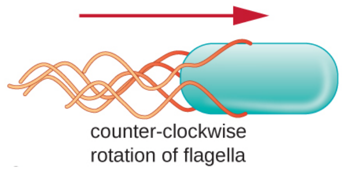
III B. Bacterial chemotaxis

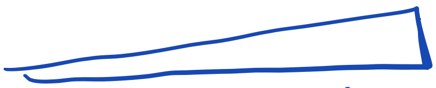
1. Biological background

Many bacterial species move around in aqueous environment by swimming using flagella.



E. coli:

swim speed $v \simeq 25\ \mu m/s \simeq 10\ cm/h$



nutrient gradient $\frac{\Delta n}{\Delta x} = g$ $\Rightarrow$ $v \cdot g = \frac{\Delta n}{\Delta t}$ = nutrient "gain"

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

$\Rightarrow$ movement can sustain growth of population

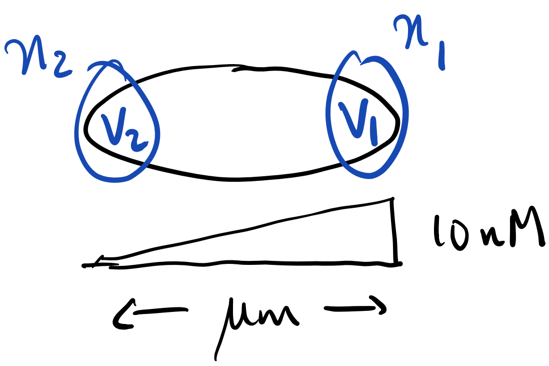
$v \cdot g = r \cdot \rho / Y$

gradient required: $g = \underbrace{\frac{r}{v \cdot Y}}_{\sim \frac{5\,mM}{10\,cm \cdot OD} = 50\,nM/\mu m \cdot OD} \cdot \rho$

$r = 1/hr$

$Y^{-1} = 5\,mM/OD$

Q: can bacteria detect gradient $\sim 10\,nM/\mu m$



$n_1 - n_2 = 10\,nM$.

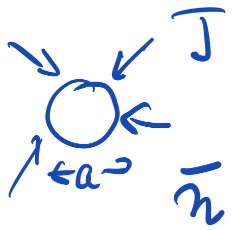
let $V_1 = V_2 = \frac{1}{10}\ \mu m^3$

since $1\,nM \simeq 1$ molecule$/\mu m^3$

$N_1 - N_2 = 1$ molecule!

requires a detection system with $\Delta N \ll 1$

→ can be done by accumulating over time



flux of molecules impinging in volume of radius a: $J = 4\pi a D \cdot \bar{n}$

molecule detected in time τ: $\bar{N} = J \cdot \tau$

$$\rightarrow \quad \bar{N} = 4\pi a D \bar{n} \cdot \tau$$

more careful calc: (Berg + Purcell, 1977)

$$\bar{N} = \underbrace{\pi a D \cdot (1-\bar{p})}_{100\,\mu m^3/sec} \bar{n} \tau$$

receptor occup.

$D = 600\ \mu m^2/s$ (glucose)

$a = 0.1\ \mu m$

detection limit: $\frac{\Delta n}{\bar{n}} = \frac{\Delta N}{\bar{N}} = \frac{1}{\sqrt{\bar{N}}} = \frac{1}{\sqrt{(100\frac{\mu m^3}{s}) \cdot \bar{n} \cdot \tau}}$

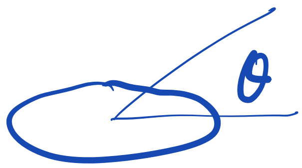
$$\Delta n \ll 10\,nM \Rightarrow \bar{n} \ll (10\,nM)^2 \cdot (100\tfrac{\mu m^3}{s} \cdot \tau)$$
$$= 10\ \mu M/s \cdot \tau$$

Want to detect gradient when nutrient level high

$\bar{n} = 1\,mM$ requires $\tau \sim 100s$

problem: brownian motion of cell

rotational diffusivity of object of size R



$$\langle(\Delta\theta)^2\rangle = 2D_\theta \cdot \tau$$

$$D_\theta = \frac{k_B T}{8\pi\eta R^3}$$

η: kinetic viscosity $= 10^{-2}$ dyn-s/cm^2 for water.

for $R = 1\,\mu m$, $D_\theta = 0.16/s$.

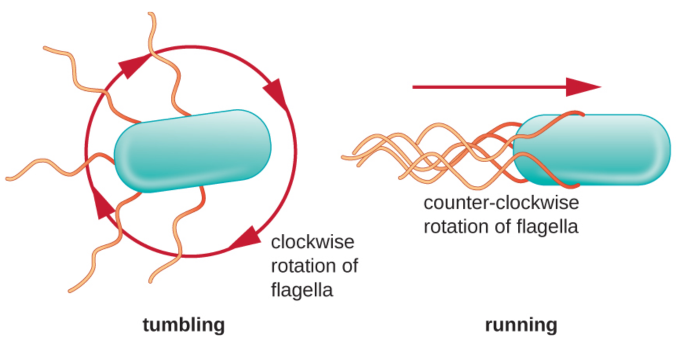
$\Rightarrow \Delta\theta \simeq 30^\circ$ for measurement time $\tau = 1s$.

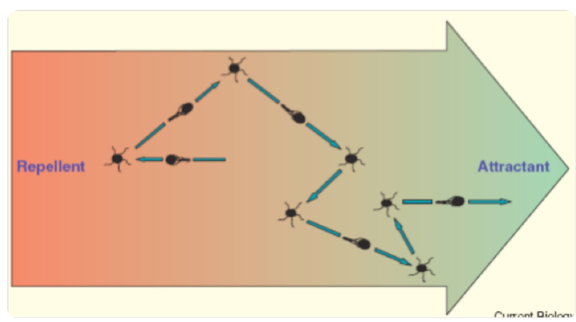
$(r < 10\,\mu M)$

Bacterial strategy:

measure difference in time rather than space

- take $\tau \sim 1$ sec to measure local conc.
  (knows general direction of motion)
- move according to temporal change in measured conc.
  - conc increases: $p > 0.5$ to continue in same direction
  - conc decrease: $p > 0.5$ to "tumble" and move in random new direction

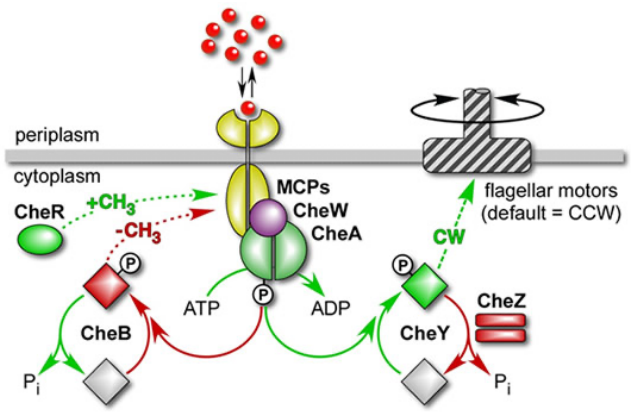


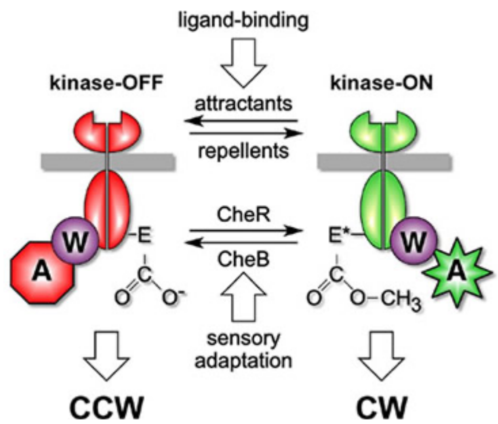


$\Rightarrow$ net result "biased random walk"

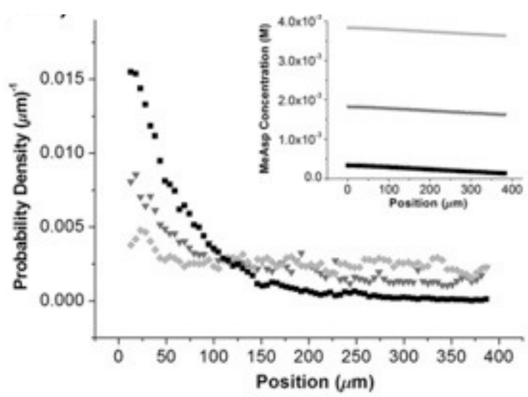
Comments:

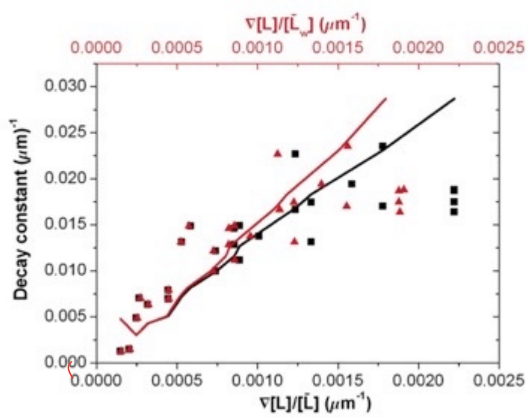
* entire cell used as detector: $a = 0.1\,\mu m \to 1\,\mu m$ in $\tau = 1\,\text{sec}$, $\Delta n = 10\,nM$ for $\bar{n} = 100\,\mu M$.
* must have memory element to compare conc in time
  → adaptation dynamics via covalent modification of the chemoreceptors (methylation/demethylation)





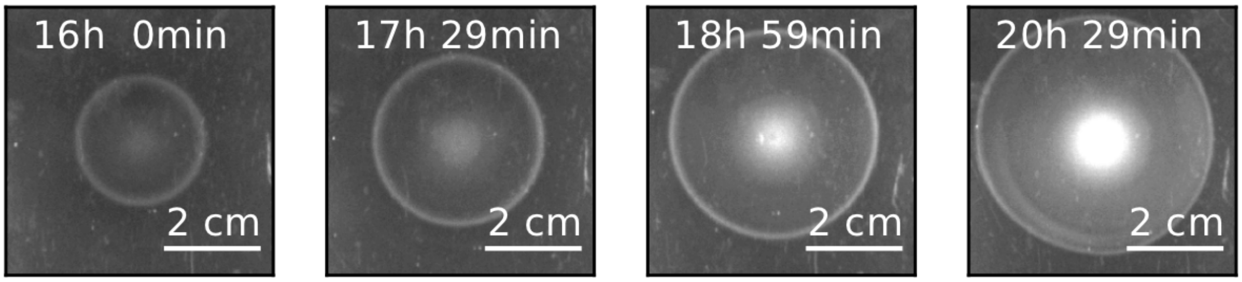
* adaptation system also provides "proportional sensing": response $\propto \frac{\Delta n}{n}$





2. Population dynamics

Chemotactic bacteria in soft agar (rich medium)



$\Rightarrow$ linear propagation of "swarm ring" (Adler, 1966)

At the population level, biased random walk is described by diffusion equation with drift

$$\frac{\partial \rho}{\partial t} = D \vec{\nabla}^2 \rho - \vec{\nabla} \cdot (\vec{v} \rho) \, , \quad \vec{v} = \text{drift velocity}$$

if $\vec{v}$ is constant, then $\tilde{\rho}(\vec{\xi}, t) = \rho(\vec{x} - \vec{v}t, t)$

follows the diffusion eqn: $\frac{\partial}{\partial t} \tilde{\rho} = D \nabla_{\xi}^2 \tilde{\rho}$

Note RHS is in the form $-\vec{\nabla} \cdot \vec{J}$,

where $\vec{J} = -D \vec{\nabla} \rho + \vec{v} \rho$ is the cell flux.

$\rightarrow$ ρ conserved since no cell growth/death

a) Keller-Segel Model (KS, 1971)

propose $\vec{v} = \chi \frac{\vec{\nabla} a}{a}$ perfect proportional sensing; Weber's law.

a = attractant conc.

χ = chemotactic coefficient.

then in 1D: $\partial_t \rho = D \partial_x^2 \rho - \chi \partial_x (\rho \partial_x a / a)$

Note 1: $\rho(x,t)$ still conserved (no growth)

Note 2: χ has same dimension as D.

Supplement with the effect of cells on a:

$\partial_t a = D_a \partial_x^2 a - k(a) \rho$

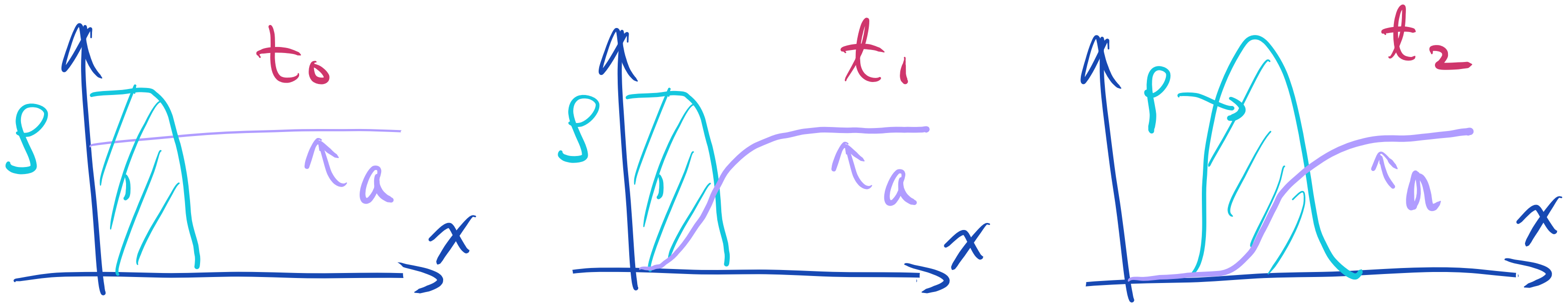
$k(a)$: attractant uptake rate (KS set to const)

D_a: attractant diff coeff. (KS set to zero)

$$\Rightarrow \begin{cases} \partial_t \rho = D \partial_x^2 \rho - \chi \partial_x (\rho \partial_x a / a) \\ \partial_t a = -k \cdot \rho \end{cases}$$ Keller-Segel eqn

main idea:

- bacterial pop. create attractant gradient through their own consumption
- pop chase the receding att. gradient



$\Rightarrow$ expect a traveling band of bacteria

init cond: $a(x,0)=a_0$ b.c.: $\frac{\partial a}{\partial x}=0$ and $\frac{\partial \rho}{\partial x}=0$

$\rho(x,0)=\rho_0(x)$ $a(x\to\infty)=a_0$, $\rho(x\to\infty)=0$

look for $\rho(x,t)=\tilde{\rho}(z)$, $a(x,t)=\hat{a}(z)$, with $z=x-ct$

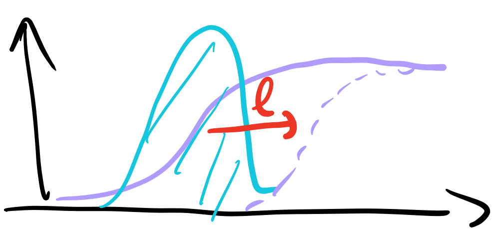
$$\begin{cases} -c\rho' = D\rho'' - \chi(\rho\, a'/a)' & \text{①} \\ -ca' = -k\rho & \text{②} \end{cases}$$

$\Rightarrow$ c obtained from conservation of ρ : (Note: same with $D\partial_x^2 a$)

Integrate ②: $c\cdot\left(a(\infty)-a(-\infty)\right) = k\int_{-\infty}^{\infty} dz\,\rho(z) = k\int_{-\infty}^{\infty} dx\,\rho_0(x) \equiv N$

$c = kN/a_0$ init # cells

Geometric interpretation:



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

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

$\Rightarrow$ problem: KS sol'n cannot accommodate cell growth

b) Sol'n of K S eqn: asymptotics

$$\begin{cases} -c\rho' = D\rho'' - \chi(\rho\, a'/a)' & (1) \\ c a' = k\rho & (2) \end{cases}$$

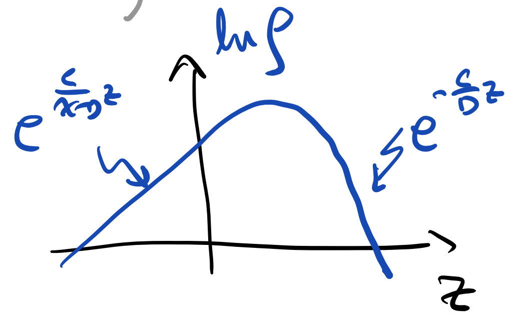
look for $\rho = \rho_1 e^{-\lambda z}$, $a = a_0 - a_1 e^{-\lambda z}$ as $z \to \infty$

(2): $c\lambda a_1 \cancel{e^{-\lambda z}} = k\rho_1 \cancel{e^{-\lambda z}} \rightarrow a_1 = \frac{k\rho_1}{c\lambda}$

(1): $c\lambda\rho_1 e^{-\lambda z} = D\lambda^2\rho_1 e^{-\lambda z} - \cancel{\chi\left(\rho_1 e^{-\lambda z}\frac{a_1\lambda}{a_0}e^{-\lambda z}\right)'}$

$c\lambda = D\lambda^2$

$\rightarrow \boxed{\lambda = c/D.}$



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

(2): $c\lambda a_1 = k\rho_1$

(1): $-c\lambda\rho_1 = D\lambda^2\rho_1 - \chi\lambda^2\rho_1 \rightarrow \boxed{\lambda = \frac{c}{\chi - D}}$

c) Full sol'n by Keller and Segel:

integrate (1): $-c\rho = D\rho' - \chi\rho\, a'/a + \cancel{\text{const}} \to 0$ (b.c.)

$\rightarrow D\frac{\rho'}{\rho} = \chi\frac{a'}{a} - c$ (3)

shift of coord z

integrate (3): $D\ln\rho = \chi\ln a - cz + \text{const}$

$\rho(z) = Q\, a^{\frac{\chi}{D}} e^{-cz/D}$ (4)

Insert (4) into (2) and integrate:

$$c\frac{d}{dz}a = Qk\cdot a^{\frac{\chi}{D}} e^{-cz/D}$$

$$a^{-\frac{\chi}{D}}\, da = Q\frac{k}{c} e^{-cz/D}\, dz$$

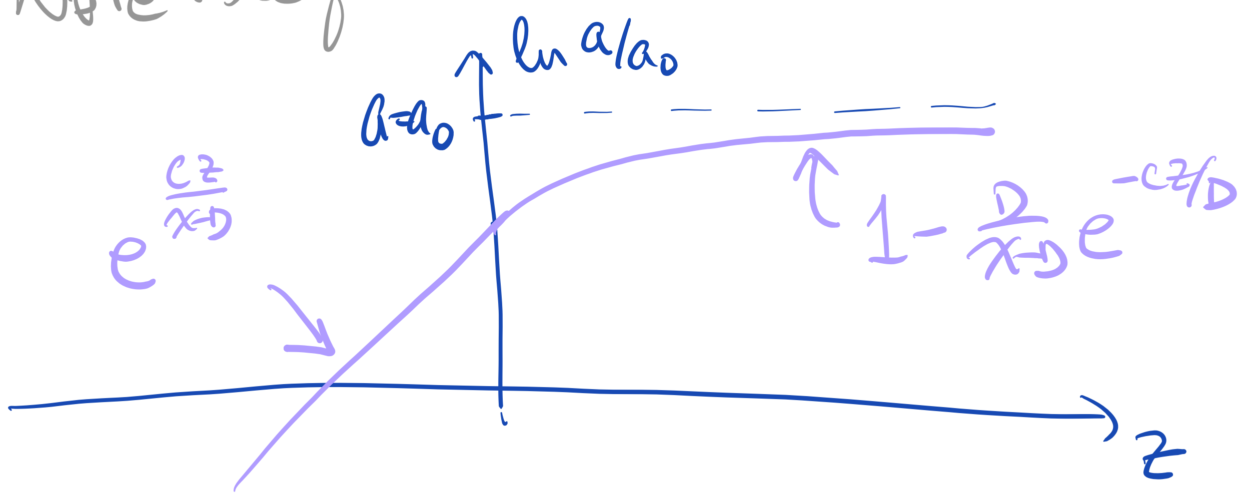
$$\left.\frac{(a')^{1-\frac{\chi}{D}}}{1-\frac{\chi}{D}}\right|_{a(z)}^{a(\infty)} = -Q\frac{kD}{c^2}\, e^{-cz/D}\Big|_{z}^{\infty}$$

$$a_0^{1-\frac{\chi}{D}} - a(z)^{1-\frac{\chi}{D}} = Q\frac{k(D-\chi)}{c^2}\, e^{-cz/D}$$

$$\frac{a(z)}{a_0} = \left[1 + \underbrace{a_0^{\frac{\chi}{D}-1} Q\, \frac{k(\chi-D)}{c^2}}_{\text{Set to 1 via choice of } Q}\, e^{-cz/D}\right]^{-\frac{D}{\chi-D}}$$

$$\boxed{a(z) = a_0\left[1+e^{-cz/D}\right]^{-\frac{D}{\chi-D}}}$$

Note: requires $\chi > D$



Corresponding expression for $\rho(z)$

$$\rho(z) = Q\, a_0^{\frac{\chi}{D}} \cdot \left[1+e^{-cz/D}\right]^{-\frac{\chi}{\chi-D}} \cdot e^{-cz/D}$$

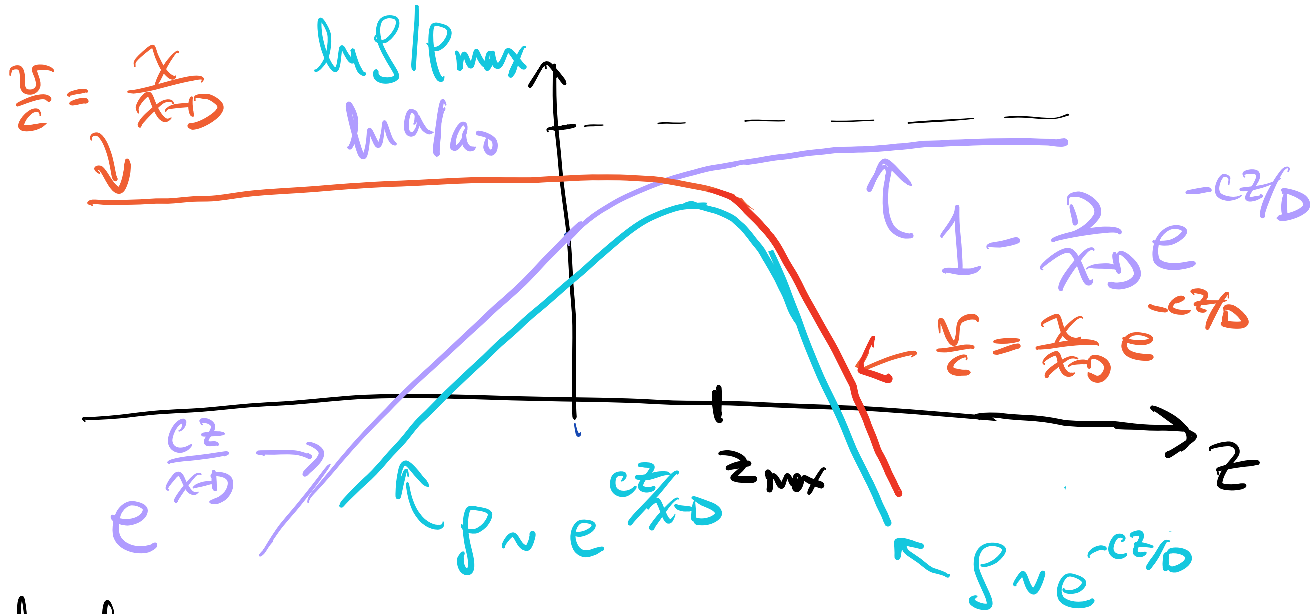
used exp for Q and c.

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

$$= \begin{cases} \dfrac{Nc}{\chi-D}\, e^{-cz/D} & z \to \infty \\[2ex] \dfrac{Nc}{\chi-D}\, e^{\frac{cz}{\chi-D}} & z \to -\infty \end{cases}$$

max ρ at $e^{-cz_{max}/D} = \frac{\chi-D}{D}$

$$\rho_{max} = \frac{Nc}{D}\left(\frac{\chi}{D}\right)^{-\frac{\chi}{\chi-D}} = \frac{c^2 a_0}{\kappa D}\left(\frac{\chi}{D}\right)^{-\frac{\chi}{\chi-D}}$$



drift speed:

$$v(z) = \chi\frac{a'}{a} = \begin{cases} \dfrac{c\chi}{\chi-D}\, e^{-cz/D} & z \to +\infty \\[2ex] \dfrac{c\chi}{\chi-D} & z \to -\infty \end{cases}$$

larger than c; needed to counter back diffusion

3. Limit in proportional sensing

Note: Const v for small z (behind the pulse) arise from perfect proportional sensing

In reality, there is a conc cutoff to adaptation

$$v = \chi \frac{a'}{a + a^*}$$

$a^* \simeq 1\,\mu M$ (Asp, E. coli)

for $a \ll a^*$, $v \propto a' \to 0$ for $z \to -\infty$.

let the position where $a(z) = a^*$ be z^*

then cells for $z \ll z^*$ are left behind

i.e., they are removed from the traveling band

→ since total pop size N determines wave speed c, expect the leakage to slow down propagation

⇒ Quantitative effect of leakage on c?

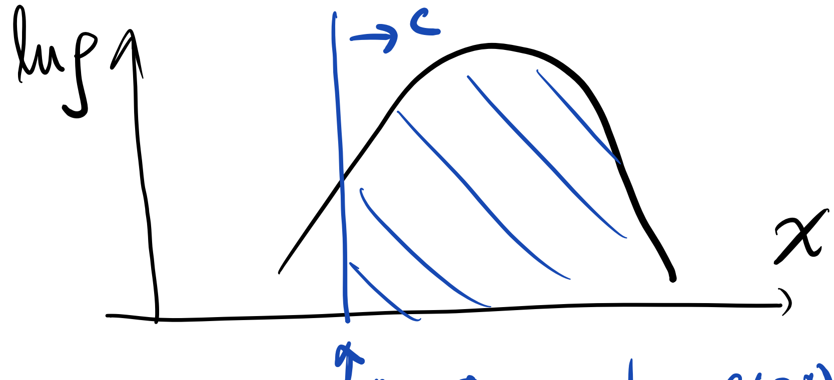
Novick-Cohen + Segal ('84): systematic expansion in D/χ

Here: heuristic analysis (to be expanded below)

* Assume KS sol'n to be unaffected for $a \geq a^*$

At $z = z^*$, $v^* \equiv \chi \frac{a'}{a + a^*} = \frac{v_{KS}}{2}$.

⇒ reduction in speed: $\Delta v \equiv v_{KS} - v^* = \frac{v_{KS}}{2} = \frac{1}{2} \frac{\chi c}{\chi - D}$



$x^* = z^* + ct$ where $a(z^*) = a^*$

$v(z^*) = v^* < v_{KS}$

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

- loss rate due to leakage

$$\frac{dN}{dt} = \frac{d}{dt}\int_{z^*+ct}^{\infty} dx\, \rho(x,t)$$

$$= -c \cdot \rho(z^*+ct, t) + \int_{z^*+ct}^{\infty} dx\, \frac{\partial \rho}{\partial t}$$

- Compute 2nd term using KS eqn:

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

$$\int_{z^*+ct}^{\infty} dx\, \frac{\partial \rho}{\partial t} = D \left.\frac{\partial \rho}{\partial x}\right|_{z^*+ct}^{\infty} - (v\rho)\Big|_{z^*+ct}^{\infty}$$

$$= -D\rho'(z^*+ct, t) + v(z^*+ct, t)\,\rho(z^*+ct, t)$$

used shorthand $\tilde{\rho}(z) = \rho(z+ct, t)$ and then writing $\tilde{\rho}(z)$ as $\rho(z)$

$$= -D\rho'(z^*) + (v_{KS} - \Delta v)\rho(z^*)$$

Since $-D\rho' + v_{KS}\rho = c\rho$

$$\Rightarrow \quad \frac{dN}{dt} = -\Delta v\, \rho(z^*)$$

using $\rho(z) = \frac{Nc}{\chi - D} e^{-cz/\chi - D}$ (for $z^* \ll \hat{z}$)

$$\Delta v = \frac{1}{2} v_{ks}(z^*) = \frac{1}{2} \frac{c\chi}{\chi - D}.$$

$$\rightarrow \frac{dN}{dt} = -\frac{\chi N}{2} \left(\frac{c}{\chi - D}\right)^2 e^{cz^*/\chi - D}.$$

Note: $\Delta v = \frac{1}{2} v_{ks}$ from a simple approx. with step function effect on drift speed

More generally, expect reduction to be

$\Delta v = b\, v_{ks} = b \frac{\chi c}{\chi - D}$. with $b < 1$

(detailed calc showed $b = \frac{1}{4}$; see below)

$\Rightarrow$ loss rate across boundary at $z = z^*$

$$\boxed{\frac{dN}{dt} = -b\chi N \left(\frac{c}{\chi - D}\right)^2 e^{cz^*/\chi - D}.}$$

further, from $a(z^*) = a^*$, and $a(z) = a_0 e^{cz/\chi - D}$

$\rightarrow a^* \simeq a_0 e^{cz^*/\chi - D}$ (for $z \ll z_{max}$)

$$\Rightarrow \frac{dN}{dt} = -b\chi N \left(\frac{c}{\chi - D}\right)^2 \frac{a^*}{a_0}$$

[Note: since $e^{c z_{max}/D} = \frac{D}{\chi - D}$,

$$z^*/z_{max} = \frac{\chi - D}{c} \ln\left(\frac{a^*}{a_0}\right) / \frac{D}{c} \ln\left(\frac{D}{\chi - D}\right)$$

$|z^*| \gg |z_{max}|$ corresponds to $\chi \gg D$]

from $c = kN/a_0$, we have

$$\frac{dN}{dt} = -b\chi \left(\frac{k/a_0}{\chi - D}\right)^2 \frac{a^*}{a_0} N^3 \equiv -\alpha N^3; \quad \alpha \equiv b\chi \frac{a^*}{a_0}\left(\frac{k/a_0}{\chi-D}\right)^2$$

→ Solve ODE with init cond $N(t=0) = N_0$

$$-\int_{N_0}^{N(t)} \frac{dN'}{(N')^3} = \int_0^t \alpha\, dt' \rightarrow \frac{1}{N(t)^2} - \frac{1}{N_0^2} = 2\alpha t$$

$$\rightarrow N(t) = \frac{N_0}{\sqrt{1+2N_0^2 \alpha t}} \propto \frac{1}{\sqrt{2\alpha t}}$$

insert into $c(t) = kN(t)/a_0$

$$c(t) = c_0 \cdot \left(1 + \frac{2b\chi c_0^2}{(\chi-D)^2} \frac{a^*}{a_0} t\right)^{-\frac{1}{2}}$$

where $c_0 = kN_0/a_0$ is speed if $a^* = 0$.

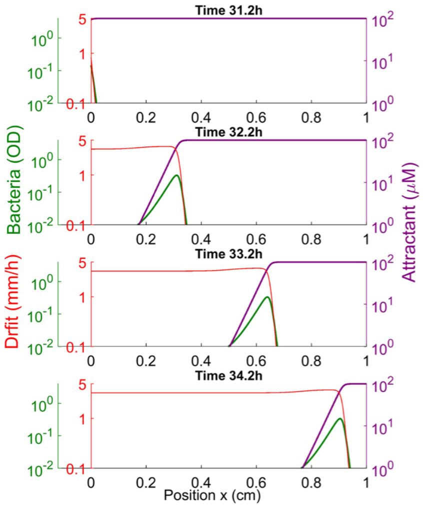
Systematic expansion (Novick-Cohen + Segel, '84)

$$\frac{c(t)}{c(0)} \rightarrow \left(\frac{\chi c_0^2}{2(\chi-D)^2} \frac{a^*}{a_0} t\right)^{-\frac{1}{2}}$$ (Corresponds to $b = \frac{1}{4}$ instead of $\frac{1}{2}$)

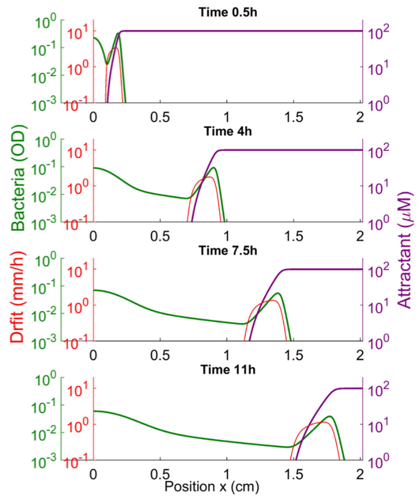
⇒ no steady propagation due to leakage behind the density pulse

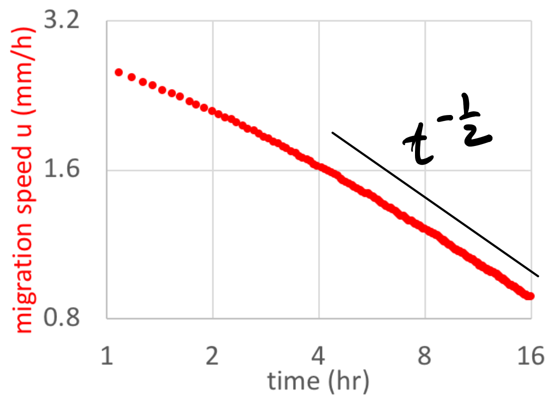
Numerical Simulation

KS eqn



KS eqn with leakage





4. Include population growth

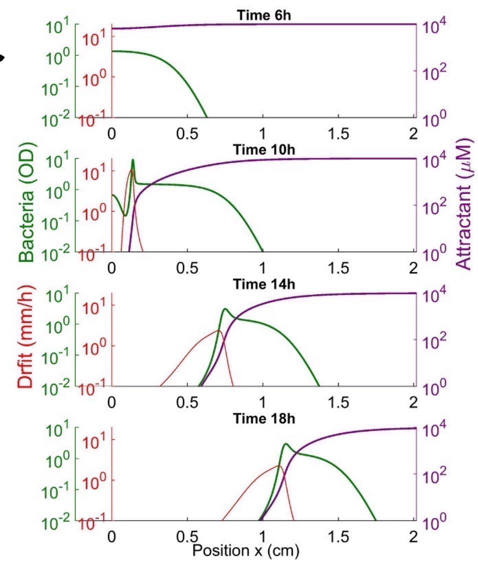
a) background: inclusion of pop growth attempted immediately after KS

$$\begin{cases} \dfrac{\partial \rho}{\partial t} = D\dfrac{\partial^2}{\partial x^2}\rho - \dfrac{\partial}{\partial x}(v\cdot\rho) + r(a)\rho \\ \dfrac{\partial a}{\partial t} = D_a\dfrac{\partial^2}{\partial x^2}a - k(a)\rho \end{cases}$$

→ never worked well (too slow)

$c_{KS} = kN/a_0$

- fast expansion favored by small a_0
- large a_0 needed to support growth



$c < c_{FK}$

→ What sets "N" for a growing population?

→ Origin of Adler ring prop. remained mysterious

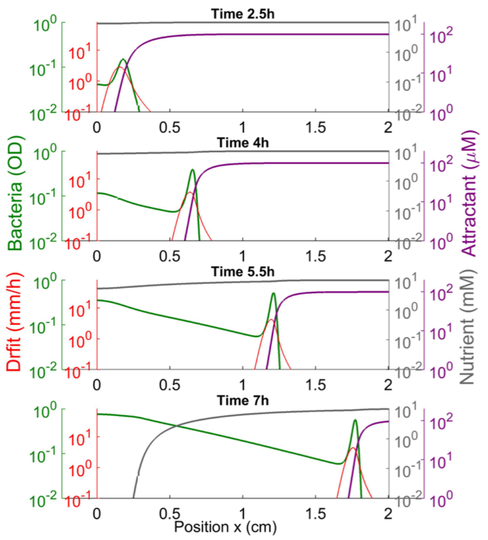
b) biological picture (Cremer et al, 2019)

Separate growth from chemotaxis

i.e., attractant $\neq$ nutrient (significance later)

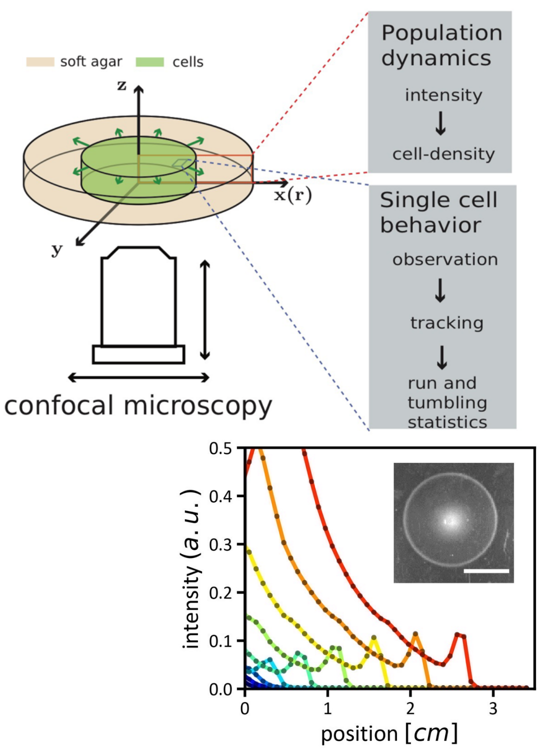
$$\begin{cases} \partial_t \rho = \overbrace{r\rho\left(1-\rho/\rho_c\right)}^{\text{logistic growth}} + D\partial_x^2\rho - \partial_x(v\rho); \quad v = \chi\,\dfrac{\partial_x a}{a+a^*} \\ \partial_t a = D_a\partial_x^2 a - k(a)\rho; \qquad k(a) = k\cdot\dfrac{a}{a+a_K} \end{cases}$$

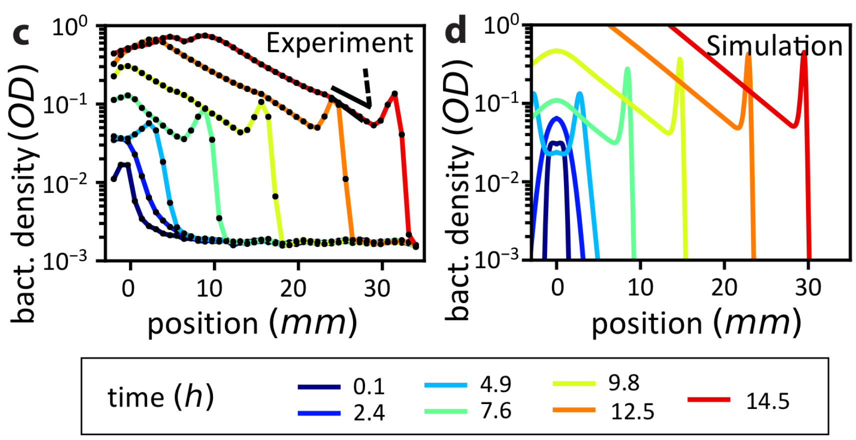
cutoff



Numerical simulation yields steady propagation with a density peak at front followed by a trailing plateau

Directly measure density profile in agar

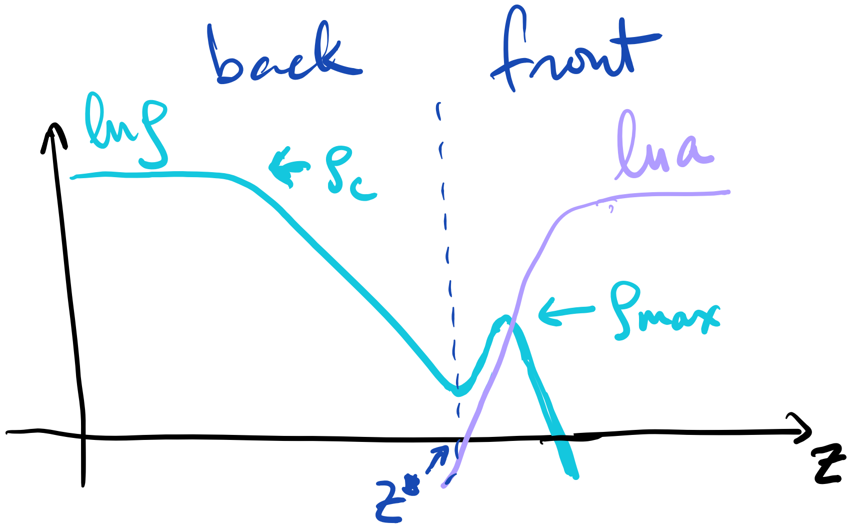




Adler "ring"? optical illusion!

c) Heuristic sol'n:

* Sol'n composed of two regions



front ($z > z^*$):

KS with leakage + growth

back ($z < z^*$):

$v = 0 \rightarrow$ Fisher wave

(ρ and a decoupled)

* front region:

for $\rho_{max} < \rho_c$, can neglect ρ^2 term in growth

for $a_k < a^*$, $k(a) = k \frac{a}{a + a_k} \simeq k$ (const)

further neglect D_a as in KS (will restore later)

$\rightarrow$ front dynamics = KS + leakage + const growth

$$\begin{cases} \partial_t \rho = r\rho + D\partial_x^2 \rho - \partial_x(v\rho); \quad v = \chi \dfrac{\partial_x a}{a + a^*} \\ \partial_t a = -k\rho; \end{cases}$$

let N = # cells in the front bulge.

$$\frac{dN}{dt} = rN - \underbrace{b\chi\left(\frac{c}{\chi - D}\right)^2 \frac{a^*}{a_0}}_{\gamma(c) = \text{leakage rate}} N$$

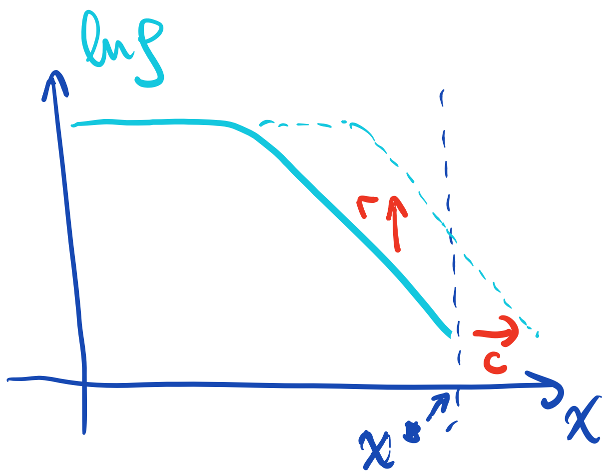
Steady propagating state $\Rightarrow r = \gamma(c)$

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

$$= \sqrt{\frac{1}{4b}\frac{a_0}{a^*}\frac{\chi}{D}}\left(1-\frac{D}{\chi}\right)\cdot c_{FK}\,; \qquad c_{FK} = 2\sqrt{r\cdot D}$$

- boost of expansion speed by $\sqrt{\chi/D}$ compared to Fisher wave. (for $\chi \gg D$)
- c increases with a_0 — opposite of KS.
  (however if a_0 too large, ρ_{max} exceeds ρ_c)

* back region:



$$\partial_t \rho = r\rho + D\partial_x^2\rho \quad (\rho^2 \text{ term neglected})$$

$$\rho \propto e^{-\lambda(x-ct)}$$

$$+\lambda c = r + D\lambda^2.$$

$$\lambda = \frac{c \pm \sqrt{c^2 - 4rD}}{2D} \rightarrow \quad c \gtrsim 2\sqrt{rD}$$

marginal stability $\rightarrow c = 2\sqrt{rD} \equiv c_{FK}$

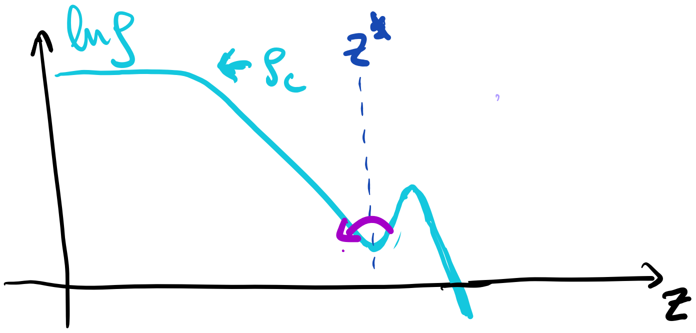
But in the above sol'n for c,

$$c \gg 2\sqrt{rD} \quad \text{if} \quad \frac{\chi}{D} \gg 1 \quad \text{and} \quad \frac{a_0}{a^*} \gg 1$$

$\rightarrow$ How do bacteria beat "marginal stability"?

or, how is prop. speed c "passed on" to the trailing region?

d) Connection between front and back region:



leakage rate from front:

$$\frac{dN}{dt} = \Delta v \cdot \rho(z^*)$$

where $\Delta v = v_{KS} - v^* = b\frac{\chi c}{\chi - D}$.

$\Rightarrow$ "Source" of new cells for trailing region

$$S(x,t) = S_0 \cdot \delta(x-(z^*+ct)); \quad S_0 = \rho_{KS}(z^*)\cdot \Delta v$$

dynamics in the back region:

$$\frac{\partial \rho}{\partial t} = \underbrace{\cancel{D\partial_x^2\rho}}_{\text{neglect}} + r\rho + S_0 \cdot \delta(x-ct-z^*)$$

let $\rho(x,t) = e^{rt}\cdot y(x,t)$

then $\frac{\partial y}{\partial t} = S_0\, e^{-rt}\, \delta(x-ct-z^*)$

$$y(x,t) = \frac{S_0}{c}\, e^{-r\cdot(x-z^*)/c}$$

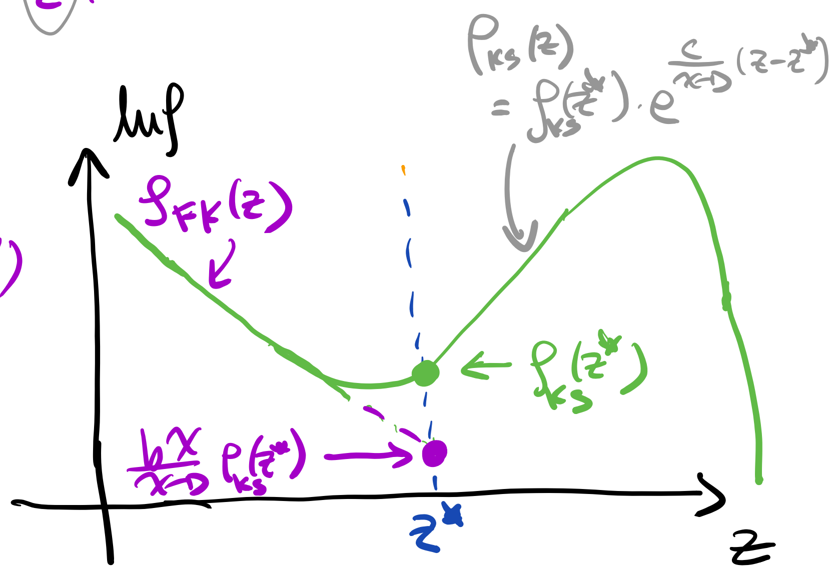
Correction of $\Theta\left(\frac{D\cdot r}{c^2} \sim \frac{D}{\chi}\right)$

$$\Rightarrow \rho(x,t) = \frac{S_0}{c}\, e^{-\frac{r}{c}(x-ct-z^*)}$$

in moving frame:

$$\rho_{FK}(z) = \frac{\Delta V}{c}\rho_{KS}(z^*)\, e^{-\frac{r}{c}(z-z^*)}$$

$\uparrow$ $b\chi/(\chi-D)$



Apparent "gap" between ρ_{FK} and ρ_{KS} $\rightarrow$ width of trough region

5. Compare to numerics (test of heuristic sol'n)

Simulation difficult with $D_a = 0$.

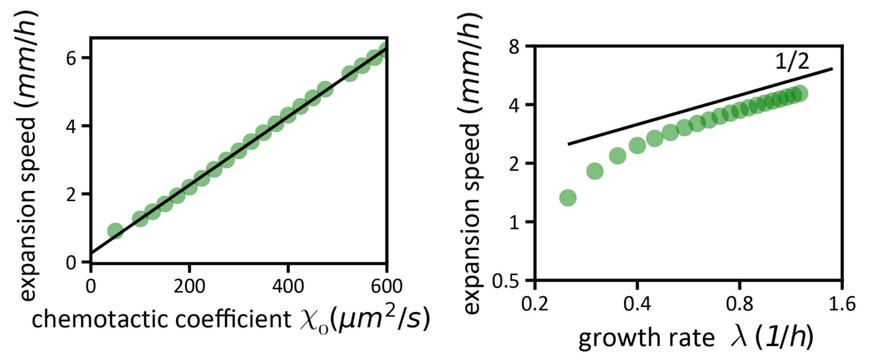
→ repeat heuristics for finite D_a.

obtain $$C = C_{FK} \cdot \sqrt{\frac{1}{4b}\frac{a_0}{a^*}\frac{\chi}{D}} \cdot \left(1-\frac{D}{\chi}\right)\sqrt{\frac{\chi-D}{D_a+\chi-D}}$$

$$\propto \frac{\chi}{\sqrt{D\cdot D_a}} C_{FK} \quad \text{for } D_a < \chi < D$$

50 μm²/s   300 μm²/s   500 μm²/s

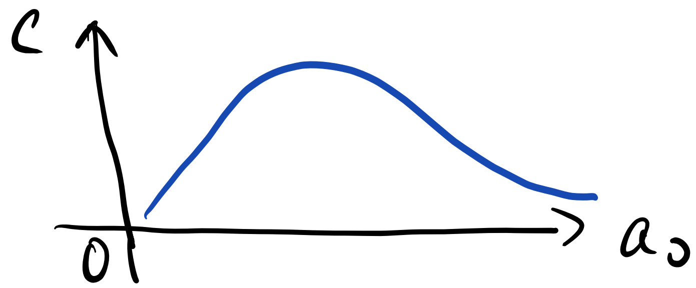
Compares well with numerics ✓

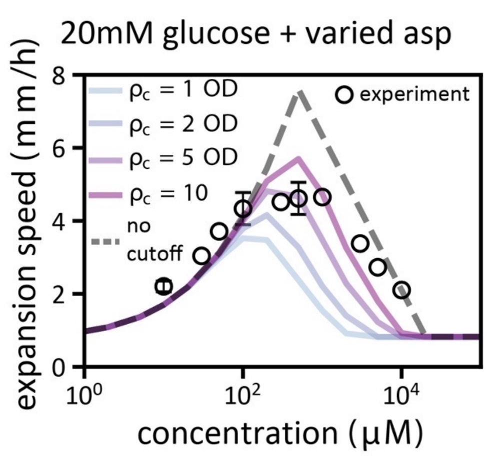


A few more notes:

- the case $k(a) \propto a$ can also be treated ($\chi \to \chi + D$)
- include carrying capacity: $a_c = \frac{k\rho_c}{r} \simeq 2mM \cdot \rho_c$ (in OD)

$$\frac{c^2}{C_{FK}^2} = \frac{1}{4b}\frac{a_0}{a^*}\frac{\chi}{D}\left(1-\frac{D}{\chi}\right)^2 \Big/ \left[1 + \frac{D_a}{\chi-D} + \frac{1}{b}\frac{a_0^2}{a_c a^*}\left(1-\frac{D}{\chi}\right)\right]$$

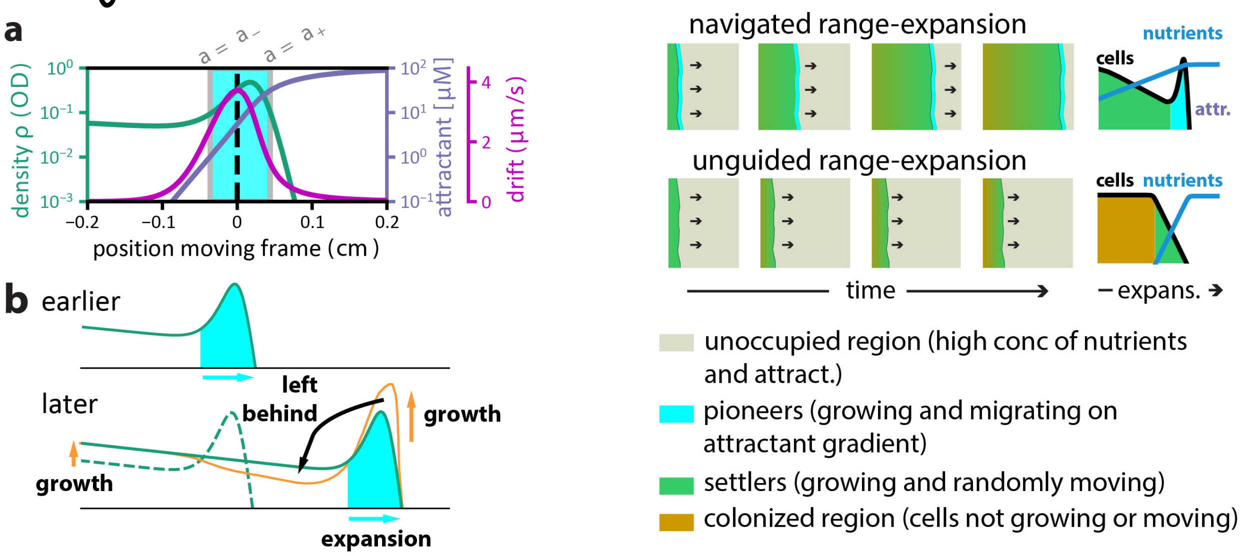




⇒ peak attr. conc.

⇒ attractant not necessary used as nutrient!
⇒ refutes classical notion of chemotaxis
for nutrient scavenging

New picture for chemotaxis (Cremer et al, 2019)
- bacterial pop. employ chemotaxis
in nutrient-replete condition
- boost of range expansion (by factor $\left(\frac{\chi}{D}\right)^{\frac{1}{2}} \sim \left(\frac{\chi}{D}\right)^{1}$)
- requires low attr. conc. (attr. ≠ nutrient)



⇒ attractant is an environmental "marker", whose destruction provides directional cue to navigate chemotaxis
⇒ expand the pop. even with exp. growth; faster GR, faster expansion

Extra 1: include the effect of finite D_a

KS eqn with $D_a \neq 0$

$$\partial_t \rho = D \partial_x^2 \rho - \chi \partial_x (\rho \, \partial_x a / a)$$
$$\partial_t a = D_a \partial_x^2 a - k \cdot \rho$$

with $\rho \to \rho(x-ct)$, $a \to a(x-ct)$

we have:

$$-c\rho' = D\rho'' - \chi(\rho \, a'/a)' \quad (1)$$
$$-ca' = D_a a'' - k \cdot \rho. \quad (2)$$

Speed still given by $c = kN/a_0$

→ with $D_a a''$ term, it is not possible to solve eq (1)+(2) in close form;

let's look for the asymptotics (important, $z \to -\infty$)

$z \to -\infty$: $\rho = \rho_1 e^{\lambda z}$, $a = a_1 e^{\lambda z}$

(1): $-c\lambda \rho_1 = D\lambda^2 \rho_1 - \chi \lambda^2 \rho_1$

$$\lambda = \frac{c}{\chi - D}$$

(2): $k\rho_1 = D_a \lambda^2 a_1 + c\lambda a_1$

$$a_1 = \frac{k\rho_1}{\lambda(D_a \lambda + c)} = \frac{k\rho_1}{\frac{c^2}{\chi - D}\left(1 + \frac{D_a}{\chi - D}\right)}$$

need to work out $\rho(z)$ for $z > z_{max}$

estimate ρ_1: $\int_{-\infty}^{\infty} dz\, \rho(z) = N$.

if $\rho(z)$ falls off much steeper for $z > z_{max}$

then $N \simeq \int_{-\infty}^{z_{max}} dz\, \rho(z) \simeq \rho_1 \int_{-\infty}^{z_{max}} e^{-\lambda z}$

$$\rightarrow \quad \rho_1^- = \frac{cN}{\chi - D} \quad \text{and} \quad a_1^- = \frac{a_0}{1 + D_a/\chi - D}$$

$$\begin{cases} \rho(z) \simeq \dfrac{cN}{\chi - D} e^{cz/\chi - D} \\ a(z) \simeq a_0 \dfrac{\chi - D}{\chi - D + D_a} e^{cz/\chi - D} \end{cases} \quad \text{for } z \to -\infty$$

Next: find leakage at $a(z^*) = a^*$

$$\rightarrow \quad a^* = a_0 \frac{\chi - D}{\chi - D + D_a} e^{cz^*/\chi - D}$$

$$\frac{dN}{dt} = -b\chi \left(\frac{c}{\chi - D}\right)^2 N e^{cz^*/\chi - D}$$

$$= \underbrace{-b\chi \left(\frac{c}{\chi - D}\right)^2 \cdot \frac{a^*}{a_0} \left(1 + \frac{D_a}{\chi - D}\right)}_{\gamma(c)} N$$

* Include growth: $\dfrac{dN}{dt} = rN - \gamma(c) N$

$$r = \gamma(c) \Rightarrow \boxed{\frac{c^2}{c_{FK}^2} = \frac{1}{4b} \frac{a_0}{a^*} \frac{\chi}{D} \cdot \left(1 - \frac{D}{\chi}\right)^2 \cdot \frac{\chi - D}{D_a + \chi - D}}$$

Extra 2: Include the effect of carrying capacity

* if N is the # cells in the front bulge

then $\frac{dN}{dt} = rN\left(1-\frac{N}{N_c}\right) - \gamma(c)N$

where $\gamma(c) = b\chi\left(\frac{c}{\chi-D}\right)^2 \frac{a^*}{a_0}\frac{D_a+\chi-D}{\chi-D} = \frac{c^2}{\chi}\cdot\tilde{b}$

is the leakage rate

$\tilde{b} = b\cdot\left(\frac{\chi}{\chi-D}\right)^2 \frac{a^*}{a_0}\frac{D_a+\chi-D}{\chi-D}$

take $N_c \simeq \rho_c/\lambda = \rho_c\cdot\frac{\chi-D}{c}$

$\frac{dN}{dt} = 0 \rightarrow r - r\frac{N\cdot c}{\rho_c(\chi-D)} = \frac{c^2}{\chi}\cdot\tilde{b}$

use $ca_0 = kN$ for N.

$r = \frac{c^2}{\chi}\tilde{b} + r\frac{c^2 a_0/k}{\rho_c(\chi-D)}$

$\frac{1.5\,mM/OD/hr}{0.7/hr} \simeq 2\,mM/OD$

$r\chi = c^2\left(\tilde{b} + \frac{ra_0}{k\cdot\rho_c}\frac{\chi}{\chi-D}\right)$

$a_0/a_c,\ a_c \equiv \frac{k}{r}\rho_c$

$c^2 = r\chi \Big/ \left[b\frac{a^*}{a_0}\left(\frac{\chi}{\chi-D}\right)^2\frac{D_a+\chi-D}{\chi-D} + \frac{ra_0}{k\cdot\rho_c}\frac{\chi}{\chi-D}\right]$

$\frac{c^2}{c_{FK}^2} = \frac{\chi}{4D}\left(1-\frac{D}{\chi}\right)^2 \Big/ \left[b\frac{a^*}{a_0}\cdot\left(1+\frac{D_a}{\chi-D}\right) + \frac{a_0}{a_c}\left(1-\frac{D}{\chi}\right)\right]$

peak: $a_0^{max} \simeq \sqrt{a^*\cdot a_c} = \sqrt{1\,\mu M\cdot 2\,mM/OD\cdot\rho_c}$

if $\rho_c \sim 2\,OD$, then $a_0^{max} \simeq 50\text{-}100\,\mu M$.

Extra 3: realistic uptake $k(a) = k_0 \frac{a}{a+a_K}$

* we must have $k(a) \to 0$ as $a \to 0$ for the model with growth, because ρ is large behind the front.

* Consider KS eqn with $k(a) = \nu \cdot a$; $\nu \equiv k_0/a_K$

$$\partial_t \rho = D \partial_x^2 \rho - \chi \partial_x (\rho \, \partial_x a / a)$$
$$\partial_t a = - \nu a \cdot \rho$$

with $\rho \to \rho(x-ct)$, $a \to a(x-ct)$

we have: $-c\rho' = D\rho'' - \chi (\rho \, a'/a)'$ (1)

$c a' = \nu a \cdot \rho$ (2)

* direct sol'n following KS:

integrate (1): $-c\rho = D\rho' - \chi \rho a'/a + \cancel{\text{const}}^{\to 0 \text{ (b.c.)}}$

$\to \quad D \frac{\rho'}{\rho} = \chi \frac{a'}{a} - c$ (3)

shift of coord z

integrate (3): $D \ln \rho = \chi \ln a - cz + \text{const}$

$\rho(z) = Q \, a^{\chi/D} e^{-cz/D}$ (4)

Insert (4) into (2) and integrate:

$$c\frac{d}{dz}a = Q\,\nu\, a^{1+\frac{\chi}{D}} e^{-cz/D}$$

$$a^{-(1+\frac{\chi}{D})}da = Q\frac{\nu}{c}e^{-cz/D}dz$$

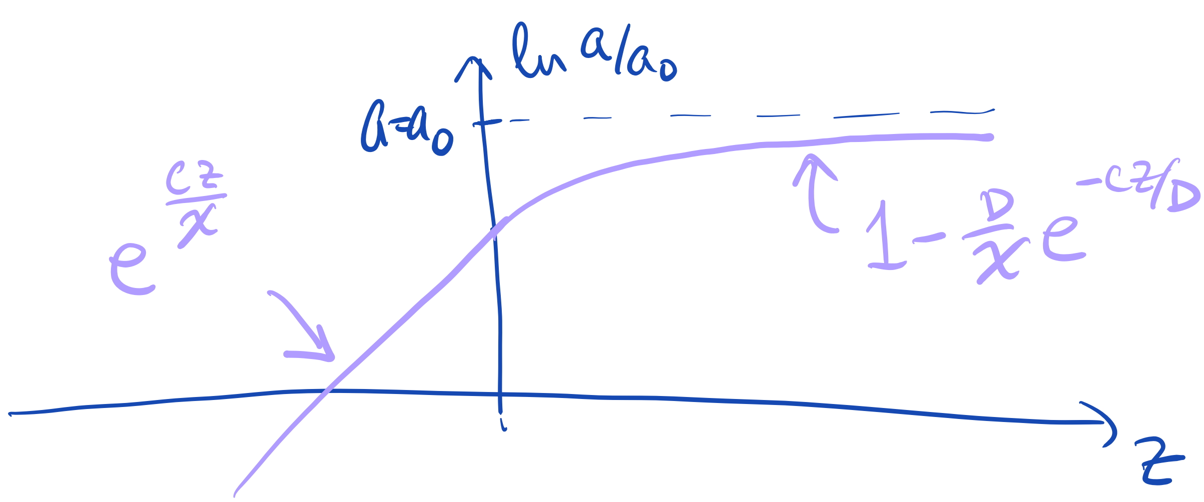
$$\left.\frac{(a')^{-\frac{\chi}{D}}}{-\frac{\chi}{D}}\right|_{a(z)}^{a_0} = \left.-Q\frac{\nu D}{c^2}e^{-cz/D}\right|_{z}^{\infty}$$

$$a_0^{-\frac{\chi}{D}} - a(z)^{-\frac{\chi}{D}} = Q\frac{\nu(-\chi)}{c^2}e^{-cz/D}$$

$$\frac{a(z)}{a_0} = \Big[1 + \underbrace{a_0^{\frac{\chi}{D}}Q\frac{\nu\chi}{c^2}}_{\text{Set to 1 via choice of } Q}e^{-cz/D}\Big]^{-\frac{D}{\chi}}$$

$$\boxed{a(z) = a_0\left[1+e^{-cz/D}\right]^{-\frac{D}{\chi}}}$$

not $\frac{D}{\chi-D}$



Corresponding expression for $\rho(z)$

$$\rho(z) = Q\, a_0^{\frac{\chi}{D}} \cdot \left[1+e^{-cz/D}\right]^{-1} e^{-cz/D}$$

used exp for Q

$$= \frac{c^2}{\nu\chi} \Big/ \left[1+e^{cz/D}\right]$$

problem : $\rho(z) \to$ finite for $z \to -\infty$

no propagating sol'n !

However, the above sol'n is okay for the front, if the back is taken care of by FK dynamics

Suppose $\rho(z) = \frac{c^2}{\nu\chi} \Big/ \left[1+e^{cz/D}\right]$ for $z \geq z^*$

z^* at $a(z^*) = a^*$

or $\quad a_0 \left[1+e^{-cz^*/D}\right]^{-\frac{D}{\chi}} = a^*$

$$e^{cz^*/D} = \left(\frac{a^*}{a_0}\right)^{\frac{\chi}{D}}$$

for $a^* \ll a_0$, $e^{cz^*/D} \ll 1$ & $\rho(z^*) \simeq \frac{c^2}{\nu\chi}$

$$v = \chi \frac{a'}{a} = c$$

$$v^* = \chi \frac{a'}{a+a^*} = \frac{c}{2}$$

leakage rate: $\frac{dN}{dt} = -\Delta v \cdot \rho(z^*) = -bc\,\rho(z^*)$

in front bulge:

$$N = \int_{z^*}^{\infty} dz\, \rho(z) = \int_{z^*}^{\infty} dz \frac{c^2/\nu\chi}{1+e^{cz/D}} = \frac{cD}{\nu\chi}\underbrace{\int_{cz^*/D}^{\infty} \frac{dy}{1+e^{y}}}_{\Theta(1)+\frac{\chi}{D}\ln\left(\frac{a_0}{a^*}\right)}$$

$\frac{cz^*}{D} = \frac{\chi}{D}\ln\left(\frac{a^*}{a_0}\right)$

for large χ/D: $N \simeq \frac{c}{\nu}\ln\frac{a_0}{a^*} = \frac{c\,a_K}{k_0}\ln\frac{a_0}{a^*}$

or $c = \nu N / \ln(a_0/a^*)$

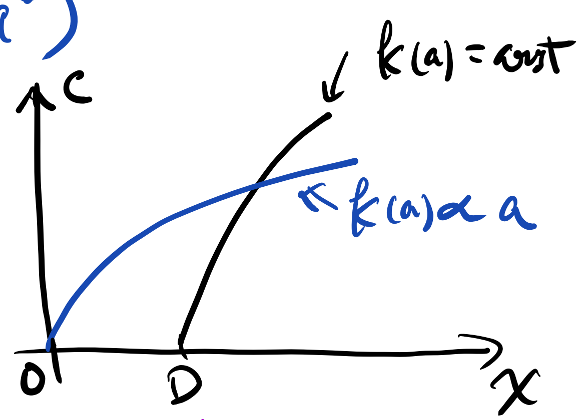
$$\rightarrow \quad \frac{dN}{dt} = -bc\,\rho(z^*) = -\underbrace{\frac{b\nu\rho(z^*)}{\ln(a_0/a^*)}}_{\gamma = bc^2/\chi\ln(a_0/a^*)} N$$

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

$\gamma(c) = r \rightarrow c^2 = b^{-1} r \chi \ln(a_0/a^*)$

Compare to $k(a) = \text{const}$:

$$c^2 = b^{-1} r \chi \left(1 - \frac{D}{\chi}\right)^2 \cdot \frac{a_0}{a^*}$$



Actual system: $k(a) = k_0 \frac{a}{a+a_K}$ with $a_K = a^*$

should be "in between" the two cases?

Repeat the above analysis for $k(a) = k_0 \frac{a}{a+a_k}$

$$\partial_t \rho = D\partial_x^2 \rho - \chi\, \partial_x (\rho\, \partial_x a/a)$$

$$\partial_t a = -k(a)\cdot \rho$$

moving frame: $\rho(x,t) \to \rho(\underbrace{x-ct}_{z})$, $a(x,t) \to a(\underbrace{x-ct}_{z})$

$$-c\rho' = D\rho'' - \chi(\rho\, a'/a)' \quad (1)$$

$$c a' = k(a)\cdot \rho \quad (2)$$

integrate eq (1) as before

$$\to \rho(z) = Q\, a^{\frac{\chi}{D}}\, e^{-cz/D} \quad (4)$$

Insert (4) into (2) and integrate:

$$c\frac{d}{dz}a = Q\, k_0 \frac{a^{1+\frac{\chi}{D}}}{a+a_k}\, e^{-cz/D}$$

$$a^{-\frac{\chi}{D}} + a_k\, a^{-(1+\frac{\chi}{D})}\, da = Q\frac{k_0}{c}\, e^{-cz/D}\, dz$$

$$\left.\frac{a^{1-\frac{\chi}{D}}}{\frac{\chi}{D}-1} + \frac{a_k\, a^{-\frac{\chi}{D}}}{\frac{\chi}{D}}\right|_{a(z)}^{a_0} = \left. Q\frac{k_0 D}{c^2}\, e^{-cz/D}\right|_{z}^{\infty}$$

$$\frac{a(z)^{1-\frac{\chi}{D}}}{\frac{\chi}{D}-1} + \frac{a_k\, a(z)^{-\frac{\chi}{D}}}{\frac{\chi}{D}} - \frac{a_0^{1-\frac{\chi}{D}}}{\frac{\chi}{D}-1} - \frac{a_k\, a_0^{-\chi/D}}{\chi/D} = Q\frac{k_0 D}{c^2}\, e^{-cz/D}$$

We are interested in the value z^* at $a(z^*) = a^*$

for $a_K = a^* \ll a_0$, the above eqn becomes

$$(a^*)^{1-\frac{\chi}{D}} \left[\frac{1}{\frac{\chi}{D}-1} + \frac{1}{\frac{\chi}{D}} \right] - \frac{a_0^{1-\frac{\chi}{D}}}{\frac{\chi}{D}-1} \simeq Q \frac{k_0 D}{c^2} e^{-cz^*/D}$$

$$\left(\frac{a^*}{a_0}\right)^{1-\frac{\chi}{D}} \left(1 + 1 - \frac{D}{\chi}\right) = 1 + \underbrace{Q\, a_0^{\frac{\chi}{D}-1} \frac{k_0 D}{c^2} \left(\frac{\chi}{D}-1\right)}_{\text{Set to } 1} e^{-cz^*/D}$$

$$\frac{a^*}{a_0} = \left(2 - \frac{D}{\chi}\right)^{+\frac{D}{\chi-D}} \left(1 + e^{-cz^*/D}\right)^{-\frac{D}{\chi-D}}$$

in the vicinity $z \simeq z^*$ (and z^* large, -ve), expect

$$a(z) \simeq a_0 \left(2 - \frac{D}{\chi}\right)^{\frac{D}{\chi-D}} e^{\frac{cz}{\chi-D}}.$$

$$v = \chi \frac{a'}{a} = \frac{\chi c}{\chi - D} \quad \Rightarrow \quad \boxed{\Delta v = -b \frac{\chi c}{\chi - D}}$$

Next, evaluate

$$\rho^* \equiv \rho(z^*) = Q \cdot (a^*)^{\frac{\chi}{D}} e^{-cz^*/D}$$

$$= \frac{a_0^{\frac{\chi}{D}} \cdot \left(2 - \frac{D}{\chi}\right)^{\frac{\chi}{\chi-D}}}{a_0^{\frac{\chi}{D}-1} \frac{k_0 D}{c^2} \left(\frac{\chi}{D}-1\right)} \cdot e^{\frac{cz^*}{\chi-D} \cdot \frac{\chi}{D}} \cdot e^{-cz^*/D}$$

$$= \frac{a_0 c^2}{k_0} \cdot \frac{\left(2 - \frac{D}{\chi}\right)^{\frac{\chi}{\chi-D}}}{\chi - D} e^{cz^*/\chi-D}$$

relate ρ^* to $N = \int_{z^*}^{\infty} dz\, \rho(z)$

for much of range $z > z^*$, $a(z) > a^*$

So we have $a(z)^{1-\frac{\chi}{D}} - a_0^{1-\frac{\chi}{D}} = \left(\frac{\chi}{D} - 1\right) Q \frac{k_0 D}{c^2} e^{-cz/D}$

as in the original KS problem.

there $\rho(z) = \frac{a_0 c^2}{k_0(\chi - D)} \left[1 + e^{-cz/D}\right]^{\frac{-\chi}{\chi - D}} \cdot e^{-cz/D}$

$$\simeq \frac{a_0 c^2}{k_0(\chi - D)} e^{cz/\chi - D} \quad (\text{large}, -\text{ve } z)$$

$$N \simeq \int_{z^*}^{0} dz\, \rho(z) = \frac{a_0 c}{k_0} \left[\text{const} - e^{cz^*/\chi - D}\right]$$

$$\Rightarrow \rho^* \simeq \frac{a_0 c^2}{k_0} \cdot \frac{\left(2 - \frac{D}{\chi}\right)^{\frac{\chi}{\chi - D}}}{\chi - D} e^{cz^*/\chi - D}$$

$$= \# \frac{Nc}{\chi - D} \left(2 - \frac{D}{\chi}\right)^{\frac{\chi}{\chi - D}} e^{cz^*/\chi - D}$$

$$= \# \frac{Nc}{\chi - D} \left(2 - \frac{D}{\chi}\right)^{\frac{\chi}{\chi - D}} \cdot \frac{a^*}{a_0} \cdot \left(2 - \frac{D}{\chi}\right)^{-\frac{D}{\chi - D}}$$

$$\frac{dN}{dt} = -\Delta v \cdot \rho^* = -\overbrace{b \frac{\chi c^2}{(\chi - D)^2} \left(2 - \frac{D}{\chi}\right) \frac{a^*}{a_0}}^{\gamma(c)} N$$

$$\gamma(c) = r \Rightarrow c^2 = \frac{r\chi}{b} \frac{a^*}{a_0} \left(1 - \frac{D}{\chi}\right)^2 \cdot \left(2 - \frac{D}{\chi}\right)$$

approx same as $a_k = 0$

Further extension : attractant = nutrient

$$\partial_t \rho = D \partial_x^2 \rho - \partial_x (v \rho) + r(a) \rho$$

$$v = \chi \frac{\partial_x a}{a + a^*} \qquad r(a) = r_0 \frac{a}{a + a_K}$$

$$\partial_t a = D_a \partial_x^2 a - k(a) \rho ; \quad k(a) = k_0 \frac{a}{a + a_K}$$

Realistic parameters : $\underset{1\,\mu M}{a^*} \ll \underset{50\,\mu M}{a_K} \ll \underset{1-10\,mM}{a_0}$.

$\rightarrow$ approx used on prev. page $k(a) \sim a$ applies