Kinetic Transport Simulation of Chemotactic Bacteria

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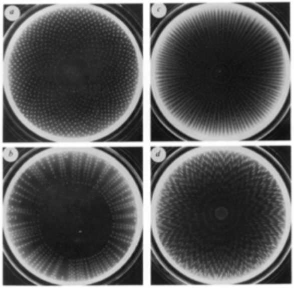
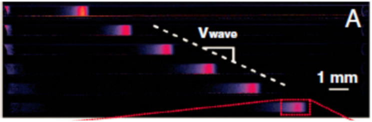
Collective Motion of Bacteria

- Colony Pattern *E. Coli*



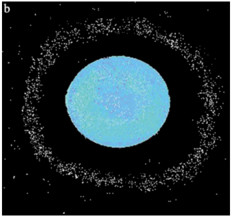
Budrene & Berg, Nature 349 (1990).

- Traveling Pulse in Micro Channel



J. Saragosti, et al., PNAS (2011).

- Swarm Band Marine Bacteria

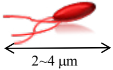


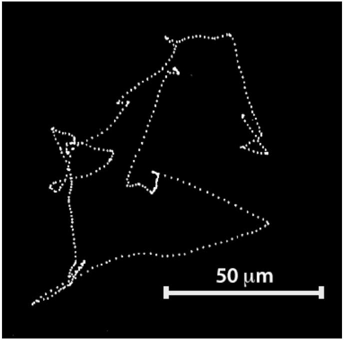
Barbara & Mitchell, Microb. Ecol. (2003).

Aggregation, Traveling Wave, Swarm...

Individual Motion

Escherichia coli





http://www.rowland.harvard.edu

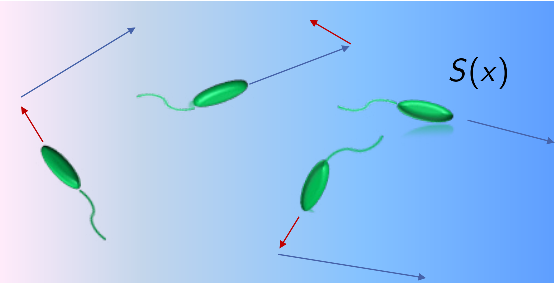
Run-and-Tumble motion

1. *Run*
2. Chemical Sensing
3. (Occasionally) *Tumble*

Chemotaxis

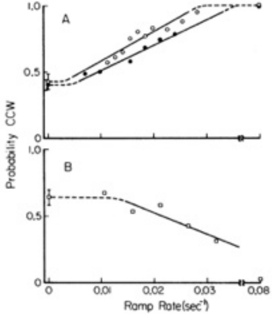
Schematic of Chemotaxis

$S(x)$ Chemoattractant



Change run length according to the temporal sensing along pathway.

Chemotactic response of E. Coli



[Block, Segall, &Berg, (1983).]

Stiff & Bounded Response

Computational and Mathematical Challenges

Understanding the multiscale mechanism between collective phenomena and individual motions.

- *How the chemotactic response strategy affects the pattern formation?*
- *Which traits are important for efficient collective motions?*
- *How macroscopic models are derived from microscopic or mesoscopic models?*

Kinetic Transport Theory of Bacteria

- Kinetic transport equation for run-and-tumble bacteria

$$\underbrace{\partial_t f(t,\boldsymbol{x},\boldsymbol{v}) + \boldsymbol{v}\cdot\nabla_x f}_{\text{Run with velocity } \boldsymbol{v}} = \int [\underbrace{\Lambda(\boldsymbol{v},\boldsymbol{v}',\boldsymbol{C})f(\boldsymbol{v}')}_{\text{Gain Term: } \boldsymbol{v}'\to\boldsymbol{v}} - \underbrace{\Lambda(\boldsymbol{v}',\boldsymbol{v},\boldsymbol{C})f(\boldsymbol{v})}_{\text{Loss Term: } \boldsymbol{v}\to\boldsymbol{v}'}]d\boldsymbol{v}$$

$f(t,\boldsymbol{x},\boldsymbol{v})$: Density of Bacteria with Velocity $\boldsymbol{v}$; $\Lambda(\boldsymbol{v},\boldsymbol{v}',\boldsymbol{C})$: Tumble from $\boldsymbol{v}'$ to $\boldsymbol{v}$; $\boldsymbol{C}=\{S(t,\boldsymbol{x}),N(t,\boldsymbol{x}),\cdots\}$: External Chemical Cues.

- Reaction Diffusion Equation

$$\partial_t S(t,\boldsymbol{x}) = \underbrace{D_S\Delta_x S}_{\text{Diffusion}} - \underbrace{\alpha S}_{\text{Degeneration}} + \underbrace{\beta\rho(t,\boldsymbol{x})}_{\text{Production}},$$

$$\partial_t N(t,\boldsymbol{x}) = D_N\Delta_x N - \underbrace{\gamma N\rho(t,\boldsymbol{x})}_{\text{Consumption}}.$$

$S(t,\boldsymbol{x})$:Concentration of Chemical product; $N(t,\boldsymbol{x})$:Concentration of Food; $\rho(t,\boldsymbol{x})=\int f(t,\boldsymbol{x},\boldsymbol{v})d\boldsymbol{v}$: Population Density of Bacteria.

Multiscale Aspect

From Meso (kinetic) to Macro (continuum)

- Internal states m and velocity v (Erban & Othmer (2004))

$$\partial_t g(t,x,v,m) + v\nabla_x g + \frac{1}{t_a}\nabla_m \dot{M}(m,S)g = \Lambda(m,S)(\int g(v')dv' - g(v)).$$

- Fast adaptation $t_a \ll 1$ (Dolak & Schmeiser (2005),Perthame, Tang, Vauchelet (2016))

$$\partial_t f(t,x,v) + v\cdot\nabla_x f = \frac{1}{k}(\int \lambda(D_t S|_{v'})f(v')dv' - \lambda(D_t S|_v)f(v)).$$

- Sequential tumbling $k \ll 1$, Keller-Segel type equation (Hillen & Othmer (2000, 2002), Chalub, Markowich, Perthame, Schmeiser (2004), Tang & Yang (2014), etc.)

$$\partial_t \rho(t,x) + \nabla_x\cdot(U(\nabla_x S)\rho) = \Delta\rho.$$

Contents

Basic Equation

Kinetic Chemotaxis Model (KCM)

$$\partial_t f + v \cdot \nabla_x f = \int_V \lambda(v', S, N) K(v, v') f' dv' - \lambda(v, S, N) f(v),$$

$$\lambda(v, S, N) = \lambda_0 \left(1 - \chi_S \tanh\left(\frac{D_t \log S|_v}{\delta}\right) - \chi_N \tanh\left(\frac{D_t \log N|_v}{\delta}\right)\right),$$

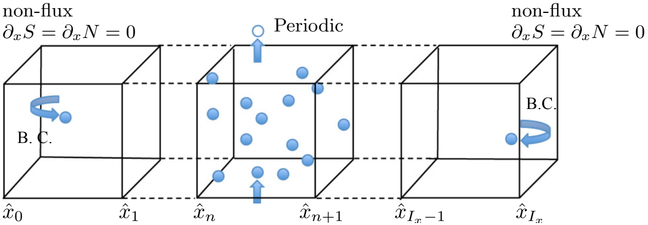
$$K(v, v') \propto \exp\left(\frac{1 - v \cdot v'}{\sigma^2}\right), \quad \text{(Probability Density, i.e., } \int K(v, v') dv = 1),$$

λ_0: Mean Tumbling Rate; χ: Modulation Amplitude; δ: Stiffness; σ: Variance;

Logarithmic sensing: $D_t \log S|_{\boldsymbol{v}} = \dfrac{\partial_t S + \boldsymbol{v} \cdot \nabla_x S}{S}$ (Kalinin, et.al, Biophys. J. (2009))

DSMC-like MC method

- Divide the spatial domain into a lattice system.
- MC particles are distributed according to $f(x_i, v)$.
- Chemical concentrations $S(\boldsymbol{x}_i)$, $N(\boldsymbol{x}_i)$ are calculated by Finite Volume method on the lattice system.



0 Initial positions and velocities, $\boldsymbol{r}_l^0$ and $\boldsymbol{v}_l^0$ are stochastically determined according to $f^0(\boldsymbol{x}_i, \boldsymbol{v})$.

1. Move particles in Δt, i.e., $\boldsymbol{r}_l^{n+1} = \boldsymbol{r}_l^n + \boldsymbol{v}_l^n \Delta t$.
2. Count the population density $\rho^{n+1}(x_i)$.
3. Calculate chemical cues $S^{n+1}(x_i)$ and $N^{n+1}(x_i)$ by FVM.
4. Judge tumbles by $\lambda(D_t \log S,\ N|_{\boldsymbol{v}})k^{-1}\Delta t$.

   The material derivative is calculated as

$$D_t \log S|_{\boldsymbol{v}} \simeq \frac{\log S^{n+1}(\boldsymbol{r}_l^{n+1}) - \log S^n(\boldsymbol{r}_l^n)}{\Delta t}.$$

5. New velocities $\boldsymbol{v}_l^{n+1}$ are given by the probability $K(\boldsymbol{v}_l^{n+1}, \boldsymbol{v}_l^n)$.

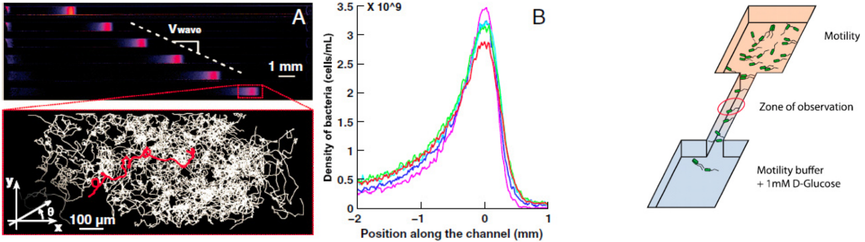
6 Division or Death of each particle is judged by $P(\rho_i)\Delta t$.

7. Return to 1.

Application to Traveling Pulse

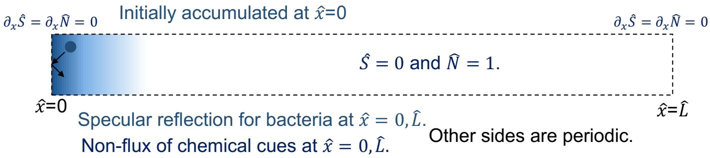
- Traveling pulse of chemotactic bacteria in micro channel

  by J. Saragosti, V. Calvez, N. Bournaveas, B. Perthame, A. Buguinn, and P. Silberzan, PNAS (2011)



Simulation Condition

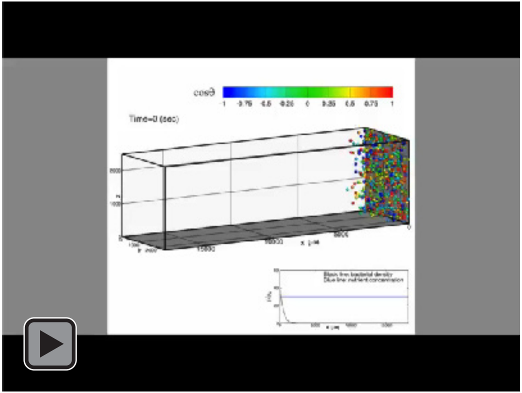
- Initial and Boundary Conditions



- Parameters

λ_0= 3.0 [1/s], χ_S=0.2, χ_N=0.6, δ=0.125 [1/s], L=1.8 cm.

Monte Carlo Result



Traveling Speed V_{wave}=4.0 μm/s (4.1 μm/s in Experiment).

Comparison to Keller-Segel equation

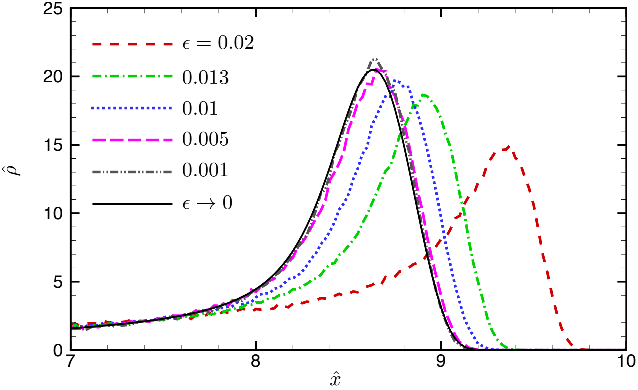


Fig. 1: Comparison of MC vs. K-S model. MC results asymptotically approach to the KS result.

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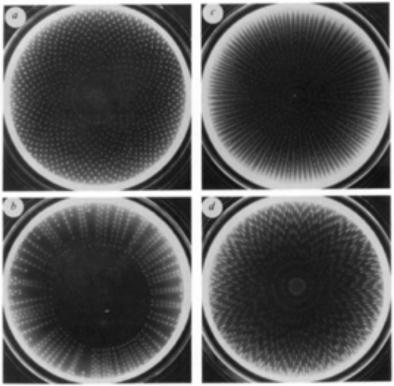
Colony Pattern of *E. Coli*

Variety of Pattern

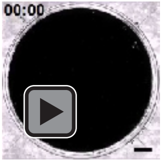


Budrene & Berg, Nature 349 (1990).

Pattern Formation Dynamics

- 1D Channel

- Petri Dish



Lie et. al., Science 334 (2011).

Aggregation (Instability) & Traveling Wave

Basic Equation

- Kinetic Chemotaxis Model

$$\partial_t f(t, \boldsymbol{x}, \boldsymbol{v}) + \boldsymbol{v} \cdot \nabla f =$$

$$\frac{1}{k} \left\{ \int_{|\boldsymbol{v}'|=1} \lambda(D_t \log S|_{\boldsymbol{v}'}) f(\boldsymbol{v}') d\boldsymbol{v}' - \lambda(D_t \log S|_{\boldsymbol{v}}) f(\boldsymbol{v}) \right\} + P(\rho) f(\boldsymbol{v}).$$

Uniform Scattering $K(v, v')$=const. $k = \lambda_0^{-1}$.

- Response Function

$$\lambda(X) = 1 - F_\delta(X),$$

$$F_\delta(X) = F\left(\frac{X}{\delta}\right), \quad F'(X) > 0, \quad F(X) \to \pm\chi.$$

- Proliferation ($\rho < 1$) and Saturation ($\rho = 1$)

$$P(\rho) = \begin{cases} > 0 & (0 \leq \rho \leq 1) \\ < 0 & (1 < \rho). \end{cases}$$

Ex) $P(\rho) = 1 - \rho$.

- Chemoattractant S

$$-D_s \Delta S + S = \rho.$$

- Key Parameters related to the instability
  k^{-1} (Tumbling Rate), χ_S (Modulation), δ^{-1} (Stiffness), D_S (Diffusion).

Stiff-Response-Induced Instability

Perthame & Yasuda, Nonlinearity (2018)

The uniform state $\rho = S = 1$ is linearly unstable when the stiffness of the response $F'_\delta(0)$ is so large as,

$$\frac{F'_\delta(0)}{k} > \left(1 + \frac{k}{\frac{k\lambda}{\arctan(k\lambda)} - 1}\right)(1 + D_S\lambda^2).$$

Furthermore, the unstable mode λ is always bounded as in *Turing instability*.

Linear Instability Analysis

- Take small perturbation and linearize the kinetic chemotaxis equation

$$
\begin{aligned}
f(t,\boldsymbol{x},\boldsymbol{v}) &= 1 + g(\boldsymbol{x},\boldsymbol{v})e^{\mu t},\\
S(t,\boldsymbol{x}) &= 1 + S_g(\boldsymbol{x})e^{\mu t},\\
\rho(t,\boldsymbol{x}) &= 1 + \rho_g(\boldsymbol{x})e^{\mu t}.
\end{aligned}
$$

  Seek the instability condition $\mathrm{Re}(\mu) > 0$.

- $\cdots$

Instability Diagram

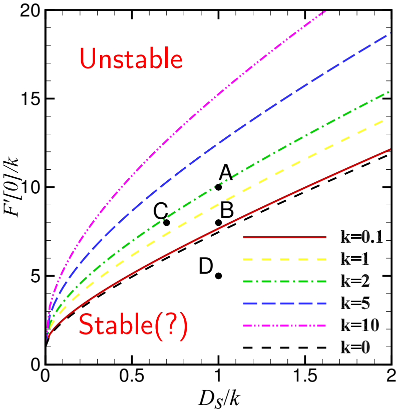


Fig. 2: Neutral curves for different k. The upper side of the curve is the instability regime.

Monte Carlo Results

1D lattice system (i.e., $\partial_y S = \partial_z S = 0$), Periodic B.C.

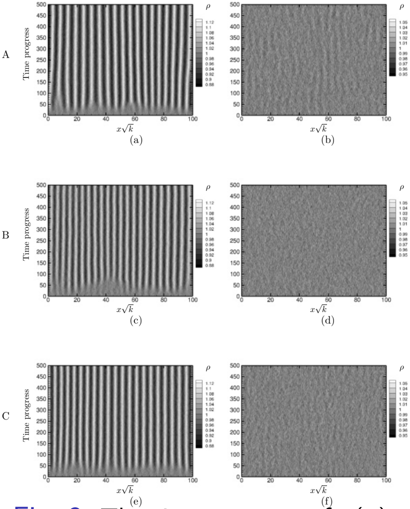
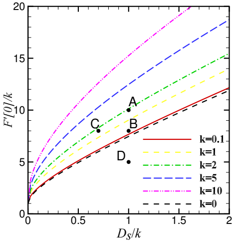


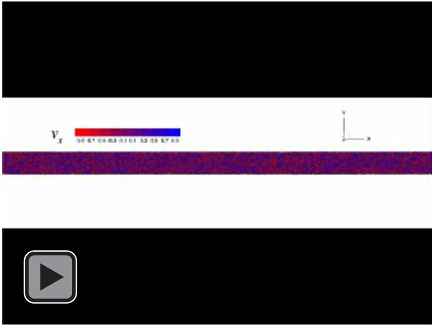
Fig. 3: The time progress of $\rho(x)$.



k	A	B	C
0.1	–	■	–
1.0	■	□	■
2.0	□	–	□

Table 1: The parameter sets.

Motions of MC particles in one-dimensional lattice system (i.e, $\partial_y S = \partial_z S = 0$).
The case with strong chemical response ($\chi/\sqrt{k} = 2.06$, $k = 0.1$).

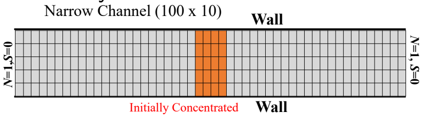


Narrow Channel

Dirichlet in x, Neumann in y.

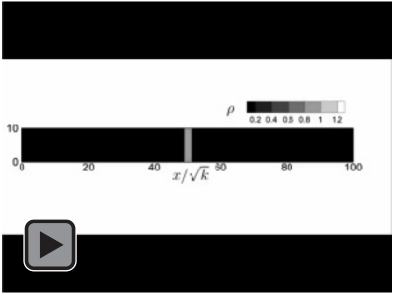
k=0.04, δ=0.25, $\chi_{S,N}$=0.1, $D_{S,N}$=0.04.

Geometry



10^3 particles in each lattice site

Time evolution of population density



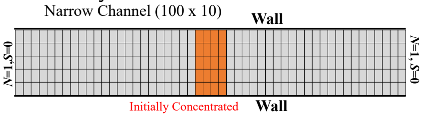
Two Dimensional Results

Narrow Channel

Dirichlet in x, Neumann in y.

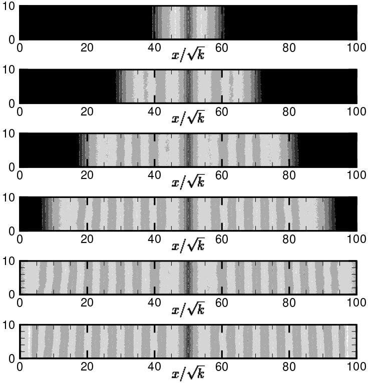
k=0.04, δ=0.25, $\chi_{S,N}$=0.1, $D_{S,N}$=0.04.

Geometry



10^3 particles in each lattice site

Time evolution of population density



Snapshots for different prameters

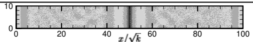
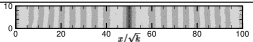
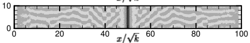
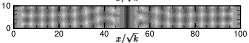
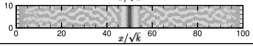
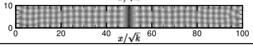
$\sqrt{k}\delta$	D_S/k	$\chi_S/\sqrt{k}$	$k = 1$	$k = 0.04$
0.05	1	0.5		
0.02	1	0.5		
0.05	0.1	0.5		

Table 2: Pattern formation in narrow channel. The channel width $W/\sqrt{k} = 10$ and channel length $L/\sqrt{k} = 100$ are fixed. The snapshots of population density at $t = 50$ are shown in the third and forth columns for different parameters.

Square

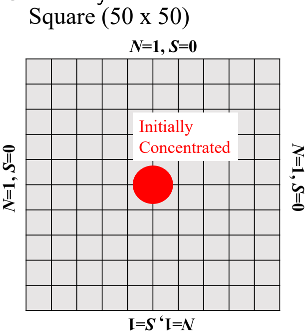
Dirichlet B.C. in x and y.

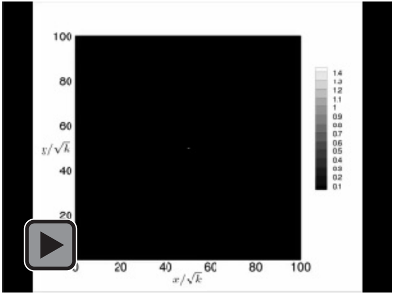
$k = 0.02$, $D_S = 0.04$, $\chi_S = 0.1$,

$\delta = 0.25$.

Time evolution

Geometry





10^3 particles in each lattice site

Square

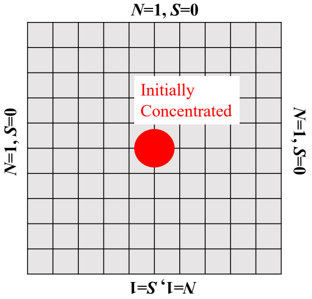
Dirichlet B.C. in x and y.

$k = 0.02$, $D_S = 0.04$, $\chi_S = 0.1$,

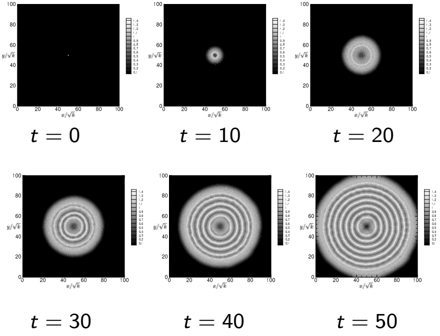
$\delta = 0.25$.

Geometry

Square (50 x 50)

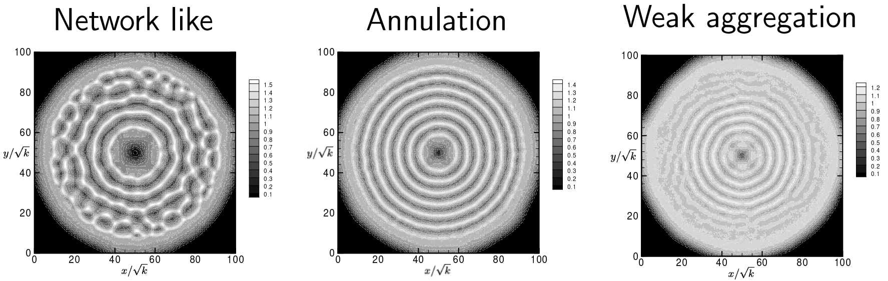


10^3 particles in each lattice site



Dependence on k

$D_{S,N} = 0.04$, $\chi_{S,N} = 0.1$, $\delta = 0.25$ are fixed.



(a) $k = 0.01$ (b) $k = 0.02$ (c) $k = 0.04$

Contents

Summary

- MC simulation for run-and-tumble chemotactic bacteria was developed based on a kinetic chemotaxis model.
- Some collective behaviors of chemotactic bacteria were well reproduced by the MC simulation.
- Comparison to the theoretical analysis verified the accuracy of the MC method.
- A novel instability mechanism, i.e., *stiff-response-induced instability*, was discovered both theoretically and numerically.

Thank you for your attention

Collaborators: Benoît PERTHAME (LJLL, Paris06), Vincent Calvez (ENS, Lyon)

References

- B. Perthame and SY, "Stiff-response-induced instability for chemotactic bacteria and flux-limited Keller-Segel equation", Nonlinearity **31**, 4065–89 (2018).
- V. Calvez, B. Perthame, and SY, "Traveling wave and aggregation in a flux-limited Keller-Segel model", Kinet. Relat. Mod. **11**, 891–909 (2018).
- SY, "Monte Carlo simulation for kinetic chemotaxis model: an application to the traveling population wave", J. Comput. Phys. **330**, 1022–42 (2017).