Nonlinear diffusion as a model mechanism for pattern formation in yeast biofilms

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Yeast

- Single-cell fungal micro-organisms ($\sim 10^{-6}$ m).
- Important model organism in cell biology research.
- Used in food and drink production.
- Responsible for pathogenic infections in humans.
- Biofilms often grow on medical devices.

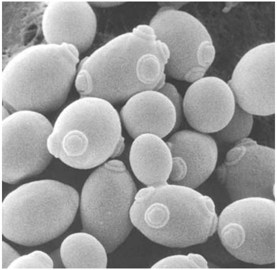

Figure: Yeast cells.

Pattern formation

- Biofilms grown *in vitro* by populating agar with yeast cells and glucose.
- Initially circular colonies develop petal-like structures.
- Two factors hypothesised to affect growth:
  - Nutrient consumption and diffusion.
  - Biofilm mechanics (e.g. extracellular fluid flow, cell-cell adhesion).

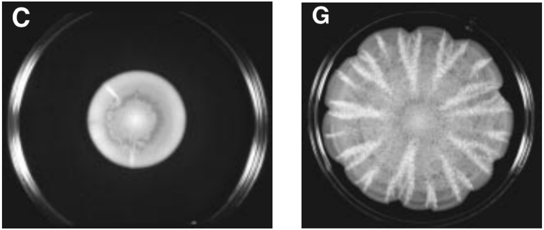

Figure: A floral yeast biofilm experiment[1]. Left: 5 days. Right: 13 days.

[1] T. B. Reynolds and G. R. Fink. "Bakers' yeast, a model for fungal biofilm formation". *Science* 291.5505 (2001), pp. 878–881.

Dimensionless Model

- Coupled reaction-diffusion system with nonlinear diffusion term[2] for cell movement.

$$\frac{\partial n}{\partial t} = D\nabla \cdot (n^k \nabla n) + ng,$$

$$\frac{\partial g}{\partial t} = \nabla^2 g - cng.$$

- $n(\boldsymbol{x}, t)$: yeast cell density.
- $g(\boldsymbol{x}, t)$: glucose concentration.
- D : ratio of cell to nutrient diffusion coefficients.
- c : quantity of glucose consumed per new cell.
- k : degree of diffusion nonlinearity.

[2] M. J. Simpson, R. E. Baker, and S. W. McCue. "Models of collective cell spreading with variable cell aspect ratio: a motivation for degenerate diffusion models". *Physical Review E* 83.2 (2011), p. 0121901.

Travelling wave analysis

- Transform to the travelling wave co-ordinate $z = x - vt$.

$$\frac{dg}{dz} = w,$$
$$n^k \frac{dn}{dz} = \frac{1}{cD}\left(v - w - vg - cvn\right),$$
$$\frac{dw}{dz} = cng - vw.$$

- For $n > 0, z < 0$: Three ODEs.
  - Equilibrium behind the wave front at $z \to -\infty$: $(g, n, w) = (0, 1/c, 0)$.
- For $n = 0, z \geq 0$: Two ODEs, algebraic equation.
  - Equilibrium ahead of wave front at $z \to \infty$: $(g, n, w) = (1, 0, 0)$.
  - Analytic solution.
- We construct solutions connecting the equilibria that are continuous at the regular singular point $z = 0$.

Travelling wave solution

- Shooting method solves a two-point BVP for $z < 0$, and determines the unique wave speed, v.

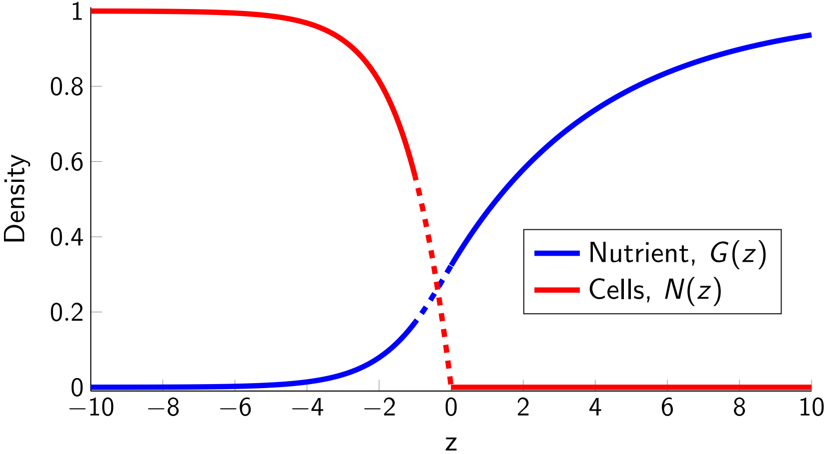

Figure: Travelling wave solution for $D = 0.3$, $c = 1$, $k = 1$, with $v = 0.2367$.

Wave speed dependence

- Travelling wave solutions reveal the effect of model variables on speed of biofilm growth.

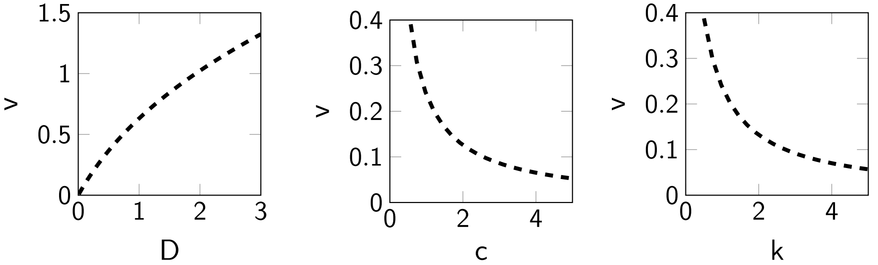

Figure: Effect of model variables on the travelling wave speed. When held constant, we use $D = 0.3$, $c = 1$, $k = 1$.

2D pattern formation

- So far we have neglected that the biofilm changes shape as it grows.

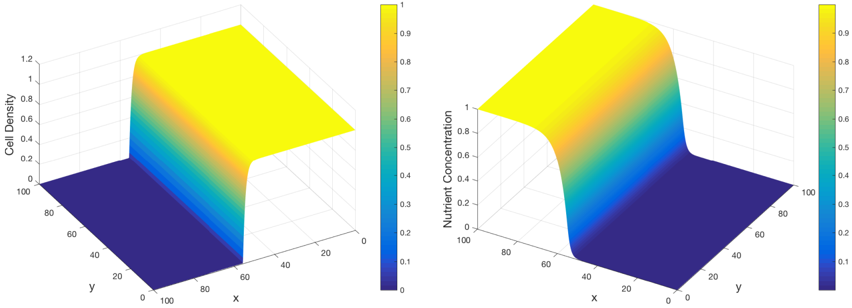

Figure: 2D planar travelling waves.

- We investigate non-planar perturbations to the planar waves.

Linear stability analysis

- Introduce co-ordinate tracking perturbed wave position,

$$\xi = z + \epsilon e^{iqy+\omega t}.$$

- Expand variables, $\epsilon \ll 1$,

$$n(\xi, y, t) = N(\xi) + \epsilon \hat{n}(\xi) e^{iqy+\omega t} + \mathcal{O}(\epsilon^2),$$
$$g(\xi, y, t) = G(\xi) + \epsilon \hat{g}(\xi) e^{iqy+\omega t} + \mathcal{O}(\epsilon^2).$$

- At $\mathcal{O}(1)$, we recover the travelling wave ODEs for $N(\xi)$ and $G(\xi)$.
- At $\mathcal{O}(\epsilon)$, we obtain a system of second order ODEs of the form[3]

$$\mathcal{L}\begin{pmatrix} \hat{n} \\ \hat{g} \end{pmatrix} = \begin{pmatrix} \omega + DN^k q^2 & 0 \\ 0 & \omega + q^2 \end{pmatrix} \begin{pmatrix} N + \frac{dN}{d\xi} \\ G + \frac{dG}{d\xi} \end{pmatrix}.$$

[3] J. Müller and W. van Saarloos. "Morphological instability and dynamics of fronts in bacterial growth models with nonlinear diffusion". *Physical Review E* 65.6 (2002), p. 061111.

Linear stability solution

- Shooting method for $\xi < 0$ determines the unique growth rate, ω.

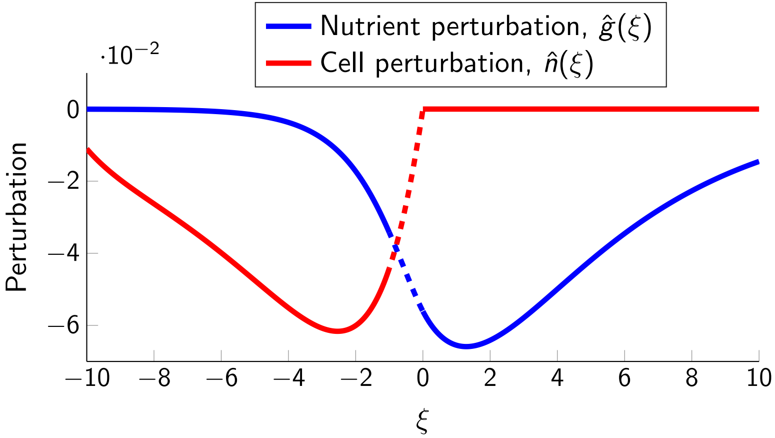

Figure: Perturbation functions for $D = 0.3$, $c = 1$, $k = 1$, $q = 0.377$, with $\omega = 0.0185$.

Linear stability: effect of D

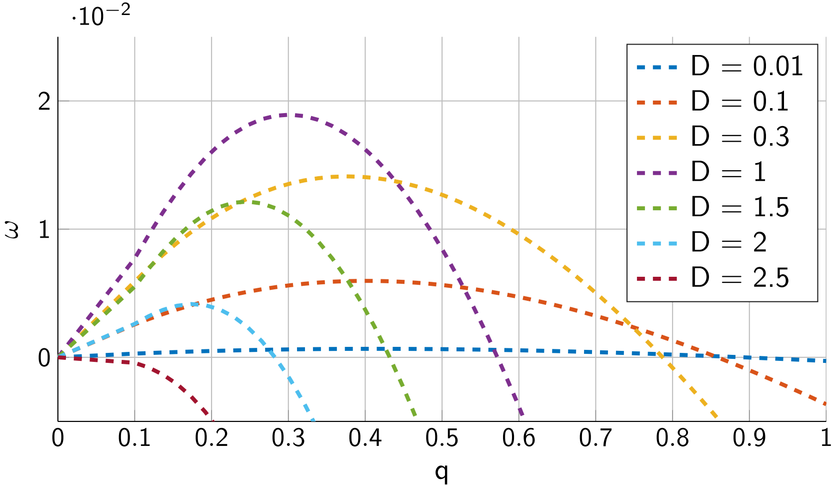

Figure: Dispersion curves for $c = 1$, $k = 2$, and varying D.

Linear stability: effect of c

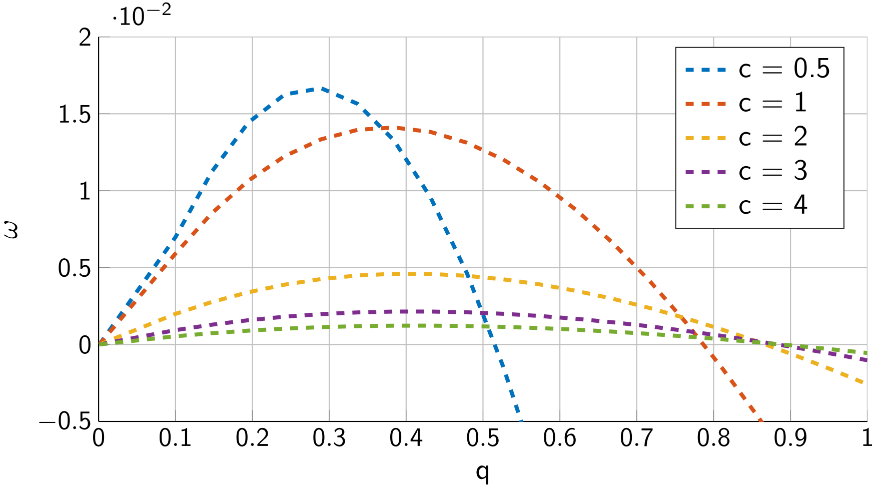

Figure: Dispersion curves for $D = 0.3$, $k = 2$, and varying c.

Linear stability: effect of k

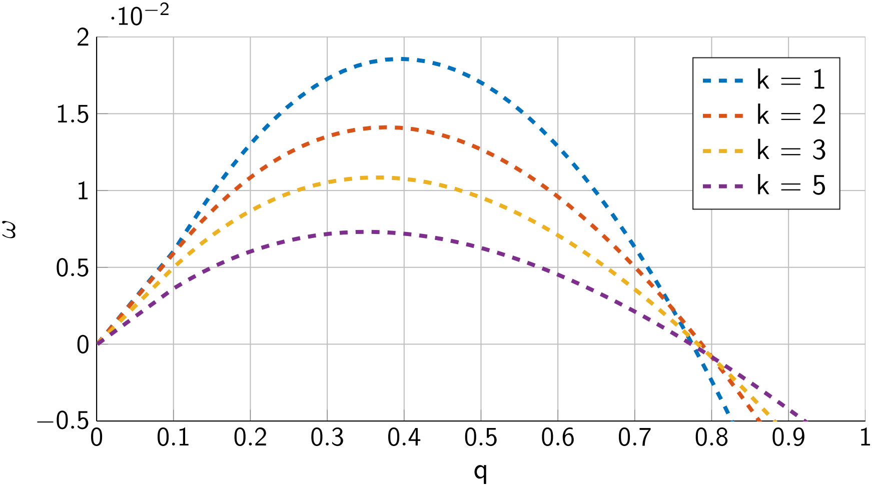

Figure: Dispersion curves for $D = 0.3$, $c = 1$, and varying k.

Numerical simulation

- Alternating-direction implicit (ADI) scheme.
- $n(\xi, y, 0) = N(\xi) + \epsilon\hat{n}(\xi)\cos(qy)$, $g(\xi, y, 0) = G(\xi) + \epsilon\hat{g}(\xi)\cos(qy)$.

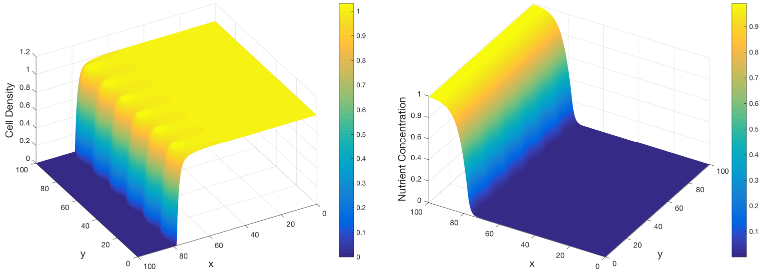

Figure: Numerical simulation for $D = 0.3$, $c = 1$, $k = 1$, $q = 0.377 = 3\pi/25$, $\epsilon = 0.01$, $\Delta x_i = 0.1$, $\Delta t = 0.01$, $t = 250$.

$$\omega = \frac{1}{t}\log\left[1 + \frac{n(\xi, y, t) - n(\xi, y, 0)}{\epsilon\hat{n}(\xi)\cos(qy)}\right].$$

- Theory: $\omega = 0.0185$. Numerical simulation: $\omega = 0.0182$.

Summary

- Yeast biofilms can form floral patterns influenced by nutrient consumption and diffusion.
- Travelling wave solutions give speed of biofilm expansion.
- Linear stability analysis indicates whether floral patterns will form.

Future work:

- Compare theory with yeast growth experiments.
  - Simulations in circular geometry.
  - Process experimental images.
- Include biofilm mechanics in the model.