

Flow and nutrient transport problems in rotating bioreactor systems



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For my parents, Jyoti and Pankajroy,
to whom I owe everything.

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Motivated by applications in tissue engineering, this thesis is concerned with the flow through and around a free-moving porous tissue construct (TC) within a high-aspect-ratio vessel (HARV) bioreactor. We formalise and extend various results for flow within a Hele-Shaw cell containing a porous obstacle. We also consider the impact of the flow on related nutrient transport problems.

The HARV bioreactor is a cylinder with circular cross-section which rotates about its axis at a constant rate, and is filled with a nutrient-rich culture medium. The porous TC is modelled as a rigid porous cylinder with circular cross-section and is fully saturated with the fluid.

We formulate the flow problem for a porous TC (governed by Darcy's equations) within a HARV bioreactor (governed by the Navier-Stokes equations). We couple the two regions via appropriate interfacial conditions which are derived by consideration of the intricate boundary-layer structure close to the TC surface. By exploiting various small parameters, we simplify the system of equations by performing an asymptotic analysis, and investigate the resulting system for the flow due to a prescribed TC motion.

The motion of the TC is determined by analysis of the force and torque acting upon it, and the resulting equations of motion (which are coupled to the flow) are investigated. The short-time TC behaviour is periodic, but we are able to study the long-time drift from this periodic solution by considering the effect of inertia using a multiple-scale analysis. We find that, contrary to received wisdom, inertia affects TC drift on a similar timescale to tissue growth.

Finally, we consider the advection of nutrient through the bioreactor and TC, and investigate the problem of nutrient advection-diffusion for a simplified model involving nutrient uptake.

Contents

1	Introduction	1
1.1	Tissue engineering	1
1.1.1	<i>In vivo</i> and <i>in vitro</i> tissue engineering	4
1.1.2	Types of bioreactor	6
1.2	Mathematical models of tissue engineering	8
1.2.1	Mathematical modelling of rotating bioreactors	12
2	Fluid flow	17
2.1	Biological problem	17
2.1.1	Model setup	18
2.2	Governing equations	21
2.2.1	Dimensional equations	21
2.2.2	Dimensionless equations	23
2.2.3	Boundary conditions	25
2.3	Reduced flow problem	26
2.3.1	Reduced governing equations	28
2.3.2	Reduced boundary conditions	29
2.4	Solving the $O(1)$ equations	31
2.4.1	Bipolar transformation	32
2.5	Solving the $O(\epsilon Re)$ equations	34
2.5.1	Bipolar transformation	35
3	Boundary regions for steady 2D flow	39
3.1	Introduction	40
3.2	Model setup for 2D steady channel flow	41
3.2.1	Boundary conditions	42
3.3	Asymptotic structure	43

3.3.1	Outer regions	44
3.3.2	Inner regions	47
3.4	Large Reynolds number: $1 \ll Re \ll \epsilon^{-1}$	52
3.4.1	Inflow	52
3.4.2	Outflow	65
4	Boundary layers for unsteady 3D flow	75
4.1	Formulation	75
4.1.1	Boundary conditions	77
4.2	Asymptotic structure	78
4.3	Outer regions	79
4.4	Inner regions	80
4.4.1	Inflow: regions II and III	85
4.4.2	Outflow: regions V and VI	90
4.5	Outer coupling conditions	100
5	Tissue construct trajectory	103
5.1	Trajectory model	104
5.1.1	Linear momentum	105
5.1.2	Angular momentum	106
5.1.3	Dimensionless equations	107
5.2	Short-time behaviour: $t = O(1)$	112
5.2.1	Angular velocity	112
5.2.2	Periodic solutions for the trajectory	113
5.3	Long-time drift	115
5.3.1	Toy model	115
5.3.2	Full solutions	125
5.4	Results	129
5.4.1	Short and intermediate-time behaviour	130
5.4.2	Long-time solutions	139
6	Nutrient transport	146
6.1	Advective transport	146
6.1.1	Particle path outside the tissue construct	148
6.1.2	Particle path inside the tissue construct	149

6.2	Effect of diffusion and uptake	152
6.2.1	Flow past circular cylinder	156
6.2.2	General shape	163
7	Conclusions and future work	167
7.1	Summary of work	167
7.2	Future work	169
A	Darcy flow in a moving frame	173
B	Transforming to bipolar coordinates	176
C	Calculations for the fluid flow	178
C.1	Deriving the $O(\epsilon Re)$ flow equations	178
C.2	Solving the $O(1)$ flow equations	181
C.3	Integral calculations	182
D	Integral calculations for trajectory	183
E	Additional boundary layers	184
E.1	Small Reynolds number: $\epsilon \ll Re \ll 1$	184
E.1.1	2D flow	185
E.1.2	3D flow	186
E.2	Inflow wall boundary layer - region IIb	188
E.3	Modified Sturm-Liouville calculations	194
E.4	Region IIc	195
E.5	Region IId	197
E.6	Region IIe	198
E.7	Region VI	199
E.8	Regions VIb and VIc	201
E.8.1	2D flow	201
E.8.2	Region VIb for 3D flow	204
E.9	Small $\tilde{X}$ analysis in region VIa	205
E.9.1	2D flow	205
E.9.2	3D flow	206
E.10	Thin gaps	207

E.11 Higher-order average flux	211
E.12 Converting the coupling conditions between frames	213
F Navier-Stokes in curvilinear coordinates	215
G Linear and angular momentum	217
G.1 Linear momentum	217
G.2 Angular momentum	219
H Algebra for multiple scales	221
I Error analysis for numerical schemes	223
Bibliography	227

List of Figures

1.1	Different types of bioreactor	6
2.1	Schematic of bioreactor in (x, y) -plane	19
2.2	Schematic of bioreactor in z -direction	20
2.3	Schematic diagram of boundary layers	26
2.4	The bipolar transformation	32
2.5	Streamlines for a prescribed trajectory	38
3.1	Model geometry for channel flow	41
3.2	Boundary-layer structure for $Re = O(1)$	44
3.3	Inner inflow problem for $Re = O(1)$	50
3.4	Inner outflow problem for $Re = O(1)$	51
3.5	Inflow boundary layer structure	54
3.6	Streamlines for inflow near the interface	59
3.7	Pressure drop for inflow	60
3.8	Interfacial stress due to inflow	64
3.9	Outflow boundary-layer structure	66
3.10	Asymptotic result for outflow pressure	72
3.11	Pressure drop for outflow	73
4.1	General tissue construct in (x, y) -plane	76
4.2	Curvilinear coordinate system	81
4.3	The function Π	96
4.4	The functions Λ_1 , Λ_2 and Λ_3	99
5.1	The function $\gamma_1(R)$	111
5.2	Coordinate change from (R, φ) to (r, θ)	115
5.3	Settling to orbital motion using the model defined in (5.34) for $\epsilon_2 \epsilon Re =$ 0.01	124

5.4	Orbital motion tending to a limit cycle using the model defined in (5.34) for $\epsilon_2 Re = 0.01$	126
5.5	Orbital motion tending to a limit cycle using the model defined in (5.34) for $\epsilon_2 Re = 0.1$	127
5.6	Phase plane showing the TC trajectory for different starting positions with $b = 0.15, \epsilon_2 = 0$ and $\overline{B} = 0.4$	131
5.7	Phase plane showing the TC trajectory for different starting positions with $b = 0.15, \epsilon_2 = 0.1, \overline{B} = 0.4$, and $K = 0.1$	132
5.8	Phase plane showing the TC trajectory for different starting positions with $b = 0.15, \epsilon_2 = 0.1, \overline{B} = 0.4$, and $K = 1$	133
5.9	Non-uniformity of short-time solution	135
5.10	Streamlines in settling regime	136
5.11	Streamlines in orbital regime	137
5.12	Streamlines in steady regime	138
5.13	Contour plot of R_T with $\overline{B} = 0$	141
5.14	Contour plot of r_{0T} with $\overline{B} = 0.1(\bar{\rho} - 1)$	143
5.15	Contour plot of r_{0T} with $\overline{B} = \bar{\rho} - 1$	144
5.16	Contour plot of r_{0T} with $\overline{B} = 10(\bar{\rho} - 1)$	145
6.1	Particle path with initial position towards bioreactor edge	150
6.2	Particle path with initial position towards bioreactor centre	151
6.3	Nutrient advection and uptake past a porous circular cylinder	158
6.4	Numerical solution of nutrient diffusion	160
6.5	Comparison of asymptotic to numerical solutions for nutrient diffusion	161
E.1	Interfacial stress for a small Reynolds number	187
E.2	Contour deformation for inversion of the Fourier integral	201
E.3	Schematic diagram of thin gap	208
E.4	Conformal mapping for region IX	210
I.1	Error tolerance check for t	224
I.2	Error tolerance check for β	225
I.3	Error tolerance check for infinite series	226

Chapter 1

Introduction

In this introduction we begin by giving a general overview of tissue engineering, discussing the current successes and limitations of the field. Of the two main branches of tissue engineering, we discuss the *in vitro* method in detail. We then review the role of mathematical models in tissue engineering generally, before discussing previous mathematical models for tissue growth in rotating bioreactors, noting specifically where the work can be extended. We end with a description of the model to be analysed in this thesis and, in particular, where we build on previous work.

1.1 Tissue engineering

Population ageing is an unprecedented global phenomenon in the modern world, and is predicted to present even greater challenges in the coming century. In 2000, the percentage of the global population aged over 60 was 10%; in 2050 it will be at 21.8%, and by 2100 it will have risen to 32.2% [39]. As the body's ability to repair itself diminishes with age [61], there will be an increased demand for replacement body parts in the future. A common way to replace organs is via donors, but within the context of an ageing population crisis there will be an even smaller supply to demand ratio than currently exists. This all leads to the conclusion that a viable alternative is required to avoid a global organ shortage.

Tissue engineering is a fast growing discipline whose general aim is to repair or replace damaged body tissue or organs via the engineering of artificial tissues or organs. Henceforth, we use the term 'tissue' to refer to both body tissue and organs. An obvious use of tissue engineering is growing and then directly transplanting tissue; one could envision a laboratory of the future growing row after row of artificial body tissue in bubbling vats ready for transplant into waiting patients. However, the

Organ Type	Time interval				
	3 Months	1 Year	3 Years	5 Years	10 Years
Kidney: Deceased Donor	95.3%	91.0%	80.1%	69.3%	43.3%
Kidney: Living Donor	98.1%	96.3%	89.6%	81.4%	59.3%
Liver: Deceased Donor	91.2%	84.3%	74.2%	68.4%	54.1%
Liver: Living Donor	90.9%	86.0%	79.0%	72.9%	62.6%
Heart	92.8%	87.9%	80.6%	73.7%	54.2%
Lung	91.6%	81.6%	63.5%	51.5%	26.2%

Table 1.1: The graft survival rate after various organ transplants in the USA for different time intervals. Data from 2009 Organ Procurement and Transplantation Network/Scientific Registry of Transplant Recipients Annual Report [3].

ability to grow body tissue from a given source has a more subtle advantage. Whilst donor tissue is no doubt useful, it comes with some drawbacks; as Table 1.1 suggests, a significant proportion of donated organs are rejected by the recipient body. Furthermore, even if the body grudgingly accepts the foreign organ, in the majority of cases the new owner must take a multitude of immunosuppressants for the rest of their life [60]. This can, however, be avoided if the donated organ comes from a donor who is genetically identical to the host. Unfortunately, most people do not have a spare identical twin. This is where the potential of tissue engineering is promising; growing tissue from the eventual host’s own cells produces tissue which is genetically identical to the host, making many rejection issues redundant [48]. There are also further potential applications; being able to grow organs, or even tumours, in the laboratory accelerates the process of testing viable drugs. This reduces the overall need for replacement tissues within the body [28] and also removes the need for animal testing [29].

There has already been success in engineering several different types of tissue. The most promising of these is skin, with over 25 years of clinical use and, more recently, commercial viability [43, 46]. Artificially engineered tracheae are another success. The first synthetic trachea transplant was carried out by Macchiarini *et al.* [42], and a systematic review of all trachea transplants since is given in Crowley *et al.* [17]. There have also been clinical trials to repair surface cartilage damage, via implantation of externally-grown chondrocytes (cartilage cells) onto the affected cartilage [11, 32]. There are many other tissue-types including bladders, corneas, blood vessels and bronchial tubes which have been involved in clinical trials [33], and numerous others which have been involved in pre-clinical trials [81].

Tissue engineers have made a lot of progress in determining the basic principles of engineering artificial tissues, such as investigating how different cell types respond to various environments [33]. However, one current challenge is to produce large tissues. The successes of tissue engineering mentioned above have one common property: none of the engineered tissues require an integrated vascular system to supply nutrients to and remove waste products from the cells. In the body, the vascular system makes up for the deficiency of diffusion as a transport mechanism by ensuring that all cells are no more than 100 μm from a blood supply, and hence shortening the distance over which diffusion has to occur [4, 33]. However, due to its complexity, the effect of the vascular system is very difficult to mimic in the laboratory [33, 71]. Providing an efficient transport mechanism is vital to avoid necrotic centres (areas of dead cell matter) within the tissue and to produce tissue that can viably be used inside a living body [23, 81].

In general, to engineer artificial tissue it is necessary to: harvest cells from a cell source (e.g. a living body of the same species), seed these cells onto a biomaterial on which to grow them (e.g. a porous scaffold), and place this seeded biomaterial inside a bioreactor to grow (e.g. an engineered vessel or a living body) [18, 44, 81].

There are many different possible sources of cells which can be harvested for growth. These can be categorised into three main types [28]: autologous, where the cells come directly from the patient (e.g. cartilage repair via autologous chondrocyte implantation where the tissue is initially grown within a scaffold [14, 32]); allogeneic, where the cells come from a donor of the same species but are not genetically identical to the patient (e.g. hepatocyte transplantation for many liver diseases [53]); and finally xenogeneic, where the cells come from a donor that is not the same species as the patient (e.g. transplanting porcine aortic valves for heart disease [67]).

The choice and shape of biomaterial used to act as a scaffold for the growing tissue is very important. We henceforth refer to the combination of the scaffold seeded with cells as the tissue construct (TC). The scaffold provides a platform on which the cells can grow and gives mechanical integrity to the whole TC [20, 81]. A common scaffold is made using the connective fibres of a natural tissue whose cells have been removed, known as decellularized tissue [33], but man-made materials can also be used; Curtis and Riehle [20] list modified collagen, artificially engineered polypeptides, and synthetic biodegradable polymers amongst others. Many scaffolds are porous; this allows the culture medium to reach the insides of the growing tissue, removing waste and providing nutrients. This provides a potential solution to the problem of enabling an efficient transport mechanism [23, 68, 81].

The scaffold can also guide cell migration, either physically or chemically. By designing a scaffold with a specific internal structure, e.g. cylindrical guidance channels in the case of neural regeneration [26], the collection of cells can be guided to grow in a specific shape, often one that matches the shape of the tissue within the body. The same effect can be achieved by modifying the scaffold surface chemically to provide cues to guide cell migration or cell differentiation (a process known as chemical patterning). This can be done by imbuing a scaffold surface with specific protein fragments which attract certain types of cells whilst rejecting others [38].

Scaffolds have also been designed that gradually degrade. Ideally, the rate of the extra-cellular matrix deposition by the cells within the scaffold matches the rate of degradation of the tissue scaffold, leaving a tissue that has enough structural integrity to support itself [30]. This is advantageous because reducing the foreign matter present within an artificially engineered tissue has a positive effect on tissue acceptance.

1.1.1 *In vivo* and *in vitro* tissue engineering

Once the tissue scaffold has been seeded with cells, there are two main ways to cultivate the TC. These are denoted as *in vivo* and *in vitro*, which relate to whether the tissue is being cultivated inside or outside a living body respectively.

The *in vivo* method uses a living body to grow the cell population. The body naturally tries to reject any foreign bodies, and so to increase the chance of being accepted by the body, the scaffold (ideally made with host material) is placed directly inside the host body at an earlier stage in tissue development, combined with anti-rejection medicines, and the tissue is allowed to grow from within [83]. Zdrahala and Zdrahala [83] use the poetic metaphor of the genesis of an artificial coral reef to describe *in vivo* tissue engineering; the body is represented by the sea, the scaffold is represented by a shipwreck and the organ or tissue to be replaced is represented by the coral reef that the shipwreck will eventually become. The wreck erodes and biodegrades, creating sites for coral and plant matter to live. The sea washes away waste and brings in nutrients, and eventually sea creatures are attracted to the system, coexist with the coral and become part of the whole structure. Thus the coral reef structure is complete. There has been some success in *in vivo* methods for repairing heart valve tissue [70] and cultivating musculoskeletal tissue [45]. However, in this thesis we concentrate on *in vitro* methods, which we now describe below.

A bioreactor is a system in which cells can be artificially cultured, and the simplest examples are a test tube or a petri dish. The *in vitro* method grows the cell population within a bioreactor that is external to a living body, and this approach has the advantage that the cultivation process can take place in an environment which can be carefully controlled. Further, a bioreactor is a much better environment than a living body to systematically study how tissues respond to different effects. For example, many growing tissues respond to and are stimulated by a mechanical stress [63, 69], and being able to control the mechanical conditions that the cells within the scaffold experience has the potential to optimise tissue growth. This relationship between local stress and local growth rate is one aspect of a process known as mechanotransduction and has been noted in several experiments [63, 69]. Mechanotransduction works via a three step process: initially there will be a mechanical trigger, often a shear or compression, on some primary cells in the tissue; these primary cells then relay a signal to secondary cells in the tissue which may or may not have physically felt the trigger. Finally, these secondary cells exhibit a response, thus ensuring that the entire tissue responds in a manner appropriate to the initial trigger [34]. Different responses include cell growth, cell differentiation, cell alignment and hormone release [47].

In vitro tissue engineering is a very wide umbrella term. There are so many possible biophysical or biochemical processes at play in tissue growth that it is no surprise that the engineering of different tissues will require vastly different experimental setups. Bioreactors have been developed for numerous specific applications, from exploring tissue vibration effects on vocal folds [73] to the effects of cyclical strain on flexor tendons [63]. Despite the many different bioreactor setups, there is common ground. Most bioreactors are systems in which a culture medium, containing nutrients and growth factors, is brought into contact with the TC in some way [16]. There are several reasons to stimulate a flow within the bioreactor; it not only sets up a stress experienced by the TC but also means that nutrient-delivery and waste removal may be enhanced via advection. Further, as the fluid is in constant motion, a fluid flow reduces the likelihood of nutrient-deprived areas appearing within the culture medium [16]. This ties in with the current challenge of engineering larger tissues. As nutrient-transport via diffusion is only effective for relatively small tissues, enhanced transport via advection can result in nutrient penetrating deeper into the tissue and the successful engineering of larger tissues.

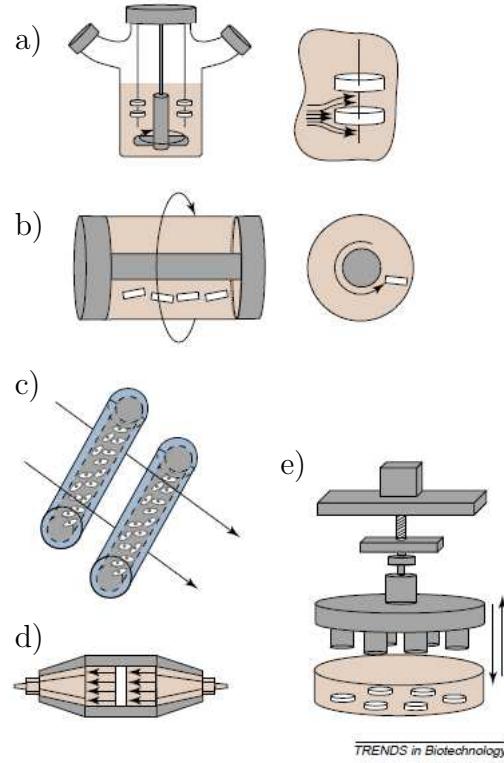


Figure 1.1: Different types of bioreactor; a) spinner-flask bioreactor, b) rotating-wall vessel (RWV) bioreactor, c) hollow-perfusion bioreactor, d) direct-perfusion bioreactor, and e) bioreactor applying a controlled mechanical force to the TCs. Reprinted from Martin *et al.* [44], with permission from Elsevier.

1.1.2 Types of bioreactor

In this section, we describe the common types of bioreactor and note that a comprehensive review is given in Chen and Hu [16].

We first consider the spinner-flask bioreactor (see Figure 1.1a). In these systems the TC is submerged, often suspended, within the nutrient-rich culture medium inside the flask, and the fluid is mixed by a magnetically-driven stir bar, inducing a flow. One problem with this approach is that the edges of the stir bar create eddies which can increase the shear stress experienced by the TC due to the induced fluid flow, and also result in unpredictable flow [16]. However, there are ways to address this, including modifying the bioreactor walls to be wavy [12]. The wavy walls reduce the effect of the eddies, and this has been shown to result in increased cell proliferation in engineered cartilage constructs [13].

A variant on the spinner flask bioreactor is the rotating-wall vessel (RWV) bioreactor (see Figure 1.1b). In such systems, the entire fluid-filled bioreactor is rotated

about its longitudinal axis in an effort to create a fluid flow that will both exert a controlled shear stress on the TC and also keep the nutrient-rich culture medium well-mixed. According to Chen and Hu [16], “The most commonly used bioreactor that exploits the benefit of low shear stress is a RWV wherein the cells are grown in a microgravity environment.” Whilst the idea of this statement is correct, from a mathematical perspective we would say that it occurs in an environment of *rotating gravity*, not microgravity. The buoyancy effect of the fluid on the TC may also result in reduced gravitational effects, but this is different to microgravity. It is likely that the confusion over the terms started when the RWV was first designed, as the initial experiments were devised and carried out by NASA in actual microgravity environments, i.e. space [35]. An added benefit of the ‘low shear stress’ mentioned is that it can be controlled via bioreactor geometry and rotation speed; as the wall rotates the TC and fluid around, there are none of the eddies that a spinner flask would create, leading to a more predictable flow.

There are several types of RWV, and two of the most common types are the slow-turning lateral vessel (STLV) and the high-aspect-ratio vessel (HARV). The STLV is essentially a large hollow cylinder with a smaller concentric solid cylinder inside. The entire bioreactor is filled with a nutrient-rich fluid culture medium and TCs, and the outer cylinder rotates. The HARV is a single rotating cylinder with a large ratio between radius and depth. The bioreactor is filled with a nutrient-rich fluid culture medium and the TC is placed inside.

In a direct-perfusion system the TC is placed within the bioreactor and the nutrient-rich culture medium is pumped directly through the TC (see Figure 1.1d and, to a lesser extent, Figure 1.1c). This means that the nutrient-rich culture medium can generally reach the interior of the TC, avoiding the problem that can occur in static conditions when the centre of the TC does not always receive an adequate nutrient supply [16]. It has been demonstrated that, compared to static or spinner-flask methods, direct perfusion yields a significant improvement on both the proportion of live to dead cells inside the scaffold and the uniformity of cell distribution within the tissue scaffold [77]. The perfusion system can also be used to initially seed the scaffold (in a more uniform manner) and then this scaffold can be placed into another bioreactor system (if a different level of shear stress is required).

1.2 Mathematical models of tissue engineering

As the field of tissue engineering has grown, it has become apparent that a multidisciplinary approach is vital, and mathematically modelling various experiments plays a key role in this. Indeed, the many types of bioreactor and tissues considered provides a wide scope for the development of novel mathematical models. For an in-depth review into the role that continuum modelling can and does play within *in vitro* tissue engineering, see O’Dea *et al.* [55]. We begin with an overview of the more relevant literature.

As the well-known Navier-Stokes equations for fluid flow have been heavily studied [54], *in vitro* tissue engineering and, in particular, bioreactors containing a fluid culture medium are good candidates for successful mathematical models. If there is a region whose microscale structure is a complicated mixture of pore space and solid matrix, it may be prohibitively difficult to determine the details of the flow on the microscale. If the exact details of the microscale flow are not required, and a macroscale knowledge of the flow is sufficient, it is possible to use the Darcy equations to determine the locally-averaged fluid velocity [54]. Though the Darcy equations were originally posed as a constitutive relationship [21], they have since been derived from the Navier-Stokes equations via a homogenization process for fluids with a small Reynolds number, where the typical pore size is used as the relevant lengthscale, see e.g. [49, 78].

The general idea of this homogenization process is to average the local fluid velocity over a representative volume (which is larger than the pore scale, but smaller than the characteristic length of the entire porous medium). This volume includes the solid matrix, leading to the resulting velocity average being a *bulk*-volume average rather than a *pore*-volume average. After this averaging procedure, the pore space and solid matrix are no longer considered to be distinct regions (as they would be for the full problem when considering the pointwise velocity). Instead, the averaging procedure results in a spatial continuum with a proportion of the pore space and solid matrix present at every point in space.

The Darcy equations are one example of a ‘multiphase flow’ model (as opposed to ‘single-phase flow’ modelled by the Navier-Stokes equations). In saturated Darcy flow, there are two phases: the fluid within the pore space, and the solid matrix. In multiphase flow models, there can be an arbitrary number of phases corresponding to, for example, fluid, pore space, solid matrix, or growing cells. Then, in a similar manner to theoretical derivations of Darcy flow, each variable is subjected to a bulk-volume

averaging procedure. Hence, a spatial continuum is obtained whereby a proportion of each phase is present at every point in space. This approach is described in Lemon *et al.* [37], where a general framework for the development of multiphase flow models is built, with an assumption of negligible inertial terms. The authors consider an arbitrary number of phases and demonstrate the potential of the multiphase framework by considering a specific case of three phases relevant to tissue engineering: water, proliferating cells, and a solid porous matrix of constant volume fraction. Transfer of mass between the cell and water phases accounts for cell proliferation.

It is also possible to couple a region (or regions) of multiphase flow with a region (or regions) of single-phase flow (also known as ‘bulk flow’), as occurs when there is a saturated porous region fully surrounded by a single fluid. In this case, the equations describing the single-phase flow outside the porous region (e.g. the Navier-Stokes equations) must be coupled to the equations describing the multiphase flow inside the porous region (e.g. the Darcy flow equations) via appropriate boundary conditions. In the specific case of the Navier-Stokes equations coupled to the Darcy equations, the form that these boundary conditions take is a relatively open question. Whilst continuity of normal flux and normal stress are relatively straightforward, we must take care with the boundary condition for the bulk tangential velocity on the porous interface. For a fluid-solid interface, the appropriate boundary condition is usually that of no slip, and for a fluid-fluid interface the appropriate boundary condition is usually continuity of tangential velocity. As a porous interface consists of pores and solid matrix, the correct pointwise boundary condition must vary between no slip and continuity of tangential velocity depending on the exact structure of the interface. Clearly, this formulation is difficult to deal with analytically, and it cannot be easily reconciled with Darcy’s equations, which have a loss of pointwise information (due to the use of the locally-averaged velocity).

Historically, the boundary condition used at such an interface has been no slip, with the underlying assumption that the interface of the porous material mainly consists of the solid matrix, and hence that the porous medium is fairly impermeable. However, this view was changed in the landmark paper by Beavers and Joseph [5], where it was found experimentally that the tangential slip between bulk and porous regions appears to be proportional to the rate of change of the bulk tangential velocity in the direction normal to the interface, evaluated on the interface. The corresponding constant of proportionality depends on the porous material, yielding one experimentally-determined parameter in the boundary condition. This boundary condition was given a theoretical justification in Saffman [64], using the method of

matched asymptotic expansions close to the interface. There have been efforts to improve upon the Beavers and Joseph (BJ) slip condition since, but due to its agreement with experiments and ease of use, it is generally accepted as the *de rigueur* boundary condition for the tangential velocity on a fluid-porous interface. The BJ slip condition, its historical background, and other possibilities for the tangential boundary condition are discussed in, e.g. Nield [50] and Nield and Bejan [51].

A coupled multiphase to single-phase approach was used to model a fibre-perfusion bioreactor for growing bone and cartilage in Whittaker *et al.* [79]. The authors consider an entirely porous cylindrical bioreactor chamber with circular cross-section filled with a fluid culture medium. Flow is pushed through the chamber via inlet and outlet pipes as well as through slender hollow porous-walled fibres where the flow is forced through one end of the fibre and the fibre is sealed at the other end, so that the fluid is forced to disperse into the scaffold. There is one single-phase region; the (thin) hollow core of the fibre, in which the fluid is governed by the Navier-Stokes equations, which are subsequently simplified using lubrication theory. There are also two multiphase regions; the porous-fibre wall, where the flow is modelled using Darcy's equations, and the porous bioreactor chamber, which also uses Darcy's equations to model the flow, but with a different permeability parameter to the porous-fibre wall. The boundary condition for the bulk fluid tangential velocity, imposed between the bulk and porous flow regions, is no slip. The authors solve for the flow and the nutrient transport through the bioreactor. These results are used to estimate the shear stress acting on the tissue cells (contained within the porous bioreactor chamber), as follows. Experimental data for the average pore size and permeability is used in conjunction with the Darcy flow model to estimate the average flow within one pore. Using this with the assumption of Poiseuille flow through each pore, the shear exerted by the flow on the internal surface of the pores may be estimated. The authors then discuss the advantage of using analytical methods compared to performing computational fluid dynamics (CFD) simulations (e.g. in Boschetti *et al.* [7], Porter *et al.* [58]), and conclude that, whilst the use of a macroscale Darcy model causes an inevitable loss of information, the ease of calculation in providing good estimates of the global flow field and nutrient transport make reduced mathematical modelling an important tool in bioreactor design.

An extension to Darcy's equation which has received a lot of attention is the Darcy-Brinkman equation, which adds a macroscale viscous term to the Darcy equation. This was proposed in Brinkman [10], and assumes that the porous material is very

porous. In the case of a porous region coupled to a single-phase region, the Darcy-Brinkman equations also have the added bonus of being able to be applied to both domains, thus bypassing any issues in choosing suitable boundary conditions with which to couple the regions. In this approach, the porosity decreases from 1 in the bulk flow (where the Darcy-Brinkman equations reduce to Stokes flow) to its value within the porous medium. The presence of the (Laplacian) viscous term also adds a regularizing/smoothing effect to the partial differential equation. However, the addition of these macroscale viscous effects also makes the resulting equations significantly more difficult to solve, and requires another free parameter (the effective viscosity) to be experimentally determined. In Nield and Bejan [51], the authors state “for many practical purposes there is no need to include the Laplacian term”, adding that the only need appears to be if applying a continuous tangential velocity and tangential stress at the interface between single-phase and porous medium flow is imperative.

The Darcy-Brinkman equations in a single-domain (where the porosity decreases from 1 in the bulk region to a constant value within the porous medium) are considered more formally in Le Bars and Worster [36], where they are derived using a volume-averaging method. The authors then solve various analytically tractable problems using these equations. The results are compared to those obtained using Darcy’s equations in the porous medium and the Stokes flow equations in the single-phase fluid. In the latter case, the two regions are coupled via either the BJ slip condition on the interface, or by imposing continuity of velocity on a ‘phantom’ interface taken to be a short distance within the porous medium (essentially allowing a slip velocity on the original interface). In the case of Poiseuille flow through a channel with one porous wall, it is found that there is little difference between all three formulations. However, in the case of vertical flow imposed a finite distance away from a semi-infinite porous strip placed horizontally in a 90° corner, imposing the BJ slip condition yields different results compared to the other two approaches. This difference manifests in the fluid flux within the bulk fluid, which is larger when using the BJ slip condition. The authors suggest that experimental data are required to determine which modelling approach provides a more accurate result.

For the reasons above, it is unclear what benefits the Darcy-Brinkman modification of the Darcy model has in our application, though we concede that it may be easier to implement numerically the Darcy-Brinkman modification on a single domain, rather than coupling several different regions together. As the Brinkman model adds a non-trivial complexity to a model, and our intention is to maximise analytic

progress (and proceeding under the philosophy of doing the ‘simplest case first’), we do not consider the Brinkman model further in this thesis.

1.2.1 Mathematical modelling of rotating bioreactors

In this thesis, we mainly consider a specific tissue engineering method; the *in vitro* method using a porous rigid scaffold which is seeded with tissue cells within a nutrient-rich fluid culture medium and placed within a high-aspect-ratio vessel (HARV) bioreactor. The HARV bioreactor is a hollow cylinder with circular cross-section, and is a type of rotating wall vessel (RWV) bioreactor that rotates about its axis at a constant rate. It is pertinent, therefore, to review the literature on mathematical models for rotating bioreactors.

A mainly numerical approach is taken in Lappa [35], which uses CFD to take on, and solve for specific cases, the problem of cultivating cartilage in a rotating-wall perfusion vessel. The specific aims are to introduce a detailed mathematical model for the growth problem and describe the fluid flow within the bioreactor as the tissue grows. The model accounts for the fluid flow past the solid TC and its subsequent growth, which occurs on a much slower timescale to fluid flow. The author finds excellent agreement with experimental results. However, this paper does not consider formal multiphase flow as used in Lemon *et al.* [37] (as the volume fraction of the cells is not accounted for), or multiphase flow coupled to a single-phase flow as used in Whittaker *et al.* [79] (as one system of equations is solved throughout the domain). In fact, Lappa [35] uses a phase-field model whereby the two phases in the model (the fluid and the solid TC mass) are accounted for by use of a phase-field variable, which is a measure of the fraction of solid mass (and is a function of time and space). This means there is a thin (but finite) region between the TC and the fluid flow where the fraction of the solid matrix rapidly falls to zero instead of introducing a mathematical boundary of zero thickness. In a similar manner to the Darcy-Brinkman equations, this method is used to account for the growing tissue, and to avoid the numerical problems associated with a moving-boundary problem.

A different system is considered in Pisu *et al.* [57], where the aim is to simulate the growth of engineered tissue cartilage in a typical RWV. This is investigated by consideration of various physical variables within the tissue. These variables are oxygen consumption, glycosaminoglycan (GAG) production (GAG is an important component of cartilage), and cell growth. The model considers nutrient and waste product transport within the growing tissue (which is cylindrical with circular cross-section)

using reaction-diffusion type equations with additional sink and source terms. A cell distribution function is considered, which is a measure of the density of cells at any given point in space and time. The oxygen, GAG, and cells do not take up any volume in the model and are, instead, concentrations of the relevant variable. The authors assume that the culture medium external to the tissues is well-mixed, and therefore Dirichlet boundary conditions are imposed for the oxygen and GAG concentrations on the tissue boundary. The derived governing equations and boundary conditions are solved numerically. The results are compared to experimental data and previous theoretical models for the spatial concentration of GAG within a growing tissue. A similar model was considered in Nikolaev *et al.* [52], and validated by comparisons to experimental data. The paper considered the growth of cartilage tissue in a typical RWV by considering the pointwise concentration of oxygen, unbound and bound GAG and density of cells. Here, unbound GAG refers to newly created GAG, which is free to move around the tissue, and bound GAG refers to GAG which has been confined by collagen fibres within the tissue. The authors consider tissue growth to be a function of bound GAG, resulting in a moving-boundary problem. The model is solved numerically, and agrees with the available experimental data for spatial GAG concentration and cell density. We note that neither of the models mentioned in this paragraph [52, 57] consider the fluid flow (either external or internal to the tissue).

1.2.1.1 High-aspect-ratio vessel bioreactor

We now consider mathematical models of the HARV bioreactor. Before this, however, we note some further behaviour and terminology relating to the TC within a HARV bioreactor.

In the HARV bioreactor, three different regimes of TC motion are observed experimentally: steady, settling, and orbital motion [19]. In the steady regime, the TC occupies a stationary position in the bioreactor with respect to the laboratory frame of reference. In the settling regime, the TC executes a periodic orbit that does not encircle the bioreactor centre. In the orbital regime, the TC executes a periodic orbit that does encircle the bioreactor centre. Experimentally, the steady or settling regime is preferred as it is believed to enhance nutrient transfer [19, 35]. A successful model will go some way towards explaining the flow and nutrient transport properties of these three motion regimes.

Another experimental phenomenon is that the TC tends to drift over time in a spiralling motion towards the bioreactor edge. Many experimental papers state that the angular velocity of the bioreactor must be varied over time in order to

counteract the TC spiralling out from what appears to be a periodic trajectory [25, 27, 31]. In general, this effect is attributed to the change in density of the TC that occurs via tissue growth. However, this growth typically occurs on a timescale of tens of hours [24, 27, 31] and it is plausible that fluid and TC inertial effects could actually play a more important role than the TC growth in the spiralling behaviour noted by experimentalists. Again, the development and solution of an appropriate mathematical model will provide insight into the underlying drift mechanism.

There have been some mathematical models that specifically consider the HARV bioreactor, and exploit the small aspect ratio to make analytic progress. In Waters *et al.* [76], a cylindrical bioreactor with circular cross-section rotating about its axis is considered for different geometries, including a HARV bioreactor. The TC in this case is modelled by a viscous fluid separated from the external viscous fluid by a membrane. Under this assumption, the linear stability of an initially circular interface between two immiscible fluids within the rotating bioreactor is explored. This paper provides a potential explanation for the irregular nature of some types of tissue grown within such systems.

In Cummings and Waters [18], the work in Waters *et al.* [76] is extended by specific consideration of a rotating HARV bioreactor containing a solid cylindrical TC with circular cross-section. The TC is free to move around the bioreactor according to the forces acting upon it. Initially, the TC trajectory is prescribed and the flow within the bioreactor is solved analytically for two cases: where the angular velocity of the TC about the bioreactor centre is far from and near to the bioreactor angular velocity respectively. The angular velocity of the TC about its own centre is not considered. Subsequently, the correct trajectory of the TC is determined via consideration of the force balance (which is coupled to the flow). The paper successfully describes the three different regimes of tissue motion mentioned above. Furthermore, partial progress is made in investigating the effect of inertia on the drift problem. This is carried out by considering the specific case where the short-term behaviour of the TC is to move entirely with the flow. The paper continues by investigating the growth problem for the case in which the TC is statically suspended within the rotating bioreactor. This case corresponds to the steady regime mentioned above. This paper was followed by Cummings *et al.* [19], in which the model in Cummings and Waters [18] is extended by introducing one free parameter. This parameter corresponds to the position where the TC sits between the flat sides of the bioreactor, and is determined via a fit to experimental data for the TC trajectory.

Whilst a lot of progress has been made in these papers [18, 19, 76], several key features are missing. The TC has previously been modelled as either fully liquid (and separated from the bulk flow via a membrane) or fully solid, which means that it has not been possible to consider nutrient transport via advection between the TC and its exterior. Additionally, the flow is modelled solely using the lubrication equations, exploiting the thin geometry of the HARV bioreactor. Whilst these are a good approximation for the flow away from the TC surface, they break down when the thin geometry cannot be exploited. This occurs in ‘inner’ regions whose distance from the TC surface is of the same order as the height of the bioreactor. As these important inner regions have not been studied, it is not immediately clear what the correct interfacial conditions to impose for the lubrication equations (in the ‘outer’ regions) are. Furthermore, the fully three-dimensional effects that contribute to the shear stress acting on the TC surface cannot be determined.

In this thesis, we specifically extend previous work [18, 19] by considering a rotating HARV with a moveable TC that, in this case, is assumed to be porous. The TC porosity enables the nutrient-rich fluid culture medium to penetrate the TC, potentially avoiding the problem of the tissue growing with a necrotic centre. We mathematically model the problem by describing the fluid flow within the porous and bulk regions of the bioreactor. The flow in these regions is coupled via appropriate boundary conditions (which we also derive). We make several simplifying assumptions, reliant on the fact that we are modelling a HARV bioreactor. We assume that the ratio of the bioreactor depth to its radius is small, and furthermore that the reduced Reynolds number of the culture medium is small. By considering boundary layers close to the TC surface, we are able to determine appropriate interfacial conditions to impose for the bulk and porous outer regions, i.e. where the lubrication equations hold. Following Cummings and Waters [18], we initially solve the resulting equations for the simplified flow system for a prescribed TC trajectory. The correct trajectory is then determined via consideration of a force and torque balance. This allows us to determine the angular velocity of the TC about its own centre. We make further progress on the drift problem by considering the effect of inertia for a general TC trajectory. Having determined the fluid flow throughout the system, we are then able to determine the nutrient transport through the porous TC.

The structure of the thesis is as follows. In Chapter 2, we formulate the flow problem for a porous TC within a HARV bioreactor. By making various assumptions, we simplify the system of equations by performing an asymptotic analysis, and solve analytically for the flow due to a prescribed TC motion. The interfacial conditions

used to couple the bulk and TC flows are subsequently derived in Chapters 3 and 4, where we consider the boundary layers close to the porous TC surface. In Chapter 3, we investigate the simpler problem of a two-dimensional porous obstacle within a channel with stationary walls. A rich boundary-layer structure is uncovered and, in Chapter 4, this work is extended to consider a three-dimensional porous obstacle within a Hele-Shaw cell with moving walls. This enables the correct interfacial conditions applied in Chapter 2 to be determined. In Chapter 5, we use the knowledge of the flow determined in previous Chapters to evaluate the TC trajectory and angular velocity about its own centre. This work is then extended to consider the effect of inertia upon TC drift. Using a multiple-scale analysis on the system of equations, we determine differential equations that govern the long-time behaviour of the TC, and subsequently investigate these. In Chapter 6, we begin by exploiting the results of previous Chapters to determine the advection of nutrient through the bioreactor and TC. We then investigate the problem of nutrient transport via the combined effects of advection and diffusion within a toy problem. Finally, in Chapter 7, we summarise the main results of this thesis and suggest future avenues of work.

Chapter 2

Fluid flow

2.1 Biological problem

In this thesis we consider a specific type of rotating wall vessel bioreactor; the high-aspect-ratio vessel (HARV) bioreactor. We consider a porous scaffold seeded with tissue cells, which we refer to as a tissue construct (TC), and this is placed within a fluid culture-medium in the HARV bioreactor. The HARV bioreactor rotates about its longitudinal axis at a constant rate. Throughout this thesis, we always assume that two dimensionless parameters are small: the ratio of the bioreactor depth to its radius, and the reduced Reynolds number of the culture-medium fluid. Both these assumptions facilitate simplification of the governing system of equations.

The rotation keeps the TC suspended in a continuous free-fall under rotating-gravity conditions. Our goal is to determine how the bioreactor rotation affects the flow and TC trajectory. The bioreactor rotation serves two main purposes, and the goal of both is to enhance TC growth. Firstly, the bioreactor rotation ensures the nutrient-rich fluid inside the bioreactor is well-mixed. Ideally, this will remove any possibility of nutrient-depleted zones, thus allowing the TC to grow in nutrient-rich conditions. One aim of our model is to set up a framework that allows us to determine whether this is actually the case. Secondly, the bioreactor rotation drives the flow which imparts a shear stress upon the TC. The shear stress acting on the tissue is an important factor in the growth rate for many tissue types [16]. This stress will depend on several experimentally controllable variables, and another aim is to determine the shear stress distribution around the TC for a given rotation rate and bioreactor geometry. This could ultimately lead to optimisation of these variables for enhanced tissue growth.

Flow within the porous TC is modelled using the Darcy equations, and is coupled

to the external flow, modelled by the incompressible Navier-Stokes equations, via appropriate boundary conditions. In contrast to Cummings and Waters [18], who considered the behaviour of a solid impermeable cylinder with circular cross-section (representing the TC) within the rotating bioreactor, we note it is now necessary to solve equations within the TC. In Chapter 4, we determine boundary conditions to couple the flow within a cylindrical porous obstacle with a *general* cross-section to an exterior bulk flow, but the application in the rest of the thesis will be for a cylindrical porous obstacle with *circular* cross-section.

In this Chapter, we set up the mathematical model for the bioreactor system and solve the fluid flow problem for a prescribed TC trajectory. In Chapter 5, we couple the TC trajectory to the fluid flow by considering the force and torque acting upon the TC.

2.1.1 Model setup

We model the fluid culture-medium as an incompressible fluid with constant viscosity μ and constant density ρ . The fluid is contained within a HARV bioreactor, which we model as a rotating cylinder of height h and to have a circular cross-section of radius a . The TC is modelled as a porous cylinder of height d and circular cross-section of radius l contained within the bioreactor, as illustrated in Figures 2.1 and 2.2. The cylindrical bioreactor rotates with a constant angular velocity of Ω about its axis.

We assume that the TC has been cultivated in impermeable sheets and hence the flat circular sides are solid boundaries, but the curved boundary is fully porous. As the TC is contained within the bioreactor, we must have $l < a$ and $d < h$. We take the ratio between the bioreactor height and radius to be small, i.e. $h/a = \epsilon \ll 1$.

There are several frames of reference in which we could work, but we end up using two frames, both with their origin at the centre of the bioreactor: a stationary laboratory frame, and a frame rotating with the TC centre. We now discuss both of these in turn. We consider the Cartesian coordinate system (x, y, z) to be the (stationary) laboratory frame. This frame is aligned such that gravity acts in the negative y -direction, as indicated in Figure 2.1. The unit vectors in the positive x and y -directions are denoted by $\mathbf{e}_x$ and $\mathbf{e}_y$ respectively, and are indicated in Figure 2.1. The z -direction is the longitudinal axis of the bioreactor and has unit vector $\mathbf{e}_z = \mathbf{e}_x \times \mathbf{e}_y$ in the positive z -direction. The origin of the laboratory frame is located at the bioreactor centre projected onto the lower (with respect to z) flat surface of the bioreactor. We define the orthogonal (X, Y) -frame with origin at the bioreactor

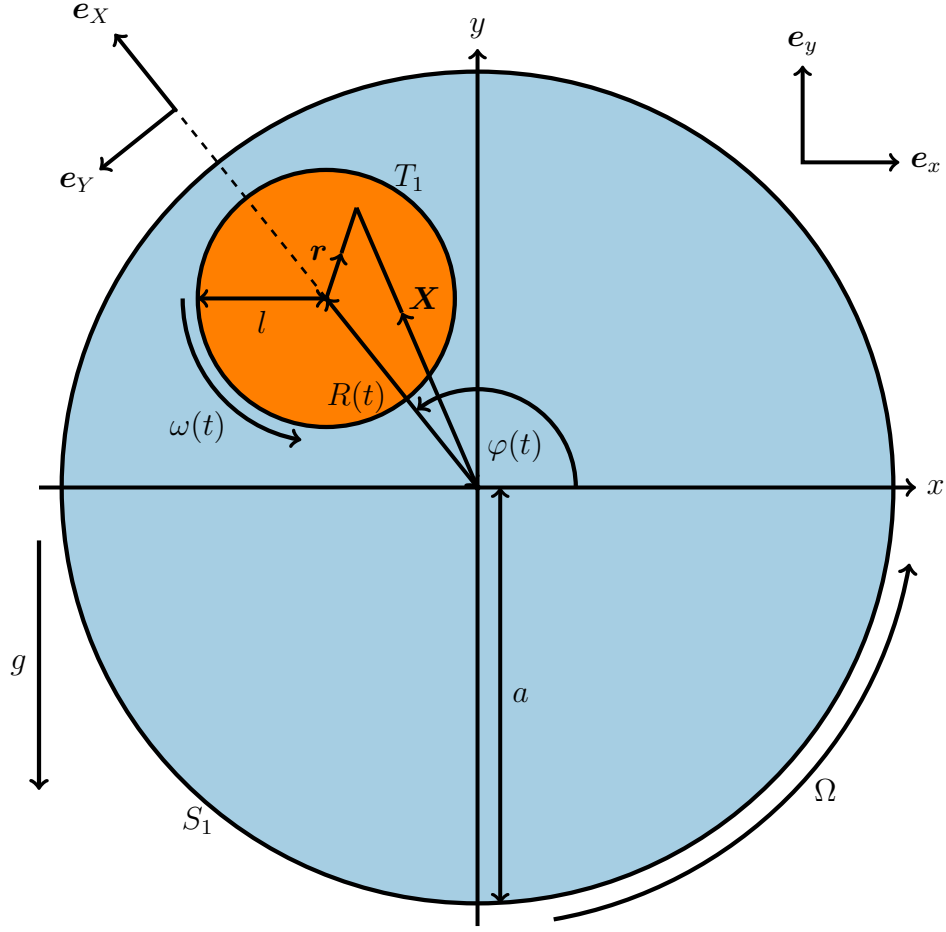


Figure 2.1: Schematic of bioreactor model. This is the face of the bioreactor with the z -axis coming out of the page. The bioreactor rotates anti-clockwise with constant angular velocity $\Omega \mathbf{e}_z$. The TC centre is a distance $R(t)$ away from the bioreactor centre, and the line joining these two centres makes an angle $\varphi(t)$ with the positive x -axis. The TC rotates with an angular velocity $\omega(t)$ around its own centre. The position vector with origin at the bioreactor centre is $\mathbf{X}$ and the position vector with origin at the TC centre is $\mathbf{r}$. Gravity acts in the negative y -direction.

centre, and to rotate with the TC centre. This means that the TC movement is solely along the X -axis in this frame, the z -direction being unchanged. The unit vectors in the positive X and Y -directions are denoted by $\mathbf{e}_X$ and $\mathbf{e}_Y$ respectively, and are indicated in Figure 2.1.

The TC movement is assumed to have no component in the $\mathbf{e}_z$ direction, and the gaps between the flat circular sides of the TC and bioreactor are taken to be the same height - which we define as $\epsilon_1 l$, as illustrated in Figure 2.2. These assumptions imply a symmetry in the problem around $z = h/2$. We further assume that these gaps are small, that is $\epsilon_1 l \ll h$, throughout this thesis.

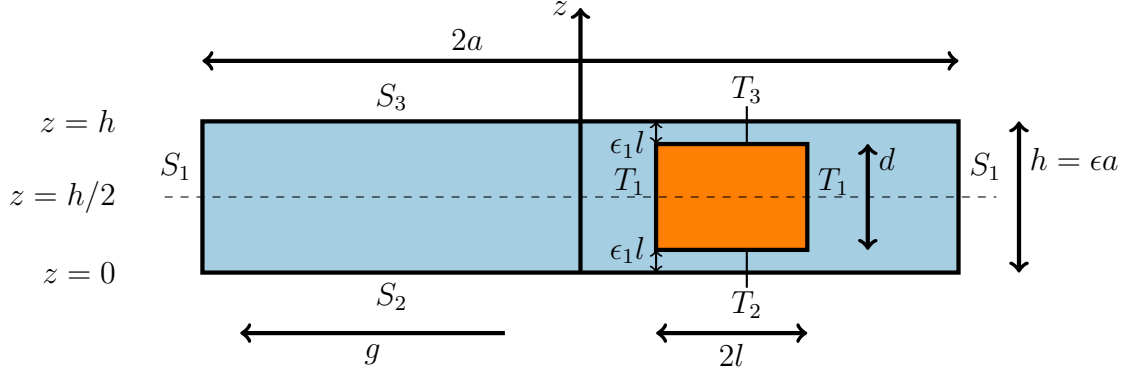


Figure 2.2: A cross-section of the bioreactor showing the detail in the z -direction. The TC has a depth of d which leaves a small gap of length $\epsilon_1 l$ between the TC and bioreactor. This gap allows relative movement between the TC and bioreactor. The dotted line at $z = h/2$ indicates a line of symmetry for the bioreactor geometry and TC movement.

As illustrated in Figure 2.1, the functions we use to describe the position of the TC centre are: $R(t)$, the distance between the centres of the bioreactor and TC, and $\varphi(t)$, the angle that the vector between the bioreactor and TC centres make with the positive x -axis. The TC also rotates about its own centre, and we denote this angular velocity by $\boldsymbol{\omega}(t) = \omega(t)\mathbf{e}_z$. Therefore, in the laboratory frame the velocity of a point within the TC is $\mathbf{V}_{\text{TC}}$, given by

$$\mathbf{V}_{\text{TC}} = \dot{\mathbf{a}} + \boldsymbol{\omega} \times \mathbf{r}, \quad \dot{\mathbf{a}} = \dot{R}\mathbf{e}_X + R\dot{\varphi}\mathbf{e}_Y, \quad \mathbf{r} = \mathbf{X} - R\mathbf{e}_X, \quad (2.1a, b, c)$$

where $\dot{\mathbf{a}}$ is the velocity of the TC centre of mass, $\mathbf{r}$ is the position vector of a point in the TC relative to the TC centre, and $\mathbf{X}$ is the position vector of the same point relative to the bioreactor centre.

In general, $R(t)$, $\varphi(t)$, and $\omega(t)$ are functions of time that will have to be solved for, but in this Chapter we assume that these are prescribed functions, and we solve for the corresponding fluid flow. In Chapter 5, we couple the flow to the trajectory and determine the functions $R(t)$, $\varphi(t)$, and $\omega(t)$ by considering the force and torque acting upon the TC.

Gravity, $\mathbf{g}$, is perpendicular to the bioreactor axis of rotation, and is given by

$$\mathbf{g} = -g(\sin \varphi \mathbf{e}_X + \cos \varphi \mathbf{e}_Y), \quad (2.2)$$

where g is the magnitude of the (constant) gravitational force.

In general, we work in the frame (X, Y, z) rotating with the TC, which shares an origin with the laboratory frame. This is to facilitate solving the governing equations

Parameter	Symbol	Typical Value
HARV radius	a	22 – 76 mm
HARV height	h	3.4 – 25 mm
TC radius	l	2 – 5.35 mm
TC depth	d	2.5 – 3.1 mm
HARV angular velocity	Ω	0.2 – 2 s ⁻¹
Gravity	g	9.81 m s ⁻²
Fluid density	ρ	1 g cm ⁻³
Fluid viscosity	μ	10 ⁻² g cm ⁻¹ s ⁻¹

Table 2.1: A table to show typical experimental parameter values. Data taken from Sams *et al.* [65], Freed and Vunjak-Novakovic [25], Anderson and Schwarz [2], Yu *et al.* [82] and Cummings *et al.* [19]. The bioreactor dimensions do not necessarily scale in proportion, and it is possible to have $h \sim 3.4$ mm, with $a \sim 76$ mm.

we discuss in §2.2. Occasionally, we refer back to the laboratory frame in order to discuss the implications of our results. It is also helpful to refer to the laboratory frame when discussing boundary conditions.

Typical values of experimental parameters are given in Table 2.1.

2.2 Governing equations

2.2.1 Dimensional equations

In this section we give the dimensional governing equations and boundary conditions in a frame rotating with the TC, and discuss how to move between the rotating and laboratory frame.

We refer to the fluid exterior to the TC as the ‘bulk fluid/flow’, and the fluid within the TC as the ‘interior fluid/flow’ or ‘porous flow’. We further emphasise that the following governing equations and fluid velocities (in both the bulk and interior fluid) are given in the frame rotating with the TC. The bulk fluid is incompressible and satisfies the Navier-Stokes equations

$$\rho (\dot{\mathbf{u}} + (\mathbf{u} \cdot \nabla) \mathbf{u} + 2\dot{\varphi} \mathbf{e}_z \times \mathbf{u} + \ddot{\varphi} \mathbf{e}_z \times \mathbf{X} - \dot{\varphi}^2 \mathbf{X}^\perp) = -\nabla \tilde{p} + \mu \nabla^2 \mathbf{u} + \rho \mathbf{g}, \quad (2.3a)$$

$$\nabla \cdot \mathbf{u} = 0, \quad (2.3b)$$

where $\mathbf{u} = (u, v, w)$ is the bulk fluid velocity, $\tilde{p}$ is the pressure in the bulk fluid, $\mathbf{X}^\perp = X\mathbf{e}_X + Y\mathbf{e}_Y$ is the projection of $\mathbf{X}$ into the (X, Y) -plane, and an overdot represents differentiation with respect to time. The interior flow is incompressible

and satisfies the Darcy equations

$$\mathbf{Q} - R\mathbf{e}_X + (\dot{\varphi} - \omega)\mathbf{e}_z \times (\mathbf{X} - R\mathbf{e}_X) = -\frac{k}{\mu} \left(\nabla \tilde{P} - \rho \mathbf{g} \right), \quad (2.4a)$$

$$\nabla \cdot \mathbf{Q} = 0, \quad (2.4b)$$

where $\mathbf{Q} = (U, V, W)$ is the Darcy velocity of the interior fluid, $\tilde{P}$ is the pressure in the interior fluid, and k is the experimentally determined permeability of the TC. We discuss the derivation of the Darcy equations in a moving frame in Appendix A.

The transformation of the bulk flow and Darcy velocity from the rotating to laboratory frame is given by

$$\mathbf{u}_{\text{LF}} = \mathbf{u} + \dot{\varphi}\mathbf{e}_z \times \mathbf{X}, \quad \mathbf{Q}_{\text{LF}} = \mathbf{Q} + \dot{\varphi}\mathbf{e}_z \times \mathbf{X}, \quad (2.5a, b)$$

where $\mathbf{u}_{\text{LF}}$ and $\mathbf{Q}_{\text{LF}}$ are the bulk flow and Darcy velocity in the laboratory frame respectively. When discussing flow through a porous medium in a macroscale context, one of two velocities is used: the Darcy velocity or the pore velocity. We use the Darcy velocity here, and present a discussion of the two terms and their relationship in Appendix A.

2.2.1.1 Boundary conditions

In order to define the boundary conditions, we formally define the boundaries of the fluid domain. The entire bioreactor surface is defined to be $S = S_1 \cup S_2 \cup S_3$, where

$$S_1 = \{(X, Y, z) \in \mathbb{R}^3 : X^2 + Y^2 = a^2, 0 \leq z \leq h\}, \quad (2.6a)$$

$$S_2 = \{(X, Y, z) \in \mathbb{R}^3 : X^2 + Y^2 < a^2, z = 0\}, \quad (2.6b)$$

$$S_3 = \{(X, Y, z) \in \mathbb{R}^3 : X^2 + Y^2 < a^2, z = h\}, \quad (2.6c)$$

and the entire TC surface is defined to be $T = T_1 \cup T_2 \cup T_3$, where

$$T_1 = \{(X, Y, z) \in \mathbb{R}^3 : (X - R)^2 + Y^2 = l^2, \epsilon_1 l \leq z \leq h - \epsilon_1 l\}, \quad (2.7a)$$

$$T_2 = \{(X, Y, z) \in \mathbb{R}^3 : (X - R)^2 + Y^2 < l^2, z = \epsilon_1 l\}, \quad (2.7b)$$

$$T_3 = \{(X, Y, z) \in \mathbb{R}^3 : (X - R)^2 + Y^2 < l^2, z = h - \epsilon_1 l\}. \quad (2.7c)$$

These boundaries are marked in Figures 2.1 and 2.2.

In the laboratory frame, we impose a no-slip condition on the solid bioreactor boundary S , given by

$$\mathbf{u}_{\text{LF}} = \Omega \mathbf{e}_z \times \mathbf{X} \quad \text{on } S. \quad (2.8)$$

Using (2.5a), in the rotating frame (2.8) becomes

$$\mathbf{u} = (\Omega - \dot{\varphi}) \mathbf{e}_z \times \mathbf{X} \quad \text{on } S. \quad (2.9)$$

Due to the different nature of the TC surfaces (i.e. T_1 being porous, and $T_2 \cup T_3$ being solid), the boundary conditions on T are split accordingly. We start with the simpler boundary condition and discuss $T_2 \cup T_3$ first.

The solid nature of $T_2 \cup T_3$ means that the normal velocity vanishes for both the bulk and interior fluid, and that the bulk slip velocity must be equal to the TC velocity on $T_2 \cup T_3$ - a no-slip condition. Due to the order of the partial differential equations involved in Darcy flow, we cannot impose any conditions on the tangential interior flow on the boundaries. Therefore, in the rotating frame, the boundary conditions on $T_2 \cup T_3$ for the exterior and interior flow respectively, are

$$\mathbf{u} = \dot{R}\mathbf{e}_X + (\omega - \dot{\varphi}) \mathbf{e}_z \times (\mathbf{X} - R\mathbf{e}_X), \quad W = 0 \quad \text{on } T_2 \cup T_3. \quad (2.10a, b)$$

We now give the boundary conditions on T_1 , the curved interface between the bulk and interior fluid, in the rotating frame. On this interface, we impose continuity of normal flux, continuity of normal stress and a Beavers and Joseph (BJ) tangential slip condition

$$\mathbf{u} \cdot \mathbf{n} = \mathbf{Q} \cdot \mathbf{n} \quad \text{on } T_1, \quad (2.11a)$$

$$-\tilde{p} + \mu \mathbf{n} \cdot \nabla (\mathbf{u} \cdot \mathbf{n}) = -\tilde{P} \quad \text{on } T_1, \quad (2.11b)$$

$$\mathbf{n} \cdot \nabla (\mathbf{u} \cdot \mathbf{s}_i) = \frac{\lambda}{\sqrt{k}} (\mathbf{u} - \mathbf{Q}) \cdot \mathbf{s}_i \quad \text{on } T_1, \quad (2.11c)$$

where $\mathbf{n}$ is the unit normal pointing out of the TC, $\mathbf{s}_i$ is any unit tangent vector to the surface (there are two linearly independent vectors that span the entire surface T_1 - we generally use $\mathbf{e}_z$ and $\mathbf{e}_z \times \mathbf{n}$), and λ is the experimentally determined (dimensionless) Beavers and Joseph slip coefficient. The BJ slip condition is a semi-constitutive relationship, and is discussed in §1.2.

2.2.2 Dimensionless equations

We nondimensionalize as follows

$$\left. \begin{aligned} (X, Y, z) &= a(X^*, Y^*, \epsilon z^*), & (l, R) &= a(b^*, R^*), \\ t &= \Omega^{-1} t^*, & \omega &= \Omega \omega^*, \\ (u, v, w) &= a\Omega(u^*, v^*, \epsilon w^*), & (U, V, W) &= a\Omega(U^*, V^*, \epsilon W^*), \\ (\tilde{p}, \tilde{P}) &= \mu\Omega\epsilon^{-2}(\tilde{p}^*, \tilde{P}^*), \end{aligned} \right\} \quad (2.12)$$

where asterisks denote dimensionless variables, and immediately drop asterisks for convenience. In dimensionless variables, we continue to use the vector notation $\mathbf{X} = (X, Y, z)$, $\mathbf{u} = (u, v, w)$ and $\mathbf{Q} = (U, V, W)$. Therefore, in component form the governing equation (2.3) becomes

$$\epsilon Re (\dot{u} + (\mathbf{u} \cdot \nabla) u - 2\dot{\varphi}v - \ddot{\varphi}Y - \dot{\varphi}^2 X) = -p_X + \epsilon^2 \nabla_{\perp}^2 u + u_{zz}, \quad (2.13a)$$

$$\epsilon Re (\dot{v} + (\mathbf{u} \cdot \nabla) v + 2\dot{\varphi}u + \ddot{\varphi}X - \dot{\varphi}^2 Y) = -p_Y + \epsilon^2 \nabla_{\perp}^2 v + v_{zz}, \quad (2.13b)$$

$$\epsilon^3 Re (\dot{w} + (\mathbf{u} \cdot \nabla) w) = -p_z + \epsilon^4 \nabla_{\perp}^2 w + \epsilon^2 w_{zz}, \quad (2.13c)$$

$$\nabla \cdot \mathbf{u} = 0, \quad (2.13d)$$

where an overdot now represents differentiation with respect to dimensionless time, subscripts denote spatial derivatives, the scalar operator $\nabla_{\perp}^2 = \partial_{XX} + \partial_{YY}$, and the Reynolds number, $Re = \rho h(a\Omega)/\mu$, is a measure of the ratio of inertial forces to viscous forces. We emphasise that the lengthscale in the Reynolds number adopted here is the bioreactor height and not its radius.

We note that, compared to Cummings and Waters [18], we have eliminated the need for a Strouhal number - a measure of the ratio of the characteristic times of fluid flow and bioreactor rotation, as these characteristic times are similar. We show that we can still obtain the flow and trajectory behaviour in Cummings and Waters [18], thus eschewing the need for the Strouhal number and reducing the number of free parameters in the model. Finally, the reduced pressure p is given by

$$p = \tilde{p} + B(X \sin \varphi + Y \cos \varphi), \quad (2.14)$$

where the Bond number (sometimes called the Eötvös number), $B = \epsilon^2 \rho a g / (\mu \Omega)$, is a measure of the ratio of gravity to the fluid viscosity.

In a similar manner, the governing equations (2.4) within the TC become

$$U - \dot{R} - (\dot{\varphi} - \omega)Y = -K P_X, \quad (2.15a)$$

$$V + (\dot{\varphi} - \omega)(X - R) = -K P_Y, \quad (2.15b)$$

$$\epsilon^2 W = -K P_z, \quad (2.15c)$$

$$\nabla \cdot \mathbf{Q} = 0, \quad (2.15d)$$

where $K = k/(\epsilon a)^2$ is the Darcy number, and we make the assumption that $K = O(1)$. Physically, this corresponds to a fairly permeable TC (e.g. similar to a kitchen sponge), and is markedly different from the permeabilities encountered in mathematical geoscience, which will be several orders of magnitude smaller. The reduced pressure P is given by

$$P = \tilde{P} + B(X \sin \varphi + Y \cos \varphi). \quad (2.16)$$

From Table 2.1, we see that typical values of the dimensionless parameters are: $\epsilon \approx 0.04 - 0.15$, $Re \approx 2 - 10^3$, and $B \approx 10^3$. Whilst the Bond number is very large, it is absorbed into the reduced pressure, and only plays a role in the TC force balance in Chapter 5 where we consider a much reduced Bond number as it is multiplied by a small parameter (which arises due to the small gap between flat sides of the TC and bioreactor). Furthermore, we consider the problem when the Reynolds number is at the lower end of its range.

2.2.3 Boundary conditions

Before giving the dimensionless boundary conditions, we describe the new boundaries in dimensionless form. The bioreactor surface $S = S_1 \cup S_2 \cup S_3$, which was originally given in (2.6), is now

$$S_1 = \{(X, Y, z) \in \mathbb{R}^3 : X^2 + Y^2 = 1, 0 \leq z \leq 1\}, \quad (2.17a)$$

$$S_2 = \{(X, Y, z) \in \mathbb{R}^3 : X^2 + Y^2 < 1, z = 0\}, \quad (2.17b)$$

$$S_3 = \{(X, Y, z) \in \mathbb{R}^3 : X^2 + Y^2 < 1, z = 1\}, \quad (2.17c)$$

and the TC surface $T = T_1 \cup T_2 \cup T_3$, originally given in (2.7), is now

$$T_1 = \{(X, Y, z) \in \mathbb{R}^3 : (X - R)^2 + Y^2 = b^2, \epsilon_2 \leq z \leq 1 - \epsilon_2\}, \quad (2.18a)$$

$$T_2 = \{(X, Y, z) \in \mathbb{R}^3 : (X - R)^2 + Y^2 < b^2, z = \epsilon_2\}, \quad (2.18b)$$

$$T_3 = \{(X, Y, z) \in \mathbb{R}^3 : (X - R)^2 + Y^2 < b^2, z = 1 - \epsilon_2\}, \quad (2.18c)$$

where $\epsilon_2 = \epsilon_1 b / \epsilon$ is the ratio of the gap distance between the flat sides of the TC and bioreactor, and the height of the bioreactor.

On the bioreactor boundary S , the no slip boundary condition (2.9) becomes

$$\mathbf{u} = (1 - \dot{\varphi}) \mathbf{e}_z \times \mathbf{X} \quad \text{on } S. \quad (2.19)$$

The boundary conditions on $T_2 \cup T_3$, the flat surfaces of the TC, are given by (2.10). They are invariant to the nondimensionalization, but we give them for completeness

$$\mathbf{u} = \dot{R} \mathbf{e}_X + (\omega - \dot{\varphi}) \mathbf{e}_z \times (\mathbf{X} - R \mathbf{e}_X), \quad W = 0, \quad \text{on } T_2 \cup T_3. \quad (2.20a, b)$$

The boundary conditions on T_1 , the curved surface of the TC, are given by (2.11) and become

$$\mathbf{u} \cdot \mathbf{n} = \mathbf{Q} \cdot \mathbf{n} \quad \text{on } T_1, \quad (2.21a)$$

$$-p + \epsilon^2 \mathbf{n} \cdot \nabla (\mathbf{u} \cdot \mathbf{n}) = -P \quad \text{on } T_1, \quad (2.21b)$$

$$\epsilon \mathbf{n} \cdot \nabla (\mathbf{u} \cdot \mathbf{s}_i) = \frac{\lambda}{\sqrt{K}} (\mathbf{u} - \mathbf{Q}) \cdot \mathbf{s}_i \quad \text{on } T_1. \quad (2.21c)$$

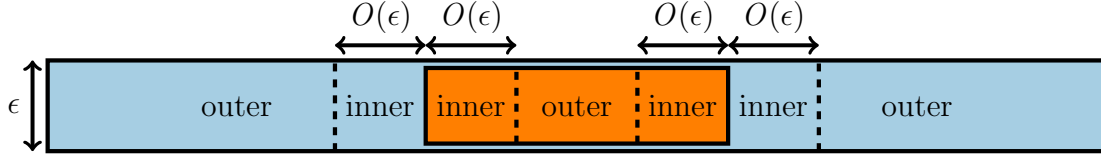


Figure 2.3: Schematic diagram of the boundary layers near the TC surface. The blue region is the bulk fluid and the orange region is the porous obstacle. The bioreactor height is exaggerated for illustrative purposes.

In the next section we formulate asymptotic expansions for the variables of interest in the limit $\epsilon \ll 1$ and $1 \ll Re \ll \epsilon^{-1}$, and solve the resulting flow problem. However, we can immediately see from (2.13) that the limit as $\epsilon \rightarrow 0$ is a singular problem (as the order of the partial differential equations is reduced in X and Y), and so we must proceed with caution. We expect the neglected viscous terms to become important within ‘inner’ regions close to the interface, whose length is of the same order as the bioreactor height, i.e. within a distance of $O(\epsilon)$ from the interface (as indicated in Figure 2.3).

We proceed by considering the flow in the ‘outer’ regions indicated in Figure 2.3. From the boundary conditions (2.21), one may naively expect that continuity of normal flux and normal stress are the correct conditions to couple the outer regions. However, we show that this only holds at leading order, and the full boundary layer structure is more subtle than it initially appears.

To give this intricate boundary layer problem our full consideration, we delay its analysis until Chapters 3 and 4, where we investigate the relevant ‘inner’ problems (as indicated in Figure 2.3): the boundary layers that are induced and the effect they have on the conditions to couple the outer regions. In the remainder of this Chapter, we use the coupling conditions derived in Chapter 4, and present these after we formalize the relevant asymptotic expansions.

2.3 Reduced flow problem

Thus far, we have given the governing equations and boundary conditions for the full flow problem. We now solve these equations by exploiting the small parameters involved in the problem.

The first assumption we make is that $\epsilon \ll 1$. This corresponds to the bioreactor height being much smaller than its radius, and is an intrinsic characteristic of the HARV bioreactor that we are modelling. We further assume that $Re \ll \epsilon^{-1}$. This

corresponds to the flow being dominated by a balance between pressure and viscosity rather than inertial effects.

For the flow problem, the leading-order solution is of the most interest, but in Chapter 5 we investigate the effect of inertia on the TC trajectory. In order to include all relevant terms, we require knowledge of the effect of inertia on the flow. That is, we must determine the flow up to $O(\epsilon Re)$. To this end, it will be convenient to assume that $Re \gg \epsilon$ (as we require $\epsilon^2 \ll \epsilon Re$) in order to consider the inertial terms in the first correction.

The last assumptions are on the size of $\epsilon_2 = \epsilon_1 b / \epsilon$, the ratio between the length of the gap between flat sides of the TC and bioreactor, and the bioreactor height. We first assume that $\epsilon_2 \ll \epsilon Re$. This means that the effect of the thin gap between TC and bioreactor on the fluid flow is much smaller than the effect of inertia, and we therefore ignore the thin gap for the rest of this Chapter, solving in the outer regions which we define below. We further assume that $\epsilon_2 Re \ll 1$, which implies that the inertial terms do not become relevant within the thin gap (as discussed in Appendix E.10).

To clarify, the assumptions we make are: $\epsilon \ll 1$, $\epsilon_2 \ll \epsilon Re \ll 1$, $\epsilon_2 Re \ll 1$, and $\epsilon \ll Re$, and we expand all of our variables in the following asymptotic expansion

$$f = f_0 + \epsilon Re f_1 + o(\epsilon Re). \quad (2.22)$$

where $f \in \{\mathbf{u}, \mathbf{Q}, p, P\}$. We have not expanded the functions that determine the TC position (R , φ , and ω), as we determine in Chapter 5 that the first correction to the TC position is $O(\epsilon_2)$ (and recall that $\epsilon_2 \ll \epsilon Re$). Therefore, we leave them as $O(1)$ variables in this Chapter, and expand them into smaller correction terms when necessary in Chapter 5.

We formally define the outer regions we consider as follows. We denote the bulk region to be D_1 , and the porous region to be D_2 . The bioreactor surface is still given by $S = S_1 \cup S_2 \cup S_3$, but the TC surface is now given by $\bar{T} = \bar{T}_1 \cup \bar{T}_2 \cup \bar{T}_3$, which neglects the small gap above and below the TC. Mathematically, the regions we work in are given by

$$D_1 = \{(X, Y, z) \in \mathbb{R}^3 : X^2 + Y^2 < 1, (X - R)^2 + Y^2 > b^2, 0 \leq z \leq 1\}, \quad (2.23a)$$

$$D_2 = \{(X, Y, z) \in \mathbb{R}^3 : (X - R)^2 + Y^2 < b^2, 0 \leq z \leq 1\}, \quad (2.23b)$$

with TC surfaces given by

$$\overline{T}_1 = \{(X, Y, z) \in \mathbb{R}^3 : (X - R)^2 + Y^2 = b^2, 0 \leq z \leq 1\}, \quad (2.24a)$$

$$\overline{T}_2 = \{(X, Y, z) \in \mathbb{R}^3 : (X - R)^2 + Y^2 < b^2, z = 0\}, \quad (2.24b)$$

$$\overline{T}_3 = \{(X, Y, z) \in \mathbb{R}^3 : (X - R)^2 + Y^2 < b^2, z = 1\}. \quad (2.24c)$$

2.3.1 Reduced governing equations

We now form the relevant asymptotic equations by substituting the asymptotic expansions (2.22) into the relevant governing equations and equating asymptotic orders. The $O(1)$ bulk flow equations (2.13) are

$$p_{0X} = u_{0zz}, \quad p_{0Y} = v_{0zz}, \quad 0 = -p_{0z}, \quad \nabla \cdot \mathbf{u}_0 = 0, \quad (2.25a, b, c, d)$$

and the $O(\epsilon Re)$ bulk flow equations (2.13) are given by

$$\dot{u}_0 + (\mathbf{u}_0 \cdot \nabla) u_0 - 2\dot{\varphi}v_0 - \ddot{\varphi}Y - \dot{\varphi}^2X = -p_{1X} + u_{1zz}, \quad (2.26a)$$

$$\dot{v}_0 + (\mathbf{u}_0 \cdot \nabla) v_0 + 2\dot{\varphi}u_0 + \ddot{\varphi}X - \dot{\varphi}^2Y = -p_{1Y} + v_{1zz}, \quad (2.26b)$$

$$0 = -p_{1z}, \quad (2.26c)$$

$$\nabla \cdot \mathbf{u}_1 = 0. \quad (2.26d)$$

The $O(1)$ interior flow equations (2.15) are

$$U_0 - \dot{R} - (\dot{\varphi} - \omega)Y = -KP_{0X}, \quad (2.27a)$$

$$V_0 + (\dot{\varphi} - \omega)(X - R) = -KP_{0Y}, \quad (2.27b)$$

$$0 = -KP_{0z}, \quad (2.27c)$$

$$\nabla \cdot \mathbf{Q}_0 = 0, \quad (2.27d)$$

and the $O(\epsilon Re)$ interior flow equations (2.15) are

$$U_1 = -KP_{1X}, \quad (2.28a)$$

$$V_1 = -KP_{1Y}, \quad (2.28b)$$

$$0 = -KP_{1z}, \quad (2.28c)$$

$$\nabla \cdot \mathbf{Q}_1 = 0. \quad (2.28d)$$

2.3.2 Reduced boundary conditions

We have already discussed the singular nature of our small parameter assumptions. The practical effects of this are that we are unable to impose slip conditions on S_1 and $\bar{T}_1$ due to the reduction in the order of the governing partial differential equations (2.25) compared to the full equations (2.13). Furthermore, neglecting the small gap above and below the TC (using the assumption $\epsilon_2 \ll \epsilon Re$) means that the boundary condition (2.20a) on the flat surfaces of the TC is not required for the reduced system. Therefore, we are only able to impose conditions (2.20b) for the porous flow on these boundaries. In Chapter 4, we formally consider the boundary layers within this problem, with further details included in Appendices E.2–E.9. In this context, we consider the flow within the thin gaps in Appendix E.10.

Within the bioreactor, the no-slip boundary conditions (2.19) on the flat surfaces of the bioreactor, S_2 and S_3 , remain unchanged, and are given by

$$\mathbf{u}_0 = (1 - \dot{\varphi}) \mathbf{e}_z \times \mathbf{X}, \quad \mathbf{u}_1 = \mathbf{0} \quad \text{on } S_2 \cup S_3. \quad (2.29a, b)$$

Within the TC, the no-flux boundary conditions (2.20b) on the flat surfaces of the TC, $\bar{T}_2$ and $\bar{T}_3$, are also unchanged, and are given by

$$W_0 = 0, \quad W_1 = 0 \quad \text{on } \bar{T}_2 \cup \bar{T}_3. \quad (2.30a, b)$$

We now give the coupling conditions for the reduced problem, which are formally derived in Chapter 4. To present them, we define the one-dimensional curves ∂D_1 and ∂D_2 as follows

$$\partial D_1 = \{(X, Y) \in \mathbb{R}^2 : X^2 + Y^2 = 1\}, \quad (2.31a)$$

$$\partial D_2 = \{(X, Y) \in \mathbb{R}^2 : (X - R)^2 + Y^2 = b^2\}, \quad (2.31b)$$

where ∂D_1 corresponds to the curved bioreactor boundary surface S_1 and ∂D_2 corresponds to the curved TC boundary surface $\bar{T}_1$, both projected onto curves in (X, Y) -space.

On the bioreactor boundary ∂D_1 , the relevant boundary conditions are derived from the continuity of flux condition (2.19). These are given in (E.137), and are

$$\int_0^1 \mathbf{u}_0 \cdot \mathbf{n} \, dz = 0, \quad \int_0^1 \mathbf{u}_1 \cdot \mathbf{n} \, dz = 0 \quad \text{on } \partial D_1, \quad (2.32a, b)$$

where $\mathbf{n}$ is the outward pointing unit normal on ∂D_1 .

On the TC boundary ∂D_2 , the relevant coupling conditions are derived from the continuity of flux condition (2.21a) and the continuity of normal stress condition

(2.21b). The higher-order coupling conditions contain a Heaviside function because they only deviate from no jump in their respective variables for outflow (which occurs when $-P_{0n} > 0$, as shown in (E.133)). The continuity of flux conditions are given in (E.135), and are

$$\int_0^1 (\mathbf{u}_0 - \mathbf{Q}_0) \cdot \mathbf{n} \, dz = 0 \quad \text{on } \partial D_2, \quad (2.33a)$$

$$\int_0^1 ((\mathbf{u}_1 - \mathbf{Q}_1) \cdot \mathbf{n}) \, dz = -K \frac{\partial}{\partial s} (P_{0n} \Lambda) H(-P_{0n}) \quad \text{on } \partial D_2, \quad (2.33b)$$

where Λ is a function of space and time that arises due to the entrainment of fluid in the direction tangential to the TC surface (and is defined in (4.89)), $\partial/\partial n$ is the normal derivative, $H(x)$ is the Heaviside function, and $\mathbf{n}$ is the outward pointing unit normal on the TC boundary ∂D_2 . The coupling conditions for the normal velocity (2.33) are all given as functions averaged over z because we integrate the continuity equation to derive them. This is not the loss of information that it appears to be. There are two reasons for this: firstly, the fluid velocity is linearly dependent on the pressure gradient, and secondly, the pressure is independent of z (both of these follow from (2.25)–(2.28)). This means that the normal fluid velocity at a boundary, averaged over z , is equivalent to a Neumann condition on the pressure. Therefore, conditions on the averaged normal velocities are enough to obtain well-posed problems for the bulk and interior fluid pressures.

The continuity of normal stress conditions are given in (4.90), and are

$$p_0 - P_0 = 0 \quad \text{on } \partial D_2, \quad (2.34a)$$

$$p_1 - P_1 = (K P_{0n})^2 \Pi H(-P_{0n}) \quad \text{on } \partial D_2, \quad (2.34b)$$

where Π is a function of space and time due to the pressure change within the inner regions (and is defined in (4.71)). We find that imposing continuity of normal stress leads to continuity of pressure at leading order, and also at first correction for inflow (when $-P_{0n} < 0$). In fact, we show in §4.4.2.1 that the right-hand side of (2.34b) is not due to the normal stress term $\mathbf{n} \cdot \nabla(\mathbf{u} \cdot \mathbf{n})$ in (2.21b), rather the variation in pressure within the inner regions. Therefore, up to the orders we consider, imposing continuity of stress at the interface is equivalent to imposing continuity of pressure.

We remark that the last boundary condition on the interface, the BJ slip condition (2.21c), cannot be imposed in the outer bulk flow region due to neglecting the in-plane viscous terms. Furthermore, we note that the BJ slip condition has no effect on the coupling conditions we have presented. In Chapters 3 and 4, we investigate regions close to the TC surface that allow the BJ slip condition to be satisfied.

2.4 Solving the $O(1)$ equations

We have now formulated the leading-order governing equations (2.25) and (2.27) with correct leading-order boundary conditions ((2.29–2.34)a).

Solving (2.25a–c) subject to (2.29a) in the X and Y direction, we obtain

$$(u_0, v_0) = (1 - \dot{\varphi})(-Y, X) + f_1(z)(p_{0X}, p_{0Y}), \quad f_1(z) = \frac{z(z-1)}{2}. \quad (2.35a, b)$$

Substituting this into (2.25d), integrating with respect to z , and using (2.29a) in the z -direction, we obtain

$$w_0 \equiv 0, \quad 0 = \nabla_{\perp}^2 p_0. \quad (2.36a, b)$$

As (2.27a–b) already gives the Darcy velocity in terms of the pressure inside the TC, our task is to formulate a governing equation for P_0 and determine W_0 . Using a similar method as for the bulk flow, we substitute (2.27a–b) into (2.27d), integrate with respect to z , and use (2.30a) to determine

$$W_0 \equiv 0, \quad 0 = \nabla_{\perp}^2 P_0. \quad (2.37a, b)$$

Thus we are required to solve Laplace's equation for the pressures p_0 and P_0 , coupled via the interfacial conditions. We therefore transform the remaining boundary conditions involving the velocity into boundary conditions for the normal pressure derivatives.

Substituting (2.35) into (2.32a), the no flux boundary condition on ∂D_1 becomes

$$\frac{\partial p_0}{\partial n} = 0. \quad (2.38)$$

Substituting (2.35) and (2.27a–b) into (2.33a), the continuity of flux boundary condition on ∂D_2 becomes

$$-\frac{1}{12} \frac{\partial p_0}{\partial n} + K \frac{\partial P_0}{\partial n} = b^{-1} \left(\dot{R}(X - R) - (1 - \dot{\varphi}) Y R \right). \quad (2.39)$$

We note that as the governing equations (2.36b) and (2.37b), and boundary conditions (2.34a), (2.38), and (2.39) are independent of z , our problem is posed on a two-dimensional (2D) domain (as briefly discussed in §2.3.2). With regard to this 2D domain, we refer to the bulk flow domain as region I, and the porous domain as region IV (the non-consecutive numbering is for consistency with Chapters 3 and 4, where we introduce boundary layer regions).

In the next section, we solve this system of equations analytically via use of a bipolar transformation.

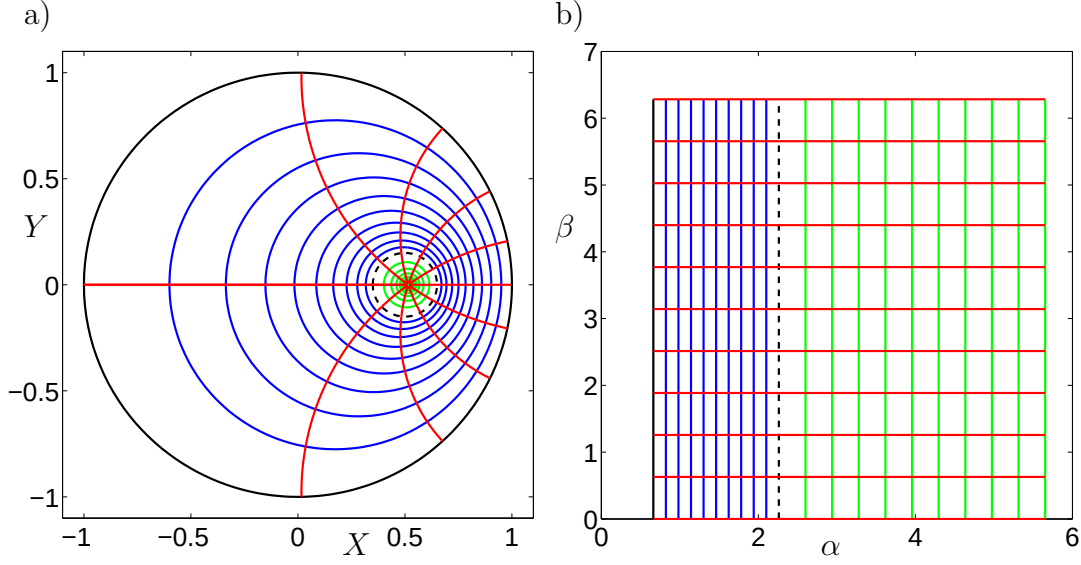


Figure 2.4: Constant lines in α and β showing the transformation from a) (X, Y) -space to b) (α, β) -space. In both cases, the blue lines correspond to constant α within the bioreactor, the green lines correspond to constant α within the TC and the red lines correspond to constant β in both regions. The solid black line is the bioreactor boundary $\alpha = \alpha_1$, and the dashed black line is the TC to bioreactor boundary $\alpha = \alpha_2$. We have terminated α after it reaches $2.5\alpha_2$, but emphasize that $\alpha \rightarrow \infty$ in the full transformation.

2.4.1 Bipolar transformation

We solve the leading order governing equations by following Cummings and Waters [18] and transforming to bipolar coordinates (α, β) , defined by

$$X = \cosh \alpha_1 - \frac{\sinh \alpha_1 \sinh \alpha}{\cosh \alpha - \cos \beta}, \quad Y = \frac{\sinh \alpha_1 \sin \beta}{\cosh \alpha - \cos \beta}, \quad (2.40a, b)$$

where

$$b = \frac{\sinh \alpha_1}{\sinh \alpha_2}, \quad R = \cosh \alpha_1 - \sinh \alpha_1 \coth \alpha_2. \quad (2.41a, b)$$

In Appendix B, we discuss the scale factors for this transformation, and relate the unit vectors between each coordinate system.

Region I now corresponds to the finite rectangle satisfied by $0 < \alpha_1 < \alpha < \alpha_2$ and $0 < \beta < 2\pi$, and region IV corresponds to the semi-infinite rectangle satisfied by $\alpha_2 < \alpha < \infty$ and $0 < \beta < 2\pi$, where both regions have periodic boundary conditions at $\beta = 0, 2\pi$. Hence, the bioreactor boundary ∂D_1 corresponds to $\alpha = \alpha_1$, and the TC boundary ∂D_2 corresponds to $\alpha = \alpha_2$. We show this transformation for $R = 0.5$ and $b = 0.15$ in Figure 2.4.

With respect to the bipolar coordinate system (α, β) , and using (B.10b), the governing equations (2.36b) and (2.37b) are now

$$\nabla^2 p_0 = 0, \quad \alpha_1 < \alpha < \alpha_2, \quad 0 < \beta < 2\pi, \quad (2.42a)$$

$$\nabla^2 P_0 = 0, \quad \alpha_2 < \alpha < \infty, \quad 0 < \beta < 2\pi. \quad (2.42b)$$

These must be solved subject to the boundary condition (2.38) on $\alpha = \alpha_1$, given by

$$\frac{\partial p_0}{\partial \alpha} = 0, \quad (2.43)$$

along with the coupling conditions (2.34a) and (2.39) on $\alpha = \alpha_2$, which become

$$p_0 = P_0, \quad (2.44a)$$

$$-\frac{1}{12} \frac{\partial p_0}{\partial \alpha} + K \frac{\partial P_0}{\partial \alpha} = \frac{\sinh \alpha_1 \left(R(1 - \dot{\varphi}) \sin \beta \sinh \alpha_2 + \dot{R}(\cos \beta \cosh \alpha_2 - 1) \right)}{(\cosh \alpha_2 - \cos \beta)^2}. \quad (2.44b)$$

Using separation of variables, the fact that p_0 and P_0 are periodic in β , the boundary condition (2.43), and the fact that the Darcy velocity (i.e. ∇P_0) must be finite as $\alpha \rightarrow \infty$, we find that (2.42) is solved by

$$p_0 = \sum_{n=1}^{\infty} \cosh(n(\alpha - \alpha_1)) (A_n \cos n\beta + B_n \sin n\beta), \quad (2.45a)$$

$$P_0 = \sum_{n=1}^{\infty} \exp(-n(\alpha - \alpha_2)) (C_n \cos n\beta + D_n \sin n\beta), \quad (2.45b)$$

and these are unique up to an arbitrary constant which, without loss of generality, we set to zero. In Appendix C.2, we solve for A_n , B_n , C_n , and D_n to obtain

$$A_n = L_n \operatorname{sech}(n(\alpha_2 - \alpha_1)) \dot{R}, \quad (2.46a)$$

$$B_n = L_n \operatorname{sech}(n(\alpha_2 - \alpha_1)) R(1 - \dot{\varphi}), \quad (2.46b)$$

$$C_n = L_n \dot{R}, \quad (2.46c)$$

$$D_n = L_n R(1 - \dot{\varphi}), \quad (2.46d)$$

where

$$L_n = -\frac{24 \sinh \alpha_1 \exp(-n\alpha_2)}{\tanh(n(\alpha_2 - \alpha_1)) + 12K}. \quad (2.46e)$$

In Cummings and Waters [18], the case $K = 0$ (which corresponds to a solid TC) is considered. We see that, in this limit, we attain the same coefficients A_n and B_n as Cummings and Waters [18].

Using the explicit solutions for p_0 and P_0 , it is straightforward to use (2.35a) and (2.27a–b) to determine $\mathbf{u}_0$ and $\mathbf{Q}_0$. To plot the results, it is useful to determine streamfunctions in the laboratory frame for the 2D flow averaged over z . Consider an arbitrary vector function $\mathbf{v}$, that only has components in the $\mathbf{e}_X$ and $\mathbf{e}_Y$ directions. If $\nabla \cdot \mathbf{v} = 0$, this implies that there exists a streamfunction ψ , such that $\mathbf{v} = \nabla \times \psi \mathbf{e}_z$. If, in addition, $\mathbf{v} = \nabla F$, this tells us that

$$(F_\alpha, F_\beta) = (\psi_\beta, -\psi_\alpha). \quad (2.47)$$

Using this fact, we can find streamfunctions in the laboratory frame for the z -averaged velocity by considering the flow due to the rotation and the reduced pressure separately. Using the transformation between laboratory and rotating frames (2.5), the streamfunctions in regions I and IV are

$$\psi_I = -\frac{1}{2}(X^2 + Y^2) - \frac{1}{12}\Psi_I, \quad (2.48a)$$

$$\psi_{IV} = \dot{R}Y - \dot{\phi}RX - \frac{\omega}{2}((X - R)^2 + Y^2) - K\Psi_{IV}, \quad (2.48b)$$

respectively, where

$$\Psi_I = \sum_{n=1}^{\infty} \sinh(n(\alpha - \alpha_1)) (A_n \sin n\beta - B_n \cos n\beta), \quad (2.49a)$$

$$\Psi_{IV} = \sum_{n=1}^{\infty} \exp(-n(\alpha - \alpha_2)) (-C_n \sin n\beta + D_n \cos n\beta), \quad (2.49b)$$

and the coefficients are given in (2.46). We show the streamlines for a prescribed trajectory in Figure 2.5.

2.5 Solving the $O(\epsilon Re)$ equations

We have now solved the governing equations at leading order. In Chapter 5 we require knowledge of the stress exerted by the flow on the TC at $O(\epsilon Re)$. Therefore, we solve the flow equations at this order to obtain this information.

The $O(\epsilon Re)$ equations are given by (2.26) and (2.28), subject to boundary conditions ((2.29–2.34)b). In Appendix C.1, we solve these equations for the velocities in terms of the pressures, and determine that the governing equations to be solved for the pressures are

$$\nabla^2 \phi = 0 \quad \text{in region I}, \quad \nabla^2 P_1 = 0 \quad \text{in region IV}, \quad (2.50a, b)$$

where

$$\phi = p_1 - \frac{1}{2} (X^2 + Y^2) + \frac{3}{560} |\nabla p_0|^2. \quad (2.51)$$

The boundary condition (2.32b) on ∂D_1 becomes

$$\frac{\partial \phi}{\partial n} = \frac{(1 - \dot{\varphi})}{10} \frac{\partial}{\partial n} \frac{\partial p_0}{\partial s} - \frac{1}{5} \frac{\partial p_0}{\partial s}, \quad (2.52)$$

where $\partial/\partial n$ is the normal derivative, and $\partial/\partial s$ is the tangential derivative, with tangential direction $\mathbf{s}$ defined by $\mathbf{n} \times \mathbf{s} = \mathbf{e}_z$. We note that if the transformation does not preserve arc length along the boundary (which is the case for the bipolar transformation), $\partial/\partial n$ and $\partial/\partial s$ are not commutative.

The boundary conditions (2.34b) and (2.33b) on ∂D_2 are

$$\phi - P_1 = -\frac{1}{2} (X^2 + Y^2) + \frac{3}{560} |\nabla p_0|^2 + \Pi(s, t) \left(K \frac{\partial P_0}{\partial n} \right)^2 H \left(-\frac{\partial P_0}{\partial n} \right), \quad (2.53a)$$

$$\frac{\partial \phi}{\partial n} - 12K \frac{\partial P_1}{\partial n} = \frac{\mathbf{n} \cdot \mathbf{B}(s, t)}{10} + 12K \frac{\partial}{\partial s} \left(\frac{\partial P_0}{\partial n} \Lambda(s, t) \right) H \left(-\frac{\partial P_0}{\partial n} \right), \quad (2.53b)$$

where $\mathbf{B}$ is defined in (C.4c), $H(x)$ is the Heaviside function, the unit normal $\mathbf{n}$ points towards the bulk fluid, and s parameterizes the boundary.

2.5.1 Bipolar transformation

We solve the $O(\epsilon Re)$ equations in a similar manner to the $O(1)$ equations, by transforming to the bipolar coordinate system described by (2.40)–(2.41).

As with the $O(1)$ equations, it will be convenient to solve this problem using Fourier series. Therefore, in order to simplify notation, we solve for the boundary conditions

$$\frac{\partial \phi}{\partial n} = g_1(\beta) \quad \text{on } \partial D_1, \quad (2.54a)$$

$$\phi - P_1 = g_2(\beta) \quad \text{on } \partial D_2, \quad (2.54b)$$

$$\frac{\partial \phi}{\partial n} - 12K \frac{\partial P_1}{\partial n} = g_3(\beta) \quad \text{on } \partial D_2, \quad (2.54c)$$

where

$$g_1(\beta) = \frac{\cosh \alpha_1 - \cos \beta}{\sinh \alpha_1} \left(a_{10} + \sum_{n=1}^{\infty} (a_{1n} \cos n\beta + b_{1n} \sin n\beta) \right), \quad (2.55a)$$

$$g_2(\beta) = a_{20} + \sum_{n=1}^{\infty} (a_{2n} \cos n\beta + b_{2n} \sin n\beta), \quad (2.55b)$$

$$g_3(\beta) = -\frac{\cosh \alpha_2 - \cos \beta}{\sinh \alpha_1} \left(a_{30} + \sum_{n=1}^{\infty} (a_{3n} \cos n\beta + b_{3n} \sin n\beta) \right), \quad (2.55c)$$

and the coefficients a_{in} and b_{in} can be determined numerically from boundary conditions (2.52) and (2.53). We note that the coefficients a_{in} and b_{in} are independent of β , but will depend on time. Using (B.10a), and noting that the unit normal pointing into the bulk fluid on ∂D_1 is $\mathbf{e}_\alpha$, the boundary condition (2.54a) on $\alpha = \alpha_1$ becomes

$$\frac{\partial \phi}{\partial \alpha} = a_{10} + \sum_{n=1}^{\infty} (a_{1n} \cos n\beta + b_{1n} \sin n\beta). \quad (2.56)$$

Noting that the unit normal pointing into the bulk fluid on ∂D_2 is $-\mathbf{e}_\alpha$, the boundary conditions (2.54b) and (2.54c) on $\alpha = \alpha_2$ become

$$\phi - P_1 = a_{20} + \sum_{n=1}^{\infty} (a_{2n} \cos n\beta + b_{2n} \sin n\beta), \quad (2.57a)$$

$$\frac{\partial \phi}{\partial \alpha} - 12K \frac{\partial P_1}{\partial \alpha} = a_{30} + \sum_{n=1}^{\infty} (a_{3n} \cos n\beta + b_{3n} \sin n\beta). \quad (2.57b)$$

The general form of ϕ and P_1 is given by

$$\phi = \phi_1 + \phi_2, \quad (2.58a)$$

$$\phi_1 = \frac{a_{10} - a_{30}}{12K} \alpha_2 + \sum_{n=1}^{\infty} \cosh(n(\alpha - \alpha_2)) (\bar{A}_n \cos n\beta + \bar{B}_n \sin n\beta), \quad (2.58b)$$

$$\phi_2 = a_{10} (\alpha - \alpha_2) + a_{20} + \sum_{n=1}^{\infty} \sinh(n(\alpha - \alpha_2)) (\bar{C}_n \cos n\beta + \bar{D}_n \sin n\beta), \quad (2.58c)$$

$$P_1 = \frac{a_{10} - a_{30}}{12K} \alpha + \sum_{n=1}^{\infty} \exp(-n(\alpha - \alpha_2)) (\bar{E}_n \cos n\beta + \bar{F}_n \sin n\beta), \quad (2.58d)$$

where the terms in (2.58) that are not contained within the infinite sums take care of a_{10} , a_{20} and a_{30} in (2.56) and (2.57). As with the $O(1)$ solution, these forms are unique up to an arbitrary constant which we take to be zero without loss of generality.

Substituting (2.58) into (2.56), multiplying by $\cos k\beta$ or $\sin k\beta$ and integrating from $\beta = 0$ to 2π , we obtain

$$\cosh(k(\alpha_2 - \alpha_1)) \bar{C}_n - \sinh(k(\alpha_2 - \alpha_1)) \bar{A}_n = \frac{a_{1n}}{n}, \quad (2.59a)$$

$$\cosh(k(\alpha_2 - \alpha_1)) \bar{D}_n - \sinh(k(\alpha_2 - \alpha_1)) \bar{B}_n = \frac{b_{1n}}{n}. \quad (2.59b)$$

In the same manner with the boundary condition (2.57a), we obtain

$$\bar{A}_n - \bar{E}_n = a_{2n}, \quad \bar{B}_n - \bar{F}_n = b_{2n}, \quad (2.60a, b)$$

and with the boundary condition (2.57b) we obtain

$$\overline{C}_n + 12K\overline{E}_n = \frac{a_{3n}}{n}, \quad \overline{D}_n + 12K\overline{F}_n = \frac{b_{3n}}{n}. \quad (2.61a, b)$$

Therefore, in (2.59)–(2.61) we have six linear equations for six unknowns. In fact, as we have separated odd and even harmonic modes, this can be further reduced to two isomorphic groups of three linear equations for three unknowns, $\{\overline{A}_n, \overline{C}_n, \overline{E}_n\}$ and $\{\overline{B}_n, \overline{D}_n, \overline{F}_n\}$. These are solved by

$$\overline{A}_n = \overline{L}_n (a_{3n} - a_{1n} \operatorname{sech}(n(\alpha_2 - \alpha_1)) + 12Kna_{2n}), \quad (2.62a)$$

$$\overline{B}_n = \overline{L}_n (b_{3n} - b_{1n} \operatorname{sech}(n(\alpha_2 - \alpha_1)) + 12Kn b_{2n}), \quad (2.62b)$$

$$\overline{C}_n = \overline{L}_n ((a_{3n} + 12Kna_{2n}) \tanh(n(\alpha_2 - \alpha_1)) + 12Ka_{1n} \operatorname{sech}(n(\alpha_2 - \alpha_1))), \quad (2.62c)$$

$$\overline{D}_n = \overline{L}_n ((b_{3n} + 12Kn b_{2n}) \tanh(n(\alpha_2 - \alpha_1)) + 12Kb_{1n} \operatorname{sech}(n(\alpha_2 - \alpha_1))), \quad (2.62d)$$

$$\overline{E}_n = \overline{L}_n (a_{3n} - a_{1n} \operatorname{sech}(n(\alpha_2 - \alpha_1)) - na_{2n} \tanh(n(\alpha_2 - \alpha_1))), \quad (2.62e)$$

$$\overline{F}_n = \overline{L}_n (b_{3n} - b_{1n} \operatorname{sech}(n(\alpha_2 - \alpha_1)) - nb_{2n} \tanh(n(\alpha_2 - \alpha_1))), \quad (2.62f)$$

$$\overline{L}_n = (n (\tanh(n(\alpha_2 - \alpha_1)) + 12K))^{-1}. \quad (2.62g)$$

We have now solved the flow problem presented for the prescribed motion of the TC up to $O(\epsilon Re)$. This work will allow the flow to be predicted by experimentalists who are able to observe the trajectory of the TC. We note that although the asymptotic approximations we have made restrict these results to certain bioreactor shapes and rotation rates, the mathematically allowed range (as seen from Table 2.1) does fall within the experimental range. It may even be the case that the mathematical approximations hold for experimental values that are not within the allowed mathematical range, but we would require experimental validation to make any statement of this kind.

In Chapters 3 and 4, we validate the coupling conditions imposed by investigating the flow near the TC boundary, using the method of matched asymptotic expansions. This allows us to determine the shear stress acting on the TC, which is important in models where the tissue growth is coupled to the shear stress experienced by the TC.

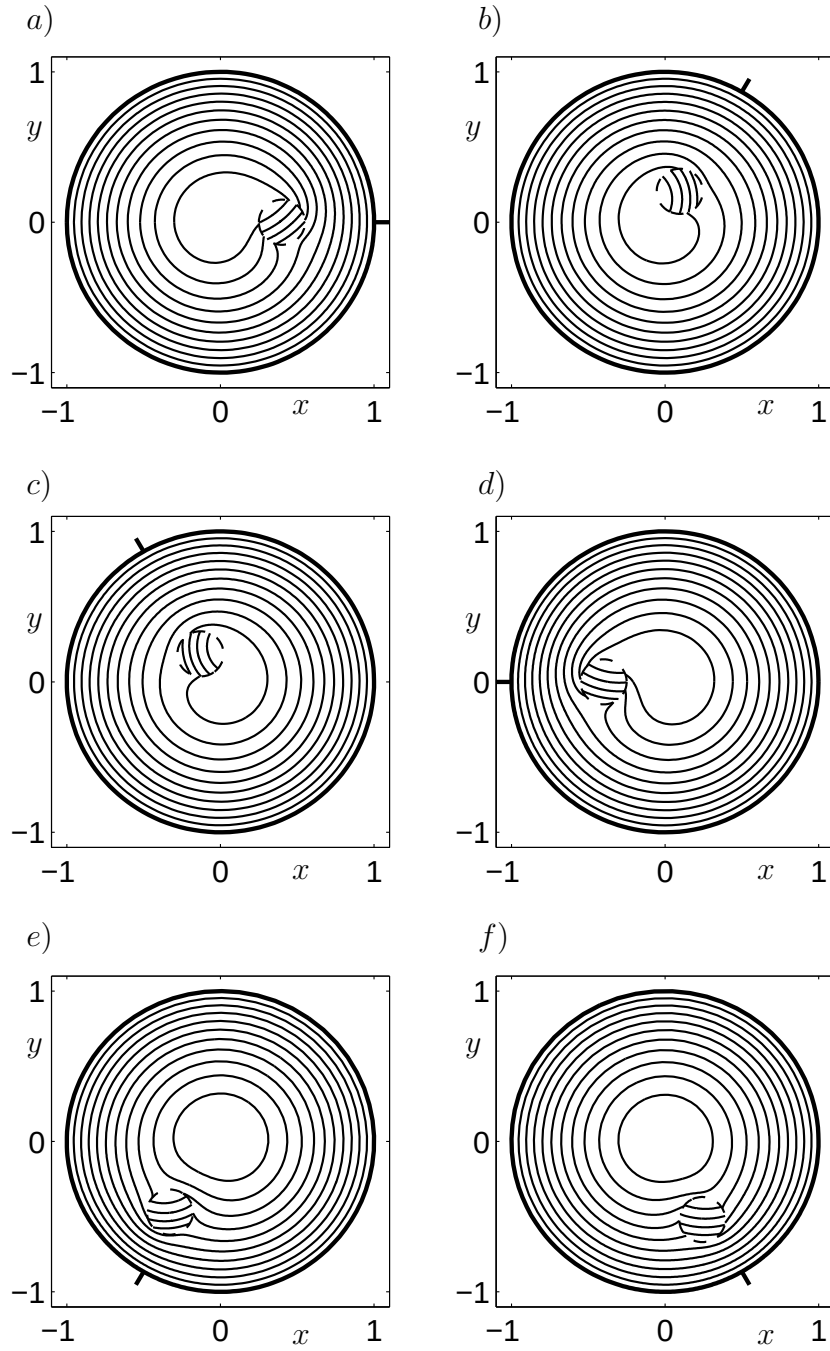


Figure 2.5: The streamlines for a prescribed trajectory, using $b = 0.15$, $K = 0.1$, $R(t) = 0.4 + 0.2 \sin 5t$, $\varphi(t) = t + 0.1 \sin 7t$, and $\omega(t) = 1 + 0.3 \sin 3t$. The images shown are for a) 0, b) $\pi/3$, c) $2\pi/3$, d) π , e) $4\pi/3$ and f) $5\pi/3$ of the way through a full cycle.

Chapter 3

Boundary regions for steady 2D flow

In Chapter 2, we calculate the flow profile within the bioreactor by adopting a lubrication assumption, i.e. that the bioreactor height is much smaller than its radius, and that inertial effects are negligible. Whilst the resulting equations are a good approximation for the flow in the regions away from the bioreactor and tissue construct (TC) surfaces (we refer to these as the ‘outer’ regions, and make this nomenclature precise in §3.3), they are not valid everywhere. One major issue is that the tangential velocity boundary conditions on the TC surface (a Beavers and Joseph (BJ) slip condition given in (2.11c)) and curved bioreactor surface (a no-slip condition given in (2.9)) cannot be satisfied in general due to the neglect of the in-plane viscous terms in the lubrication limit. Moreover, it is not immediately clear how neglect of the tangential velocity conditions affects the boundary conditions coupling the outer-flow regions. Furthermore, the behaviour of the flow near the TC surface is important experimentally. A large change in velocity near the interface could lead to a shear stress that significantly affects the TC trajectory.

We refer to the single-phase fluid governed by the Navier-Stokes equations as the ‘bulk fluid’, and the flow within the porous medium governed by the Darcy equations as the ‘interior fluid’ or ‘porous flow’. In this Chapter we analyse the flow near the interface between the bulk and interior fluid for a two-dimensional (2D) flow. We consider the canonical example of 2D flow through a thin channel which is fully blocked by a finite-length porous plug. Due to the lubrication approximation, there is a boundary layer close to the interface where the small aspect-ratio assumption for the channel breaks down. We fully explore this boundary layer structure in detail. We begin with a short review on the key strands of the literature relevant to this Chapter.

3.1 Introduction

Due to its similarity to a case we consider in §3.4.2, a problem that is particularly relevant to our application is the development of Poiseuille flow within a channel at a large Reynolds number. The asymptotic structure for this problem, with uniform flow as an initial condition, was considered in Van Dyke [74] and Wilson [80], and numerical solutions are given in, e.g. Bodoia and Osterle [6] and Brandt and Gillis [9]. It was found that standard Prandtl boundary layers form at the top and bottom of the channel to flank the inviscid core, and grow in thickness proportionally to the square root of the distance from the channel entrance. Then, once the boundary layers on the channel wall have grown such that they are no longer asymptotically small compared to the inviscid core, a new asymptotic region comes into play, and it is this region in which the transition from plug to Poiseuille flow occurs. We discuss this in more detail in §3.4.2, where we have plug flow leaving the porous TC.

In Chapter 4, we extend our results concerning flow through a 2D channel to flow past a general three-dimensional (3D) porous cylindrical obstacle within a Hele-Shaw cell with moving walls. In Thompson [72], the problem of uniform flow past a solid cylindrical obstacle with circular cross-section in a Hele-Shaw cell with stationary walls was considered. In the outer region away from the interface, the flow is well described by the lubrication equations, while in an inner region near the interface (of width comparable to the thickness of the cell), additional viscous effects become important. Since the normal velocity becomes small close to the interface, the inertial terms are small and the flow in the inner region is governed by Stokes flow at leading order. The flow in both the outer and inner regions is determined up to an asymptotic order which includes inertial corrections, and a macroscale boundary condition for the outer flow is obtained.

Our work extends the work in Thompson [72] to consider a porous obstacle. We do not consider the small permeability limit that is presumably a regular perturbation of Thompson [72], as this is not relevant to our application. Rather, we consider the case where the obstacle is very permeable, and the inertial terms are significant at the asymptotic first-correction to the flow (which is the case relevant to this thesis). Due to the porosity of the obstacle, the normal flow does not vanish on the interface for the problem we consider, and we therefore have more complicated, coupled equations at leading order within the boundary layers. We find that the presence of a normal flow combined with inertial effects induces additional boundary layers, and their structure depends on whether we are considering inflow or outflow.

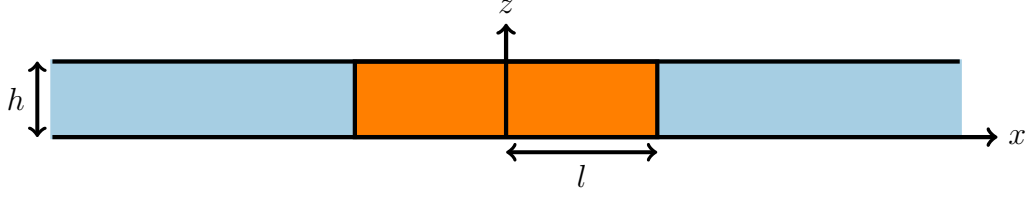


Figure 3.1: The model geometry for channel flow. The blue region is the bulk fluid and the orange region is the porous obstacle.

3.2 Model setup for 2D steady channel flow

We begin by considering steady incompressible Newtonian fluid with density ρ and viscosity μ in an infinitely long channel of height h , which contains a rectangular porous plug of permeability k , height h and length $2l$, where $\epsilon = h/l \ll 1$. We use Cartesian coordinates (x, z) , as illustrated in Figure 3.1, and the plug is placed at $x \in [-l, l]$ and $z \in [0, h]$ within the channel.

The bulk flow, which corresponds to the single-phase flow external to the porous plug (the blue regions in Figure 3.1), is governed by the incompressible steady Navier-Stokes equations with no external force. The bulk fluid velocity and pressure are denoted by $\mathbf{u} = u\mathbf{e}_x + w\mathbf{e}_z$ and p respectively, where $\mathbf{e}_x$ and $\mathbf{e}_z$ are the unit vectors in the x and z -directions respectively. The fluid interior to the porous plug, which corresponds to the orange region in Figure 3.1, is governed by the incompressible Darcy equations with no external force. We denote by $\mathbf{Q} = U\mathbf{e}_x + W\mathbf{e}_z$ and by P the Darcy velocity and pressure respectively. The bulk flow is driven by a pressure gradient in the far-field, which drives a Poiseuille flow whose cross-sectionally averaged velocity has magnitude q , and is coupled to the interior flow via boundary conditions, which we describe after nondimensionalizing.

We nondimensionalize and scale the variables by $x \sim l$, $z \sim \epsilon l$, $(p, P) \sim \mu q / (\epsilon h)$, $(u, U) \sim q$, and $(w, W) \sim \epsilon q$, thus balancing the axial (i.e. along the channel length) pressure gradient with transverse (i.e. across the channel height) viscous terms at leading order in ϵ within the bulk fluid. We note that these dimensionless variables are different to those in Chapter 2 (the relevant lengthscale here is the porous obstacle length, and not the bioreactor radius), and we take care to compensate for this difference when applying the results in this Chapter to the work in Chapter 2.

The dimensionless governing equations in the bulk flow are the scaled Navier-

Stokes equations

$$\epsilon Re (uu_x + wu_z) = -p_x + u_{zz} + \epsilon^2 u_{xx}, \quad (3.1a)$$

$$\epsilon^3 Re (uw_x + ww_z) = -p_z + \epsilon^2 w_{zz} + \epsilon^4 w_{xx}, \quad (3.1b)$$

$$0 = u_x + w_z, \quad (3.1c)$$

which are valid for $|x| > 1$, $0 < z < 1$, and in which $Re = \rho h q / \mu$ is the Reynolds number, using the channel height as the reference length. We use subscripts to denote derivatives. The governing equations in the porous plug are given by the scaled Darcy equations

$$U = -K P_x, \quad (3.2a)$$

$$\epsilon^2 W = -K P_z, \quad (3.2b)$$

$$0 = U_x + W_z, \quad (3.2c)$$

which are valid for $|x| < 1$, $0 < z < 1$, and where $K = k/h^2$. We assume that $K = O(1)$ to retain as many physical effects as possible at leading order in ϵ , corresponding to the distinguished limit in which the plug is very permeable. This is the same limit as we considered in Chapter 2.

3.2.1 Boundary conditions

On the channel walls at $z = 0, 1$, we impose no-slip conditions in the bulk flow and a no-flux condition in the porous flow, with

$$\mathbf{u} = \mathbf{0} \quad \text{on } z = 0, 1 \quad \text{for } |x| > 1, \quad (3.3a)$$

$$W = 0 \quad \text{on } z = 0, 1 \quad \text{for } |x| < 1. \quad (3.3b)$$

On the fluid-porous interfaces at $x = \pm 1$, we impose continuity of normal flux, continuity of normal stress and a BJ tangential slip condition. As the BJ condition is dependent on the unit normal of the relevant interface, we give the interfacial conditions separately for each interface. On the inflow interface, we have

$$u = U, \quad p - 2\epsilon^2 \frac{\partial u}{\partial x} = P, \quad \epsilon \frac{\partial w}{\partial x} = \frac{\lambda}{\sqrt{K}} (W - w) \quad \text{on } x = -1 \text{ for } 0 < z < 1, \quad (3.4a, b, c)$$

and on the outflow interface, we have

$$u = U, \quad p - 2\epsilon^2 \frac{\partial u}{\partial x} = P, \quad \epsilon \frac{\partial w}{\partial x} = \frac{\lambda}{\sqrt{K}} (w - W) \quad \text{on } x = 1 \text{ for } 0 < z < 1, \quad (3.5a, b, c)$$

where λ is the BJ slip coefficient, and is experimentally determined. The flow is driven by imposing a constant pressure gradient in the far-field, with

$$p \sim -12x - (12 - K^{-1}) \quad \text{as } x \rightarrow -\infty, \quad (3.6)$$

where the first term drives the flow (the factor of 12 ensures that the cross-sectionally averaged horizontal component of velocity has magnitude 1 in the far-field), and the second term imparts a symmetry to the eventual solution and has been included for convenience.

3.3 Asymptotic structure

The dimensionless problem defined in (3.1)–(3.6) is characterised by two lengthscales: the porous obstacle half-length, 1, and the channel height, ϵ . We proceed by considering the case $\epsilon \ll 1$, where the channel height is much smaller than the half-length of the porous obstacle (as is the case considered throughout this thesis). For now, we analyse the distinguished limit in which $Re = O(1)$, but we consider the physically relevant asymptotic sub-limit $1 \ll Re \ll \epsilon^{-1}$ in §3.4, and (for completeness) we consider the asymptotic sub-limit $\epsilon \ll Re \ll 1$ in Appendix E.1.

We seek a solution using the method of matched asymptotic expansions, in terms of the small parameter ϵ . The asymptotic structure is shown in Figure 3.2a, where each of the seven asymptotic regions are labelled. We describe the regions as follows, noting that in each case the relevant transverse lengthscale is the channel height, ϵ . There are three ‘outer’ regions characterised by an $O(1)$ axial lengthscale: two for the bulk fluid (regions I and VII) where we have Poiseuille flow at leading order, and one for the interior fluid (region IV) where we have plug flow at leading order. A flow schematic is shown in Figure 3.2b. The inflow transition from Poiseuille to plug flow occurs near the interface $x = -1$, where there are two ‘inner’ regions, one on each side of the interface, each characterised by an axial lengthscale of $O(\epsilon)$, which is the same as the transverse lengthscale. The bulk inflow inner region is region II, and the porous inflow inner region is region III. In a similar manner, the outflow transition from plug to Poiseuille flow occurs near the interface $x = 1$, where again there are two inner regions, one on each side of the interface, and each characterised by an axial lengthscale of $O(\epsilon)$, which is the same as the transverse lengthscale. The porous outflow inner region is region V, and the bulk outflow inner region is region VI.

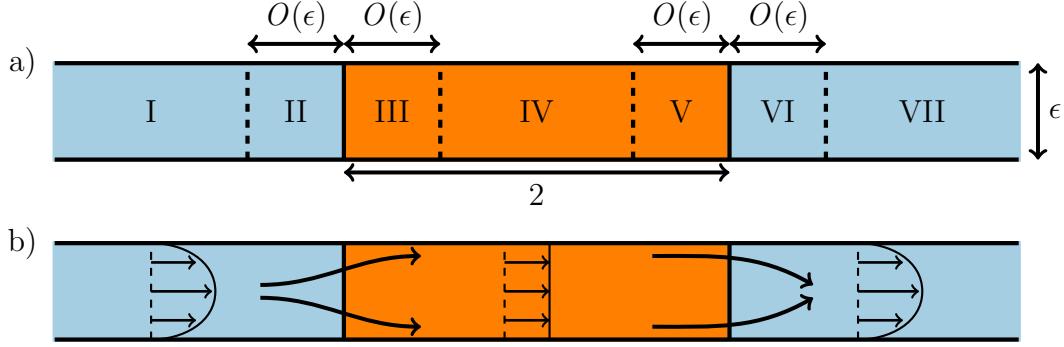


Figure 3.2: The boundary-layer structure for $Re = O(1)$. The blue region is the bulk fluid and the orange region is the porous obstacle. a) The different asymptotic regions are indicated and labelled in Roman numerals. b) A schematic representation of the flow.

3.3.1 Outer regions

In the outer regions, we consider asymptotic expansions

$$(\mathbf{u}, \mathbf{Q}, p, P) = (\mathbf{u}_0, \mathbf{Q}_0, p_0, P_0) + \epsilon(\mathbf{u}_1, \mathbf{Q}_1, p_1, P_1) + O(\epsilon^2), \quad (3.7)$$

as $\epsilon \rightarrow 0$. Substituting (3.7) into the bulk flow equations (3.1), the leading-order bulk-flow governing equations become

$$0 = -p_{0x} + u_{0zz}, \quad 0 = -p_{0z}, \quad 0 = u_{0x} + w_{0z} \quad \text{for } |x| > 1 \text{ for } 0 < z < 1. \quad (3.8a, b, c)$$

Substituting (3.7) into the porous flow equations (3.2), the leading-order interior fluid governing equations become

$$U_0 = -KP_{0x}, \quad 0 = -KP_{0z}, \quad 0 = U_{0x} + W_{0z} \quad \text{for } |x| < 1 \text{ for } 0 < z < 1. \quad (3.9a, b, c)$$

The channel wall boundary conditions (3.3) at leading-order are as follows

$$\mathbf{u}_0 = \mathbf{0} \quad \text{on } z = 0, 1 \quad \text{for } |x| > 1, \quad (3.10a)$$

$$W_0 = 0 \quad \text{on } z = 0, 1 \quad \text{for } |x| < 1, \quad (3.10b)$$

and the far-field condition (3.6) at leading order is

$$p_0 \sim -12x - (12 - K^{-1}) \quad \text{as } x \rightarrow -\infty. \quad (3.11)$$

We are unable to impose the interfacial boundary conditions (3.4) and (3.5) in the outer regions; they are satisfied within the inner regions described in §3.3.2. For the outer problems, we must impose matching conditions between regions instead, and we

use Van Dyke's matching rule [75] throughout this thesis to match solutions within asymptotic regions. These are determined in §3.3.2, and we give them here to close the problem. We find that we must impose continuity of flux and pressure at each interface, with

$$\int_0^1 u_0 \, dz = \int_0^1 U_0 \, dz, \quad p_0 = P_0 \quad \text{on } |x| = 1. \quad (3.12a, b)$$

It is a standard application of lubrication theory (see e.g. Ockendon and Ockendon [54]), to solve the system (3.8)–(3.12) in each region as follows. In region I, we have

$$u_0 = 6z(1 - z), \quad w_0 = 0, \quad p_0 = -12x - (12 - K^{-1}) \quad \text{for } x < -1, 0 < z < 1, \quad (3.13a, b, c)$$

in region IV we have

$$U_0 = 1, \quad W_0 = 0, \quad P_0 = -\frac{x}{K} \quad \text{for } |x| < 1, 0 < z < 1, \quad (3.14a, b, c)$$

and in region VII we have

$$u_0 = 6z(1 - z), \quad w_0 = 0, \quad p_0 = -12x + (12 - K^{-1}) \quad \text{for } x > 1, 0 < z < 1. \quad (3.15a, b, c)$$

We remark that the presence of the porous plug introduces a jump in pressure of $24 - 2K^{-1}$ by comparison to the case in which there is no plug. This could have applications in determining the permeability of porous blockages in pipes. However, a more pressing issue is that the horizontal components of velocity (3.13a) and (3.14a) are clearly incompatible with the continuity of flux condition (3.4a) on the interfacial inflow boundary for the full problem, similarly for outflow, we find that (3.14a) and (3.15a) are incompatible with (3.5a). In the next section we introduce inner regions to resolve this issue, but for the remainder of this section we consider the higher-order terms in the outer regions.

Using the leading-order solutions (3.13) and (3.15), the $O(\epsilon)$ terms in the bulk flow equations (3.1) become

$$0 = -p_{1x} + u_{1zz}, \quad 0 = -p_{1z}, \quad 0 = u_{1x} + w_{1z} \quad \text{for } |x| > 1, 0 < z < 1. \quad (3.16a, b, c)$$

Similarly, using the leading-order solutions (3.14), the $O(\epsilon)$ terms in the interior fluid equations (3.2) become

$$U_1 = -K P_{1x}, \quad 0 = -K P_{1z}, \quad 0 = U_{1x} + W_{1z} \quad \text{for } |x| < 1, 0 < z < 1. \quad (3.17a, b, c)$$

The channel wall boundary conditions (3.3) at this order are as follows

$$\mathbf{u}_1 = \mathbf{0} \quad \text{on } z = 0, 1 \quad \text{for } |x| > 1, \quad (3.18a)$$

$$W_1 = 0 \quad \text{on } z = 0, 1 \quad \text{for } |x| < 1, \quad (3.18b)$$

and the far-field condition (3.6) is

$$p_1 \rightarrow 0 \quad \text{as } x \rightarrow -\infty. \quad (3.19)$$

However, in contrast to the leading-order problem, we are unable to analytically determine enough matching conditions across the interface to couple the outer flows at this order. This is because we are unable to analytically solve the relevant inner problem that would allow us to determine suitable coupling conditions between outer regions for $Re = O(1)$. We note that it is possible to proceed numerically, but our goal is to maximise analytic progress. We show in §3.3.2 that the only interfacial boundary condition we are able to determine analytically is that of continuity of flux, with

$$\int_0^1 u_1 \, dz = \int_0^1 U_1 \, dz \quad \text{on } |x| = 1. \quad (3.20)$$

Despite the fact that the system given by (3.16)–(3.20) is incomplete, we are able to determine the general solution. We are left with two free parameters for the full system, as we are missing two boundary conditions (one from each interface). In region I, we have

$$\mathbf{u}_1 = \mathbf{0}, \quad p_1 = 0 \quad \text{for } x < -1, 0 < z < 1, \quad (3.21a, b)$$

in region IV we have

$$\mathbf{Q}_1 = \mathbf{0}, \quad P_1 = \text{constant} \quad \text{for } |x| < 1, 0 < z < 1, \quad (3.22a, b)$$

and in region VII we have

$$\mathbf{u}_1 = \mathbf{0}, \quad p_1 = \text{constant} \quad \text{for } x > 1, 0 < z < 1, \quad (3.23a, b)$$

where the two constant values taken in (3.22b) and (3.23b) are the two undetermined free parameters. For two dimensions, knowing the solution up to a constant in the pressure is not too problematic for the task of determining the flow. However, if we require knowledge of the force that the fluid imparts upon the obstacle, it is an issue. Furthermore, in three dimensions the higher-order general solution is more

complicated, and we may not be able to determine the outer flow correction without knowledge of the flow behaviour within the inner regions. Fully understanding the 2D problem will allow us to make progress in the 3D case considered in Chapter 4. We proceed by considering the inner regions, highlighting the problems that would need to be solved numerically to determine the drop in pressure across each interface.

3.3.2 Inner regions

The inner regions have an axial lengthscale of $O(\epsilon)$. To preserve the continuity equations (3.1c) and (3.2c), we must therefore scale $w, W \sim \epsilon^{-1}$. We present the full governing equations for inflow and outflow together (as they are equivalent), then present the leading-order flow problems for inflow and outflow separately (as the boundary conditions render them different).

The appropriate scalings in the inflow and outflow inner regions are $x = \mp 1 + \epsilon X^\mp$ respectively and $(w, W) = \epsilon^{-1}(\bar{w}, \bar{W})$. We also use $(u, U) = (\bar{u}, \bar{U})$, $(p, P) = (\bar{p}, \bar{P})$ and $(\bar{\mathbf{u}}, \bar{\mathbf{Q}}) = (\bar{u}, \bar{U})\mathbf{e}_x + (\bar{w}, \bar{W})\mathbf{e}_z$ where we employ overbars to indicate that we are working in the inner regions. Then, the bulk fluid governing equations (3.1) (using vector operators in terms of $X^\mp$ and z) become

$$Re(\bar{\mathbf{u}} \cdot \nabla) \bar{\mathbf{u}} = -\epsilon^{-1} \nabla \bar{p} + \nabla^2 \bar{\mathbf{u}}, \quad 0 = \nabla \cdot \bar{\mathbf{u}} \quad \text{in regions II and VI}, \quad (3.24a, b)$$

which are valid when $X^- < 0$ for inflow (region II) and $X^+ > 0$ for outflow (region VI), with $0 < z < 1$ in both cases. The interior fluid governing equations (3.2) become

$$\bar{\mathbf{Q}} = -\epsilon^{-1} K \nabla \bar{P}, \quad 0 = \nabla \cdot \bar{\mathbf{Q}} \quad \text{in regions III and V}, \quad (3.25a, b)$$

which are valid for $X^- > 0$ for inflow (region III) and $X^+ < 0$ for outflow (region V), with $0 < z < 1$ in both cases. The boundary conditions on the channel walls (3.3) are now given by

$$\bar{\mathbf{u}} = \mathbf{0} \quad \text{on } z = 0, 1 \quad \text{for } X^- < 0 \text{ and } X^+ > 0, \quad (3.26a)$$

$$\bar{W} = 0 \quad \text{on } z = 0, 1 \quad \text{for } X^- > 0 \text{ and } X^+ < 0. \quad (3.26b)$$

On the interface at $X^- = 0$, the interfacial conditions (3.4) become

$$\bar{u} = \bar{U}, \quad \bar{p} - 2\epsilon \bar{u}_{X^-} = \bar{P}, \quad \bar{w}_{X^-} = \frac{\lambda}{\sqrt{K}} (\bar{W} - \bar{w}) \quad \text{on } X^- = 0 \text{ for } 0 < z < 1, \quad (3.27a, b, c)$$

and on the interface at $X^+ = 0$, the interfacial conditions (3.5) become

$$\bar{u} = \bar{U}, \quad \bar{p} - 2\epsilon\bar{u}_{X^+} = \bar{P}, \quad \bar{w}_{X^+} = \frac{\lambda}{\sqrt{K}} (\bar{w} - \bar{W}) \quad \text{on } X^+ = 0 \text{ for } 0 < z < 1, \quad (3.28a, b, c)$$

Similarly to (3.7), we form inner expansions in powers of ϵ as follows

$$(\bar{\mathbf{u}}, \bar{\mathbf{Q}}, \bar{p}, \bar{P}) = (\bar{\mathbf{u}}_0, \bar{\mathbf{Q}}_0, \bar{p}_0, \bar{P}_0) + \epsilon(\bar{\mathbf{u}}_1, \bar{\mathbf{Q}}_1, \bar{p}_1, \bar{P}_1) + O(\epsilon^2), \quad (3.29)$$

as $\epsilon \rightarrow 0$. Substituting the asymptotic series (3.29) into the inner bulk flow equations (3.24), the $O(\epsilon^{-1})$ problem is

$$\mathbf{0} = -\nabla \bar{p}_0 \quad \text{in regions II and VI}, \quad (3.30)$$

and substituting the asymptotic expansions (3.29) into the inner porous flow equations (3.25), the $O(\epsilon^{-1})$ problem is

$$\mathbf{0} = -K\nabla \bar{P}_0 \quad \text{in regions III and V}. \quad (3.31)$$

The appropriate interfacial conditions on $X^\mp = 0$ for the leading-order pressure are given by the leading-order terms in (3.27b) and (3.28b), which become

$$\bar{p}_0 = \bar{P}_0 \quad \text{on } X^\mp = 0. \quad (3.32)$$

The governing equations (3.30)–(3.31) imply that the leading-order pressure is unchanged within the inner regions. Further, from (3.32), there is no pressure jump across either interface. By matching with the outer solutions (3.13)–(3.14), the (constant) leading-order pressures within the inner inflow regions are given by

$$\bar{p}_0 = K^{-1} \quad \text{in region II}, \quad \bar{P}_0 = K^{-1} \quad \text{in region III}, \quad (3.33a, b)$$

and by matching with the outer solutions (3.14)–(3.15), the (constant) leading-order pressures within the inner outflow regions are given by

$$\bar{P}_0 = -K^{-1} \quad \text{in region V}, \quad \bar{p}_0 = -K^{-1} \quad \text{in region VI}. \quad (3.34a, b)$$

The continuity condition (3.12b), which we imposed on the outer problem, is then deduced from (3.33)–(3.34).

As the leading-order fluid pressures are constant within each inner region, the leading-order flow is driven by the first correction to pressure. This is because the outer flow is driven by $\partial p / \partial x$ and, using the inner scalings $x = \mp 1 + \epsilon X^\mp$, it is consistent for the inner flow to be driven by the $O(\epsilon)$ pressure. The leading-order

flow problem is given by the $O(1)$ equations after substituting the asymptotic expansions (3.29) into the inner governing equations (3.24)–(3.25). The bulk flow governing equations are

$$Re(\bar{\mathbf{u}}_0 \cdot \nabla) \bar{\mathbf{u}}_0 = -\nabla \bar{p}_1 + \nabla^2 \bar{\mathbf{u}}_0, \quad 0 = \nabla \cdot \bar{\mathbf{u}}_0 \quad \text{in regions II and VI,} \quad (3.35a, b)$$

and the interior flow governing equations are

$$\bar{\mathbf{Q}}_0 = -K \nabla \bar{P}_1, \quad 0 = \nabla \cdot \bar{\mathbf{Q}}_0 \quad \text{in regions III and V.} \quad (3.36a, b)$$

The boundary conditions on the channel walls (3.26) are

$$\bar{\mathbf{u}}_0 = \mathbf{0} \quad \text{on } z = 0, 1 \quad \text{for } X^- < 0 \text{ and } X^+ > 0, \quad (3.37a)$$

$$\bar{W}_0 = 0 \quad \text{on } z = 0, 1 \quad \text{for } X^- > 0 \text{ and } X^+ < 0, \quad (3.37b)$$

and on the interface at $X^- = 0$, the interfacial conditions (3.27) become

$$\bar{u}_0 = \bar{U}_0, \quad \bar{p}_1 - 2\bar{u}_{0X^-} = \bar{P}_1, \quad \bar{w}_{0X^-} = \frac{\lambda}{\sqrt{K}} (\bar{W}_0 - \bar{w}_0) \quad \text{on } X^- = 0 \text{ for } 0 < z < 1, \quad (3.38a, b, c)$$

and on the interface at $X^+ = 0$, the interfacial conditions (3.28) become

$$\bar{u}_0 = \bar{U}_0, \quad \bar{p}_1 - 2\bar{u}_{0X^+} = \bar{P}_1, \quad \bar{w}_{0X^+} = \frac{\lambda}{\sqrt{K}} (\bar{w}_0 - \bar{W}_0) \quad \text{on } X^+ = 0 \text{ for } 0 < z < 1. \quad (3.39a, b, c)$$

The far-field conditions are obtained through matching with the outer regions. In region II, the matching conditions with region I are given by

$$\bar{\mathbf{u}}_0 \sim 6z(1-z)\mathbf{e}_x, \quad \bar{p}_1 \sim -12X^- + p_1(-1) \quad \text{as } X^- \rightarrow -\infty, \quad (3.40a, b)$$

and, in region III, the matching conditions with region IV are given by

$$\bar{\mathbf{Q}}_0 \sim \mathbf{e}_x, \quad \bar{P}_1 \sim -K^{-1}X^- + P_1(-1) \quad \text{as } X^- \rightarrow \infty. \quad (3.41a, b)$$

In region V, the matching conditions with region IV are given by

$$\bar{\mathbf{Q}}_0 \sim \mathbf{e}_x, \quad \bar{P}_1 \sim -K^{-1}X^+ + P_1(1) \quad \text{as } X^+ \rightarrow -\infty, \quad (3.42a, b)$$

and, in region VI, the matching conditions with region VII are given by

$$\bar{\mathbf{u}}_0 \sim 6z(1-z)\mathbf{e}_x, \quad \bar{p}_1 \sim -12X^+ + p_1(1) \quad \text{as } X^+ \rightarrow \infty. \quad (3.43a, b)$$

We illustrate these leading-order flow problems in Figure 3.3 for inflow, and in Figure 3.4 for outflow. In both cases, the inner flow transition problem is governed by the

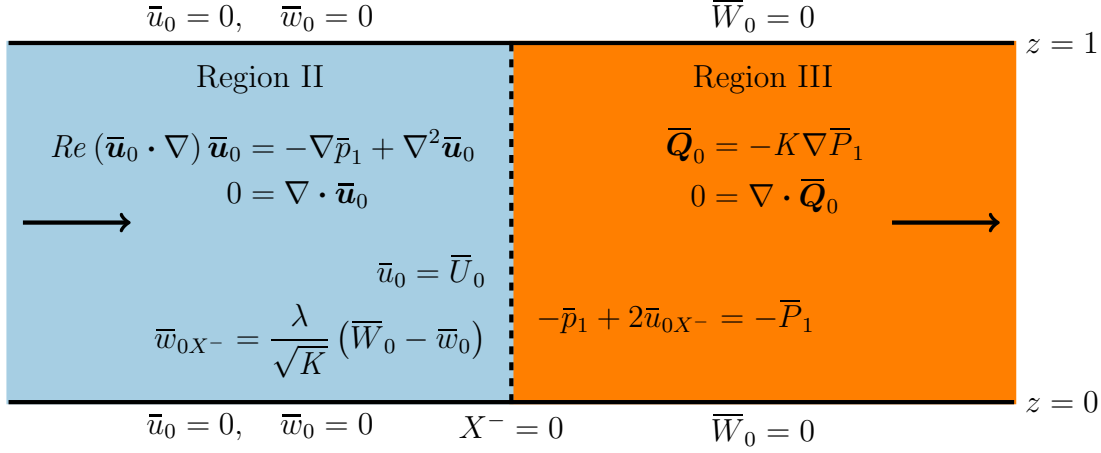


Figure 3.3: The leading-order inner inflow problem for $Re = O(1)$. The arrows indicate the direction of flow. In addition, the matching conditions within region II are: $\bar{\mathbf{u}}_0 \sim 6z(1-z)\mathbf{e}_x$ and $\bar{p}_1 \sim -12X^- + p_1(-1)$ as $X^- \rightarrow -\infty$, and the matching conditions within region III are: $\bar{\mathbf{Q}}_0 \sim \mathbf{e}_x$ and $\bar{P}_1 \sim -K^{-1}X^- + P_1(-1)$ as $X^- \rightarrow \infty$.

full 2D steady Navier-Stokes equations coupled to the Darcy equations. Due to their complexity, it will be difficult to make analytic progress with these inner problems.

To couple the outer regions across each interface, we require two coupling conditions at each interface. Although we are unable to determine analytically the pressure jump across the inner regions to couple the outer regions, we are able to deduce another suitable coupling condition for the flux without having to solve the full inner problem.

By integrating the continuity equations for the full problem (3.24b) and (3.25b) across the channel height, and using the no-flux conditions on the channel walls (3.26), we see that the averaged horizontal components of velocity for inflow/outflow remain constant in $X^\mp$ respectively. Combining this result with the continuity of flux boundary conditions on the interfaces (given in (3.27a) and (3.28a) for the full inner problem) and matching with the outer solutions, we deduce the following condition for the outer horizontal components of velocity

$$\int_0^1 u_0 dz = \int_0^1 U_0 dz, \quad \int_0^1 u_1 dz = \int_0^1 U_1 dz \quad \text{on } |x| = 1. \quad (3.44a, b)$$

To summarise, we have been able to deduce suitable conditions to couple the leading-order flow (3.44a) and pressure (3.32) in the outer regions. For the higher-order flow, we have presented the problems that would have to be solved in order to determine conditions to couple the outer regions. However, for the higher-order terms, we are only able to determine analytically one condition to couple the flow (3.44b),

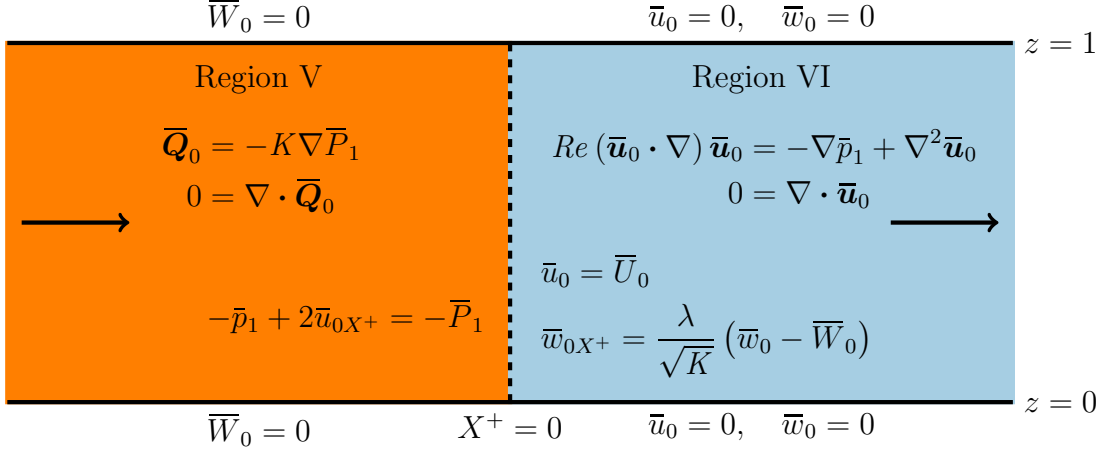


Figure 3.4: The leading-order inner outflow problem for $Re = O(1)$. The arrows indicate the direction of flow. In addition, the matching conditions within region V are: $\bar{\mathbf{Q}}_0 \sim \mathbf{e}_x$ and $\bar{P}_1 \sim -K^{-1}X^+ + P_1(1)$ as $X^+ \rightarrow -\infty$, and the matching conditions within region VI are: $\bar{\mathbf{u}}_0 \sim 6z(1-z)\mathbf{e}_x$ and $\bar{p}_1 \sim -12X^+ + p_1(1)$ as $X^+ \rightarrow \infty$.

and are unable to determine analytically the higher-order pressure jump to close the outer problem. We proceed by working in the physically relevant asymptotic sub-limit $1 \ll Re \ll \epsilon^{-1}$ to investigate the inflow and outflow problems presented in this section using analytic methods, thus allowing an asymptotic approximation of the pressure jump for large Re . This sub-limit is consistent with the flow assumptions made in Chapters 2 and 5 for the rotating HARV bioreactor problem. The asymptotic sub-limit $\epsilon \ll Re \ll 1$ is considered in Appendix E.1 for completeness.

We finish this section by giving the general expressions for the dimensionless stress (scaled with $\mu q/l$) on the interface in region II and region VI variables for later ease of reference

$$\sigma_{xx} = -\epsilon^{-2}\bar{p} + 2\epsilon^{-1}\bar{u}_{X^\mp}, \quad (3.45a)$$

$$\sigma_{xz} = \epsilon^{-1}(\bar{u}_z + \bar{w}_{X^\mp}). \quad (3.45b)$$

We denote the stress acting on the interface by $\mathbf{t}(\mathbf{n})$, where $\mathbf{n}$ is the unit normal on the interface in the direction of the fluid. On the inflow boundary at $x = -1$, the stress acting on the interface is given by

$$\mathbf{t}(-\mathbf{e}_x) = -\sigma_{xx}\mathbf{e}_x - \sigma_{xz}\mathbf{e}_z, \quad (3.46)$$

and on the outflow boundary at $x = 1$, the stress acting on the interface is given by

$$\mathbf{t}(\mathbf{e}_x) = \sigma_{xx}\mathbf{e}_x + \sigma_{xz}\mathbf{e}_z. \quad (3.47)$$

3.4 Large Reynolds number: $1 \ll Re \ll \epsilon^{-1}$

In this section, our goal is to obtain the asymptotic solution to the problems shown in Figures 3.3 and 3.4 (which are independent of ϵ) in the limit $Re \gg 1$. It will be useful to work with the (small) inverse Reynolds number $\delta = Re^{-1} \ll 1$ for ease of notation.

In the limit $\delta \rightarrow 0$, the asymptotic structure for the outer regions is unchanged, with the next-order terms being of $O(\delta^{-1})$ to remain consistent with the new inner structure (as the next-order terms in the outer regions are driven by the leading-order terms in the inner regions). Within the inner regions there is a significant change, as suggested from the inner bulk flow equations (3.35), where we see that the viscous terms are asymptotically small in the inner regions II and VI. Therefore, the limit $\delta \rightarrow 0$ is a singular problem, and we expect viscous effects to become important in regions near each boundary. Furthermore, as fluid momentum dominates within regions II and VI, the flow direction is vitally important. Indeed, we obtain a topologically different boundary layer structure for inflow and outflow, and therefore split the analysis into these two cases. Due to their complexity, we delay a full description of each boundary layer until that boundary layer is analysed in detail.

As mentioned above, the first-correction terms $\mathbf{u}_1$, $\mathbf{Q}_1$, p_1 , and P_1 from the asymptotic series in the outer regions (3.7) are now scaled with δ^{-1} to be consistent with the new inner scalings as follows

$$(\mathbf{u}_1, \mathbf{Q}_1, p_1, P_1) = \delta^{-1}(\mathbf{u}_{10}, \mathbf{Q}_{10}, p_{10}, P_{10}) + (\mathbf{u}_{11}, \mathbf{Q}_{11}, p_{11}, P_{11}) + O(\delta). \quad (3.48)$$

Though we have not yet fully described the inner asymptotic structure, we give the asymptotic expansions within each region (of the regions considered in the main thesis text) in Table 3.1 for ease of reference, and repeat the relevant information the first time it is required in the analysis of each boundary layer. We now consider the inflow problem.

3.4.1 Inflow

The inflow inner problem in the asymptotic sub-limit $1 \ll Re \ll \epsilon^{-1}$ (within regions II and III) is governed by the system (3.35)–(3.38) and (3.40)–(3.41), and is shown in Figure 3.3. The (dimensionless) lengthscales have all been scaled to 1, and now the relevant small parameter is δ . As before, we proceed by seeking a solution via the method of matched asymptotic expansions.

Region	Expansions	Relative scalings
I	$(\mathbf{u}, p) = (\mathbf{u}_0, p_0) + \epsilon(\mathbf{u}_1, p_1) + O(\epsilon^2)$ $(\mathbf{u}_1, p_1) = \delta^{-1}(\mathbf{u}_{10}, p_{10}) + (\mathbf{u}_{11}, p_{11}) + O(\delta)$	
II	$(\bar{\mathbf{u}}, \bar{p}) = (\bar{\mathbf{u}}_0, \bar{p}_0) + \epsilon(\bar{\mathbf{u}}_1, \bar{p}_1) + O(\epsilon^2)$ $\bar{\mathbf{u}}_0 = \bar{\mathbf{u}}_{00} + \delta\bar{\mathbf{u}}_{01} + O(\delta^{4/3})$ $\bar{p}_1 = \delta^{-1}\bar{p}_{10} + \bar{p}_{11} + O(\delta^{1/3})$	$u = \bar{u}, w = \epsilon^{-1}\bar{w}$ $x = \epsilon X, p = \bar{p}$
IIa	$(\hat{\mathbf{u}}, \hat{p}) = (\hat{\mathbf{u}}_0, \hat{p}_0) + \epsilon(\hat{\mathbf{u}}_1, \hat{p}_1) + O(\epsilon^2)$ $\hat{u}_0 = \hat{u}_{00} + \delta\hat{u}_{01} + O(\delta^{4/3})$ $\hat{w}_0 = \hat{w}_{00} + O(\delta^{1/3})$ $\hat{p}_1 = \delta^{-1}\hat{p}_{10} + \hat{p}_{11} + O(\delta^{1/3})$	$u = \hat{u}, w = \epsilon^{-1}\delta\hat{w}$ $x = \epsilon\delta\hat{X}, p = \hat{p}$
III	$(\bar{\mathbf{Q}}, \bar{P}) = (\bar{\mathbf{Q}}_0, \bar{P}_0) + \epsilon(\bar{\mathbf{Q}}_1, \bar{P}_1) + O(\epsilon^2)$ $\bar{\mathbf{Q}}_0 = \bar{\mathbf{Q}}_{00} + \delta\bar{\mathbf{Q}}_{01} + O(\delta^{4/3})$ $\bar{P}_1 = \delta^{-1}\bar{P}_{10} + \bar{P}_{11} + O(\delta^{1/3})$	$U = \bar{U}, W = \epsilon^{-1}\bar{W}$ $x = \epsilon X, P = \bar{P}$
IV	$(\mathbf{Q}, P) = (\mathbf{Q}_0, P_0) + \epsilon(\mathbf{Q}_1, P_1) + O(\epsilon^2)$ $(\mathbf{Q}_1, P_1) = \delta^{-1}(\mathbf{Q}_{10}, P_{10}) + (\mathbf{Q}_{11}, P_{11}) + O(\delta)$	
V	$(\bar{\mathbf{Q}}, \bar{P}) = (\bar{\mathbf{Q}}_0, \bar{P}_0) + \epsilon(\bar{\mathbf{Q}}_1, \bar{P}_1) + O(\epsilon^2)$ $\bar{\mathbf{Q}}_0 \sim \bar{\mathbf{Q}}_{00} + \delta^{1/2}\bar{\mathbf{Q}}_{0a}$ $\bar{P}_1 \sim \delta^{-1}\bar{P}_{10} + \delta^{-1/2}\bar{P}_{1a} + \bar{P}_{11} + \delta^{1/2}\bar{P}_{1b}$	$U = \bar{U}, W = \epsilon^{-1}\bar{W}$ $x = \epsilon X, P = \bar{P}$
VI	$(\bar{\mathbf{u}}, \bar{p}) = (\bar{\mathbf{u}}_0, \bar{p}_0) + \epsilon(\bar{\mathbf{u}}_1, \bar{p}_1) + O(\epsilon^2)$ $\bar{\mathbf{u}}_0 \sim \bar{\mathbf{u}}_{00} + \delta^{1/2}\bar{\mathbf{u}}_{0a}$ $\bar{p}_1 \sim \delta^{-1}\bar{p}_{10} + \delta^{-1/2}\bar{p}_{1a}$	$u = \bar{u}, w = \epsilon^{-1}\bar{w}$ $x = \epsilon X, p = \bar{p}$
VIa	$(\tilde{\mathbf{u}}, \tilde{p}) = (\tilde{\mathbf{u}}_0, \tilde{p}_0) + \epsilon(\tilde{\mathbf{u}}_1, \tilde{p}_1) + O(\epsilon^2)$ $\tilde{u}_0 = \tilde{u}_{00} + O(\delta^{1/2})$ $\tilde{w}_0 = \tilde{w}_{01} + O(\delta^{1/2})$ $\tilde{p}_1 = \delta^{-1}\tilde{p}_{10} + O(\delta^{-1/2})$	$u = \tilde{u}, w = \epsilon^{-1}\delta\tilde{w}$ $x = \epsilon\delta^{-1}\tilde{X}, p = \tilde{p}$
VII	$(\mathbf{u}, p) = (\mathbf{u}_0, p_0) + \epsilon(\mathbf{u}_1, p_1) + O(\epsilon^2)$ $(\mathbf{u}_1, p_1) = \delta^{-1}(\mathbf{u}_{10}, p_{10}) + O(\delta^{-1/2})$	

Table 3.1: Asymptotic expansions within each boundary layer.

The limit as $\delta \rightarrow 0$ yields inviscid flow in region II at leading-order away from the boundaries, with five additional boundary layers being required to satisfy all of the boundary conditions, as we shall now describe. Two of the viscous boundary layers are on the channel wall and porous interface boundaries, whilst the three remaining boundary layers occur in the corner between the channel wall and porous interface. The boundary layer structure for the inflow problem is shown in Figure 3.5.

We start by considering the inner coupled regions II and III, where we have inviscid flow coupled to Darcy flow at leading order. We show that the transition to Poiseuille

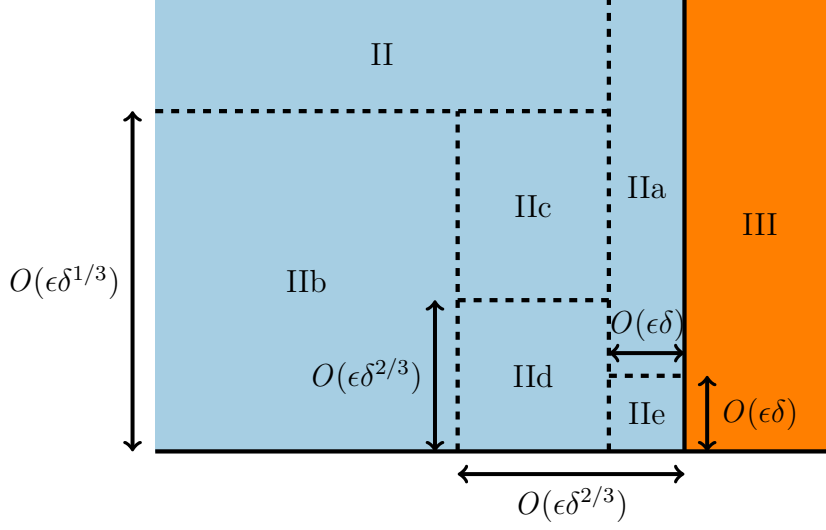


Figure 3.5: Schematic diagram of the inner regions IIa-e within the inflow boundary region II. The blue region is the bulk fluid and the orange region is the porous obstacle.

flow occurs solely within region III.

3.4.1.1 Inner regions II and III

Within regions II and III, using the benefit of hindsight, we take the following asymptotic expansions

$$(\bar{\mathbf{u}}_0, \bar{\mathbf{Q}}_0) = (\bar{\mathbf{u}}_{00}, \bar{\mathbf{Q}}_{00}) + \delta(\bar{\mathbf{u}}_{01}, \bar{\mathbf{Q}}_{01}) + \delta^{4/3}(\bar{\mathbf{u}}_{02}, \bar{\mathbf{Q}}_{02}) + O(\delta^{5/3}), \quad (3.49a)$$

$$(\bar{p}_1, \bar{P}_1) = \delta^{-1}(\bar{p}_{10}, \bar{P}_{10}) + (\bar{p}_{11}, \bar{P}_{11}) + \delta^{1/3}(\bar{p}_{12}, \bar{P}_{12}) + O(\delta^{2/3}), \quad (3.49b)$$

as $\delta \rightarrow 0$. We note that the non-integer powers of δ come from corrections to the flow that arise due to the presence of a boundary layer near the channel walls (region IIb in Figure 3.5), and the terms at that order are used in Appendix E.2, but are not required further in this section.

Substituting the asymptotic expansions (3.49) into the bulk flow governing equations (3.35), we obtain the following $O(\delta^{-1})$ (leading-order) equations

$$(\bar{\mathbf{u}}_{00} \cdot \nabla) \bar{\mathbf{u}}_{00} = -\nabla \bar{p}_{10}, \quad 0 = \nabla \cdot \bar{\mathbf{u}}_{00} \quad \text{in region II}, \quad (3.50a, b)$$

and from the interior flow governing equations (3.36), we obtain the following $O(\delta^{-1})$ (leading-order) equation

$$\mathbf{0} = -K \nabla \bar{P}_{10} \quad \text{in region III.} \quad (3.51)$$

The boundary conditions we impose in region II are all obtained via matching with relevant asymptotic regions. On the channel walls $z = 0, 1$, through matching (carried out in Appendix E.2) with region IIb (whose position within region II is shown in Figure 3.5), we are able to impose no flux through the channel walls

$$w_{00} = 0 \quad \text{on } z = 0, 1 \quad \text{for } X^- < 0. \quad (3.52)$$

In the far-field, as $X^- \rightarrow -\infty$, we use (3.40) (obtained via matching with region I), which becomes

$$\bar{u}_{00} \sim 6z(1-z)\mathbf{e}_x, \quad \bar{p}_{10} \rightarrow p_{10}(-1) \quad \text{as } X^- \rightarrow -\infty \quad \text{for } 0 < z < 1. \quad (3.53)$$

In region III, the far-field condition as $X^- \rightarrow \infty$ is given by (3.41) (obtained via matching with region IV), which becomes

$$\bar{P}_{10} \rightarrow P_{10}(-1) \quad \text{as } X^- \rightarrow \infty \quad \text{for } 0 < z < 1. \quad (3.54)$$

In order to couple regions II and III, we formally consider an ‘inner-inner’ boundary layer closer to the interface (region IIa in Figure 3.5) in §3.4.1.2 in which the interfacial conditions (3.38) are all satisfied. From this analysis, we are able to deduce that the leading-order pressure is unchanged within the inner-inner region. Then, lifting the result (3.80b) from this future section, the correct condition to couple the pressures within regions II and III is continuity of pressure

$$\bar{p}_{10} = \bar{P}_{10} \quad \text{on } X^- = 0 \quad \text{for } 0 < z < 1. \quad (3.55)$$

Whilst the full leading-order system (3.50)–(3.55) for regions II and III is non-linear, the information travels with the flow and we are able to deduce that the leading-order flow travels through region II without varying. Therefore, the solution in region II is given by

$$\bar{u}_{00} = 6z(1-z), \quad \bar{w}_{00} = 0, \quad \bar{p}_{10} = p_{10}(-1), \quad (3.56a, b, c)$$

and the solution in region III is given by

$$\bar{P}_{10} = P_{10}(-1). \quad (3.57)$$

Therefore, the pressure does not vary within the inner regions up to $O(\epsilon\delta^{-1})$, and the correct coupling condition between regions I and IV at $O(\epsilon\delta^{-1})$ on $x = -1$ can be deduced from the interfacial boundary condition (3.55) as follows

$$p_{10} = P_{10} \quad \text{on } x = -1. \quad (3.58)$$

We additionally note that the leading-order horizontal component of velocity (3.56a) in region II vanishes on the channel walls, even though we are only able to impose a condition on the normal velocity (3.52). This does not occur at the next order in region II, there being an $O(\delta)$ tangential slip on the channel walls. This slip is remedied by a boundary layer close to the channel walls (region IIb in Figure 3.5).

We now consider the $O(1)$ equations obtained by substituting the asymptotic expansions (3.49) into the governing equations (3.35) and (3.36), in order to determine how the flow transitions from Poiseuille to plug flow. In the bulk fluid, using the leading-order solution (3.56), we obtain the following $O(1)$ equations

$$\bar{u}_{00}\bar{u}_{01X} + \bar{u}_{00z}\bar{w}_{01} = -\bar{p}_{11X} - 12, \quad \bar{u}_{00}\bar{w}_{01X} = -\bar{p}_{11z}, \quad \nabla \cdot \bar{\mathbf{u}}_{01} = 0 \quad \text{in region II.} \quad (3.59a, b, c)$$

and from the porous flow governing equations (3.36), we obtain the following $O(1)$ equations

$$\bar{\mathbf{Q}}_{00} = -K\nabla\bar{P}_{11}, \quad 0 = \nabla \cdot \bar{\mathbf{Q}}_{00} \quad \text{in region III.} \quad (3.60a, b)$$

The boundary conditions we impose at this order in region II are again obtained via matching. On the channel walls (via matching with region IIb in Appendix E.2), we have no flux through the walls, as follows

$$w_{01} = 0 \quad \text{on } z = 0, 1 \quad \text{for } X^- < 0, \quad (3.61)$$

and in the far-field we match with region I using (3.40), to obtain

$$\bar{\mathbf{u}}_{01} \rightarrow \mathbf{0}, \quad \bar{p}_{11} \sim -12X^- + p_{11}(-1) \quad \text{as } X^- \rightarrow -\infty \quad \text{for } 0 < z < 1. \quad (3.62a, b)$$

The boundary conditions in region III are: no flux on the channel walls (3.37b), given by

$$\bar{\mathbf{W}}_{00} = 0 \quad \text{on } z = 0, 1 \quad \text{for } X^- > 0, \quad (3.63)$$

and a matching condition with region IV as follows

$$\bar{P}_{11} \sim -\frac{X^-}{K} + P_{11}(-1) \quad \text{as } X^- \rightarrow \infty \quad \text{for } 0 < z < 1; \quad (3.64)$$

we note that the far-field expansion $\bar{\mathbf{Q}}_{00} \sim \mathbf{e}_x$ as $X^- \rightarrow \infty$ follows consistently from (3.64) using (3.60a).

The conditions to couple regions II and III are formally derived from consideration of the inner-inner boundary layer in §3.4.1.2, within which we find that the leading-order flow $\bar{u}_{00}$ and the first correction to pressure $\bar{p}_{11}$ are unchanged. Then, lifting the

results (3.80a) and (3.86) from this future section, the correct conditions to couple regions II and III are continuity of flux and stress

$$6z(1-z) = \bar{U}_{00}, \quad \bar{p}_{11} = \bar{P}_{11} \quad \text{on } X^- = 0 \quad \text{for } 0 < z < 1, \quad (3.65a, b)$$

noting that there is no normal viscous stress term in (3.65b) (the inclusion of which might be expected from the full normal stress interfacial condition (3.38b)) due to the leading-order bulk flow remaining unchanged. Therefore, the continuity of stress condition becomes continuity of pressure at this order.

We remark that the system (3.59)–(3.65), which governs the first-correction variables in regions II and III, decouples between the regions. Therefore, we can solve for the region III variables by consideration of the governing equation (3.60), with boundary conditions (3.65a), (3.63), and (3.64), to obtain the system

$$\nabla^2 \bar{P}_{11} = 0 \quad \text{in region III,} \quad (3.66a)$$

$$-K \bar{P}_{11X^-} = 6z(1-z) \quad \text{on } X^- = 0 \quad \text{for } 0 < z < 1, \quad (3.66b)$$

$$-K \bar{P}_{11z} = 0 \quad \text{on } z = 0, 1 \quad \text{for } X^- > 0, \quad (3.66c)$$

$$\bar{P}_{11} \sim -\frac{X^-}{K} + P_{11}(-1) \quad \text{as } X^- \rightarrow \infty \quad \text{for } 0 < z < 1, \quad (3.66d)$$

noting that we have turned conditions on the Darcy velocity into conditions on the Darcy pressure using (3.60a). The system (3.66) has solution

$$-K \bar{P}_{11} = -K P_{11}(-1) + X^- + \sum_{k=1}^{\infty} A_k \exp(-2k\pi X^-) \cos(2k\pi z), \quad A_k = \frac{3}{(\pi k)^3}. \quad (3.67)$$

As $\bar{u}_{00}$ is unchanged in region II, the leading order inflow transition from Poiseuille to plug flow occurs entirely within the porous medium in region III. From the values of $\bar{w}_{00}$ and $\bar{W}_{00}$, which are given by (3.56b) and (3.67), we also deduce that we are unable to satisfy the BJ slip condition (3.27c). This issue is resolved in the inner-inner boundary layer region IIa in §3.4.1.2.

We now complete the solution in region II by determining $\bar{u}_{01}$ and $\bar{p}_{11}$, and find that this generates a slip velocity on the channel walls which must be remedied by another boundary layer (analysed in Appendix E.2). We go to this higher order for two main reasons. Firstly, knowledge of $\bar{p}_{11}$ allows us to determine the normal stress acting on the interface up to $O(\epsilon^{-1})$. Secondly, showing that $\bar{p}_{11}$ varies continuously from its value at the interface $X^- = 0$ to its value as $X^- \rightarrow -\infty$ provides some confidence in the asymptotic analysis we have carried out so far.

By taking the curl and gradient of (3.59a,b), and using (3.59c) where necessary, we obtain

$$z(1-z)\nabla^2\bar{w}_{01} + 2\bar{w}_{01} = 0 \quad \text{in region II,} \quad (3.68a)$$

$$\nabla^2\bar{p}_{11} = -2\bar{u}_{00z}\bar{w}_{01X^-} \quad \text{in region II.} \quad (3.68b)$$

The relevant boundary conditions are given by: no flux on the channel walls (3.61), continuity of pressure at the interface (3.65b), and matching conditions with region I (3.62). We restate these all for convenience

$$\bar{w}_{01} = 0 \quad \text{on } z = 0, 1 \quad \text{for } X^- < 0, \quad (3.69a)$$

$$\bar{p}_{11} = P_{11}(-1) - \frac{1}{K} \sum_{k=1}^{\infty} A_k \cos(2k\pi z) \quad \text{on } X^- = 0 \quad \text{for } z \in (0, 1), \quad (3.69b)$$

$$\bar{w}_{01} \rightarrow 0 \quad \text{as } X^- \rightarrow -\infty \quad \text{for } z \in (0, 1), \quad (3.69c)$$

$$\bar{p}_{11} \sim -12X^- + p_{11}(-1) \quad \text{as } X^- \rightarrow -\infty \quad \text{for } z \in (0, 1). \quad (3.69d)$$

We solve for $\bar{w}_{01}$ first, then use its solution to solve for $\bar{p}_{11}$. As (3.68a) is an elliptic equation, we require conditions on each boundary. We use (3.69a) on $z = 0, 1$ and (3.69c) as $X^- \rightarrow -\infty$, but require a boundary condition for $\bar{w}_{01}$ on $X^- = 0$. We can derive a consistent boundary condition for $\bar{w}_{01}$ on $X^- = 0$ using the boundary condition for the pressure on $X^- = 0$ (3.69b) in combination with the governing equation (3.59b). Using this method, we deduce that

$$\bar{w}_{01X^-} = -\frac{1}{K\bar{u}_{00}} \sum_{k=1}^{\infty} 2k\pi A_k \sin(2k\pi z) \quad \text{on } X^- = 0. \quad (3.70)$$

The boundary condition (3.70) ensures that $\bar{w}_{01}$ does not vanish on $X^- = 0$ and so there is a slip velocity on this interface within region II. This issue is taken care of in an inner-inner boundary layer closer to the interface (region IIa in Figure 3.5) in §3.4.1.2.

We have preserved enough of the analytic nature of this work to determine that $\bar{w}_{01}$ scales exactly with K^{-1} . We note that $\bar{w}_{01}$ satisfies a linear equation (3.68a), whose coefficients are independent of K , and $\bar{w}_{01}$ only has one inhomogeneous boundary condition (3.70). From its definition in (3.67), we see that A_k is independent of K and therefore, from (3.70), $\bar{w}_{01}$ scales with K^{-1} . Further, from the continuity equation (3.59c) it follows that $\bar{u}_{01}$ also scales with K^{-1} .

We solve equation (3.68a) with boundary conditions (3.69a), (3.69c), and (3.70) numerically, using a standard central finite difference scheme. By numerically integrating $\bar{w}_{01}$ with respect to X^- , we are able to plot the streamlines in Figure 3.6.

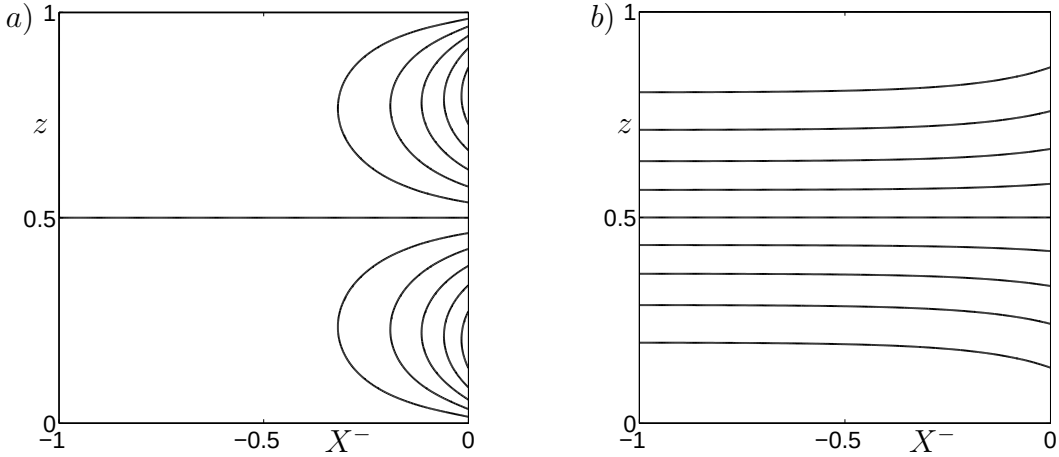


Figure 3.6: The streamlines for inflow near the interface with $K = 0.1$. a) The streamlines for the first-correction velocity $\bar{\mathbf{u}}_{01}$. The fluid moves from the centre of the channel to the channel walls. b) The streamlines for the full velocity up to first-correction $\bar{\mathbf{u}}_{00} + \delta \bar{\mathbf{u}}_{01}$ (with $\delta = 0.2$). The fluid moves from left to right.

In Figure 3.6a, we show the streamlines for the first-correction to velocity, and in Figure 3.6b, we show the streamlines for the full velocity up to first-correction. We see that the fluid moves from the centre of the channel towards the channel walls, as expected. Therefore, we do see some flow adjustment in region II, but it occurs at higher-orders. This movement induces a horizontal slip velocity on the channel walls. This is expected because we cannot impose any tangential conditions on the channel walls in region II. We resolve this issue in Appendix E.2 by introducing a boundary layer near the channel walls in which $z = O(\delta^{1/3})$ on the bottom wall, with similar on the top wall, and we show that the flow near $z = 0$ has the form

$$\bar{u}_0 \sim 6z(1-z) + \delta \sum_{k=1}^{\infty} C_k \exp(\mu_k X^-) g'_k(0) \frac{\int_0^{z/\delta^{1/3}} \text{Ai}(a_k v) dv}{\int_0^{\infty} \text{Ai}(a_k s) ds}, \quad (3.71)$$

where C_k and μ_k are the values taken in (E.15a), Ai is the Airy function of the first kind, and a_k are defined in (E.35b). From (3.71), we see that the leading-order solution is preserved near the channel wall. In fact, the slip is resolved within higher-order terms in the boundary layer, and does not affect the leading-order solution in region II.

The problem for $\bar{p}_{11}$ is given by (3.68b) with boundary conditions (3.69b), and (3.69d). In a similar manner to the derivation of (3.70), we obtain consistent boundary conditions for $\bar{p}_{11}$ on the channel walls by substituting the leading-order flow solution (3.56a) into the governing equation (3.59b) to obtain

$$\bar{p}_{11z} = 0 \quad \text{on } z = 0, 1 \quad \text{for } X^- < 0. \quad (3.72)$$

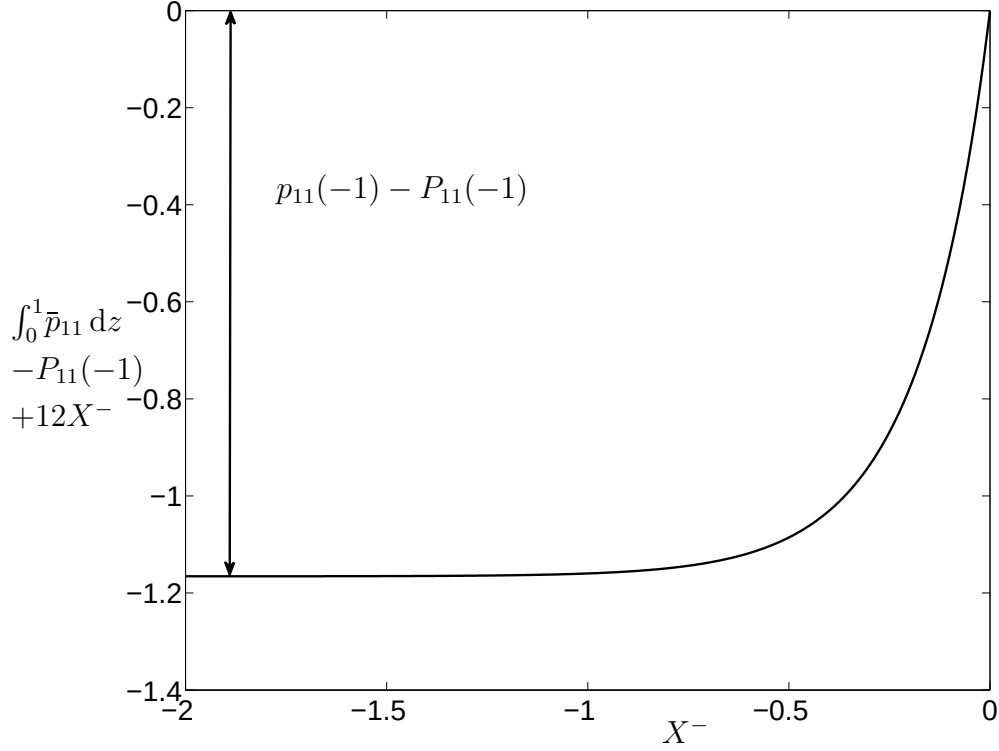


Figure 3.7: A plot showing $\int_0^1 \bar{p}_{11} dz - P_{11}(-1) + 12X^-$ for varying X^- in region II which, using (3.69d), allows us to calculate $p_{11}(-1) - P_{11}(-1)$ as indicated by the drop signalled by the arrow. We use $K = 0.1$, and note that the pressure drop scales with K^{-1} .

We solve the full system for $\bar{p}_{11}$, given by (3.68b) with boundary conditions (3.69b), (3.69d), and (3.72) numerically using a central finite-difference scheme. Using a similar scaling argument as for $\bar{w}_{01}$, we find that $\bar{p}_{11} - P_{11}(-1)$ is equal to $-12X^-$ plus a function that scales with K^{-1} . We are then able to calculate $p_{11}(-1) - P_{11}(-1)$ by plotting $\bar{p}_{11} - P_{11}(-1) + 12X^-$, and by using the matching condition (3.69d). Noting that $p_{11}(-1) - P_{11}(-1)$ is independent of z , and to more easily show the pressure drop on a graph, we plot $\bar{p}_{11} - P_{11}(-1) + 12X^-$ averaged over z for varying X^- in Figure 3.7.

In Figure 3.7, we show a graph of the result and deduce that the pressure jump condition between outer regions is given by $p_{11}(-1) - P_{11}(-1) = -\alpha K^{-1}$, where $\alpha = 0.117$ to three significant figures.

3.4.1.2 Inner-inner region IIa

We now investigate the inner-inner boundary layer closer to the interface. We denote this as region IIa, and its position within region II is shown in Figure 3.5. This boundary layer is required in order to satisfy the BJ slip condition (3.38c) on the interface, and occurs due to the viscous terms induced by the presence of the porous interface balancing the relevant inertial terms. Our interest is in the tangential velocity $\bar{w}_0$, and ensuring that it is able to satisfy a boundary condition on $X^- = 0$, but we are also able to determine higher orders of $\bar{u}_0$ and $\bar{p}_1$ within this region with little extra effort.

The relevant scalings are $X^- = \delta \hat{X}$ and $\bar{w}_0 = \delta \hat{w}_0$, and we introduce the new variables $\bar{u}_0 = \hat{u}_0$ and $\bar{p}_1 = \hat{p}_1$ to signify that we are working in region IIa. Under these scalings, in region IIa the governing equations (3.35) become

$$\delta^{-1} \hat{u}_0 \hat{u}_{0\hat{X}} + \delta \hat{w}_0 \hat{u}_{0z} = -\hat{p}_{1\hat{X}} + \delta^{-1} \hat{u}_{0\hat{X}\hat{X}} + \delta \hat{u}_{0zz}, \quad (3.73a)$$

$$\hat{u}_0 \hat{w}_{0\hat{X}} + \delta^2 \hat{w}_0 \hat{w}_{0z} = -\delta \hat{p}_{1z} + \hat{w}_{0\hat{X}\hat{X}} + \delta^2 \hat{w}_{0zz}, \quad (3.73b)$$

$$0 = \hat{u}_{0\hat{X}} + \delta^2 \hat{w}_{0z}, \quad (3.73c)$$

and the interfacial boundary conditions (3.27) become

$$\hat{u}_0 = \bar{U}_0, \quad \hat{p}_1 - 2\delta^{-1} \hat{u}_{0\hat{X}} = \bar{P}_1, \quad \hat{w}_{0\hat{X}} = \frac{\lambda}{\sqrt{K}} (\bar{W}_0 - \delta \hat{w}_0) \quad \text{on } \hat{X} = 0. \quad (3.74a, b, c)$$

We form asymptotic expansions as follows

$$\hat{u}_0 = \hat{u}_{00} + \delta \hat{u}_{01} + O(\delta^{4/3}), \quad (3.75a)$$

$$\hat{w}_0 = \hat{w}_{01} + O(\delta^{1/3}), \quad (3.75b)$$

$$\hat{p}_1 = \delta^{-1} \hat{p}_{10} + \hat{p}_{11} + O(\delta^{1/3}), \quad (3.75c)$$

as $\delta \rightarrow 0$. Substituting the asymptotic expansions (3.75) into the governing equations (3.73) and equating powers of δ , in region IIa we obtain the following leading-order equations

$$\hat{u}_{00} \hat{u}_{00\hat{X}} = -\hat{p}_{10\hat{X}} + \hat{u}_{00\hat{X}\hat{X}}, \quad (3.76a)$$

$$\hat{u}_{00} \hat{w}_{01\hat{X}} = -\hat{p}_{10z} + \hat{w}_{01\hat{X}\hat{X}}, \quad (3.76b)$$

$$0 = \hat{u}_{00\hat{X}}, \quad (3.76c)$$

and the leading-order interfacial boundary conditions (3.74) become

$$\hat{u}_{00} = \bar{U}_{00}, \quad \hat{p}_{10} - 2\hat{u}_{00\hat{X}} = \bar{P}_{10}, \quad \hat{w}_{01\hat{X}} = -\lambda\sqrt{K}\bar{P}_{11z} \quad \text{on } \hat{X} = 0, \quad (3.77a, b, c)$$

where $\bar{P}_{11z}$ can be determined from (3.67).

The far-field conditions as $\hat{X} \rightarrow -\infty$ arise via matching with region II, giving

$$\hat{u}_{00} \sim 6z(1-z), \quad \hat{w}_{01} \sim \bar{w}_{01}(0, z), \quad \hat{p}_{10} \rightarrow \bar{p}_{10} \quad \text{as } \hat{X} \rightarrow -\infty, \quad (3.78a, b, c)$$

where $\bar{w}_{01}$ is solved for numerically in §3.4.1.1. Due to the reduction of order in z of the partial differential equations (3.76) from the full equations (3.73), we are unable to impose any conditions on the channel walls. This issue is resolved in another boundary layer close to the channel walls in a region we define as region IIe (as shown in Figure 3.5), and this is considered in Appendix E.6.

The solution to the leading-order system (3.76)–(3.78) is given by

$$\hat{u}_{00} = 6z(1-z), \quad \hat{w}_{01} = \bar{w}_{01}(0, z) - \frac{\lambda\sqrt{K}\bar{P}_{11z}(0, z)}{\hat{u}_{00}} \exp(\hat{u}_{00}\hat{X}), \quad \hat{p}_{10} = \bar{p}_{10}, \quad (3.79a, b, c)$$

from which we see that the leading-order pressure and horizontal component of velocity are unchanged within region IIa. Therefore, the correct coupling conditions between regions II and III (in their respective variables) used in §3.4.1.1, are given by

$$\bar{u}_{00} = \bar{U}_{00}, \quad \bar{p}_{10} = \bar{P}_{10} \quad \text{on } X^- = 0. \quad (3.80a, b)$$

Additionally, we see that (3.79b) can only be a solution for inflow, as we require $\hat{u}_{00}\hat{X} < 0$ as we move back into region II. For outflow, this inner-inner region is not a valid boundary layer, and we must tackle the problem in a different manner. Finally, we note that, were we to impose no-slip with $\hat{w} = 0$ on the interface $\hat{X} = 0$, instead of the BJ slip condition (3.77c), the solution would be given by

$$\hat{w}_{01} = \bar{w}_{01}(0, z) \left(1 - \exp(\bar{u}_{00}\hat{X})\right), \quad (3.81)$$

and hence the boundary layer structure persists.

We are further able to solve for $\hat{u}_{01}$ and $\hat{p}_{11}$ in region IIa, by substituting the asymptotic expansions (3.75) into the governing equations (3.73a,c). In region IIa, the first-correction equations are

$$\hat{u}_{00}\hat{u}_{01\hat{X}} = -\hat{p}_{11\hat{X}} + \hat{u}_{01\hat{X}}\hat{X}, \quad (3.82a)$$

$$0 = \hat{u}_{01\hat{X}}, \quad (3.82b)$$

with relevant interfacial conditions obtained from (3.74), giving

$$\hat{u}_{01} = \bar{U}_{01}, \quad \hat{p}_{11} - 2\hat{u}_{01\hat{X}} = \bar{P}_{11} \quad \text{on } \hat{X} = 0, \quad (3.83a, b)$$

and far-field conditions obtained via matching with region II

$$\widehat{u}_{01} \sim \bar{u}_{01}(0, z), \quad \widehat{p}_{11} \sim \bar{p}_{11}(0, z) \quad \text{as } \widehat{X} \rightarrow -\infty. \quad (3.84a, b)$$

The system (3.82)–(3.84) is solved by

$$\widehat{u}_{01} = \bar{u}_{01}(0, z), \quad \widehat{p}_{11} = \bar{p}_{11}(0, z), \quad (3.85a, b)$$

and, using (3.85) with the interfacial condition (3.83b), we are able to give the final coupling condition required between regions II and III in §3.4.1.1, which is

$$\bar{p}_{11} = \bar{P}_{11} \quad \text{on } X^- = 0. \quad (3.86)$$

We have also deduced that $\widehat{u}_{01}$ does not vary with respect to $\widehat{X}$ in region IIa, but this result is not needed in this thesis.

Using the general result for the stress acting on the interface (3.45) (and adjusting to the change of variables from region II to region IIa), it is straightforward to calculate that the components of stress on the interface at $x = -1$ are given by

$$\sigma_{xx} = -\epsilon^{-1} \bar{p}_{11}(0, z) + O(\delta^{1/3} \epsilon^{-1}), \quad (3.87a)$$

$$\sigma_{xz} = \epsilon^{-1} \left(6(1 - 2z) - \lambda K^{1/2} \bar{P}_{11z}(0, z) \right) + O(\delta^{1/3} \epsilon^{-1}), \quad (3.87b)$$

where the $\bar{p}_{11}$ term in the normal stress (3.87a) is obtained via a boundary layer analysis in region II in §3.4.1.1. The $\bar{P}_{11z}$ term in the shear stress (3.87b) comes from calculating $\widehat{w}_{\widehat{X}}$ via (3.79b), and is therefore dependent on a boundary layer analysis in region IIa, which was carried out in this section. In Figure 3.8, we give the calculated normal and shear stresses (3.87) at $O(\epsilon^{-1})$, comparing them to the stresses predicted by the outer solutions (i.e. dropping the two terms mentioned above). We see that there is a significant difference between the two, highlighting the importance of the boundary layer analysis.

Using the solution (3.81), obtained by imposing no tangential slip on the interface instead of the BJ slip condition, the shear stress is given by

$$\sigma_{xz} = 6\epsilon^{-1} ((1 - 2z) - z(1 - z)\bar{w}_{01}(0, z)) + O(\delta^{1/3} \epsilon^{-1}), \quad (3.88)$$

and we note that this is the same order of magnitude as the stress induced by imposing the BJ slip condition, given in (3.87b).

We have now solved for the flow variables within the inflow boundary layers for the regions which affect the stress and the pressure drop. As shown in Figure 3.5,

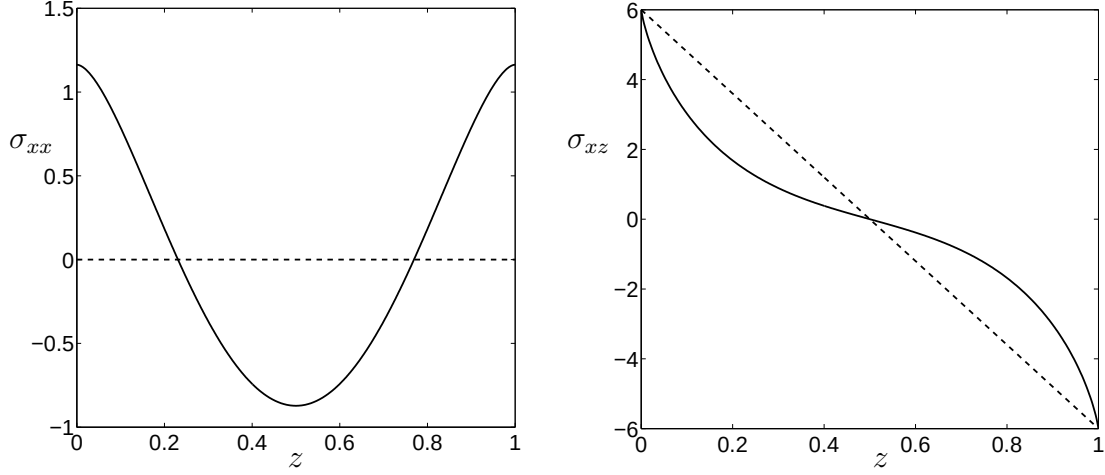


Figure 3.8: The $O(\epsilon^{-1})$ normal (left) and shear (right) stresses on the interface $X^- = 0$ as given in (3.87) using parameter values of $K = 0.1$, $\lambda = 1$. The solid black line is the stress calculated using boundary layer theory and the dashed black line is the stress calculated using the outer solution. As $\bar{p}_{11}$ is unique up to a constant, we choose the constant such that $\int_0^1 \bar{p}_{11} dz = 0$ on the interface $X = 0$.

there are further boundary layers which are important for inflow, and we discuss them in Appendices E.2–E.6.

However, the main part of the leading-order flow is described by the work carried out in §3.4.1 as follows. The leading-order axial flow and pressure are unchanged until they reach the interface, after which they transition to plug flow inside the porous obstacle in region III, whose length is comparable to the channel height. This has an effect on the correction to normal flow and pressure in region II. Meanwhile, the tangential velocity satisfies the boundary condition on the TC surface in region IIa – a boundary layer of even smaller width, which is comparable to the length of the channel height multiplied by the reciprocal of the Reynolds number.

Combining the original asymptotic expansion (3.29) with the asymptotic expansion in region II (3.49b), we deduce that the pressure jump between outer inflow regions I and IV is $O(\epsilon)$. Specifically, we have determined that

$$p(-1) - P(-1) \sim -\epsilon \frac{\alpha}{K}, \quad (3.89)$$

as $\epsilon, \delta \rightarrow 0$, with the constraint $\epsilon \ll \delta \ll 1$. As we are only concerned with the flow up to $O(\epsilon\delta^{-1})$, we do not require the full condition (3.89) in Chapter 2.¹

¹We present it here because it is an interesting result and, once the boundary layer structure is known, can be obtained with little further effort.

We note that the argument presented will not hold if the fluid is leaving the TC rather than entering. This is because the boundary layer region IIa, induced by a boundary condition on the tangential velocity, is only valid for $\bar{u}_{00} > 0$ (as can be seen from (3.79b)). In the case of outflow, we must reconsider our approach and do so in the next section.

3.4.2 Outflow

The outflow inner problem in the asymptotic sub-limit $1 \ll Re \ll \epsilon^{-1}$ (within regions V and VI) is governed by the system (3.35)–(3.37), (3.39), (3.42)–(3.43), and is shown in Figure 3.4. The (dimensionless) lengthscales have all been scaled to 1, and we proceed by seeking a solution via the method of matched asymptotic expansions for small δ .

The asymptotic structure for outflow is shown schematically in Figure 3.9, and is as follows. The flow in region V is unchanged at leading order and reaches the interface as uniform plug flow with magnitude 1. There is an inviscid core in the centre of region VI, flanked by Prandtl boundary layers near $z = 0, 1$ whose height is of $O((\delta X^+)^{1/2})$. These boundary layers (region VIb) grow downstream, and we show that the transition to Poiseuille flow occurs when their thickness becomes $O(1)$, on a horizontal lengthscale of $O(\delta^{-1})$, in a transition region we denote region VIa. There is a third boundary layer, denoted region VIc, which occurs in the corner between the channel wall and the porous interface. This region deals with a singularity at the corner that arises in region VIb, as in the classic Prandtl problem.

In this section, we consider the regions VI and VIa in detail, which allows us to understand the transition from plug to Poiseuille flow and to determine the pressure jump between the outer regions IV and VII. Regions VIb and VIc are discussed in Appendix E.8.1. Recall that, from (3.89), we calculated an $O(\epsilon)$ pressure jump between outer regions I and IV for inflow. We show that the pressure jump between outer regions IV and VII is $O(\epsilon\delta^{-1})$ for outflow.

As mentioned in §3.1, the problem of plug flow transitioning to Poiseuille flow in a 2D channel is a classical problem, with the asymptotic structure examined in Van Dyke [74] and Wilson [80], and numerical solutions given in, e.g. Brandt and Gillis [9], Bodoia and Osterle [6]. These papers considered various inlet conditions for the transverse velocity, but never a BJ slip condition. This is due to two factors. Firstly, a transition from plug to Poiseuille flow was considered solely in the context of a theoretical bulk plug flow, and coupling this with porous media was not the object

Substituting the asymptotic expansions (3.90) into the interior flow equations (3.36), and equating powers of δ up to $O(1)$, we obtain

$$\mathbf{0} = -K\nabla\bar{P}_{10}, \quad \mathbf{0} = -K\nabla\bar{P}_{1a}, \quad \bar{\mathbf{Q}}_{00} = -K\nabla\bar{P}_{11}, \quad 0 = \nabla \cdot \bar{\mathbf{Q}}_{00} \quad \text{in region V.} \quad (3.91a, b, c, d)$$

As the bulk flow equations are more complicated, we analyse their leading-order equations before moving onto the higher-order equations. Substituting (3.90) into the bulk flow equations (3.35), the leading-order equations are

$$(\bar{\mathbf{u}}_{00} \cdot \nabla) \bar{\mathbf{u}}_{00} = -\nabla\bar{p}_{10}, \quad 0 = \nabla \cdot \bar{\mathbf{u}}_{00} \quad \text{in region VI.} \quad (3.92a, b)$$

In region V, the leading-order boundary conditions on the channel walls (3.37b) are given by

$$\bar{W}_{00} = 0 \quad \text{on } z = 0, 1 \text{ for } X^+ < 0, \quad (3.93)$$

while the far-field conditions are obtained by matching with region IV, and are given by

$$\bar{P}_{10} \rightarrow 0, \quad \bar{P}_{1a} \rightarrow 0, \quad \bar{P}_{11} \sim -\frac{X^+}{K} \quad \text{as } X^+ \rightarrow -\infty \text{ for } 0 < z < 1. \quad (3.94a, b, c)$$

In region VI, the boundary conditions on the channel walls are obtained by matching with region VIb (carried out in Appendix E.8.1), and are given by

$$\bar{w}_{00} = 0 \quad \text{on } z = 0, 1 \text{ for } X^+ > 0. \quad (3.95)$$

Finally, the leading-order interfacial conditions (3.28) between regions V and VI become

$$\bar{u}_{00} = \bar{U}_{00}, \quad \bar{p}_{10} = \bar{P}_{10}, \quad \bar{w}_{00X^+} = \frac{\lambda}{\sqrt{K}} (\bar{w}_{00} - \bar{W}_{00}) \quad \text{on } X^+ = 0 \text{ for } 0 < z < 1. \quad (3.96a, b, c)$$

The solution to the system (3.91)–(3.96) governing the leading-order flow in region V is given by

$$\bar{P}_{10} = 0, \quad \bar{P}_{1a} = 0, \quad \bar{P}_{11} = -\frac{X^+}{K}, \quad \bar{U}_{00} = 1, \quad \bar{W}_{00} = 0, \quad (3.97a, b, c, d, e)$$

and, in region VI, is given by

$$\bar{u}_{00} = 1, \quad \bar{w}_{00} = 0, \quad \bar{p}_{10} = 0. \quad (3.98a, b, c)$$

We now consider the next-order variables in regions V and VI, which are required to match with region VIa. Substituting the asymptotic expansions (3.90) into the interior flow equations (3.36), we obtain the $O(\delta^{1/2})$ interior flow equations, given by

$$\bar{\mathbf{Q}}_{0a} = -K\nabla\bar{P}_{1b}, \quad 0 = \nabla \cdot \bar{\mathbf{Q}}_{0a} \quad \text{in region V.} \quad (3.99a, b)$$

Substituting the asymptotic expansions (3.90) into the bulk flow equations (3.35), we obtain the first-correction to the bulk flow equations, namely

$$\bar{u}_{0aX^+} = -\bar{p}_{1aX^+}, \quad \bar{w}_{0aX^+} = -\bar{p}_{1az}, \quad 0 = \bar{u}_{0aX^+} + \bar{w}_{0az} \quad \text{in region VI.} \quad (3.100a, b, c)$$

In region V, the first-correction to the boundary conditions on the channel walls (3.37b) are given by

$$\bar{W}_{0a} = 0 \quad \text{on } z = 0, 1 \text{ for } X^+ < 0, \quad (3.101)$$

while the far-field conditions are obtained by matching with region IV to yield

$$\bar{P}_{1b} \rightarrow 0, \quad \bar{\mathbf{Q}}_{0a} \rightarrow \mathbf{0} \quad \text{as } X^+ \rightarrow -\infty \text{ for } 0 < z < 1. \quad (3.102a, b)$$

In region VI, the boundary conditions on the channel walls are obtained by matching with region VIb (carried out in Appendix E.8.1), which induces a ‘leakage flux’ into region VI. The boundary conditions are given by

$$\bar{w}_{0a} = \frac{\tilde{\beta}}{2(X^+)^{1/2}} \quad \text{on } z = 0 \text{ for } X^+ > 0, \quad (3.103a)$$

$$\bar{w}_{0a} = -\frac{\tilde{\beta}}{2(X^+)^{1/2}} \quad \text{on } z = 1 \text{ for } X^+ > 0. \quad (3.103b)$$

We note that $\tilde{\beta} \approx 1.721$ is a famous result that is numerically determined from a nonlinear ordinary differential equation (discussed further in Appendix E.8.1), and that the parameter β used in Van Dyke [74] and Wilson [80] is related to $\tilde{\beta}$ via $\tilde{\beta} = 2^{1/2}\beta$. Finally, the interfacial conditions (3.28) become

$$\bar{u}_{0a} = \bar{U}_{0a}, \quad \bar{p}_{1a} = 0, \quad \bar{w}_{0aX^+} = \frac{\lambda}{\sqrt{K}} (\bar{w}_{0a} - \bar{W}_{0a}) \quad \text{on } X^+ = 0 \text{ for } 0 < z < 1. \quad (3.104a, b, c)$$

The coupled system of equations (3.99)–(3.104) is difficult to solve analytically, and we do not solve it fully. Instead, we acquire the necessary information for the far-field matching, and deduce the asymptotic order of the stress acting on the outflow

interface. We first note that, by differentiating and rearranging, it follows from (3.100) that

$$\nabla^2 \bar{w}_{0a} = 0 \quad \text{in region VI.} \quad (3.105)$$

We remark that $\bar{p}_{1a}$ is the harmonic conjugate of $\bar{w}_{0a}$, and that $\bar{p}_{1a} + \bar{u}_{1a}$ is independent of X^+ .

We implicitly solve for $\bar{w}_{0a}$ in Appendix E.7. However, we only require the leading-order far-field behaviour of $\bar{w}_{0a}$, which we can obtain by considering the governing equation (3.105) together with the channel wall boundary conditions (3.103a) and (3.103b). A straightforward analysis reveals that the far-field behaviour of $\bar{w}_{0a}$ is given by

$$\bar{w}_{0a} \sim \frac{\tilde{\beta}(1-2z)}{2(X^+)^{1/2}} \quad \text{as } X^+ \rightarrow \infty \text{ for } 0 < z < 1. \quad (3.106)$$

Using the far-field condition (3.106) in the governing equations (3.100a,c), we further deduce that

$$\bar{u}_{0a} \sim 2\tilde{\beta}(X^+)^{1/2}, \quad \bar{p}_{1a} \sim -2\tilde{\beta}(X^+)^{1/2} \quad \text{as } X^+ \rightarrow \infty \text{ for } 0 < z < 1. \quad (3.107a, b)$$

Thus, the far-field behaviour of the region VI variables can be obtained via the leading-order solutions (3.98) and the far-field expansions of the first-correction variables (3.106) and (3.107). Knowledge of these far-field expansions will allow us to determine matching conditions with region VIa for use in the next section. We carry out this matching in Appendix E.9.1.

We note that the far-field expansions (3.106)–(3.107) have no dependence on the permeability K or the BJ slip coefficient λ . As we will see that the outflow pressure drop occurs (at highest asymptotic magnitude) in region VIa, we deduce that neither the permeability nor the BJ slip coefficient have any effect on the pressure drop at $O(\epsilon\delta^{-1})$. However, when we consider 3D outflow in §4.4.2, we see that the permeability does have an effect on both coupling conditions at $O(\epsilon\delta^{-1})$. This is due to an entrainment effect of the azimuthal flow moving fluid through the inner regions.

We can use the expressions for the stress (3.45) to deduce that the components of stress on the interface at $x = 1$ are given by

$$\sigma_{xx} = -\epsilon^{-1}\delta^{-1/2}\bar{p}_{1a} + o(\epsilon^{-1}\delta^{-1/2}), \quad (3.108a)$$

$$\sigma_{xz} = \epsilon^{-1}\delta^{1/2}(\bar{u}_{0az} + \bar{w}_{0aX^+}) + o(\epsilon^{-1}\delta^{1/2}), \quad (3.108b)$$

where we have not explicitly calculated any of the above terms. We find that the normal stress (3.108a) for outflow is a factor of $O(\delta^{-1/2})$ larger than for inflow (3.87a), while the shear stress (3.108b) for outflow is a factor of $O(\delta^{1/2})$ smaller than for inflow (3.87b).

3.4.2.2 Transition region VIa

We now consider the region in which the flow transitions from plug to Poiseuille flow. This occurs when the growing Prandtl boundary layers of thickness $O((\delta X^+)^{1/2})$ become $O(1)$, i.e. when $X^+ = O(\delta^{-1})$, bringing about a balance in the governing equations (3.35) between fluid momentum and viscosity across the full channel width. Recall that we have called this region VIa, as shown in Figure 3.9.

The relevant scalings are $X^+ = \delta^{-1}\tilde{X}$ and $\bar{w}_0 = \delta\tilde{w}_0$, and we introduce the new variables $\bar{u}_0 = \tilde{u}_0$ and $\bar{p}_1 = \tilde{p}_1$ to signify that we are working in region VIa. Then, in region VIa the governing equations (3.35) become

$$\tilde{u}_0\tilde{u}_{0\tilde{X}} + \tilde{w}_0\tilde{u}_{0z} = -\delta\tilde{p}_{1\tilde{X}} + \delta^2\tilde{u}_{0\tilde{X}\tilde{X}} + \tilde{u}_{0zz}, \quad (3.109a)$$

$$\delta^2(\tilde{u}_0\tilde{u}_{0\tilde{X}} + \tilde{w}_0\tilde{w}_{0z}) = -\delta\tilde{p}_{1z} + \delta^4\tilde{w}_{0\tilde{X}\tilde{X}} + \delta^2\tilde{w}_{0zz}, \quad (3.109b)$$

$$\tilde{u}_{0\tilde{X}} + \tilde{w}_{0z} = 0. \quad (3.109c)$$

We pose the asymptotic expansions

$$\tilde{u}_0 = \tilde{u}_{00} + O(\delta^{1/2}), \quad \tilde{w}_0 = \tilde{w}_{01} + O(\delta^{1/2}), \quad \tilde{p}_1 = \delta^{-1}\tilde{p}_{10} + O(\delta^{-1/2}), \quad (3.110a, b, c)$$

as $\delta \rightarrow 0$, and substitute them into the governing equations (3.109) to yield the following leading-order governing equations in region VIa:

$$\tilde{u}_{00}\tilde{u}_{00\tilde{X}} + \tilde{w}_{01}\tilde{u}_{00z} = -\tilde{p}_{10\tilde{X}} + \tilde{u}_{00zz}, \quad 0 = -\tilde{p}_{10z}, \quad \tilde{u}_{00\tilde{X}} + \tilde{w}_{01z} = 0. \quad (3.111a, b, c)$$

The boundary conditions on the channel walls, given by (3.37), become

$$\bar{\mathbf{u}}_{00} = \mathbf{0} \quad \text{on } z = 0, 1 \text{ for } \tilde{X} > 0. \quad (3.112)$$

The leading-order matching conditions are derived in Appendix E.9.1. They are obtained by forming composite expansions between regions VI and VIb, then using Van Dyke's matching rule to match. We use the composite expansions to ensure that the matching condition for the velocity satisfies the no-slip condition on the channel

walls. This allows a greater accuracy when we solve numerically the resulting system. The matching conditions are given by

$$\tilde{u}_{00} \sim \left(1 + 2\tilde{\beta}\tilde{X}^{1/2}\right) f'(\tilde{\eta}_{(0)}) f'(\tilde{\eta}_{(1)}), \quad (3.113a)$$

$$\tilde{w}_{01} \sim \frac{(1-2z)}{2\tilde{\beta}\tilde{X}^{1/2}} (\tilde{\eta}_{(0)} f'(\tilde{\eta}_{(0)}) - f(\tilde{\eta}_{(0)})) (f(\tilde{\eta}_{(1)}) - \tilde{\eta}_{(1)} f'(\tilde{\eta}_{(1)})), \quad (3.113b)$$

$$\tilde{p}_{10} \sim -2\tilde{\beta}\tilde{X}^{1/2} + P_{10}(1), \quad (3.113c)$$

as $\tilde{X} \downarrow 0$, where f is the standard Blasius similarity solution (defined in (E.87)), $\tilde{\eta}_{(0)} = z/\tilde{X}^{1/2}$ and $\tilde{\eta}_{(1)} = (1-z)/\tilde{X}^{1/2}$. The matching conditions between regions VIa and VII are given by

$$\tilde{u}_{00} \sim 6z(1-z), \quad \tilde{w}_{01} \rightarrow 0, \quad \tilde{p}_{10} \sim -12\tilde{X} + p_{10}(1) \quad \text{as } \tilde{X} \rightarrow \infty \quad (3.114a, b, c)$$

where $p_{10}(1)$ is determined from the solution in region VIa. The full system for the flow in region VIa is given by (3.111)–(3.114).

We note that the translational invariance of $\tilde{p}_{10}$ in the governing equations (3.111) means that we are able to simplify the boundary condition (3.113c). That is, we subtract $P_{10}(1)$ from $\tilde{p}_{10}$, which turns (3.113c) into

$$\tilde{p}_{10} = -2\tilde{\beta}\tilde{X}^{1/2} \quad \text{as } \tilde{X} \downarrow 0, \quad (3.115)$$

whilst the matching condition (3.114c) with region VII becomes

$$\tilde{p}_{10} \sim -12\tilde{X} + \Pi_0 \quad \text{as } \tilde{X} \rightarrow \infty, \quad (3.116)$$

where $\Pi_0 = p_{10}(1) - P_{10}(1)$. Therefore, we do not have to solve for every value of $P_{10}(1)$ in (3.113c) to determine the pressure jump Π_0 , we can just impose (3.115) instead of (3.113c), and read Π_0 off from (3.116).

In Bodoia and Osterle [6], this same transition region was considered (though was not derived formally through asymptotic methods), and the authors used the boundary conditions

$$\tilde{u}_{00} = 1, \quad \tilde{w}_{01} = 0, \quad \tilde{p}_{10} = 0 \quad \text{on } \tilde{X} = 0, \quad (3.117a, b, c)$$

instead of the matching conditions (3.113a) and (3.115).³ Apart from (3.117b), these are equivalent to (3.113a) and (3.115) in the limit $\tilde{X} \downarrow 0$. In Bodoia and Osterle [6], it was found that the pressure jump $\Pi_0 \approx -0.338$.

³It is likely that these conditions were selected as a formal asymptotic procedure was not carried out.

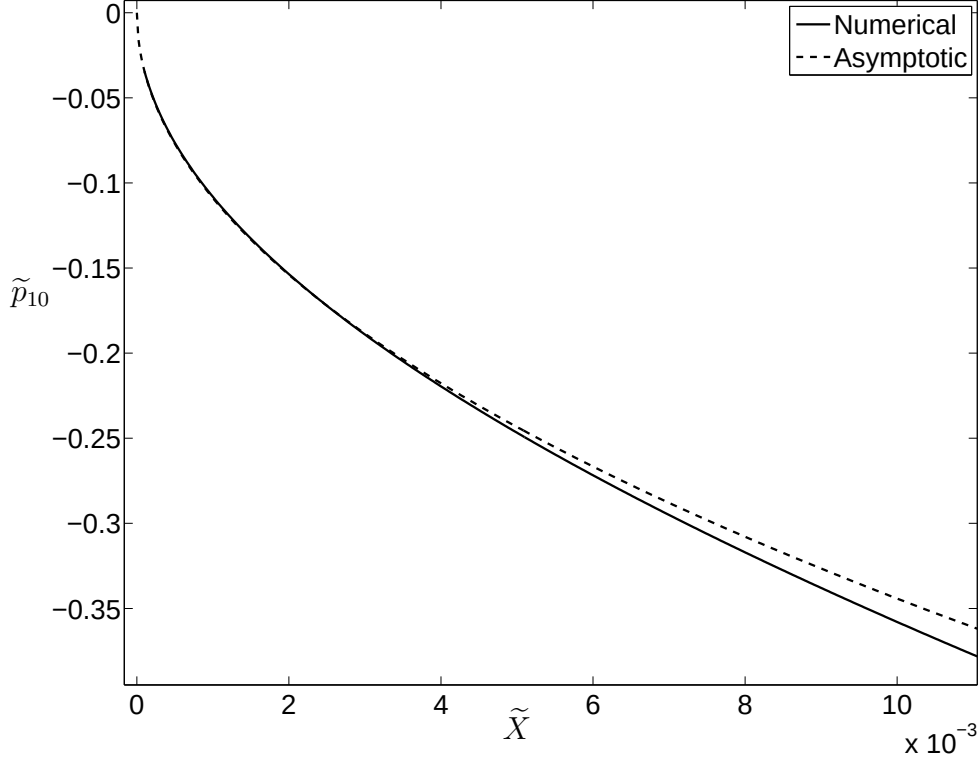


Figure 3.10: Comparing the asymptotic result with the numerics for the pressure for small $\tilde{X}$. See text for details.

We now perform two tasks. Firstly, we validate the matching conditions (3.113a,b) and (3.115) (which are obtained from the far-field expansions in region VI and are equivalent to the small- $\tilde{X}$ expansions in region VIa) by comparing them to numerical simulations of the governing equations (3.111) in region VIa. Secondly, we calculate the pressure jump Π_0 using the formal matching conditions and compare this to the result obtained in Bodoia and Osterle [6].

To validate the matching conditions (3.113), we solve numerically the governing equations (3.111) in region VIa using the finite-difference scheme described in Bodoia and Osterle [6] and, due to the square-root singularity in the pressure gradient, start the simulation at $\tilde{X} = 10^{-4}$. These numerical results are compared to the asymptotic small- $\tilde{X}$ solution for the pressure (given in (3.115)) in Figure 3.10. We see excellent agreement between asymptotics and numerics for $10^{-4} \lesssim \tilde{X} \lesssim 5 \times 10^{-3}$, after which the solutions start to diverge.⁴ We can therefore be confident in the accuracy of the small- $\tilde{X}$ asymptotic approximation.

⁴From the matching condition (3.116), we see that the numerical solution will eventually end up as a linear function of $\tilde{X}$.

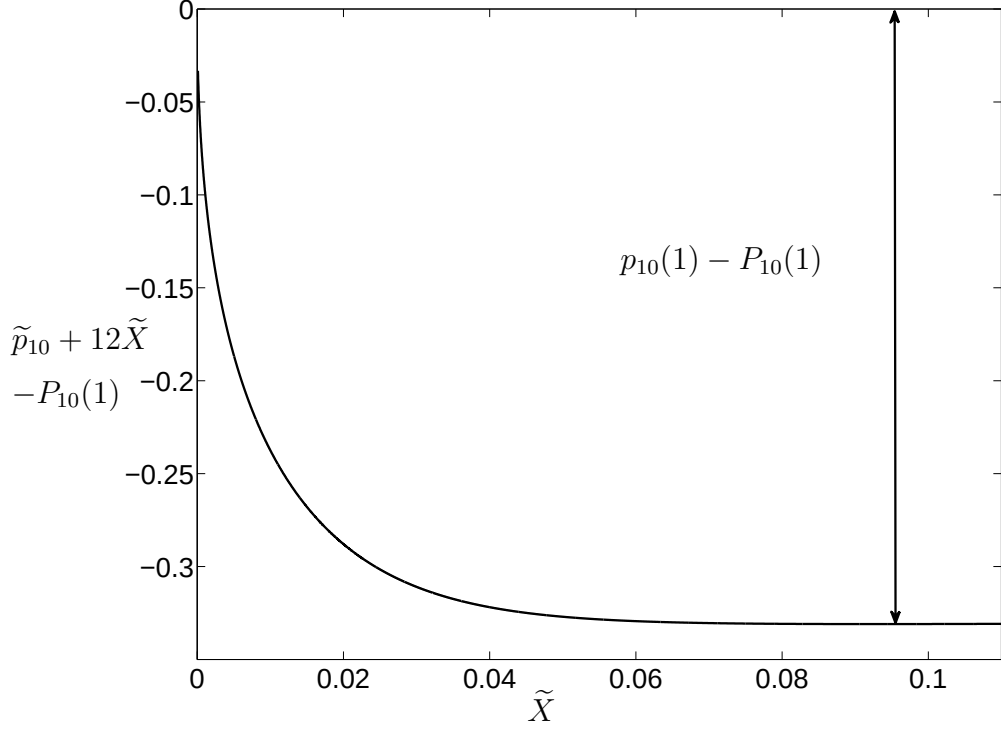


Figure 3.11: Calculating the outflow pressure drop along the channel by plotting $\tilde{p}_{10} + 12\tilde{X} - P_{10}(1)$. See text for details.

To calculate Π_0 using the freshly verified formal matching conditions (3.113), we again start the numerical simulation at $\tilde{X} = 10^{-4}$ to avoid the square-root singularity in the pressure gradient. In Figure 3.11, we show the numerical solutions for $\tilde{p}_{10} - P_{10}(1) + 12\tilde{X}$ as a function of $\tilde{X}$. Using this calculation, and the matching condition (3.114c) we determine that the value of the pressure jump between outer regions IV and VII is given by

$$\Pi_0 = -0.331, \quad (3.118)$$

to 3 significant figures. Combining the original asymptotic expansion (3.29) with the asymptotic expansion in region VIa (3.110c), we deduce that the pressure jump between outer outflow regions IV and VII is $O(\delta^{-1}\epsilon)$. Specifically, we have determined that

$$p(1) - P(1) \sim \frac{\epsilon}{\delta} \Pi_0, \quad (3.119)$$

as $\epsilon, \delta \rightarrow 0$, with the constraint $\epsilon \ll \delta \ll 1$.

We see that the calculated drop in pressure (3.118) only differs by about 2% from the value found by Bodoia and Osterle [6] using the naive boundary conditions (3.117). It is likely that the function $\tilde{w}_{01}$ (and its apparent singularity near the channel entrance) has little effect on the pressure jump, and we conclude that the naive boundary conditions are viable alternatives to a formal matching procedure in this case. However, the naive boundary conditions are unsuitable if a high level of accuracy is required in the far-field, or if information about the flow near the interface is required.

Combining the outflow pressure jump condition (3.118) with the inflow pressure jump condition (3.58), we deduce that the jump in the first-correction outer pressures is given by

$$p_{10} - P_{10} = \Pi_0 H(\mathbf{u}_0 \cdot \mathbf{n}) \quad \text{on } |x| = 1, \quad (3.120)$$

where $H(x)$ is the Heaviside function, and $\mathbf{n}$ is the outward pointing unit normal on the interface.

Therefore, under the asymptotic sub-limit $\epsilon \ll \delta \ll 1$, we are able to calculate the pressure jump between outer regions, which is given by (3.120). This closes the outer problem, and enables us to calculate the first-correction terms in the outer regions (3.21)–(3.23). Therefore, the $O(\epsilon\delta^{-1})$ terms in the outer regions are given by

$$\mathbf{u}_{10} = \mathbf{0}, \quad p_{10} = 0 \quad \text{in region I,} \quad (3.121a)$$

$$\mathbf{Q}_{10} = \mathbf{0}, \quad P_{10} = 0 \quad \text{in region IV,} \quad (3.121b)$$

$$\mathbf{u}_{10} = \mathbf{0}, \quad p_{10} = \Pi_0 \quad \text{in region VII.} \quad (3.121c)$$

To summarise, in this Chapter we determined the boundary-layer structure for 2D flow through a channel with stationary walls containing a porous obstacle. We formulated the full problem for an $O(1)$ Reynolds number, then considered the physically relevant sub-limit in which $1 \ll Re \ll \epsilon^{-1}$. In this sub-limit, a rich boundary-layer structure was unveiled, which differed for inflow and outflow. We solved the problem of how flow transitions from Poiseuille to plug for inflow and from plug back to Poiseuille for outflow, which allowed us to determine the leading-order shear stress acting on the interfaces. Further, we determined coupling conditions for the outer regions. In the next Chapter, we extend the work in this Chapter to a 3D flow in a Hele-Shaw domain where the cell walls and porous medium are moving.

Chapter 4

Boundary layers for unsteady 3D flow

4.1 Formulation

In Chapter 3, we consider the problem of two-dimensional (2D) steady flow through a channel with stationary walls containing a finite-length porous obstacle. In this Chapter, we consider the problem of three-dimensional (3D) unsteady flow within a Hele-Shaw cell which we refer to as the bioreactor.

The bioreactor contains a moving 3D porous cylindrical obstacle of arbitrary cross-section which we refer to as the tissue construct (TC). The TC axis (which we denote as the z -axis) is normal to the two parallel flat sides of the bioreactor, and the bioreactor rotates about the z -axis. A view of the system in a plane with normal in the z -direction is shown in Figure 4.1. We assume that the cross-sectional boundary ∂D of the TC is smooth, the typical half-length of the TC is l , and that the bioreactor height is h , where $\epsilon = h/l \ll 1$. The bioreactor rotates with a constant angular velocity $\Omega \mathbf{e}_z$, where $\mathbf{e}_z$ is the unit vector in the positive z -direction, and the fluid has viscosity μ and density ρ . The distance between the bioreactor and TC centres $R(t)$ is a prescribed function of time t , and the TC rotates about its own centre with a prescribed angular velocity $\omega(t)\mathbf{e}_z$. There are thin gaps between the flat sides of the bioreactor and the TC of height $\epsilon_2 l$ (where $\epsilon_2 \ll \epsilon$) (these are analogous to the thin gaps shown in Figure 2.2). We show in Appendix E.10 that the thin gaps do not affect the flow up to the asymptotic orders we consider. Therefore, we do not consider them further for the flow problem, but note that they contribute a significant friction term for the trajectory problem considered in Chapter 5.

For convenience, we work in the frame in which the TC is stationary, and where the coordinate origin is at the TC centre of mass projected onto $z = 0$. The change

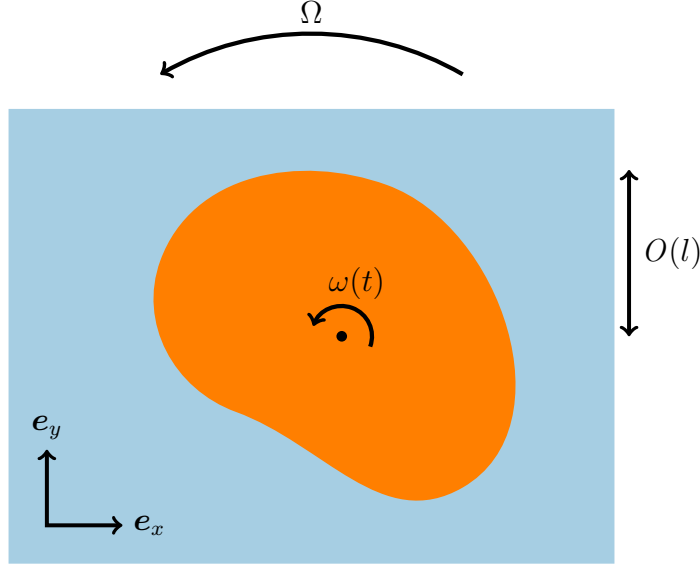


Figure 4.1: Schematic of general TC model. The z -axis points out of the page. The Hele-Shaw cell has a depth of length h in the z -direction, but this is not shown here.

in origin from the bioreactor centre to the TC centre is achieved via a translation of $R(t)\mathbf{e}_X$ (in the notation of Chapter 2). Then, we rotate about the centre of mass of the TC at an angular velocity of $\omega(t)\mathbf{e}_z$ in order to work in a frame in which the TC is stationary.

The difference between this model and the model presented in Chapter 2 is that, in this section, the cylindrical TC has an arbitrary cross section, whereas in Chapter 2 the cylindrical TC has a circular cross-section. The work in this Chapter relies heavily upon the work in Chapter 3, and we find that the 3D model shares most of the boundary layer structure of the 2D model.

We initially work in Cartesian coordinates (x, y, z) , with origin at the TC centre of mass, for ease of notation. We use $\mathbf{r}$ to denote the position vector of a point with respect to this origin. When we investigate the flow close to the fluid-porous interface we move into local curvilinear coordinates (n, s, z) , where n and s measure distance normal and tangential to the interface, the z -axis remaining the same. The bulk and interior fluid velocities in the TC frame are $\mathbf{u}^{\text{rel}} = u^{\text{rel}}\mathbf{e}_x + v^{\text{rel}}\mathbf{e}_y + w^{\text{rel}}\mathbf{e}_z$ and $\mathbf{Q}^{\text{rel}} = U^{\text{rel}}\mathbf{e}_x + V^{\text{rel}}\mathbf{e}_y + W^{\text{rel}}\mathbf{e}_z$ respectively, where $\mathbf{e}_x$ and $\mathbf{e}_y$ are the unit vectors in the x and y -directions respectively. Their relation to the velocities in the inertial frame is given in (F.1). The bulk and interior fluid pressures are p and P respectively, and we assume that any external force is conservative and can be absorbed into the pressure, e.g. gravity.

We nondimensionalize as follows $(x, y, R) \sim l$, $z \sim \epsilon l$, $t \sim \Omega^{-1}$, $\omega \sim \Omega$, $(p, P) \sim \mu l \Omega / (\epsilon h)$, $(u^{\text{rel}}, v^{\text{rel}}, U^{\text{rel}}, V^{\text{rel}}) \sim l \Omega$, and $(w^{\text{rel}}, W^{\text{rel}}) \sim \epsilon l \Omega$. We note that, in contrast to the steady 2D problem considered in Chapter 3, we are now considering a time-dependent problem. We therefore scale time with Ω^{-1} and use this timescale in the fluid velocity scale. We additionally note that this nondimensionalization is different to the nondimensionalization considered in Chapter 2 (but is more convenient for the purposes of this Chapter), and we take care to discuss the results of this Chapter in the context of the Chapter 2 scalings in §4.5. With these scalings, the dimensionless Navier-Stokes equations, which hold outside the TC, are given by

$$\epsilon Re \left(\frac{\partial u^{\text{rel}}}{\partial t} + (\mathbf{u}^{\text{rel}} \cdot \nabla) u^{\text{rel}} + \mathbf{f}^{\text{rel}} \cdot \mathbf{e}_x \right) = -p_x + \epsilon^2 \nabla_{\perp}^2 u^{\text{rel}} + u_{zz}^{\text{rel}}, \quad (4.1a)$$

$$\epsilon Re \left(\frac{\partial v^{\text{rel}}}{\partial t} + (\mathbf{u}^{\text{rel}} \cdot \nabla) v^{\text{rel}} + \mathbf{f}^{\text{rel}} \cdot \mathbf{e}_y \right) = -p_y + \epsilon^2 \nabla_{\perp}^2 v^{\text{rel}} + v_{zz}^{\text{rel}}, \quad (4.1b)$$

$$\epsilon^3 Re \left(\frac{\partial w^{\text{rel}}}{\partial t} + (\mathbf{u}^{\text{rel}} \cdot \nabla) w^{\text{rel}} \right) = -p_z + \epsilon^4 \nabla_{\perp}^2 w^{\text{rel}} + \epsilon^2 w_{zz}^{\text{rel}}, \quad (4.1c)$$

$$0 = \nabla \cdot \mathbf{u}^{\text{rel}}, \quad (4.1d)$$

where $Re = \rho h(l\Omega)/\mu$ is the Reynolds number, the operator $\nabla_{\perp}^2 = \partial_{xx} + \partial_{yy}$, and $\mathbf{f}^{\text{rel}}$ accounts for the fictitious forces due to the change of frame, as follows

$$\mathbf{f}^{\text{rel}} = 2\omega \mathbf{e}_z \times \mathbf{u}^{\text{rel}} - \omega^2 \mathbf{r} + \frac{d\omega}{dt} \mathbf{e}_z \times \mathbf{r} - \frac{d^2}{dt^2} (Re \mathbf{e}_x). \quad (4.2)$$

The dimensionless Darcy equations, which hold inside the TC, are given by

$$U^{\text{rel}} = -K P_x, \quad V^{\text{rel}} = -K P_y, \quad \epsilon^2 W^{\text{rel}} = -K P_z, \quad 0 = \nabla \cdot \mathbf{Q}^{\text{rel}}, \quad (4.3a, b, c, d)$$

where $K = k/h^2$.

4.1.1 Boundary conditions

The boundary conditions on the walls at $z = 0, 1$ are no-slip on the moving Hele-Shaw cell walls for the bulk flow and no-flux on the TC flat surfaces, given by

$$\mathbf{u}^{\text{rel}} = \mathbf{u}^{\text{slip}}(x, y, t) \quad \text{on } z = 0, 1 \quad \text{outside the TC}, \quad (4.4a)$$

$$W = 0 \quad \text{on } z = 0, 1 \quad \text{inside the TC}. \quad (4.4b)$$

We use the prescribed $\mathbf{u}^{\text{slip}}$ in (4.4a) to keep the analysis general in this section, but give the dimensional wall slip for the problem considered in the rest of this thesis in (F.6).

On the interface ∂D , we impose the same interfacial conditions as in Chapter 2. These are given in (2.21), and are continuity of normal flux, continuity of normal stress and a Beavers and Joseph (BJ) tangential slip condition, as follows

$$\mathbf{u}^{\text{rel}} \cdot \mathbf{n} = \mathbf{Q}^{\text{rel}} \cdot \mathbf{n} \quad \text{on } \partial D, \quad (4.5a)$$

$$-p + \epsilon^2 \mathbf{n} \cdot \nabla (\mathbf{u}^{\text{rel}} \cdot \mathbf{n}) = -P \quad \text{on } \partial D, \quad (4.5b)$$

$$\epsilon \mathbf{n} \cdot \nabla (\mathbf{u}^{\text{rel}} \cdot \mathbf{s}_i) = \frac{\lambda}{\sqrt{K}} (\mathbf{u}^{\text{rel}} - \mathbf{Q}^{\text{rel}}) \cdot \mathbf{s}_i \quad \text{on } \partial D. \quad (4.5c)$$

where $\mathbf{n}$ is the unit normal pointing out of the TC into the bulk fluid, $\mathbf{s}_i$ is any unit tangent vector to the surface (there are two linearly independent vectors that span the entire surface ∂D ; we use $\mathbf{e}_z$ and $\mathbf{e}_z \times \mathbf{n}$), and λ is the experimentally determined BJ slip coefficient. To close the system, we need a flow condition on the external bioreactor boundary (or in the far-field if the model assumes the bioreactor has an infinite domain). A relevant example is no slip on the external bioreactor boundary. For a stationary bioreactor, this corresponds to $\mathbf{u}^{\text{rel}} = \mathbf{0}$. For the infinite bioreactor case, a relevant far-field condition is an imposed pressure gradient. For a stationary bioreactor, imposing $p \rightarrow -12x$ corresponds to a unidirectional far-field flow of magnitude 1. In this Chapter, we do not specify any condition on the external boundary, aiming to provide general coupling conditions for a wide class of bioreactor models. However, in Chapter 2 we impose a no-slip condition on the external boundary.

4.2 Asymptotic structure

The dimensionless problem (4.1)–(4.5) is characterised by two lengthscales: the typical TC half-length, 1, and the Hele-Shaw cell height, $\epsilon \ll 1$. We seek a solution using the method of matched asymptotic expansions, in terms of the small parameter ϵ . We initially consider the distinguished limit $Re = O(1)$, then investigate the physically relevant asymptotic sub-limit $1 \ll Re \ll \epsilon^{-1}$ (similarly to Chapter 3).

The outer problems are characterised by an $O(1)$ lengthscale in the (x, y) -plane (with the Hele-Shaw cell height, ϵ , being the lengthscale in the z -direction), where we have Poiseuille and plug flow in the bulk and interior regions respectively. The inner regions are characterised by an $O(\epsilon)$ lengthscale in the (x, y) -plane, which is the same as the lengthscale in the z -direction. These inner regions occur on either side of the interface ∂D . As the TC is a cylinder with smooth cross-section, the local surface topology near a point on the TC boundary is well-approximated by its tangent plane.

Therefore, we find that the inner problems are very similar to those considered in the 2D case in Chapter 3, and we have a similar boundary layer structure.

4.3 Outer regions

In the outer regions, we consider asymptotic expansions

$$(\mathbf{u}^{\text{rel}}, \mathbf{Q}^{\text{rel}}, p, P) = (\mathbf{u}_0^{\text{rel}}, \mathbf{Q}_0^{\text{rel}}, p_0, P_0) + \epsilon(\mathbf{u}_1^{\text{rel}}, \mathbf{Q}_1^{\text{rel}}, p_1, P_1) + O(\epsilon^2), \quad (4.6)$$

as $\epsilon \rightarrow 0$. Substituting the asymptotic expansions (4.6) into the bulk flow equations (4.1), the leading-order bulk-flow governing equations become

$$0 = -p_{0x} + u_{0zz}^{\text{rel}}, \quad 0 = -p_{0y} + v_{0zz}^{\text{rel}}, \quad 0 = -p_{0z}, \quad 0 = \nabla \cdot \mathbf{u}_0^{\text{rel}}. \quad (4.7a, b, c, d)$$

Substituting the asymptotic expansions (4.6) into the interior flow equations (4.3), the leading-order interior fluid governing equations become

$$U_0^{\text{rel}} = -K P_{0x}, \quad V_0^{\text{rel}} = -K P_{0y}, \quad 0 = -K P_{0z}, \quad 0 = \nabla \cdot \mathbf{Q}_0^{\text{rel}}. \quad (4.8a, b, c)$$

The Hele-Shaw cell wall boundary conditions (4.4) at leading-order are as follows

$$\mathbf{u}_0^{\text{rel}} = \mathbf{u}^{\text{slip}} \quad \text{on } z = 0, 1 \quad \text{outside the TC}, \quad (4.9a)$$

$$W_0 = 0 \quad \text{on } z = 0, 1 \quad \text{inside the TC}. \quad (4.9b)$$

As with the 2D case considered in Chapter 3, the interfacial boundary conditions are satisfied within the inner regions. In the outer problems, we must impose matching conditions between regions instead, from which suitable coupling conditions can be determined. From the inner region analysis in §4.4, we find that we must impose

$$p_0 = P_0, \quad \int_0^1 \mathbf{u}_0^{\text{rel}} \cdot \mathbf{n} \, dz = \int_0^1 \mathbf{Q}_0^{\text{rel}} \cdot \mathbf{n} \, dz \quad \text{on } \partial D, \quad (4.10a, b)$$

for the leading-order variables. Obtaining the coupling conditions for the higher-order terms is more complicated, and we delay their presentation until we are able to give them a proper context.

We solve the leading-order bulk flow equations (4.7) with the wall boundary conditions (4.9a) to obtain the leading-order fluid velocity in terms of the pressure as follows

$$u_0^{\text{rel}} \mathbf{e}_x + v_0^{\text{rel}} \mathbf{e}_y = \frac{z(z-1)}{2} \nabla p_0 + \mathbf{u}^{\text{slip}}, \quad w_0^{\text{rel}} = 0, \quad (4.11)$$

and, in the same manner, the interior fluid velocities are given by

$$U_0^{\text{rel}} \mathbf{e}_x + V_0^{\text{rel}} \mathbf{e}_y = -K \nabla P_0, \quad W_0^{\text{rel}} = 0. \quad (4.12)$$

The bulk and interior fluid pressures satisfy Laplace's equation as follows

$$0 = \nabla_{\perp}^2 p_0 \quad \text{outside the TC}, \quad 0 = \nabla_{\perp}^2 P_0 \quad \text{inside the TC}, \quad (4.13a, b)$$

and the coupling conditions (4.10) on ∂D become

$$-\frac{1}{12} \frac{\partial p_0}{\partial n} + \mathbf{u}^{\text{slip}} \cdot \mathbf{n} = -K \frac{\partial P_0}{\partial n}, \quad p_0 = P_0 \quad \text{on } \partial D, \quad (4.14a, b)$$

where $\partial/\partial n$ is the normal derivative with direction into the bulk fluid. We reiterate that we require another condition on the external bioreactor boundary (or a suitable far-field condition) to fully close the system.

The $O(\epsilon)$ terms could be evaluated by substituting the asymptotic expansions (4.6) into the bulk flow equations (4.1) and the interior flow equations (4.3), equating terms of $O(\epsilon)$, and solving the resulting equations. In fact, this is what we do in §2.5 for a similar system. We do not repeat this here, as the details are not relevant to the structure of the inner problem which we now present.

4.4 Inner regions

As the inner regions occur close to the TC boundary ∂D , it will be convenient to work in general curvilinear coordinates (n, s, z) such that $n = 0$ on ∂D . Increasing n moves into the bulk fluid, and s is the distance along the anticlockwise azimuthal direction as shown in Figure 4.2. The dimensional Navier-Stokes and Darcy equations in the curvilinear coordinate system described above are given in Appendix F.

The inner problems occur in regions of distance $O(\epsilon)$ normal to the interface ∂D . To preserve the continuity equations (4.1d) and (4.3d), we must also scale $w^{\text{rel}}, W^{\text{rel}} \sim \epsilon^{-1}$ in these regions. Therefore, the relevant inner scalings are $n = \epsilon N$ and $(w^{\text{rel}}, W^{\text{rel}}) = \epsilon^{-1}(\bar{w}, \bar{W})$. We also use $(p, P) = (\bar{p}, \bar{P})$ to signify that we are working in the inner regions, and define the components of fluid velocity in curvilinear coordinates as $\bar{\mathbf{u}} = \bar{u} \mathbf{n} + \bar{v} \mathbf{s} + \bar{w} \mathbf{e}_z$ and $\bar{\mathbf{Q}} = \bar{U} \mathbf{n} + \bar{V} \mathbf{s} + \bar{W} \mathbf{e}_z$ in the bulk and porous regions respectively (where $\mathbf{n} = \mathbf{e}_n$ and $\mathbf{s} = \mathbf{e}_s$ are the unit vectors in the normal and azimuthal directions respectively). Under these scalings, and up to the order that we

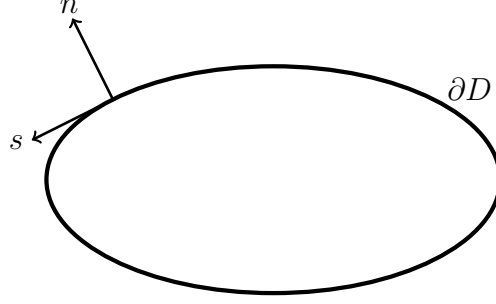


Figure 4.2: Schematic diagram of the curvilinear (n, s) -coordinate system on the boundary of a general obstacle.

shall require for an asymptotic analysis, the bulk-flow equations (4.1) become

$$Re(\bar{u}\bar{u}_N + \bar{w}\bar{u}_z) + O(\epsilon Re) = -\epsilon^{-1}\bar{p}_N + \bar{u}_{NN} + \bar{u}_{zz} + O(\epsilon), \quad (4.15a)$$

$$Re(\bar{u}\bar{v}_N + \bar{w}\bar{v}_z) + O(\epsilon Re) = -\bar{p}_s + \bar{v}_{NN} + \bar{v}_{zz} + O(\epsilon), \quad (4.15b)$$

$$Re(\bar{u}\bar{w}_N + \bar{w}\bar{w}_z) + O(\epsilon Re) = -\epsilon^{-1}\bar{p}_z + \bar{w}_{NN} + \bar{w}_{zz} + O(\epsilon), \quad (4.15c)$$

$$0 = \bar{u}_N + \bar{w}_z + \epsilon(\kappa(s)\bar{u} + \bar{v}_s) + O(\epsilon^2). \quad (4.15d)$$

Note that $\kappa(s)$ denotes the curvature of the boundary ∂D . Similarly, the porous-flow equations (4.3) become

$$\epsilon\bar{U} = -K\bar{P}_N, \quad (4.16a)$$

$$\bar{V} = -K\bar{P}_s + O(\epsilon), \quad (4.16b)$$

$$\epsilon\bar{W} = -K\bar{P}_z, \quad (4.16c)$$

$$0 = \bar{U}_N + \bar{W}_z + \epsilon(\kappa(s)\bar{U} + \bar{V}_s) + O(\epsilon^2). \quad (4.16d)$$

The boundary conditions on the Hele-Shaw cell walls (4.4) become

$$\bar{\mathbf{u}} = \mathbf{u}^{\text{slip}}(\epsilon N, s, t) \quad \text{on } z = 0, 1 \text{ for } N > 0, \quad (4.17a)$$

$$\bar{W} = 0 \quad \text{on } z = 0, 1 \text{ for } N < 0, \quad (4.17b)$$

On the interface ∂D (equivalent to $N = 0$), the interfacial conditions (4.5) become

$$\bar{u} = \bar{U} \quad \text{on } N = 0, \quad (4.18a)$$

$$-\bar{p} + \epsilon \frac{\partial \bar{u}}{\partial N} = -\bar{P} \quad \text{on } N = 0, \quad (4.18b)$$

$$\frac{\partial \bar{v}}{\partial N} = \frac{\lambda}{\sqrt{K}}(\bar{v} - \bar{V}) \quad \text{on } N = 0, \quad (4.18c)$$

$$\frac{\partial \bar{w}}{\partial N} = \frac{\lambda}{\sqrt{K}}(\bar{w} - \bar{W}) \quad \text{on } N = 0. \quad (4.18d)$$

Similarly to (4.6), we form inner expansions in powers of ϵ as follows

$$(\bar{\mathbf{u}}, \bar{\mathbf{Q}}, \bar{p}, \bar{P}) = (\bar{\mathbf{u}}_0, \bar{\mathbf{Q}}_0, \bar{p}_0, \bar{P}_0) + \epsilon(\bar{\mathbf{u}}_1, \bar{\mathbf{Q}}_1, \bar{p}_1, \bar{P}_1) + O(\epsilon^2); \quad (4.19)$$

substituting these into the inner bulk-flow equations (4.15) and equating powers of ϵ yields the leading-order pressure equations

$$0 = -\bar{p}_{0N}, \quad 0 = \bar{p}_{0z}, \quad (4.20a, b)$$

and the leading-order flow equations

$$Re(\bar{u}_0 \bar{u}_{0N} + \bar{w}_0 \bar{u}_{0z}) = -\bar{p}_{1N} + \bar{u}_{0NN} + \bar{u}_{0zz}, \quad (4.21a)$$

$$Re(\bar{u}_0 \bar{v}_{0N} + \bar{w}_0 \bar{v}_{0z}) = -\bar{p}_{0s} + \bar{v}_{0NN} + \bar{v}_{0zz}, \quad (4.21b)$$

$$Re(\bar{u}_0 \bar{w}_{0N} + \bar{w}_0 \bar{w}_{0z}) = -\bar{p}_{1z} + \bar{w}_{0NN} + \bar{w}_{0zz}, \quad (4.21c)$$

$$0 = \bar{u}_{0N} + \bar{w}_{0z}. \quad (4.21d)$$

Substituting the asymptotic expansions (4.19) into the inner porous-flow governing equations (4.16) and equating powers of ϵ yields the leading-order pressure equations

$$0 = -\bar{P}_{0N}, \quad 0 = \bar{P}_{0z}, \quad (4.22a, b)$$

and the leading-order flow equations

$$\bar{U}_0 = -K\bar{P}_{1N}, \quad (4.23a)$$

$$\bar{V}_0 = -K\bar{P}_{0s}, \quad (4.23b)$$

$$\bar{W}_0 = -K\bar{P}_{1z}, \quad (4.23c)$$

$$0 = \bar{U}_{0N} + \bar{W}_{0z}. \quad (4.23d)$$

The boundary conditions on the Hele-Shaw cell wall (4.17) become

$$\bar{\mathbf{u}}_0 = \mathbf{u}^{\text{slip}}(0, s, t) \quad \text{on } z = 0, 1 \text{ for } N > 0, \quad (4.24a)$$

$$\bar{W}_0 = 0 \quad \text{on } z = 0, 1 \text{ for } N < 0, \quad (4.24b)$$

On the interface ∂D , the interfacial condition for the leading-order pressure can be determined from (4.18b), and is given by

$$\bar{p}_0 = \bar{P}_0 \quad \text{on } N = 0 \quad (4.25)$$

while the conditions for the leading-order flow and for the first-correction to the pressure are determined from (4.18), and are given by

$$\bar{u}_0 = \bar{U}_0 \quad \text{on } N = 0, \quad (4.26a)$$

$$-\bar{p}_1 + \frac{\partial \bar{u}_0}{\partial N} = -\bar{P}_1 \quad \text{on } N = 0, \quad (4.26b)$$

$$\frac{\partial \bar{v}_0}{\partial N} = \frac{\lambda}{\sqrt{K}} (\bar{v}_0 - \bar{V}_0) \quad \text{on } N = 0, \quad (4.26c)$$

$$\frac{\partial \bar{w}_0}{\partial N} = \frac{\lambda}{\sqrt{K}} (\bar{w}_0 - \bar{W}_0) \quad \text{on } N = 0. \quad (4.26d)$$

We also have matching conditions between inner and outer regions. For the bulk flow, the matching conditions for the pressure are

$$\bar{p}_0 \sim p_0(0, s, t), \quad \bar{p}_1 \sim N p_{0n}(0, s, t) + p_1(0, s, t) \quad \text{as } N \rightarrow \infty, \quad (4.27a, b)$$

while the matching conditions for the flow velocities are

$$\bar{u}_0 \sim \mathbf{n} \cdot \mathbf{u}_0^{\text{rel}}(0, s, z, t) = \frac{z(z-1)}{2} p_{0n}(0, s, t) + \mathbf{n} \cdot \mathbf{u}^{\text{slip}}(0, s, t) \quad \text{as } N \rightarrow \infty, \quad (4.28a)$$

$$\bar{v}_0 \sim \mathbf{s} \cdot \mathbf{u}_0^{\text{rel}}(0, s, z, t) = \frac{z(z-1)}{2} p_{0s}(0, s, t) + \mathbf{s} \cdot \mathbf{u}^{\text{slip}}(0, s, t) \quad \text{as } N \rightarrow \infty, \quad (4.28b)$$

$$\bar{w}_0 \rightarrow w_0^{\text{rel}}(0, s, z, t) = 0 \quad \text{as } N \rightarrow \infty, \quad (4.28c)$$

where we use the leading-order outer solutions (4.11) to determine the right-hand sides of (4.28). For the interior flow, the matching conditions for the pressure are

$$\bar{P}_0 \sim P_0(0, s, t), \quad \bar{P}_1 \sim N P_{0n}(0, s, t) + P_1(0, s, t) \quad \text{as } N \rightarrow -\infty, \quad (4.29a, b)$$

while the matching conditions for the flow velocities are

$$\bar{U}_0 \sim \mathbf{n} \cdot \mathbf{Q}_0^{\text{rel}}(0, s, t) = -K P_{0n}(0, s, t) \quad \text{as } N \rightarrow -\infty, \quad (4.30a)$$

$$\bar{V}_0 \sim \mathbf{s} \cdot \mathbf{Q}_0^{\text{rel}}(0, s, t) = -K P_{0s}(0, s, t) \quad \text{as } N \rightarrow -\infty, \quad (4.30b)$$

$$\bar{W}_0 \rightarrow W_0^{\text{rel}}(0, s, t) = 0 \quad \text{as } N \rightarrow -\infty, \quad (4.30c)$$

where now we use the leading-order outer solutions (4.12) to evaluate the right-hand sides of (4.30).

The full inner system, up to the orders we require, is defined in (4.20)–(4.30). Notably, we see that the azimuthal velocities $\bar{v}_0, \bar{V}_0$ are decoupled in this 3D system and, though the resultant system is dependent on the azimuthal coordinate s and time t (via the boundary conditions (4.24)–(4.30)), these are now parameters in the

problems for $\bar{p}_0, \bar{P}_0, \bar{p}_1, \bar{P}_1, \bar{u}_0, \bar{U}_0, \bar{w}_0$, and $\bar{W}_0$ which are functions of the independent variables N and z . Furthermore, with the exception of the Hele-Shaw cell wall boundary condition (4.24a), this problem is equivalent to the 2D system considered previously in Chapter 3 (in which we consider the case where $\mathbf{u}^{\text{slip}} \equiv 0$ in (4.24a)). We proceed by considering a 2D slice through the TC and bioreactor (with coordinates N and z), which is parameterized by s . In this 2D slice of the 3D problem, we refer to the regions in the same way as the corresponding ‘fully 2D case’ (which we use to refer to the scenario considered in Chapter 3). Thus region II refers to the inflow inner bulk region which is within a distance of $O(\epsilon)$ to the interface, and region III refers to the inflow inner porous region which is within a distance of $O(\epsilon)$ to the interface (as shown in Figure 3.2a).

We note that the slip condition (4.24a) played no part in obtaining the leading-order coupling conditions between outer regions in the fully 2D case considered in Chapter 3, given by no jump in pressure and no jump in the normal flux averaged over the cell height in (3.12). We therefore deduce that these conditions also hold for the 3D case, and we are justified in writing (4.10).

To determine the correct higher-order conditions to couple the outer regions, we have three main tasks. The first task concerns the flux condition, and the last two tasks allow us to determine the pressure jump condition by solving for the leading-order inner flow. The tasks are as follows. Firstly, determine a 3D coupling condition equivalent to the flux condition in 2D (3.44). Secondly, adapt the previous flow results for the fully 2D case to take the wall slip (4.24a) into account. Thirdly, evaluate the azimuthal flow $\bar{v}_0$ within the inner regions. The first task is carried out in Appendix E.11, where we determine

$$\int_0^1 ((\mathbf{u}_1^{\text{rel}} - \mathbf{Q}_1^{\text{rel}}) \cdot \mathbf{n})|_{n=0} dz = - \int_0^\infty \int_0^1 (\bar{v}_{0s} - \mathbf{s} \cdot \mathbf{u}_{0s}^{\text{rel}}|_{n=0}) dz dN, \quad (4.31)$$

and we see that there is an entrainment effect at this order. That is, the jump in the $O(\epsilon)$ average normal velocity between outer regions across the interface has a contribution from the leading-order azimuthal velocity in the inner regions. This contribution is due to the variation of azimuthal velocity within the inner regions, which causes fluid to move perpendicular to the 2D slices which characterize the inner flow, acting thereby as a source/sink in a given 2D slice.

In the next few sections we determine the leading-order flow and first-correction to the pressures in the inner regions in the asymptotic sub-limit in which $1 \ll Re \ll \epsilon^{-1}$. As with the 2D case in Chapter 3, we use $\delta := Re^{-1} \ll 1$ and consider inflow and

outflow separately, starting with inflow. As we are considering the large Reynolds number limit, the first-correction terms $\mathbf{u}_1^{\text{rel}}$, $\mathbf{Q}_1^{\text{rel}}$, p_1 , and P_1 from the asymptotic series in the outer regions (4.6) are now scaled with δ^{-1} , to be consistent with the new inner scalings, as follows

$$(\mathbf{u}_1^{\text{rel}}, \mathbf{Q}_1^{\text{rel}}, p_1, P_1) = \delta^{-1}(\mathbf{u}_{10}^{\text{rel}}, \mathbf{Q}_{10}^{\text{rel}}, p_{10}, P_{10}) + O(1), \quad (4.32)$$

as $\delta \rightarrow 0$. We note that the asymptotic expansions (4.32) turn the averaged normal flux condition (4.31) into

$$\int_0^1 ((\mathbf{u}_{10}^{\text{rel}} - \mathbf{Q}_{10}^{\text{rel}}) \cdot \mathbf{n})|_{n=0} dz = -\delta \int_0^\infty \int_0^1 (\bar{v}_{0s} - \mathbf{s} \cdot \mathbf{u}_{0s}^{\text{rel}}|_{n=0}) dz dN. \quad (4.33)$$

We note that the magnitude of the right-hand side may not be $O(\delta)$ if we further scale $\bar{v}_0$ or N with some power of δ (in fact, we scale N in the following sections). For completeness, we solve for the azimuthal velocity (and discuss the procedure for solving for the other variables) in the asymptotic sub-limit $\epsilon \ll Re \ll 1$ in Appendix E.1.2.

Finally, to determine the shear stress acting on the TC interface, we give expressions for the dimensionless components of the stress tensor (scaled with $\mu\Omega$) on the interface in inner variables

$$\sigma_{nn} = -\epsilon^{-2}\bar{p} + 2\epsilon^{-1}\bar{u}_N, \quad (4.34a)$$

$$\sigma_{ns} = \epsilon^{-1}\bar{v}_N + O(1), \quad (4.34b)$$

$$\sigma_{nz} = \epsilon^{-1}(\bar{u}_z + \bar{w}_N). \quad (4.34c)$$

4.4.1 Inflow: regions II and III

Inflow occurs in a similar manner to §3.4.1, but due to the change in coordinate system, is now characterised by $\bar{u}_0 < 0$. The possibility exists of $\bar{u}_0$ being both positive and negative for two different values of $z \in (0, 1)$ (e.g. if the pressure gradient is large enough to drive flow in the opposite direction to the wall movement). However, for the system we are considering this is not an issue, as we confirm in Chapter 5 that the movement of the bioreactor walls and the fluid pressure both act in the same direction - to oppose the motion of the TC. We therefore proceed under the assumption that $\bar{u}_0$ is either entirely positive or entirely negative for $z \in (0, 1)$ for a given s and t .

In regions II and III we have the governing equations (4.21) and (4.23) respectively, with wall boundary conditions (4.24), interfacial conditions (4.26), and matching

conditions (4.27b), (4.28), (4.29b), and (4.30). We form the asymptotic expansions

$$(\bar{\mathbf{u}}_0, \bar{\mathbf{Q}}_0) = (\bar{\mathbf{u}}_{00}, \bar{\mathbf{Q}}_{00}) + O(\delta), \quad (4.35a)$$

$$(\bar{p}_1, \bar{P}_1) = \delta^{-1}(\bar{p}_{10}, \bar{P}_{10}) + (\bar{p}_{11}, \bar{P}_{11}) + O(\delta^{1/3}), \quad (4.35b)$$

as $\delta \rightarrow 0$. It is possible to determine further terms, but we restrict ourselves to presenting the terms relevant for our goals of determining coupling conditions between the outer regions and deducing the leading-order azimuthal flow. Substituting the asymptotic expansions (4.35) into the bulk flow equations (4.21), in region II we obtain the following leading-order bulk flow equations

$$\bar{u}_{00}\bar{u}_{00N} + \bar{w}_{00}\bar{u}_{00z} = -\bar{p}_{10N}, \quad (4.36a)$$

$$\bar{u}_{00}\bar{v}_{00N} + \bar{w}_{00}\bar{v}_{00z} = 0, \quad (4.36b)$$

$$\bar{u}_{00}\bar{w}_{00N} + \bar{w}_{00}\bar{w}_{00z} = -\bar{p}_{10z}, \quad (4.36c)$$

$$0 = \bar{u}_{00N} + \bar{w}_{00z}. \quad (4.36d)$$

Substituting the asymptotic expansions (4.35) into the porous flow equations (4.23), in region III we obtain the following equations for the leading-order interior pressure

$$0 = -K\bar{P}_{10N}, \quad (4.37a)$$

$$0 = -K\bar{P}_{10z}, \quad (4.37b)$$

and the following equations for the leading-order interior flow

$$\bar{U}_{00} = -K\bar{P}_{11N}, \quad (4.38a)$$

$$\bar{V}_{00} = -K\bar{P}_{0s}, \quad (4.38b)$$

$$\bar{W}_{00} = -K\bar{P}_{11z}, \quad (4.38c)$$

$$0 = \bar{U}_{00N} + \bar{W}_{00z}. \quad (4.38d)$$

We are only able to impose conditions on the normal velocity in regions II and III on the Hele-Shaw cell walls. These come from (4.24), and are given by

$$\bar{w}_{00} = 0 \quad \text{on } z = 0, 1 \text{ for } N > 0, \quad (4.39a)$$

$$\bar{W}_{00} = 0 \quad \text{on } z = 0, 1 \text{ for } N < 0. \quad (4.39b)$$

To impose the interfacial conditions (4.26), we must consider an inner-inner region closer to the interface (denoted as region IIa and shown in Figure 3.5), and we do this

in §4.4.1.1. By matching between regions II and IIa, we obtain the following coupling conditions between regions II and III

$$\bar{u}_{00} = \bar{U}_{00} \quad \text{on } N = 0, \quad (4.40a)$$

$$\bar{p}_{10} = \bar{P}_{10} \quad \text{on } N = 0. \quad (4.40b)$$

The matching conditions between region II and the outer bulk flow are given by (4.27b) and (4.28) as follows

$$\bar{u}_{00} \sim \frac{z(z-1)}{2} p_{0n}(0, s, t) + \mathbf{n} \cdot \mathbf{u}^{\text{slip}}(0, s, t) \quad \text{as } N \rightarrow \infty, \quad (4.41a)$$

$$\bar{v}_{00} \sim \frac{z(z-1)}{2} p_{0s}(0, s, t) + \mathbf{s} \cdot \mathbf{u}^{\text{slip}}(0, s, t) \quad \text{as } N \rightarrow \infty, \quad (4.41b)$$

$$\bar{w}_{00} \rightarrow 0 \quad \text{as } N \rightarrow \infty, \quad (4.41c)$$

$$\bar{p}_{10} \sim p_{10}(0, s, t), \quad \text{as } N \rightarrow \infty, \quad (4.41d)$$

and the matching conditions between region III and the outer porous flow are given by (4.29b) and (4.30) as follows

$$\bar{P}_{10} \sim P_{10}(0, s, t) \quad \text{as } N \rightarrow -\infty, \quad (4.42a)$$

$$\bar{P}_{11} \sim NP_{0n}(0, s, t) + P_{11}(0, s, t) \quad \text{as } N \rightarrow -\infty, \quad (4.42b)$$

$$\bar{U}_{00} \sim -K P_{0n}(0, s, t) \quad \text{as } N \rightarrow -\infty, \quad (4.42c)$$

$$\bar{U}_{00} \sim -K P_{0s}(0, s, t) \quad \text{as } N \rightarrow -\infty, \quad (4.42d)$$

$$\bar{W}_{00} \rightarrow 0 \quad \text{as } N \rightarrow -\infty. \quad (4.42e)$$

The region II variables in the system (4.36)–(4.42) are solved by

$$\bar{u}_{00} = \frac{z(z-1)}{2} p_{0n}(0, s, t) + \mathbf{n} \cdot \mathbf{u}^{\text{slip}}(0, s, t), \quad (4.43a)$$

$$\bar{v}_{00} = \frac{z(z-1)}{2} p_{0s}(0, s, t) + \mathbf{s} \cdot \mathbf{u}^{\text{slip}}(0, s, t), \quad (4.43b)$$

$$\bar{w}_{00} = 0, \quad (4.43c)$$

$$\bar{p}_{10} = p_{10}(0, s, t), \quad (4.43d)$$

and we see that these leading-order variables are constant in N within region II. The region III variables in the system (4.36)–(4.42) are solved by

$$\bar{V}_{00} = -K P_{0s}(0, s, t), \quad (4.44a)$$

$$\bar{P}_{10} = P_{10}(0, s, t), \quad (4.44b)$$

$$\bar{P}_{11} = NP_{0n}(0, s, t) + P_{11}(0, s, t) - \frac{p_{0n}(0, s, t)}{4K\pi^3} \sum_{k=1}^{\infty} k^{-3} \exp(2\pi k N) \cos(2\pi k z), \quad (4.44c)$$

where $\overline{U}_{00}$ and $\overline{W}_{00}$ can be deduced from (4.44c) by differentiating with respect to N and z respectively, then using the governing equations (4.38a) and (4.38c).

Using the interfacial condition (4.40b) with the bulk and interior pressures (4.43d) and (4.44b), we are able to give the coupling condition between outer regions for the $O(\delta^{-1}\epsilon)$ pressure for inflow, as follows

$$p_{10} = P_{10} \quad \text{on } \partial D. \quad (4.45)$$

In the next section we consider the inner-inner region IIa, which is necessary to satisfy the BJ slip conditions (4.26c,d). This region also allows us to impose the continuity of stress interfacial condition (4.26b), to determine the shear stress acting on the interface for inflow, and to determine the coupling conditions between outer regions for inflow.

4.4.1.1 Inner-inner inflow: region IIa

The relevant scalings in the inner-inner region are $N = \delta \hat{N}$ and $\bar{w}_0 = \delta \hat{w}_0$. We also use $\bar{u}_0 = \hat{u}_0$, $\bar{v}_0 = \hat{v}_0$ and $\bar{p}_1 = \hat{p}_1$ to indicate that we are in the inner-inner region, which is defined as region IIa. We use the following asymptotic expansions

$$\hat{u}_0 = \hat{u}_{00} + O(\delta), \quad (4.46a)$$

$$\hat{v}_0 = \hat{v}_{00} + O(\delta), \quad (4.46b)$$

$$\hat{w}_0 = \hat{w}_{01} + O(\delta^{1/3}), \quad (4.46c)$$

$$\hat{p}_1 = \delta^{-1} \hat{p}_{10} + O(1), \quad (4.46d)$$

as $\delta \rightarrow 0$. Using the scalings described above, and the asymptotic expansions (4.46) in the inner bulk flow equations (4.21), the leading-order equations in region IIa are given by

$$\hat{u}_{00} \hat{u}_{00\hat{N}} = -\hat{p}_{10\hat{N}} + \hat{u}_{00\hat{N}\hat{N}}, \quad (4.47a)$$

$$\hat{u}_{00} \hat{v}_{00\hat{N}} = \hat{v}_{00\hat{N}\hat{N}}, \quad (4.47b)$$

$$\hat{u}_{00} \hat{w}_{01\hat{N}} = -\hat{p}_{10z} + \hat{w}_{01\hat{N}\hat{N}}, \quad (4.47c)$$

$$0 = \hat{u}_{00\hat{N}}. \quad (4.47d)$$

The interfacial conditions on $\hat{N} = 0$ are given in (4.26) and, at leading-order, become

$$\hat{u}_{00} = \bar{U}_0 \quad \text{on } \hat{N} = 0, \quad (4.48a)$$

$$\hat{p}_{10} - 2\hat{u}_{00\hat{N}} = \bar{P}_{10} \quad \text{on } \hat{N} = 0, \quad (4.48b)$$

$$\hat{v}_{00\hat{N}} = 0 \quad \text{on } \hat{N} = 0, \quad (4.48c)$$

$$\hat{w}_{01\hat{N}} = \lambda\sqrt{K}\bar{P}_{11z}(0, s, z, t) \quad \text{on } \hat{N} = 0. \quad (4.48d)$$

The matching conditions with region II are given by

$$\hat{u}_{00} \sim \bar{u}_{00}(0, s, z, t) \quad \text{as } \hat{N} \rightarrow -\infty, \quad (4.49a)$$

$$\hat{v}_{00} \sim \bar{v}_{00}(0, s, z, t) \quad \text{as } \hat{N} \rightarrow -\infty, \quad (4.49b)$$

$$\hat{w}_{01} \sim \bar{w}_{01}(0, s, z, t) \quad \text{as } \hat{N} \rightarrow -\infty, \quad (4.49c)$$

$$\hat{p}_{10} \sim \bar{p}_{10}(0, s, t) \quad \text{as } \hat{N} \rightarrow -\infty, \quad (4.49d)$$

where $\bar{w}_{01}(0, s, z, t)$ is not solved for within region II in the 3D case, and so is left as a general function here. If required, $\bar{w}_{01}$ could be solved for in region II in the same manner as in §3.4.1.1.

The system (4.47)–(4.49) is solved by

$$\hat{u}_{00} = \bar{u}_{00}(0, s, z, t), \quad (4.50a)$$

$$\hat{v}_{00} = \bar{v}_{00}(0, s, z, t), \quad (4.50b)$$

$$\hat{w}_{01} = \bar{w}_{01}(0, s, z, t) + \frac{\lambda\sqrt{K}\bar{P}_{11z}(0, s, z, t)}{\bar{u}_{00}(0, s, z, t)} \exp(\hat{N}\bar{u}_{00}(0, s, z, t)), \quad (4.50c)$$

$$\hat{p}_{10} = \bar{p}_{10}(0, s, t). \quad (4.50d)$$

We note that the normal and azimuthal velocities (4.50a,b) and the pressure (4.50d) are unchanged within region IIa. This justifies the coupling conditions (4.40) imposed between regions II and III, and hence justifies the coupling condition between outer regions for the $O(\delta^{-1}\epsilon)$ pressure (4.45) for inflow.

We note that $\hat{w}_{01}$ (given in (4.50c)) does change in this region and, from the shear stress (4.34c), yields an $O(\epsilon^{-1})$ contribution to the stress (an $O(\delta)$ quantity varying in a region of length $O(\epsilon\delta)$). As $\hat{v}_{00}$ does not vary in $\hat{N}$, one might think that the azimuthal velocity does not contribute to the stress (4.34b) at this order. However, if we were to carry on with the expansion (4.46b), it would be the $O(\delta)$ azimuthal term that would vary in region IIa, and it would contribute another $O(\epsilon^{-1})$ term to the stress for the same reason as above. We note that we do not need to calculate

the next-order azimuthal velocity term explicitly to calculate this stress, as it can be determined directly from the BJ slip condition (4.26c). Therefore, from the general stress expressions (4.34) and in terms of the outer variables (using the solutions in regions II, IIa, and III given by (4.43), (4.50), and (4.44) respectively), we deduce that the stress acting on the TC due to inflow is given by

$$\sigma_{nn} = -\epsilon^{-2}p_0(0, s, t) - \epsilon^{-1}\delta^{-1}p_{10}(0, s, t) + O(\epsilon^{-1}), \quad (4.51a)$$

$$\sigma_{ns} = \epsilon^{-1}\frac{\lambda}{\sqrt{K}}\left(\frac{z(z-1)}{2}p_{0s}(0, s, t) + \mathbf{s} \cdot \mathbf{u}^{\text{slip}}(0, s, t) + KP_{0s}(0, s, t)\right) + O(1), \quad (4.51b)$$

$$\sigma_{nz} = \epsilon^{-1}p_{0n}(0, s, t)\left(z - \frac{1}{2} + \frac{\lambda}{2K\pi^2}\sum_{k=1}^{\infty}k^{-2}\sin(2k\pi z)\right) + O(1), \quad (4.51c)$$

in the asymptotic limit in which $\epsilon \ll \delta \ll 1$.

The final task for inflow is to determine the coupling condition between outer regions for the averaged normal flux, given by (4.33). From the solutions for the azimuthal velocity in regions II and IIa, given by (4.43b) and (4.50b) respectively, we see that the azimuthal velocity is constant in N at leading-order for inflow (given by its matching condition (4.28b)). As the coupling condition (4.33) is a measure of the change in the azimuthal velocity, the contribution from the leading-order azimuthal velocity is zero. We note that were we to continue the asymptotic expansions (4.35a) and (4.46b), the azimuthal velocity would vary in N within regions II and IIa at $O(\delta)$. Therefore, the right-hand side of the coupling condition (4.33) is $O(\delta^2)$, and we deduce that the condition to couple the outer average normal velocities for inflow is given by

$$\int_0^1 ((\mathbf{u}_{10}^{\text{rel}} - \mathbf{Q}_{10}^{\text{rel}}) \cdot \mathbf{n})|_{n=0} dz = 0. \quad (4.52)$$

Therefore, the relevant coupling conditions for inflow are no jump in pressure, given by (4.45), and no jump in averaged normal velocity, given by (4.52).

4.4.2 Outflow: regions V and VI

Outflow occurs in a similar manner to §3.4.2 but, due to the change in coordinate system, is now characterised by $\bar{u}_0 > 0$. The porous inner outflow region is defined as region V and the bulk inner outflow region is defined as region VI (shown in Figure 3.2a). In regions V and VI we have the governing equations (4.23) and (4.21), with wall boundary conditions (4.24), interfacial conditions (4.26), and matching

conditions (4.27b), (4.28), (4.29b), and (4.30). In regions V and VI we form the following asymptotic expansions

$$(\bar{\mathbf{u}}_0, \bar{\mathbf{Q}}_0) \sim (\bar{\mathbf{u}}_{00}, \bar{\mathbf{Q}}_{00}) + \delta^{1/2}(\bar{\mathbf{u}}_{0a}, \bar{\mathbf{Q}}_{0a}), \quad (4.53a)$$

$$\bar{p}_1 \sim \delta^{-1}\bar{p}_{10} + \delta^{-1/2}\bar{p}_{1a}, \quad (4.53b)$$

$$\bar{P}_1 = \delta^{-1}\bar{P}_{10} + \bar{P}_{11} + O(\delta^{1/2}), \quad (4.53c)$$

as $\delta \rightarrow 0$. In this section we only evaluate the leading-order terms and $\bar{P}_{11}$ (which drives the leading-order flow in region V) from (4.53). However, we make use of the far-field limits of the correction terms in Appendix E.9.2, where we determine matching conditions into the intermediate transition region VIa (shown in Figure 3.9). The leading-order terms in the asymptotic expansions for outflow (4.53) are the same as for inflow (4.35). As the lengthscales are the same in region V as for region III, and the same in region VI as for region II, the governing equations and some boundary conditions are shared. For brevity, we do not repeat them here, but instead indicate where they can be found.

The governing equations in region V are given by (4.37) and (4.38). The governing equations in region VI are given by (4.36). The Hele-Shaw cell wall boundary conditions we are able to impose (which are conditions on the normal velocities) are given by (4.39). We are able to impose the full set of interfacial conditions, which are continuity of flux and continuity of stress (4.40) and the two BJ slip conditions (4.26c) and (4.26d), which become

$$\bar{v}_{00N} = \frac{\lambda}{\sqrt{K}} (\bar{v}_{00} - \bar{V}_{00}) \quad \text{on } N = 0, \quad (4.54a)$$

$$\bar{w}_{00N} = \frac{\lambda}{\sqrt{K}} (\bar{w}_{00} - \bar{W}_{00}) \quad \text{on } N = 0. \quad (4.54b)$$

We also require matching conditions between region V and the outer porous flow, which are given by (4.42). The matching conditions between region VI and the intermediate transition region VIa are determined from the solution in region VI. For the system outlined above, the solutions in region V are given by

$$\bar{U}_{00} = -K P_{0n}(0, s, t), \quad (4.55a)$$

$$\bar{V}_{00} = -K P_{0s}(0, s, t), \quad (4.55b)$$

$$\bar{W}_{00} = 0, \quad (4.55c)$$

$$\bar{P}_{10} = P_{10}(0, s, t), \quad (4.55d)$$

$$\bar{P}_{11} = N P_{0n}(0, s, t) + P_{11}(0, s, t). \quad (4.55e)$$

Therefore, the leading-order variables in region V are all constant in N (and are given by their matching conditions with region IV), and the pressure $\bar{P}_{11}$ drives the flow. The solutions in region VI are given by

$$\bar{u}_{00} = -K P_{0n}(0, s, t), \quad (4.56a)$$

$$\bar{v}_{00} = -K P_{0s}(0, s, t), \quad (4.56b)$$

$$\bar{w}_{00} = 0, \quad (4.56c)$$

$$\bar{p}_{10} = P_{10}(0, s, t), \quad (4.56d)$$

and we find that there is also no change in leading-order variables in region VI. This is equivalent to the behaviour in the 2D case in Chapter 3, where the transition to Poiseuille flow occurs in an intermediate region which we investigate in the next section. Note that $\bar{u}_{00}$ and $\bar{v}_{00}$ do not, in general, satisfy the slip condition (4.24a) on the Hele-Shaw cell walls, and this issue is resolved in Appendix E.8.2 in a boundary layer close to the walls.

Finally, we determine the shear stress acting on the outflow interface. The general form for the stress given in (4.34) becomes

$$\sigma_{nn} = -\epsilon^{-2} P_0 - \epsilon^{-1} \delta^{-1} P_{10} + O(\epsilon^{-1} \delta^{-1/2}), \quad (4.57a)$$

$$\sigma_{ns} = O(\epsilon^{-1} \delta^{1/2}), \quad (4.57b)$$

$$\sigma_{nz} = O(\epsilon^{-1} \delta^{1/2}), \quad (4.57c)$$

in the asymptotic limit in which $\epsilon \ll \delta \ll 1$. We see that the shear stress on the TC is asymptotically smaller by a factor of $O(\delta^{1/2})$ for outflow (4.57) than for inflow (4.51). This is because the leading-order tangential flow does not vary within region VI for outflow, as the flow leaving the TC satisfies the BJ slip condition (4.54) automatically. The inflow does not have this luxury, which is reflected in the presence of a boundary layer close to the interface (region IIa) where the tangential velocity varies and thus causes a larger shear stress. Therefore, we have analytically determined the stress acting on the interface up to $O(\epsilon^{-1} \delta^{-1})$ for the normal stress and up to $O(\epsilon^{-1})$ for the shear stress (and we note that the contribution to the shear stress from outflow is zero at this order).

4.4.2.1 Intermediate outflow: region VIa

The relevant scalings for the intermediate region are $N = \delta^{-1} \tilde{N}$ and $\bar{w}_0 = \delta \tilde{w}$. We also use $\bar{u}_0 = \tilde{u}_0$, $\bar{v}_0 = \tilde{v}_0$ and $\bar{p}_1 = \tilde{p}_1$ to indicate that we are in the intermediate

region, which is defined as region VIa. We use the following asymptotic expansions

$$\tilde{u}_0 = \tilde{u}_{00} + O(\delta^{1/2}), \quad (4.58a)$$

$$\tilde{v}_0 = \tilde{v}_{00} + O(\delta^{1/2}), \quad (4.58b)$$

$$\tilde{w}_0 = \tilde{w}_{01} + O(\delta^{1/2}), \quad (4.58c)$$

$$\tilde{p}_1 = \delta^{-1}\tilde{p}_{10} + O(\delta^{-1/2}). \quad (4.58d)$$

As the problem for the azimuthal velocity decouples from the rest of the system, we proceed by solving for $\tilde{u}_{00}$, $\tilde{w}_{00}$ and $\tilde{p}_{10}$, before returning to $\tilde{v}_{00}$. Substituting (4.58) into the governing equations (4.21), in region VIa we obtain the leading-order equations

$$\tilde{u}_{00}\tilde{u}_{00\tilde{N}} + \tilde{w}_{01}\tilde{u}_{00z} = -\tilde{p}_{10\tilde{N}} + \tilde{u}_{00zz}, \quad (4.59a)$$

$$0 = -\tilde{p}_{10z}, \quad (4.59b)$$

$$0 = \tilde{u}_{00\tilde{N}} + \tilde{w}_{01z}. \quad (4.59c)$$

The Hele-Shaw cell wall boundary conditions are obtained by substituting the asymptotic expansion (4.58) into the boundary conditions (4.24a), and are given by

$$\tilde{u}_{00} = \mathbf{n} \cdot \mathbf{u}^{\text{slip}}(0, s, t), \quad \tilde{w}_{01} = 0, \quad \text{on } z = 0, 1 \text{ for } \tilde{N} > 0. \quad (4.60a, b)$$

The interfacial boundary conditions are given by matching with region VI. In Appendix E.9.2, we determine the matching conditions by considering further terms in region VI. The matching conditions with region VI are given by

$$\tilde{u}_{00} \sim \left(-K P_{0n}(0, s, t) + 2w^l \left(-K P_{0n}(0, s, t) \tilde{N} \right)^{1/2} \right) g'(\tilde{\eta}_{(0)}) g'(\tilde{\eta}_{(1)}), \quad (4.61a)$$

$$\tilde{w}_{01} \sim w^l \frac{(1-2z)(-K P_{0n}(0, s, t))^{1/2}}{2\tilde{N}^{1/2}} (\tilde{\eta}_{(0)} g'(\tilde{\eta}_{(0)}) - g(\tilde{\eta}_{(0)})) (\tilde{\eta}_{(1)} g'(\tilde{\eta}_{(1)}) - g(\tilde{\eta}_{(1)})), \quad (4.61b)$$

$$\tilde{p}_{10} \sim P_{10}(0, s, t) - 2w^l \left(-K P_{0n}(0, s, t) \tilde{N} \right)^{1/2}, \quad (4.61c)$$

as $\tilde{N} \downarrow 0$, where w^l is defined in (E.97) and $g(\eta)$ is defined in (E.95) with $\tilde{\eta}_{(0)} = z/\tilde{N}^{1/2}$ and $\tilde{\eta}_{(1)} = (1-z)/\tilde{N}^{1/2}$. The function g is a Blasius-type similarity solution with a boundary condition that takes into account the moving wall. We note that, from the governing equations (4.59), the far-field behaviour of the relevant variables satisfies the matching conditions, which are given by

$$\tilde{u}_{00} \sim \mathbf{n} \cdot \mathbf{u}^{\text{slip}}(0, s, t) + \frac{z(z-1)}{2} p_{0n}(0, s, t) \quad \text{as } \tilde{N} \rightarrow \infty, \quad (4.62a)$$

$$\tilde{w}_{01} \rightarrow 0 \quad \text{as } \tilde{N} \rightarrow \infty, \quad (4.62b)$$

$$\tilde{p}_{10} \sim p_{0n}(0, s, t) \tilde{N} + p_{10}(0, s, t) \quad \text{as } \tilde{N} \rightarrow \infty. \quad (4.62c)$$

To determine $p_{10}(0, s, t) - P_{10}(0, s, t)$ for the coupling condition between outer regions, we must solve the full system (4.59)–(4.62) numerically, and determine the coupling condition using the matching conditions (4.61c) and (4.62c). There are three parameters on which the solution depends: $-KP_{0n}$, $\mathbf{n} \cdot \mathbf{u}^{\text{slip}}$, and P_{10} . However, we can simplify our task by noting that the governing equations (4.59) are invariant to the transformations

$$\tilde{N} = \mathcal{U}\mathbf{n}, \quad \tilde{u}_{00} = \mathcal{U}u, \quad \tilde{p}_{10} = \mathcal{P} + \mathcal{U}^2\mathbf{p}, \quad (4.63a, b, c)$$

where $\mathcal{U}$ and $\mathcal{P}$ are independent of $\tilde{N}$ and z . Using the scalings (4.63) in the governing equations (4.59) yields

$$\mathbf{u}\mathbf{u}_{\mathbf{n}} + \tilde{w}_{01}\mathbf{u}_z = -\mathbf{p}_{\mathbf{n}} + \mathbf{u}_{zz}, \quad (4.64a)$$

$$0 = -\mathbf{p}_z, \quad (4.64b)$$

$$0 = \mathbf{u}_{\mathbf{n}} + \tilde{w}_{01z}, \quad (4.64c)$$

within region VIa. The translational invariance of the pressure in (4.63c) allows a reduction in the system to a two-parameter family of solutions (removing P_{10}). However, we are not able to exploit the scaling invariance in (4.63), as the boundary conditions (4.61) are not amenable to such a scaling, and it might appear that we must leave this path of attack. In fact, we can make use of this scaling by recalling the work carried out for region VIa in the 2D case. In §3.4.2.2 we calculated that the difference in $p_{10}(0, s, t) - P_{10}(0, s, t)$ obtained when using the formal matching conditions with region VI (3.113) and using the naive boundary conditions (3.117) was very small (around 2%). As the scaling in (4.63) allows us to reduce the problem to a one-parameter family of solutions (with the relevant parameter given below), we proceed by using the naive boundary conditions (defined below), accepting a 2% error as a fair price to pay for this parameter reduction.

The naive boundary conditions are obtained by taking the limit of the formal matching conditions (4.61) as $\tilde{N} \rightarrow 0$, and setting $\tilde{w}_{01} = 0$ as follows

$$\hat{u}_{00} = -KP_{0n}(0, s, t) \quad \text{on } \mathbf{n} = 0, \quad (4.65a)$$

$$\tilde{w}_{01} = 0 \quad \text{on } \mathbf{n} = 0, \quad (4.65b)$$

$$\tilde{p}_{10} = P_{10}(0, s, t) \quad \text{on } \mathbf{n} = 0. \quad (4.65c)$$

For the invariant scalings (4.63), we take $\mathcal{U} = -KP_{0n}(0, s, t)$ (which is positive due to the outflow assumption) and $\mathcal{P} = P_{10}(0, s, t)$. Under this transformation, the naive

boundary conditions (4.65) become

$$\mathbf{u} = 1 \quad \text{on } \mathbf{n} = 0, \quad (4.66a)$$

$$\tilde{w}_{01} = 0 \quad \text{on } \mathbf{n} = 0, \quad (4.66b)$$

$$\mathbf{p} = 0 \quad \text{on } \mathbf{n} = 0, \quad (4.66c)$$

and the wall boundary conditions (4.60) become

$$\mathbf{u} = \frac{\mathcal{A}}{\mathcal{U}}, \quad \tilde{w}_{01} = 0, \quad \text{on } z = 0, 1 \text{ for } \mathbf{n} > 0, \quad (4.67a, b)$$

where we introduce the notation $\mathcal{A} = \mathbf{n} \cdot \mathbf{u}^{\text{slip}}(0, s, t)$ for convenience. Using the leading-order outer coupling condition (4.14a), we are able to deduce that

$$p_{0n}(0, s, t) = 12(\mathcal{A} - \mathcal{U}), \quad (4.68)$$

which allows us to write the scaled far-field matching conditions (4.62) as

$$\mathbf{u} \sim \frac{\mathcal{A}}{\mathcal{U}} + 6z(1-z) \left(1 - \frac{\mathcal{A}}{\mathcal{U}}\right) \quad \text{as } \mathbf{n} \rightarrow \infty, \quad (4.69a)$$

$$\tilde{w}_{01} \rightarrow 0 \quad \text{as } \mathbf{n} \rightarrow \infty, \quad (4.69b)$$

$$\mathbf{p} \sim -12 \left(1 - \frac{\mathcal{A}}{\mathcal{U}}\right) \mathbf{n} + \frac{1}{\mathcal{U}^2} (p_{10}(0, s, t) - P_{10}(0, s, t)) \quad \text{as } \mathbf{n} \rightarrow \infty. \quad (4.69c)$$

The scaled problem in $\mathbf{u}$, $\tilde{w}_{01}$, and $\mathbf{p}$ (dependent on the variables $\mathbf{n}$ and z) has governing equations (4.64) and boundary conditions (4.66), (4.67) and (4.69). Therefore, we see that the natural (sole) parameter of the problem is the ratio $\mathcal{A}/\mathcal{U}$, which is the ratio of the channel wall velocity to the normal outflow velocity at the interface. From (4.69c), we see that the pressure coupling condition between outer regions is given by

$$p_{10}(0, s, t) - P_{10}(0, s, t) = \mathcal{U}^2 \Pi \left(\frac{\mathcal{A}}{\mathcal{U}}; s, t \right), \quad (4.70)$$

where the function $\Pi(\mathcal{A}/\mathcal{U}; s, t)$ is defined as follows

$$\Pi \left(\frac{\mathcal{A}}{\mathcal{U}}; s, t \right) = \lim_{\mathbf{n} \rightarrow \infty} \left(\mathbf{p} \left(\frac{\mathcal{A}(s, t)}{\mathcal{U}(s, t)} \right) + 12 \left(1 - \frac{\mathcal{A}(s, t)}{\mathcal{U}(s, t)} \right) \mathbf{n} \right), \quad (4.71)$$

and we note that $\Pi(0; s, t) = \Pi_0 \approx -0.331$, calculated in (3.118) where we considered a stationary channel wall, and $\Pi(1; s, t) = 0$, which corresponds to pure plug flow with no pressure-driven component, i.e. the pressure remains constant. We calculate the function Π using the central finite difference scheme described in Bodoia and Osterle

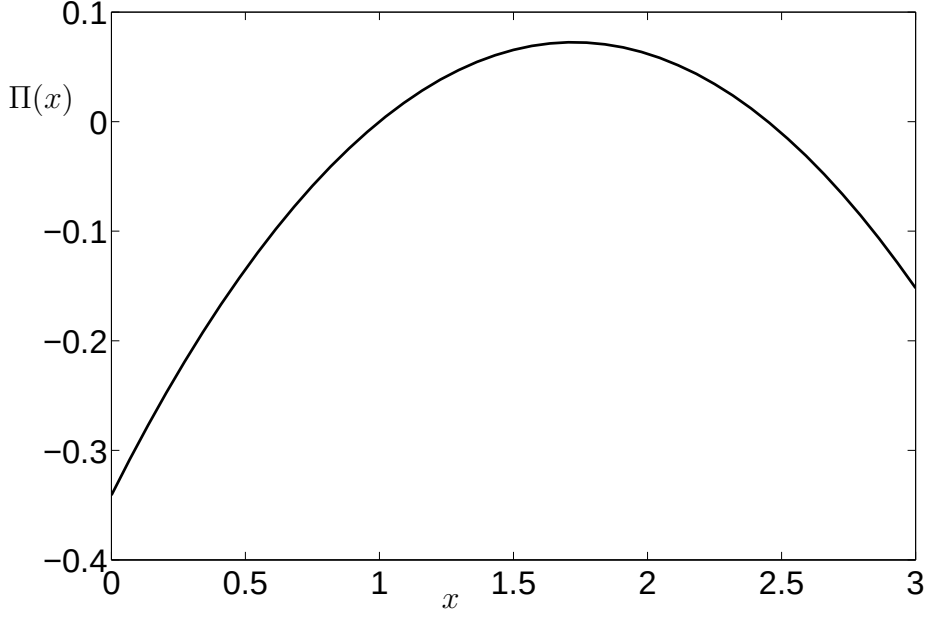


Figure 4.3: The function Π , defined in (4.71).

[6], but implement moving channel walls. We show the graph of Π in Figure 4.3. We take a range of $\mathcal{A}/\mathcal{U} \in [0, 3]$ for the argument, the upper bound being the limit where the velocity in the centre of the channel first becomes negative (as can be deduced from (4.69a)) and the lower bound being where the wall velocity first becomes negative, as our numerical scheme is unable to deal with a negative velocity.

To complete the analysis of the leading-order 3D flow, we now consider the azimuthal velocity $\tilde{v}_{00}$. Once we have determined $\tilde{v}_{00}$, we then evaluate the remaining outer coupling condition for the averaged normal flux. In region VI variables, this coupling condition is given by (4.33), and in region VIa variables (and using the transformation (4.63)) it becomes

$$\int_0^1 ((\mathbf{u}_{10}^{\text{rel}} - \mathbf{Q}_{10}^{\text{rel}}) \cdot \mathbf{n})|_{n=0} dz = -\mathcal{U} \int_0^\infty \int_0^1 (\tilde{v}_{00s}(\mathbf{n}) - \mathbf{s} \cdot \mathbf{u}_{00s}^{\text{rel}}|_{n=0}) dz d\mathbf{n}. \quad (4.72)$$

The governing equation for $\tilde{v}_{00}$ is obtained by substituting the asymptotic expansion (4.58) into the governing equation (4.21b) which, using the transformation (4.63a,b), is given by

$$\mathbf{u}\tilde{v}_{00n} + \tilde{w}_{01}\tilde{v}_{00z} = -\tilde{p}_{0s} + \tilde{v}_{00zz} \quad \text{in region VIa.} \quad (4.73)$$

The boundary conditions on the channel walls (4.24a) become

$$\tilde{v}_{00} = \mathbf{s} \cdot \mathbf{u}^{\text{slip}}(0, s, t) \quad \text{on } z = 0, 1 \text{ for } \tilde{N} > 0, \quad (4.74)$$

and the matching conditions with region VI are determined in Appendix E.9.2, as follows

$$\tilde{v}_{00} \sim -K P_{0s}(0, s, t) h(\tilde{\eta}_{(0)}) h(\tilde{\eta}_{(1)}) \quad \text{as } \tilde{N} \downarrow 0, \quad (4.75)$$

where $h(\eta)$ is defined in (E.103), $\tilde{\eta}_{(0)} = z/\tilde{N}^{1/2}$, and $\tilde{\eta}_{(1)} = (1-z)/\tilde{N}^{1/2}$. The function h allows $\tilde{v}_{00}$ to attain the value of the wall slip near the channel wall in region VI. In this sense, it is similar to the Blasius function, though it satisfies a different equation (given in (E.103)).

Finally, the far-field behaviour can be determined from the governing equation (4.73), and satisfies the relevant matching condition given by

$$\tilde{v}_{00} \sim \mathbf{s} \cdot \mathbf{u}^{\text{slip}}(0, s, t) + \frac{z(z-1)}{2} p_{0s}(0, s, t) \quad \text{as } \tilde{N} \rightarrow \infty, \quad (4.76)$$

and is obtained naturally from the governing equation (4.73). The full system is given by (4.73)–(4.76), and is dependent on three parameters: $\mathcal{A}/\mathcal{U}$ (from the dependence on $\mathbf{u}$, $\mathbf{n}$ and $h(\eta)$), K , and $p_{0s}(0, s, t)$ (which is equivalent to $P_{0s}(0, s, t)$ using the pressure coupling condition between outer regions (4.14)). Therefore, to fully evaluate the outer coupling condition (4.72), it appears as though we have a three-parameter family of solutions.

However, we are able to significantly simplify the number of required computations because the system (4.73)–(4.76) is linear in $\tilde{v}_{00}$. We can exploit the linearity using the scaling

$$\tilde{v}_{00} = \mathcal{V} \mathbf{v} + \mathcal{B}, \quad (4.77)$$

where we use $\mathcal{V} = -p_{0s}(0, s, t)$ and $\mathcal{B} = \mathbf{s} \cdot \mathbf{u}^{\text{slip}}(0, s, t)$ for convenience. The scaling (4.77) turns the governing equation (4.73) into

$$L(\mathbf{v}) = 1, \quad (4.78)$$

where the linear operator L is defined as

$$L = \mathbf{u} \frac{\partial}{\partial \mathbf{n}} + \tilde{w}_{01} \frac{\partial}{\partial z} - \frac{\partial^2}{\partial z^2}, \quad (4.79)$$

while the boundary conditions on the channel walls (4.74) become

$$\mathbf{v} = 0 \quad \text{on } z = 0, 1 \text{ for } \mathbf{n} > 0; \quad (4.80)$$

matching conditions (4.75) become

$$\mathbf{v} \sim K h(\tilde{\eta}_{(0)}) h(\tilde{\eta}_{(1)}) - \frac{\mathcal{B}}{\mathcal{V}} \quad \text{as } \tilde{N} \downarrow 0; \quad (4.81)$$

and the far-field condition (4.76) becomes

$$\mathbf{v} \sim \frac{z(1-z)}{2} \quad \text{as } \mathbf{n} \rightarrow \infty. \quad (4.82)$$

The system (4.78)–(4.82) has a linear dependence on two parameters: K and $\mathcal{B}/\mathcal{V}$. We can explicitly see this linear dependence by taking

$$\mathbf{v} = \mathbf{v}_1 + K\mathbf{v}_2 + \mathcal{B}/\mathcal{V}\mathbf{v}_3, \quad (4.83)$$

where $\mathbf{v}_i$ satisfy the following governing equations:

$$L(\mathbf{v}_1) = 1, \quad L(\mathbf{v}_2) = 0, \quad L(\mathbf{v}_3) = 0 \quad \text{in region VIa}; \quad (4.84a, b, c)$$

with the boundary conditions on the channel walls

$$\mathbf{v}_i = 0 \quad \text{for } i \in \{1, 2, 3\} \quad \text{on } z = 0, 1 \text{ for } \mathbf{n} > 0; \quad (4.85a, b, c)$$

the matching conditions with region VI

$$\mathbf{v}_1 \rightarrow 0, \quad \mathbf{v}_2 \sim h(\tilde{\eta}_{(0)})h(\tilde{\eta}_{(1)}), \quad \mathbf{v}_3 \sim -1 \quad \text{as } \mathbf{n} \downarrow 0; \quad (4.86a, b, c)$$

and the far-field conditions

$$\mathbf{v}_1 \sim \frac{z(1-z)}{2}, \quad \mathbf{v}_2 \rightarrow 0, \quad \mathbf{v}_3 \rightarrow 0 \quad \text{as } \mathbf{n} \rightarrow \infty. \quad (4.87a, b, c)$$

The systems (4.84)–(4.87) are only dependent on one parameter: $\mathcal{A}/\mathcal{U}$. Therefore, we have demonstrated the linear dependence of $\mathbf{v}$ on the parameters K and $\mathcal{B}/\mathcal{V}$. We are rewarded in this effort by the parameter reduction of (4.72). Accounting for the change of variable to $\mathbf{n}$ being dependent on s , the scaling (4.77), the splitting (4.83), and the far-field result for $\tilde{v}_{00}$ (4.76), the outer coupling condition (4.72) becomes

$$\int_0^1 ((\mathbf{u}_{10}^{\text{rel}} - \mathbf{Q}_{10}^{\text{rel}}) \cdot \mathbf{n}) \, dz = -K \frac{\partial}{\partial s} \left(P_{0n}(0, s, t) \Lambda \left(\frac{\mathcal{A}}{\mathcal{U}}; s, t \right) \right) \quad \text{on } n = 0, \quad (4.88)$$

where

$$\begin{aligned} \Lambda \left(\frac{\mathcal{A}}{\mathcal{U}}; s, t \right) &= p_{0s}(0, s, t) \left(\Lambda_1 \left(\frac{\mathcal{A}}{\mathcal{U}}; s, t \right) + K \Lambda_2 \left(\frac{\mathcal{A}}{\mathcal{U}}; s, t \right) \right. \\ &\quad \left. - \mathbf{s} \cdot \mathbf{u}^{\text{slip}}(0, s, t) \Lambda_3 \left(\frac{\mathcal{A}}{\mathcal{U}}; s, t \right) \right), \end{aligned} \quad (4.89a)$$

$$\Lambda_1 \left(\frac{\mathcal{A}}{\mathcal{U}}; s, t \right) = \int_0^\infty \int_0^1 \left(\mathbf{v}_1 \left(\frac{\mathcal{A}(s, t)}{\mathcal{U}(s, t)} \right) - \frac{z(1-z)}{2} \right) \, dz \, d\mathbf{n}, \quad (4.89b)$$

$$\Lambda_2 \left(\frac{\mathcal{A}}{\mathcal{U}}; s, t \right) = \int_0^\infty \int_0^1 \mathbf{v}_2 \left(\frac{\mathcal{A}(s, t)}{\mathcal{U}(s, t)} \right) \, dz \, d\mathbf{n}, \quad (4.89c)$$

$$\Lambda_3 \left(\frac{\mathcal{A}}{\mathcal{U}}; s, t \right) = \int_0^\infty \int_0^1 \mathbf{v}_3 \left(\frac{\mathcal{A}(s, t)}{\mathcal{U}(s, t)} \right) \, dz \, d\mathbf{n}, \quad (4.89d)$$

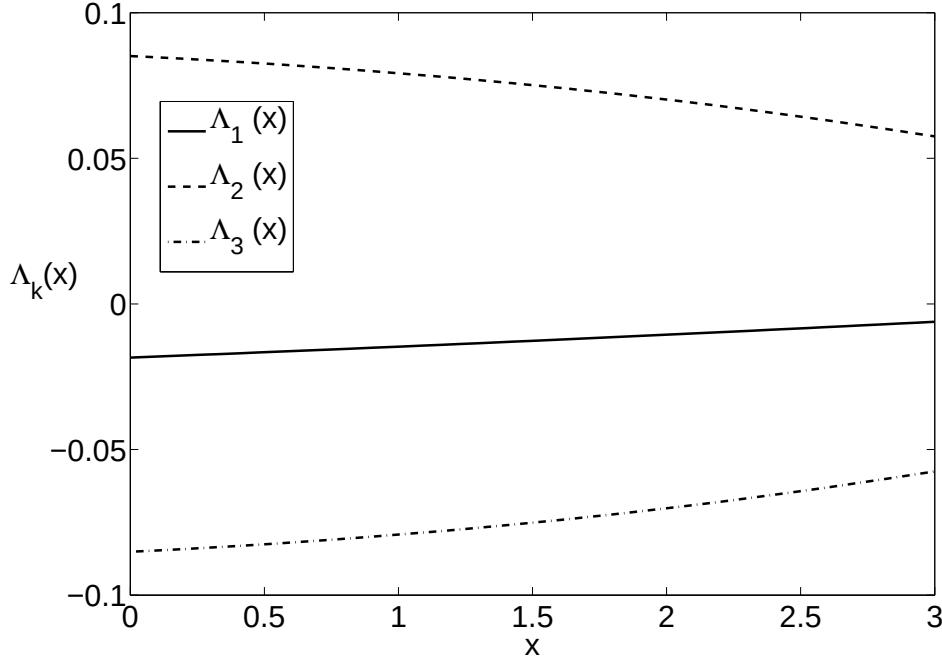


Figure 4.4: Calculating the functions Λ_1 , Λ_2 and Λ_3 defined in (4.89b-d).

and we have made explicit the dependence of $\mathbf{v}_i$ on the single parameter given by $\mathcal{A}/\mathcal{U} = \mathbf{n} \cdot \mathbf{u}^{\text{slip}}(0, s, t) / (-K P_{0n}(0, s, t))$. This means that instead of solving one problem (4.73)–(4.76) for a three-dimensional parameter space and evaluating (4.72), we now only need to solve three problems (4.84)–(4.87) for a one-dimensional parameter space $\mathcal{A}/\mathcal{U}$ and evaluate (4.89b-d).

We show graphs of the three functions (4.89b-d) in Figure 4.4. These are evaluated using a central finite difference scheme, and the coefficients $\mathbf{u}$ and $\tilde{w}_{01}$ in the linear operator (4.79) are obtained above when solving for Π (defined in (4.71)), using the central finite difference scheme described in Bodoia and Osterle [6].

This concludes the determination of the inner problem for outflow in the asymptotic limit in which $\delta \ll \epsilon \ll 1$. The coupling conditions for the outer outflow problems are given by (4.70) and (4.88).

To summarise, we have calculated the macroscale boundary conditions for flow past a porous cylindrical obstacle with an arbitrary smooth cross-section. In the next section, we consider the coupling conditions determined thus far in the context of the flow problem considered in Chapter 2.

4.5 Outer coupling conditions

In this section we collate the coupling conditions determined in this Chapter, and discuss their use in the rest of this thesis. The coupling conditions between outer regions are given by (4.10) at leading order, and we find there is no pressure or average flux jump within the inner regions, with

$$p_0 - P_0 = 0 \quad \text{on } \partial D, \quad (4.90a)$$

$$\int_0^1 ((\mathbf{u}_0^{\text{rel}} - \mathbf{Q}_0^{\text{rel}}) \cdot \mathbf{n}) \, dz = 0 \quad \text{on } \partial D. \quad (4.90b)$$

The coupling conditions between the $O(\epsilon\delta^{-1})$ higher-order corrections are different for inflow and outflow. For inflow, we again find that there is no pressure or average flux jump, and these conditions are given in (4.45) and (4.52). However, for outflow the situation is more complicated. We find that there is a jump in both pressure and average flux across the inner regions. The pressure jump for outflow is given in (4.70), and the average flux jump for outflow is given in (4.88). Using a Heaviside function, we can combine the first-correction outer coupling conditions for inflow and outflow as follows

$$p_{10} - P_{10} = (-KP_{0n})^2 \Pi(s, t) H \left(\int_0^1 \mathbf{u}_0^{\text{rel}} \cdot \mathbf{n} \, dz \right) \quad \text{on } \partial D, \quad (4.91a)$$

$$\int_0^1 ((\mathbf{u}_{10}^{\text{rel}} - \mathbf{Q}_{10}^{\text{rel}}) \cdot \mathbf{n}) \, dz = -K \frac{\partial}{\partial s} (P_{0n} \Lambda(s, t)) H \left(\int_0^1 \mathbf{u}_0^{\text{rel}} \cdot \mathbf{n} \, dz \right) \quad \text{on } \partial D. \quad (4.91b)$$

We note that, since $-KP_{0n} = \int_0^1 \mathbf{u}_0^{\text{rel}} \cdot \mathbf{n} \, dz$ (as seen from the integrated form of the outer coupling conditions (4.10b) and (4.14)), the coupling conditions (4.91) are continuous in $-KP_{0n}$, i.e. there is no jump *in the pressure jump* between outer regions as we move from inflow to outflow. There is an interesting problem (and another boundary layer) around any transition point from inflow to outflow but, as we have continuous coupling conditions in $\int_0^1 \mathbf{u}_0^{\text{rel}} \cdot \mathbf{n} \, dz$, and we have closed systems within all of the asymptotic regions we have introduced, we do not consider this additional boundary layer further.

We can also determine the boundary conditions to impose on an impermeable boundary (such as the curved bioreactor edge S_1 defined in (2.17a)). One can proceed formally, in which case the normal flow near the boundary is of $o(1)$, and the inertial terms within the boundary layers are negligible at leading-order. This analysis is

similar to the case considered in Thompson [72], i.e. flow in a Hele-Shaw cell past a solid obstacle. However, we are interested in the coupling conditions between outer regions, and not the exact details of the flow. Therefore, for our purposes it is enough to take the limit as $K \rightarrow 0$ in (4.90b) and (4.91b), from which we obtain

$$\int_0^1 \mathbf{u}_0^{\text{rel}} \cdot \mathbf{n} \, dz = 0, \quad \int_0^1 \mathbf{u}_{10}^{\text{rel}} \cdot \mathbf{n} \, dz = 0, \quad (4.92)$$

where $\mathbf{u}^{\text{rel}}$ is the fluid velocity relative to the (possibly moving) boundary.

Therefore, all the outer coupling conditions for the flow as required in Chapter 2 are obtained from (4.90)–(4.92). In Appendix E.12, we convert these into the variables used in Chapter 2.

Finally, we give the stress acting on the TC surface for use in Chapter 5. In terms of the outer variables, the stress expressions for inflow and outflow are given in (4.51) and (4.57) respectively. To the order required in Chapter 5, these combined stress expressions are given by

$$\boldsymbol{\sigma} \cdot \mathbf{n} = -\epsilon^{-2} P_0 \mathbf{n} - \epsilon^{-1} \delta^{-1} P_{10} \mathbf{n} + O(\epsilon^{-1} \delta^{-1/2}), \quad (4.93)$$

where we have used the interior instead of bulk fluid pressure for later convenience.

To summarise, in this Chapter we determined the coupling conditions between outer regions for a porous cylindrical obstacle with arbitrary cross-section within a rotating Hele-Shaw cell. The boundary layer structure is very similar to the 2D case considered in Chapter 3, and our main tasks were to account for the moving channel walls and to solve for the flow component in the azimuthal direction. We found that the conditions to couple the leading-order outer variables (4.90) were unchanged from the fully 2D case (given in (3.12b) and (3.44a)), but that the conditions to couple the higher-order variables in the outer flow (4.91) were significantly different to the fully 2D case (given in (3.44b) and (3.120)).

We emphasise that the intricate boundary layer structure we have found does depend on the governing equations that we impose within the porous medium. Were we to have used the Darcy-Brinkman equations within the TC, we would have to impose additional boundary conditions on the tangential component of fluid velocity on the interior boundaries of the TC. This may alter the higher-order coupling conditions (4.91), and could potentially induce further boundary layers within the porous medium. Whilst the Darcy-Brinkman extension is beyond the scope of this thesis, we highlight this issue as an interesting problem that bears further study.

In the next Chapter, where the TC and bioreactor walls are moving, we use the flow results we have determined so far to formulate and solve equations of motion for the TC trajectory.

Chapter 5

Tissue construct trajectory

In Chapter 2, we determined the flow that results when a tissue construct (TC) undergoes a prescribed trajectory within a rotating high-aspect-ratio vessel (HARV) bioreactor. Specifically, we determined the flow in the ‘outer regions’ (the regions whose distance from the TC surface is much larger than the height of the bioreactor) coupled via appropriate boundary conditions. The correct form of these boundary conditions was determined in Chapters 3 and 4 via a boundary layer analysis in which the flow within the ‘inner regions’ (the regions whose distance from the TC surface is the same order as the height of the bioreactor) was resolved.

The work in Chapters 2–4 was performed under the assumption of a prescribed TC trajectory, which is a key observable dynamic feature of the experiments. One goal of our model, that has been achieved in Chapters 2–4, is to use this experimentally measured trajectory as an input into the model. This will enable us to give a detailed description of the flow and resulting hydrodynamical forces acting on the TC that cannot easily be measured experimentally.

However, the difficulty in obtaining experimental data for spatial and temporal details of the flow also means that the model will be hard to validate as it currently stands. It therefore follows that a prediction of the TC trajectory would be very useful towards the goal of providing experimental validation of the model.

As discussed in §1.2.1.1, the spiralling drift associated with the TC motion is an interesting phenomenon. In particular, we would like to investigate whether experimentalists are correct to assert that a change in tissue mass (e.g. due to tissue growth) is the cause of drift. We further recall the three different regimes of TC motion observed experimentally in HARV bioreactors: steady, settling and orbital motion [19] (described in detail in §1.2.1.1). We use our model to predict regions of parameter space in which each of these regimes occur. Moreover, a comprehensive knowledge of

the TC trajectory will allow the development of algorithms to control the trajectory and keep the TC in an appropriate motion regime.

Cummings and Waters [18] considered the ‘short-time’ ($t = O(1)$) periodic orbits of a solid TC, neglecting the effect of TC rotation around its own centre. They also made a conjecture concerning the long-term behaviour of the TC motion in one particular orbital regime. Our aim is to significantly extend this work in several ways. Firstly, to determine the effect of TC porosity on its trajectory. Secondly, to include the motion of TC rotation around its own centre. Lastly, to formally account for the effect of inertia and the resultant drift in all possible motion regimes.

In this Chapter, we determine the TC trajectory and angular velocity by equating the force and torque experienced by the TC to the rate of change of its linear and angular momentum respectively. The forces acting on the TC are due to the hydrodynamical stress and (reduced) gravity. In particular, the fluid dynamical stress will be coupled to the flow.

In §5.1, we set up the model for the TC trajectory, exploiting expressions for the flow calculated in previous Chapters, and nondimensionalize the system to obtain the equations of motion. In §5.2.1, we solve for the angular velocity of the TC around its own axis, and in §5.2.2 we analytically solve for the leading-order trajectory of the TC. The solution is not uniformly valid for all time, and in §5.3 we deduce the ‘intermediate-time’ ($t = O(1/\epsilon_2)$) and ‘long-time’ ($t = O(1/(\epsilon_2 \epsilon Re))$) behaviour. The intermediate-time behaviour is verified numerically, and the long-time behaviour is tackled by first considering a toy model (retaining the key features of the full model), which we are able to solve analytically and verify numerically. This allows us to deduce the physical relevance of several terms in the governing equations, as well as set-up the framework for a multiple-scale analysis. We then solve the full governing equations using the framework developed for the toy model and discuss the results in §5.4.

5.1 Trajectory model

The model set-up in this Chapter is the same as in Chapter 2, and we use the same fluid and geometrical parameters defined in §2.1.1. A schematic diagram of the HARV bioreactor is given in Figures 2.1 and 2.2, where we see that the functions defining the TC centre of mass are given by $R(t)$ - the distance between bioreactor and TC centres, and $\varphi(t)$ - the angle between the positive x -axis and the vector joining the bioreactor centre to the TC centre. The TC also rotates about its own centre with

angular velocity $\boldsymbol{\omega}(t)$. The goal of this Chapter is to determine the functions $R(t)$, $\varphi(t)$, and $\boldsymbol{\omega}(t)$.

We assume that the geometry and the flow within the bioreactor and TC are symmetric about $z = h/2$. This ensures that the two gaps between each circular face of the bioreactor and TC are the same width (as illustrated in Figure 2.2), and that the rotation of the TC about its own centre has its axis of rotation in the z -direction. That is, $\boldsymbol{\omega}(t) = \omega(t)\mathbf{e}_z$. The intuitive idea behind this modelling assumption is that a TC which is closer to one circular face of the bioreactor than the other will experience a force pushing it towards the centre-line $z = h/2$. By taking the problem to be symmetric around $z = h/2$, we are assuming that the system has settled into this state. Whilst it is beyond the scope of this thesis, it would be mathematically and experimentally interesting to investigate the stability of this state in further work. We consider conservation of linear and angular momentum separately, starting with the linear momentum, which we denote by $\mathbf{P}$.

5.1.1 Linear momentum

The rate of change of linear momentum of the TC in the inertial frame is given by

$$\frac{d\mathbf{P}}{dt} = M_c \frac{d^2}{dt^2} (R(t)\mathbf{e}_X), \quad (5.1)$$

where M_c is the mass of the wetted TC, and can be determined by integrating the effective TC density ρ_c over the TC volume to obtain

$$M_c = \rho_c \pi l^2 d. \quad (5.2)$$

Here, ρ_c is defined to be

$$\rho_c = \rho\phi + \rho_s(1 - \phi), \quad (5.3)$$

where $\phi \in [0, 1]$ is the porosity of the TC (where $\phi = 0$ for a solid TC, and $\phi = 1$ for a fully fluid TC), and ρ_s is the density of the solid matrix within the TC.¹

By Newton's second law, we can relate the rate of change of linear momentum of the TC to the force acting on the TC to obtain an equation of motion for the TC

¹We must take care to consider the momentum change of the TC due to the motion of fluid within and across the boundary of the TC. This is carried out in Appendix G.1, where it is concluded that the momentum change due to the relative motion between the TC and the flow within, and also the resulting momentum flux, are actually negligible compared to the rate of change of momentum of the entire TC.

centre of mass, $R(t)$, as follows

$$\mathbf{f}_c + \mathbf{f}_f + \mathbf{f}_g = M_c \frac{d^2}{dt^2} (R(t) \mathbf{e}_X), \quad (5.4)$$

where $\mathbf{f}_c$ is the hydrodynamical force on the curved TC surface T_1 , $\mathbf{f}_f$ is the hydrodynamical force on the flat TC surfaces T_2 and T_3 , and $\mathbf{f}_g$ is the weight of the wet mass of the TC. The TC surfaces T_i are defined in (2.7), and we repeat them here for convenience

$$T_1 = \{(X, Y, z) \in \mathbb{R}^3 : (X - R)^2 + Y^2 = l^2, z \in [\epsilon_1 l, h - \epsilon_1 l]\}, \quad (5.5a)$$

$$T_2 = \{(X, Y, z) \in \mathbb{R}^3 : (X - R)^2 + Y^2 < l^2, z = \epsilon_1 l\}, \quad (5.5b)$$

$$T_3 = \{(X, Y, z) \in \mathbb{R}^3 : (X - R)^2 + Y^2 < l^2, z = h - \epsilon_1 l\}, \quad (5.5c)$$

where (in dimensional terms) l is the radius of the TC, h is the height of the bioreactor, and $\epsilon_1 l$ is the width of the gaps between the flat sides of the TC and bioreactor.

The forces in (5.4) are given by

$$\mathbf{f}_c = \iint_{T_1} \boldsymbol{\sigma} \cdot \mathbf{n} dS, \quad (5.6a)$$

$$\mathbf{f}_f = \iint_{T_2 \cup T_3} \boldsymbol{\sigma} \cdot \mathbf{n} dS, \quad (5.6b)$$

$$\mathbf{f}_g = -M_c g (\sin \varphi(t) \mathbf{e}_X + \cos \varphi(t) \mathbf{e}_Y), \quad (5.6c)$$

where $\boldsymbol{\sigma}$ is the Newtonian stress tensor of the bulk fluid and $\mathbf{n}$ is unit normal pointing into the bulk fluid on the TC surface.

We now consider conservation of angular momentum about the centre of mass of the TC, which we denote by $\mathbf{L}$, to derive a governing equation for the angular velocity of the TC.

5.1.2 Angular momentum

The rate of change of angular momentum of the TC in the inertial frame is given by

$$\frac{d\mathbf{L}}{dt} = \frac{M_c l^2}{2} \frac{d\omega}{dt} \mathbf{e}_z, \quad (5.7)$$

in dimensional terms.²

²As before, we must take care to account for the motion of fluid within and across the boundary of the TC. However, we again deduce (in Appendix G.2) that the change in angular momentum due to the relative fluid motion is negligible compared to the rate of change of angular momentum of the entire TC.

The rate of change of angular momentum is equal to the torque experienced by the TC, and is determined by taking the cross product of $\mathbf{r}$ (the position vector with origin taken at the TC centre of mass, defined in (2.1c)), with the force acting on the TC. Practically, this means taking the cross product of $\mathbf{r}$ with the stress $\boldsymbol{\sigma} \cdot \mathbf{n}$, and integrating over the TC surfaces. As gravity acts through the centre of mass, it does not contribute to the torque. Therefore, the equation of motion for the angular velocity of the TC about its own axis is given by

$$\boldsymbol{\tau}_c + \boldsymbol{\tau}_f = \frac{M_c l^2}{2} \frac{d\omega}{dt} \mathbf{e}_z, \quad (5.8)$$

where

$$\boldsymbol{\tau}_c = \iint_{T_1} \mathbf{r} \times (\boldsymbol{\sigma} \cdot \mathbf{n}) \, dS, \quad (5.9a)$$

$$\boldsymbol{\tau}_f = \iint_{T_2 \cup T_3} \mathbf{r} \times (\boldsymbol{\sigma} \cdot \mathbf{n}) \, dS. \quad (5.9b)$$

We now nondimensionalize the conservation of linear and angular momentum equations and use the asymptotic expressions for the fluid velocity and pressure derived in previous Chapters to evaluate the force and torque acting on the TC.

5.1.3 Dimensionless equations

We use the same dimensionless variables as in (2.12). However, previously we made no mention of $\boldsymbol{\sigma}$, $\mathbf{f}_i$ or $\boldsymbol{\tau}_j$ (where $i \in \{c, f, g\}$ and $j \in \{c, f\}$), and nondimensionalize them as follows

$$\boldsymbol{\sigma} = \mu \Omega \boldsymbol{\sigma}^*, \quad \mathbf{f}_i = \mu \Omega a^2 \mathbf{f}_i^*, \quad \boldsymbol{\tau}_i = \mu \Omega a^3 \boldsymbol{\tau}_i^*, \quad (5.10a, b, c)$$

before immediately dropping the asterisks for convenience.

The dimensionless linear and angular momentum equations (5.4) and (5.8) become

$$\mathbf{f}_c + \mathbf{f}_f + \mathbf{f}_g = Re \bar{\rho} (\pi b^2) (1 - 2\epsilon_2) \frac{d^2}{dt^2} (R(t) \mathbf{e}_X), \quad (5.11a)$$

$$\boldsymbol{\tau}_c + \boldsymbol{\tau}_f = Re \bar{\rho} (\pi b^2) (1 - 2\epsilon_2) \frac{b^2}{2} \frac{d\omega}{dt} \mathbf{e}_z, \quad (5.11b)$$

where $Re = \rho h(a\Omega)/\mu$ is the Reynolds number (as defined in §2.2.2), $\bar{\rho} = \rho_c/\rho$ is the ratio between the effective density of the TC and the density of the nutrient fluid, $\epsilon_2 = \epsilon_1 b/\epsilon$ is the dimensionless width of the gap between the flat sides of the

bioreactor and TC relative to the bioreactor height (as defined in §2.2.3), and $b = l/a$ is the ratio of the TC and bioreactor radii (as defined in (2.12)).

We now determine the individual contributions to the force and torque on the left-hand sides of (5.11). We start with $\mathbf{f}_g$ (defined in (5.6c)) which, in dimensionless form, becomes

$$\mathbf{f}_g = -\frac{B\bar{\rho}}{\epsilon}(\pi b^2)(1 - 2\epsilon_2)(\sin \varphi \mathbf{e}_X + \cos \varphi \mathbf{e}_Y), \quad (5.12)$$

where $B = \epsilon^2 a \rho g / (\mu \Omega)$ is the Bond number (as defined in §2.2.2).

We now consider $\mathbf{f}_f$ and $\boldsymbol{\tau}_f$. In Appendix E.10, we consider the flow between the flat sides of the TC and bioreactor. We calculate the stress $\boldsymbol{\sigma} \cdot \mathbf{n}$ acting on T_2 and T_3 , the flat surfaces of the TC, as follows

$$\boldsymbol{\sigma} \cdot \mathbf{n} = \frac{1}{\epsilon \epsilon_2} \left(-\dot{R} \mathbf{e}_X + R(1 - \dot{\varphi}) \mathbf{e}_Y + (1 - \omega) \mathbf{e}_z \times \mathbf{r} \right) + O(\epsilon^{-1} \epsilon_2), \quad (5.13)$$

which acts as a frictional effect to oppose the motion of the TC relative to the bioreactor, as would be physically expected. We note that (5.13) is naturally separated into the motion of the TC centre of mass (the first two terms on the right-hand side of (5.13)), and a rotation about the TC centre (the third term on the right-hand side of (5.13)). Therefore, the motion of the TC centre will have no effect on the torque $\boldsymbol{\tau}_f$ and, likewise, the rotation about the TC centre will have no effect on the force $\mathbf{f}_f$. Substituting the stress tensor (5.13) into the expressions for the force (5.6b) and torque (5.9b) acting on the flat surfaces of the TC, it is a simple task to calculate that

$$\mathbf{f}_f = \frac{2\pi b^2}{\epsilon \epsilon_2} \left(-\dot{R} \mathbf{e}_X + R(1 - \dot{\varphi}) \mathbf{e}_Y \right) + O(\epsilon^{-1} \epsilon_2), \quad (5.14a)$$

$$\boldsymbol{\tau}_f = \frac{\pi b^4}{\epsilon \epsilon_2} (1 - \omega) \mathbf{e}_z + O(\epsilon^{-1} \epsilon_2). \quad (5.14b)$$

Finally, we consider $\mathbf{f}_c$ and $\boldsymbol{\tau}_c$. On T_1 , the curved surface of the TC, the stress tensor is given in (4.93), which becomes

$$\boldsymbol{\sigma} \cdot \mathbf{n} = \frac{1}{\epsilon^2} (B(X \sin \varphi + Y \cos \varphi) - (P_0 + \epsilon R e P_1)) \mathbf{n} + O(\epsilon^{-1} R e^{1/2}), \quad (5.15)$$

where the first term on the right-hand side is due to the difference between the actual and reduced pressure (using (2.16)), and contributes to the buoyancy force acting on the TC.

To find the force and torque produced by the stress given in (5.15), we must integrate the stress over T_1 . We start with the simpler case of $\boldsymbol{\tau}_c$, for which we use

two facts. Firstly, the right-hand side of (5.15) is independent of z . Secondly, the TC cross-section is circular, and so $\mathbf{r}$ is parallel to $\mathbf{n}$. From this, we infer that any net torque acting on the TC due to the stress on the curved boundary T_1 is entirely due to the error term in (5.15) multiplied by ϵ to take care of the TC height - that is

$$\boldsymbol{\tau}_c = O(Re^{1/2}). \quad (5.16)$$

The force $\mathbf{f}_c$ can be evaluated directly by integrating the stress (5.15) over T_1 to obtain

$$\begin{aligned} \mathbf{f}_c = (\pi b^2) \frac{1 - 2\epsilon_2}{\epsilon} & \left(B(\sin \varphi \mathbf{e}_X + \cos \varphi \mathbf{e}_Y) \right. \\ & \left. - \frac{1}{\pi b^2} \oint_{\partial D_2} (P_0 + \epsilon Re P_1) \mathbf{n} ds \right) + O(Re^{1/2}), \end{aligned} \quad (5.17)$$

where the first term on the right-hand side is the buoyancy force which can be calculated via direct integration or Stokes' theorem, and the integral on the right-hand side is integrated over the one-dimensional boundary curve defined in (2.31b).

We calculate the integral in (5.17) directly by noting that, in bipolar coordinates (α, β) defined in (2.40) and (2.41), P_0 and P_1 evaluated on ∂D_2 (which is equivalent to $\alpha = \alpha_2$) are each given by a Fourier series in β (see equations (2.45b) and (2.58d)). These Fourier series are given by

$$P_0 = \sum_{n=1}^{\infty} (C_n \cos n\beta + D_n \sin n\beta), \quad (5.18a)$$

$$P_1 = \frac{a_{10} - a_{30}}{12K} \alpha_2 + \sum_{n=1}^{\infty} (\bar{E}_n \cos n\beta + \bar{F}_n \sin n\beta), \quad (5.18b)$$

where C_n , D_n , $\bar{E}_n$, and $\bar{F}_n$ are defined in (2.46c), (2.46d), (2.62e), and (2.62f) respectively. To determine the integrals in (5.17), we note that, on ∂D_2 , the element of arc-length is given by $ds = h_\beta d\beta$, and the unit normal pointing into the bulk fluid is given by $\mathbf{n} = -\mathbf{e}_\alpha$, where h_β and $\mathbf{e}_\alpha$ are defined in (B.7) and (B.8a) respectively. Using the bipolar transformation, we find that

$$\oint_{\partial D_2} P_0 \mathbf{n} ds = \sinh \alpha_1 \sum_{n=1}^{\infty} \left(\int_0^{2\pi} X_n(\beta) \mathbf{e}_X + Y_n(\beta) \mathbf{e}_Y d\beta \right), \quad (5.19a)$$

where

$$X_n(\beta) = \frac{1 - \cosh \alpha_2 \cos \beta}{(\cosh \alpha_2 - \cos \beta)^2} (C_n \cos n\beta + D_n \sin n\beta), \quad (5.19b)$$

$$Y_n(\beta) = \frac{\sinh \alpha_2 \sin \beta}{(\cosh \alpha_2 - \cos \beta)^2} (C_n \cos n\beta + D_n \sin n\beta), \quad (5.19c)$$

and for the integral of P_1 , we just replace C_n with $\overline{E}_n$, and D_n with $\overline{F}_n$. Then, using the integral identities from (C.17), and standard trigonometric identities, we deduce that

$$\oint_{\partial D_2} P_0 \mathbf{n} \, ds = 2\pi \sinh \alpha_1 \sum_{n=1}^{\infty} n \exp(-n\alpha_2) (-C_n \mathbf{e}_X + D_n \mathbf{e}_Y), \quad (5.20a)$$

$$\oint_{\partial D_2} P_1 \mathbf{n} \, ds = 2\pi \sinh \alpha_1 \sum_{n=1}^{\infty} n \exp(-n\alpha_2) (-\overline{E}_n \mathbf{e}_X + \overline{F}_n \mathbf{e}_Y). \quad (5.20b)$$

Replacing C_n and D_n using the expressions (2.46c) and (2.46d), (5.20a) can be written in the slightly more compact form of

$$\frac{1}{\pi b^2} \oint_{\partial D_2} P_0 \mathbf{n} \, ds = 2 \left(\dot{R} \mathbf{e}_X - R(1 - \dot{\varphi}) \mathbf{e}_Y \right) \gamma_1(R), \quad (5.21a)$$

$$\gamma_1(R) = 24 \sinh^2 \alpha_2(R) \sum_{n=1}^{\infty} \frac{n \exp(-2n\alpha_2(R))}{\tanh(n(\alpha_2(R) - \alpha_1(R))) + 12K}, \quad (5.21b)$$

where we have made explicit the dependence of α_1 and α_2 on R . We note that $\gamma_1(R)$ is a monotonically increasing function of R , as shown in Figure 5.1 for various values of the dimensionless permeability K . For $K = 0$, the function $\gamma_1(R) \rightarrow \infty$ as $R \rightarrow 1 - b$. This effect was noted in Cummings and Waters [18] (who considered a solid TC), and corresponds to the fluid pressure getting very large as the TC gets close to the bioreactor wall.³

As we evaluate the coefficients $\overline{E}_n$ and $\overline{F}_n$ numerically, we cannot be as precise with (5.20b). We therefore write

$$\frac{1}{\pi b^2} \oint_{\partial D_2} P_1 \mathbf{n} \, ds = -2 (\gamma_2(R) \mathbf{e}_X - \gamma_3(R) \mathbf{e}_Y), \quad (5.22a)$$

$$\gamma_2(R, \varphi, \dot{R}, \dot{\varphi}, \ddot{R}, \ddot{\varphi}) = \frac{\sinh \alpha_2(R)}{b} \sum_{n=1}^{\infty} n \exp(-n\alpha_2(R)) \overline{E}_n(R, \varphi, \dot{R}, \dot{\varphi}, \ddot{R}, \ddot{\varphi}), \quad (5.22b)$$

$$\gamma_3(R, \varphi, \dot{R}, \dot{\varphi}, \ddot{R}, \ddot{\varphi}) = \frac{\sinh \alpha_2(R)}{b} \sum_{n=1}^{\infty} n \exp(-n\alpha_2(R)) \overline{F}_n(R, \varphi, \dot{R}, \dot{\varphi}, \ddot{R}, \ddot{\varphi}). \quad (5.22c)$$

We have now fully determined the dimensionless force and torque acting on the TC up to $O(\epsilon_2 \epsilon R e)$. Substituting (5.14), (5.16), (5.17), (5.21), and (5.22) into the governing equations (5.11), we obtain our equations of motion. The dimensionless

³The canonical example of this is a standard squeeze-film analysis.

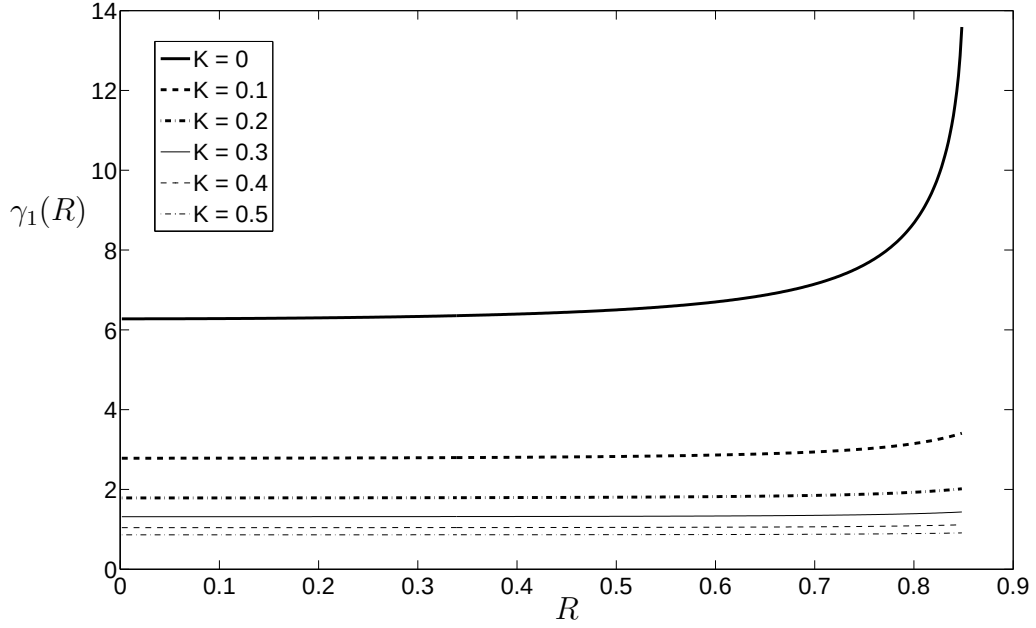


Figure 5.1: The function $\gamma_1(R)$ for various values of K , taking $b = 0.15$ in each. The functions stop at $R = 1 - b$, which corresponds to where the TC hits the bioreactor edge.

linear momentum equation (5.11a) becomes

$$\begin{aligned}
& -\overline{B} (\sin \varphi \mathbf{e}_X + \cos \varphi \mathbf{e}_Y) + (1 + \epsilon_2 \gamma_1(R)) \left(-\dot{R} \mathbf{e}_X + R(1 - \dot{\varphi}) \mathbf{e}_Y \right) \\
& + (\epsilon_2 \epsilon Re) \left(\gamma_2(R, \varphi, \dot{R}, \dot{\varphi}, \ddot{R}, \ddot{\varphi}) \mathbf{e}_X - \gamma_3(R, \varphi, \dot{R}, \dot{\varphi}, \ddot{R}, \ddot{\varphi}) \mathbf{e}_Y \right) \\
& = (\epsilon_2 \epsilon Re) \frac{\bar{\rho}}{2} \left(\left(\ddot{R} - R\dot{\varphi}^2 \right) \mathbf{e}_X + \left(2\dot{\varphi}\dot{R} + \ddot{\varphi}R \right) \mathbf{e}_Y \right) + O(\epsilon \epsilon_2 Re^{1/2}), \quad (5.23)
\end{aligned}$$

where the modified Bond number $\overline{B}$ is defined to be

$$\overline{B} = \frac{\epsilon_2 B (\bar{\rho} - 1) (1 - 2\epsilon_2)}{2}. \quad (5.24)$$

We note that the sign of $\overline{B}$ depends on the sign of $\bar{\rho} - 1$, i.e. whether the TC is lighter or heavier than the surrounding fluid, and reiterate that we make the assumption $\epsilon_2 \ll \epsilon Re \ll 1$ in §2.3. In (5.23), the left-hand side consists of the forces acting on the TC, and the right-hand side is the rate of change of linear momentum. On the left-hand side of (5.23), the first term is due to the reduced gravity acting on the entire TC, the second term is split into an $O(1)$ term due to the fluid friction acting on the flat surfaces of the TC and an $O(\epsilon_2)$ term due to the leading-order fluid pressure acting on the curved surface of the TC, and the third term is due to the first correction to the fluid pressure acting on the curved surface of the TC.

The dimensionless angular momentum equation (5.11b) becomes

$$1 - \omega = (\epsilon_2 \epsilon Re) \frac{\bar{\rho}}{2} \frac{d\omega}{dt} + O(\epsilon \epsilon_2 Re^{1/2}), \quad (5.25)$$

where the left-hand side of (5.25) is due to the fluid friction acting on the flat surfaces of the TC, and the right-hand side is the rate of change of angular momentum. We further note that $\omega(t)$ does not affect $R(t)$ and $\varphi(t)$ up to the orders considered.

We solve the governing equations (5.23) and (5.25) in the next sections and discuss their physical implications. We see that there is a distinguished limit, corresponding to $\bar{B} = O(1)$, at leading order in (5.23) in which gravity and fluid friction (due to the thin gaps neighbouring the flat sides of the TC) balance; we assume this order of magnitude henceforth. We first consider the equations when $t = O(1)$, and refer to this as the ‘short-time’. Longer timescales will be introduced later. We start with the simplest equation, and solve (5.25) first.

5.2 Short-time behaviour: $t = O(1)$

5.2.1 Angular velocity

The governing equation for the angular velocity of the TC is given in (5.25). Up to $O(\epsilon_2 \epsilon Re)$, this is a linear ordinary differential equation with constant coefficients and has solution

$$\omega(t) = 1 + (\omega(0) - 1) \exp\left(-\frac{2t}{(\epsilon_2 \epsilon Re) \bar{\rho}}\right). \quad (5.26)$$

Thus, we see that the angular velocity of the TC will always tend to 1 with an exponentially small error. Physically, this means that the angular velocity of the TC will always tend to the angular velocity of the bioreactor, no matter what value the initial angular velocity of the TC takes.

We further note that as $\bar{\rho}$ gets larger/smaller, the angular velocity of the TC tends to its ‘steady-state’ value of $\omega = 1$ more slowly/quickly. This is expected physically, as the heavier an object (i.e. the larger ρ_c , and hence $\bar{\rho}$) the more resistant it is to a change in angular velocity.

The TC will rotate at the same angular velocity as the bioreactor because the leading order torque on the TC is due to the relative angular velocity between the TC and the bioreactor, which acts in a stabilising manner. We note, however, that our results are only valid away from $\omega - 1 = O(\epsilon \epsilon_2 Re^{1/2})$; near this limit, the error terms in (5.16)) may come into play. Therefore, despite the angular velocity tending

to 1 at leading order, it may be that the actual steady state angular velocity differs from 1 by $O(\epsilon\epsilon_2 Re^{1/2})$. We do not pursue this matter further, as the leading-order angular velocity is acceptable for our purposes. We now determine the trajectory of the TC centre.

5.2.2 Periodic solutions for the trajectory

The governing equation for the trajectory of the TC centre of mass is given by (5.23). Unlike (5.25), we cannot spot an analytic solution, so we instead perform an asymptotic analysis to make analytic progress.

There is, however, a more fundamental difference between the two solutions. If we had wished, we could have solved (5.25) using the method of matched asymptotic expansions. There would be an ‘outer’ region in time (where $t = O(1)$: the so-called short-time solution), and an ‘inner’ region in time (where $t = O(\epsilon_2\epsilon Re)$). The inner region allows the initial TC angular velocity to rapidly transition to its steady state value of $\omega = 1$.

We could proceed for the TC trajectory by seeking a similar type of solution. For the inner and outer regions (in time) mentioned above, this method is fine. However, we are interested in longer timescales for the TC trajectory and we show in this section that the $t = O(1)$ solution for the TC trajectory is (non-trivially) periodic. Therefore, in order to determine a uniformly accurate representation of the long-time solution (which we use to refer to the solution for $t = O((\epsilon_2\epsilon Re)^{-1})$), we use the method of multiple scales, and this is the subject of §5.3.

For now, we consider the leading order equations by taking the following asymptotic expansions

$$R(t) = R_0(t) + O(\epsilon_2), \quad (5.27a)$$

$$\varphi(t) = \varphi_0(t) + O(\epsilon_2). \quad (5.27b)$$

Substituting these into the governing equation (5.23), we obtain

$$0 = \dot{R}_0 + \overline{B} \sin \varphi_0, \quad (5.28a)$$

$$0 = R_0(1 - \dot{\varphi}_0) - \overline{B} \cos \varphi_0, \quad (5.28b)$$

which represents a balance between gravity and friction. We see that there are steady solutions for $(R_0, \varphi_0) = (\overline{B}, 0)$ when $\overline{B} > 0$ and for $(R_0, \varphi_0) = (-\overline{B}, \pi)$ when $\overline{B} < 0$. These occur within the bioreactor as long as $\overline{B} \leq |1 - b|$, with equality when the TC

touches the bioreactor edge. We reiterate that the sign of $\overline{B}$ is positive when $\bar{\rho} > 1$ and negative when $\bar{\rho} < 1$.

We solve (5.28) by introducing a polar coordinate system (r, θ) centred around this steady point (as shown in Figure 5.2). Thus we define

$$R \cos \varphi = \overline{B} + r \cos \theta, \quad (5.29a)$$

$$R \sin \varphi = r \sin \theta, \quad (5.29b)$$

and we expand r and θ in similar asymptotic expansions to (5.27). In Appendix H, we show that in the new variables, the governing equations (5.28) become

$$r_0 \dot{r}_0 + \overline{B} \left(\dot{r}_0 \cos \theta_0 + r_0 \left(1 - \dot{\theta}_0 \right) \sin \theta_0 \right) = 0, \quad (5.30a)$$

$$r_0^2 \left(1 - \dot{\theta}_0 \right) + \overline{B} \left(r_0 \left(1 - \dot{\theta}_0 \right) \cos \theta_0 - \dot{r}_0 \sin \theta_0 \right) = 0, \quad (5.30b)$$

with unique solution

$$r_0 = r(0), \quad \theta_0 = t + \theta(0). \quad (5.31a, b)$$

Therefore, at leading order we have circular motion around the steady point. Furthermore, we can deduce that we will be in the steady regime if $r = 0$, the settling regime if $r < |\overline{B}|$, and in the orbital regime if $r > |\overline{B}|$. A settling trajectory is illustrated in Figure 5.2.

To summarise, we have determined the leading-order solution analytically for the TC trajectory. Furthermore, we have deduced that the motion regime of the TC is only dependent on its starting position. We note that the full system (5.23) is second-order in R and φ , while the leading-order approximation (5.28) is only first-order in R_0 and φ_0 (or equivalently - in r_0 and θ_0). This implies that there is a boundary layer in early time (for $t = O(\epsilon_2 \epsilon Re)$) in which the initial velocities will adjust to the $O(1)$ solution; this is a similar situation to the equation of motion for ω (5.25).

Neglecting the infinite sums γ_1 , γ_2 , and γ_3 , it is an exercise in boundary layer theory to obtain the early time solution for (5.23) as

$$r \sim r(0) + (\epsilon_2 \epsilon Re) \frac{\bar{\rho} \dot{r}(0)}{2} \left(1 - \exp \left(-\frac{2t}{(\epsilon_2 \epsilon Re) \bar{\rho}} \right) \right), \quad (5.32a)$$

$$\theta \sim \theta(0) + t + (\epsilon_2 \epsilon Re) \frac{\bar{\rho} (\dot{\theta}(0) - 1)}{2} \left(1 - \exp \left(-\frac{2t}{(\epsilon_2 \epsilon Re) \bar{\rho}} \right) \right). \quad (5.32b)$$

By comparison of the early-time solution (5.32) to the full equations (5.23) with the leading-order approximation to the solution (5.31), we see that we generate an $O(\epsilon_2 \epsilon Re)$ error in position by imposing the initial position as a boundary condition for the first-order differential equations (5.30), and ignoring the initial velocity.

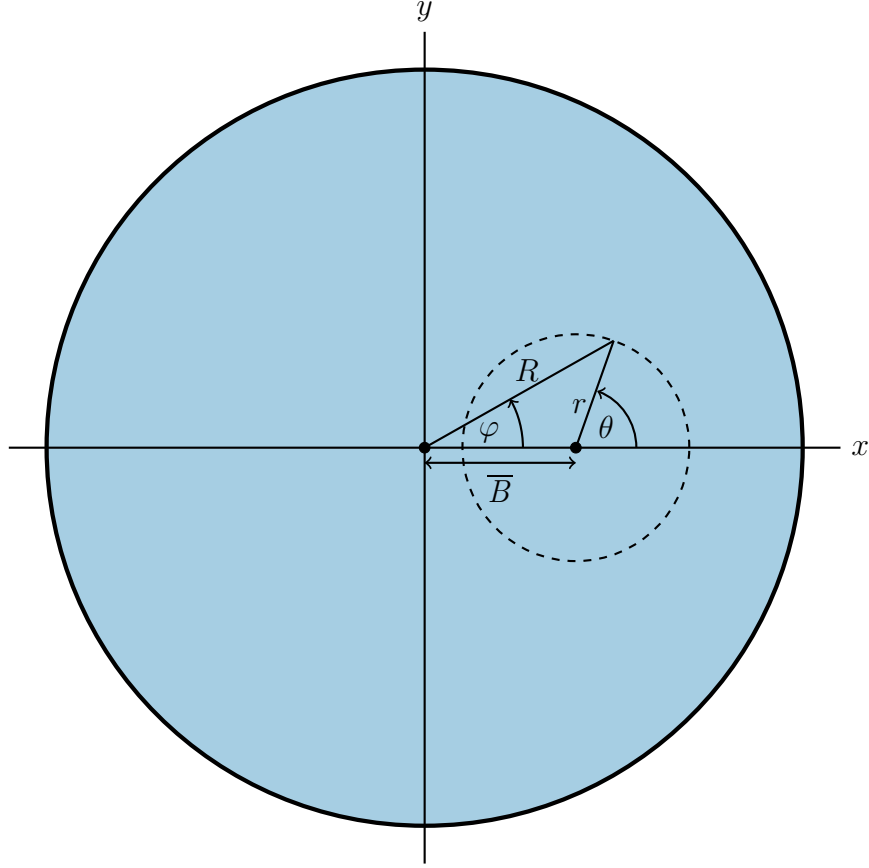


Figure 5.2: Diagram of the coordinate change from (R, φ) to (r, θ) . The dashed line is an example of the leading-order trajectory for the TC centre, i.e. $r = \text{constant}$, in the settling regime. The new coordinate system (r, θ) is shifted from the old coordinate system (R, φ) along the x -axis by $\overline{B}$, a modified Bond number defined in (5.24). If $r < |\overline{B}|$, the TC is in the settling regime, and if $r > |\overline{B}|$ the TC is in the orbital regime.

5.3 Long-time drift

5.3.1 Toy model

As the infinite sums γ_1 , γ_2 and γ_3 (defined in (5.21b), (5.22b), and (5.22c) respectively), which are all due to the fluid pressure acting on the curved surface of the TC, must be determined numerically, it is difficult to obtain a fully analytic solution to (5.23). Therefore, to gain some physical insight into the equations before we solve them in full, we interrogate a toy model that contains analytically tractable terms representing the physical effects in the full system of governing equations. We do not expect the toy model to completely describe the TC motion, but it will allow us to set up the machinery used to solve the full coupled equations using the method of

multiple scales (MMS).

We see from the full governing equations (5.23) that by dropping the infinite sums, the forces left are due to gravity and friction. If these were the only forces included in the model, we would physically expect the TC to spiral out until it hits the bioreactor edge due to the centrifugal force from the inertial terms on the right-hand side of (5.23) - no matter where the TC starts in the bioreactor or what value $\bar{\rho}$ takes. This is because we have made no effort to consider the force exerted on the TC by the surrounding fluid, which we expect to cause the TC to spiral inwards if it is lighter than the surrounding fluid (i.e. $\bar{\rho} < 1$). This behaviour is due to the centrifugal force of the surrounding fluid, and if it is larger than the centrifugal force induced by the rotation of the TC around the bioreactor centre, it will push the TC inwards.

We take the centrifugal force acting on the TC due to the fluid to have the same form as the centrifugal force that appears in the $O(\epsilon Re)$ Navier-Stokes equations (2.26). That is, we integrate $-\epsilon Re \dot{\varphi}^2 (X^2 + Y^2) \mathbf{n}/2$ around the TC boundary. Noting that

$$\frac{1}{\pi b^2} \oint_{\partial D_2} (X^2 + Y^2) \mathbf{n} \, ds = 2R \mathbf{e}_X, \quad (5.33)$$

we take the centrifugal force in our toy model to be $-\epsilon Re \dot{\varphi}^2 R \mathbf{e}_X$, which pushes the TC towards the bioreactor centre as required. Following this *ad hoc* introduction of the centrifugal force, we emphasise again that we do not expect this model to fully describe the actual TC motion, just to aid with our physical understanding of the model.

In summary, we use (5.23) for the basis of our toy model, but remove the infinite sums by replacing $\gamma_2 \mathbf{e}_X - \gamma_3 \mathbf{e}_Y$ with $-\dot{\varphi}^2 R/2 \mathbf{e}_X$, and we completely neglect $\gamma_1(R)$. We then obtain the following coupled ODEs for $R(t)$ and $\varphi(t)$

$$\begin{aligned} & -\bar{B} (\sin \varphi \mathbf{e}_X + \cos \varphi \mathbf{e}_Y) - \dot{R} \mathbf{e}_X + R(1 - \dot{\varphi}) \mathbf{e}_Y = \\ & \frac{\epsilon_2 \epsilon Re}{2} \left(\bar{\rho} \left(\left(\ddot{R} - \dot{\varphi}^2 R \right) \mathbf{e}_X + \left(2\dot{\varphi} \dot{R} + \ddot{\varphi} R \right) \mathbf{e}_Y \right) + \dot{\varphi}^2 R \mathbf{e}_X \right). \end{aligned} \quad (5.34)$$

Using the change of coordinates described in (5.29) and, in particular, using (H.6) with (H.2) and (H.8) to convert $R(t)$ and $\varphi(t)$ into $r(t)$ and $\theta(t)$, the governing

equations (5.34) become

$$\begin{aligned}
& -r\dot{r} - \overline{B} \left(\dot{r} \cos \theta + r \left(1 - \dot{\theta} \right) \sin \theta \right) = \\
& (\epsilon_2 \epsilon Re) \frac{\bar{\rho}}{2} \left(r \left(\ddot{r} - r\dot{\theta}^2 \right) + \overline{B} \left(\left(\ddot{r} - r\dot{\theta}^2 \right) \cos \theta - \left(2\dot{r}\dot{\theta} + r\ddot{\theta} \right) \sin \theta \right) \right) \\
& + \frac{(\epsilon_2 \epsilon Re)}{2} \left(\frac{\left(r\dot{\theta} (r + \overline{B} \cos \theta) + \overline{B}\dot{r} \sin \theta \right)^2}{r^2 + 2r\overline{B} \cos \theta + \overline{B}^2} \right), \tag{5.35a}
\end{aligned}$$

$$\begin{aligned}
& r^2 \left(1 - \dot{\theta} \right) + \overline{B} \left(r \left(1 - \dot{\theta} \right) \cos \theta - \dot{r} \sin \theta \right) = \\
& (\epsilon_2 \epsilon Re) \frac{\bar{\rho}}{2} \left(r \left(2\dot{r}\dot{\theta} + r\ddot{\theta} \right) + \overline{B} \left(\left(\ddot{r} - r\dot{\theta}^2 \right) \sin \theta + \left(2\dot{r}\dot{\theta} + r\ddot{\theta} \right) \cos \theta \right) \right), \tag{5.35b}
\end{aligned}$$

where overdots represent differentiation with respect to t , and the only small parameter is $\epsilon_2 \epsilon Re$.

We are now ready to formally solve the full toy problem. To determine the long-time solution valid when $t = O((\epsilon_2 \epsilon Re)^{-1})$, we use the MMS on (5.35) and introduce a slow timescale $T = (\epsilon_2 \epsilon Re) t = O(1)$. The time derivative then becomes

$$\frac{d}{dt} = \frac{\partial}{\partial t} + (\epsilon_2 \epsilon Re) \frac{\partial}{\partial T}, \tag{5.36}$$

and (avoiding the subscript 1 so as to use notation that is consistent with §5.3.2) we seek an asymptotic expansion of the form

$$r(t, T) \sim r_0(t, T) + (\epsilon_2 \epsilon Re) r_2(t, T), \tag{5.37a}$$

$$\theta(t, T) \sim \theta_0(t, T) + (\epsilon_2 \epsilon Re) \theta_2(t, T). \tag{5.37b}$$

At $O(1)$, (5.35) becomes

$$r_0 r_{0t} + \overline{B} (r_{0t} \cos \theta_0 + r_0 (1 - \theta_{0t}) \sin \theta_0) = 0, \tag{5.38a}$$

$$r_0^2 (1 - \theta_{0t}) + \overline{B} (r_0 (1 - \theta_{0t}) \cos \theta_0 - r_{0t} \sin \theta_0) = 0, \tag{5.38b}$$

which is the same equation as (5.30), and is uniquely solved by

$$r_{0t} = 0, \quad \theta_{0t} = 1. \tag{5.39a, b}$$

Therefore, we find that

$$r_0 = r_0(T), \quad \theta_0 = t + \phi(T), \tag{5.40a, b}$$

and the solutions are periodic on the short timescale t . This hugely simplifies the $O(\epsilon_2 \epsilon Re)$ terms in (5.35), which become

$$r_0 r_{2t} + \overline{B} (r_{2t} \cos \theta_0 - r_0 \theta_{2t} \sin \theta_0) = \eta(r_0, \theta_0), \tag{5.41a}$$

$$r_0^2 \theta_{2t} + \overline{B} (r_0 \theta_{2t} \cos \theta_0 + r_{2t} \sin \theta_0) = \nu(r_0, \theta_0), \tag{5.41b}$$

where

$$\begin{aligned} \eta(r_0, \theta_0) = & \frac{\bar{\rho}}{2} r_0 (r_0 + \bar{B} \cos \theta_0) - r_{0T} (r_0 + \bar{B} \cos \theta_0) + r_0 \theta_{0T} \bar{B} \sin \theta_0 \\ & - \frac{(r_0 (r_0 + \bar{B} \cos \theta_0))^2}{2 (r_0^2 + 2r_0 \bar{B} \cos \theta_0 + \bar{B}^2)}, \end{aligned} \quad (5.42a)$$

$$\nu(r_0, \theta_0) = \frac{\bar{\rho}}{2} r_0 \bar{B} \sin \theta_0 - r_0 \theta_{0T} (r_0 + \bar{B} \cos \theta_0) - r_{0T} \bar{B} \sin \theta_0. \quad (5.42b)$$

To determine $r_0(T)$ and $\phi(T)$, we need to impose the secularity condition induced by the assumption that the solution to (5.41) is periodic in t . This is equivalent to imposing orthogonality of the solutions of the adjoint problem under periodic boundary conditions via the Fredholm Alternative Theorem (FAT). Since this procedure is less well known for systems, we first describe it in abstract terms.

Consider the linear system

$$L(x) = \begin{pmatrix} L_1 & L_2 \\ L_3 & L_4 \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \end{pmatrix} = \begin{pmatrix} f_1 \\ f_2 \end{pmatrix} = f, \quad (5.43)$$

where f_1, f_2, x_1, x_2 are functions of $t \in (a, b)$ and the L_i are linear operators. We impose periodic boundary conditions on $t = a, b$. We see that (5.41) satisfies this form for $t \in (0, 2\pi)$ with linear operators defined later in (5.51). We further define an inner product for the system as

$$\langle u, v \rangle = \int_a^b u(t)v(t) dt. \quad (5.44)$$

Then, with $y = (y_1, y_2)^\top$

$$\begin{aligned} \langle L(x), y \rangle &= \int_a^b (L_1(x_1) + L_2(x_2)) y_1 + (L_3(x_1) + L_4(x_2)) y_2 dt, \\ &= \int_a^b x_1 L_1^*(y_1) + x_2 L_2^*(y_1) + x_1 L_3^*(y_2) + x_2 L_4^*(y_2) dt, \\ &= \int_a^b x_1 (L_1^*(y_1) + L_3^*(y_2)) + x_2 (L_2^*(y_1) + L_4^*(y_2)) dt, \\ &= \langle x, L^*(y) \rangle, \end{aligned} \quad (5.45)$$

where the adjoint of the system is given by

$$L^* = \begin{pmatrix} L_1^* & L_3^* \\ L_2^* & L_4^* \end{pmatrix}, \quad (5.46)$$

and the individual adjoint operators L_i^* are defined in the usual manner via

$$\int_a^b L_i(u)w dt = \int_a^b u L_i^*(w) dt. \quad (5.47)$$

Lastly, we note that the periodic boundary conditions on x have been transferred to y in the second line of (5.45).

Then, invoking FAT, if there is a non-trivial solution of the adjoint problem

$$L^*(y) = 0, \quad (5.48)$$

with periodic boundary conditions, the original problem has a solvability condition given by

$$\langle f, y \rangle = \langle L(x), y \rangle = \langle x, L^*(y) \rangle = \langle x, 0 \rangle = 0, \quad (5.49)$$

which, in terms of our inner product, is given by

$$\int_a^b (y_1 f_1 + y_2 f_2) dt = 0. \quad (5.50)$$

If there are two linearly independent non-trivial solutions, there are two solvability conditions. We further note that this method is easily generalizable to a system of N linear differential equations by taking the adjoint operator $L^* = (L^\top)^*$, that is - the adjoint of each element of the transpose of the initial operator.

For the toy problem (5.41), the operators L_1 , L_2 , L_3 and L_4 are as follows

$$L_1(x_1) = \xi(r_0, \theta_0) \frac{\partial x_1}{\partial t}, \quad (5.51a)$$

$$L_2(x_2) = -r_0 \sigma(r_0, \theta_0) \frac{\partial x_2}{\partial t}, \quad (5.51b)$$

$$L_3(x_1) = \sigma(r_0, \theta_0) \frac{\partial x_1}{\partial t}, \quad (5.51c)$$

$$L_4(x_2) = r_0 \xi(r_0, \theta_0) \frac{\partial x_2}{\partial t}, \quad (5.51d)$$

where

$$\xi(r_0, \theta_0) = r_0 + \bar{B} \cos \theta_0, \quad \sigma(r_0, \theta_0) = \bar{B} \sin \theta_0. \quad (5.52a, b)$$

The adjoint operators are given by

$$L_1^*(y_1) = -\frac{\partial}{\partial t} (\xi y_1), \quad (5.53a)$$

$$L_2^*(y_1) = \frac{\partial}{\partial t} (r_0 \sigma y_1), \quad (5.53b)$$

$$L_3^*(y_2) = -\frac{\partial}{\partial t} (\sigma y_2), \quad (5.53c)$$

$$L_4^*(y_2) = \frac{\partial}{\partial t} (r_0 \xi y_2). \quad (5.53d)$$

Seeking a non-trivial solution to the adjoint problem (5.48), we obtain the equations

$$0 = \frac{\partial}{\partial t} (\xi y_1 + \sigma y_2), \quad (5.54a)$$

$$0 = \frac{\partial}{\partial t} (r_0 (-\sigma y_1 + \xi y_2)), \quad (5.54b)$$

which can be integrated and rearranged for y_1 and y_2 to obtain

$$\begin{pmatrix} y_1 \\ y_2 \end{pmatrix} = \frac{1}{r_0 (\xi^2 + \sigma^2)} \begin{pmatrix} r_0 \xi & -\sigma \\ r_0 \sigma & \xi \end{pmatrix} \begin{pmatrix} A \\ B \end{pmatrix}, \quad (5.55)$$

where $\xi^2 + \sigma^2 = \bar{B}^2 + 2r_0\bar{B}\cos\theta_0 + r_0^2 = R_0^2$, and A and B are arbitrary constants. Substituting our newly found adjoint functions (5.55) along with the forcing functions (5.42), into the solvability condition (5.50), the secularity conditions are found by setting the coefficients of A and B to vanish. Equivalently, we first set $(A, B) = (1, 0)$ and then $(A, B) = (0, 1)$, giving, respectively

$$0 = \int_0^{2\pi} \frac{\xi\eta + \sigma\nu}{\xi^2 + \sigma^2} dt, \quad (5.56a)$$

$$0 = \int_0^{2\pi} \frac{\xi\nu - \sigma\eta}{r_0(\xi^2 + \sigma^2)} dt. \quad (5.56b)$$

Using this result for our toy problem, i.e. substituting (5.42) and (5.52) into (5.56), the secularity conditions become

$$0 = \int_0^{2\pi} \left(\frac{\bar{\rho}}{2} r_0 - r_{0T} - \frac{r_0^2 (r_0 + \bar{B} \cos \theta_0)^3}{2 (r_0^2 + 2r_0\bar{B} \cos \theta_0 + \bar{B}^2)^2} \right) dt, \quad (5.57a)$$

$$0 = \int_0^{2\pi} \left(-r_0 \theta_{0T} + \frac{\bar{B} \sin \theta_0 (r_0 (r_0 + \bar{B} \cos \theta_0))^2}{2 (r_0^2 + 2r_0\bar{B} \cos \theta_0 + \bar{B}^2)^2} \right) dt. \quad (5.57b)$$

We consider (5.57b) first as it is the easier condition. The second term integrates to zero since the integrand is odd around $t = \pi - \theta(0)$. Therefore, the secularity condition for the angular velocity is given by

$$r_0 \theta_{0T} = 0, \quad (5.58)$$

so that θ_0 is constant in T .

We now consider (5.57a). The third term in the integral is evaluated in Appendix D using complex contour integration, and the result is given by

$$\int_0^{2\pi} \frac{(r_0 + \overline{B} \cos \theta_0)^3}{(r_0^2 + 2r_0\overline{B} \cos \theta_0 + \overline{B}^2)^2} dt = \begin{cases} 0 & \text{if } r_0 < |\overline{B}|, \\ \frac{\pi}{r_0^3} (2r_0^2 - \overline{B}^2) & \text{if } r_0 > |\overline{B}|. \end{cases} \quad (5.59)$$

We note that the result depends on whether $r_0 < |\overline{B}|$ or $r_0 > |\overline{B}|$, i.e. whether the TC is in settling or orbital motion. This is because the third term stems from the centrifugal force of the fluid acting on the TC (introduced as $-\dot{\varphi}^2 R/2\mathbf{e}_X$), and the discontinuity in the integral arises because the effect of centrifugal force averaged over one periodic orbit is discontinuous as we move from $r_0 < |\overline{B}|$ (settling) to $r_0 > |\overline{B}|$ (orbital). To get a sense of why this is the case, note that we have $\varphi \in (-\pi/2, \pi/2)$ for settling motion, and $\varphi \in (0, 2\pi)$ for orbital motion (modulo 2π). Therefore, the average of $\dot{\varphi}$ over one orbit will be 0 for settling motion, and 1 for orbital motion. Although the introduced centrifugal force has a factor of $\dot{\varphi}^2$ and not $\dot{\varphi}$, this discontinuity across motion regimes will transfer from $\dot{\varphi}$ to $\dot{\varphi}^2$.

Using the integral result (5.59) in the secularity condition (5.57a), we obtain the governing equation

$$\frac{dr_0}{dT} = \begin{cases} \frac{\bar{\rho}}{2} r_0 & \text{if } r_0 < |\overline{B}|, \\ \frac{\bar{\rho} - 1}{2} r_0 + \frac{\overline{B}^2}{4r_0} & \text{if } r_0 > |\overline{B}|. \end{cases} \quad (5.60)$$

We can obtain the limiting behaviour of r_0 as $T \rightarrow \infty$, by exploring the sign of the right-hand side of (5.60) as follows. When in settling motion ($r_0 < |\overline{B}|$), the TC will always spiral out until it reaches the boundary between settling and orbital motion at $r_0 = |\overline{B}|$. From this point, the TC will continue to move in a manner consistent with its behaviour in orbital motion.

When in orbital motion ($r_0 > |\overline{B}|$) and if $\bar{\rho} > 1$, the right-hand side of (5.60) is positive, and therefore the TC will always spiral out until it hits the bioreactor edge. For $\bar{\rho} < 1$, we must take care to determine if or when r_0 reaches $|\overline{B}|$ in the right-hand side of (5.60). We note that $r_{0T} < 0$ (and hence the TC will spiral in towards settling motion) if $\bar{\rho} < 1/2$. Therefore, the TC will tend towards the orbit which lies on the boundary between settling and orbital motion if $\bar{\rho} < 1/2$. For $\bar{\rho} \in (1/2, 1)$, there is a critical value

$$r_0^c = (2(1 - \bar{\rho}))^{-1/2} |\overline{B}|, \quad (5.61)$$

for which $r_{0T} = 0$, and this value is a stable limit cycle for the trajectory.

To make sense of how the critical value r_0^c varies as $\bar{\rho}$ varies within $(1/2, 1)$, recall from (5.24) that $\bar{B}$ is a linear function of $\bar{\rho} - 1$. Therefore, even though the critical point given in (5.61) starts at $r_0^c = |\bar{B}|$ for $\bar{\rho} = 1/2$, and the coefficient multiplying $|\bar{B}|$ tends to infinity as $\bar{\rho} \uparrow 1$, the physical value of r_0^c behaves like $(1 - \bar{\rho})^{1/2}$. Thus, even though r_0^c is shrinking as $\bar{\rho}$ grows from $\bar{\rho} = 1/2$ to $\bar{\rho} = 1$, it is still larger than $\bar{B}$ (which shrinks linearly as $\bar{\rho}$ grows from $\bar{\rho} = 1/2$ to $\bar{\rho} = 1$), and so we have a stable limit cycle within the orbital regime.

Furthermore, in the limit $\bar{\rho} \rightarrow 1$, we obtain $\bar{B} \rightarrow 0$, and the TC motion is centred around the bioreactor centre. The TC motion in this case is then spiralling out to the bioreactor edge for $\bar{\rho} > 1$, and spiralling into the bioreactor centre for $\bar{\rho} < 1$. This is equivalent to the informal conjecture made in Cummings and Waters [18] for $\bar{B} = 0$. Our toy model supports this conjecture, and extends it to $\bar{B} \neq 0$.

The physical effect of the centrifugal force of the fluid acting on the TC is to oppose the motion of the TC towards the bioreactor edge (though this only fully manifests within the orbital regime). For $\bar{\rho} < 1/2$, our toy model suggests that this opposition allows the TC to reach a stable limit cycle which passes through the bioreactor centre. For $\bar{\rho} > 1$, the centrifugal force of the fluid is too weak to stop the TC reaching the bioreactor edge, but does slow it down compared to if it were not included. For $\bar{\rho} \in (1/2, 1)$, the centrifugal force of the fluid will balance the centrifugal force of the TC at a finite value of r_0 , causing a stable limit cycle within the orbital regime.

Though we have already determined the long-time behaviour of the TC trajectory, we can also solve (5.60) analytically as follows

$$r_0 = \begin{cases} r_0(0) \exp\left(\frac{\bar{\rho}T}{2}\right) & \text{if } r_0 < |\bar{B}|, \\ \left(\left(r_0^2(0) + \frac{\bar{B}^2}{2(\bar{\rho}-1)}\right) \exp((\bar{\rho}-1)T) - \frac{\bar{B}^2}{2(\bar{\rho}-1)}\right)^{1/2} & \text{if } r_0 > |\bar{B}|. \end{cases} \quad (5.62)$$

From this solution we can determine the time it takes for various events to happen.

If we start in the settling regime, we find that $r_0 = |\bar{B}|$ when

$$T = \frac{2}{\bar{\rho}} (\log |\bar{B}| - \log r_0(0)). \quad (5.63)$$

If starting in the orbital regime, we find that $r_0 = |\bar{B}|$ when

$$T = \frac{1}{1-\bar{\rho}} \log \left(\frac{2(1-\bar{\rho})r^2(0)/\bar{B}^2 - 1}{1-2\bar{\rho}} \right), \quad (5.64)$$

for $\bar{\rho} < 1/2$. Additionally, we find that $r_0 = 1$ when

$$T = \frac{1}{\bar{\rho} - 1} \log \left(\frac{2(\bar{\rho} - 1) + \bar{B}^2}{2r^2(0)(\bar{\rho} - 1) + \bar{B}^2} \right), \quad (5.65)$$

for $\bar{\rho} > 1$. Finally, we can deduce that $r_0 \rightarrow r_0^c$ as $T \rightarrow \infty$ if $\bar{\rho} \in (1/2, 1)$.

This toy model suggests that the TC will never remain within the settling regime, and will always tend to the orbital regime in finite time. Further, if $\bar{\rho} > 1$, the TC will hit the bioreactor edge in finite time no matter where it starts. If $\bar{\rho} < 1$, the long-time behaviour will depend on the value of $\bar{\rho}$. If $\bar{\rho} \in (1/2, 1)$, the TC will tend to a stable limit cycle in the orbital regime in infinite time. If $\bar{\rho} < 1/2$, the TC trajectory will attain the trajectory on the boundary between settling and orbital motion in finite time. Since none of these long-term outcomes has the TC within the steady or settling regimes that experimentalists prefer, our toy model suggests that it will be difficult to keep the TC in these regimes, unless the angular velocity of the bioreactor is slowly varied during the experiment to avoid these long-term solutions. Notably, our toy model suggests that it is possible to move from the settling to orbital regime, but it is never possible to move from the orbital to settling regime.

We now present some results to show how the analytical results compare to a numerical simulation of the model system (5.34). We note that on the boundary between settling and orbital motion (where $r_0 = |\bar{B}|$), there is a jump in both φ , the angle that the TC makes with the x -axis, from $\pi/2$ to $3\pi/2$, and the radial velocity $\dot{R}$ from $-|\bar{B}|$ to $|\bar{B}|$ as the TC centre traverses $R = 0$. These jumps can occur because R is a coefficient of the ODEs, leading to a degeneracy when the TC centre passes through the bioreactor origin. In order to ensure that the simulation does not run into problems near this singularity, we run all simulations with the mapping $R \mapsto R + \delta$, where we take δ to be very small (typically $\sim 10^{-8}$), and use error tolerances (typically $\sim 10^{-10}$) that are able to recognise δ .

In Figure 5.3, we show how r_0 varies in time for a trajectory starting in settling motion and moving to orbital motion as predicted by the parameter values $\bar{B} = 0.2$, $\bar{\rho} = 1.2$, $\epsilon_2 \epsilon Re = 0.01$, and initial position $(R, \varphi) = (0.3, 0)$. We see that the numerical and analytical results are very close, with the small difference only being noticeable when zoomed in. The error between solutions is an oscillation about the MMS solution, and is due to the $O(\epsilon_2 \epsilon Re)$ terms determined by r_2 . We could determine these oscillations by solving for the first correction to the trajectory (5.41) if required. We do not solve for these further terms analytically as they do not give any additional insight.

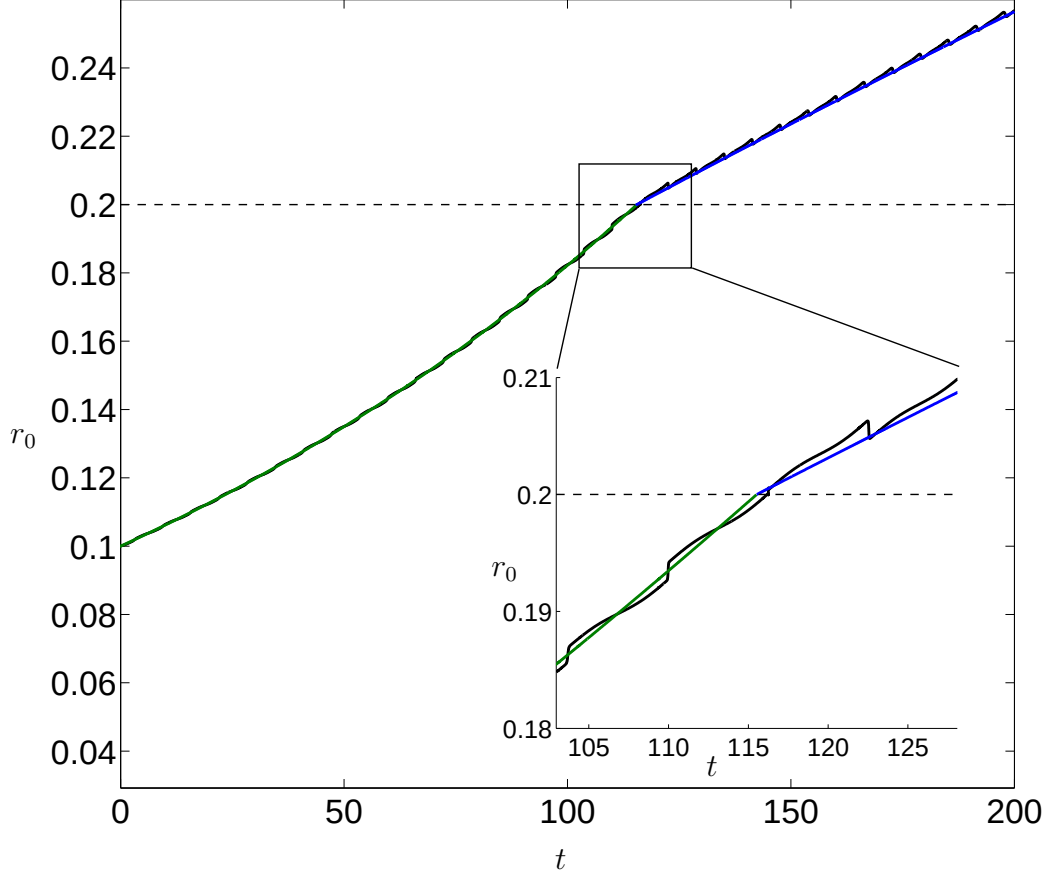


Figure 5.3: Comparing the numerics and asymptotics for the long-time behaviour of r_0 using the model defined in (5.34). For this simulation, the steady point $\overline{B} = 0.2$, the ratio of TC and fluid density $\bar{\rho} = 1.2$, the small parameter $\epsilon_2 \epsilon Re = 0.01$, and the initial position is $(x, y) = (0.3, 0)$. The black line is the numerical result, the green and blue lines are the analytical results in the settling and orbital regime respectively. The dashed black line denotes the boundary between settling and orbital motion. In the inset, we zoom into the trajectory as it crosses from settling to orbital motion.

In Figure 5.4 and 5.5 we show how r_0 varies in time for a trajectory starting in orbital motion and tending to the limit cycle predicted by (5.61). For both Figures, we take $\bar{B} = -0.2$, $\bar{\rho} = 0.9$, and initial position $(R, \varphi) = (0.1, 0)$. However, in Figure 5.4 we use $\epsilon_2 \epsilon Re = 0.01$, and in Figure 5.5 we use $\epsilon_2 \epsilon Re = 0.1$. As expected, for a larger value of $\epsilon_2 \epsilon Re$ the periodic variation away from the predicted long-term behaviour is much larger and the limit cycle is approached more quickly. From Figure 5.5, we further see that the larger value of $\epsilon_2 \epsilon Re$ also means that the analytically predicted limit cycle is crossed by the numerical solution. This is due to the $O(\epsilon_2 \epsilon Re)$ first-correction term, which has the effect of slightly moving the limit cycle in the negative y -direction (as shown in the inset). The agreement between our asymptotic and numerical results is within the error predicted by the former.

It is also possible to slightly alter the model (5.34) by using a centrifugal force of the form $-\epsilon Re Re_X$ instead of $-\epsilon Re \dot{\varphi}^2 Re_X$, i.e. taking the angular velocity of the fluid to be due to the bioreactor, and not the TC. Using this different approximation of the centrifugal force, we obtain a solution $r_0 = r(0) \exp((\bar{\rho} - 1)T/2)$ everywhere within the bioreactor. This result suggests there is no difference to the TC behaviour as we cross from orbital to settling, and that the only long-time behaviour of the TC is to tend to the bioreactor centre or to hit the bioreactor edge. This qualitative change in model prediction tells us that the effect of the fluid on the TC is likely to be very important in determining the correct behaviour of the TC. We should also not be surprised if the MMS analysis for the full problem suggests a discontinuity in behaviour across the settling and orbital regimes.

In the next section, we analyse the full problem as defined in (5.23) using the method of multiple scales. We then discuss the results and how they compare to the model described in this section.

5.3.2 Full solutions

In the previous section we analysed a toy model designed to provide some physical insight into the TC trajectory. In this section, we derive solvability conditions for the full model that result in the equations that govern the long-term behaviour of the TC. In §5.4 we present the results and discuss their physical relevance.

We analyse (5.23) using the method of multiple scales (MMS), and use both coordinate systems (R, φ) and (r, θ) depending on which is more convenient (the transformation is defined in (5.29), and shown in Figure 5.2). The presence of an $O(\epsilon_2)$ term in the full equations motivates the introduction of an intermediate timescale

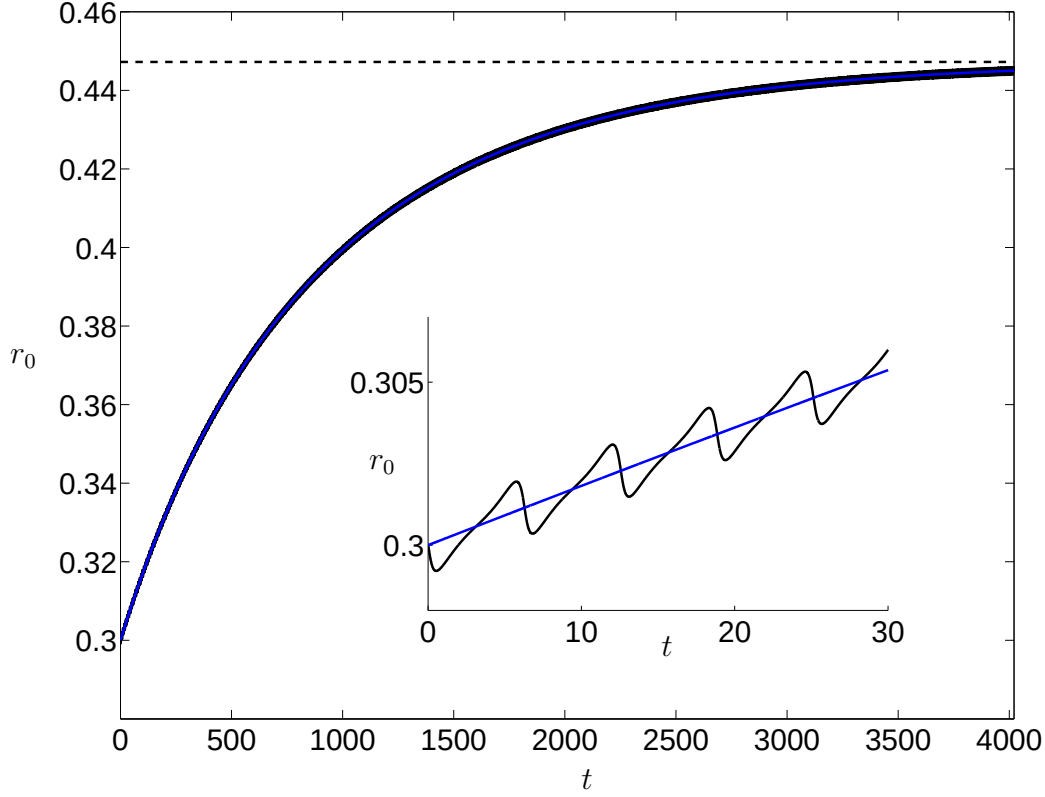


Figure 5.4: Comparing the numerics and asymptotics for the long-time behaviour of r_0 using the model defined in (5.34). For this simulation, the steady point $\bar{B} = -0.2$, the ratio of TC and fluid density $\bar{\rho} = 0.9$, the small parameter $\epsilon_2 \epsilon Re = 0.01$, and the initial position is $(x, y) = (0.1, 0)$. The solid black line is the numerical result, the blue line is the analytical result. The dashed black line is the limit to which r_0 will reach as predicted by the analytic model. In the inset, we show the trajectory for early time.

$\tau = \epsilon_2 t$, along with the long timescale $T = (\epsilon_2 \epsilon Re)t$ used in the previous section. The time derivative then becomes

$$\frac{d}{dt} = \frac{\partial}{\partial t} + \epsilon_2 \frac{\partial}{\partial \tau} + (\epsilon_2 \epsilon Re) \frac{\partial}{\partial T} \quad (5.66)$$

and we seek asymptotic expansions (consistent with the expansions given in (5.37)) of the form

$$r(t, \tau, T) \sim r_0(t, \tau, T) + \epsilon_2 r_1(t, \tau, T) + (\epsilon_2 \epsilon Re) r_2(t, \tau, T), \quad (5.67a)$$

$$\theta(t, \tau, T) \sim \theta_0(t, \tau, T) + \epsilon_2 \theta_1(t, \tau, T) + (\epsilon_2 \epsilon Re) \theta_2(t, \tau, T), \quad (5.67b)$$

and we use similar expansions for R and φ . We note that one of the assumptions in

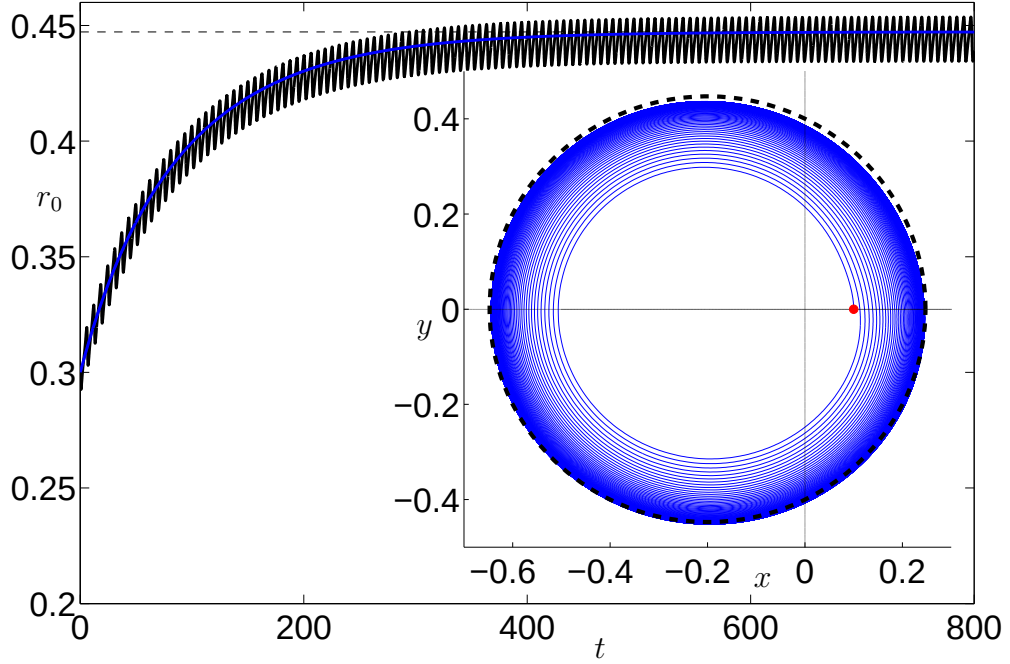


Figure 5.5: Comparing the numerics and asymptotics for the long-time behaviour of r_0 using the model defined in (5.34). For this simulation, the steady point $\overline{B} = -0.2$, the ratio of TC and fluid density $\bar{\rho} = 0.9$, the small parameter $\epsilon_2 \epsilon Re = 0.1$, and the initial position is $(x, y) = (0.1, 0)$. The black line is the numerical result, the blue line is the analytical result. The dotted black line is the limit to which r_0 will reach as predicted by the analytic model. In the inset, we show the TC trajectory in the laboratory frame of the bioreactor (centred on the trajectory, not the bioreactor). The red circle is the initial position of the TC centre, and the dashed black line is the predicted limit cycle.

Chapter 2 was that $\epsilon_2 \ll \epsilon Re$. This means that we will not have to consider terms of $O(\epsilon_2^2)$.

At $O(1)$, the governing equations (5.23) yield the same equations as in §5.3.1, given by (5.39) which, as before, can be rearranged into $r_{0t} = 0$ and $\theta_{0t} = 1$, leading to

$$r_0 = r_0(\tau, T), \quad \theta_0 = t + \phi_0(\tau, T). \quad (5.68a, b)$$

Using (5.29) to write r_0 and θ_0 in terms of R_0 and φ_0 , we obtain

$$R_0 = \left(r_0^2 + \overline{B}^2 + 2r_0\overline{B} \cos(t + \phi_0) \right)^{1/2}, \quad (5.69a)$$

$$\varphi_0 = \tan^{-1} \left(\frac{r_0 \sin(t + \phi_0)}{\overline{B} + r_0 \cos(t + \phi_0)} \right). \quad (5.69b)$$

We therefore have circular motion around the point $(R, \varphi) = (\overline{B}, 0)$ on the short time-scale.

The form of the leading-order solution (5.69) facilitates a simplification of the $O(\epsilon_2)$ terms in (5.23). The linear operators acting on r_1 and θ_1 are the same as for the toy problem (5.41), the $O(\epsilon_2)$ equations from (5.23) being given by

$$r_0 r_{1t} + \overline{B} (r_{1t} \cos \theta_0 - r_0 \theta_{1t} \sin \theta_0) = \eta_1(r_0, \theta_0), \quad (5.70a)$$

$$r_0^2 \theta_{1t} + \overline{B} (r_0 \theta_{1t} \cos \theta_0 + r_{1t} \sin \theta_0) = \nu_1(r_0, \theta_0), \quad (5.70b)$$

where

$$\eta_1(r_0, \theta_0) = \gamma_1(R_0) r_0 \overline{B} \sin \theta_0 - r_{0\tau} (r_0 + \overline{B} \cos \theta_0) + \overline{B} r_0 \theta_{0\tau} \sin \theta_0, \quad (5.71a)$$

$$\nu_1(r_0, \theta_0) = \gamma_1(R_0) \overline{B} (\overline{B} + r_0 \cos \theta_0) - r_{0\tau} \theta_{0\tau} (r_0 + \overline{B} \cos \theta_0) - r_{0\tau} \overline{B} \sin \theta_0. \quad (5.71b)$$

From the framework developed in the previous section, we deduce that the solvability conditions are given by substituting η_1 and ν_1 (defined in (5.71)) into (5.56) in place of their unsubscripted counterparts. This yields

$$0 = \int_0^{2\pi} (-r_{0\tau} + \overline{B} \gamma_1(R_0) \sin \theta_0) dt, \quad (5.72a)$$

$$0 = \int_0^{2\pi} (-r_0 \theta_{0\tau} + \overline{B} \gamma_1(R_0) \cos \theta_0) dt. \quad (5.72b)$$

The second term in (5.72a) is odd around $t = \pi + \phi_0(\tau, T)$, and therefore does not contribute to the integral. Therefore, we deduce that

$$r_0 = r_0(T), \quad r_0 \frac{\partial \phi_0}{\partial \tau} = \frac{\overline{B}}{2\pi} \int_0^{2\pi} \gamma_1(R_0) \cos \theta_0 dt. \quad (5.73a, b)$$

Thus there is no spiralling due to the effect of the fluid on the TC at $O(\epsilon_2)$ (i.e. due to the effect of the leading-order fluid pressure), but there is a change in rotation rate. Furthermore, from (5.69a) we see that $R_0(t)$ is 2π -periodic with the same phase as $\cos \theta_0$, and from (5.21b) we see that $\gamma_1(R_0) > 0$. Therefore, we can deduce that $\partial \phi_0 / \partial \tau \geq 0$, with equality if $\overline{B} = 0$, i.e. if R_0 is constant over the short timescale t . Hence, the actual angular velocity of the TC centre around the steady point is slightly larger than the $O(1)$ equations predict.

At $O(\epsilon_2 \epsilon Re)$, the governing equations (5.23) give

$$r_0 r_{2t} + \overline{B} (r_{2t} \cos \theta_0 - r_0 \theta_{2t} \sin \theta_0) = \eta_2(r_0, \theta_0), \quad (5.74a)$$

$$r_0^2 \theta_{2t} + \overline{B} (r_0 \theta_{2t} \cos \theta_0 + r_{2t} \sin \theta_0) = \nu_2(r_0, \theta_0), \quad (5.74b)$$

where

$$\eta_2(r_0, \theta_0) = R_0 \gamma_2(R_0) + \left(\frac{\bar{\rho}}{2} r_0 - r_{0T}\right) (r_0 + \bar{B} \cos \theta_0) + r_0 \theta_{0T} \bar{B} \sin \theta_0, \quad (5.75a)$$

$$\nu_2(r_0, \theta_0) = -R_0 \gamma_3(R_0) + \left(\frac{\bar{\rho}}{2} r_0 - r_{0T}\right) \bar{B} \sin \theta_0 - r_0 \theta_{0T} (r_0 + \bar{B} \cos \theta_0). \quad (5.75b)$$

Then, substituting η_2 and ν_2 into (5.56) in place of their unsubscripted counterparts yields

$$r_{0T} - \frac{\bar{\rho}}{2} r_0 = \frac{1}{2\pi} \int_0^{2\pi} \frac{(\gamma_2(t) (r_0 + \bar{B} \cos \theta_0) - \gamma_3(t) \bar{B} \sin \theta_0)}{R_0} dt, \quad (5.76a)$$

$$-r_0 \theta_{0T} = \frac{1}{2\pi} \int_0^{2\pi} \frac{(\gamma_3(t) (r_0 + \bar{B} \cos \theta_0) + \gamma_2(t) \bar{B} \sin \theta_0)}{R_0} dt, \quad (5.76b)$$

where the functions γ_2 and γ_3 are defined in (5.22b) and (5.22c), and are dependent on the position, velocity and acceleration of the TC at $O(1)$. The more important condition (and the one that we focus on in §5.4) is (5.76a), as this will determine whether the TC spirals inwards or outwards. We solve (5.76a) numerically in the next section to determine the long-time behaviour of the TC.

5.4 Results

We now present and discuss the behaviour of the TC trajectory on the short ($O(1)$), intermediate ($O(\epsilon_2)$) and long-timescales ($O(\epsilon_2 \epsilon Re)$). The short-time results are obtained from the exact solution for (R_0, φ_0) given in (5.69).

The intermediate-time behaviour is determined by substituting the analytic result for the leading-order trajectory (5.69) into the infinite sum $\gamma_1(R_0)$ (from (5.21b)), then using the MATLAB program `trapz` to evaluate the solvability conditions (5.73b). These are validated numerically, using the MATLAB program `ode15s` to solve (5.23) (neglecting the $O(\epsilon_2 \epsilon Re)$ terms), and comparing these numerical results with those obtained using the multiple-scale analysis.

We determine the long-term behaviour by evaluating r_{0T} from the solvability condition (5.76a). The right-hand side of (5.76a) is determined by numerically evaluating the integral using the MATLAB program `trapz`. The infinite sums γ_2 and γ_3 (defined in (5.22b) and (5.22c) respectively) within the integrand are obtained by determining $\bar{E}_n$ and $\bar{F}_n$ (from (2.62e) and (2.62f) respectively). This requires the knowledge of a_{in} and b_{in} (where $i \in \{1, 2, 3\}$ and $n \in \mathbb{Z}$) obtained from (2.52)–(2.55). Finally, these coefficients can be determined numerically from the calculation of p_0 (given in (2.45a))

and its derivatives, which can be calculated using the analytic result (5.69) to determine the coefficients A_n and B_n (defined in (2.46a) and (2.46b)) of p_0 . This requires a discretization of β in bipolar coordinates.

There are several numerical discretizations involved in the procedure described above. We perform an error analysis for each of these in Appendix I, and note that the results for r_{0T} are accurate to around $O(10^{-4})$.

5.4.1 Short and intermediate-time behaviour

We consider the short and intermediate-time solutions together by neglecting terms of $O(\epsilon_2 \epsilon Re)$ in (5.23) to obtain

$$0 = (1 + \epsilon_2 \gamma_1(R)) \dot{R} + \overline{B} \sin \varphi, \quad (5.77a)$$

$$0 = (1 + \epsilon_2 \gamma_1(R)) R(1 - \dot{\varphi}) - \overline{B} \cos \varphi. \quad (5.77b)$$

The short-time equations are found by taking $\epsilon_2 = 0$.

Recall from the equation for the steady point (5.24) that $\overline{B}$ linearly depends on $\bar{\rho} - 1$. This means that for $\bar{\rho} > 1$, the steady point will be on the right-hand side of the bioreactor, and for $\bar{\rho} < 1$ it will be on the left-hand side. In Figures 5.6 and 5.7 we plot the TC trajectories in the (x, y) laboratory frame for varying initial position with $b = 0.15$, $\overline{B} = 0.4$, and $K = 0.1$. In Figure 5.6 we take $\epsilon_2 = 0$, and in Figure 5.7 we take $\epsilon_2 = 0.1$.

In all of the Figures in this section, we observe the three different types of periodic motion. The phase paths that do not contain the bioreactor origin correspond to the settling regime, the phase paths that contain the bioreactor origin correspond to the orbital regime, and the unique critical point of (5.77) corresponds to the steady regime.

We note that in both Figures the solution breaks down as $R \rightarrow 1 - b$. This limit corresponds to the TC hitting the bioreactor boundary, where the bipolar coordinate transformation breaks down. Additionally, our modelling assumptions mean that the calculations are not valid for a TC close to the bioreactor wall, as neglected terms (e.g. the in-plane viscous terms) become important. However, in Cummings *et al.* [19], experimental results show TCs hitting the curved bioreactor wall. After collision, the TCs continue to move along the wall before leaving the wall to continue on a circular motion away from the wall. We can conclude that whilst our model does not account for the behaviour of a TC near the bioreactor wall, our model does seem to reflect TC behaviour away from the wall as seen in Cummings *et al.* [19].

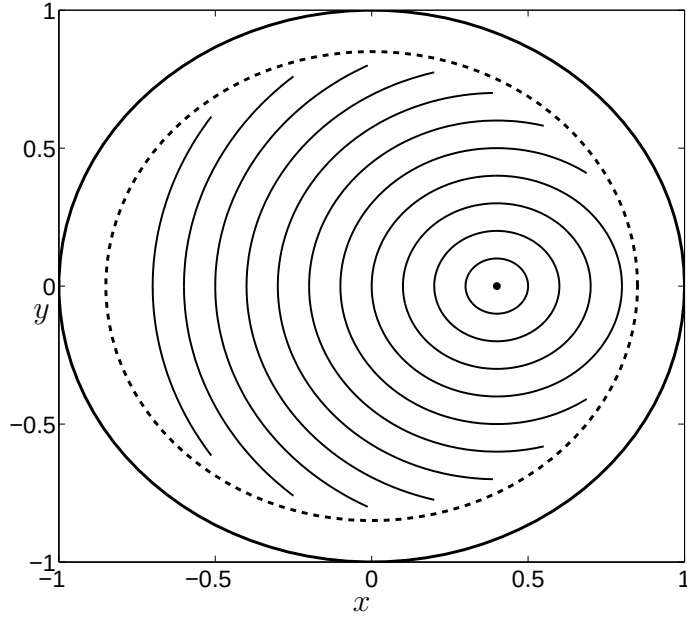


Figure 5.6: Phase plane showing the TC trajectory for different starting positions with $b = 0.15$, $\epsilon_2 = 0$, $\bar{B} = 0.4$, and $K = 0.1$. All trajectories are anti-clockwise around the steady point, located at $(x, y) = (0.4, 0)$.

To determine how varying certain parameters affects the TC trajectory, it is useful to consider the pressure contribution (5.21) in more detail. We see that every term in the infinite sum γ_1 is positive, and note that

$$\frac{1}{1 + 12K} \leq \frac{1}{\tanh(n(\alpha_2 - \alpha_1)) + 12K} \leq \frac{1}{12K}. \quad (5.78)$$

Additionally, we note that taking the derivative of

$$\sum_{n=1}^{\infty} \exp(-2n\alpha_2) = \frac{1}{\exp(2\alpha_2) - 1}, \quad (5.79)$$

with respect to α_2 implies that

$$\sum_{n=1}^{\infty} n \exp(-2n\alpha_2) = \frac{1}{4 \sinh^2 \alpha_2}, \quad (5.80)$$

so we can deduce that

$$\frac{6}{1 + 12K} \leq \gamma_1(R) \leq \frac{1}{2K}, \quad (5.81)$$

i.e. there is little variation in $\gamma_1(R)$ unless $K \rightarrow 0$. The limit $K \rightarrow 0$ corresponds a solid TC, and in this limit $\gamma_1 \rightarrow \infty$ as $R \rightarrow 1 - b$. That is, the pressure exerted by

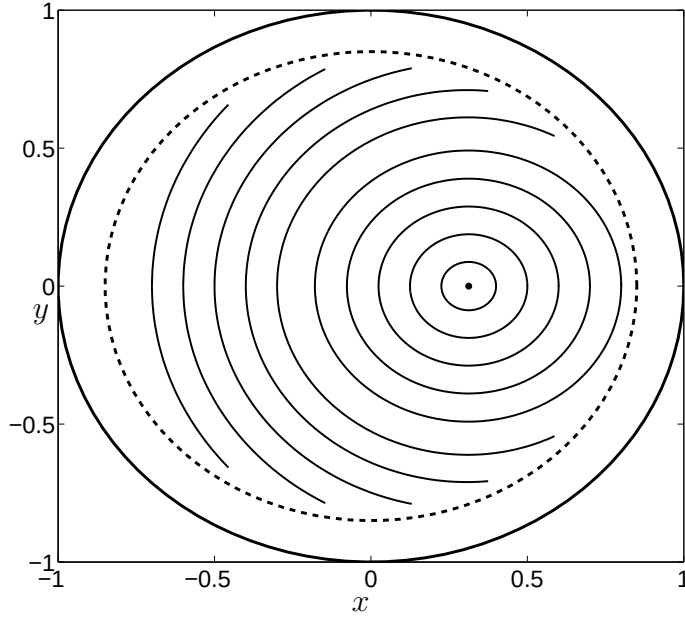


Figure 5.7: Phase plane showing the TC trajectory for different starting positions with $b = 0.15$, $\epsilon_2 = 0.1$, $\overline{B} = 0.4$, and $K = 0.1$. All trajectories are anti-clockwise around the steady point, located at $(x, y) \approx (0.3126, 0)$.

the fluid on the TC gets very large as the solid TC comes close to the bioreactor wall, as we would expect.

From the periodicity of the TC trajectory, we note that the average of $\dot{R}$ over one period is 0 in both regimes. However, in the settling regime the average of $\dot{\varphi}$ over one period is 0, whereas in the orbital regime, the average of $\dot{\varphi}$ over one period is 1. From the form of the leading-order fluid pressure (5.21), we see that its contribution to the TC trajectory (averaged over one orbit) is roughly proportional to $R\mathbf{e}_Y$ in the settling regime, but will be much smaller in the orbital regime. As $\mathbf{e}_Y$ is perpendicular to $\mathbf{e}_X$ (in the anti-clockwise direction), and the average of $\mathbf{e}_X$ over one period in the settling regime is $\mathbf{e}_x$ (the unit vector in the laboratory x -axis), we expect that the average effect of the leading-order fluid pressure over one orbit acts roughly in the direction of the positive y -axis. That is, we expect the averaged effect of the leading-order fluid pressure to oppose the gravitational effect in the settling regime, and to have a much smaller effect in the orbital regime.

We can see this $O(\epsilon_2)$ effect in Figures 5.6 and 5.7. That is, the point around which the trajectories orbit in the settling regime is slightly closer to the bioreactor centre when $\epsilon_2 = 0.1$, and there does not appear to be much difference in the orbital

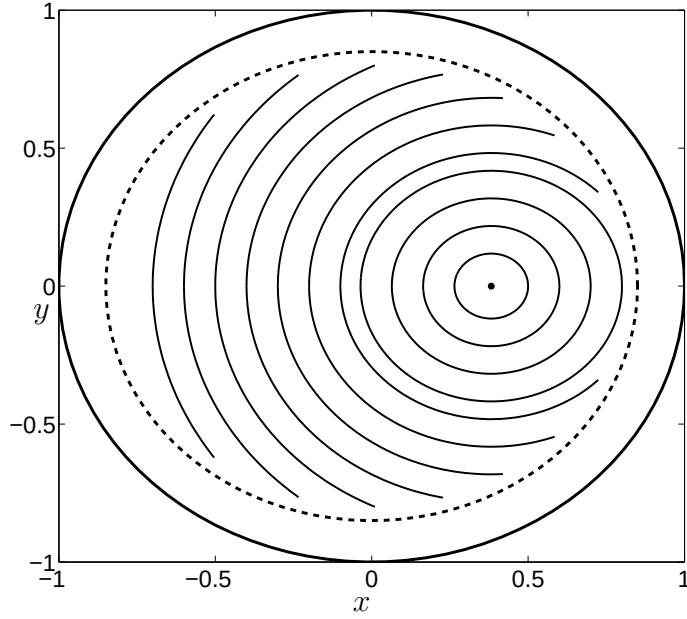


Figure 5.8: Phase plane showing the TC trajectory for different starting positions with $b = 0.15$, $\epsilon_2 = 0.1$, $\bar{B} = 0.4$, and $K = 1$. All trajectories are anti-clockwise around the steady point, located at $(x, y) \approx (0.3823, 0)$.

trajectories. In Figure 5.6, the steady point is located at $(x, y) = (0.4, 0)$, and in Figure 5.7, the steady point is located at $(x, y) \approx (0.3126, 0)$.

From (5.78), we expect that the trajectory will not be very sensitive to K , though an increase in K will lead to the fluid pressure having less of an effect on the TC, i.e. boost the gravitational effect in the settling regime. We see this in Figure 5.8, where we have the same parameters as Figure 5.7, but change from $K = 0.1$ to $K = 1$. We see that the steady point is slightly to the right in Figure 5.8 (where it is located at $(x, y) \approx (0.3823, 0)$) compared to its position in Figure 5.7 (located at $(x, y) \approx (0.3126, 0)$).

We can calculate the proportion of the bioreactor which contains trajectories in the settling regime by determining the trajectory that passes through the origin. Taking this trajectory as our boundary trajectory, the area inside is given by $\pi \bar{B}^2$ at leading-order if none of the settling trajectories hit the bioreactor edge, and is modified otherwise. If the initial position of the TC had a known random distribution (e.g. the likely scenario that experimentalists had a non-perfect control over the initial position of the TC), we could calculate the probability of a TC being in a given movement regime.

From the numerical results, we see that the contribution from $O(\epsilon_2)$ terms is to slightly change the position of the steady point. This was not calculated in our multiple-scale analysis, as we did not calculate the $O(\epsilon_2)$ terms in the governing equations (5.77) on r_1 and θ_1 (just the effect of the $O(\epsilon_2)$ terms on r_0 and θ_0). More importantly, the numerical results of (5.77) for finite ϵ_2 suggest that the TC trajectories are periodic, which is in agreement with the prediction of our multiple-scale analysis.

We can see directly from (5.77) that its solutions are periodic, as there exists a first integral of the system (obtained by forming and integrating $d\varphi/dR$), as follows

$$H + \overline{B}R \cos \varphi = \frac{R^2}{2} + \epsilon_2 \int_0^R \hat{R} \gamma_1(\hat{R}) d\hat{R}, \quad (5.82)$$

where H is a constant. The right-hand side of (5.82), and its derivative (with respect to R), are positive and monotonically increasing from a value of 0 when $R = 0$. For a given φ (working modulo 2π), the left-hand side is linear in R with a vertical translation depending on the value of H . Therefore, on a particular trajectory, and for a given value of φ , the number of values that R can take can only be zero, one or two. As the critical point is a centre, this implies that the solutions to (5.77) must be periodic (as spiralling must allow an infinite number of values for R). Indeed, we expect the solutions to (5.77) to be periodic, as we have not yet included any inertial effects. This follows from the time reversibility of Stokes flow, and the fact that the external forces within the problem (due to gravitational effects and the rotation of the bioreactor) are time invariant. This mathematically justifies our decision to include inertial effects at first correction - any correction terms due to the small Reynolds number limit would only produce periodic orbits.

Although the solutions to (5.77) must be periodic, our $O(1)$ solutions are not uniformly valid, and break down when $t = O(\epsilon_2^{-1})$. We resolve this breakdown in the previous section by using a multiple-scale analysis, and deduce that the correction in $\theta(t)$ for $t = O(\epsilon_2^{-1})$ can be determined from (5.72b). In Figure 5.9, we show this effect, and how our multiple-scale analysis can predict the phase difference using a value of $\epsilon_2 = 0.01$. We see that at around $t = 6300$, the short-time solution is completely out of phase with the numerical solution, but the multiple-scale analysis remains uniformly valid. This corresponds to around 1000 rotations of the bioreactor which, at a typical rotation rate of 15 rotations per minute, takes a dimensional time of about an hour. If the value of ϵ_2 is larger, this effect will be more pronounced and occur more quickly. As these experiments run over a few days, this effect should be

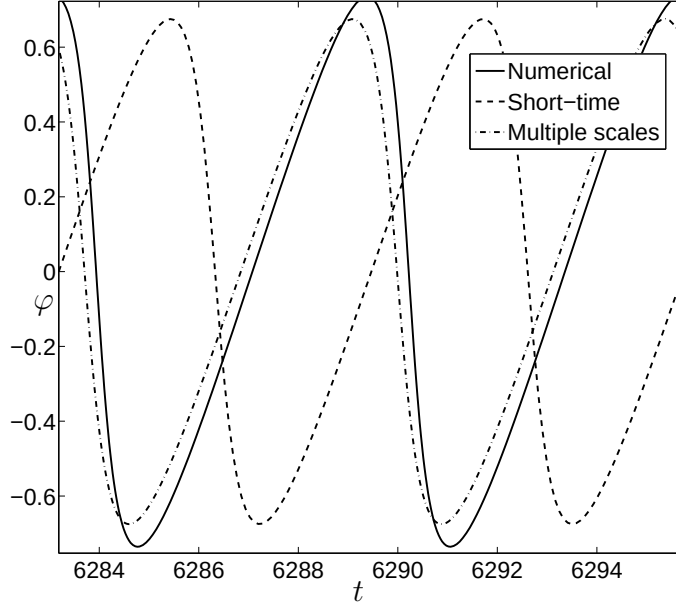


Figure 5.9: The drift in φ over an intermediate time. We take $b = 0.15$, $K = 0.1$, $\overline{B} = 0.4$, $r = 0.25$, and $\epsilon_2 = 0.01$. After around 6300 dimensionless time units the short time solution is almost out of phase with the numerical solution. However, the multiple-scale analysis can capture this effect, and keep the analytic approximation uniformly valid.

taken into account if past estimates or future predictions are to be made from the current state of rotation.

In Figures 5.10 and 5.11, we show instantaneous streamlines at various times throughout the periodic cycle for selected parameter values in the settling and orbital regimes respectively. We use the streamfunctions determined in (2.48) and (2.49), whose coefficients are given by (2.46).

We see that the streamlines within the TC in the orbital regime (in Figure 5.11) show that the fluid does not vary much from rigid-body rotation, which is in stark contrast to the corresponding streamlines within the settling regime (in Figure 5.10). This suggests that there will be a greater mixing of convection-dominated nutrient transport in the settling regime, which agrees with physical intuition and current experimental practise (to keep the TC in the settling regime near to the steady regime). Intuitively this difference is because, in settling motion, the TC moves in the opposite direction to the bulk flow at some point during its trajectory, causing greater mixing. Mathematically, we explain this difference as follows. From the leading-order flow solutions (2.35) and (2.27a–b), we see that it is the fluid pressure

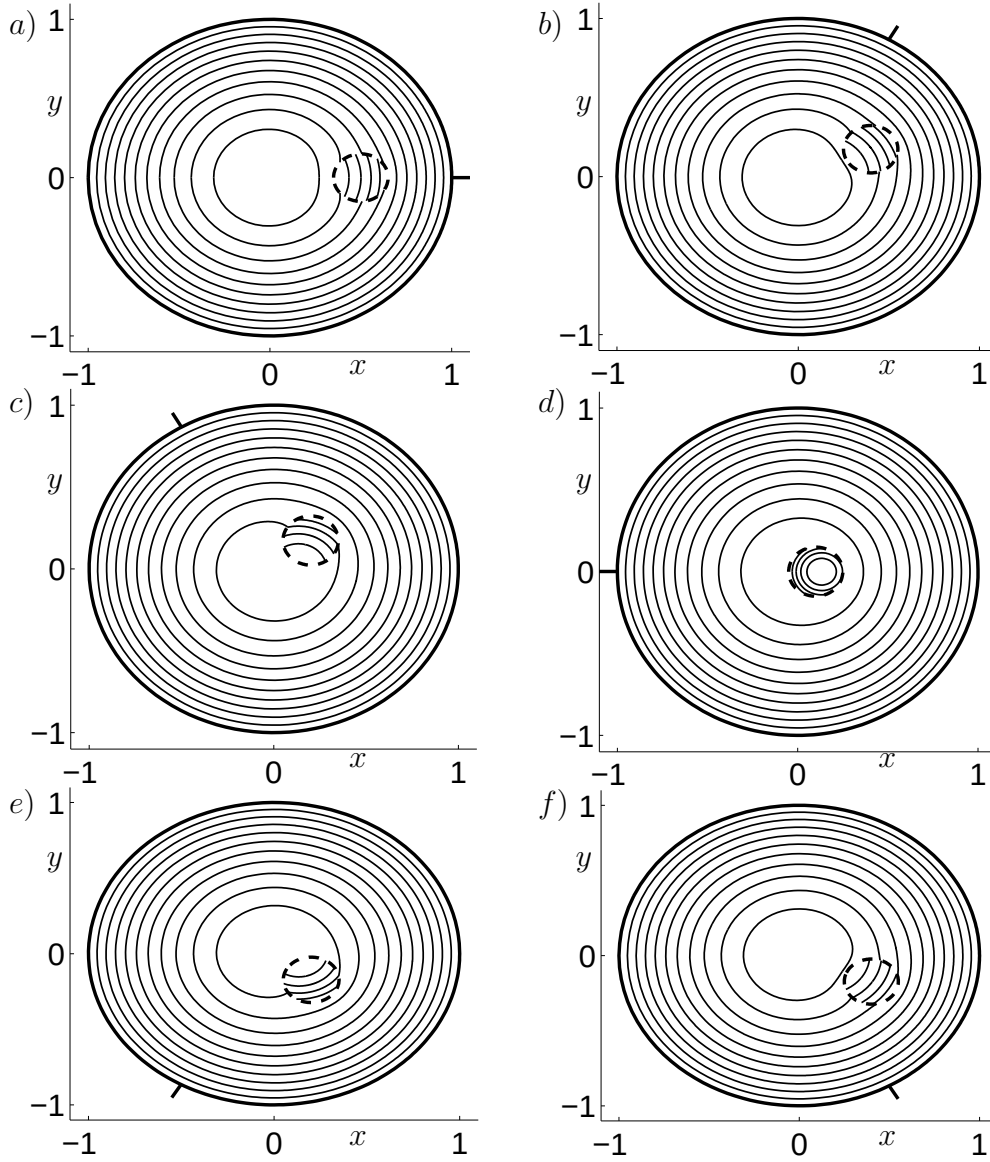


Figure 5.10: Typical streamlines for the bioreactor flow with a porous TC, illustrating a periodic motion in the settling regime, shown in the inertial frame. The images shown are for a) 0, b) $\pi/3$, c) $2\pi/3$, d) π , e) $4\pi/3$ and f) $5\pi/3$ of the way through a full cycle, and the small line protruding out of the bioreactor signifies this. The dashed line is the TC boundary. The parameter values are $b = 0.15$, $\epsilon_2 = 0$, $K = 0.1$, and $\overline{B} = 0.3$; and (5.77) are solved subject to $R(0) = 0.5$, $\varphi(0) = 0$.

which drives the flow away from a rigid-body rotation with the bioreactor. The fluid pressure is far lower when the TC is in the orbital regime compared to when it is in the settling regime (as can be seen from the fluid pressure coefficients in (2.46)). Therefore, the flow is close to rigid-body rotation when the TC is in orbital motion.

In Figure (5.10d), we see that the instantaneous streamlines within the TC are

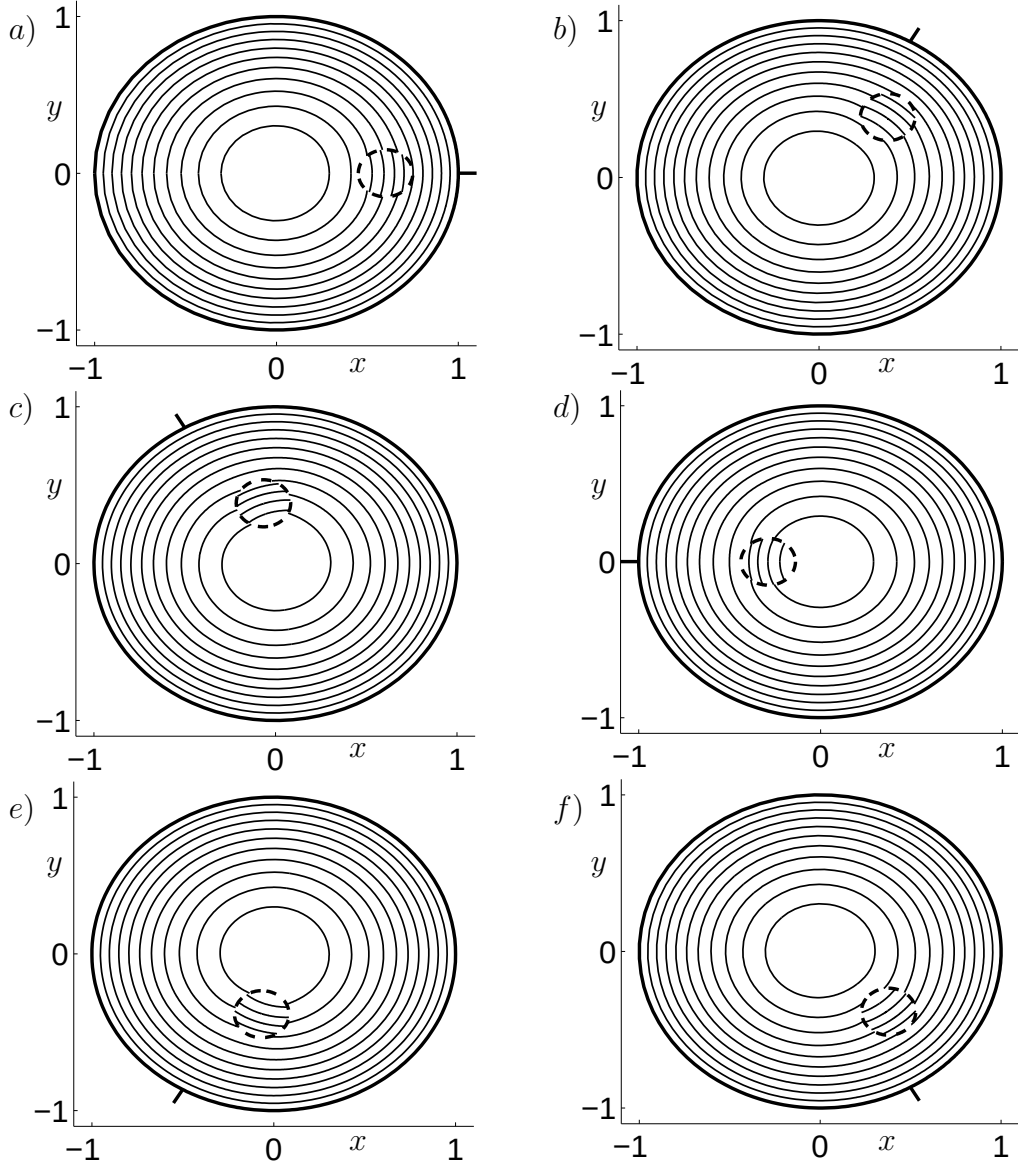


Figure 5.11: Typical streamlines for the bioreactor flow with a porous TC, illustrating a periodic motion in the orbital regime, shown in the inertial frame. The images shown are for a) 0, b) $\pi/3$, c) $2\pi/3$, d) π , e) $4\pi/3$ and f) $5\pi/3$ of the way through a full cycle, and the small line protruding out of the bioreactor signifies this. The dashed line is the TC boundary. The parameter values are $b = 0.15$, $\epsilon_2 = 0.1$, $K = 0.1$, and $\overline{B} = 0.2$; and (5.77) are solved subject to $R(0) = 0.6$, $\varphi(0) = 0$.

different compared to the streamlines in the other Figures. This is because R and $\dot{R}$ are small when the TC is close to the bioreactor centre in the settling regime, and so from (2.48b) we see that the rotation of the TC about its own centre ($\omega \approx 1$) dominates the streamlines within the TC. This manifests in streamlines which are roughly circular around the TC centre. Note that this only occurs instantaneously;

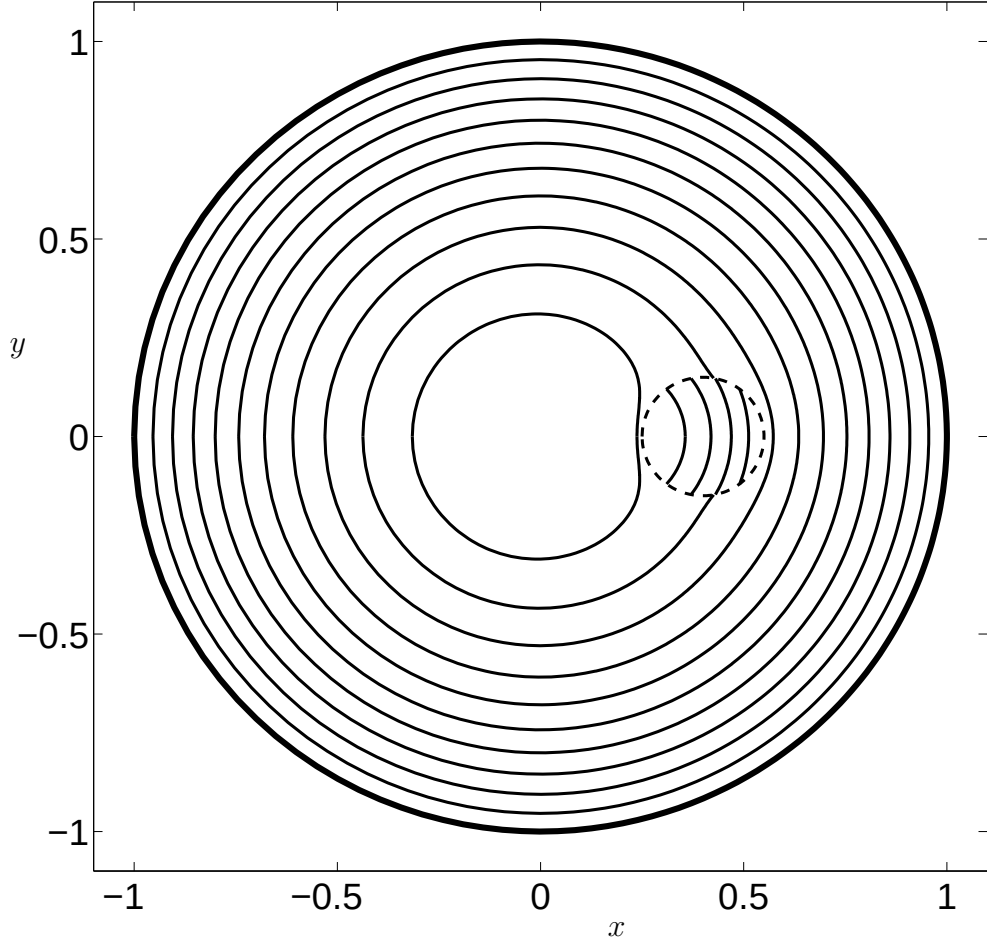


Figure 5.12: Typical streamlines for the bioreactor flow with a porous TC, illustrating the steady regime, shown in the inertial frame. The parameter values are $b = 0.15$, $\epsilon_2 = 0$, $K = 0.1$, and $\overline{B} = 0.4$; and (5.77) are solved subject to $R(0) = 0.4, \varphi(0) = 0$.

the streamlines here are not particle paths, and we do not expect particles to circle around inside the TC.

In Figure 5.12, we show the streamlines for a TC in the steady regime. The streamlines are now equivalent to the particle paths. We see that the proportion of the fluid that enters the TC is quite small compared to the total amount of fluid within the bioreactor. This suggests that, in a convection-dominated nutrient transport regime, steady motion may not be the best way to deliver nutrient to the TC due to the lack of mixing of nutrient in this regime.

5.4.2 Long-time solutions

We now discuss the solutions to the long-time problem obtained from the solvability condition (5.76a). We present the results by showing contour plots for r_{0T} over varying $\bar{\rho}$ and r_0 . As the steady point $\bar{B}$ defined in (5.24) is linearly dependent on $\bar{\rho} - 1$, we keep $\bar{B}/(\bar{\rho} - 1)$ constant in Figures 5.13–5.16. Varying $\bar{\rho}$ will change the regions of the bioreactor which are in the settling and orbital TC motion regimes, and we indicate these regions on the Figures. Physically, varying $\bar{\rho}$ corresponds to keeping all experimental parameters constant, but allowing the density of the TC to change (e.g. to model TC growth).

To check that we are numerically calculating the integral (5.76a) correctly, we start by ensuring that we obtain the same value of r_{0T} when starting at different positions on the same trajectory, i.e. that we obtain the same value of r_{0T} when r_0 is the same but $\theta_0(0)$ is varied. Secondly, we compute the numerical results for a simplified model and compare them with analytical results that we are able to obtain in this simplified case. We do this by sending $\bar{B} \rightarrow 0$ independently of $\bar{\rho}$ as follows. From (5.29) or (5.69) (see Figure 5.2 for a schematic), we see that letting $\bar{B} \rightarrow 0$ means that $R = r$, and $\varphi = \theta$, giving $\dot{R}_0 = 0$ and $\dot{\varphi}_0 = 1$, so that the TC rotates about the bioreactor centre in a rigid-body rotation. This is apparent from (2.45a) and (2.46), from which we see that the fluid pressure vanishes, i.e. there is no motion relative to the rotation of the bioreactor. This causes most of the terms in (2.54), the boundary conditions for the first correction to the fluid flow, to vanish. The remaining term in the boundary conditions (2.54) is the force due to the rotation of the bioreactor, and so (2.55) becomes

$$g_1(\beta) = 0, \quad (5.83a)$$

$$g_2(\beta) = -\frac{1}{2}(X^2 + Y^2), \quad (5.83b)$$

$$g_3(\beta) = 0. \quad (5.83c)$$

Then, using the bipolar transformation defined in (2.40)–(2.41) and contour integration, we can determine the Fourier series

$$-\frac{1}{2}(X^2 + Y^2) = \text{constant} + 2 \sinh \alpha_1 R \sum_{n=1}^{\infty} \exp(-n\alpha_2) \cos n\beta, \quad (5.84)$$

and we can deduce from (2.62) and (5.22b) that

$$\gamma_2 = -2 \sinh^2 \alpha_2 R \sum_{n=1}^{\infty} \frac{\tanh(n(\alpha_2 - \alpha_1))}{\tanh(n(\alpha_2 - \alpha_1)) + 12K} (n \exp(-2n\alpha_2)), \quad (5.85a)$$

$$\gamma_3 = 0. \quad (5.85b)$$

From an alternative description of the bipolar transformation (B.5), we can see that $\alpha_1, \alpha_2 \rightarrow \infty$ as $R \rightarrow 0$. Using this information with the identity (2.41a), we can deduce that

$$\alpha_2 - \alpha_1 = -\log b + O(R^2) \quad \text{as } R \rightarrow 0, \quad (5.86)$$

which implies that

$$\tanh(n(\alpha_2 - \alpha_1)) = \frac{1 - b^{2n}}{1 + b^{2n}} + O(R^2) \quad \text{as } R \rightarrow 0. \quad (5.87)$$

Using the fact that

$$\sinh^2 \alpha_2 \exp(-2\alpha_2) = \frac{1}{4} + O(R^2) \quad \text{as } R \rightarrow 0, \quad (5.88)$$

we deduce that in the limit of $R \rightarrow 0$, (5.85a) becomes

$$\gamma_2 \sim -\frac{R}{2 \left(1 + 12K \left(\frac{1+b^2}{1-b^2} \right) \right)} + O(R^3). \quad (5.89)$$

Therefore, as $R \rightarrow 0$, the solvability condition (5.76a) becomes

$$R_T = \left(\bar{\rho} - \frac{1}{1 + 12K \left(\frac{1+b^2}{1-b^2} \right)} \right) \frac{R}{2}, \quad (5.90)$$

and, near $R = 0$, our numerics should produce a critical line of $R_T = 0$ near

$$\bar{\rho} = \frac{1}{1 + 12K \left(\frac{1+b^2}{1-b^2} \right)}. \quad (5.91)$$

In fact, using the summation result (5.80) in (5.85a) for $K = 0$, the limiting result (5.89) (without the error term) is true for all values of R . Then, the solution to the resultant governing equation (5.90) with $K = 0$ is $R = R(0) \exp((\bar{\rho} - 1)T/2)$. This is the same as the conjectured result in Cummings and Waters [18], i.e. for $\bar{B} = 0$ and $K = 0$ we have $R_T > 0$ for $\bar{\rho} > 1$ and $R_T < 0$ for $\bar{\rho} < 1$.

We present the results of the numerical calculation for R_T from (5.76a) (imposing $\bar{B} = 0$, resulting in $r = R$) in Figure 5.13 for $b = 0.15$ and $K = 0.1$; from the above analysis we anticipate a critical line near $\bar{\rho} \approx 0.4434$. We see excellent agreement between the numerical and asymptotic result for the critical line near $R = 0$. There is another critical line on $R = 0$, which corresponds to the bioreactor centre. As the

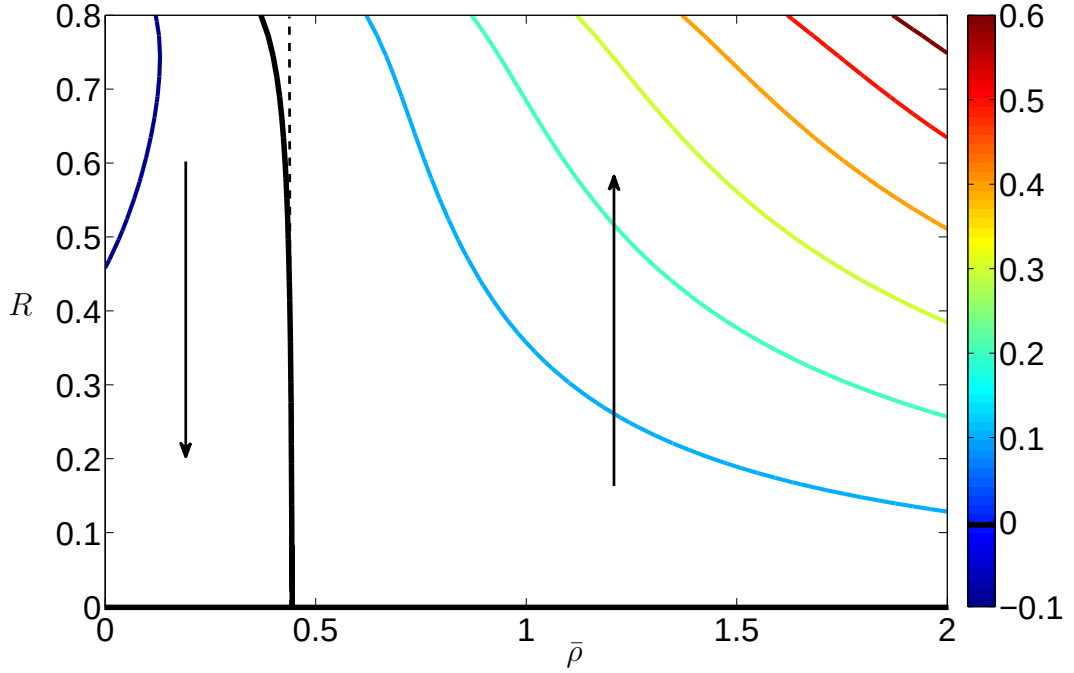


Figure 5.13: The contours indicate the value of R_T for varying $\bar{\rho}$ and R , taking $\bar{B} = 0$ and $K = 0.1$. The black line denotes the critical line $R_T = 0$. The vertical dashed line denotes the asymptotic approximation to the critical line. The arrows denote the sign of R_T in each region by pointing in the direction that R will change. In the region to the right of the critical line the TC will spiral out until it hits the bioreactor edge. In the region to the left of the critical line the TC will spiral inwards towards the bioreactor centre.

value of the contours in Figure 5.13 represent the value of R_T , and the y -axis is R , all motion due to R_T is represented by movement in the y -direction within this diagram. We note that $R_T < 0$ to the left of the critical line, and $R_T > 0$ to the right of the critical line (indicated by arrows in Figure 5.13). Therefore, we deduce that the bioreactor centre is a stable limit point if the TC has a small enough relative density $\bar{\rho}$, otherwise it is unstable and the TC will spiral out until it hits the bioreactor edge.

We note that as $\bar{B} = 0$, the entire bioreactor region is in the orbital regime, and there is a critical line which propagates into this regime. By considering any perturbation away from this critical line, we see that any point on the critical line represents an unstable limit cycle. Furthermore, there is only a narrow range of $\bar{\rho}$ for which this limit cycle exists.

We perform similar simulations as above for r_{0T} from (5.76a), but now taking $\bar{B}/(\bar{\rho} - 1) = 0.1, 1$ and 10 , with the results shown in Figures 5.14, 5.15 and 5.16

respectively, plotting contours of constant r_{0T} for varying r_0 and $\bar{\rho}$. The physically realistic parameter is $\bar{B}/(\bar{\rho} - 1) = 10$, but the other values are mathematically interesting. As the value of the contours represents the value of r_{0T} , and the y -axis is r_0 , all motion due to r_{0T} is represented by movement in the y -direction within this diagram. Furthermore, as $\bar{B}$ now varies, we have settling as well as orbital regimes. As suggested by the toy model considered in §5.3.1, there is a discontinuity in r_{0T} across the boundary between the orbital and settling regimes in Figures 5.14–5.16. To avoid errors in plotting contours of constant r_{0T} (resulting from the discontinuities across these lines), we plot the results from the orbital and settling regimes separately.

The large triangle within which all contours are located represents the possible trajectories of the TC within the bioreactor. The two upper boundaries, the lines $r_0 = (1 - b) - \bar{B}$ and $r_0 = (1 - b) + \bar{B}$ (with $r_0 \in (0, 1 - b)$), represent the TC touching the bioreactor edge at some point in its trajectory. The lower boundary $r_0 = 0$ represents the short-time steady regime, where the TC appears to stay at one point in the laboratory frame. The dashed lines within this larger triangle separate the settling (lower left and right triangles) and orbital (higher central diamond) regimes. We mark the critical lines r_{0T} with a thick black line, and indicate which direction the TC will move on the long timescale using arrows. For $\bar{B}/(\bar{\rho} - 1) = 0.1$, the lowest value that the steady point can take is $\bar{B} = -0.1$, and so Figure 5.14 does not show as much of the triangle as is seen in Figures 5.15 and 5.16 for the possible locations of the steady point.

From Figure 5.14, we see that there does not appear to be much difference between settling and orbital regimes. The discontinuity between regimes is slight, and the critical line where $r_{0T} = 0$ is almost independent of $\bar{\rho}$. For $\bar{\rho} \gtrsim 0.45$, the TC always spirals out towards the bioreactor edge, and for $\bar{\rho} \lesssim 0.45$, the point $r_0 = 0$ is a steady attractor. Therefore, the choice of long-time behaviour is between steady and hitting the bioreactor edge.

In Figure 5.15, where $\bar{B}/(\bar{\rho} - 1) = 1$, we see that the critical line now slightly varies in $\bar{\rho}$. Furthermore, as the location of the critical line increases in $\bar{\rho}$ as r_0 increases (i.e. it moves to the right in Figure 5.15 as r_0 increases), the critical line represents a stable limit cycle. Therefore, we are able to attain three types of long-term behaviour. These are: steady (if $\bar{\rho} \lesssim 0.45$), settling (if $0.45 \lesssim \bar{\rho} \lesssim 0.52$), and hitting the bioreactor edge (if $\bar{\rho} \gtrsim 0.52$). Note that, in general, the time taken to hit the bioreactor edge in Figure 5.15 will be much larger than in Figure 5.14. This is because r_{0T} is much larger in Figure 5.14 (where it attains a maximum of 0.9) than in Figure 5.15 (where it attains a maximum of 0.2).

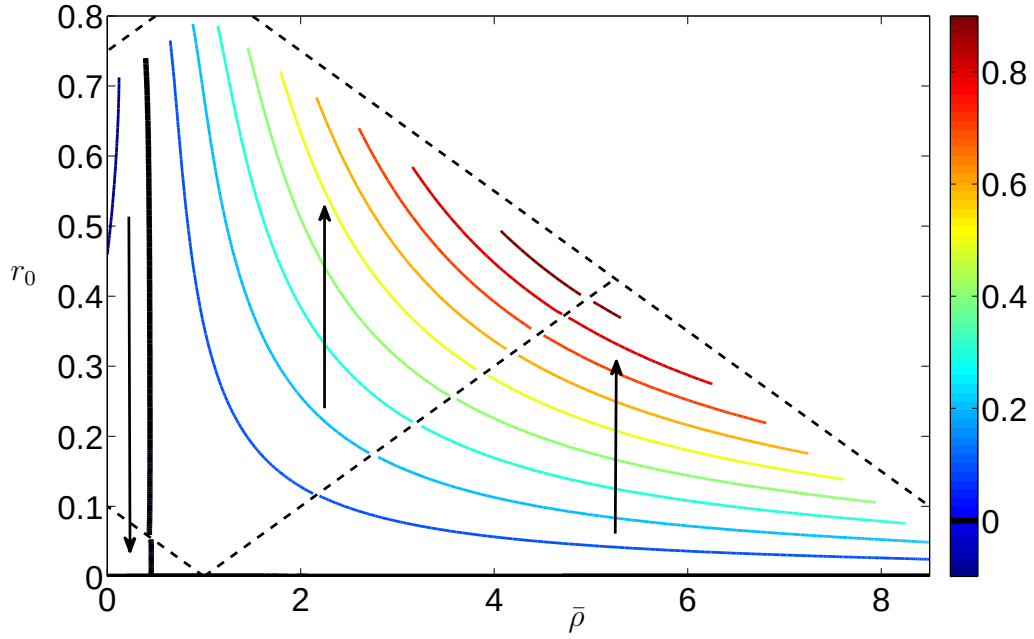


Figure 5.14: The contours indicate the value of r_{0T} for varying $\bar{\rho}$ and r_0 , taking $\bar{B} = 0.1(\bar{\rho} - 1)$, $b = 0.15$, and $K = 0.1$. The solid black line denotes the critical line $r_{0T} = 0$. The arrows denote the sign of r_{0T} in each region by pointing in the direction that r_0 will change. The exterior dashed black lines denote where the TC will hit the bioreactor edge, and the interior dashed lines denote the boundary between settling and orbital motion.

The parameters used in Figure 5.16 are the most physically relevant cases. In this Figure the TC behaviour is more straightforward, and we see that a TC located anywhere within the bioreactor will drift out to the bioreactor edge. The drift to the edge will be slower than in Figures 5.14 and 5.15 as r_{0T} is smaller. In addition, the discontinuities between orbital and settling motion are more apparent here.

Therefore, we see that on the long timescale it is very difficult to obtain a limit cycle within the settling regime. This is unfortunate for experimentalists, as we suggested in §5.4.1 that the settling regime promotes nutrient mixing more than the orbital regime. For the three different values of $\bar{B}/(\bar{\rho} - 1)$ we considered, we were only able to obtain settling orbits for a narrow band of values of $\bar{\rho}$ in the case where $\bar{B}/(\bar{\rho} - 1) = 1$. As being in orbital motion will result in a minimal nutrient transfer and eventually hitting the bioreactor edge, the next best option is to tend to the steady point. For the physically relevant case of $\bar{B}/(\bar{\rho} - 1) = 10$, even this is not possible. For the less physically relevant cases of $\bar{B}/(\bar{\rho} - 1) = 0.1, 1$, it is only possible to reach the steady regime if $\bar{\rho} \lesssim 0.45$. As with the settling case, this is difficult to

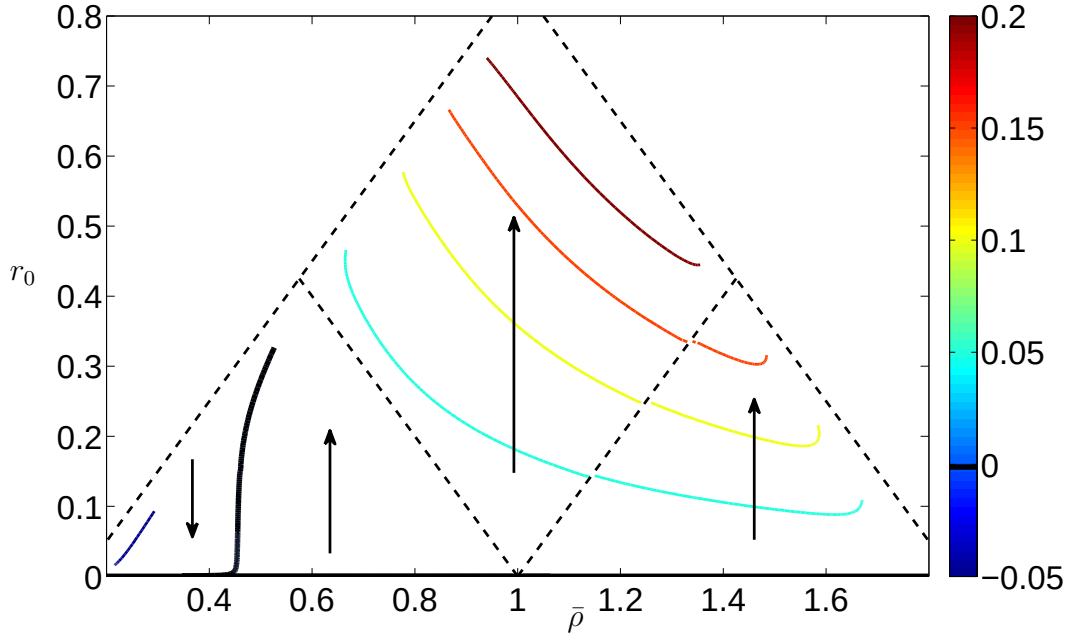


Figure 5.15: The contours indicate the value of r_{0T} for varying $\bar{\rho}$ and r_0 , taking $\bar{B} = \bar{\rho} - 1$, $b = 0.15$, and $K = 0.1$. The solid black line denotes the critical line $r_{0T} = 0$. The arrows denote the sign of r_{0T} in each region by pointing in the direction that r_0 will change. The exterior dashed black lines denote where the TC will hit the bioreactor edge, and the interior dashed lines denote the boundary between settling and orbital motion.

impose experimentally, as it requires the solid matrix within the porous scaffold to be far lighter than the surrounding fluid.

To conclude, in this Chapter we derived equations of motion for the TC that were coupled to the fluid flow determined in Chapters 2–4. To make physical sense of these equations, we formulated and analyzed a toy model for the TC motion. We then analyzed the full problem via the method of multiple scales, plotting leading-order solutions for the TC trajectories and streamlines using the flow results determined in Chapter 2. We then performed a multiple-scale analysis to determine the long-time drift from the short-time periodic TC trajectory. This required calculating integrals via numerical quadrature, which is far less computationally intensive than would be required for numerically solving the entire system. We then presented these results for the TC drift for various parameter values which illustrated the typical behaviour that may be observed experimentally, comparing them with analytic results where possible to verify the simulations.

It is our recommendation that experimentalists pay careful attention to the param-

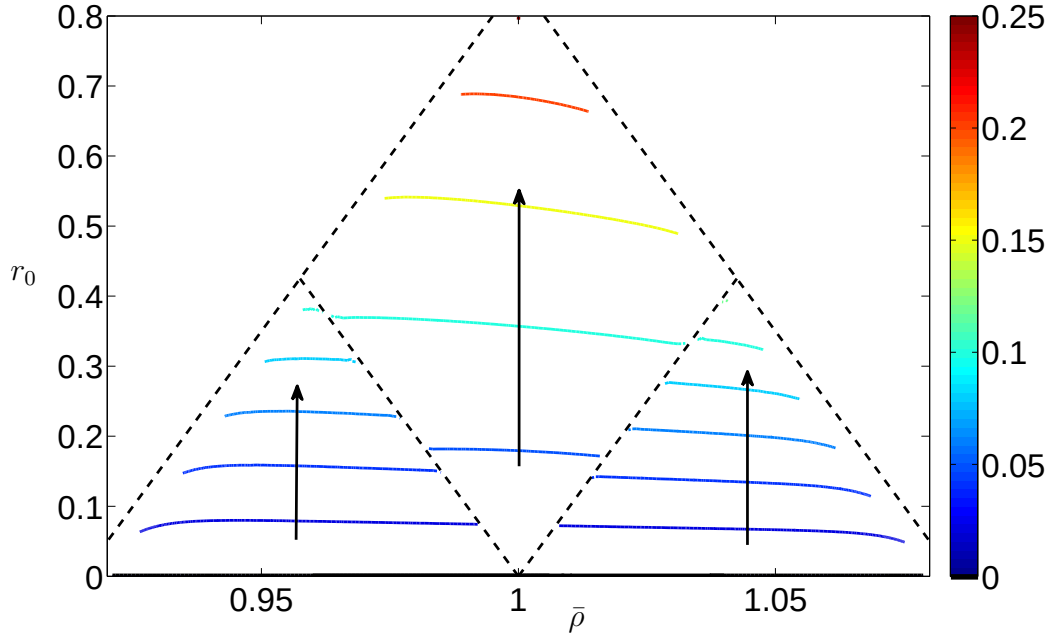


Figure 5.16: The contours indicate the value of r_{0T} for varying $\bar{\rho}$ and r_0 , taking $\bar{B} = 10(\bar{\rho} - 1)$, $b = 0.15$, and $K = 0.1$. The solid black line denotes the critical line $r_{0T} = 0$. The arrows denote the sign of r_{0T} in each region by pointing in the direction that r_0 will change. The exterior dashed black lines denote where the TC will hit the bioreactor edge, and the interior dashed lines denote the boundary between settling and orbital motion.

eter values they are working with, and adjust the initial position of the TC accordingly. The spiralling of the TC can occur due to inertia on a timescale of $t = O((\epsilon_2 \epsilon Re)^{-1})$, and therefore not just due to the tissue growth as hypothesized by experimentalists. Using experimental parameters, the timescale of drift due to inertia corresponds to hours, whereas tissue growth can take tens of hours, if not days.

We note that experimental data would be required to validate any of the predictions made by our model, especially to achieve the eventual goal of having the model used by experimentalists. It is our hope that experiments could be carried out by using a non-reactive porous material with no tissue cells for the TC. This would explore the effect of inertia and remove the complicating effect of TC growth, thus providing a useful comparison for our model. Similar experiments have been carried out for a solid (unreactive) TC in Cummings *et al.* [19], and it would be immensely useful to have similar experimental data with which to compare our model.

In the next Chapter, we consider nutrient transport within the bioreactor system, and discuss the physical implications of our results.

Chapter 6

Nutrient transport

In the thesis so far, we have considered the coupled problem of the flow through a rotating high-aspect-ratio vessel (HARV) bioreactor that contains a free-moving porous tissue construct (TC). As a result, we are now able to describe the flow of the nutrient-rich fluid and the motion of the TC.

In this Chapter, we consider how nutrient is transported around the bioreactor. In §6.1, we consider nutrient transport due to advection within the HARV bioreactor, and in §6.2 we consider how the additional effects of diffusion and nutrient uptake affect the nutrient distribution in a simpler toy model (that still considers advection). We begin with advective transport by considering the particle paths within the bioreactor. This case is the physically most important to consider because advection is the dominant nutrient transport mechanism within a HARV bioreactor at typical operating conditions [18].

6.1 Advective transport

In Chapter 2 we determine the fluid flow within a rotating HARV bioreactor for a prescribed TC motion, and in Chapter 5 we determine the TC motion. We now use the leading-order analytic results from both Chapters to investigate the particle path problem. By a ‘particle’, we mean a particle in the fluid with position vector $\mathbf{x}(t) = X(t)\mathbf{e}_X + Y(t)\mathbf{e}_Y$ with respect to the rotating frame, which is advected by, but does not alter, the flow. We use the same notation and nondimensionalization that is used in Chapters 2 and 5 and scale $|\mathbf{x}| \sim a$, the bioreactor radius. In this section we work at leading order in the outer-flow regions, and drop the subscript 0 (denoting leading-order terms) for convenience. As there is no fluid velocity in the z -direction at leading order in the outer regions, we work with the fluid flow averaged

over the z -direction and consider motion in a two-dimensional plane.

Essentially, in the inertial frame, we solve the dimensionless problem

$$\frac{d\mathbf{x}}{dt} = \begin{cases} \int_0^1 \mathbf{u}_{\text{LF}} dz & \text{if } \mathbf{x} \text{ is outside the TC,} \\ \int_0^1 \mathbf{U}_{\text{LF}} dz & \text{if } \mathbf{x} \text{ is inside the TC,} \end{cases} \quad (6.1)$$

where $\mathbf{x}$ is the position vector of the particle, $\mathbf{u}_{\text{LF}}$ is the fluid velocity in the bulk flow, and we emphasise that $\mathbf{U}_{\text{LF}}$ is the *pore velocity* in the inertial frame and not $\mathbf{Q}_{\text{LF}}$, which is the Darcy velocity in the inertial frame (the difference is discussed in Appendix A). From (A.3), $\mathbf{Q}_{\text{LF}}$ and $\mathbf{U}_{\text{LF}}$ are related via

$$\mathbf{Q}_{\text{LF}} = \phi \mathbf{U}_{\text{LF}} + (1 - \phi) \mathbf{V}_{\text{TC}}, \quad (6.2)$$

where $\phi \in [0, 1]$ is the pore fraction of the TC (assumed constant), and $\mathbf{V}_{\text{TC}}$ is the velocity of the TC defined in (2.1).

We start by working in the rotating frame, though end up converting the governing equations to the bipolar coordinate system introduced in §2.4.1. This is because the majority of our vectors are in terms of $\mathbf{e}_X$ and $\mathbf{e}_Y$, but the reduced pressures, p and P , are functions of the bipolar coordinates $\alpha(t)$ and $\beta(t)$, and inverting the bipolar transformation (2.40) so that $\alpha(t)$ and $\beta(t)$ can be represented in terms of $X(t)$ and $Y(t)$ is a nonlinear task.

As we are in a rotating frame, there is a contribution to the particle velocity from the effect of the rotation

$$\frac{d\mathbf{x}}{dt} = \frac{dX}{dt} \mathbf{e}_X + \frac{dY}{dt} \mathbf{e}_Y + \dot{\varphi} (-Y \mathbf{e}_X + X \mathbf{e}_Y), \quad (6.3)$$

and from (2.5), (2.27a,b), and (2.35), we see that the averaged flows in the inertial frame are given by

$$\int_0^1 \mathbf{u}_{\text{LF}} dz = -Y \mathbf{e}_X + X \mathbf{e}_Y - \frac{1}{12} \nabla p, \quad (6.4a)$$

$$\int_0^1 \mathbf{U}_{\text{LF}} dz = \mathbf{V}_{\text{TC}} - \frac{K}{\phi} \nabla P, \quad (6.4b)$$

Hence, outside the TC we have

$$\dot{X} \mathbf{e}_X + \dot{Y} \mathbf{e}_Y = (1 - \dot{\varphi}) (-Y \mathbf{e}_X + X \mathbf{e}_Y) - \frac{1}{12} \nabla p, \quad (6.5a)$$

and inside the TC we have

$$\dot{X} \mathbf{e}_X + \dot{Y} \mathbf{e}_Y = \dot{R} \mathbf{e}_X + (\omega - \dot{\varphi}) (-Y \mathbf{e}_X + (X - R) \mathbf{e}_Y) - \frac{K}{\phi} \nabla P, \quad (6.5b)$$

where p and P are given in (2.45) and (2.46) respectively.

We now convert (6.5) into the bipolar coordinate system. The transformation from (X, Y) to (α, β) is given in (2.40) and (2.41), and several useful transformation quantities are given in Appendix B. Before rewriting the right-hand side of (6.5) with respect to the bipolar coordinate system, we start by calculating $\dot{X}$ and $\dot{Y}$. As α_1 depends on $R(t)$, this must be considered along with α and β . To this end, we use (B.5a) to deduce

$$\frac{d}{dt}(\cosh \alpha_1) = -\frac{\dot{R}b}{R} \cosh \alpha_2, \quad (6.6)$$

and by using $\cosh^2 z - \sinh^2 z = 1$, we also obtain

$$\frac{d}{dt}(\sinh \alpha_1) = \coth \alpha_1 \frac{d}{dt}(\cosh \alpha_1) = -\frac{\dot{R}b}{R} \coth \alpha_1 \cosh \alpha_2. \quad (6.7)$$

We can now evaluate $\dot{X}$ and $\dot{Y}$

$$\dot{X} = \frac{\sinh \alpha_1 (CC\dot{\alpha} + SS\dot{\beta})}{(\cosh \alpha - \cos \beta)^2} - \frac{\dot{R} \coth \alpha_2}{R} \left(\sinh \alpha_1 - \frac{\sinh \alpha \cosh \alpha_1}{\cosh \alpha - \cos \beta} \right), \quad (6.8a)$$

$$\dot{Y} = \frac{\sinh \alpha_1 (-SS\dot{\alpha} + CC\dot{\beta})}{(\cosh \alpha - \cos \beta)^2} - \frac{\dot{R} \coth \alpha_2}{R} \left(\frac{\cosh \alpha_1 \sin \beta}{\cosh \alpha - \cos \beta} \right), \quad (6.8b)$$

where

$$SS(\alpha, \beta) = \sinh \alpha \sin \beta, \quad (6.9a)$$

$$CC(\alpha, \beta) = \cosh \alpha \cos \beta - 1. \quad (6.9b)$$

6.1.1 Particle path outside the tissue construct

We first consider particle paths outside the TC, governed by (6.5a). Using (B.8) and (B.10a), we see that

$$\nabla p(\alpha, \beta) = \frac{1}{\sinh \alpha_1} ((CCp_\alpha + SS p_\beta) \mathbf{e}_X + (CCp_\beta - SS p_\alpha) \mathbf{e}_Y). \quad (6.10)$$

Substituting (2.40), (6.8) and (6.10) into (6.5a) and taking components in the $\mathbf{e}_X$ and $\mathbf{e}_Y$ directions, we determine governing equations for $\dot{\alpha}$ and $\dot{\beta}$

$$\dot{\alpha} = f_{\text{out}}(\alpha, \beta, t) - \frac{(\cosh \alpha - \cos \beta)^2}{12 \sinh^2 \alpha_1} p_\alpha, \quad (6.11a)$$

$$\dot{\beta} = g_{\text{out}}(\alpha, \beta, t) - \frac{(\cosh \alpha - \cos \beta)^2}{12 \sinh^2 \alpha_1} p_\beta, \quad (6.11b)$$

which govern the particle paths with respect to the bipolar coordinate system, and where f_{out} and g_{out} are

$$f_{\text{out}}(\alpha, \beta, t) = (1 - \dot{\varphi}) \sin \beta (\cosh \alpha - \coth \alpha_1 \sinh \alpha) + \frac{\dot{R}}{R} \coth \alpha_2 ((\cosh \alpha - \coth \alpha_1 \sinh \alpha) \cos \beta - 1), \quad (6.12a)$$

$$g_{\text{out}}(\alpha, \beta, t) = (1 - \dot{\varphi}) ((\coth \alpha_1 \cosh \alpha - \sinh \alpha) \cos \beta - \coth \alpha_1) + \frac{\dot{R}}{R} \coth \alpha_2 \sin \beta (\sinh \alpha - \cosh \alpha \coth \alpha_1), \quad (6.12b)$$

noting that α_1 and α_2 are functions of $R(t)$. We also note that the equations for rigid-body motion within the (α, β) coordinate system are given by $\dot{\alpha} = f_{\text{out}}$ and $\dot{\beta} = g_{\text{out}}$.

6.1.2 Particle path inside the tissue construct

We now consider particle paths inside the TC, governed by (6.5b). Similarly to §6.1.1, we note that

$$\nabla P(\alpha, \beta) = \frac{1}{\sinh \alpha_1} ((CCP_\alpha + SSP_\beta) \mathbf{e}_X + (CCP_\beta - SSP_\alpha) \mathbf{e}_Y). \quad (6.13)$$

Substituting (2.40), (6.8), and (6.10) into (6.5b) and taking components in the $\mathbf{e}_X$ and $\mathbf{e}_Y$ directions, we determine governing equations for $\dot{\alpha}$ and $\dot{\beta}$

$$\dot{\alpha} = F_{\text{out}}(\alpha, \beta, t) - K \frac{(\cosh \alpha - \cos \beta)^2}{\phi \sinh^2 \alpha_1} P_\alpha, \quad (6.14a)$$

$$\dot{\beta} = G_{\text{out}}(\alpha, \beta, t) - K \frac{(\cosh \alpha - \cos \beta)^2}{\phi \sinh^2 \alpha_1} P_\beta, \quad (6.14b)$$

where F_{out} and G_{out} are

$$F_{\text{out}}(\alpha, \beta, t) = (\omega - \dot{\varphi}) \sin \beta (\cosh \alpha - \coth \alpha_2 \sinh \alpha) + \frac{\dot{R}}{\sinh \alpha_1} (\cosh \alpha \cos \beta - 1) - \frac{\dot{R}}{R} \coth \alpha_2 \left(1 + \frac{\cos \beta \sinh(\alpha - \alpha_1)}{\sinh \alpha_1} \right), \quad (6.15a)$$

$$G_{\text{out}}(\alpha, \beta, t) = (\omega - \dot{\varphi}) (\coth \alpha_2 (\cos \beta \cosh \alpha - 1) - \cos \beta \sinh \alpha) + \frac{\dot{R}}{\sinh \alpha_1} \sinh \alpha \sin \beta - \frac{\dot{R}}{R} \coth \alpha_2 \frac{\sin \beta \cosh(\alpha - \alpha_1)}{\sinh \alpha_1}, \quad (6.15b)$$

noting that the equations for moving in rigid-body motion with the TC within the (α, β) coordinate system are given by $\dot{\alpha} = F_{\text{out}}$ and $\dot{\beta} = G_{\text{out}}$.

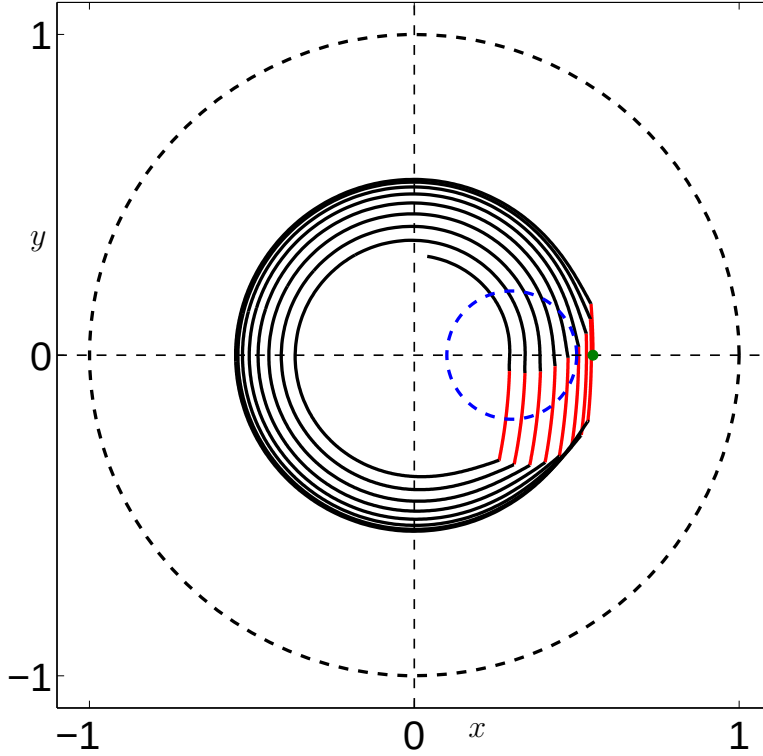


Figure 6.1: Particle path for initial position $(x, y) = (0.55, 0)$ (indicated by a green dot). The path is denoted by a black curve when the particle is outside the TC and a red curve when the TC is inside the TC. The TC starts with centre at $(x, y) = (0.5, 0)$ and its trajectory is marked by a dotted blue line and the bioreactor edge is given by a dotted black line. We use parameter values $\bar{B} = 0.3$, $K = 0.1$, $b = 0.15$, $\phi = 0.1$. We give the results for $t = [0, 16\pi]$, which is equivalent to eight orbits of the TC.

We now have simultaneous ordinary differential equations in $\alpha(t)$ and $\beta(t)$ for a particle both inside and outside the TC, so we can couple these and solve numerically to find particle paths for any given starting position of both the TC and a particle moving with the fluid flow. We give examples of this in Figures 6.1 and 6.2, where we see particle paths over eight orbits of the TC for two starting positions.

In summary, we have constructed a framework to determine how nutrient is advected through the bioreactor and TC via the flow. From this, we could determine experimentally useful quantities, such as the proportion of the fluid within the bioreactor that will enter the TC in a given time. This would allow us to calculate the amount of nutrient that the TC has access to via the mechanism of advection alone. In fact, assuming that the cells within the TC absorb a prescribed fraction of the

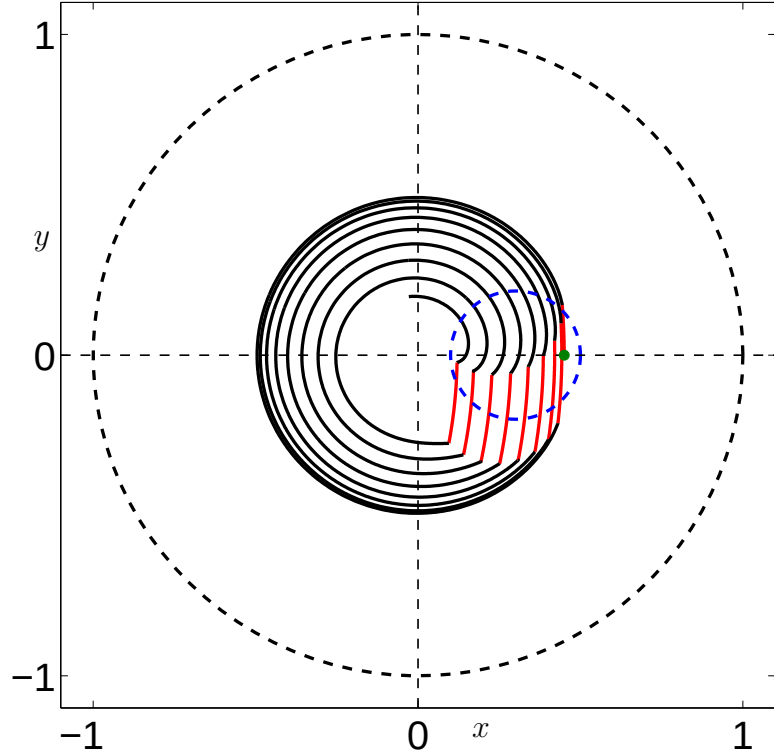


Figure 6.2: Particle path for initial position $(x, y) = (0.45, 0)$ (indicated by a green dot). The path is denoted by a black curve when the particle is outside the TC and a red curve when the TC is inside the TC. The TC starts with centre at $(x, y) = (0.5, 0)$ and its trajectory is marked by a dotted blue line and the bioreactor edge is given by a dotted black line. We use parameter values $\bar{B} = 0.3$, $K = 0.1$, $b = 0.15$, $\phi = 0.1$. We give the results for $t = [0, 16\pi]$, which is equivalent to eight orbits of the TC.

nutrient they are exposed to, it would be possible to calculate the uptake of nutrient within the TC. In the next section, we consider a toy problem that includes this type of proportional nutrient uptake as well as weak diffusion.

We remark that it may be possible to reduce the computations required to determine the above, by numerically constructing a map between particle position at the beginning and end of one TC orbit. As the leading-order flow and trajectory are 2π -periodic, this map is the same for the first orbit as it would be for the n th orbit. It therefore follows that a map between initial particle position and particle position after one TC orbit could be iterated to give the particle position after n orbits of the TC, without having to further calculate the particle motion between iterations. This would enable us to determine the long-time behaviour of the system in a numerically

efficient manner.

6.2 Effect of diffusion and uptake

In this section we consider the effect of diffusion and nutrient uptake for a toy model of flow past an obstacle within an infinite domain. We consider the steady case for the high-Peclet-number limit (corresponding to a small effect of diffusion compared with advection). We highlight a few relevant examples of previous work in the high-Peclet-number regime.

Lynch and Knessl [40, 41] considered the combined effects of advection and diffusion for nutrient transport in a uniform flow through and past through a circular obstacle within an infinite domain; the limit of high Peclet number was considered. For convenience, the flow was assumed to be unaffected by the obstacle, but the nutrient was assumed to be completely absorbed on the obstacle boundary, which resulted in a shadow region behind the obstacle where the nutrient concentration was far less than in the far-field. There are several boundary layers in this problem, near the obstacle and on the shadow boundary, and the authors solved for the concentration in each region of interest.

A lot of previous work on modelling nutrient transport and uptake within bioreactors has been numerical e.g. Lappa [35], but the example most relevant to our work is from Cummings and Waters [18], where the nutrient problem is considered analytically for a solid TC within a HARV bioreactor. The problem considered is in the steady regime, where the TC is stationary with respect to the laboratory frame. The Peclet number is very large so the nutrient is mainly advected with the flow, but diffusion acts to smooth out the concentration gradient induced by the nutrient uptake which occurs on the boundary of the solid TC at a rate proportional to the local nutrient concentration. The authors use this model to make predictions on the rate of tissue growth. To calculate the effect of the processes described above, the authors exploit the separation of timescales to decouple each process and investigate each effect in turn.

We build on these models by considering a porous obstacle and consider nutrient uptake within the entire obstacle rather than just on the boundary. We proceed by discussing the appropriate governing equations and boundary conditions for this problem. We then form dimensionless variables and give the resulting equations. We first consider an obstacle with circular cross-section, then extend the analysis to an obstacle with a general cross-section, both within a Hele-Shaw cell. In both cases

we take the typical half-length of the porous obstacle (which we also refer to as the tissue construct or ‘TC’) to be L (which is the exact radius in the cylindrical case), and the height of the TC and Hele-Shaw cell to be ϵL . Therefore, the TC completely fills the height of the Hele-Shaw cell. We use a Cartesian coordinate system (x, y, z) with corresponding unit vectors $\mathbf{e}_x$, $\mathbf{e}_y$ and $\mathbf{e}_z$, and the Hele-Shaw cell height varies in the z -direction.

The bulk flow is governed by the incompressible steady Navier-Stokes equations

$$\rho(\mathbf{u} \cdot \nabla) \mathbf{u} = -\nabla p + \mu \nabla^2 \mathbf{u}, \quad \nabla \cdot \mathbf{u} = 0, \quad (6.16a, b)$$

where $\mathbf{u} = u\mathbf{e}_x + v\mathbf{e}_y + w\mathbf{e}_z$ is the bulk fluid velocity, p is the pressure, ρ is the fluid density, and μ is the fluid viscosity. The flow within the TC is incompressible and satisfies the Darcy equations

$$\phi \mathbf{U} = -\frac{k}{\mu} \nabla P, \quad \nabla \cdot (\phi \mathbf{U}) = 0, \quad (6.17a, b)$$

where $\mathbf{U} = U\mathbf{e}_x + V\mathbf{e}_y + W\mathbf{e}_z$ is the *pore velocity* (and not the Darcy velocity) of the interior fluid (used so that the concentration can be taken as continuous across the TC boundary), P is the interior fluid pressure, $\phi \in [0, 1]$ is the porosity of the TC, and k is the experimentally determined permeability of the TC.

We assume that the nutrient is dissolved within the fluid, and can therefore be represented by its concentration $c(x, y)$. For simplicity, we ignore any effect of Taylor dispersion, and look for a solution of c which does not vary in z . We model nutrient transport in the bulk and porous flow by a standard advection-diffusion-reaction equation

$$\mathbf{u} \cdot \nabla c = D \nabla^2 c + F(\mathbf{x}, c), \quad (6.18)$$

where D is the diffusion coefficient, and $F(\mathbf{x}, c)$ is an uptake function. We use the following form for the sink function, assuming that nutrient uptake occurs solely within the porous region, and is proportional to the concentration

$$F(\mathbf{x}, c) = \begin{cases} -\eta c & \text{inside the TC,} \\ 0 & \text{outside the TC,} \end{cases} \quad (6.19)$$

which is a linearization of the Michaelis-Menton uptake rate typically used, corresponding to a large saturation limit of the cells (with respect to nutrient concentration); our implicit assumption is that this limit is never approached.

The boundary conditions on the Hele-Shaw cell walls are no-slip/flux in the bulk flow, and no-flux in the porous region on $z = 0, \epsilon L$

$$\mathbf{u} = \mathbf{0} \quad \text{outside the TC} \quad \text{on } z = 0, \epsilon L, \quad (6.20a)$$

$$W = 0 \quad \text{inside the TC} \quad \text{on } z = 0, \epsilon L. \quad (6.20b)$$

The boundary conditions for the flow at the interface are those given in (2.11), and we delay their discussion in this section until we have taken the asymptotic limit of small aspect-ratio and small reduced Reynolds number. In the far-field, we impose a prescribed concentration c_∞ and pressure gradient $-12(\mu U_\infty)/(\epsilon L)^2$ (which drives a far-field flow with magnitude U_∞) as $|\mathbf{x}| \rightarrow \infty$, given by

$$c \rightarrow c_\infty, \quad p \rightarrow -12 \frac{\mu U_\infty}{(\epsilon L)^2} x. \quad (6.21a, b)$$

We nondimensionalize as follows

$$\left. \begin{aligned} (x, y, z) &= L(x^*, y^*, \epsilon z^*), & c &= c_\infty c^*, \\ (u, v, w) &= U_\infty(u^*, v^*, \epsilon w^*), & (U, V, W) &= U_\infty(U^*, V^*, \epsilon W^*), \\ (p, P) &= \frac{\mu U_\infty}{\epsilon^2 L}(p^*, P^*). \end{aligned} \right\} \quad (6.22)$$

where asterisks denote dimensionless quantities, and we highlight that the lengthscale is due to the TC and not any Hele-Shaw lengthscale. We immediately drop the asterisks for convenience.

The bulk flow equations (6.16) become

$$\epsilon^2 Re (\mathbf{u} \cdot \nabla) u = -p_x + \epsilon^2 \nabla_\perp^2 u + u_{zz}, \quad (6.23a)$$

$$\epsilon^2 Re (\mathbf{u} \cdot \nabla) v = -p_y + \epsilon^2 \nabla_\perp^2 v + v_{zz}, \quad (6.23b)$$

$$\epsilon^4 Re (\mathbf{u} \cdot \nabla) w = -p_z + \epsilon^4 \nabla_\perp^2 w + \epsilon^2 w_{zz}, \quad (6.23c)$$

$$\nabla \cdot \mathbf{u} = 0, \quad (6.23d)$$

where $Re = (\rho U_\infty L)/\mu$, and the scalar operator $\nabla_\perp^2 = \partial_{xx} + \partial_{yy}$. The Darcy flow equations (6.17) become

$$U = -K P_x, \quad (6.24a)$$

$$V = -K P_y, \quad (6.24b)$$

$$\epsilon^2 W = -K P_z, \quad (6.24c)$$

$$\nabla \cdot \mathbf{U} = 0, \quad (6.24d)$$

where $K = k/(\phi(\epsilon L)^2)$ (which is different to previous Chapters by a factor of ϕ^{-1}) is taken to be $O(1)$ to keep as many terms in at leading-order as possible. The concentration equation (6.18) becomes

$$\mathbf{u} \cdot \nabla c = Pe^{-1} \nabla^2 c + f(\mathbf{x}, c), \quad (6.25)$$

where $Pe = (U_\infty L)/D$ is the Peclet number (a measure of advective to diffusive nutrient transport), and f is the dimensionless sink function given by

$$f(\mathbf{x}, c) = \begin{cases} -\lambda c & \text{inside the TC,} \\ 0 & \text{outside the TC,} \end{cases} \quad (6.26)$$

where $\lambda = \eta L/U_\infty$, and we assume that $\lambda = O(1)$ to retain as many terms in at leading-order as possible.

The far-field conditions are given by

$$c \rightarrow 1, \quad p \rightarrow -12x \quad \text{as } |\mathbf{x}| \rightarrow \infty, \quad (6.27a, b)$$

and the boundary conditions on the Hele-Shaw walls are still given by (6.20) but now evaluated on $z = 0, 1$. We delay discussion of the dimensionless interfacial conditions (2.21) until we have formed the asymptotic limit of small aspect-ratio and small reduced Reynolds number, and have the relevant governing equations. Note that we only consider the leading-order equations, so avoid the use of a subscript 0 for convenience.

We proceed by considering the limit where $\epsilon, \epsilon^2 Re \ll 1$. With this assumption, the bulk flow equations (6.23) become

$$p_x = u_{zz}, \quad p_y = v_{zz}, \quad 0 = -p_z, \quad \nabla \cdot \mathbf{u} = 0, \quad (6.28a, b, c, d)$$

which are equivalent to (2.25) and, using the no-slip/flux conditions (6.20b), are solved by

$$\mathbf{u} = \frac{z(z-1)}{2} \nabla p, \quad 0 = \nabla_\perp^2 p. \quad (6.29a, b)$$

In the same limit, the Darcy equations are solved by (6.24a,b) and

$$W \equiv 0, \quad 0 = \nabla_\perp^2 P. \quad (6.30a, b)$$

From the work in Chapter 4, we note that although the boundary conditions (2.21) are satisfied within a region close to the TC interface, the correct coupling conditions to impose on the outer regions considered in this section are given in (4.90). Therefore,

the relevant forms of the boundary conditions on the bulk-porous interface are given by

$$\int_0^1 \mathbf{u} \cdot \mathbf{n} \, dz = \phi \int_0^1 \mathbf{U} \cdot \mathbf{n} \, dz, \quad p = P. \quad (6.31a, b)$$

We note that the effects of the boundary layers close to the interface are small, and will not affect the leading-order concentration.

6.2.1 Flow past circular cylinder

We now consider flow in a Hele-Shaw cell past a porous cylinder (TC) with circular cross-section (of dimensionless radius 1) in an infinite domain. Therefore, the cylinder boundary is located at $r = 1$, and we now work in standard cylindrical polar coordinates (r, θ, z) , with the origin located at the TC centre projected onto $z = 0$ for convenience.

To determine the nutrient distribution, we require knowledge of the flow. The solution to the coupled set of equations (6.29b) and (6.30b) with boundary conditions (6.31) on $r = 1$ and (6.27b) as $r \rightarrow \infty$ is

$$p = -12\left(r + \frac{A}{r}\right) \cos \theta, \quad P = Br \cos \theta. \quad (6.32a, b)$$

where $A = (1 - 12\phi K)/(1 + 12\phi K)$ and $B = -24/(1 + 12\phi K) < 0$. Similarly to §6.1, we simplify the problem by working with the variables averaged over the z -direction and considering motion in a two-dimensional plane. Therefore, using (6.29a) and (6.32a) in the bulk flow we use the averaged velocity $\bar{\mathbf{u}}$ defined as

$$\bar{\mathbf{u}} = \int_0^1 \mathbf{u} \, dz = \mathbf{e}_x - \frac{A}{r^2} (\cos \theta \mathbf{e}_r + \sin \theta \mathbf{e}_\theta), \quad (6.33)$$

and note that, from (6.24a,b) and (6.32b), the flow inside the TC is

$$\mathbf{U} = -KB\mathbf{e}_x, \quad (6.34)$$

which does not vary in z .

Having determined the flow, we are now in a position to investigate the nutrient concentration within the system. We consider the asymptotic limit $Pe \gg 1$ which, outside the obstacle and using the averaged velocity (6.33), turns the governing equation for the nutrient concentration (6.25) into

$$(\bar{\mathbf{u}} \cdot \nabla) c = 0, \quad (6.35)$$

at leading order. Equation (6.35) implies that the concentration is advected with the flow and, as the flow is travelling from negative infinity, the concentration takes its far-field value of $c = 1$ (at leading-order) upstream of the TC.

At leading order within the TC, (6.25) becomes

$$-KBc_x = -\lambda c, \quad (6.36)$$

which is solved by an exponential decay of concentration (as $B < 0$). This decay is proportional to the arc-length of the streamlines inside the TC. As the streamlines are just lines of constant y -value, this is a decay in x , starting at a certain y for each streamline. Formally, this is

$$c(x, y) = \exp\left(\nu\left(x + \sqrt{1 - y^2}\right)\right), \quad \text{for } x^2 + y^2 \leq 1, \quad (6.37)$$

where $\nu = \lambda/(KB) < 0$. From this, we can deduce that on the outflow boundary the concentration is given by

$$c(\sqrt{1 - y^2}, y) = \exp\left(2\nu\sqrt{1 - y^2}\right). \quad (6.38)$$

Moreover, as the concentration equation (6.35) outside the TC implies that the nutrient concentration is constant along streamlines, we can solve the problem for the full domain using a combination of this fact and (6.38). Moving to polar coordinates, (6.38) becomes

$$c(1, \theta_0) = \exp(2\nu \cos \theta_0) \quad \text{on } r = 1, \quad \theta_0 \in [-\pi/2, \pi/2]. \quad (6.39)$$

Furthermore, the harmonic conjugate of the pressure (given in (6.32a)) implies that the streamfunction ψ is

$$\psi = -12\left(r - \frac{A}{r}\right) \sin \theta. \quad (6.40)$$

Therefore, we can determine the concentration downstream of the TC from (6.39) and (6.40). That is, the concentration at any point (r, θ) is given by following the streamline (given by constant values of (6.40)) back to the outflow boundary (where $r = 1$), where it takes the value given by (6.39), and we give an example of the nutrient field (for parameter values $K = 0.1$, $\phi = 0.2$, and $\lambda = 0.1$) in Figure 6.3.

We now determine the concentration distribution as $x \rightarrow \infty$. From (6.40), we see that $\psi \rightarrow -12y$ as $x \rightarrow \infty$, and $\psi = -12(1 - A) \sin \theta_0$ on $r = 1$ (using the same

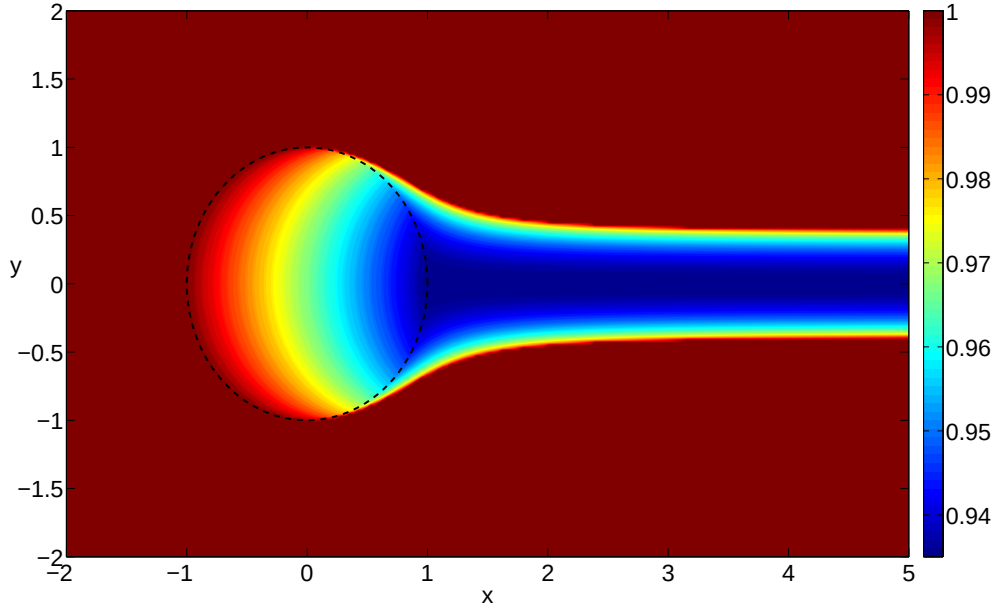


Figure 6.3: The concentration of nutrient under the influence of advection and uptake past and through a porous circular cylinder for parameter values $K = 0.1$, $\phi = 0.2$, and $\lambda = 0.1$. The cylinder is marked by a dashed black line.

notation on the outflow boundary as (6.39)). Therefore, the streamlines from the outflow boundary and the far-field are linked via the relationship

$$y/(1 - A) = \sin \theta_0 \quad \text{as } x \rightarrow \infty. \quad (6.41)$$

As concentration is constant along streamlines (outside the TC), we can use (6.41) to determine the downstream concentration from the outflow boundary concentration distribution (6.39) as $x \rightarrow \infty$, which is given by

$$c \rightarrow g(y) = \begin{cases} 1 & \text{for } y > l, \\ \exp \left(2\nu \left(1 - \left(\frac{y}{l} \right)^2 \right)^{1/2} \right) & \text{for } y \in [-l, l], \\ 1 & \text{for } y < -l, \end{cases} \quad (6.42)$$

where $l = 1 - A$.

We note that (6.42) does not satisfy the far-field condition (6.27a). Physically, we expect this to be satisfied by the effect of diffusion spreading out the concentration over a long lengthscale, i.e. we expect a ‘boundary layer at infinity’. We also expect there to be boundary layers close to the boundary between depleted and non-depleted regions (due to the sharp concentration gradient apparent in (6.42)), but we do not consider these.

We can investigate this boundary layer at infinity by considering the lengthscale $X = Pe^{-1}x$, where $X = O(1)$. One possible experimental set-up is to place several porous TCs within a bioreactor, and determining the far-field nutrient concentration for a single TC may have applications in determining the correct spacing for multiple TCs. In addition, it may be useful to know the far-field concentration profile for a given shape of TC, and we extend this work to consider a general shape in §6.2.2. In the far-field, the velocity $\bar{\mathbf{u}} \rightarrow \mathbf{e}_x$ (from (6.33)), and the concentration equation (6.25) becomes

$$\frac{\partial c}{\partial X} = \frac{\partial^2 c}{\partial y^2} + Pe^{-2} \frac{\partial^2 c}{\partial X^2}, \quad (6.43)$$

therefore a new dominant balance occurs. From a simple Prandtl matching condition, the ‘initial condition’ at $X = 0$ is the far-field condition (6.42) for the convection problem. The leading-order problem is therefore equivalent to solving the heat equation on the right half-plane with initial condition (6.42), which has solution

$$c(X, y) = \frac{1}{\sqrt{4\pi X}} \int_{-\infty}^{\infty} \exp\left(-\frac{(y-s)^2}{4X}\right) g(s) ds. \quad (6.44)$$

We can therefore resolve the concentration field by solving the integral in (6.44) numerically (as shown in Figure 6.4). We can also make several statements about various asymptotic limits.

Firstly, we consider the case where $X = O(1)$ and $|y| \gg 1$. We note that were we to apply Laplace’s method for integrals to (6.44), the leading-order contribution would be from the region near $s = y$. For $|y| \gg 1$, $g(s)$ is analytic in a neighbourhood of $s = y$ and equivalent to 1. Therefore, Laplace’s method implies that $c - 1$ is exponentially small for $X = O(1)$ and $|y| \gg 1$.

We now consider the concentration on the line $y = 0$ for small and large X . After scaling $s \sim 2X^{1/2}$, the concentration on the line $y = 0$ (via (6.44)) is given by

$$c(X, 0) = \frac{1}{\sqrt{\pi}} \int_{-\infty}^{\infty} \exp(-s^2) g(2X^{1/2}s) ds. \quad (6.45)$$

For small X , the main contribution will come from the shadow region directly downstream of the cylinder. As the non-depleted regions (where $g(2X^{1/2}s) = 1$ within the integrand in (6.45)) are now defined at $|s| \geq l/(2X^{1/2}) \gg 1$, their contribution to (6.45) will be exponentially small. As the main contribution to (6.45) will come from a region near $s = 0$, we expand $g(t)$ for small t (via (6.42)) to obtain

$$g(t) \sim \exp\left(2\nu \left(1 - \left(\frac{t}{l}\right)^2\right)^{1/2}\right) = \exp(2\nu) \left(1 - \frac{\nu t^2}{l^2} + O(t^4)\right). \quad (6.46)$$

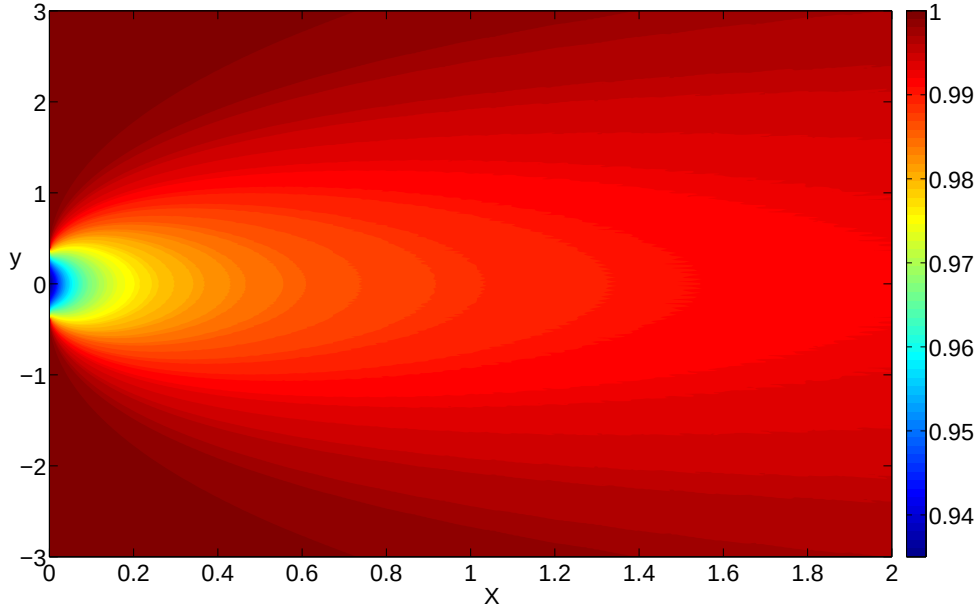


Figure 6.4: The concentration of nutrient (taking the long-term effect of diffusion into account) determined by numerically solving the integral in (6.44) for parameter values $K = 0.1$, $\phi = 0.2$, and $\lambda = 0.1$.

Then, we can use (6.46) in (6.45), and deduce that for small X we obtain

$$c(X, 0) \sim \frac{1}{\sqrt{\pi}} \exp(2\nu) \int_{-\infty}^{\infty} \exp(-s^2) \left(1 - \frac{4\nu X s^2}{l^2} + O(X^2) \right) ds. \quad (6.47)$$

To evaluate the integrals in (6.47), we note that

$$\int_{-\infty}^{\infty} s^{2n} \exp(-s^2) ds = \int_0^{\infty} t^{n-1/2} \exp(-t) dt \quad \text{for } n \in \mathbb{N}, \quad (6.48a)$$

and that the right-hand side of (6.48a) is the Gamma function $\Gamma(z)$, which is defined in general to be

$$\Gamma(z) = \int_0^{\infty} s^{z-1} \exp(-s) ds. \quad (6.48b)$$

We further note that

$$\Gamma\left(n + \frac{1}{2}\right) = \frac{(2n)! \sqrt{\pi}}{4^n (n!)}, \quad (6.48c)$$

for $n \in \mathbb{N}$ [56]. The equation (6.48c) is a famous result for $n = 0$ (most easily evaluated via the left-hand side of (6.48a)), and the full result for (6.48c) follows via induction, using the property $\Gamma(z + 1) = z\Gamma(z)$.

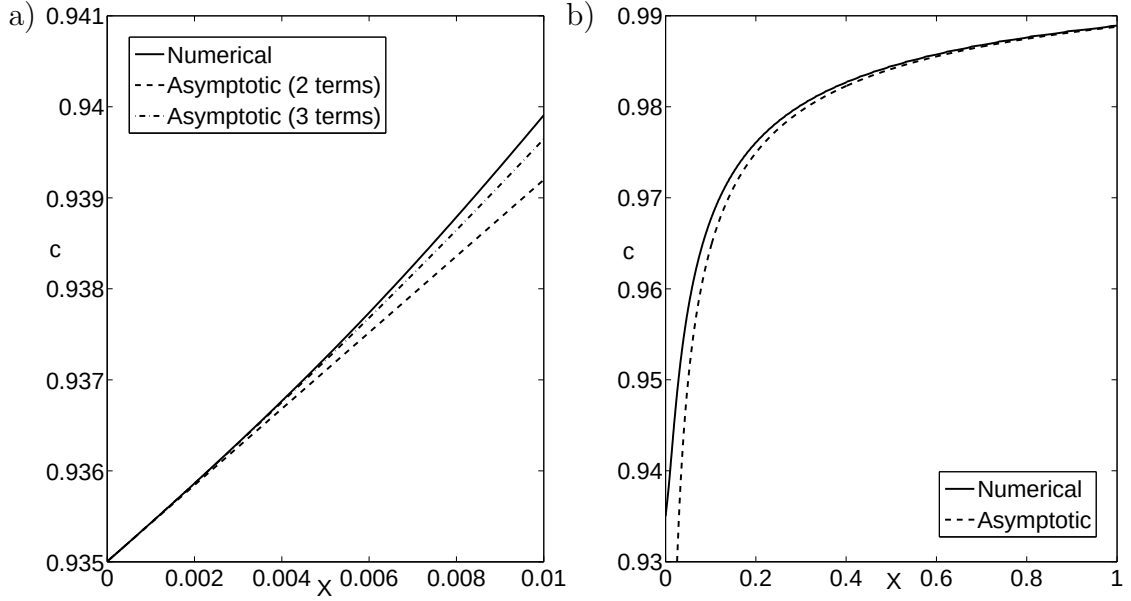


Figure 6.5: A comparison of asymptotic to numerical solutions for the nutrient field under the effect of diffusion. We use parameter values $K = 0.1$, $\phi = 0.2$, and $\lambda = 0.1$. The numerical solution in both cases is obtained by numerically evaluating the integral (6.45). a) the solution for $X \ll 1$, using (6.49) and (6.64) for the two and three-term asymptotic solutions. b) the solution for $X \gg 1$, using (6.58) for the asymptotic solution.

Using (6.48), the integrals in (6.47) can be integrated exactly to yield

$$c(X, 0) \sim \exp(2\nu) \left(1 - \frac{2\nu X}{l^2} + O(X^2) \right). \quad (6.49)$$

In Figure 6.5a, we compare the numerical and asymptotic solutions for $X \ll 1$. We see that the asymptotic solution very quickly becomes inaccurate, even when using additional terms (which are determined from the general solution in (6.64), calculated in the next section).

The large X case is marginally more complicated. We split the integral (6.45) as follows

$$\begin{aligned} c(X, 0) &= \frac{2}{\sqrt{\pi}} \int_{l/2X^{1/2}}^{\infty} \exp(-s^2) ds \\ &+ \frac{1}{\sqrt{\pi}} \int_{-l/2X^{1/2}}^{l/2X^{1/2}} \exp \left(2\nu \left(1 - 4X \left(\frac{s}{l} \right)^2 \right)^{1/2} \right) \exp(-s^2) ds. \end{aligned} \quad (6.50)$$

and scale the second integral in (6.50) by $s \sim l/(2X^{1/2})$ to obtain

$$c(X, 0) = \frac{2}{\sqrt{\pi}} \int_{l/2X^{1/2}}^{\infty} \exp(-s^2) ds + \frac{l}{\sqrt{4\pi X}} \int_{-1}^1 \exp(2\nu(1-s^2)^{1/2}) \exp\left(-\frac{l^2 s^2}{4X}\right) ds. \quad (6.51)$$

The first integral in (6.51) can be further split as follows

$$\frac{2}{\sqrt{\pi}} \int_{l/2X^{1/2}}^{\infty} \exp(-s^2) ds = \frac{2}{\sqrt{\pi}} \int_0^{\infty} \exp(-s^2) ds - \frac{2}{\sqrt{\pi}} \int_0^{l/2X^{1/2}} \exp(-s^2) ds. \quad (6.52)$$

The first term in (6.52) can be evaluated exactly using (6.48c) (in the case $n = 0$), and the second term can be approximated by expanding the integrand in a Taylor series (recalling that $X \gg 1$), to obtain

$$\frac{2}{\sqrt{\pi}} \int_{l/2X^{1/2}}^{\infty} \exp(-s^2) ds = 1 - \frac{2}{\sqrt{\pi}} \left(\int_0^{l/2X^{1/2}} 1 + O(s^2) ds \right). \quad (6.53)$$

Then, we can integrate (6.53) to yield

$$\frac{2}{\sqrt{\pi}} \int_{l/2X^{1/2}}^{\infty} \exp(-s^2) ds = 1 - \frac{l}{\sqrt{\pi X}} + O(X^{-3/2}). \quad (6.54)$$

We use the large X limit to expand the second exponential in the integrand of the second term in (6.51) via a Taylor series to obtain

$$\int_{-1}^1 \exp(2\nu(1-s^2)^{1/2}) \exp\left(-\frac{l^2 s^2}{4X}\right) ds = \int_{-1}^1 \exp(2\nu(1-s^2)^{1/2}) ds + O(X^{-1}). \quad (6.55)$$

Using Mathematica, the integral on the right-hand side of (6.55) can be written in terms of the modified Bessel function of the first kind I_1 and the modified Struve function L_{-1} as follows

$$\int_{-1}^1 \exp(2\nu(1-s^2)^{1/2}) \exp\left(-\frac{l^2 s^2}{4X}\right) ds = \pi (I_1(2\nu) + L_{-1}(2\nu)) + O(X^{-1}). \quad (6.56)$$

In series form, I_1 and L_{-1} are given by [56]

$$I_1(z) = \frac{z}{2} \sum_{k=0}^{\infty} \frac{(z/2)^{2k}}{k!(k+1)!}, \quad (6.57a)$$

$$L_{-1}(z) = \sum_{k=0}^{\infty} \frac{(z/2)^{2k}}{\Gamma(k+1/2)\Gamma(k+3/2)}. \quad (6.57b)$$

Finally, we can use (6.54) and (6.56) to evaluate (6.51) and determine that, for large X , the concentration on $y = 0$ is given by

$$c(X, 0) \sim 1 - \frac{l}{\sqrt{\pi X}} \left(1 - \frac{\pi}{2} (I_1(2\nu) + L_{-1}(2\nu)) \right) + O(X^{-3/2}), \quad (6.58)$$

and we note that this is algebraically close to the far-field limit of the concentration (where $c \rightarrow 1$) compared to the limit as $|y| \rightarrow \infty$, which is exponentially close. In Figure 6.5b, we compare the numerical and asymptotic solutions for $X \gg 1$. We see that the asymptotic solution is very accurate, even for moderate values of X . In the next section we perform the same far-field analysis for a general shape, but now evaluate the higher-order terms.

6.2.2 General shape

For a general shape, the exact velocity profile will be difficult to obtain analytically, as we are now required to solve the coupled set of equations (6.29b) and (6.30b) with boundary conditions (6.31) on the general TC boundary and (6.27b) as $|\mathbf{x}| \rightarrow \infty$. However, we can make some progress by noting that the flow is uniform in the far-field, thus yielding the governing equation (6.43).

For a given initial condition $c(0, y) = g(y)$, the leading-order problem is solved by (6.44). This initial condition will depend on the shape of the porous obstacle and the uptake of nutrient, but we can make analytic progress in various spatial limits if we assume a fairly general form, such as

$$g(y) = \begin{cases} 1 & |y| > l, \\ h(y) & |y| \leq l, \end{cases} \quad (6.59)$$

where we note that $g(y)$ is not necessarily continuous at $|y| = l$ (e.g. in the case of complete uptake within the TC), but we do assume that $h(y)$ is smooth up to any required derivative (as we wish to Taylor expand), and symmetric around $y = 0$ for simplicity (though the analysis could be extended to the non-symmetric case in a systematic manner). We note that if we were to use a sink function such as (6.26), the nutrient concentration at the outflow boundary of the TC will be an exponential decay with argument proportional to the arc-length of the streamline within the TC.

As we are considering the same asymptotic problem as before, but replacing the given form (6.42) with a general function $h(y)$, the analysis proceeds in the same manner. Therefore, for $|y| \gg 1$ and $X = O(1)$, we use exactly the same argument and obtain the same result: that $c \sim 1 + \text{exponentially small terms}$.

We now consider the line $y = 0$. We can split the limits of integration within the general solution (6.45), to rewrite the solution as

$$c(X, 0) = \frac{2}{\sqrt{\pi}} \int_{l/2X^{1/2}}^{\infty} \exp(-s^2) ds + \frac{1}{\sqrt{\pi}} \int_{-l/2X^{1/2}}^{l/2X^{1/2}} \exp(-s^2) h(2X^{1/2}s) ds. \quad (6.60)$$

We note that the first term in (6.60) is more commonly known as the complementary error function $\text{erfc}(l/(2X^{1/2}))$, defined in general as

$$\text{erfc}(x) = \frac{2}{\sqrt{\pi}} \int_x^{\infty} \exp(-s^2) ds, \quad (6.61)$$

which has asymptotic behaviour [56]

$$\text{erfc}(x) \sim \frac{\exp(-x^2)}{x\sqrt{\pi}} \quad \text{as } x \rightarrow \infty. \quad (6.62)$$

For $X \ll 1$, we can Taylor expand $h(2X^{1/2}s)$ and write (6.60) as

$$c(X, 0) = \text{erfc}\left(\frac{l}{\sqrt{4X}}\right) + \frac{1}{\sqrt{\pi}} \int_{-l/2X^{1/2}}^{l/2X^{1/2}} \exp(-s^2) \sum_{k=0}^{\infty} \frac{(2X^{1/2}s)^k}{k!} \frac{\partial^k h}{\partial y^k} \Big|_{y=0} ds. \quad (6.63)$$

Then, in the $X \ll 1$ limit, we introduce exponentially small errors by extending the range of integration for the integral in (6.63) across the entire real line, and evaluate (6.63) (using (6.62) to approximate the first term, and (6.48) to evaluate the second term) to obtain

$$c(X, 0) \sim \sqrt{\frac{4X}{\pi}} \frac{\exp(-l^2/4X)}{l} + \sum_{k=0}^{\infty} \frac{X^k}{k!} \frac{\partial^{2k} h}{\partial y^{2k}} \Big|_{y=0}, \quad (6.64)$$

where the odd powers of s in the integral vanish by anti-symmetry. We keep the first term in (6.64), even though it is an exponentially small term obtained from the far-field limit of $\text{erfc}(l/(2X^{1/2}))$. This is because it is the contribution from the non-depleted region, and will be the leading order term if $h(y) \equiv 0$ (which occurs in the case of complete uptake), as the exponentially small error terms induced by changing the limits of the integral will also vanish.

We now consider the case where $X \gg 1$. Due to symmetry in the integrand, we note that the first term in (6.60) can be rewritten as

$$\frac{2}{\sqrt{\pi}} \int_{l/2X^{1/2}}^{\infty} \exp(-s^2) ds = 1 - \frac{1}{\sqrt{\pi}} \int_{-l/2X^{1/2}}^{l/2X^{1/2}} \exp(-s^2) ds. \quad (6.65)$$

Then, scaling $s \sim l/(2X^{1/2})$, (6.65) further becomes

$$\frac{2}{\sqrt{\pi}} \int_{l/2X^{1/2}}^{\infty} \exp(-s^2) ds = 1 - \frac{l}{\sqrt{4\pi X}} \int_{-1}^1 \exp(-l^2 s^2/4X) ds. \quad (6.66)$$

Using the same scaling ($s \sim l/(2X^{1/2})$), and defining $\bar{h}(s) = h(ls)$, the second term in (6.60) can be rewritten as

$$\frac{1}{\sqrt{\pi}} \int_{-l/2X^{1/2}}^{l/2X^{1/2}} \exp(-s^2) h(2X^{1/2}s) ds = \frac{l}{\sqrt{4\pi X}} \int_{-1}^1 \exp(-l^2 s^2/4X) \bar{h}(s) ds. \quad (6.67)$$

By combining (6.65) and (6.67), then Taylor expanding the argument of the exponential (using $X \gg 1$), we can rewrite the solution for the concentration (6.60) as

$$c(X, 0) \sim 1 - \frac{l}{\sqrt{4\pi X}} \sum_{k=0}^{\infty} \frac{(-1)^k l^{2k}}{k!(4X)^k} \int_{-1}^1 s^{2k} (1 - \bar{h}(s)) ds, \quad (6.68)$$

for large x . As with the circular obstacle (which is a specific case of this general shape), we note that the decay to the far-field condition is algebraic for large X rather than exponential as is the case when $|y| \rightarrow \infty$.¹

We have therefore determined how diffusion and nutrient uptake affect advection of nutrient dissolved in fluid that moves through and around a porous obstacle in the large Peclet number limit. The nutrient concentration is unchanged until it reaches the obstacle. Inside the TC, the concentration will decay exponentially along the streamlines. When the nutrient leaves the porous obstacle, a shadow region is produced and advected with the fluid. However, on a lengthscale of $O(Pe)$ the effect of diffusion becomes noticeable and acts to smooth out the shadow. We have further shown that the far-field concentration limit is attained algebraically on the line $y = 0$ as $X \rightarrow \infty$, and that the effect of the shadow region on the concentration far from the TC (which never entered the TC) is exponentially small.

Although the problem considered here was a toy problem, it provides physical insight into the smoothing nature of diffusion, and suggests a lengthscale ($x \sim Pe$) over which the effect of diffusion becomes important. The next important step for this model would be to tie it back to the HARV bioreactor problem considered in the rest of this thesis. One way this could be approached is by using the mapping suggested at the end of §6.1 and considering the effect of diffusion upon this map.

¹On a practical note, we remark that for a large (but finite) value of X , there will be some stage within the infinite series representation (6.68) at which the (given) algebraic terms are smaller than the (omitted) exponentially small correction. However, we give all the terms as there is some satisfaction to be gained in writing down the general term in an asymptotic series.

This would be a small effect for every iteration of the map, but it would build up over a long time to smooth the concentration. If the timescale for diffusion was far larger than the timescale for nutrient uptake, the nutrient concentration profile due to the effect of both could be determined by calculating the limiting concentration profile after full nutrient uptake and then calculating the effect of diffusion on this profile. If the timescale for diffusion was far less than the timescale for nutrient uptake, the nutrient concentration will be fairly uniformly distributed. There is a mathematically interesting case when the timescales are similar. This could be tackled by considering the effect of diffusion on the iterative mapping discussed in §6.1, but it is less clear whether analytic progress will be possible in this case. One way to proceed may be to consider a toy model in a finite domain with periodic boundary conditions, as the full moving TC problem may be difficult to implement.

Chapter 7

Conclusions and future work

7.1 Summary of work

In this thesis, we consider the fluid flow and trajectory of a porous tissue construct (TC) within a high-aspect-ratio vessel (HARV) rotating bioreactor and related nutrient transport problems. We refer to the flow outside the TC as the bulk flow (which we assume to be governed by the Navier-Stokes equations with a small reduced Reynolds number), and we refer to the flow inside the TC as the interior fluid or the porous flow (which we assume to be governed by Darcy's equations).

In Chapter 2, we investigate the flow in the bulk and porous 'outer' regions. We refer to the 'inner' regions as the regions close to the interface between bulk and porous flow (within a distance comparable to the bioreactor height). The outer regions are the regions within the bioreactor and TC that do not include the inner regions, and where the lubrication equations are appropriate approximations of the flow at leading order. We determine the outer flows by considering an asymptotic expansion in the (small) reduced Reynolds number, and use boundary conditions that we determine in Chapter 4 to couple the two regions. We solve for the leading-order and first-correction terms by assuming a prescribed motion of the TC. We achieve this analytically by working in the frame rotating with the TC, and using a bipolar transformation to turn the non-concentric circular bulk and porous regions into finite and semi-infinite rectangular regions respectively. We are then able to calculate the fluid pressure (and hence the fluid velocity) within the bioreactor and TC for any prescribed TC motion.

In Chapters 3 and 4 we are concerned with deriving appropriate boundary conditions to couple the outer-flow regions considered in Chapter 2. To this end, in Chapter 3 we consider the canonical problem of flow through a two-dimensional (2D)

channel with stationary walls fully blocked by a permeable obstacle. Using boundary layer theory, we investigate the flow close to the interface where the lubrication approximation breaks down. The intricate structure of the boundary layers is shown to depend on the Reynolds number and, in the case of a large Reynolds number but a small reduced Reynolds number (corresponding to the experimental regime of interest), we find that the boundary layer structure also depends on whether the fluid is travelling into or out of the porous obstacle.

In Chapter 4, we extend the work of Chapter 3 by considering flow past a general three-dimensional (3D) cylindrical porous obstacle within a Hele-Shaw cell with moving walls. As long as the obstacle has a cross-section which is smooth, the local topology around any point on the boundary is equivalent to its tangent plane at leading order. Therefore, the analysis for the 2D problem is similar to this 3D problem. By considering the azimuthal flow (which is new to the 3D problem) and the entrainment that it can induce in the normal flow at higher asymptotic orders, we determine the flow structure for a wide class of obstacles. We obtain two important results. Firstly, we are able to calculate the stress exerted by the fluid on the obstacle boundary and, secondly, we obtain coupling conditions between the outer regions.

In Chapter 5, we investigate the TC motion by constructing a force and torque balance for the TC. As the flow imparts a stress on the TC, the equations of motion for the TC are coupled to the fluid flow. We determine that the leading-order torque is due to the flow in the thin gaps between the flat sides of the TC and bioreactor (which imparts a frictional effect), and hence the TC rotates about its own centre at the same rotation rate as the bioreactor at leading order. For the force balance, the flow in the thin gaps between the flat sides of the TC and bioreactor again contributes at leading order, and we consider the dominant balance where the effect of reduced gravity balances the friction arising from the flow in the thin gaps. We solve the leading-order problem analytically, and deduce that the effect of reduced gravity is to translate the point about which the TC centre orbits. We then consider the effect of inertia upon the TC. Before tackling the full problem, we consider a toy model which captures the key features of the full model. We investigate this toy model analytically, using a multiple-scale analysis, and verify the results by comparing them to numerical solutions. This toy model prepares us for the analysis of the full system by presenting the relevant framework, and highlighting some potential hazards (such as the discontinuity in velocity between various motion regimes). Finally, we analyse the full problem using a multiple-scale analysis, and determine the long-time drift of the TC due to the effect of inertia. We highlight the effect of key parameters (e.g.

the ratio of the TC density to the fluid density) on the long-time behaviour of the TC, and discuss the implications of these results for experimentalists.

Finally, in Chapter 6 we consider the problem of nutrient transport. In the first part, we determine the nutrient transport within the HARV bioreactor solely due to advection. Using the analytic results for the flow and TC trajectory, we derive ODEs for particle paths within the bipolar coordinate system. We neglect the effect of nutrient uptake within the TC in this section, but discuss how it could be included within the framework that we have built, including a suggestion of how to reduce the computational effort required to determine long-term effects. In the second part of this Chapter, we consider the effect of advection, uptake and weak diffusion on nutrient transport by investigating a toy problem with a simplified geometry. We consider the nutrient distribution for flow past a stationary porous cylinder with a circular cross-section within a Hele-Shaw cell. We determine the nutrient uptake within the cylinder, and investigate how weak diffusion acts to replenish the nutrient loss downstream. Finally, we extend the weak diffusion analysis to flow past a stationary porous cylinder with a general cross-section within a Hele-Shaw cell, and determine some asymptotic results for various spatial limits. This Chapter forms the framework for future work beyond the scope of this thesis. It will enable investigation of the long-term nutrient transport (and uptake) problem within the HARV bioreactor, and eventually allow consideration of tissue growth.

7.2 Future work

Whilst we have made significant progress in understanding the fluid mechanics of a HARV bioreactor and the nutrient transport within a simplified system, there are several open questions that follow directly from this work. These are questions of interest for both experimentalists and applied mathematicians.

Perhaps the most easily answerable (within the context of the framework laid out in this thesis) of these questions is what effect does the fluid mechanics have on nutrient delivery within the porous TC, and is there any way in which nutrient delivery can be enhanced? We have provided a framework to calculate the nutrient transport due to advection in §6.1, and it should be possible to combine this with a sink term in the nutrient transport equation (included in §6.2) to model nutrient uptake. In fact, we have used the results from §6.2 to determine that, when nutrient uptake is proportional to nutrient concentration, the uptake of nutrient is proportional to the arc-length of the particle path within the TC.

As it may be numerically expensive to run long-time simulations to determine the nutrient transport, one idea that may speed things up considerably is the iterative mapping suggested in Chapter 6, and we reiterate that idea here. The idea relies on the fact that the TC orbit and resultant fluid flow are 2π -periodic for $t = O(1)$. Due to this periodicity, a map between particle position at the beginning and end of the first TC orbit will also be a map for the same movement in the general n th TC orbit. Therefore, a numerically intensive long-time computation can be reduced to iterating a short-time computation. In fact, if the nutrient concentration for a particle is also tracked, and the fraction of nutrient removed from the particle is proportional to the arc-length of the particle path within the TC (as in §6.2), it will also be possible to determine an iterative map that governs the concentration distribution. It may also be possible to include the effect of diffusion within this iterative map, which will act as a smoothing mechanism for the concentration distribution. However, as the periodic solution for the TC trajectory is not uniformly valid for all time, there will come a point where the accuracy of this iterative map breaks down.

Once the nutrient uptake is fully understood, we can begin to answer a more fundamental question. How does the tissue grow within the HARV bioreactor? To answer this question, the tissue growth must be coupled to the nutrient uptake. The exact details of this coupling will be tissue-dependent, but a first model should consider the case where the tissue growth is proportional to the nutrient uptake. Using the framework of this thesis, the simplest first model would be to assume that the tissue cells occupy a negligible volume, and calculate their growth according to their nutrient uptake. As one assumption in this model was that the cells occupy a negligible volume, this growth will not affect the flow, but the model could take into account the larger nutrient demands from a larger cell population. However, the assumption of negligible cell volume is only physically relevant for the early stages in tissue development, and a more realistic model would take the tissue cell volume into account by considering a multiphase approach, or by modelling the tissue growth as a change in TC permeability. For the second of these ideas, we could use the model in this thesis to consider spatially uniform growth across the entire TC (as this would correspond to the dimensionless permeability K taking a different constant value), but would have to extend the model in order to consider a spatially or temporally-varying permeability. As the timescales involved with fluid flow and tissue growth are well separated, it may suffice to consider permeabilities with a weak spatial or temporal variation, and an asymptotic approach may be possible. Furthermore, as a decrease in local permeability leads to less local flow and hence less nutrient uptake, it

may be possible to analyse the stability of the spatial or temporal variation in tissue growth. We could even follow Cummings and Waters [18] and consider a physical outwards growth of tissue (i.e. enlarging the TC), although physically we only expect a small outwards growth, as the underlying scaffold provides a surface to which the tissue cells can adhere. Further work on tissue growth could involve including various forms of mechanotransduction, e.g. coupling growth to shear stress.

Throughout this thesis, we have made the assumption that the TC has been cultivated within and cut from impermeable sheets. Thus we have not needed to consider flow through the flat sides of the TC. It would be interesting to relax this assumption and consider a fully permeable TC boundary. Preliminary work suggests that there will still be no flow through a large area of the flat sides, and that the main effect of imposing permeability is to reduce the friction that these sides offer. Considering a new dominant balance in (5.23), we find that it is the leading-order pressure acting on the curved boundary which now balances gravity. From the form of the pressure contribution in (5.21), we expect a qualitatively similar trajectory, but the exact quantitative details may be of importance to experimentalists. Furthermore, for an impermeable boundary on the flat sides of the TC, we expect the repellant force that the TC experiences if it moves towards one bioreactor boundary (e.g. as with flow in a squeeze film) to stabilise the TC, and keep the TC an equal distance away from either flat surface of the bioreactor. In the case of a porous boundary, it is not clear whether this force will manifest, and this bears further investigation.

On a related note, it would also be interesting to relax the assumption that the problem is symmetric around $z = h/2$ and, in particular, the stability of the TC about this steady state would bear further study. Intuitively, one might expect the TC to be stable to small perturbations for a small relative movement of the TC to the bioreactor, but to be unstable for a large relative movement. It would be useful to investigate this effect: to check whether this intuition is qualitatively correct, and to obtain quantitative details on the nature of any bifurcation.

We have also assumed throughout this thesis that the TC has a circular cross-section. Though this is often the shape aimed for experimentally, there are likely to be small imperfections in the manufacturing process. It would therefore be interesting to consider the effect of small imperfections upon the flow and TC trajectory. The imperfections could be modelled as a small perturbation to the boundary, in order to estimate how large the perturbations must be to cause significant errors in the model considered in this thesis. Furthermore, the small imperfections may affect the TC growth by changing the flow, and the stability of this process could be investigated.

Finally, there are many interesting canonical problems that are natural extensions to the work in Chapter 3. It would be useful to investigate how the governing equations within the TC affect the coupling conditions between outer regions. In particular, if we were to change the governing equations to the Darcy-Brinkman equations, the higher-order coupling conditions (4.91) may yield slightly different results and there may be additional boundary layers that appear within the TC. The two-dimensional work could be extended from a long porous obstacle to consider a thin porous obstacle (so the boundary layers may not be able to fully form), and this could then be extended to consider a periodic array of thin porous obstacles (which has potential applications in filtration membranes). We could also consider the implications of the interface being slightly curved across the height of the bioreactor. These canonical problems may have applications in broader fields such as separation science, as well as tissue engineering. The three-dimensional problem of flow through and around a three-dimensional cylindrical porous obstacle with a smooth boundary within a Hele-Shaw cell could also be extended. Specifically, to relax the assumptions on the cross-section boundary, drawing on the 2D work described above. Furthermore, investigating the boundary layers induced by flow past a porous wedge may be of canonical interest.

In conclusion, we have developed exciting theoretical results with which to inform experimental work. The combination of these two approaches could lead to an experimentally-validated predictive modelling tool, which could be used to automate the HARV bioreactor operating conditions. The automation would be underpinned via the development of algorithms which would determine how, for example, the rotation rate of the bioreactor should be varied as the TC moves and grows, in order to maintain the ‘optimum’ flow and nutrient distribution.

Appendix A

Darcy flow in a moving frame

In this thesis we work in many different frames of reference, e.g. laboratory, rotating with the tissue construct (TC) around the bioreactor origin, moving with the TC centre, moving with the TC centre and rotating around the TC centre. It is therefore useful to discuss the relationship between these various frames. We also include an explanation of the Darcy and pore velocities, as they are key to understanding the meaning of the dependent variables in a given frame.

We start by defining the Darcy and pore velocities. We take the pointwise velocity within the TC and in the non-moving laboratory frame (which we also refer to as the inertial frame) to be $\mathbf{v}(\mathbf{x}, t)$. Then, in the inertial frame, the Darcy velocity $\mathbf{Q}_{\text{LF}}$, and pore velocity $\mathbf{U}_{\text{LF}}$ are defined as

$$\mathbf{Q}_{\text{LF}}(\mathbf{x}, t) = \frac{\int_{\Omega(\mathbf{x}, t)} \mathbf{v} \, dV}{\int_{\Omega(\mathbf{x}, t)} dV}, \quad \mathbf{U}_{\text{LF}}(\mathbf{x}, t) = \frac{\int_{\Omega_f(\mathbf{x}, t)} \mathbf{v} \, dV}{\int_{\Omega_f(\mathbf{x}, t)} dV}, \quad (\text{A.1a, b})$$

where the integrals are meant as an ensemble average around the point $\mathbf{x}$. The region $\Omega(\mathbf{x}, t)$ is the entire volume considered around $\mathbf{x}$, and the region $\Omega_f(\mathbf{x}, t)$ is the pore volume considered around $\mathbf{x}$; that is, the region consisting of just fluid with no solid matrix. The pore volume fraction is given by

$$\phi = \frac{\int_{\Omega_f(\mathbf{x}, t)} dA}{\int_{\Omega(\mathbf{x}, t)} dA}. \quad (\text{A.2})$$

We assume that the size of the regions $\Omega(\mathbf{x}, t)$ and $\Omega_f(\mathbf{x}, t)$ is small enough that there is a separation of scales between the pointwise velocity and the macroscale variables we end up using, e.g. the Darcy pressure, yet large enough to ensure a continuous field for the velocity. Essentially, this is the same as requiring a separation of scales between the porescale and the macroscale, as is required for any derivation of Darcy's equations using a homogenisation argument (e.g. [49, 78]), and we therefore

we do not require any additional assumptions if we accept that the Darcy equations are a valid model here.

There is a question as to what the pointwise velocity $\mathbf{v}(\mathbf{x}, t)$ should be within the solid matrix (i.e. $\mathbf{x} \in \Omega \setminus \Omega_f$). In order to preserve continuity of velocity, it is sensible to take $\mathbf{v}(\mathbf{x}, t)$ to be the velocity of the solid matrix. That is, if the porous medium is moving with velocity $\mathbf{V}_{\text{TC}}(\mathbf{x}, t)$ (defined for the problem considered in this thesis in (2.1)), then we say $\mathbf{v}(\mathbf{x}, t) = \mathbf{V}_{\text{TC}}(\mathbf{x}, t)$ for $\mathbf{x} \in \Omega \setminus \Omega_f$, and the relationship between velocity and flux becomes

$$\mathbf{Q}_{\text{LF}} = \phi \mathbf{U}_{\text{LF}} + (1 - \phi) \mathbf{V}_{\text{TC}}(\mathbf{x}, t). \quad (\text{A.3})$$

This may seem unusual, but recall that the Darcy velocity is averaged over the entire material, not just the pore space. Hence, the physical interpretation of (A.3) is just that the average velocity of material for a moving TC is the sum of the average velocity of the fluid and the average velocity of the solid.

If we consider the problem within a frame moving with the TC, with Darcy and pore velocity given as $\mathbf{Q} = \mathbf{Q}_{\text{LF}} - \mathbf{V}_{\text{TC}}$ and $\mathbf{U} = \mathbf{U}_{\text{LF}} - \mathbf{V}_{\text{TC}}$, we deduce that (A.3) can be written in the more familiar form

$$\mathbf{Q} = \phi \mathbf{U}. \quad (\text{A.4})$$

We have resolved the question of how the Darcy and pore velocity relate in (A.3), but what is the governing law that relates any one of those quantities to the fluid pressure within the TC? For the frame moving with the TC, the usual relationship is given by Darcy's law for an incompressible fluid

$$\mathbf{Q} = -\frac{k}{\mu} \nabla P, \quad \nabla \cdot \mathbf{Q} = 0, \quad (\text{A.5a, b})$$

where P is the fluid pressure within the porous medium. In (A.5a), P is the averaged interstitial pressure, i.e. the ensemble average over Ω_f , and not the pressure averaged over Ω . The historical reason for the form of (A.5) is that the experimentally measurable quantities are $\mathbf{Q}$ and P [64].

There are many plausible derivations of Darcy's equations using homogenisation techniques [49, 78], but all require a negligible inertia within the TC pores. As we are interested in the effect that inertia has on the TC trajectory, this may seem at odds with our purpose. However, we emphasise that it is the inertia on the TC *pore-scale* that must be negligible. Therefore, for a small enough typical pore size, it is entirely

consistent to neglect the pore inertia of the fluid within the TC, whilst considering the effective inertia of the entire TC. We now formalise this physical argument.

We work in a frame such that the solid matrix in the TC is stationary. Therefore, the Navier-Stokes equations for the pointwise velocity within the TC are

$$\rho \left(\frac{D\mathbf{V}}{Dt} + 2\boldsymbol{\omega} \times \mathbf{V} + \dot{\boldsymbol{\omega}} \times \mathbf{r} + \boldsymbol{\omega} \times (\boldsymbol{\omega} \times \mathbf{r}) + \ddot{\mathbf{a}} \right) = -\nabla p + \mu \nabla^2 \mathbf{V}, \quad (\text{A.6a})$$

$$0 = \nabla \cdot \mathbf{V}, \quad (\text{A.6b})$$

where overdots represent differentiation with respect to time, $\mathbf{V} = \mathbf{v} - \mathbf{V}_{\text{TC}}$, and $D\mathbf{V}/Dt$ is the convective derivative. We form dimensionless parameters as follows

$$\mathbf{r} = r_p \mathbf{r}^*, \quad \mathbf{a} = a \mathbf{a}^*, \quad t = \Omega^{-1} t^*, \quad \boldsymbol{\omega} = \Omega \boldsymbol{\omega}^*, \quad \mathbf{V} = r_p \Omega \mathbf{V}^*, \quad p = \frac{a\mu\Omega}{r_p} p^*, \quad (\text{A.7})$$

where r_p is a typical porescale length, a and Ω are typical scales for the macroscale problem (and are first described in Chapter 2), and the porescale length is small compared to the TC radius, i.e. $\delta_p := r_p/a \ll 1$. We note that the velocity is scaled with $r_p\Omega$ and not $a\Omega$ - this is because we physically expect the typical lengthscale to be the porescale when the surrounding solid matrix is stationary. Further, the pressure is scaled such that

$$\frac{[p]}{a} \sim \frac{\mu[V]}{r_p^2}, \quad (\text{A.8})$$

i.e. the pressure varies on the longer lengthscale and balances the viscous stresses.

Dropping the asterisks for convenience, equation (A.6a) becomes

$$\frac{\delta_p^2 Re}{\epsilon} \left(\frac{D\mathbf{V}}{Dt} + 2\boldsymbol{\omega} \times \mathbf{V} + \dot{\boldsymbol{\omega}} \times \mathbf{r} + \boldsymbol{\omega} \times (\boldsymbol{\omega} \times \mathbf{r}) \right) + \frac{\delta_p Re}{\epsilon} \ddot{\mathbf{a}} = -\frac{1}{\delta_p} \nabla p + \nabla^2 \mathbf{V}, \quad (\text{A.9})$$

where Re is the Reynolds number defined in Chapter 2 as $Re = \epsilon \rho a^2 \Omega / \mu$. Therefore, as long as $\delta_p Re / \epsilon \ll 1$ we can always drop the momentum terms within a porous medium - even if it is moving. From this point, a homogenisation argument to obtain the Darcy equations (as in, e.g. Neuman [49], Whitaker [78]) is permitted and we obtain (A.5). We note that any further scaling of the pressure (as occurs in our macroscale problem) will be absorbed into the permeability constant k , and does not affect any of the above.

We have therefore justified the form of (A.5), and it is a simple task to move from (A.5) back into the inertial frame to obtain the dimensional governing equations for a moving porous medium as follows

$$\mathbf{Q}_{\text{LF}} - \mathbf{V}_{\text{TC}} = -\frac{k}{\mu} \nabla P, \quad \nabla \cdot (\mathbf{Q}_{\text{LF}} - \mathbf{V}_{\text{TC}}) = 0. \quad (\text{A.10a, b})$$

Appendix B

Transforming to bipolar coordinates

For any transformation $(X, Y) \mapsto (\alpha, \beta)$, a system of basis vectors in the new coordinate system can be written as

$$\mathbf{h}_\alpha = \frac{\partial \mathbf{r}}{\partial \alpha}, \quad \mathbf{h}_\beta = \frac{\partial \mathbf{r}}{\partial \beta}, \quad (\text{B.1})$$

where $\mathbf{r} = X\mathbf{e}_X + Y\mathbf{e}_Y$ [62]. To normalise these, we define $h_\alpha = |\mathbf{h}_\alpha|$, and $h_\beta = |\mathbf{h}_\beta|$ which are called ‘scale factors’ for the transformation. Then, we have basis unit vectors in the new coordinate system as follows

$$\mathbf{e}_\alpha = \frac{\mathbf{h}_\alpha}{h_\alpha}, \quad \mathbf{e}_\beta = \frac{\mathbf{h}_\beta}{h_\beta}. \quad (\text{B.2})$$

The general form for the divergence and gradient are given by

$$\nabla \cdot \mathbf{v} = \frac{1}{h_\alpha h_\beta} \left(\frac{\partial}{\partial \alpha} (h_\beta v_\alpha) + \frac{\partial}{\partial \beta} (h_\alpha v_\beta) \right), \quad (\text{B.3a})$$

$$\nabla \phi = \frac{1}{h_\alpha} \frac{\partial \phi}{\partial \alpha} \mathbf{e}_\alpha + \frac{1}{h_\beta} \frac{\partial \phi}{\partial \beta} \mathbf{e}_\beta, \quad (\text{B.3b})$$

where $\mathbf{v}$ is a vector, and ϕ is a scalar. From these, we can see that the Laplacian operator is given by

$$\nabla^2 \phi = \frac{1}{h_\alpha h_\beta} \left(\frac{\partial}{\partial \alpha} \left(\frac{h_\alpha}{h_\beta} \frac{\partial \phi}{\partial \alpha} \right) + \frac{\partial}{\partial \beta} \left(\frac{h_\beta}{h_\alpha} \frac{\partial \phi}{\partial \beta} \right) \right). \quad (\text{B.4})$$

In Section 2.4.1 we transform to bipolar coordinates (α, β) , defined by (2.40) and (2.41). An equivalent definition of α_1 and α_2 is given by

$$\cosh \alpha_1 = \frac{1 + R^2 - b^2}{2R}, \quad \cosh \alpha_2 = \frac{1 - R^2 - b^2}{2Rb}. \quad (\text{B.5a, b})$$

We find that for the bipolar transformation defined in (2.40), we obtain

$$\frac{\partial X}{\partial \alpha} = \frac{\sinh \alpha_1}{(\cosh \alpha - \cos \beta)^2} (\cosh \alpha \cos \beta - 1), \quad (\text{B.6a})$$

$$\frac{\partial X}{\partial \beta} = \frac{\sinh \alpha_1}{(\cosh \alpha - \cos \beta)^2} \sinh \alpha \sin \beta, \quad (\text{B.6b})$$

$$\frac{\partial Y}{\partial \alpha} = -\frac{\sinh \alpha_1}{(\cosh \alpha - \cos \beta)^2} \sinh \alpha \sin \beta, \quad (\text{B.6c})$$

$$\frac{\partial Y}{\partial \beta} = \frac{\sinh \alpha_1}{(\cosh \alpha - \cos \beta)^2} (\cosh \alpha \cos \beta - 1), \quad (\text{B.6d})$$

The scale factors for this transformation are

$$h_\alpha = \frac{\sinh \alpha_1}{\cosh \alpha - \cos \beta}, \quad h_\beta = \frac{\sinh \alpha_1}{\cosh \alpha - \cos \beta}. \quad (\text{B.7})$$

Then, the unit vectors in the positive α and β directions, $\mathbf{e}_\alpha$ and $\mathbf{e}_\beta$ respectively, are

$$\mathbf{e}_\alpha = \frac{(\cosh \alpha \cos \beta - 1)\mathbf{e}_X - \sinh \alpha \sin \beta \mathbf{e}_Y}{\cosh \alpha - \cos \beta}, \quad (\text{B.8a})$$

$$\mathbf{e}_\beta = \frac{\sinh \alpha \sin \beta \mathbf{e}_X + (\cosh \alpha \cos \beta - 1)\mathbf{e}_Y}{\cosh \alpha - \cos \beta}. \quad (\text{B.8b})$$

Rearranging these, we can also deduce that

$$\mathbf{e}_X = \frac{(\cosh \alpha \cos \beta - 1)\mathbf{e}_\alpha + \sinh \alpha \sin \beta \mathbf{e}_\beta}{\cosh \alpha - \cos \beta}, \quad (\text{B.9a})$$

$$\mathbf{e}_Y = \frac{-\sinh \alpha \sin \beta \mathbf{e}_\alpha + (\cosh \alpha \cos \beta - 1)\mathbf{e}_\beta}{\cosh \alpha - \cos \beta}. \quad (\text{B.9b})$$

The useful vector operators (the gradient and Laplacian operator) for the bipolar transformation are then given by

$$\nabla \phi = \frac{\cosh \alpha - \cos \beta}{\sinh \alpha_1} \left(\frac{\partial \phi}{\partial \alpha} \mathbf{e}_\alpha + \frac{\partial \phi}{\partial \beta} \mathbf{e}_\beta \right), \quad (\text{B.10a})$$

$$\nabla^2 \phi = \left(\frac{\cosh \alpha - \cos \beta}{\sinh \alpha_1} \right)^2 \left(\frac{\partial^2 \phi}{\partial \alpha^2} + \frac{\partial^2 \phi}{\partial \beta^2} \right). \quad (\text{B.10b})$$

Appendix C

Calculations for the fluid flow

C.1 Deriving the $O(\epsilon Re)$ flow equations

The $O(\epsilon Re)$ flow equations in Chapter 2 are given by (2.26) and (2.28), and have boundary conditions ((2.29–2.34)b). In this Appendix, we use these equations to derive the governing equations for the bulk and porous pressure. These are the equations considered in (2.50). To aid with this, we use the vector identity

$$\frac{1}{2}\nabla(\mathbf{v} \cdot \mathbf{v}) = \mathbf{v} \times (\nabla \times \mathbf{v}) + (\mathbf{v} \cdot \nabla)\mathbf{v}, \quad (\text{C.1})$$

and the 2D projection of the standard vectors into (X, Y) -space to simplify notation. Therefore $\mathbf{u}_1 = (u_1, v_1, 0)$, $\mathbf{X} = (X, Y, 0)$, and $\nabla = (\partial_X, \partial_Y, 0)$. Then, we can rewrite (2.26a-b) as

$$\dot{\mathbf{u}}_0 + (\mathbf{u}_0 \cdot \nabla)\mathbf{u}_0 + 2\dot{\varphi}\mathbf{e}_z \times \mathbf{u}_0 + \ddot{\varphi}\mathbf{e}_z \times \mathbf{X} - \dot{\varphi}^2\mathbf{X} = -\nabla p_1 + \mathbf{u}_{1zz}, \quad (\text{C.2})$$

From (2.35a), we note that

$$\dot{\mathbf{u}}_0 + \ddot{\varphi}\mathbf{e}_z \times \mathbf{X} = f_1(z)\nabla\dot{p}_0, \quad (\text{C.3a})$$

and using (C.1) we deduce that

$$(\mathbf{u}_0 \cdot \nabla)\mathbf{u}_0 = \frac{1}{2}\nabla(\mathbf{u}_0 \cdot \mathbf{u}_0) + 2(1 - \dot{\varphi})\mathbf{e}_z \times \mathbf{u}_0. \quad (\text{C.3b})$$

We can simplify the convective derivative in (C.3b) by substituting in (2.35a) to obtain

$$\frac{1}{2}\nabla(\mathbf{u}_0 \cdot \mathbf{u}_0) = (1 - \dot{\varphi})^2\mathbf{X} + (1 - \dot{\varphi})f_1(z)\nabla((\mathbf{e}_z \times \mathbf{X}) \cdot \nabla p_0) + \frac{(f_1(z))^2}{2}\nabla|\nabla p_0|^2 \quad (\text{C.3c})$$

Finally, we also note that

$$\mathbf{e}_z \times \mathbf{u}_0 = -(1 - \dot{\varphi})\mathbf{X} - f_1(z)\nabla \times (p_0\mathbf{e}_z), \quad (\text{C.3d})$$

Then, substituting (C.3) into (C.2), we obtain

$$\mathbf{u}_{1zz} = \mathbf{A}(\mathbf{X}, t) + f_1(z)\mathbf{B}(\mathbf{X}, t) + (f_1(z))^2\mathbf{C}(\mathbf{X}, t), \quad (\text{C.4a})$$

$$\mathbf{A}(\mathbf{X}, t) = \nabla \left(p_1 - \frac{1}{2}|\mathbf{X}|^2 \right), \quad (\text{C.4b})$$

$$\mathbf{B}(\mathbf{X}, t) = \nabla (\dot{p}_0 + (1 - \dot{\varphi})(\mathbf{e}_z \times \mathbf{X}) \cdot \nabla p_0) - 2\nabla \times (p_0\mathbf{e}_z), \quad (\text{C.4c})$$

$$\mathbf{C}(\mathbf{X}, t) = \nabla \left(\frac{1}{2}|\nabla p_0|^2 \right). \quad (\text{C.4d})$$

We note that $\mathbf{B}$ is a solenoidal vector field (i.e. $\nabla \cdot \mathbf{B} = 0$), which will simplify matters later. To see this, note that when the divergence of (C.4c) is taken, the first term in (C.4c) vanishes due to p_0 being harmonic, and the last term in (C.4c) vanishes by the divergence of the curl property. Taking the divergence of the middle term, we obtain

$$\nabla^2(-Y p_{0X} + X p_{0Y}) = -Y \partial_X \nabla^2 p_0 + X \partial_Y \nabla^2 p_0, \quad (\text{C.5})$$

which vanishes due to p_0 being harmonic.

Then, integrating (C.4a) twice with respect to z and using the no slip conditions (2.29b), we find that (C.4a) has solution

$$\mathbf{u}_1 = f_1(z)\mathbf{A} + f_2(z)\mathbf{B} + f_3(z)\mathbf{C}, \quad (\text{C.6a})$$

$$f_1(z) = \frac{z(z-1)}{2}, \quad (\text{C.6b})$$

$$f_2(z) = \frac{f_1(z)}{12} (z^2 - z - 1), \quad (\text{C.6c})$$

$$f_3(z) = \frac{f_1(z)}{120} (2z^4 - 4z^3 + z^2 + z + 1). \quad (\text{C.6d})$$

We note that $f_1(z) < 0$, $f_2(z) > 0$, and $f_3(z) < 0$ for $z \in (0, 1)$, and that the only real roots for all three polynomials are located at $z = 0, 1$.

We can obtain the solution for w_1 by substituting (C.6a) into (2.26d) and using the solenoidal condition on $\mathbf{B}$ to obtain

$$w_1 = -\nabla^2 \left(\left(p_1 - \frac{1}{2}(X^2 + Y^2) \right) \int_0^z f_1(\hat{z}) d\hat{z} + \frac{1}{2}|\nabla p_0|^2 \int_0^z f_3(\hat{z}) d\hat{z} \right), \quad (\text{C.7})$$

We can now obtain a workable governing equation for p_1 by setting $z = 1$ in equation (C.7), and using the results

$$\int_0^1 f_1(z) dz = -\frac{1}{12}, \quad \int_0^1 f_2(z) dz = \frac{1}{120}, \quad \int_0^1 f_3(z) dz = -\frac{1}{1120}, \quad (\text{C.8a, b, c})$$

to yield

$$\nabla^2 \left(p_1 - \frac{1}{2} (X^2 + Y^2) + \frac{3}{560} |\nabla p_0|^2 \right) = 0, \quad (\text{C.9})$$

which has general solution

$$p_1 = \frac{1}{2} (X^2 + Y^2) - \frac{3}{560} |\nabla p_0|^2 + \phi, \quad (\text{C.10})$$

where ϕ satisfies

$$\nabla^2 \phi = 0, \quad (\text{C.11})$$

and will be determined by applying appropriate boundary conditions.

The pressure inside the TC is much simpler to work with, as the governing equations (2.28) already give the Darcy velocity in terms of the pressure. By substituting (2.28a-b) into (2.28d), integrating with respect to z and applying the boundary conditions (2.30b) on $z = 0$ and 1, we deduce

$$W_1 \equiv 0, \quad \nabla^2 P_1 = 0. \quad (\text{C.12a}, b)$$

In order to apply boundary conditions (2.32b) and (2.33b), we average (C.6a) over z , and express the equation in terms of ϕ instead of p_1 to obtain

$$\int_0^1 \mathbf{u}_1 \, dz = -\frac{1}{12} \nabla \phi + \frac{\mathbf{B}}{120}, \quad (\text{C.13})$$

Then, working in terms of ϕ and P_1 , the no flux boundary condition (2.32b) on S_1 is given by

$$\frac{\partial \phi}{\partial n} = \frac{1}{10} \left(\frac{\partial \dot{p}_0}{\partial n} + (1 - \dot{\varphi}) \frac{\partial}{\partial n} \mathbf{s} \cdot \nabla p_0 - 2\mathbf{n} \cdot \nabla \times (p_0 \mathbf{e}_z) \right). \quad (\text{C.14})$$

where the tangential direction $\mathbf{s} = (-Y, X, 0)$ on S_1 . Using the boundary condition (2.38) on S_1 for p_0 , we deduce that the first term vanishes. We also note that for a boundary contained within the (X, Y) -plane (or (α, β) -plane), the curl relates the normal and tangential directions as follows: $\mathbf{n} \cdot (\nabla \times \phi \mathbf{e}_z) = \mathbf{s} \cdot \nabla \phi$ for any function ϕ . Using these, we obtain the boundary condition (2.52) for p_1 on S_1 .

In a similar manner, the continuity of normal stress and flux boundary conditions (2.33b) and (2.34b) on $\bar{T}_1$ are given in (2.53).

Therefore, the $O(\epsilon Re)$ problem is governed by the coupled equations (C.11) and (C.12b), with boundary conditions (2.52) and (2.53).

C.2 Solving the $O(1)$ flow equations

In this section we obtain the coefficients for the leading-order fluid pressures given in (2.45) by invoking the boundary conditions (2.44).

Substituting (2.45) into (2.44a), multiplying by $\cos k\beta$ or $\sin k\beta$ and integrating from $\beta = 0$ to 2π , we obtain

$$\cosh(k(\alpha_2 - \alpha_1))A_k = C_k, \quad (\text{C.15a})$$

$$\cosh(k(\alpha_2 - \alpha_1))B_k = D_k. \quad (\text{C.15b})$$

Substituting (2.45) into (2.44b), multiplying by $\sin k\beta$, and integrating from $\beta = 0$ to 2π , we obtain

$$\begin{aligned} & -k\pi \left(\sinh(k(\alpha_2 - \alpha_1)) \frac{B_k}{12} + KD_k \right) \\ &= \sinh \alpha_1 \left(R(1 - \dot{\varphi}) \sinh \alpha_2 \int_0^{2\pi} \frac{\sin k\beta \sin \beta d\beta}{(\cosh \alpha_2 - \cos \beta)^2} \right. \\ & \quad \left. + \dot{R} \cosh \alpha_2 \int_0^{2\pi} \frac{\sin k\beta \cos \beta d\beta}{(\cosh \alpha_2 - \cos \beta)^2} - \dot{R} \int_0^{2\pi} \frac{\sin k\beta d\beta}{(\cosh \alpha_2 - \cos \beta)^2} \right), \end{aligned} \quad (\text{C.16a})$$

and doing the same with $\cos k\beta$, we obtain

$$\begin{aligned} & -k\pi \left(\sinh(k(\alpha_2 - \alpha_1)) \frac{A_k}{12} + KC_k \right) \\ &= \sinh \alpha_1 \left(R(1 - \dot{\varphi}) \sinh \alpha_2 \int_0^{2\pi} \frac{\cos k\beta \sin \beta d\beta}{(\cosh \alpha_2 - \cos \beta)^2} \right. \\ & \quad \left. + \dot{R} \cosh \alpha_2 \int_0^{2\pi} \frac{\cos k\beta \cos \beta d\beta}{(\cosh \alpha_2 - \cos \beta)^2} - \dot{R} \int_0^{2\pi} \frac{\cos k\beta d\beta}{(\cosh \alpha_2 - \cos \beta)^2} \right). \end{aligned} \quad (\text{C.16b})$$

Transforming the integration contour into one around the unit circle in complex space, it is straightforward to deduce the following integrals

$$\int_0^{2\pi} \frac{\cos m\beta}{(\cosh \alpha_2 - \cos \beta)^2} d\beta = \frac{2\pi \exp(-m\alpha_2)}{\sinh^2 \alpha_2} (m + \coth \alpha_2), \quad (\text{C.17a})$$

$$\int_0^{2\pi} \frac{\sin m\beta}{(\cosh \alpha_2 - \cos \beta)^2} d\beta = 0, \quad (\text{C.17b})$$

for every non-negative integer m . This is carried out in Appendix C.3.

Using standard trigonometric identities on (C.16), and using (C.17) to evaluate the integrals, we obtain

$$\sinh(k(\alpha_2 - \alpha_1))B_k + 12KD_k = -24R(1 - \dot{\varphi}) \sinh \alpha_1 \exp(-k\alpha_2), \quad (\text{C.18a})$$

$$\sinh(k(\alpha_2 - \alpha_1))A_k + 12KC_k = -24\dot{R} \sinh \alpha_1 \exp(-k\alpha_2). \quad (\text{C.18b})$$

Hence, for each positive integer k , we end up with four linear equations, as given by (C.15) and (C.18), for four unknowns, A_k, B_k, C_k and D_k . These are solved by (2.46).

C.3 Integral calculations

In this section, we derive the integral calculations for (C.17). Consider the following integral

$$I_1 = \int_0^{2\pi} \frac{\exp(im\beta)}{(\cosh \alpha_2 - \cos \beta)^2} d\beta. \quad (\text{C.19})$$

Taking real and imaginary parts, we obtain the left-hand sides of (C.17). By considering the transformation into complex space given by $z = \exp(i\beta)$, which has Jacobian $dz = iz d\beta$, the integral I becomes

$$\begin{aligned} I_1 &= \frac{1}{i} \oint_{|z|=1} \frac{z^m dz}{z (\cosh \alpha_2 - \frac{1}{2}(z + z^{-1}))^2}, \\ &= \frac{4}{i} \oint_{|z|=1} \frac{z^{m+1} dz}{(z - \exp(\alpha_2))^2 (z - \exp(-\alpha_2))^2}. \end{aligned} \quad (\text{C.20})$$

As $m \in \mathbb{N}$, the residues of the integrand are located at $z = \exp(\alpha_2)$ and $z = \exp(-\alpha_2)$. Further, as $\alpha_2 > 0$, the only residue located within the integration contour is at $z = \exp(-\alpha_2)$, and is a double pole. Therefore, using Cauchy's residue theorem, the integral I is given by

$$I_1 = 8\pi \frac{d}{dz} \left(\frac{z^{m+1}}{(z - \exp(\alpha_2))^2} \right), \quad (\text{C.21})$$

evaluated at $z = \exp(-\alpha_2)$. We note that

$$\frac{d}{dz} \left(\frac{z^{m+1}}{(z - \exp(\alpha_2))^2} \right) = \frac{z^m (z(m-1) - (m+1)\exp(\alpha_2))}{(z - \exp(\alpha_2))^3}, \quad (\text{C.22})$$

and then, evaluating this at $z = \exp(-\alpha_2)$, we deduce that

$$I_1 = \frac{2\pi \exp(-m\alpha_2)}{\sinh^2 \alpha_2} (m + \coth \alpha_2). \quad (\text{C.23})$$

Taking real and imaginary parts, we obtain (C.17).

Appendix D

Integral calculations for trajectory

In this Appendix, we calculate the following integral from (5.59)

$$I_2 = \int_0^{2\pi} \frac{(r_0 + \overline{B} \cos(t + \phi_0))^3}{(r_0^2 + 2r_0\overline{B} \cos(t + \phi_0) + \overline{B}^2)^2} dt. \quad (\text{D.1})$$

We first note that the function ϕ_0 (which is constant in t) has no effect in this integral as $\cos t$ is 2π -periodic. We therefore take $\phi_0 \equiv 0$ here without loss of generality. Making the transformation $z = \exp(it)$, which has scale factor $dz = iz dt$, the integral I becomes

$$I_2 = \frac{1}{i} \oint_{|z|=1} \frac{\left(r_0 + \frac{\overline{B}}{2}(z + z^{-1})\right)^3 dz}{z(\overline{B}^2 + r_0\overline{B}(z + z^{-1}) + r_0^2)^2} = \frac{1}{8i} \oint_{|z|=1} f(z) dz, \quad (\text{D.2})$$

where

$$f(z) = \frac{(\overline{B}z^2 + 2r_0z + \overline{B})^3}{z^2(r_0z + \overline{B})^2(\overline{B}z + r_0)^2}. \quad (\text{D.3})$$

We see that $f(z)$ has singularities at $z = 0$, $-\overline{B}/r_0$ and $-r_0/\overline{B}$. Therefore, the value of the integral will depend on whether $r_0 < |\overline{B}|$ or $r_0 > |\overline{B}|$. The residues at each of these singularities are given by

$$\text{Res}(f(z), 0) = \frac{2}{r_0^3} (2r_0^2 - \overline{B}^2), \quad (\text{D.4a})$$

$$\text{Res}\left(f(z), -\frac{r_0}{\overline{B}}\right) = \frac{2}{r_0^3} (\overline{B}^2 - 2r_0^2), \quad (\text{D.4b})$$

$$\text{Res}\left(f(z), -\frac{\overline{B}}{r_0}\right) = \frac{2}{r_0^3} (2r_0^2 - \overline{B}^2), \quad (\text{D.4c})$$

and hence the integral I_2 is solved by (5.59), and is discontinuous at $r_0 = |\overline{B}|$.

Appendix E

Additional boundary layers

In this Appendix we expand on the work considered in Chapters 3 and 4. We present the sections within this Appendix in the order they are required in the main thesis. In Appendix E.1, we consider the asymptotic sub-limit $\epsilon \ll Re \ll 1$, which is different to the sub-limit considered in detail in Chapters 3 and 4.

In the remainder of the Appendix we consider the asymptotic sub-limit $1 \ll Re \ll \epsilon^{-1}$, which is the sub-limit considered in Chapters 3 and 4. In Appendices E.2–E.6, we consider the additional boundary layers that occur for inflow. In Appendices E.7–E.9, we consider the additional boundary layers that occur for outflow. In each of these sections we give the relevant governing equations within each region of interest. We solve for these equations analytically where possible and, where we are unable to give an analytic solution, resign ourselves to simply presenting the full system to be solved.

In Appendix E.10, we investigate the flow through the thin gaps present within the HARV bioreactor problem. This allows us to determine the shear stress acting on the TC due to the thin gaps. In Appendix E.11, we consider the continuity of flux condition for higher-order corrections. This is a key result in determining the coupling conditions between the outer regions. Finally, in Appendix E.12 we collate the coupling conditions between outer regions, and convert them into a frame of reference suitable for use in the rest of this thesis.

E.1 Small Reynolds number: $\epsilon \ll Re \ll 1$

In this section, we discuss the inner regions discussed in §3.3.2 and §4.4 in the asymptotic sub-limit where $\epsilon \ll Re \ll 1$. We first consider the 2D case and then the 3D case.

E.1.1 2D flow

The full inner problem in §3.3.2 is governed by the system (3.35)–(3.38) for inflow (shown in Figure 3.3), and the system (3.35)–(3.37), (3.39) for outflow (shown in Figure 3.4). In the asymptotic sub-limit of small Reynolds number $\epsilon \ll Re \ll 1$, we do not obtain further boundary regions, as with the large Reynolds number sub-limit, and the asymptotic structure is as discussed in §3.3. We note that the inertial terms are now negligible at leading order and, as such, the flow equations become reversible. Hence, inflow and outflow behave equivalently, and it suffices to solely consider inflow. For convenience, we use $X^- = X$.

We use the following asymptotic expansions

$$(\bar{\mathbf{u}}_0, \bar{\mathbf{Q}}_0, \bar{p}_1, \bar{P}_1) = (\bar{\mathbf{u}}_{00}, \bar{\mathbf{Q}}_{00}, \bar{p}_{11}, \bar{P}_{11}) + O(Re). \quad (E.1)$$

Substituting the asymptotic expansions (E.1) into the bulk flow equations (3.35), we obtain

$$0 = -\nabla \bar{p}_{11} + \nabla^2 \bar{\mathbf{u}}_{00}, \quad 0 = \nabla \cdot \bar{\mathbf{u}}_{00} \quad \text{in region II}, \quad (E.2a, b)$$

and the interior flow equations (3.36) are unchanged, to obtain

$$\bar{\mathbf{Q}}_{00} = -K \nabla \bar{P}_{11}, \quad 0 = \nabla \cdot \bar{\mathbf{Q}}_{00} \quad \text{in region III}, \quad (E.3a, b)$$

thus yielding Stokes flow (E.2) coupled with Darcy flow (E.3) at leading order. Substituting the asymptotic expansions (E.1) into the boundary conditions on the channel walls (3.37) yields

$$\bar{\mathbf{u}}_{00} = \mathbf{0} \quad \text{on } z = 0, 1 \quad \text{for } X < 0, \quad (E.4a)$$

$$\bar{W}_{00} = 0 \quad \text{on } z = 0, 1 \quad \text{for } X > 0, \quad (E.4b)$$

and on the interface at $X = 0$, the interfacial conditions (3.27) become

$$\bar{u}_{00} = \bar{U}_{00}, \quad \bar{p}_{11} - 2\bar{u}_{00X} = \bar{P}_{11}, \quad \bar{w}_{00X} = \frac{\lambda}{\sqrt{K}} (\bar{W}_{00} - \bar{w}_{00}) \quad \text{on } X = 0 \text{ for } z \in (0, 1). \quad (E.5a, b, c)$$

The matching conditions between regions I and II are

$$\bar{u}_{00} \sim 6z(1-z), \quad \bar{w}_{00} \rightarrow 0, \quad \bar{p}_{11} \sim -12X \quad \text{as } X \rightarrow -\infty \text{ for } z \in (0, 1), \quad (E.6a, b, c)$$

and the matching conditions between regions III and IV are

$$\bar{U}_{00} \sim 1, \quad \bar{W}_{00} \rightarrow 0, \quad \bar{P}_{11} \sim -K^{-1}X \quad \text{as } X \rightarrow \infty \text{ for } z \in (0, 1). \quad (E.7a, b, c)$$

By introducing a streamfunction $\psi \mathbf{e}_y = \nabla \times \bar{\mathbf{u}}_0$, where $\mathbf{e}_y = \mathbf{e}_x \times \mathbf{e}_z$, we can replace (E.2) by

$$\nabla^4 \psi = 0 \quad \text{in region II.} \quad (\text{E.8})$$

Similarly, we can rearrange (E.3) to obtain

$$\nabla^2 \bar{P}_{11} = 0 \quad \text{in region III.} \quad (\text{E.9})$$

We solve the system (E.4)–(E.9) numerically, using an iterative central finite difference scheme to bypass some of the cost of solving the fully coupled problem in one step. That is, we iterate between solving Laplace’s equation (E.9) in region III and the biharmonic equation (E.8) in region II (both via a standard centred finite difference scheme), and use the solution found in the previous iteration for boundary conditions in the current iteration. The iteration is halted once the difference between solutions (using a suitable matrix norm) is less than 10^{-10} .

From the general expression for the stress (3.45), we deduce that the normal and shear stresses on the interface are given by

$$\sigma_{xx} = \epsilon^{-1} (-\bar{p}_{11} + 2\psi_{Xz}) + O(\epsilon^{-1} Re), \quad (\text{E.10a})$$

$$\sigma_{xz} = \epsilon^{-1} (\psi_{zz} - \psi_{XX}) + O(\epsilon^{-1} Re), \quad (\text{E.10b})$$

respectively, and are evaluated at $X = 0$.

We present the stress at the interface at $O(\epsilon^{-1})$ for typical parameter values in Figure E.1. We see that the inner regions contribute leading-order terms to the stress. For models where the stress is important (e.g. in cell models where mechanotransduction plays a large role), proceeding without information about the inner regions could induce avoidable errors. We note that the normal stress does not vanish on $z = 0, 1$ as might be expected from taking the limit of $\bar{u}_{00X}$ along the channel wall from (E.4a), but instead tends to a finite limit. This is because the stress is discontinuous at the corners $X = 0$ and $z = 0, 1$ due to the BJ slip condition (E.5c) imposed on the interface at $X = 0$.

E.1.2 3D flow

We now consider the small Reynolds number limit for the 3D flow considered in §4. We use the asymptotic expansion given in (E.1) where, now, $\bar{\mathbf{u}}_0 = \bar{u}_0 \mathbf{n} + \bar{v}_0 \mathbf{s} + \bar{w}_0 \mathbf{e}_z$ and $\bar{\mathbf{Q}}_0 = \bar{U}_0 \mathbf{n} + \bar{V}_0 \mathbf{s} + \bar{W}_0 \mathbf{e}_z$. The procedure for obtaining $\bar{u}_{00}$, $\bar{w}_{00}$, $\bar{p}_{11}$, $\bar{U}_{00}$, $\bar{W}_{00}$, and $\bar{P}_{11}$ is the same as is carried out in Appendix E.1.1 (but now imposing a non-zero

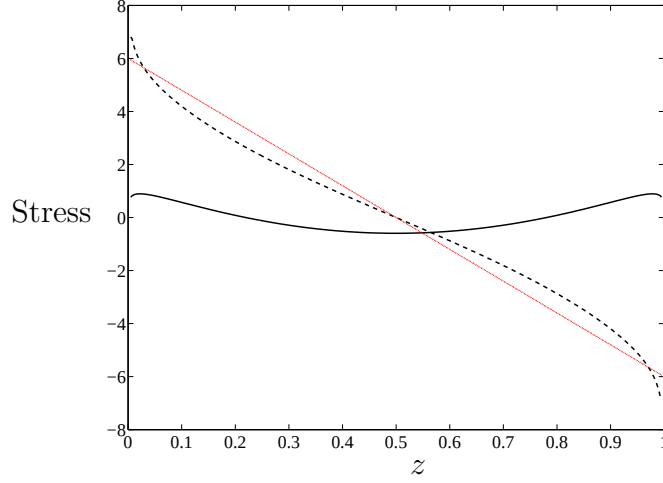


Figure E.1: The stress on the interface $X = 0$ for parameter values $K = 0.2$, $\lambda = 1$. The solid black line is the normal stress $-\bar{p}_{11} + \psi_{Xz}$ and the dashed black line is the shear stress $\psi_{zz} - \psi_{XX}$. We also plot a dotted red line to show the shear stress as estimated by the outer solution $6(1 - 2z)$.

velocity on the Hele-Shaw cell walls), and we omit it here for brevity. Therefore, in this section we solve for the leading-order azimuthal flow $\bar{v}_{00}$.

The leading-order terms in (4.15b) neglect inertial terms and yield the governing equation for the $O(1)$ velocity in the s -direction as follows

$$\bar{v}_{00NN} + \bar{v}_{00zz} = p_{0s}(0, s, t), \quad (\text{E.11})$$

The boundary conditions for $\bar{v}$ are

$$\bar{v}_{00} = \mathbf{s} \cdot \mathbf{u}^{\text{slip}}(0, s, t) \quad \text{on } z = 0, 1, \quad (\text{E.12a})$$

$$\bar{v}_{00N} = \frac{\lambda}{\sqrt{K}}(\bar{v} + KP_{0s}) \quad \text{on } N = 0, \quad (\text{E.12b})$$

$$\bar{v}_{00} \sim \frac{z(z-1)}{2}p_{0s}(0, s, t) + \mathbf{s} \cdot \mathbf{u}^{\text{slip}}(0, s, t) \quad \text{as } N \rightarrow \infty, \quad (\text{E.12c})$$

where $\bar{P}_0$ is given by evaluating P_0 on ∂D . This is solved by

$$\bar{v}_{00} = \frac{z(z-1)}{2}p_{0s}(0, s, t) + \mathbf{s} \cdot \mathbf{u}^{\text{slip}}(0, s, t) + \sum_{k=0}^{\infty} A_k \exp(-\alpha_k N) \sin \alpha_k z, \quad (\text{E.13a})$$

$$A_k = \frac{4\lambda}{\alpha_k (\lambda + \alpha_k \sqrt{K})} \left(\frac{p_{0s}}{\alpha_k^2} - KP_{0s} - \mathbf{s} \cdot \mathbf{u}^{\text{slip}}(0, s, t) \right), \quad \alpha_k = (2k+1)\pi. \quad (\text{E.13b})$$

As $\bar{v}_{00}$ changes rapidly in a region close to the boundary, it is responsible for the leading order shear stress on ∂D in the s -direction (4.34b), which becomes

$$\sigma_{ns} = -\epsilon^{-1} \sum_{k=1}^{\infty} \alpha_k A_k \sin \alpha_k z + O(\epsilon^{-1} Re). \quad (\text{E.14})$$

E.2 Inflow wall boundary layer - region IIb

We now consider problems generated in the asymptotic sub-limit $\epsilon \ll \delta \ll 1$, which is the limit considered in detail in Chapters 3 and 4.

As discussed in §3.4.1, there is an $O(\delta)$ slip velocity induced on the channel walls near $z = 0$ and 1 . Therefore, we introduce boundary layers near $z = 0$ and $z = 1$ to satisfy the slip condition on the walls. The problem is symmetric around the line $z = 1/2$, so the analysis in this section will be confined to the boundary layer near $z = 0$ for brevity, and we refer to this as region IIb. We use $X^- = X$ for convenience.

The classical Prandtl result for high Reynolds number flow past a flat plate is that a boundary layer of height $O(\delta^{1/2})$ is formed near the plate, which grows proportionally to the square root of the distance from the plate tip. This may seem like the canonical example from which to proceed (and, indeed, it plays a role in region VIb for outflow as we discuss in §3.4.2, and in Appendix E.8.1), but there are complications in our problem which mean that a different scaling and solution near the boundary are required. These complications stem from the fact that the induced slip velocity $\bar{u}_0 = O(\delta)$, and that the leading-order Poiseuille flow is linear in z near the wall. Therefore, the correct scaling comes from looking for distinguished limits when $O(\bar{u}_0) = O(z)$ close to the wall, and then scaling $\bar{w}_0$ such that we have a non-trivial incompressibility condition. The problem of induced slip is then resolved at a higher order.

Before we proceed, it will be useful to analyse the fluid velocities $\bar{u}_{01}$ and $\bar{w}_{01}$ in region II in more detail. By considering separable solutions to governing equations (3.59c) and (3.68a), the fluid velocities $\bar{u}_{01}$ and $\bar{w}_{01}$ are given by

$$\bar{u}_{01} = \sum_{k=1}^{\infty} C_k \exp(\mu_k X^-) g'_k(z), \quad \bar{w}_{01} = - \sum_{k=1}^{\infty} \mu_k C_k \exp(\mu_k X^-) g_k(z), \quad (\text{E.15a, b})$$

where the eigenfunctions $g_k(z)$ satisfy the eigenvalue problem

$$g''_k(z) + \left(\frac{2}{z(1-z)} + \mu_k^2 \right) g_k(z) = 0 \quad \text{for } z \in (0, 1), \quad (\text{E.16})$$

together with boundary conditions $g_k(0) = g_k(1) = 0$ obtained from the normal velocity boundary conditions (3.69a); the coefficients C_k would have to be determined numerically (using the orthogonality of the eigenfunctions) if we used this form of the solution.

We note that the eigenvalue problem (E.16) is in Sturm-Liouville form. However, as there are singularities in the coefficients within (E.16) at the end-points of the domain, we cannot blindly apply the standard results of Sturm-Liouville theory. In Appendix E.3, we modify certain Sturm-Liouville results to determine that $\mu_k^2 \geq 0$ in general, and that $\mu_k^2 > 0$ for the expansion used in (E.15). We are then able to use the complete spectrum of positive roots in (E.15). We now continue with the solution in region IIb.

The relevant scalings are $\bar{u}_0 = \delta^{1/3}\dot{u}$, $\bar{w}_0 = \delta^{2/3}\dot{w}$, and $z = \delta^{1/3}Z$, and we introduce the new variable $\bar{p}_1 = \dot{p}$ to signify that we are working in region IIb. Under these scalings, the governing equations (3.35) become

$$\dot{u}\dot{u}_X + \dot{w}\dot{u}_Z = -\delta^{1/3}\dot{p}_X + \dot{u}_{ZZ} + \delta^{2/3}\dot{u}_{XX} \quad \text{in region IIb}, \quad (\text{E.17a})$$

$$\delta^{1/3}(\dot{u}\dot{w}_X + \dot{w}\dot{w}_Z) = -\dot{p}_Z + \delta^{1/3}\dot{w}_{ZZ} + \delta\dot{w}_{XX} \quad \text{in region IIb}, \quad (\text{E.17b})$$

$$0 = \dot{u}_X + \dot{w}_Z \quad \text{in region IIb}. \quad (\text{E.17c})$$

The boundary conditions on the channel wall (3.37a) can be fully imposed in this region

$$\dot{\mathbf{u}} = 0 \quad \text{on } Z = 0 \text{ for } X < 0, \quad (\text{E.18})$$

but once we form asymptotic expansions, we are unable to impose any conditions on the interfacial boundary within region IIb. This issue is resolved in region IIc in Appendix E.4. We give suitable matching conditions between regions II and IIb after we define asymptotic expansions of the form

$$\dot{u} \sim \dot{u}_0 + \delta^{1/3}\dot{u}_1 + \delta^{2/3}\dot{u}_2 + O(\delta), \quad (\text{E.19a})$$

$$\dot{w} \sim \dot{w}_0 + \delta^{1/3}\dot{w}_1 + \delta^{2/3}\dot{w}_2 + O(\delta), \quad (\text{E.19b})$$

$$\dot{p} \sim \delta^{-1}\dot{p}_{10} + \delta^{-1/3}\dot{p}_{1c} + \dot{p}_{11} + \delta^{1/3}\dot{p}_{12} + O(\delta^{2/3}), \quad (\text{E.19c})$$

and we show that the $O(\delta)$ slip in region II is resolved by $\dot{u}_2$, $\dot{w}_2$, and $\dot{p}_{12}$ in region IIb. We further note that the flow of matching information is as follows. At a given order, the horizontal slip velocity in region II gives enough information to close the problem in region IIb. The solution in region IIb then yields next-order boundary conditions

for the vertical velocity and pressure in region II. The next-order solution in region II then yields a higher-order horizontal slip velocity, and the cycle continues.

The leading-order equations are obtained via substitution of (E.19) into (E.17a) and (E.17b) to obtain

$$\dot{p}_{10X} = 0, \quad \dot{p}_{10Z} = 0 \quad \text{in region IIb.} \quad (E.20a, b)$$

The leading-order pressure $\dot{p}_{10}$ has matching condition

$$\dot{p}_{10} \rightarrow 0 \quad \text{as } Z \rightarrow \infty, \quad (E.21)$$

and the solution to (E.20)–(E.21) is trivially given by

$$\dot{p}_{10} = 0. \quad (E.22)$$

The next-order equations via substitution of (E.19) into (E.17) in region IIb are given by

$$\dot{u}_0 \dot{u}_{0X} + \dot{w}_0 \dot{u}_{0Z} = -\dot{p}_{1cX} + \dot{u}_{0ZZ}, \quad (E.23a)$$

$$0 = -\dot{p}_{1cZ}, \quad (E.23b)$$

$$0 = \dot{u}_{0X} + \dot{w}_{0Z}, \quad (E.23c)$$

with the channel wall boundary condition (E.18) given by

$$\dot{\mathbf{u}}_0 = \mathbf{0} \quad \text{on } Z = 0 \text{ for } X < 0, \quad (E.24)$$

and matching conditions with region II given by

$$\dot{u}_0 \sim 6Z, \quad \dot{w}_0 \rightarrow 0, \quad \dot{p}_{1c} \rightarrow 0 \quad \text{as } Z \rightarrow \infty, \quad (E.25a, b, c)$$

where (E.25a) follows in a standard manner from the leading-order solution (3.56) in region II, and (E.25c) is deduced from consideration of the governing equation (3.59a) on the boundary $z = 0$, using the boundary condition (3.61) and the leading-order solution (3.56a). We note that (E.25b) determines the correct boundary condition to impose in region IIb.

Although the system (E.23)–(E.25) is nonlinear, the solution is trivially given by the matching conditions (E.25) as follows

$$\dot{u}_0 = 6Z, \quad \dot{w}_0 = 0, \quad \dot{p}_{1c} = 0. \quad (E.26a, b, c)$$

The $O(\delta^{1/3})$ flow equations in region IIb are obtained via substitution of (E.19) into (E.17) (using the flow solution (E.26)), and are given by

$$6Z\dot{u}_{1X} + 6\dot{w}_1 = -\dot{p}_{11X} + \dot{u}_{1ZZ}, \quad (\text{E.27a})$$

$$0 = -\dot{p}_{11Z}, \quad (\text{E.27b})$$

$$0 = \dot{u}_{1X} + \dot{w}_{1Z}, \quad (\text{E.27c})$$

with the channel wall boundary condition (E.18) given by

$$\dot{\mathbf{u}}_1 = \mathbf{0} \quad \text{on } Z = 0 \text{ for } X < 0, \quad (\text{E.28})$$

and matching conditions with region II given by

$$\dot{u}_1 \sim -6Z^2, \quad \dot{w}_1 \rightarrow 0, \quad \dot{p}_{11} \rightarrow -12X \quad \text{as } Z \rightarrow \infty, \quad (\text{E.29a, b, c})$$

where (E.29b) determines the correct boundary condition to impose in region IIb.

The solution to the system (E.27)–(E.29) is (again) trivially given by the matching conditions (E.29) as follows

$$\dot{u}_1 = -6Z^2, \quad \dot{w}_1 = 0, \quad \dot{p}_{11} = -12X. \quad (\text{E.30a, b, c})$$

We now consider the terms which allow the $O(\delta)$ slip in region II to satisfy the no-slip boundary conditions (E.18) in region IIb. The $O(\delta^{2/3})$ flow equations in region IIb are obtained via substitution of (E.19) into (E.17) (using the flow solution (E.26)), and are given by

$$6(Z\dot{u}_{2X} + \dot{w}_2) = -\dot{p}_{12X} + \dot{u}_{2ZZ}, \quad (\text{E.31a})$$

$$0 = -\dot{p}_{12Z}, \quad (\text{E.31b})$$

$$0 = \dot{u}_{2X} + \dot{w}_{2Z}, \quad (\text{E.31c})$$

and the channel wall boundary condition (E.18) is given by

$$\dot{\mathbf{u}}_2 = \mathbf{0} \quad \text{on } Z = 0 \text{ for } X < 0, \quad (\text{E.32})$$

and, from the general form of the flow solution in region II (E.15), the matching condition with the horizontal velocity in region II is given by

$$\dot{u}_2 \sim \sum_{k=1}^{\infty} C_k \exp(\mu_k X) g'_k(0) \quad \text{as } Z \rightarrow \infty, \quad (\text{E.33})$$

where C_k , μ_k , and g_k are described as part of (E.15).

We solve the system (E.31)–(E.33) by introducing a streamfunction $\mathring{\psi}$ such that $\mathring{u}_2 = \mathring{\psi}_Z$ and $\mathring{w}_2 = -\mathring{\psi}_X$. Considering the form of the matching condition (E.33), we seek solutions in the form

$$\mathring{\psi} = \sum_{k=1}^{\infty} \exp(\mu_k X) f_k(Z), \quad (\text{E.34})$$

where $f_k(Z)$ are to be determined. Differentiating (E.31a) with respect to Z , we obtain

$$f_k^{(\text{IV})}(Z) - a_k^3 Z f_k''(Z) = 0, \quad a_k^3 = 6\mu_k > 0, \quad (\text{E.35a, b})$$

with boundary conditions

$$f_k(0) = 0, \quad f_k'(0) = 0, \quad f_k'(\infty) = C_k g_k'(0). \quad (\text{E.36a, b, c})$$

We note that this is three boundary conditions for a fourth-order ODE, and we discuss this issue in time.

The solution to (E.35) with boundary conditions (E.36) is given by

$$f_k(Z) = C_k g_k'(0) \frac{\int_0^Z \int_0^u \text{Ai}(a_k v) \, dv \, du}{\int_0^\infty \text{Ai}(a_k s) \, ds}. \quad (\text{E.37})$$

where Ai is the Airy function of the first kind. Therefore, the asymptotic solution for the velocity in this boundary layer is given by

$$\mathring{u} \sim 6Z(1 - \delta^{1/3} Z) + \delta^{2/3} \sum_{k=1}^{\infty} C_k g_k'(0) \exp(\mu_k X) \frac{\int_0^Z \text{Ai}(a_k v) \, dv}{\int_0^\infty \text{Ai}(a_k s) \, ds} + O(\delta), \quad (\text{E.38a})$$

$$\mathring{w} \sim -\delta^{2/3} \sum_{k=1}^{\infty} \mu_k C_k g_k'(0) \exp(\mu_k X) \frac{\int_0^Z \int_0^u \text{Ai}(a_k v) \, dv \, du}{\int_0^\infty \text{Ai}(a_k s) \, ds} + O(\delta), \quad (\text{E.38b})$$

and we note that it is possible to evaluate the integral in the denominators of (E.37) and (E.38) as

$$\int_0^\infty \text{Ai}(a_k s) \, ds = \frac{1}{3a_k}. \quad (\text{E.39})$$

As we differentiated (E.31a) in order to obtain (E.35), we have artificially introduced a problem in which there are only three boundary conditions for a linear fourth-order ODE. However, if we consider the behaviour of (E.35) as $Z \rightarrow \infty$, the single boundary condition (E.36c) removes two degrees of freedom from the solution. A naive boundary condition count then suggests that all is well. However, two wrongs do not make a right, and this is not a valid resolution to what is actually a more subtle issue.

The resolution hinges on the flow of information within this problem, specifically the value of $\bar{p}_{12}$ in region II and $\mathring{p}_{12}$ in region IIb, and their matching. We show this via the following. The eigenfunctions for $\bar{p}_{12}$ in region II will be the same as those determined in the general solution to the $O(\delta)$ velocities in region II (E.15) and (E.16) (as the linearised operators of the underlying full problem (3.50) will be equivalent). This means that we can denote $\mathring{p}_{12X}$ by

$$\mathring{p}_{12X} = \sum_{k=1}^{\infty} b_k \exp(\mu_k X), \quad (\text{E.40})$$

for some constants b_k , and re-write the relevant governing equation in region IIb, given by (E.31a), as

$$f_k'''(Z) - a_k^3 (Z f_k'(Z) - f_k(Z)) = b_k. \quad (\text{E.41})$$

The general solution to (E.41) is

$$f_k(Z) = \frac{b_k}{a_k^3} + B_{k1}Z + B_{k2}h_1(Z) + B_{k3}h_2(Z), \quad (\text{E.42})$$

where the behaviour of h_1 and h_2 as $Z \rightarrow \infty$ can be determined using a standard WKBJ analysis to obtain

$$h_1 \sim \frac{\exp\left(\frac{2}{3}(a_k Z)^{3/2}\right)}{Z^{5/4}}, \quad h_2 \sim \frac{\exp\left(-\frac{2}{3}(a_k Z)^{3/2}\right)}{Z^{5/4}}. \quad (\text{E.43})$$

Applying the boundary condition (E.36c) imposes $B_{k1} = C_k g'_k(0)$ and $B_{k2} = 0$. Then, we are left to impose the remaining boundary conditions (E.36a,b) as follows

$$0 = \frac{b_k}{a_k^3} + B_{k3}h_2(0), \quad 0 = C_k g'_k(0) + B_{k3}h'_2(0), \quad (\text{E.44a, b})$$

which appears to be two equations for one unknown: B_{k3} . However, this is not quite correct. We never stated how b_k were derived. They are, in fact, currently free parameters and, along with B_{k3} , are therefore determined from (E.44). Therefore, the matching conditions between regions II and IIb for the vertical component of velocity and the pressure arise in region IIb and provide information to region II. From the streamfunction (E.34), the general (E.42) and far-field behaviour (E.43), we obtain a matching condition for $\bar{w}_{02}$ in region II as follows

$$\bar{w}_{02}(X, 0) = - \sum_{k=1}^{\infty} \frac{\mu_k b_k}{a_k^3} \exp(\mu_k X), \quad (\text{E.45})$$

and the matching condition for $\bar{p}_{12}$ in region II can be determined from (E.40).

We have therefore resolved the slip along the channel walls for inflow. We note that whilst we have resolved the no-slip condition on $z = 0$, we have not resolved the interfacial BJ condition on $X = 0$ for $\bar{w}$ when $z = O(\delta^{1/3})$, as we cannot impose any extra conditions on $X = 0$. In Appendix E.4, we resolve this by considering a region where $X = O(\delta^{2/3})$ and $\bar{w} = O(1)$. In this region (denoted region IIc), the leading-order governing equations are the same as in region IIa, where we find that any general outer condition can be matched for inflow.

E.3 Modified Sturm-Liouville calculations

In this section, we investigate the eigenvalue problem (E.16), and deduce that $\mu_k \geq 0$.

Even though we are unable to invoke standard Sturm-Liouville theory, we are still able to deduce that $\mu_k \in \mathbb{R}$ (as the linear operator in (E.16) is real). We also note that the general solution to (E.16) (without taking the boundary conditions into account) near $z = 0$ is given by

$$g_k(z) \sim a_0 + \sum_{n=1}^{\infty} z^n (a_n + b_n \log z), \quad (\text{E.46})$$

which is bounded near $z = 0$ (and we can obtain a similar result near $z = 1$).

We are able to make further progress by forming the Rayleigh quotient

$$\mu_k^2 = \frac{\int_0^1 \left((g'_k)^2 - \frac{2g_k^2}{z(1-z)} \right) dz}{\int_0^1 g_k^2 dz}. \quad (\text{E.47})$$

As the solution to (E.16) is bounded, we are able to impose a normalization condition $\int_0^1 g_k^2 dz = 1$. This enables us to write (E.47) as

$$\mu_k^2 = \int_0^1 \left((g'_k)^2 - \frac{2g_k^2}{z(1-z)} \right) dz, \quad (\text{E.48})$$

with boundary conditions $g_k(0) = g_k(1) = 0$. We proceed by considering the right-hand side of (E.48) as a functional for all possible values of $g_k(z)$ (which may not necessarily satisfy (E.16)). We argue that any stationary value of the functional in (E.48) is a minimum, as we can increase the value of the functional without bound by considering very oscillatory (bounded) functions. Finding the minimum value that the functional can take will give us a lower bound on the value of μ_k^2 (note that the

only information we have about μ_k^2 is that it is real - we currently know nothing about its sign).

Using the Euler-Lagrange equation, we determine that the function $g(z)$ which gives the minimum value of (E.48) satisfies the following equation

$$g''(z) + \frac{2}{z(1-z)}g(z) = 0, \quad (\text{E.49})$$

and is solved by

$$g(z) = \sqrt{30}z(1-z). \quad (\text{E.50})$$

In fact, this is a solution to (E.16) with $\mu_k = 0$. Therefore, we deduce that $\mu_k \geq 0$, and there is a null eigenfunction $g_0 = \sqrt{30}z(1-z)$ with null eigenvalue $\mu_k = 0$. We further note that $\bar{w}_{01}$ is anti-symmetric around $z = 1/2$, and so we require functions of $g_k(z)$ which are anti-symmetric around $z = 1/2$. Therefore, we do not include the null eigenfunction in the expansion of (E.15b).

The eigenfunctions and eigenvalues can be determined numerically using, e.g. the eigenfunction/eigenvalue solver in Chebfun [22] up to arbitrary accuracy, and the coefficients C_k determined using the interfacial condition (3.70). Using Chebfun, we are able to numerically determine that the smallest eigenvalue is $\mu_1 \approx 5.1783$.

E.4 Region IIc

As discussed in Appendix E.2, we are unable to satisfy a BJ boundary condition on the interface $X = 0$ in region IIb. Therefore, in this section we introduce a boundary layer near $X = 0$ in order to determine how $\hat{w}$ changes near the interface. The problem is symmetric around the line $z = 1/2$, so we proceed as with Appendix E.2 and confine the analysis in this section to the boundary layer near $z = 0$, and denote this as region IIc.

The relevant scalings from region II to region IIc are $X = \delta^{2/3}X^c$, $z = \delta^{1/3}Z$, $\bar{u} = \delta^{1/3}u^c$, and $\bar{w} = \delta w^c$. We note that $\bar{w}$ is larger within region IIc than region IIb, and this is because it is induced via the BJ slip condition (3.38c). We also take $\bar{p} = p^c$ to signify that we are working in region IIc. Under these scalings, the bulk flow governing equations (3.35) in region IIc become

$$u^c u_{X^c}^c + \delta w^c u_Z^c = -\delta^{1/3} p_{X^c}^c + u_{X^c X^c}^c + \delta^{2/3} u_{ZZ}^c, \quad (\text{E.51a})$$

$$u^c w_{X^c}^c + \delta w^c w_Z^c = -p_Z^c + w_{X^c X^c}^c + \delta^{2/3} w_{ZZ}^c, \quad (\text{E.51b})$$

$$0 = u_{X^c}^c + \delta w_Z^c. \quad (\text{E.51c})$$

The main purpose of this region is satisfy the BJ slip condition (3.38c) on the interface $X = 0$ which, in region IIc scalings, becomes

$$\delta^{1/3} w_{X^c}^c = \frac{\lambda}{\sqrt{K}} (\bar{W}_0(0, \delta^{1/3} Z) - \delta w^c) \quad \text{on } X^c = 0. \quad (\text{E.52})$$

Substituting asymptotic expansions

$$u^c \sim u_0^c + O(\delta^{1/3}), \quad (\text{E.53a})$$

$$w^c \sim w_0^c + O(\delta^{1/3}), \quad (\text{E.53b})$$

$$p^c \sim \delta^{-1} p_{10}^c + \bar{p}_{11} + O(\delta^{1/3}), \quad (\text{E.53c})$$

into (E.51c), we deduce that u^c is constant in X^c up to $O(\delta)$. Using this information in (E.51a) further tells us that p^c is constant in X^c up to $O(\delta^{2/3})$. By matching with region IIb, we deduce that

$$u_0^c = 6Z, \quad p_{10}^c = 0, \quad p_{11}^c = 0. \quad (\text{E.54a, b, c})$$

Using (E.54), the governing equation (E.51b) becomes

$$6Z w_{0X^c}^c = w_{0X^c X^c}^c, \quad (\text{E.55})$$

with the BJ slip condition on the interface obtained from (E.52), and is given by

$$w_{0X^c}^c = \frac{\lambda}{\sqrt{K}} Z \bar{W}_{00z}(0, 0) \quad \text{on } X^c = 0, \quad (\text{E.56})$$

and the matching condition with region IIb given by

$$w_0^c \rightarrow 0 \quad \text{as } X^c \rightarrow -\infty. \quad (\text{E.57})$$

The system (E.55)–(E.57) is solved by

$$w_0^c = \frac{\lambda \bar{W}_{00z}(0, 0)}{6\sqrt{K}} \exp(6ZX^c), \quad (\text{E.58})$$

and we note that an $O(\delta)$ (in terms of the region II variables) flux is induced on the channel wall. This issue requires a further boundary layer near $Z = 0$, and we discuss this in Appendix E.5 in a boundary region we denote region IId.

E.5 Region II_d

In Appendix E.4 we determined how the BJ slip condition on $X^c = 0$ was satisfied close to the interface and near the channel wall in region II_c. However, we further showed that this resolution would cause an apparent flux on the channel wall. This is resolved in a further boundary layer which we denote as region II_d.

The relevant scalings from region II to region II_d are $X = \delta^{2/3}X^c$ (which is the same as in region II_c), $z = \delta^{2/3}Z^d$, $\bar{u} = \delta^{2/3}u^d$, and $\bar{w} = \delta w^d$. We also take $\bar{p} = p^d$ to signify that we are working in region II_d. Under these scalings, the bulk flow governing equations (3.35) in region II_d become

$$\delta^{1/3}u^d u_{X^c}^d + \delta^{2/3}w^d u_{Z^d}^d = -p_{X^c}^d + u_{X^c X^c}^d + u_{Z^d Z^d}^d, \quad (\text{E.59a})$$

$$\delta^{2/3}u^d w_{X^c}^d + \delta w^d w_{Z^d}^d = -p_{Z^d}^d + \delta^{1/3}(w_{X^c X^c}^d + w_{Z^d Z^d}^d), \quad (\text{E.59b})$$

$$0 = u_{X^c}^d + \delta^{1/3}w_{Z^d}^d, \quad (\text{E.59c})$$

and we can impose boundary conditions on the channel wall (3.37a) as follows

$$\mathbf{u}^d = \mathbf{0} \quad \text{on } Z = 0 \text{ for } X < 0. \quad (\text{E.60})$$

The condition as $X \uparrow 0$ will be determined via matching with region II_e once we have given the asymptotic expansions we are working with. We consider region II_e in Appendix E.6.

Substituting asymptotic expansions

$$u^d \sim u_0^d + O(\delta^{1/3}), \quad (\text{E.61a})$$

$$w^d \sim w_0^d + O(\delta^{5/3}), \quad (\text{E.61b})$$

$$p^d \sim \delta^{-1}p_{10}^d + p_{11}^d + O(\delta^{1/3}), \quad (\text{E.61c})$$

into (E.59c), we can deduce that u_0^d is constant in X^c up to $O(\delta^{1/3})$ and given by its matching condition. We obtain similar results for the pressure, to obtain

$$u_0^d = 6Z^d, \quad p_{10}^d = 0, \quad p_{11}^d = 0. \quad (\text{E.62a, b, c})$$

Were we to continue with the asymptotic expansion in the pressure (which would involve going into further orders in previous regions), we would find that the $O(\delta^{1/3})$ pressure vanishes. Therefore, the problem to solve that allows the vertical component of velocity to satisfy the correct boundary condition (E.60) is

$$0 = w_{0X^c X^c}^d + w_{0Z^d Z^d}^d \quad \text{in region II}_d, \quad (\text{E.63})$$

with boundary conditions obtained from (E.60) on the channel walls

$$w_0^d = 0 \quad \text{on } Z^d = 0 \text{ for } X^c < 0. \quad (\text{E.64})$$

The condition as $X \uparrow 0$ is determined via matching with region IIe in Appendix E.6 to obtain

$$w_0^d = \lim_{\hat{X} \rightarrow -\infty} w_0^e(\hat{X}, z) \quad \text{on } X^c = 0 \text{ for } Z^d > 0, \quad (\text{E.65})$$

where w_0^e and $\hat{X}$ are defined in Appendix E.6, and finally a matching condition with region IIc from (E.58), given by

$$w_0^d \sim \frac{\lambda \overline{W}_{00z}(0, 0)}{6\sqrt{K}} \quad \text{as } Z^d \rightarrow \infty \text{ for } X^c < 0. \quad (\text{E.66})$$

We do not solve for w_0^d , but it may be numerically determined from (E.63)–(E.66).

E.6 Region IIe

In this Appendix we resolve the tangential slip induced on the channel walls in region IIa in §3.4.1.2. Therefore, we introduce a boundary layer near $z = 0$ in order to satisfy the no slip condition on the boundary. Again, we confine our analysis to the boundary layer near $z = 0$ for brevity which we denote as region IIe.

The relevant scalings (from region II to region IIe) are $\bar{u}_0 = \delta u^e$, $\bar{w}_0 = \delta w^e$, $X = \delta \hat{X}$ (also used in region IIa) and $z = \delta \hat{z}$, and we introduce the new variable $\bar{p}_1 = p^e$ to signify that we are working in region IIe. With these scalings, the governing equations (3.35) become

$$\delta (u^e u_{\hat{X}}^e + w^e u_{\hat{z}}^e) = -p_{\hat{X}}^e + u_{\hat{X}\hat{X}}^e + u_{\hat{z}\hat{z}}^e, \quad (\text{E.67a})$$

$$\delta (u^e w_{\hat{X}}^e + w^e w_{\hat{z}}^e) = -p_{\hat{z}}^e + w_{\hat{X}\hat{X}}^e + w_{\hat{z}\hat{z}}^e, \quad (\text{E.67b})$$

$$0 = u_{\hat{X}}^e + w_{\hat{z}}^e. \quad (\text{E.67c})$$

Substituting asymptotic expansions

$$u^e \sim u_0^e + O(\delta^{1/3}), \quad (\text{E.68a})$$

$$w^e \sim w_0^e + O(\delta^{1/3}), \quad (\text{E.68b})$$

$$p^e \sim p_{11}^e + O(\delta^{1/3}), \quad (\text{E.68c})$$

into (E.67), we find that the leading-order equations are Stokes flow, as follows

$$0 = -p_{11\hat{X}}^e + u_{0\hat{X}\hat{X}}^e + u_{0\hat{z}\hat{z}}^e, \quad (\text{E.69a})$$

$$0 = -p_{11\hat{z}}^e + w_{0\hat{X}\hat{X}}^e + w_{0\hat{z}\hat{z}}^e, \quad (\text{E.69b})$$

$$0 = u_{0\hat{X}}^e + w_{0\hat{z}}^e. \quad (\text{E.69c})$$

We impose boundary conditions on the channel wall boundary (3.37a) as follows

$$u_0^e = 0, \quad w_0^e = 0, \quad \text{on } \hat{z} = 0 \text{ for } \hat{X} < 0, \quad (\text{E.70a, b})$$

with continuity of normal stress and BJ slip boundary conditions (3.38b,c) on the interface $X = 0$ which, in region IIe scalings, become

$$p_{11}^e - 2u_{0\hat{X}}^e = \bar{P}_{11}(0, 0), \quad w_{0\hat{X}}^e = 0, \quad \text{on } \hat{X} = 0 \text{ for } \hat{z} > 0, \quad (\text{E.71a, b, c})$$

matching conditions between regions IIa and IIe given by

$$u_0^e \sim 6\hat{z}, \quad w_0^e \sim \frac{\lambda}{6\sqrt{K}} \bar{W}_{00z}(0, 0), \quad p_{11}^e \rightarrow 0 \quad \text{as } \hat{z} \rightarrow \infty \text{ for } \hat{X} < 0, \quad (\text{E.72a, b, c})$$

and matching conditions between regions IIId and IIe given by

$$u_0^e \sim 6\hat{z}, \quad w_0^e \sim w_0^d(0, z), \quad p_{11}^e \rightarrow 0 \quad \text{as } \hat{X} \rightarrow -\infty \text{ for } Z^d > 0, \quad (\text{E.73a, b, c})$$

noting that (E.73b) is equivalent to (E.65). We therefore have Stokes flow at leading order in the corner near the interface with appropriate boundary conditions. We do not solve for u_0^e , w_0^e , or p_{11}^e , but they may be numerically determined from (E.69)–(E.73).

E.7 Region VI

In this Appendix, we implicitly solve for the correction to the transverse velocity $\bar{w}_{0a}$ in region VI.

We proceed by following Wilson [80], and solve for $\bar{w}_{0a}$ using a Fourier transform in X^+ . We will be unable to solve for $\bar{w}_{0a}$ explicitly, instead formulating and analysing an implicit representation. We define the Fourier transform of $y(X^+, z)$ in X^+ , denoted $\mathcal{F}(y(X^+, z))$, as follows

$$\mathcal{F}(y(X^+, z)) = \int_0^\infty y(X^+, z) \exp(ikX^+) dX^+. \quad (\text{E.74})$$

The Fourier transform of (3.105) is given by

$$(\mathcal{F}(\bar{w}_{0a}))_{zz} - k^2 \mathcal{F}(\bar{w}_{0a}) = f(k, z), \quad (\text{E.75})$$

where

$$f(k, z) = \frac{\lambda}{\sqrt{K}} (\bar{w}_{0a}(0, z) - \bar{W}_{0a}(0, z)) - ik\bar{w}_{0a}(0, z), \quad (\text{E.76})$$

is evaluated using the BJ slip condition (3.104b). Using the integral identity [56]

$$\int_0^\infty s^{-1/2} \exp(ias) ds = \exp(i\pi/4) \sqrt{\frac{\pi}{a}}, \quad (\text{E.77})$$

to evaluate the Fourier transform of the channel wall boundary conditions (3.103), we can solve (E.75) using variation of parameters to obtain

$$\mathcal{F}(\bar{w}_{0a}) = \frac{g(k, z)}{k \sinh k} - \frac{\tilde{\beta} \sqrt{\pi} \exp(i\pi/4)}{2} h(k, z), \quad (\text{E.78})$$

where the first term in (E.78) is the particular integral due to the right-hand side of (E.75) (present due to the boundary conditions on the porous interface), the second term is the contribution due to the channel walls, and

$$g(k, z) = \sinh k(z-1) \int_0^z f(k, s) \sinh ks ds + \sinh kz \int_z^1 f(k, s) \sinh k(s-1) ds, \quad (\text{E.79a})$$

$$h(k, z) = \frac{\sinh kz + \sinh k(z-1)}{k^{1/2} \sinh k}. \quad (\text{E.79b})$$

We note that the branch cut for $k^{-1/2}$ in (E.79b) is taken along the negative imaginary axis, and we use the branch which is positive along the positive real axis. Therefore, we can obtain an implicit representation of $\bar{w}_{0a}$ by inverting the solution in Fourier space (E.78) to obtain

$$\bar{w}_{0a}(X^+, z) = \frac{1}{2\pi} \int_{-\infty}^{\infty} \left(\frac{g(k, z)}{k \sinh k} - \frac{\tilde{\beta} \sqrt{\pi} \exp(i\pi/4)}{2} h(k, z) \right) \exp(-ikX^+) dk. \quad (\text{E.80})$$

Whilst the implicit nature of (E.80) does not seem to have helped matters much, it does allow us to evaluate the relative importance of the conditions on the porous interface compared to the leakage flux induced via matching with region VIb. We begin by deforming the integration contour for (E.80) into the complex k -plane as shown in Figure E.2. From (E.78), we see that all singularities induced by the porous interface are located at $k = in\pi$ (with the important singularities for the deformation

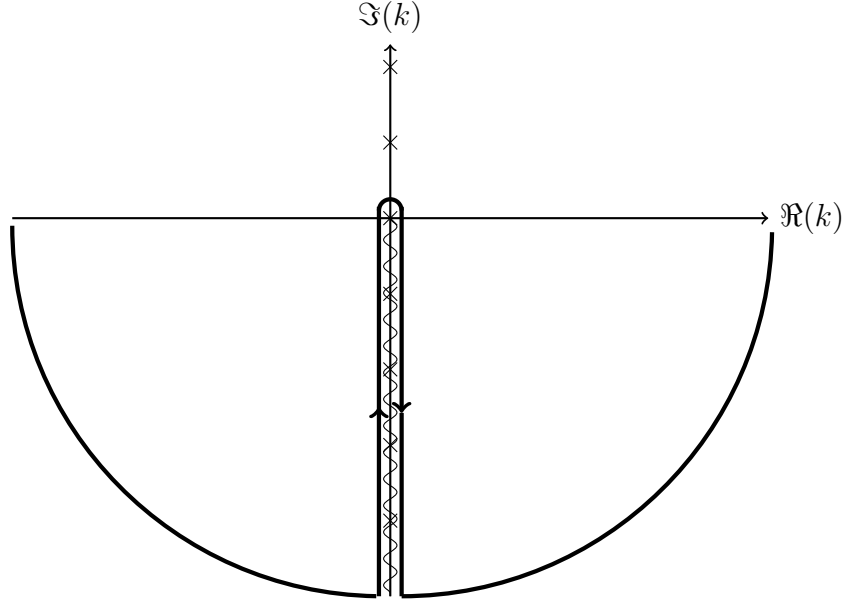


Figure E.2: Contour deformation for inversion of the Fourier integral. The singularities are marked by crosses, and are located at $in\pi$ for $n \in \mathbb{Z}$.

located at $n \in \mathbb{Z}^-$, as we are considering $X^+ > 0$), and that the singularity at $k = 0$ is removable. Therefore, in the limit $X^+ \rightarrow \infty$, the contribution from these singularities (using Cauchy's Residue Theorem) is exponentially small in X^+ with largest exponential $\exp(-\pi X^+)$. However, as there is a branch cut in k along the negative imaginary semi-axis for the second term in the solution (E.78) (which arises due to the channel walls), we do not obtain the same exponentially small terms that we obtain via inversion of the first term in (E.78) as $X^+ \rightarrow \infty$. In fact, if we neglect the first term in (E.80) in the limit $X^+ \rightarrow \infty$ (as its contribution is exponentially small), we obtain an explicit representation for $\bar{w}_{0a}$ which we could invert up to as many algebraic terms as we required.

E.8 Regions VIb and VIc

E.8.1 2D flow

In this section we solve for the flow near the outflow channel wall, in regions we denote region VIb and region VIc (as shown in Figure 3.9). The work in this section is a classic result in boundary layer theory, first outlined in Prandtl [59], and is an excellent candidate for the birth of singular perturbation theory. We emphasise that the work in this section is not original, it is provided for reference and for matching

purposes. As a result, we are fairly brief with the details. We use $X^+ = X$ for convenience.

The relevant scalings from region VI to region VIb are: $z = \delta^{1/2}\check{z}$ and $\bar{w}_0 = \delta^{1/2}\check{w}$. We also use $\bar{u}_0 = \check{u}$ and $\bar{p}_1 = \check{p}$ to signify that we are working in region VIb. With these scalings, the bulk flow governing equations (3.35) in region VIb become

$$\check{u}\check{u}_X + \check{w}\check{u}_z = -\delta\check{p}_X + \check{u}_{zz} + \delta\check{u}_{XX}, \quad (\text{E.81a})$$

$$\check{u}\check{w}_X + \check{w}\check{w}_z = -\check{p}_z + \check{w}_{zz} + \delta\check{w}_{XX}, \quad (\text{E.81b})$$

$$0 = \check{u}_X + \check{w}_z. \quad (\text{E.81c})$$

Then, substituting the asymptotic expansions

$$\check{u} = \check{u}_0 + O(\delta^{1/2}), \quad (\text{E.82a})$$

$$\check{w} = \check{w}_0 + O(\delta^{1/2}), \quad (\text{E.82b})$$

$$\check{p} = \check{p}_{10} + O(\delta^{1/2}), \quad (\text{E.82c})$$

into bulk flow governing equations (E.81), we obtain the following leading-order equations

$$\check{u}_0\check{u}_{0X} + \check{w}_0\check{u}_{0z} = -\check{p}_{10X} + \check{u}_{0zz} \quad \text{in region VIb}, \quad (\text{E.83a})$$

$$0 = -\check{p}_{10z} \quad \text{in region VIb}, \quad (\text{E.83b})$$

$$0 = \check{u}_{0X} + \check{w}_{0z} \quad \text{in region VIb}. \quad (\text{E.83c})$$

The boundary conditions on the channel wall $\check{z} = 0$ are given by

$$\check{u}_0 = 0, \quad \check{w}_0 = 0 \quad \text{on } \check{z} = 0 \text{ for } X > 0, \quad (\text{E.84a, b})$$

and the matching conditions into region VI are given by

$$\check{u}_0 \sim 1, \quad \bar{p}_{10} \rightarrow 0 \quad \text{as } \check{z} \rightarrow \infty \text{ for } X > 0. \quad (\text{E.85a, b})$$

The governing equation (E.83b) in conjunction with the matching condition (E.85b) tell us that $\bar{p}_{10} \equiv 0$ throughout region VIb. The remaining equations and boundary conditions have a similarity solution as follows

$$\check{u}_0 = f'(\eta), \quad \check{w}_0 = \frac{1}{2X^{1/2}} (\eta f'(\eta) - f(\eta)) \quad \text{where } \eta = \check{z}X^{-1/2}, \quad (\text{E.86a, b})$$

where $f(\eta)$ satisfies the following Blasius ODE

$$f''' + \frac{1}{2}ff'' = 0, \quad f(0) = f'(0) = 0, \quad f'(\infty) = 1. \quad (\text{E.87})$$

The function f is well studied (see, e.g. Boyd [8]), its behaviour as $\eta \rightarrow \infty$ is given by

$$f \sim \eta - \tilde{\beta} + \text{exponentially small terms} \quad \text{as } \eta \rightarrow \infty, \quad (\text{E.88})$$

where $\tilde{\beta} \approx 1.721$, and its behaviour for small η is given by

$$f = \frac{f''(0)}{2}\eta^2 + O(\eta^5) \quad \text{as } \eta \rightarrow 0, \quad (\text{E.89})$$

where $f''(0) \approx 0.332$ is a famous result known because it used to calculate the shear stress acting on the channel wall. Substituting (E.88) into the solution for $\check{w}_0$ (E.86b) yields the matching conditions with region VI (3.103a) and (3.103b).

We have calculated the leading-order solution in region VIb but, from the form of (E.86), we see that there appears to be a singularity in the solution as $X \rightarrow 0$. This requires another boundary layer to remedy, and we denote this as region VIc.

The relevant scalings from region VI to region VIc are: $z = \delta z$, $X = \delta X$, and $\bar{p}_1 = \delta^{-1}p$. We also use $\bar{u}_0 = u$, and $\bar{w}_0 = w$ to signify that we are working in region VIc. With these scalings, the bulk flow governing equations (3.35) become

$$uu_X + ww_z = -p_X + u_{zz} + u_{XX} \quad \text{in region VIc}, \quad (\text{E.90a})$$

$$uw_X + ww_z = -p_z + w_{zz} + w_{XX} \quad \text{in region VIc}, \quad (\text{E.90b})$$

$$0 = u_X + w_z \quad \text{in region VIc}, \quad (\text{E.90c})$$

and we therefore have the full 2D steady Navier-Stokes equations. We will not be able to solve these analytically, but give the relevant boundary conditions for completeness. The boundary conditions on the channel wall (3.37a) become

$$u = 0, \quad w = 0 \quad \text{on } z = 0 \text{ for } X > 0, \quad (\text{E.91a, b})$$

the interfacial boundary conditions (3.39) are

$$u = 1, \quad p - 2u_X = 0, \quad w_X = 0 \quad \text{on } X = 0 \text{ for } z > 0, \quad (\text{E.92a, b, c})$$

and the matching conditions into region VIb are given by

$$u \sim f'(\bar{\eta}), \quad w \sim \frac{\bar{\eta}f'(\bar{\eta}) - f(\bar{\eta})}{2\bar{\chi}^{1/2}}, \quad p \rightarrow 0 \quad \text{as } X^2 + z^2 \rightarrow \infty, \quad (\text{E.93a, b, c})$$

where $\bar{\eta} = zX^{-1/2}$.

E.8.2 Region VIb for 3D flow

In this section we consider the flow in region VIb for the 3D problem where the channel walls are moving. The problem for the azimuthal velocity decouples, so we proceed by first solving for the new problem of a moving boundary, and then for the azimuthal velocity.

Using the same scalings for region VIb as in §E.8.1 (and using the same notation for brevity), we obtain the same leading-order governing equations (E.83). Using the same methodology, we obtain a similarity solution to the 3D problem which satisfies the same Blasius differential equation as for the 2D case (E.87). However, for the 3D case, the boundary conditions are different. They are given by

$$f(0) = 0, \quad f'(0) = \mathbf{n} \cdot \mathbf{u}^{\text{slip}}(0, s, t), \quad f'(\infty) = -K P_{0n}(0, s, t) > 0. \quad (E.94a, b, c)$$

Therefore, this problem has two free parameters, the far-field velocity and the wall velocity. We can scale out one of these free parameters by noting that $f(\eta) = ag(a\eta)$, where $a^2 = -K P_{0n}(0, s, t)$, and $g(\eta)$ satisfies the following

$$g''' + \frac{1}{2}gg'' = 0, \quad g(0) = 0, \quad g'(0) = \frac{\mathbf{n} \cdot \mathbf{u}^{\text{slip}}(0, s, t)}{(-K P_{0n}(0, s, t))}, \quad g'(\infty) = 1. \quad (E.95)$$

We therefore deduce that the velocities in this region are given by

$$\check{u}_0 = a^2 g'(\eta), \quad \check{w}_0 = \frac{a}{2X^{1/2}} (\eta g'(\eta) - g(\eta)) \quad \text{where } \eta = \check{z}X^{-1/2}. \quad (E.96a, b)$$

In §E.8.1, we considered the case where $\mathbf{n} \cdot \mathbf{u}^{\text{slip}} = 0$ and $-K P_{0n} = 1$, which had far-field behaviour (E.88). The far-field behaviour for the Blasius differential equation (E.87) using the generalised boundary condition (E.94) is given by

$$g(\eta) \sim \eta - w^l \left(\frac{\mathbf{n} \cdot \mathbf{u}^{\text{slip}}(0, s, t)}{(-K P_{0n}(0, s, t))} \right) + \text{exponentially small terms} \quad \text{as } \eta \rightarrow \infty, \quad (E.97)$$

where we see from (E.95) that w^l is a function of $\mathbf{n} \cdot \mathbf{u}^{\text{slip}}(0, s, t)/(-K P_{0n}(0, s, t))$.

Therefore, from the expression for $\check{w}_0$ (E.96b) and the far-field behaviour (E.97), we can deduce that there is a leakage flux from region VIb, given by

$$\check{w}_0 \sim \frac{w^l (-K P_{0n}(0, s, t))^{1/2}}{2X^{1/2}} \quad \text{as } \check{z} \rightarrow \infty. \quad (E.98)$$

Similarly, the leakage flux on the upper channel wall near $z = 1$ will be (E.98) but with the opposite sign.

We now consider the azimuthal velocity. Using $\bar{v}_0 = \check{v}_0$ to indicate we are working in region VIb, and the same scalings as above, the relevant equation for the azimuthal velocity is obtained from (4.21b), which becomes

$$\check{u}_0 \check{v}_{0X} + \check{w} \check{v}_{0\check{z}} = \check{v}_{0\check{z}\check{z}}, \quad (\text{E.99})$$

with boundary conditions

$$\check{v}_0 = \mathbf{s} \cdot \mathbf{u}^{\text{slip}}(0, s, t) \quad \text{on } \check{z} = 0, \quad (\text{E.100a})$$

$$\check{v}_0 \sim -K P_{0s}(0, s, t) \quad \text{as } \check{z} \rightarrow \infty. \quad (\text{E.100b})$$

The system (E.99)–(E.100) admits a similarity solution

$$\check{v} = -K P_{0s}(0, s, t) h(\eta), \quad \eta = \check{z} X^{-1/2}, \quad (\text{E.101})$$

such that

$$h''(\eta) + \frac{g(\eta)}{2} h'(\eta) = 0, \quad h(0) = \frac{\mathbf{s} \cdot \mathbf{u}^{\text{slip}}(0, s, t)}{(-K P_{0s}(0, s, t))}, \quad h(\infty) = 1, \quad (\text{E.102})$$

which is solved by

$$h(\eta) = \frac{\mathbf{s} \cdot \mathbf{u}^{\text{slip}}(0, s, t)}{(-K P_{0s}(0, s, t))} + \left(1 + \frac{\mathbf{s} \cdot \mathbf{u}^{\text{slip}}(0, s, t)}{K P_{0s}(0, s, t)} \right) \frac{\int_0^\eta \exp\left(-\frac{1}{2} \int_0^\tau g(s) ds\right) d\tau}{\int_0^\infty \exp\left(-\frac{1}{2} \int_0^\tau g(s) ds\right) d\tau}, \quad (\text{E.103})$$

and we note that the solution near the channel wall at $z = 1$ is the same as (E.103), but with the scaling $z = 1 - \delta^{1/2} \check{z}$.

E.9 Small $\tilde{X}$ analysis in region VIa

E.9.1 2D flow

In this section, we provide a small $\tilde{X}$ analysis for the variables in region VIa. This allows us to avoid the singularity at $\tilde{X} = 0$ when we solve the system (3.111)–(3.114) numerically in §3.4.2.2. When discussing the abscissa in region VI, we use $X^+ = X$ for convenience.

We start by calculating the far-field expansion in region VI, from the leading-order solution (3.98), and the far-field $O(\delta^{1/2})$ correction velocities (3.107). The region VI variables up to $O(\delta^{1/2})$ for the flow and up to $O(\delta^{-1/2})$ for the pressure are given by

$$\bar{u}_0 \sim 1 + 2\tilde{\beta}(\delta X)^{1/2}, \quad \bar{w}_0 \sim \frac{\tilde{\beta}(1-2z)}{2(X/\delta)^{1/2}}, \quad \bar{p}_1 \sim \delta^{-1} P_{10}(1) - 2\tilde{\beta}(X/\delta)^{1/2} \quad \text{as } X \rightarrow \infty. \quad (\text{E.104a, b, c})$$

The solution near the channel wall $z = 0$ is given by (E.86) as follows

$$\bar{u}_0 \sim f'(\eta), \quad \bar{w}_0 \sim \frac{\eta f'(\eta) - f(\eta)}{2(X/\delta)^{1/2}} \quad \text{where } \eta = z(\delta X)^{-1/2}, \quad (\text{E.105a, b})$$

with similar near $z = 1$ (essentially taking $\eta = (1 - z)(\delta X)^{-1/2}$ instead and reversing the sign on $\bar{w}_0$). To obtain the small $\tilde{X}$ behaviour in region VIa, we write the far-field expansions (E.104) and (E.105) in terms of $\tilde{X} = \delta X$. Furthermore, it will be useful to form a composite expansion between regions VI and VIb (which is notationally easier in the limit as $X \rightarrow \infty$). We form the multiplicative composite expansion so we can impose no-slip on the channel walls. Then, the combination of composite expansion and far-field limit yields the following

$$\tilde{u}_0 = \left(1 + 2\tilde{\beta}\tilde{X}^{1/2}\right) f'(\tilde{\eta}_{(0)}) f'(\tilde{\eta}_{(1)}) \quad \text{as } \tilde{X} \downarrow 0, \quad (\text{E.106a})$$

$$\tilde{w}_0 = \frac{(1 - 2z)}{2\tilde{\beta}\tilde{X}^{1/2}} (\tilde{\eta}_{(0)} f'(\tilde{\eta}_{(0)}) - f(\tilde{\eta}_{(0)})) (\tilde{\eta}_{(1)} f'(\tilde{\eta}_{(1)}) - f(\tilde{\eta}_{(1)})) \quad \text{as } \tilde{X} \downarrow 0, \quad (\text{E.106b})$$

$$\tilde{p}_{10} = -2\tilde{\beta}\tilde{X}^{1/2} + P_{10}(1) \quad \text{as } \tilde{X} \downarrow 0, \quad (\text{E.106c})$$

where $\tilde{\eta}_{(0)} = z/\tilde{X}^{1/2}$ and $\tilde{\eta}_{(1)} = (1 - z)/\tilde{X}^{1/2}$.

E.9.2 3D flow

In this section we determine suitable matching conditions for the 3D problem in region VIa. To this end, it will be useful to determine the far-field behaviour of the correction terms in region VI.

The analysis follows the 2D case studied in §3.4.2.1, in which we determined the far-field behaviour of the vertical component of velocity using the leakage flux conditions (3.103a) and (3.103b) combined with the far-field limit of the governing equation for the vertical component of velocity (3.105). From this, we used the continuity equation (3.100c) and an equation coupling the velocity to the pressure (3.100a) to deduce the far-field behaviour of all the variables.

The leakage flux from region VIb into region VI is given in (E.98) and, using the same methodology as in §3.4.2.1, we use it to deduce that the far-field behaviour of $\bar{w}_{0a}$ is given by

$$\bar{w}_{0a} \sim w^l \frac{(1 - 2z) (-K P_{0n}(0, s, t))^{1/2}}{2N^{1/2}} \quad \text{as } N \rightarrow \infty. \quad (\text{E.107})$$

Then, using the 3D equivalent of equations (3.100a,c), we determine that

$$\bar{u}_{0a} \sim 2w^l (-K P_{0n}(0, s, t)N)^{1/2} \quad \text{as } N \rightarrow \infty, \quad (\text{E.108a})$$

$$\bar{p}_{0a} \sim -2w^l (-K P_{0n}(0, s, t)N)^{1/2} \quad \text{as } N \rightarrow \infty, \quad (\text{E.108b})$$

which are essentially scaled versions of their 2D equivalents given in (3.106)–(3.107).

Combining (E.107) and (E.108) with the leading order solutions given in (4.56), we obtain the following far-field behaviour in region VI

$$\bar{u}_{0a} \sim -K P_{0n}(0, s, t) + 2w^l (-K P_{0n}(0, s, t)\delta N)^{1/2} \quad \text{as } N \rightarrow \infty, \quad (\text{E.109a})$$

$$\bar{w}_{0a} \sim w^l \frac{(1-2z)(-K P_{0n}(0, s, t))^{1/2}}{2(N/\delta)^{1/2}} \quad \text{as } N \rightarrow \infty, \quad (\text{E.109b})$$

$$\bar{p}_{0a} \sim P_{10}(0, s, t) - 2w^l (-K P_{0n}(0, s, t)\delta N)^{1/2} \quad \text{as } N \rightarrow \infty. \quad (\text{E.109c})$$

Finally, forming multiplicative composite expansions with the solutions in region VIb, given by (E.96), the matching condition for the small $\tilde{N}$ behaviour in region VIa (using region VIa notation) is given by

$$\tilde{u}_0 \sim \left(-K P_{0n}(0, s, t) + 2w^l \left(-K P_{0n}(0, s, t)\tilde{N} \right)^{1/2} \right) g'(\tilde{\eta}_{(0)}) g'(\tilde{\eta}_{(1)}), \quad (\text{E.110a})$$

$$\tilde{w}_0 \sim w^l \frac{(1-2z)(-K P_{0n}(0, s, t))^{1/2}}{2\tilde{N}^{1/2}} \left(\tilde{\eta}_{(0)} g'(\tilde{\eta}_{(0)}) - g(\tilde{\eta}_{(0)}) \right) \left(\tilde{\eta}_{(1)} g'(\tilde{\eta}_{(1)}) - g(\tilde{\eta}_{(1)}) \right), \quad (\text{E.110b})$$

$$\tilde{p}_1 \sim P_{10}(0, s, t) - 2w^l \left(-K P_{0n}(0, s, t)\tilde{N} \right)^{1/2}, \quad (\text{E.110c})$$

as $\tilde{N} \downarrow 0$, and where $g(\eta)$ is defined in (E.95) with $\tilde{\eta}_{(0)} = z/\tilde{N}^{1/2}$ and $\tilde{\eta}_{(1)} = (1-z)/\tilde{N}^{1/2}$.

We can determine the matching conditions for the azimuthal velocity by forming the composite expansion of the solution in region VI (4.56b) with the solution near the channel walls (E.101) and (E.103). Then, the matching condition between region VI and region VIa is

$$\tilde{v}_{00} \sim -K P_{0s}(0, s, t) h(\tilde{\eta}_{(0)}) h(\tilde{\eta}_{(1)}) \text{ as } \tilde{N} \downarrow 0, \quad (\text{E.111})$$

as given in (4.75).

E.10 Thin gaps

We now consider the flow within the thin gaps of dimensionless height ϵ_2 between the tissue construct (TC) and bioreactor. This induces two boundary layers which we define as regions VIII and IX as shown in Figure E.3.

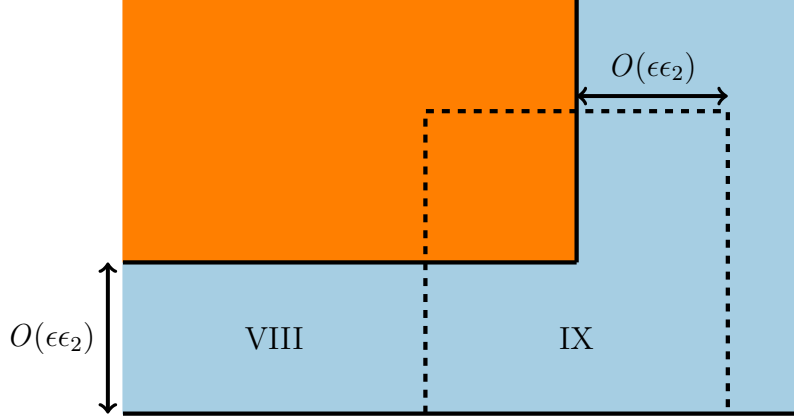


Figure E.3: Schematic diagram of the thin gap boundary layer structure for regions VIII and IX. The blue region is the bulk fluid and the orange region is the porous obstacle.

We start with region VIII, where we scale $z = \epsilon_2 \hat{z}$, and $w = \epsilon_2 \hat{w}$. Then, governing equations (2.13) become

$$O(\epsilon Re) = -p_X + \epsilon_2^{-2} u_{\hat{z}\hat{z}}, \quad (\text{E.112a})$$

$$O(\epsilon Re) = -p_Y + \epsilon_2^{-2} v_{\hat{z}\hat{z}}, \quad (\text{E.112b})$$

$$0 = -\epsilon_2^{-1} p_{\hat{z}} + O(\epsilon^2 \epsilon_2^{-1}), \quad (\text{E.112c})$$

$$0 = u_X + v_Y + \hat{w}_{\hat{z}}, \quad (\text{E.112d})$$

with boundary conditions of no slip and flux on $\hat{z} = 0$ given by (2.19) and on $\hat{z} = 1$ given by (2.20a).

The solution of (E.112) up to $O(\epsilon_2^2)$ is

$$\mathbf{u} = \epsilon_2^2 \frac{\hat{z}(\hat{z} - 1)}{2} \nabla p + ((1 - \dot{\varphi}) \mathbf{e}_z \times \mathbf{X})(1 - \hat{z}) + \left(\dot{R} \mathbf{e}_X + (\omega - \dot{\varphi}) \mathbf{e}_z \times \mathbf{r} \right) \hat{z}, \quad (\text{E.113})$$

where the pressure satisfies

$$\nabla^2 p = 0. \quad (\text{E.114})$$

Using the dimensionless stress tensor defined in (5.10a), we can deduce that the stress of the fluid acting on the TC surface T_2 is given by

$$\boldsymbol{\sigma} \cdot \mathbf{n} = -\frac{1}{\epsilon \epsilon_2} \frac{\partial \mathbf{u}}{\partial \hat{z}} - \frac{1}{\epsilon^2} p \mathbf{n} - \epsilon \epsilon_2 \nabla \hat{w}, \quad (\text{E.115})$$

where $\mathbf{n} = \mathbf{e}_z$.

By differentiating (E.113) with respect to $\hat{z}$, we obtain

$$\frac{\partial \mathbf{u}}{\partial \hat{z}} = \epsilon_2^2 \left(\hat{z} - \frac{1}{2} \right) \nabla p + \dot{R} \mathbf{e}_X - R(1 - \dot{\varphi}) \mathbf{e}_Y - (1 - \omega) \mathbf{e}_z \times \mathbf{r}. \quad (\text{E.116})$$

On T_3 , the stress of the fluid acting on the TC is given by (E.115) but with opposite sign due to $\mathbf{n} = \mathbf{e}_z$. The velocity of the fluid adjacent to T_3 (with a suitable translation for $\hat{z}$) is given by (E.113) but with the opposite sign. Therefore, the effect of pressure on (E.115) will cancel, but the effect of the shear stress due to the fluid will double. The effective shear stress on the TC due to the flat sides is then given by

$$\boldsymbol{\sigma} \cdot \mathbf{n} = -\frac{2}{\epsilon \epsilon_2} \left(\dot{R} \mathbf{e}_X - R(1 - \dot{\varphi}) \mathbf{e}_Y - (1 - \omega) \mathbf{e}_z \times \mathbf{r} \right) + O(\epsilon_2 \epsilon^{-1}). \quad (\text{E.117})$$

We now consider region IX. It will be convenient to work in cylindrical polar coordinates (r, θ, z) with origin at the TC centre where $\mathbf{u} = u \mathbf{e}_r + v \mathbf{e}_\theta + w \mathbf{e}_z$, and we scale $z = \epsilon_2 \hat{z}$, $r = b + \epsilon \epsilon_2 \hat{R}$, and $w = \epsilon^{-1} \hat{w}$. Then, the governing equations (2.13) in these scaled cylindrical coordinates become

$$O(\epsilon_2 Re) = -\frac{\epsilon_2}{\epsilon} p_{\hat{R}} + u_{\hat{z}\hat{z}} + u_{\hat{R}\hat{R}}, \quad (\text{E.118a})$$

$$O(\epsilon_2 Re) = v_{\hat{z}\hat{z}} + v_{\hat{R}\hat{R}}, \quad (\text{E.118b})$$

$$O(\epsilon_2 Re) = -\frac{\epsilon_2}{\epsilon} p_{\hat{z}} + \hat{w}_{\hat{z}\hat{z}} + \hat{w}_{\hat{R}\hat{R}}, \quad (\text{E.118c})$$

$$0 = u_{\hat{R}} + \hat{w}_{\hat{z}} + O(\epsilon \epsilon_2). \quad (\text{E.118d})$$

We note that this is the first point at which we have required the assumption that $\epsilon_2 Re \ll 1$ described in §2.3. We further note that a dominant balance is obtained when $\epsilon_2 = O(\epsilon)$, and that this is consistent with $\epsilon_2 Re \ll 1$. In this case, (E.118) is Stokes flow at leading order. If we integrate the continuity equation (E.118d) across $\hat{z}$ within the channel for $\hat{R} < 0$, we see that the effect of the thin gaps in the outer bulk flow is to provide a source at the corners of strength $O(\epsilon \epsilon_2)$. This is smaller than any term of the asymptotic expansions we investigate, and we can therefore deduce that the thin gaps have no effect on the flow at the orders which we have investigated.

We further note that if we wished to solve these, we could use complex variable theory. The complex mapping

$$\zeta(z) = \frac{1}{\pi} \left(2(z+1)^{1/2} + \log \left(\frac{(z+1)^{1/2} + 1}{(z+1)^{1/2} - 1} \right) \right), \quad (\text{E.119})$$

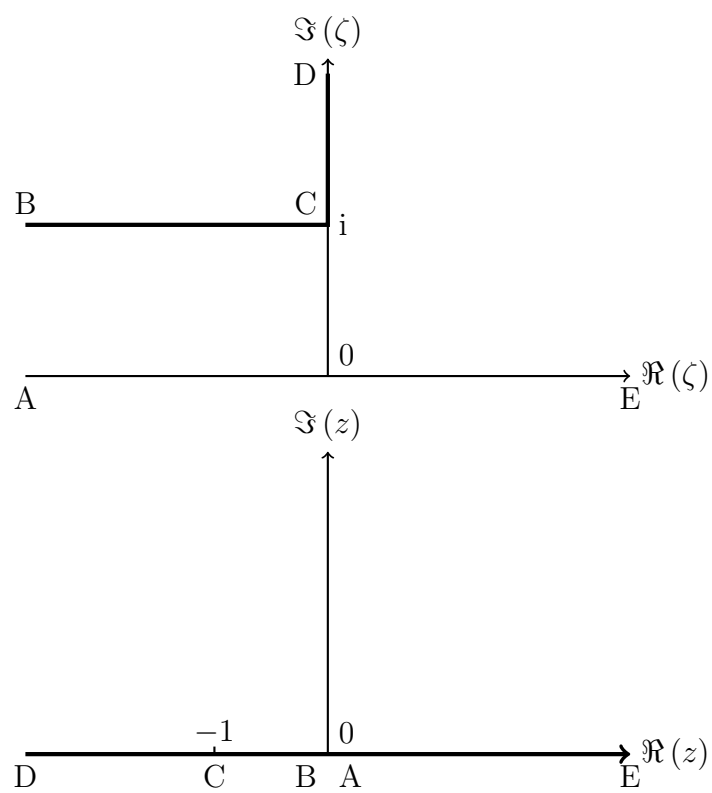


Figure E.4: Schematic diagram of the conformal mapping $\zeta(z)$ described in (E.119).

turns the upper half-plane (in terms of $z = \hat{R} + i\hat{z}$) into the region shown in Figure E.4 (in terms of $\zeta = \xi + i\eta$). Then, using a streamfunction ψ such that $\psi_{\hat{z}} = u$ and $\psi_{\hat{R}} = -\hat{w}$, the governing equation for u and $\hat{w}$ becomes

$$\nabla^4 \psi = 0, \quad (\text{E.120})$$

which is solved by [15]

$$\psi = \Im(\bar{z}f(z) + g(z)), \quad (\text{E.121})$$

where $f(z)$ and $g(z)$ are analytic functions that satisfy the correct boundary conditions.

E.11 Higher-order average flux

In this section we determine a higher-order averaged normal flux condition to couple the outer regions in the 3D problem considered in Chapter 4. The leading-order continuity equations are given in (4.21d) and (4.23d), and by integrating these over the cell height, and imposing the no-flux boundary conditions (4.24), we deduce that

$$\frac{\partial}{\partial N} \int_0^1 \bar{u}_0(N, s, z, t) dz = 0, \quad \frac{\partial}{\partial N} \int_0^1 \bar{U}_0(N, s, z, t) dz = 0. \quad (\text{E.122})$$

The $O(\epsilon)$ versions of the continuity equations, obtained by substituting (4.19) into (4.15d) and (4.16d), then equating powers of $O(\epsilon)$, are given by

$$0 = \bar{u}_{1N} + \bar{w}_{1z} + \kappa(s)\bar{u}_0 + \bar{v}_{0s} \quad \text{outside the TC}, \quad (\text{E.123a})$$

$$0 = \bar{U}_{1N} + \bar{W}_{1z} + \kappa(s)\bar{U}_0 + \bar{V}_{0s} \quad \text{inside the TC}. \quad (\text{E.123b})$$

The relevant boundary conditions on the Hele-Shaw cell wall are for $\bar{w}_1$ and $\bar{W}_1$, and are obtained from (4.17) at $O(\epsilon)$, which yield

$$\bar{w}_1 = 0 \quad \text{on } z = 0, 1 \text{ for } N > 0, \quad (\text{E.124a})$$

$$\bar{W}_1 = 0 \quad \text{on } z = 0, 1 \text{ for } N < 0. \quad (\text{E.124b})$$

The relevant interfacial conditions for $\bar{u}_1$ and $\bar{U}$ are obtained from (4.18a) at $O(\epsilon)$, and yield

$$\bar{u}_1 = \bar{U}_1 \quad \text{on } N = 0. \quad (\text{E.125})$$

To investigate the continuity equations (E.123), we also require matching conditions for $\bar{u}_1$ and $\bar{U}_1$ into the outer regions. For the bulk and porous flow, these are given by

$$\bar{u}_1 \sim (N \mathbf{u}_{0n}^{\text{rel}}(0, s, z, t) + \mathbf{u}_1^{\text{rel}}(0, s, z, t)) \cdot \mathbf{e}_n \quad \text{as } N \rightarrow -\infty, \quad (\text{E.126a})$$

$$\bar{U}_1 \sim (N \mathbf{Q}_{0n}^{\text{rel}}(0, s, z, t) + \mathbf{Q}_1^{\text{rel}}(0, s, z, t)) \cdot \mathbf{e}_n \quad \text{as } N \rightarrow \infty. \quad (\text{E.126b})$$

In a similar manner to the $O(1)$ coupling condition, we integrate the continuity equations (E.123) over the cell height, and imposing the no-flux boundary conditions (E.124), we deduce that

$$\int_0^1 \bar{u}_{1N}(N, s, z, t) dz + \kappa(s) \int_0^1 \bar{u}_0(N, s, z, t) dz + \int_0^1 \bar{v}_{0s}(N, s, z, t) dz = 0, \quad (\text{E.127a})$$

$$\int_0^1 \bar{U}_{1N}(N, s, z, t) dz + \kappa(s) \int_0^1 \bar{U}_0(N, s, z, t) dz + \int_0^1 \bar{V}_{0s}(N, s, z, t) dz = 0. \quad (\text{E.127b})$$

Using the matching conditions (4.28), (4.30), and (E.126), we can determine the far-field limit of (E.127) is given by

$$\int_0^1 \mathbf{e}_n \cdot (\mathbf{u}_{0n}^{\text{rel}}(0, s, z, t) + \kappa(s) \mathbf{u}_0^{\text{rel}}(0, s, z, t)) dz + \int_0^1 \mathbf{e}_s \cdot \mathbf{u}_{0s}^{\text{rel}}(0, s, z, t) dz = 0, \quad (\text{E.128a})$$

$$\int_0^1 \mathbf{e}_n \cdot (\mathbf{Q}_{0n}^{\text{rel}}(0, s, z, t) + \kappa(s) \mathbf{Q}_0^{\text{rel}}(0, s, z, t)) dz + \int_0^1 \mathbf{e}_s \cdot \mathbf{Q}_{0s}^{\text{rel}}(0, s, z, t) dz = 0. \quad (\text{E.128b})$$

Subtracting (E.128) from (E.127), using the fact that the leading-order averaged normal velocities are constant in N (E.122), and that $\bar{V}_0$ is constant in N (from (4.22) and (4.23b)), we obtain

$$\int_0^1 (\bar{u}_{1N}(N) - \mathbf{e}_n \cdot \mathbf{u}_{0n}^{\text{rel}}|_{n=0}) dz + \int_0^1 (\bar{v}_{0s}(N) - \mathbf{e}_s \cdot \mathbf{u}_{0s}^{\text{rel}}|_{n=0}) dz = 0, \quad (\text{E.129a})$$

$$\int_0^1 (\bar{U}_{1N}(N) - \mathbf{e}_s \cdot \mathbf{Q}_{0n}^{\text{rel}}|_{n=0}) dz = 0, \quad (\text{E.129b})$$

where we have suppressed all arguments apart from N for ease of notation. Integrating (E.129) with respect to N , we deduce that

$$\begin{aligned} \int_0^1 (\bar{u}_1(N) - N \mathbf{e}_n \cdot \mathbf{u}_{0n}^{\text{rel}}|_{n=0}) dz &= - \int_0^N \int_0^1 (\bar{v}_{0s}(\xi) - \mathbf{e}_s \cdot \mathbf{u}_{0s}^{\text{rel}}|_{n=0}) dz d\xi \\ &\quad + \int_0^1 \bar{u}_1(0) dz, \end{aligned} \quad (\text{E.130a})$$

$$\int_0^1 (\bar{U}_1(N) - N \mathbf{e}_n \cdot \mathbf{Q}_{0n}^{\text{rel}}|_{n=0}) dz = \int_0^1 \bar{U}_1(0) dz. \quad (\text{E.130b})$$

Then, taking the limit as $N \rightarrow \infty$ in (E.130a), and the limit as $N \rightarrow -\infty$ in (E.130b), we obtain

$$\int_0^1 \mathbf{e}_n \cdot \mathbf{u}_1^{\text{rel}} dz = - \int_0^\infty \int_0^1 (\bar{v}_{0s}(\xi) - \mathbf{e}_s \cdot \mathbf{u}_{0s}^{\text{rel}}|_{n=0}) dz d\xi + \int_0^1 \bar{u}_1(0) dz, \quad (\text{E.131a})$$

$$\int_0^1 \mathbf{e}_n \cdot \mathbf{Q}_1^{\text{rel}} dz = \int_0^1 \bar{U}_1(0) dz. \quad (\text{E.131b})$$

Finally, integrating the interfacial continuity of flux condition (E.125) across the Hele-Shaw cell height, we can equate (E.131a) and (E.131b) to obtain (4.31).

E.12 Converting the coupling conditions between frames

In this section we convert the coupling conditions (4.90)–(4.92), derived in Chapter 4, into the frame and variables used in Chapter 2.

For the boundary layer work in Chapters 3 and 4, it was convenient to nondimensionalize using the TC radius as the typical lengthscale. However, in Chapter 2, we use the bioreactor radius as the typical lengthscale. Therefore, we must take care when applying the boundary layer results to Chapter 2. We note, however, that as there are no dimensional constants present in the coupling conditions (4.90)–(4.92), we are able to use the conditions as they stand, replacing the dimensionless variables from Chapter 4 with the dimensionless variables from Chapter 2.

Therefore, to write the outer coupling conditions (4.90), (4.91) and (4.92) in terms of Chapter 2 variables, our only task is to move from the frame where the TC is stationary (as used in this Chapter), to the frame which is rotating with the TC (which is used in Chapter 2). For this task, we use the conversion from laboratory frame to the frame where the TC is stationary (F.1), and the conversion from the laboratory frame to the frame which is rotating with the TC (2.5). Then, the conversion from the frame where the TC is stationary to the frame which is rotating with the TC is given by

$$\mathbf{u}^{\text{rel}} = \mathbf{u} - \dot{R}\mathbf{e}_X + (\dot{\varphi} - \omega)\mathbf{e}_z \times \mathbf{r}, \quad \mathbf{Q}^{\text{rel}} = \mathbf{Q} - \dot{R}\mathbf{e}_X + (\dot{\varphi} - \omega)\mathbf{e}_z \times \mathbf{r}. \quad (\text{E.132a, b})$$

We note that pressure is a scalar function, and is therefore invariant to a change in frame. In particular, this means that the relationship between interior pressure and averaged velocity (obtained via integration of the outer coupling conditions (4.10b)

and (4.14)) holds in general, and is given by

$$-K \frac{\partial P_0}{\partial n} = \int_0^1 \mathbf{u}_0^{\text{rel}} \cdot \mathbf{n} \, dz, \quad (\text{E.133})$$

which will be useful in simplifying the coupling conditions. As $K \geq 0$, it may be dropped on the left-hand side of (E.133) if we are only interested in the sign of (E.133) (as is the case for the argument within the Heaviside function).

Then, in terms of Chapter 2 variables, the pressure coupling conditions (4.90a) and (4.91a) become

$$p_0 - P_0 = 0, \quad (\text{E.134a})$$

$$p_1 - P_1 = (K P_{0n})^2 \Pi \left(-\frac{\mathbf{n} \cdot \mathbf{u}^{\text{slip}}}{K P_{0n}} \right) H(-P_{0n}), \quad (\text{E.134b})$$

where the function Π is defined in (4.71). The averaged normal flux coupling conditions (4.90b) and (4.91b) become

$$\int_0^1 ((\mathbf{u}_0 - \mathbf{Q}_0) \cdot \mathbf{n}) \, dz = 0, \quad (\text{E.135a})$$

$$\int_0^1 ((\mathbf{u}_1 - \mathbf{Q}_1) \cdot \mathbf{n}) \, dz = -K \frac{\partial}{\partial s} (P_{0n} \Lambda(s, t)) H(-P_{0n}), \quad (\text{E.135b})$$

where the function Λ is defined in (4.89). Finally, we note that in terms of the Chapter 2 frame and variables, the wall slip can be determined from its value in the frame where the TC is stationary (F.6), and is given by

$$\mathbf{u}^{\text{slip}}(0, s, t) = (1 - \omega) \mathbf{e}_z \times \mathbf{r} - \dot{R} \mathbf{e}_X + (1 - \dot{\varphi}) R \mathbf{e}_Y. \quad (\text{E.136})$$

We note that $\mathbf{n} \cdot (\mathbf{e}_z \times \mathbf{r}) = 0$ for a circular boundary, though we additionally determine in Chapter 5 that $\omega = 1$ at leading-order, so this point is moot. Finally, we obtain the boundary conditions on the curved bioreactor wall from (4.92), which are

$$\int_0^1 \mathbf{u}_0 \cdot \mathbf{n} \, dz = 0, \quad \int_0^1 \mathbf{u}_1 \cdot \mathbf{n} \, dz = 0. \quad (\text{E.137})$$

Appendix F

Navier-Stokes in curvilinear coordinates

In §4, it will be useful to work in curvilinear coordinates which have one family parallel to the porous obstacle (TC) boundary ∂D . We use the coordinate system (n, s, z) such that $n = 0$ on ∂D , increasing n moves in the outward normal direction, and s is in the anticlockwise tangential direction. Therefore, we are in a frame in which the TC is stationary. The fluid velocity external to and relative to the motion of the TC is $\mathbf{u}^{\text{rel}} = u\mathbf{e}_n + v\mathbf{e}_s + w\mathbf{e}_z$, and the fluid velocity internal to and relative to the motion of the TC is $\mathbf{Q}^{\text{rel}} = U\mathbf{e}_n + V\mathbf{e}_s + W\mathbf{e}_z$. In terms of variables defined in Chapter 2, note that

$$\mathbf{u}^{\text{rel}} = \mathbf{u}_{\text{LF}} - \mathbf{V}_{\text{TC}}, \quad \mathbf{Q}^{\text{rel}} = \mathbf{Q}_{\text{LF}} - \mathbf{V}_{\text{TC}}. \quad (\text{F.1a}, b)$$

The general Navier-Stokes equations in a frame where the TC is stationary are adapted from Schlichting and Gersten [66], and are

$$\begin{aligned} & \rho \left(\frac{\partial u}{\partial t} + u \frac{\partial u}{\partial n} + \frac{v}{1 + \kappa n} \frac{\partial u}{\partial s} - \frac{\kappa}{1 + \kappa n} v^2 + w \frac{\partial u}{\partial z} + \mathbf{f}^{\text{rel}} \cdot \mathbf{e}_n \right) \\ &= -\frac{\partial p}{\partial n} + \frac{1}{1 + \kappa n} \frac{\partial}{\partial n} ((1 + \kappa n) \tau_{nn}) + \frac{1}{1 + \kappa n} \frac{\partial \tau_{ns}}{\partial s} - \frac{\kappa}{1 + \kappa n} \tau_{ss} + \frac{\partial \tau_{nz}}{\partial z}, \end{aligned} \quad (\text{F.2a})$$

$$\begin{aligned} & \rho \left(\frac{\partial v}{\partial t} + u \frac{\partial v}{\partial n} + \frac{v}{1 + \kappa n} \frac{\partial v}{\partial s} + \frac{\kappa}{1 + \kappa n} uv + w \frac{\partial v}{\partial z} + \mathbf{f}^{\text{rel}} \cdot \mathbf{e}_s \right) \\ &= -\frac{1}{1 + \kappa n} \frac{\partial p}{\partial s} + \frac{1}{(1 + \kappa n)^2} \frac{\partial}{\partial n} ((1 + \kappa n)^2 \tau_{ns}) + \frac{1}{1 + \kappa n} \frac{\partial \tau_{ss}}{\partial s} + \frac{\partial \tau_{sz}}{\partial z}, \end{aligned} \quad (\text{F.2b})$$

$$\begin{aligned} & \rho \left(\frac{\partial w}{\partial t} + u \frac{\partial w}{\partial n} + \frac{v}{1 + \kappa n} \frac{\partial w}{\partial s} + w \frac{\partial w}{\partial z} \right) \\ &= -\frac{\partial p}{\partial z} + \frac{1}{1 + \kappa n} \frac{\partial}{\partial n} ((1 + \kappa n) \tau_{nz}) + \frac{1}{1 + \kappa n} \frac{\partial \tau_{sz}}{\partial s} + \frac{\partial \tau_{zz}}{\partial z}, \end{aligned} \quad (\text{F.2c})$$

$$0 = \frac{1}{1 + \kappa n} \frac{\partial}{\partial n} ((1 + \kappa n) u) + \frac{1}{1 + \kappa n} \frac{\partial v}{\partial s} + \frac{\partial w}{\partial z}, \quad (\text{F.2d})$$

where ρ is the density of the fluid and $\kappa = \kappa(s)$ is the curvature of the obstacle. The viscous stresses are given by

$$\tau_{nn} = 2\mu \frac{\partial u}{\partial n}, \quad (\text{F.3a})$$

$$\tau_{ss} = \mu \left(\frac{2}{1 + \kappa n} \left(\frac{\partial v}{\partial s} + \kappa u \right) \right), \quad (\text{F.3b})$$

$$\tau_{zz} = 2\mu \frac{\partial w}{\partial z} \quad (\text{F.3c})$$

$$\tau_{ns} = \mu \left(\frac{\partial v}{\partial n} - \frac{\kappa v}{1 + \kappa n} + \frac{1}{1 + \kappa n} \frac{\partial u}{\partial s} \right), \quad (\text{F.3d})$$

$$\tau_{nz} = \mu \left(\frac{\partial w}{\partial n} + \frac{\partial u}{\partial z} \right), \quad (\text{F.3e})$$

$$\tau_{sz} = \mu \left(\frac{1}{1 + \kappa n} \frac{\partial w}{\partial s} + \frac{\partial v}{\partial z} \right), \quad (\text{F.3f})$$

where μ is the viscosity of the fluid. The fictitious forces from the moving reference frame are given by

$$\mathbf{f}^{\text{rel}} = 2\omega \mathbf{e}_z \times \mathbf{u}^{\text{rel}} - \omega^2 \mathbf{r} + \dot{\omega} \mathbf{e}_z \times \mathbf{r} - \frac{d^2}{dt^2} (R \mathbf{e}_X). \quad (\text{F.4})$$

where R is the distance between bioreactor origin and TC centre of mass, ω is the angular velocity of the TC about its centre of mass, and $\mathbf{r}$ is the position vector with TC centre of mass as the origin.

From (A.10), the general Darcy equations in a frame where the obstacle centre of mass is stationary are given by

$$U = -\frac{k}{\mu} \frac{\partial P}{\partial n}, \quad (\text{F.5a})$$

$$V = -\frac{k}{\mu} \left(\frac{1}{1 + \kappa n} \frac{\partial P}{\partial s} \right), \quad (\text{F.5b})$$

$$W = -\frac{k}{\mu} \frac{\partial P}{\partial z}, \quad (\text{F.5c})$$

$$0 = \frac{1}{1 + \kappa n} \frac{\partial}{\partial n} ((1 + \kappa n) U) + \frac{1}{1 + \kappa n} \frac{\partial V}{\partial s} + \frac{\partial W}{\partial z}, \quad (\text{F.5d})$$

where k is the permeability of the porous medium.

The boundary conditions for the Navier-Stokes flow on the Hele-Shaw cell walls $z = 0, \epsilon$ are given by (2.8). We can transform this into a condition on $\mathbf{u}^{\text{rel}}$ by using (F.1) to determine that on $z = 0, \epsilon$ we have

$$\mathbf{u}^{\text{rel}} = (\Omega - \omega) \mathbf{e}_z \times \mathbf{r} - \dot{R} \mathbf{e}_X + (\Omega - \dot{\varphi}) R \mathbf{e}_Y. \quad (\text{F.6})$$

Appendix G

Linear and angular momentum

In this appendix, we discuss the form of the rate of change of momentum in the force balance equation. The entire tissue construct (TC) region is denoted as $V(t)$, the fluid part of the TC is denoted as $V_f(t)$ and the solid part of the TC is denoted as $V_s(t)$. We note that $|V_f|/|V| = \phi$, and $|V_s|/|V| = 1 - \phi$, where $\phi \in [0, 1]$ is the porosity of the TC.

G.1 Linear momentum

Recalling that the velocity of a point in the TC is given by $\mathbf{V}_{\text{TC}}(\mathbf{x}, t) = \dot{\mathbf{a}} + \boldsymbol{\omega} \times \mathbf{r}$ (defined fully in (2.1)), the rate of change of the linear momentum $\mathbf{P}$ of the TC is given by

$$\frac{d\mathbf{P}}{dt} = \frac{d}{dt} \left(\iiint_{V_f(t)} \rho \mathbf{v} dV + \iiint_{V_s(t)} \rho_s \mathbf{V}_{\text{TC}} dV \right) + \iint_{\partial V_f(t)} \rho \mathbf{v} ((\mathbf{v} - \mathbf{V}_{\text{TC}}) \cdot \mathbf{n}) dV, \quad (\text{G.1})$$

where $\mathbf{v}$ is the pointwise fluid velocity in the inertial frame (as discussed in Appendix A), ρ is the density of the fluid, and ρ_s is the density of the solid matrix inside the TC.

The first bracketed term in (G.1) is the rate of change of the momentum of material within the TC, and the second term is the flux of momentum through the boundary of the TC. This ‘momentum flux’ is equal to the total momentum of the fluid multiplied by the flux through the boundary. Considering the rate of change of momentum within a region and the momentum carried through the boundary is one way to derive the Navier-Stokes equations when considering a fixed boundary in space rather than a fluid blob moving with the flow [1]. Here, we are performing a similar procedure,

but for a region moving with a prescribed velocity rather than a fixed region or a region specifically moving with the fluid.

The second term on the right-hand side of (G.1) is easily dealt with as there are no spatially varying terms in the integrand. The rotating terms vanish as the origin of the position vector is the centre of mass, and so we write the second term as

$$\frac{d}{dt} \iiint_{V_s(t)} \rho_s \mathbf{V}_{TC} dV = \frac{d}{dt} \iiint_{V(t)} \rho_s (1 - \phi) \dot{\mathbf{a}} dV, \quad (\text{G.2})$$

for later ease of use.

The first term on the right-hand side of (G.1) needs more thought. It will be helpful to think about the velocity in a frame moving with the solid matrix, and so we subtract and add the TC velocity

$$\frac{d}{dt} \iiint_{V_f(t)} \rho \mathbf{v} dV = \frac{d}{dt} \iiint_{V_f(t)} \rho (\mathbf{v} - \mathbf{V}_{TC}) dV + \frac{d}{dt} \iiint_{V_f(t)} \rho \mathbf{V}_{TC} dV. \quad (\text{G.3})$$

The second integral on the right-hand side is easily dealt with as before, and we obtain

$$\frac{d}{dt} \iiint_{V_f(t)} \rho \mathbf{V}_{TC} dV = \frac{d}{dt} \iiint_{V(t)} \rho \phi \dot{\mathbf{a}} dV. \quad (\text{G.4})$$

Then, we can re-write (G.1) as

$$\begin{aligned} \frac{d\mathbf{P}}{dt} = & \frac{d}{dt} \iiint_{V(t)} (\rho \phi + \rho_s (1 - \phi)) \dot{\mathbf{a}} dV \\ & + \frac{d}{dt} \iiint_{V_f(t)} \rho (\mathbf{v} - \mathbf{V}_{TC}) dV + \iint_{\partial V_f(t)} \rho \mathbf{v} ((\mathbf{v} - \mathbf{V}_{TC}) \cdot \mathbf{n}) dV, \end{aligned} \quad (\text{G.5})$$

The last two terms on the right-hand side of (G.5) are then exactly the rate of change of fluid momentum within the TC in a frame moving with the TC. To put it another way, if we were to derive the Navier-Stokes equations by considering a force balance equation on a region moving with velocity $\mathbf{V}_{TC}$, we would obtain the last two terms term on the right-hand side of (G.5).

However, these are exactly the terms that are neglected in a Darcy model of flow through porous media, in which the assumption is that the pore-scale Reynolds number is negligible. This has been discussed in Appendix A.

Therefore, in a manner consistent with the assumption that Darcy's equations hold, the rate of change of linear momentum can be approximated by the first term

of (G.5). We define an effective density of $\rho_c = \rho\phi + \rho_s(1 - \phi)$, and note that M_c , the mass of the TC, is given by $M_c = \rho_c\pi b^2 d$.

Therefore, the form of (G.5) that we use is

$$\frac{d\mathbf{P}}{dt} = M_c \frac{d^2\mathbf{a}}{dt^2}. \quad (\text{G.6})$$

G.2 Angular momentum

The rate of change of the angular momentum $\mathbf{L}$ of the TC is given by

$$\begin{aligned} \frac{d\mathbf{L}}{dt} = & \frac{d}{dt} \left(\iiint_{V_f(t)} \rho \mathbf{r} \times \mathbf{v} dV + \iiint_{V_s(t)} \rho_s \mathbf{r} \times \mathbf{V}_{\text{TC}} dV \right) \\ & + \iiint_{\partial V_f(t)} \rho \mathbf{r} \times \mathbf{v} ((\mathbf{v} - \mathbf{V}_{\text{TC}}) \cdot \mathbf{n}) dV. \end{aligned} \quad (\text{G.7})$$

We note that for the same reasons as in the previous section, the angular momentum of the fluid relative to the movement of the solid matrix will be negligible. Therefore, we can deduce that

$$\frac{d\mathbf{L}}{dt} = \frac{d}{dt} \left(\iiint_{V(t)} \rho_c \mathbf{r} \times \mathbf{V}_{\text{TC}} dV \right). \quad (\text{G.8})$$

As is expected with the angular velocity, the term due to the movement of the centre of mass will vanish. We therefore obtain

$$\frac{d\mathbf{L}}{dt} = \frac{d}{dt} \left(\iiint_{V(t)} \rho_c \mathbf{r} \times (\boldsymbol{\omega} \times \mathbf{r}) dV \right). \quad (\text{G.9})$$

As $\boldsymbol{\omega} = \omega \mathbf{e}_z$, and the TC has a plane of symmetry on $z = 1/2$, we can deduce that the term in the brackets of the right-hand side of (G.9) is given by

$$\iiint_{V(t)} \rho_c \mathbf{r} \times (\boldsymbol{\omega} \times \mathbf{r}) dV = \int_{\epsilon_1 b}^{h - \epsilon_1 b} \int_0^{2\pi} \int_0^b \rho_c r^3 \omega \mathbf{e}_z dr d\theta dz, \quad (\text{G.10})$$

where the integral can be solved to deduce that

$$\iiint_{V(t)} \rho_c \mathbf{r} \times (\boldsymbol{\omega} \times \mathbf{r}) dV = \frac{M_c b^2 \omega(t)}{2} \mathbf{e}_z. \quad (\text{G.11})$$

Therefore, we can write (G.9) as

$$\frac{d\mathbf{L}}{dt} = \frac{M_c b^2}{2} \frac{d\omega}{dt} \mathbf{e}_z. \quad (\text{G.12})$$

Therefore, both the linear and angular momentums are what would have been expected for a solid cylinder of mass M_c . This is possibly what could have been written down as a guess for the respective momenta, but in this appendix we have theoretically justified the neglect of the moving fluid within the TC using the same assumptions as required for Darcy flow.

Appendix H

Algebra for multiple scales

We present the algebra for section 5.2.2 and 5.3 which involves the coordinate transform defined in (5.29) i.e. moving to polar coordinates whose origin is defined to be the steady point of motion.

Differentiating (5.29) with respect to time, we obtain

$$\dot{R} \sin \varphi + R \dot{\varphi} \cos \varphi = \dot{r} \sin \theta + r \dot{\theta} \cos \theta, \quad (\text{H.1a})$$

$$\dot{R} \cos \varphi - R \dot{\varphi} \sin \varphi = \dot{r} \cos \theta - r \dot{\theta} \sin \theta. \quad (\text{H.1b})$$

We can multiply these by $R \cos \varphi$ or $R \sin \varphi$ and take linear combinations to obtain

$$R \dot{R} = r \dot{r} + \overline{B} \left(\dot{r} \cos \theta - r \dot{\theta} \sin \theta \right), \quad (\text{H.2a})$$

$$R^2(1 - \dot{\varphi}) = r^2(1 - \dot{\theta}) + \overline{B} (\overline{B} + r \cos \theta) + \overline{B} \left(r(1 - \dot{\theta}) \cos \theta - \dot{r} \sin \theta \right). \quad (\text{H.2b})$$

Multiplying (5.28) through by R_0 , we substitute in the $O(1)$ version of (H.2) to obtain (5.30), which can be rewritten as

$$\dot{r}_0 (r_0 + \overline{B} \cos \theta_0) + r_0 \overline{B} (1 - \dot{\theta}_0) \sin \theta_0 = 0, \quad (\text{H.3a})$$

$$r_0 (r_0 + \overline{B} \cos \theta_0) (1 - \dot{\theta}_0) - \dot{r}_0 \overline{B} \sin \theta_0 = 0. \quad (\text{H.3b})$$

Multiplying (H.3) by $r_0 + \overline{B} \cos \theta_0$ or $\overline{B} \sin \theta_0$ and taking linear combinations, we find that

$$\dot{r}_0 R_0^2 = 0, \quad (\text{H.4a})$$

$$r_0 (1 - \dot{\theta}_0) R_0^2 = 0, \quad (\text{H.4b})$$

where $R_0^2 = r_0^2 + 2r_0 \overline{B} \cos \theta_0 + \overline{B}^2$. In general, $R \neq 0$. However, when it is, (5.28) force us to take $r \equiv 0$ and $\overline{B} \equiv 0$. Therefore, we can conclude that the unique solution

to (H.3) is given by

$$\dot{r}_0 = 0, \quad (\text{H.5a})$$

$$\dot{\theta}_0 = 1. \quad (\text{H.5b})$$

We now calculate the acceleration term on the right-hand side of (5.23) under the same coordinate transform. Firstly, we expand the acceleration term to obtain

$$\frac{d^2}{dt^2} (R \mathbf{e}_X) = (\ddot{R} - \dot{\varphi}^2 R) \mathbf{e}_X + (2\dot{\varphi}\dot{R} + \ddot{\varphi}R) \mathbf{e}_Y. \quad (\text{H.6})$$

If we differentiate (H.1) with respect to time, we obtain

$$(\ddot{R} - R\dot{\varphi}^2) \sin \varphi + (2\dot{R}\dot{\varphi} + R\ddot{\varphi}) \cos \varphi = (\ddot{r} - r\dot{\theta}^2) \sin \theta + (2\dot{r}\dot{\theta} + r\ddot{\theta}) \cos \theta, \quad (\text{H.7a})$$

$$(\ddot{R} - R\dot{\varphi}^2) \cos \varphi - (2\dot{R}\dot{\varphi} + R\ddot{\varphi}) \sin \varphi = (\ddot{r} - r\dot{\theta}^2) \cos \theta - (2\dot{r}\dot{\theta} + r\ddot{\theta}) \sin \theta. \quad (\text{H.7b})$$

In the same manner as before, if we multiply (H.7) by $R \cos \varphi$ or $R \sin \varphi$, and take linear combinations, we find that

$$R(\ddot{R} - R\dot{\varphi}^2) = r(\ddot{r} - r\dot{\theta}^2) + \overline{B} \left((\ddot{r} - r\dot{\theta}^2) \cos \theta - (2\dot{r}\dot{\theta} + r\ddot{\theta}) \sin \theta \right), \quad (\text{H.8a})$$

$$R(2\dot{R}\dot{\varphi} + R\ddot{\varphi}) = r(2\dot{r}\dot{\theta} + r\ddot{\theta}) + \overline{B} \left((\ddot{r} - r\dot{\theta}^2) \sin \theta + (2\dot{r}\dot{\theta} + r\ddot{\theta}) \cos \theta \right). \quad (\text{H.8b})$$

Substituting (H.5) into (H.8) at $O(1)$, we obtain

$$R_0(\ddot{R}_0 - R_0\dot{\varphi}_0^2) = -r_0(r_0 + \overline{B} \cos \theta_0), \quad (\text{H.9a})$$

$$R_0(2\dot{R}_0\dot{\varphi}_0 + R_0\ddot{\varphi}_0) = -r\overline{B} \sin \theta_0. \quad (\text{H.9b})$$

We must also calculate $R_0^2\dot{\varphi}_0^2$ in terms of r_0 and θ_0 . From (H.2b) we can calculate

$$R^2\dot{\varphi}^2 = \frac{(R^2\dot{\varphi})^2}{R^2} = \frac{(r\dot{\theta}(r + \overline{B} \cos \theta) + \overline{B}\dot{r} \sin \theta)^2}{r^2 + 2r\overline{B} \cos \theta + \overline{B}^2}, \quad (\text{H.10})$$

then using (H.5), we deduce that

$$R_0^2\dot{\varphi}_0^2 = \frac{(r_0(r_0 + \overline{B} \cos \theta_0))^2}{r_0^2 + 2r_0\overline{B} \cos \theta_0 + \overline{B}^2}. \quad (\text{H.11})$$

Appendix I

Error analysis for numerical schemes

We now perform an error analysis for each of the discretizations discussed in §5.4. This is carried out by increasing the number of grid points involved in one discretization whilst keeping the other discretizations constant, and calculating r_{0T} from the solvability condition (5.76a). We take the value of r_{0T} at the finest discretization to the value we compare against, X_∞ , and define the relative error, η , to be a function of the number of grid points, n , as follows

$$\eta(n) = \left| \frac{X(n) - X_\infty}{X_\infty} \right|. \quad (\text{I.1})$$

In Figure I.1, we perform an error analysis on the number of points used to approximate the interval $t \in [0, 2\pi]$. Based on this analysis, we use 100 points in t , leaving an error of around $O(10^{-4})$. In Figure I.2, we perform an error analysis on the number of points used to approximate the interval $\beta \in [0, 2\pi]$, and in Figure I.3, we perform an error analysis on the number of terms used to approximate the infinite series γ_1 , γ_2 and γ_3 . We see in both that there is an exponential convergence. The slowest convergence occurs when the TC orbit passes close to the bioreactor edge, but this is still exponential (results not shown). We therefore make the choice to use 10 points in β and 10 terms in the infinite series, satisfied with an error of around $O(10^{-8})$. We see that the convergence for the discretisation of time is far slower, and does not appear to be exponential. The discretization of time is the most significant error in our numerics, and very fine time discretizations would be required for better accuracy than $O(10^{-4})$. Therefore, the total error in calculating r_{0T} from the solvability condition (5.76a) is likely to be around $O(10^{-4})$.

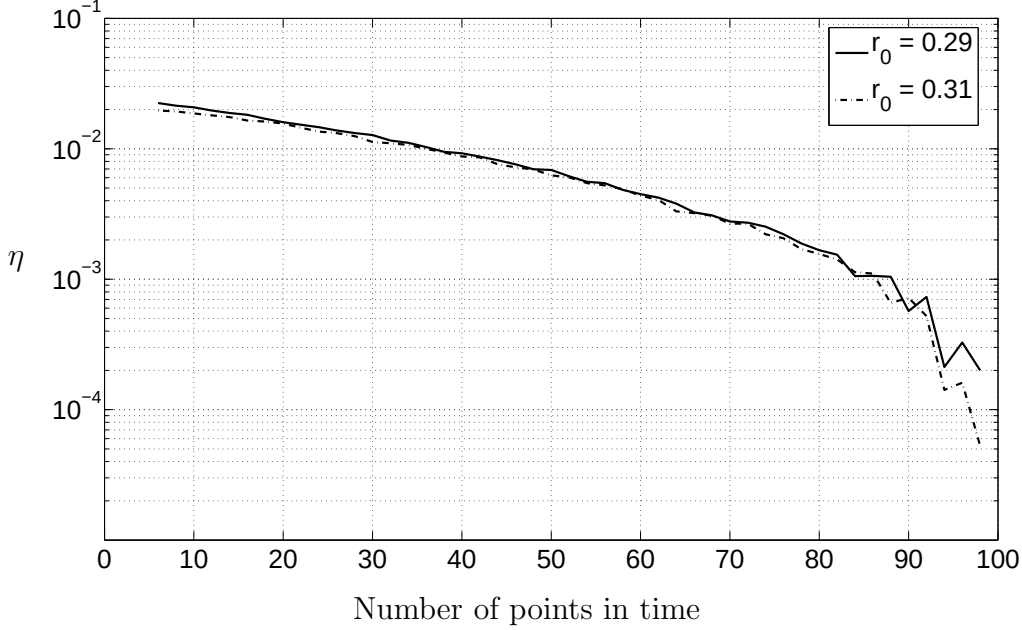


Figure I.1: Error tolerance check for the number of points required in t to evaluate the solvability condition (5.76a). We only use an even number of points in t to fully capture the even nature of the integrand. We use parameter values $\overline{B} = 0.3$, $b = 0.15$, $K = 0.1$, with 25 points used in β , and 30 terms used in each infinite series. We show results for $r_0 = 0.29$ and $r_0 = 0.31$, which are on either side of the boundary between settling and orbital motion.

The main reason why it is difficult to get a better accuracy with respect to time without significant computational expense is due to the discontinuities in the higher-order boundary conditions. The first-correction to the continuity of flux boundary condition (2.33b) has a discontinuous derivative at the transition points between inflow and outflow, and the first-correction to the continuity of normal stress boundary condition (2.34b) has a discontinuous second derivative at the transition points. Therefore, our solution has a larger error than it would if the boundary conditions were smooth. This is apparent from the work in §4.4.2.1, where we managed to reduce certain required computations to a one-parameter family ((4.71) and (4.89)) by normalising with respect to the normal flow (averaged over the Hele-Shaw cell height) leaving the TC. In doing this, we created an issue near points where the flow transitions from inflow to outflow (as the averaged flow passes through zero here). Whilst this does not affect the solution up to a reasonable accuracy (around $O(10^{-4})$), it does mean that an enhanced accuracy will require significantly more computational effort.

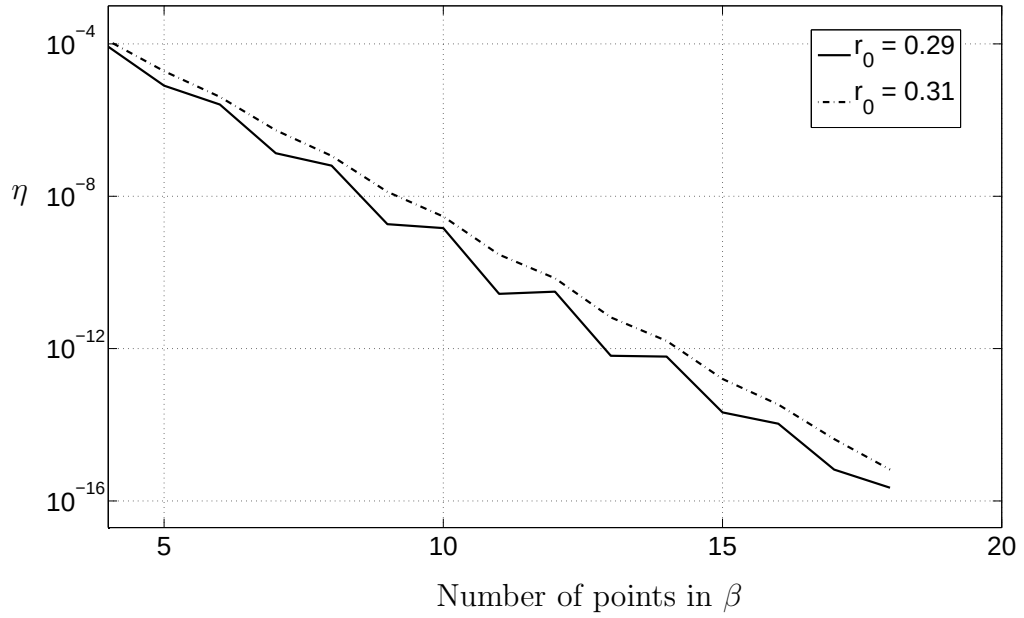


Figure I.2: Error tolerance check for the number of points required in β to evaluate the solvability condition (5.76a). We use parameter values $\overline{B} = 0.3$, $b = 0.15$, $K = 0.1$, with 100 grid points used for the time interval, and 30 terms used in each infinite series. We show results for $r_0 = 0.29$ and $r_0 = 0.31$, which are on either side of the boundary between settling and orbital motion.

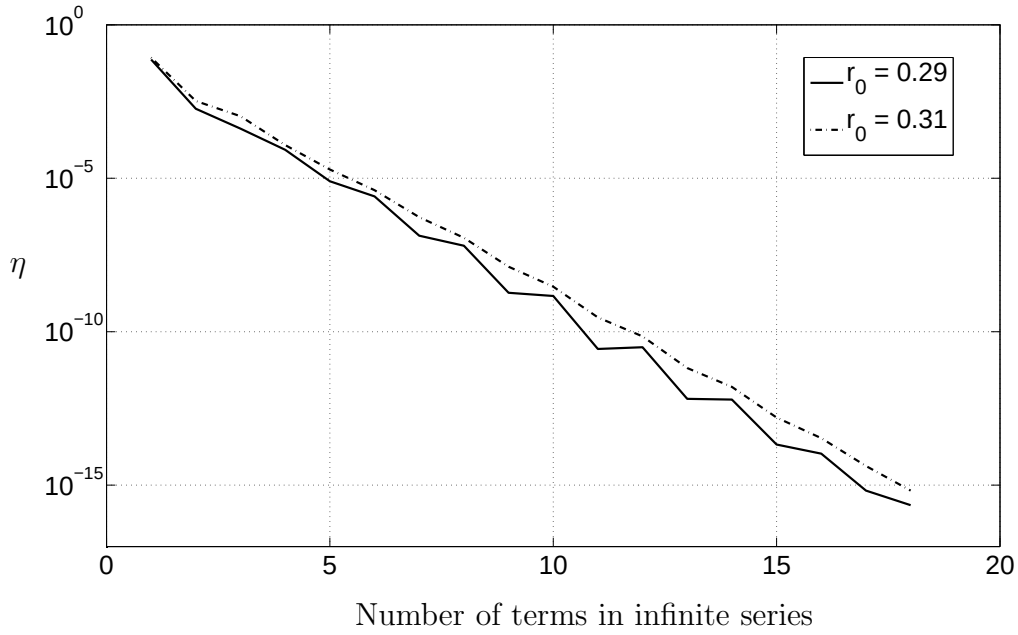


Figure I.3: Error tolerance check for the number of terms required in the infinite series γ_1 , γ_2 and γ_3 to evaluate the solvability condition (5.76a). We use parameter values $\overline{B} = 0.3$, $b = 0.15$, $K = 0.1$, with 100 grid points used for the time interval, and 25 points used in β . We show results for $r_0 = 0.29$ and $r_0 = 0.31$, which are on either side of the boundary between settling and orbital motion.

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