MATHEMATICAL MODELS OF CELL MOTION

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OUTLINE OF THE LECTURE

I. Introduction

II. Chemotaxis

III. Initiation of angiogenesis

IV. Kinetic picture

V. Angiogenesis

COLLABORATORS

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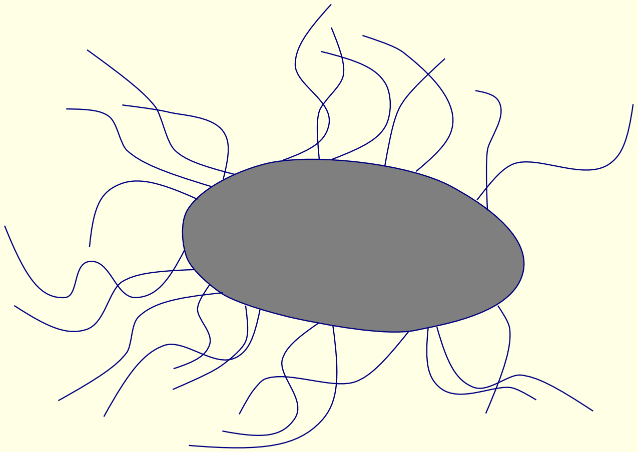
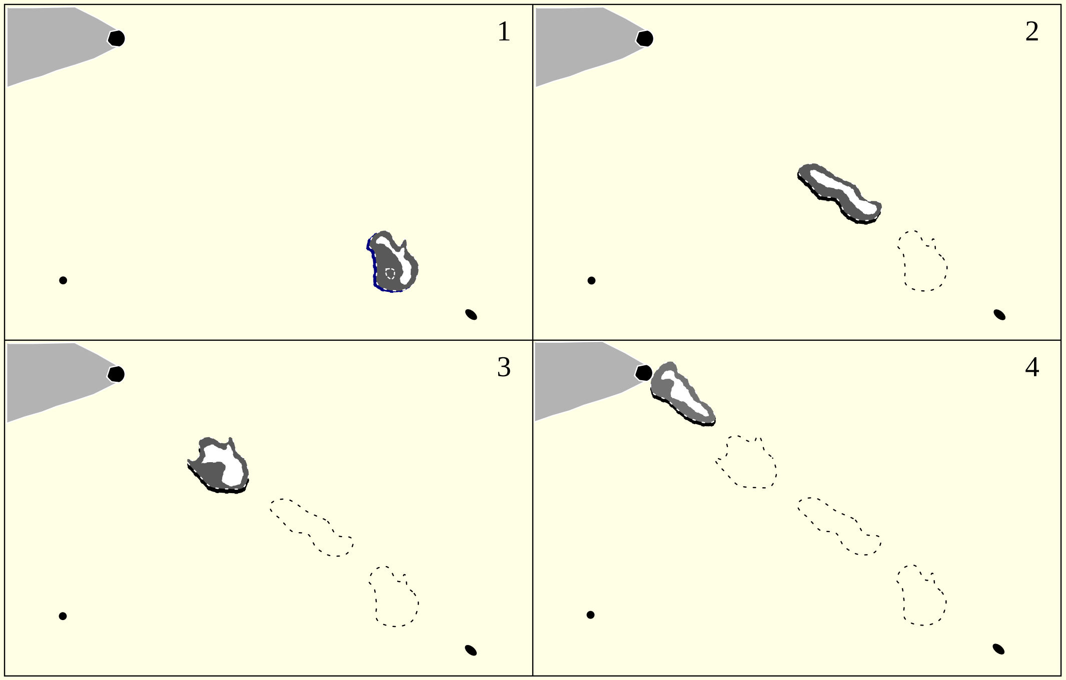
Introduction: how do cells move?

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



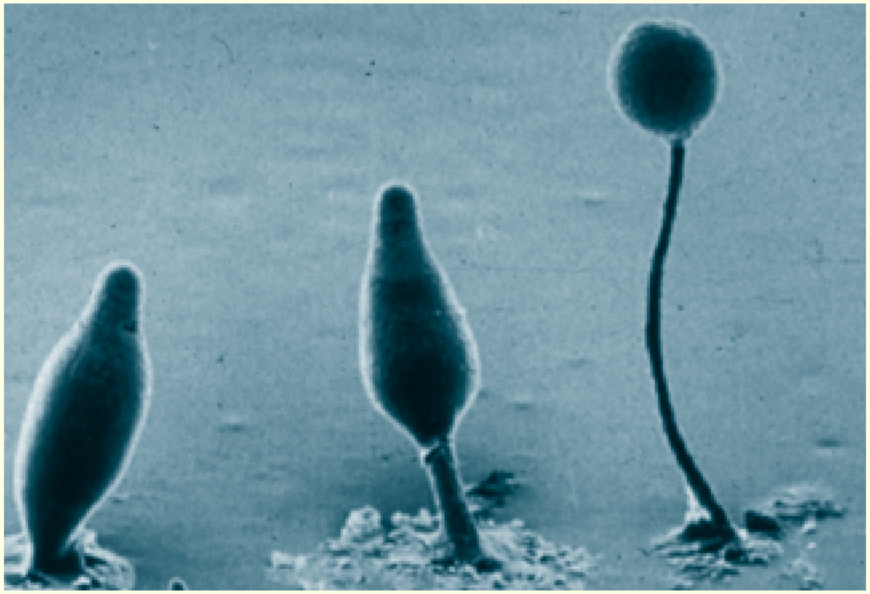
A representation of bacterium Escherichia Coli and its flagella

... to the prokariotic amoeba Dictyostelium Discoïdeum



Motion of Dictyostelium Discoïdeum in reaction to a chemoattractant emited from the dark point (upper left corner)

This hability to move allows for a collective behavior of Dictyostelium Discoïdeum and create a fruting body when nutriments are lacking



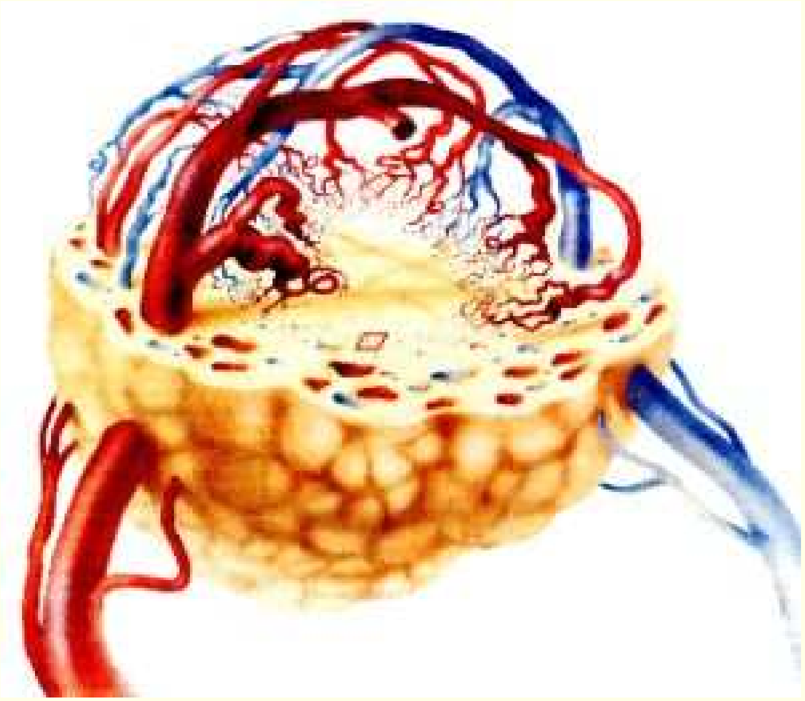
Introduction: which cells move?

Human endothelial cells are usually at rest.

But when aggregates of a few hundred of cancerous cells are formed, they emit a chemical signal (VEGF) that is able to attract endothelial cells.

A new capillary vasculature is created that develops in the direction the tumor and brings nutriments.

Introduction: which cells move?



Vascularized tumor (from M. Chaplain)

Chemotaxis: mathematical models

The modelling goes back to Patlak (1953), E. Keller and L. Segel (70's)

$$\begin{aligned} n(t,x) &= \text{ density of cells at time t and position x,} \\ c(t,x) &= \text{concentration of chemoattractant,} \end{aligned}$$

In a collective motion, the chemoattractant is emited by the cells that react according to biased random walk.

$$\begin{cases} \frac{\partial}{\partial t} n(t,x) - \Delta n(t,x) + \mathrm{div}(n\chi\nabla c) = 0, \quad x \in R^d, \\ -\Delta c(t,x) = n(t,x), \end{cases}$$

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

This model, although very simple, exhibits a deep mathematical structure and especially "chemotactic collapse".

Chemotaxis: mathematical models

$$
\begin{cases}
\frac{\partial}{\partial t} n(t,x) - \Delta n(t,x) + \mathrm{div}(n\chi\nabla c) = 0, \quad x \in R^d, \\
\\
-\Delta c(t,x) = n(t,x), \\
\\
n(t=0) = n^0(x) \geq 0, \quad n^0 \in L^1(R^d).
\end{cases}
$$

This is the reason why it has attracted a number of authors

-Childress, Parcus (84); Jäger, Luckhaus (92),
-Rascle, Zitti (95); Nagai (95); Biler, Nadzieja(93),
-Herrero, Medina, Velazquez (96-03);
-Brenner, Constantin, Kadanoff, Schenkel, Venkatarami (98);
-Horstmann (00); Corrias, Perthame, Zaag (04);

Chemotaxis: mathematical theory

Theorem (dimensions $d \geq 2$)

(i) for $\|n^0\|_{L^{d/2}(R^d)}$ small, then there are weak solutions,

(ii) these small solutions propagate L^p regularity,

(iii) for $(\int |x|^2 n^0)^{(d-2)} < C\|n^0\|^d_{L^{d/2}(R^d)}$ with C small, there is blow-up time T^*,

(iv) (d>2) various (stable or unstable) radial blow-up profiles,

(iv) (d=2) with radial symmetry $n(t) \to \frac{8\pi}{\chi}\delta(x=0) + R$.

Proof (d=2)(1st step)

$$\frac{d}{dt}\int n(t,x)\log n(t,x) \quad = -4\int |\nabla\sqrt{n}|^2 + \underbrace{\int \nabla(\ln n)\, n\,\chi\,\nabla c}_{\chi\int \nabla n\cdot\nabla c = -\chi\int n\Delta c}$$

$$= \underbrace{-4\int |\nabla\sqrt{n}|^2}_{\text{entropy dissipation}} + \underbrace{\chi\int n^2}_{\text{hyperbolic effect}}$$

Using Gagliardo-Nirenberg-Sobolev ineq. on the quantity $u(x)=\sqrt{n}$, we obtain

$$\int u^4 \leq C_{GNS}\int |\nabla u|^2 \int u^2,$$

Since mass is conserved, we arrive at

$$\frac{d}{dt}\int n(t,x)\, log\, n(t,x) \quad \leq -4\int |\nabla\sqrt{n}|^2 + \chi\, C_{GNS}\ \int n(t,x)\ \int |\nabla\sqrt{n}|^2$$

$$\leq 0$$

for

$$\chi\, C_{GNS}\ \int n^0 \leq 4.$$

And this gives equiintegrability of $n(t,x)$ for small mass.

Proof (d=2)(2nd step)

$$\frac{d}{dt}\int\big(n(t,x)-k\big)_+^p \quad = -C(p)\int|\nabla(n-k)_+^{p/2}|^2+\chi\,C(p)\int(n-k)_+^{p+1}$$

$$\leq -C(p)\int|\nabla(n-k)_+^{p/2}|^2$$
$$+\chi\,C_{GNS}(p)\int(n-k)_+\int|\nabla(n-k)_+^{p/2}|^2$$

But since we have, thanks to equiintegrability proved in the 1st step

$$\int(n-k)_+ \underset{k\to\infty}{\longrightarrow} 0,$$

and we arrive, for k large enough at

$$\frac{d}{dt}\int\big(n(t,x)-k\big)_+^p \leq 0.$$

And this proves L^p regularity of $n(t,x)$ for small mass.

Chemotaxis: mathematical models

Keller and Segel model:

$$\begin{cases} \frac{\partial}{\partial t} n(t,x) - \Delta n(t,x) + \mathrm{div}(n\chi\nabla c) = 0, \quad x \in R^d, \\ \\ -\Delta c(t,x) = n(t,x), \end{cases}$$

Theorem (dimension d=2)
(i) for $\|n^0\|_{L^1(R^2)} \leq \frac{4\pi \times 1.822}{\chi}$, then there are smooth solutions,
(iii) for $\|n^0\|_{L^1(R^2)} > \frac{8\pi}{\chi}$ and $\int |x|^2 n^0 < \infty$ there is blow-up time,

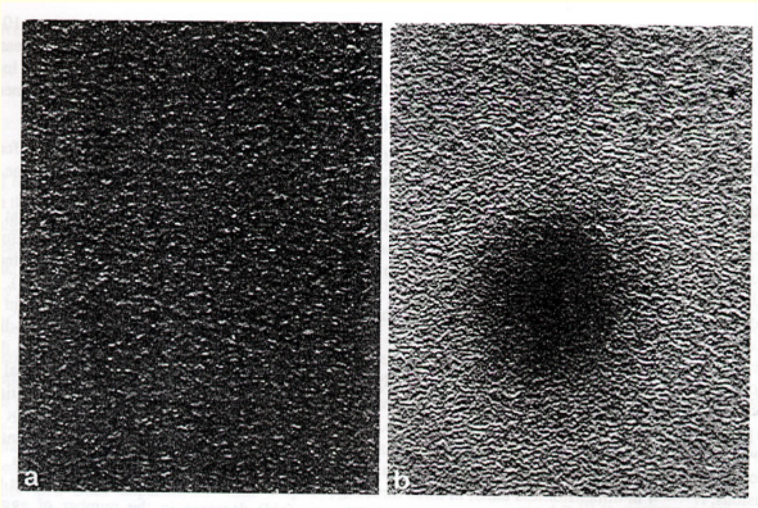
Is this what is observed in experiments?

Chemotaxis: and experiments?

-) Aggregation is very well reported for amoeba Dictyostelium Discoïdeum and the phenomenon is fast.

-) For bacteria it can also be observed

Chemotaxis: and experiments?



Mechanism for chemotactic pattern formation by bacteria (from M. P. Brenner, L. S. Levitov and E. O. Budrene)

But we also have... From J. Newell in Höfer, Sherratt and Maini