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Dynamics of the Tear Film

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Abstract In this paper, current understanding of tear film physiology and mathematical models for some its dynamics are discussed. First, a brief introduction to the tear film and the ocular surface is given. Next, mathematical models for the tear film are discussed, with an emphasis on models that describe the formation and relaxation of the tear film from blinking. Finally, future issues in tear film modeling are listed.

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1 INTRODUCTION

Why study the tear film that forms on the front of the eye every time we blink? Within a very brief time post-blink, the ocular surface must establish a sufficiently smooth outer surface through which we can see. The outermost surface is that of the tear film. The tear film must provide a high-quality optical surface for refraction, since it is the highest power interface in the ocular system (Oyster, 1999). This multi-layered fluid structure also keeps the ocular surface moist, provides protection against dust and bacteria, helps transport waste away from the ocular surface, and does all this while being able to re-form rapidly after each blink (Fatt & Weissman, 1992). Remarkably, the tear film does this on corneal, conjunctival and contact lens surfaces, though the dynamics is different in each case.

Contributing to medical knowledge for diseased states is important as well. Dry eye syndrome (DES) is recognized to be a collection of problems associated with the insufficient or malfunctioning tear film, among other causes (Lemp et al., 2007). Based on data from the two largest studies of dry eye up to 2007, it is estimated that 4.91 million Americans suffer from dry eye syndrome (Smith et al., 2007). According to one recent review (Johnson & Murphy, 2004), most large studies have estimated that significant DES occurs in about 10 to 20% of the adult population. Thus, new understanding and suggestions for treatment will benefit a large number of people. Also according to Johnson & Murphy (2004):

“The structure and function of the tear film are far from being understood... It is a prerequisite that the normal tear film is better understood if we are to move on in our ability to effectively manage DES.”

There are three main classifications for the tear film. The tear film on the cornea is often called the pre-corneal tear film or PCTF. When a contact lens is present, it divides the tear film into a pre-lens tear film (PLTF) and a post-lens tear film (PoLTF). The pre-conjunctival tear film has been studied less than the others because sight does not occur through it, and it will not have its own acronym. This review will focus mainly on the PCTF.

Away from the lids, the tear film has a ratio of thickness to length that is approximately 10^{-3} and so it is a thin film. Thin films have been the subject of many studies; we will not duplicate recent extensive reviews in thin film research (Oron et al., 1997; Craster & Matar, 2009). Though many ideas developed elsewhere in the thin film literature may be applied to tear films, new ideas will continue to be needed to explain and understand the tear film and its dynamics.

This review will focus on describing relevant experimental and theoretical results for the tear film. The experimental parts will focus on the dynamics and properties from select in vivo and in vitro results. These results provide important input for fluid dynamics modeling as well as define challenges and opportunities for understanding the tear film. The mathematical modeling will emphasize results from the formation and drainage of the tear film as a whole, though treatment of local rupture phenomena will be included as well.

The paper begins with a survey of the tear film structure and experimental observations in Section 2. Subsequently, some aspects of its geometry, and properties of whole tears as well as some components, are discussed. Next, the

dynamics of the eyelids as well as the tear film are surveyed. The paper proceeds to mathematical models for the tear film in Section 3. The discussion will focus on a model of a single-layer fluid with an insoluble surfactant on and evaporation from its free surface, as well as transport of solutes within the tear film. Bilayer models with surfactants will be briefly discussed as well. Finally, the situation is summarized, and future challenges are outlined in Section 4.

2 EXPERIMENTAL RESULTS

2.1 Structure Of The Tear Film

The human tear film is sometimes described as a three-layer film that plays a number of roles to maintain the health and function of the eye (Ehlers, 1965; Mishima, 1965). A sketch of the eye and the overlying tear film are shown in Figure 1.

There are three types of mucins present in the tear film and ocular surface. Soluble mucins are secreted from goblet cells and appear principally to float in the aqueous layer. Transmembrane mucins protrude through the apices of the epithelial cells at the front of the cornea (Gipson, 2004; Govindarajan & Gipson, 2010). The mucus is thought (Bron et al., 2004) to be a concentration of gel-forming mucins that are found among the microvilli and among those long transmembrane mucins (Gipson, 2004; Govindarajan & Gipson, 2010). In the classical outlook, mucus is thought to provide the first, separate layer above the epithelial cells (Sharma et al., 1999). However, the view that there is a distinct, well-defined mucus layer appears to be out of favor in the ocular science community (Bron et al., 2004; Gipson, 2004; Govindarajan & Gipson, 2010).

A long-held view was that the corneal surface itself was not wettable by water

and that a mucus layer was necessary for the wetting of the cornea (e.g., Holly 1973). This view is now largely discredited, and it is generally accepted that both the healthy cornea and the highly-glycosylated transmembrane mucins are hydrophilic (Sharma, 1998). Measurements of wettability of the cornea support the latter view (Tiffany, 1990a,b).

The aqueous layer is primarily water (about 98%, with a variety of components forming the balance) and lies above the mucus layer (Mishima, 1965; Fatt & Weissman, 1992). The aqueous layer is, essentially, what is commonly thought of as tears. Opinion regarding the amount of mucins that are in the aqueous part of the film has varied over the years (Bron et al., 2004; Holly, 1973; Holly & Lemp, 1977), though there are certainly soluble and gel-forming mucins that play a number of roles in the aqueous layer (Gipson, 2004). The interface between the aqueous and possible mucus layers, if there is a sharp interface, is not observed experimentally in humans in vivo (King-Smith et al., 2000, 2004); whether the mucus film is a separate layer is still a matter of debate.

The outermost (lipid) layer is composed of a non-polar layer above the aqueous layer with polar lipids acting as surfactants at the aqueous/lipid interface (McCulley & Shine, 1997; Bron et al., 2004). The lipid layer decreases the surface tension of the air/tear film interface and reduces evaporation, with both stabilizing the tear film against rupture (“tear film breakup” in the eye literature).

2.2 Tear Film Geometry

The tear film is a very thin layer over most of the ocular surface. It covers the cornea, which is closely approximated by a prolate spheroid (Read et al., 2006). In principle, this corneal surface shape could generate pressure gradients and drive

flow, but this effect is thought to be negligible (Berger & Corrsin, 1974; Braun et al., 2011). The remainder of the globe, or eyeball, is closely approximated by a sphere of radius $10^{-2}m$ (e.g., Fatt & Weissman 1992).

The PCTF thickness has been measured by interferometry only in the last 25 years. An in vivo interferometer was developed by Doane (1989); he subsequently found PLTF thicknesses of $1.5 - 2\mu m$ (Doane & Gleason, 1994). The thinner range of available PCTF measurements from $1.5 - 5\mu m$ are generally considered the most accurate and representative values for the tear film thickness; they are from interferometry (King-Smith et al., 2004) and optical coherence tomography (OCT; Wang et al. 2003). The PLTF and PoLTF both have similar thicknesses; see King-Smith et al. (2004, 2006) for a discussion. We emphasize that the tear film is dynamic; however, a typical thickness is important for understanding and mathematical modeling of the tear film.

The meniscus of the tear film is a region of increased thickness at the lid margin. The tear film wets the lid margin to the mucocutaneous junction, which is the boundary separating wettable conjunctival surface from less wettable skin surface; it separates the anterior and posterior parts of the lid. The mucocutaneous junction is just posterior the meibomian orifices where lipids are expressed from the meibomian glands located within the lids. The tear meniscus width (TMW) is the distance the tear film occupies along the lid margin normally (anteriorly) to the ocular surface. The TMW has reported average values from $6 \times 10^{-5}m$ (Mainstone et al., 1996; Golding et al., 1997) to $3.65 \times 10^{-4}m$ (Gaffney et al., 2010), though it apparently changes at times with tear film volume (Palakru et al., 2007). Gaffney et al. (2010) chose a representative value is $2.7 \times 10^{-4}m$. The tear meniscus radius (or TMR) is sometimes, unfortunately, labeled the tear

meniscus curvature or TMC; however, the reported values in such papers are a TMR. If one assumes a constant curvature of the meniscus adjacent to the lid margins, then TMR values can be measured by several means. Average TMR values have been reported as $5.45 \times 10^{-4}\text{m}$ (Mainstone et al., 1996), $3.65 \times 10^{-4}\text{m}$ (Yokoi et al., 1999) and about $2.50 \times 10^{-4}\text{m}$ (Wang et al., 2006b) for normals; reduced values have been found for dry eye subjects of 190 to $240\mu\text{m}$ (Yokoi et al., 2000).

The tear meniscus height (or TMH) is the distance the tear film meniscus extends along the ocular surface normal to the lid margin. Average values have been measured from about $100\mu\text{m}$ to the range of $250\mu\text{m}$ to $600\mu\text{m}$ (Mainstone et al., 1996; Johnson & Murphy, 2005; Wang et al., 2006b,a). The larger values in the range only seem to appear for the inferior meniscus. Wang et al. (2006b) found that the superior and inferior TMH were closely correlated to roughly equal size under normal conditions; however, there are times when it is clearly visible that the inferior meniscus is larger, e.g., after installation of artificial tears (Palakru et al., 2007). The measurements presented in the literature may be a vertical distance from the mucocutaneous junction to the superior edge of the meniscus rather than the distance along the ocular surface, though these quantities may be close in value and difficult to distinguish experimentally.

2.3 Properties Of Tear Fluid

In a series of papers by Tiffany and coworkers, the human tear film has been shown to have non-Newtonian properties (Tiffany 1991, 1994; Pandit et al. 1999). Tiffany (1991) found that whole tears, that is, tear sampled directly from the eye, are shear thinning. He fit the viscosity variation with shear rate using a four-

parameter Cross model (Cross, 1966); that fit has been approximated by power law or Ellis fluids over smaller ranges of shear rates in more recent theoretical models (discussed in Sections 3.2.2 and 3.3 below). Tiffany (1994) also found weak elastic effects. The non-Newtonian properties are due to the presence of large protein and mucin molecules in the tear film; Tiffany & Nagyová (1998) found that removing all lipids from tears caused tear fluid to become Newtonian.

The effect of the lipid layer on the surface tension of tears illustrates some challenges of tear film research. The surface tension of tears was indirectly measured by Miller (1969). Using a special contact lens and a wire ring, he found that tears had $2/3$ of the surface tension of water, or about 0.0462N/m . In this view of the tear film, there is a single interface between tear fluid and air, and the surface tension is lumped onto it (rather than treating the tear film as having separate but closely spaced air-lipid and lipid-aqueous interfaces). Pandit et al. (1999) measured the surface tension of whole tears with a capillary tube and obtained 0.043N/m for unstimulated tears and 0.046mN/m for stimulated tears; these are a generally accepted values for the surface tension of tears and 45mN/m is often used in theoretical studies. Comparing the two methods suggests that Miller (1969) measured surface tension for stimulated tears. The components responsible for lowering the surface tension from that of pure water is a subject of ongoing research (Nagyová & Tiffany, 1999; Tiffany & Nagyová, 1998; Mudgil & Millar, 2006, 2008). The difficulty in establishing the dependence of surface tension on chemical species complicates attempts to understand the details of the Marangoni effect in the tear film.

2.3.1 LIPID LAYER Tiffany & Dart (1981) measured values of the viscosity for human meibum (the material expressed from the meibomian glands inside

the lids) using a capillary tube and they estimated values from 9.7 to 19.5 Pa·s at 308K. This is a representative value for the temperature on the surface of the tear film (Purslow & Wolffsohn, 2005). The rheology of the lipid layer could be expected to depend significantly on temperature given that the melting temperature of lipids is near this temperature (Tiffany, 1987). Leiske et al. (2010a) used multiple techniques to measure fluid dynamics properties and the structure of an in vitro meibomian lipid layer from humans and desert marsupials. Their room-temperature results indicated gel behavior of the lipids and that domains of lipid could form even at zero surface pressure; they explained that this occurs because the cholesterol ester species have long chains which prevent the formation of a two-dimensional gas phase of surfactant (Leiske et al., 2010a; Butovich, 2008). The surface pressure increases and a gel forms upon compression (with both surface elasticity and viscosity) because of the increasing density of these islands. Leiske et al. (2010b) found that the elasticity and viscosity of the meibomian lipid layer decreases with increasing temperature and the elasticity appears to be small above 305K. King-Smith et al. (2010b) used high-resolution microscopy to observe lipid layer dynamics, and they saw fine structure of the lipid layer during the interblink period that included islands of lipids.

2.3.2 THE LIPID LAYER AND EVAPORATION An important function of the lipid layer is to impede evaporation of water from the aqueous layer (Craig & Tomlinson, 1997) and this has been the subject of numerous studies. Mishima & Maurice (1961) inferred the evaporation rate from observations of the cornea in rabbits. They found increased evaporation if the lipid layer was removed. Special goggles were developed by subsequent authors for use in humans (for recent reviews see Mathers 2004; Tomlinson et al. 2005, 2009). The measured

rates from using goggle-based approaches range from roughly 2 to $60 \times 10^{-6} \text{kg m}^{-2} \text{s}^{-1}$ for dry eyes (e.g., Tomlinson et al. 2009). In Craig & Tomlinson (1997) and Goto et al. (2007), evaporation rates were linked to the structure of the lipid layer as assessed from the visual appearance with interference patterns. Lower quality lipid layers with large thickness variation or apparent gaps had larger evaporation rates.

Recently, measurements of the thinning rate of the the tear film have been used to estimate the evaporation rate of water from the tear film (Nichols et al., 2005; King-Smith et al., 2008). This method avoids constraining the air flow around the eye, but does not directly measure the mass of water that leaves the tear film. In Nichols et al. (2005), a bimodal distribution of thinning rates was found in the seconds following a blink, with the lower mode peaked at about $2.5 \mu/\text{min}$ and the upper mode peaked at about $10 \mu/\text{min}$. King-Smith et al. (2010a) quantified lipid layer thickness and evaporation rate; they found modest correlation between the two indicating that both the thickness of the lipid layer and its composition are important in limiting evaporation.

Tomlinson et al. (2009) reviewed evaporation rates from the literature and found that measurements of the thinning rate typically yield larger evaporation rates than those found from the methods involving goggles. They offered some possible reasons for the discrepancy. Subsequently, Kimball et al. (2010) made interferometric measurements of of thinning rates with and without air-tight goggles and showed that the goggles stopped thinning of the tear film. They concluded that the constraint of air flow and water vapor diffusion by the goggles stopped evaporation, and so evaporation must be major cause of tear film thinning. McCulley et al. (2006) and Uchiyama et al. (2007) quantified the increase

in evaporation from eyes that occurred when the relative humidity of the surrounding air was reduced. The significance of these different measurement types is an area of active research.

Faced with the complexity of the composition, structure and function of the lipid layer *in vivo*, a number of model or analog systems have been studied. Holly (1974) combined bovine tear film components with buffered solution and oxidized mineral oil in order to study tear film breakup. Sharma et al. (1999) developed a multilayer model with water on top of silicon oil, which in turn was above a silicone wafer with a small polymer brush at the surface to mimic the transmembrane mucins; they wanted to emulate breakup and subsequent dewetting. Recently, Cerretani & Radke (2010) studied a system similar to that of Holly (1974) with oxidized mineral oil spread with bovine submaxillary mucin on a buffered water layer in a small heated Langmuir trough. They varied the amount of oil and found that increasing the oil layer thickness slowed down evaporation, but not as efficiently as the healthy lipid layer *in vivo*. Generally the *in vitro* evaporation rates of model systems have been faster than *in vivo* tear films (Brown & Dervichian, 1969; Herok et al., 2008); essential components of *in vivo* lipid layers appear to be missing in model systems.

2.4 Tear Film Dynamics

2.4.1 LID MOTION The motion of the lids during “unforced” or spontaneous blinks was filmed using high speed photography by Doane (1980). Frame by frame analysis indicated that a typical unforced blink nominally lasts 0.258s, with the downstroke of the upper lid lasting 0.082s and the upstroke lasting 0.176s. Maximum lid speeds ranged from 10 to 30cm/s during the downstroke; the up-

stroke is about half as fast. He also found that many blinks were incomplete, with a few subjects never executing complete blinks in the 45s filming period; understanding partial blinks as well as full blinks is significant (Harrison et al., 2008). Measurements of lid and contact lens motion have been made for subjects blinking on command (Fatt & Weissman 1992, Ch. 10); generally forced blinks are slower than spontaneous blinks. For a recent review of blink-related data, see Cruz et al. (2011).

2.4.2 SUPPLY AND DRAINAGE It is generally agreed that the bulk of tear fluid comprising the aqueous portion of tears is supplied from the lacrimal gland that is located superiorly and temporally to the globe Oyster (1999). The fluid secreted into the superior fornix and then (typically) reaches the exposed surface of the eye by entering the meniscus in the same area (Maurice, 1973; Harrison et al., 2008). Fraunfelder (1976) used technetium as a tracer to image flow under the eyelids and in the lacrimal drainage system; in some instances, the tracers appeared to be swept from the edge of the conjunctival sac (the fornices) toward the menisci at the lid margins in concentrated streams or rivi. MacDonald & Maurice (1991) also reported some results on flow under the lids.

The flow of tear fluid from the supply region around the menisci to the puncta on the superior and inferior lids near the nasal canthus was visualized by Maurice using lampblack and a slit lamp (Maurice, 1973). Just after a blink, those fine soot particles in the superior and temporal supply region diverged with some moving along the superior lid and some around the temporal canthus and along the inferior lid. In both cases, the particles generally traveled toward the nasal canthus with some going down the puncta. Similar flows were observed by Khanal & Millar (2010) using fluorescent hydrophilic InGaP quantum dots and by Har-

rison et al. (2008) using fluorescein. The term “hydraulic connectivity” is used here to denote the tear flow from the superior meniscus to the lower meniscus through the temporal canthus.

Doane (1981) proposed a model for how tears are subsequently drained from the anterior eye. Zhu & Chauhan (2005b) developed a model for drainage through the canaliculi, though their model relies on boundary conditions and elastic properties of the canaliculus to generate low pressures to drive drainage, rather than Horner’s muscle as described in Doane (1981). Khanal & Millar (2010) confirmed that aqueous tear fluid drained down the puncta. When they used lipophilic quantum dots, they observed that the dots did not go down the puncta but were adsorbed onto nearby skin and lashes.

2.4.3 THE LIPID LAYER The lipid layer exhibits many fascinating dynamics; only a small sample is given here. Particles in the lipid layer have been observed to move superiorly after a blink, and this effect has been shown to be driven by the Marangoni effect arising from polar lipid concentration gradients (Berger & Corrsin, 1974; Owens & Phillips, 2001; King-Smith et al., 2009). Interferometry (DiPasquale et al., 2004) and fluorophotometry (Jones et al., 2006) have been used to image horizontal lines moving up the tear film after a blink. King-Smith et al. (2008) used interferometry to image a bursting bubble in the lipid layer; the subsequent superior movement and simultaneous spreading are suggestive of insoluble surfactant spreading (Williams & Jensen, 2001; Warner et al., 2004).

Cerretani & Radke (2010) noticed that after a sufficiently long time, the mineral oil in their model layer would no longer stay spread on the water substrate and would separate into droplets. They observed a time sequence that resembles

high-resolution microscopy observations of humans in vivo during the interblink (King-Smith et al., 2010b).

2.4.4 BREAKUP The tear film eventually ruptures, or breaks up, even for healthy eyes. For some subjects, the initial BUT can take minutes (Norn 1969; Haen & Marx 1926; King-Smith et al. 2000). For most subjects the BUT is well under a minute (Norn, 1969) and may even be a few seconds to no time at all for those with severe dry eye conditions (Liu et al., 2006). The BUT and subsequent patterns of dry-out on the cornea have been measured or inferred by many methods, including: fluorescence (Norn 1969; Bitton & Lovasik 1998; Begley et al. 2006); interferometric methods of different types imaging of the lipid layer (Doane 1989; King-Smith et al. 1999, 2009); and other optical methods (Liu et al., 2010). Narrow-band interferometry applied to the pre-lens tear film can give accurate relative thickness changes because of the high contrast interface between the lens and the tear film (Doane, 1989; King-Smith et al., 2004).

The optical science community has labeled observed breakup patterns on the cornea as different phenomena, for example, as dots, streaks and pools as in Bitton & Lovasik (1998). However, this notion is at odds with theoretical results for thin films that rupture on flat impermeable substrates (Witelski & Bernoff, 2000). In theory, rupture always occurs at a point (or dot); these points grow and groups of them merge to form one dimensional streaks and curves. Those streaks may widen and merge to form wider areas which have dewet (for a review, see Craster & Matar 2009). On the corneal surface, the progression is less clear, but observations in vivo do not always seem to follow theoretically predicted patterns or are not reported that way. Initial point breakup may be difficult or impossible to observe in practice, e.g., when the BUT is effectively zero or because the ocular

surface is far from being an ideal plane. The growth of “dry” areas on the cornea has been observed (Liu et al., 2006).

2.4.5 OSMOSIS FROM THE OCULAR SURFACE The osmolarity is the concentration of a collection of solutes (primarily salts and proteins) that induce transport to and from the ocular surface. The chronic elevation of the osmolarity is thought to be important in the development of the symptoms of dry eye (Lemp et al., 2007). The cornea is relatively impermeable to solutes or foreign materials in order to protect its optical function (Oyster, 1999); the conjunctiva is more susceptible to transport across it for both solutes and water (Dartt, 2002). Transport across the corneal epithelium is often neglected in models of ocular function for normal interblink times of a few seconds (Gaffney et al., 2010). However, for long interblink times as in controlled staring experiments, the contribution appears to be significant in thinning experiments (King-Smith et al., 2007, 2010c; Braun et al., 2010). Klyce & Russell (1979) and others have studied the permeability of rabbit and steer corneas and scaled the results to apply them to human eyes (Fatt & Weissman, 1992). Levin & Verkman (2004) used microfluorometry and a compartment model to determine mouse corneal water permeability; the model appears promising for use with human models. The details of ion and water transport continue to be an active area of research (Hill, 2008).

3 MODELING AND COMPUTATION

In nearly all models for the fluid dynamics of the tear film, the substrate under the tear film (the cornea or a contact lens) is assumed to be flat. Berger & Corrsin (1974) are often cited for this and they refer to Berger (1973). This approximation

is made based on the small thickness of the tear film (a few 10^{-6}m) compared to the average radius of curvature of the globe (about 10^{-2}m); however, they do not give any details for this simplification. Braun et al. (2011) analyzed thin film flow on a prolate spheroidal substrate for Newtonian and Ellis fluids, and concluded that the contribution to thinning on the cornea was negligible compared other causes of thinning in vivo (King-Smith et al., 2009). However, projecting the surface area of the ocular surface to a plane reduces the area by about 29% on average (Tiffany et al., 1998).

3.1 A Model Framework

To simplify the discussion, we develop a formulation for a single layer of Newtonian fluid representing the aqueous layer as a vehicle for discussing mathematical models for the tear film. The lipid layer will be simplified to transport of an insoluble surfactant and to limiting evaporation in this formulation. The model will include evaporation from the aqueous layer, and transport of insoluble surfactants on the free surface. The insoluble surfactant here is one of the polar components of the lipid layer, for example, a suitable phospholipid (McCulley & Shine, 1997); the surfactant is thought to be located at the aqueous-lipid interface in vivo. The evaporation is modified from kinetic theory to be a one-sided model that assumes that all contributions from the air outside the tear film are small.

The film may be subject to van der Waals type forces (Israelachvili, 2010; Oron & Bankoff, 1999; Ajaev, 2005; Ajaev & Homsy, 2001); we discuss both wetting and dewetting cases. Heat transfer through the tear film is included for the evaporation model as well (much simplified from Scott 1988, e.g.). This approach is intended for eyes that are exposed to an environment that is unaffected by

evaporation rather than goggle experiments.

The cornea behind the tear film will be treated as a semipermeable membrane which responds by osmosis to higher osmolarity in the tear film (Fatt & Weissman, 1992). The osmolarity is treated as a concentration of a single solute with appropriate properties. We shall generally use the properties of ions from salts. Tear fluid supplied from the lacrimal gland and the aqueous humor, which is hypothesized to supply fluid to the tear film through the cornea, is assumed to be isotonic with concentration $c_0 = 300\text{mOsM}$. We will use this as a reference concentration.

We discuss bilayer models of the tear film in Section 3.3; none of those models include any thermal effects or evaporation but do include effects of mucus or lipid layers explicitly.

3.1.1 SCALES We now state our non-dimensionalization and parameters, and give the governing equations as the leading contributions from lubrication theory. We assume that $\epsilon = d/L \ll 1$ and that $\epsilon Re \ll 1$, where $Re = \rho U d / \mu$ is the Reynolds number. $d = 5\mu\text{m}$ is a typical tear film thickness away from the menisci, though we shall discuss other values as well. The half width of the palpebral fissure (eye opening) is $L = 5\text{mm}$ and it is the length scale in the x direction. The length scale ratio $\epsilon = d/L = 10^{-3}$ is satisfactory for lubrication theory (e.g., Craster & Matar 2009; Oron et al. 1997). We assume that the density $\rho = 10^3\text{kg/m}^3$ (effectively water), and $\mu = 1.3 \times 10^{-3} \text{ Pa}\cdot\text{s}$ is close to the large shear rate asymptote for whole tears (Tiffany, 1991). U is the velocity scale along the film. We use either $U = 5 \times 10^{-3}\text{m/s}$ or the maximum lid speed during a blink $U = 0.1\text{m/s}$ (Doane, 1980; Berke & Mueller, 1998). (The average blink speed over a cycle, say 0.04m/s could be used after Jones et al. 2005, 2006

as well.) In the worst case away from the menisci, $\epsilon \text{Re} \approx 5 \times 10^{-4}$, which is satisfactory. The menisci may increase to up to $3.65 \times 10^{-4} \text{m}$ at the lid margin, and so ϵRe may become close to unity if the characteristic speed is unchanged in this region. To date, all lubrication models including the ends of the tear film have proceeded with the thin film approximation.

The characteristic speed across the film is ϵU and the time scale is L/U . The pressure scale is viscous, namely $\mu U/(L\epsilon^2)$, and the pressure is referred to the outside vapor pressure p_v . The temperature scale is referred to the saturation temperature difference of the surrounding air T_s , so that the dimensional temperature T' becomes $T = (T' - T_s)/(T_{eye} - T_s)$ with $T_{eye} = 308^\circ \text{K}$. The reference value of the surface tension is $\sigma_0 = 0.045 \text{N/m}$ (Miller, 1969; Nagyová & Tiffany, 1999); reference values are indicated with a subscript 0. The osmolarity c' is made dimensionless with the isotonic concentration $c_0 = 300 \text{mOsM}$ so that $c = c'/c_0$. The insoluble surfactant concentration Γ is made dimensionless by the reference value Γ_0 .

3.1.2 LUBRICATION THEORY Let (x, z) be the nondimensional coordinate directions along and through the film, respectively, with $X(t) < x < 1$, the aqueous layer in $0 < z < h(x, t)$ and the film thickness given by $z = h(x, t)$. Positive x points inferiorly; z points anteriorly through the tear film. The origin is located in the center of the eye opening. The function $X(t)$ simulates the upper lid position. The eyelid motion of a blink is simplified to a time-periodic domain length with specified film thickness and flux at each end; it is assumed that only the left end of the domain moves, corresponding to the upper eyelid moving with each blink. When the interblink period is studied, $X = -1$ for the duration of the simulation.

Let (u, w) be the respective velocity components in the (x, z) directions. The leading order parallel flow problem is, in $0 < z < h$,

$$\partial_x u + \partial_z w = 0, \partial_z^2 u - \partial_x p = 0, \partial_z p = 0, \quad (1)$$

$$\partial_z^2 T = 0, \text{ and} \quad (2)$$

$$\partial_t c + u \partial_x c + v \partial_z c = \text{Pe}_c^{-1} \left(\partial_x^2 c + \epsilon^{-2} \partial_z^2 c \right), \quad (3)$$

respectively, for mass conservation and momentum conservation in the x and z directions (1), heat conservation (2) and osmolarity (solute) conservation (3).

$\text{Pe}_c = UL/D_c$ where D_c is the diffusivity of the osmolarity on an average basis.

The solute conservation equation will be simplified to the lubrication approximation shortly.

At $z = 0$, corresponding to the corneal surface, we have conditions on the velocity components, the temperature and osmolarity. We allow for slip on this surface, osmosis of water through the cornea, fix the temperature and conserve solute there. The boundary conditions on $z = 0$ are then

$$u = \beta \partial_z u, \quad (4)$$

$$w = P_c(c - 1), \quad (5)$$

$$T = 1, \quad (6)$$

$$(\text{Pe}_c \epsilon^2)^{-1} \partial_z c = wc. \quad (7)$$

The slip parameter $\beta = L_s/d$ is the ratio of the slip length to the film thickness.

According to (5), osmosis from the ocular surface causes w to be nonzero if there is a concentration difference from the isotonic value. The nondimensional permeability of the cornea is defined as

$$P_c = \frac{RT_{\text{eye}} c_0}{S_c R_t \epsilon U} \quad (8)$$

where $R = 8.314 \text{ J/mol/K}$ is the ideal gas constant, and $S_c = 1.47 \times 10^{-4} \text{ m}^2$ is the surface area of the cornea (using a factor of 1.3 based on Tiffany's surface area increase over a 2D image (Tiffany et al., 1998)). R_t is the resistance to flow through the cornea posterior to the film. For the whole cornea an estimate of Fatt & Weissman (1992) estimated $R_t = 2.15 \times 10^{18} \text{ N s/m}^5$ for the cornea and $R_t = 1.42 \times 10^{18} \text{ N s/m}^5$ for the corneal epithelium from in vitro measurements. King-Smith et al. (2010b) estimated $R_t = 7.24 \times 10^{18} \text{ N s/m}^5$ from recent thinning rate measurements in vivo. For the purposes of this model, the interpretation of epithelium or whole cornea is the same. Conservation of solute at $z = 0$, (7), requires a balance between diffusion of solute and the influx of water there (Probstein 1994, p. 72). In the absence of osmosis, we have $P_c = 0$, and the boundary at $z = 0$ is impermeable to both fluid motion and solutes.

At the surface of the film $z = h(x, t)$, we have

$$\partial_t h + u \partial_x h - w = -EJ, \quad (9)$$

$$p = -S \partial_x^2 h - \phi, \quad (10)$$

$$\partial_z u = -M \partial_x \Gamma, \quad (11)$$

$$J = -\partial_z T, \quad (12)$$

$$\bar{K} J = \delta p + T, \quad (13)$$

$$\partial_t \Gamma + \partial_x (u_s \Gamma) = \text{Pe}_s^{-1} \partial_x^2 \Gamma \quad (14)$$

$$\left(\text{Pe}_c \epsilon^2 \right)^{-1} \left(\partial_z c - \epsilon^2 \partial_x h \partial_x c \right) = EJc. \quad (15)$$

The equations represent, respectively, the kinematic condition (9), the normal (10) and tangential (11) stress conditions, the thermal energy balance (12), the constitutive equation for the evaporative mass flux (13), conservation of the insoluble polar lipid concentration (14) and conservation of osmolarity (15). Consider

$\phi = Ah^{-3}$, an unretarded van der Waals force. The nondimensional parameters from these equations represent the contributions of surface tension, van der Waals forces, the Marangoni effect, evaporation, and advection of insoluble surfactant:

$$S = \frac{\sigma_0 \epsilon^3}{\mu U}, \quad G = \frac{\rho g d^2}{\mu U}, \quad A = \frac{A^*}{\mu U d l}, \quad M = \frac{\epsilon \sigma_0 (\partial_\Gamma \sigma)_0}{\mu U}, \quad (16)$$

$$E = \frac{k(T_{\text{eye}} - T_s)}{\epsilon \rho U d L_m}, \quad \bar{K} = \frac{k K^*}{d L_m}, \quad \delta = \frac{\alpha \mu U}{\epsilon^2 L (T_{\text{eye}} - T_s)} \quad \text{Pe}_s = \frac{U L}{D_s}. \quad (17)$$

$L_m = 2.3 \times 10^6 \text{ J/kg}$ is the latent heat of vaporization of water on a mass basis. Values for the Hamaker constant $A^* = 3.5 \times 10^{-19} \text{ J}$ and the constant $\alpha = 0.036^\circ \text{K/Pa}$, which relates pressure to evaporative mass flux, are estimated from Winter et al. (2010) for a given temperature difference. Here we used $T_{\text{eye}} - T_s = 10 \text{ K}$ and $U = 5 \times 10^{-3} \text{ m/s}$. The constant δ is the nondimensional form of α . The constant $K^* = 1.5 \times 10^5 \text{ K m}^2 \text{ s/kg}$ relates the mass flux to temperature and pressure differences at the film surface with saturation conditions in the passive gas outside the film; this value is chosen to match a $4 \times 10^{-6} \text{ m/min}$ thinning rate. The thermal conductivity for tear fluid is assumed to be that of water, $k = 0.68 \text{ W/m/K}$. Pe_s is the surface Péclet number and D_s is the surface diffusivity of Γ . With $D_s = 3 \times 10^{-8} \text{ m}^2 \text{ s}$ (Sakata & Berg, 1969), $U = 5 \times 10^{-3} \text{ m/s}$ and $L = 5 \times 10^{-3} \text{ m}$, we estimate $\text{Pe}_s \approx 833$ during the interblink; it is 20 times larger during the blink itself, and surface diffusion has been neglected in models of blinks with surfactant transport (Jones et al., 2006; Aydemir et al., 2010).

Equation (15) has important consequences for the osmolarity. This boundary condition states that evaporation will act as a source term that increases the osmolarity inside the tear film as water is lost to the surrounding environment.

When $M = 0$, the dynamics of the surfactant are completely decoupled from the film dynamics, and the film surface is stress free. This is designated the stress free limit (SFL). When $M \gg 1$, the surfactant transport equation simplifies and Γ

can be eliminated, although a strong effect of the surfactant remains; we call this the uniform stretching limit (USL) when the end moves, or tangentially immobile if the end does not move ($X(t) = -1$). For a derivation of the USL, see Braun & King-Smith (2007) or Heryudono et al. (2007).

In order to solve the leading order parallel flow problem, we note that the pressure is independent of z , so that the pressure through the film depth is specified by the normal stress condition (10). Then, we may solve for the linear thermal field through the film; applying the boundary conditions (6) and (12), yields $T = 1 - Jz$. Substituting into the constitutive equation for the evaporative mass flux (13) gives

$$J = (1 + \delta p)/(\bar{K} + h). \quad (18)$$

Next, we can integrate mass conservation in the z direction from $z = 0$ to h and apply Leibnitz rule to obtain

$$w(x, h, t) - u(x, h, t)\partial_x h - w(x, 0, t) + \partial_x \int_0^h u dx = 0. \quad (19)$$

The first two terms may be eliminated using the kinematic condition (9) and the third term can be eliminated using (5); we obtain

$$\partial_t h + EJ - P_c[c(x, 0, t) - 1] + \partial_x(h\bar{u}) = 0, \quad (20)$$

where

$$q = \int_0^h u(x, z, t) dz, \text{ and } \bar{u} = q/h. \quad (21)$$

We still need the approximate velocity component $u(x, z, t)$ from lubrication theory. It must satisfy $\partial_z^2 u = \partial_x p$ from (1) subject to (4) and (11); we obtain

$$u = \partial_x p \left(\frac{z^2}{2} - (z + \beta)h \right) - M\partial_x \Gamma(z + \beta), \quad (22)$$

$$q = -\partial_x p \left(\frac{h^3}{3} + \beta h^2 \right) - M\partial_x \Gamma \left(\frac{h^2}{2} + \beta h \right). \quad (23)$$

Finally, a lubrication approximation for the osmolarity c is needed. The problem for the osmolarity is to solve (3) subject to the boundary conditions (7) and (15). Diffusion across the thin layer is assumed to be fast compared to diffusion along its length; the leading order concentration is then independent of z . Following Jensen & Grotberg (1993), one obtains

$$h(\partial_t c + \bar{u}\partial_x c) = \text{Pe}_c^{-1}\partial_x(h\partial_x c) + EJc - P_c(c-1)c. \quad (24)$$

Thus, the general equations for most of the following discussion are as follows:

$$\partial_t h + EJ - P_c(c-1) = -\partial_x(\bar{u}h), \quad (25)$$

$$h(\partial_t c + \bar{u}\partial_x c) = \text{Pe}_c^{-1}\partial_x(h\partial_x c) + EJc - P_c(c-1)c, \quad (26)$$

$$\partial_t \Gamma + \partial_x(u_s \Gamma) = \text{Pe}_s^{-1}\partial_x^2 \Gamma, \quad (27)$$

$$p = -S\partial_x^2 h - \phi. \quad (28)$$

J is given by (18), $u_s = u(x, h, t)$ and appropriate expressions for ϕ will be given in subsequent sections.

3.1.3 DOMAINS FOR THE MODELS These equations are most generally to be solved on the time dependent domain $X(t) < x < 1$ with $-1 \leq X \leq 1 - 2\lambda$, where λ is the fraction of the domain remaining when it is at its smallest extent (corresponding to when the lids are most closed).

Formulas for the eyelid motion $X(t)$ (at the widest separation line) were developed by Berke & Mueller (1998) from the data of Doane (1980) and their own measurements of lid motion. Their formulas were for complete blinks and used decaying exponentials for lid position. Subsequent modeling efforts to study the deposition and draining of the tear film (Jones et al., 2005; Aydemir et al., 2010) and for complete blink cycles including partial blinks (Heryudono et al., 2007) have developed their own lid motion equations.

3.1.4 BOUNDARY AND INITIAL CONDITIONS At the ends of the film, one typically specifies the tear film thickness $h = h_0$ at $x = X(t)$ and $x = 1$ as well as either p (pressure) or q (flux). The flux is generally thought to be what is controlled in vivo. The last boundary condition is challenging for numerical solution because $h_0 > 1$ and multiplies the third derivative at the boundary, and usually numerical discretization errors are largest at the boundary.

The temperature is not specified at the ends because it has been eliminated from the equations. The surfactant boundary conditions have been either no flux at both ends or a specified concentration corresponding to the inferior lid and no flux on the moving superior lid as discussed in more detail in Section 3.2.3.

The osmolarity may be specified to be isotonic ($c = 1$) at the ends, which approximates the value for new tear fluid supplied there from under the lids.

For initial conditions, it is common to specify piecewise polynomial initial conditions with the thickness being essentially constant in the middle for domains corresponding to the open eye $-1 \leq x \leq 1$. A constant or quadratic thickness is common for the simulations beginning with domain corresponding to a closed eye, $X(0) = 1 - 2\lambda \leq x \leq 1$. $\lambda = 0.1$ and 0.2 have been used in the literature for the closed lid position and $\lambda \leq 0.5$ for partial blinks.

We now discuss results for subsets of these lubrication models.

3.2 Single Layer Models

3.2.1 MODELS WITH STATIONARY ENDS There have been a number of mathematical studies of PCTF drainage or relaxation after a blink (Wong et al., 1996; Sharma et al., 1998; Miller et al., 2002); all of these used Newtonian film properties and treated the the tangentially immobile case without evapora-

tion and with stationary ends. The equation for these models takes the form

$$\partial_t h + \partial_x q = 0, \quad q = \frac{h^3}{12} \left[S \partial_x \left(\frac{\partial_x^2 h}{[1 + (\epsilon \partial_x h)^2]^{3/2}} \right) + G \right]. \quad (29)$$

The full curvature was retained from the normal stress condition here. In Wong et al. (1996) and Braun & Fitt (2003), $\epsilon = 0$; the full curvature with $\epsilon \neq 0$ was retained in Sharma et al. (1998) and Miller et al. (2002) in an effort to better approximate the menisci. This class of models corresponds to $\beta = A = P_c = J = 0$, $c = 1$ and $X(t) = -1$. We note that Wong et al. (1996) were the first to use the tangentially immobile approximation for the tear film surface, corresponding to $M \gg 1$ and replacing the tangential stress boundary condition with $u = 0$ on $z = h$. In Miller et al. (2002), the boundary condition $\partial_x^3 h = 0$ was used rather than $q = 0$ for the no-flux condition at the film ends.

All of these authors found reasonable times to breakup were possible in the lubrication models; in these papers, breakup is defined as reaching a predetermined cutoff thickness. A representative result is shown in Figure 2. The meniscus, with its large thickness, is at the edge of the domain. The thin region next to it corresponds to the black line seen in vivo. All these papers found t^α thinning near the end of the domain, approximating the black line region in the eye, with $\alpha = -0.45$ or $\alpha = -0.46$, at the thinnest point in the film (located near the menisci). Though they did not study the tear film, Bertozzi et al. (1994) found both analytically and computationally a $t^{-0.5}$ thinning solution for the capillary-pressure driven case of Wong et al. (1996). The $t^{-0.5}$ result is for asymptotically long time and may not be achievable in tear film conditions with a typical interblink time of 10s or so.

In Braun & Fitt (2003), gravitational and evaporative effects were added; they

studied

$$\partial_t h + \frac{E}{\bar{K} + h} + \partial_x q = 0, \quad q = (h^3/12)(S\partial_x^3 h + G). \quad (30)$$

In that work, $\bar{K}$ was chosen to fit the upper end of evaporation rates measured in eyes (Mathers, 2004). It was shown that evaporation could combine with capillary-driven thinning to accelerate breakup.

Representative results for the drainage problem are shown in Figure 3 from Braun & Fitt (2003); in this case $G = 0$, but evaporation is active and matched to upper end of experimental values from Mathers (2004). In the current scalings, this plot is for $d = 10^{-5}\text{m}$, $L = 5 \times 10^{-3}\text{m}$, $S = 5.5 \times 10^{-5}$, $E = 29.6$, $\bar{K} = 4.43 \times 10^3$, and $h_0 = 13$. The overall thinning with increasing time is caused by evaporation. The tear film thickness decreases faster than for capillary driven thinning alone and can break up in finite time according to the model (Braun & Fitt, 2003).

3.2.2 MOVING ENDS: FORMATION AND BLINKING Wong et al. (1996) were the first to cast the formation of the tear film as a modified dip coating problem (Levich, 1962; Probstein, 1994). They used separate models to study both drainage and formation. The formation mode is an application of the Landau-Levich dip coating problem, with the matching onto a meniscus with constant radius. They predicted a reasonable range of thicknesses from their theory but the values were typically larger than subsequent direct measurements (King-Smith et al., 2004). Creech et al. (1998) used the theory to derive tear film thicknesses from meniscus radius measurements and a wide range of tear film thicknesses was found, from 2.8 to $24 \times 10^{-6}\text{m}$.

Jones et al. (2005, 2006) developed lubrication models that combined film formation and drainage. In one case, Jones et al. (2005) assume a strong insoluble

surfactant on the aqueous layer surface ($M \gg 1$); in this USL, the surfactant transport equation and the shear stress condition simplify to yield a spatially-uniform surfactant concentration to leading order and so surfactant transport yields $u_s = -\dot{X}(1-x)/(1-X)$, where the dot indicates ordinary differentiation with respect to time. Together with the normal stress condition, the tangentially immobile case with $\beta = J = A = 0$ and $c = 1$ requires

$$q = \frac{h^3}{12}(S\partial_x^3 h + G) + \frac{h}{2} \frac{1-x}{1-X} \dot{X}. \quad (31)$$

Thus in this case, the tear film thickness is governed by the single PDE; the first term on the right is from pressure-driven Poiseuille flow, while the second is from shear-driven Couette flow due to the USL. They assumed that only superior eyelid moved via an exponential expression for $X(t)$ and they specified the film thickness $h = h_0$ at both ends. They also specified the flux $q(-1, t) = 0$ and $q(X, t) = \dot{X}h_e$; the flux from under the upper lid that arises from exposing a pre-existing layer of thickness h_e under the lid. We label this last condition “Flux Proportional to Lid Motion” (FPLM). Two models were studied corresponding to pure tear film or stress-free film (lipid layer has no effect) and the USL (strong insoluble surfactant). Jones et al. (2005) found it to be impossible to form a PCTF without influxes from the upper lid during the upstroke. In particular, film breakup occurs in both models near the upper meniscus with only 80% of the cornea exposed. This agrees with the finding of King-Smith et al. (2004), based on cross-sectional area measurements, that supply or exposure of the tear film from under the lids is required to adequately deposit the pre-corneal tear film.

Maki et al. (2008) studied tear film formation and relaxation subject to reflex tearing and evaporation. This model corresponds to $\beta = A = 0$, $c = 1$ in the

USL, and it treated the dynamics of the tear film thickness subject to reflex tearing (e.g., from cutting an onion) and evaporation in a 1D model (Maki et al., 2008). Comparison with measured thickness data from the center of the cornea (King-Smith et al., 2000) was favorable; results are shown in Figure 4. The flux boundary conditions of Heryudono et al. (2007) were modified to include a pulse of incoming fluid due to reflex tearing during the interblink. During the computation, capillary-driven thinning creates black lines near each lid; the additional fluid from reflex tearing and the effect of gravity cause a bulge of fluid to drain down the cornea from the superior meniscus. Good qualitative agreement with experimental observation was found for the increase and subsequent thinning at the film's center. In most circumstances, the black line is a barrier to flow; however, in our 1D simulations the extra flux from reflex tearing coupled with gravity can supply fluid through the black line region. Once some fluid has pushed through the black line, a relatively small flux can continue to flow from the meniscus. In two dimensions, there is less resistance to fluid flow along the meniscus rather than directly through the black line; this is discussed further in Section 3.4.

Jossic et al. (2009) studied an SFL model combining formation and drainage using a shear thinning Ellis fluid (Myers, 2005). In that paper, parameters were fit to tear fluid properties at the lower end of the shear thinning range for the Ellis fluid. They used their model to optimize eye drop properties, such as the viscosity, to make the tear film as uniform as possible.

3.2.3 FORMATION AND DRAINAGE WITH INSOLUBLE SURFACTANT The upward motion of particles in the tear film just after a blink was observed by Berger & Corrsin (1974); the particles moved upward for 1-2s, and they slowed during

the motion. They constructed a linearized theory in a Lagrangian framework for the motion of the particles, the theory corresponds to setting $\beta = G = A = J = 0$ and $c = 1$. They considered an extended domain, so there were no menisci or ends of the film. Their theory showed that the Marangoni effect was consistent with the observed motion. This notion was later confirmed by Owens & Phillips (2001) and King-Smith et al. (2009) experimentally.

Jones et al. (2006) considered the mobile surface with an insoluble surfactant with a nonlinear equation of state. They studied a model with an exponential equation of state for the surface tension, $\sigma = 1 - e^{-\Gamma(-1 + \sigma_w/\sigma_0)}$, where σ_w is the surface tension for air/pure water interface. In our notation, this case has $\beta = A = \text{Pe}_s = 0$, $\lambda = 0.2$ and $c = 1$, with all other effects present, and a different form for the Marangoni term (proportional to M). By appropriately choosing parameters, they found upward motion of the film surface after the upstroke of the upper lid with speed and duration that compared well with experimental results from Owens & Phillips (2001). Formation of the tear film during the upstroke tended to leave a high concentration of tear fluid at the end corresponding to the lower lid, and to decrease as the superior lid was approached. During the first 3 seconds of the interblink, the concentration distribution flattened out and a bulge of fluid propagated up the film, which mimics observations in vivo. Results from their paper are shown in Figure 5. The upward motion is driven by the Marangoni effect. They also considered the half blink by modeling it with lipid present only in the inferior half of the tear film together with a spike of lipid concentration at the center of the domain. Subsequent dynamics left the superior half of the tear film with smaller thickness than the inferior half. Those dynamics agree qualitatively with their fluorescence observations, but the thin film model did

not show a valley in the center of the film as observed in vivo (Heryudono et al., 2007).

Aydemir et al. (2010) studied the problem from the general formulation above without evaporation, osmolarity or van der Waals forces ($J = A = \text{Pe}_s = 0$, $\lambda = 0.2$, $c = 1$). They used a linearized equation of state for $\sigma(\Gamma)$ as above, and their theory was based on a 10^{-5}m film thickness with 10^{-3}m TMW at each end. For boundary conditions, they specified h at the boundary along with no flux boundary conditions on both h and Γ . They found a significant gradient of concentration, and thus surface tension, though the nascent black line region, indicating a contribution from the Marangoni effect. As shown in Figure 6, the lipid concentration tended to separate during the upstroke and with larger values at the film ends, but then started to spread toward the center of the film during the interblink period. They also found that, in the absence of any flux from under the moving end, a thin film could formed across the entire domain, in opposition to the result of Jones et al. (2006). We note that their specified thickness at the end was 10^{-3}m and that the nominal tear film thickness was 10^{-5}m , which are both large for the tear film; these large values are favorable for film formation without influx from under the lids.

Jones et al. (2006) noted that the boundary conditions at the film ends ($x = X(t)$ and $x = 1$) should be chosen with care. At each end, one may wish to control four quantities: h , u_s , q and one of either the surfactant flux $q^{(\Gamma)} = u^{(s)}\Gamma - \Gamma_x/\text{Pe}_s$ or Γ . Only three such quantities may be specified at each end; this is because lubrication theory reduced the dimensionality of the problem. Jones et al. (2006) and Aydemir et al. (2010) made particular choices that gave useful results. There may be other good choices possible in light of discussions of the lipid layer's supply

and dynamics (DiPasquale et al., 2004; Tiffany, 1987; Bron et al., 1991; Bron & Tiffany, 1998; Tiffany, 1995) as well as requirements for blink cycles.

3.2.4 BLINK CYCLES Braun & King-Smith (2007) and Heryudono et al. (2007) were the first to compute full blink cycles; they used single-equation models similar to those in Jones et al. (2005) but including slip at $z = 0$. In the terms of this paper, they used $J = A = 0$, $c = 1$ and $0.1 \leq \lambda \leq 0.5$. Heryudono et al. (2007) studied single equation models for the USL and SFL film surfaces over multiple blink cycles as well as partial or half blinks. They solved $\partial_t h + \partial_x q = 0$, where for the SFL q is from (23) with $M = 0$, and for the USL,

$$q = -\frac{h^3}{12} \left(1 + \frac{3\beta}{h + \beta} \right) (S\partial_x p - G) + \dot{X} \frac{1-x}{1-X} \frac{h}{2} \left(1 + \frac{\beta}{h + \beta} \right). \quad (32)$$

The complete problem is specified with $h = h_0$ and q specified at the ends ($x = X(t)$ and $x = 1$) and a smooth initial condition. They used realistic lid motion functions fit from observed lid motion data by modifying results from Berke & Mueller (1998) to include partial blinks. They developed generalized FPLM boundary conditions, namely $q(X, t) = q_{top} + h_e \dot{X}$, and $q(-1, t) = -q_{bot}$, where q_{top} and q_{bot} are specified functions of time designed to mimic supply from the lacrimal gland and drainage through the puncta (see Heryudono et al. 2007 for details).

In their numerical study, better comparisons to in vivo measured partial blink data were found when using the uniform stretching limit model coupled with the generalized flux boundary conditions. An image of a PLTF just after a half-blink is shown at left in Figure 7. The interference fringes shown in the photo indicate a change of $0.16 \times 10^{-6} \text{m}$ for each change between light and dark. The absolute thickness of the tear film along the vertical line (dots at right) can be found from the interference fringes using two different methods simultaneously (King-

Smith et al., 1999, 2000, 2006); comparison with computed results are shown at right. Jones et al. (2006) also saw valleys experimentally, via fluorescence and tearscope (lipid) imaging, but Heryudono et al. (2007) made a quantitative comparison. The model showed some sensitivity to slip at relatively large values of β .

Both Braun & King-Smith (2007) and Heryudono et al. (2007) found that the solutions for the tear film became periodic once the lids became close enough together at the end of the downstroke (about 1/8 or 12% open). They interpreted this to mean that any state that had occurred in the last blink cycle had been erased, and that this was the fluid dynamic equivalent of a full blink. Thus an incomplete blink that is within 1/8 of being fully closed is just as good as full blink in those models. This may help rationalize why there are so many incomplete blinks and why they may be so effective (Doane, 1980; Harrison et al., 2008).

3.2.5 SINGLE LAYER MODELS OF BREAKUP The existence of a separate mucus layer has been argued in the eye literature (Holly, 1973; Holly & Lemp, 1977). The hypothesis was that the hydrophilic mucus layer allows wetting of a nonwetting cornea; if the mucus layer were to break up, then the aqueous layer would dewet from the cornea. Some models have been developed to describe this situation. Lin & Brenner (1982) studied a linearized model of a single fluid layer on cylindrical substrate with a strong surfactant which was subject to an instability driven by van der Waals forces. For our nondimensionalization, the unretarded van der Waals term, a disjoining pressure, would be

$$\phi = -\frac{A}{h^3}, \quad A = \frac{A^*}{6\pi\mu U\epsilon L^2}. \quad (33)$$

Their linear theory, which was not in the lubrication approximation, predicted rupture. Gorla & Gorla (2000) studied the corresponding nonlinear theory, and

estimated BUTs, though their computations suffered from low resolution in the spatial coordinate. Gorla & Gorla (2004) studied breakup using a power law fluid on a cylindrical substrate to model the eye and treated it similarly.

The nonlinear model was extended by Zhang et al. (2003b) to one that included van der Waals forces, transport of an insoluble surfactant on the air-aqueous interface, and slip at the corneal surface to model the presence of mucins there. They considered $G = 0$ and a periodic domain without menisci. They found that breakup was accelerated by increasing slip, e.g., with shorter BUTs, and that the variation of surface velocity and film thickness was increased by slip. Increasing surface tension was stabilizing and the effect was quantified for a range of values.

Winter et al. (2010) considered a single layer model together with evaporation for the aqueous layer, with a tangentially immobile surface and van der Waals forces that cause wetting of the corneal surface (conjoining pressure). They numerically solved the equation

$$\partial_t h + EJ + \partial q_x = 0, \quad q = \frac{h^3}{12} \partial_x (S \partial_x^2 h + \phi). \quad (34)$$

They specified h and p at each end. The evaporation model is that of Ajaev and Homsy Ajaev (2005); Ajaev & Homsy (2001), and for our nondimensionalization, we have

$$\phi = \frac{A}{h^3}, \quad \text{and} \quad J = \left[1 - \delta (S \partial_x^2 h + \phi) \right] (\bar{K} + h)^{-1}. \quad (35)$$

The additional terms for non-planar interfaces of Wu & Wong (2004) do not appear to contribute for the conditions studied by Winter et al. (2010). This conjoining pressure term prevents dewetting, and can arrest thinning due to evaporation at a uniform equilibrium thickness $h_{eq} = (\delta A)^{1/3}$. This thickness was chosen to be same size as the microvilli and glycocalix; thus in this model, breakup means that $h = h_{eq}$. This equilibrium value mimics the wetting behavior

of the glycocalix by stopping evaporation and forcing relatively slow motion and large resistance to flow. They chose h_{eq} to correspond to about $0.2 \times 10^{-6}\text{m}$.

In the model of Winter et al. (2010), breakup first occurred at the black line and holes opened from there. Later, a hole could also form in the middle of the film. The opening rates of experimentally observed holes (from an imaging interferometer for lipids, P.E. King-Smith, unpublished research) were estimated, and the parameters of the theoretical model explored to estimate reasonable values for δ and A , which yielded the α and A^* given above. This is a simple model that has promise for mimicking tear film breakup, but the tear film has large molecules and dissolved salts present, so screening and retardation of the van der Waals forces may be important (Israelachvili, 2010). Those effects are yet to be incorporated in eye models.

3.3 Bilayer models

The different cases discussed here all require for each fluid that the flux is given by

$$q^{(1)} = \int_0^{h^{(1)}} u^{(1)}(x, z, t) dz \quad \text{and} \quad q^{(2)} = \int_{h^{(1)}}^{h^{(2)}} u^{(2)}(x, z, t) dz, \quad (36)$$

where $u^{(i)}(x, z, t)$ is the approximate velocity field from lubrication theory. The two fluid layers are in $0 < z < h^{(1)}(x, t)$ and $h^{(1)}(x, t) < z < h^{(2)}(x, t)$ for $i = 1, 2$.

Using the kinematic condition and mass conservation, the free surface evolution is given by the forms

$$\partial_t h^{(i)} + \partial_x q^{(i)} = 0. \quad (37)$$

In the models discussed below, surfactant transport may be on either on the surface between the two layers or the top of the bilayer, and in either case are

governed by

$$\partial_t \Gamma^{(i)} + \partial_x \left(u_s^{(i)} \Gamma^{(i)} \right) = \left(\text{Pe}_s^{(i)} \right)^{-1} \partial_x^2 \Gamma^{(i)}, \quad (38)$$

where $\Gamma^{(i)}$ and $u_s^{(i)}$ are located on $h^{(i)}$.

3.3.1 MUCUS AND AQUEOUS LAYERS Sharma and Ruckenstein extended tear film models with van der Waals driven rupture to linear (Sharma & Ruckenstein, 1986b) and nonlinear (Sharma & Ruckenstein, 1985, 1986a) theories that included a separate mucus layer between the aqueous layer and the epithelium. The models were derived with shear forces dominating in both layers. Surfactant transport on the hypothesized mucus-aqueous interface ($h^{(1)}$) was also included. Thus, they considered equations for $h^{(i)}$, $i = 1, 2$ and $\Gamma^{(1)}$ in their most general case. The expressions for the $q^{(i)}$ and $u_s^{(1)}$ are complicated; see those papers for details. The mucus layer was unstable to van der Waals forces in the model. All of the theories could give reasonable BUT ranges.

The two-layer film theory was generalized to include van der Waals forces in both mucus and aqueous layers, and surfactant transport on the aqueous-lipid interface (Zhang et al., 2003a, 2004). The mucus layer, with top surface $h^{(1)}$ in our notation, was treated as a power-law fluid with a fit to experimental data for whole tears (Pandit et al., 1999) over a range of shear rates up to 5s^{-1} being used to determine the power $n = 0.81$. The aqueous layer was assumed to be Newtonian, and the lipid layer was simplified to the transport of an insoluble surfactant, so that they considered equations $h^{(i)}$ and $\Gamma^{(2)}$. (See their papers for expressions for $q^{(i)}$ and $u_s^{(2)}$.) They found that the tear film could be unstable with rupture driven by van der Waals forces. Thinner mucus layers in the model led to reduced BUTs, and increased Marangoni effect (stronger surfactant) led to increased rupture times. Related papers, which may apply to eyes via analogy

with lung surfactants, include Matar et al. (2002) which is discussed further in Section 3.3.3. For a comprehensive review of related bilayer work, see Craster & Matar (2009).

3.3.2 MULTILAYER FILMS THAT WET THE CORNEA The current thinking for the mucus distribution in the tear film does not currently posit a separate layer for the gel-forming mucins (Gipson, 2004; Bron et al., 2004; Govindarajan & Gipson, 2010), though there could be a relatively mucin-rich area near the glycocalix and the microvilli. However, there may still be validity to treating the region near the corneal surface differently than the main part of the aqueous layer. The transmembrane mucins that form the forest-like glycocalix are thought to trap toxic or damaging molecules or other debris (Sharma, 1998) and then the ectodomain (part anterior to the corneal epithelium) can break off and be transported away from the corneal surface (Govindarajan & Gipson, 2010). Alternatives for treating this $0.2\text{--}0.5 \times 10^{-6}\text{m}$ region include separate fluid layers as in the previous section or with slip (Zhang et al., 2003b; Heryudono et al., 2007). Winter et al. (2010) used the simple model of unretarded van der Waals forces to model the hydrating properties of the glycocalix to stop evaporation at an appropriate thickness while using a single layer model. Alternative treatments could include a thin soft porous medium with varying porosity or a film on a soft substrate (Skotheim & Mahadevan, 2004). More physiologically realistic and detailed models may be helpful, and it is expected that this will remain an active area of research.

3.3.3 LIPID AND AQUEOUS LAYERS Another bilayer approach to the tear film is to treat the lipid and aqueous layers. Let (2) denote lipid and (1) the aqueous layer. The polar lipids at the lipid-aqueous (i.e., (1)-(2)) interface will

affect flow via the Marangoni effect (McCulley & Shine, 1997; Owens & Phillips, 2001; Jones et al., 2006; King-Smith et al., 2009). Bruna-Estrach (2009) derived a model that incorporated the large viscosity contrast $\mu_0^{(2)}/\mu_0^{(1)} \approx 10^4$ (Tiffany (1987), p. 35), and the surface tension contrast $\sigma_0^{(2)}/\sigma_0^{(1)} \approx 1$. The approach resulted in a model with equations governing $h^{(1)}$, $h^{(2)}$ and $\Gamma^{(1)}$ where the viscous (2) layer is extensional, the (1) layer is dominated by shear, and the insoluble surfactant transport equation is on the interface between them. The development closely parallels that of Matar et al. (2002); the latter model has a very viscous layer that is extensional overlying a shear dominated layer, but the surfactant $\Gamma^{(2)}$ is located on $h^{(2)}$. Matar et al. (2002) derived their model for the liquid lining in the lung's airways rather than the tear film. The lipid distribution for Bruna-Estrach's computed results with the bilayer was similar to that of Aydemir et al. (2010) for the upstroke and interblink. Bruna-Estrach (2009) found different limiting cases, including one where the surfactant concentration and lipid layer thickness were proportional, one where the surface viscosity remained when the lipid layer thickness was small, and one where the surface tension of a simplified aqueous-air interface is the sum of the surface tensions of the aqueous-lipid and lipid-air interfaces. This work should appear in the literature in the near future (M. Bruna-Estrach, V.S. Zubkov, C.J.W. Breward and E.A. Gaffney, in preparation).

3.4 Two-dimensional Models

To our knowledge, Maki et al. (2010a,b) the first papers published the first two-dimensional computations of tear film dynamics. Using a stationary eye shape created from an image of an eye, the dynamics were computed for the model

(now written as a system with $A = \beta = 0$, $\Gamma = c = 1$)

$$h_t + \nabla \cdot \left[-\frac{h^3}{12} \nabla (p + Gy) \right] = 0, \text{ and } p + S\nabla^2 h = 0. \quad (39)$$

Here $\nabla = (\partial_x, \partial_y)$ where x now points temporally and y points superiorly. Only surface tension, viscosity and gravity may be present in the model; the difficulty is in the boundary geometry in this case.

The boundary conditions specified values for the film thickness and either the pressure (p , Maki et al. 2010a) or the flux of fluid normal to the boundary ($\mathbf{n} \cdot \nabla p$ with $\mathbf{n}$ being the outward normal to the domain, Maki et al. 2010b). The initial condition was exponential decay from the boundary to a flat surface in the middle. Results for specified nonzero flux on the boundary with $G = 0$ are shown here. The results are for a model problem where the supply from the lacrimal gland is time-independent and set to its estimated average (basal) value, and it enters from the superior lid margin (domain edge) above the temporal canthus. The model problem also has constant drainage out of the puncta near the nasal canthus, leaving the net tear volume unchanged.

In Figure 8 for $t = 1$, the black line region forms (shown as dark blue here) near the lid margin, and the meniscus is clearly wider near the temporal canthus. For $t = 10$, the black line region is pushed out from influx from the lacrimal gland (wider dark red region), and it is pulled toward the lid margin near the puncta. In Figure 9, the flux direction vectors are plotted with shading to indicate their relative magnitudes, where darker is slower. The influx of fluid above the temporal canthus splits with some traveling along the upper lid nasally, and more going temporally and to the lower lid. This flow is in accord with in vivo observations (Maurice, 1973; Harrison et al., 2008). With either flux or pressure boundary conditions, Maki and coworkers found that the canthi promote flow

along the menisci toward themselves, aiding flow toward the puncta on the nasal side of the eye, where fluid drains at the end of a blink (e.g., Doane 1981; Zhu & Chauhan 2005b).

3.5 Osmolarity and solute models

Gaffney et al. (2010) developed a compartment model that is a mass and solute balance of the tear film that focuses on osmolarity. The model accounts for osmolarity in discrete regions of the tear film, such as the broad middle, the menisci near the lids and fornices (areas under the lids). Input parameters include the tear supply from the lacrimal gland, the tear evaporation rate, and the blink rate. The model indicates that the osmolarity should increase over most of the eye from evaporation, possibly to high enough levels to cause noticeable sensation (Liu et al., 2009). Parameters relevant for dry eye predict more elevated concentration than for normals. The model will not ever-increasing osmolarity for aqueous deficient dry eye (ADDE) as it appears to predict an unstable tear film because the meniscus radius of curvature may take on values outside the empirically observed range. Parameters appropriate for evaporative dry eye (EDE) or hybrid ADDE and EDE indicate increased osmolarity and a tear film that remains stable according to the model. Results from the model also suggest that increased blink rate, in an effort to supply more tears, may have a limited benefit for ADDE given the constraint of a stable tear film with a meniscus radius of curvature within empirical bounds.

Zhu & Chauhan (2005a) studied a mass and solute balance compartment model for the tear film that focused on drug delivery and residence time. They considered the dynamics of a passive tracer that is not absorbed by the ocular surface

and a solute that is absorbed by the ocular surface. Evaporation, tear supply and drainage via the canaliculus model of Zhu & Chauhan (2005b) were included. They explored the effect of instilling a $15\mu\text{l}$ drop into the tear film via this model for various parameters including the surface tension and viscosity.

Recent tear film thinning measurements for long interblink periods suggest that osmosis from the ocular surface may help slow thinning due to evaporation King-Smith et al. (2007, 2010c). As a first step, consider the general system that is uniform in space with $\Gamma = 1$ and $G = 0$, namely

$$\dot{h} + EJ = P_c(c - 1), \quad h\dot{c} + P_c(c - 1)c = EJc, \quad J = (1 - \delta Ah^{-3})/(\bar{K} + h). \quad (40)$$

Here we give results for measured value of permeability from King-Smith et al. (2010c) given in Section 3.1.2; they determined the permeability and evaporation rate from thinning measurements and a single-equation model for $h(t)$ resulting from (40) with $A = 0$ and $EJ = E_0$ (a constant). Figure 10 shows results for $d = 3.5 \times 10^{-6}\text{m}$, $P_c = 0.0206$, $E = 241$, $\bar{K} = 2.03 \times 10^4$, $\delta = 0.95$, $A = 3.06 \times 10^{-6}$, corresponding to an evaporative thinning rate of $2.5 \times 10^{-6}\text{m/min}$. The results show that osmotic supply may arrest tear film thinning on a time scale of a minute, and may affect the thinning rate on the order of tens of seconds. The thickness results shown in Figure 10 are indistinguishable from those of King-Smith et al. (2010c) for the single equation case. Extending these results to include spatial variation as in the model framework and to include the influence of lipid layer dynamics is an important future research direction; work in this direction is underway (Braun et al., 2010).

4 Summary and Future Directions

The tear film is a complex and dynamic biological structure of great importance for our sight. It cannot be controlled as precisely as, say, systems that have been studied profitably in dewetting on Si wafers (Craster & Matar, 2009). Model systems, both experimental and theoretical, may be able to significantly aid our understanding. A long history of biologically based experimental models, from a variety of mammals, to in vitro models that use components from some of these species as well as humans, have aided understanding. Recent models show promise for understanding complex issues related to surface rheology and evaporation from the tear film. Sophisticated in vivo measurements continue to be developed for basic research as well as clinical use, and closely aligning theory with these methods is appropriate. Theoretical models can vary parameters that experiment is unable to control in vivo or in vitro; they may contribute greatly to understanding the tear film.

Future Issues

1. The dynamics of osmolarity are thought to be an important variable in the cause and progression of dry eye (Lemp et al., 2007). While some mathematical directions are currently being explored, more studies that include lipid layer dynamics and evaporation as well as transport to and from the ocular surface and its response to hyperosmolarity are desirable.
2. Two dimensional simulations of tear film dynamics can shed more light on the roles of mensici, canthi and central regions in the fluid motion and osmolarity variation as well. Current osmolarity measurements rely on the samples from the temporal canthus (e.g., Benelli et al. 2010), but that loca-

tion is thought to be somewhat separate, fluid dynamically, from the central region (Miller et al., 2002). While the measured osmolarity values from the meniscus are well-correlated to dry-eye conditions (Tomlinson et al., 2006), two-dimensional approaches can help understand elevated values of osmolarity over the whole ocular surface (Liu et al., 2009).

3. Tear film dynamics under the lids and coupling to the visible tear film is a virtually unexplored area from a theoretical (mathematical) viewpoint. To our knowledge, there is only one paper published on the fluid dynamics under the lids, and it attempts to model the flow under the eyelid wiper region near the lid margin on the posterior side of the lid (Jones et al., 2008).
4. Some details of evaporation through the lipid layer are not well understood at this time. Decreased amounts of lipid have been demonstrated to increase evaporation (Mishima & Maurice, 1961; Craig & Tomlinson, 1997); King-Smith et al. (2010a) quantified this effect for the rate of thinning. Incorporating these and other experimental results into mathematical models that simultaneously treat tear film dynamics remains to be done. Incorporating vapor diffusion outside the film is doubt be important in some situations; the approach of Sultan et al. (2004) seems appropriate in those cases.

Related Resources

1. Fluid Mechanics of the Eye, Jennifer H. Siggers and C. Ross Ethier, *Annu. Rev. Fluid Mech.* 44 (2012), this issue.

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LIST OF ACRONYMS

PCTF: Pre-Corneal Tear Film.

PLTF: Pre-Lens Tear Film (anterior to a contact lens).

PoLTF: Post-Lens Tear Film (posterior to contact lens but anterior to the cornea).

OCT: Optical Coherence Tomography

BUT: Break-up time (a.k.a., time to rupture).

TMH: Tear Meniscus Height.

TMW: Tear Meniscus Width.

TMR: Tear Meniscus Radius.

FPLM: Flux Proportional to Lid Motion.

ADDE: Aqueous Deficient Dry Eye.

EDE: Evaporative Dry Eye.

LIST OF TERMS

Superior: A direction or location toward the top of the body.

Inferior: A direction or location toward the bottom of the body.

Temporal: A direction or location toward the outside of the body (a.k.a. lateral).

Nasal: A direction or location toward the nose (a.k.a. medial).

Anterior: A direction or location toward the front of the body.

Posterior: A direction or location toward the rear of the body.

Sagittal plane: A plane, often meaning a cross-section, whose normals point temporally or nasally.

Cornea: The clear central portion of the anterior of the eye, about 10^{-2}m in diameter.

Canthus: A corner of the eye, where upper and lower eyelids meet.

Puncta: Drain holes through which tears drain, located near the nasal canthus, on superior and inferior lid margins.

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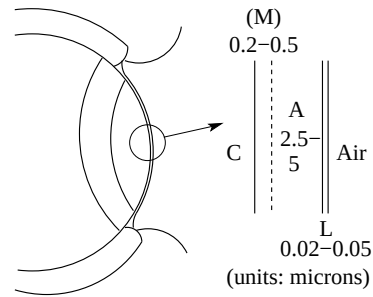


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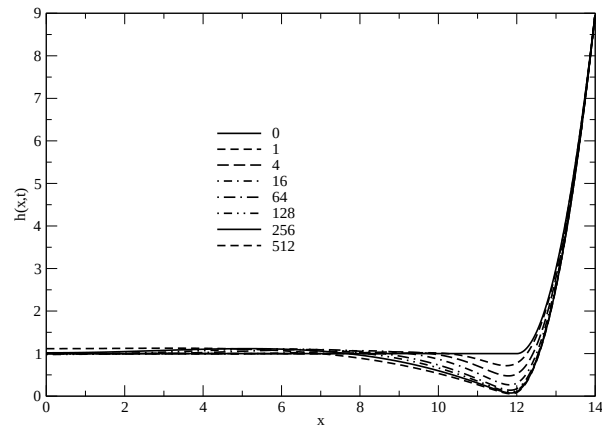


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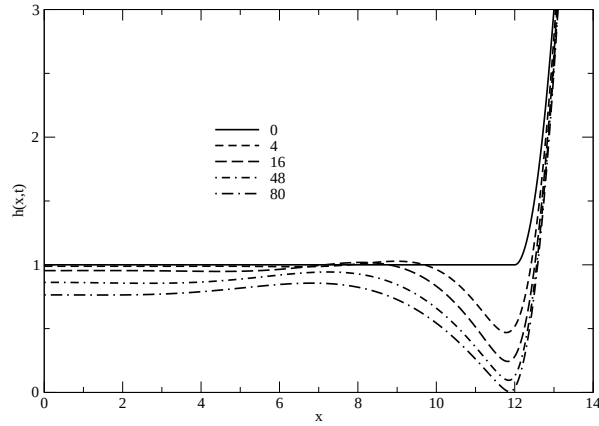


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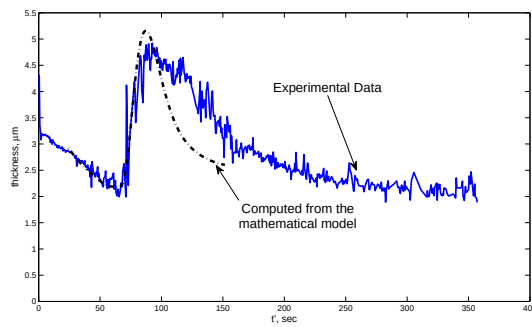


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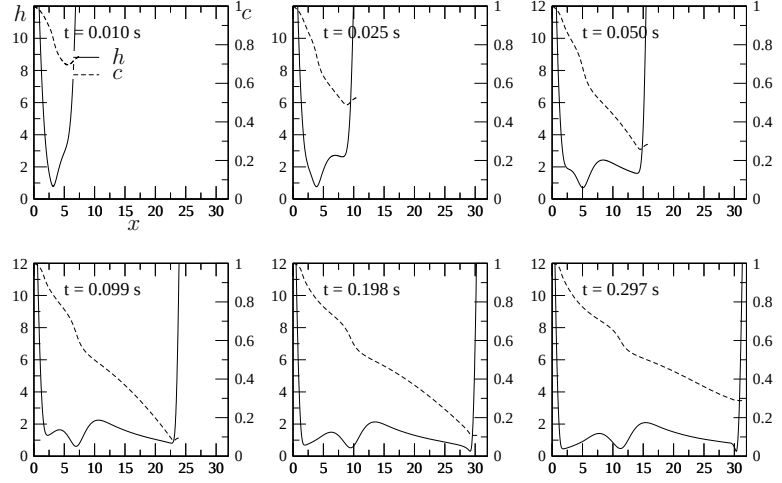


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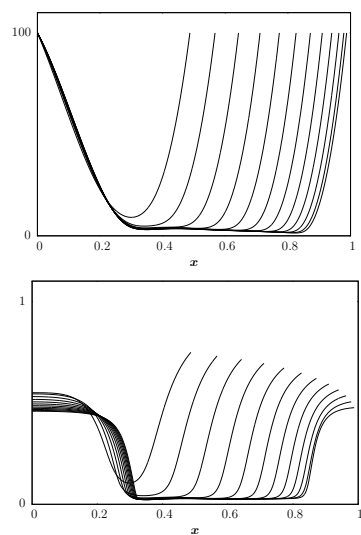


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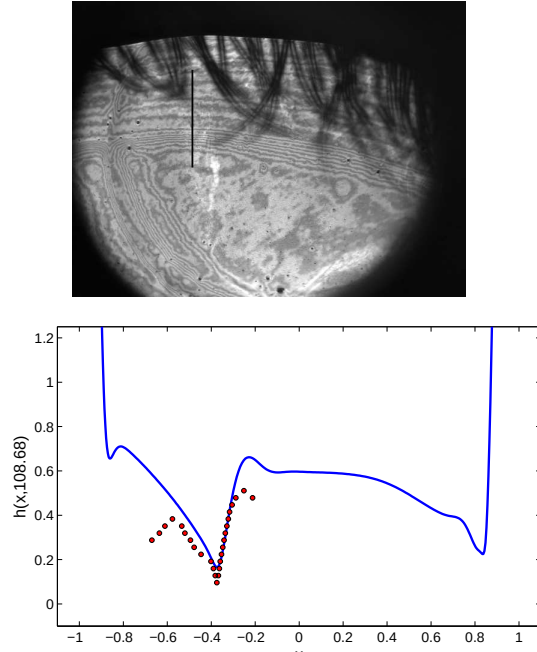


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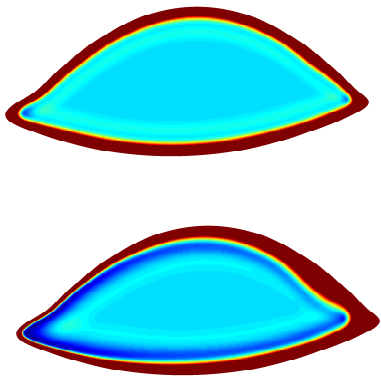


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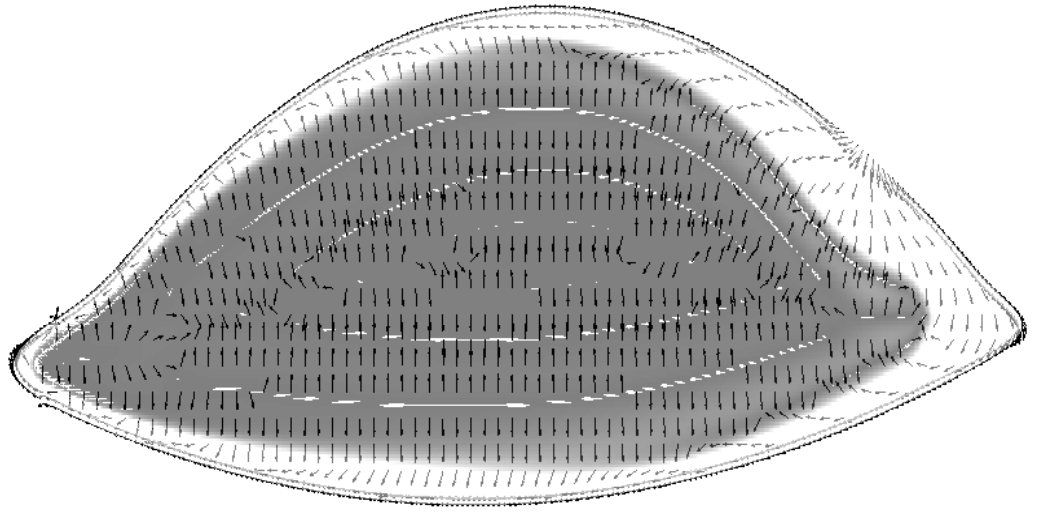


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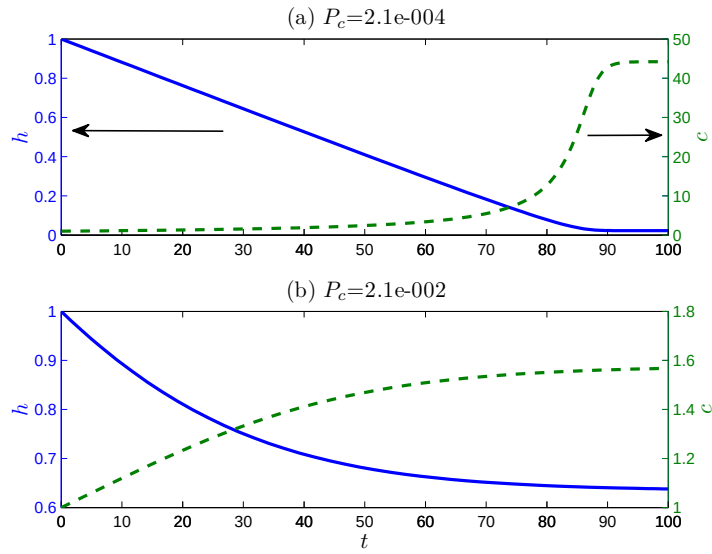


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