Biological and Soft Matter Physics

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Microscopic Physics

Fluctuations and Fluctuation-Induced Forces

Elasticity

Chemical Kinetics and Pattern Formation

REG

Electrokinetic Phenomena

A Survey of Experimental Techniques

- **AFM**
- **Optical Trapping**
- **Magnetic Tweezers**

UFK

Central Course Web Page

http://www.damtp.cam.ac.uk/user/gold/teaching_biophysicsIII.html

Course Hand-out and Lecture Notes

Lecture notes:
You can obtain a pdf-file of the preliminary lecture notes on the course webpage.
These will be updated periodically and we aim to provide printouts in the following week.

Lectures will be given primarily with powerpoint slides. These will be available online as well as in printed form.

This course contains a significant amount of material that is taken from the primary literature, and you will be expected to read some of these original journal articles.

To facilitate this process you will find essentially all required articles on the course webpage.

Question Sheets & Examples Classes

There will be 4 examples sheets.

The questions will have a range of difficulties. It would be advisable to consult e.g. Riley, Hobson and Bence , “Mathematical Methods for Physics and Engineering” or a similar book if you are unfamiliar with mathematical issues discussed in the lecture.
This book is used in the first year of the natural sciences tripos and is available as an ebook. Sections on special functions will be of particular relevance.

For some questions you will have to read research articles from the primary literature; these are already available on the teaching webpage.

Solutions for the question sheets will be made available about one week after the sheet is posted.

The question sheets will be discussed during Examples classes, as announced on the course webpage.

Other Material

Throughout the course we will quote from experimental results. Many will be illustrated by videos for specific experiments.

These will be made available on the course webpage.

There will be also links to other external webpages of other labs that discuss experimental data or explain their measurements in more detail.

Please use these resources to help your understanding of the material of the course.

Exam(s)

The course is taught between the physics and math departments.

Due to the structure of the examinations there will be TWO exams.

The Physics exam will be held in January 2015, like the other major option exams, with a similar structure, and will be designed by Ulrich Keyser.

The Math exam will be held in the usual time at the end of the academic year in May/June. It will be designed by Ray Goldstein.

There will be TWO DIFFERENT exams for the physics and math students, respectively. They will take into account the respective mathematical inclinations.

HOWEVER, the material from the whole course is examinable for all students.
(Unless single slides or topics are marked as non-examinable.)

Reading Material

Introductory reading

Murray “Mathematical Biology I. & II.” (Math)

Nelson, “Biological Physics” (Physics)

Philips et al. “Physical Biology of the Cell” (Biology & Physics)

Alberts et al., “Molecular Biology of the Cell” (Biology)

Advanced and Complementary Reading

Parsegian, “van der Waals Forces” (Fluctuation induced forces)

Verwey & Overbeek, “Theory of the Stability of Lyophobic Colloids” (see above)

Israelachvilli, “Intermolecular and Surface Forces”
Rubinstein “Polymer Physics”
Strobl, “Polymer Physics”

Heimburg, “Thermal Membrane Biophysics”
Andelman & Poon “Soft Condensed Matter Physics in Molecular and Cell Biology” (Poisson Boltzmann Equation)

Popular Science Books

- E. Schroedinger: “What is Life?”
- M. Haw: “The Middle World”

Overview (first part)

Start (today) with review of length scales and basic definitions (Reynolds numbers, Péclet, diffusion, Stokes-Einstein etc.)

Molecular Interactions
(van der Waals, screened electrostatic interactions)

Fluctuations and associated forces
(review of statistical physics, polymers chains, interfaces, Brownian motion, diffusion)

Worm-like chain model for polymers

Dynamics
(Stokes problem, elasto-hydrodynamics, instabilities)

Chemical kinetics and pattern formation

Overview (second part)

Test of polymer models with experimental techniques

Using Brownian motion to calibrate molecular forces

Optical tweezers, magnetic tweezers, atomic force microscopy

Protein (un-)folding
(Loading rate dependence)

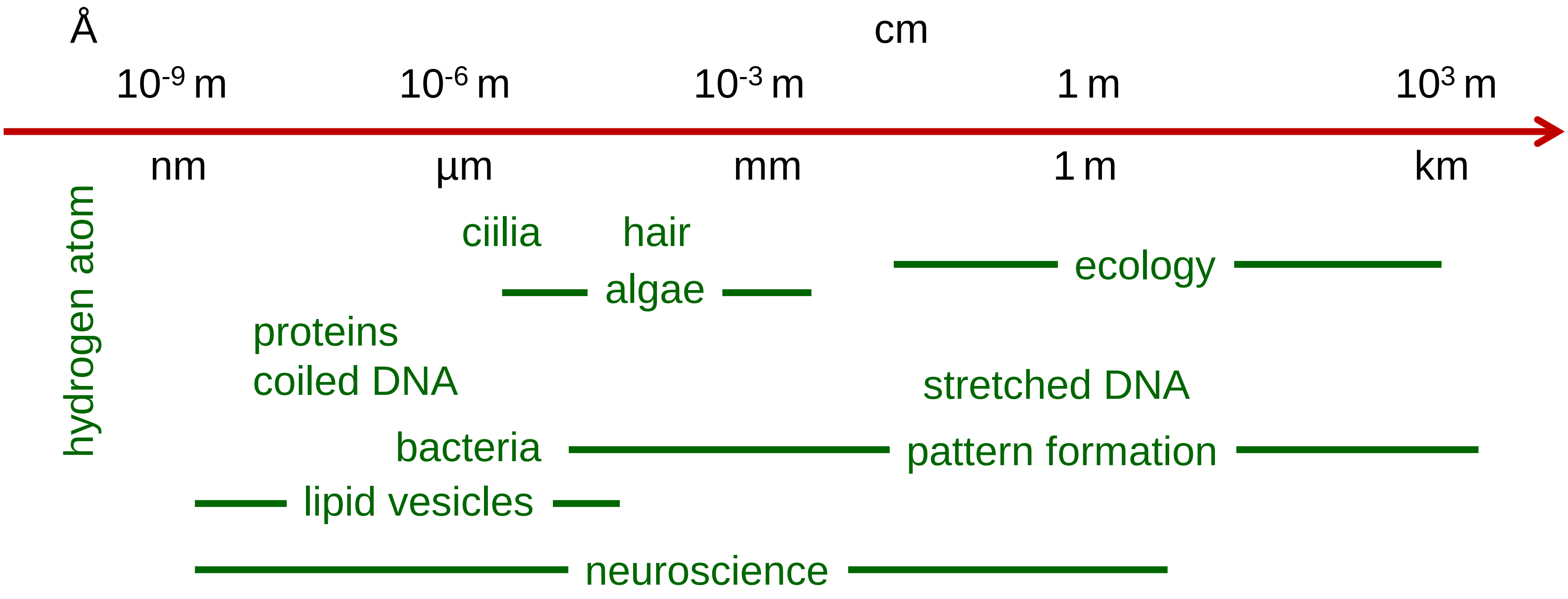
Electrokinetic phenomena
(Electrophoresis, electro-osmosis, damped oscillators)

Polymers in gels and in electric fields
(Gel electrophoresis, Entropic forces, hydrodynamic interactions)

Molecular machines and membrane pores
(Lipid membranes, torque of molecular motors)

Announcement

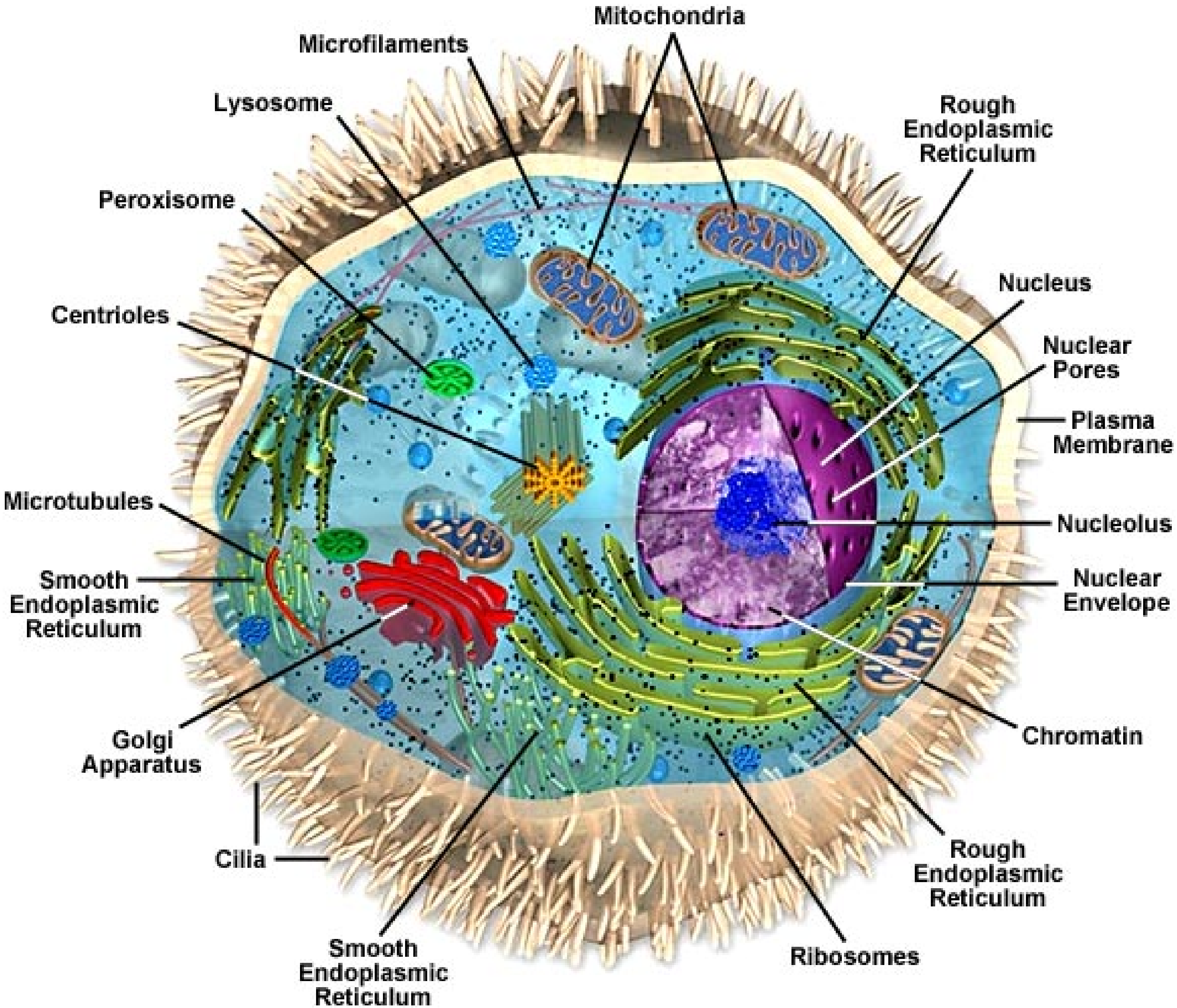
Numbers Matter!



Thermal fluctuations **Other forms of noise**

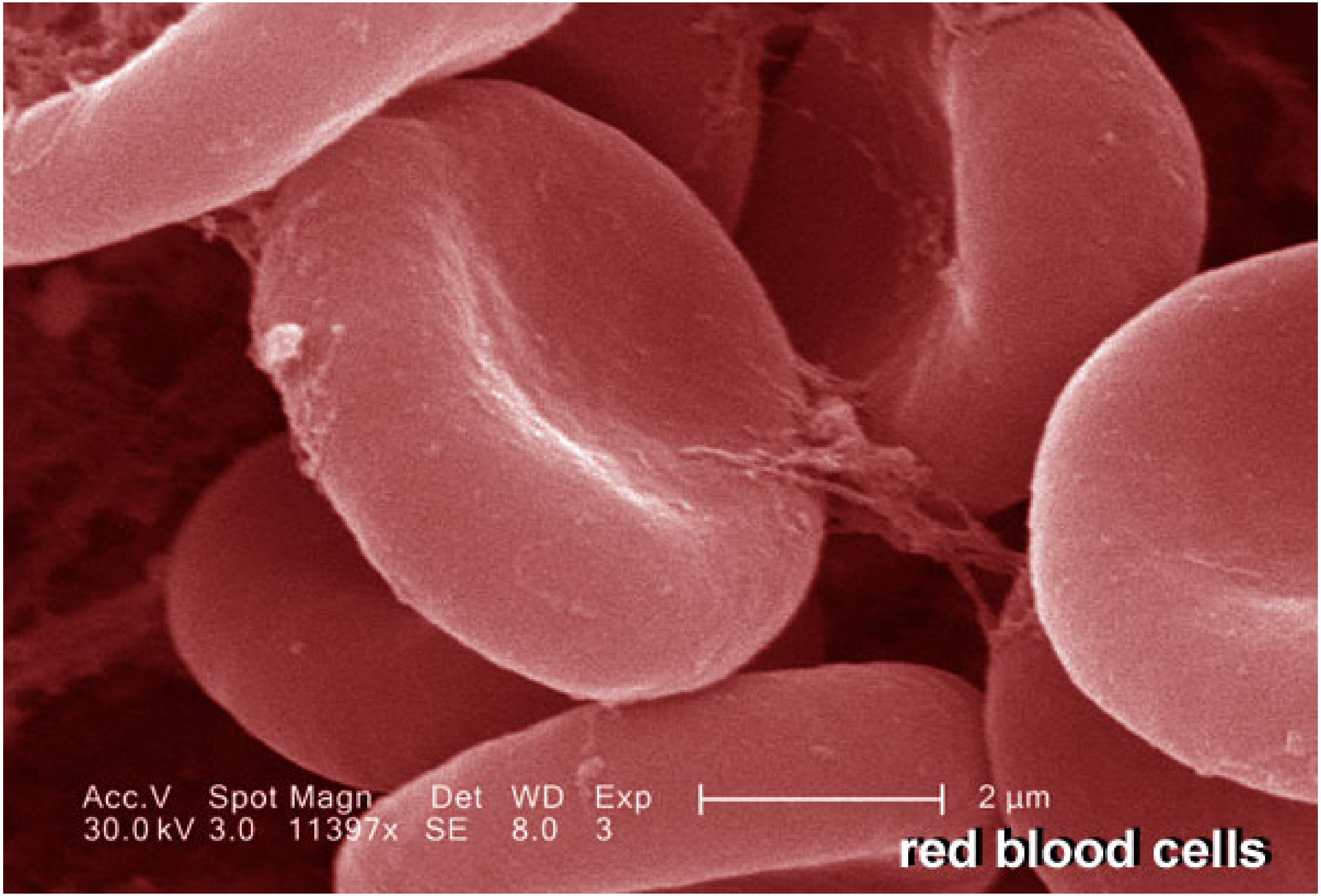
$$\mu\mathrm{m} = \sqrt{\mathrm{\AA} \cdot \mathrm{cm}}$$

Cells are complicated objects



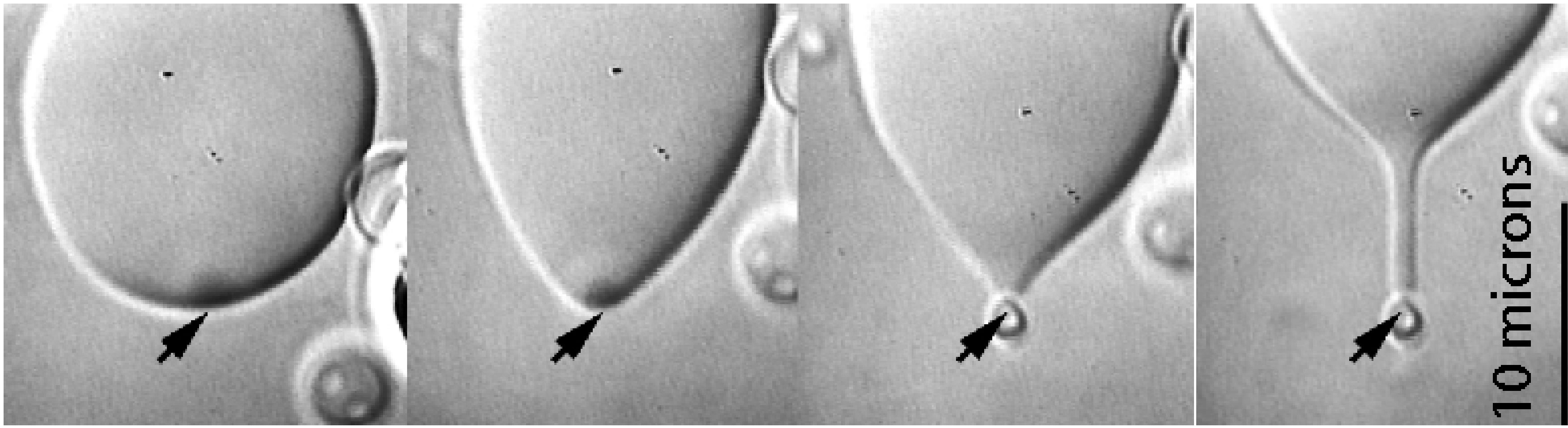
Hierarchical Chromosome Organization

Erythrocytes (Red Blood Cells)



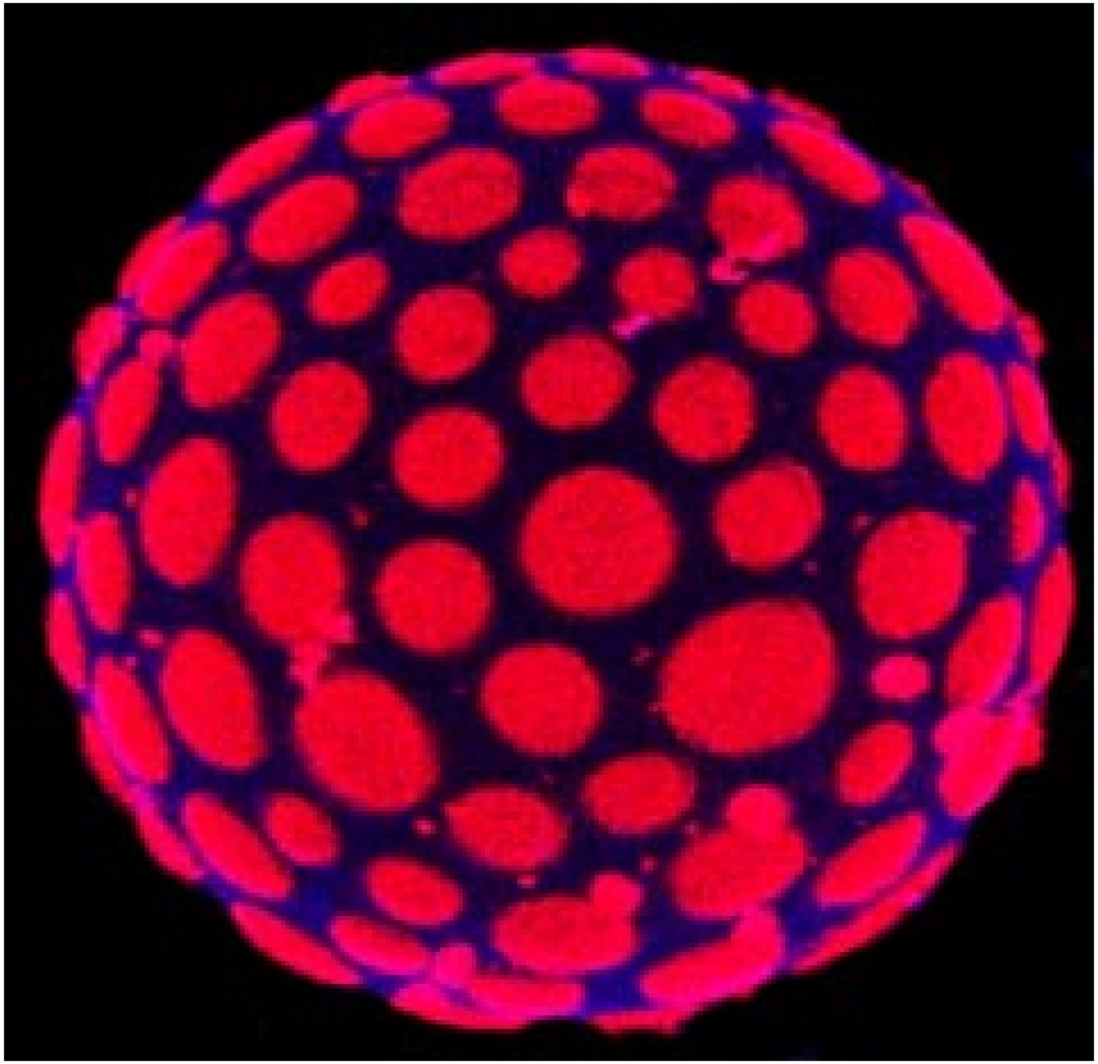
Fluctuating Lipid Vesicle

Artificial Lipid Vesicles – Membrane Tethers



D. Fygenson (UCSB)

Domains on a GUV (Giant Unilamellar Vesicle)



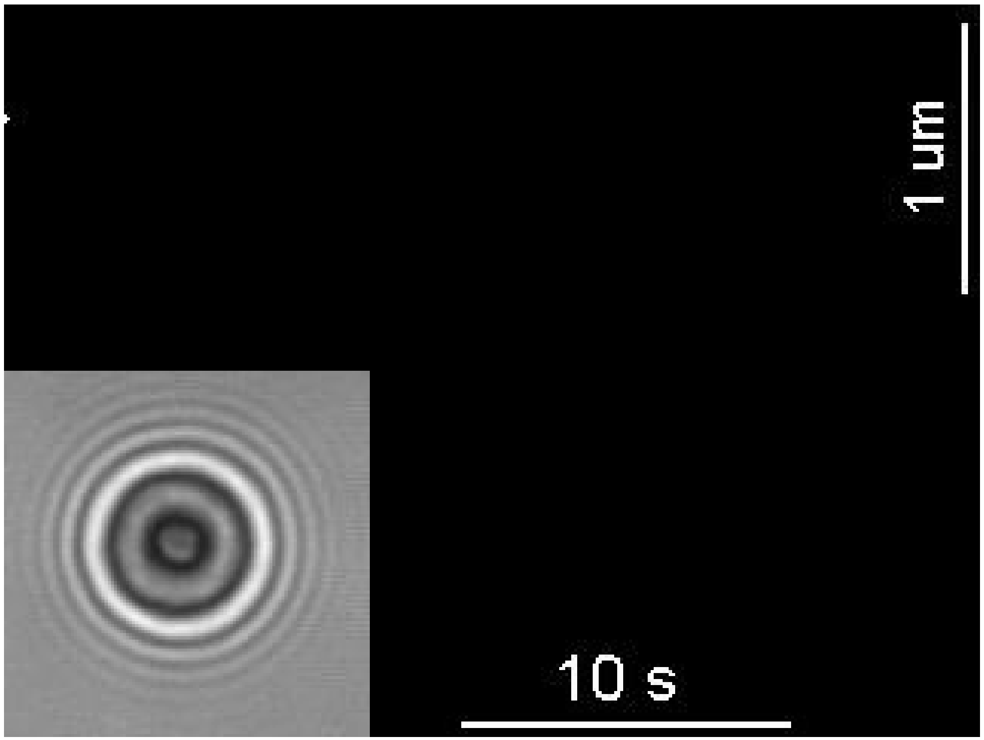
W. Webb (Cornell)

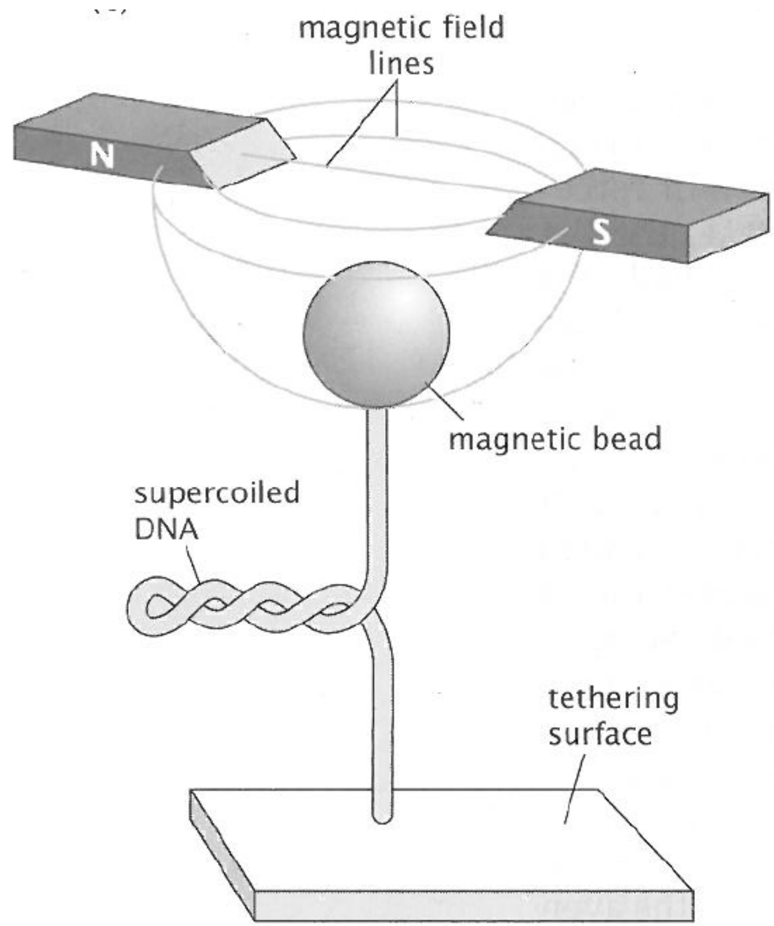
Optical Tweezers: Manipulating Single Molecules

Optical Tweezers: Controlling Particles

Magnetic Tweezers: Coiling DNA

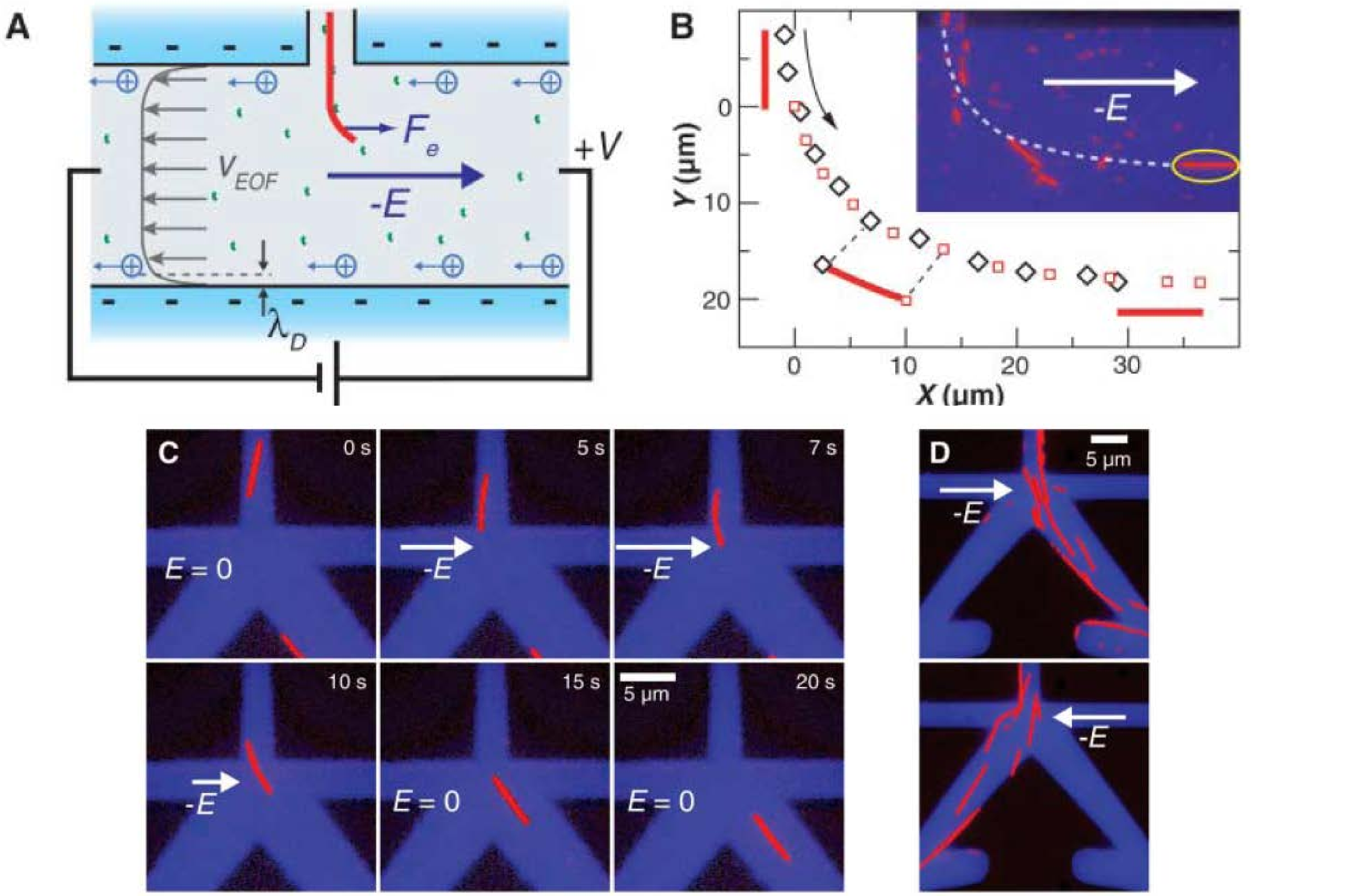
(Seidel 2005)





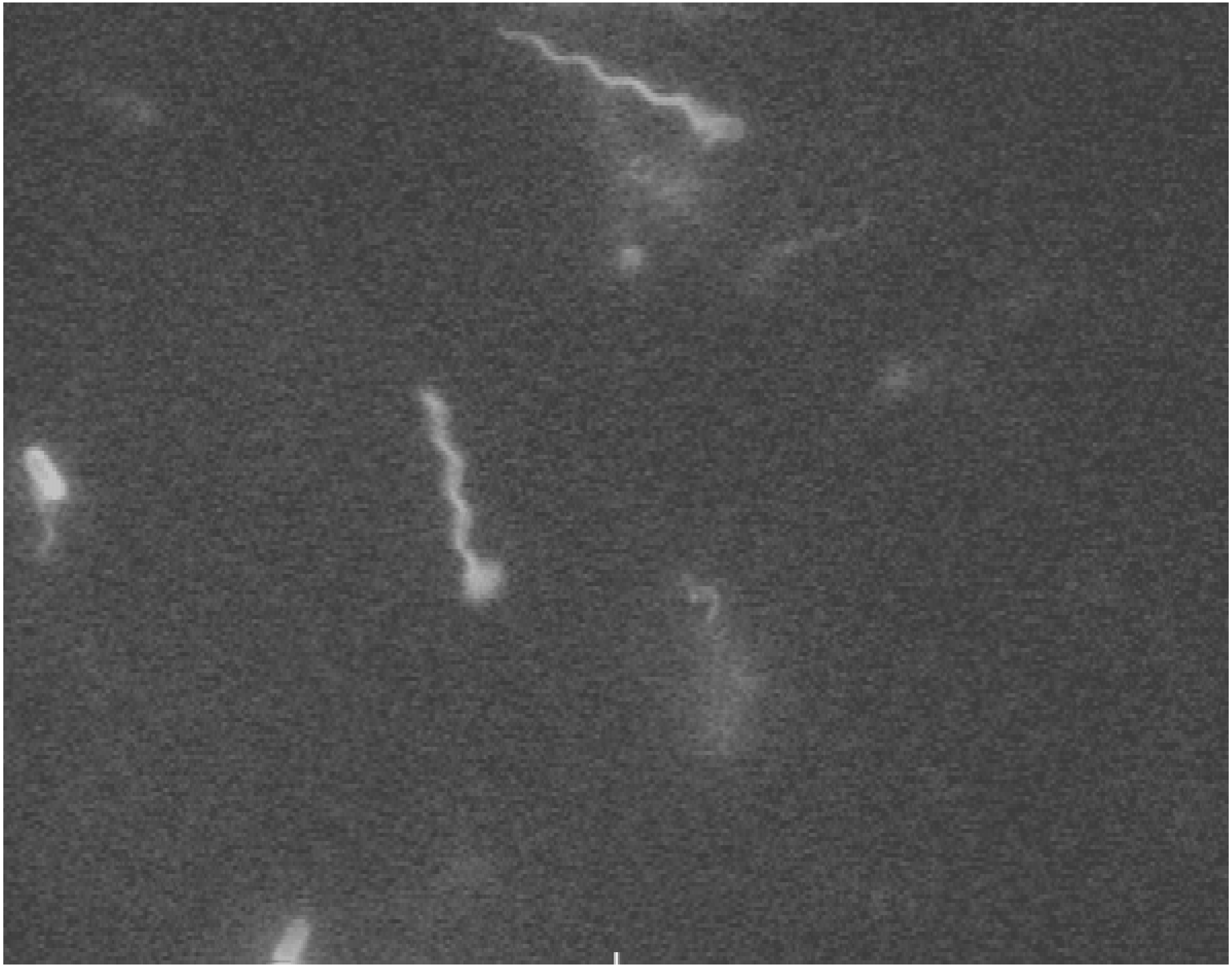
Electrokinetic Effects: Steering Microtubules

Van den Heuvel et al. Science (2006)

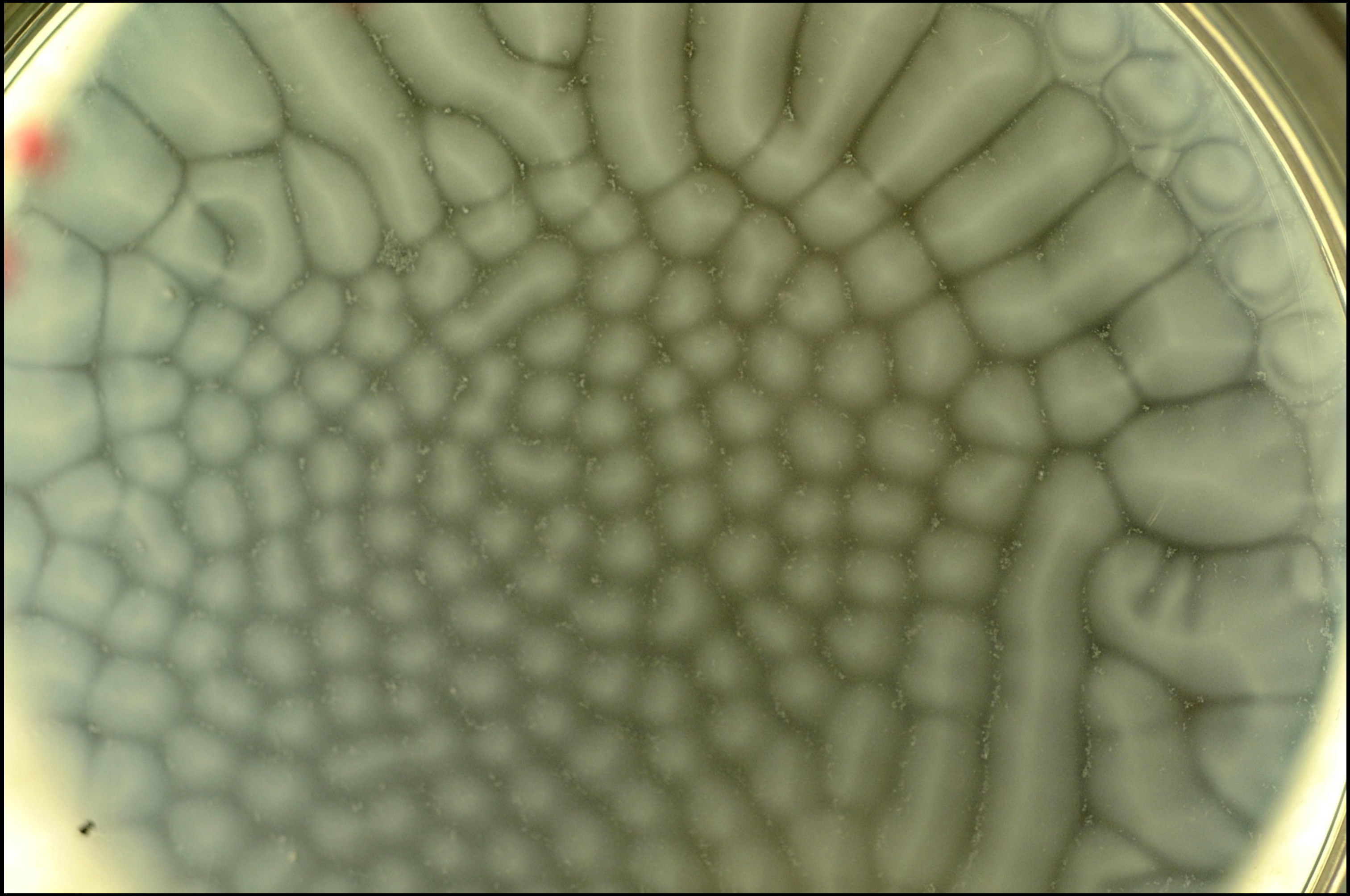


Beating Eukaryotic Flagella

Molecular Motors: Swimming Bacteria



Bioconvective Rolls



Bioconvection (J.O. Kessler)

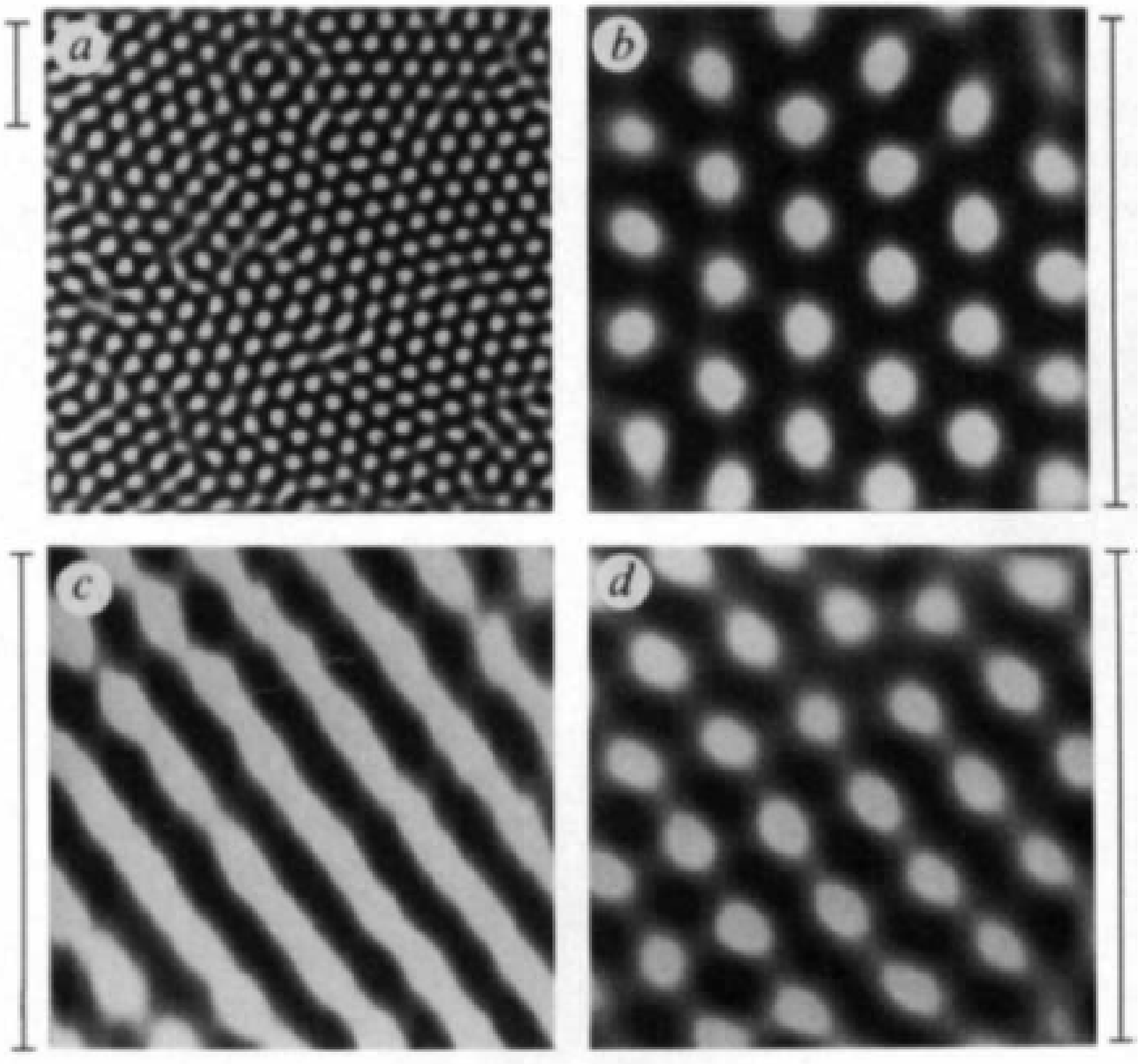
Transition from a uniform state to hexagonal and striped Turing patterns

Q. Ouyang & Harry L. Swinney

Center for Nonlinear Dynamics and Department of Physics,
The University of Texas, Austin, Texas 78712, USA

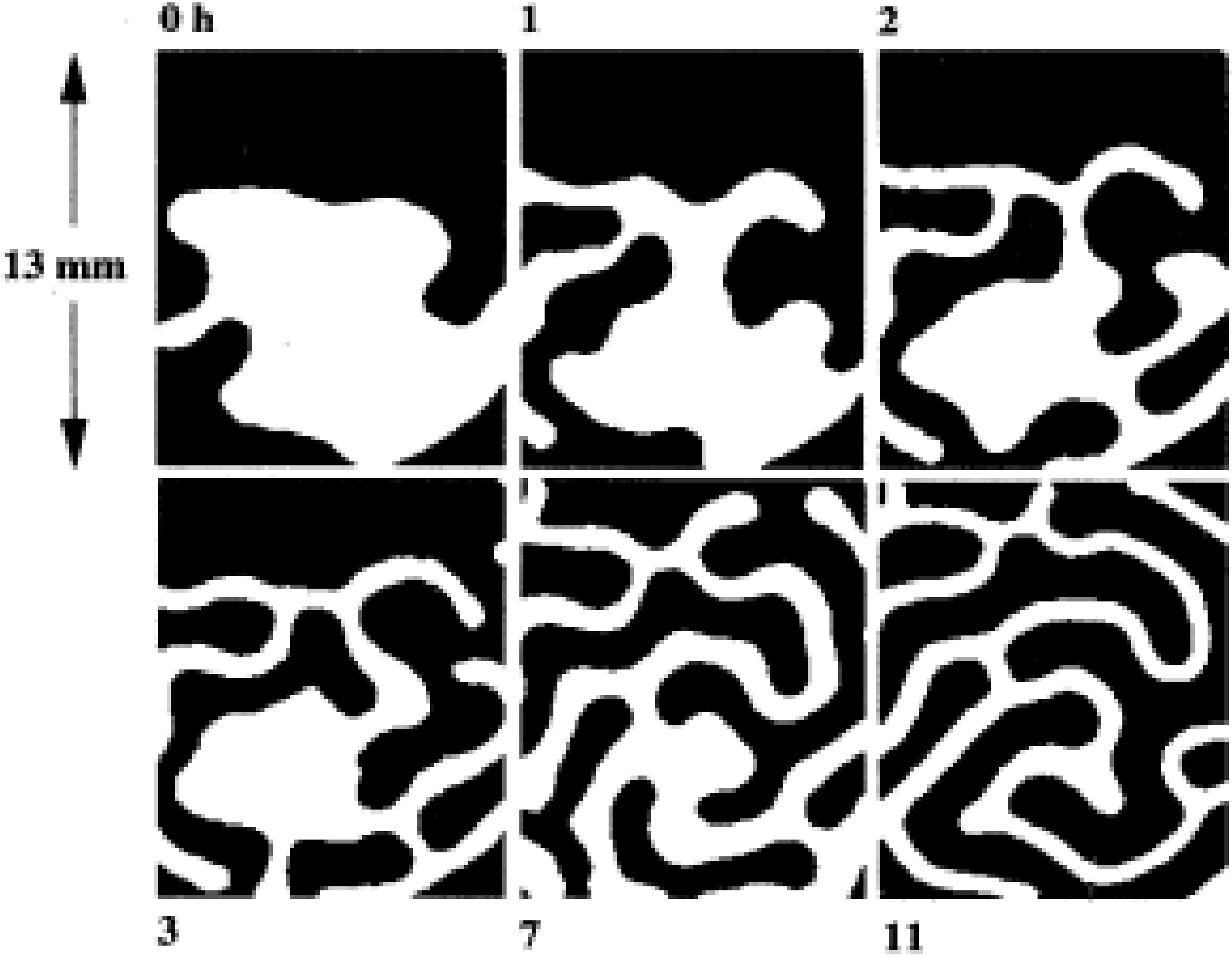
CHEMICAL travelling waves have been studied experimentally for more than two decades[1–5], but the stationary patterns predicted by Turing[6] in 1952 were observed only recently[7–9], as patterns localized along a band in a gel reactor containing a concentration gradient in reagents. The observations are consistent with a mathematical model for their geometry of reactor[10] (see also ref. 11). Here we report the observation of extended (quasi-two-dimensional) Turing patterns and of a Turing bifurcation—a transition, as a control parameter is varied, from a spatially uniform state to a patterned state. These patterns form spontaneously in a thin disc-shaped gel in contact with a reservoir of reagents of the chlorite–iodide–malonic acid reaction[12]. Figure 1 shows examples of the hexagonal, striped and mixed patterns that can occur. Turing patterns have similarities to hydrodynamic patterns (see, for example, ref. 13), but are of particular interest because they possess an intrinsic wavelength and have a possible relationship to biological patterns[14–17].

Classical Turing Patterns



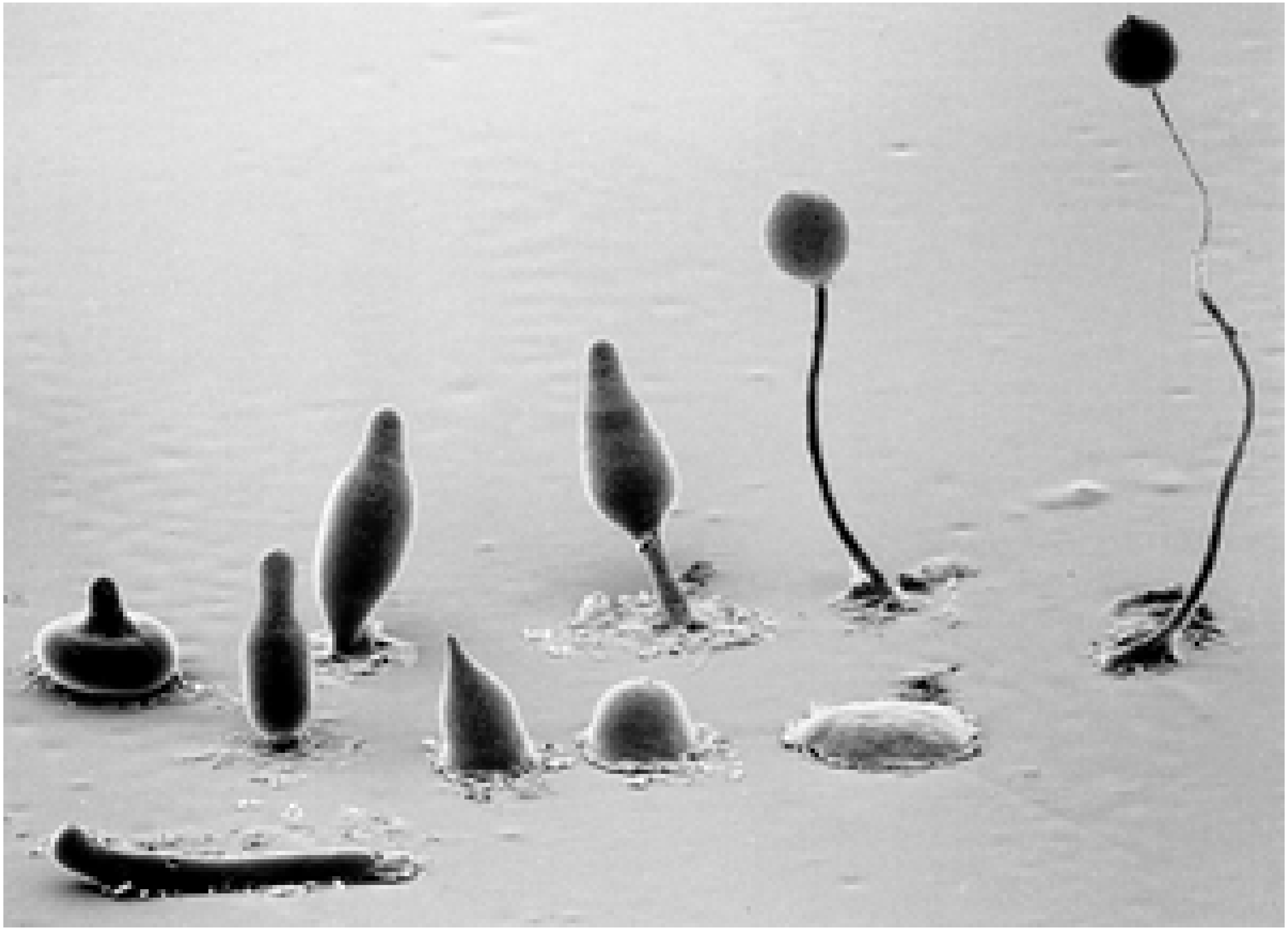
Ouyang and Swinney, 1991 (CIMA)

Unconventional Patterns

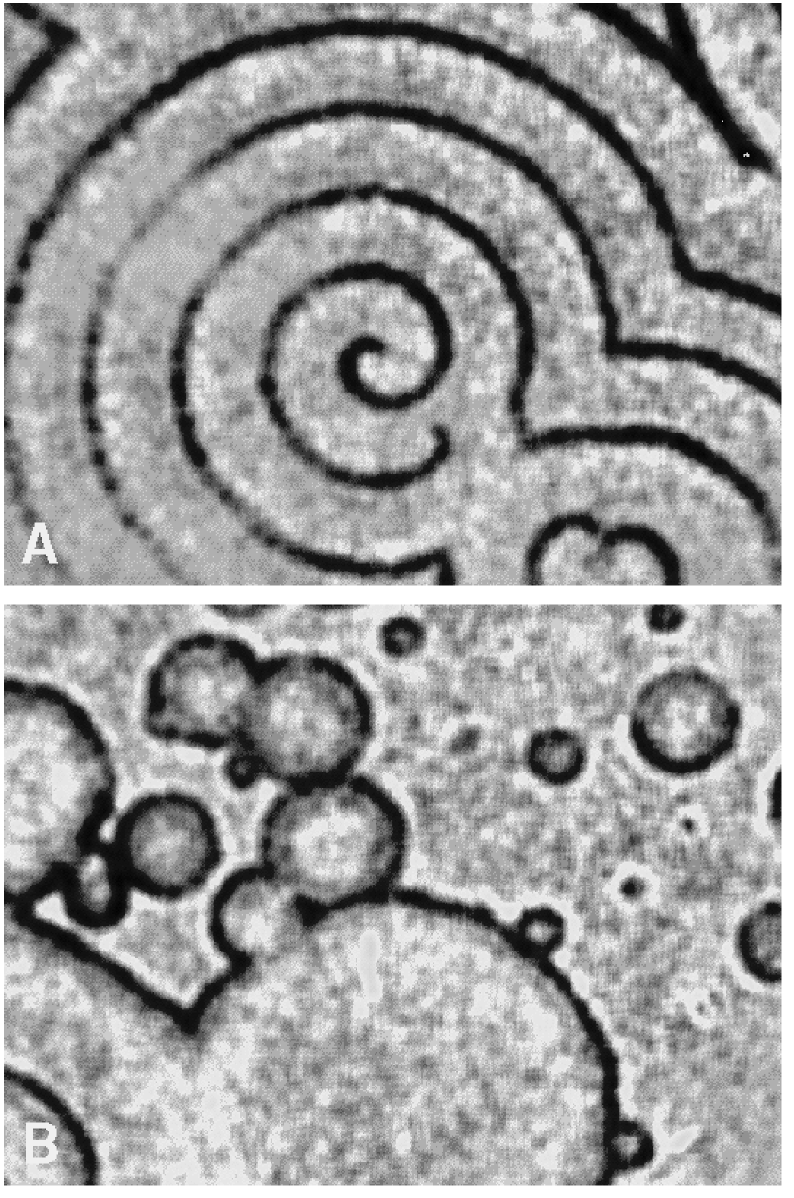


Lee, McCormick, Ouyang, and Swinney, 1993 (CIMA)

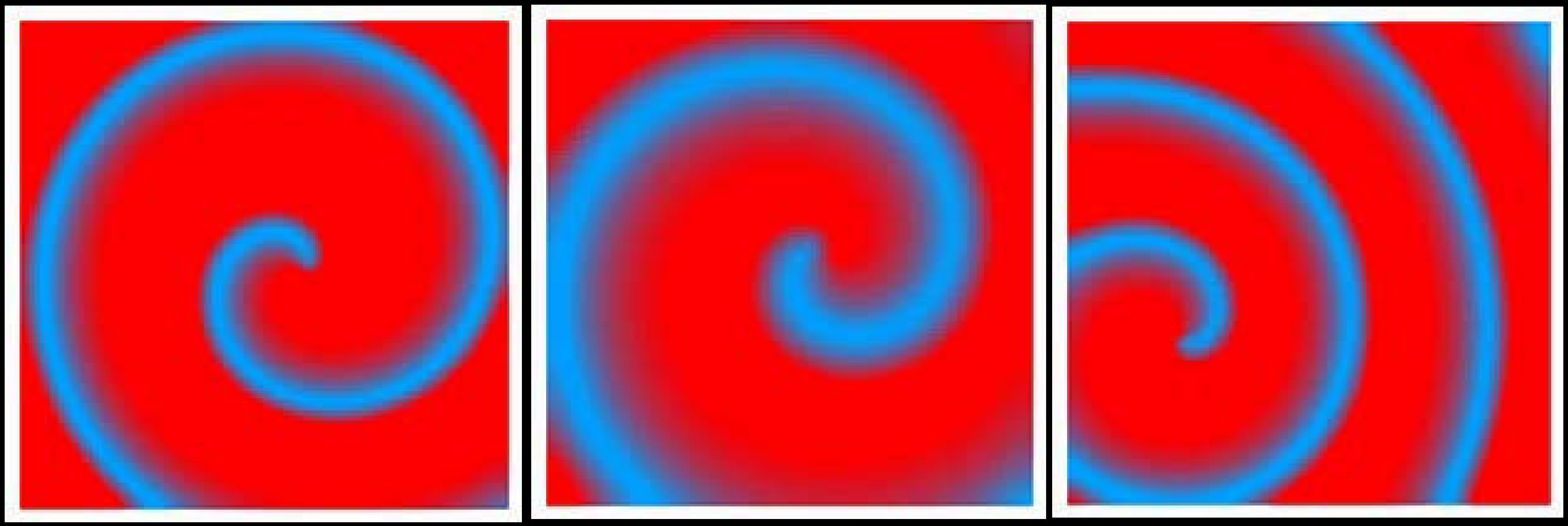
Dictyostelium discoideum



Chemical Waves



Spiral Waves in Theory



Back-of-the-envelope thinking

- Size of an atom (in 'cgs' units):

$$\mathcal{E} = \frac{\hbar^2}{2m}\frac{1}{\ell^2} - \frac{e^2}{\ell}$$

$$\frac{\partial \mathcal{E}}{\partial \ell} \rightarrow \frac{\hbar^2}{m\ell^3} = \frac{e^2}{\ell^2}$$

$$\Rightarrow \quad \boxed{\ell = \frac{\hbar^2}{me^2} \simeq 0.05 \text{ nm}}$$

$$\hbar = 10^{-27} erg\ s$$

$$m \sim 10^{-27} g$$

$$e \sim 5 \cdot 10^{-10} erg^{1/2} cm^{1/2}$$

- Calculate Energy using minimizer:

$$\boxed{\mathcal{E}(\ell^*) = -\frac{me^4}{2\hbar^2} \simeq -13.6 \text{ eV}}$$

No Laguerre polynomials needed…

The Viscous Regime

Typical forces and voltages

Let us estimate the typical force encountered by a swimming bacterium. Suppose it is in a fluid of viscosity η (0.01 for water), has a radius *a* on the order of a micron and swims at a speed *v* on the order of 10 μm/s. Using the Stokes drag law for a sphere the force on it is

$$F = 6\pi\eta a v \simeq 2 \times 10^{-8}\mathrm{dyne} \simeq 2 \times 10^{-13}\mathrm{N} = 0.2\ \mathrm{pN}$$

Forces on the cellular scale are on the order of pN. A very useful way to think about this is to convert thermal energy into pN nm

$$k_B T = 4 \times 10^{-14}\mathrm{erg} \qquad [k_B = 1.38 \times 10^{-16}\mathrm{erg/K}]$$

$$k_B T = 4 \times 10^{-21}\mathrm{J} = 4 \times 10^{-12}\mathrm{N} \times 10^{-9}\mathrm{m} = 4\ \mathrm{pN} \cdot \mathrm{nm}$$

With a very similar approach we can also estimate the typical voltages as

$$\frac{k_B T}{e} = \frac{4 \times 10^{-14}\mathrm{erg}}{5 \times 10^{-10}\mathrm{esu}} \simeq 25\mathrm{mV}$$

The Reynolds Number

Consider a fluid of density ρ in which there is a characteristic speed U and a length scale L. Then it is natural to scale velocities by U and time by L/U.

Acceleration term of Navier-Stokes equation:

$$\rho \frac{\partial u}{\partial t} \sim \frac{\rho U}{L/U} \sim \frac{\rho U^2}{L}$$

Note: this is nonlinear in U

Viscous dissipation term:

$$\eta \frac{\partial^2 u}{\partial y^2} \sim \frac{\eta U}{L^2}$$

$$\boxed{\frac{\text{inertial}}{\text{viscous}} = \frac{UL}{\nu} \equiv Re}$$

$$\nu = \eta/\rho$$

Kinematic viscosity

For a bacterium in water, with $U \sim 10\ \mu\text{m/s}$, $L \sim 1\ \mu\text{m}$, and $\nu \sim 0.01\ \text{cm}^2/\text{s}$, $Re \sim 10^{-5}$!!

No Coasting at Low Reynolds Number

Ignoring any detailed fluid mechanics, we might imagine the equation of motion of a bacterium that has just switched off its flagellar motion to be of the form:

$$\frac{4}{3}\pi R^3 \rho \frac{d^2x}{dt^2} = -6\pi\eta R \frac{dx}{dt}$$

Hence we deduce there is a characteristic time and distance

$$\boxed{\tau \sim \frac{2}{9}\frac{R^2}{\eta/\rho}}$$

$$\boxed{\ell = v_0\tau \sim \frac{2}{9}\frac{R^2 v_0}{\nu}}$$

For a bacterium in water, with $v_0 \sim 10^{-3}$ cm/s, $R \sim 10^{-4}$ cm, and $\nu \sim 0.01$ cm^2/s, $\tau \sim 10^{-7}$ s and $\ell \sim 10^{-10}$ cm!!

Advection & Diffusion

If a fluid has a typical velocity **U**, varying on a length scale **L**, with a molecular species of diffusion constant **D**. Then there are two times:

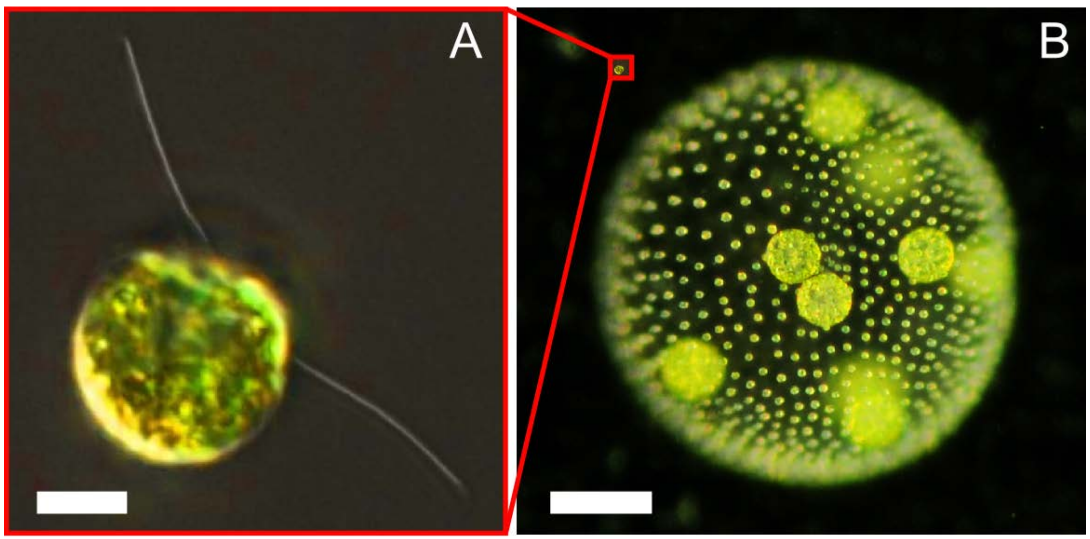
$$\boxed{\begin{aligned} t_{advection} &= \frac{L}{U} \\ t_{diffusion} &= \frac{L^2}{D} \end{aligned}}$$

We define the Péclet number as the ratio:

$$\boxed{Pe = \frac{t_{diffusion}}{t_{advection}} = \frac{UL}{D}}$$

This is like the Reynolds number comparing inertia to viscous dissipation:

$$Re = \frac{UL}{\nu}$$



If U=10 µm/s, L=10 µm,
Re ~ 10^{-4}, Pe ~ 10^{-1}
At the scale of an individual cell, diffusion dominates advection.

The opposite holds for ***multicellularity****…*

Diffusion and the Stokes-Einstein Relation

If molecules have a diffusion constant D, concentration c, and are advected with speed u, then the flux is:

$$\boxed{J = -D\frac{dc}{dx} + uc}$$

In the low-Re regime we expect a force balance of the form $\zeta u = \text{force} = -d\phi/dx$, where ϕ is a suitable potential energy.

At equilibrium, we must have $J = 0$, so $0 = -D\frac{dc}{dx} - \frac{1}{\zeta}c\frac{d\phi}{dx}$, or

$$\boxed{c \sim \exp(-\phi/D\zeta)}$$

If equilibrium statistical mechanics holds then we must conclude that

$$\boxed{D\zeta = k_B T \quad \text{or} \quad D = \frac{k_B T}{\zeta}}$$

If we is the Stokes drag coefficient for a molecule of radius 2 $\mathring{A}$ we obtain

$$D \sim \frac{4 \times 10^{-14}}{20 \cdot 0.01 \cdot 2 \times 10^{-8}} \sim 10^{-5}\text{cm}^2/s$$

Diffusional Time Scales

From the diffusion equation

$$\frac{\partial c}{\partial t} = D\nabla^2 c$$

we see by dimensional analysis the scaling

$$Dt \sim \ell^2 \quad \text{or} \quad \boxed{t \sim \frac{\ell^2}{D}}$$

On the scale of a bacterium ($\ell \sim 10^{-4}$ cm), $t \sim 10^{-3}$s, but on the scale of a plant ($\ell \sim 10$ cm), $t \sim 10^{7}$ s, or about 3-4 months!)

Something must take over as a transport mechanism beyond Several hundred microns for life to function.

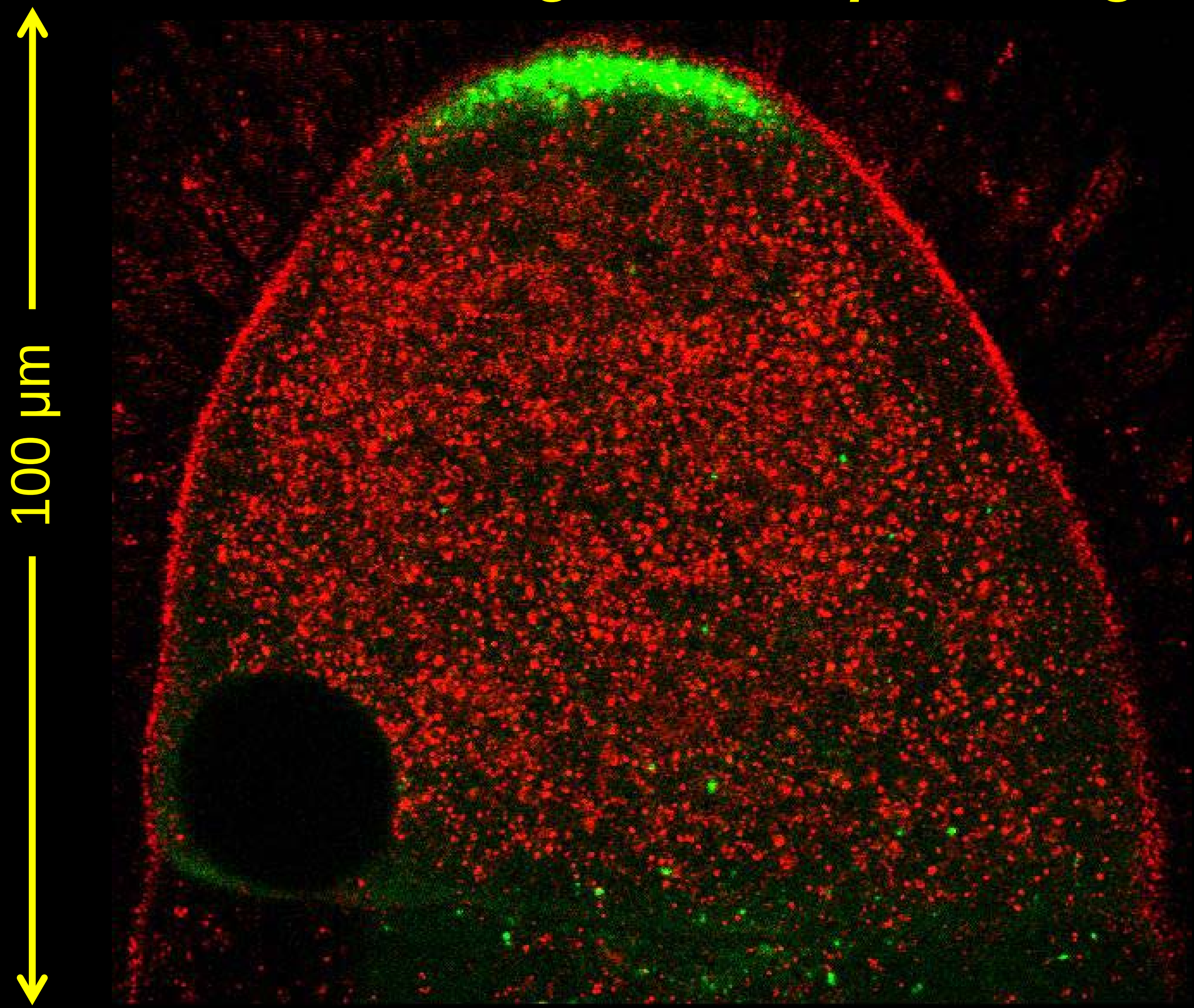
See J.B.S. Haldane, “On Being the Right Size”

The Aquatic Plant *Chara corallina*

Cytoplasmic Streaming (the Movie)

Goldstein, Tuval, van de Meent, *PNAS* 105, 3663 (2008)

Streaming in *Drosophila* oogenesis



Kinesin-based movement of cargo along microtubules

speed ~30 nm/s

Viscosity very high

Ganguly, Williams, Palacios , Goldstein, *PNAS* **109**, 15109 (2012)