Kinetic models of chemotaxis

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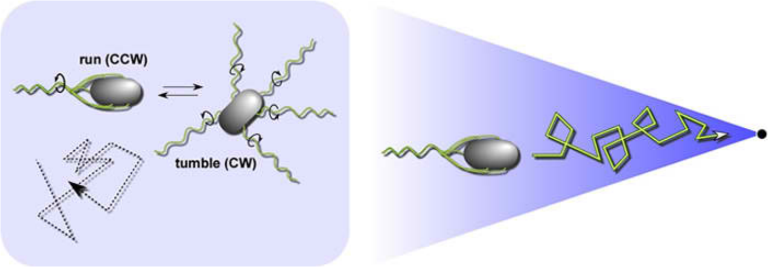
'Run and tumble' of *Escheria coli*

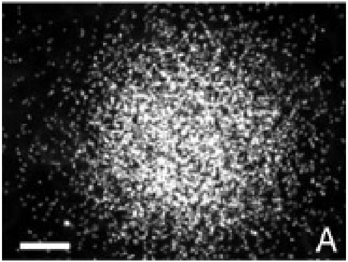


Parkinson lab, Univ. Utah

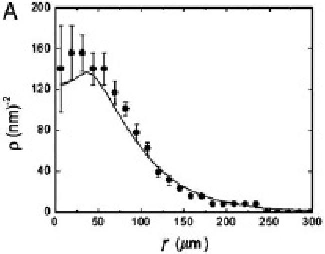
Left: unbiased random motion in an isotropic environment

Right: chemotaxis in a chemo-attractant gradient by longer runs in the favorable direction

Aggregation by chemotaxis



Mittal et al., PNAS 100 (2003), 13259–13263



Cell-cell signalling by production of a diffusing chemo-attractant

Kinetic transport models for chemotaxis

Cell distribution in phase space: $f(x, v, t)$
Position $x \in \mathbb{R}^d$, velocity $v \in V \subset \mathbb{R}^d$, time t

$$\partial_t f + v \cdot \nabla_x f = Q(f)$$

with $Q(f) := \int_V [T[S](v' \to v)f' - T[S](v \to v')f]dv'$

$T[S](v \to v')$: rate of change from velocity v to v' in the presence of a chemo-attractant with density $S(x, t)$

Macroscopic cell density: $\rho_f(x, t) = \int_V f(x, v, t)dv$

Global existence and macroscopic limit

$$\varepsilon^2\partial_t f + \varepsilon v\cdot\nabla_x f = Q_\varepsilon(f) = Q_0(f) + \varepsilon Q_1[S]f$$
$$-\Delta_x S = \rho_f$$

with $Q_\varepsilon(f) := \int_V [T_\varepsilon[S](v'\to v)f' - T_\varepsilon[S](v\to v')f]dv'$

Theorem: Let $T_\varepsilon[S] \le c(1 + S(x+v) + S(x-v))$ and $V\subset\mathbb{R}^3$ bounded. Then there exists a global bounded solution (with an ε-dependent bound).

Theorem: Let $Q_0(F) = 0$, $\int_V F\,dv = 1$, $\int_V vF\,dv = 0$. Then $f(x,v,t)\to\rho(x,t)F(v)$ as $\varepsilon\to 0$ locally in time, where ρ solves a convection-diffusion equation (Keller-Segel for various appropriate choices of $T_\varepsilon[S]$).

Chalub, Markowich, Perthame, CS, *Monatsh. Math.* (2004)

The Patlak (1953) Keller-Segel (1970) model

Assumptions: 2D, elliptic-parabolic (i.e. fast chemoattractant diffusion)

$$\partial_t \rho + \nabla \cdot (\rho \nabla S - \nabla \rho) = 0$$

$$S = -\frac{1}{2\pi} \ln(|x|) * \rho$$

Theorem (Jäger, Luckhaus, Blanchet, Dolbeault, Perthame, Calvez, Carrillo, Masmoudi, Biler, Laurencot, Suzuki, Sugiyama, Herrero, Velazquez, ..., 1992–)

Let $(1+|x|^2)\rho(t=0) \in L^1(\mathbb{R}^2)$, $M = \int \rho(t=0)dx$. Then

$M < 8\pi \implies$ global existence, self similar dispersion

$M > 8\pi \implies$ concentration in finite time

$M = 8\pi \implies$ concentration in infinite time

Global measure solutions

Theorem (Dolbeault, CS, 2008): Existence of global solutions $\rho(t) \in \mathcal{M}_1^+(\mathbb{R}^2)$, $t \geq 0$, for arbitrary M. Distributional definition of the convective flux due to Poupaud (2002).

Strong formulation: Assume

$$\rho(x,t) = \overline{\rho}(x,t) + \sum_n M_n(t)\delta(x - x_n(t))$$

with smooth $\overline{\rho}, M_n, x_n$. Then $M_n(t) \geq 8\pi$ and

$$\partial_t \overline{\rho} + \nabla \cdot (\overline{\rho}\nabla S[\overline{\rho}] - \nabla \overline{\rho}) - \frac{1}{2\pi}\nabla\overline{\rho} \cdot \sum_n M_n(t)\frac{x - x_n}{|x - x_n|^2} = 0$$

$$\dot{M}_n = M_n\overline{\rho}(x = x_n), \quad \dot{x}_n = \nabla S[\overline{\rho}](x = x_n) - \frac{1}{2\pi}\sum_{m \neq n} M_m \frac{x_n - x_m}{|x_n - x_m|^2}$$

Local-in-time well posedness by Velazquez (2004).

Approximation by a stochastic many particle system

$$dx_n = -\frac{M}{2\pi N} \sum_{n\neq m\leq N} \frac{x_n - x_m}{|x_n - x_m|^2} dt + \sqrt{2}\, dB_n\,, \quad 1 \leq n \leq N$$

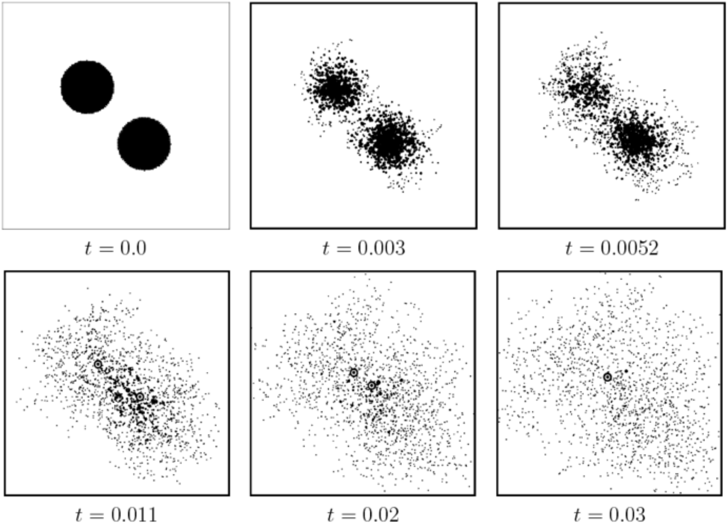
with $B_1, \dots, B_N$ independent normalized 2D Brownian motions.

The N-particle probability density $p(t, x_1, \dots, x_N)$ satisfies

$$\partial_t p = \sum_{n=1}^{N} \nabla_{x_n} \cdot \left(\frac{M}{2\pi N} \sum_{n\neq m\leq N} \frac{x_n - x_m}{|x_n - x_m|^2} p + \nabla_{x_n} p \right)$$

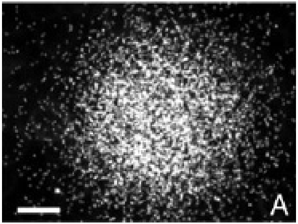
Theorem: (Haskovec, CS, 2008) Existence of global measure solutions. Convergence of
$\rho^N(t, x_1) := \int p(t, x_1, \dots, x_N) dx_2 \dots dx_N$
as $N \to \infty$ to a measure solution of Keller-Segel.

Stochastic particle simulation



Aggregation and fragmentation allowed

Distributed aggregates in kinetic models?



In other words: Is there a stable (rotationally symmetric?) steady state of a system of the form

$$\partial_t f + v \cdot \nabla_x f = Q[S](f), \quad \rho = \int f\, dv$$
$$\partial_t S = D_S \Delta S + \alpha\rho - \beta S$$

A simplified (linearized, 1D) problem

Assumptions:

- There is a fixed chemo-attractant distribution with a unique maximum at $x = 0$ ($x \in \mathbb{R}$).
- Bacterial velocities v lie in a bounded interval, symmetric with respect to $v = 0$.
- Velocity jump rates depend on pre-jump velocities with higher rates for velocities pointing away from $x = 0$.
- Velocity jump rates are independent from the distance to $x = 0$.

$$\partial_t f + v\,\partial_x f = Q(f) = \int_V \left(K(x,v')f' - K(x,v)f\right) dv'$$

with $\quad K(x,v) = 1 + \chi\,\mathrm{sign}(xv), \quad 0 < \chi < 1, \quad V = [-1/2, 1/2].$

Existence of a nontrivial steady state

Ansatz: $g(x,v) \approx e^{-\alpha|x|} G(v) \quad \text{as } |x| \to \infty$

Lemma: The eigenvalue problem $-\alpha v G = Q(G)$ (with a normalization condition for G) has a unique solution with $\alpha, G > 0$.

Theorem: Existence of a steady state g satisfying

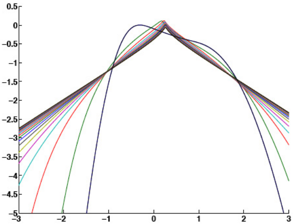
$$ce^{-\alpha|x|} \le g(x,v) \le Ce^{-\alpha|x|} \,.$$

Stability of the steady state

By mass conservation,

$$\frac{d}{dt}\int_{\mathbb{R}}\int_V f(x,v,t)dv\,dx = 0\,,$$

we expect $f(x,v,t) \to \mu_\infty g(x,v)$ as $t \to \infty$



with $\mu_\infty = \int f\,dv\,dx / \int g\,dv\,dx$, w.l.o.g.: $\mu_\infty = 0$.

A Lyapunov functional: (relative entropy, Markov process)

$$\frac{1}{2}\frac{d}{dt}\int_{\mathbb{R}}\int_V \frac{f^2}{g}dv\,dx = -\int_{\mathbb{R}}\int_V\int_V gK\left(\frac{f'}{g'}-\frac{f}{g}\right)^2 dv'\,dv\,dx$$

Problem: lack of coercivity of the entropy dissipation.
It vanishes for $f(x,v,t) = \mu(x,t)g(x,v)$.

Hypocoercivity

Abstract 'kinetic equation' in a Hilbert space:

$$\frac{df}{dt} + \mathsf{T}f = \mathsf{L}f$$

with L symmetric, negative semidefinite ('collision operator'),
T antisymmetric ('transport operator'), and $\mathcal{N}(\mathsf{L}) \cap \mathcal{N}(\mathsf{T}) = \{0\}$.

Entropy: $\frac{1}{2}\frac{d}{dt}\|f\|^2 = \langle \mathsf{L}f, f\rangle \le 0$

Hypocoercivity (trade mark C. Villani): $\lim_{t\to\infty} f(t) = 0$, although the entropy dissipation vanishes for $f \in \mathcal{N}(\mathsf{L}) \ne \{0\}$

C. Villani, *Hypocoercivity*, Mem. AMS 202, 2009

An abstract approach for proving hypocoercivity

Assumptions: (Π ... orthogonal projection to $\mathcal{N}(\mathsf{L})$)

- Microscopic coercivity: $-\langle \mathsf{L}f, f\rangle \geq \lambda_m \|(1-\Pi)f\|^2$
- Macroscopic coercivity: $\|\mathsf{T}\Pi f\|^2 \geq \lambda_M \|\Pi f\|^2$
- Diffusive macroscopic behavior: $\Pi\mathsf{T}\Pi = 0$

Modified entropy:

$$\mathsf{H}[f] = \frac{1}{2}\|f\|^2 + \varepsilon\langle \mathsf{A}f, f\rangle\,, \quad \mathsf{A} := (1 + (\mathsf{T}\Pi)^*\mathsf{T}\Pi)^{-1}(\mathsf{T}\Pi)^*$$

$$\frac{d}{dt}\mathsf{H}[f] = \langle \mathsf{L}f, f\rangle - \varepsilon\,\langle \mathsf{A}\mathsf{T}\Pi f, f\rangle - \varepsilon\,\langle \mathsf{A}\mathsf{T}(1-\Pi)f, f\rangle$$
$$+\varepsilon\,\langle \mathsf{T}\mathsf{A}f, f\rangle + \varepsilon\,\langle \mathsf{A}\mathsf{L}f, f\rangle\,.$$

Theorem: Let $\mathsf{AT}(1-\Pi)$ and AL be bounded and $\varepsilon > 0$ small enough. Then $\|f(t)\|$ decays exponentially.

J. Dolbeault, C. Mouhot, CS, *Trans. AMS* (2015)

Back to chemotaxis

$$\partial_t f + v\,\partial_x f = Q(f)$$

The choice $\mathsf{L} = Q$ and $\mathsf{T} = v\,\partial_x$ **does not work** since $Q(g), v\,\partial_x g \neq 0$. Also Q is not symmetric and $v\partial_x$ not antisymmetric in $L^2(dv\,dx/g)$.

The choice

$$\begin{aligned} \mathsf{L}f &:= \frac{1}{2}(Q - v\partial_x + (Q - v\partial_x)^*)f \\ &= \int_V \frac{g'K' + gK}{2}\left(\frac{f'}{g'} - \frac{f}{g}\right) dv'\,, \end{aligned}$$

$\mathsf{T} := (Q - v\partial_x - (Q - v\partial_x)^*)/2$ **works**.

V. Calvez, G. Raoul, CS, *KRM* (2015)

A nonlinear system

$$\partial_t f + v\partial_x f = \int_{\mathbb{R}} \big(S(x+v)f' - S(x+v')f \big) dv'$$

$$-\partial_x^2 S = \rho_f - S$$

ODE systems for the moments

$$A_{m,n}(t) := \int_{\mathbb{R}} \int_{\mathbb{R}} x^m v^n f(x,v,t) dx\, dv$$

are closed at any order: $A_{0,0}(t) = M$, $A_{1,0}(t) = A_{0,1}(t) = 0$.
For $N \geq 2$:

$$\dot{A}_{N-n,n} = (N-n)A_{N-n-1,n+1} + ((-1)^n + \delta_{n,N})\, MA_{N,0} - MA_{N-n,n} + l.o.t.$$

Results for the moment systems

Lemma: a) The second order moments tend to infinity for $M < 2$.
b) For $M > 2$,

$$A_{2,0}(t) \to \frac{2M}{M-2}, \quad A_{1,1}(t) \to 0, \quad A_{0,2}(t) \to \frac{2M^2}{M-2}.$$

c) For fixed N and for M large enough, the moments of order up to N converge to finite limits.
d) For fixed M and N large enough, some moments of order N tend to infinity, in general.

Conjecture: For $M > 2$, there exists a steady state with total mass M and with algebraic decay in x and v, becoming stronger with increasing M.

The formal limit $M \to \infty$

The rescaling $f \to Mf$, $S \to MS$ leads to

$$\partial_t f + v\partial_x f = M\big(S[\rho_f](x+v)\rho_f(x) - f\big)$$

Thus, $M \to \infty$ is a macroscopic limit. Formally,

$$f(x,v,t) \to f_0(x,v,t) = \rho_0(x,t)S[\rho_0](x+v,t)$$

with

$$\partial_t \rho_0 - \partial_x(x\,\rho_0) = 0$$

Large time limit:

$$\lim_{t\to\infty} f_0(x,v,t) = \frac{1}{2}\delta(x)e^{-|v|}$$

The Fourier transform

The Fourier transform $\widehat{f}(\xi, k, t) = \int_{\mathbb{R}} \int_{\mathbb{R}} f(x, v, t) e^{-i(\xi x + kv)} dv\, dx$ satisfies

$$\partial_t \widehat{f} - \xi \partial_k \widehat{f} = \frac{\widehat{\rho}_f(k) \widehat{\rho}_f(\xi - k)}{1 + k^2} - M \widehat{f}$$

The Duhamel formula can now be used to prove regularization results (both in x and v).

Existence of a steady state – open problems

Theorem: For every $M > 2$, there exists an even steady state $g \in L^1_+(\mathbb{R}_x \times \mathbb{R}_v) \cap C^\infty(\mathbb{R}_x \times \mathbb{R}_v)$ with total mass M.

A. Nouri, CS, *KRM* (2017)

- Is the steady state unique?
- What is its decay behavior in x and v?
- Is it stable?
- Higher dimensional problems (rotational symmetry)?