

Multiscale modelling shows how cell-ECM interactions impact ECM fibre alignment and cell detachment

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Table 1. Model parameters. Description and values of the parameters used in our simulations.

General parameters	
$\eta = 50 \text{ pN}\cdot\text{s}\cdot\mu\text{m}^{-1}$	Viscous coefficient. Estimated
ECM parameters	
$L_{l,m}^0$	Natural length of the fibre. Determined by the initial condition
$k_{l,m}^{\text{el}} = \frac{E_{l,m}A_{l,m}}{L_{l,m}^0}$	Elastic constant of the fibre
$E_{l,m}$ $E_{l,m} = E_t = 10 - 100 \text{ MPa}$ $E_{l,m} = E_c = 0.1E_t \text{ MPa}$	Young's modulus of the fibres. Reference value from [1,2] Young's modulus of extended fibres Young's modulus of compressed fibres [2]
$A_{l,m}$ Fibre diameter = 10^{-7} m	Cross-sectional area of the fibres [3, 4]
Crosslink density, $0.2 \mu\text{m}^{-2}$	[2]
Mean fibre length density, $0.6 - 0.7 \mu\text{m} \cdot \mu\text{m}^{-2}$	[2]
Cell parameters	
$\kappa_i^{\text{el}} = 5 \cdot 10^3 \text{ pN}\cdot\mu\text{m}^{-1}$	Elastic constant of cell viscoelastic elements. Estimated
$\kappa_i^{\text{vi}} = 10^3 \text{ pN}\cdot\text{s}\cdot\mu\text{m}^{-1}$	Damping constant of cell viscoelastic elements. Estimated
$l_i^c = 15 \mu\text{m}$	Natural length of viscoelastic elements. Estimated from cell sizes.
$\kappa_i^{\text{el}} = 1 \text{ pN}\cdot\text{rad}^{-1}$	Angular elastic constant of the viscoelastic elements. Estimated
$\theta_{i,j}^0$	Natural angle between viscoelastic elements. Determined by initial cell shape.
$F^{\text{co}} = 10^3 - 5 \times 10^4 \text{ pN}$	Estimated. Reference values [5–7].
Integrin and FAs parameters	
$k^{\text{i}} = 10^6 \text{ pN} \cdot \mu\text{m}^{-1}$	Elastic constant of the integrins, see [8].
$K_{\text{on}} = 0.2 \text{ s}^{-1}$	Integrins binding rate, estimated value. Reference value for estimation [7, 9]
$K_{\text{off}}(F_{i,l}^{\text{i}}) = 0.4 \exp(-0.04F_{i,l}^{\text{i}}) + 4 \times 10^{-7} \exp(0.2F_{i,l}^{\text{i}})$	Integrin unbinding rate, [9]
$N = \frac{6000}{N_n^c} \text{ integrins}$	Estimated available integrins per FA site. N_n^c is the number of FA sites in the n -th cell

References

1. Tsingos E, Bakker BH, Keijzer KA, Hupkes HJ, Merks RM. Hybrid cellular Potts and bead-spring modeling of cells in fibrous extracellular matrix. *Biophysical Journal*. 2023;122(13):2609–2622.
2. Humphries D, Grogan J, Gaffney E. Mechanical cell–cell communication in fibrous networks: the importance of network geometry. *Bulletin of Mathematical Biology*. 2017;79:498–524.

3. Lindström SB, Vader DA, Kulachenko A, Weitz DA. Biopolymer network geometries: Characterization, regeneration, and elastic properties. *Physical Review E*. 2010;82(5):051905.
4. Liang L, Jones C, Chen S, Sun B, Jiao Y. Heterogeneous force network in 3D cellularized collagen networks. *Physical Biology*. 2016;13(6):066001.
5. Elosegui-Artola A, Oria R, Chen Y, Kosmalska A, Pérez-González C, Castro N, et al. Mechanical regulation of a molecular clutch defines force transmission and transduction in response to matrix rigidity. *Nature cell biology*. 2016;18(5):540–548.
6. Novikova EA, Storm C. Contractile fibers and catch-bond clusters: a biological force sensor? *Biophysical journal*. 2013;105(6):1336–1345.
7. Sabass B, Schwarz US. Modeling cytoskeletal flow over adhesion sites: competition between stochastic bond dynamics and intracellular relaxation. *Journal of Physics: Condensed Matter*. 2010;22(19):194112.
8. Lepzelter D, Bates O, Zaman M. Integrin clustering in two and three dimensions. *Langmuir*. 2012;28(12):5379–5386.
9. Li Y, Bhimalapuram P, Dinner AR. Model for how retrograde actin flow regulates adhesion traction stresses. *Journal of Physics: Condensed Matter*. 2010;22(19):194113.