B. Bacterial Chemotaxis

1. biological background

- Swimming speed of bacteria: 10–100 μm/s (3–30 cm/h)
- at such speeds, cells can grow on small nutrient gradient

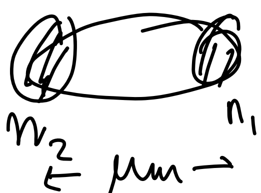
$$\frac{\Delta n}{\Delta x} = g. \qquad v \cdot g = \frac{\Delta n}{\Delta t} = \text{"nutrient gain"}$$

nutrient uptake: $\frac{dn}{dt} = r \cdot \rho / Y$

gradient needed to sustain growth at density ρ

$$g = \frac{r \cdot \rho}{v Y} \sim 10\,\text{nM}/\mu\text{m at } \rho = 0.2\,\text{OD}.$$

- to detect such a gradient for μm-size cell



Need to detect conc difference between front & back to 1nM accuracy

- require long accumulation time (~ 100 s for conc $= 1$ mM)
- problem: Brownian motion randomizes the orientation of cell ($\Delta\theta \simeq 30°$ in 1s)

$\Rightarrow$ bacterial strategy: measure conc difference in <u>time</u> rather than space

$\Rightarrow$ modulate change in direction according to conc diff = biased diffusion

* Molecular system for chemotaxis:
  - require memory (to compare difference in time)
  - adaptation dynamics: detects $\frac{\Delta n}{n}$

2. Population dynamics (no growth)

$$\frac{\partial \rho}{\partial t} = D \nabla^2 \rho - \vec{\nabla} \cdot (\vec{v} \rho)$$

- drift velocity: $v = \chi \frac{\vec{\nabla} a}{a}$

  a = attractant conc

  χ = chemotactic coeff (same dim as D)

  (χ / D = chemotactic bias; E. coli: $\chi/D \sim 5$)

- Consumption of attractant

$$\frac{\partial}{\partial t} a = D_a \nabla^2 a - k(a) \cdot \rho$$

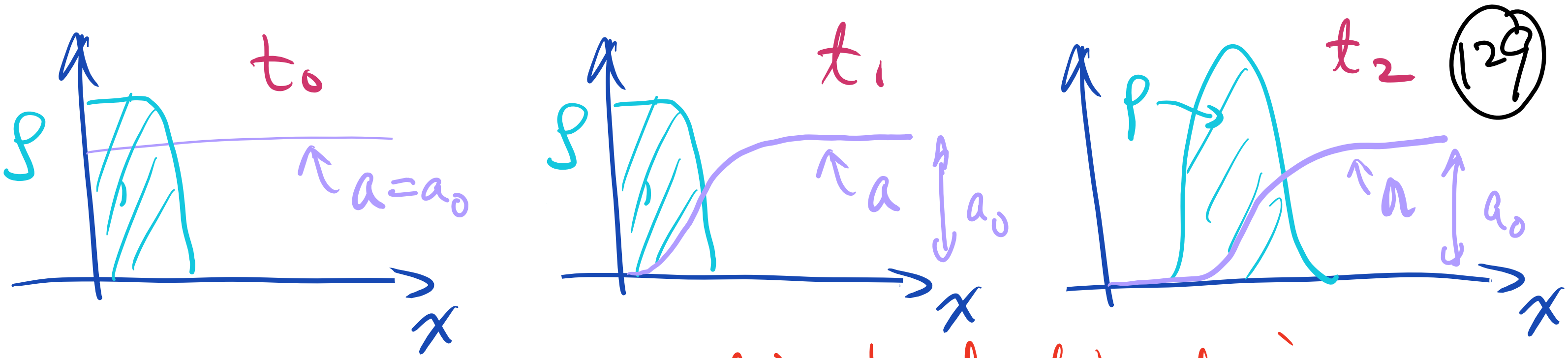
$k(a)$ ↑ attractant uptake rate

⇒ Keller-Segel eqn

$$\frac{\partial \rho}{\partial t} = D \frac{\partial^2}{\partial x^2} \rho - \chi \frac{\partial}{\partial x} \left(\frac{1}{a} \frac{\partial a}{\partial x} \cdot \rho \right)$$

$$\frac{\partial a}{\partial t} = - k \cdot \rho$$

- bacterial pop. generates attractant gradient through consumption
- population chase receding gradient



$\Rightarrow$ expect a traveling band of bacteria

$\rho(x,t) = \tilde\rho(x-ct)$, $a(x,t) = \tilde a(x-ct)$

$$-c\tilde\rho' = D\tilde\rho'' - \chi\cdot\left(\tilde\rho\,\tilde a'/\tilde a\right)' \qquad (1)$$

$$-c\tilde a' = k\tilde\rho \qquad (2)$$

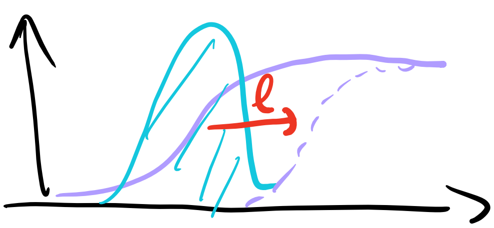
– propagation speed of KS eqn from conservation of ρ

integrate (2): $-c\int_{-\infty}^{\infty} dz\,\tilde a' = -c\left(\tilde a(+\infty) - \tilde a(-\infty)\right)$
$= -c\,a_0$

$k\int_{-\infty}^{\infty} dz\,\tilde\rho = k\cdot N$ ← total # of cells.
(conserved due to lack of growth)

$\rightarrow$ $\boxed{c = kN/a_0}$

Geometric interpretation:

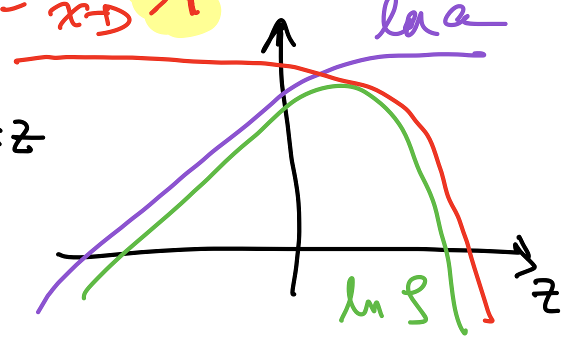


- in time τ, $a(x)$ has receded by a distance $\ell = c\cdot\tau$.
- the loss of $\Delta a \simeq a_0\cdot\ell$ is given by the total uptake $= k\cdot N\tau$

$\rightarrow$ $a_0\cdot\ell = kN\cdot\tau$, or $c = kN/a_0$

- Sol'n of the KS eqn

$\frac{v}{c} = \frac{\chi}{\chi - D} > 1$



front ($z \to \infty$): $\lambda = c/D$

look for $\tilde{\rho} = \rho_1 e^{-\lambda z}$, $\tilde{a} = a_0 - a_1 e^{-\lambda z}$

back ($z \to -\infty$): $\lambda = \frac{c}{\chi - D}$.

look for $\tilde{a} = a_1 e^{\lambda z}$, $\tilde{\rho} = \rho_1 e^{\lambda z}$

full sol'n: $\tilde{a}(z) = a_0 \left[1 + e^{-cz/D}\right]^{-\frac{D}{\chi - D}}$

$$\tilde{\rho}(z) = \frac{Nc}{\chi - D}\left[1 + e^{-cz/D}\right]^{-\frac{\chi}{\chi - D}} \cdot e^{-cz/D}$$

drift velocity: $v = \chi \frac{1}{\tilde{a}}\frac{\partial \tilde{a}}{\partial x} = \begin{cases} \frac{c\chi}{\chi - D} e^{-cz/D} & z \to +\infty \\ \frac{c\chi}{\chi - D} & z \to -\infty \end{cases}$

Note: $v > c$ in the back
(needed to push against diffusion)

3. Limit of proportional sensing

→ worst v as $z \to -\infty$ due to perfect prop. sensing
(unrealistic)

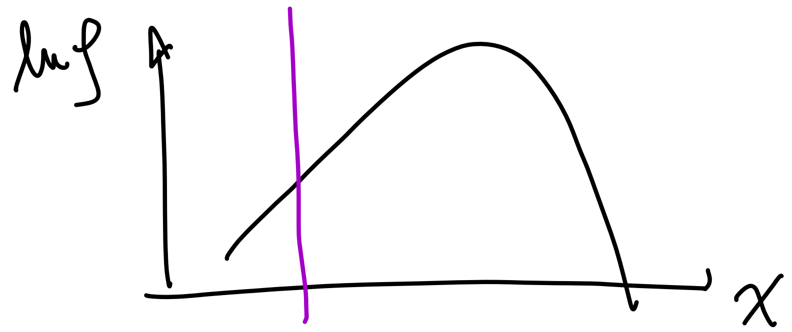
→ Cutoff in reality: $v = \chi \frac{1}{a + a^*}\frac{\partial a}{\partial x}$

$a^* \sim 1\,\mu M$ for E. coli

- for $a(z) < a^*$, $v \to 0$ and cells are lost from the propagating population

- lost of population would slow down propagation speed since $c = kN/a_0$

Quantitative analysis of population loss:



$x^* = z^* + ct$: where $\tilde{a}(z^*) = a^*$
$v(z^*) = v^* < v_{KS}$

\# cells remaining in the front: $N(t) = \int_{z^*+ct}^{\infty} dx\, \rho(x,t)$

Assume the $\rho(x,t) = \tilde{\rho}(x-ct)$ is not affected for $z > z^*$

$$\Rightarrow \frac{dN}{dt} = -(v_{KS} - v^*) \cdot \tilde{\rho}(z^*)$$

$$\frac{dN}{dt} = -\gamma(c) N \; ; \quad \gamma(c) = \frac{\chi}{4}\left(\frac{c}{\chi - D}\right)^2 \frac{a^*}{a_0}$$

since $c \sim N$, then $\gamma(c) \sim N^2$.

$$\frac{dN}{dt} \sim -\alpha N^3 \rightarrow N(t) \sim \frac{1}{\sqrt{2\alpha t}}$$

$$c(t) \sim N(t) \sim \frac{1}{\sqrt{2\alpha t}}$$

4. Include population growth (132)

Early attempt (1970s): attractant = nutrient.

$$\begin{cases} \frac{\partial \rho}{\partial t} = D\frac{\partial^2}{\partial x^2}\rho - \frac{\partial}{\partial x}(v\cdot\rho) + r(a)\cdot\rho\,; \quad v = \chi\frac{\frac{\partial a}{\partial x}}{a+a^*} \\ \frac{\partial a}{\partial t} = D_a\frac{\partial^2}{\partial x^2}a - k(a)\cdot\rho \end{cases}$$

→ too slow: fast expansion favored by small a_0
but large a_0 needed to sustain large pop.
(large pop → fast depletion of a → fast expansion)

Cremer et al: attractant ≠ (sole) nutrient

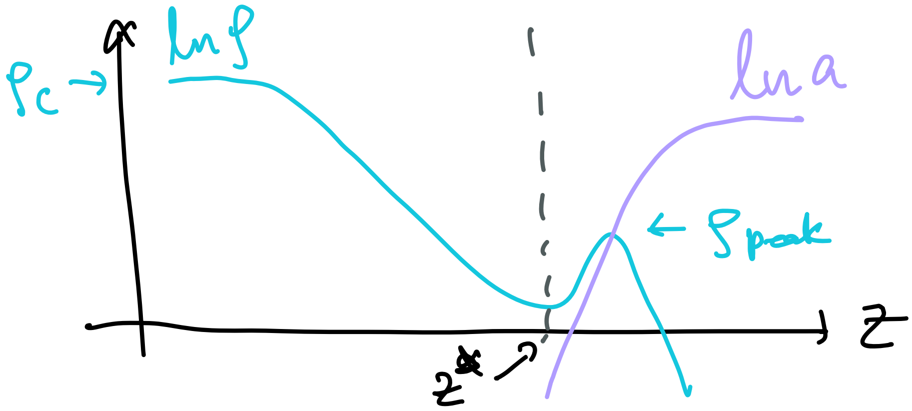
$$\frac{\partial \rho}{\partial t} = D\frac{\partial^2}{\partial x^2}\rho - \frac{\partial}{\partial x}(v\rho) + r\rho(1-\rho/\rho_c)\,; \quad v = \chi\frac{\frac{\partial a}{\partial x}}{a+a^*}$$

$$\frac{\partial a}{\partial t} = D_a\frac{\partial^2 a}{\partial x^2} - k(a)\cdot\rho\,; \quad k(a) = k\cdot\frac{a}{a+a_k}$$

→ propagating soln, with density peak
followed by a trailing plateau

Adler ring (optical illusion)

→ explicit sol'n (Narla et al, 2021)



• Heuristic sol'n for propagation speed (for $\rho \ll \rho_c$)

focus on # cells in the front bulge: $N(t)$

$$\frac{dN}{dt} = -\gamma(c)N + rN$$

leakage rate from front bulge

$$\to \quad c = (\chi - D)\left(\frac{r}{4\chi}\frac{a_0}{a^*}\right)^{1/2}$$

$$= \sqrt{\frac{a_0}{a^*}\frac{\chi}{D}} \cdot \left(1-\frac{D}{\chi}\right) c_{FK}, \quad c_{FK} = 2\sqrt{r \cdot D}$$

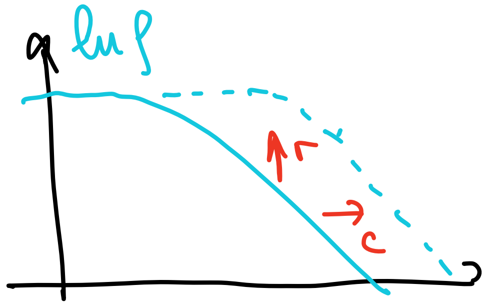
• boost of expansion speed from FK speed by a factor $\propto \sqrt{\chi/D}$ (for $\chi \gg D$)

• c increases with a_0 (but for very large a_0, $\rho_{peak} > \rho_c$)

• propagating sol'n at the back:

for $z \ll z^*$, $a \to 0$. hence $v \to 0$

recover FK eqn: $\frac{\partial \rho}{\partial t} = D\frac{\partial^2}{\partial x^2}\rho + r\rho(1-\rho/\rho_c)$



effective propagation from growth (r).

for $\chi \gg D$, $c \gg c_{FK}$.

this is possible because the profile of ρ is much flatter than that of FK: marginal stability broken