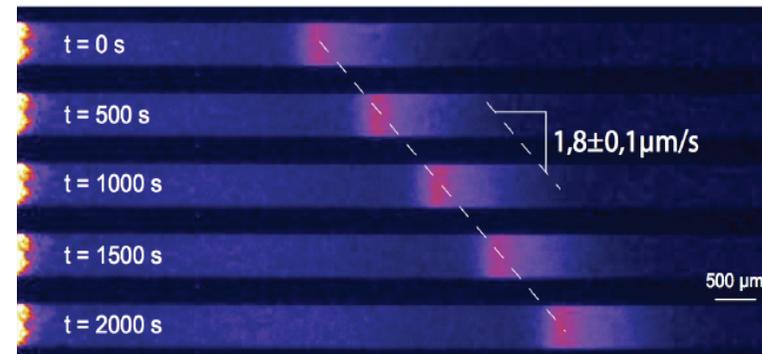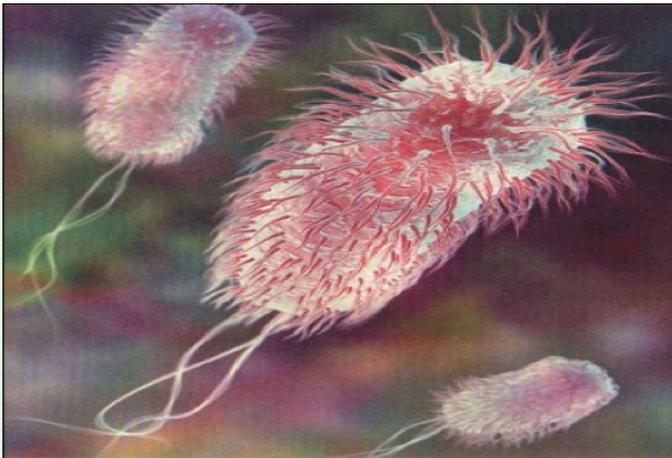# Kinetic models of chemotaxis and Traveling Bands
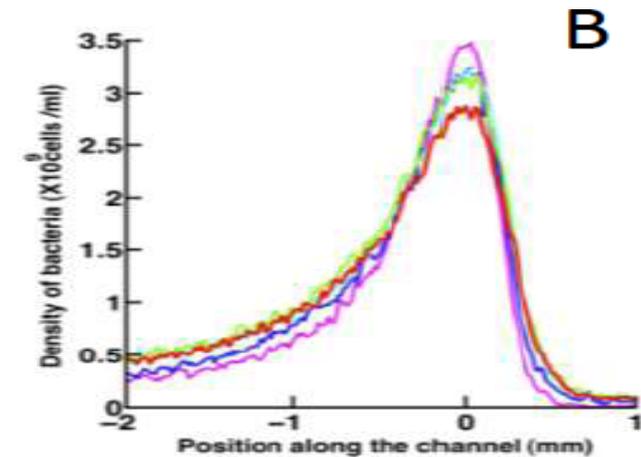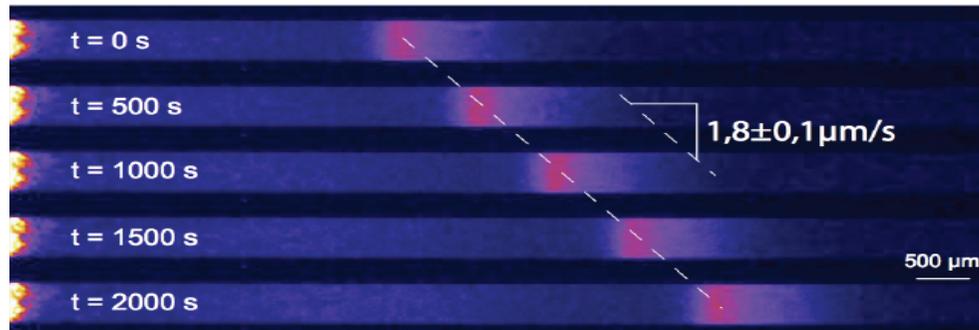
Benoît Perthame
Laboratoire J.-L. Lions, UPMC and INRIA

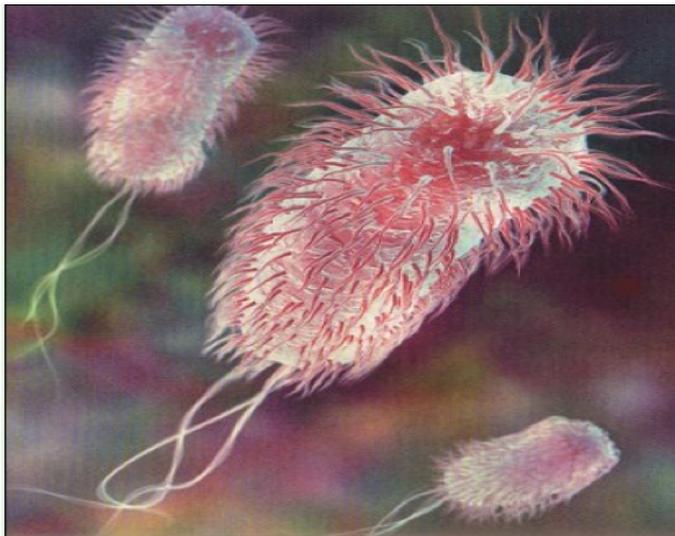- Adler's famous experiment for E. Coli (1966)

- Explain this pattern ; its asymmetry (Buguin, Saragosti, Silberzan, Curie institute)

- Is it a phenomena explanable at the macroscopic scale ?

MOTIVATION

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

E. coli, size $\approx 1\mu m$
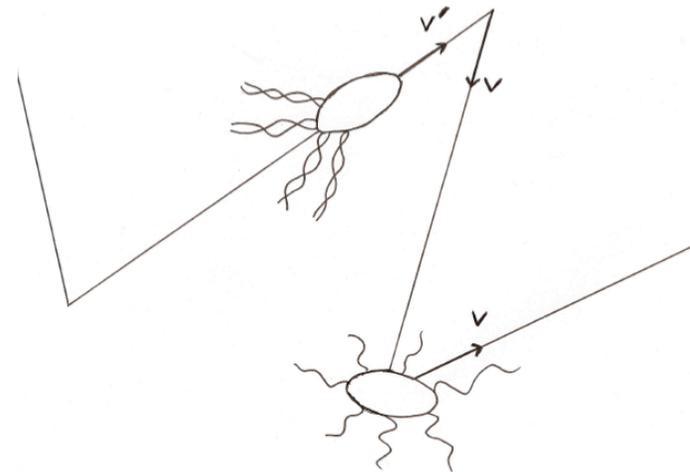
Run size $\approx 10\mu m$

MOTIVATION

Another remarkable pattern for E. coli

Mittal, Budrene, Brenner, van Oudenaarden : PNAS 2003
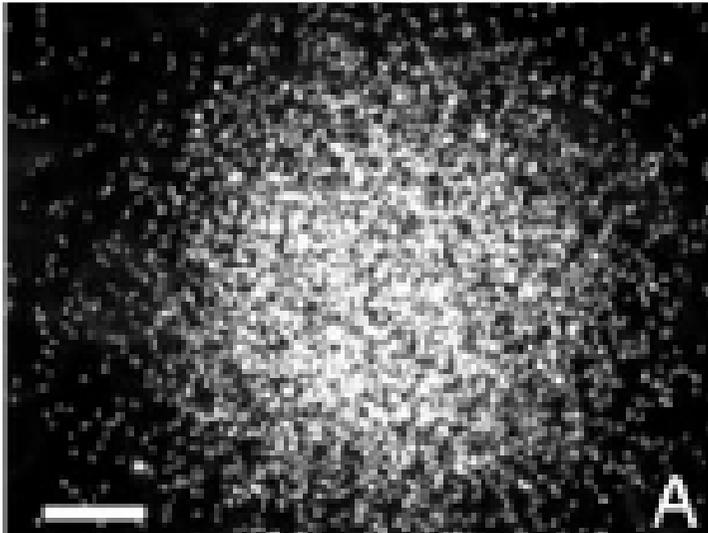
Cluster of bacteria (scale $100\mu m$)
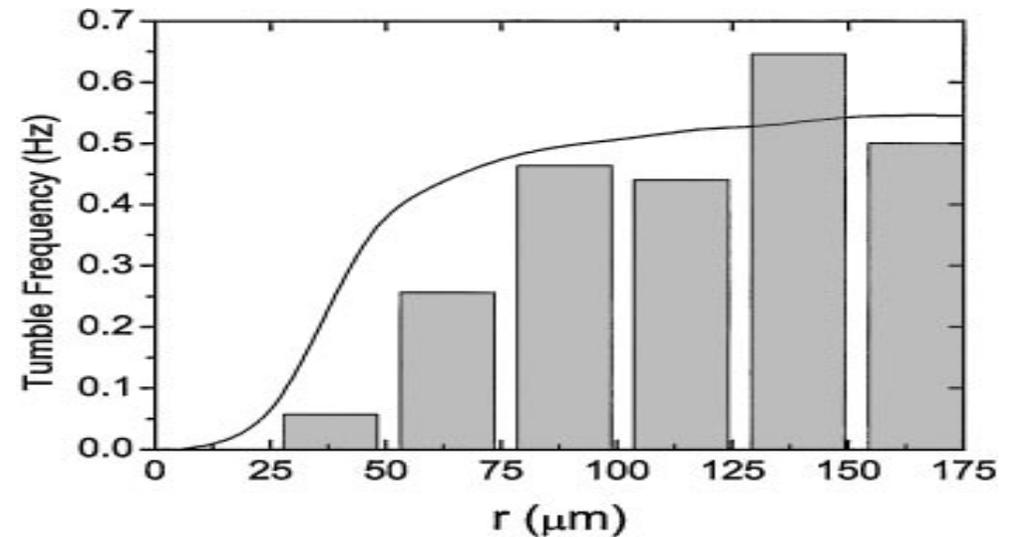
Tumbling frequency as a function of cell position

MOTIVATION
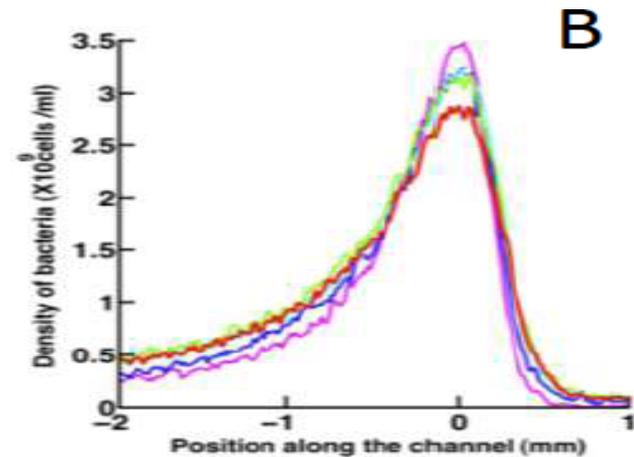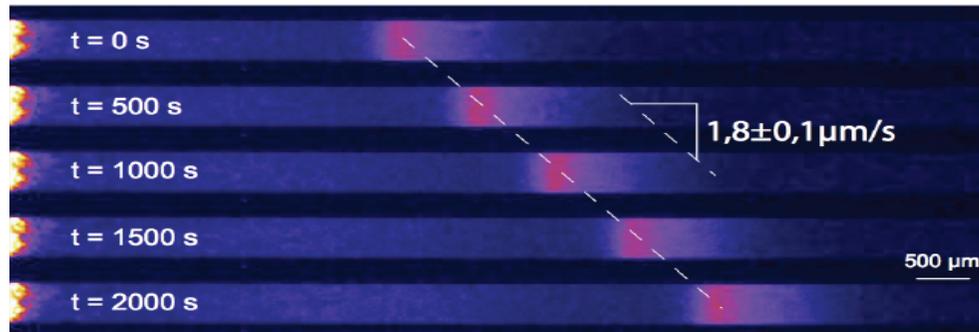
- *E. coli* is a chemotactic bacterium

- Time scale is too short for cell multiplication

- Medium contains various chemicals (chemoattractant, nutrients)

- Interaction with fluid is not an important effect here

- Several strains are used ; the phenomena is robust

METHOD

- The standard Keller-Segel model does not sustain such solutions

- Even the many variants introduced for other patterns

- Use extensions 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

OUTLINE OF THE LECTURE

I.   Macroscopic models (Keller-Segel)

II. Kinetic models

III. Hyperbolic and diffusion limits

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Work with :   N. Bournaveas, V. Calvez

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

PLOS Computational Biology 2010

PNAS 2011

CHEMOTAXIS : Keller-Segel model (macroscopic)

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

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

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

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

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

CHEMOTAXIS : Keller-Segel model

$$\frac{\partial}{\partial t}n(t,x) - \Delta n(t,x) + \operatorname{div}(n\chi\nabla c) = 0,$$

$$-\Delta c(t,x) = n(t,x),$$
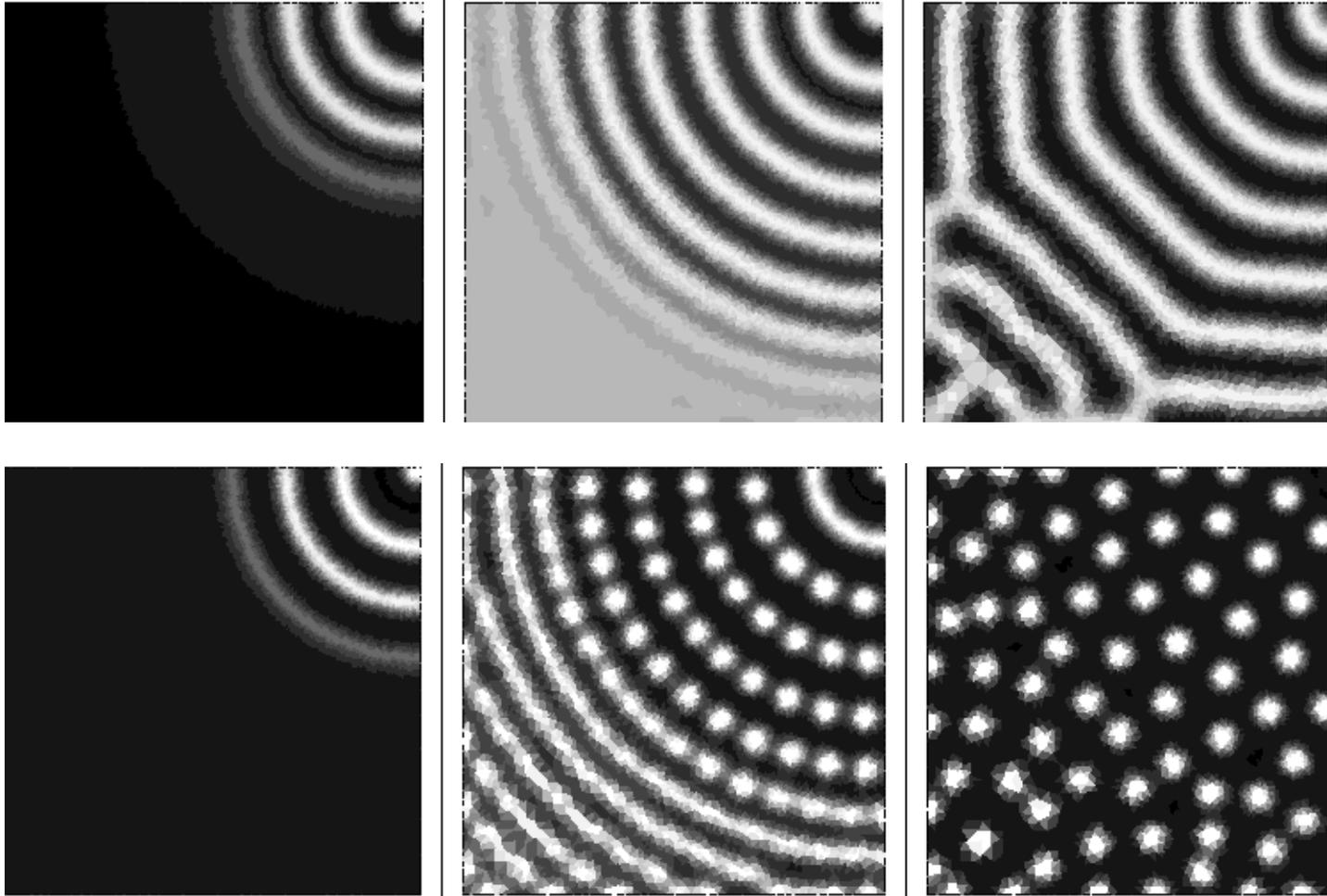
Theorem (Blanchet, Dolbeault, Perthame)

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

Claim Singularities are pointwise Dirac masses

This is proved in many situations M. Herrero, J.-L. Velazquez

From J. Murray's book ; computations by A. Marrocco (INRIA, BANG)

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

CHEMOTAXIS : Keller-Segel model

Traveling waves of speed σ are 1-D solutions $n(x - \sigma t), c(x - \sigma t)$

$$\begin{cases} -\sigma n' &= n'' - \chi(nc')' \\ -c'' &= nf - rc ... etc, \end{cases}$$

CHEMOTAXIS : Keller-Segel model

Traveling waves of speed σ are 1-D solutions $n(x - \sigma t), c(x - \sigma t)$

$$\begin{cases} -\sigma n' & = \ n'' - \chi(nc')' \\[2mm] -c'' & = \ nf - rc...etc, \end{cases}$$

$$-\sigma n = n' - \chi n c'$$

CHEMOTAXIS : Keller-Segel model

Traveling waves of speed σ are 1-D solutions $n(x - \sigma t), c(x - \sigma t)$

$$\begin{cases} -\sigma n' &=& n'' - \chi(nc')' \\ -c'' &=& nf - rc...etc, \end{cases}$$

$$-\sigma n = n' - \chi n c'$$

$$\ln(n)' = -\sigma + \chi c'$$

CHEMOTAXIS : Keller-Segel model

Traveling waves of speed σ are 1-D solutions $n(x - \sigma t), c(x - \sigma t)$

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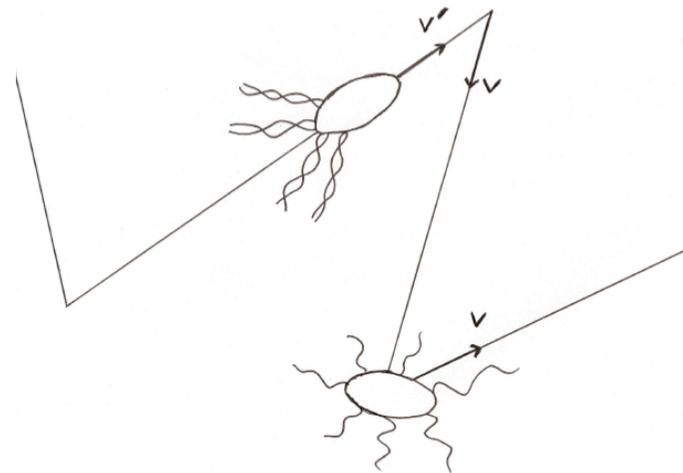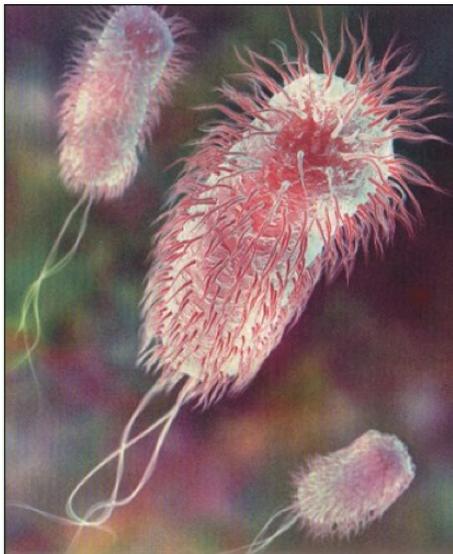
$$-\sigma n = n' - \chi n c'$$

$$\ln(n)' = -\sigma + \chi c'$$

$$\ln(n) = -\sigma x + \chi c + \mu$$
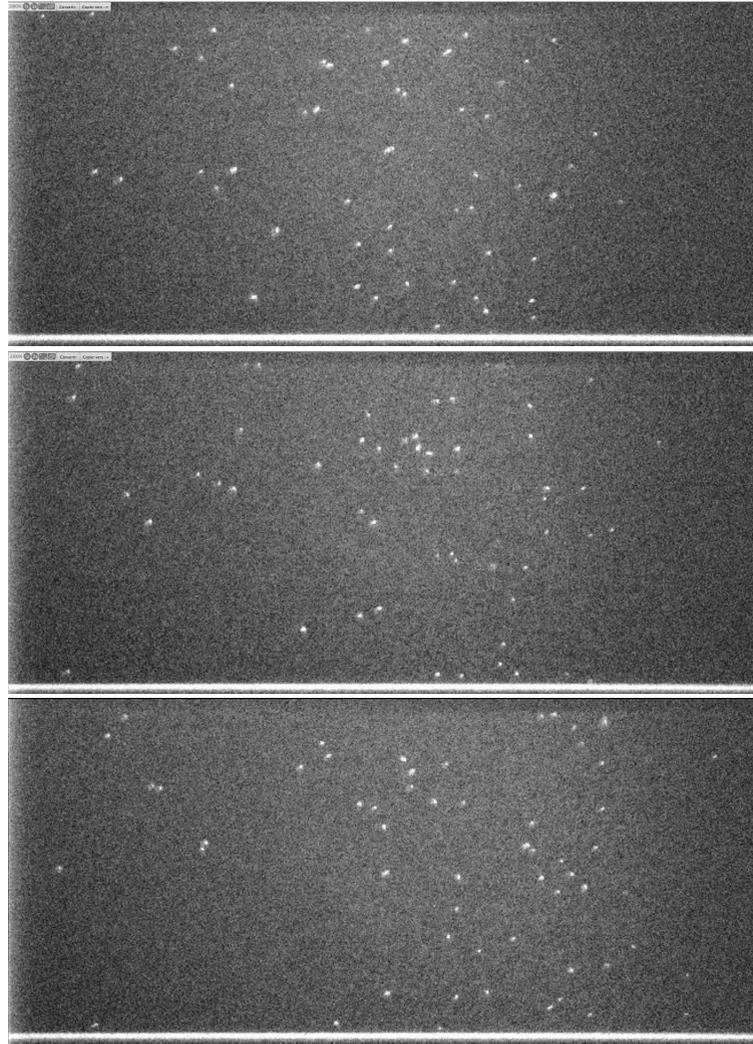
This is incompatible with any rule for the production/regulation of c

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)

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

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

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

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

- 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 (see also Hwang, Kang and Stevens)

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

-) Related questions Internal variables (Erban-Othmer, M. Tang), 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, Filbet)

KINETIC MODELS : diffusion limit

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

$$\begin{cases} \mathcal{K}[f] = \int K(c;\xi,\xi')f'd\xi' - \int K(c;\xi',\xi)d\xi'\, f, \\[2mm] K(c;\xi,\xi') = k_-\big(c(x - \varepsilon\xi')\big) + k_+\big(c(x + \varepsilon\xi)\big). \end{cases}$$

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

Diffusion scaling law : $K(\xi,\xi') = $ symmetric $+\ \varepsilon$ anti-symmetric

KINETIC MODELS : diffusion limit

Theorem With the same assumptions, as $\varepsilon \to 0$, then for short times,

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

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

and the transport coefficients are given by

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

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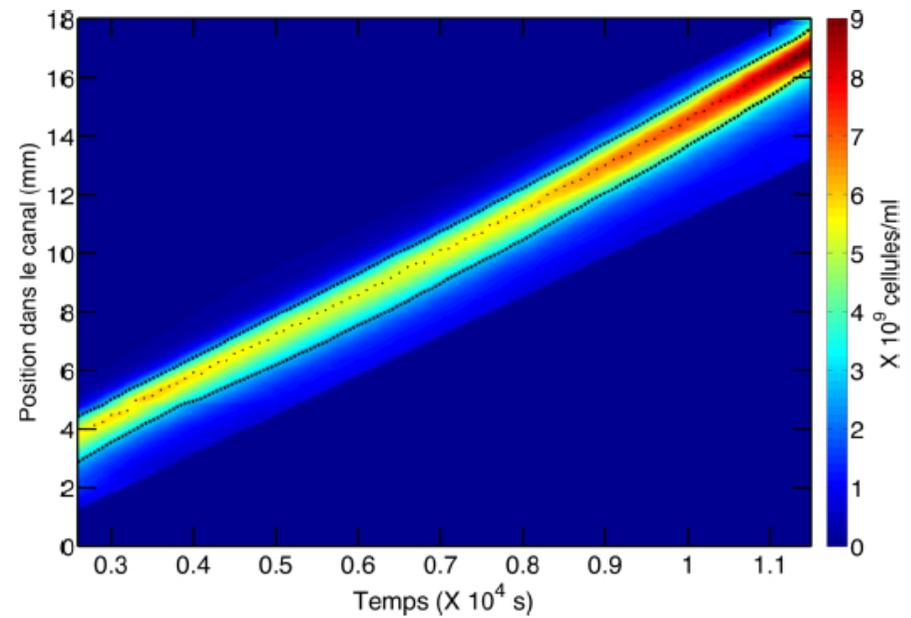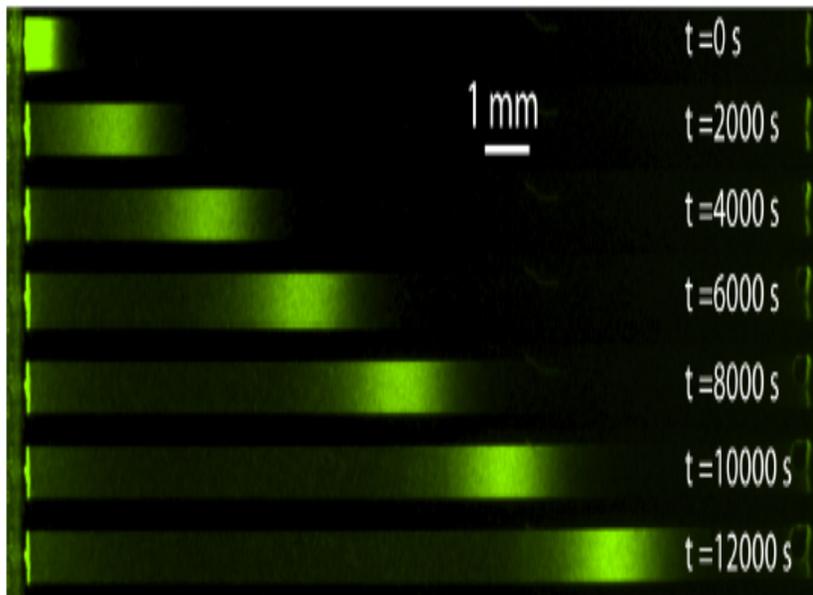
KINETIC MODELS : hyperbolic limit

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

Then the scaling is different

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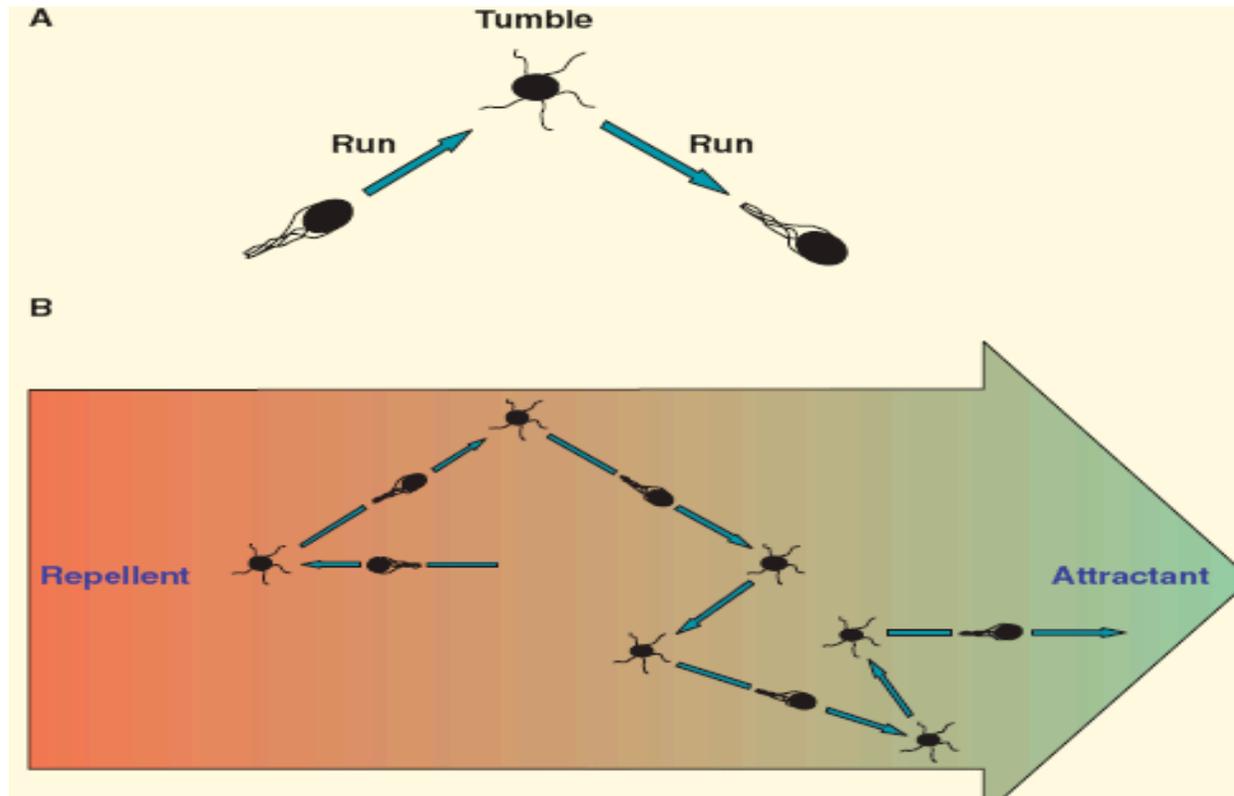-\Delta c(t, x) = n(t, x) := \int f(t, x, \xi) d\xi.
\end{cases}
$$

$$
\begin{cases}
\frac{\partial}{\partial t} n(t, x) + \operatorname{div}[n\, U(c)] = 0, \\[2ex]
-\Delta c(t, x) = n(t, x).
\end{cases}
$$

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 leads Dolak and Schmeiser to choose

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

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 $\mathbf{k}(\cdot)$.

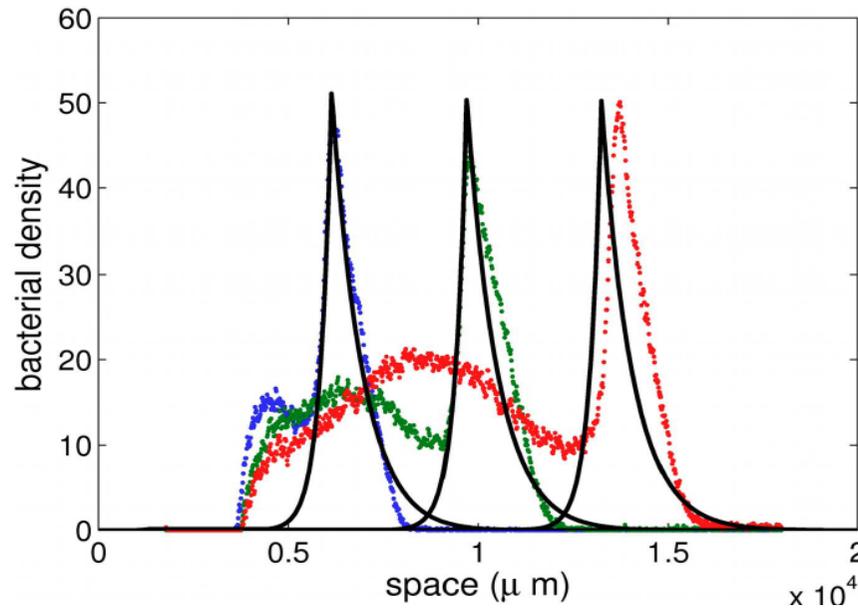With a nutrient and a chemoattractant and in one dimension

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

See also Caselles, Mazón, Bellomo, Bellouquid, Nieto and Soler
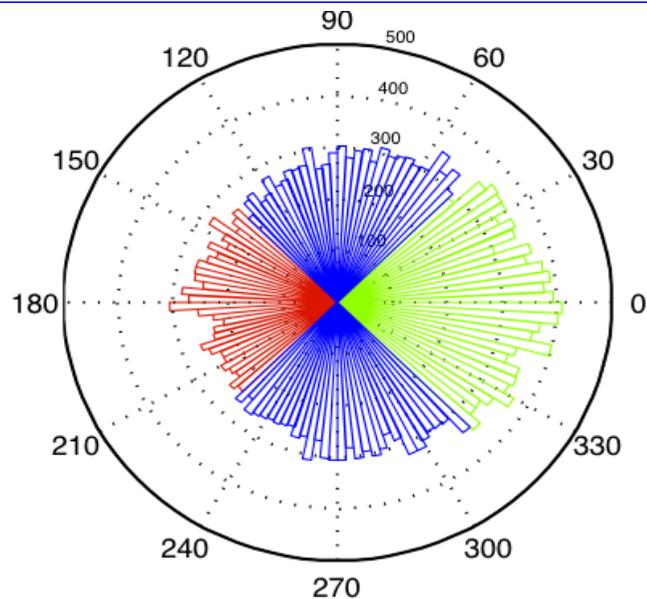James, Vauchelet

Pulse waves

Theorem Asymmetric traveling pulses to the FLKS model exist with

- stiff response
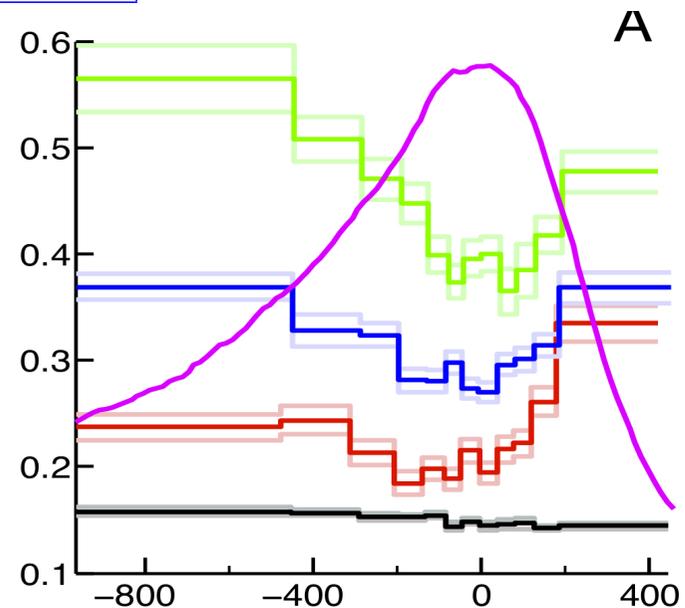- both chemoatraction and nutrient.

Superimposition of the FLKS solution and the experimental concentration profiles
at three different times.
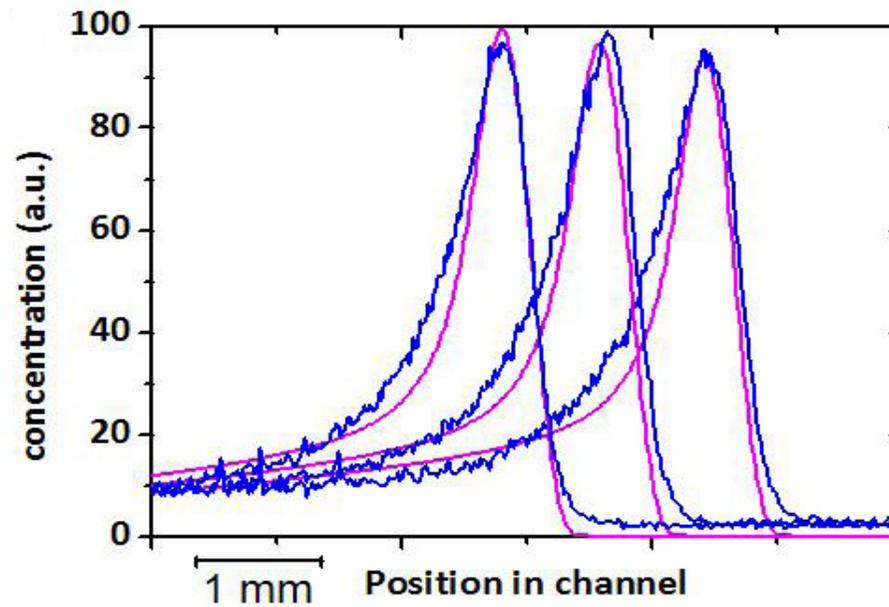
Run/tumble

Left : angular distribution of runs

Right : duration of runs w.r. position

Tumbling events : K depend on ξ also (post-tumble velocity depends on velocity before tumbles) ; not included in

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

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

Conclusion

- Kinetic models explain quantitatively collective motion by chemotaxis

- Detailed rules at the individual scale explain flux limitations in the Keller-Segel equations

- Follow-up : accelerating waves (E. Bouin, V. Calvez, G. Nadin, F. Filbet, N. Vauchelet)

Conclusion

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THANK YOU