Derivation and Approximation of Hyperbolic Models for Chemotaxis

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Ph. Laurencot, B. Perthame (Model derivation)
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Outline of the talk:

- How do cells move?
- Modelling chemotaxis
  - Macroscopic models: parabolic models, hyperbolic models
  - Mesoscopic or kinetic models: an intermediate approach between micro and macro models.
- Kinetic equations to make the link between the different models:
  - Cattaneo system for chemotaxis
  - Nonlinear hyperbolic model.
- Overview of the well-balanced algorithm
- Simulation of hyperbolic models
- Conclusions and perspectives
How do cells move?

Nearly all cells are endowed with devices allowing them to move. From E. Coli (bacteria)...

Figure 1: A representation of bacterium Escherichia Coli.
How do cells move?

the Dictyostelium Discoideum (amoeboid cells)

Figure 2: Motion of Dictyostelium in reaction to a chemoattractant emitted at a certain point (upper left corner).
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T=0, 2H, 4H, 6H, 20H
In the simple situation where we only consider cells and a chemical substance (the chemo-attractant), a model for the space and time evolution of the density $n = n(t, x)$ of cells and the chemical concentration $c = c(t, x)$ at time $t$ and position $x \in \Omega \subset \mathbb{R}^d$ has been introduced by Patlak and Keller & Segel and reads

$$\frac{\partial n}{\partial t} - \text{div}(\nabla n - \chi n \nabla c) = 0,$$

coupled with the chemoattractant equation for $c$

$$\frac{\partial c}{\partial t} - \Delta c = g(n, c).$$
(i) for $\|n_0\|_{L^1}$ small enough ($8\pi$), then there exist weak solutions.

(ii) these weak solutions propagate $L^p$ regularity.

(iii) for $\left(\int |x|^2 n_0 \right)$ is finite, then there is blow-up\(^a\) time $T^*$

(iv) $(d = 2)$ with radial symmetry\(^b\) $n(t) \to 8\pi \delta_0(x) + R$.

(v) $(d > 2)$ various (stable or unstable) radial blow-up profiles.

\(^a\)Herrero, Medina and Velazquez; Nonlinearity (1997), Dolbeault-Perthame; CRAS (2004)

Kinetic framework

We start from the transport equation for the distribution function $f = f(t, x, v)^a$

$$\frac{\partial f}{\partial t} + \frac{1}{\varepsilon} v \cdot \nabla_x f = \frac{1}{\varepsilon^2} \mathcal{T}(c, f).$$

The density of cells $n$ is given by

$$n(t, x) = \int_V f(t, x, v) dv.$$

and we assume herein that the turning operator is of the form

$$\mathcal{T}(c, f) = \mathcal{T}_0(f) + \varepsilon \mathcal{T}_1(c, f).$$

It is possible to derive rigorously the PKS model: large time$^b$.

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$^a$Othmer, Dunbar & Alt, JMB (1988), A. Stevens SIAM JAM

$^b$Hillen & Othmer SIAM JAM (2000); Chalub et al. (Monast.)
Run and tumble process:

We assume that cells move, stop and suddenly change their directions.

$\mathcal{T}(c, f)$ describes this change of direction:

$$
\mathcal{T}(c, f) = \int_V K(v, v', c) f(v') \, dv' - \int_V K(v', v, c) \, dv' \, f(v),
$$

where $K(v, v', c)$ is the rate of change of direction.

Now, we consider the following scaling:

$$
\frac{\partial f}{\partial t} + v \cdot \nabla_x f = \frac{1}{\varepsilon} \mathcal{T}(c, f).
$$
• The turning operators $\mathcal{T}_0$ and $\mathcal{T}_1$ preserve the local mass

$$\int_V \mathcal{T}_0(f) \, dv = \int_V \mathcal{T}_1(c, f) \, dv = 0,$$

for any $c \geq 0$.

• In addition, $\mathcal{T}_0$ conserves the population flux, that is,

$$\int_V \mathcal{T}_0(f) \, v \, dv = 0.$$

• For all $n \in [0, +\infty)$ and $u \in \mathbb{R}^d$, there exists a unique function $F_{n,u} \in L^1(V; (1 + |v|) \, dv)$ such that

$$\mathcal{T}_0(F_{n,u}) = 0, \quad \int_V F_{n,u}(v) \, dv = n, \quad \int_V F_{n,u}(v) \, v \, dv = n \, u.$$
Let $f$ be a solution to the kinetic equation and set

$$n(t, x) = \int_V f(t, x, v) dv, \quad n(t, x) u(t, x) = \int_V f(t, x, v) v dv.$$

We introduce $f_1$ such that

$$\varepsilon f_1(t, x, v) = f(t, x, v) - F_{n(t,x),u(t,x)}(v),$$

We integrate the KE over $v \in V$ and use the conservation of mass

$$\frac{\partial n}{\partial t} + \text{div}(n u) = 0.$$

Owing to the conservation of momentum by the turning operator $T_0$

$$\frac{\partial (nu)}{\partial t} + \text{div} \left( \int_V v \otimes v F_{n,u}(v) dv \right) = \int_V T_1(c, F_{n,u}) v dv + O(\varepsilon).$$
Next, we compute

\[ \int_V v \otimes v \, F_{n,u} \, dv = \int_V (v-u) \otimes (v-u) \, F_{n,u} \, dv + n u \otimes u, = P + n u \otimes u \]

where the pressure tensor is given by

\[ P(t, x) = \int_V (v - u(t, x)) \otimes (v - u(t, x)) \, F_{n(t,x),u(t,x)} \, dv. \]

Then,

\[
\begin{align*}
\frac{\partial n}{\partial t} + \text{div}(n \, u) &= 0, \\
\frac{\partial (n u)}{\partial t} + \text{div}(n u \otimes u + P) &= \int_V (v - u) \, T_1(c, F_{n,u}) \, dv,
\end{align*}
\]
Then, the turning operator $\mathcal{T}_0$ is like a BGK operator

$$\mathcal{T}_0(f)(v) = \lambda \left( \frac{n}{\vartheta(n)} F \left( \frac{v - u}{\vartheta^{1/2}(n)} \right) - f(v) \right).$$

where

$$\int_V F(v) \, dv = 1, \quad \int_V v F(v) \, dv = 0.$$ 

$$\Rightarrow P = n \int_V (v - u) \otimes (v - u) F \left( \frac{v - u}{\vartheta^{1/2}(n)} \right) \, dv = n \vartheta(n) \, p,$$

Moreover, let $\mathcal{T}_1$ be such that

$$\mathcal{T}_1(c, f) = \int_V K_1(v, v', \nabla c) \, f(v') \, dv' - \int_V K_1(v', v, \nabla c) \, dv' \, f(v).$$
From these assumptions on $T_1$, we get the following nonlinear model

\[
\begin{align*}
\frac{\partial n}{\partial t} + \text{div}(n u) &= 0, \\
\frac{\partial (nu)}{\partial t} + \text{div}(nu \otimes u + n\vartheta(n)p) &= -\sigma n u + n \vartheta^{3/2}(n) \chi' \nabla c,
\end{align*}
\]

coupled with the concentration equation for $c$.

- already obtained by Serini & al\textsuperscript{a}:

\textsuperscript{a}Serini et al. EMBO J. (2003)
What about entropy inequality?

For the PKS model \( \frac{\partial \tilde{\eta}}{\partial t} + \text{div} \tilde{G} \leq 0 \), where
\[
\tilde{\eta} = n(\log n - 1 - c) + \frac{c^2}{2} + \frac{(\nabla c)^2}{2},
\]
\[
\tilde{G} = (n \nabla c - \nabla n)(\log n - c) - (n - c + \Delta c) \nabla c,
\]

For the hyperbolic model when \( \chi(c) = c \)
\[
\frac{\partial \eta}{\partial t} + \text{div} G = -\sigma n u^2 - \left( \frac{\partial c}{\partial t} \right)^2 \leq 0,
\]
\[
\eta = n(\log n - 1) + \frac{1}{2} n u^2 - nc + \frac{1}{2} \left( c^2 + \left( \frac{\partial c}{\partial x} \right)^2 \right),
\]
\[
G = n u (\log n + \frac{1}{2} u^2) - nu c - \frac{\partial c}{\partial t} \frac{\partial c}{\partial x}.
\]
Cells are not interacting: Cattaneo model

Since cells are not interacting, the turning operator is linear

\[ T_0(f)(t, x, v) = \int_V (T_0(v, v') f(t, x, v') - T_0(v', v) f(t, x, v)) \, dv'. \]

with \( V = S^1 \)

\[ T_0(v, v') = (1 + C_0 v \cdot v') \]

The steady state is a linear combination of \( 1, v_1, \ldots, v_d \)

\[ F_{n,u}(v) = \left( n + C_1 n \sum_{i=1}^{d} v_i u_i \right), \]
\[
\begin{aligned}
\frac{\partial n}{\partial t} + \text{div}(n \, u) &= 0, \\
\frac{\partial (n u)}{\partial t} + \nabla n &= -\sigma n \, u + n \, \nabla c
\end{aligned}
\]

• another model (Hillen and Othmer\(^a\)) can be also obtained using a similar technique.

• linear with respect to \((n, n \, u)\)

\(^a\)Othmer-Dunbar Alt JMB (1988); Hillen M3AS (2002)
Write the discrete version of the system in the following form

$$\Delta x_i \frac{d}{dt} U_i(t) + F_{i+1/2} - F_{i-1/2} = \Delta x_i S_i$$

where $\Delta x_i$ denotes the mesh size $\Delta x_i = x_{i+1/2} - x_{i-1/2}$, and the cell-average vector of discrete unknowns is

$$U_i(t) = \begin{pmatrix} n_i(t) \\ n_i(t) u_i(t) \end{pmatrix},$$

and $S_i$ is a “smart” approximation of the source.
For a first order scheme, we get

\[ F_{i+1/2} = \mathcal{F}(U_i(t), U_{i+1}(t)), \]

and you want to preserve \( \log(n_i) - \chi(c_i) = c^{te}, \ u_i = 0. \) Then replace\(^a\) \( F_{i+1/2} \) by

\[ F_{i+1/2} = \mathcal{F}(U_{i+1/2}^-, U_{i+1/2}^+), \]

The source term is discretized as \((\sigma = 0.)\)

\[ S_i = \frac{1}{\Delta x_i} \begin{pmatrix} 0 \\ n_{i+1/2}^- - n_{i-1/2}^+ \end{pmatrix}. \]

This ansatz is motivated by the balancing requirement. Indeed, when steady state holds \( \nabla n = n \chi'(c) \nabla c = n e^{-\chi(c)} \nabla (e^{\chi(c)}). \)

To ensure steady state conservation (with zero population flux), we must choose
\[ n_{i+1/2}^- = n_{i+1/2}^+, \quad u_i = 0. \]

From this observation, we take
\[ n_{i+1/2}^- = n_i e^{\chi_{i+1/2}^- - \chi(c_i)} \]
and
\[ n_{i+1/2}^+ = n_{i+1} e^{\chi_{i+1/2}^+ - \chi(c_{i+1})}. \]

Here we could choose for instance
\[ \chi_{i+1/2} = \max (\chi(c_i), \chi(c_{i+1})). \]
Theorem: consistency and well-balancing

Consider a numerical flux $\mathcal{F}$ for the homogeneous problem, which preserves nonnegativity of $n_i(t)$. Then, the scheme with periodic boundary conditions satisfies the following

(i) preserves the nonnegativity of $n_i(t)$

(ii) preserves the steady state: $\log(n_i) - \chi(c_i) = c^{te}$

(iii) is consistent with the Hyperbolic system with a source term.

(iv) there is a discrete entropy property.
Flux Splitting Scheme

To approximate the flux function, we use a flux splitting scheme

\[ F(U_l, U_r) = F^+(U_l) + F^-(U_r), \quad \text{and} \quad F(U, U) = F(U) \]

In most applications the simple Lax-Friedrichs flux splitting

\[ F_{LF}^\pm(U) = \frac{1}{2} (F(U) \pm \alpha U), \quad \alpha = \max_{m, U} |\lambda_m(U)|, \]

Local characteristic Lax-Friedrichs flux splitting and get a \( k \)-th order approximation of the flux \( \hat{F}_{i+1/2} \) via a WENO reconstruction.

\[ \hat{F}_{i+1/2} = \hat{F}_{i+1/2}^+ + \hat{F}_{i+1/2}^- , \]

where

\[ \hat{F}_{i+1/2}^+ = R_{i+1/2} \left( R_{i+1/2}^{-1} (F(U) + \alpha U) \right)_{i,r} . \]
We perform a well-balanced reconstruction not of the density $n$ but of the numerical fluxes $\hat{F}^{\pm}_{i+1/2}$

$$F^+_{i+1/2} = \hat{F}^+_i (e^{\chi(c)})^{i+1/2}_{i,r} - \hat{F}^-_i (e^{\chi(c)})^{i+1/2}_{i,l},$$

$$F^-_{i+1/2} = \hat{F}^-_i (e^{\chi(c)})^{i+1/2}_{i+1,l},$$

with

$$(e^{\chi(c)})^{i+1/2} = \max \left( (e^{\chi(c)})_{i,r}, (e^{\chi(c)})^{i+1/2}_{i+1,l} \right)$$

and $(e^{\chi(c)})_{i,r}$ is a right hand side $k$-th order approximation of $e^{\chi(c)}$ on the interval $(x_{i-1/2}, x_{i+1/2})$.

The source term is approximated as

$$S_i = \frac{1}{\Delta x} n_i e^{-\chi(c_i)} \left( (e^{\chi(c)})^{i+1/2} - (e^{\chi(c)})^{i-1/2} \right).$$
WENO reconstruction properties

1. The scheme is proven to be **uniformly fifth order accurate** including at smooth extrema, and this is verified numerically.

2. Near discontinuities the scheme **behaves very similarly to an ENO scheme**, namely the solution has a sharp and non-oscillatory discontinuity transition.

3. The numerical flux has the same smoothness dependency on its arguments as that of the physical flux $F(U)$. This helps in a convergence analysis for smooth solutions and in steady state convergence.

4. The approximation is self similar. That is, when fully discrete with Runge-Kutta methods, the scheme **is invariant when the spatial and time variables are scaled by the same factor**.
THEOREM. Consider the Lax-Friedrich flux splitting scheme $\mathcal{F}$ coupled with the $k$-th order ENO or WENO reconstruction for the homogeneous problem. Then, this scheme with periodic boundary conditions

(i) preserves the steady state for the ENO reconstruction:

$$\log(n_i) - \chi(c_i) = c^{te},$$

whereas it preserves steady state up to $t\varepsilon$ for the WENO reconstruction.

(ii) is $k$-th order accurate with the system Hyperbolic system with source term.
Numerical simulations

- Justification of the Well Balanced Algorithm in 1d.
- Illustration of chemosensitive movement.
- Network formation of Endothelial cells and early stage of blood vessel formation.
### Tests 1: one dimensional model

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<th>Well-balanced Finite Volume</th>
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</table>
Figure 3: Accuracy test for well-balanced steady state resolution: cell density $n(t, x)$ (left) and population flux $n(t, x) u(t, x)$ (right) at time $T = 20$. Solid lines: WENO scheme with the well-balanced reconstruction; dotted lines: WENO schemes with a centered approximation of the source term.
Simulation of the PKS model

t = 0.0003

t = 0.0009

35
Simulation of the PKS model

t = 0.0012

t = 0.0018
Simulation of the hyperbolic model
Simulation of the hyperbolic model
Simulation of the hyperbolic model
Simulation of the hyperbolic model
Network formation: early blood vessel formation

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T=0, 2H, 4H, 6H, 20H
Network formation: early blood vessel formation
Conclusion and Discussion

- Nonlinear hyperbolic model arises when we consider interactions between cells.

- Blow-up of solution to the hyperbolic system: there is blow-up for Euler-Poisson.

- Play with the pressure to prevent blow-up \( \equiv \) play with the diffusion on PKS

- The kinetic model does not blow-up!!

- Construct kinetic models describing cell interactions.


[H] F. Filbet, Ph. Laurençot & B. Perthame, Derivation of Hyperbolic Models for Chemotaxis, with Shu Approximation. *Preprint*

