Pathway-based mean-field models for E.Coli chemotaxis

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Joint work with
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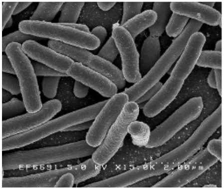
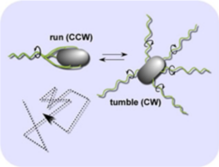
Movement

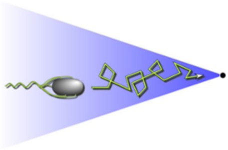
E. coli, most studied, most understood



- $0.5\mu m \times 2\mu m$, rod shape, $5-10$ flagella
- 4500 gene, 50 genes related to chemotaxis
- replicate every 20–30 minutes, $20\mu m/s$



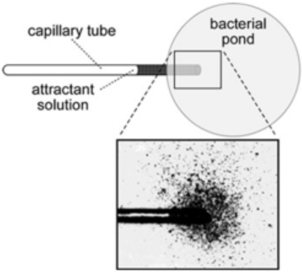
Tumble

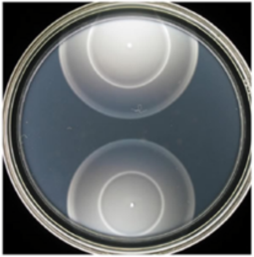


Run

E.coli Chemotaxis

- **Chemotaxis:** the migration of cells toward attractant chemical or away from repellent.





[Pfeffer et al. 1880s]; [Adler,1969]

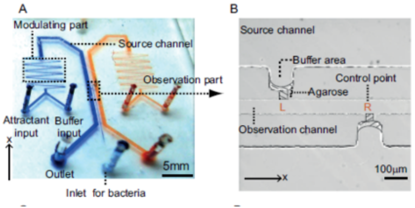
- **Population** level model for E.coli chemotaxis, Keller and Segel, 1970.

$$\frac{\partial n}{\partial t} = \nabla \cdot (\mu(s)\nabla n) - \nabla \cdot (\kappa(s) n \nabla s) + g(n,s) - h(n,s)$$
$$\frac{\partial s}{\partial t} = D\Delta s - f(n,s)$$

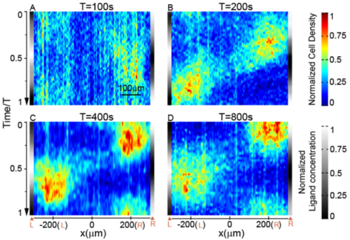
New experiments

X. Zhu, G. Si, N. Deng, Q. Ouyang, T. Wu, Z. He, L. Jiang, C. Luo, and Y. Tu, Phys. Rev. Lett. 108, 128101 (2012).

- **The devices**



- **Observations**

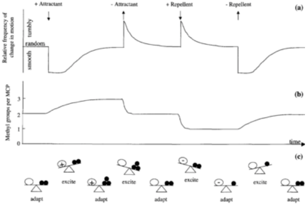


Outline

1. Chemotatic sensory system of E.coli
2. The transport model for E. coli collective motion
3. Derivation of the mean field model
4. The keller-Segel limit and physical impacts
5. Discussion and Future work

Intracellular signaling pathways

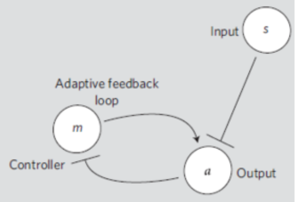
- Temporal sensing: excitation and adaptation

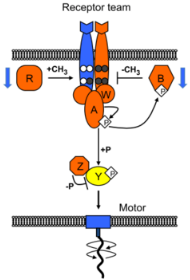


- E. coli chemotaxis network

Sourjik, V. and Berg, H. (2002). PNAS

Cluzel, P. , Surette, M. , Leibler S. (2000) Science





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The transport model $\partial_t P = -\mathbf{v} \cdot \partial_{\mathbf{x}} P - \partial_m (f(a)P) + Q(P, z)$.

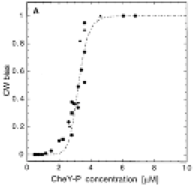
- $P(t, \mathbf{x}, \mathbf{v}, m)$ is the **probability density function** of bacteria at **time** t, **position x**, moving with the **velocity v** and **methylation level** m.
- $a(m, [L])$ is the receptor activity.
- $Q(p, z)$ is the tumbling term

$$Q(P,z) = \int_\Omega z(a, \mathbf{v}, \mathbf{v}')P(t, \mathbf{x}, \mathbf{v}', m)d\mathbf{v}' - \int_\Omega z(a, \mathbf{v}', \mathbf{v})d\mathbf{v}' P(t, \mathbf{x}, \mathbf{v}, m),$$

- $z(a)$ is the tumbling rate function

$$z = z_0 + \tau^{-1}(a/a_0)^H$$

z_0 rotational diffusion,
H Hill coefficient,
τ average run time



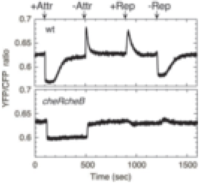
A great many works done by H. Othmer and his collaborators on a linear model for methylation dynamics.

Intracelluar adaptation dynamics

- **Dynamics of the methylation level:**

$$\frac{dm}{dt} = f(a) = k_R(1 - a/a_0)$$

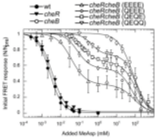
k_R the methylation rate,
a_0 the receptor preferred activity



- **The receptor activity:**

$$a = \left(1 + \exp(NE)\right)^{-1}$$

The free energy



$$E = -\alpha(m - m_0) + f_0([L]),$$

$$f_0([L]) = \ln\left(\frac{1 + [L]/K_I}{1 + [L]/K_A}\right).$$

N, m_0, K_I, K_A represent respectively the number of tightly coupled receptors, the base methylation level, dissociation constant for inactive and active receptors.

Purposes

- Look for easily simulated models – moment system?
- Can explain the new experimental observation?
  SPECS, L. Jiang, Q. Ouyang, and Y. Tu, PLoS Comput. Biol. 6, e1000735 (2010)
- Relations with Keller-Segel equations?

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One dimensional model[1]

- **The two flux model:**

$$\frac{\partial P^+}{\partial t} = -\frac{\partial (v_0 P^+)}{\partial x} - \frac{\partial (f(a)P^+)}{\partial m} - \frac{z(m)}{2}(P^+ - P^-),$$
$$\frac{\partial P^-}{\partial t} = \frac{\partial (v_0 P^-)}{\partial x} - \frac{\partial (f(a)P^-)}{\partial m} + \frac{z(m)}{2}(P^+ - P^-).$$

Each single cell of E. coli moves either in the "+" or "−" direction with a constant velocity v_0.

- **Macroscopic quantities:** Density ρ, density flux J_ρ, momentum q, momentum flux J_q

$$\rho(x,t) = \int (P^+ + P^-)dm, \quad J_\rho(x,t) = \int v_0(P^+ - P^-)dm;$$
$$q(x,t) = \int m(P^+ + P^-)dm, \quad J_q(x,t) = \int v_0 m(P^+ - P^-)dm.$$

[1] Si-Tang-Y., SIAM MMS, 2015

Model derivation I

- The continuity equation:

$$\frac{\partial \rho}{\partial t} + \frac{\partial J_\rho}{\partial x} = 0$$

- The equation for density flux J_ρ:

$$\begin{aligned}
\frac{\partial J_\rho}{\partial t} &= -v_0^2 \frac{\partial \rho}{\partial x} - v_0 \int z(m)(P^+ - P^-)\,\mathrm{d}m \\
&\approx -v_0^2 \frac{\partial \rho}{\partial x} - v_0 \int \left(z(M) + \frac{\partial z}{\partial m}\Big|_{m=M} (m - M) \right)(P^+ - P^-)\,\mathrm{d}m \\
&= -v_0^2 \frac{\partial \rho}{\partial x} - Z J_\rho + \frac{\partial Z}{\partial m} M J_\rho - \frac{\partial Z}{\partial m} J_q,
\end{aligned}$$

Assumption

We need the following conditions to close the moment system,

$$\int (m - M)^2 P^{\pm}\,\mathrm{d}m \ll 1,$$

Model derivation II

- The momentum equation

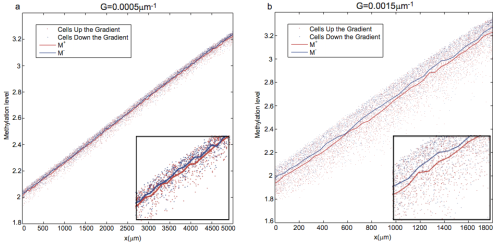
$$\begin{aligned}\frac{\partial q}{\partial t} &= -\frac{\partial J_q}{\partial x} + \int f(a)(P^+ + P^-)\,\mathrm{d}m \\ &\approx -\frac{\partial J_q}{\partial x} + \int \left(f(a)|_{m=M} + \frac{\partial f}{\partial m}\Big|_{m=M}(m-M)\right)(P^+ + P^-)\,\mathrm{d}m \\ &= -\frac{\partial J_q}{\partial x} + F\rho + \frac{\partial F}{\partial m}(q - M\rho) \\ &= -\frac{\partial J_q}{\partial x} + F\rho,\end{aligned}$$

- The equation for momentum flux

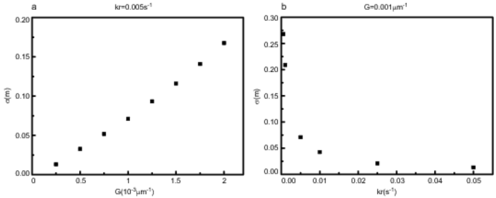
$$\frac{\partial J_q}{\partial t} = -v_0^2\frac{\partial q}{\partial x} + FJ_\rho + \frac{\partial F}{\partial m}(J_q - MJ_\rho) - ZJ_q - \frac{\partial Z}{\partial m}M(J_q - MJ_\rho).$$

Assumption justification

Numerical evidence: if $K_I \ll [L] \ll K_A$, $f_0[L] \approx \ln([L]/K_I)$,
Let $[L] = [L]_0 \exp(Gx)$, effect of G:



The variance with respect to G and the adaptation rate k_R:



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The parabolic scaling

$$\varepsilon = (z_0 + \tau^{-1})^{-1}, \quad Z = Z_\varepsilon/\varepsilon, \quad \text{and} \quad t \to t/\varepsilon.$$

The system becomes

$$\varepsilon \frac{\partial \rho}{\partial t} = -\frac{\partial J_\rho}{\partial x},$$
$$\varepsilon \frac{\partial J_\rho}{\partial t} = -v_0^2 \frac{\partial \rho}{\partial x} - \frac{Z_\varepsilon}{\varepsilon} J_\rho + \frac{1}{\varepsilon}\frac{\partial Z_\varepsilon}{\partial m}(MJ_\rho - J_q),$$
$$\varepsilon \frac{\partial q}{\partial t} = -\frac{\partial J_q}{\partial x} + F\rho,$$
$$\varepsilon \frac{\partial J_q}{\partial t} = -v_0^2 \frac{\partial q}{\partial x} + FJ_q + \frac{\partial F}{\partial m}(J_q - MJ_\rho) - \frac{Z_\varepsilon}{\varepsilon} J_q - \frac{1}{\varepsilon}\frac{\partial Z_\varepsilon}{\partial m} M(J_q - MJ_\rho).$$

The asymptotic expansion

$$\rho = \rho^{(0)} + \varepsilon\rho^{(1)} + \cdots, \qquad J_\rho = J_\rho^{(0)} + \varepsilon J_\rho^{(1)} + \cdots;$$
$$q = q^{(0)} + \varepsilon q^{(1)} + \cdots, \qquad J_q = J_q^{(0)} + \varepsilon J_q^{(1)} + \cdots;$$
$$M = M^{(0)} + \varepsilon M^{(1)} + \cdots, \quad F = F^{(0)} + \varepsilon F^{(1)} + \cdots.$$

The Keller Segel equation

$$\varepsilon = (z_0 + \tau^{-1})^{-1}, \quad Z = Z_\varepsilon/\varepsilon, \quad \text{and} \quad t \to t/\varepsilon.$$

The system becomes

$$\varepsilon \frac{\partial \rho}{\partial t} = -\frac{\partial J_\rho}{\partial x},$$
$$\varepsilon \frac{\partial J_\rho}{\partial t} = -v_0^2 \frac{\partial \rho}{\partial x} - \frac{Z_\varepsilon}{\varepsilon} J_\rho + \frac{1}{\varepsilon}\frac{\partial Z_\varepsilon}{\partial m}(MJ_\rho - J_q),$$
$$\varepsilon \frac{\partial q}{\partial t} = -\frac{\partial J_q}{\partial x} + F\rho,$$
$$\varepsilon \frac{\partial J_q}{\partial t} = -v_0^2 \frac{\partial q}{\partial x} + FJ_q + \frac{\partial F}{\partial m}(J_q - MJ_\rho) - \frac{Z_\varepsilon}{\varepsilon} J_q - \frac{1}{\varepsilon}\frac{\partial Z_\varepsilon}{\partial m} M(J_q - MJ_\rho).$$

The Keller Segel limit

$$\frac{\partial \rho^{(0)}}{\partial t} = v_0^2 \frac{\partial}{\partial x}\left(Z_\varepsilon^{-1}\frac{\partial \rho^{(0)}}{\partial x}\right) - v_0^2 \frac{\partial}{\partial x}\left(Z_\varepsilon^{-2}\frac{\partial Z_\varepsilon}{\partial m}\frac{\partial M^{(0)}}{\partial x}\rho^{(0)}\right).$$

One model used in experiments

G. Si, T. Wu, Q. Ouyang, and Y. Tu, A pathway-based mean-field model for Escherichia coli chemotaxis, Phys. Rev. Lett. 109 (2012), 048101.

$$\frac{\partial \rho}{\partial t} = -\frac{\partial J}{\partial x},$$
$$\frac{\partial J}{\partial t} \approx -v_0^2 \frac{\partial \rho}{\partial x} - ZJ - v_0 \frac{\partial Z}{\partial M} \Delta M \rho,$$
$$\frac{\partial M}{\partial t} \approx F - \frac{J}{\rho}\frac{\partial M}{\partial x} - \frac{1}{\rho}\frac{\partial}{\partial x}(v_0 \Delta M \rho),$$

under the physical assumption $\Delta M \approx -\frac{\partial M}{\partial x} Z^{-1} v_0$.

$\rho(t,x)$ density,
$J(t,x)$ the density current,
$M(t,x)$ the averaged methylation,
$\Delta M(t,x)$ methylation deviation.

Assumption

Define the drift velocity $v_d = J/\rho$, we assumes

$$v_d \ll v_0.$$

Under this assumption

$$MJ_\rho - J_q \approx -v_0 \Delta M \rho, \qquad Z >> \left| \frac{1}{\rho}\frac{\partial J}{\partial x} + \frac{\partial F}{\partial m} \right|$$

The equation for momentum flux becomes

$$v_0 \rho \frac{\partial \Delta M}{\partial t} \approx \frac{J^2}{\rho}\frac{\partial M}{\partial x} + \frac{J}{\rho}\frac{\partial}{\partial x}(v_0 \rho \Delta M) + v_0 \Delta M \frac{\partial J}{\partial x} - v_0^2 \rho \frac{\partial M}{\partial x} + v_0 \rho \Delta M \left(\frac{\partial F}{\partial M} - Z \right).$$

$$\Delta M = v_0 \frac{\partial M}{\partial x} \frac{1}{\frac{1}{\rho}\frac{\partial J}{\partial x} + \frac{\partial F}{\partial m} - Z} \Rightarrow \Delta M \approx -\frac{\partial M}{\partial x} Z^{-1} v_0.$$

Methylation dynamics for different driving periods

$T = 80$ $T = 1200$

Augmented Keller-Segel equations[2]

The system consists of an equation for the bacteria density ρ with drift velocity and diffusion coefficients determined by the macroscopic average methylation level M governed by an additional dynamic equation:

$$\frac{\partial \rho}{\partial t} = v_0^2 \frac{\partial}{\partial x}\left(Z^{-1}\frac{\partial \rho}{\partial x}\right) - v_0^2 \frac{\partial}{\partial x}\left(Z^{-2}\frac{\partial Z}{\partial m}\frac{\partial M}{\partial x}\rho\right);$$

$$\frac{\partial M}{\partial t} = \kappa F.$$

Advantage:

- can explain the experimental observation of phase-shift between the maxima of ligand concentration and density of *E. coli* in fast-varying environments at the population level;
- a necessary complement to the original PBMFT where the phase-shift can only be modeled by moment systems.

[2] Li-Tang-Y., CMS, accepted.

Oriented moment system

Denote the right (left)-traveling densities: $\int p^+ \,\mathrm{d}m$ and the right (left)-oriented moments of methylation m: $\int mp^+ \,\mathrm{d}m$ as ρ^+ (ρ^-) and q^+ (q^-) respectively. They satisfy the following four-equation hyperbolic system:

$$
\begin{aligned}
\frac{\partial \rho^+}{\partial t} &= -v_0 \frac{\partial \rho^+}{\partial x} - \frac{1}{2}\left(Z^+\rho^+ - Z^-\rho^-\right), \\
\frac{\partial \rho^-}{\partial t} &= v_0 \frac{\partial \rho^-}{\partial x} + \frac{1}{2}\left(Z^+\rho^+ - Z^-\rho^-\right), \\
\frac{\partial q^+}{\partial t} &= -v_0 \frac{\partial q^+}{\partial x} + F^+\rho^+ - \frac{1}{2}\left(Z^+q^+ - Z^-q^-\right), \\
\frac{\partial q^-}{\partial t} &= v_0 \frac{\partial q^-}{\partial x} + F^-\rho^- + \frac{1}{2}\left(Z^+q^+ - Z^-q^-\right).
\end{aligned}
$$

Here $M^\pm = q^\pm/\rho^\pm$ is the right (left) oriented average methylation level, and $F^\pm = F\left(a(M^\pm, [L])\right)$, $Z^\pm = Z\left(a(M^\pm, [L])\right)$.

Asymptotic scaling

Long time, strong tumbling frequency, but a separation of time-scales on methylation.

$$\varepsilon\frac{\partial\rho^+}{\partial t} = -v_0\frac{\partial\rho^+}{\partial x} - \frac{1}{2\varepsilon}\left(Z^+\rho^+ - Z^-\rho^-\right),$$

$$\varepsilon\frac{\partial\rho^-}{\partial t} = v_0\frac{\partial\rho^-}{\partial x} + \frac{1}{2\varepsilon}\left(Z^+\rho^+ - Z^-\rho^-\right),$$

$$\kappa\rho^+\frac{\partial M^+}{\partial t} + \varepsilon M^+\frac{\partial\rho^+}{\partial t} = -v_0\frac{\partial q^+}{\partial x} + F^+\rho^+ - \frac{1}{2\varepsilon}\left(M^+Z^+\rho^+ - M^-Z^-\rho^-\right),$$

$$\kappa\rho^-\frac{\partial M^-}{\partial t} + \varepsilon M^-\frac{\partial\rho^-}{\partial t} = v_0\frac{\partial q^-}{\partial x} + F^-\rho^- + \frac{1}{2\varepsilon}\left(M^+Z^+\rho^+ - M^-Z^-\rho^-\right).$$

Derivation

Consider the following asymptotic expansion

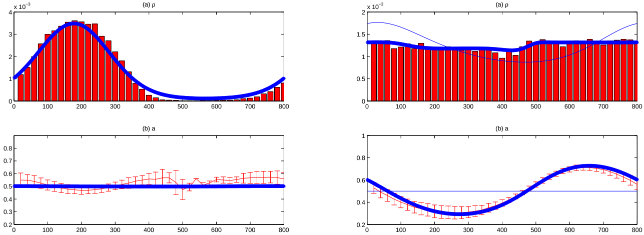
$$\rho^{\pm} = \rho^{\pm(0)} + \varepsilon \rho^{\pm(1)} + \cdots, \qquad q^{\pm} = q^{\pm(0)} + \varepsilon q^{\pm(1)} + \cdots,$$
$$F^{\pm} = F^{\pm(0)} + \varepsilon F^{\pm(1)} + \cdots, \qquad Z^{\pm} = Z^{\pm(0)} + \varepsilon Z^{\pm(1)} + \cdots,$$
$$M^{\pm} = M^{\pm(0)} + \varepsilon M^{\pm(1)} + \cdots.$$

Matching at the orders of ε gives

$$\frac{\partial \rho}{\partial t} = v_0^2 \frac{\partial}{\partial x}\left(Z^{-1} \frac{\partial \rho}{\partial x} \right) - v_0^2 \frac{\partial}{\partial x}\left(Z^{-2} \frac{\partial Z}{\partial m} \frac{\partial M}{\partial x} \rho \right);$$
$$\frac{\partial M}{\partial t} = \kappa F.$$

Numerical comparison to SPECS[3]

Parameters for E.coli chemotaxis are $\alpha = 1.7$, $m_0 = 1$, $K_I = 18.2\mu M$, $K_A = 3mM$, $N = 6$, $k_R = 0.01s^{-1}$, $a_0 = 0.5$, $z_0 = 0.14s^{-1}$, $\tau = 0.8s$, $H = 10$. 20000 cells are simulated in SPECS. Parameters for the environment used here are $[L]_0 = 500\mu M$, $[L]_A = 100\mu M$, $\lambda = 800\mu m$. The steady state profiles of ρ (top) and $a(M)$ (bottom) are presented.
Left: $u = 0.4\mu m/s$; Right: $u = 8\mu m/s$.



[3] Jiang-Ouyang-Tu, PLoS Comput. Biol., (2010)

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High order moment system

Further introduce

$$e(x,t) = \int (m-M)^2 (P^+ + P^-)\,\mathrm{d}m, \qquad J_e(x,t) = v_0 \int (m-M)^2 (P^+ - P^-)\,\mathrm{d}m$$

Find a system of six variables ρ, q, e, J_ρ, J_q and J_e.

$$\begin{aligned}
\frac{\partial \rho}{\partial t} &= \frac{\partial J_\rho}{\partial x}, \\
\frac{\partial J_\rho}{\partial t} &= -v_0^2 \frac{\partial \rho}{\partial x} - Z J_\rho + \frac{\partial Z}{\partial m} M J_\rho - \frac{\partial Z}{\partial m} J_q - \frac{1}{2} \frac{\partial^2 Z}{\partial m^2} J_e, \\
\frac{\partial q}{\partial t} &= -\frac{\partial J_q}{\partial x} + F\rho + \frac{1}{2} \frac{\partial^2 F}{\partial m^2} e, \\
\frac{\partial J_q}{\partial t} &= -v_0^2 \frac{\partial q}{\partial x} + F J_\rho + \frac{\partial F}{\partial m} (J_q - M J_\rho) - Z J_q - \frac{\partial Z}{\partial m} M (J_q - M J_\rho) \\
&\quad - \frac{1}{2} \Big(-\frac{\partial^2 F}{\partial m^2} + M \frac{\partial^2 Z}{\partial m^2} + 2 \frac{\partial Z}{\partial m} \Big) J_e, \\
\frac{\partial (e + Mq)}{\partial t} &= -\frac{\partial (J_e + 2 M J_q - M^2 J_\rho)}{\partial x} + 2 M F \rho + \big(M \frac{\partial^2 F}{\partial m^2} + 2 \frac{\partial F}{\partial m} \big) e, \\
\frac{\partial (J_e + 2 M J_q - M^2 J_\rho)}{\partial t} &= -v_0^2 \frac{\partial (e + Mq)}{\partial x} + 2 M F J_\rho + 2 \big(M \frac{\partial F}{\partial m} + F \big) (J_q - M J_\rho) + \big(M \frac{\partial^2 F}{\partial m^2} + 2 \frac{\partial F}{\partial m} \big) J_e \\
&\quad - M^2 Z J_\rho - \big(2 M Z + M^2 \frac{\partial Z}{\partial m} \big) (J_q - M J_\rho) - \frac{1}{2} \big(\frac{\partial^2 Z}{\partial m^2} M^2 + 4 M \frac{\partial Z}{\partial m} + 2 Z \big) J_e.
\end{aligned}$$

Two dimensional model

In two dimensions, $\boldsymbol{v} = v_0(\cos\theta, \sin\theta)$. The tumbling term

$$\begin{aligned} Q(P,z) &= \fint_V z(m,[L],\theta,\theta')P(t,\mathbf{x},\theta',m)\,\mathrm{d}\theta' \\ &\quad - \fint_V z(m,[L],\theta',\theta)\,\mathrm{d}\theta' P(t,\mathbf{x},\theta,m), \end{aligned}$$

$$g(t,\mathbf{x},\theta) = \int P(t,\mathbf{x},\theta,m)\,\mathrm{d}m; \qquad h(t,\mathbf{x},\theta) = \int mP(t,\mathbf{x},\theta,m)\,\mathrm{d}m$$

$$M(t,\mathbf{x},\theta) = \frac{h(t,\mathbf{x},\theta)}{g(t,\mathbf{x},\theta)}, \qquad \overline{M}(t,\mathbf{x}) = \frac{\int_V h(t,\mathbf{x},\theta)\,\mathrm{d}\theta}{\int_V g(t,\mathbf{x},\theta)\,\mathrm{d}\theta}.$$

We define the density, density flux, momentum, and momentum flux

$$\rho(t,\mathbf{x}) = \fint_V g(t,\mathbf{x},\theta)\,\mathrm{d}\theta, \quad J_\rho(t,\mathbf{x}) = \fint_V \mathbf{v}g(t,\mathbf{x},\theta)\,\mathrm{d}\theta;$$

$$q(t,\mathbf{x}) = \fint_V h(t,\mathbf{x},\theta)\,\mathrm{d}\theta, \quad J_q(t,\mathbf{x}) = \fint_V \mathbf{v}h(t,\mathbf{x},\theta)\,\mathrm{d}\theta.$$

Two dimensional moment closure

Assumption

$$P(t,\mathbf{x},\theta,m) = g(t,\mathbf{x},\theta)\delta\big(m - M(t,\mathbf{x},\theta)\big).$$

$$\frac{\partial \rho(t,\mathbf{x})}{\partial t} = -\partial_{\mathbf{x}} \cdot J_\rho.$$

$$\frac{\partial J_\rho}{\partial t} = -\int_V \mathbf{v} \otimes \mathbf{v} \partial_{\mathbf{x}} g \, \mathrm{d}\theta - Z J_\rho - \frac{\partial Z}{\partial M}\big(J_q - \overline{M} J_\rho\big),$$

$$\frac{\partial q(\mathbf{x},t)}{\partial t} = -\partial_{\mathbf{x}} J_q + F\rho.$$

$$\frac{\partial J_q}{\partial t} == -\int_V \mathbf{v} \otimes \mathbf{v} \partial_{\mathbf{x}} h \, \mathrm{d}\theta + F J_\rho + \frac{\partial F}{\partial M}(J_q - \overline{M} J_\rho) - Z J_q - \frac{\partial Z}{\partial M} \overline{M}(J_q - \overline{M} J_\rho).$$

$$\overline{M} = \frac{q}{\rho}$$

Two dimensional model

Assumption

$$\begin{aligned} g(t,\mathbf{x},\theta) &\approx g_1(t,\mathbf{x}) + g_c(t,\mathbf{x})\cos\theta + g_s(t,\mathbf{x})\sin\theta, \\ h(t,\mathbf{x},\theta) &\approx h_1(t,\mathbf{x}) + h_c(t,\mathbf{x})\cos\theta + h_s(t,\mathbf{x})\sin\theta. \end{aligned}$$

$$\begin{aligned} \rho(t,\mathbf{x}) &\approx \fint_V \left(g_1 + g_c\cos\theta + g_s\sin\theta\right) \mathrm{d}\theta = g_1, \\ J_\rho(t,\mathbf{x}) &\approx \fint_V \mathbf{v} g(t,\mathbf{x},\theta)\,\mathrm{d}\theta = \frac{v_0}{2}(g_c, g_s)^T, \\ q(t,\mathbf{x}) &\approx \fint_V \left(h_1 + h_c\cos\theta + h_s\sin\theta\right) \mathrm{d}\theta = h_1 \\ J_q(t,\mathbf{x}) &\approx \fint_V \mathbf{v}\left(h_1 + h_c\cos\theta + h_s\sin\theta\right) \mathrm{d}\theta = \frac{v_0}{2}(h_c, h_s)^T. \end{aligned}$$

$$\fint_V \mathbf{v}\otimes\mathbf{v}\partial_{\mathbf{x}} g\,\mathrm{d}\theta \approx \frac{v_0^2}{2}\partial_{\mathbf{x}}\rho, \qquad \fint_V \mathbf{v}\otimes\mathbf{v}\partial_{\mathbf{x}} h\,\mathrm{d}\theta \approx \frac{v_0^2}{2}\partial_{\mathbf{x}} q.$$

Summary

- Develop the model based on moment system that can capture the phase shift between the oscillations of E. Coli's methylation level and chemical concentration in rapid-changing environment.
- Agree with the agent-based model (particle simulation), but is much easier to be solved.
- Provide an explicit explanation for the assumption made on the methylation difference in PBMFT (Si et al, PRL 2012).
- The new system is hyperbolic, and thus has some numerical advantage than the diffusion model in PBMFT.
- The KS limit is obtained by considering the moment system in the regime of long time and strong tumbling.
- Develop an augmented Keller-Segel equation with a capture of phase-shift in fast-varying environments.

Future work

- Find the volcano effect experimentally
- Introduce Tumbling term into the model
- Understand the cell level mechanism to prevent the model blow up
- Understand the cell-cell interaction by comparing the experimental data and the model prediction (long term...)

Some important references:

- H.C. Berg and D.A. Brown, Nature 239 (1972), 500-504.
- N. Mittal, E.O. Budrene, M.P. Brenner, A. Van Oudenaarden, Proc. Natl. Acad. Sci., 100 (2003) 13259-13263.
- J.E. Simons and P.A. Milewski, Math. Comput. Model. 53 (2011), 1374-1388.
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