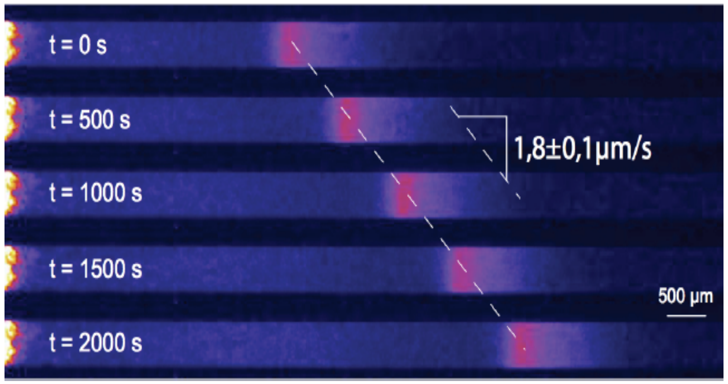
Bacterial movement by run and tumble : models, patterns, pathways, scales

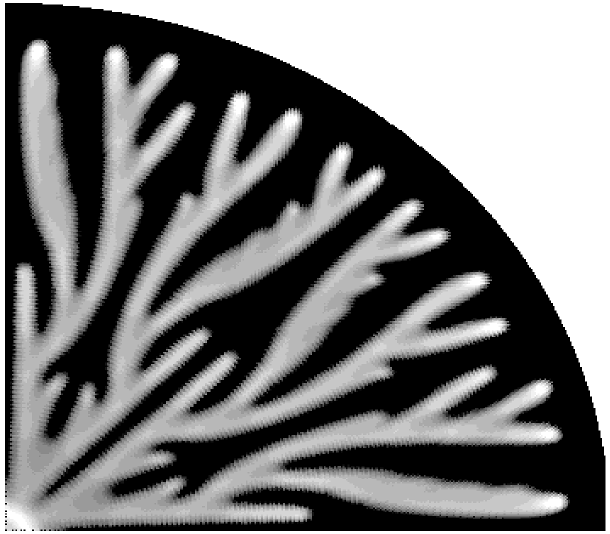
Benoît Perthame



Motivation

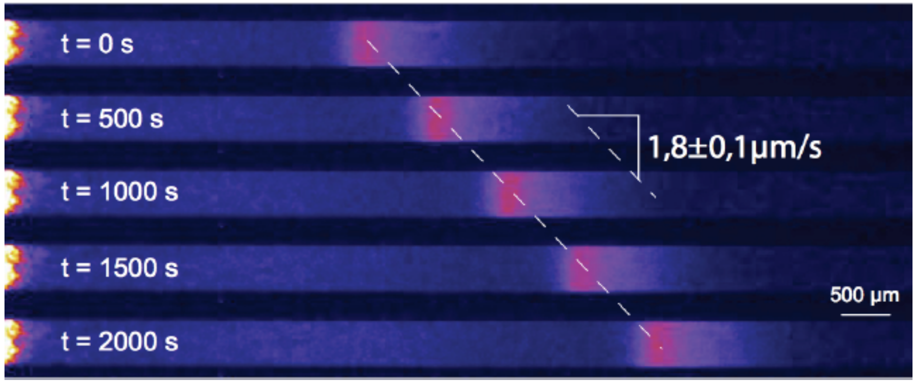
Paradigm for collective organisation

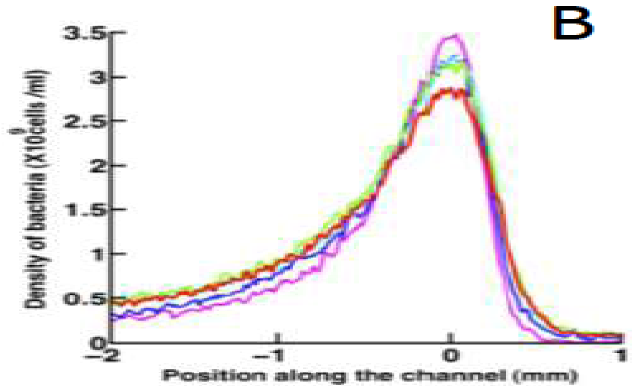
Courtesy S. Seror, B. Holland (Paris-Sud),



Numerical simulation of a mathematical model

Motivation





- Adler's famous experiment for *E. Coli* (1966)
- Self-attraction + attraction towards fresh nutrient
- Explain this pattern ; its asymmetry (experiments Curie institute)

- *E. coli* is a chemotactic bacterium
- Several strains are used ; the phenomena is robust
- Fluid dynamics is not dominant

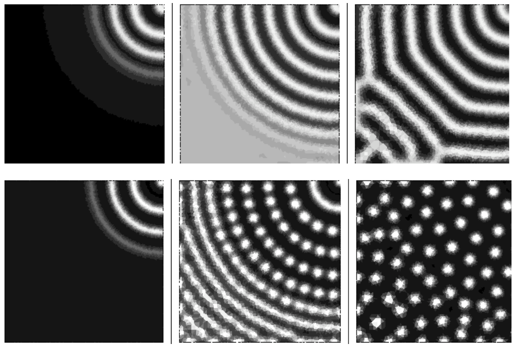
Chemotaxis : Keller-Segel

$$\frac{\partial}{\partial t} n(t,x) - \underbrace{\Delta n(t,x)}_{\text{brownian motion}} + \underbrace{\mathrm{div}(n\chi\nabla(c+S))}_{\text{oriented drift}} = 0, \quad \text{cell population density}$$

$$\tau \frac{\partial c}{\partial t} - \underbrace{\Delta c(t,x)}_{\text{molecular diffusion}} + \underbrace{rc(t,x)}_{\text{degradation}} = \underbrace{n(t,x)}_{\text{production}}, \quad \text{concentration of chemoattractant}$$

$$\tau_S \frac{\partial S}{\partial t} - \underbrace{\Delta S(t,x)}_{\text{molecular diffusion}} + \underbrace{r_S n(t,x) S(t,x)}_{\text{consumption}} = 0, \quad \text{nutrient}$$

- Internal mathematical interest
- Finite time blow-up
- **Cannot sustain robust traveling bands**
- In opposition with kinetic/hyperbolic models



Chemotaxis : Flux Limited K.-S.

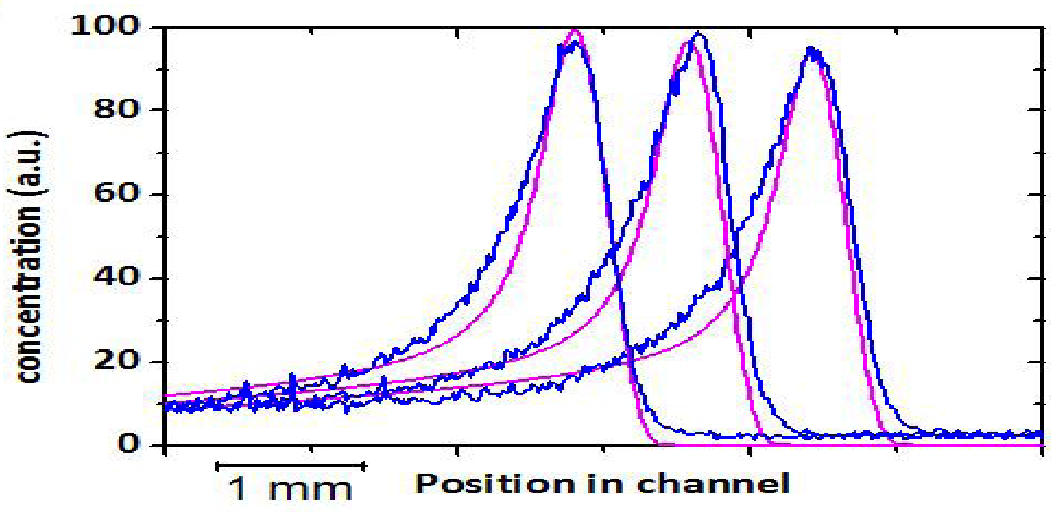
The Flux Limited Keller-Segel (Dolak-Schmeiser, Erban-Othmer)

$$\begin{cases} \frac{\partial}{\partial t} n(t,x) - \Delta n(t,x) + \mathrm{div}(nU) = 0, \\ \qquad\qquad U = \chi_c(c_t, c_x)\,\frac{\nabla c}{|\nabla c|} - \chi_S(S_t, S_x)\,\frac{\nabla S}{|\nabla S|} \\ \frac{\partial}{\partial t} c - D_c \Delta c = n(t,x) \\ \frac{\partial}{\partial t} S - D_S \Delta S = -n(x,t)\; S(t,x) \end{cases}$$

admits traveling band solutions

Can be fit to the experimental data

Chemotaxis : Flux Limited K.-S.

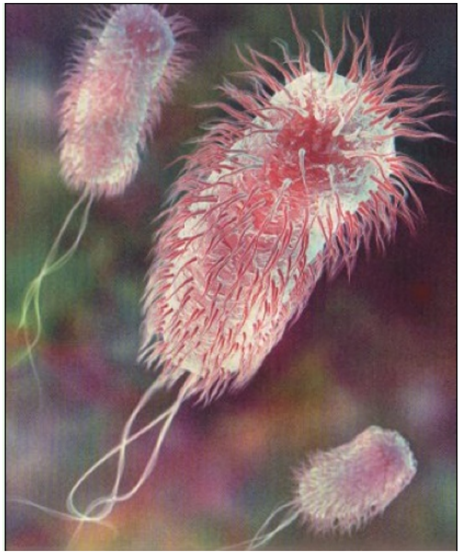


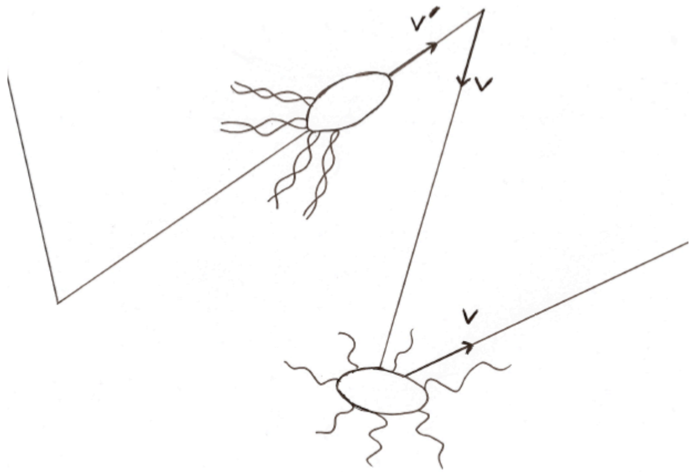
Superimposition of the calculated (pink) and the experimental (blue) concentration profiles at three different times.

- Where does the FLKS comes from ?
- The kinetic formalism uses rules for individual behaviour

Kinetic models (80-90's)

E. Coli is known to move by run and tumble Alt, Dunbar, Othmer, Stevens, Hillen...





A beautiful example of multiscale motion

Kinetic models (80-90's)

- $f(t,x,\xi)$ the population density of cells moving with the velocity ξ
- $c(t,x)$ the chemoattractant concentration

$$\frac{\partial}{\partial t} f(t,x,\xi) + \underbrace{\xi \cdot \nabla_x f}_{\textbf{run}} = \underbrace{\mathcal{K}[c,S]f}_{\textbf{tumble}},$$

$$\mathcal{K}[c,S]f = \int_B K(c,S;\xi,\xi')f(\xi')d\xi' - \int_B K(c,S;\xi',\xi)d\xi'\, f,$$

- Various forms of the tumbling kernel $\mathcal{K}[c,S]$ have been proposed
- Typical $K(c;\xi,\xi') = k\Big(c(x-\varepsilon\xi')\Big)$ (with chemoattractant only)

Kinetic models : asymptotic

Based on the run time ε : $\qquad K(c;\xi,\xi') = k\Big(c(x-\varepsilon\xi')\Big)$

$$\frac{\partial}{\partial t} f_\varepsilon(t,x,\xi) + \frac{\xi\cdot\nabla_x f_\varepsilon}{\varepsilon} = \frac{\mathcal{K}[c]}{\varepsilon^2},$$

Before blow-up time

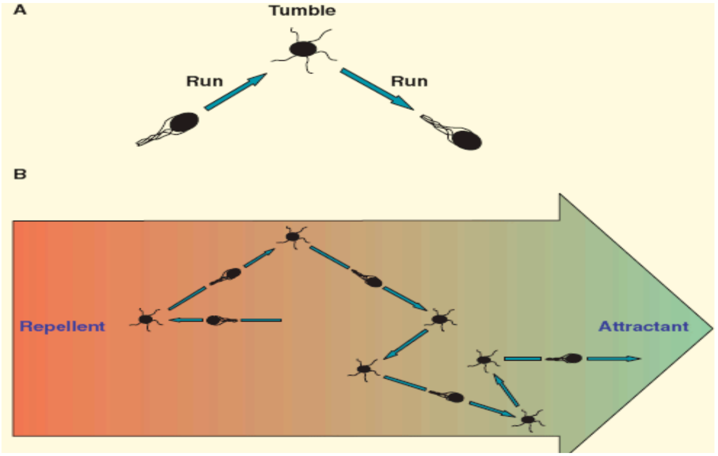
$$f_\varepsilon(t,x,\xi) \to n(t,x), \qquad c_\varepsilon(t,x) \to c(t,x),$$

$$\frac{\partial}{\partial t} n(t,x) - \mathrm{div}[D\nabla n(t,x)] + \mathrm{div}(n\chi\nabla c) = 0,$$

and the transport coefficients are given by

$$D(c) = \frac{D_0}{k(c)}, \qquad \chi(c) = \chi_0\,\frac{k'(c)}{k(c)}\,.$$

Pulse waves



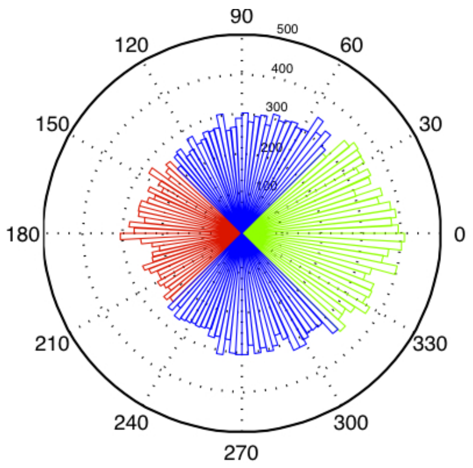
When c increases, jumps are longer

$$\frac{\partial}{\partial t} f(t,x,\xi) + \xi \cdot \nabla_x f = \mathcal{K}[c] f$$

$$K(c;\xi,\xi') = \mathbf{K}_\varepsilon \Big(\frac{\partial c}{\partial t} + \xi' . \nabla c \Big)$$

- Macroscopic limit is the Flux Limited K.-S. system

Pulse waves



angular distribution and mean run time

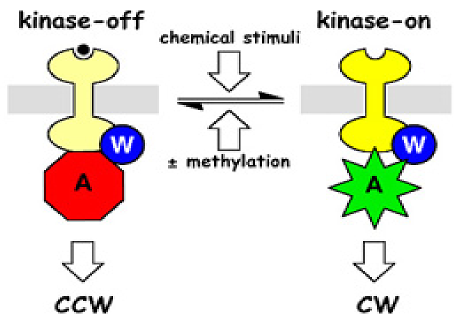
$$\frac{\partial}{\partial t} f(t,x,\xi) + \xi \cdot \nabla_x f = \mathcal{K}[c]f$$

$$K(c;\xi,\xi') = \mathbf{K}_{\varepsilon}\Big(\frac{\partial c}{\partial t} \; + \xi'.\nabla c\Big)$$

- Can one explain the tumbling rate

Biochemical pathways

Can one explain the tumbling rate $\mathbf{K}_\varepsilon\left(\frac{\partial c}{\partial t} + \xi'.\nabla c\right)$?



Use the internal biochemical pathway controling tumbling (Erban-Othmer, Dolak-Schmeiser),

$g(t, x, \xi, m)$ receptor methylation level (internal state).

Biochemical pathways

Principle : internal state m adapts to the external state

$$m \approx M(c)$$

$$\frac{\partial}{\partial t} g_\varepsilon(t,x,\xi,m) + \xi \cdot \nabla_x g_\varepsilon + \frac{1}{\varepsilon}\frac{\partial}{\partial m}[R(m - M(c))g_\varepsilon] = \mathcal{K}_\varepsilon[m,c][g_\varepsilon]$$

$$\mathcal{K}_\varepsilon[m,c][g_\varepsilon] = \int \Big[K(\frac{m - M(c)}{\varepsilon}, \xi, \xi')g_\varepsilon(x,\xi',m) - K(\ldots,\xi',\xi)g_\varepsilon(t,x,\xi,m)\Big]d\xi'$$

Fast adaptation, stiff response

Theorem The limit $\varepsilon \to 0$ gives

$$g_\varepsilon \to \delta(m - M(c))f(s,\xi,t) \qquad \text{and} \qquad \mathbf{K}\Big(\frac{\partial c}{\partial t} + \xi'.\nabla c\Big)$$

Abnormal diffusions

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Swarming bacteria migrate by Lévy Walk

Gil Ariel[1], Amit Rabani[2], Sivan Benisty[2], Jonathan D. Partridge[3], Rasika M. Harshey[3] & Avraham Be'er[2]

$$\varepsilon^{1+\mu}\frac{\partial}{\partial t}g(t,x,\xi,m)+\varepsilon\xi\cdot\nabla_x g+\varepsilon^s\Delta_m g=\mathcal{K}[m,c][g]$$

When $\mathcal{K}[m,c][g]$ degenerates,

$$\mathcal{K}[m,c][g]\approx 0 \quad \text{as} \quad m\to\infty,$$

the limiting behaviour is fractional Laplacian

$$\frac{\partial n}{\partial t}-\Delta^\alpha n=0$$

Conclusion

- Flux-Limited Keller-Segel system relies on a multiscale approach (molecule to cell to population)

- It is possible to fit quantitatively the experimental data

- Numerous mathematical questions (singularities, asymptotic, fractional derivatives, waves...)

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