A new mathematical model for chemotactic bacterial colony growth

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Abstract A new continuum model for the growth of a single species biofilm is proposed. The geometry of the biofilm is described by the interface between the biomass and the surrounding liquid. Nutrient transport is given by the solution of a semi-linear Poisson equation. In this model we study the morphology of a chemotactic bacterial colony, which grows in the direction of increasing nutrient concentration. Numerical simulations using the level set method and finite difference schemes are presented. The results show rich heterogeneous morphology.

Keywords Biofilm; continuum model; diffusion; level set method; mass conservation; simulations

Introduction

Biofilm morphology has been a very active area of research ever since the rich geometrical structures of biofilms were first observed around 1990 using confocal scanning laser microscopy. The interest in biofilm morphology has increased the demand for mathematical models to aid the understanding of experimental results and (ideally) to accurately predict the behaviour of biofilms.

Among the earliest models for biofilm growth is the one proposed by Wanner and Gujer (1986). Their model is essentially one-dimensional, so even though it can predict the amount of biomass correctly, it cannot account for the spatial irregularities in real biofilms. Since then several biofilm models, all of which are capable of producing spatially heterogeneous solutions, have been put forth. Eberl et al. (2001) have proposed a continuum model, where both the nutrient and the biomass are described by scalar fields which satisfy a system of partial differential equations of the reaction-diffusion type. Picioreanu et al. (1999) use a model where the nutrient concentration satisfies a reaction-diffusion equation and the growth of the biofilm is modelled by cellular automata (see Kreft et al., 1998). It has recently been proposed by Dockery and Klapper (2001) that the biofilm should be modelled as a viscous fluid. The transport of the nutrients is still given by a reaction-diffusion equation.

The complex morphology of biofilms raises the following question: which rule governs the development of such structures? Some candidates are: (a) the interaction with the surrounding liquid, (b) cell-to-cell signalling, and (c) the dynamics of transport and consumption of nutrients. It is most likely due to a combination of these mechanisms. To devise a model for biofilm growth which includes all of these factors is probably very difficult. To fully understand biofilms one should also take care to estimate the material properties of the biomass and incorporate them into the model, see Klapper et al. (2001). The model proposed in this paper focuses entirely on mechanism (c).

The model

The following model intends to describe an idealized single species bacterial colony whose preferred growth, induced by chemotaxis, is in the direction of greater nutrient concentrations. This is the same assumption used in Ben Jacobs et al. (1994, page 41). The model can
be formulated in any number of spatial dimensions, but our simulations are carried out in
the two-dimensional case. For accuracy, we therefore only present the two-dimensional
version of our model.

We consider a system (liquid and biofilm) which is contained in an open rectangle:

$$\Omega = \{ \mathbf{x} = (x_1, x_2) : 0 < x_1 < W, 0 < x_2 < H \}$$

For later use, we divide the boundary of $\Omega$ into two parts $\partial \Omega = \Gamma_1 \cup \Gamma_2$, where $\Gamma_1 = \{ \mathbf{x} : x_2 = 0 \} \cup \{ \mathbf{x} : x_1 = 0 \} \cup \{ \mathbf{x} : x_1 = W \}$ consists of the bottom and the sides, and $\Gamma_2 = \{ \mathbf{x} : x_2 = H \}$ is the top of $\Omega$. The biofilm is attached to the bottom of the rectangle, i.e. the set $\{ \mathbf{x} : x_2 = 0 \}$ is the sub-
stratum. We may imagine the sides of $\Omega$ to be in contact with similar systems, or to consist of
walls that are impermeable to the nutrients, so that there will be no net transport of nutri-
ents through $\Gamma_1$. We also assume that $\Gamma_2$ is the interface to a large reservoir of nutrients,
where the concentration of the nutrient is held at a fixed positive value.

Since the biofilm consists of a single species of bacteria, we assume that it may be ade-
quately described by its density $\rho = \rho(\mathbf{x}, t), \mathbf{x} \in \Omega, t \geq 0$. We furthermore assume that the
density can only assume two distinct values: zero and $\rho_0 \geq 0$. Thus, if $B_t$ denotes the subset
of $\Omega$ which is occupied by the biofilm at time $t \geq 0$, then

$$\rho(t,x) = \begin{cases} 
\rho_0 & \text{for } \mathbf{x} \in B_t, \\
0 & \text{for } \mathbf{x} \in \Omega \setminus B_t. \end{cases}$$

(1)

This assumption is essential to our model, and it implies that the biofilm growth is com-
pletely described by tracking the boundary $\partial B_t$ of the biofilm at any time $t \geq 0$.

The transport of nutrients

The bacteria in our model are assumed to consume a single kind of nutrient, whose concen-
tration (measured in mass per unit volume) is given by a non-negative scalar function $c =
c(\mathbf{x}, t), \mathbf{x} \in \Omega, t \geq 0$. The nutrients are transported through the system by diffusion, and are
consumed at a rate $f = f(c, \rho)$ within the biofilm. Thus $c$ must satisfy a reaction-diffusion
equation of the form:

$$\nabla \cdot (D \nabla c) - \frac{\partial c}{\partial t} = f(c, \rho),$$

(2)

where $D = D(c, \rho)$ is the diffusivity. In our calculations it is assumed that $D = D_0$ is constant
throughout $\Omega$. The nutrient uptake is assumed to follow the so called Monod kinetics:

$$f(c, \rho) = \frac{k_1 c \rho}{k_2 + c}$$

where $k_1, k_2 > 0$ are constants. Since the biofilm growth is much slower than the diffusion
process, we may, at any time $t \geq 0$, use the steady state solution of (2) to model the distribu-
tion of the nutrient in the system. Thus, for a given biofilm density $\rho$, we take $c$ to be the
solution of the semi-linear Poisson equation:

$$\begin{cases}
D \Delta c = f(c, \rho) & \text{in } \Omega, \\
\frac{\partial c}{\partial n} = 0 & \text{on } \Gamma_1, \\
c = c_0 & \text{on } \Gamma_2.
\end{cases}$$

(3)

The boundary condition $\frac{\partial c}{\partial n} = 0$ means that there is no (net) flux of nutrients through
the bottom and the sides of the domain. The condition $c = c_0$ corresponds to the assumption that
our system is in contact with a large reservoir of nutrients at $\Gamma_2$.  

\begin{align*}
\text{E. Alpkvist et al.} & \\
\text{188} & \\
\end{align*}
Biofilm growth

The growth of the biofilm is assumed to induce a flow of biomass in the system. This volumetric flow is modelled by a time-varying vector field $\mathbf{u} = \mathbf{u}(x, t)$ defined in $\Omega$. The consumed nutrients are transformed into biomass through a function describing the substrate uptake rate $q$. We assume conservation of mass in our model, expressed by the equation of continuity:

$$\frac{\partial \rho}{\partial t} + \nabla \cdot (\rho \mathbf{u}) = q(f(c, \rho)).$$

We also assume the flow to be in the direction of the gradient of the nutrients:

$$\mathbf{u} = g \nabla c$$

where $g = g(x, t)$ is a scalar function. We express this assumption verbally by saying that the biofilm grows in the direction of increasing nutrient concentration. The rate of uptake is assumed to satisfy the linear function

$$q(f) = \gamma f,$$

where $0 < \gamma < 1$. An important point to our model is that it is possible to choose $g$ in (5) such that the equation of continuity (4) holds. In fact, if we recall the assumption in (1), that $\rho = \rho_0$ in $B$, then we conclude that $\partial \rho/\partial t = 0$ inside $B$. Hence it follows from (3) and (4) that

$$\rho_0 \nabla \cdot (g \nabla c) = \gamma f(c, \rho_0) = \gamma D_0 \Delta c$$

in $B$. This equation is clearly satisfied if we take $g = \gamma D_0 / \rho_0$. This argument shows that we have conservation of mass if we choose the flow field to be

$$\mathbf{u} = \frac{\gamma D_0}{\rho_0} \nabla c.$$

Methods

To compute the growth of the biofilm $B_t$ in a small time increment $\Delta t$, we first compute $c$ from (3), using the density $\rho$ given in (1) as input. Then we propagate the boundary $\delta B_t$ along the vector $\mathbf{u} \Delta t$, with $\mathbf{u}$ given by (6), to obtain the points of $\delta B_{t+\Delta t}$. How this is achieved in practice is the content of this section.

The level set method

To get a handy description of $B_t$, we use the so called level set method introduced by Osher and Sethian (1988). We give a brief outline of the theory which is adapted to the problem at hand. For a more complete introduction to the level set method the reader should consult one of the recent monographs on the subject, such as Sethian (1996), or Osher and Fedkiw (2003).

By a level set function for $B_t$ we mean a continuous function $\phi = \phi(x, t)$ such that

$$B_t = \{ x \in \Omega; \phi(x, t) < 0 \}.$$

In particular we have $\phi(x, t) = 0$ for $x \in \delta B_t$, and $t > 0$. The biofilm growth is now encoded in the time evolution $t \rightarrow \phi(\cdot, t)$ of the level set function. Suppose we have a fictitious point $\mathbf{x} = \mathbf{x}(t)$ which follows the boundary $\delta B_t$. Then $\phi(\mathbf{x}, (t), t) = 0$ for all $t$, so if we differentiate with respect to time we find that
In our model a point $x \in \delta B_t$ moves with the velocity $u(x, t) = \gamma \left( \frac{D_0}{\rho_0} \right) \nabla c (x, t)$. If we substitute the velocity field $u$ for the particle velocity $x'(t)$ in the equation above, then we get the following partial differential equation, which is the level set equation for biofilm growth:

$$\frac{\partial \phi}{\partial t}(x, t) + \gamma \frac{D_0}{\rho_0} \nabla \phi(x, t) \cdot \nabla c(x, t) = 0$$

(7)

The initial condition for (7) is $\phi(\cdot, 0) = \phi_0(\cdot)$, where $\phi_0$ is determined by the initial biofilm $B_0$.

**Numerical methods**

The rectangular computational domain $\Omega$ is discretized with a Cartesian grid. The indices for the grid points are $i = 1, \ldots, N$ and $j = 1, \ldots, N$ for the $x_1$ and $x_2$ spatial dimension with a grid point distance of $h$. At time $t = 0$ we randomize a distribution of biomass at the grid points on the substratum. For each time $t^n$ with $t^{n+1} = t^n + k$ we find the nutrient concentration by a second-order finite difference scheme combined with a Gauss-Newton method for the nonlinearity in (3). We construct the initial condition for (7) using the signed Euclidian distance from every point to the interface of a randomized distribution of biomass $B_0$ on the substratum. Now we solve (7) by an explicit Euler scheme

$$\frac{\phi_{i,j}^{n+1} - \phi_{i,j}^n}{k} = \gamma \frac{D_0}{\rho_0} \nabla c^n \cdot \nabla \phi^n.$$

The discretizations for the spatial derivatives of $\phi$ for a point $x_{i,j}$ are performed using a first-order forward and backward difference technique:

$$
\begin{cases}
\frac{\partial \phi}{\partial x_1} \frac{\phi_{i+1,j}^n - \phi_{i,j}^n}{h} & \text{if } \left( \frac{\partial c}{\partial x_1} \right)_{i,j}^n < 0 \\
\frac{\partial \phi}{\partial x_1} \frac{\phi_{i,j}^n - \phi_{i-1,j}^n}{h} & \text{if } \left( \frac{\partial c}{\partial x_1} \right)_{i,j}^n < 0
\end{cases}
$$

for the spatial dimension $x_2$ the discretization is chosen in a similar manner. The ratio between $k$ and $h$ should be limited, this limit is known as the CFL number or the Courant number and is determined by the maximal flow of information. Choosing $k$ to satisfy this condition is a necessary condition for stability of our numerical scheme. We need to ensure $|\nabla \phi| \approx 1$ to make $\phi$ smooth enough to approximate its spatial derivatives within some degree of accuracy. For this reason it is always advisable to reinitialize the level set function between the time steps. For further reading on this reinitialization procedure see Sussman et al. (1994).

**Results and discussion**

For all simulations a stopping criterion is implemented. This criterion is fulfilled when the distance between the top boundary $\Gamma_2$ and some point in $B_t$ is less than a fifth of the height of $\Omega$. Without stopping criteria our model would eventually grow outside of its computational box.

We see from Figure 1 that the model generates typical biofilm structures such as channels and mushroom-like fingerings. Although not seen in this simulation the model sometimes tends to develop holes. Until this model is compared to experimental data one possible confirmation is comparison with existing models. Picioreanu et al. (1999)
grouped a number of parameters to a nondimensional quantity \( G = \frac{W^2 f(c_0)}{D_0 c_0} \). With an increasing \( G \)-number several other models show the morphological structure of the biofilm becoming more heterogeneous. The influence of high and low \( G \)-number for our model was investigated. Presented here are results varying the uptake rate \( k_1 \). With an increasing \( k_1 \) the consumption of nutrient will increase and thus make nutrient availability in \( B_t \) drop. Some simulations with varying \( k_1 \) for the same initial state were performed on a \([100 \times 100]\) grid with other parameters set equal to 1.

For our simulations an increasing \( G \)-number shows the same impact as other models on the simulated biofilm morphology, as seen in Figure 2.

**Conclusions**

We have presented a new continuum model for a single species chemotactic bacterial colony growth. Simulations show that the proposed model admits spatially heterogeneous solutions with fingerings. Given the rule for biomass growth in our model (growth is in the direction of greater nutrient concentrations) such structures seem to be favourable for nutrient availability. Moreover, the predicted morphology becomes more heterogeneous for lower nutrient availability. This is in agreement with previous models.

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**Figure 1** Simulation of an evolving biofilm. Level sets for biomass and iso-concentration contours of the nutrient are shown. Simulated at \([170 \times 170]\) grid points. All parameter values set to 1. From the top left to the bottom right iteration number [25, 100, 200, 286]

**Figure 2** Level sets for biomass and iso-concentration contours of the nutrient are shown. Simulations of the same initial state with varying parameter \( k_1 \) with other parameters kept equal to 1. From left to right \( k_1 = 0.1, 1, 10 \)
References