Run-and-tumble motion and differential dynamic microscopy

Zhao Yongfeng

Department of Physics, The University of Hong Kong

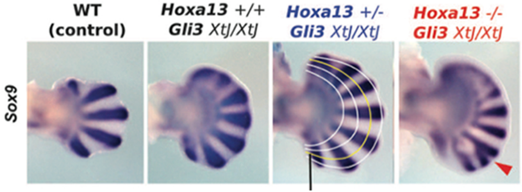
Octobor 24, 2016

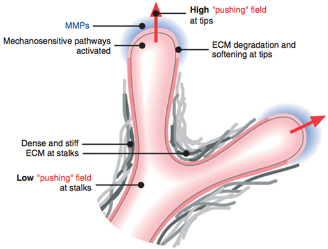
Outline

Patterns

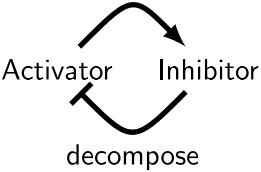



Patterns

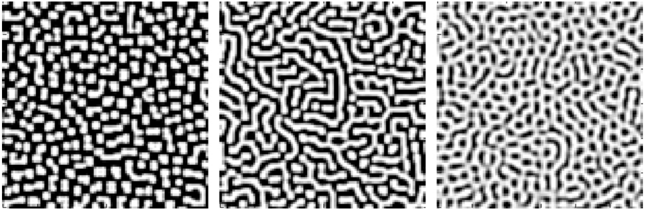

WT
(control)
Hoxa13 +/+
Gli3 XtJ/XtJ
Hoxa13 +/-
Gli3 XtJ/XtJ
Hoxa13 -/-
Gli3 XtJ/XtJ
Sox9


High "pushing" field
at tips
MMPs
Mechanosensitive pathways
activated
ECM degradation and
softening at tips
Dense and stiff
ECM at stalks
Low "pushing" field
at stalks

Turing pattern (1952)

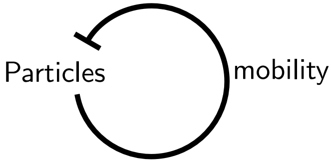


$$\frac{\partial A}{\partial t} = D_A \nabla^2 A + f(A, I)$$
$$\frac{\partial I}{\partial t} = D_I \nabla^2 I + g(A, I)$$

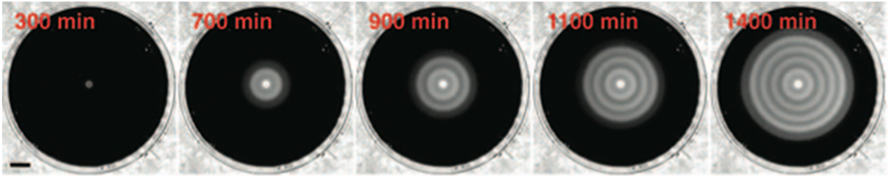


(*Wikipedia.org*)

Density-dependent mobility induced pattern



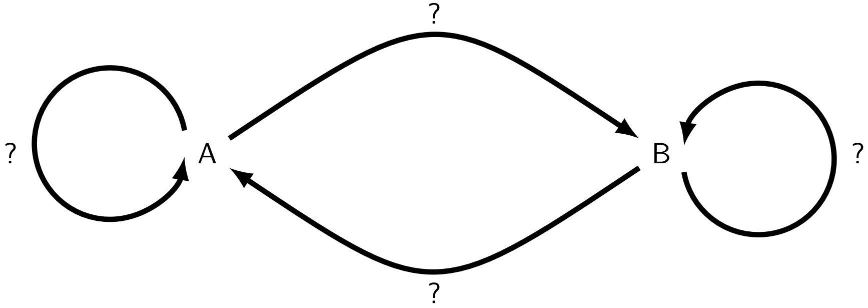
$$\frac{\partial \rho}{\partial t} = \nabla[D(\rho)\nabla\rho]$$



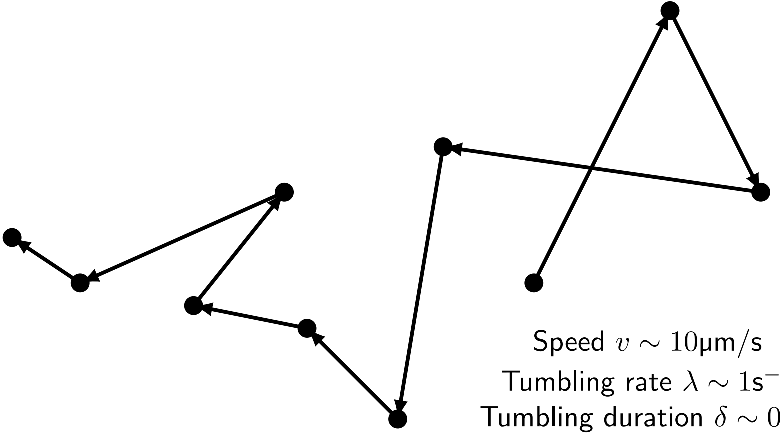
(*2011, Chenli Liu, Xiongfei Fu, et al, Science*)

Outline

Interactions among two species



Run-and-tumble motion of *E. coli*



Speed $v \sim 10$μm/s
Tumbling rate $\lambda \sim 1\text{s}^{-1}$
Tumbling duration $\delta \sim 0.1$s

$$\frac{\partial \rho}{\partial t} = \nabla \cdot (D \nabla \rho) + \nabla \left[\frac{v}{d\lambda} \nabla \left(\frac{v}{1 + \lambda\delta} \rho \right) \right] .$$

Linear stability analysis

$$\frac{\partial \rho_a}{\partial t} =\nabla \left[\frac{v_a^2}{d\lambda_a(\rho_b)(1+\lambda_a(\rho_b)\delta_a)} \nabla \rho_a - \frac{v_a^2 \delta_a \lambda_a'(\rho_b)\rho_a}{d\lambda_a(\rho_b)(1+\lambda_a(\rho_b)\delta_a)^2} \nabla \rho_b \right],$$

$$\frac{\partial \rho_b}{\partial t} =\nabla \left[\frac{v_b^2}{d\lambda_b(\rho_a)(1+\lambda_b(\rho_a)\delta_b)} \nabla \rho_b - \frac{v_b^2 \delta_b \lambda_b'(\rho_a)\rho_b}{d\lambda_b(\rho_a)(1+\lambda_b(\rho_a)\delta_b)^2} \nabla \rho_a \right].$$

Bifurcation condition

$$\lambda_a'(\rho_{b0})\lambda_b'(\rho_{a0}) > \frac{(1+\lambda_a(\rho_{a0})\delta_a)(1+\lambda_b(\rho_{b0})\delta_b)}{\delta_a\delta_b\rho_{a0}\rho_{b0}}.$$

Eigenvector

$$\left(\frac{v_a^2}{d\lambda_a(\rho_{b0})(1+\lambda_a(\rho_{b0})\delta_a)} + \eta \right) \delta\rho_a = \frac{v_a^2 \delta_a \lambda_a'(\rho_{b0})\rho_{a0}}{d\lambda_a(\rho_{b0})(1+\lambda_a(\rho_{b0})\delta_a)^2} \delta\rho_b .$$

Linear stability analysis

$$\frac{\partial \rho_a}{\partial t} =\nabla \left[\frac{v_a^2}{d\lambda_a(\rho_b)(1+\lambda_a(\rho_b)\delta_a)} \nabla \rho_a - \frac{v_a^2 \delta_a \lambda_a'(\rho_b)\rho_a}{d\lambda_a(\rho_b)(1+\lambda_a(\rho_b)\delta_a)^2} \nabla \rho_b \right] ,$$
$$\frac{\partial \rho_b}{\partial t} =\nabla \left[\frac{v_b^2}{d\lambda_b(\rho_a)(1+\lambda_b(\rho_a)\delta_b)} \nabla \rho_b - \frac{v_b^2 \delta_b \lambda_b'(\rho_a)\rho_b}{d\lambda_b(\rho_a)(1+\lambda_b(\rho_a)\delta_b)^2} \nabla \rho_a \right] .$$

Bifurcation condition

$$\lambda_a'(\rho_{b0})\lambda_b'(\rho_{a0}) > \frac{(1+\lambda_a(\rho_{a0})\delta_a)(1+\lambda_b(\rho_{b0})\delta_b)}{\delta_a \delta_b \rho_{a0}\rho_{b0}} .$$

Eigenvector

$$\left(\frac{v_a^2}{d\lambda_a(\rho_{b0})(1+\lambda_a(\rho_{b0})\delta_a)} + \eta \right) \delta\rho_a = \frac{v_a^2 \delta_a \lambda_a'(\rho_{b0})\rho_{a0}}{d\lambda_a(\rho_{b0})(1+\lambda_a(\rho_{b0})\delta_a)^2} \delta\rho_b .$$

Two general principles

$$\lambda'_a(\rho_{b0})\lambda'_b(\rho_{a0}) > \frac{(1+\lambda_a(\rho_{a0})\delta_a)(1+\lambda_b(\rho_{b0})\delta_b)}{\delta_a\delta_b\rho_{a0}\rho_{b0}} \Longrightarrow$$

$$\lambda'_a(\rho_{b0}) > 0,\ \lambda'_b(\rho_{a0}) > 0 \text{ or } \lambda'_a(\rho_{b0}) < 0,\ \lambda'_b(\rho_{a0}) < 0.$$

- $\lambda'_a(\rho_{b0}) > 0,\ \lambda'_b(\rho_{a0}) > 0$: **mutual inhibition**
  $\delta\rho_a \propto \delta\rho_b$: co-migrating pattern.
- $\lambda'_a(\rho_{b0}) < 0,\ \lambda'_b(\rho_{a0}) < 0$: **mutual activation**
  $\delta\rho_a \propto -\delta\rho_b$: segregating pattern.

The similar conclusions hold for density dependent speed (from Curatolo) or tumbling duration.

Two general principles

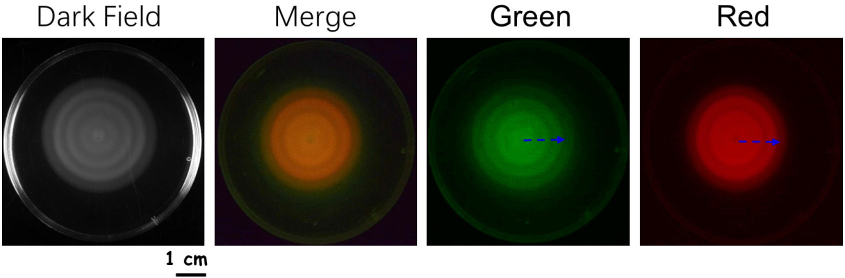
$$\lambda'_a(\rho_{b0})\lambda'_b(\rho_{a0}) > \frac{(1+\lambda_a(\rho_{a0})\delta_a)(1+\lambda_b(\rho_{b0})\delta_b)}{\delta_a\delta_b\rho_{a0}\rho_{b0}} \Longrightarrow$$

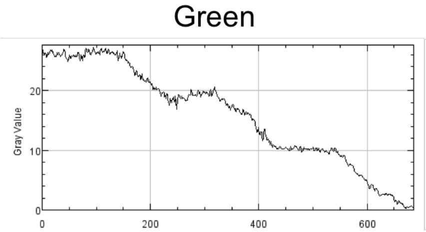
$$\lambda'_a(\rho_{b0}) > 0,\ \lambda'_b(\rho_{a0}) > 0 \text{ or } \lambda'_a(\rho_{b0}) < 0,\ \lambda'_b(\rho_{a0}) < 0.$$

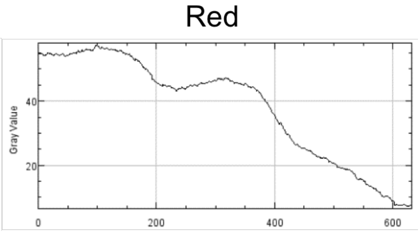
- $\lambda'_a(\rho_{b0}) > 0,\ \lambda'_b(\rho_{a0}) > 0$: **mutual inhibition**
  $\delta\rho_a \propto \delta\rho_b$: co-migrating pattern.
- $\lambda'_a(\rho_{b0}) < 0,\ \lambda'_b(\rho_{a0}) < 0$: **mutual activation**
  $\delta\rho_a \propto -\delta\rho_b$: segregating pattern.

The similar conclusions hold for density dependent speed (from Curatolo) or tumbling duration.

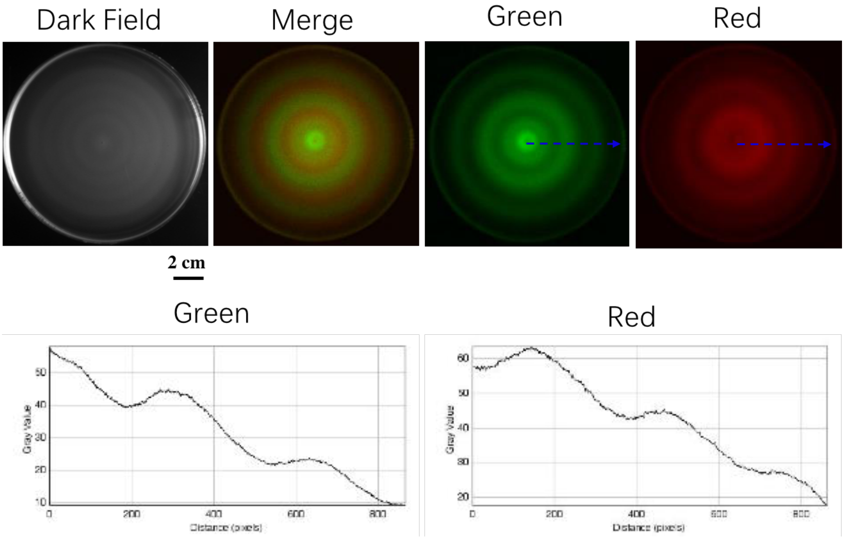
Experiments - mutual inhibition







Experiments - mutual activation



A question

How do we know the designed system works as we expected?

$\Longrightarrow$ How can we measure the speed/tumbling rate/tumbling duration of *E. coli* ?

Outline

Why not tracking?

- Special equipment for 3D measurement.
- Difficult to measure tumbling duration.
- Valid only for low density.
- Laborious.
- Poor statistics ($\sim 10^2$ cells).

If I am telling you there is a method:

- Usual equipment automatically doing 3D measurement.
- Easier to measure tumbling duration.
- Valid for high density.
- Easy.
- Good statistics ($\gg 10^4$ cells).

Why not tracking?

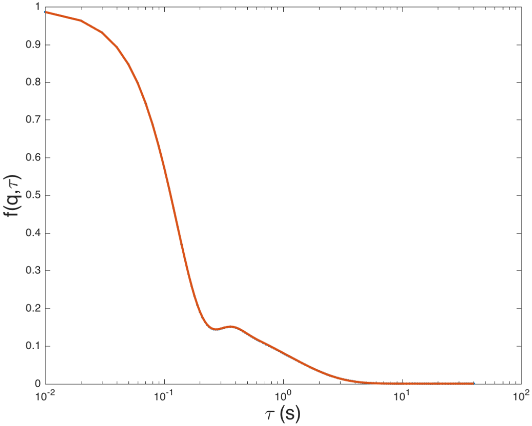
- Special equipment for 3D measurement.
- Difficult to measure tumbling duration.
- Valid only for low density.
- Laborious.
- Poor statistics ($\sim 10^2$ cells).

If I am telling you there is a method:

- Usual equipment automatically doing 3D measurement.
- Easier to measure tumbling duration.
- Valid for high density.
- Easy.
- Good statistics ($\gg 10^4$ cells).

Intermediate scattering function (ISF)

$$f(q,\tau) = \frac{\langle \Delta\rho(q,t)\Delta\rho^*(q,t+\tau)\rangle_e}{\langle \Delta\rho(q,t)\Delta\rho^*(q,t)\rangle_e}\,.$$



Differential dynamic microscopy

The principle of differential dynamic microscopy

It can be proven for ergodic point particles that

$$f(q,\tau) = \frac{\langle \Delta\rho(q,t)\Delta\rho^*(q,t+\tau)\rangle_t}{\langle \Delta\rho(q,t)\Delta\rho^*(q,t)\rangle_t} = p(q,\tau)\,,$$

which is the solution of corresponding master equation with initial condition to be $p(x,t)=\delta(x)$.

- $f(q,\tau)$ can be calculated from image intensity $I(q,t)$, via

$$g(q,\tau) = \langle |I(q,t+\tau) - I(q,t)|^2\rangle_t = A(q)(1-f(q,\tau)) + B(q)\,.$$

- $p(q,\tau)$ can be obtained from solving the master equation.

Differential dynamic microscopy

The principle of differential dynamic microscopy

It can be proven for ergodic point particles that

$$f(q,\tau) = \frac{\langle \Delta\rho(q,t)\Delta\rho^*(q,t+\tau)\rangle_t}{\langle \Delta\rho(q,t)\Delta\rho^*(q,t)\rangle_t} = p(q,\tau)\,,$$

which is the solution of corresponding master equation with initial condition to be $p(x,t) = \delta(x)$.

- $f(q,\tau)$ can be calculated from image intensity $I(q,t)$, via

$$g(q,\tau) = \langle |I(q,t+\tau) - I(q,t)|^2\rangle_t = A(q)(1 - f(q,\tau)) + B(q)\,.$$

- $p(q,\tau)$ can be obtained from solving the master equation.

Master equation of run-and-tumble particles

$$\frac{\partial p(\boldsymbol{x},\boldsymbol{v},t)}{\partial t} = D\nabla^2 p - \boldsymbol{v}\cdot\nabla p - \lambda p + \frac{\lambda}{\Omega}\int p(\boldsymbol{x},\boldsymbol{v}',t)d\Omega' \,.$$

$$p(q,v,s) = \frac{\arctan(qv/(s+Dq^2+\lambda))}{qv - \lambda\arctan(qv/(s+Dq^2+\lambda))} \,.$$

Adding a distribution of v and a contribution of dead cells,

$$f(q,\tau) = (1-\alpha)e^{-Dq^2\tau} + \alpha\int_0^\infty p(q,v,t)P(v)\,dv \,,$$

where

$$P(v) = \frac{v^Z}{\Gamma(Z+1)}\left(\frac{Z+1}{\bar{v}}\right)^{Z+1} e^{-(Z+1)v/\bar{v}} \,.$$

Master equation of run-and-tumble particles

$$\frac{\partial p(\boldsymbol{x},\boldsymbol{v},t)}{\partial t} = D\nabla^2 p - \boldsymbol{v}\cdot\nabla p - \lambda p + \frac{\lambda}{\Omega}\int p(\boldsymbol{x},\boldsymbol{v}',t)d\Omega'\,.$$

$$p(q,v,s) = \frac{\arctan(qv/(s+Dq^2+\lambda))}{qv - \lambda\arctan(qv/(s+Dq^2+\lambda))}\,.$$

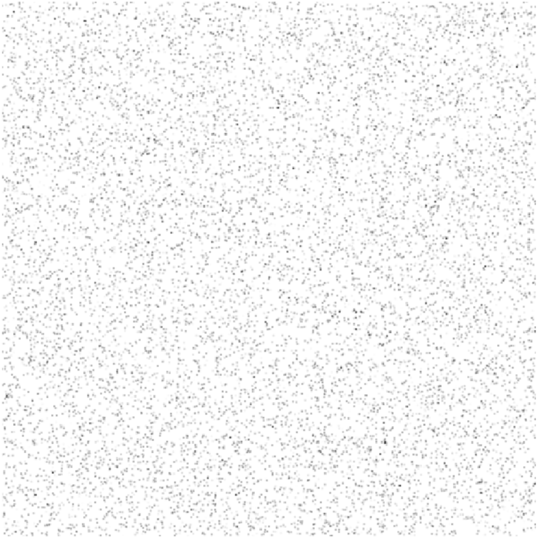
Adding a distribution of v and a contribution of dead cells,

$$f(q,\tau) = (1-\alpha)e^{-Dq^2\tau} + \alpha\int_0^\infty p(q,v,t)P(v)\,dv\,,$$

where

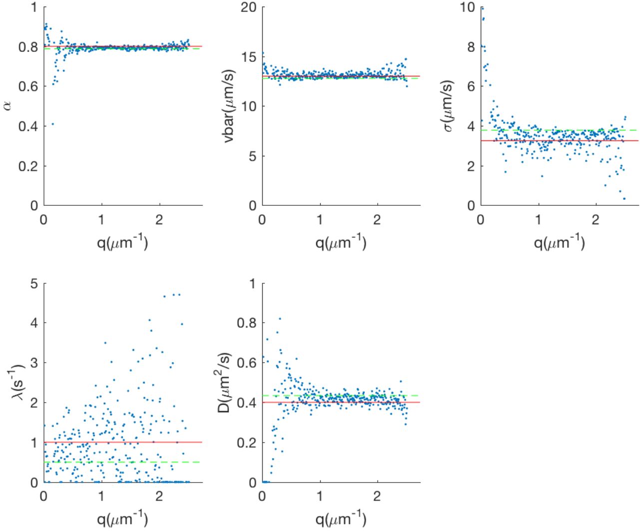
$$P(v) = \frac{v^Z}{\Gamma(Z+1)}\left(\frac{Z+1}{\bar{v}}\right)^{Z+1} e^{-(Z+1)v/\bar{v}}\,.$$

Simulation

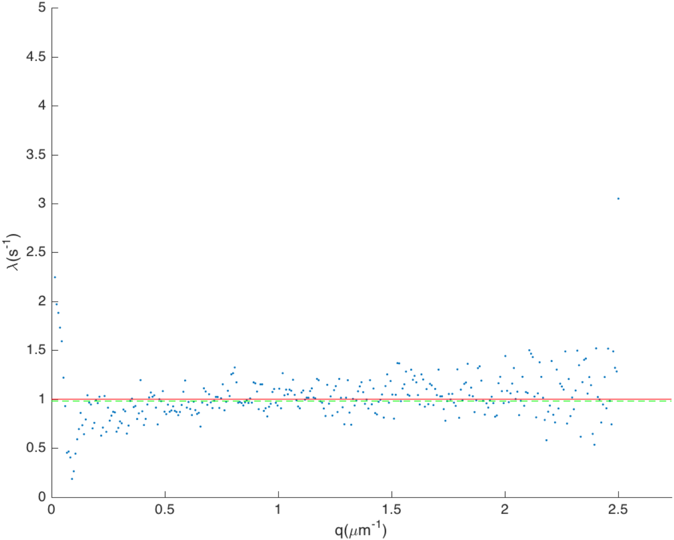


- 512×512 pixels.
- Pixel size corresponds to real microscopy systems.
- Depth of fields ~ 40 μm.
- Particle number $\sim 10^4$.

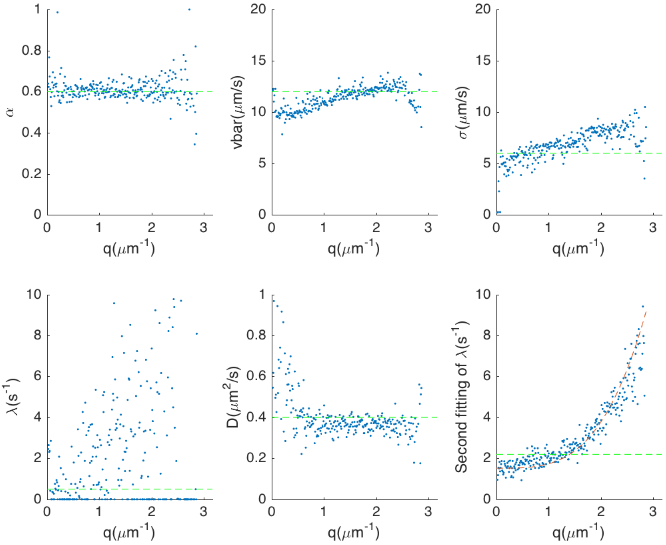
Fitting result of simulation



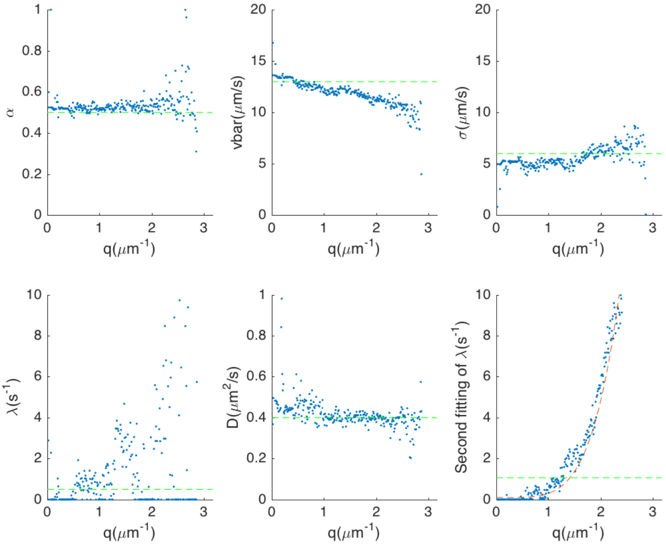
A second fitting with fixed parameters



Fitting result of experiment of wild type *E. coli*



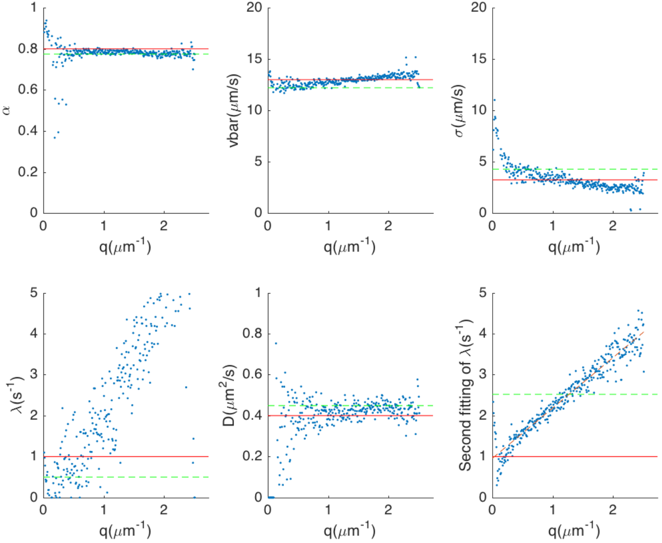
Fitting result of experiment of ΔCheY *E. coli*



What is missing?

- Finite tumbling duration.
- Rotational diffusion.
- Active rotational diffusion causing bias in tumbling.
- Lévy's walk (power law distribution in running time).

Simulation with finite tumbling duration



Finite tumbling duration

Master equation

$$\frac{\partial p_r(\boldsymbol{x}, \boldsymbol{v}, \tau)}{\partial \tau} = D\nabla^2 p_r - \boldsymbol{v} \cdot \nabla p_r - \lambda p_r + \frac{p_t}{\delta\Omega}\,,$$

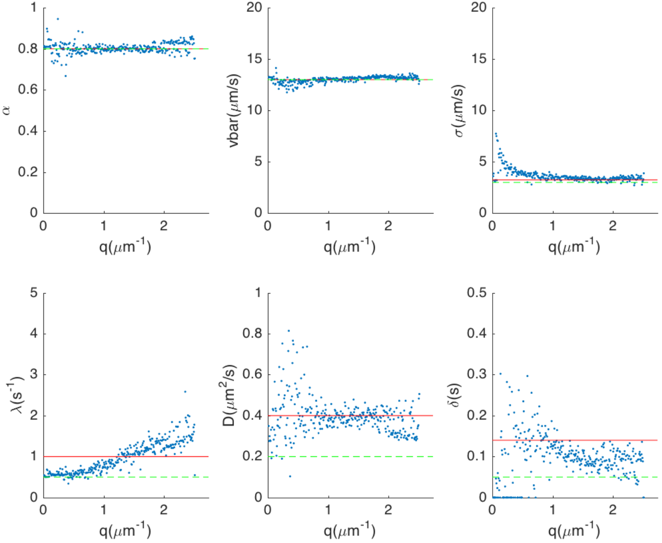
$$\frac{\partial p_t(\boldsymbol{x}, \tau)}{\partial \tau} = D\nabla^2 p_t + \lambda \int p_r(\boldsymbol{x}, \boldsymbol{v}', \tau) d\Omega' - \frac{p_t}{\delta}\,.$$

Intermediate scattering function

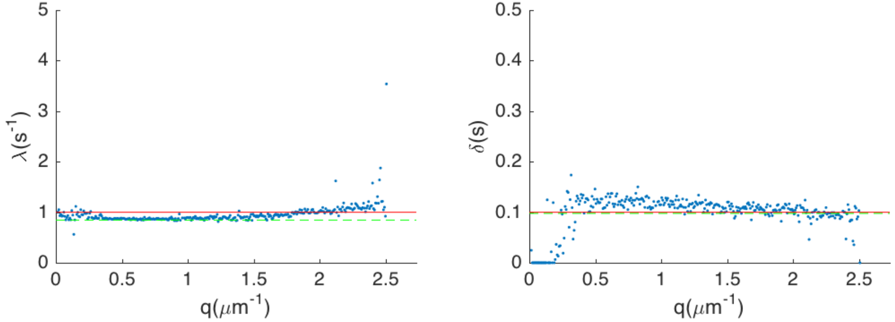
$$p(q, v, s) = \frac{1}{(\delta(s + Dq^2) + 1)(\delta\lambda + 1)} \left(\frac{(\delta(s + \lambda + Dq^2) + 1)^2 \arctan(qv/(s + \lambda + Dq^2))}{qv(\delta(s + Dq^2) + 1) - \lambda \arctan(qv/(s + \lambda + Dq^2)} + \delta^2\lambda \right)\,.$$

$$f(q, \tau) = (1 - \alpha)e^{-Dq^2\tau} + \alpha \int_0^\infty p(q, v, t) P(v)\, dv\,.$$

Fitting with tumbling duration

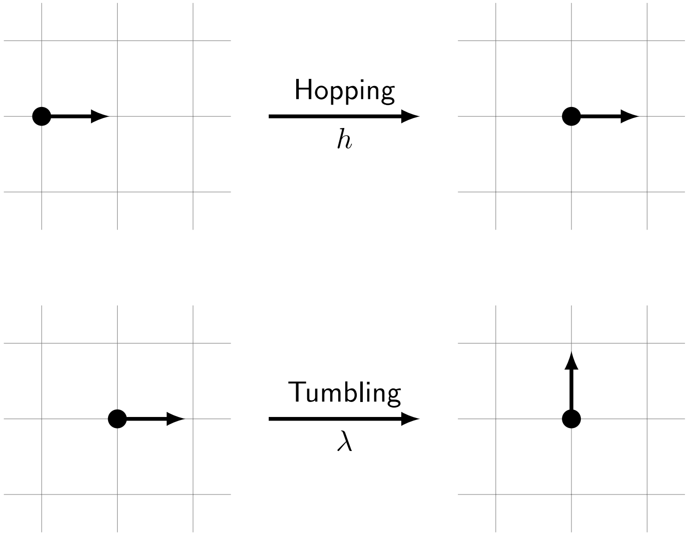


Fitting with tumbling duration

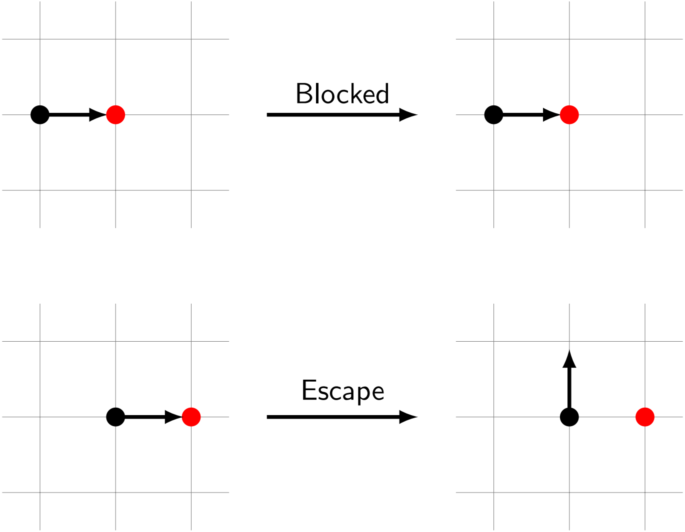


Outline

Lattice model



Lattice model



Mean field approximation

- c: Concentration of obstacles.

Master equation

$$\frac{\partial p_r(\boldsymbol{x},\hat{\boldsymbol{v}},t)}{\partial t} = -\nabla\cdot(\hat{\boldsymbol{v}}hp_r) - \lambda p_r - \gamma_d(c)hcp_r + \frac{\lambda(1-c)}{\Omega}\rho_M\,,$$

$$\frac{\partial p_b(\boldsymbol{x},\hat{\boldsymbol{v}},t)}{\partial t} = -\lambda p_b + \frac{\lambda c}{\Omega}\rho_M + \gamma_d(c)hcp_r\,,$$

$$\rho_M = \int (p_r + p_b)\, d\Omega\,.$$

Effective diffusion coefficient

$$D_{\text{eff}} = \frac{h^2\lambda(1-c)}{d[hc\gamma_d(c)+\lambda]^2}\,.$$

Mean field approximation

- c: Concentration of obstacles.

Master equation

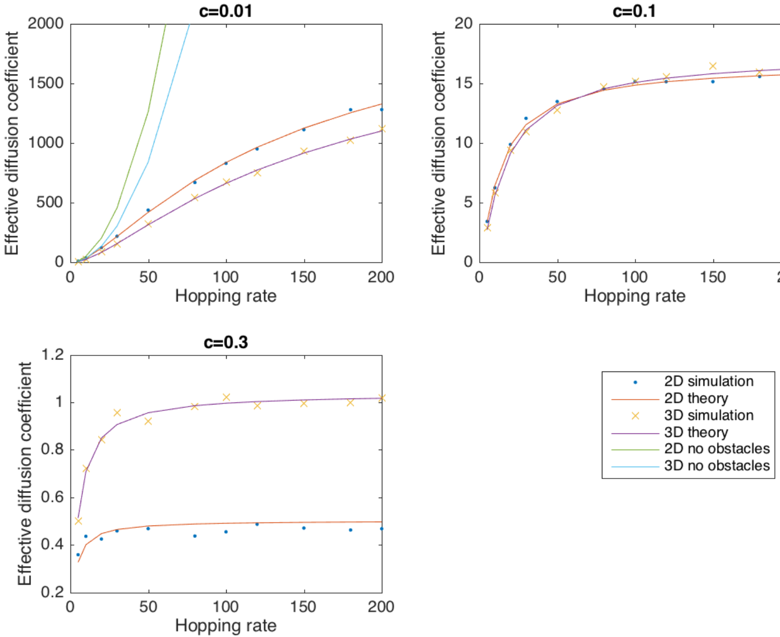
$$\frac{\partial p_r(\boldsymbol{x},\hat{\boldsymbol{v}},t)}{\partial t} = -\nabla\cdot(\hat{\boldsymbol{v}}hp_r) - \lambda p_r - \gamma_d(c)hcp_r + \frac{\lambda(1-c)}{\Omega}\rho_M\,,$$

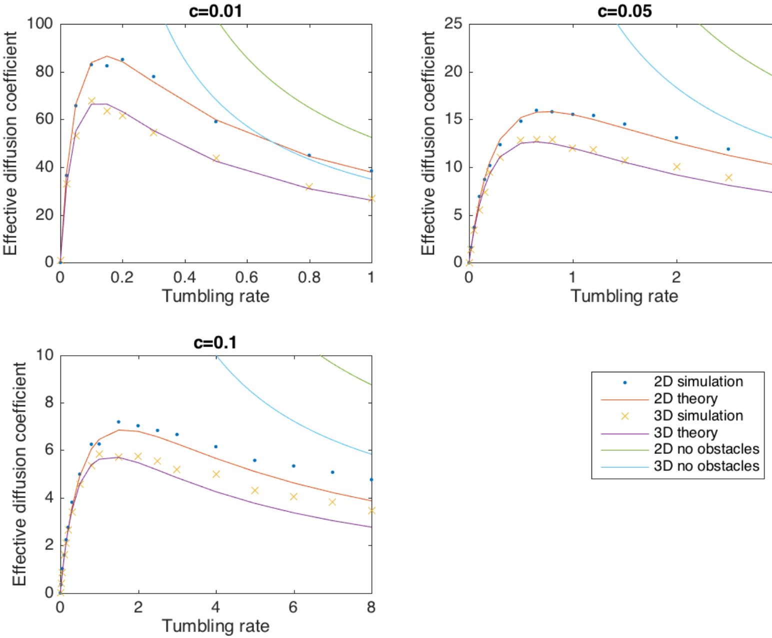
$$\frac{\partial p_b(\boldsymbol{x},\hat{\boldsymbol{v}},t)}{\partial t} = -\lambda p_b + \frac{\lambda c}{\Omega}\rho_M + \gamma_d(c)hcp_r\,,$$

$$\rho_M = \int (p_r + p_b)\,d\Omega\,.$$

Effective diffusion coefficient

$$D_{\text{eff}} = \frac{h^2\lambda(1-c)}{d[hc\gamma_d(c)+\lambda]^2}\,.$$


c=0.01
Effective diffusion coefficient
2000
1500
1000
500
0
0
50
100
150
200
Hopping rate
c=0.1
Effective diffusion coefficient
20
15
10
5
0
0
50
100
150
200
Hopping rate
c=0.3
Effective diffusion coefficient
1.2
1
0.8
0.6
0.4
0.2
0
50
100
150
200
Hopping rate
2D simulation
2D theory
3D simulation
3D theory
2D no obstacles
3D no obstacles


c=0.01
Effective diffusion coefficient
Tumbling rate
100
80
60
40
20
0
0
0.2
0.4
0.6
0.8
1
c=0.05
Effective diffusion coefficient
Tumbling rate
25
20
15
10
5
0
0
1
2
3
c=0.1
Effective diffusion coefficient
Tumbling rate
10
8
6
4
2
0
0
2
4
6
8
2D simulation
2D theory
3D simulation
3D theory
2D no obstacles
3D no obstacles

Outline

Summary

New mechanism for pattern formation

- Mutual inhibition of mobility: co-migrating pattern.
- Mutual activation of mobility: segregating pattern.

New development of differential dynamic microscopy

- Tumbling rate can be measured for run-and-tumble particles with instantaneous tumbling.
- Tumbling duration can be measured for run-and-tumble particles if the tumbling rate is known.
- The motion of *E. coli* may have some ingredients we haven't known.

New attempt for *E. coli* motion with obstacles

- A valid lattice model.
- A mean field approximation.

Summary

New mechanism for pattern formation

- Mutual inhibition of mobility: co-migrating pattern.
- Mutual activation of mobility: segregating pattern.

New development of differential dynamic microscopy

- Tumbling rate can be measured for run-and-tumble particles with instantaneous tumbling.
- Tumbling duration can be measured for run-and-tumble particles if the tumbling rate is known.
- The motion of *E. coli* may have some ingredients we haven't known.

New attempt for *E. coli* motion with obstacles

- A valid lattice model.
- A mean field approximation.

Summary

New mechanism for pattern formation

- Mutual inhibition of mobility: co-migrating pattern.
- Mutual activation of mobility: segregating pattern.

New development of differential dynamic microscopy

- Tumbling rate can be measured for run-and-tumble particles with instantaneous tumbling.
- Tumbling duration can be measured for run-and-tumble particles if the tumbling rate is known.
- The motion of *E. coli* may have some ingredients we haven't known.

New attempt for *E. coli* motion with obstacles

- A valid lattice model.
- A mean field approximation.

Future work

Pattern formation

- Experiments: tuning the pattern.
- Three-species, four-species, ...: more complex network motif.
- Growth, death, ...: more kinds of interactions.

Differential dynamic microscopy

- Way to specify the tumbling rate of run-and-tumble particles with finite tumbling duration: multi-scale imaging?
- Measure rotational diffusivity.
- Effect of Levy's walk.

E. coli moving in agar

- Existence of better continuous approximation: calculation of $\gamma_d(c)$.
- Possibility of DDM.

Future work

Pattern formation

- Experiments: tuning the pattern.
- Three-species, four-species, ...: more complex network motif.
- Growth, death, ...: more kinds of interactions.

Differential dynamic microscopy

- Way to specify the tumbling rate of run-and-tumble particles with finite tumbling duration: multi-scale imaging?
- Measure rotational diffusivity.
- Effect of Levy's walk.

E. coli moving in agar

- Existence of better continuous approximation: calculation of $\gamma_d(c)$.
- Possibility of DDM.

Future work

Pattern formation

- Experiments: tuning the pattern.
- Three-species, four-species, ...: more complex network motif.
- Growth, death, ...: more kinds of interactions.

Differential dynamic microscopy

- Way to specify the tumbling rate of run-and-tumble particles with finite tumbling duration: multi-scale imaging?
- Measure rotational diffusivity.
- Effect of Levy's walk.

E. coli moving in agar

- Existence of better continuous approximation: calculation of $\gamma_d(c)$.
- Possibility of DDM.

What's more?

- Applying DDM to study the motion of other "particles": mammalian cells, fishes, birds, sheep, humans, ...
- Studying their collective behaviour.
- Finding principles in coordination and self-organization.
- Answering questions in organ development, morphogenesis, microbe infection, ...

Acknowledgement

- Prof. Cheng, Kwong Sang
- Prof. Zhang, Fu-Chun
- Prof. Huang, Jian-Dong
- Dr. Julien Tailleur (University Paris Diderot)
- Dr. Vincent Martinez (The University of Edinburgh)
- Dr. Adrian Daerr (University Paris Diderot)
- Dr. Huang, Wei
- Prof. Peter Lenz
- Mr. Zhou, Nan
- Ms. Agnese Curatolo (University Paris Diderot)
- Dr. Alexandre Solon (MIT)
- Dr. Lina Hamouche (University Paris Diderot)

Case no obstacle: compare with continuous model

Master equation

$$\frac{\partial P(\boldsymbol{x}, \boldsymbol{e}_i, t)}{\partial t} = hP(\boldsymbol{x} - \boldsymbol{e}_i, \boldsymbol{e}_i, t) - hP - \lambda P + \frac{\lambda}{2d} \sum_i P(\boldsymbol{x}, \boldsymbol{e}_i, t)\,.$$

Mean square displacement - lattice model

$$\langle \Delta x^2(t) \rangle = \left(\frac{2h^2}{d\lambda} + \frac{h}{d} \right) t + \frac{2h^2}{d\lambda^2} (e^{-\lambda t} - 1)\,.$$

Mean square displacement - continuous model

$$\langle \Delta x^2(t) \rangle = \frac{2v^2}{d\lambda} t + \frac{2v^2}{d\lambda^2} (e^{-\lambda t} - 1)\,.$$

- Necessary condition of lattice model to be valid: $h \gg \lambda/2$.

Numerical inverse Laplace transformation - Week's method

$$\mathcal{L}\{f(t)\} = F(s)\,.$$

- Möbius transformation: $s = \sigma - b\frac{z+1}{z-1}$.
- Expand the function:

$$(s - \sigma + b)F(s) = \frac{2b}{1-z}F\left(\sigma - b\frac{z+1}{z-1}\right) = \sum_{n=0}^{\infty} a_n z^n\,.$$

- Laplace transformation of Laguerre polynomial: $\mathcal{L}[L_n(2bt)] = \frac{(s-2b)^n}{s^{n+1}}$.
- $\mathcal{L}^{-1}[F(s)] = f(t) = \sum_{n=0}^{\infty} a_n e^{(\sigma-b)t} L_n(2bt)\,.$
-

$$a_n = \frac{1}{2\pi}\int_0^{2\pi} e^{-in\theta}\frac{2b}{1-e^{i\theta}}F\left(\sigma - b\frac{e^{i\theta}+1}{e^{i\theta}-1}\right)d\theta\,.$$