From Crawlers to Swimmers- Mathematical and Computational Problems in Cell Motility

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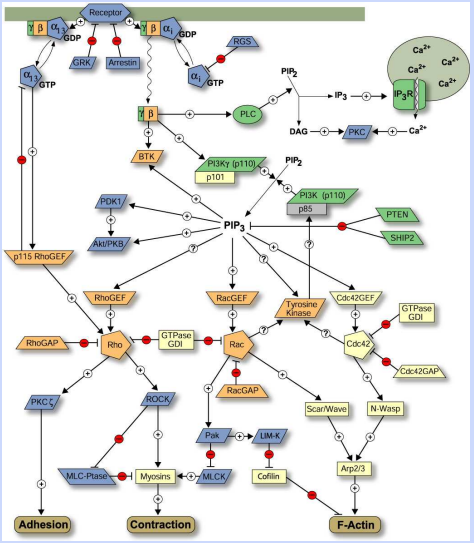
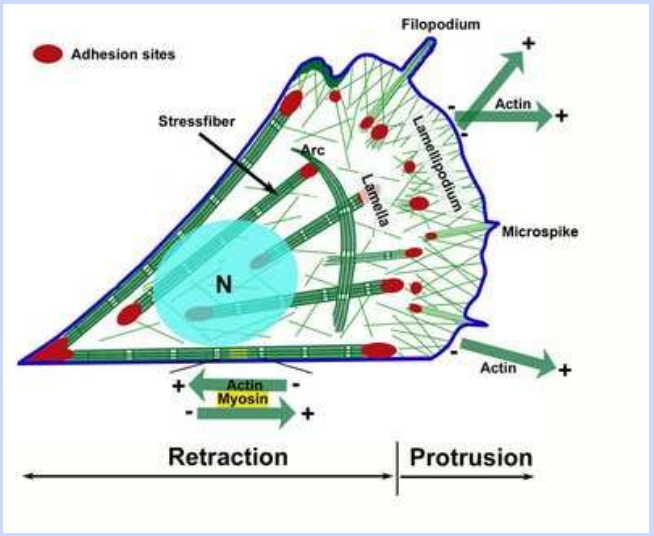
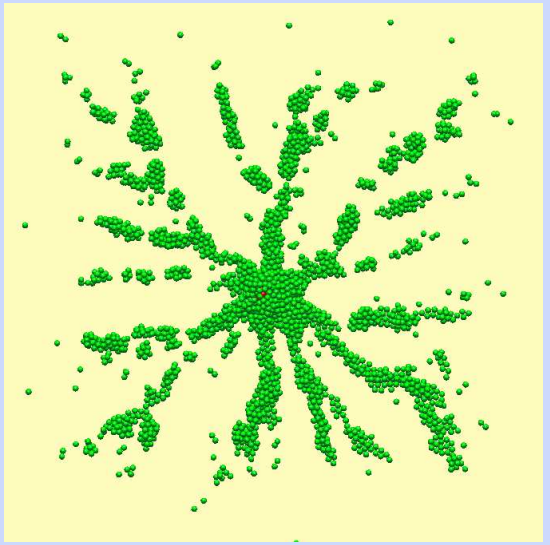


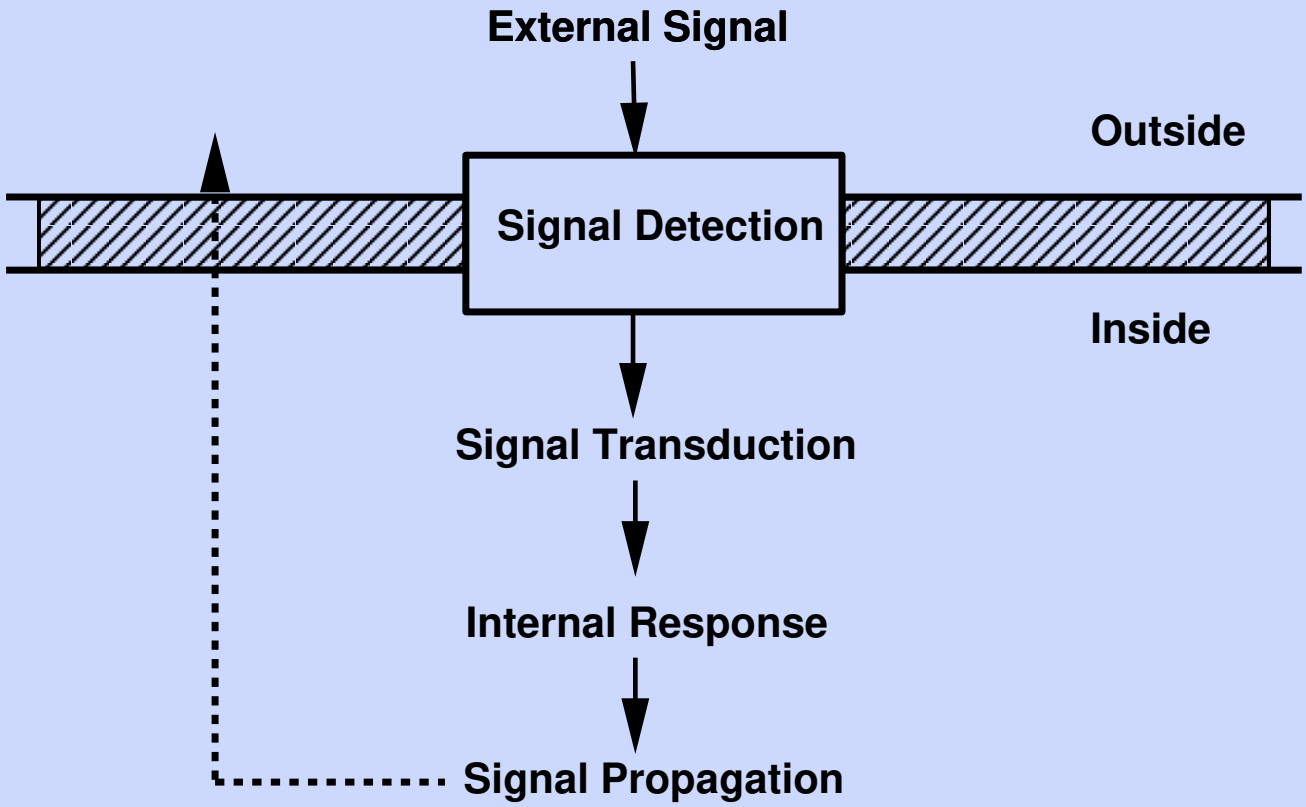




Edinburgh – Oct. 2017 – Lecture 3

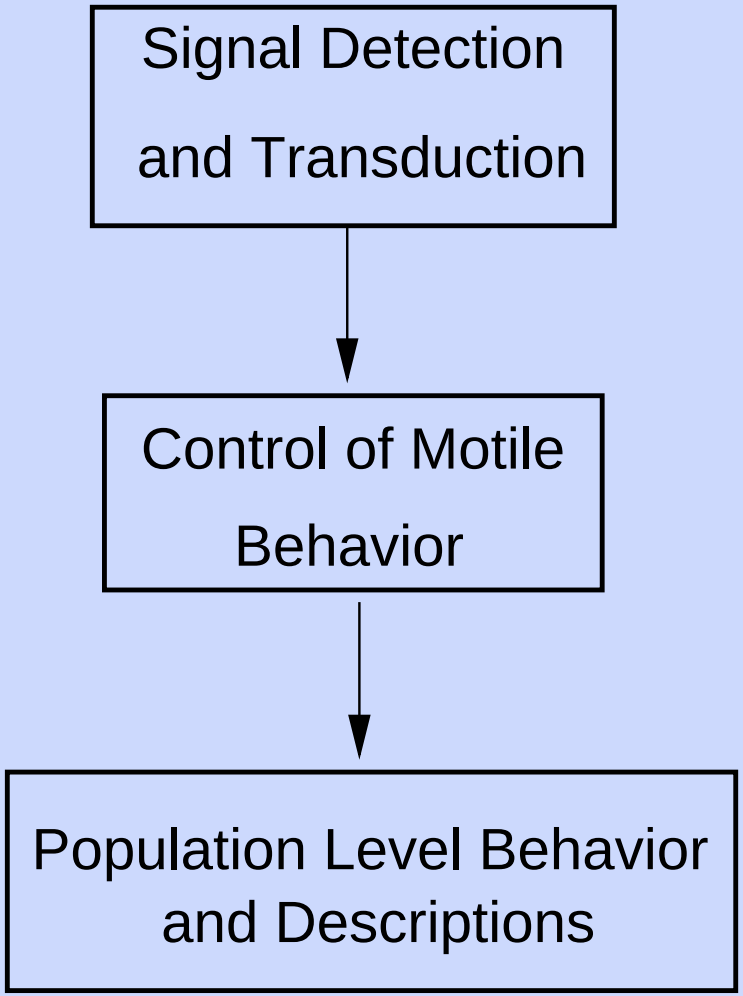
Recall the basic processes at the individual level

- A signal of some sort
- Transduction of the signal into ‘information’ that can affect movement



- Movement – which of course involves mechanics

The components in an integrated description

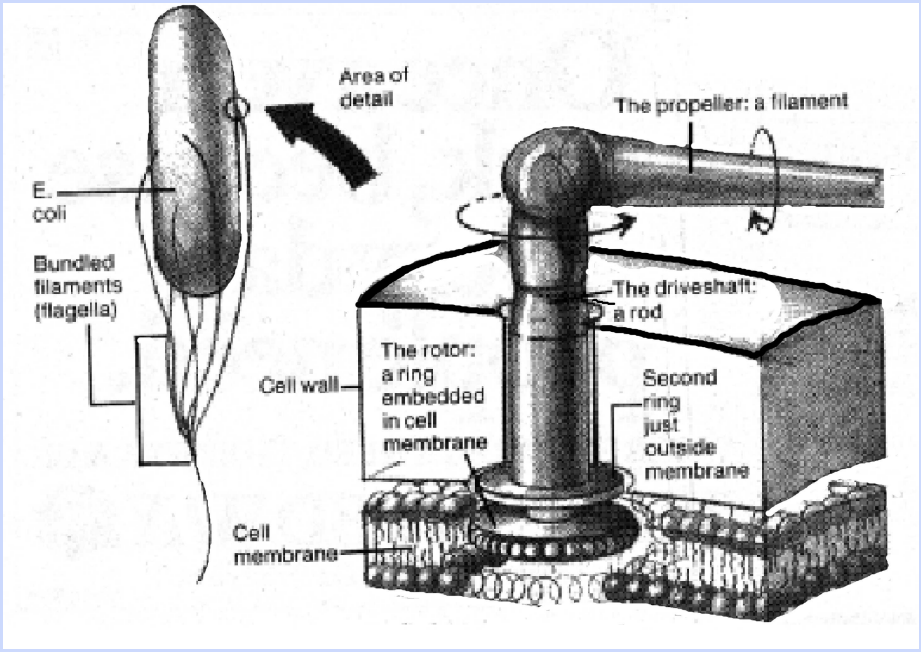


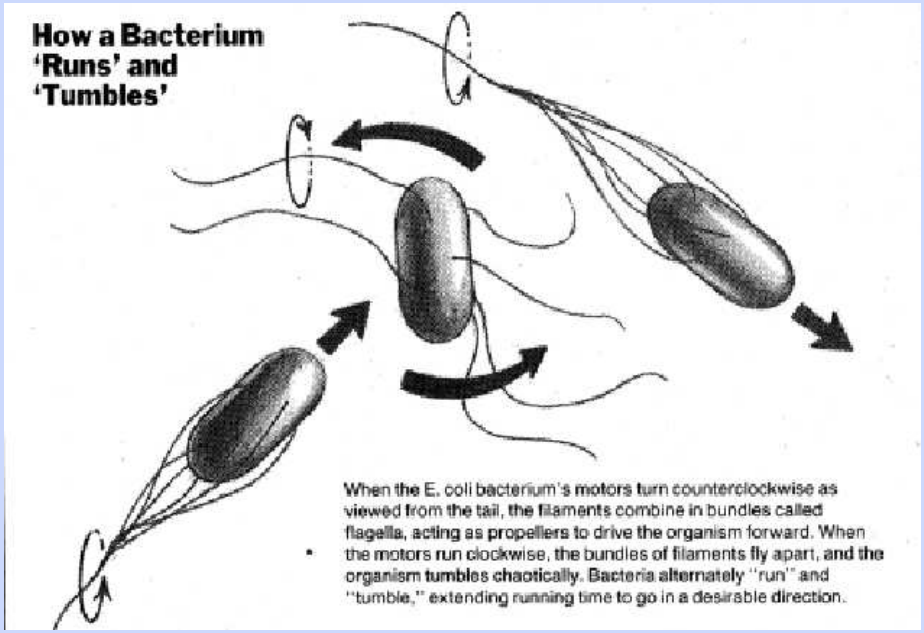
Some basic questions posed by the modelling process

- How does one obtain ‘simple’, stereotypical dynamical behavior from complex networks *reliably*? Is there a canonical topological structure in the networks or must one analyze each individually? Is there a heirarchy of feedbacks that produces this?
- How does one determine when stochastic effects are important in signal transduction, gene control, etc? What are the mechanisms that have evolved to cope with noisy signals? Is noise ever advantageous?
- Once we understand the normal or standard behavior, can we predict how changes in inputs, parameters, and the pattern of interactions affect this behavior? Are there tools we can use to understand the different effects of parametric *versus* structural changes?
- Can one develop hierarchical averaging or homogenization techniques that enable us to embed information about microscopic-level processes into ‘population-level’ descriptions?
- More generally, what new mathematical and computational tools are needed to analyze complex biological systems ?

From micro- to macro- in *E. Coli*

*E. coli*as a model system

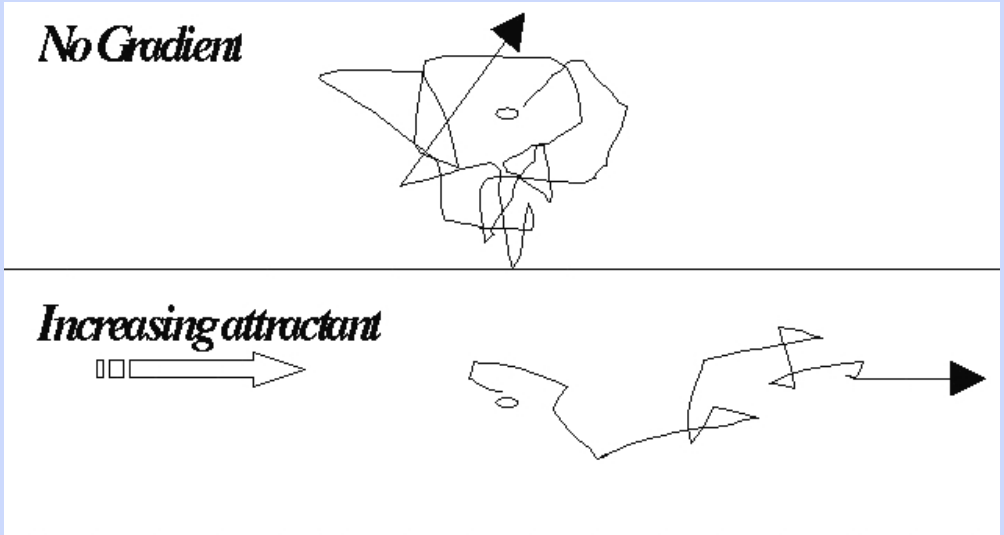




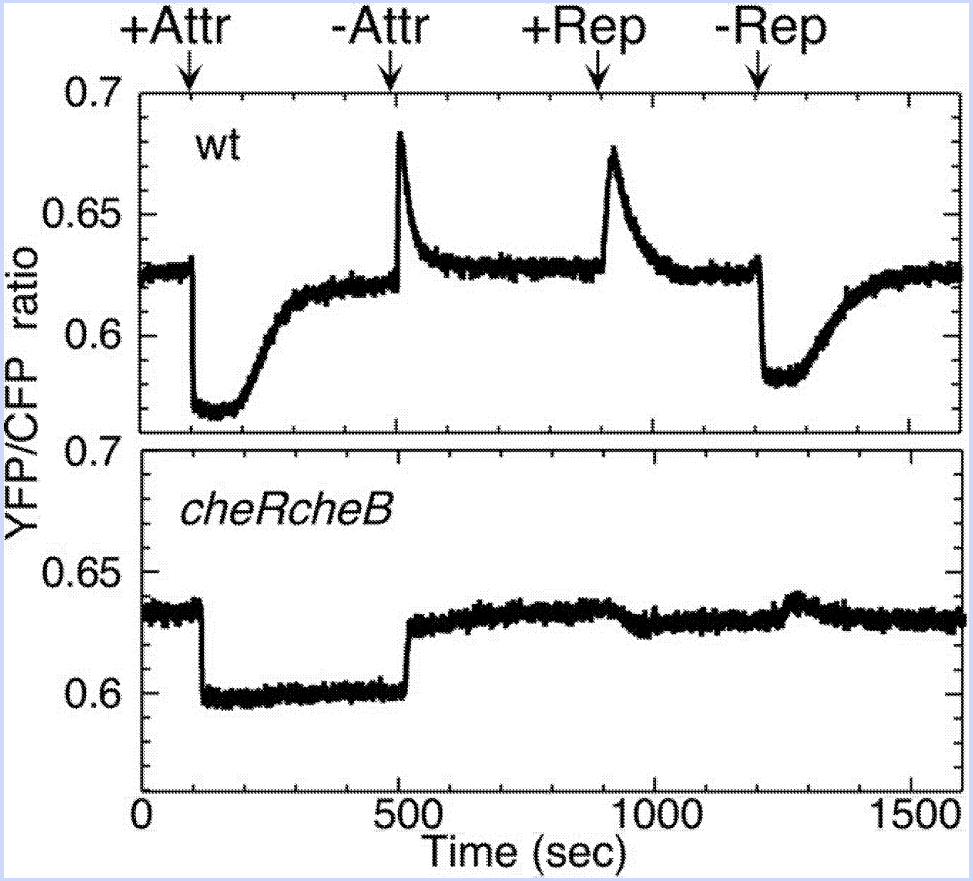
Counterclockwise rotation (CCW): 'runs'

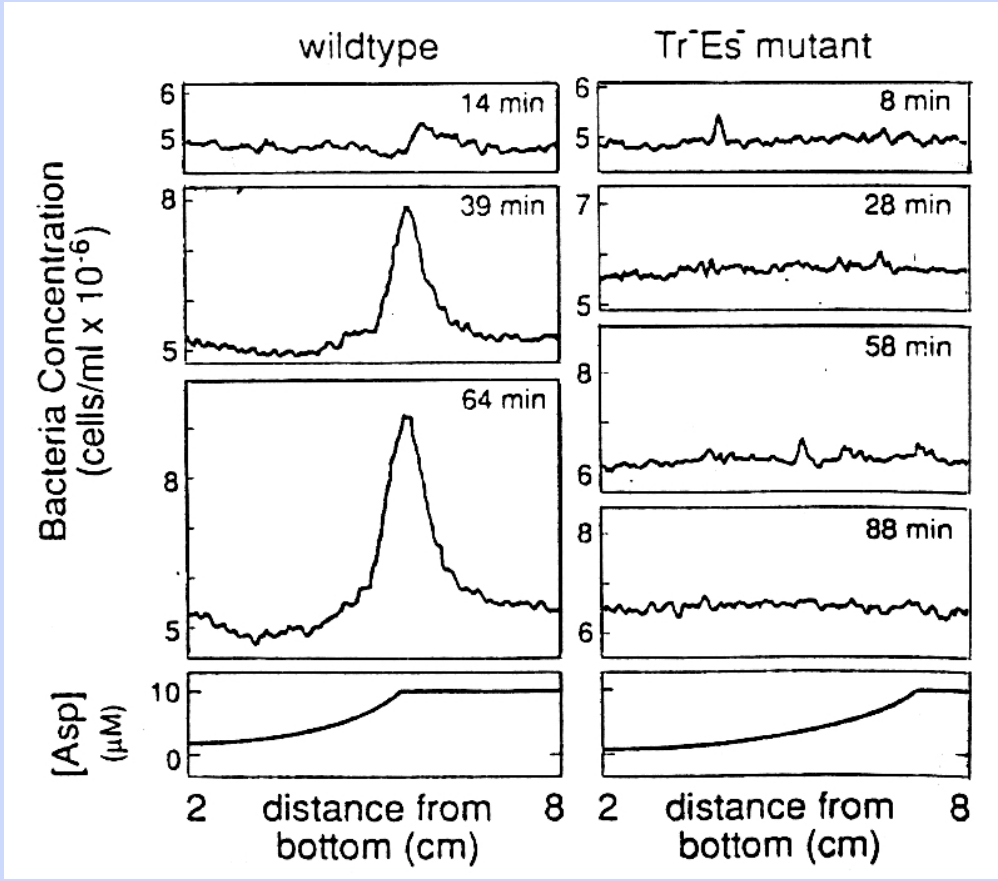
Clockwise rotation (CW) : 'tumbles'

Bias: Probability of CCW *i.e.,* probability of running



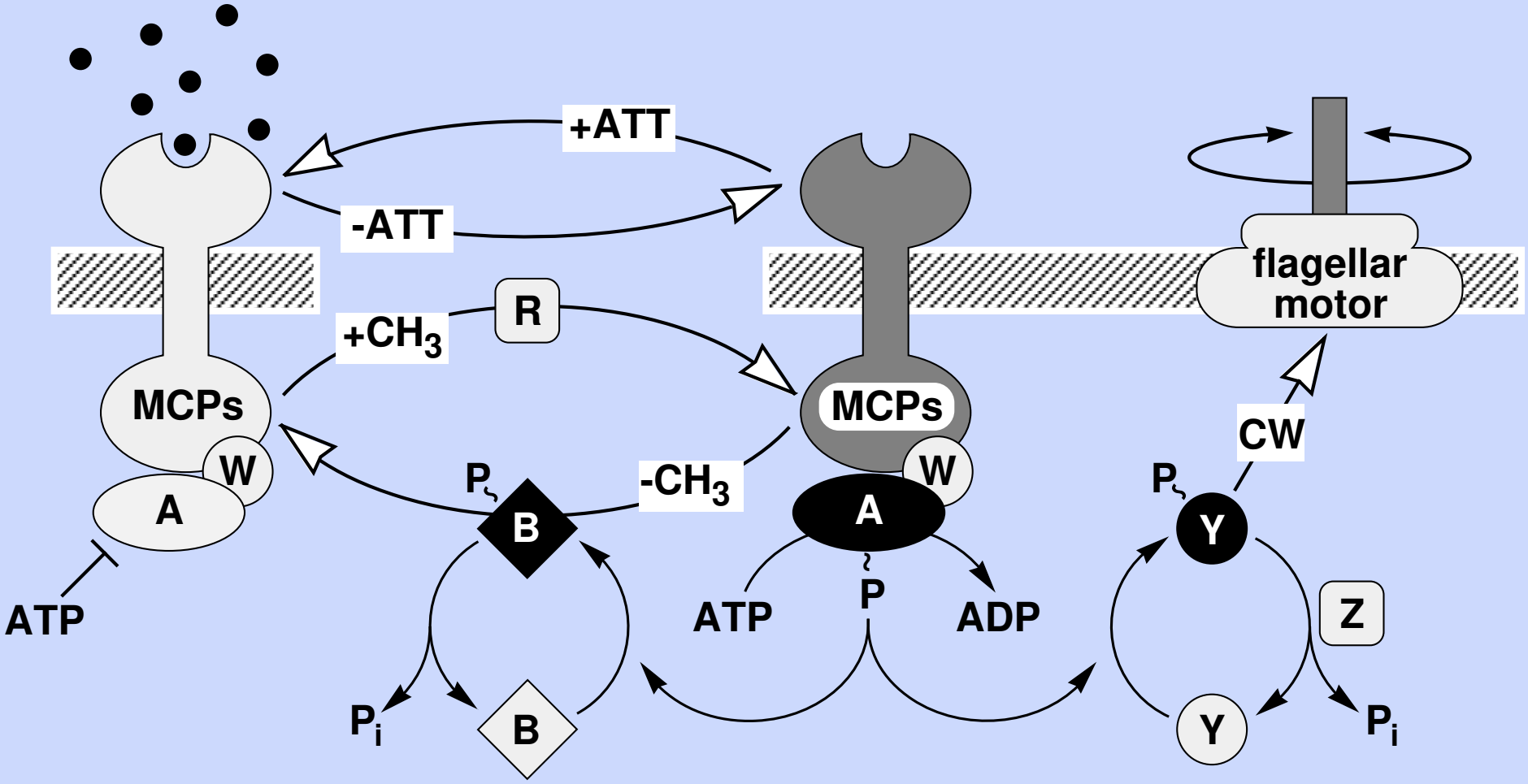
E. coli also adapt to constant stimuli





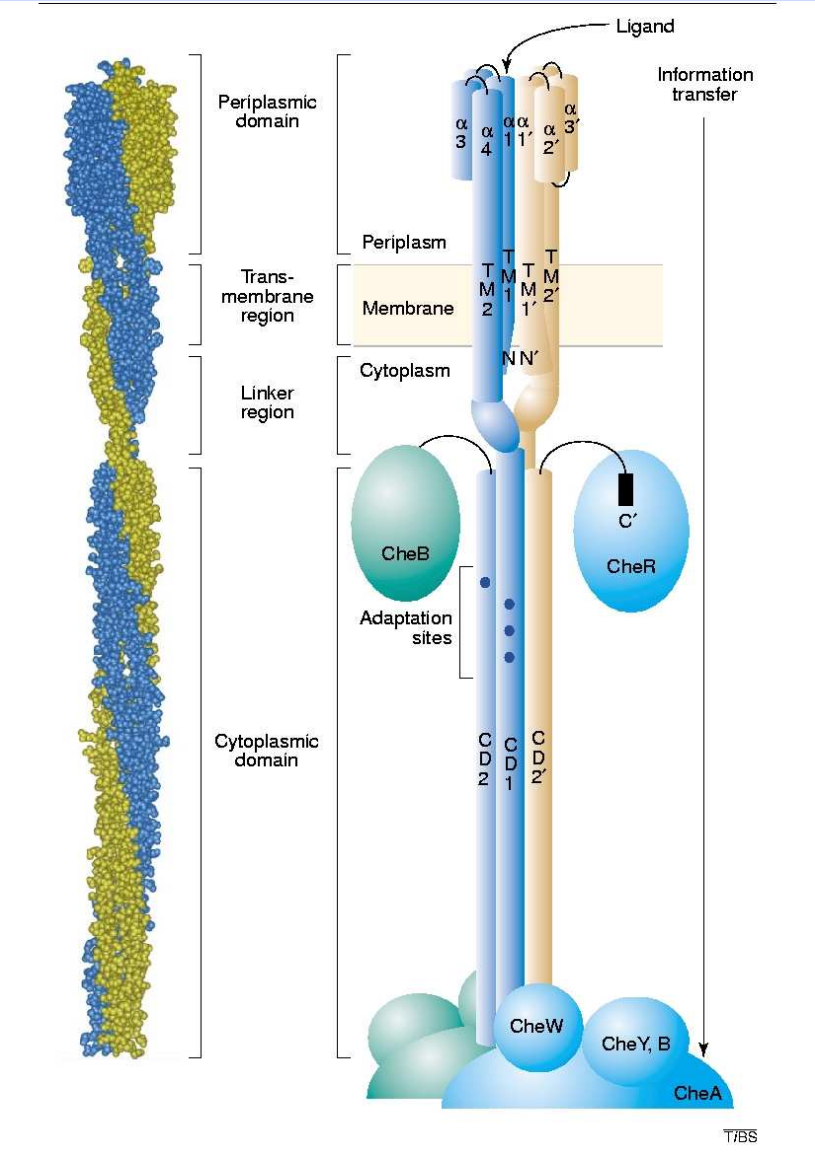
Clearly adaptation is essential for aggregation! This is probably also the case for *P. mirabilis* but is not the case for amoeboid cells; they can aggregate in steady gradients without adaptation, but not in periodic waves of attractant.

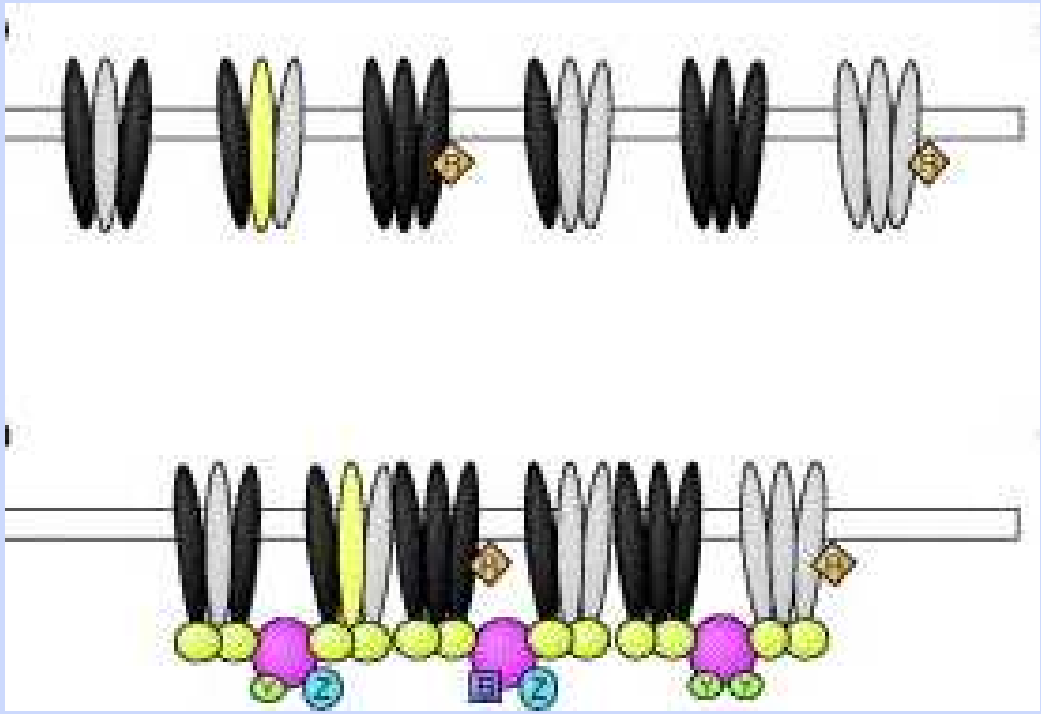
Signal transduction in *E. coli*

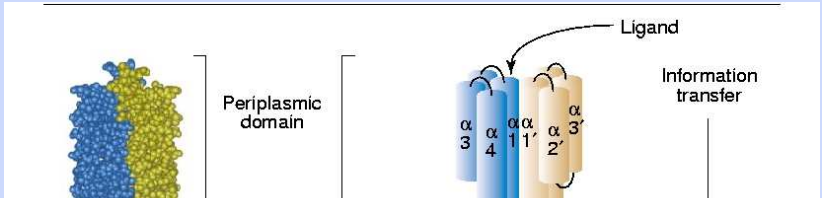


P. Spiro, et al., A model of excitation and adaptation in bacterial chemotaxis, PNAS, 94, 7263-7268, (1997).

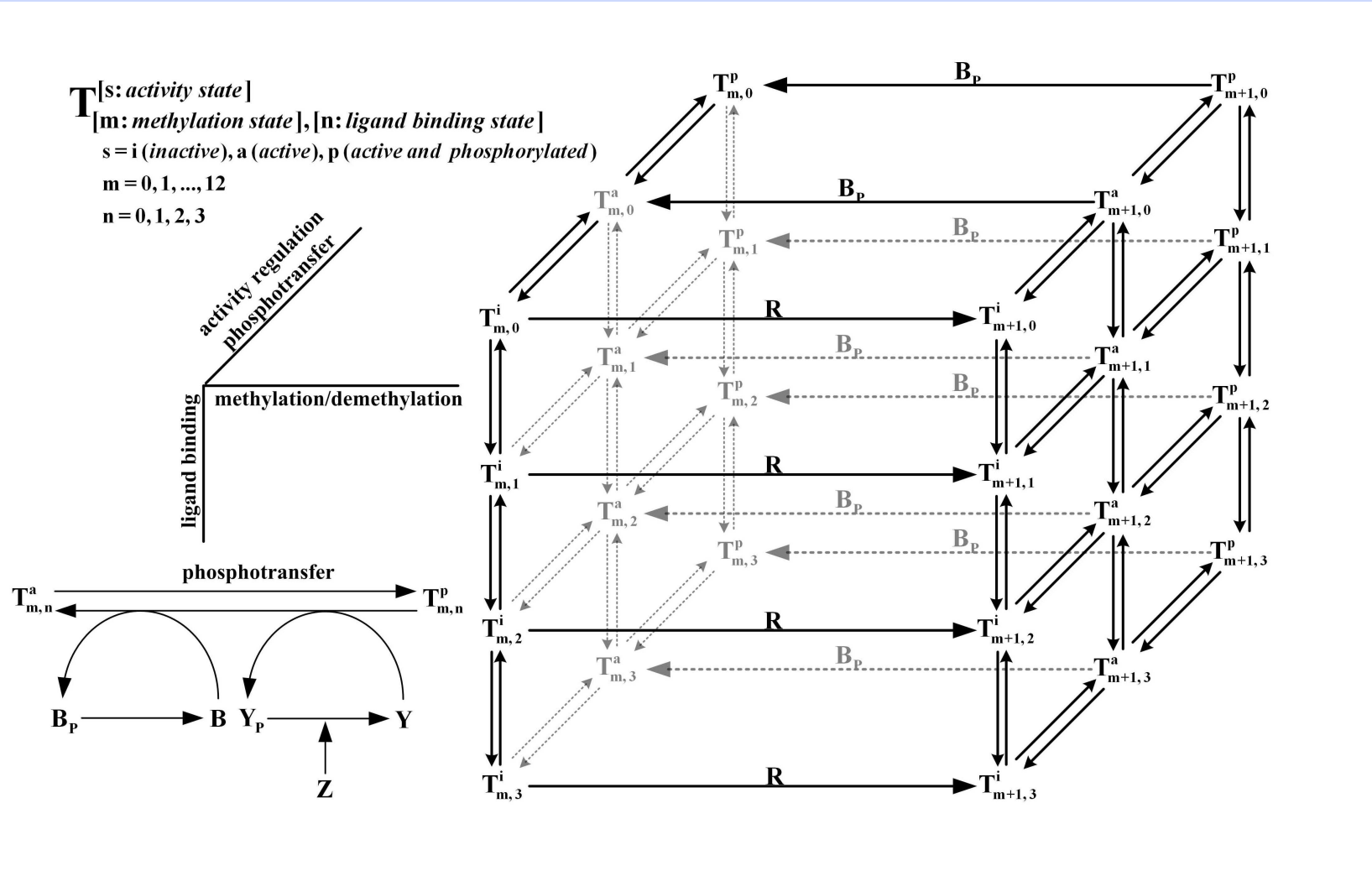
The Tar receptor







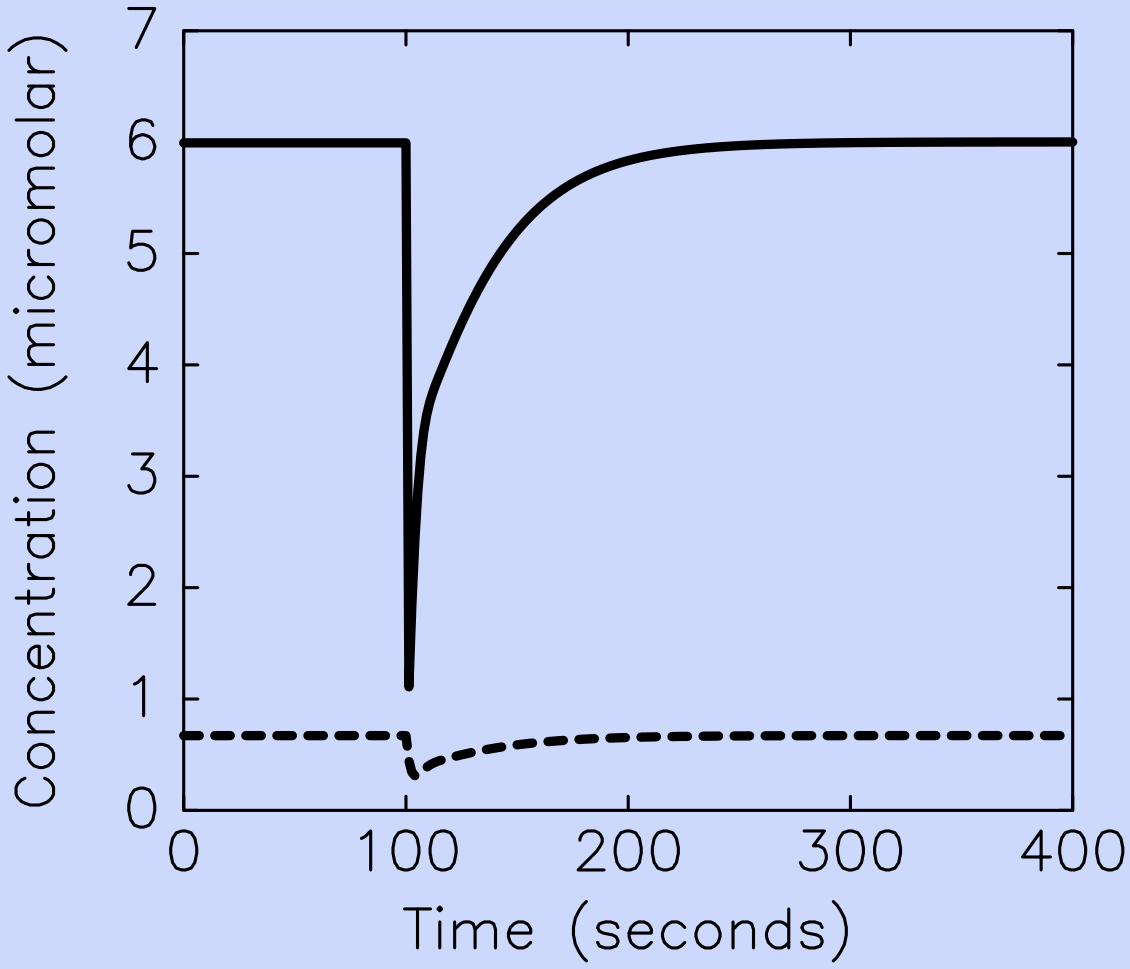
The underlying network



There are 158 variables, but on a relevant time scale this can be reduced to 16, and with some approximation, to 4.

Xiangrong Xin and Hans G. Othmer A 'trimer of dimers'- based model for the chemotactic signal transduction network in bacterial chemotaxis, Bull Math Biol (2012).

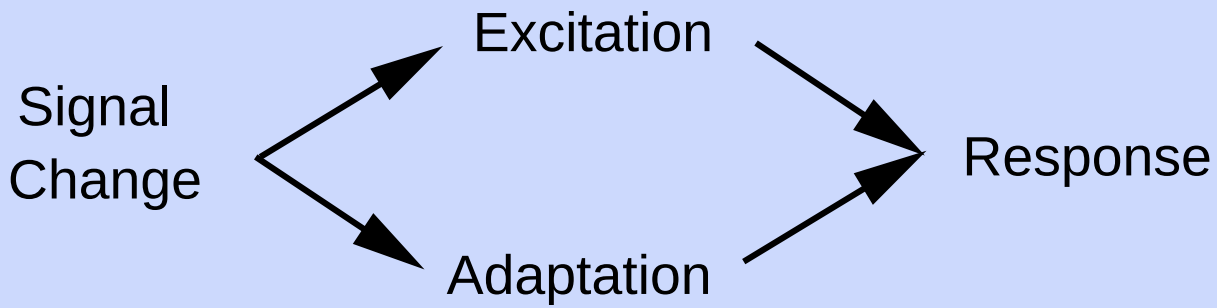
Simple response from a complex network



Even though the network is very complicated, the input-output behavior is very simple! This may be a common (and highly adaptive) phenomenon in signal transduction networks.

The big question is how to extract this from the full model!

A cartoon model for internal dynamics



$$\frac{dy_1}{d\tau} = \frac{g(S(\tau)) - (y_1 + y_2)}{\tau_E}, \qquad \frac{dy_2}{d\tau} = \frac{g(S(\tau)) - y_2}{\tau_A}, \qquad Response = h(y_1)$$

If $\tau_E << \tau_A$, then for $\tau >> \tau_E$, y_1 relaxes to $y_1 \sim \tau_A \dot{y}_2$. In a steady linear gradient of attractant

$$\frac{dS}{dt} = v \cdot \nabla S,$$

and $u \equiv \dot{y}_2$ is given by

$$u(T) = e^{-T/\tau_A} u(0) \pm \Omega f(T)$$

$$\Omega \equiv |v| S' \qquad f(T) = (1 - e^{-T/\tau_A})$$

Now we can see why adaptation is essential ..

For steps of fixed length we can write

$$u_n \equiv u(nT) = \lambda_0 u_{n-1} \pm \lambda_1$$

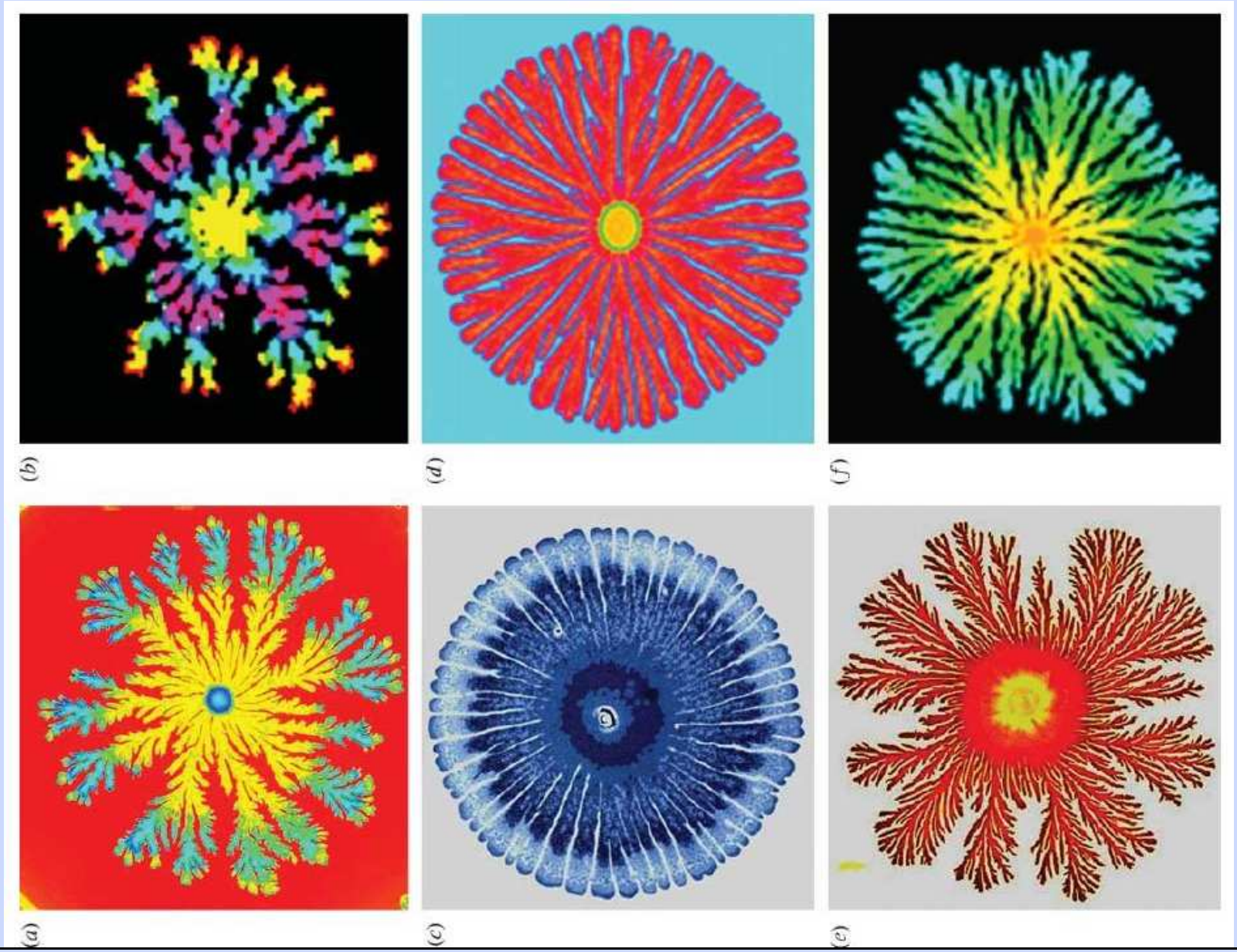
$$u_n = \lambda_0^n u_0 + \lambda_1 \left[\pm \lambda_0^{n-1} \pm \lambda_0^{n-2} + \cdots \pm \lambda_0 \right]$$

Consider two realizations, right-left and left-right:

$$\begin{aligned} u^-(2T) &= e^{-T/\tau_A} u^+(T) - \Omega f(T) \\ &= e^{-2T/\tau_A} u(0) - \Omega f^2(T) \end{aligned}$$

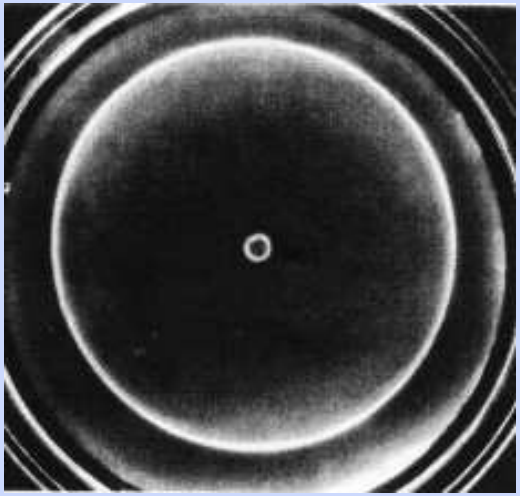
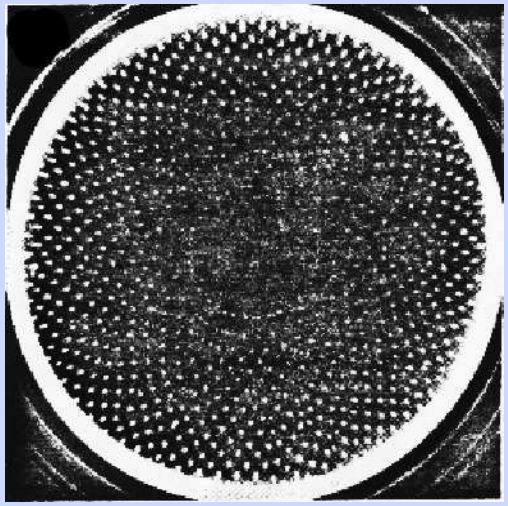
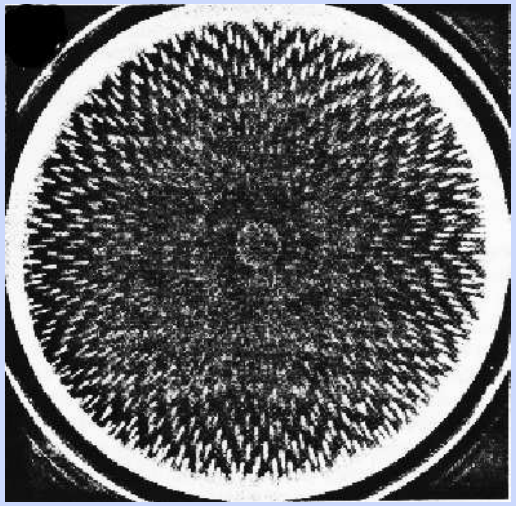
$$\begin{aligned} u^+(2T) &= e^{-T/\tau_A} u^-(T) + \Omega f(T) \\ &= e^{-2T/\tau_A} u(0) + \Omega f^2(T). \end{aligned}$$

Spatial pattern formation in bacteria



E. Ben-Jacob and H. Levine, Self-engineering capabilities of bacteria, J. R. Soc. Interface, 3, 197-214, (2006)

Pattern formation in *E. coli*

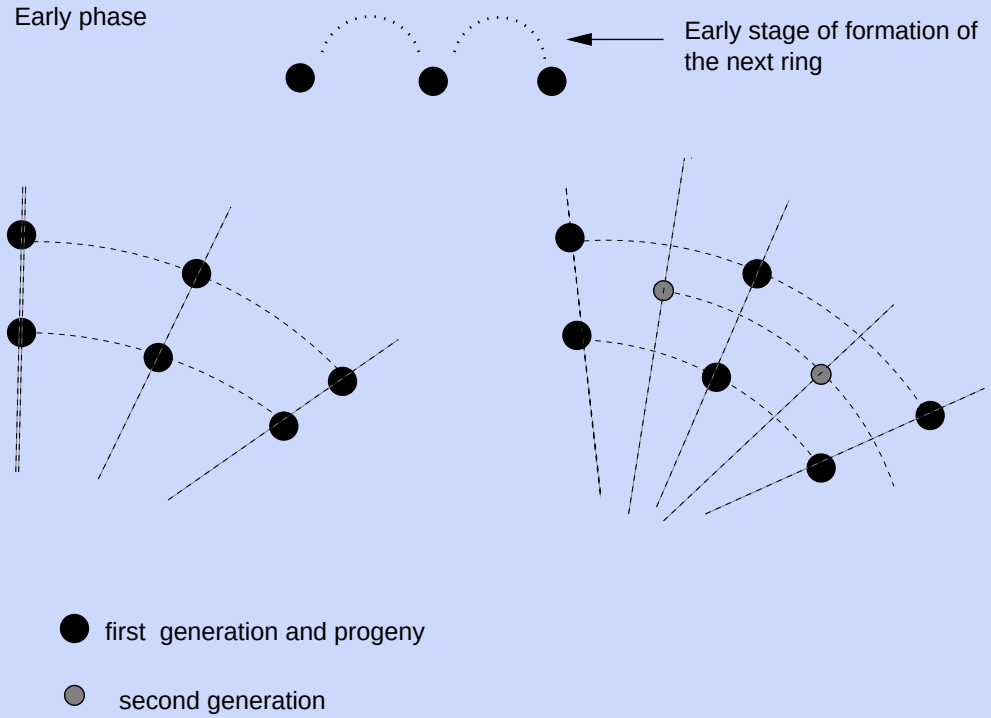




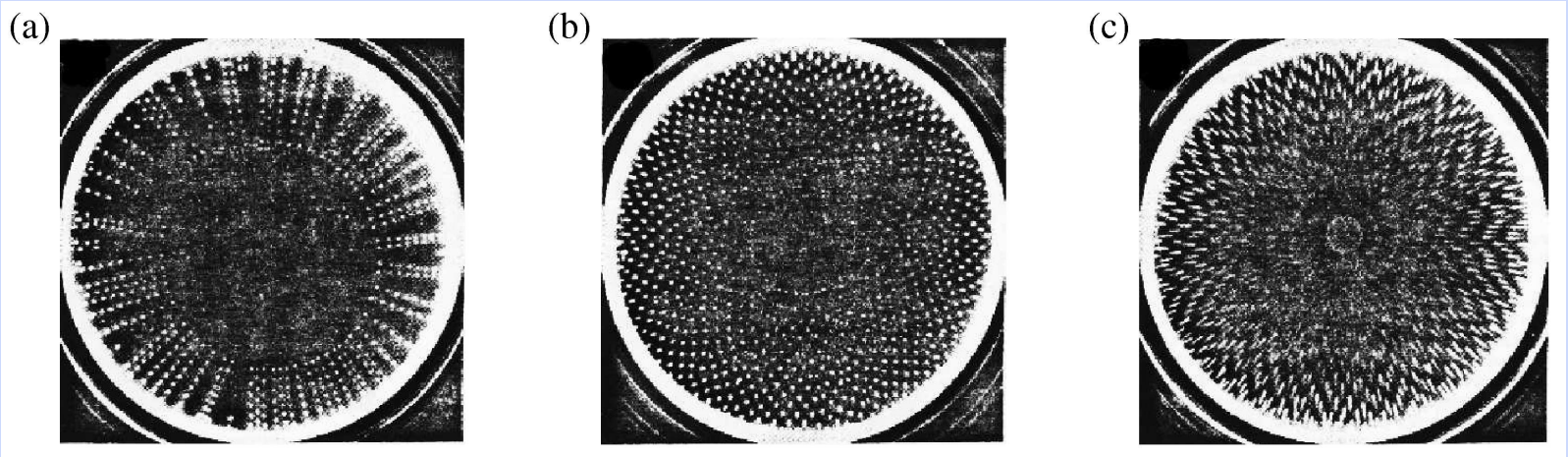
Basic experimental facts

- Cells are chemotactic towards aspartate; asp$^-$ cells do not aggregate
- Cells still use the ‘run-and-tumble’ strategy
- Cells can become nonmotile, which leads to stable spots
- Succinate is the primary carbon source
- Cells produce and secrete aspartate via the TCA cycle, but when starved they consume it
- Cells double every 2 hours

E. O. Budrene and H. C. Berg, Dynamics of formation of symmetrical patterns by chemotactic bacteria, Nature, 376, 49–53 (1995).

Spatial pattern formation in bacteria





E. O. Budrene and H. C. Berg – Complex patterns formed by motile cells of *E. coli* Nature 349 630-3 (1991).

Are cell-based computational models feasible?

- For a single bacterium certainly ! We have one ...
- What about for spatial patterns?

  Consider the Budrene-Berg experiments, and suppose we innoculate with 1000 cells in a spot. Cells divide every two hours, so after 3 days we have

  $$10^3 \cdot 2^{36} \quad \sim \quad \times 10^{15} \text{ cells}$$

  Suppose we also need 10 internal variables for each cell.

  Thus .....

  A Monte Carlo simulation of the stochastic process may be feasible for the first few division cycles, but certainly not later !!

- We need a higher-level description .....

The phenomenological approach to chemotaxis

Let $\Omega \subset R^n$ be compact with smooth boundary, let n be the 'particle' density, and let v be the 'attractant' density.

$$
\begin{aligned}
n_t &= \nabla \cdot (\nabla n - n \nabla \Phi(v)) \\
&= \nabla \cdot (\nabla n - n \chi \nabla v) \\
v_t &= D \Delta v + f(n, v) \\
& n_n = v_n = 0
\end{aligned}
$$

Chemotactic Sensitivity: $\chi \equiv \Phi_v(n, v, x, \dots)$

Chemotactic Velocity: $\mathbf{u}_c = \nabla \Phi = \chi \nabla v$

Fundamental question: Given a microscopic model of individual cells, how does one obtain the chemotactic sensitivity ?

A brief history of work on chemotaxis ..

(1) Patlak BMB (1952) - 'First' derivation of equations

(2) Keller/Segel JTB (1970) - Applications to bacterial chemotaxis

(3) Childress/Percus MBS (1981) - First analysis of blowup

(4) Alt (1982) Diffusion limits of a stochastic process

(5) Rivero, *et al.* (1989) Incorporation of adaptation

(6) Jager/Luckhaus, (1992) - Blowup

(7) Rascle/Ziti (1995) - Blowup

(7) Herrero/Velazquez (1996) - Blowup

(7) Othmer/Stevens (1997) - Aggregation/blowup w/o diffusion of attractant

(9) Hillen/Othmer (2000,02) - Diffusion limits of the velocity-jump process

(10) Stevens (2000) - Derivation from interacting particle systems

(11) Dirk Horstmann (2003) Jahresber. Deutsch. Math.-Verein.,— review articles

12) Erban /Othmer (2004,2005) - Embedding microscopic behavior into macroscopic equations

(13) Erban, Othmer, Kevrekidis (2006)- A new computational approach to particle systems

(14) Dolak/Schmeiser (2004), Erban /Othmer (2007) The 'back-of-the-wave' problem

(15) Xue/Othmer (2009) A new moment method

Most of these do not address the question of how one embeds microscopic (e.g, cell-level) behavior into macroscopic equations, or they do so phenomenologically!

A 1D example of a velocity-jump process

$$\frac{\partial p^+}{\partial t} + \frac{\partial (s^+ p^+)}{\partial x} = -\lambda^+ p^+ + \lambda^- p^- \qquad x \in (0, L)$$

$$\frac{\partial p^-}{\partial t} - \frac{\partial (s^- p^-)}{\partial x} = \lambda^+ p^+ - \lambda^- p^- .$$

Case I: λ and $s^\pm = s =$ const $\quad p \equiv p^+ + p^- \quad j \equiv (s^+ p^+ - s^- p^-)\ \lambda^+ = \lambda^-$

$$\frac{\partial p}{\partial t} + \frac{\partial j}{\partial x} = 0$$

$$\frac{\partial j}{\partial t} + 2\lambda j = -s^+ \frac{\partial}{\partial x}(s^+ p^+) - s^- \frac{\partial}{\partial x}(s^- p^-) + \lambda(s^+ p^- - s^- p^+)$$

$$\boxed{\frac{\partial^2 p}{\partial t^2} + 2\lambda \frac{\partial p}{\partial t} = s^2 \frac{\partial^2 p}{\partial x^2}}$$

The diffusion equation results by formally taking the limit $\lambda \to \infty, s \to \infty$ with $s^2/\lambda \equiv 2D$ constant, but this can be made more precise.

Reduction to a diffusion process

The solution when the spatial domain is the entire line is

$$p(x,t) = \begin{cases} \dfrac{e^{-\lambda t}}{2}\left(\delta(x-st)+\delta(x+st)+\dfrac{\lambda}{s}\left[I_0(\Lambda)+\dfrac{\lambda t}{\Lambda}I_1(\Lambda)\right]\right) & |x|<st \\ 0 & |x|>st \end{cases}$$

Here I_0 and I_1 are modified Bessel functions of the first kind. If we make use of the asymptotic expansions

$$I_0(z) = \frac{e^z}{\sqrt{2\pi z}} + \mathcal{O}\left(\frac{1}{z}\right) \qquad I_1(z) = \frac{e^z}{\sqrt{2\pi z}} + \mathcal{O}\left(\frac{1}{z}\right) \qquad \text{as } z \to \infty$$

we see that

$$p(x,t) = \frac{1}{\sqrt{4\pi Dt}} e^{-\dfrac{x^2}{4Dt}} + e^{-\lambda t}\mathcal{O}(\xi^2) \qquad \xi^2 \equiv (x/st)^2$$

Reduction to a diffusion process

Thus the telegraph process reduces to a diffusion process on short space scales and long time scales. This fact was known to Einstein and this process has since been studied by many.
If we define $\tau = \epsilon^2 t$ and $\xi = \epsilon x$, where ϵ is a small parameter, then we obtain

$$\epsilon^2 \frac{\partial^2 n}{\partial \tau^2} + 2\lambda \frac{\partial n}{\partial \tau} = s^2 \frac{\partial^2 n}{\partial \xi^2}. \tag{1}$$

The diffusion regime defined by the exact solution now becomes

$$\frac{x}{st} = \epsilon \frac{\xi}{s\tau}$$

and this requires only that $\xi/(s\tau) \leq \mathcal{O}(1)$. This shows that the approximation of the telegraph process by a diffusion process hinges on the appropriate relation between the space and time scales, not necessarily on the limit of speed and turning rate tending to infinity

Theorem For Neumann data on the boundary there are no nonconstant time-invariant solutions when the speed and turning rate are constant.

Other cases

Case II: λ constant, speed dependent on direction

Here one finds that the time-independent solutions are given by

$$p^+(x) = \left[\frac{s^+(0)p^+(0)}{s^+(x)}\right] e^{\lambda \int_0^x \frac{s^+ - s^-}{s^+ s^-} d\xi} \equiv p^+(0)F^+(x),$$

$$p^-(x) = \left[\frac{s^+(0)p^+(0)}{s^-(x)}\right] e^{\lambda \int_0^x \frac{s^+ - s^-}{s^+ s^-} d\xi} \equiv p^+(0)F^-(x).$$

where the constant $p^+(0)$ is determined by the conservation of walkers. Clearly the flux vanishes pointwise, as it must at steady state. It is also clear that these distributions differ if $s^+(x) \neq s^-(x)$.

However there is no evidence that the bacterial speed changes with direction.

Other cases

Case III: constant speed, $\lambda^+ \neq \lambda^-$

$$\lambda^{\pm} = \frac{\lambda^+ + \lambda^-}{2} \pm \frac{\lambda^+ - \lambda^-}{2} \equiv \lambda_0 \pm \lambda_1$$

$$\boxed{\begin{aligned} \frac{\partial p}{\partial t} + \frac{\partial j}{\partial x} &= 0 \\ \frac{\partial j}{\partial t} + 2\lambda_0 j &= -s^2 \frac{\partial p}{\partial x} - 2s\lambda_1 p \end{aligned}}$$

As $t \to \infty$

$$p(x,t) \to \frac{N_0 e^{-\frac{2}{s}\int_0^x \lambda_1(\xi)d\xi}}{\int_0^1 e^{-\frac{2}{s}\int_0^x \lambda_1(\xi)d\xi} dx}$$

Chemotactic velocity:

$$\boxed{u_c = -\frac{s\lambda_1}{\lambda_0}}$$

The transport equation for a velocity-jump process

The transport equation in the absence of internal dynamics and signals

$$\frac{\partial}{\partial t}p(x,v,t) + v \cdot \nabla p(x,v,t) = -\lambda_0 p(x,v,t) + \lambda_0 \int_V T(v,v')p(x,v',t)dv' \quad (2)$$

$$= -\lambda_0 p(x,v,t) + \mathcal{T}p(x,v,t) \equiv \mathcal{L}p(x,v,t) \quad (3)$$

G. C Papanicolaou – Asymptotic analysis of transport processes, Bull. AMS, 81, 330-392 (1975).

- Identify the correct time and space scalings for the parabolic limit so that there are new time and space scales for which $\tau = \epsilon^2 t \qquad \xi = \epsilon x$
- Analyze the spectral properties of the turning operator $\mathcal{L}$
- Construct the outer solution:

$$p(\xi,\tau,v) = \sum_{k=0}^{\infty} \epsilon^k p_k(\xi,\tau,v)$$

The time and space scales for bacteria

We estimate a diffusion time scale as

$$\tau_{DIFF} \sim \frac{L^2}{D} = \frac{L^2 \lambda}{s^2}.$$

We can also define a characteristic drift time as

$$\tau_{DRIFT} = \frac{L}{s},$$

and we assume that the space scale L is such that the time scales are related as follows:

$$\tau_{RUN} \equiv \lambda^{-1} \ll \tau_{DRIFT} \ll \tau_{DIFF}. \tag{4}$$

For example, a characteristic speed for bacteria such as *E. coli* is $10 - 20\mu/\mathrm{sec}$, and $\lambda^{-1} \sim \mathcal{O}(1)$ second. On a length scale of 1 mm, $\tau_{DRIFT} \sim 50 - 100\,\mathrm{seconds}$ and $\tau_{DIFF} \sim 2500 - 10^4\,\mathrm{seconds}$. Therefore we have $\tau_{RUN} \sim \mathcal{O}(1)$ on the dimensional scale, and

$$\begin{aligned} \tau_{DRIFT} &\sim O(1/\epsilon), \\ \tau_{DIFF} &\sim O(1/\epsilon^2), \end{aligned}$$

Some technical hypotheses on $\mathcal{T}$

(T1) $T(v,v') \geq 0, \quad \int_V T(v,v')dv = 1, \quad$ and $\quad \int_V \int_V T^2(v,v')dv'dv < \infty$.

(T2) *There are functions u_0, ϕ, and $\psi \in \mathcal{K}$ with the properties that $u_0 \not\equiv 0$ and ϕ and ψ vanish at most on a set of Lebesgue measure zero, and such that for all $(v,v') \in V \times V$*

$$u_0(v)\phi(v') \leq \ T(v',v) \ \leq u_0(v)\psi(v').$$

(T3) $\|\mathcal{T}\|_{\langle 1 \rangle^\perp} < 1$, where $\langle 1 \rangle^\perp$ is the orthogonal complement in $L^2(V)$ of the span of 1.

(T4) $\int_V T(v,v')dv' = 1$

The effect of all these conditions is to make $\mathcal{L}_0$ a Perron-Froebenius operator, so that we can prove the following.

Theorem

Define $\mu_2 \equiv \lambda_0 \left(1 - \|\mathcal{T}\|_{\langle 1 \rangle^\perp}\right)$

Assume **(T1)-(T4)**; then

1. 0 is a simple eigenvalue of $\mathcal{L}_0$ and the corresponding eigenfunction is $\phi(v) \equiv 1$.
2. All nonzero eigenvalues satisfy $-2\lambda_0 < \text{Re } \mu \leq -\mu_2 < 0$, and to within scalar multiples there is no other positive eigenfunction.
3. There is a decomposition $L^2(V) = \langle 1 \rangle \oplus \langle 1 \rangle^\perp$.
4. $\|\mathcal{L}_0\|_{\mathbf{L}(L^2(V), L^2(V))} \leq 2\lambda_0$.
5. $\mathcal{L}_0$ restricted to $\langle 1 \rangle^\perp \subset L^2(V)$ has an inverse $\mathcal{F}_0$ with norm

$$\|\mathcal{F}_0\|_{\mathbf{L}(\langle 1 \rangle^\perp, \langle 1 \rangle^\perp)} \leq \frac{1}{\mu_2}.$$

The rest is easy!

$$\frac{\partial p(x,v,t)}{\partial t} + v \cdot \nabla p(x,v,t) = -\lambda_0 p(x,v,t) + \lambda_0 \int_V T(v,v') p(t,x,v') dv'$$

$$\tau = \epsilon^2 t \qquad \xi = \epsilon x, \qquad p = p_0 + \epsilon p_1 + \epsilon^2 p_2 + \epsilon^n \cdots$$

$$\begin{aligned}
\epsilon^0 : \qquad \mathcal{L}_0 p_0 &\equiv -\lambda_0 p_0 + \lambda_0 \int_V T(\mathbf{v},\mathbf{v}') p_0 dv' = 0 \\
\epsilon^1 : \qquad \mathcal{L}_0 p_1 &= v \cdot \nabla p_0 \\
\epsilon^2 : \qquad \mathcal{L}_0 p_2 &= \frac{\partial p_0}{\partial \tau} + v \cdot \nabla p_1
\end{aligned}$$

$$\mathcal{L}_0 p_1 = v \cdot \nabla p_0 : \qquad \int_V (v \cdot \nabla p_0) dv = 0,$$

$$\boxed{p_1 = \mathcal{F}_0 \left(v \cdot \nabla p_0 \right)}$$

$$\mathcal{L}_0 p_2 = \frac{\partial p_0}{\partial \tau} + v \cdot \nabla p_1 : \qquad \int_V \left[\frac{\partial p_0}{\partial \tau} + v \cdot \nabla \left(\mathcal{F}_0 \left(v \cdot \nabla p_0 \right) \right) \right] dv = 0$$

$$\frac{\partial n_0}{\partial \tau} = \nabla \cdot \left(D \nabla n_0 \right)$$

Diffusion tensor:

$$D \equiv \frac{1}{\omega} \int_V v \mathcal{F}_0 v dv$$

If $T(\mathbf{v}, \mathbf{v}') = 1/\omega, \omega = |V|$ i.e. the redistribution is uniform, then

$$D = \frac{1}{\omega} \int_V \frac{vv}{\lambda_0} dv = \frac{s^2}{\lambda_0 n} I$$

General results

One can

- *prove in general that the diffusion tensor is positive definite*
- *derive necessary and sufficient conditions for* $D = \delta I$
- *derive error estimates for the diffusion approximation*
- add bias in the turning kernel to obtain the classical chemotaxis equation

1. Thomas Hillen and H. G. Othmer, SIAM JAM, 61, 751-775, (2000).
2. H. G. Othmer and T. Hillen, SIAM JAM, 62, 1222-1250, (2002).

The parabolic limit

Assume (T1)-(T4), and for $k \geq 2$ define $p_0, p_1, ..., p_k$ via :

$$(a1) \qquad \frac{\partial p_0}{\partial \tau} = \nabla \cdot \big(D \nabla p_0\big) \qquad\qquad p_0(\xi, 0) = \int_V p(\xi, v, 0) dv$$

$$(a2) \qquad \int_V p_j(\xi, v, \tau) dv = 0, \text{ for all } 1 \leq j \leq k,$$

$$(a3) \qquad \int_V v\, p_j(\xi, v, \tau) dv = 0, \text{ for all } 2 \leq j \leq k,$$

$$(a4) \qquad p_j(\xi, v, \tau) \equiv \mathcal{F}(p_{j-2,\tau} + v \cdot \nabla p_{j-1}), \text{ for all } 2 \leq j \leq k,$$

Then for each $\vartheta/\epsilon^2 < t < \infty$ and each $x \in \Omega$, $\quad q_k \equiv \sum_{j=0}^{k} \epsilon^j p_j$ satisfies

$$\|p(x, ., t) - q_k(x, ., t)\|^2_{L^2(V)} \leq C\, \epsilon^{k+1}$$

where C depends on μ_2, ω, powers of s of highest order $2k$ and on C_0.

The jump process with internal states and forces

Suppose that the internal variables $y \subset R^m$ involved in signal transduction evolve according the equations

$$\frac{dy}{dt} = f(y, S)$$

where S is the external signal. Inclusion of internal state variables y and external forces F in the jump process leads to the following transport equation.

$$\frac{\partial}{\partial t}p(x, v, y, t) + \ v \cdot \nabla_x p(x, v, y, t) + \ \nabla_v \cdot (Fp(x, v, y, t))$$

$$+\nabla_y \cdot (f_i(y, S)p(x, v, y, t)) = -\lambda(y)p(x, v, y, t) + \lambda(y) \int_V T_0(v, v', y)p(x, v', y2, t)dv'$$

The micro to macro step via moments

Assumptions

- Use the cartoon two-variable model described previously.
- Assume that excitation is fast, and define $z_2 = y_2 - S(x)$.
- Scale time and space as before, and assume that the turning rate depends on z_2.

Then we have to solve

$$\epsilon^2 \frac{\partial p}{\partial t} + \epsilon \nabla_x \cdot (vp) + \frac{\partial}{\partial z_2}\left(-\frac{z_2}{t_a} - G'(S)\left(\epsilon \nabla S \cdot v + \epsilon^2 \frac{\partial S}{\partial t}\right) p\right)$$

$$= (\lambda_0 + a_1 z_2 + a_2 z_2^2 + \cdots)\left(-p + \int_V T(v, v') p(v')\, dv'\right)$$

Moments

Define internal state moments as follows.

$$M_j = \int z_2^j \, p \, dz_2 \quad \forall \, j = 0, 1, 2, 3, \ldots, \qquad M = (M_0, M_1, M_2, \ldots)^t.$$

$$\epsilon^2 \frac{\partial}{\partial t} \mathbf{\Lambda M} + \epsilon \mathbf{v} \cdot \nabla_x \mathbf{\Lambda M} = \epsilon^2 \mathbf{B M} + \epsilon \mathbf{C M} + \mathbf{D M}.$$

Here

$$\mathbf{B} = -G'(S) \frac{\partial S}{\partial t} \mathbf{J}^t, \qquad \mathbf{C} = -G'(S)(\nabla S \cdot \mathbf{v}) \mathbf{J}^t,$$

and

$$\mathbf{D} = -\frac{1}{t_a} \text{diag}\,\{0, 1, 1, \ldots\} + \mathcal{L}\mathbf{\Lambda}(\lambda_0 \mathbf{I} + a_1 \mathbf{J} + a_2 \mathbf{J}^2 + \cdots),$$

where $\mathcal{L}$ is the turning operator, $\mathbf{\Lambda} : l^\infty(L^2(V)) \to l^\infty(L^2(V))$ is a diagonal scaling operator $\mathbf{\Lambda} = \text{diag}\left\{1, 1, \frac{1}{2}, \frac{1}{3}, \cdots\right\}$, and $\mathbf{J} : l^\infty(L^2(V)) \to l^\infty(L^2(V))$ is the shift operator.

The asymptotic analysis

Write $\mathbf{M}$ as an expansion in powers of ϵ as

$$\mathbf{M} = \mathbf{M}^0 + \epsilon \mathbf{M}^1 + \epsilon^2 \mathbf{M}^2 + \cdots$$

Define:

$$D_n = -\frac{1}{|V|\lambda_0} \int_V v \otimes \mathcal{B}v \, dv$$

and

$$\chi(S) = -\frac{a_1 t_a}{|V|\lambda_0} G'(S) \int_V v \otimes (t_a \lambda_0 \mathcal{L} - 1)^{-1} v dv,$$

For unbiased re-orientation

$$T(v, v') = \frac{1}{|V|}.$$

and

$$D_n = \frac{s^2}{N\lambda_0} I, \qquad \chi(S) = G'(S) \frac{a_1 s^2 t_a}{N\lambda_0(1 + t_a\lambda_0)}.$$

The classical chemotaxis equation

$$\frac{\partial n}{\partial t} = \nabla_x \cdot \left(\frac{s^2}{N\lambda_0} \nabla_x n - G'(S) \frac{a_1 s^2 t_a}{N\lambda_0(1 + t_a\lambda_0)} n \nabla_x S \right).$$

If we include finite excitation time and directional persistence we obtain

$$\chi(S) = \frac{a_1 t_a}{|V|\lambda_0} G'(S) \int_V v \otimes (t_e\lambda_0\mathcal{A} - 1)^{-1} (t_a\lambda_0\mathcal{A} - 1)^{-1} v dv,$$

and this reduces to

$$\chi(S) = \frac{a_1 s^2 t_a G'(S)}{N\lambda_0(1 + (1 - \psi_d)t_a\lambda_0)(1 + (1 - \psi_d)t_e\lambda_0)}.$$

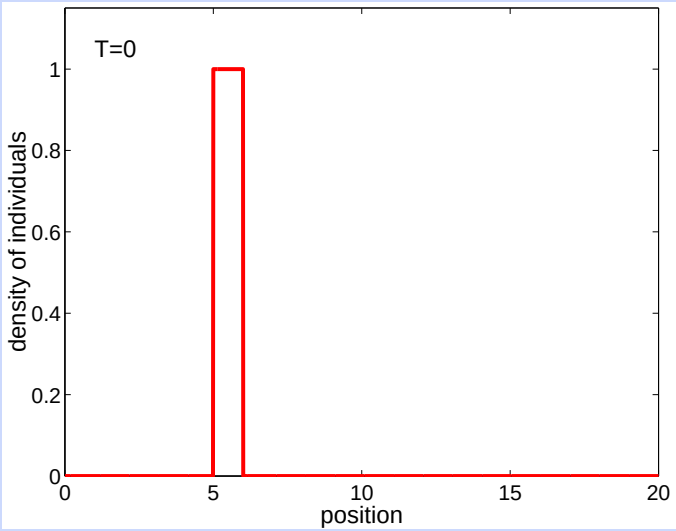
Thus

$$\frac{\partial}{\partial t} n = \nabla \cdot \left(\frac{s^2}{N(1 - \psi_d)\lambda_0} \nabla n - \frac{a_1 s^2 t_a G'(S)}{N\lambda_0(1 + (1 - \psi_d)t_a\lambda_0)(1 + (1 - \psi_d)t_e\lambda_0)} n \nabla S \right)$$

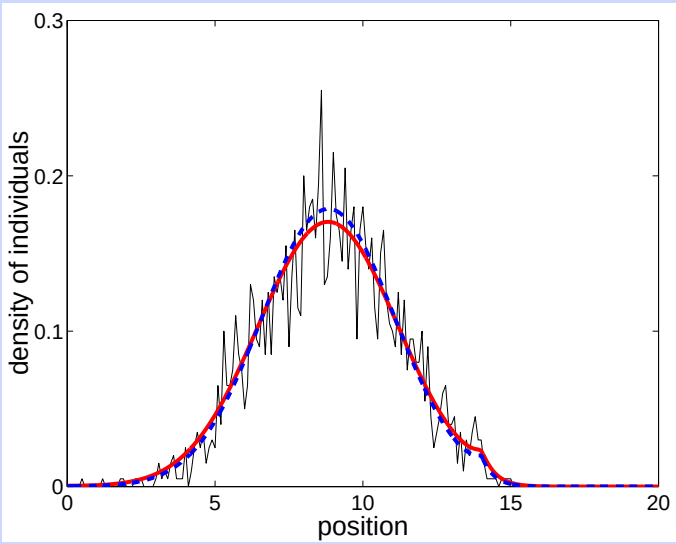
C. Xue and H. G. Othmer Multiscale models of taxis-driven patterning in bacterial populations, SIAM JAM, 70, 1, 133-167, (2009).

Numerical results

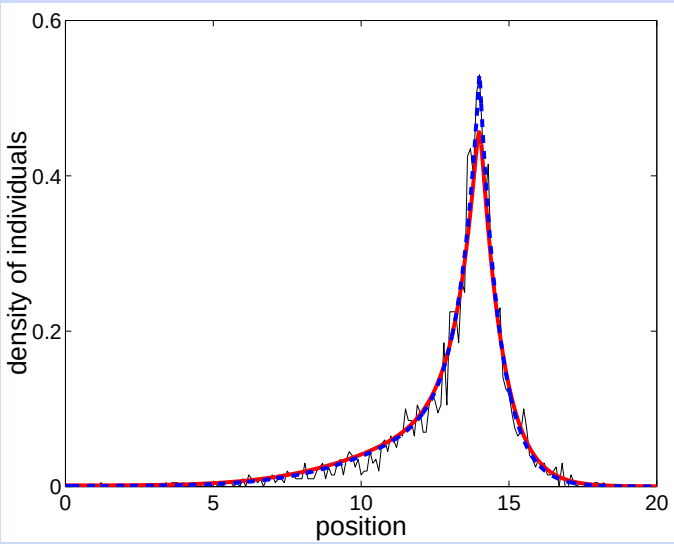
T=0



T=500



T=1500



black: stochastic simulation of the velocity jump process

red: macroscopic moment equations (and hyperbolic chemotaxis equation)

blue: classical chemotaxis equation

R. Erban and H. G. Othmer, SIAM JAM, 65, 361-391 , (2004).

R. Erban and H. G. Othmer, Multiscale Modeling and Simulation, 3, 362-394, (2005).

Conclusions ..

- For simple systems such as bacteria one can derive PKS equations from the transport equation with internal state variables, and thereby derive the chemotactic sensitivity in terms of characteristics of the microscopic motion.

- For amoeboid cells such as Dd, its harder to obtain reduced equations, but the moment equations reflect the population-level behavior well.

- Whether PKS can be obtained from the transport equations is still open ...