Mathematical models for cell movement
Part II

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Overview

- Biological background
- Keller-Segel model
- Kinetic models
- Scaling up and down

Overview – Today

- The Keller-Segel model.
- Variations on the same theme. Models with global existence.
- Kinetic models

The Keller-Segel Model

For $x \in \mathbb{R}^2$, we call the *classical Keller-Segel model*:

$$\begin{aligned} \partial_t \rho &= \nabla \cdot (\nabla \rho - \chi \rho \nabla S) \ , \\ \Delta S &= -\rho \ , \end{aligned}$$

with

$$\rho(\cdot, 0) = \rho^{\mathrm{I}} \ ,$$

with $\chi = \chi_0 = \text{const.}$

Keller-Segel Models

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- *if* $M < 8\pi/\chi$*: global existence of solutions,*
- *if* $M > 8\pi/\chi$*: finite-time-blow-up.*

Keller-Segel Models

Consider the following Keller-Segel model (with *prevention of overcrowding*) (Hillen-Painter model):

$$\begin{aligned} \partial_t \rho &= \nabla \cdot (\nabla \rho - \chi(\rho)\rho \nabla S) \\ \Delta S &= -\rho \ , \end{aligned}$$

where

$$\chi(\rho) = 0 \ , \quad \rho \geq \bar{\rho} > 0 \ .$$

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$$\chi(\rho) = 0 \,, \quad \rho \geq \bar{\rho} > 0 \,.$$

Theorem. *(Hillen, Painter, 2002) Solutions of the HP model exist globally.*

Keller-Segel Models

Define the *non-local* gradient

$$\mathring{\nabla}_R f(x,t) = \frac{1}{\omega_{n-1} R^{n-1}} \int_{S^{n-1}} f(x + yR) dy \; .$$

Keller-Segel Models

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Then the Hillen-Schmeiser-Painter model

$$\partial_t \rho = \nabla \cdot \left(\nabla \rho - \chi \rho \overset{\circ}{\nabla}_R S \right) \; ,$$

has global existence of solutions.

Keller-Segel Models

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- For any $\mu > 0$, ρ_μ exists for any time t.

Kinetic Models

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- The set of all possible velocities is given by a compact, spherically symmetric set V.

Kinetic Models

We define an equilibrium distribution $F = F(v)$:

$$F > 0\ , \quad \int_V F dv = 1\ , \quad \int_V vF dv = 0\ ,$$

if $S = S_0 \implies T[S_0, \rho](x, v, v', t)F(v') = T[S_0, \rho](x, v', v, t)F(v)$.

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Two possible turning kernels:

$$\begin{aligned} T[S, \rho](x, v, v', t) &= \lambda(S, \rho)(x, t)F(v) + a(S, \rho)F(v)v \cdot \nabla S(x, t)\,, \\ T[S, \rho](x, v, v', t) &= \psi(S(x + vt, t) - S(x, t))F(v)\,. \end{aligned}$$

Kinetic Models

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

$$\int_V (T[S,\rho](x,v,v',t) f(x,v',t) - T[S,\rho](x,v',v,t) f(x,v,t)) dv' \, .$$

Kinetic Models

Notation

$$
\begin{aligned}
f &= f(x, v, t)\ , \\
f' &= f(x, v', t)\ , \\
T[S,\rho] &= T[S,\rho](x, v, v', t)\ , \\
T^*[S,\rho] &= T[S,\rho](x, v', v, t).
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Kinetic Models

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Equation

$$\partial_t f + v\cdot\nabla f = \int_V (T[S,\rho]f' - T^*[S,\rho]f)dv'\ .$$

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Proof: (Let us suppose $n = 3$, the case $n = 2$ is technically more complicated but similar.)

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Theorem. *(C., Markowich, Perthame, Schmeiser, 2004; Hwang, Kang, Stevens, 2005) If $\psi(y) \leq Ay + B$ then solutions of the kinetic model exist globally.*

Proof: (Let us suppose $n = 3$, the case $n = 2$ is technically more complicated but similar.) We divide

$$S(x,t) = \frac{1}{4\pi} \int_{\mathbb{R}^3} \frac{1}{|x-y|} \rho(y,t)\,dy \,,$$

in $S = S^S + S^L$, where

$$S^S = \frac{1}{4\pi|\cdot|} \mathbb{I}_{\{|x|<1\}} * \rho \,, \qquad S^L = \frac{1}{4\pi|\cdot|} \mathbb{I}_{\{|x|\geq 1\}} * \rho \,.$$

Kinetic Models

Mass conservation:

$$||\rho(\cdot,t)||_{L^1(\mathbb{R}^3)} = ||f(\cdot,\cdot,t)||_{L^1(\mathbb{R}^3\times V)} = ||f^{\mathrm{I}}||_{L^1(\mathbb{R}^3\times V)}\ .$$

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From Young's inequality:

$$||S^L(\cdot,t)||_{L^\infty(\mathbb{R}^3)} \le \frac{1}{4\pi}||f^{\mathrm{I}}||_{L^\infty(\mathbb{R}^3\times V)} \,.$$

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Possibly changing the bounds on the turning kernels, we can change S by S^S.

Kinetic Models

Now, we have that

$$\partial_t f + v \cdot \nabla f \leq \int_V T[S(x, v, v', t) f(x, v', t) dv' \,.$$

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$$\partial_t f + v \cdot \nabla f \leq \int_V T[S(x,v,v',t) f(x,v',t) dv' \,.$$

We write $T[S(x,v,v',t) \leq C(1 + S^S(x+v,t))$, and then

$$f(x,v,t) \leq f^{\mathrm{I}}(x - vt, t) + C \int_0^t \rho(x - vs, t - s) ds + C f^1(x,v,t) \,,$$

where

$$\partial_t f(x,v,t) + v \cdot \nabla f(x,v,t) = \int_V S^S(x+v,t) f(x,v',t) dv' \,,$$

$$f(x,v,0) = 0 \,.$$

Kinetic Models

$$f^1(x,v,t) = \int_0^t S(x-vs+v,t-s)\rho(x-vs,t-s)ds\ .$$

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$$f^1(x,v,t) = \int_0^t S(x - vs + v, t - s)\rho(x - vs, t - s)ds \ .$$

$$||f^1(\cdot,\cdot,t)||_{L^p} \leq \sup_{s\in[0,t]} ||S^S(\cdot,s)||_{L^p} \int_0^t ||\rho(\cdot, t - s)||_{L^p} ds \ .$$

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$$||\rho(\cdot,t)||_{L^p} \le C(V)||f(\cdot,\cdot,t)||_{L^p} \ .$$

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$$f^1(x,v,t) = \int_0^t S(x - vs + v, t - s)\rho(x - vs, t - s)ds \; .$$

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$$||\rho(\cdot,t)||_{L^p} \leq C(V)||f(\cdot,\cdot,t)||_{L^p} \; .$$

We put everything together and find for $p \geq 2$

$$||f(\cdot,\cdot,t)||_{L^p} \leq ||f^{\mathrm{I}}||_{L^p} +$$

$$C\left(1 + \sup_{s\in[0,t]} ||S^S(\cdot,s)||_{L^p}\right) \int_0^t ||f(\cdot,\cdot,s)||_{L^p} ds \; .$$

Kinetic Models

In the previous equation, fix $p = 2$. In this case

$$\frac{1}{4\pi|x|}\mathbb{I}_{\{|x|\leq 1\}} \in L^2 \ .$$

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Then, from Young's inequality:

$$||S^S(\cdot,t)||_{L^2} \leq c||f^{\mathrm{I}}||_{L^1} \ ,$$

and from Gronwall's inequality we conclude a bound for $||f(\cdot,\cdot,t)||_{L^2}$.

Kinetic Models

Still, from Young's inequality, we have

$$||S^S(\cdot,t)||_{L^\infty} \leq c||f(\cdot,\cdot,t)||_{L^2} \leq C(t) \ ,$$

and again from Young's inequality, we have a bound for $||f(\cdot,\cdot,t)||_{L^\infty}$.

Kinetic Models

Let us consider the following turning kernels (with prevention of overcrowding):

$$
\begin{aligned}
T_\varepsilon[S,\rho] &= \lambda(S,\rho)F + \varepsilon a(S,\rho) F v \cdot \nabla S \,, \\
T_\varepsilon[S,\rho] &= \psi(S(x+\varepsilon\mu(\rho)v,t) - S(x,t))F
\end{aligned}
$$

with

$$
a(S,\rho) = 0 \,, \quad \mu(\rho) = 0 \,, \quad \rho \geq \bar{\rho} > 0 \,,
$$

and $\varepsilon > 0$ is a small parameter.

Kinetic Models

Theorem. *(C., Rodrigues, 2005) The kinetic models associated to these turning kernels have global existence of solutions. Furthermore,*

$$||\rho(\cdot,t)||_{L^\infty(\mathbb{R}^n)} \leq \max\{\bar{\rho}, ||\rho^{\mathrm{I}}||_{L^\infty(\mathbb{R}^n)}\} \, .$$

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- We prove only the first case, the second is similar.
- We consider initial conditions given by $f^{\mathrm{I}} = \rho^{\mathrm{I}} F$ and $S = 0$ and that λ is constant.

Kinetic Models

Lemma. *First note that*

$$\sup_{s\in[0,t]} ||\nabla S(\cdot,s)||_{L^\infty} \leq c \left(\sup_{s\in[0,t]} ||\rho(\cdot,s)||_{L^\infty} + \sup_{s\in[0,t]} ||\rho(\cdot,s)||_{L^1} \right) .$$

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Lemma. *First note that*

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Lemma. *Now, consider a time $t_* > 0$ such that $T[S,\rho] \ge 0, \forall (x,v,v',t) \in \mathbb{R}^n \times V \times V \times [0,t_*]$. Then,*

$$\sup_{s\in[0,t_*]} ||\rho(\cdot,s)||_{L^\infty} \le \max\{||\rho^{\mathrm{I}}||_{L^\infty}, \bar{\rho}\} .$$

Kinetic Models

Proof: First consider initial conditions such that $||\rho^{\mathrm{I}}||_{L^\infty} \leq \bar{\rho}$.

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Proof: First consider initial conditions such that $||\rho^{\mathrm{I}}||_{L^\infty} \leq \bar{\rho}$. We define

$$\begin{aligned}
\tilde{f} &= \bar{\rho}F - f \;, \\
\tilde{\rho} &= \int_V \tilde{f}\,dv = \bar{\rho} - \rho \;, \\
\tilde{S} &= \bar{\rho}t - S \;, \\
\tilde{a}(\tilde{S}, \tilde{\rho}) &= a(S, \rho)\frac{\rho}{\bar{\rho} - \rho} \;.
\end{aligned}$$

Kinetic Models

$(\tilde{f}, \tilde{S})$ is solution of

$$\begin{aligned} \partial_t \tilde{f} + v \cdot \nabla \tilde{f} &= \lambda F \tilde{\rho} + a(\tilde{S}, \tilde{\rho}) v \cdot \nabla \tilde{S} \tilde{\rho} - \lambda \tilde{f} \,, \\ \Delta \tilde{S} &= -\tilde{\rho} \,. \end{aligned}$$

with initial conditions given by $\tilde{\rho}^{\mathrm{I}} = (\bar{\rho} - \rho^{\mathrm{I}}) F > 0$ and $\tilde{S} = 0$.

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with initial conditions given by $\tilde{\rho}^{\mathrm{I}} = (\bar{\rho}-\rho^{\mathrm{I}})F > 0$ and $\tilde{S}=0$. The turning kernels is

$$\tilde{T}[\tilde{S},\tilde{\rho}] = \lambda F + \varepsilon\tilde{a}(\tilde{S},\tilde{\rho})Fv\cdot\tilde{S} \geq 0\,,$$

$\forall(x,v,v',t)\in\mathbb{R}^n\times V\times V\times[0,t_*]$. We conclude the positivity of $\tilde{f}$, then $0\leq\bar{\rho}F-f$, which implies $\rho\leq\bar{\rho}$.

Kinetic Models

Now consider x such that $\rho^{\mathrm{I}}(x) > \bar{\rho}$ in a neighbourhood U of x we have

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This implies

$$e^{\lambda t} f(x, v, t) = f\left(x - vt, v, t\right) + \int_0^t e^{\lambda s} \lambda F \rho\left(x - v(t-s), s\right) \, ds \ ,$$

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and then

$$e^{\lambda t} \rho(x, t) \leq ||\rho^{\mathrm{I}}||_{L^\infty} + \int_0^t e^{\lambda s} \lambda ||\rho(\cdot, s)||_{L^\infty(U)} ds\ .$$

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Kinetic Models

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$$e^{\lambda t}\rho(x,t) \leq ||\rho^{\mathrm{I}}||_{L^\infty} + \int_0^t e^{\lambda s}\lambda||\rho(\cdot,s)||_{L^\infty(U)}ds\ .$$

Finally, using Gronwall's lemma:

$$||\rho(\cdot,t)||_{L^\infty(U)} \leq ||\rho^{\mathrm{I}}||_{L^\infty}$$

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- $||\nabla S||_{L^\infty}$ is bounded by $||\rho||_{L^\infty}$.
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- This implies the $||\nabla S||_{L^\infty}$ is uniformly in time bounded.
- Then, $T_\varepsilon[S, \rho] = \lambda F + \varepsilon a(S, \rho) F v \cdot \nabla S$ is positive for small ε, for any time.

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- Then, $T_\varepsilon[S, \rho] = \lambda F + \varepsilon a(S, \rho) F v \cdot \nabla S$ is positive for small ε, for any time.
- We do everything again!

Kinetic Models

Theorem. *(C., Kang) With*

$$T_{\varepsilon,\mu}[S,\rho] = \psi\left(S\left(x + \frac{\varepsilon}{1+\mu\rho}v\right) - S\left(x,t\right)\right)$$

the solution exists globally.

General Picture

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Let us define the limit

$$\Phi := \lim_{\varepsilon \to 0} (\rho_\varepsilon, S_\varepsilon) \ .$$

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Question:

Which is the set of equations that Φ obey?

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Time evolution	$\mathcal{M}_\varepsilon[\Psi_\varepsilon] = 0$		$\mathcal{M}[\Phi] = 0$
	$\downarrow$		$\downarrow$
Final state	$\Psi_\varepsilon(T)$	**?**	$\Phi(T)$

General Picture

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	$\downarrow$		$\downarrow$
Time evolution	$\mathcal{M}_\varepsilon[\Psi_\varepsilon] = 0$		$\mathcal{M}[\Phi] = 0$
	$\downarrow$		$\downarrow$
Final state	$\Psi_\varepsilon(T)$	**?**	$\Phi(T)$

If

$$\Phi(t) = \lim_{\varepsilon\to 0} \Phi_\varepsilon(t)\ , \quad t < T$$

(in some sense) then $\mathcal{M}$ is the limit model of $\mathcal{M}_\varepsilon$.