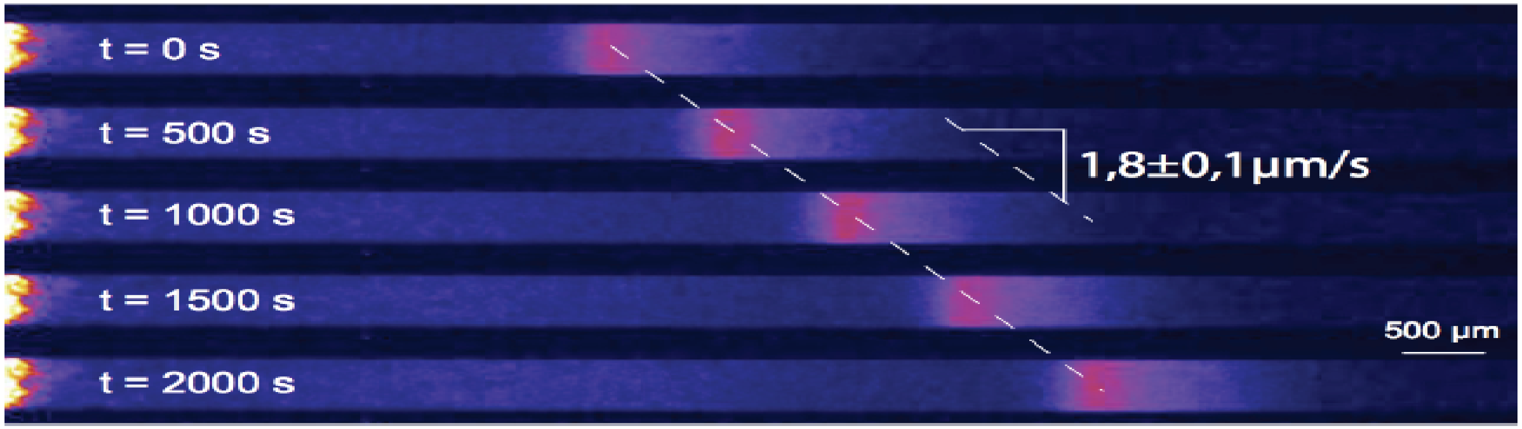
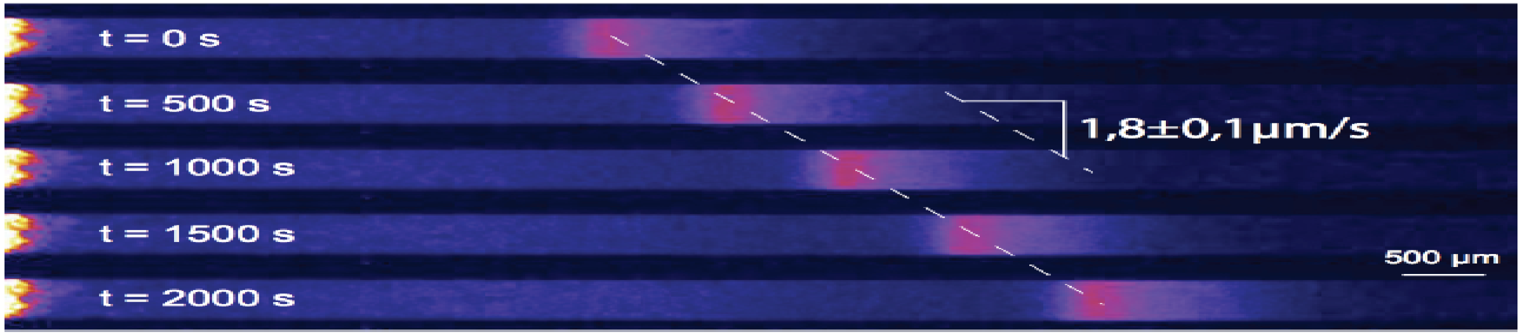
Traveling Pulses and chemotaxis

Benoît Perthame
Laboratoire J.-L. Lions, UPMC and INRIA



MOTIVATION



- Adler's famous experiment for E. Coli
- Time scale is too short for cell multiplication
- Medium contains various nutrients
- Explain this pattern ; its asymmetry

METHOD

- The Keller-Segel model does not sustain such solutions
- Even the many variants introduced for other patterns

- Derive extension of the Keller-Segel system from kinetic theory
- Based on refined experimental measurements on run-tumble phenomena

OUTLINE OF THE LECTURE

I. Macroscopic models (Keller-Segel)

II. Kinetic models

III. Hyperbolic and diffusion limits

IV. Back to experiments

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Work with : N. Bournaveas, V. Calvez

A. Buguin, J. Saragosti, P. Silberzan (Curie Intitute)

Plos Computational Biology 2010

CHEMOTAXIS : Keller-Segel model

$$n(t,x) \;=\; \text{density of cells at time t and position } x,$$

$$c(t,x) \;=\; \text{concentration of chemoattractant,}$$

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

$$\tau \frac{\partial c}{\partial t} - \Delta c(t,x) + rc(t,x) = n(t,x),$$

The parameter χ is the sensitivity of cells to the chemoattractant.

CHEMOTAXIS : Keller-Segel model

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

$$-\Delta c(t,x) = n(t,x),$$

Theorem (Blanchet, Dolbeault, Perthame)
In $\mathbb{R}^2$ we have

For $M^0 < \frac{8\pi}{\chi}$ there are global smooth solutions, that disperse to 0

For $M^0 > \frac{8\pi}{\chi}$ solutions blow-up in finite time

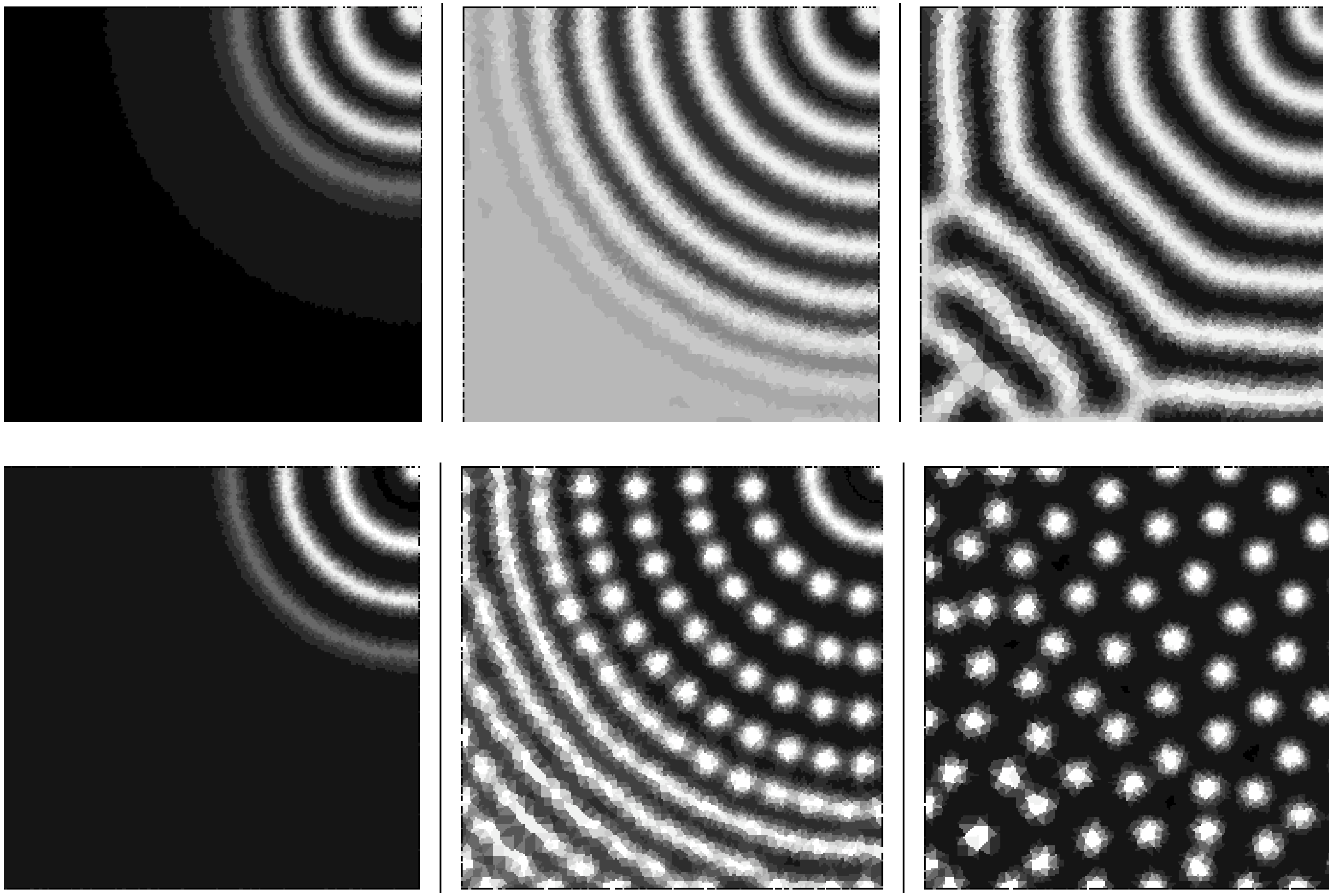
CHEMOTAXIS : Keller-Segel model

Biologists and biomathematicians have proposed variants as Maini, Murray, Budrene and Berg, Brenner et al...

$$
\begin{cases}
\dfrac{\partial n}{\partial t} = \Delta n - \nabla \cdot (n\chi\nabla c) \\
-\Delta c = nf - rc, \\
\dfrac{\partial f}{\partial t} = -nf.
\end{cases}
$$

See analysis in Calvez and Perthame, BIT Num. Math 2006

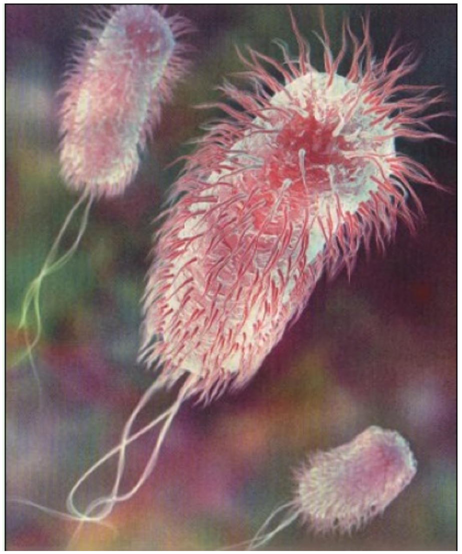
These models do not exhibit robust Traveling Pulses

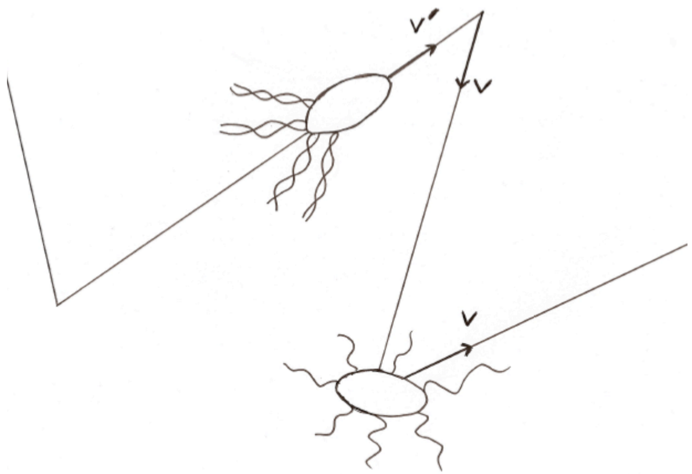


From A. Marrocco (INRIA, BANG)

KINETIC MODELS

E. Coli is known (since the 80's) to move by run and tumble depending on the coordination of motors that control the flagella





See Alt, Dunbar, Othmer, Stevens, Hillen....

KINETIC MODELS

Denote by $f(t, x, \xi)$ the density of cells moving with the velocity ξ.

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

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

$$-\Delta c(t, x) = n(t, x) := \int_B f(t, x, \xi) d\xi,$$

- There are now TWO variables x, ξ (difficult to compute)
- Used to derive macroscopic models (Boltzmann $\rightarrow$ Navier-Stokes)

KINETIC MODELS

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

$$-\Delta c(t,x) = n(t,x) := \int_B f(t,x,\xi) d\xi,$$

- Various forms of the tumbling kernel have been proposed
- Most probably K only depends on ξ

KINETIC MODELS

Simplest example

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

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

$$-\Delta c(t,x) = n(t,x) := \int_B f(t,x,\xi) d\xi,$$

$$K(c;\xi,\xi') = k_-(c(x-\varepsilon\xi')) + \; k_+(c(x+\varepsilon\xi)).$$

Related to linear scatering with a changing background.

KINETIC MODELS

Theorem (Chalub, Markowich, P., Schmeiser)
For $0 \leq k_{\pm}(c; \xi, \xi') \leq C(1 + c)$, there is a GLOBAL solution to the kinetic model and

$$\|f(t)\|_{L^\infty} \leq C(t)[\, \|f^0\|_{L^1} + \|f^0\|_{L^\infty}]$$

-) Situation better for a hyperbolic model !
-) Open question : Is it possible to prove a bound in L^∞ when we replace the specific form of K by

$$0 \leq K(c; \xi, \xi') \leq \|c(t)\|_{L^\infty_{\text{loc}}} \ ?$$

-) Related questions Internal variables (Erban, Othmer, Hwang, Dolak, Schmeiser), quorum sensing, mesenchymal (Hillen)

KINETIC MODELS

Idea of the proof

Use dispersive effects and change of variable

$$\xi \mapsto x - \varepsilon\xi = y$$

KINETIC MODELS

Another class of turning kernels

-) Hwang, Kang, Stevens : $k\Big(\nabla c(x-\varepsilon\xi')\Big)$ or $k\Big(\nabla c(x+\varepsilon\xi)\Big)$

$$k\Big(\nabla c(x-\varepsilon\xi')\Big)+k\Big(\nabla c(x+\varepsilon\xi)\Big).$$

Theorem (Bournaveas, Calvez, Gutierrez, P.)

For SMALL initial data, there is a GLOBAL solution.

Based on Strichartz inequalities

Blow-up

can occur with spherically symmetric data (Bournaveas, Calvez)

Numerics indicates different type of blow-up (Vauchelet)

KINETIC MODELS : diffusion limit

One can perform a parabolic rescaling **based on the memory scale**

$$\begin{cases} \mathcal{K}[f] = \int K(c;\xi,\xi')f'd\xi' - \int K(c;\xi',\xi)d\xi'\ f, \\ K(c;\xi,\xi') = \ k_-\Big(c(x-\varepsilon\xi')\Big) + \ k_+\Big(c(x+\varepsilon\xi)\Big). \end{cases}$$

$$\begin{cases} \frac{\partial}{\partial t}f(t,x,\xi) + \frac{\xi\cdot\nabla_x f}{\varepsilon} = \frac{\mathcal{K}[c,f]}{\varepsilon^2}, \\ -\Delta c(t,x) = n(t,x) := \int f(t,x,\xi)d\xi. \end{cases}$$

Diffusion scaling law : K = symmetric + ε anti-symmetric

KINETIC MODELS : diffusion limit

Theorem (Chalub, Markowich, P., Schmeiser) With the same assumptions, as $\varepsilon \longrightarrow 0$, then locally in time,

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

$$\begin{cases} \frac{\partial}{\partial t} n(t,x) - \text{div}[D \nabla n(t,x)] + \text{div}(n\chi\nabla c) = 0, \\ -\Delta c(t,x) = n(t,x). \end{cases}$$

KINETIC MODELS : diffusion limit

and the transport coefficients are given by

$$D(n,c) = D_0 \, \frac{1}{k_-(c) + k_+(c)} \, ,$$

$$\chi(n,c) = \chi_0 \, \frac{k'_-(c) + k'_+(c)}{k_-(c) + k_+(c)} \, .$$

The drift (sensibility) term $\chi(n,c)$ comes from the memory term.

Interpretation in terms of random walk : memory is fundamental.

KINETIC MODELS : hyperbolic limit

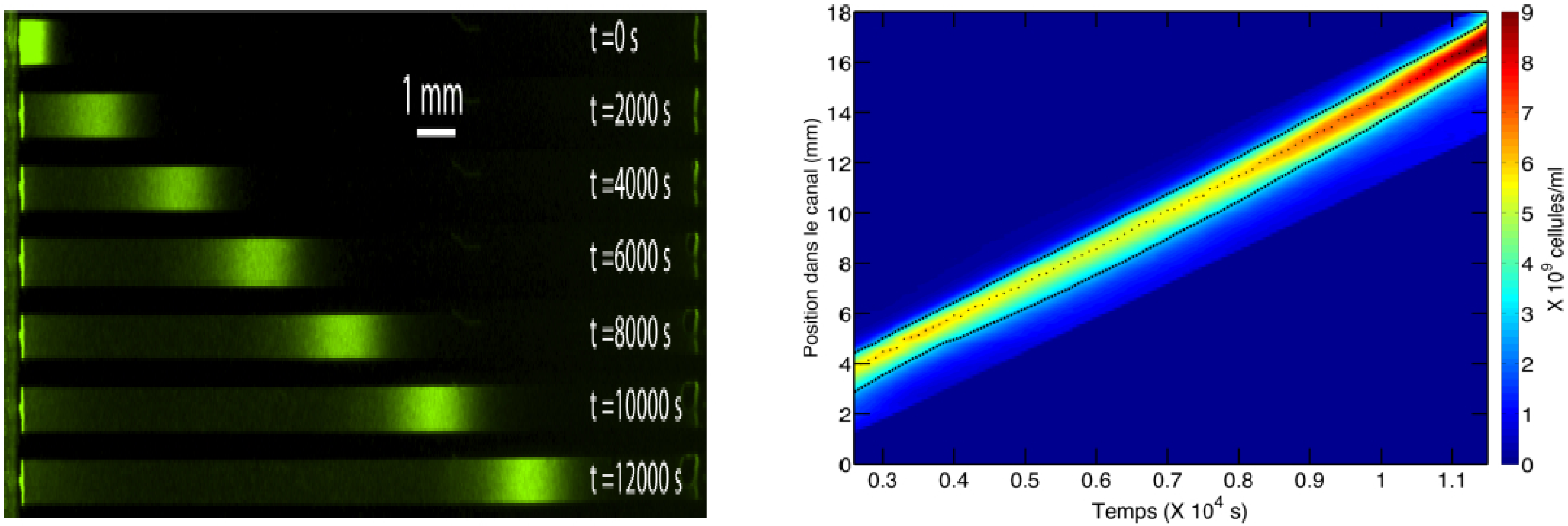
Hyperboloc scaling law : $K =$ symmetric $+ O(1)$ anti-symmetric.

Then the scaling is different

$$\begin{cases} \frac{\partial}{\partial t} f(t,x,\xi) + \xi \cdot \nabla_x f = \frac{\mathcal{K}[c,f]}{\varepsilon}, \\ -\Delta c(t,x) = n(t,x) := \int f(t,x,\xi) d\xi. \end{cases}$$

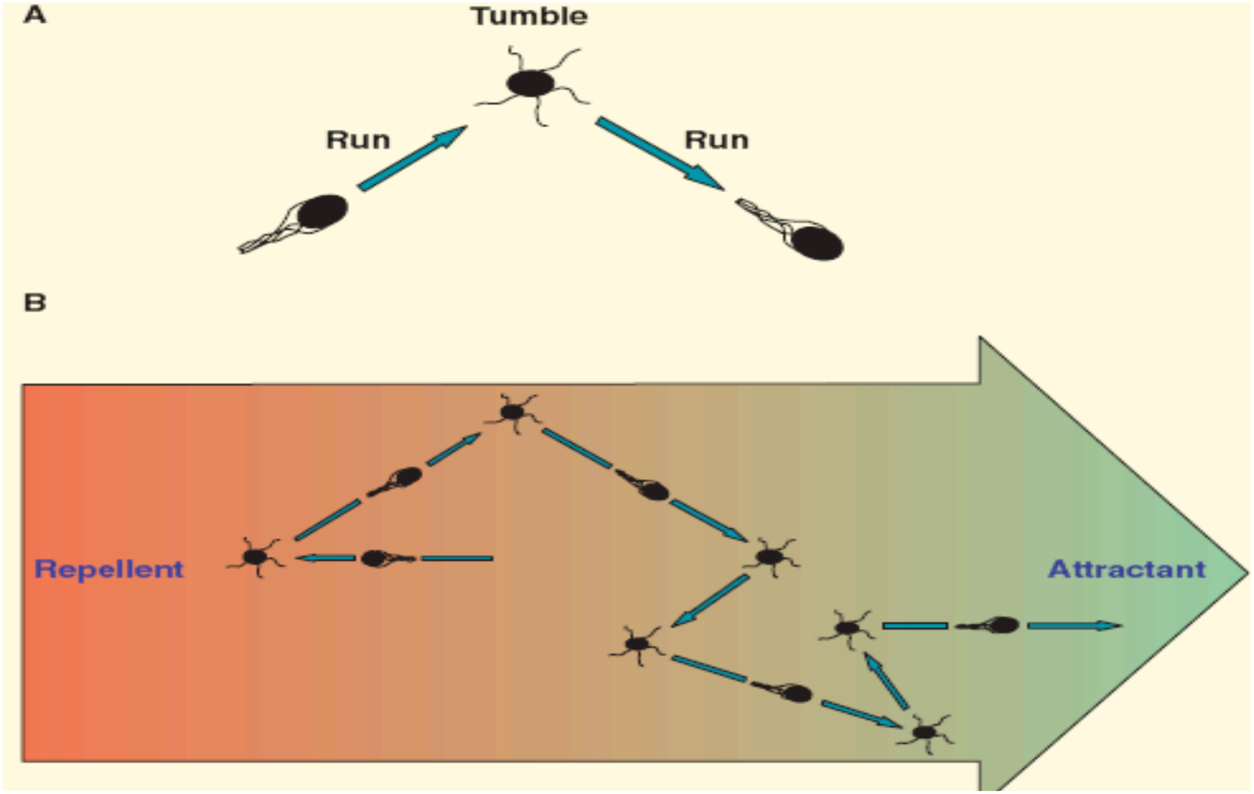
$$\begin{cases} \frac{\partial}{\partial t} n(t,x) + \text{div}[n\, U(c)] = 0, \\ -\Delta c(t,x) = n(t,x). \end{cases}$$

Pulse waves



Asymmetric pulse wave of *E. Coli* A. Buguin, P. Silberzan, J. Saragosti (Curie Institute)

Pulse waves



When c increases, jumps are longer

Pulse waves

$$\frac{\partial}{\partial t} f(t,x,\xi) + \xi \cdot \nabla_x f = \int K(c;\xi,\xi') f(\xi') d\xi' - \int K(c;\xi',\xi) d\xi' \, f,$$

$$-\Delta c(t,x) = n(t,x) := \int f(t,x,\xi) d\xi,$$

This lead Dolak and Schmeiser to choose

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

With (stiff response)

$$\mathbf{k}(z) = \begin{cases} k_- & \text{for } z < 0, \\ \\ k_+ < k_- & \text{for } z > 0. \end{cases}$$

More generally $\mathbf{k}(\cdot)$ a (smooth) decreasing function

Pulse waves

The diffusion limit is the Flux Limited Keller-Segel system

$$\begin{cases} \frac{\partial}{\partial t} n(t,x) - \Delta n(t,x) + \mathrm{div}(nU) = 0, \\ U = \chi(c_t, c_x) \, \frac{\nabla c}{|\nabla c|} \end{cases}$$

And the nonlinear sensitivity χ depends on $\mathbf{k}(\cdot)$.

With a nutrient and a chemoattractant and in one dimension

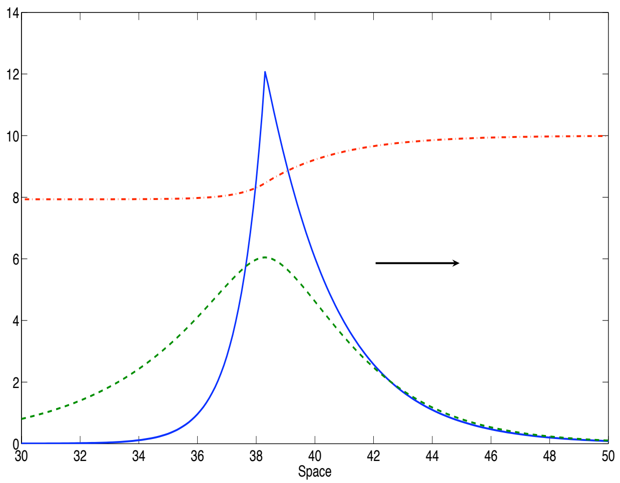
$$u = \chi_c \Big(1 - (\varepsilon \frac{c_t}{c_x})^2\Big)_+ \mathrm{sgn}(c_x) + \chi_N \Big(1 - (\varepsilon \frac{N_t}{N_x})^2\Big)_+ \mathrm{sgn}(N_x)$$

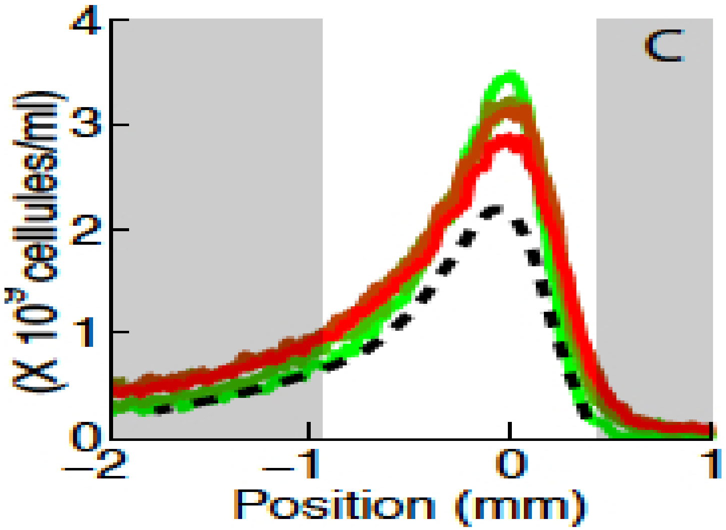
See also Bellomo, Bellouquid, Nieto and Soler

Pulse waves

Theorem There are asymmetric traveling pulses to the FLKS model with

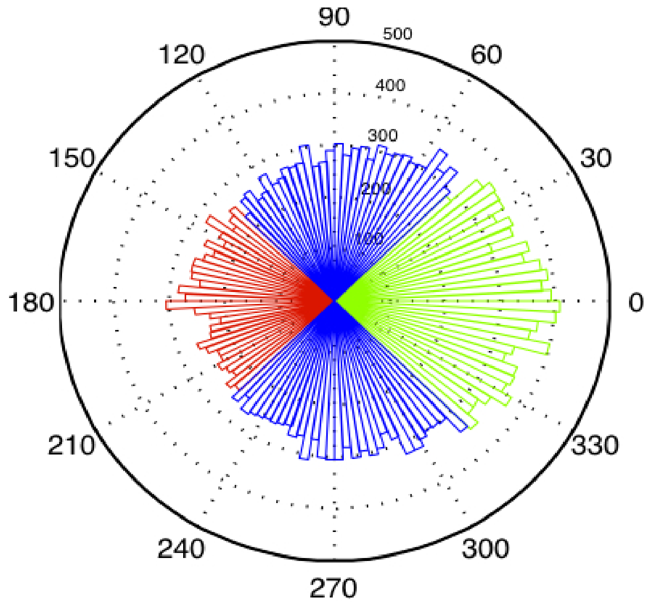
- stiff response
- both chemoattaction and nutrient.



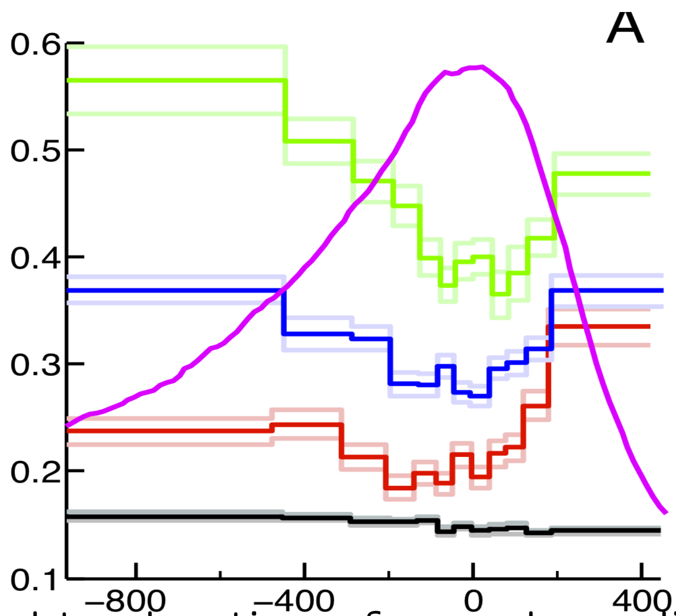


Left : analytical solution of the model   Right : experimental profile

Ongoing on run/tumble



Left : angular distribution of runs



Right : duration of runs depending on the position

Tumbling events are short but might also be important quantitatively : K might depend on ξ'.

Conclusion

- Modulation of tumbling frequency arises by longer run with increasing concentration attractant

- It was propsed (Dolak-Schmeiser) to include this effect in a kinetic model

- This generates a (Flux Limited' Keller-Segel system

- FLKS admits robust traveling pulses compatible with experiments