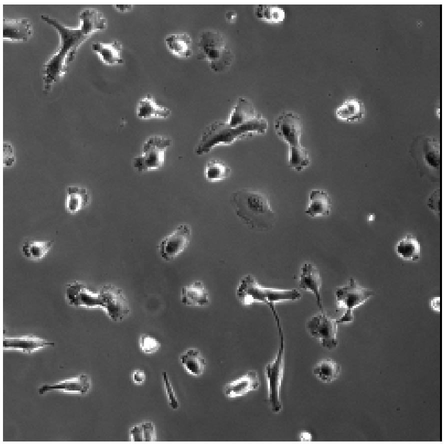
Competitive System of Chemotaxis

Takashi Suzuki

Cell Movement

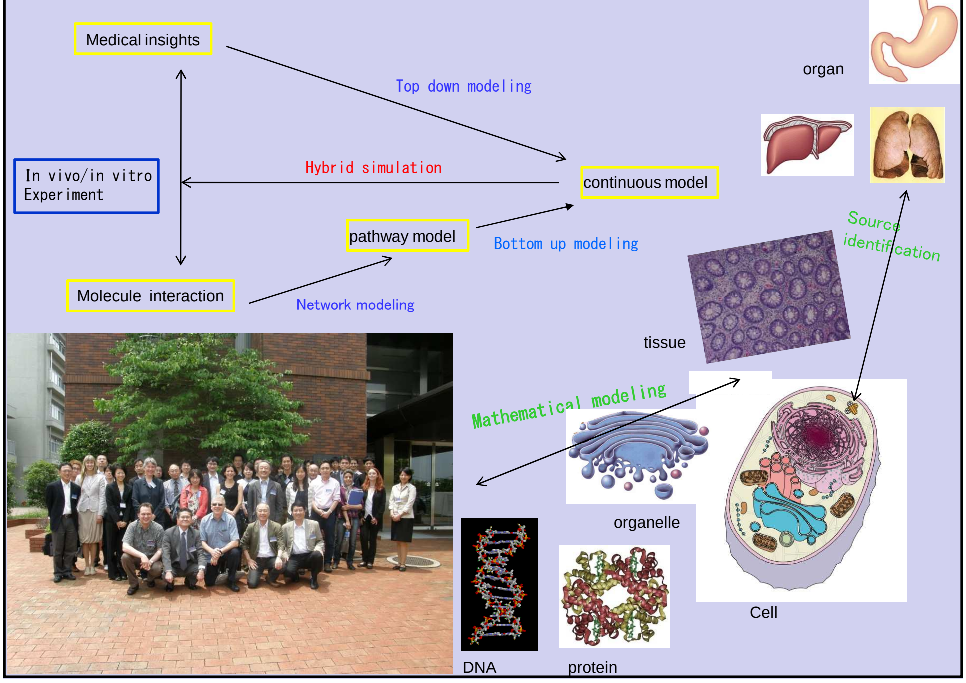


HT1080Human Adeno sarcoma Cell

Physiological
- morphogenesis
- wound healing
- cellular immunity

Pathological
- inflammation
- arteriosclerosis
- cancer invasion, metastasis

Mathematical Methods in Cancer Cell Biology



top down modeling

1) reinforce-consumption

$u_t = \alpha, \ v_t = -\beta$

2) production-extinction

$u_t = \alpha u, \ v_t = -\beta v$

3) transport

$u_t = -\nabla \cdot j$

$j \ldots$ fllux

4) gradient

$j = -d_u \nabla u \ldots$ diffusion

$j = d_v \nabla v \ldots$ chemotaxis

5) chemical reaction

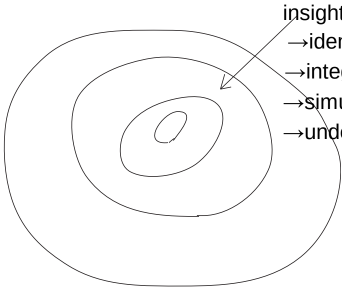
$A + B \to C \ (k)$

$\Rightarrow$ (mass action)

$$\frac{d[A]}{dt} = -k[A][B]$$

$$\frac{d[B]}{dt} = -k[A][B]$$

insight from experiments
→identify factors
→integrated formulae
→simulation check
→understand the evens as a system



complicated network
cutting individual pathways may cause opposite effects

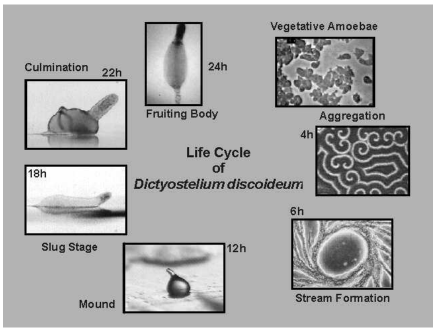
beyond the reductionism

Keller-Segel 70

$$
\begin{aligned}
u_t &= \nabla \cdot (d_1(u,v)\nabla u) - \nabla \cdot (d_2(u,v)\nabla v) \\
v_t &= d_v \Delta v - k_1 vw + k_{-1} p + f(v)u \\
w_t &= d_w \Delta w - k_1 vw + (k_{-1} + k_2)p \\
&\quad + g(v,w)u \\
p_t &= d_p \Delta p + k_1 vw - (k_{-1} + k_2)p
\end{aligned}
$$

$u = u(x,t)$ cellular slime molds
$v = v(x,t)$ chemical substances
$w = w(x,t)$ enzymes
$p = p(x,t)$ comlices

1. transport, gradient
   (a) diffusion u, v, w, p
   (b) chemotaxis $v \to u$
2. production $u \to (v, w)$



moving clustered cells   aggregating cells

3. chemical reaction v, w, p

$$
V + W \underset{\leftarrow (k_{-1})}{\overset{(k_1) \rightarrow}{}} P \overset{(k_2)}{\rightarrow} W + A
$$

$$
\begin{aligned}
v_t &= -k_1 vw + k_{-1} p \\
w_t &= -k_1 vw + (k_{-1} + k_2)p \\
p_t &= k_1 vw - (k_{-1} + k_2)p
\end{aligned}
$$

Michaelis-Menten reduction (w, p)

1. quasi-static $k_1 vw - (k_{-1} + k_2)p = 0$
2. mass conservation $w + p = c$

$\Rightarrow$

$$
\begin{aligned}
u_t &= \nabla \cdot (d_1(u,v)\nabla u) - \nabla \cdot (d_2(u,v)\nabla v) \\
v_t &= d_v \Delta v - k(v)v + f(v)u \\
k(v) &= \frac{c k_1 k_2}{(k_{-1} + k_2) + k_1 v}
\end{aligned}
$$

Nanjundiah 73

$d_1(u,v)$, $k(v)$, $f(v)$ constant
$d_2(u,v) = u\chi'(v)$

$$
\begin{aligned}
u_t &= d_u \Delta u - \nabla \cdot (u \nabla \chi(v)) \\
v_t &= d_v \Delta v - b_1 v + b_2 u
\end{aligned}
$$

Smoluchowski-Poisson system

Jäger-Luckhaus 92

$$
\begin{aligned}
& u_t = \nabla \cdot (\nabla u - u \nabla v) \\
& -\Delta v = u - \frac{1}{|\Omega|} \int_\Omega u \text{ in } \Omega \times (0,T) \\
& \frac{\partial u}{\partial \nu} - u \frac{\partial v}{\partial \nu} = \frac{\partial v}{\partial \nu} = 0 \text{ on } \partial\Omega \times (0,T) \\
& \int_\Omega v = 0
\end{aligned}
$$

zero-flux boundary condition

Smoluchowski-ODE system

$$
\begin{aligned}
& q_t = \nabla \cdot (\nabla q - q \nabla \varphi(v)) \\
& v_t = q \text{ in } \Omega \times (0,T) \\
& \left. \frac{\partial q}{\partial \nu} - q \frac{\partial \varphi(v)}{\partial \nu} \right|_{\partial\Omega} = 0
\end{aligned}
$$

Espejo-Stevens-Velazquez 09

competitive system of chemotaxis

$$\partial_t u_1 = d_1 \Delta u_1 - \chi_1 \nabla \cdot u_1 \nabla v$$
$$\partial_t u_2 = d_2 \Delta u_2 - \chi_2 \nabla \cdot u_2 \nabla v$$
$$d_1 \frac{\partial u_1}{\partial \nu} - \chi_1 u_1 \frac{\partial v}{\partial \nu} = 0$$
$$d_2 \frac{\partial u_2}{\partial \nu} - \chi_2 u_2 \frac{\partial v}{\partial \nu} = 0$$

$$u_1|_{t=0} = u_{10}(x) \geq 0$$
$$u_2|_{t=0} = u_{20}(x) \geq 0$$
$$\frac{1}{|\Omega|} \int_\Omega u_{10} + u_{20} \ dx = 1$$

$$-\Delta v = u_1 + u_2 - 1, \ \left. \frac{\partial v}{\partial \nu} \right|_{\partial \Omega} = 0$$
$$\int_\Omega v \ dx = 0$$

c.f. Jager-Luckhaus 92

full system of chemotaxis
→ (dimension analysis)
→ single u-equation

$\Omega \subset \mathbf{R}^2$ bounded domain

$\partial\Omega$ smooth

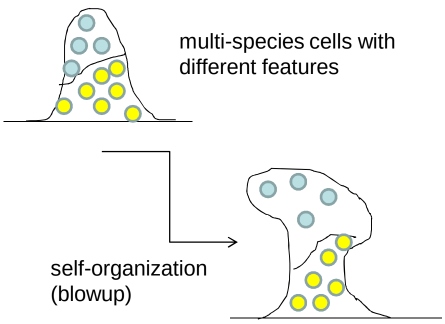
$\|u_0\|_1 \ll 1 \Rightarrow T = T_{\max} = +\infty$

$\|\exists u_0\|_1 \gg 1, \ T = T_{\max} < +\infty$

first rigorous proof of blowup and global-in-time existence of the solution

cell species in mound-fruiting body formation
→
competitive system of chemotaxis

→
blowup time discrepancy?



Mathematical results

1. general case

a. local in time well-posedness

b. global-in-time existence criterion

2. radially symmetric case

a. blowup criterion

b. simultaneous blowup at the origin

c. component-wisely different blowup mechanism (formal)

my motivation

1. tumor microenvironment in cell-tissue level
2. interaction of tumor cell and tumor associated macrophage

Hematogenous Metastasis

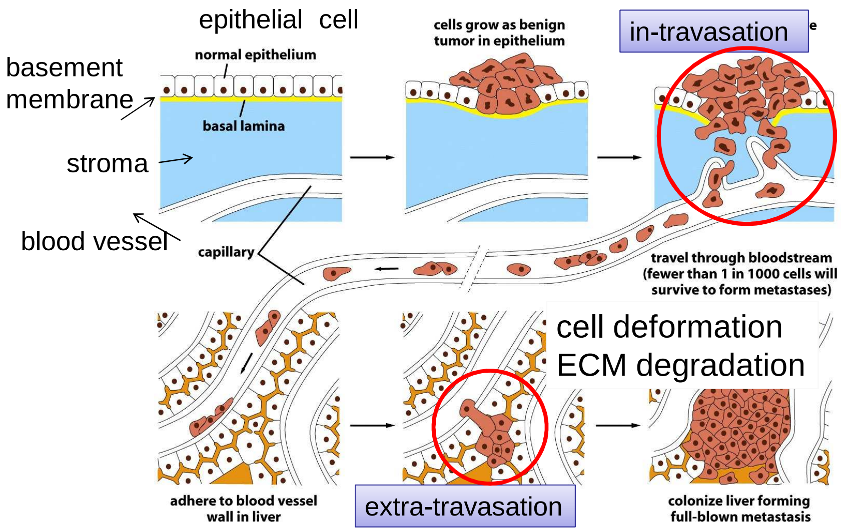
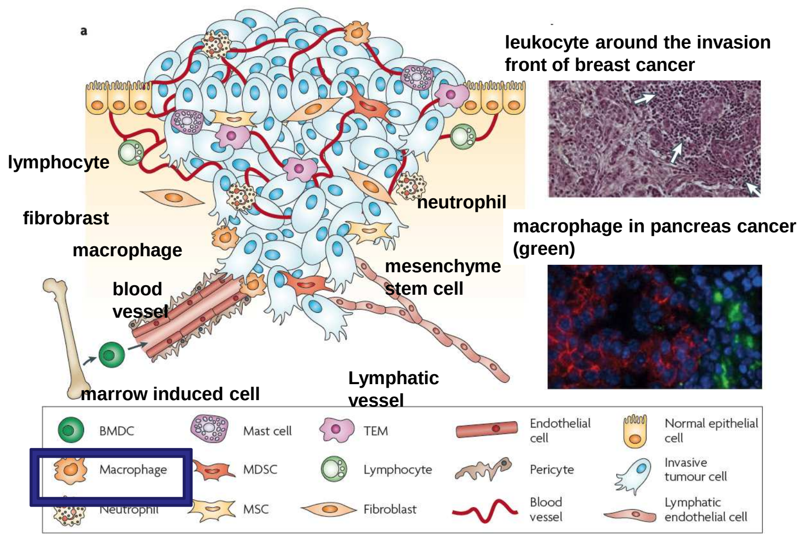


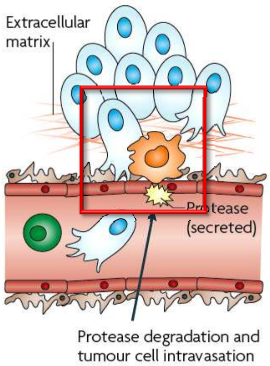
Figure 20-17 Molecular Biology of the Cell (© Garland Science 2008)

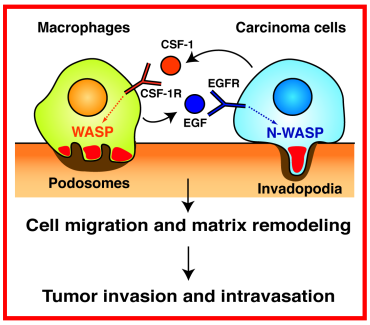
Tumor microenvironment



J. Joyce, and J. Pollard. *Nat Rev Cancer* 9: 239-252 (2009)

Tumor associated macrophage in invasion and intravasation





J. Joyce, and J. Pollard.
Nat Rev Cancer **9: 239-252 (2009)**

H. Yamaguchi et al.
Eur J Cell Biol **85: 213-218 (2006)**

competitive species → species selection

Abstract

A competitive system of chemotaxis can describe some aspects of tumor microenvironment. In this system there is formation of collapse in each component of the blowup solution. We have total mass quantiztion, subcollapse formation, and type II blowup rate. For radially symmetric solution, simultaneous blowup of two components and mass separation with quantization (formally) occur. We review the structure using the single equation, emphasize the essential difficulty in multi-component case, and describe some of the proof

I. Smoluchowski-Poisson equation

Jäger-Luckhaus 92

Smoluchowski equation

$u_t = \nabla \cdot (\nabla u - u \nabla v)$ in $\Omega \times (0,T)$

$\frac{\partial u}{\partial \nu} - u \frac{\partial v}{\partial \nu} = 0$ on $\partial\Omega \times (0,T)$

Poisson equation

$-\Delta v = u - \frac{1}{|\Omega|}\int_\Omega u, \quad \left.\frac{\partial v}{\partial \nu}\right|_{\partial\Omega} = 0$

$\int_\Omega v = 0$

$\Leftrightarrow$

$v = G * u = \int_\Omega G(\cdot, x')u(x')dx'$

1. variational structure

$\mathcal{F}(u) = \int_\Omega u(\log u - 1) - \frac{1}{2}\langle G * u, u\rangle$

Helmholtz's free energy

$\delta\mathcal{F}(u) = \log u - G * u$

$u_t = \nabla u \cdot \nabla \delta\mathcal{F}(u)$

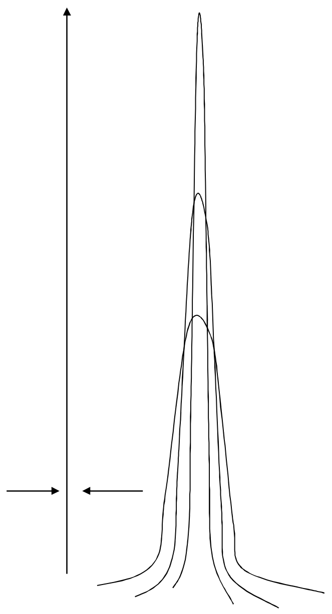
$\left.\frac{\partial}{\partial \nu}\delta\mathcal{F}(u)\right|_{\partial\Omega} = 0$ model (B) equation

$\frac{d}{dt}\|u(t)\|_1 = 0$ total mass conservation

$\frac{d}{dt}\mathcal{F}(u(t)) = -\int_\Omega u|\nabla\delta\mathcal{F}(u)|^2$

free energy decrease

2. global-in-time existence



concentration under L^1 control

$C'(\overline{\Omega}) \cong \mathcal{M}(\overline{\Omega}) \Rightarrow$ collapse formation

Theorem A1 (Nagai-Senba-Yoshida 97 Biler 98, Gajewski-Zacharias 98)

$n = 2, \ \|u_0\|_1 < 4\pi \ \Rightarrow T_{\max} = +\infty$

Proof *dual Trudinger-Moser inequality*

$\inf\{\mathcal{F}(u) \mid u \geq 0, \ \|u\|_1 = 4\pi\} > -\infty$

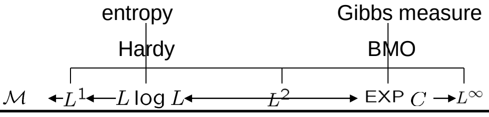
$+$ total mass conservation

1. $\lambda = \|u(t)\|_1 < 4\pi$

$\Rightarrow \sup_{t \geq 0}\|u(t)\|_{L\log L} < +\infty$

2. parabolic-elliptic regularity

$\Rightarrow T = +\infty, \ \sup_{t\geq 0}\|u(t)\|_\infty < +\infty$



3. blowup criterion

Theorem A2 (Senba-S. 01) ⟵ **symmetrization** (weak form)

$^\exists \eta > 0$ absolute constant s.t.

$x_0 \in \overline{\Omega}, \quad 0 < R \ll 1$

$$\frac{1}{R^2}\int_{\Omega \cap B_{2R}(x_0)} |x - x_0|^2 u_0(x)dx < \eta$$

$$\int_{\Omega \cap B_R(x_0)} u_0(x)dx > m_*(x_0)$$

$\Rightarrow$

$T = T_{\max} = o(R^2) < +\infty$

$$m_*(x_0) = \begin{cases} 8\pi, & x_0 \in \Omega \\ 4\pi, & x_0 \in \partial\Omega \end{cases}$$

$G(x', x) = G(x, x')$

$\Rightarrow$

$$\frac{d}{dt}\int_\Omega u(\cdot,t)\varphi = \int_\Omega u(\cdot,t)\Delta\varphi$$
$$+\frac{1}{2}\int_\Omega\int_\Omega \rho_\varphi(x,x')u(x,t)u(x',t)dxdx'$$

$$\varphi \in C^2(\overline{\Omega}), \ \left.\frac{\partial\varphi}{\partial\nu}\right|_{\partial\Omega} = 0$$

$$\rho_\varphi(x,x') = \nabla\varphi(x)\cdot\nabla_x G(x,x')$$
$$+\nabla\varphi(x')\cdot\nabla_{x'}G(x,x') \in L^\infty(\Omega\times\Omega)$$

Over mass with concentration implies blowup

Each boundary blowup point takes a half mass

4. scaling

$u_t = \nabla\cdot(\nabla u - u\nabla\Gamma * u)$

$(x,t) \in \mathbf{R}^n \times (0,T)$

$-\Delta\Gamma = \delta$

4.1 critical dimension

self-similar trasnformation

$u_\mu(x,t) = \mu^2 u(\mu x, \mu^2 t), \ \mu > 0$

$\|u(t)\|_1 = \|u_\mu(t)\|_1 \Leftrightarrow n = 2$

4.2. critical mass

$$\mathcal{F}(u) = \int_{\mathbf{R}^n} u(\log u - 1) - \frac{1}{2}\langle\Gamma * u, u\rangle$$

dual Trudinger-Moser inequality

$n = 2 \Rightarrow$

$\inf\{\mathcal{F}(u) \mid u \geq 0, \ \|u\|_1 = 8\pi\} > -\infty$

$$\Gamma(x) = \frac{1}{2\pi}\log\frac{1}{|x|}$$

$u_\mu(x) = \mu^2 u(\mu x) \geq 0, \ \mu > 0$

$\Rightarrow$

$\|u_\mu\|_1 = \|u\|_1 \equiv \lambda$

$$\mathcal{F}(u_\mu) = \left(2\lambda - \frac{\lambda^2}{4\pi}\right)\log\mu + \mathcal{F}(u)$$

critical mass $\lambda = 8\pi$

5. mathematical results

$$u_t = \nabla \cdot (\nabla u - u \nabla v)$$

$$-\Delta v = u - \frac{1}{|\Omega|}\int_\Omega u \quad \text{in } \Omega \times (0,T)$$

$$\frac{\partial u}{\partial \nu} - u\frac{\partial v}{\partial \nu} = \frac{\partial v}{\partial \nu} = 0 \text{ on } \partial\Omega \times (0,T)$$

$$\int_\Omega v = 0, \quad \Omega \subset \mathbf{R}^2$$

Theorem B1 [collapse formation]

$T = T_{\max} < +\infty \Rightarrow$

$$u(x,t)dx \rightharpoonup \sum_{x_0 \in \mathcal{S}} m(x_0)\delta_{x_0}(dx) + f(x)dx$$

as $t \uparrow T$ in $\mathcal{M}(\overline{\Omega})$,

$0 \leq f = f(x) \in L^1(\Omega) \cap C(\overline{\Omega} \setminus \mathcal{S})$

$\mathcal{S} = \{x_0 \in \overline{\Omega} \mid \exists (x_k, t_k) \to (x_0, T)$
s.t. $u(x_k, t_k) \to +\infty\}$

Theorem B2 [mass quantization]

$$m(x_0) = m_*(x_0) \equiv \begin{cases} 8\pi, & x_0 \in \Omega \\ 4\pi, & x_0 \in \partial\Omega \end{cases}$$

$[\ \|u(t)\|_1 = \|u_0\|_1 \Rightarrow$

$2\sharp(\mathcal{S} \cap \Omega) + \sharp(\mathcal{S} \cap \partial\Omega) \leq \|u_0\|_1 / (4\pi)]$

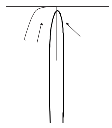
Theorem B3 [blowup rate]

$\forall x_0 \in \mathcal{S}$ type II

$$\lim_{t \uparrow T}(T-t)\|u(\cdot,t)\|_{L^\infty(\Omega \cap B(x_0, b(T-t)^{1/2}))}$$
$= +\infty, \ \forall b > 0$

total blowup mechanism is enveloped in hyper-parabola

Parabolic envelope ...
infinitely wide
parabolic region



$t = T$

Hyper-parabola ..
infinitely small parabolic region

pre-scaled
(1) collapse formation
(2) mass quantization

$$u(x,t)dx \rightharpoonup \sum_{x_0 \in \mathcal{S}} m_*(x_0)\delta_{x_0}(dx) + f(x)dx$$

$0 \leq f = f(x) \in L^1(\Omega) \cap C(\overline{\Omega} \setminus \mathcal{S})$

rescaled
(1) sub-collapse formation
(2) type II blowup rate

$z(y, s+s')dy \rightharpoonup m_*(x_0)\delta_0(dy)$
$C_*(-\infty, +\infty; \mathcal{M}_0(\mathbf{R}^2))$
$s' \uparrow +\infty$

$z(y,s) = (T-t)u(x,t)$
$y = (x - x_0)/(T-t)^{1/2}, \ s = -\log(T-t)$

$M_0(\mathbf{R}^2) = C_0(\mathbf{R}^2)'$
$C_0(\mathbf{R}^2) = \{f \in C(\mathbf{R}^2 \cup \{\infty\}) |\ f(\infty) = 0\}$

Theorem B4 [blowup in infinite time]

$T = T_{\max} = +\infty$

$t_k \uparrow +\infty, \ \|u(t_k)\|_\infty \to +\infty$

$\Rightarrow$

$\exists \{t_k'\} \subset \{t_k\}, \ u(x, t + t_k')dx \rightharpoonup \mu(dx, t)$

in $C_*(-\infty, +\infty; \mathcal{M}(\overline{\Omega}))$

$$\mu_s(dx,t) = \sum_{1 \leq i \leq N(t)} m_*(x(t))\delta_{x(t)}(dx)$$

$\lambda = 4\pi \Rightarrow N(t) = 1, \ x(t) \in \partial\Omega$

$$\frac{dx}{dt} = 2\pi\nabla_\tau R(x)$$ Hamiltonian control

$$R(x) = \left[G(x,x') + \frac{1}{\pi}\log|x - x'|\right]_{x'=x}$$

$x \in \partial\Omega$, Robin function

a recursive hierarchy

II. Mathematical Methods

1. blowup analysis

Theorem C1 [Gidas-Spruck 81]

$\Omega \subset \mathbf{R}^n$ bounded domain, $\partial\Omega$ smooth

$1 < p < \frac{n+2}{n-2}$

$\Rightarrow$

$^\exists C > 0$ s.t. $\|v\|_\infty \leq C$, $^\forall v$

$-\Delta v = v^p, \quad v > 0 \quad$ in $\Omega \subset \mathbf{R}^n$

$v = 0 \quad$ on $\partial\Omega$

<u>scaling</u>

$1 < p < \infty$, $\mu > 0$

$-\Delta v = v^p$

$v_\mu(x) = \mu^{2/(p-1)} v(\mu x)$

$\Rightarrow$

$-\Delta v_\mu = v_\mu^p$

1. assume the contrary

$\exists \{v_k\}$ solution sequence s.t.

$m_k = v_k(x_k) = \|v_k\|_\infty \to +\infty$

2. scaling $\tilde{v}_k(x) = \mu_k^{\frac{2}{p-1}} v_k(\mu_k x + x_k)$

3. scaling limit

$-\Delta v = v^p$, $0 \leq v \leq v(0) = 1$ in $\mathbf{R}^n$

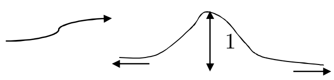
or $\exists s > 0$,

$-\Delta v = v^p$, $0 \leq v \leq v(0) = 1$ in $x_n > -s$

$v = 0$ on $x_n = -s$

4. Liouville property

$1 < p < \frac{n+2}{n-2} \Rightarrow \nexists$ scaling limit



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2. partial regularity ($\sharp\mathcal{S} < +\infty$)

<u>harmonic heat flow</u>

$\Omega = \mathbf{R}^2 / a\mathbf{Z} \times b\mathbf{Z}$

$u = u(x,t)$:

$\Omega \times [0,T) \to S^{n-1} \subset \mathbf{R}^n$

$u_t - \Delta u = u\,|\nabla u|^2$

$|u| = 1$ in $\Omega \times (0,T)$

Theorem C2 (Struwe 85)

$\exists$global-in-time H^1 solution

finite number of singularities

in $\Omega \times [0, +\infty)$

localization

$B_R = B(0,R)$

$E(u,R) = \frac{1}{2}\int_{B_R} |\nabla u|^2$

$E_0 = \frac{1}{2}\|\nabla u_0\|_2^2$

ε-regularity

$\exists \varepsilon_0 > 0$

$\sup_{t\in[0,T]} E(u(\cdot,t), B_R) < \varepsilon_0$

$\Rightarrow$

$u = u(x,t)$ regular in $B_{R/2} \times [0,T]$

monotonicity formula

$E(u(\cdot,T), B_R)$

$\leq E(u_0, B_{2R}) + CE_0T/R^2$

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scaling and monotonicity

1. blowup analysis
   (a) scale invariance
   (b) control at ∞ of scaled solution
   (c) hierarchical argument
   (d) classification of the scaling limit
2. partial regularity
   (a) ε-regularity ... parabolic local theory
   (b) monotonicity formula
   ... trade-off of space and time

Summary (1)

1. Quantized blowup mechanism aries in 2D Smoluchowski-Poisson equation
2. Fundamental factor is a variational structure which ensures total mass conservation, free energy decreasing, and weak form
3. Scaling property compatible to the variational structure chooses critical dimension and critical mass
4. There are collpase formation, mass quantization, and sub-collapse formation which results in type II blowup rate at any blowup point

II competing system of chemotaxis

1. main results $i = 1, 2, \cdots, N$

$$\partial_t u_i = d_i \Delta u_i - \chi_i \nabla \cdot u_i \nabla v$$
in $\Omega \times (0, T)$

$$d_i \frac{\partial u_i}{\partial \nu} - \chi_i u_i \frac{\partial v}{\partial \nu}\Big|_{\partial\Omega} = 0$$
$$u_i|_{t=0} = u_{i0}(x) \geq 0$$

$$-\Delta v = u - \frac{1}{|\Omega|}\int_\Omega u$$
$$u = \sum_{i=1}^N u_i$$
$$\frac{\partial v}{\partial \nu}\Big|_{\partial\Omega} = 0, \quad \int_\Omega v = 0$$

$\Omega \subset \mathbf{R}^2$ bounded domain, $\partial\Omega$ smooth

$T = T_{\max} < +\infty$
$\Rightarrow$
$\lim_{t \uparrow T} \|u(t)\|_\infty = +\infty$

$\mathcal{S} = \{x_0 \in \overline{\Omega} \mid \exists x_k \to x_0,\ t_k \uparrow T$
s.t. $u(x_k, t_k) \to +\infty\} \neq \emptyset$

Theorem 1 [finiteness of blowup points]
$\sharp \mathcal{S} < +\infty$

Theorem 2 [formation of collapse]
$u_i(x,t)dx \rightharpoonup$
$\sum_{x_0 \in \mathcal{S}} m_i(x_0)\delta_{x_0}(dx) + f_i(x)dx$ in $\mathcal{M}(\overline{\Omega})$
$t \uparrow T$, $\forall i$

$m_i(x_0) \geq 0$, $\sum_{i=1}^N m_i(x_0) > 0$

$0 \leq f_i = f_i(x) \in L^1(\Omega) \cap C(\overline{\Omega} \setminus \mathcal{S})$

Theorem 3
[total collapse mass quantization]
$\forall x_0 \in \mathcal{S}$
$$\left(\sum_{i=1}^N m_i(x_0)\right)^2 = m_*(x_0)\sum_{i=1}^N \xi_i m_i(x_0)$$
$\xi_i = d_i/\chi_i$
$$m_*(x_0) = \begin{cases} 8\pi, & x_0 \in \Omega \\ 4\pi, & x_0 \in \partial\Omega \end{cases}$$

Theorem 4 [subcollapse formation]
$z_i(y, s+s')dy \rightharpoonup m_i(x_0)\delta_0(dy)$
in $C_*(-\infty, +\infty, \mathcal{M}_0(\mathbf{R}^2))$
$s' \uparrow +\infty$

$z_i(y,s) = (T-t)u_i(x,t)$
$y = (x - x_0)/(T-t)^{1/2}$, $s = -\log(T-t)$

Question (colllapse mass separation)
$\exists k$ s.t. $m_i(x_0) = 0$, $\forall i \neq k$

Dirichlet case

1. Wolansky 02
$(\sum_{i=1}^N \lambda_i)^2 < 8\pi \sum_{i=1}^N \xi_i \lambda_i$, $\lambda_i = \|u_{i0}\|_1$
$\Rightarrow$ Some conditions missed !
$T = +\infty$
$\uparrow$ contradiction

2. (Espejo-Stevens-Velazquez 09)
$\forall i$, $u_i = u_i(|x|, t)$, $\exists k$, $\lambda_k > 8\pi\xi_k$
$\Rightarrow$
$\exists T > 0$, $\limsup_{t \uparrow T} \|u_k(\cdot, t)\|_\infty = +\infty$

2. Trudinger-Moser inequality (Shafrir-Wolansky 05)

logarithmic HLS inequality

$\Omega \subset \mathbf{R}^n$

$f, g \geq 0, \ \int_\Omega f \ dx = \int_\Omega g \ dx = 1$

$0 < \alpha < 1 \Rightarrow$

$$n \int_{\Omega \times \Omega} f(x) \cdot \log \frac{1}{|x-x'|} \cdot g(x') dx dx'$$

$$\leq \int_\Omega (1-\alpha) f \log f + \alpha g \log g \ dx + C_\alpha$$

$n = 2$

$\hat{\mathcal{F}}_{\oplus \xi_i}(\oplus u_i)$

$$= \sum_{i=1}^N \int_\Omega \xi_i (\log u_i - 1) dx - \frac{1}{2} \langle \Gamma * u, u \rangle$$

$$u = \sum_{i=1}^N u_i$$

linear programming

$$\left(\sum_{i \in K} \lambda_i \right)^2 \leq 8\pi \sum_{i \in K} \xi_i \lambda_i$$

$\forall K \subset \{1, 2, \cdots, N\}$

$\Rightarrow$

$\inf \{ \hat{\mathcal{F}}_{\oplus_i \xi_i}(\oplus_i u_i) \mid u_i \geq 0$

$\|u_i\|_1 = \lambda_i, \ i = 1, 2, \cdots, N \} > -\infty$

Hierarchical assumptions needed !

Green function estimate

Theorem D1 [Dirichlet case]

$$\left(\sum_{i \in K} \lambda_i \right)^2 < 8\pi \sum_{i \in K} \xi_i \lambda_i$$

$\forall K \subset \{1, 2, \cdots, N\} \Rightarrow T = +\infty$

3. mathematical structure

$\Omega \subset \mathbf{R}^2$ bounded domain

$\partial\Omega$ smooth $\quad i = 1, 2, \cdots, N$

$$\frac{\partial u_i}{\partial t} = d_i \Delta u_i - \chi_i \nabla \cdot u_i \nabla v$$

$$d_i \frac{\partial u_i}{\partial \nu} - \chi_i u_i \frac{\partial v}{\partial \nu} \Big|_{\partial\Omega} = 0$$

$$u_i|_{t=0} = u_{i0}(x) \geq 0$$

$$-\Delta v = u - \frac{1}{|\Omega|} \int_\Omega u$$

$$u = \sum_{i=1}^N u_i$$

$$\frac{\partial v}{\partial \nu} \Big|_{\partial\Omega} = 0, \ \int_\Omega v = 0$$

---

1. Total mass conservation

$\|u_i(t)\|_1 = \lambda_i, \forall i$

2. free energy decreasing

$$\frac{d}{dt} \mathcal{F}_{\oplus \xi_i}(\oplus u_i)$$

$$= -\sum_{i=1}^N \int_\Omega \xi_i^{-1} u_i |\nabla (d_i \log u_i - \chi_i v)|^2$$

$$\mathcal{F}_{\oplus \xi_i}(\oplus u_i) = \sum_{i=1}^N \int_\Omega \xi_i u_i (\log u_i - 1) dx$$

$$-\frac{1}{2} \langle (-\Delta)^{-1} u, u \rangle$$

3. weak fom

$$\forall \varphi \in C^2(\overline{\Omega}), \ \frac{\partial \varphi}{\partial \nu} \Big|_{\partial\Omega} = 0$$

$$\frac{d}{dt} \int_\Omega \sum_i \chi_i^{-1} u_i \varphi dx - \int_\Omega \sum_i \xi_i u_i \Delta \varphi dx$$

$$= \frac{1}{2} \int_\Omega \int_\Omega \rho_\varphi u(x,t) u(x',t) dx dx'$$

$$\rho_\varphi(x, x') = \nabla \varphi(x) \cdot \nabla_x G(x, x')$$

$$+ \nabla \varphi(x') \cdot \nabla_{x'} G(x, x')$$

Theorem D2 $\forall K \subset \{1, 2, \cdots, N\}$

$$\left(\sum_{i \in K} \lambda_i\right)^2 < 4\pi \sum_{i \in K} \xi_i \lambda_i$$

$\Rightarrow$

$T = +\infty$

$\updownarrow$ discrepancy

Theorem D3 $\exists x_0 \in \overline{\Omega}$, $\exists R > 0$

$$\left(\sum_{i=1}^N \lambda_i(x_0)\right)^2 > m_*(x_0) \sum_{i=1}^N \xi_i \lambda_i(x_0)$$

$\lambda_i(x_0) = \|u_{i0}\|_{L^1(\Omega \cap B(x_0, R))}$

$\forall i$, $\||x - x_0|^2 u_{i0}\|_{L^1(\Omega \cap B(x_0, 2R))} \ll 1$

$\Rightarrow$

$T < +\infty$

1. Behavior of the Green's function, near the boundary required

2. blowup threshold yet unknown except for $N = 2$, $u_i = u_i(|x|, t)$, $\forall i$

3. still $\exists$total mass quantization

$$\left(\sum_{i=1}^N m_i(x_0)\right)^2 = m_*(x_0) \sum_{i=1}^N \xi_i m_i(x_0)$$

by *two* types of parabolic envelop; local mass and local second moment

4. in a competitive system u be an upper bound for $\forall u_i$ although careful analysis needed for their time evolution as measures

4. proof of total mass quantization

4.1. formation of collapse

1. free energy + Trudinger-Moser

$\Rightarrow$ ε-regularity;

$$\lim_{R \downarrow 0} \limsup_{t \uparrow T} \|u(\cdot, t)\|_{L^1(\Omega \cap B(x_0, R))} < \exists \varepsilon_0$$

$\Rightarrow x_0 \notin \mathcal{S}$

2. weak fomulation

$\Rightarrow$ monotonicity formula;

$$\varphi \in C^2(\overline{\Omega}), \ \left.\frac{\partial \varphi}{\partial \nu}\right|_{\partial \Omega} = 0$$

$$\left| \frac{d}{dt} \int_\Omega \sum_i \chi_i^{-1} u_i(\cdot, t) \varphi \right| \leq C_\varphi (\lambda + \lambda^2)$$

3. $u_i \leq u$, $\forall i$

$$u_i(x, t)dx \rightharpoonup \sum_{x_0 \in \mathcal{S}} m_i(x_0) \delta_{x_0}(dx)$$
$$+ f_i(x)dx \text{ in } \mathcal{M}(\overline{\Omega}), \ t \uparrow T, \ \forall i$$

4.2. total mass quantization

1. weak scaling limit

$y = (x - x_0)/(T - t)$

$s = -\log(T - t)$, $t < T$

$z(y, s) = (T - t)u(x, t)$

$\forall s_k \uparrow +\infty$, $\exists \{s_k'\} \subset \{s_k\}$ s.t.

$z(y, s + s_k')dy \rightharpoonup \exists \zeta(dy, s)$

in $C_*(-\infty, +\infty; \mathcal{M}_0(\mathbf{R}^2))$

with 0-extension and reflection (for boundary blowup point)

weak solution to the **scaling limit equation**

$$\hat{\zeta}_s = \nabla \cdot (\nabla \tilde{\zeta} - \zeta \nabla (\Gamma * \zeta + |y|^2/4))$$
in $\mathbf{R}^2 \times (-\infty, +\infty)$

$$\hat{\zeta} = \sum_i \chi_i^{-1} \zeta_i, \ \tilde{\zeta} = \sum_i \xi_i \zeta_i, \ \zeta = \sum_i \zeta_i$$

ζ_i: individually defined eventually

2. parabolic envelope (1)

$\varphi = \varphi_{x_0,R}$, $0 < R \leq 1$

$$\left| \frac{d}{dt}\int_\Omega \sum_i \chi_i^{-1} u_i(\cdot,t)\varphi \right| \leq CR^{-2}$$

$\Rightarrow$

$$\hat{\zeta}(\mathbf{R}^2, s) = \sum_{i=1}^N \chi_i^{-1}\hat{m}_i(x_0), \ \hat{\zeta} \equiv \sum_{i=1}^N \chi_i^{-1}\zeta_i$$

$$\hat{m}_i(x_0) = \begin{cases} m_i(x_0), & x_0 \in \Omega \\ 2m_i(x_0), & x_0 \in \partial\Omega \end{cases}$$

$$u_i(x,t)dx \rightharpoonup \sum_{x_0 \in \mathcal{S}} m(x_0)\delta_{x_0}(dx)$$

$+f_i(x)dx$, $t \uparrow T$

$\zeta_i(\mathbf{R}^2, s) \leq \hat{m}_i(x_0)$

$\Rightarrow$

$\zeta_i(\mathbf{R}^2, s) = \hat{m}_i(x_0)$

$-\infty < s < +\infty$, $\forall i$

3. parabolic envelope (2)

$\varphi \approx |x - x_0|^2\varphi_{x_0,R}$, $0 < R \leq 1$

$$\left| \frac{d}{dt}\int_\Omega \sum_i \chi_i^{-1} u_i(\cdot,t)\varphi \right| \leq C$$

$\Rightarrow 0 \leq \langle |y|^2, \hat{\zeta}(dy,s)\rangle = I(s) \leq C$

scaling limit equation

$$\zeta_s = \nabla\cdot(\nabla\tilde{\zeta} - \zeta\nabla(\Gamma * \zeta + |y|^2/4))$$

$$\tilde{\zeta} = \sum_{i=1}^N \xi_i\zeta_i, \ \zeta = \sum_{i=1}^N \zeta_i \quad \Rightarrow$$

$$\frac{dI}{ds} \geq (\min_i \chi_i)I - \sigma(x_0), \ \forall s \in \mathbf{R}$$

$$\sigma(x_0) = \frac{1}{2\pi}\left(\sum_i \hat{m}_i(x_0)\right)^2 - 4\sum_i \xi_i\hat{m}_i(x_0)$$

$\Rightarrow$

$0 \leq I(s) \leq (\max_i \chi_i^{-1})\sigma(x_0)$

$\forall x_0 \in \mathcal{S}$

$$\left(\sum_{i=1}^N m_i(x_0)\right)^2 \geq m_*(x_0)\sum_{i=1}^N \xi_i m_i(x_0)$$

4. scaling back

$\zeta_i(dy,s) = e^{-s}A_i(dy', s')$

$y' = e^{-s/2}y$, $s' = -e^{-s}$

$\Rightarrow$

$\hat{A}_s = \nabla\cdot(\nabla\tilde{A} - A\nabla\Gamma * A)$

$A_i = A_i(dy,s) \geq 0$ in $\mathbf{R}^2 \times (-\infty, 0)$

$A_i(\mathbf{R}^2, s) = \hat{m}_i(x_0)$

$$\hat{A} = \sum_{i=1}^N \chi_i^{-1}A_i, \ \tilde{A} = \sum_{i=1}^N \xi_i A_i, \ A = \sum_{i=1}^N A_i$$

weak translation limit

$\forall s_k \uparrow +\infty$, $\exists\{s_k'\} \subset \{s_k\}$

$A_i(dy, s - s_k') \rightharpoonup a_i(dy,s)$

in $C_*(-\infty, +\infty; \mathcal{M}(\mathbf{R}^2))$

$\mathcal{M}(\mathbf{R}^2) = [C_0(\mathbf{R}^2) \oplus \mathbf{R}]'$ envelopes the total scaling mass

$\hat{a}_s = \nabla\cdot(\nabla\tilde{a} - a\nabla\Gamma * a)$

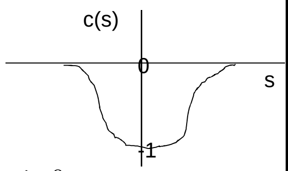
$a_i(dy,s) \geq 0$ in $\mathbf{R}^2 \times (-\infty, +\infty)$

$a_i(\mathbf{R}^2, s) = \hat{m}_i(x_0)$

$$\hat{a} = \sum_{i=1}^N \chi_i^{-1}a_i, \ \tilde{a} = \sum_{i=1}^N \xi_i a_i, \ a = \sum_{i=1}^N a_i$$

5. Kurokiba-Ogawa's scaling argument

1) local second moment



$0 \leq c'(s) \leq 1$, $s \geq 0$

$-1 \leq c(s) \leq 0$, $s \geq 0$

$$c(s) = \begin{cases} s - 1, & 0 \leq s \leq 1/4 \\ 0, & s \geq 4 \end{cases}$$

$\boxed{\sigma(x_0) > 0}$

$\Rightarrow$

$\exists C,\ \delta > 0$ s.t.

$$\frac{d}{ds}\langle c(|y|^2)+1, \hat{a}(dy,s)\rangle \leq$$
$$C\langle c(|y|^2)+1, \hat{a}(dy,s)\rangle - \delta\sigma(x_0)$$

$-\infty < s < +\infty$

$\langle c(|y|^2)+1, \hat{a}(dy,0)\rangle < \eta$

$$\eta = \frac{\delta\sigma(x_0)}{C}$$

$\Rightarrow$

$\langle c(|y|^2)+1, \hat{a}(dy,s)\rangle < 0,\ s \gg 1$

contradiction

$\boxed{\langle c(|y|^2)+1, \hat{a}(dy,0)\rangle \geq \eta}$

2) scaling invariance of the full orbit

$a_i(y,s) \mapsto a_i^\mu(y,s) = \mu^2 a_i(\mu y, \mu^2 s)$

local second moment criterion

$\langle c(|y|^2)+1, \hat{a}^\mu(dy,0)\rangle \geq \eta$

$\Rightarrow$

$\langle c(\mu^{-2}|y|^2)+1, \hat{a}(dy,0)\rangle \geq \eta,\ \forall\mu > 0$

$0 \leq c(\mu^{-2}|y|^2)+1 \leq 1$

$c(\mu^{-2}|y|^2)+1 \to 0,\ \mu \uparrow +\infty$

$\Rightarrow$ (dominated convergence theorem)

$0 \geq \eta$, contradiction

$\sigma(x_0) \leq 0 \Rightarrow$

$$\boxed{\frac{1}{2\pi}\left(\sum_i \hat{m}_i(x_0)\right)^2 \leq 4\sum_i \xi_i \hat{m}_i(x_0)}$$

5. radial case

$u_i = u_i(|x|,t),\ \forall i$

$\Rightarrow$

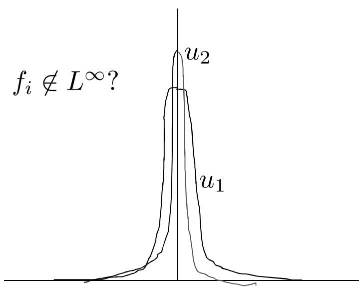
$\mathcal{S} = \{0\}$

1. [simultaneous blowup]

$\forall i,\ 0 < \forall R \ll 1$

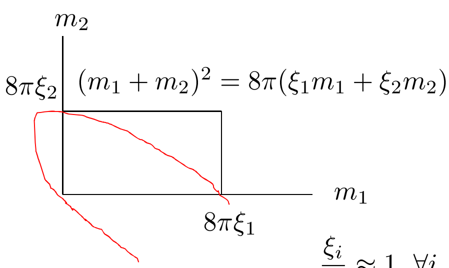
$$\limsup_{t\uparrow T} \|u_i(\cdot,t)\|_{L^\infty(B_R(0))} = +\infty$$

$f_i \notin L^\infty$?

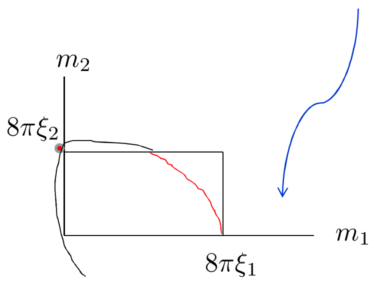


2. [mass separation?]

$\boxed{m_i = m_i(0) \leq 8\pi\xi_i,\ \forall i}$



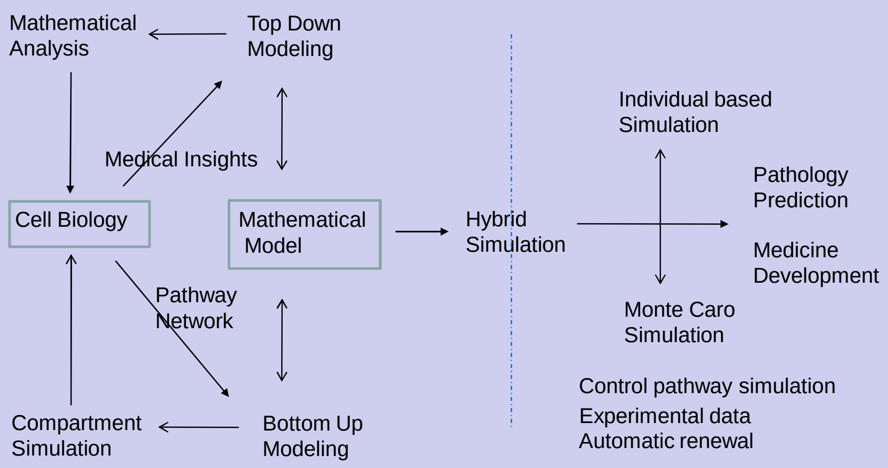
$$\frac{\xi_i}{\xi_j} \approx 1,\ \forall i,j$$



Summary (2)

1. In a competitive system of chemotaxis one has finiteness of blowup points, collapse formation, total mass quantization, and sub-collapse formation
2. First, formation of collapse is proven with ε-regularity and weak form
3. Then, total collapse mass is estimated from below using rescaled second moment applied to the weak scaling limit equation
4. Finally, a global-in-time exsitence criterion of the full orbit implies the total collapse mass estimate from above. Here scaling back and translation limit are used
5. It is the second part that is essential for multi-component systems
6. In radially symmetric case there arise a simultaneous blowup and a suggestion to collapse mass separation

Collaboration with Mathematical Modeling and Cell Biology



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