

Biofilm rots teeth and gums

A polymer-solvent model of biofilm growth

H. F. Winstanley¹, M. Chapwanya², M. J. McGuinness³, A. C. Fowler¹

1: MACSI, Department of Maths and Stats, University of Limerick, Ireland

2: Department of Maths and Applied Maths, University of Pretoria, South Africa

3: School of Maths, Stats and O.R., Victoria University of Wellington, New Zealand



Summary

We model the growth of bacterial biofilms using the concept of extra-cellular polymeric substance (EPS) as a polymer solution, whose viscoelastic rheology is described by the classical Flory-Huggins theory. We show that one-dimensional solutions exist, which take the form at large times of travelling waves, and we characterise their form and speed. Numerical solutions of the time-dependent problem converge to the travelling wave solutions.

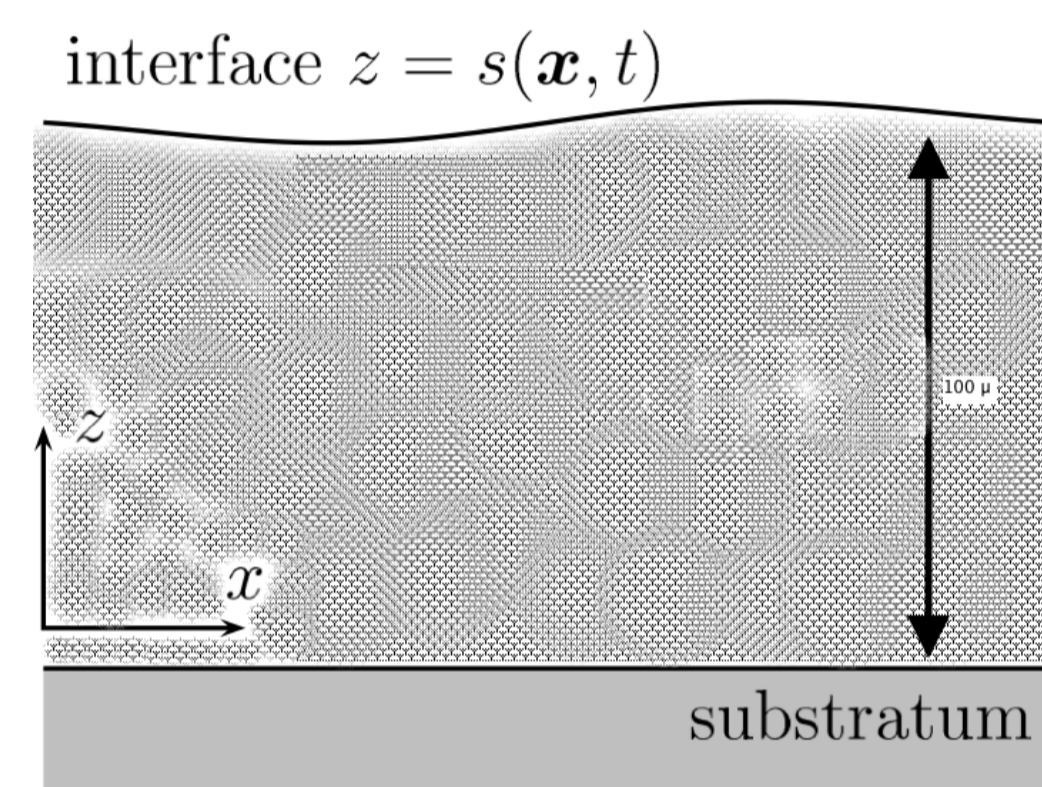
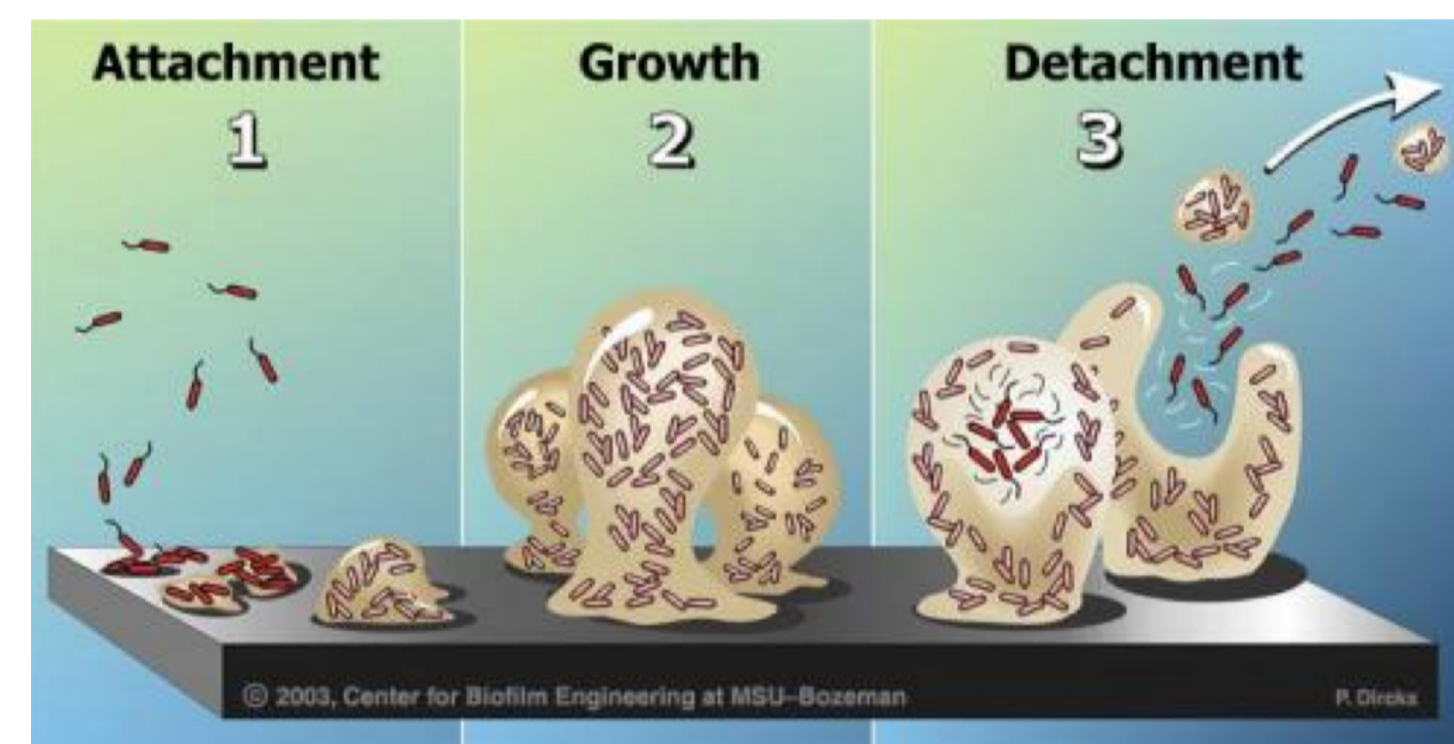


Figure 1: Geometry of the biofilm. A bacterial layer grows upwards from a wall at $z = 0$, and is bounded by its surface at $z = s$. Nutrient flows by, above this surface.



Biofilm growth sketch (thanks to Montana State University Center for Biofilm Eng.)

Previous Models

Our work is based on the conceptual model of Cogan and Keener (2004, 2005), who consider the biofilm as a biological gel consisting of EPS and water, in which bacterial cells occupy only a small volume fraction. The asymptotic limit of their two fluid continuum model uses a dominant balance between viscous stress and the osmotic pressure term. They find a 1D steady state with constant interface growth velocity and examine the instability of this solution to spatial perturbations. We also seek to provide a description of a uniformly growing biofilm. Our approach deviates markedly from theirs: we use an explicit nondimensionalisation, choosing natural scales to identify a different dominant balance.

Flory-Huggins

The Flory-Huggins free energy per unit volume is realised as an osmotic pressure – the additional pressure required to equilibrate the polymer solution with pure solvent across a semi-permeable membrane. This osmotic pressure is given in the relevant limit of large polymer volume and $\phi \ll 1$ as

$$\Psi = E_L \left[-\left(\chi - \frac{1}{2}\right)\phi^2 + \frac{1}{6}\phi^3 + O(\phi^4) \right], \quad (1)$$

where ϕ is the volume fraction of polymer.

Polymer-Solvent Model I

We consider a biofilm in $0 < z < s$ as illustrated in Fig. 1, surrounded by nutrient-rich water, behaving as a gel, and with an osmotic pressure described by the Flory-Huggins theory. We also take both the polymer and the interstitial water to be viscous, and to interact via an interfacial drag term. Biomass growth is assumed to be rate-limited by one nutrient, for example the dissolved oxygen in water acting as the electron acceptor. Biomass is lumped in with the EPS in the model, combining cellular growth and EPS production.

Mass conservation gives, noting that $1 - \phi$ is the volume fraction of water,

$$\phi_t + \nabla \cdot (\phi \mathbf{v}) = g(\phi, c), \quad -\phi_t + \nabla \cdot [(1 - \phi)\mathbf{w}] = 0, \quad (2)$$

where \mathbf{v} and \mathbf{w} denote polymer and solvent phase-averaged velocities, and g is a growth term.

Polymer-Solvent Model II

The concentration c is that of the assumed rate-limiting nutrient, and satisfies

$$[(1 - \phi)c]_t + \nabla \cdot [(1 - \phi)c\mathbf{w}] = \nabla \cdot [(1 - \phi)D\nabla c] - r(\phi, c), \quad (3)$$

with D a diffusion coefficient, and r nutrient uptake by biomass. Assuming Monod kinetics, $g = \frac{G\phi c}{K + c}$, $r = \frac{R\phi c}{K + c}$, where G , R and K are constants. Momentum equations for slow two-phase flow are

$$\begin{aligned} \mathbf{0} &= \mu \nabla \cdot [\phi(\nabla \mathbf{v} + \nabla \mathbf{v}^T)] - f\phi(1 - \phi)(\mathbf{v} - \mathbf{w}) - \nabla \Psi - \phi \nabla p, \\ \mathbf{0} &= \mu_w \nabla \cdot [(1 - \phi)(\nabla \mathbf{w} + \nabla \mathbf{w}^T)] + f\phi(1 - \phi)(\mathbf{v} - \mathbf{w}) - (1 - \phi)\nabla p. \end{aligned} \quad (4)$$

Here, p is fluid pressure, Ψ is the osmotic pressure given by (1), μ is the long-time viscosity of the polymer matrix, μ_w is the viscosity of water, and the term in f is an interfacial drag term. The solvent viscous term is negligible, so that equation (4)₂ is just Darcy's law, and f is given by $f = \frac{\mu_w(1 - \phi)}{k\phi}$, essentially defining the permeability k . We assume that f is constant.

Eqns (4) are the same as those given by Cogan and Keener (2004). Cogan and Keener now argue that since ϕ is small, the interfacial drag term can be ignored. This leads them to an approximate model which is quite different to the one we derive here, where we find that in fact the interfacial friction term is dominant.

Nondimensionalisation

If $\chi > \frac{1}{2}$, then a stable gel fraction $\phi_{eq} \approx 6(\chi - \frac{1}{2})$ can exist where $\Psi = 0$. This suggests that we balance $\Psi \sim E_L \phi^3$, expecting that this will be appropriate if the poorly constrained Flory parameter χ is close to (and greater than) one half. So we choose the scales

$$\begin{aligned} c \sim c_0, \quad \phi \sim \phi_0 = \left(\frac{fGDc_0}{RE_L}\right)^{1/3}, \quad \Psi \sim p \sim p_0 = \frac{fGDc_0}{R} \\ \mathbf{x} \sim d = \left(\frac{Dc_0}{R\phi_0}\right)^{1/2}, \quad \mathbf{v}, \mathbf{w} \sim v_0 = Gd, \quad t \sim t_0 = \frac{1}{G}. \end{aligned} \quad (5)$$

The lengthscale is based on a balancing the uptake and diffusion terms in the nutrient equation, representing the depth of the active layer of biofilm. The time and velocity scales are chosen to balance the growth rate. The pressure scale reflects a balance between the interfacial drag and pressure terms in (4)₂. The scale ϕ_0 is chosen by balancing the osmotic and interfacial drag terms in (4)₁.

The non-dimensional forms of the equations (1), (2), (3) and (4) are

$$\begin{aligned} \phi_t + \nabla \cdot (\phi \mathbf{v}) &= \frac{\phi c}{\kappa + c}, \\ -\varepsilon \phi_t + \nabla \cdot [(1 - \varepsilon)\mathbf{w}] &= 0, \\ \alpha(1 - \varepsilon)\phi[c_t + \mathbf{w} \cdot \nabla c] &= \nabla \cdot [(1 - \varepsilon)\nabla c] - \frac{\phi c}{\kappa + c}, \\ \mathbf{0} &= \beta \nabla \cdot [\phi(\nabla \mathbf{v} + \nabla \mathbf{v}^T)] - \phi(1 - \varepsilon)\phi(\mathbf{v} - \mathbf{w}) - \nabla \Psi - \varepsilon \phi \nabla p, \\ \mathbf{0} &= \gamma \nabla \cdot [(1 - \varepsilon)\phi(\nabla \mathbf{w} + \nabla \mathbf{w}^T)] + \phi(1 - \varepsilon)\phi(\mathbf{v} - \mathbf{w}) - (1 - \varepsilon)\nabla p, \\ \Psi &= -\lambda \phi^2 + \frac{1}{6}\phi^3 + O(\varepsilon). \end{aligned} \quad (6)$$

The parameters are defined by, and take the approximate values:

$$\begin{aligned} \varepsilon = \phi_0 \approx 0.37 \times 10^{-2}, \quad \kappa = \frac{K}{c_0} \approx 0.35, \quad \alpha = \frac{Gc_0}{R\phi_0} \approx 1.37 \times 10^{-4}, \\ \beta = \frac{\mu\phi_0 v_0}{d p_0} \approx 1.1 \times 10^{-4}, \quad \gamma = \frac{\mu_w v_0}{d p_0} \approx 0.76 \times 10^{-7}, \quad \lambda = \frac{\chi - \frac{1}{2}}{\phi_0} \geq O(1), \end{aligned}$$

Reduced 1D Model

In one dimension the reduced model obtained by setting small parameters to zero can be written

$$\phi_t + (\phi v)_z = \frac{\phi c}{\kappa + c}, \quad v_z + P_{zz} = 0, \quad c_{zz} = \frac{\phi c}{\kappa + c}, \quad (7)$$

where $P(\phi) = \int_{\delta\lambda}^{\phi} \frac{\Psi'(\phi) d\phi}{\phi}$, subject to

$$\phi = \delta\lambda, \quad c = 1, \quad s_t = v \text{ on } z = s; \quad \phi_z = c_z = v = 0 \text{ on } z = 0. \quad (8)$$

It follows that $v = -P_z$, and thus that ϕ satisfies the nonlinear diffusion equation

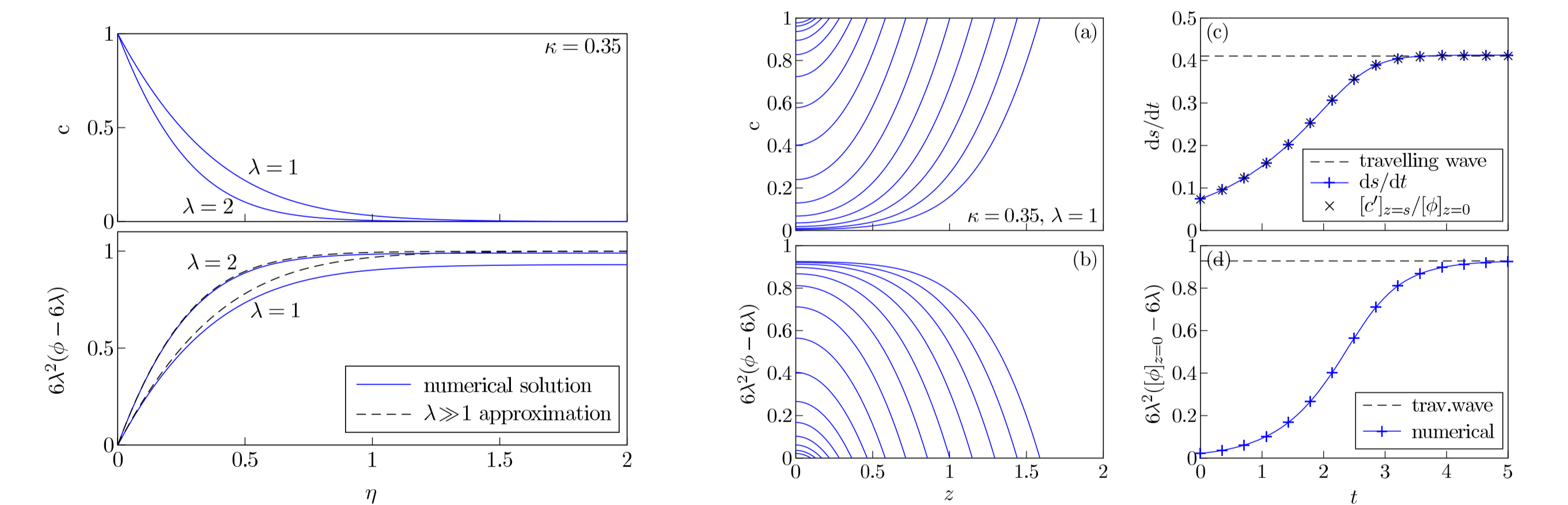
$$\phi_t = (\Lambda\phi)_z + \frac{\phi c}{\kappa + c}, \quad (9)$$

where we write $\Lambda(\phi) = \Psi'(\phi) = \frac{1}{2}\phi(\phi - 4\lambda)$ (since $\phi P' = \Psi'$). We therefore require $\phi > 4\lambda$ (no phase separation) for the current problem to be well posed.

The 1D model has travelling wave solutions, functions of $\eta = Ut - z$. The appropriate conditions in the far field are $c \rightarrow 0$, $\phi \rightarrow \phi_\infty$ as $\eta \rightarrow \infty$; both U and ϕ_∞ must be determined as part of the solution. With primes denoting differentiation with respect to η , the equations become

$$U\phi' = (\Lambda\phi)' + \frac{\phi c}{\kappa + c}, \quad c'' = \frac{\phi c}{\kappa + c}. \quad (10)$$

A first integral of these equations can be found. Numerical solutions of the resulting coupled ordinary differential equations are plotted below, alongside numerical solutions of the transient 1D equations (7). The fully time-dependent solutions approach the travelling waves as time increases. Further details may be found in [3].



Travelling-wave numerical solutions.

Fully transient numerical solutions.

Conclusions

We model biofilm growing on an impermeable substratum based on the material properties of a polymer solution. Estimates of typical scales lead to a different mathematical description to earlier work. Solutions of the model converge to a travelling wave solution strongly dependent on

the dimensionless parameter $\lambda = \frac{\phi_{eq}}{6} \left(\frac{RE_L}{fGDc_0}\right)^{1/3}$. The travelling wave solution provides the

expression $U = \frac{GD}{R} \frac{c_z|_{z=s}}{\phi|_{z=0}}$ for the growth velocity of the biofilm surface in dimensional terms.

This is also a good approximation in the time-dependent case of relatively thin biofilms for which nutrient penetrates the full biofilm depth, and thus provides reasonable scope for comparison with experiment.

REFERENCES:

- [1] Cogan N. G. and J. P. Keener (2004). The role of the biofilm matrix in structural development. *Math. Med. Biol.* **21**, 147–166.
- [2] Cogan N. G. and J. P. Keener (2005). Channel formation in gels. *SIAM J. Appl. Math.* **65**, 1,839–1,854.
- [3] H.F. Winstanley, M. Chapwanya, M.J. McGuinness, and A.C. Fowler (2011). A polymer-solvent model of biofilm growth. *Proc. Roy. Soc. Lond. A*, **467**, 2129 1449–1467. doi: 10.1098/rspa.2010.0327