Mathematical models for cell movement
Part I

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Overview

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

Overview – Today

- Biological background
  - Cells move — for what ?
  - Life and death of *Dictyostelium discoideum*
- Choosing a problem: the initiation of the aggregation
- The Keller-Segel model.

Chemotaxis

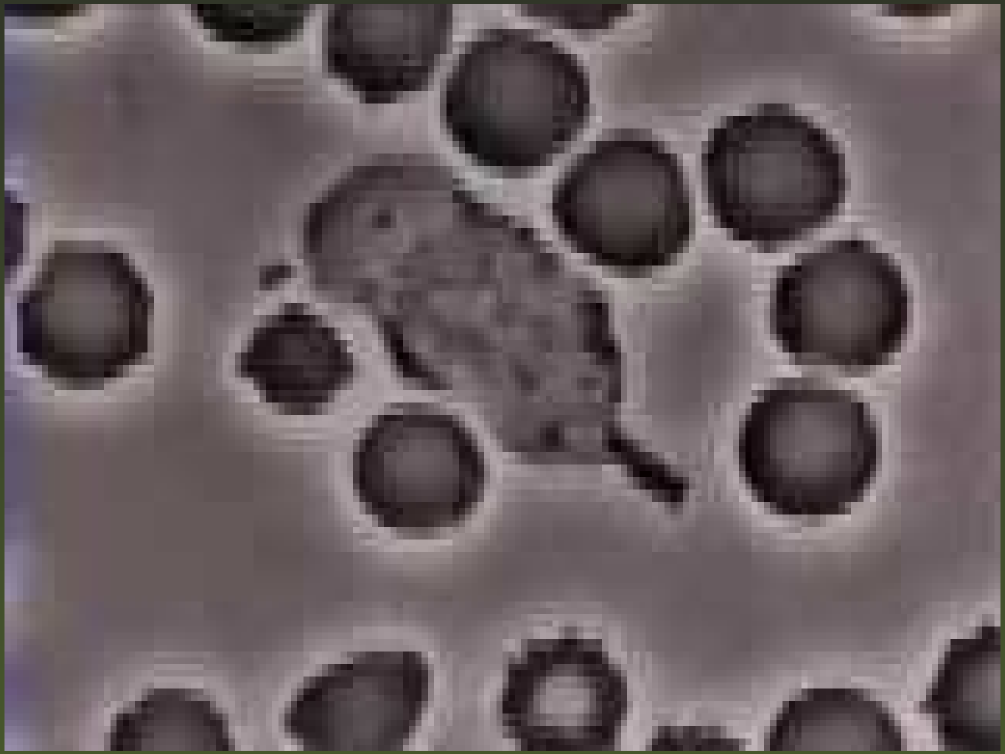

Figure 1: A neutrophil (white blood cell) chasing a bacterium. Film by Peter Devreotes.

Why do cells move?

- In general: looking for better places to live.
- Other reasons are:
  - immunology,
  - embryology and development,
  - aggregation.

One day in the life of *Dd*

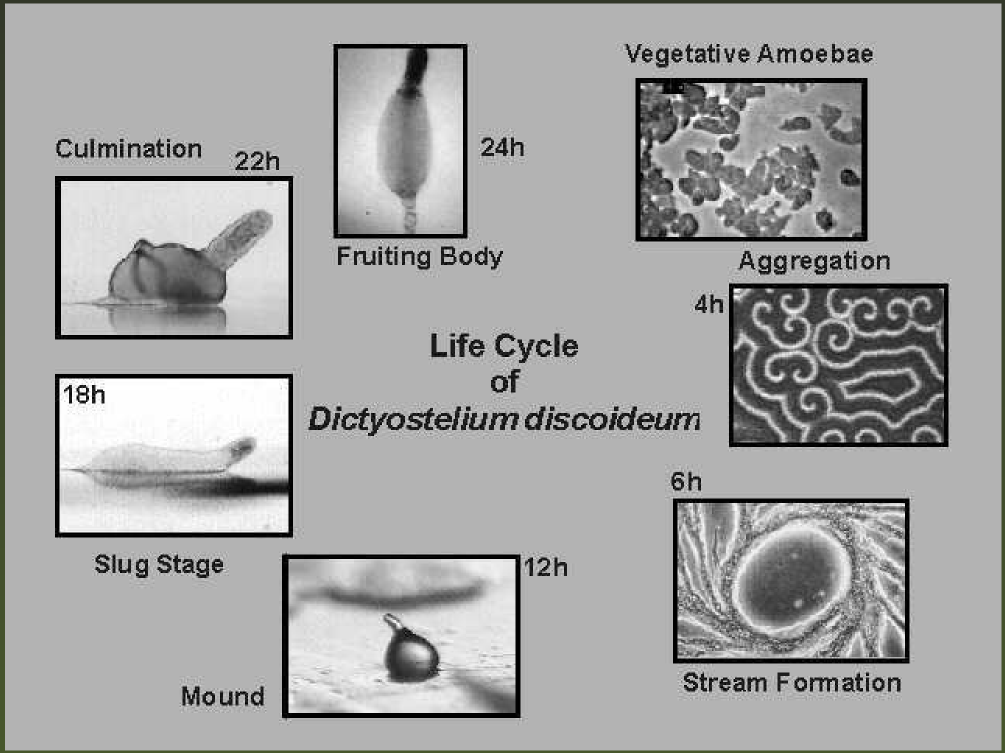

Figure 2: Life cycle of *Dictyostelium discoideum*. Picture made by Florian Seigert and Kees Wiejer (Zoologisches Institut München Ludwig-Maximilians-Universität München).

The initiation of the aggregation

The *Dictyostelium discoideum* moves toward higher concentrations of cAMP.

- Video 1 by Peter Devreotes.
- Video 2 by Peter Devreotes.

The formation of a core

Cells of *Dd* aggregates in a core.

- Video 1 by Kees Wiejer and Florian Seigert.

The slug phase

The aggregate starts to behave like a slug and migrates.

- Video 1 by Kees Wiejer and Florian Seigert.
- Video 2 by by Kees Wiejer and Florian Seigert.
- Video 3 by by Kees Wiejer and Florian Seigert.

The Culmination

The *slug* culminates with a spore on the top.

- Video 1 by Kees Wiejer and Florian Seigert.
- Video 2 by Rex Chisolm.

Why it is important to study the *Dd*?

Many reasons:

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- Cell motility,

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- Cell communication,

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Many reasons:

- Cell motility,
- Cell communication,
- Cooperation among non-clonal individuals.

Keller-Segel model

"Initiation of Slime Mold Aggregation Viewed as an Instability", Evelyn Keller and Lee Segel, *J. Theor. Biol.* (1970) **26**, 399–415.

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Variables:

- $\rho(x,t) =$ density of amoebas.

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Variables:

- $\rho(x,t) =$ density of amoebas.
- $S(x,t) =$ density of cAMP.

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- $\rho(x,t)$ = density of amoebas.
- $S(x,t)$ = density of cAMP.
- $\eta(x,t)$ = density of phosphodiesterase.

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- $c(x,t) =$ density of a certain instable substance.

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We assume $n = 2$.

Keller-Segel model

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- cAMP is degraded by an extra-cellular enzyme (phosphodiesterase) at rate $g(S, \eta)$ by amoeba.

Keller-Segel model

We shall implement:

- cAMP is produced by the amoebas at a rate $f(S, \rho)$ per amoeba.
- cAMP is degraded by an extra-cellular enzyme (phosphodiesterase) at rate $g(S, \eta)$ by amoeba.
- cAMP and phosphodiesterase react making a new unstable compound C that decays immediately in phosphodiesterase and certain degenerated product.

$$S + \eta \leftrightarrows C \to \eta + \text{product}.$$

Keller-Segel model

- cAMP, phosphodiesterase and the compound diffuse according to Fick's law.

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$$J = D\nabla\phi\,.$$

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\phi &= \text{flux} \,,
\end{aligned}
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$$J = D\nabla\phi \,.$$

- Amoebas concentration varies due to random diffusion and chemotaxis, in the positive direction of cAMP's gradient.

Keller-Segel model

For any substance with density a^i, we have a flux J^i and a creation/destruction term Q^i such that

$$\frac{\partial a^i}{\partial t} = Q^i - \nabla \cdot J^i \; .$$

Keller-Segel model

For any substance with density a^i, we have a flux J^i and a creation/destruction term Q^i such that

$$\frac{\partial a^i}{\partial t} = Q^i - \nabla \cdot J^i \ .$$

Mass conservation implies that

$$Q^\rho = 0 \ .$$

Keller-Segel model

In order to obtain Q^S, Q^η and Q^C we shall consider the production by the amoebas and the chemical reaction:

$$\begin{aligned} Q^S &= -k_1 S\eta + k_{-1}c + \rho f(S,\rho)\ , \\ Q^\eta &= -k_1 S\eta + (k_{-1}+k_2)c + \rho g(S,\eta)\ , \\ Q^c &= k_1 S\eta - (k_1+k_2)c\ . \end{aligned}$$

Keller-Segel model

Fluxes are given by the following expressions:

$$
\begin{aligned}
J^\rho &= -D_1 \nabla \rho + D_2 \nabla S \,, \\
J^S &= -D_S \nabla S \,, \\
J^\eta &= -D_\eta \nabla \eta \,, \\
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\end{aligned}
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Keller-Segel model

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Diffusion coefficients are:

$$D_i = D_i(\rho, S, \eta, c) \, .$$

Keller-Segel model

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$$\begin{aligned}
\frac{\partial \rho}{\partial t} &= \nabla \cdot (D_1 \nabla \rho) - \nabla \cdot (D_2 \nabla S) \, , \\
\frac{\partial S}{\partial t} &= -k_1 S \eta + k_{-1} c + \rho f(S, \rho) + D_S \Delta S \, , \\
\frac{\partial \eta}{\partial t} &= -k_1 S \eta + (k_{-1} + k_2) c + \rho g(S, \eta) + D_\eta \eta \, , \\
\frac{\partial c}{\partial t} &= k_1 S \eta - (k_1 + k_2) c + D_c \Delta c \, .
\end{aligned}$$

Keller-Segel model

Now, we simplify the model.

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- The substance C is in chemical equilibrium:

$$k_1 S\eta - (k_{-1} + k_2)c = 0 \ .$$

(Haldane's assumption)

Keller-Segel model

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- The substance C is in chemical equilibrium:

  $$k_1 S\eta - (k_{-1} + k_2)c = 0 \ .$$

  (Haldane's assumption)

- Enzyme concentration (in both free and bound forms) is constant

  $$\eta + c = \eta_0 \ .$$

Keller-Segel model

Solving the system, we find

$$\eta = \frac{\eta_0}{1 + K\rho} ,$$

$$K = \frac{k_1}{k_{-1} + k_2} .$$

Keller-Segel model

We write again the system:

$$\frac{\partial \rho}{\partial t} = -\nabla \cdot (D_1 \nabla \rho) + \nabla (D_2 \nabla S) ,$$
$$\frac{\partial S}{\partial t} = -k(S)S + \rho f(S, \rho) + D_S \Delta S ,$$

where $k(S) = \eta_0 k_2 K / (1 + KS)$.

Keller-Segel model

We resume the model

- Amoebas have a random and a chemotactical movement.

Keller-Segel model

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- Amoebas have a random and a chemotactical movement.
- Chemoattractant S diffuses, is created by the amoebas at rate f and decays at rate k.

Keller-Segel model

From now on, we call the following system the Keller-Segel system

$$\frac{\partial \rho}{\partial t} = \nabla \cdot (D\nabla\rho - \chi\rho\nabla S) \; ,$$
$$\frac{\partial S}{\partial t} = D_S \Delta S + \varphi(\rho, S) \; ,$$

where $D = D(S,\rho)$, $\chi = \chi(S,\rho)$ e $D_S = D_S(S,\rho)$.

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where $D = D(S, \rho)$, $\chi = \chi(S, \rho)$ e $D_S = D_S(S, \rho)$.

$\varphi(\rho, S)$ describes production and decay of the chemoattractant. Typically

$$\varphi = \alpha \rho - \beta S \; .$$

The Keller-Segel Model

- ρ=density of cells.
- S=density of chemo-attractant.

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$$\frac{\partial \rho}{\partial t} = \nabla \cdot (D\nabla \rho - \chi \rho \nabla S) \ ,$$
$$\frac{\partial S}{\partial t} = D_0 \Delta S + \alpha \rho - \beta S \ ,$$

where $D = D(S, \rho)$, $\chi = \chi(S, \rho)$, $D = D(S, \rho)$ e $D_0 = D_0(S, \rho)$, $\alpha > 0$, $\beta \geq 0$.

The Keller-Segel Model

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- The fast-diffusion limit: elliptic equation for S.

The Keller-Segel Model

Some important cases:

- The *classical* Keller-Segel model: $\chi, D, D_0 =$ const.
- The no-decay case: $\beta = 0$.
- The fast-diffusion limit: elliptic equation for S.

With these assumption the equation for S is

$$\Delta S = -\rho \, .$$

The Keller-Segel Model

Finally, consider for $x \in \mathbb{R}^2$

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

with

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

The Keller-Segel Model

Properties:

The Keller-Segel Model

Theorem. *(Perthame, Dolbeaut, 2004) Consider a solution of the KS system, such that*

- $\int_{\mathbb{R}^2} |x|^2 \rho(x,t)dx < \infty$,
- $\int_{\mathbb{R}^2} \frac{1+|x|}{|x-y|}\rho(y,t)dy \in L^\infty((0,T)\times\mathbb{R}^2)$.

Then

$$\frac{d}{dt}\int_{\mathbb{R}^2} |x|^2\rho(x,t)dx = 4M\left(1-\frac{\chi M}{8\pi}\right) .$$

The Keller-Segel Model

Proof:

$$S(x,t) \;=\; -\frac{1}{2\pi}\int_{\mathbb{R}^2} \log|x-y|\rho(y,t)dy \;,$$

The Keller-Segel Model

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\begin{aligned}
S(x,t) &= -\frac{1}{2\pi}\int_{\mathbb{R}^2} \log|x-y|\rho(y,t)dy \ , \\
\nabla S(x,t) &= -\frac{1}{2\pi}\int_{\mathbb{R}^2} \frac{x-y}{|x-y|^2}\rho(y,t)dy \ .
\end{aligned}
$$

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$$S(x,t) = -\frac{1}{2\pi}\int_{\mathbb{R}^2} \log|x-y|\rho(y,t)dy \, ,$$

$$\nabla S(x,t) = -\frac{1}{2\pi}\int_{\mathbb{R}^2} \frac{x-y}{|x-y|^2}\rho(y,t)dy \, .$$

$$\int_{\mathbb{R}^2} \rho(x)\rho(y)\frac{x\cdot(x-y)}{|x-y|^2}dydx = -\int_{\mathbb{R}^2} \rho(x)\rho(y)\frac{y\cdot(x-y)}{|x-y|^2}dydx =$$

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$$\int_{\mathbb{R}^2} \rho(x)\rho(y)\frac{x\cdot(x-y)}{|x-y|^2}dydx = -\int_{\mathbb{R}^2} \rho(x)\rho(y)\frac{y\cdot(x-y)}{|x-y|^2}dydx =$$

$$\frac{1}{2}\int_{\mathbb{R}^2} \rho(x)\rho(y)\frac{(x-y)\cdot(x-y)}{|x-y|^2}dydx = \frac{1}{2}\int_{\mathbb{R}^2} \rho(x)\rho(y)dxdy = \frac{M^2}{2} \;.$$

The Keller-Segel Model

$$\frac{1}{2}\frac{d}{dt}\int_{\mathbb{R}^2} |x|^2 \rho(x)dx \;=\; \frac{1}{2}\int_{\mathbb{R}^2} |x|^2 \nabla\cdot\left(\nabla\rho - \chi\rho\nabla S\right)dx$$

The Keller-Segel Model

$$\begin{aligned}
\frac{1}{2}\frac{d}{dt}\int_{\mathbb{R}^2}|x|^2\rho(x)dx &= \frac{1}{2}\int_{\mathbb{R}^2}|x|^2\nabla\cdot(\nabla\rho-\chi\rho\nabla S)\,dx \\
&= -\int_{\mathbb{R}^2}x\,(\nabla\rho-\chi\rho\nabla S)\,dx
\end{aligned}$$

The Keller-Segel Model

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\int_{\mathbb{R}^2}|x|^2\rho(x)dx &= \frac{1}{2}\int_{\mathbb{R}^2}|x|^2\nabla\cdot\left(\nabla\rho-\chi\rho\nabla S\right)dx\\ &= -\int_{\mathbb{R}^2}x\left(\nabla\rho-\chi\rho\nabla S\right)dx\\ = \int_{\mathbb{R}^2}2\rho dx &- \frac{\chi}{2\pi}\iint_{\mathbb{R}^2\times\mathbb{R}^2}\rho(x)\rho(y)x\cdot\frac{(x-y)}{|x-y|^2}dydx\end{aligned}$$

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&=
\end{aligned}$$

The Keller-Segel Model

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= \int_{\mathbb{R}^2} 2\rho dx &- \frac{\chi}{2\pi}\iint_{\mathbb{R}^2\times\mathbb{R}^2} \rho(x)\rho(y)x\cdot\frac{(x-y)}{|x-y|^2}dydx \\
&= 2M - \frac{\chi}{2\pi}\frac{M^2}{2}
\end{aligned}$$

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\frac{1}{2}\frac{d}{dt}\int_{\mathbb{R}^2} |x|^2 \rho(x) dx &= \frac{1}{2}\int_{\mathbb{R}^2} |x|^2 \nabla\cdot\left(\nabla\rho - \chi\rho\nabla S\right) dx \\
&= -\int_{\mathbb{R}^2} x\left(\nabla\rho - \chi\rho\nabla S\right) dx \\
= \int_{\mathbb{R}^2} 2\rho dx &- \frac{\chi}{2\pi}\iint_{\mathbb{R}^2\times\mathbb{R}^2} \rho(x)\rho(y) x\cdot\frac{(x-y)}{|x-y|^2} dy dx \\
&= 2M - \frac{\chi}{2\pi}\frac{M^2}{2} = 2M\left(1 - \frac{\chi M}{8\pi}\right) .
\end{aligned}$$

The Keller-Segel Model

Theorem. *(Perthame, Dolbeaut, 2004) Consider the KS system such that*

- $M < 8\pi/\chi$,
- $\rho^{\mathrm{I}} \in L^1(\mathbb{R}^2, (1+|x|^2)dx)$.

Then, the system has a weak solution such that

- $(1+|x|^2+\log\rho)\rho \in L^\infty_{\mathrm{loc}}(\mathbb{R}^+, L^1(\mathbb{R}^2))$,
- $\int_0^\infty \int_{\mathbb{R}^2} \rho|\nabla \log\rho - \chi\nabla S|^2 dx\, dt < \infty$,
- $\rho, \nabla\sqrt{\rho} \in L^2([0,T]\times\mathbb{R}^2), \forall T > 0$.

The Keller-Segel Model

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- Regularization of solutions,
- Estimations,
- Limits.

The Keller-Segel Model

Step 1: (Regularization) Consider

$$K_\varepsilon(z) = \begin{cases} -\frac{1}{2\pi} \log|z| & \text{if } |z| > \varepsilon\ , \\ -\frac{1}{2\pi} \log\varepsilon & \text{if } |z| \le \varepsilon\ . \end{cases}$$

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This means that, from

$$S(x,t) = -\frac{1}{2\pi}\int_{\mathbb{R}^2} \log|x-y|\rho(y,t)dy$$

we change to

$$S_\varepsilon(x,t) = \int_{\mathbb{R}^2} K_\varepsilon(x-y)\rho(y,t)dy = (K_\varepsilon * \rho_\varepsilon)(x,t)\ .$$

The Keller-Segel Model

Step 2: (Estimations) Equation:

$$\partial_t \rho_\varepsilon = \nabla \cdot \left(\nabla \rho_\varepsilon - \chi \rho_\varepsilon \nabla \left(K_\varepsilon * \rho_\varepsilon \right) \right) \ .$$

$$\frac{d}{dt}$$

The Keller-Segel Model

Step 2: (Estimations) Equation:

$$\partial_t \rho_\varepsilon = \nabla \cdot (\nabla \rho_\varepsilon - \chi \rho_\varepsilon \nabla (K_\varepsilon * \rho_\varepsilon)) \ .$$

Then:

$$\frac{d}{dt} \int_{\mathbb{R}^2} |x|^2 \rho_\varepsilon(x,t) dx \quad = \quad 4M - \frac{\chi}{2\pi} \int_{|y-x|>\varepsilon} \rho_\varepsilon(x,t) \rho_\varepsilon(y,t) dx dy$$

The Keller-Segel Model

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We prove similar ε-independent bounds and take the limit $\varepsilon \to 0$.

The Keller-Segel Model

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Corollary. *In the two dimensional case, we have:*

- *if* $M < 8\pi/\chi$*: global existence of solutions,*
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This is in agreement with the fact that aggregation occurs only if the initial density of *Dd* is above certain threshold.

The Keller-Segel Model

Corollary. *In the two dimensional case, we have:*

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

This is in agreement with the fact that aggregation occurs only if the initial density of *Dd* is above certain threshold.

What happens if $M = 8\pi/\chi$?

The Keller-Segel Model

Suppose general dimension n.

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Theorem. *(Corrias, Perthame, Zaag, 2004) There exists a constant K such that*

$$||\rho^{\mathrm{I}}||_{L^{n/2}(\mathbb{R}^n)} \leq K$$

then the KS system has a global in time weak solution such that

$$\begin{aligned} ||\rho(\cdot,t)||_{L^p(\mathbb{R}^n)} &\leq ||\rho^{\mathrm{I}}||_{L^p(\mathbb{R}^n)}\,, \quad \max\{1, \frac{n}{2}-1\} \leq p \leq \frac{n}{2}\,, \\ ||\rho(\cdot,t)||_{L^p(\mathbb{R}^n)} &\leq C(t, K, ||\rho^{\mathrm{I}}||_{L^p(\mathbb{R}^n)})\,, \quad \frac{n}{2} < p \leq \infty\,. \end{aligned}$$

The Keller-Segel Model

Theorem. *(Corrias, Perthame, Zaag, 2004) Suppose that* $n \geq 3$ *and*

$$\int_{\mathbb{R}^n} \frac{|x|^2}{2} \rho^{\mathrm{I}}(x) dx \leq C M^{n/(n-2)} \ ,$$

and assume that

$$M \geq M_0$$

for some $M_0 > 0$. *Then the KS system has no global solution with fast decay.*

Keller-Segel Models

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

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

where

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

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

Keller-Segel Models

Proof: Consider:

$$
\begin{aligned}
\mathcal{J}_+ &= \{x | \rho(x,t) > \bar{\rho}\} \ , \\
\mathcal{J}_0 &= \{x | \rho(x,t) = \bar{\rho}\} \ , \\
\mathcal{J}_- &= \{x | \rho(x,t) < \bar{\rho}\} \ ,
\end{aligned}
$$

Keller-Segel Models

Proof: Consider:

$$\begin{aligned} \mathcal{J}_+ &= \{x|\rho(x,t) > \bar{\rho}\} \,, \\ \mathcal{J}_0 &= \{x|\rho(x,t) = \bar{\rho}\} \,, \\ \mathcal{J}_- &= \{x|\rho(x,t) < \bar{\rho}\} \,, \end{aligned}$$

and define

$$\rho^+(x,t) = \begin{cases} \rho(x,t) - \bar{\rho} & \text{if } x \in \mathcal{J}_+ \,, \\ 0 & \text{otherwise.} \end{cases}$$

Keller-Segel Models

$$\frac{1}{2}\frac{d}{dt}||\rho^+(\cdot,t)||^2_{L^2(\mathbb{R}^n)} \quad = \quad \left(\int_{\mathcal{J}_+} + \int_{\mathcal{J}_0} + \int_{\mathcal{J}_-}\right)\rho^+\rho^+_t$$

Keller-Segel Models

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$$= \int_{\mathcal{J}_+}(\rho - \bar{\rho})\rho_t$$

Keller-Segel Models

$$\begin{aligned}
\frac{1}{2}\frac{d}{dt}||\rho^+(\cdot,t)||^2_{L^2(\mathbb{R}^n)} &= \left(\int_{\mathcal{J}_+} + \int_{\mathcal{J}_0} + \int_{\mathcal{J}_-}\right)\rho^+\rho^+_t \\
&= \int_{\mathcal{J}_+}(\rho - \bar{\rho})\rho_t \\
&= \int_{\mathcal{J}_+}(\rho - \bar{\rho})\nabla\cdot\left(\nabla\rho - \chi\beta(\rho)\rho\nabla S\right) \ ,
\end{aligned}$$

Keller-Segel Models

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\end{aligned}
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&= -\int_{\mathcal{J}_+}|\nabla\rho|^2 \leq 0\ .
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Keller-Segel Models

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Keller-Segel Models

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If $||\rho^{\mathrm{I}}||_{L^\infty(\mathbb{R}^n)} > \bar{\rho}$, then in a neighbourhood of a point x such that $\rho(x, t) > \bar{\rho}$, the equation is

$$\partial_t \rho = \Delta \rho$$

and the maximum principle holds.

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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Keller-Segel Models

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$$\beta(\rho) = \beta_\mu(\rho) = \frac{\rho}{1 + \mu\rho} ,$$

or more generally:

$$\begin{aligned} \beta_\mu(\rho) &= \frac{1}{\mu} Q(\mu\rho) , \\ Q(y) &\approx y - \alpha y^2 , \quad y \to \infty , \\ \lim_{y \to \infty} Q(y) &< \infty . \end{aligned}$$

Keller-Segel Models

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More precisely:

- For $t < T$, $\lim_{\mu\to 0} \rho_\mu = \rho_0$.
- This cannot be extended after T because ρ_0 no longer exists (T is the blow up time).
- For any $\mu > 0$, ρ_μ exists for any time t.

Keller-Segel Models

For any $\mu > 0$ the aggregation region is of order $\sqrt{\mu}$. We consider each of the N aggregates as a point particles, x_j, $j = 1, \cdots, N$, and consider a regular remainder which is important far from these points:

$$\rho(x,t) \approx \sum_{j=1}^{N} M_j(t)\delta(x - x_j(t)) + u_{\mathrm{reg}}(x,t) \ .$$

Keller Segel Models

The chemoattractant concentration is given by

$$S(x,t) \approx -\frac{1}{2\pi}\sum_{j=1}^{N} M_j(t)\log(|x - x_j(t)|) + S_{\rm reg}(x,t)\ ,$$

where

$$S_{\rm reg} = -\frac{1}{2\pi}\int_{\mathbb{R}^2} \log(|x-y|)u_{\rm reg}(y,t)dy\ .$$

Keller-Segel Models

Theorem. *(Velazquez, 2004) Consider a solution of the V model. If we impose the previous Ansatz, then*

$$
\begin{aligned}
\frac{\partial \rho_{\mathrm{reg}}}{\partial t} &= \Delta \rho_{\mathrm{reg}} + \frac{1}{2\pi} \sum_{j=1}^{N} M_j(t) \frac{(x - x_j(t))}{|x - x_j(t)|^2} \cdot \nabla \rho_{\mathrm{reg}} \\
&\quad - \nabla \left(\rho_{\mathrm{reg}} \nabla S_{\mathrm{reg}} \right) \ , \\
S_{\mathrm{reg}}(x,t) &= -\frac{1}{2\pi} \int_{\mathbb{R}^2} \log(|x-y|) \rho_{\mathrm{reg}}(y,t) dy \ , \\
\dot{x}_i(t) &= \Gamma(M(t)) A_i(t) \ ,
\end{aligned}
$$

Keller-Segel Models

$$
\begin{aligned}
A_i(t) &= -\sum_{j=1\ ,j\neq i}^{N} \frac{M_j(t)}{2\pi} \frac{(x_i(t)-x_j(t))}{|x_i(t)-x_j(t)|^2} \\
&\quad +\nabla S_{\text{reg}}(x_i(t),t)\ , \\
\frac{dM_i(t)}{dt} &= u_{\text{reg}} M_i(t)\ ,
\end{aligned}
$$

where $\Gamma(M)$ is a function of $M > 8\pi$.

Keller-Segel Models

After certain time, mass will be only in the aggregates, that will interact as

$$\begin{aligned} \dot{x}_i(t) &= \frac{\Gamma(M_i(t))M_j(t)}{2\pi} \cdot \frac{(x_i(t) - x_j(t))}{|x_i(t) - x_j(t)|^2}, \\ \dot{x}_j(t) &= \frac{\Gamma(M_j(t))M_i(t)}{2\pi} \cdot \frac{(x_j(t) - x_i(t))}{|x_j(t) - x_i(t)|^2} \end{aligned}$$

and after certain time they will coalesce in a single aggregate.

Keller-Segel Models

the function $\Gamma(M)$ has the following properties:

$$0 < \Gamma(M) < 1\,,$$

$$\lim_{M \to 8\pi} \Gamma(M) = 1\,,$$

$$\lim_{M \to \infty} \Gamma(M) = 0\,.$$

The Keller-Segel Model

Is the extension of the Keller-Segel model made by Velazquez general?