Modeling of Moving Cell Populations

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University of Alberta, Edmonton
How to find macroscopic models based on information on individuals?

- Two methods.
  - (1) random walk descriptions and the master equation.
  - (2) transport equations and the hydrodynamic scaling.
- Science: (1) models for volume filling.
- Science: (2) models for chemotaxis.
- Science: (3) models for cell movement in fibre networks.
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Exercises.
Lecture 1: **Random Walk Models**

(A) Method: Random Walks

(B) Science: The Volume Filling Model

(C) Exercise: 1
Outline

Lecture 1: Random Walk Models
   (A) Method: Random Walks
   (B) Science: The Volume Filling Model
   (C) Exercise: 1

Lecture 2: Transport Equations
   (A) Method: Scaling Limits
   (B) Science: Chemotaxis
   (C) Exercise: 2
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Lecture 2: **Transport Equations**

(A) Method: Scaling Limits

(B) Science: Chemotaxis

(C) Exercise: 2

Lecture 3: **Movement in Fibre Networks**

(B) Science: Mesenchymal Motion

(C) Exercise: 3
Derivation from a Master Equation

Random walk description (Othmer-Stevens 1997)

$u_i(t)$: Probability to find a particle at $x_i$ at time $t$.

$T_i^\pm$: Transitional probabilities per unit of time for one jump to the right (+) or left (−).
Derivation from a Master Equation

Random walk description (Othmer-Stevens 1997)

$u_i(t) :$ Probability to find a particle at $x_i$ at time $t$.

$T_i^\pm :$ Transitional probabilities per unit of time for one jump to the right (+) or left (-).

**Master equation:**

$$\frac{du_i}{dt} = T_{i-1}^+ u_{i-1} + T_{i+1}^- u_{i+1} - (T_i^+ + T_i^-) u_i.$$
Example: Diffusion

Assume the grid size is $h$ and

$$T_i^{±} = \alpha.$$
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$$\frac{d u_i}{d t} = \alpha(u_{i-1} + u_{i+1} - 2u_i)$$
Example: Diffusion

Assume the grid size is $h$ and

$$T_i^\pm = \alpha.$$

$$\frac{d u_i}{dt} = \alpha (u_{i-1} + u_{i+1} - 2u_i)$$

With $h \rightarrow 0$ we find for $u(t, x)$:

$$\frac{d u}{dt} = \alpha h^2 \frac{\partial^2}{\partial x^2} u + O(h^3)$$

The diffusion equation with $D_u = \lim_{h \rightarrow 0} \alpha h^2$. 
\( v_i \): Concentration of a chemical signal.

\[
T_i^\pm = \alpha + \beta (\tau(v_{i\pm1}) - \tau(v_i))
\]

\( \tau \): sensitivity function, \( \alpha, \beta \geq 0 \)
\( v_i \): Concentration of a chemical signal.

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\frac{du_i}{dt} = \alpha (u_{i+1} - 2u_i + u_{i-1}) - \beta ((u_{i+1} + u_i)(\tau_{i+1} - \tau_i) - (u_i + u_{i-1})(\tau_i - \tau_{i-1}))
\]
Now with Chemotaxis

$v_i$: Concentration of a chemical signal.

$$T_i^\pm = \alpha + \beta (\tau(v_{i+1}) - \tau(v_i))$$

$\tau$: sensitivity function, $\alpha, \beta \geq 0$

$$\frac{du_i}{dt} = \alpha (u_{i+1} - 2u_i + u_{i-1})$$

$$-\beta((u_{i+1} + u_i)(\tau_{i+1} - \tau_i) - (u_i + u_{i-1})(\tau_i - \tau_{i-1}))$$

With $h \to 0$:

$$u_t = \alpha h^2 u_{xx} - \beta h^2 (2u\tau_x)_x$$
Chemotaxis Equation

\[ u_t = D_u u_{xx} - (u\chi(v)v_x)_x, \]

\[ D_u = \lim \alpha h^2, \]

\[ \chi(v) = \lim 2h^2/\beta \frac{\partial \tau(v)}{\partial v}: \text{chemotactic sensitivity.} \]
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\[ u_t = D_u \Delta u - \nabla \cdot \{ u \chi(v) \nabla v \} \]
\[ v_t = D_v \Delta v + g(u, v) \]

(Patlak ’53, Keller + Segel ’70)
Results on Spikes and Finite Time Blow Up

\[
\begin{align*}
  u_t &= \Delta u - \chi \nabla \cdot \{u \nabla v\} \\
  v_t &= D_v \Delta v + \gamma u - \delta v
\end{align*}
\]

(Childress, Percus, Jäger, Luckhaus, Nagai, Senba, Yoshida, Herrero, Velazquez, Levine, Sleeman, Gajewski, Zacharias, Biler, Post, Horstmann, Suzuki, Yagi, Potapov, Hillen, Renclawowicz, etc )

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\[ \bar{u}_0 = \int u_0(x) \, dx \]

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1-D: Spike formation, no blow-up.

(Childress, Percus, Jäger, Luckhaus, Nagai, Senba, Yoshida, Herrero, Velazquez, Levine, Sleeman, Gajewski, Zacharias, Biler, Post, Horstmann, Suzuki, Yagi, Potapov, Hillen, Renclawowicz, etc )

\[ \bar{u}_0 = \int u_0(x) dx \]

1-D: Spike formation, no blow-up.

2-D: There exists a threshold \( \theta \) such that

\[ \bar{u}_0 \geq \theta \implies \text{blow-up} \]

\[ \frac{\theta}{2} \leq \bar{u}_0 < \theta \implies \text{boundary blow-up} \]

\[ \bar{u}_0 < \frac{\theta}{2} \implies \text{no blow-up}. \]

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n-D: There is a threshold as well (Renclawowicz, Hillen 2005).
So What?
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Question 1:
What does finite time blow-up tell us about the biology?
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Question 1:
What does finite time blow-up tell us about the biology?

Question 2:
What does finite time blow-up tell us about the modeling?
Volume Effects

- Volume Filling (H’, Painter)
Volume Effects

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- Quorum Sensing (H’, Painter)
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- Finite Sampling Radius (H’, Painter, Schmeiser)
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- Pressure (Preziosi et al.)
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- Pressure (Preziosi et al.)
- Multi-phase flow (Byrne and Owen)
(3) The Volume Filling Approach

(w. K. Painter)

Increasing chemoattractant concentration

Assumption $q(U_{max}) = 0$ and $q(u) > 0$ for all $0 < u < U_{max}$.

Standard example: $U_{max} = 1$; $q(u) = 1$ for all $0 < u$.
Introduce $q(u)$: probability to find space at a local cell density $u$
(3) The Volume Filling Approach

(w. K. Painter)

Introduce $q(u)$: probability to find space at a local cell density $u$

Assumption

$$q(U_{\text{max}}) = 0 \text{ and } q(u) \geq 0 \text{ for all } 0 \leq u < U_{\text{max}}.$$
(3) The Volume Filling Approach

(w. K. Painter)

Introduce $q(u)$: probability to find space at a local cell density $u$

Assumption

$$q(U_{\text{max}}) = 0 \text{ and } q(u) \geq 0 \text{ for all } 0 \leq u < U_{\text{max}}.$$ 

Standard example: $U_{\text{max}} = 1$, $q(u) = 1 - u$. 

The Volume Filling Model

\[ T_i^{\pm} = q(u_{i\pm 1}) (\alpha + \beta(\tau(v_{i\pm 1}) - \tau(v_i))) \]
The Volume Filling Model

\[ T_i^\pm = q(u_{i\pm 1})(\alpha + \beta(\tau(v_{i\pm 1}) - \tau(v_i))) \]

Substitute \( T_i^\pm \) into the above master equation and let \( h \to 0 \):

\[
\begin{align*}
  u_t &= \nabla(D_u(q(u) - q'(u)u)\nabla u - q(u)u\chi(v)\nabla v) \\
  v_t &= D_v \Delta v + g(u, v)
\end{align*}
\]
[1] Hillen + Painter 2000:
First mention of the volume filling model; proof of global existence for special cases; numerical pattern formation.
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If the domain is large enough we obtain non trivial steady states.
Pattern Formation in 1-D

\[ g(u, v) = u - v. \]
Pattern Formation in 2-D

\[ \bar{u}_0 = 0.5 \text{ (top), } 0.25 \text{ (middle), } 0.75 \text{ (bottom)} \]
Complete Picture [1]-[7]

- [1] Hillen + Painter 2000:
Complete Picture [1]-[7]

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- [2] Painter + Hillen 2002:
  Derivation from a random walk description, pattern formation, coarsening.
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- [3] D. Wrzosek 2003:
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- [4] D. Wrzosek 2004:
  Lyapunov function. $\omega$-limit sets are steady states.
[5] Potapov + Hillen 2004:
Bifurcation diagram, metastability, numerical estimates of leading eigenvalues, scaling analysis and pattern interaction.
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Bifurcation Diagram
[6] Dolak + Schmeiser 2004:
Asymptotic analysis of pattern interaction.
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Asymptotic analysis of pattern interaction.

[7] Dolak + Hillen 2003:
Application to Dictyostelium discoideum and to Salmonella typhimurium.
Application to *Dictyostelium discoideum*
Application to *Salmonella typhimurium*
Exercise 1
(with M. Owen)
Consider the Master equation with transitional probabilities of the form

\[ T_i^{\pm} = q(u_{i\pm1})\phi(v_i). \]

1. Give an interpretation of these \( T_i^{\pm} \).
2. Show that the continuous limit leads to a chemotaxis equation of the form

\[ u_t = (A(u,v)u_x - B(u,v)v_x)_x. \]

Find \( A(u,v) \) and \( B(u,v) \).