Mathematical models for cell movement
Part III

FABIO A. C. C. CHALUB

Centro de Matemática e Aplicações Fundamentais
Universidade de Lisboa

Overview

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

Overview – Today

- Kinetic and Keller-Segel description of chemotaxis.
- Formal and rigorous convergence of solutions.
- Keller-Segel models after blow up time.

General Picture

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Question:

Which is the set of equations that Φ obey?

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If

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

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

Re-scaling

Let us go back to the Othmer-Dunbar-Alt model:

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

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$$\begin{aligned} \bar{x} &= x/x_0 \ , & \bar{t} &= t/t_0 \ , & \bar{v} &= v/v_0 \ , \\ \bar{T} &= T/T_0 \ , & \bar{S} &= S/S_0 \ , & \bar{\rho} &= \rho/\rho_0 \ , \\ \bar{f} &= f/f_0 \ . \end{aligned}$$

Re-scaling

$$
\begin{aligned}
\frac{\partial f}{\partial t} + \frac{v_0}{x_0/t_0} v \cdot \nabla f &= T_0 v_0^n t_0 \int_V \left(T f' - T^* f\right) dv' \ , \\
\frac{\partial S}{\partial t} &= \frac{t_0}{x_0^2} D_0 \Delta S + \frac{\alpha_1 \rho_0 t_0}{S_0} \rho - \alpha_2 t_0 S \ , \\
\rho &= \frac{f_0 v_0^n}{\rho_0} \int_V f \, dv \ .
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\end{aligned}$$

We impose the *diffusive scaling*: $t_0 \approx x_0^2$, normalisations and

$$\varepsilon = \frac{x_0/t_0}{v_0}.$$

Re-scaling

$$\frac{\partial f}{\partial t} + \frac{1}{\varepsilon} v \cdot \nabla f = \frac{1}{\varepsilon^2} \int_V (T_\varepsilon f' - T_\varepsilon^* f)\, dv' ,$$

$$\frac{\partial S}{\partial t} = \Delta S + \rho - S ,$$

$$\rho = \int_V f\, dv .$$

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The solution depends on ε...

Kinetic Model

The previously defined turning kernels are written as

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T_\varepsilon[S,\rho] &= \lambda(S,\rho)F + \varepsilon a(S,\rho) v \cdot \nabla S \ , \\
T_\varepsilon[S,\rho] &= \psi(S(x + \varepsilon\mu(\rho)v, t) - S(x,t))F \ .
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$$T_\varepsilon[S,\rho] = T_0[S,\rho] + \varepsilon T_1[S,\rho] + \cdots$$

We define

$$\mathcal{T}_\kappa[f] = \int_V (T^*_\kappa[S,\rho]f - T_\kappa[S,\rho]f')dv' \ , \ \kappa = 0,1,2,\cdots$$

Kinetic Models

We also consider the ε expansion of the solutions

$$\begin{aligned} f_\varepsilon &= f_0 + \varepsilon f_1 + \cdots \ , \\ S_\varepsilon &= S_0 + \varepsilon S_1 + \cdots \ , \end{aligned}$$

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We put all these expansions in the kinetic model and solve for each order of ε.

Kinetic Models

To order ε^0:

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\begin{aligned}
0 &= \mathcal{T}_0(f_0) \ , \\
\rho_0 &= \int_V f_0 dv \ , \\
-\Delta S_0 &= \rho_0 \ .
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f_0(x,v,t) = \rho_0(x,t)F(v)\ .
$$

Examples

To order ε^1

$$\begin{aligned} v\cdot\nabla f_0 &= -(\mathcal{T}_1(f_0)+\mathcal{T}_0(f_1))\ , \\ \rho_1 &= \int_V f_1 dv\ , \\ -\Delta S_1 &= \rho_1\ . \end{aligned}$$

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We define:

$$\begin{aligned} D(S,\rho) &= \frac{1}{n\lambda[S]} \int_V v^2 F dv, \\ \Gamma(S,\rho)] &= \chi(S,\rho) \nabla S \;, \\ \chi(S,\rho) &= \frac{1}{n\lambda(S,\rho)} a(S,\rho) \int_V v^2 F dv. \end{aligned}$$

Examples

We multiply the first equation by v and integrate over V

$$D(S_0, \rho_0)\nabla\rho_0 = \chi(S_0, \rho_0)\nabla S_0\rho_0 - \int_V v f_1 dv\ .$$

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So

$$\int_v v f_1 dv = \chi(S_0, \rho_0)\nabla S_0\rho_0 - D(S_0, \rho_0)\nabla\rho_0 \; .$$

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This equation with

$$-\Delta S_0 = \rho_0$$

is the Keller-Segel model.

General Picture (again...)

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Rigorous results

Theorem. *(C., Markowich, Perthame, Schmeiser, 2004; Hwang, Kang, Stevens, 2005, C., Rodrigues, 2005): Consider turning kernels* T_ε *depending on* S_ε, ∇S_ε *and* ρ_ε *under mild assumptions. Then, the solution of the kinetic model* $(f_\varepsilon, S_\varepsilon)$ *is such that*

$$\begin{aligned} \rho_\varepsilon &\longrightarrow \rho_0 \ \textit{in } L^2_{\mathrm{loc}}(\mathbb{R}^n)\,, \\ S_\varepsilon &\longrightarrow S_0 \ \textit{in } L^q_{\mathrm{loc}}(\mathbb{R}^n)\,, 1 \le q < \infty\,, \\ \nabla S_\varepsilon &\longrightarrow \nabla S_0 \ \textit{in } L^q_{\mathrm{loc}}(\mathbb{R}^n)\,, 1 \le q < \infty. \end{aligned}$$

where (ρ_0, S_0) *is the solution of the associated Keller-Segel model.*

Rigorous Results

By *mild assumptions* we mean:

$$\phi_\varepsilon^S[\rho, S] \geq \gamma(1 - \varepsilon\Lambda(||S||_{W^{1,\infty}}))FF' ,$$

$$\int_V \frac{\phi_\varepsilon^A[\rho, S]^2}{F\phi_\varepsilon^S[\rho, S]} dv' \leq \varepsilon^2\Lambda(||S||_{W^{1,\infty}}) ,$$

where

$$\phi_\varepsilon^S := \frac{T_\varepsilon[S, \rho]F' + T_\varepsilon^*[\rho, S]F}{2} ,$$

$$\phi_\varepsilon^A := \frac{T_\varepsilon[S, \rho]F' - T_\varepsilon^*[\rho, S]F}{2} ,$$

and other more technical ones.

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We first prove that

$$||S||_{L^p} + ||S||_{C^{1,\alpha}} \leq c\left(||\rho||_{L^1} + ||\rho||_{L^q}\right) \ .$$

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Then, we prove

$$\frac{1}{q}\frac{d}{dt}\iint \frac{f_\varepsilon^q}{F} dv\, dx +$$

$$\frac{1}{4\varepsilon^2}\iint \phi_\varepsilon[S,\rho]\left(\frac{f_\varepsilon}{F} - \frac{f'_\varepsilon}{F'}\right)\left(\left(\frac{f_\varepsilon}{F}\right)^{q-1} - \left(\frac{f'_\varepsilon}{F'}\right)^{q-1}\right) dv'\, dv\, dx$$

$$\leq \frac{c_q}{2\varepsilon^2}\iint \frac{\phi_\varepsilon[S,\rho]^2}{F\phi_\varepsilon^S[S,\rho]}\frac{f_\varepsilon^q}{F^{q-1}} dv'\, dv\, dx \ .$$

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This simplifies to

$$\frac{d}{dt}\iint \frac{f_\varepsilon^q}{F^{q-1}}dv\,dx \le \frac{qc_q}{2}\Lambda\left(||S_\varepsilon(\cdot,t)||_{W^{1,\infty}}\right)\iint \frac{f_\varepsilon^q}{F^{q-1}}dv\,dx\ .$$

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We also have that

$$||S||_{C^{1,\alpha}} \le c\,(1+||\rho||_{L^q}) \le c\left(1+\left(\iint \frac{f_\varepsilon^q}{F^{q-1}}dv\,dx\right)^{1/q}\right)\ .$$

Rigorous Results

Now, we use Gronwall's inequality to prove that

$$f_\varepsilon \in L^\infty \left(0, t^*; L^1_+(\mathbb{R}^3 \times V) \cup L^q \left(\mathbb{R}^3 \times V; \frac{dx\, dv\, dt}{F}\right)\right) ,$$

$$S_\varepsilon \in L^\infty(0, t^*; L^p \cup C^{1,\alpha}(\mathbb{R}^3)) ,$$

for certain α (that depends on the regularity of the initial condition), $p \in (3, \infty)$ and ε-independent $t^* > 0$.

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and prove that

$$\int_0^{t^*} \iint_{\mathbb{R}^n \times V} \frac{r_\varepsilon^2}{F} dv\, dx\, dt \le c\ .$$

Rigorous Results

This is enough to prove the weak convergence of f_ε, S_ε, and ∇S_ε.

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This is enough to prove the weak convergence of f_ε, S_ε, and ∇S_ε.
But, as the turning kernel depends on ρ, S and ∇S, we need to prove *strong* convergence of these functions (in the limit $\varepsilon \longrightarrow 0$).

Rigorous Results

Define

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By elliptic regularity, $S_{J,\varepsilon} \in L^2(0,t^*; H^2_{\text{loc}}(\mathbb{R}^3))$ and then, from

$$\partial_t \nabla S_\varepsilon + \nabla \left(\nabla \cdot S_{J,\varepsilon} \right) = 0 \,,$$

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The strong convergence of S_ε to S_0 is proved analogously.

Rigorous Results

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$$f_\varepsilon = \rho_\varepsilon F + \varepsilon r_\varepsilon \ .$$

Rigorous Results

This implies

$$\lambda[S_0,\rho_0]D[S_0,\rho_0]\nabla\rho_\varepsilon = \rho_\varepsilon \int_V \frac{\mathcal{T}_\varepsilon[S_\varepsilon,\rho_\varepsilon](F)}{\varepsilon} v dv$$

$$+\int\int_{V\times V} \left(T_\varepsilon[S_\varepsilon,\rho_\varepsilon]r'_\varepsilon - T^*_\varepsilon[S_\varepsilon,\rho_\varepsilon]r_\varepsilon\right) v dv\, dv'$$

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$$-\varepsilon\nabla\cdot\int_V v\otimes v r_\varepsilon dv - \varepsilon\partial_t\int_V v f_\varepsilon dv\ .$$

Using the previous estimates and Rellich's theorem, we conclude that $\lambda D\nabla\rho_\varepsilon$ is in a compact set of $H^{-1}_{\mathrm{loc}}(\mathbb{R}^3\times(0,t^*))$.

Rigorous Results

Using the fact that λ is bounded from below and that D is positive defined, we conclude that $\nabla \rho_\varepsilon \in H^{-1}_{\mathrm{loc}}(\mathbb{R}^3 \times (0, t^*))$.

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Finally, we consider

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$$X_\varepsilon = (J_\varepsilon, \rho_\varepsilon)\ , \quad Y_\varepsilon = (0, \rho_\varepsilon)\ ,$$

and then

$$\begin{aligned} \text{div}_{(x,t)} X_\varepsilon &= 0\ , \\ \text{curl}_{(x,t)} Y_\varepsilon &= -\text{curl}_x \rho_\varepsilon\ . \end{aligned}$$

Rigorous Results

The RHS of both equations lie in $H^{-1}_{\text{loc}}(\mathbb{R}^3 \times (0, t^*))$.

Rigorous Results

The RHS of both equations lie in $H^{-1}_{\mathrm{loc}}(\mathbb{R}^3 \times (0, t^*))$. Now, we use the div-curl lemma and conclude the convergence of ρ_ε to ρ_0.

Consequences

- It is possible to give examples of kinetic models with global existence that converges to KS models with blow up:

$$T_\varepsilon[S](x,v,v',t) = F(v)\Psi(S(x+\varepsilon v,t) - S(x,t))$$

with $0 < \Psi_{\min} \leq \Psi(y) \leq Ay + B$.

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  with $0 < \Psi_{\min} \leq \Psi(y) \leq Ay + B$.
- For kinetic models with preventions of overcrowding it is possible to reproduce the HP results.

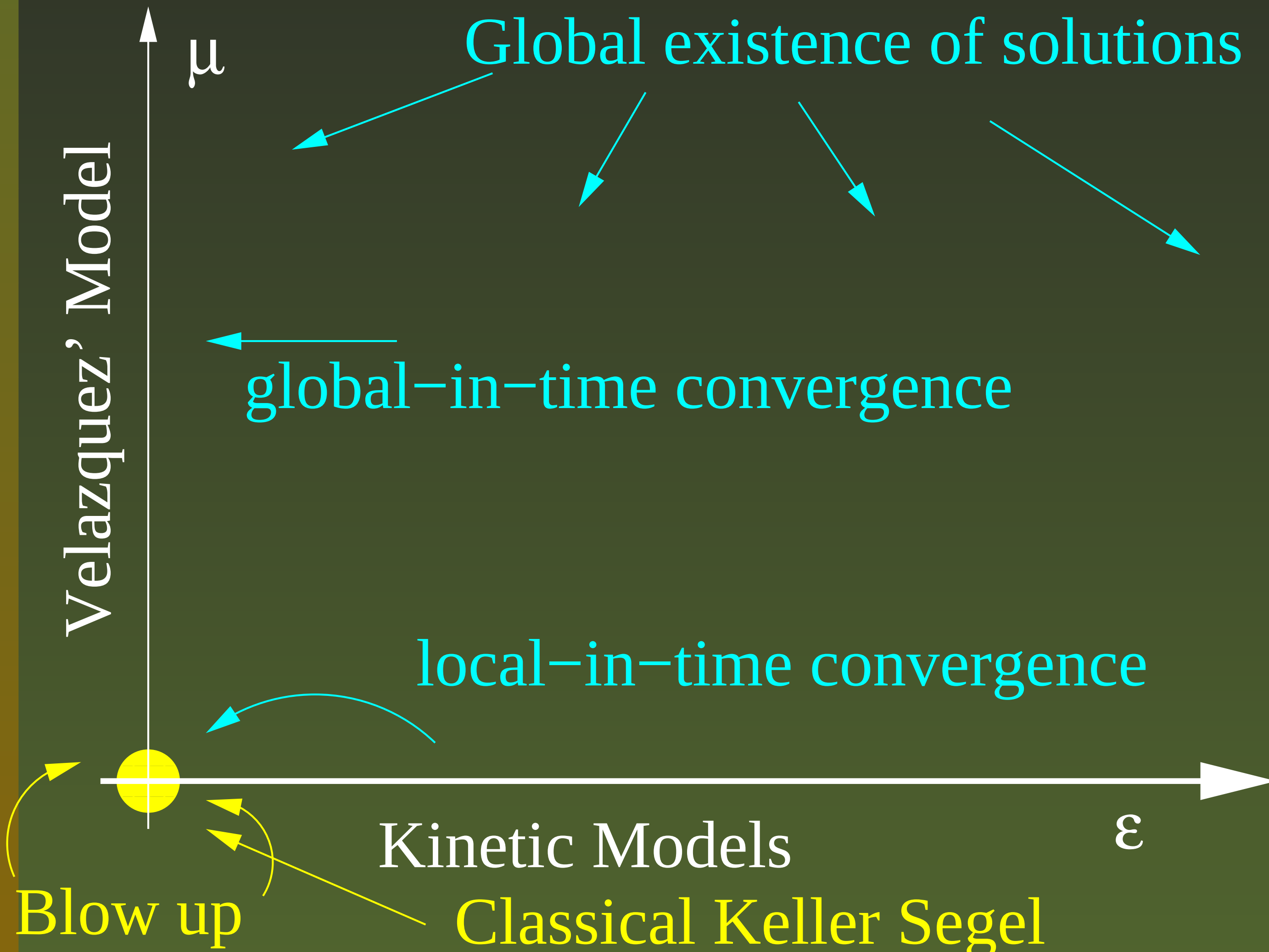
Beyond Keller-Segel

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 and the drift-diffusion limit (*globally in time*) is the Velazquez' model.*

Beyond Keller-Segel



Beyond Keller-Segel

Consider the Classical Keller-Segel model.

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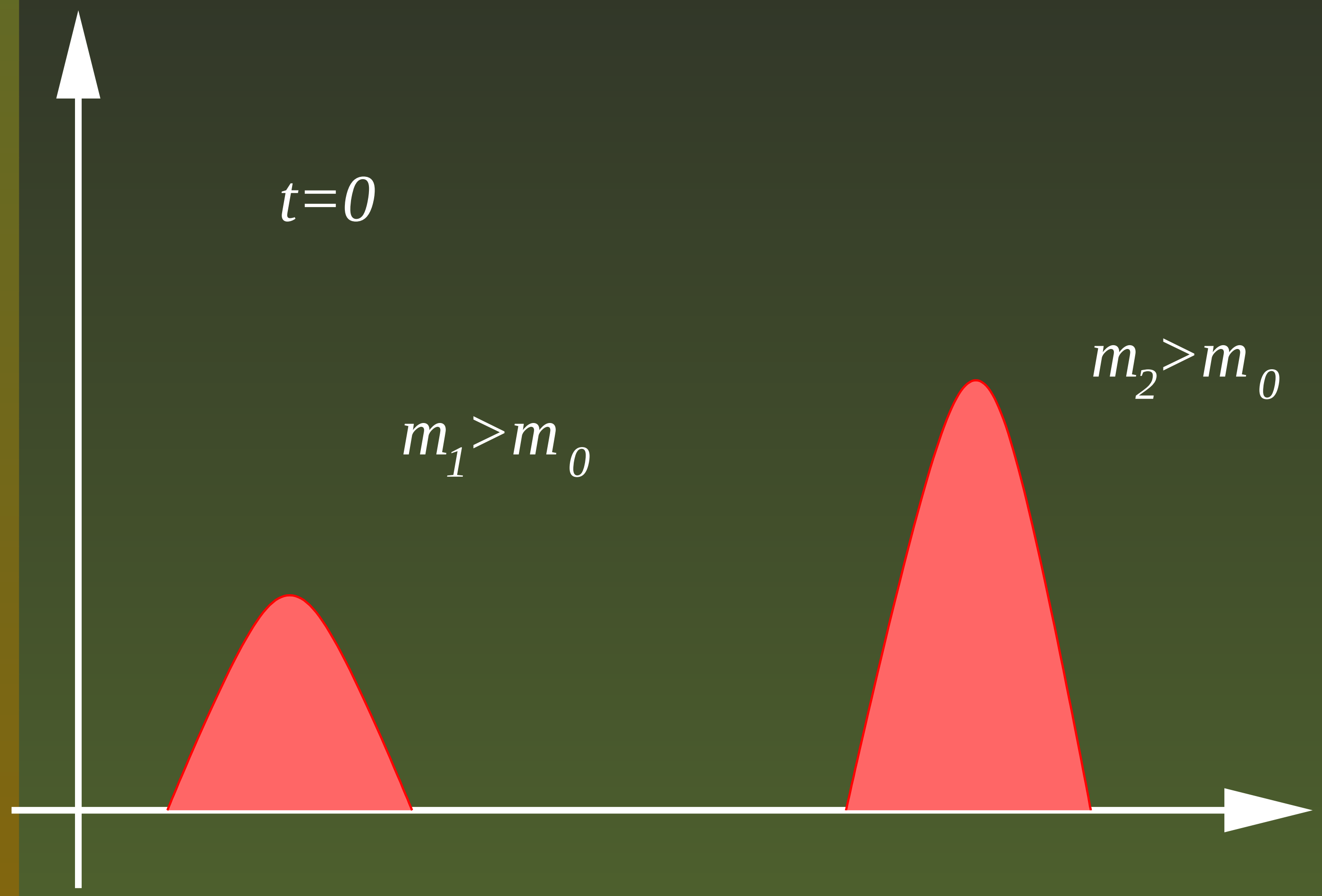
If the initial conditions are given by two small aggregates, both with mass larger than the minimal required for blow up, and these aggregates are far enough, we can expect that both will converge (in finite time) to Dirac-delta distributions.

Beyond Keller-Segel



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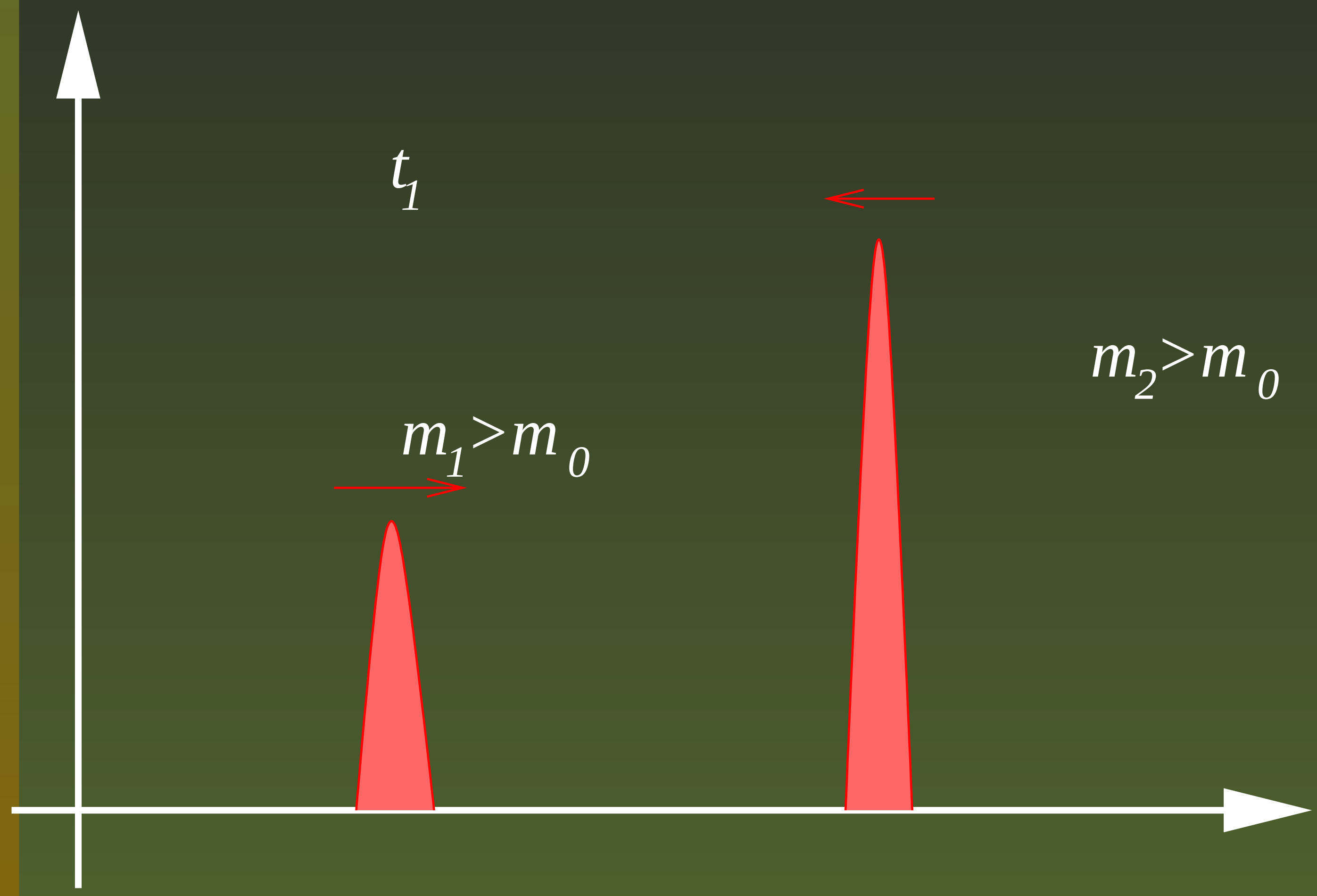

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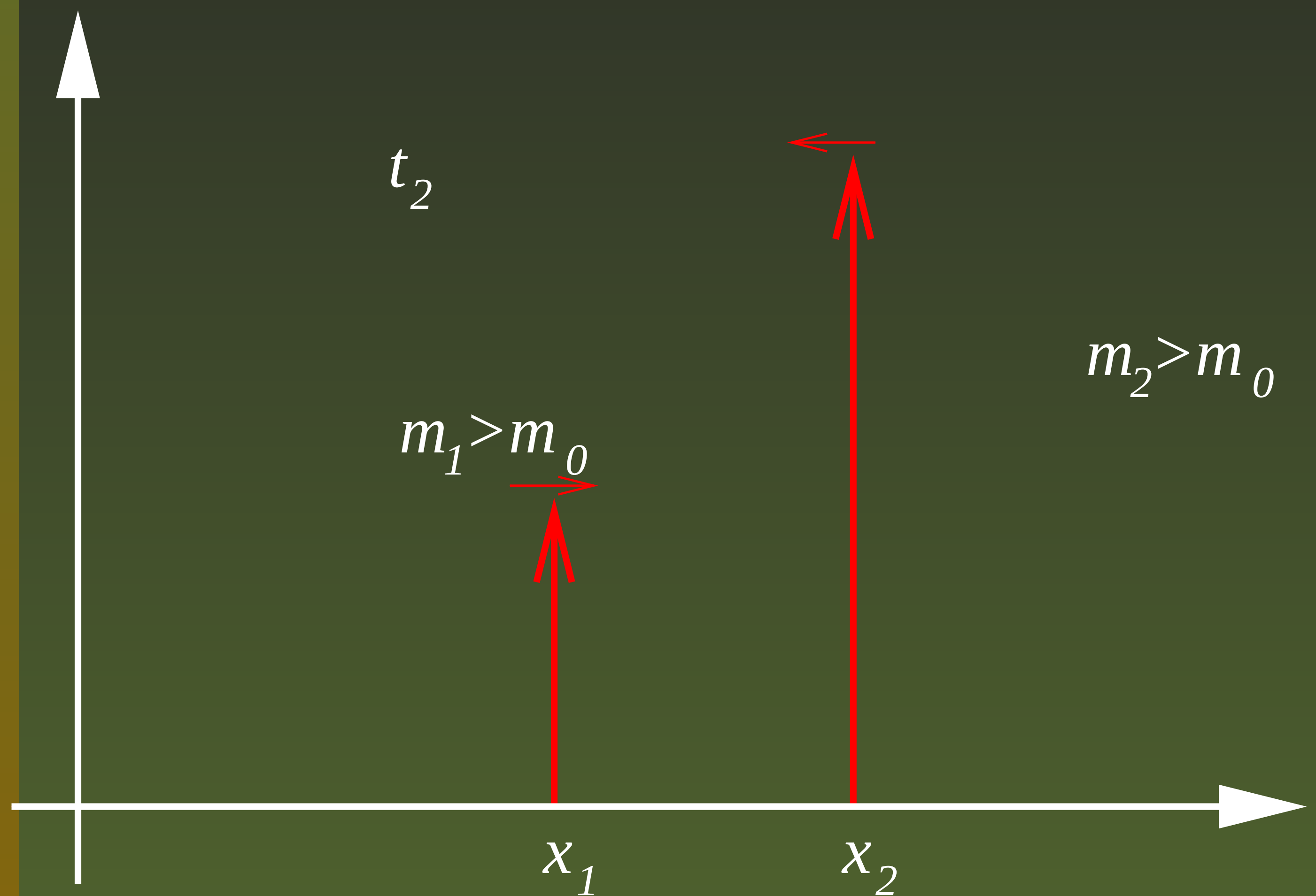

Beyond Keller-Segel

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Answer: Velázquez, 2004.

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Answer: Velázquez, 2004.

The final system of ODE (with some simplifications), for two aggregates, is given by

$$\dot{x}_1(t) = -\frac{\Gamma(m_2)m_1}{2\pi}\frac{x_1(t)-x_2(t)}{|x_1(t)-x_2(t)|^2}\,,$$
$$\dot{x}_2(t) = -\frac{\Gamma(m_1)m_2}{2\pi}\frac{x_2(t)-x_1(t)}{|x_2(t)-x_1(t)|^2}\,,$$

where $\Gamma(m) \in (0,1)$ is a given function such that

$$\lim_{m\to 8\pi^+} \Gamma(m) = 1\,,$$

Beyond Keller-Segel

Question: Can we use kinetic models to extend the Keller-Segel model after the blow up time?

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