Not Waving but Drowning: Ordering processes in Bacteria

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Introduction

Ordering mechanisms involving what might be thought of as soft particles occur in a wide variety of biological systems, ranging from bacteria to the microtubules which control the mechanical properties of complex cells. A simple example was investigated by Volfson *et al*[1], who allowed *Escherichia coli* bacteria to grow in a trough which was long and wide but only about one cell diameter high. Figure 1 shows the spatial evolution of the pattern of bacteria as they bred.

[1] Dmitri Volfson, Scott Cookson, Jeff Hasty, and Lev S. Tsimring. Biomechanical ordering of dense cell populations. *Proceedings of the National Academy of Sciences*, 105(40):15346–15351, 2008

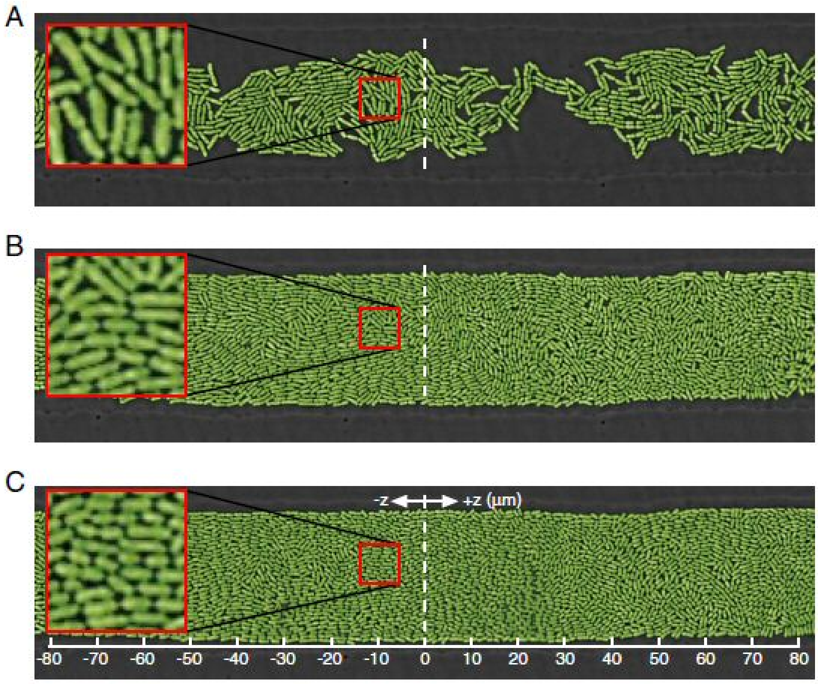

Figure 1: Snapshots of *E. coli* monolayers growing in a cavity, shown after 60 (A), 90 (B) and 138 (C) minutes. The scale bar is 10 μm long. From Volfson *et al* 2008.

Continuum Model of Ordering

The evolution of the arrangement of bacteria may be understood using similar methods to those used by Doi and Edwards[2] to describe the ordering of nematic liquid crystals. The basic idea is that each bacterium is described by a vector which gives its orientation, and this is converted after averaging over a volume containing many bacteria to an "order tensor" Q. If the population of bacteria, ν, the velocity with which they move, $\mathbf{v}$, and Q are expressed as functions of position and time, then the equations which govern

[2] M Doi and S F Edwards. *The Theory of Polymer Dynamics*. Oxford University Press, 2003

their behaviour are mass balance (including breeding at a rate α

$$\frac{\partial \nu}{\partial t} + \nabla(\nu \mathbf{v}) = \alpha \nu, \tag{1}$$

momentum balance, which includes friction with the walls of the trough,

$$\frac{D\nu\mathbf{v}}{Dt} = -\nabla.\sigma - \mu\nu\mathbf{v}, \tag{2}$$

where D/Dt is the total derivative $\partial/\partial t + \mathbf{v}.\nabla$, σ is the stress tensor and μ is the friction coefficient, and the order parameter equation

$$\frac{DQ_{\alpha\beta}}{Dt} = \kappa^a_{\alpha\gamma}Q_{\gamma\beta} - Q_{\gamma\beta}\kappa^a_{\alpha\gamma} + B\kappa^s_{\alpha\gamma} + \Gamma H_{\alpha\beta}. \tag{3}$$

In Equation 3 the κ terms are the symmetric-traceless and antisymmetric parts of the strain rate tensor, the term in B represents the way in which ordering is enhanced by symmetric flow, and the term in Γ is an entropy term.

The messy equations 1 to 3 can be simplified by assuming that flow occurs only in one direction (which we take to be x), that the only relevant order parameter is $q = Q_{xx}$, and that the stress tensor may be replaced by a pressure field p which depends on the density of bacteria,

$$p = P\exp[\xi(\nu - \nu_c)]. \tag{4}$$

With a bit more simplification we then have equations in just x and t:

$$\frac{\partial \nu}{\partial t} + \frac{\partial(\nu u)}{\partial x} = \alpha\nu, \tag{5}$$

$$\frac{\partial \nu u}{\partial t} + u\frac{\partial \nu u}{\partial x} = -\frac{\partial p}{\partial x} - \mu\nu u, \tag{6}$$

$$\frac{\partial q}{\partial t} + u\frac{\partial q}{\partial x} = B\left(1 - q^2\right)\frac{\partial u}{\partial x}. \tag{7}$$

Investigate solutions of Equations 4 to 7. Initially, use `NDSolve`, on a range of $-0.5 \le x \le 0.5$ and $0 \le t \le 100$. Investigate the effects of varying the parameters, but you may find a useful initial choice to be $\nu_c = 1$, $P = 1$, $\xi = 10$. (representing the short-range nature of the pressure exreted by one bacterium on another), $\alpha = 0.1$ and $\mu = 0.1$. You will also need to insert starting conditions: start with a 'spike' of population, $\nu(x,0) = 0.1\exp(-x^2)$, with uniform order $q(x,0) = 0.01$ and velocity $v(x,0) == 0.01$. Set boundary conditions at $x = -0.5$ for all times to match the initial conditions. You should find that the population in the middle of the trough grows to a limiting value, and that the ordering also saturates.

In reality, if the pressure gets large (as it will if the bacteria are tightly packed) bacterial growth will be inhibited. Simulate this by replacing α by $\alpha_0[1 - (p/p_c)^2]$, examine what happens to the results, and explain.

Microtubules

About 70% of the inside of a living cell is occupied by the cytosol, a complex, self-organising viscoeleastic fluid. Entangled networks of microtubules and actin filaments form the cytoskeletal scaffold of the cell, and these are constructed and repaired by molecular motors. With some simplifying assumptions[3], the dynamics of the microtubules can be reduced to a set of continuum equations, which show that with a large enough initial concentration of molecular motors and microtubules a spontaneous ordering will take place. Close to the ordering transition, where the concentration of tubules is $\nu - \nu_c$, the equations which describe the concentration and local orientation (τ) of tubules are

[3] I S Aranson and L S Tsimring. Theory of self-assembly of microtubules and motors. *Physical Review E*, 74(3):031915, 2006

$$\frac{\partial \nu}{\partial t} = \nabla^2\left[\frac{\nu}{32} - \frac{B^2\nu^2}{16}\right] - \frac{\pi B^2 H}{16}\left[3\nabla.(\tau\nabla^2\nu - \nu\nabla^2\tau) + 2\sum_{i=1,2}\sum_{j=1,2}\frac{\partial}{\partial x_i}\left(\frac{\partial \nu}{\partial x_j}\frac{\partial \tau_i}{\partial x_j} - \frac{\partial \nu}{\partial x_i}\frac{\partial \tau_j}{\partial x_j}\right)\right] - \frac{7\nu_0 B^4}{256}\nabla^4\nu \tag{8}$$

$$\frac{\partial \tau}{\partial t} = \frac{5}{192}\nabla^2\tau + \frac{1}{96}\nabla(\nabla.\tau) + b_0(\nu - \nu_c)\tau - A_0|\tau|^2\tau + H\left[\frac{\nabla\nu^2}{16\pi} - \left(\pi - \frac{8}{3}\right)\tau(\nabla.\tau) - \frac{8}{3}(\tau.\nabla)\tau\right] + \frac{B^2\nu_0}{4\pi}\nabla^2\tau, \tag{9}$$

where the distance has been scaled in units of the microtubule length ℓ and we work in two dimensions, $\tau = (\tau_1, \tau_j)$ and $(x, y) = (x_1, x_2)$. Suitable values are $b_0 = 0.273$, $A_0 = 1$, $H = 0.125$. For small values of B^2H two characteristic sorts of orientation pattern are found, vortices with spiral-like structure and asters, with tubules pointing radially away from points (see Figure 2).

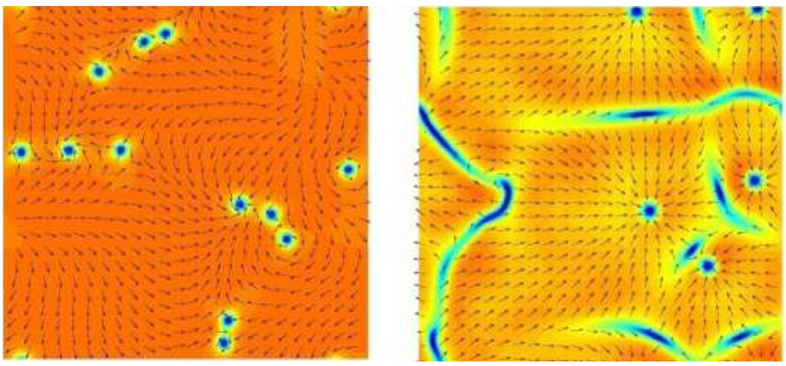

Figure 2: Orientation τ for vortices ($H = 0.006$, left) and asters ($H = 0.125$, right) obtained from numerical solution with $B^2 = 0.05$, $\nu_0 = 4$, on a domain of integration 80×80 length units, integrated for 1000 time units. From Aranson and Tsimring (2006).

Try to set up and solve these equations: you may find that it is possible to do this by specifying the spatial grid to be used by `NDSolve`. Alternatively, set up a centred finite difference scheme on a regular spatial mesh with periodic boundary conditions and use an explicit Euler scheme for the time integration – a short timestep will be necessary for stability.

References

[1] I S Aranson and L S Tsimring. Theory of self-assembly of microtubules and motors. *Physical Review E*, 74(3):031915, 2006.

[2] M Doi and S F Edwards. *The Theory of Polymer Dynamics*. Oxford University Press, 2003.

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