Active Matter: The Cell Cytoskeleton, Molecular Motors and Active Gels

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Outline

- What is active matter?
- Active matter in the cell: Examples
  - Cell membranes
  - Cell motility
  - Cytoskeletal filament dynamics
  - Molecular motors
- Motor-microtubule pattern formation: Motivation
- Hydrodynamic theory for motor-microtubule pattern formation
- Motivation for a theory of active gels
- Outline of a theory of active gels

http://cognition.ups-tlse.fr/dynactom/

A vortex in a school of barracudas

Lane formation in groups of sheep

The Structure and Function of Fish Schools

Schooling serves to reduce the risk of being eaten. Each fish employs its eyes and lateral lines, which are sensitive to the displacement of water, to match the speed and the direction of all the other fish in the school

by Brian L. Partridge

Partridge, BL. Structure and function of fish schools. 1982. *Scientific American*, v.246, no.6, pp. 114+

Evasive maneuvers in fish escaping a predator

Collective behavior even when the threat is individual

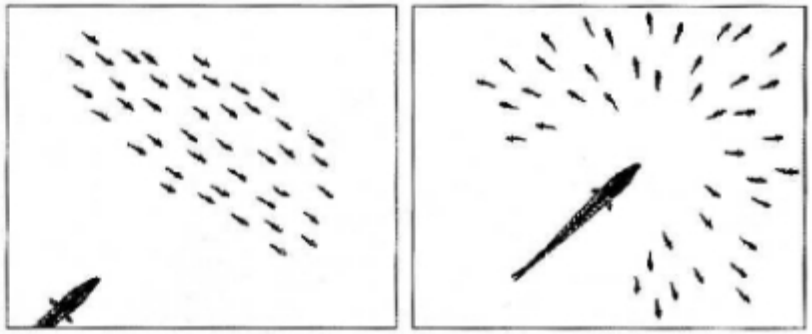


Figure 11.3 A school of fish displaying the evasive maneuver, termed *flash expansion*. (From Partridge 1982, used with permission)

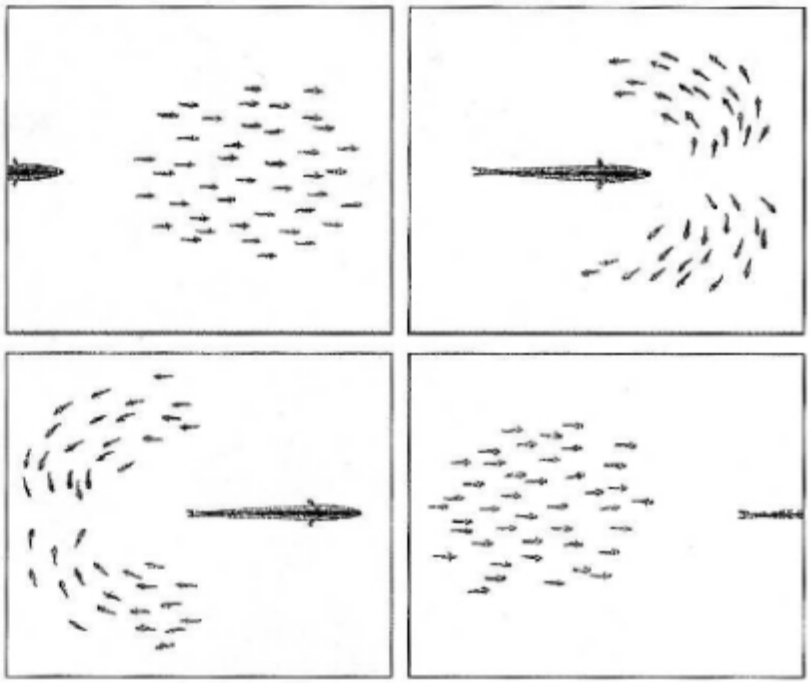


Figure 11.4 A school of fish displaying the evasive maneuver, termed the *fountain ef-*

Thinking about Active Matter

Theories to describe the seasonal migration of animal populations, the collective motion of ants, the swimming of shoals of fish and groups of bacteria and the flight of flocks of birds

Individual "agents" which evolve *via* a set of update rules while interacting with other agents

Agent-based models (Vicsek). Hydrodynamic equations (Toner, Tu . . .)

Active fluids: Subset of problems involving agents whose *mechanical* behaviour at a scale larger than the individual agent must be constrained by local conservation laws, such as the conservation of momentum.

Simha-Ramaswamy (2002), Hatwalne et al(2004). . .

Active matter is a term which describes a material (either in the continuum or naturally decomposable into discrete units), which is driven out of equilibrium through the transduction of energy derived from an internal energy source into work performed on the environment.

Such systems, interacting either directly or indirectly via the medium, are generically capable of emergent behaviour at large scales.

Different from other classes of driven systems: Energy input internal to the medium (*i.e.* located on each unit). Does not act at the boundaries or via external fields.

Active matter at the cellular and subcellular scale

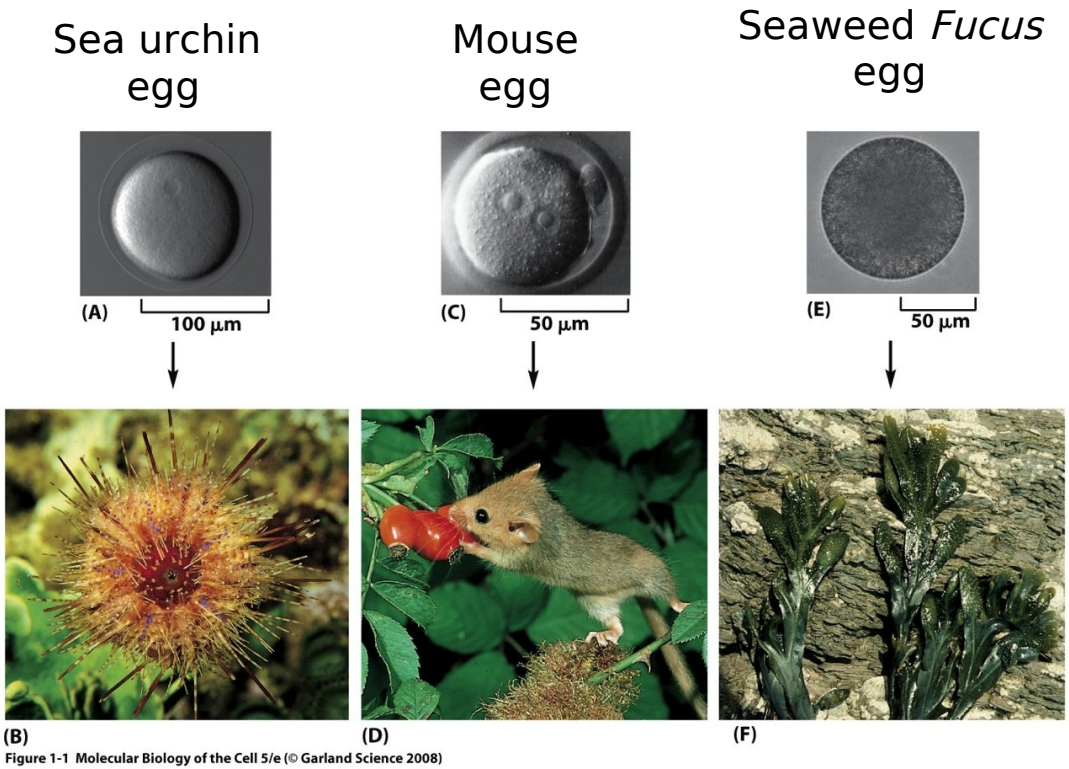


Figure 1-1 Molecular Biology of the Cell 5/e (© Garland Science 2008)

10-100 million different species on earth

Parent organism specifies features of progeny:

HEREDITY

Single CELL is the vehicle of hereditary information

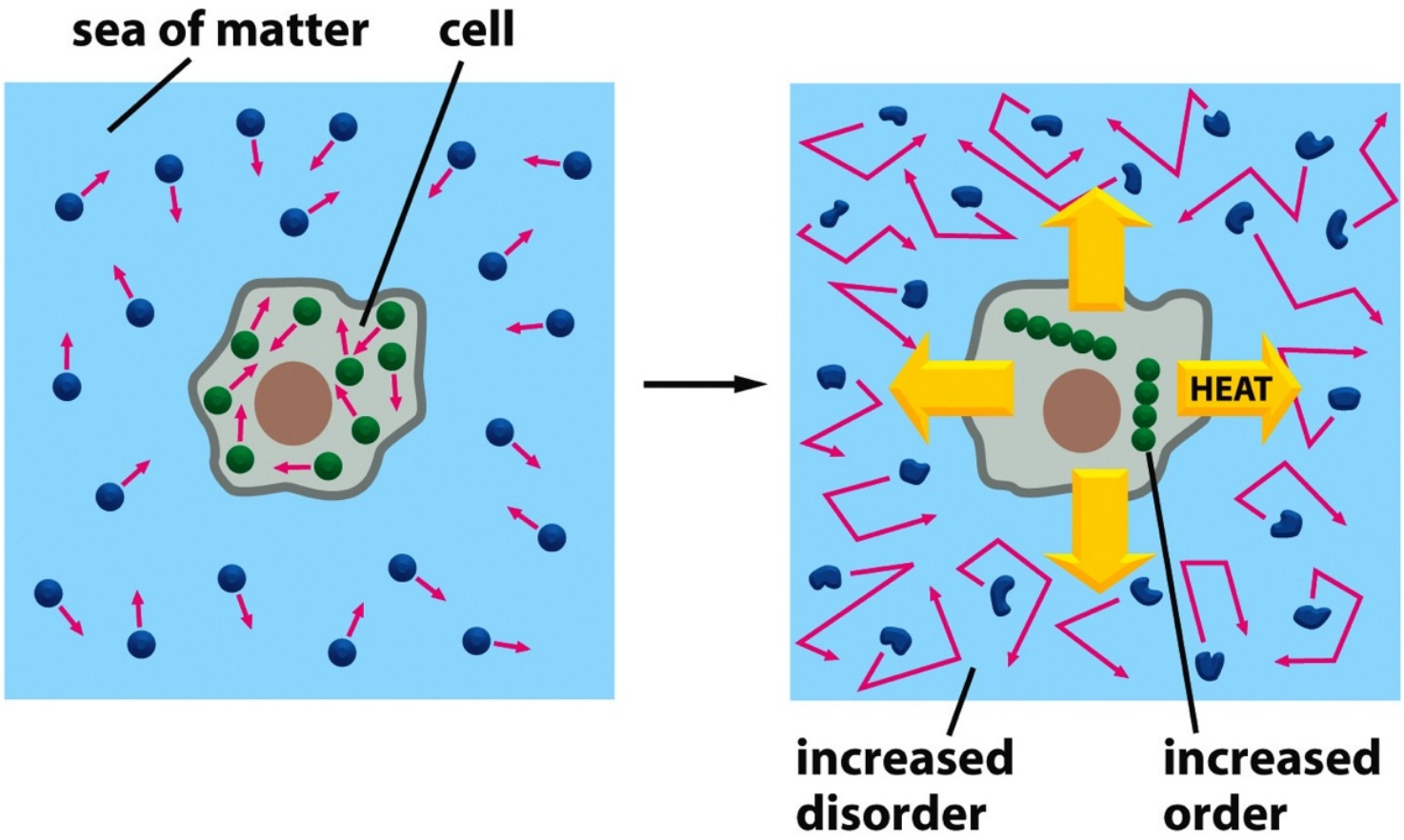


Figure 2-38 Molecular Biology of the Cell 5/e (© Garland Science 2008)

The Animal Cell

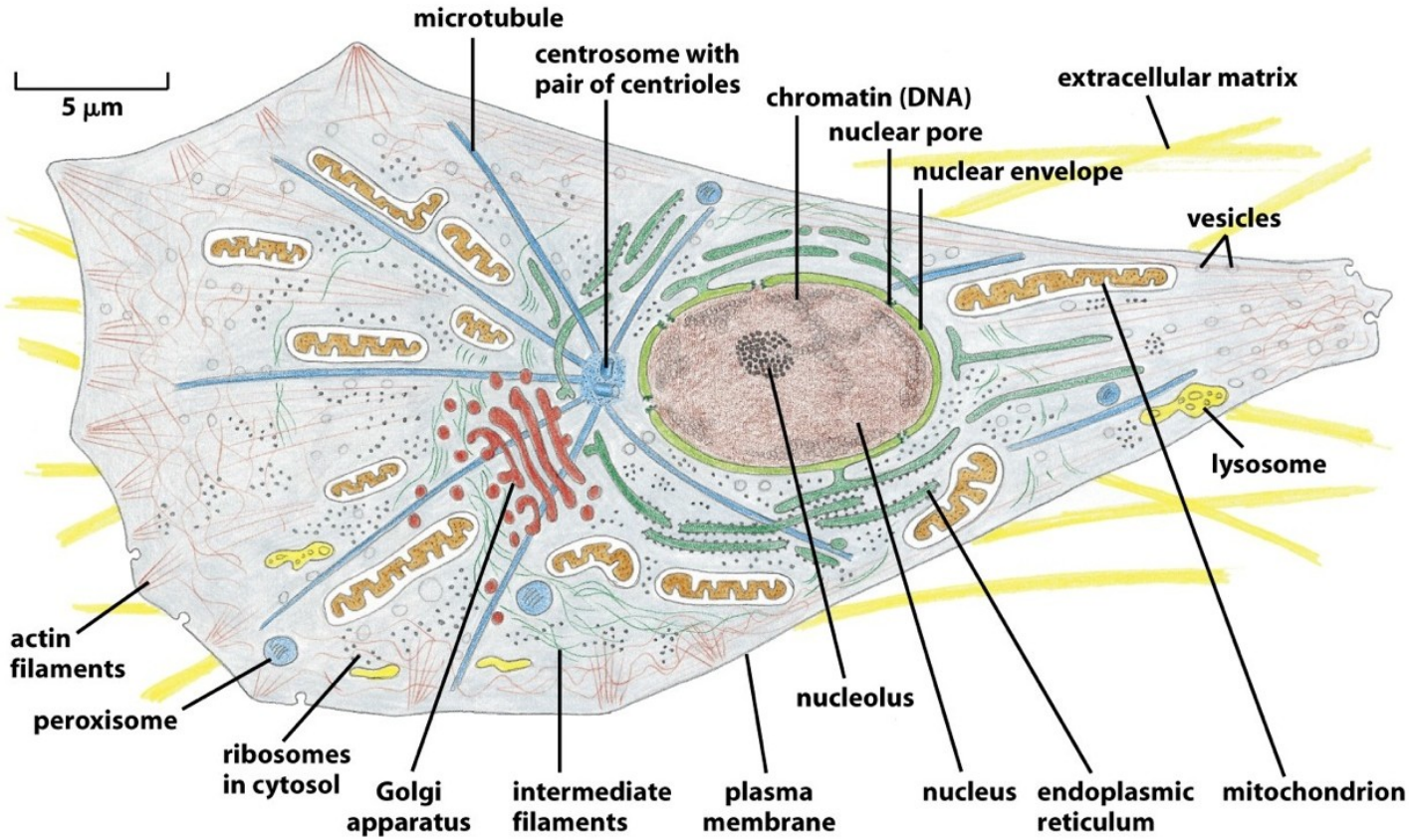


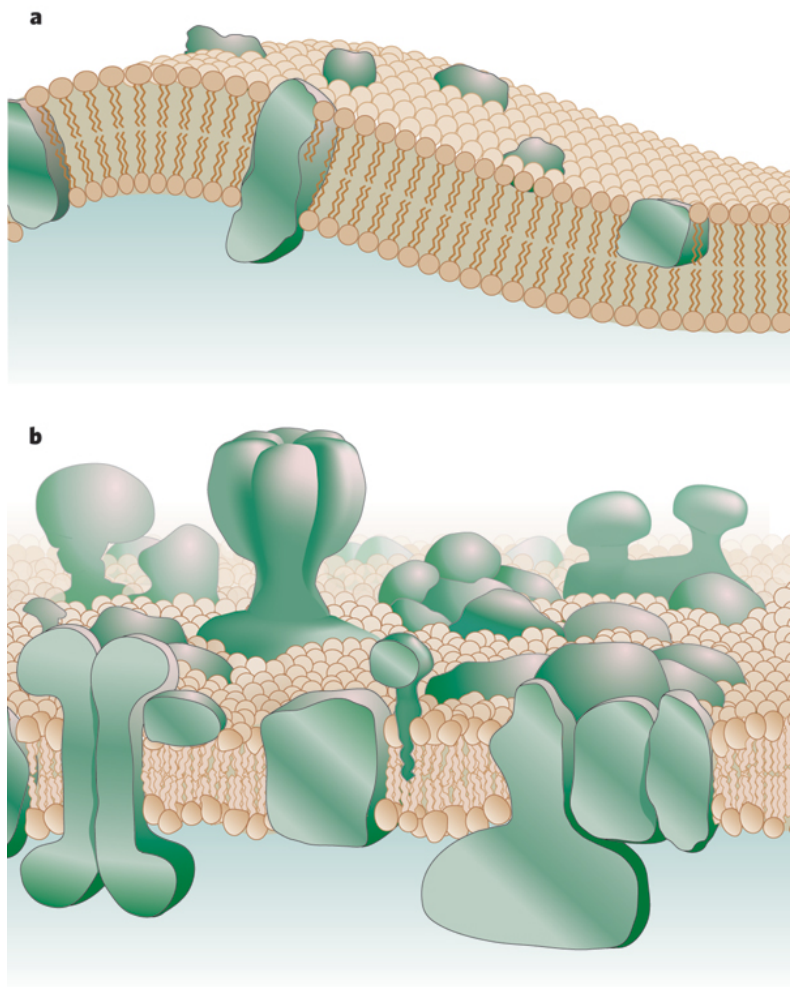
Figure 1-30 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Plant cells similar, contain chloroplasts, tough external cell wall made of cellulose

Cell Membrane and active stuff on it

- Cell membrane is fluid
- Surface of zero thickness
- Surface conformation energy
- Weight amount of surface (surface tension σ); surface curvature (mean curvature κ).
- Gaussian curvature irrelevant if no topology changes

- Membrane can carry "active" protein molecules
- Pumps, channels embedded in the bilayer
- Specific pumps have directionality



- Artificial membranes with pumps which are kept out of equilibrium
- Light-activated Bacterio-rhodopsin pumps
- Micropipette experiments measure effective fluctuation strength
- Active system, a non-equilibrium temperature
- Prost, Bruinsma, Manneville, Bassereau, Ramaswamy, Toner, Gov, Lacoste ...
- Madan Rao/Jitu Mayor: Alternative exploration of consequences of activity

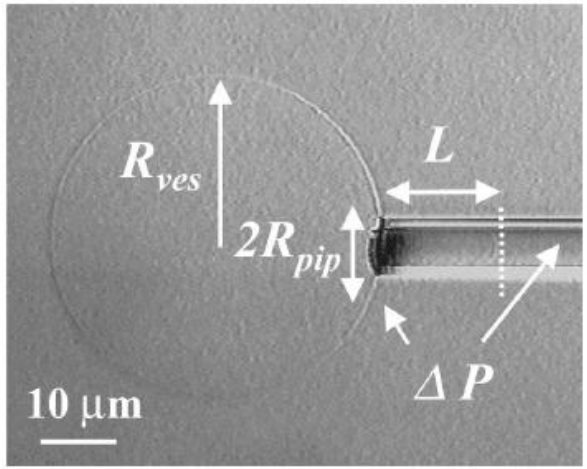


FIG. 3. Typical micropipet experiment. The pressure difference ΔP is the difference between the pressure outside and inside the pipet. The intrusion length L is the length of membrane aspirated inside the pipet when a pressure difference ΔP is applied. The bar represents 10 μm.

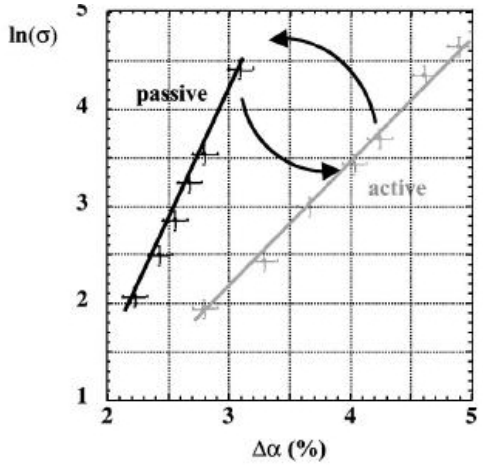
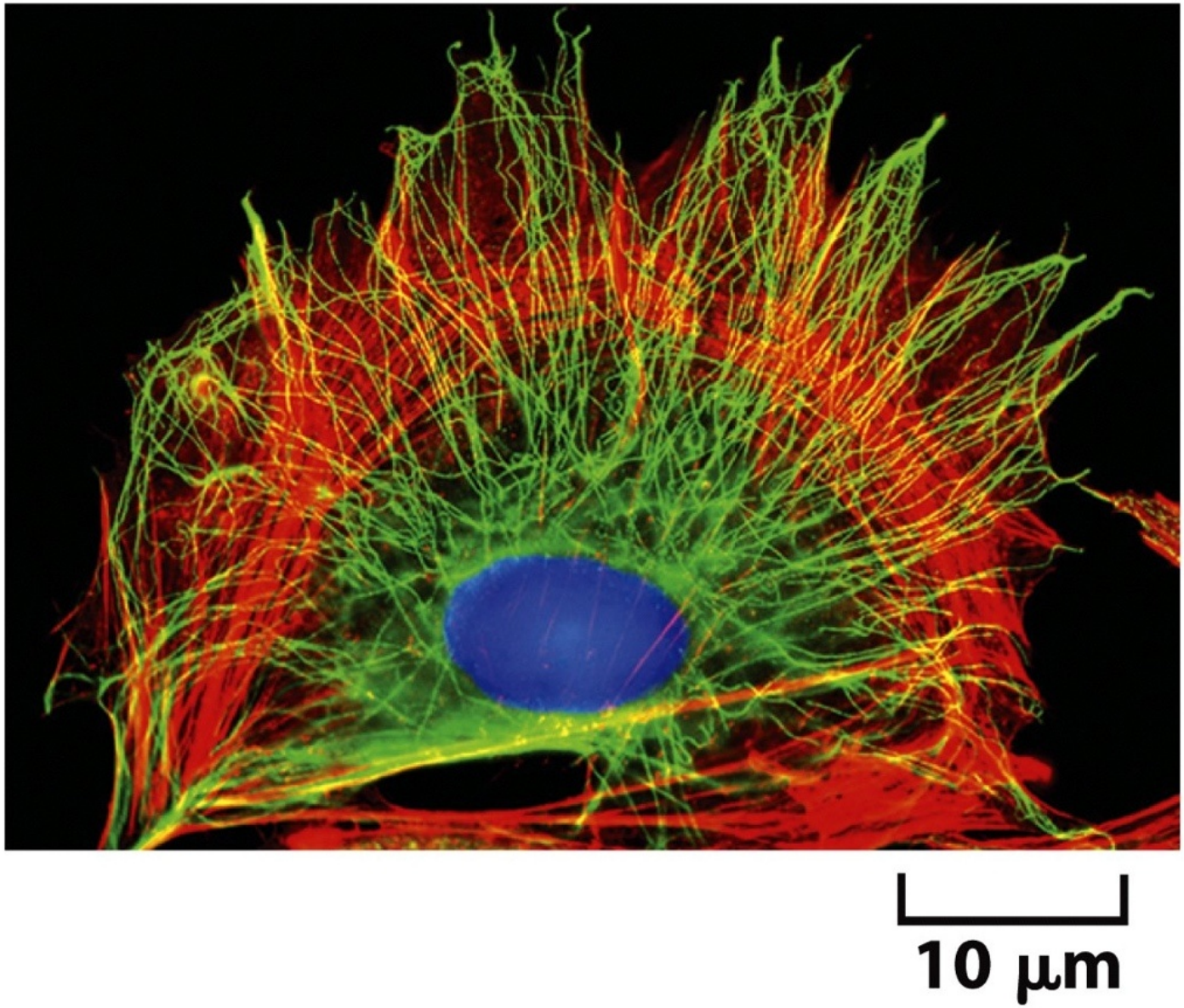
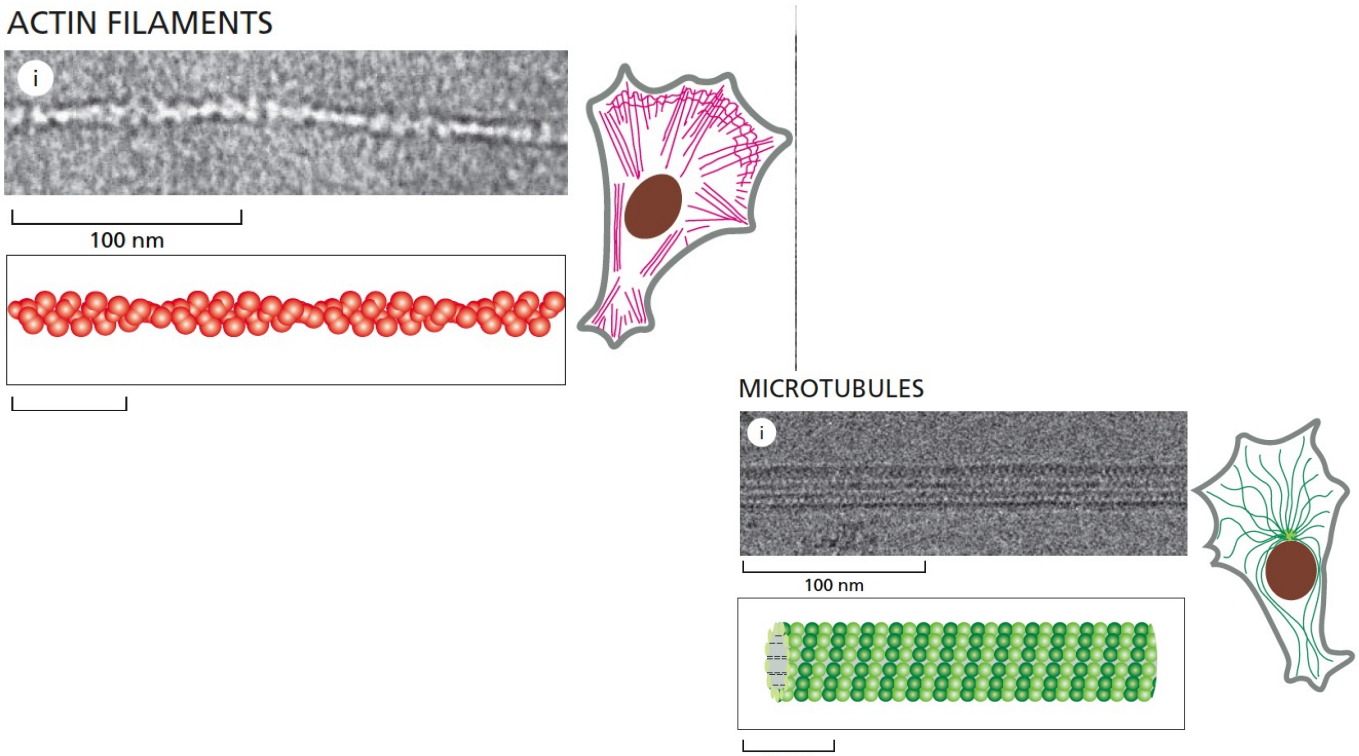


FIG. 4. Variation of the logarithm of the tension σ vs the areal strain $\Delta\alpha$ for the same vesicle containing BR, alternately passive and active.

The Cell Cytoskeleton



The Cell Cytoskeleton



The Cell Cytoskeleton: Microtubules

Microtubule structure

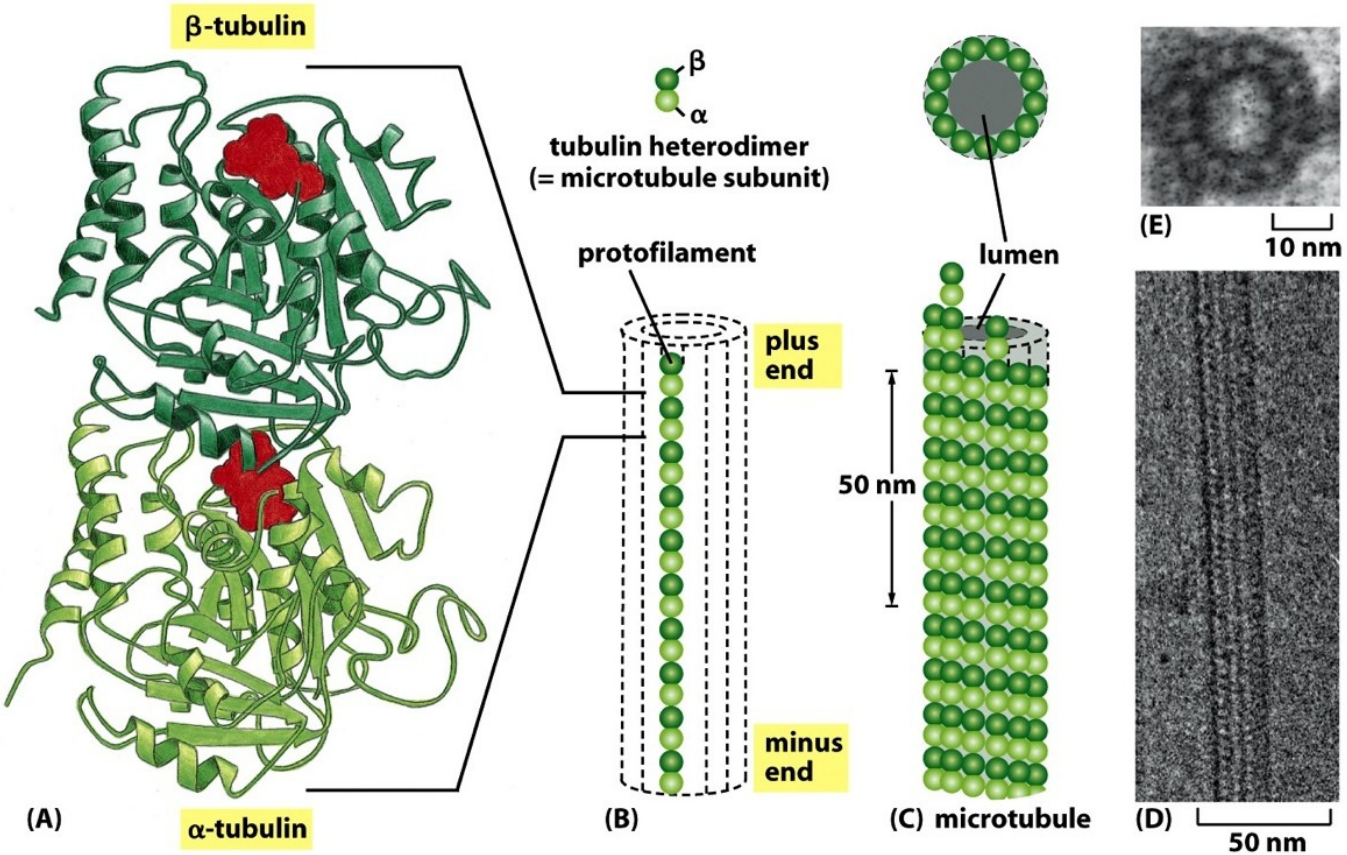


Figure 16-11 Molecular Biology of the Cell 5/e (© Garland Science 2008)

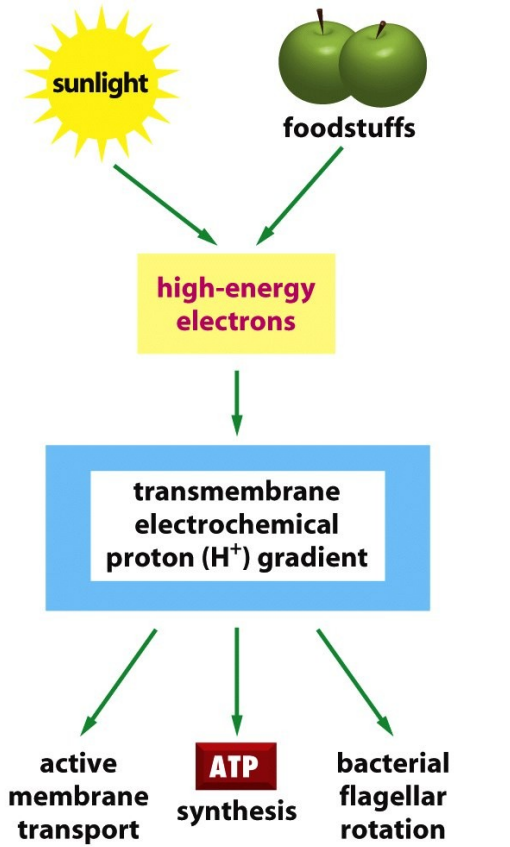


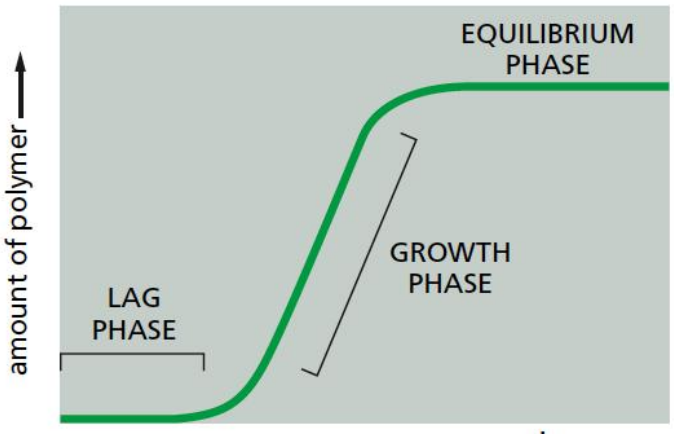
Figure 14-2 Molecular Biology of the Cell 5/e (© Garland Science 2008)

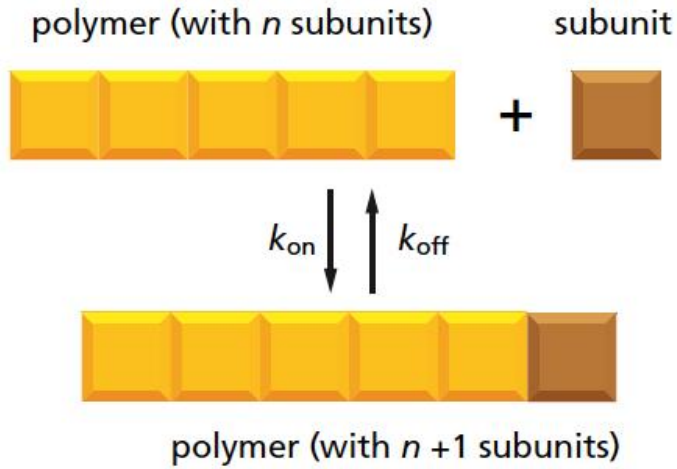
The energy currency of the cell is a molecule called ATP, synthesized in mitochondria

Energy required for cellular processes packaged in nucleoside-triphosphate molecules (NTP) e.g. ATP and GTP. Microtubules use energy derived from the hydrolysis of GTP to grow and shrink.

- Microtubules and actin are remarkable polymers
- They are fairly stiff - persistence lengths are of order several microns (actin) and millimetres (microtubules)
- They are polar objects, + end and a - end
- They polymerize and depolymerize, often rapidly, in processes that are tightly regulated by proteins which bind to them
- This polymerization and depolymerization, coupled to the fact that they are polar, lead to interesting physical phenomena, such as dynamic instability and treadmilling
- Cells use polymerization of cytoskeletal filaments to exert forces

Ppolymerization of Cytoskeletal Filaments

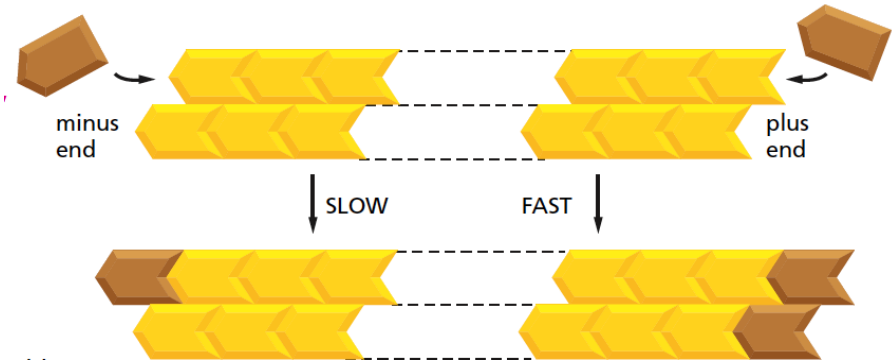




$$k_{on}\, C = k_{off}$$

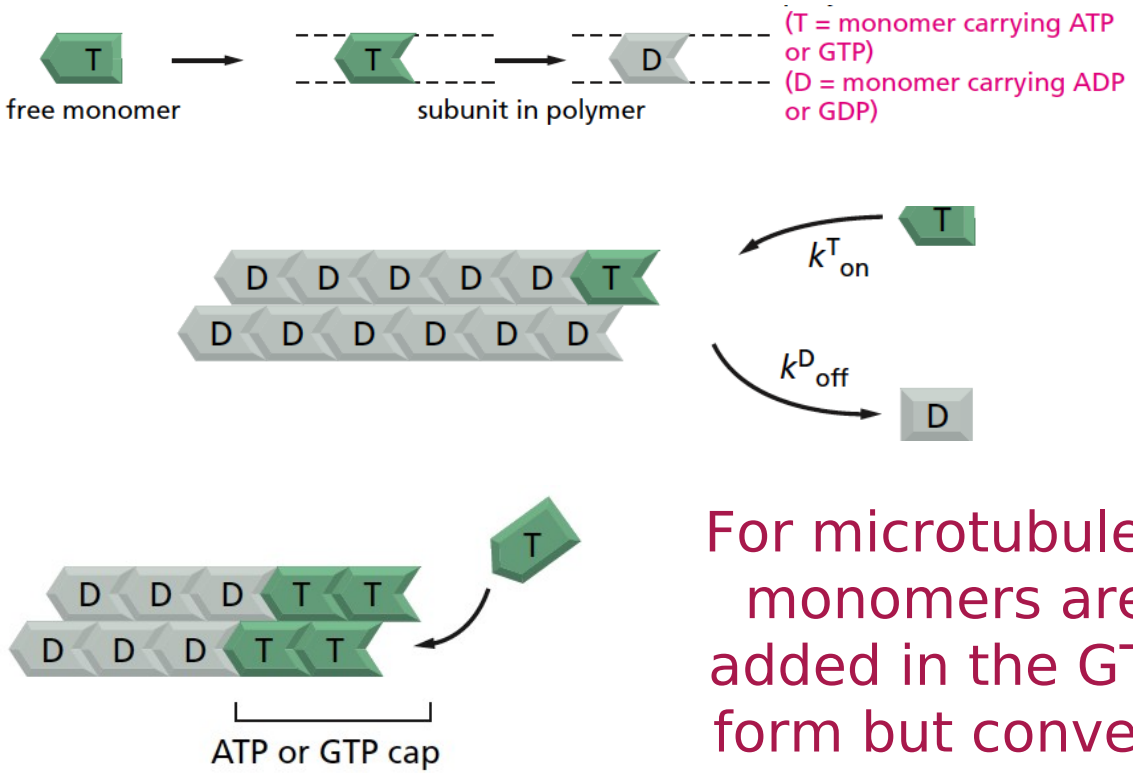
$$C_c = \frac{k_{off}}{k_{on}} = \frac{1}{K}$$

Polymerization of the Microtubule



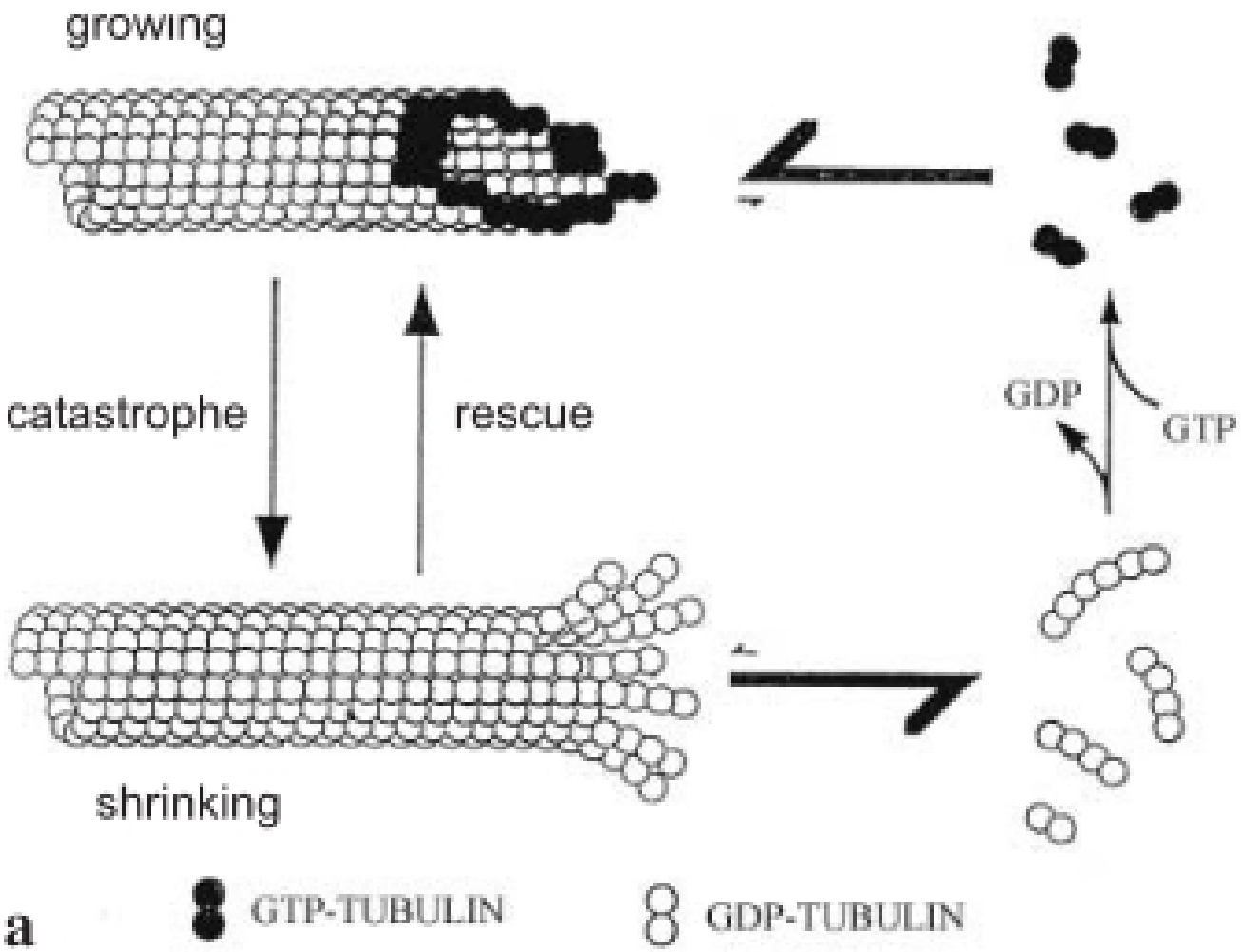
The two ends of the polymer can be chemically distinct, so the rates for addition/removal of monomers can be different at the two ends

The GTP cap



For microtubules, monomers are added in the GTP form but convert into the GDP form

Dynamic Instability



Dynamical Instability

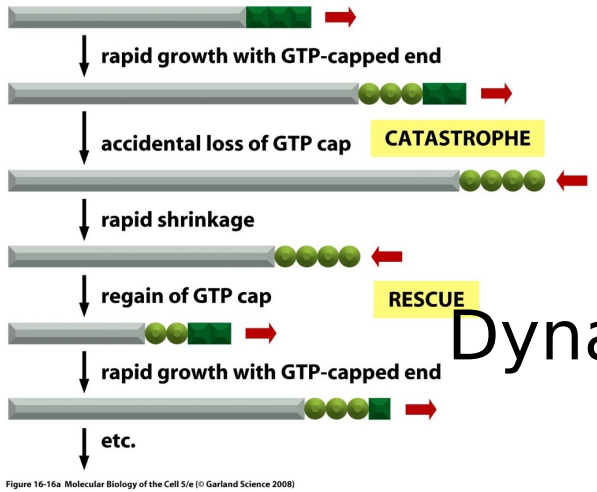


Figure 16-16a Molecular Biology of the Cell 5/e (© Garland Science 2008)

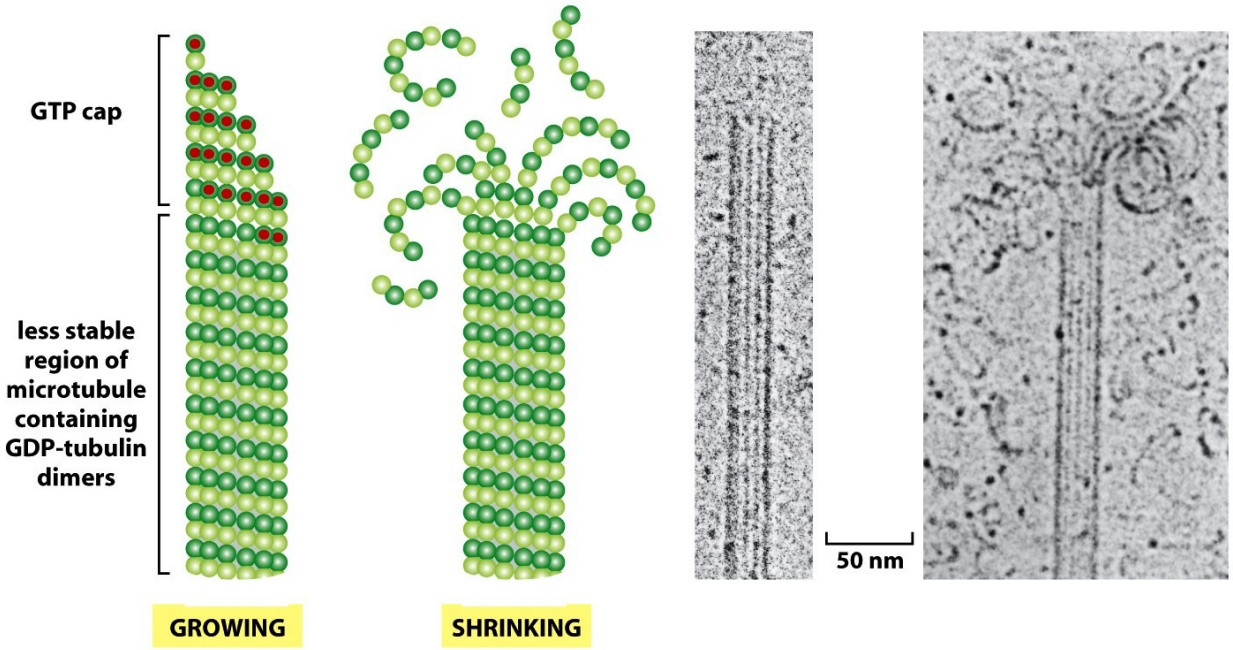
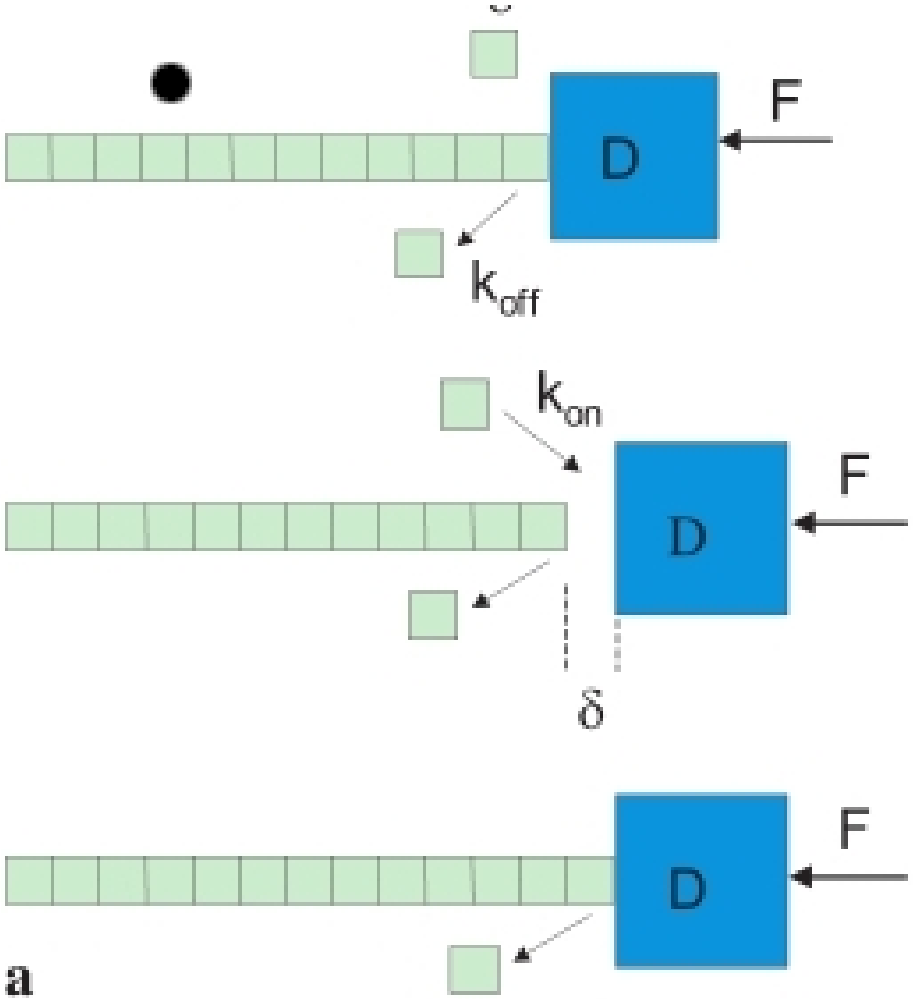
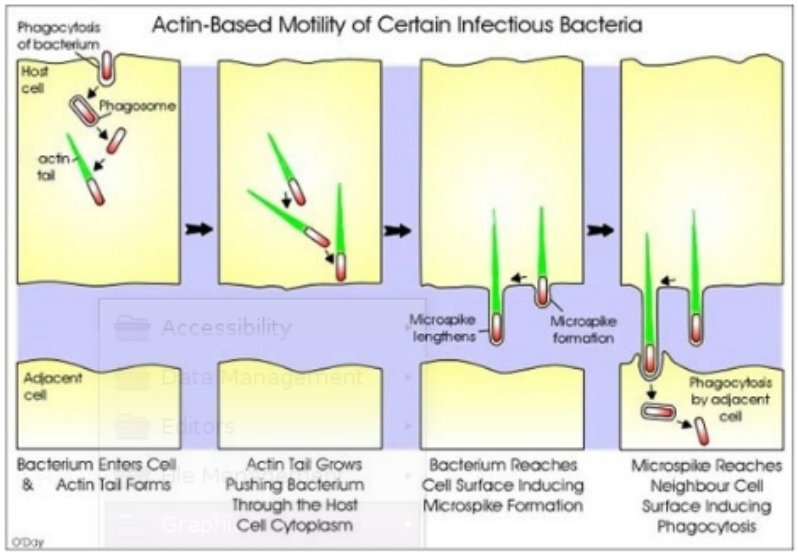


Figure 16-16c Molecular Biology of the Cell 5/e (© Garland Science 2008)

Polymerization Forces

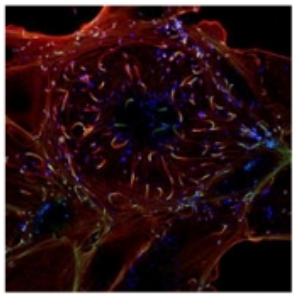


Polymerization Forces: Actin



Comet tails and the motion of *Listeria Monocytogenes*

Theriot Lab (Stanford)



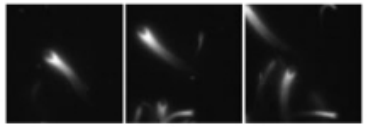
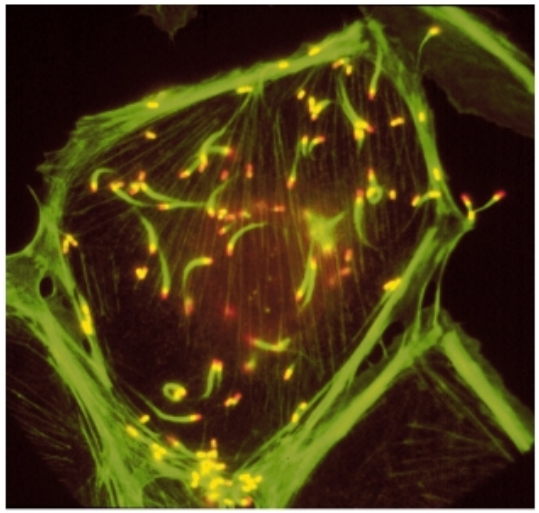
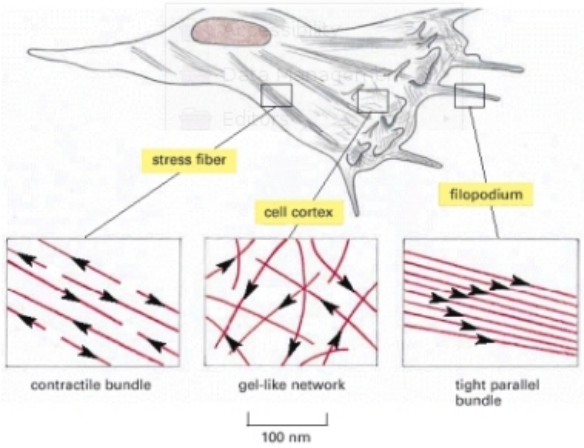


Image by Le Ma

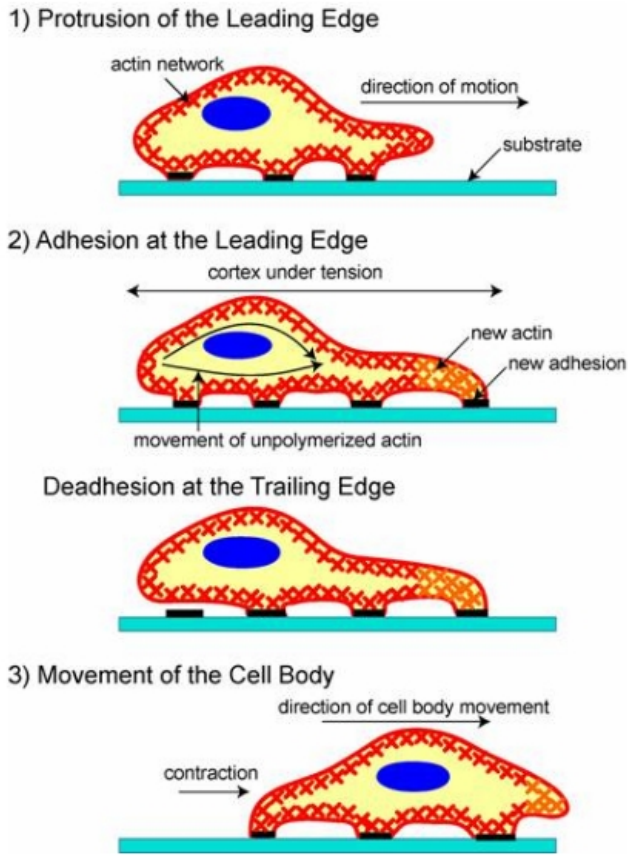


Matteo Bonazzi: Visualization of actin comet tails stained with two different antibodies against actin (Green and Red) in PtK2 cell infected with Listeria monocytogenes (Blue).

Cell Crawling



http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=mboc4&part=A2955



Gel-like state of actin filaments near the edges

Motors

Protein molecules which use energy from ATP hydrolysis to move cargo along the cell cytoskeleton, exert forces

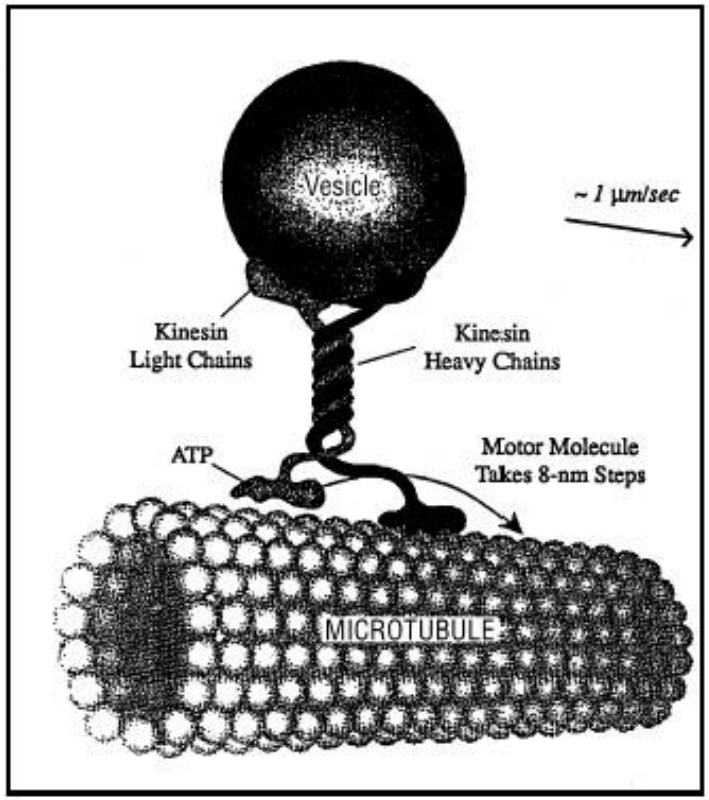
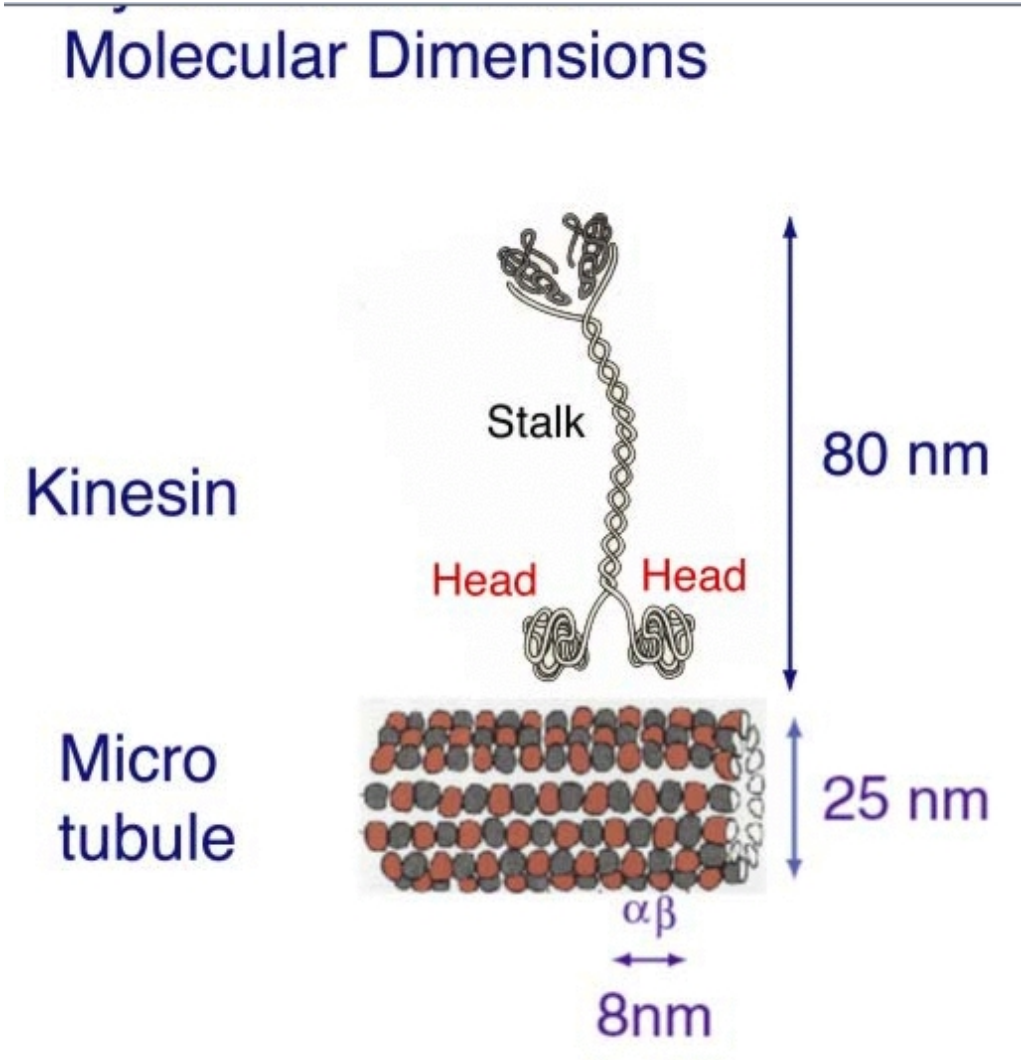
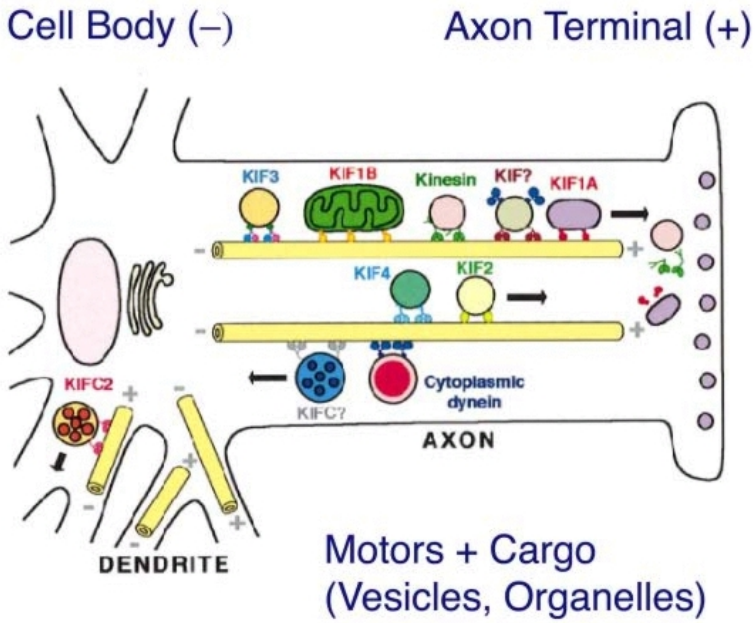


Fig. 9.32. Vesicle carried along microtubule track by kinesin transport molecule (schematic only, modified from Travis[1535]).

Scales involved



Kinesins, Dyneins and Myosins: Motors



- Three motor super families: Kinesins, Dyneins and Myosins
- Myosins: muscle action
- Motors are directional - kinesins move from - to + on microtubules, cytoplasmic dyneins move from + to -.
- Transporters, force exerters

Schematic of Motor Motion

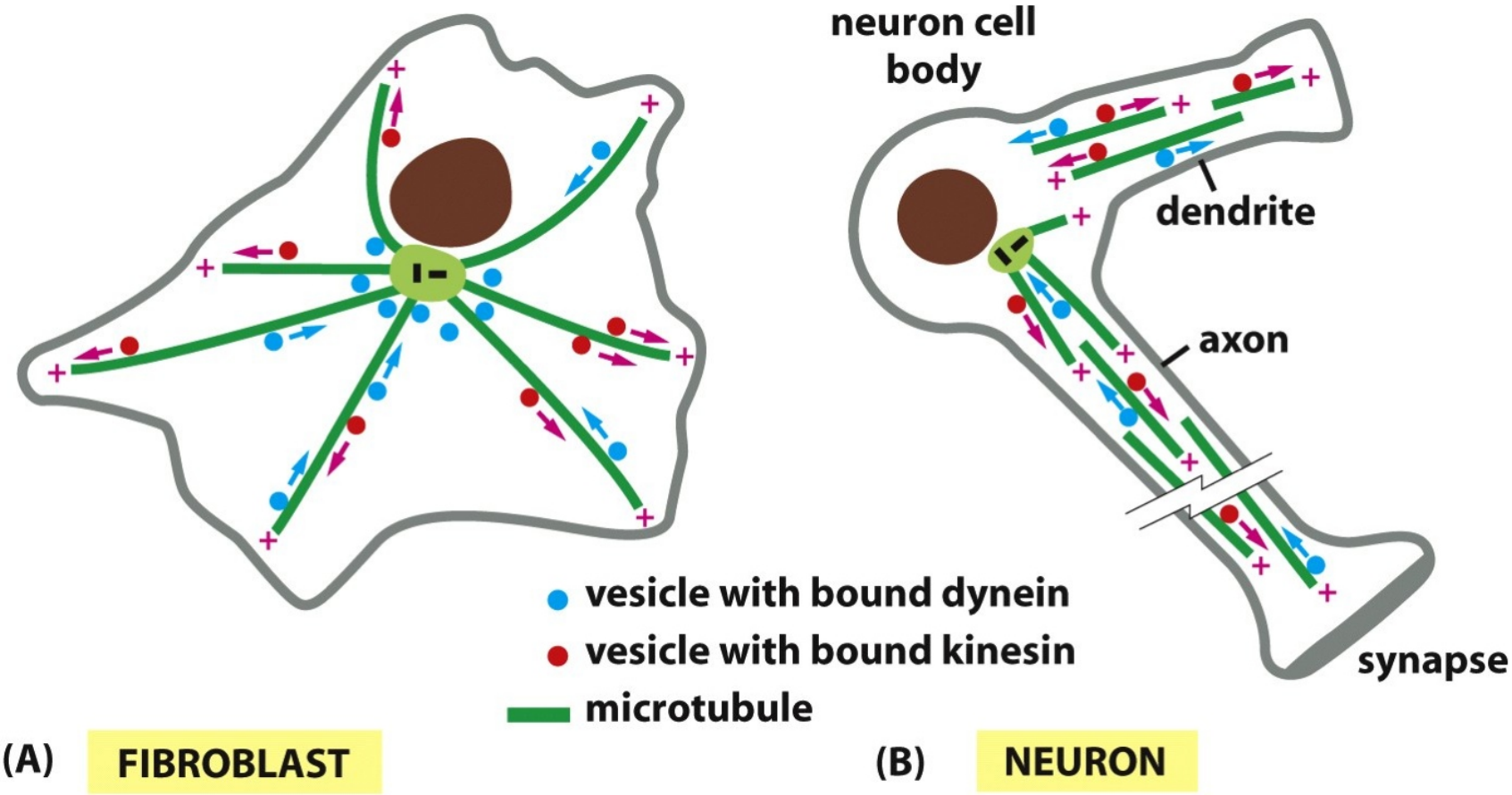


Figure 16-104 Molecular Biology of the Cell 5/e (© Garland Science 2008)

The role of ATP hydrolysis in motion

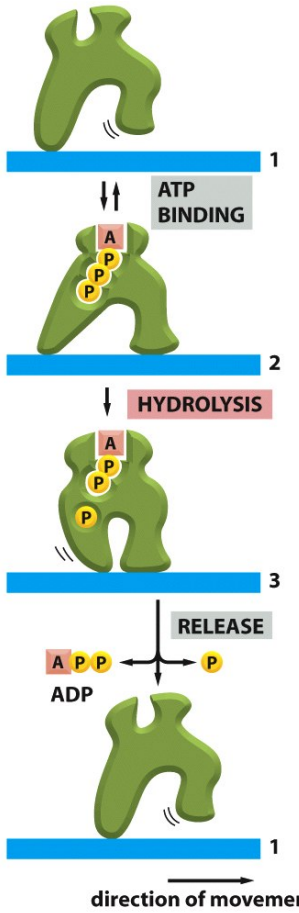
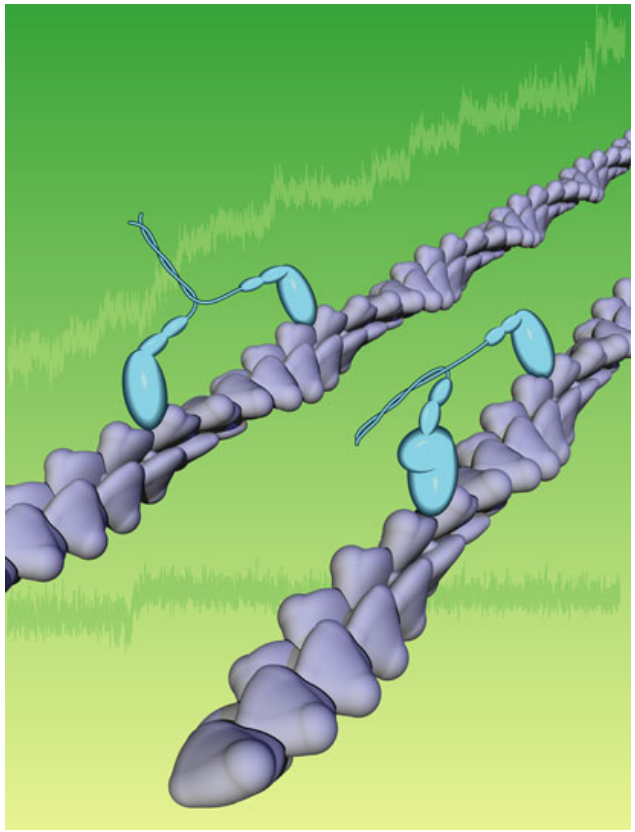


Figure 3-77 Molecular Biology of the Cell 5/e (© Garland Science 2008)

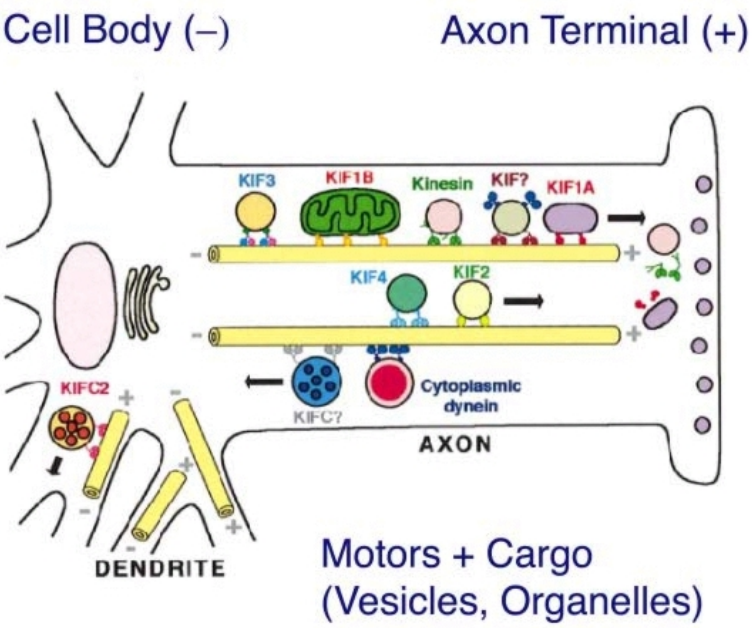
Questions

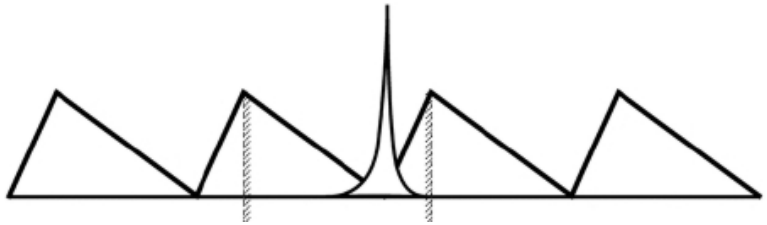
The cell is a very highly Brownian environment

- How does the motor manage to walk unidirectionally?
- Why isn't it blown off by thermal fluctuations?



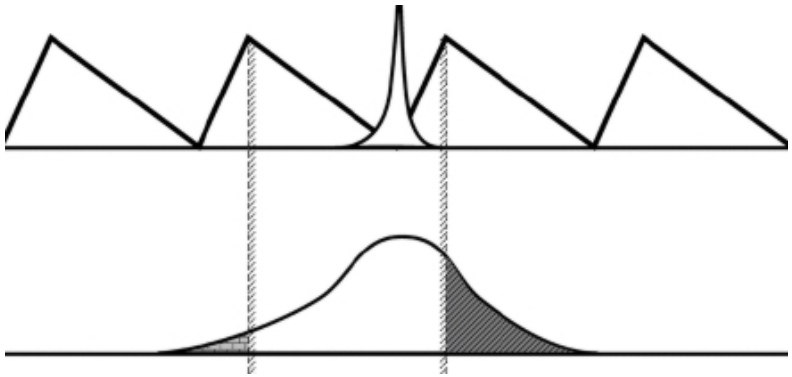
What singles out a direction?





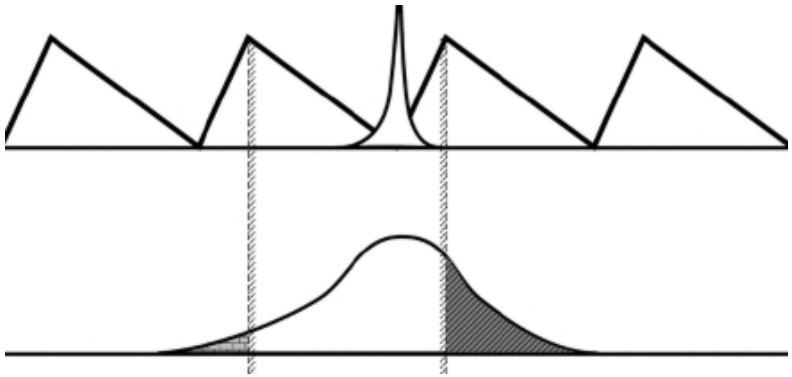
- Motor walks on a periodic track, the filament
- This track need not have reflection symmetry, could be polar. (It is!)
- This would single out a direction

Why doesn't it fly off immediately?



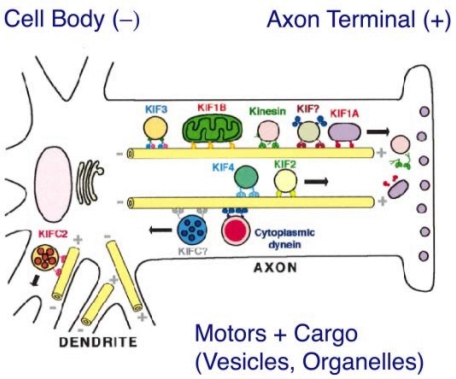
- Must be tightly bound to the filament, at least some of the time.
- But not all the time, or it wouldn't move. It would just be stuck

Signifance of the weakly bound state



- In the weakly bound state, motor should be able to move (diffuse) on the filament
- If only weakly bound state, diffusion would not lead to a net current: thermal equilibrium
- If only strongly bound, very little motion and no net current: thermal equilibrium

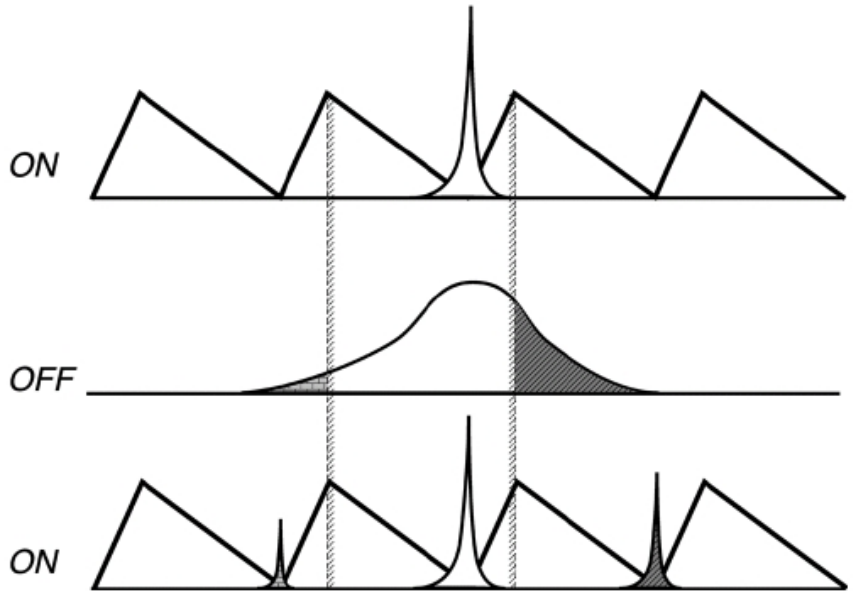
Putting it all together



- Need a periodic but asymmetric potential
- Need weakly and strongly bound states
- Need to alternate between them
- No macroscopic tilt of the potential

Will this work?

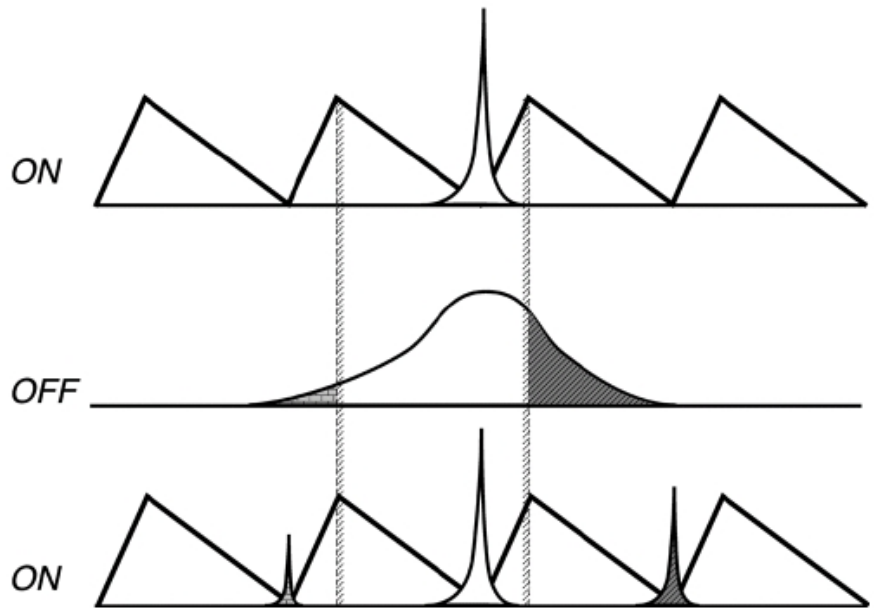
The Brownian (flashing) ratchet

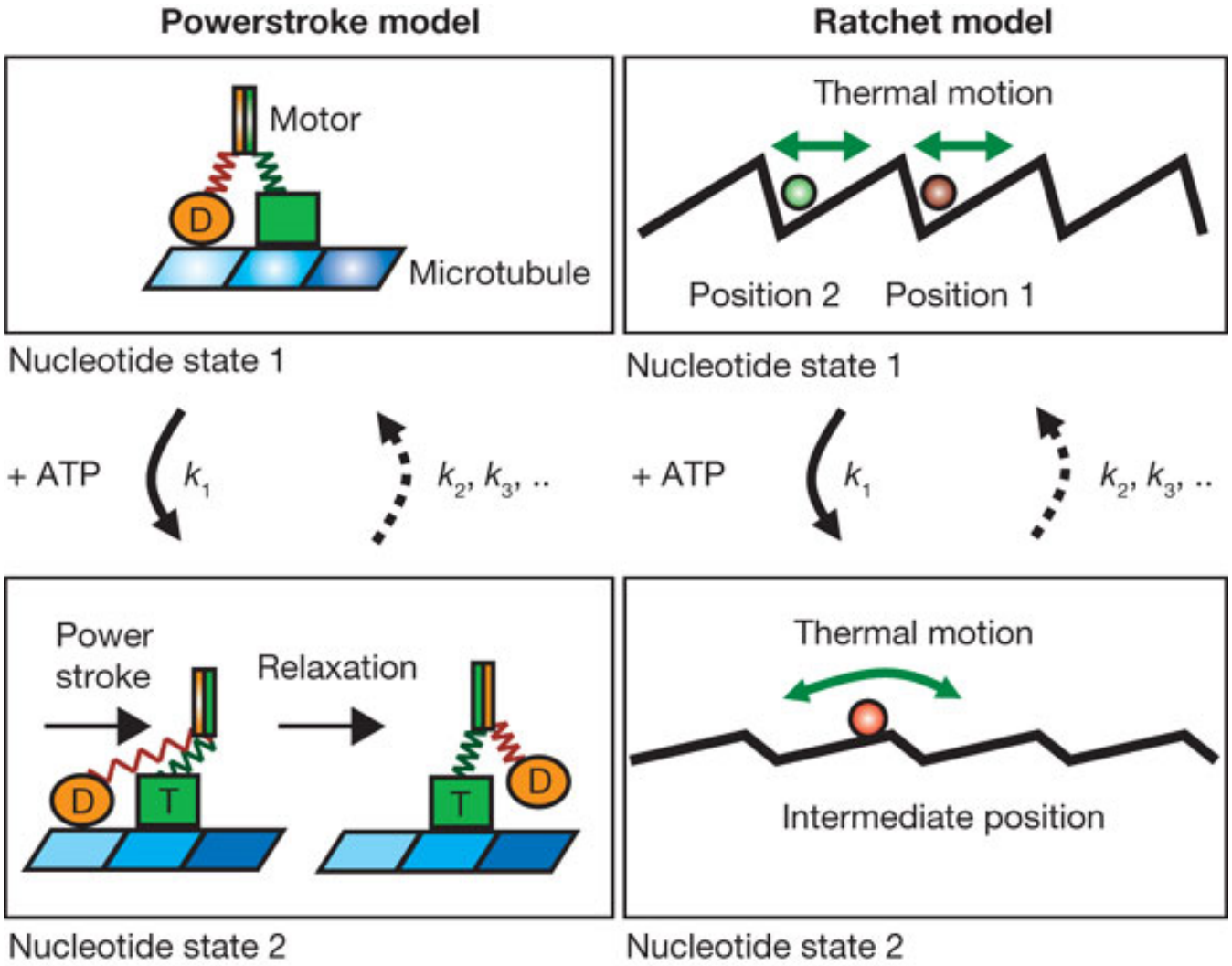


- Potential switches on/off via ATP hydrolysis
- ATP binding alters the coupling of the motor to the filament
- Detailed structure of the motor unimportant

The Brownian Motor Again

- Brownian particle in an asymmetric potential
- Particle diffuses - probability distribution broadens
- Potential is switched on and off
- Asymmetric motion of the particle
- Drive against a force, do work




Powerstroke model
Ratchet model
Motor
D
Microtubule
Thermal motion
Position 2
Position 1
Nucleotide state 1
Nucleotide state 1
+ ATP
k_1
$k_2, k_3, ..$
+ ATP
k_1
$k_2, k_3, ..$
Power stroke
Relaxation
D
T
T
D
Thermal motion
Intermediate position
Nucleotide state 2
Nucleotide state 2

The inevitability of ratchet-like mechanisms

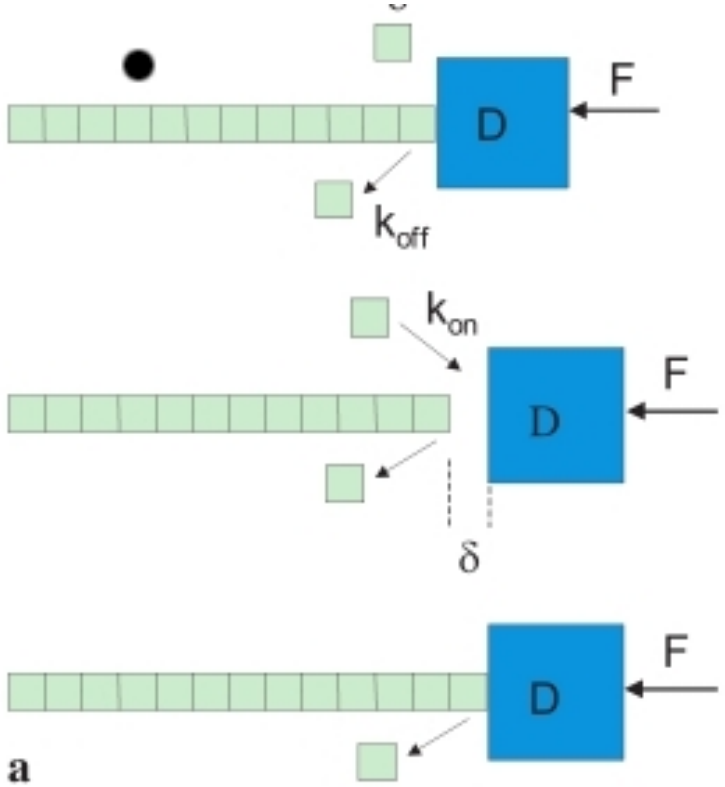
Ratchet-like mechanisms must underlie almost all of biology's machines

Physically, ratchets provide a way of biasing motion in one way.

Non-equilibrium ensures the rest. This is a very general idea.

Motors: Ajdari, Prost, Julicher RMP 1997

Polymerization Ratchet



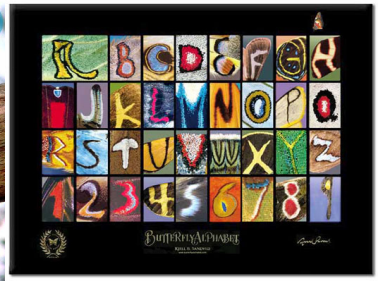
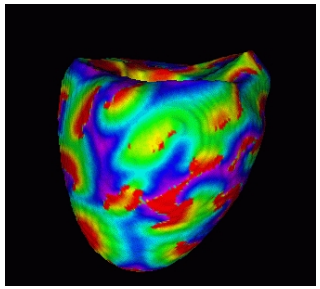
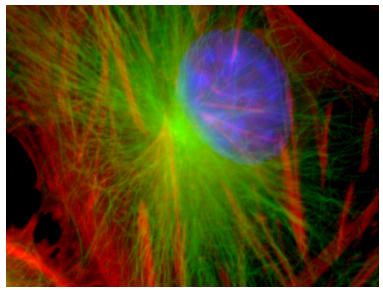
Idea that a "polymerization ratchet" mechanism is responsible for force exertion by polymerizing biofilaments (Hill, Oster, Mogilner).
Some problems with questions of principle

Things to remember for later

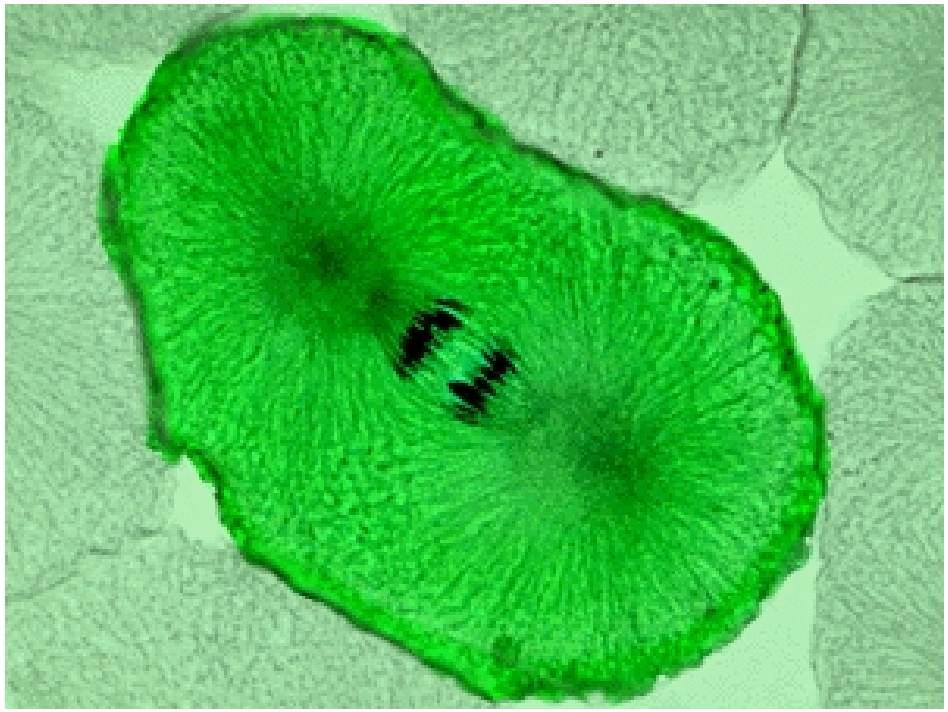
- All of this is out of thermal equilibrium. Must account for this in any theoretical description
- These systems are multicomponent and complex. Hard to see how detaile molecular specifications will help.
- Polymerization and forces exerted by polymerization are crucial to mechanical behaviour of the cell. Cytoskeletal polymers responsible for exerting forces often found in gel-like states whose fluidity is controlled tightly.
- Motors and their tracks collaborate
- The role of noise is very important. Sub-cellular processes must find a way to co-opt noise

Patterns in Nature



Fundamental Motivation



Astral (star-like) bipolar structures formed when cells divide
The Mitotic Spindle: Require motors interacting with microtubules

Pattern Formation Theories

Spatial patterns from coupled non-linear partial differential equations (Reaction-Diffusion equations)

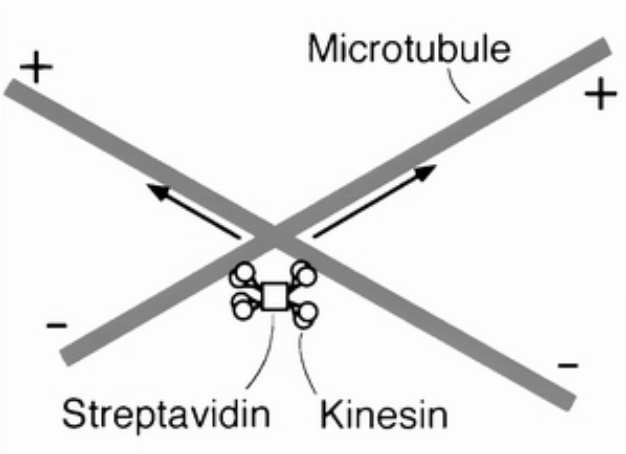
Turing patterns, BZ reactions

Components with different diffusion constants, Short-ranged amplification, long ranged inhibition

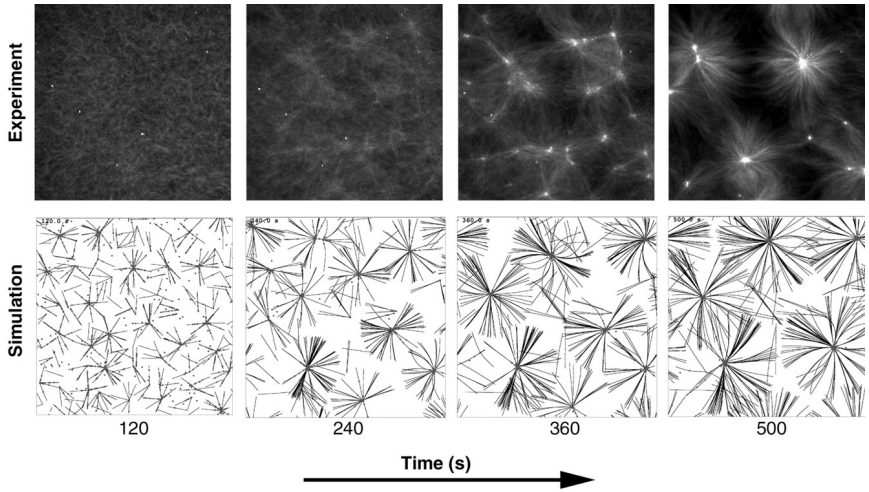
Patterns also in driven fluids, vector degrees of freedom involved. Fluid velocity field. Boundary driving. Scales set by confinement.

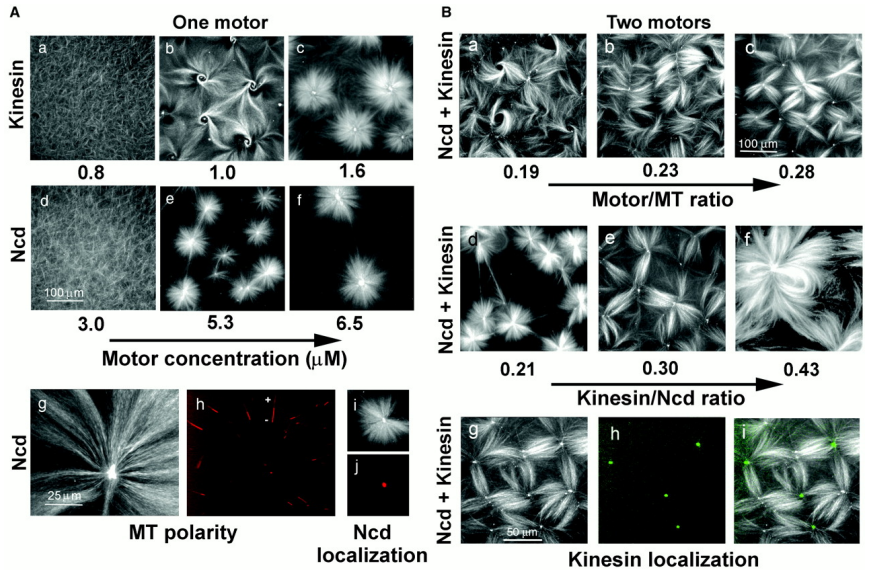
Motor-microtubule pattern formation combines some aspects of both problems. Intrinsic scales to patterns, confinement effects important in some regimes. Non-equilibrium from internal driving, not from boundary conditions.

Nedelec, Surrey, Maggs, Leibler, Karsenti, [Nature, Science] (1997,2001)

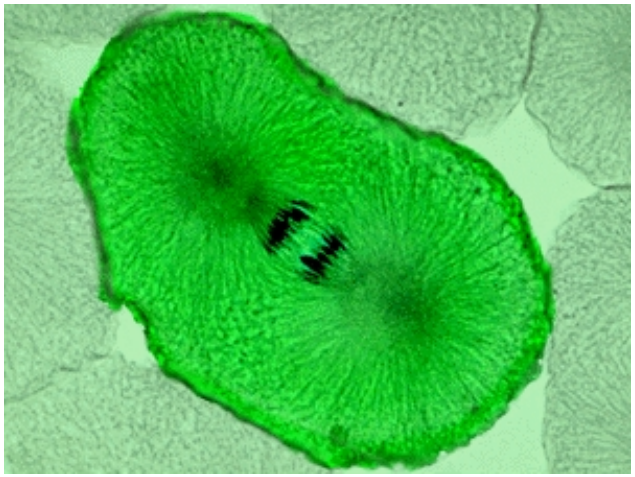


- Outside the cell: mix motors, microtubules and ATP together
- Can you reproduce the structures seen when a cell divides?



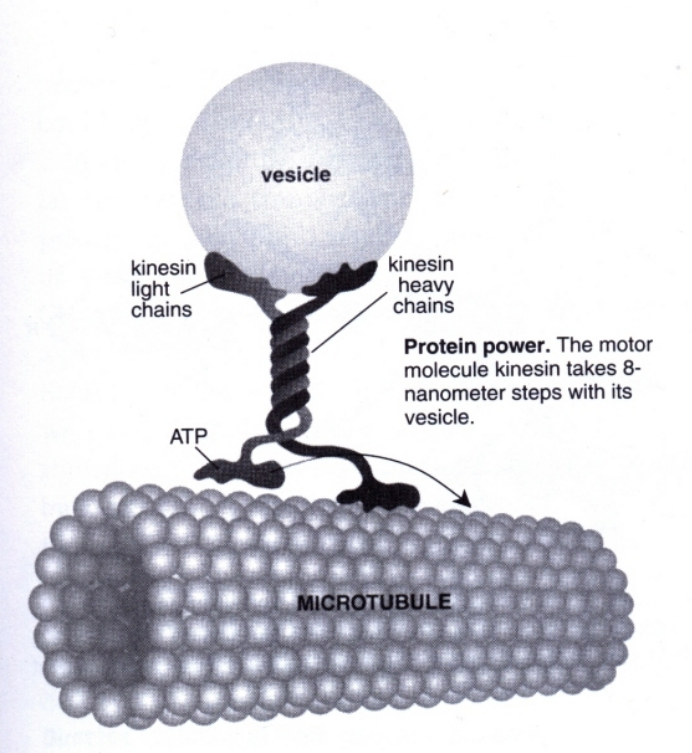


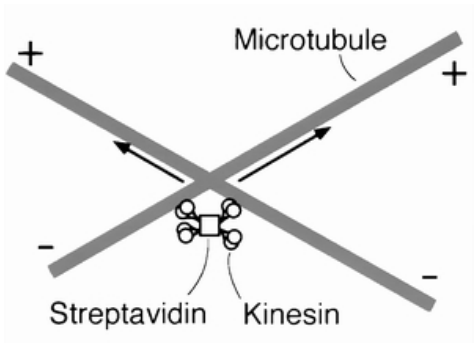
Pattern Formation in Motor-Microtubule Mixtures



- Nonequilibrium, external energy input, bounded
- Not densities (scalar) of reactants but *orientations* (vectors) Unconventional
- Nature of patterns *in vitro*?

Microtubules and Motors

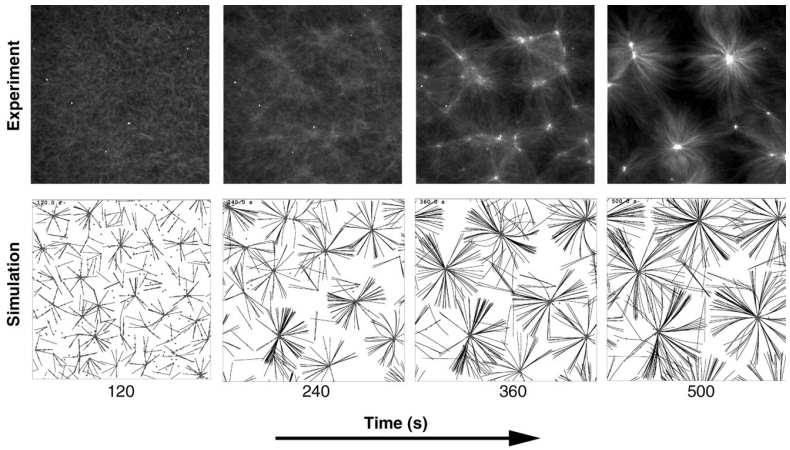




- Microtubule a polar object (+/− ends)
- Kinesin motors walk on the microtubule ($- \rightarrow +$); motion coupled to ATP hydrolysis (non-equilibrium!)
- Motors attach and detach, stabilized by loads
- Processive motors: Translocate through long distances without detaching
- Motor complexes formed by combining multiple motors

Motors and Microtubules in Vitro

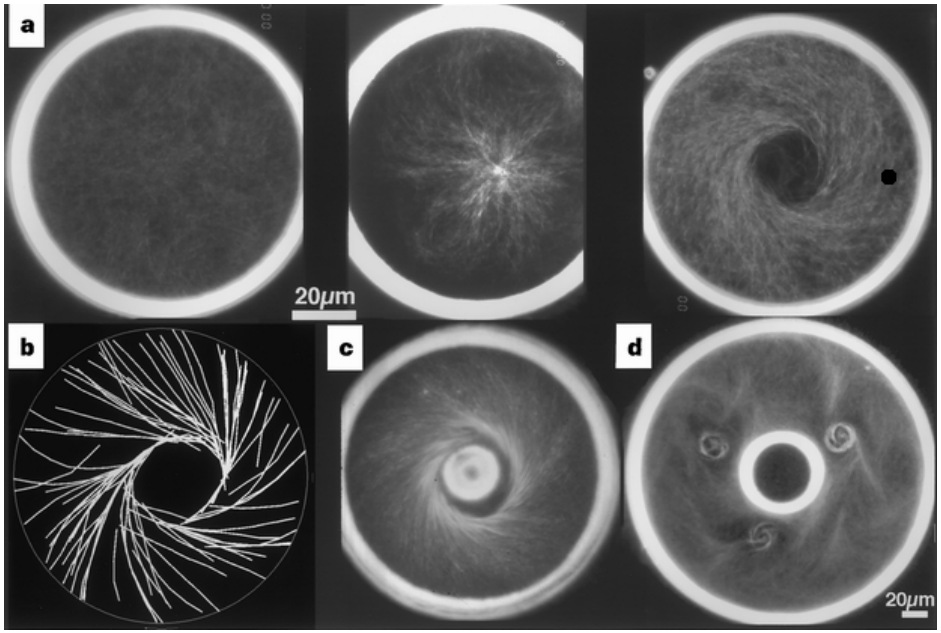
Surrey, Nedelec, Leibler, Karsenti, Science **292** 1167 (2001)



- Non-equilibrium patterns in mixtures of motor complexes and microtubules: disordered states, asters, vortices ..
- Self-organized structures; non-equilibrium, requires ATP
- Quasi-two-dimensional geometry
- Qualitative agreement with simulations
- But simulations have 19 parameters to be fixed

Self-organization: Confinement

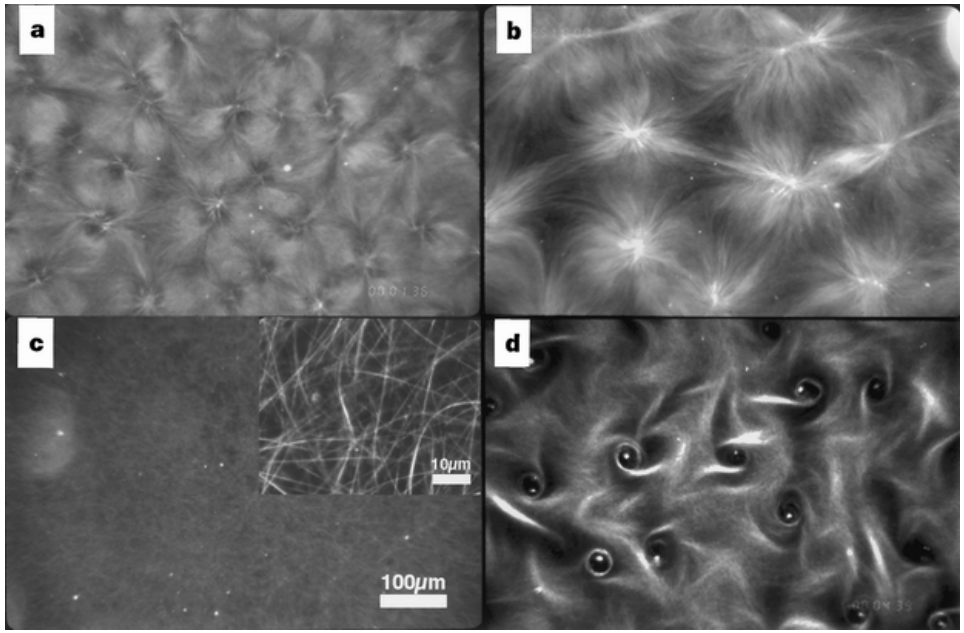
Nédélec, Surrey, Maggs, Leibler, Nature **389** (1997), 305



- Initial growth into an aster, distorts into a vortex on elongation
- Aster to vortex transformation due to boundaries
- Boundary effects important in small systems ($\sim$ 100 μm)

Patterns in large systems

Nédélec, Surrey, Maggs, Leibler, Nature **389** (1997), 305



- Larger system size ($\sim$ 1000 μm). Boundary effects unimportant
- Patterns depend on motor concentration
- Sequence (Kinesins): disordered/aster-vortex mixture $\longrightarrow$ lattice of vortices $\longrightarrow$ lattice of asters

Theoretical Approaches

Hydrodynamic, symmetry based models (Lee-Kardar, Sankararaman-Menon-Kumar)

Force and moment balance, polymer based theories (Liverpool -Marchetti)

Active Gel Models (Kruse, Julicher, Prost, Joanny ...)

Boltzmann equation-type approaches (Aranson-Tsimring)

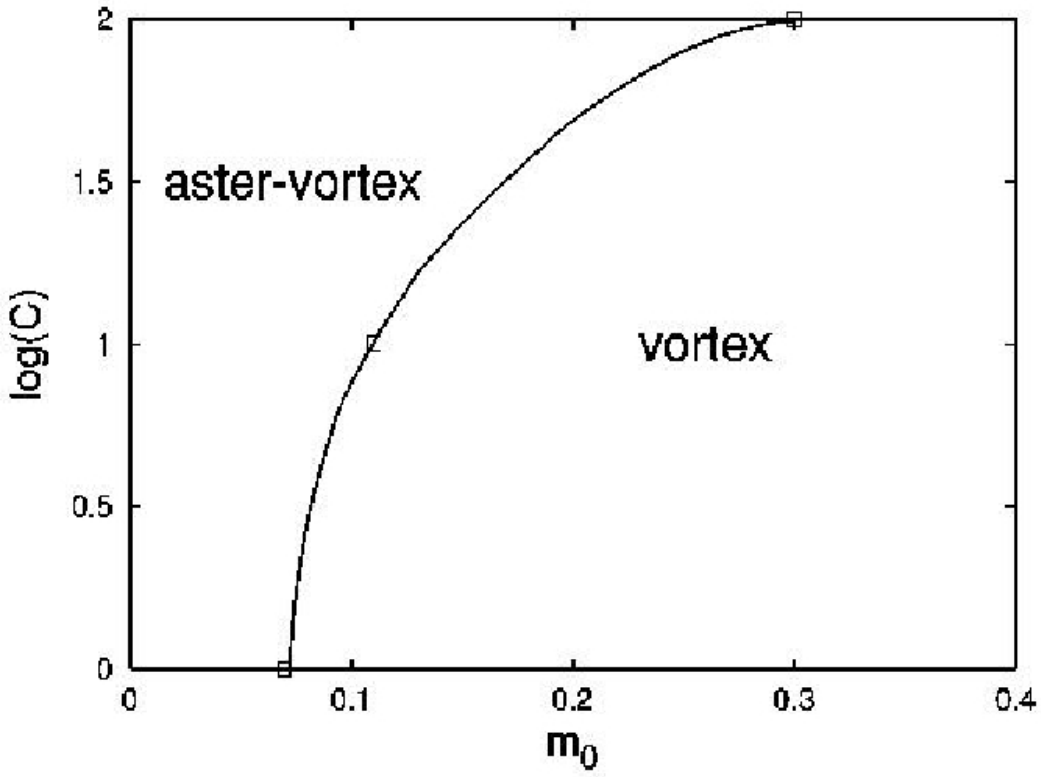
Approaches developed for the study of flocking and active nematic systems are a general background to the hydrodynamic approach [Toner, Tu, Ramaswamy and collaborators]

The Lee-Kardar (LK) Model

$$\begin{aligned} \partial_t m &= D\nabla^2 m - A\nabla\cdot(m\mathbf{T}) \\ \partial_t \mathbf{T} &= \mathbf{T}(\alpha - \beta T^2) + \gamma m\nabla^2\mathbf{T} + \gamma\nabla m\cdot\nabla\mathbf{T} \end{aligned}$$

- A (polar) field for microtubules
- A scalar field for motor molecules
- Single equation of motion for the total motor density field.
- Lowest-order symmetry allowed terms
- Non-equilibrium from convective terms

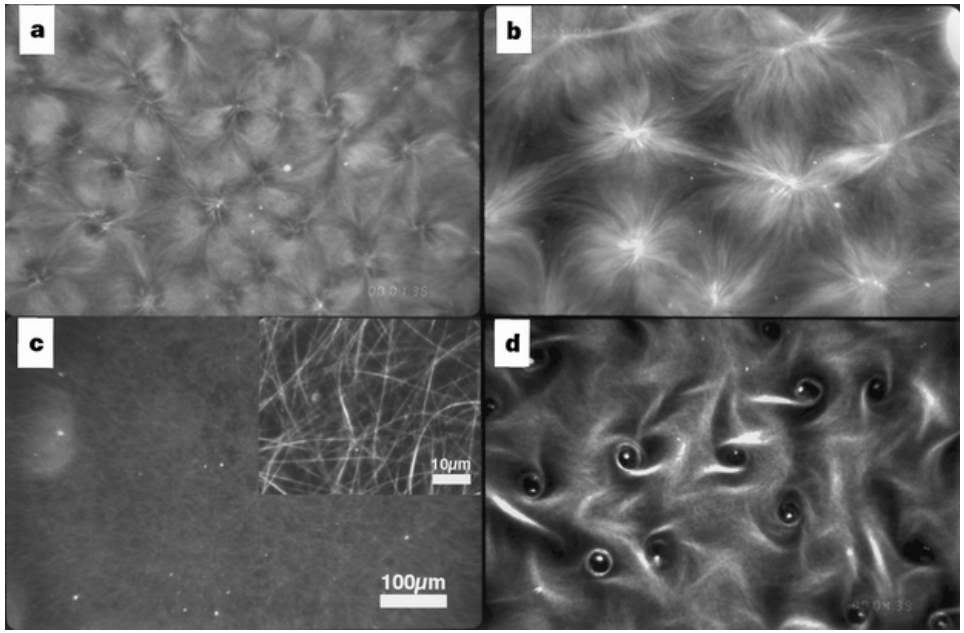
Phase Diagram of the LK Model



Phase obtained at large motor densities is always a single vortex. The y-axis is the "growth rate" for the local T field.

But experimental sequence is different

Nédélec, Surrey, Maggs, Leibler, Nature **389** (1997), 305



- Larger system size ($\sim$ 1000 μm). Boundary effects unimportant
- Patterns depend on motor concentration
- Sequence (Kinesins): disordered/aster-vortex mixture $\longrightarrow$ lattice of vortices $\longrightarrow$ lattice of asters

Equations for motor density fields

Diffusion of free motors, transport of bound motors along $\mathbf{T}$.
Free and bound motors interconvert

$$\partial_t m_f = D\nabla^2 m_f - \gamma'_{f\to b} m_f + \gamma'_{b\to f} m_b$$

$$\partial_t m_b = -A\nabla\cdot(m_b\mathbf{T}) + \gamma'_{f\to b} m_f - \gamma'_{b\to f} m_b$$

Simplest equations dictated by the physics

Equation for the tubule field

Microtubule orientation described by a 2-d vector field

$$\begin{aligned} \partial_t \mathbf{T} &= \mathbf{T}(\alpha - \beta|T|^2) + \kappa' \nabla^2 \mathbf{T} + \gamma m_b \nabla^2 \mathbf{T} \\ &+ \gamma' \nabla m_b \cdot \nabla \mathbf{T} + S' \nabla m_b \end{aligned}$$

- Tubules have preferred length
- Motor independent stiffness term for tubules. Symmetry allowed terms describing alignment of the tubules mediated by motors
- Last term is allowed by symmetry. Corresponds to a contribution to splay induced by motors. Only bound motor density field appears in the tubule equation

Compare to the Lee-Kardar Model

Putting things together

Diffusion of free motors, transport of bound motors.
Free and bound motors interconvert
Motors orient microtubules

$$
\begin{aligned}
\partial_t m_f &= D\nabla^2 m_f - \gamma'_{f\to b} m_f + \gamma'_{b\to f} m_b \\
\partial_t m_b &= -A\nabla.(m_b \mathbf{T}) + \gamma'_{f\to b} m_f - \gamma'_{b\to f} m_b \\
\partial_t \mathbf{T} &= \mathbf{T}(\alpha - \beta|T|^2) + \kappa'\nabla^2\mathbf{T} + \gamma m_b \nabla^2 \mathbf{T} \\
&+ \gamma'\nabla m_b \cdot \nabla \mathbf{T} + S'\nabla m_b
\end{aligned}
$$

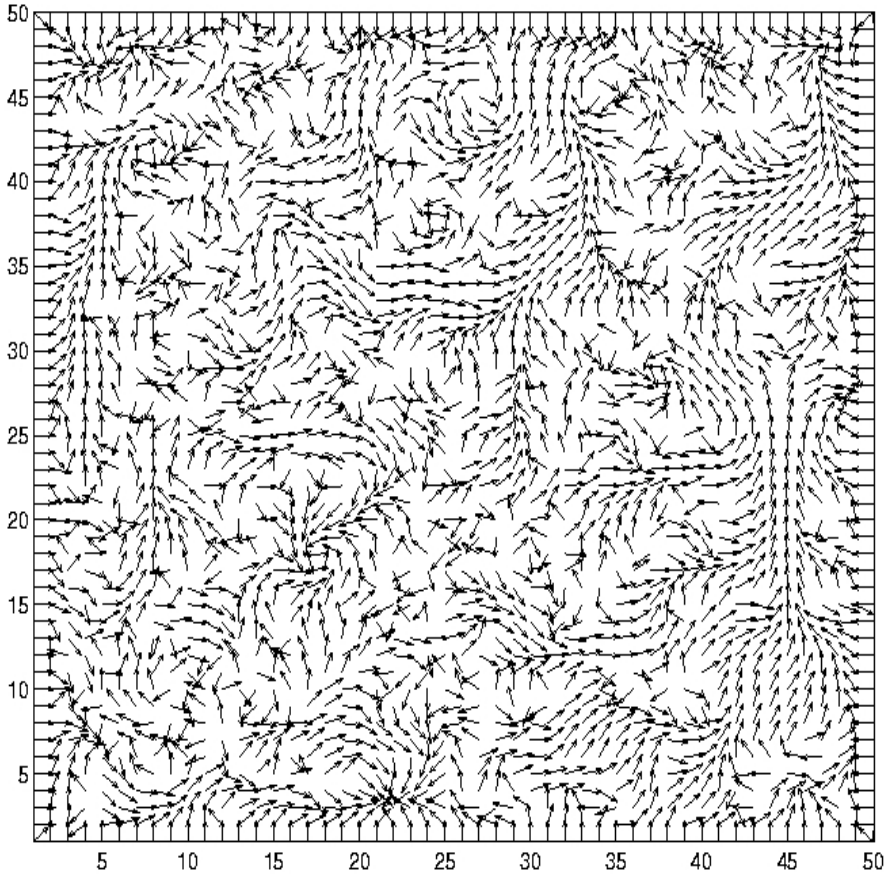
Lowest order terms dictated by symmetry appear here.
Minimal model with predictive power

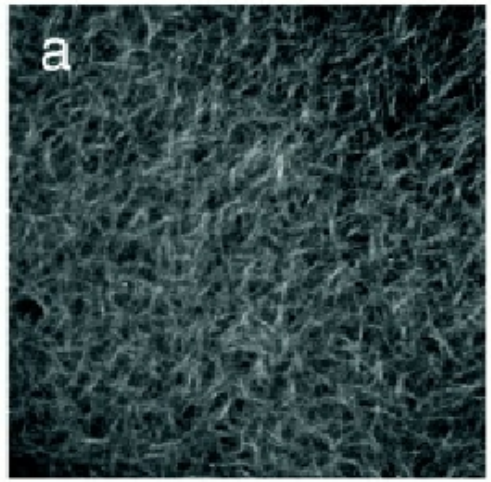
The Equations

$$
\begin{aligned}
\partial_t m_f &= D\nabla^2 m_f - \gamma'_{f\to b} m_f + \gamma'_{b\to f} m_b \\
\partial_t m_b &= -A\nabla\cdot(m_b\mathbf{T}) + \gamma'_{f\to b} m_f - \gamma'_{b\to f} m_b \\
\partial_t \mathbf{T} &= \mathbf{T}(\alpha - \beta|T|^2) + \kappa'\nabla^2\mathbf{T} + \gamma m_b \nabla^2\mathbf{T} \\
&+ \gamma'\nabla m_b\cdot\nabla\mathbf{T} + S'\nabla m_b
\end{aligned}
$$

In scaled variables

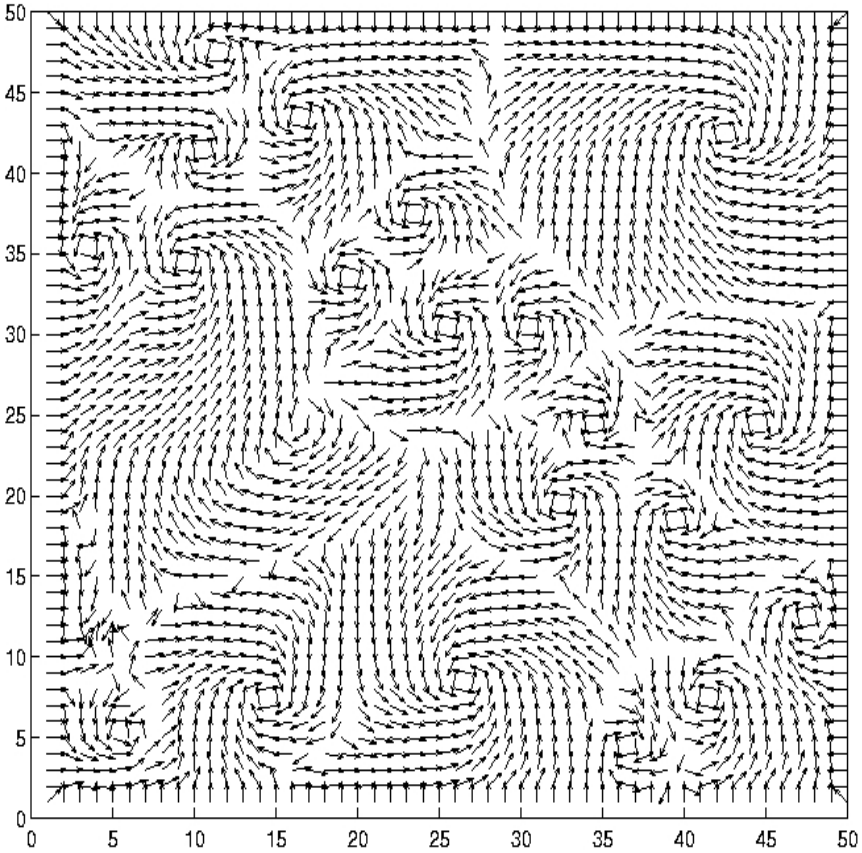
$$
\begin{aligned}
\partial_t m_f &= \nabla^2 m_f - \gamma_{f\to b} m_f + \gamma_{b\to f} m_b \\
\partial_t m_b &= -\nabla.(m_b\mathbf{T}) + \gamma_{f\to b} m_f - \gamma_{b\to f} m_b \\
\partial_t \mathbf{T} &= C\mathbf{T}(1-T^2) + \kappa\nabla^2\mathbf{T} + \\
&+ m_b\nabla^2\mathbf{T} + \epsilon\nabla m_b\cdot\nabla\mathbf{T} + S\nabla m_b
\end{aligned}
$$

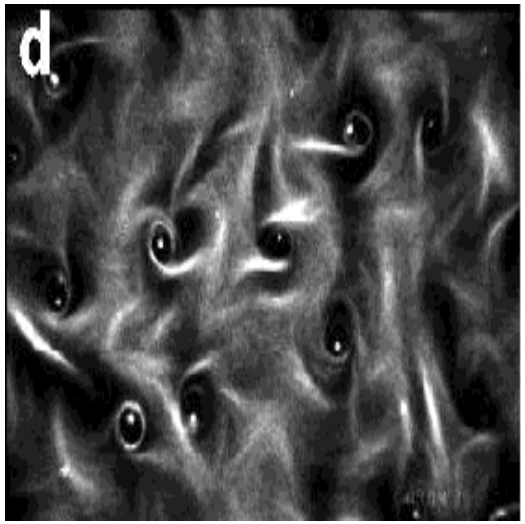




Surrey et. al. Science (2001)

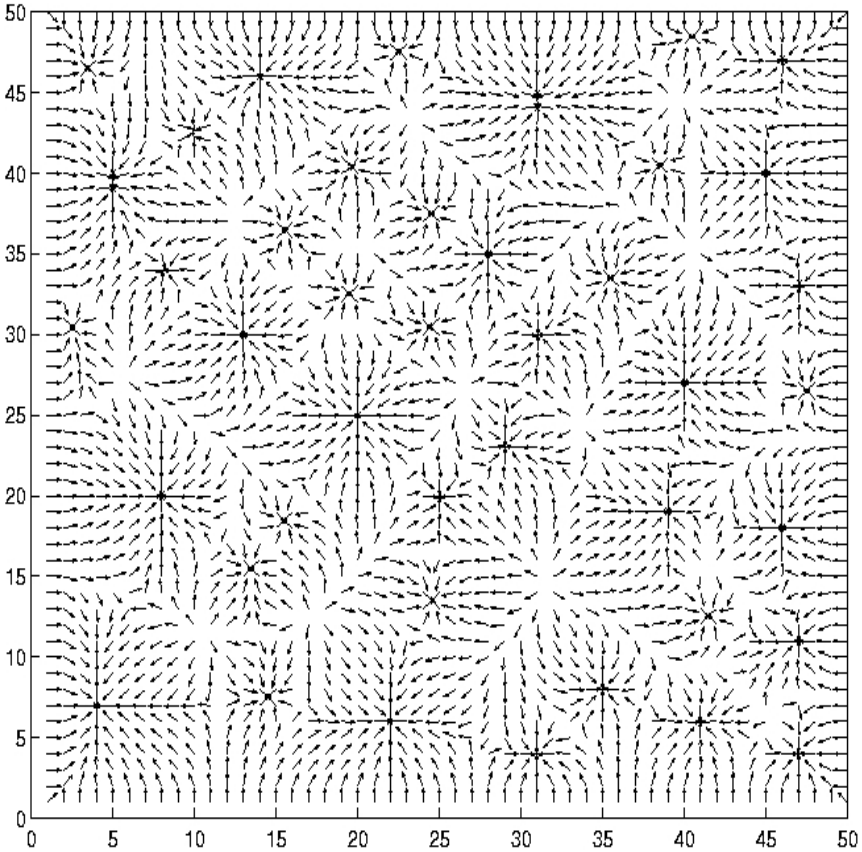
Disordered states

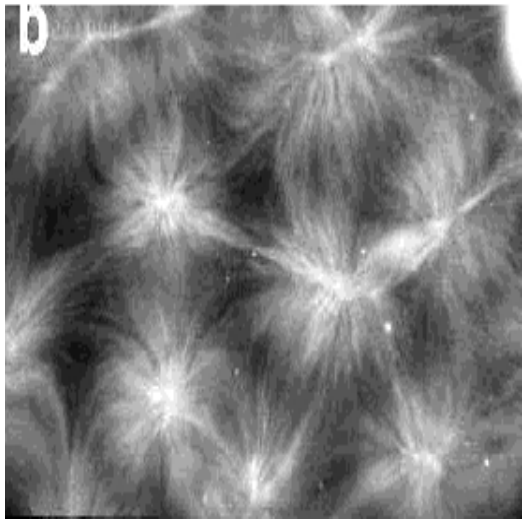




Nedelec et. al. Nature (1997)

A Lattice of vortices

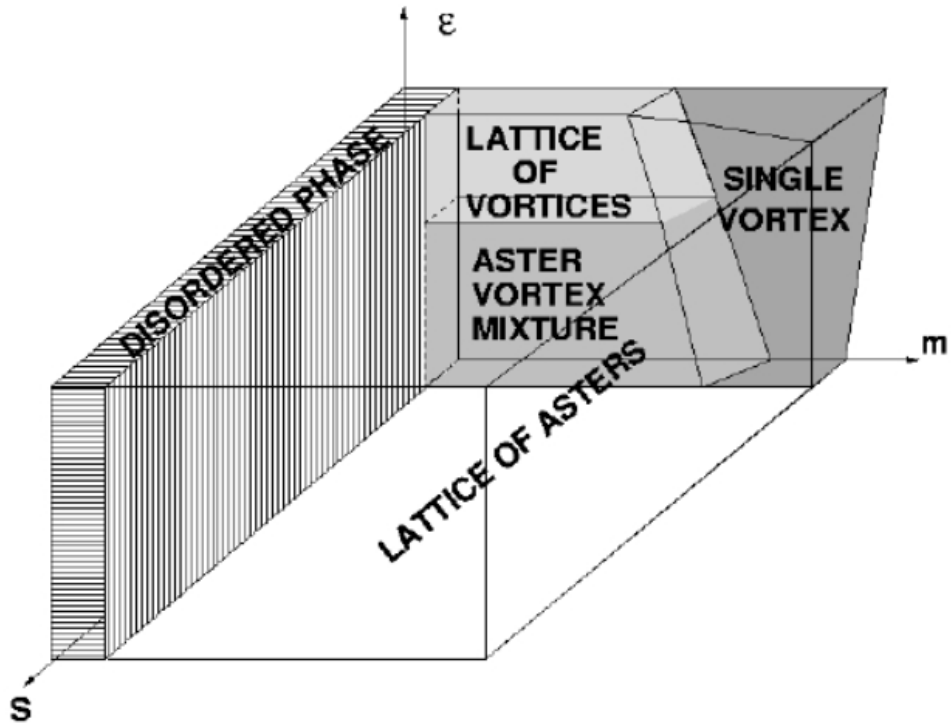




Nedelec et. al. Nature (1997)

A Lattice of asters

A Nonequilibrium "Phase Diagram"

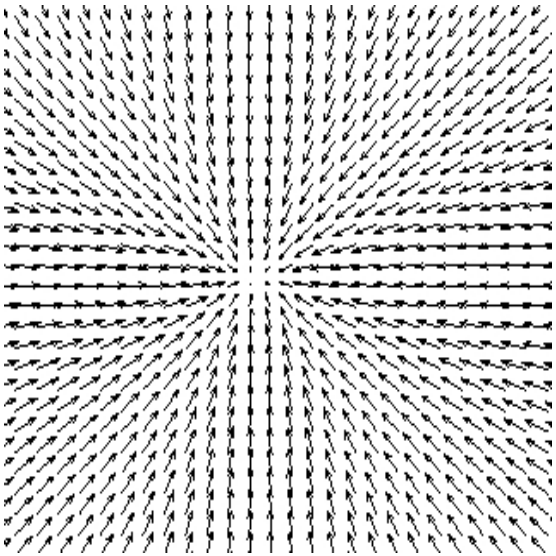


All states seen in experiments represented here. 3-parameter space. Case of unbounded systems. Confinement effects negligible.

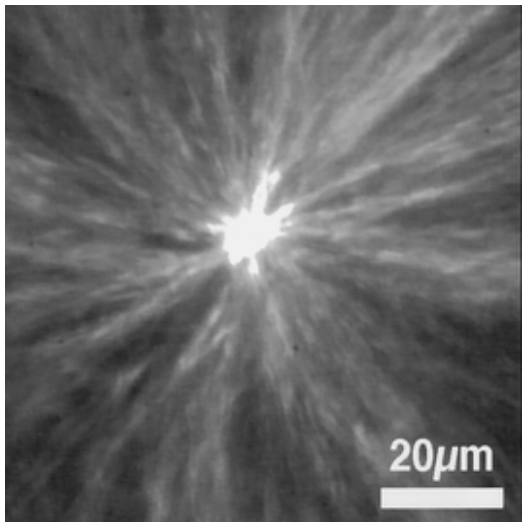
Sankararaman, GIM, Kumar (PRE,'04)

Lots of related work: Aronson & Tsimring ('05), Marchetti & Liverpool ('04,'05), Prost, Joanny, Kruse, Julicher ('04)

Confinement: Aster



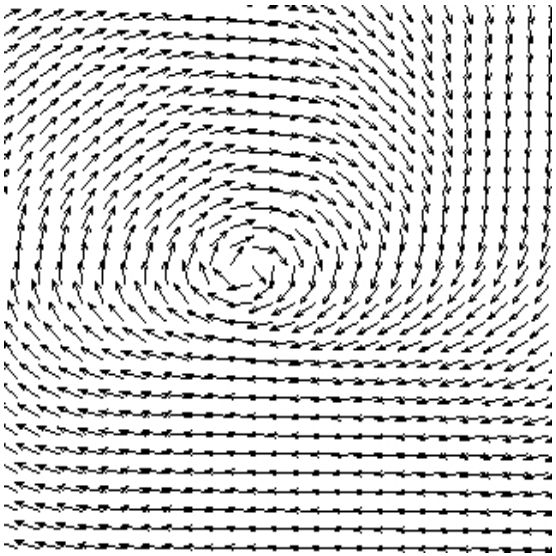
A single aster



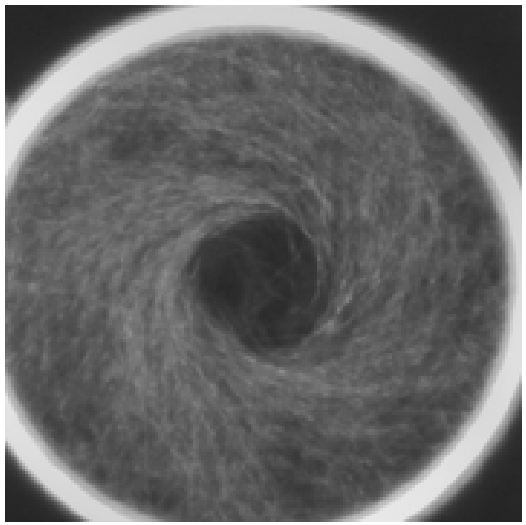
Nedelec et. al. PRL (

Asters or vortices depending on boundary conditions in small systems

Vortex



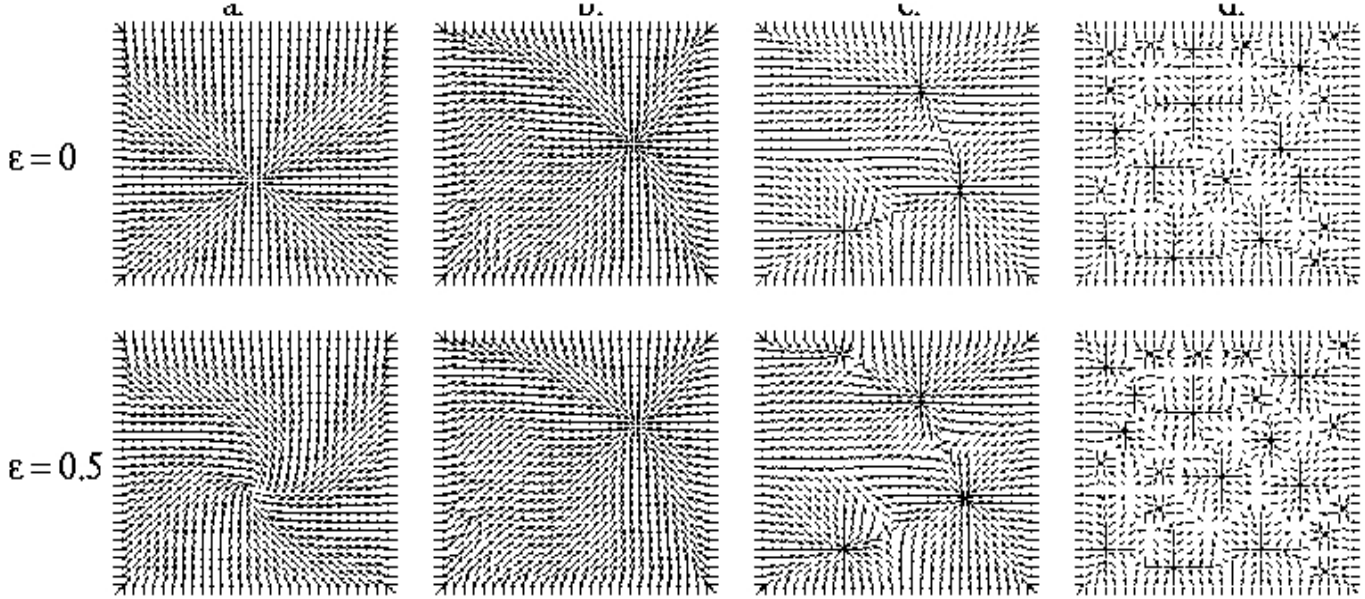
A single vortex



Nedelec et. al. Natur

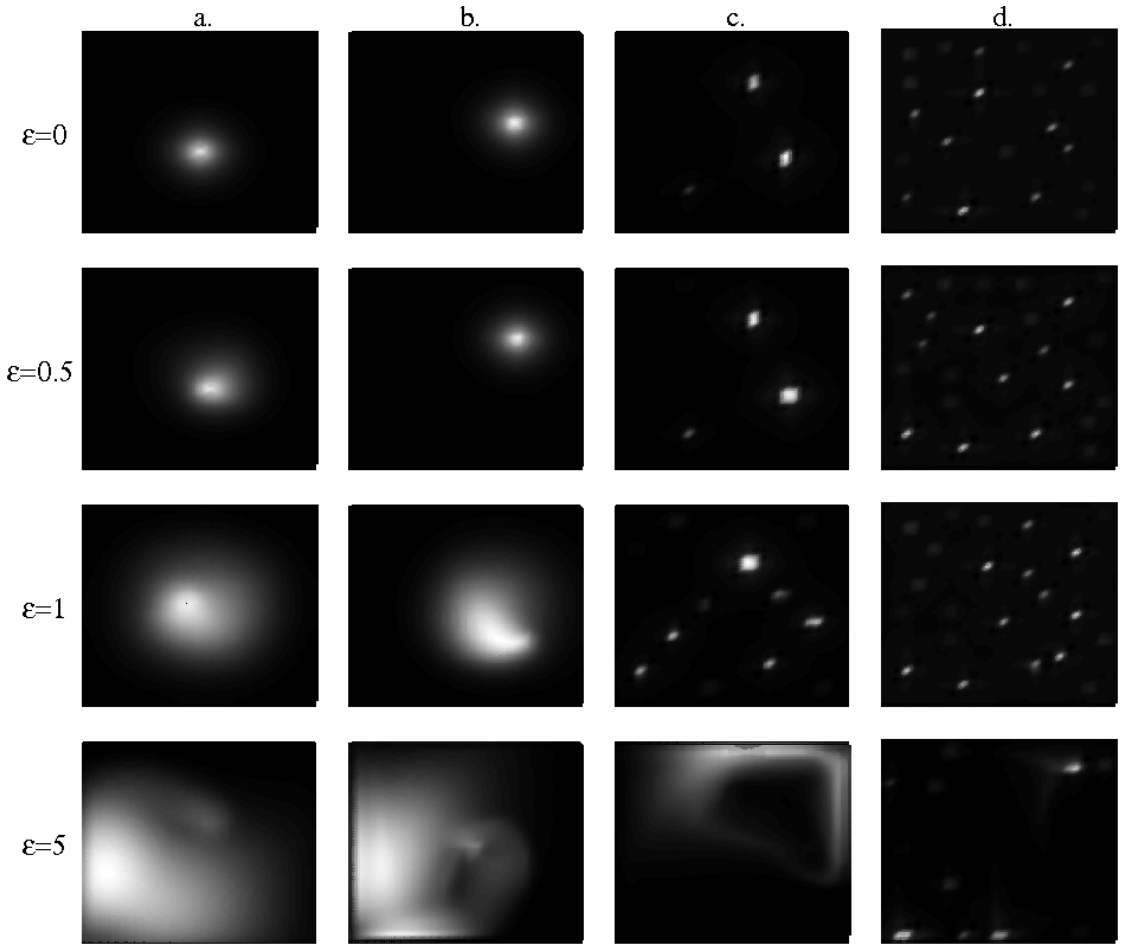
Single vortices generic at large motor densities in confined systems

Finite systems: Nonzero S



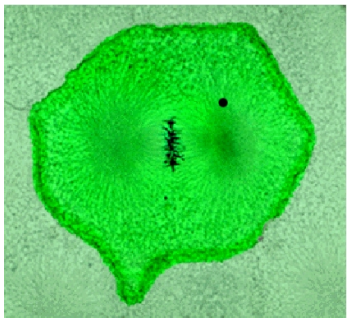
S = 0,0.05,0.5 and 2 from left to right

Free Motor densities: Nonzero S



S = 0,0.05,0.5 and 2 from left to right

All of this work is in: Physica Scripta ('03), Physical Review E('04), Physica A('06)



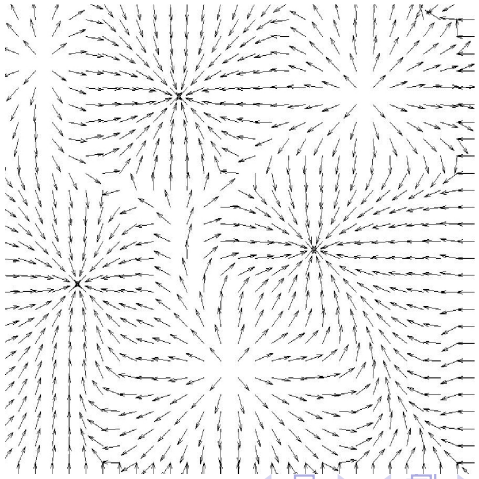
".. it may be useful to think of mitotic spindle formation as a pattern formation problem, which can be modelled using continuum hydrodynamical equations in a small number of variables. The construction of the appropriate set of simplified equations with spindle-like structures as steady state solutions remains an outstanding problem."

Sankararaman, Menon and Kumar, Phys. Scripta ('03)

Two motors: + and -

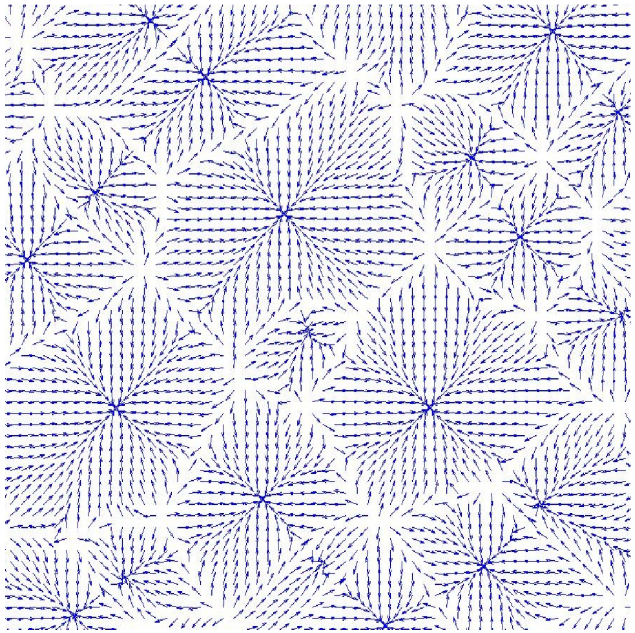
$$
\begin{aligned}
\partial_t m^+ &= D^+ \nabla^2 m^+ - A^+ \nabla \cdot (m^+ \mathbf{T}) \\
\partial_t m^- &= D^- \nabla^2 m^- + A^- \nabla \cdot (m^- \mathbf{T}) \\
\partial_t \mathbf{T} &= \mathbf{T}(\alpha - \beta T^2) + \gamma (m^+ + m^-) \nabla^2 \mathbf{T} \\
&+ \gamma \nabla (m^+ + m^-) \cdot \nabla \mathbf{T} \\
&+ -S \nabla m^+ - S' \nabla m^-
\end{aligned}
$$

- Simpler Lee-Kardar model, but with two motor species
- Outward and inward asters



Two motors: + and -

- Many scans
  1. Vary relative velocities of both motors
  2. Vary relative strength of the S term
  3. Vary relative number densities of both motors
- Fairly clear that spindle-like structures can't be generated this way
- Need new ideas
- What are the principle determinants of coarse-grained models of spindle structure?



Determinants of Spindle Structure

JCB Article

Computer simulations reveal motor properties generating stable antiparallel microtubule interactions

François Nédélec

Cell Biology and Biophysics Program, European Molecular Biology Laboratory, 69117 Heidelberg, Germany

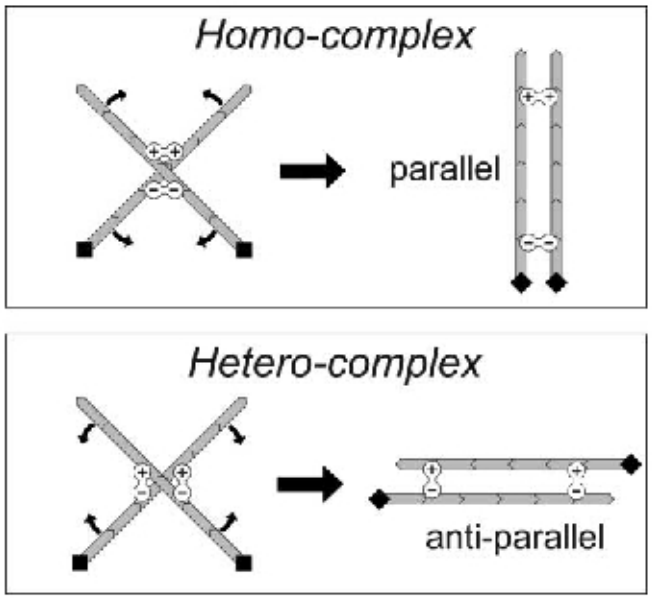


Figure 7. **The zipper effect.** Schematically, the action of homo-complexes on two microtubules produces parallel microtubule

- Role of $\pm$ motor constructs and other heterocomplexes
- Orient antiparallel microtubules
- Favour nematic order where density of $\pm$ constructs large
- Nematic order described by a tensor

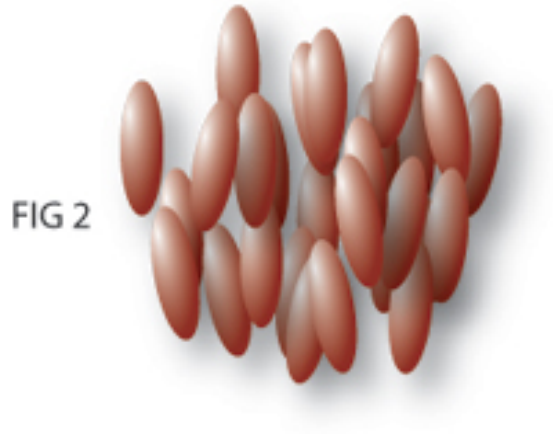
Phases of anisotropic molecules I

The Isotropic Phase

- No orientational or translational order

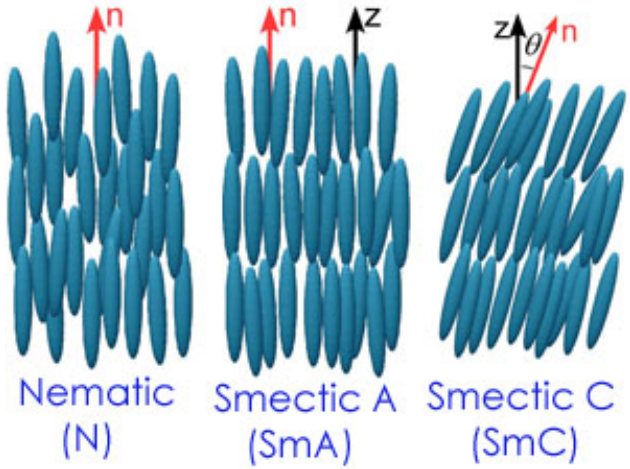
The Nematic Phase

- Nematic phase: Orientational but not translational order
- Isotropic-Nematic transition is weakly first order



Source: Kent State Liquid Crystal Lab

Phases of anisotropic molecules II



Source: http://www.atom.physics.calpoly.edu/~jfernsler

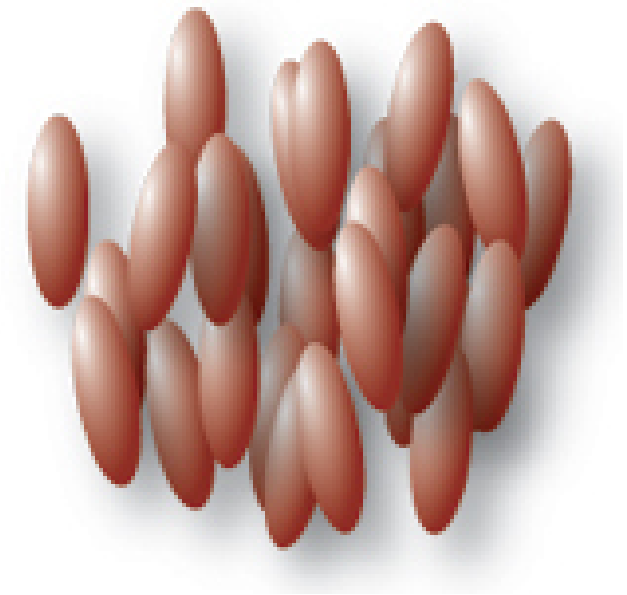
Orientational order with Director **n** description

- Order parameter amplitude ~ 1. Soft orientational degrees of freedom retained.
- Gradient (Frank free energy) cost for variations in $\mathbf{n}$.
- Symmetry $\mathbf{n} \leftrightarrow -\mathbf{n}$
- Symmetry is tensorial (rank 2 tensor), not scalar or vectorial

Parametrizing order in the Nematic Phase

Director description **n**

Order parameter amplitude ~ 1. Soft orientational degrees of freedom retained

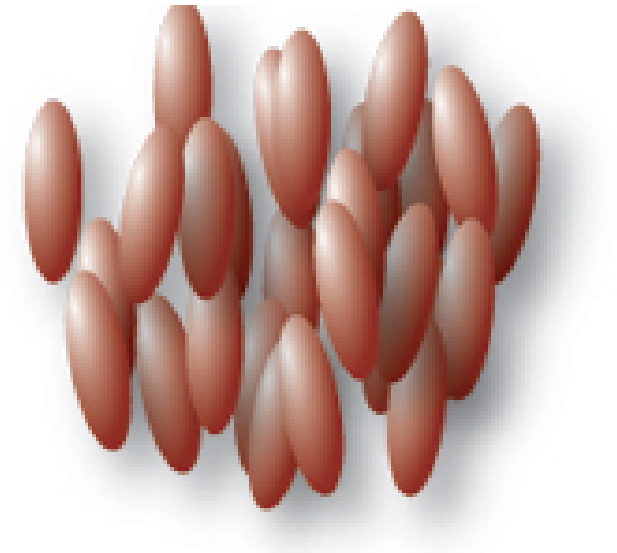


Source: http://www.atom.physics.calpoly.edu/~jfernsler

Ordering tensor $Q_{\alpha\beta}$

Order parameter amplitude can vary. Complete tensorial description with no approximations.

- Orientational order through second-rank, symmetric traceless tensor, $Q_{\alpha\beta}$.
- Principal axes specify axis of ordering.
- Principal values represent strength of ordering.
- Assuming $f(\mathbf{x}, \mathbf{u}, t)$ the molecular orientational distribution function at $\mathbf{x}, t$



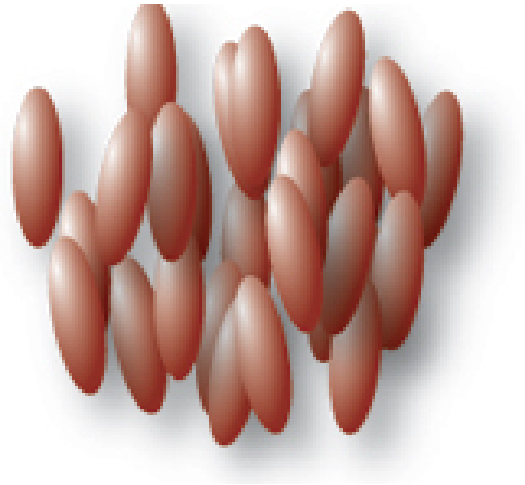
Nematic order:

$$\mathbf{Q}(\mathbf{x}, t) = \int du f(\mathbf{x}, \mathbf{u}, t) \overline{\mathbf{uu}} \equiv \langle \overline{\mathbf{uu}} \rangle$$

Source: http://www.atom.physics.calpoly.edu/~jfernsler

- $\overline{X}$: symmetric traceless part of tensor $\mathbf{X}$

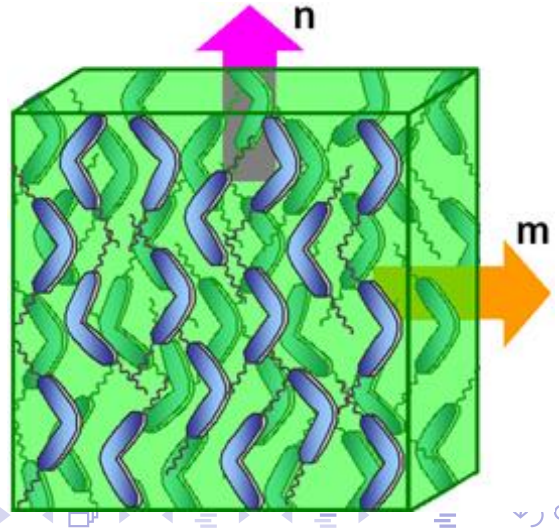
Unixiality and Biaxiality I



- Principal axes specify the director $\mathbf{n}$, the codirector $\mathbf{m}$ and joint normal $\mathbf{p}$.
- If $T \neq 0$, Biaxial Nematic
- Given principal values S and T, the order parameter is

Source: http://www.atom.physics.calpoly.edu/~jfernsler

$$Q_{\alpha\beta} = \frac{3}{2}S(n_\alpha n_\beta - \frac{1}{3}\delta_{\alpha\beta}) + \frac{1}{2}T(m_\alpha m_\beta - p_\alpha p_\beta)$$



- Measure of alignment with $-\frac{1}{3} \leq S \leq \frac{2}{3}$, $0 \leq T < 3S$
- $S = \frac{2}{3}$, $T = 0$ corresponds to uniaxial nematic. $S = 0$ is the isotropic phase.

Landau-Ginzburg-de Gennes Approach

- Landau-Ginsburg functional F from local expansion in rotationally invariant combinations of $\mathbf{Q}(\mathbf{x}, t)$,

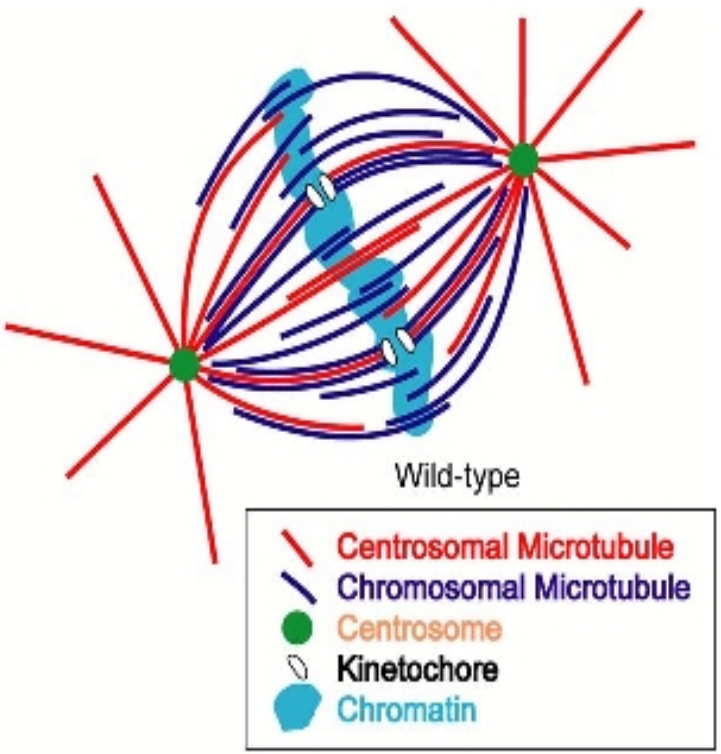
$$\mathcal{F}_h[\mathbf{Q}] = \frac{1}{2} A Tr\mathbf{Q}^2 + \frac{1}{3} B Tr\mathbf{Q}^3 + \frac{1}{4} C (Tr\mathbf{Q}^2)^2 + E'(Tr\mathbf{Q}^3)^2$$

- C and E' positive. E' non-zero for a biaxiality in the bulk
- Add non-local terms from rotationally invariant combinations of order-parameter gradients

$$\mathcal{F}_{el}[\partial\mathbf{Q}] = \frac{1}{2} L_1 (\partial_\alpha Q_{\beta\gamma})(\partial_\alpha Q_{\beta\gamma}) + \frac{1}{2} L_2 (\partial_\alpha Q_{\alpha\beta})(\partial_\gamma Q_{\beta\gamma})$$

- L_1 and L_2 are elastic constants
- Can add surface terms of the same order in gradients. Omit them here.
- $\mathrm{K}_{11} = K_{33}$ (splay = bend) at this order. Equals twist if $L_2 = 0$

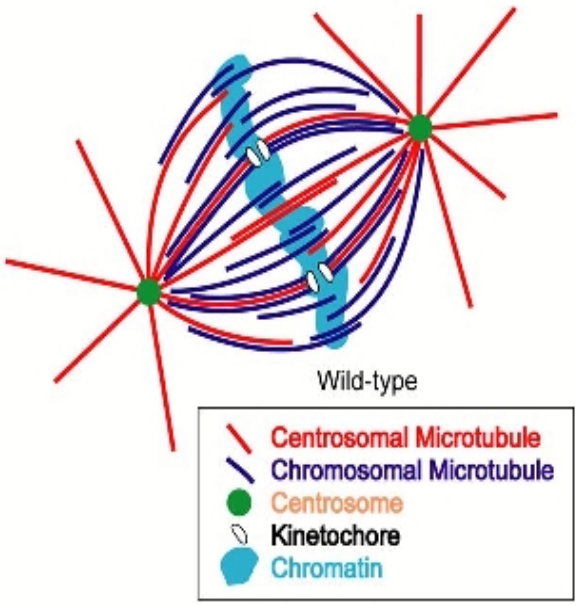
Determinants of Spindle Structure



- Oriented at the centrosomes
- Antiparallel overlap (Think of this as a nematic region)
- A polar-nematic interface
- How can this be stabilized by active processes?
- No understanding of polar-nematic interfaces.
- Isotropic-nematic interfaces (de Gennes, Sluckin, Popa-Nita . . .): Can now test many of these theories

Nedelec, *JCB* (2003)

Determinants of Spindle Structure



- A $\pm$ motor (a complex of a $+$ and a - motor) or a $+X$ motor (a $+$ directed and a cross-linking motor) could act to stabilize antiparallel alignment
- Such motors ineffective in regions of polar alignment.
- $++$ or $--$ motor complexes create regions of local polar alignment (or asters, with addition of the S term)
- Theory to accomodate nematic as well as polar order. Also two species of motor complexes

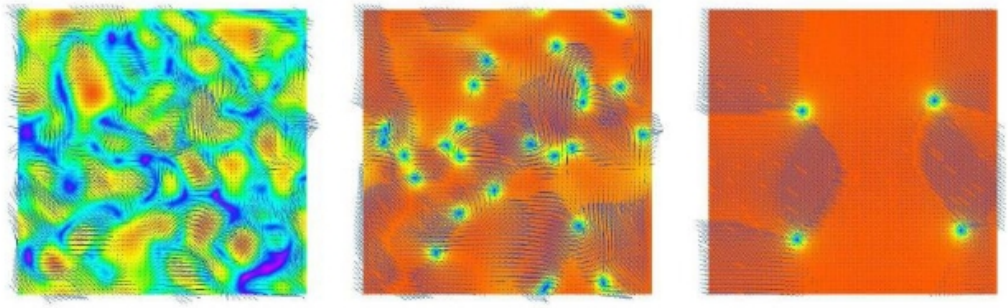
Thoughts

- Anisotropies
- Equations: Many possibilities. Test those which are physically most transparent, intuitive and lowest order in fields and gradients. The "minimal" model?
- Have developed nematic codes in 2 and 3 dimensions.
- Can simulate equations like

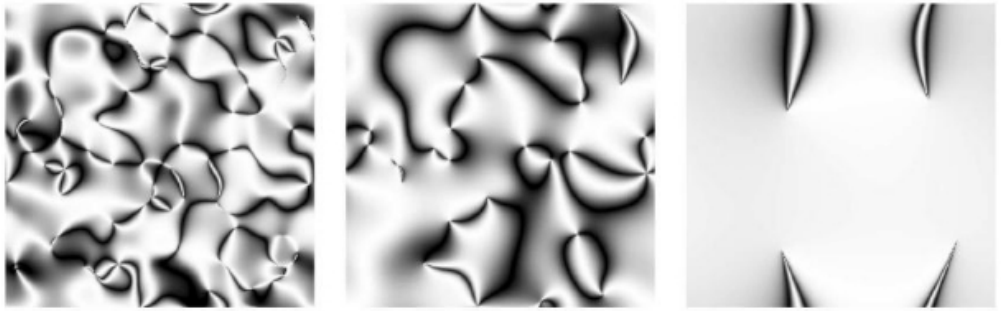
$$\partial_t Q_{ij} = -\frac{\delta F[Q]}{\delta Q_{ij}}$$

- Simulate the underlying equilibrium nematic, growth on quenching, nematic-isotropic interface, topological defect identification, visualization. [Amit Bhattacharjee, Ronojoy Adhikari]

Some illustrative examples



(a) $t = 700$ (b) $t = 2 \times 10^3$ (c) $t = 6 \times 10^4$



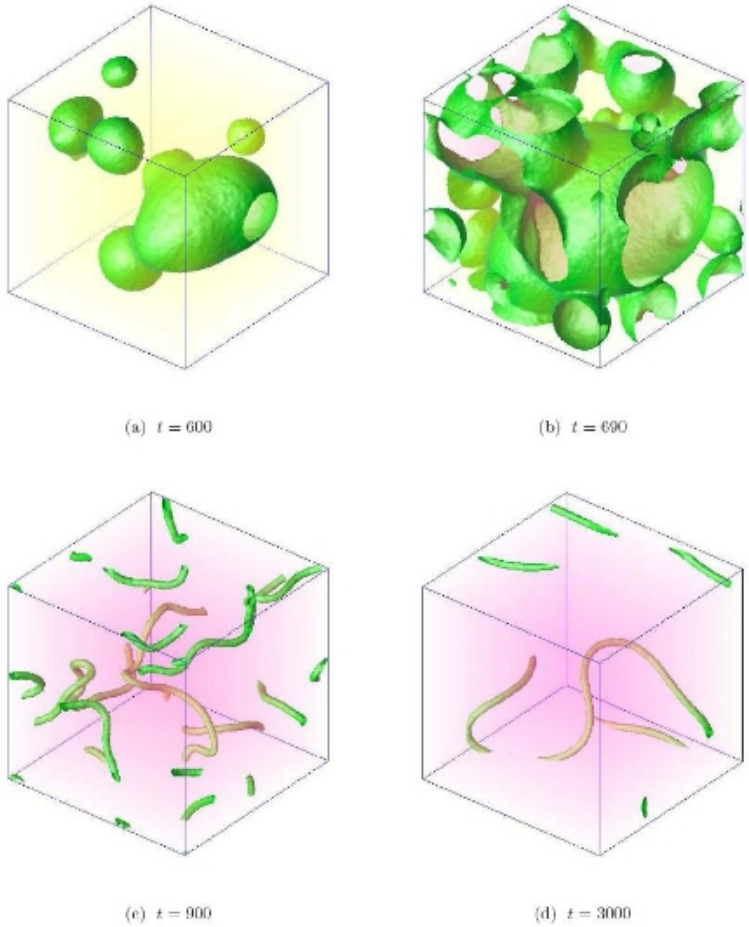
(d) $t = 700$ (e) $t = 2 \times 10^3$ (f) $t = 6 \times 10^4$

Figure 5.1: Uniaxial degree of alignment S and the nematic director field $\mathbf{n}$ on top of that and the corresponding Schlieren textures in a coarsening nematic from the isotropic phase. Topological defects of integer and half - integer charge are clearly observed, as seen in the coloured frames of S in (a)-(c) and the textures in (d)-(f). (a) Shows the formation of defects with coalesce of domains after quench from a random configuration. (c) and (f) show the defects at an early and late stage of the dynamics. The numerical parameters are $A = -0.08, B = -0.5, C = 2.67, E' = 0.0, L_1 = 1.0, L_2 = 0$ and $\Gamma = 0.1$, grid size 256^2 with unit spacing for 6×10^4 time steps.

Coarsening in a two-dimensional nematic.
Numerical identification of topological defects, Schlieren textures

+ **Bhattacharjee, Adhikari** (PRE, 2008)

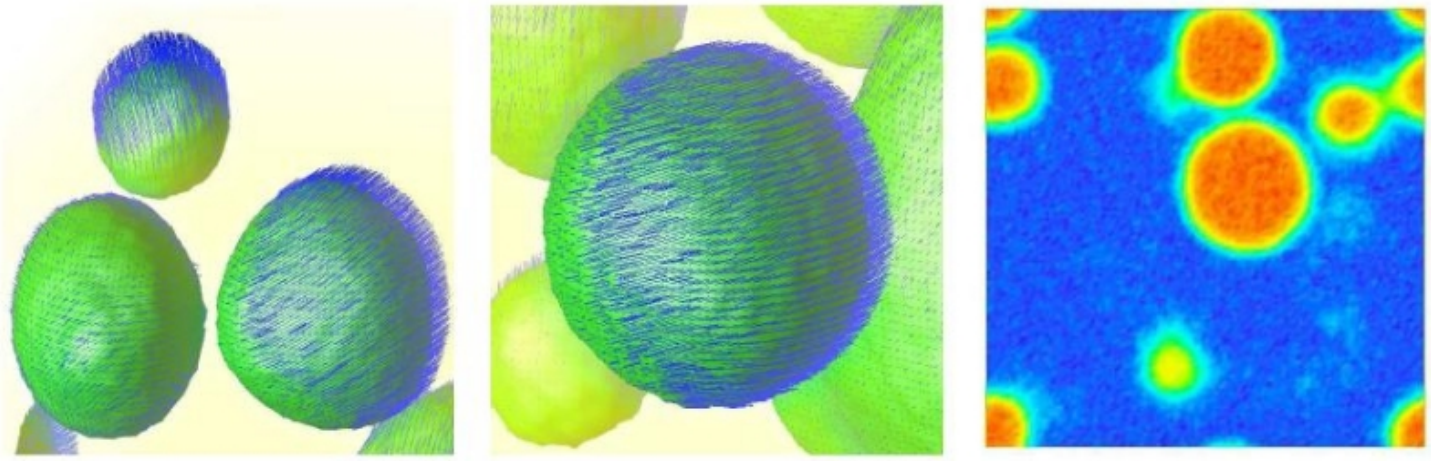
Coarseningin three-dimensional nematics



(a) $t = 600$ (b) $t = 690$

(c) $t = 900$ (d) $t = 3000$

Figure 6.5: Time evolution of uniaxial order in a three dimensional volume. Panel (a) show the emergence of uniaxial nematic droplet in the fluctuating isotropic background. Panel (b) shows the coalescence of droplets to form line defects shown in panel (c). The defects at a late of the kinetics is shown in panel (d). The numerical parameters are $A = 10^{-4}, B = -0.5, C = 2.67, E' = 0, L_1 = 0.01, L_2 = 0, \Gamma = 20.0$ and $k_BT = 2.0807 \times 10^{-7}$. The numerics is performed on a 128^3 grid upto 3×10^3 SRK4 iterations with increment $dt = 1$.



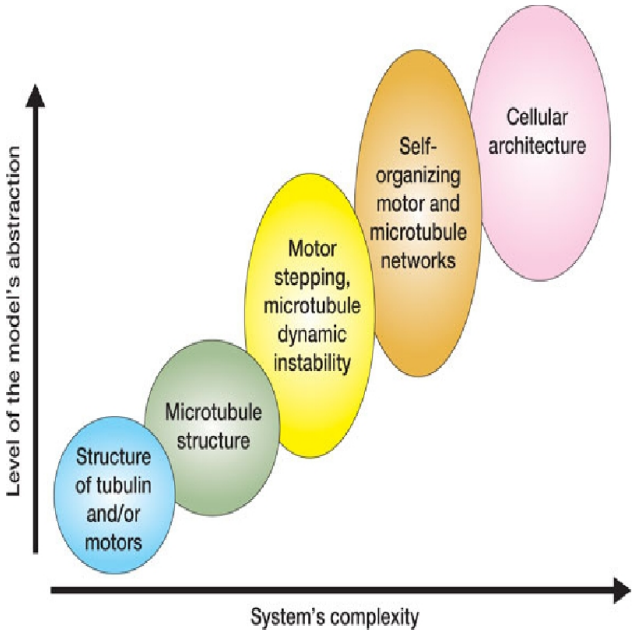
(a) $t = 600$ (b) $t = 600$ (c) $t = 600$

Figure 6.6: Panel (a) and (b) shows the uniaxial order and director field on the surface of nematic droplets in the three dimensional volume. Panel (c) shows the uniaxial order in a x-y plane that slices the three dimensional volume at $z = 20$. The numerical parameters are $A = 10^{-4}, B = -0.5, C = 2.67, E' = 0, L_1 = 0.01, L_2 = 0, \Gamma = 20.0$ and $k_B T = 2.0807 \times 10^{-7}$. The numerics is performed on 128^3 grid upto 3×10^3 SRK4 iterations with increment $dt = 1$.

Nucleation in nematics: Circular three-dimensional droplets in the absence of elastic anisotropy

+ **Bhattacharjee, Adhikari** (*unpublished*)

Where such treatments fit



- Long-wavelength treatment, symmetry based.
- "The unreasonable effectiveness of hydrodynamics .."
- Few parameters. Must appeal to more microscopic approaches to constrain them.
- Complementary to other methods
- Simple, intuitive, "right" variables

Karsenti, Nedelec, Surrey, *Nature Cell Biology* (2006)

The Importance of Coarsegraining

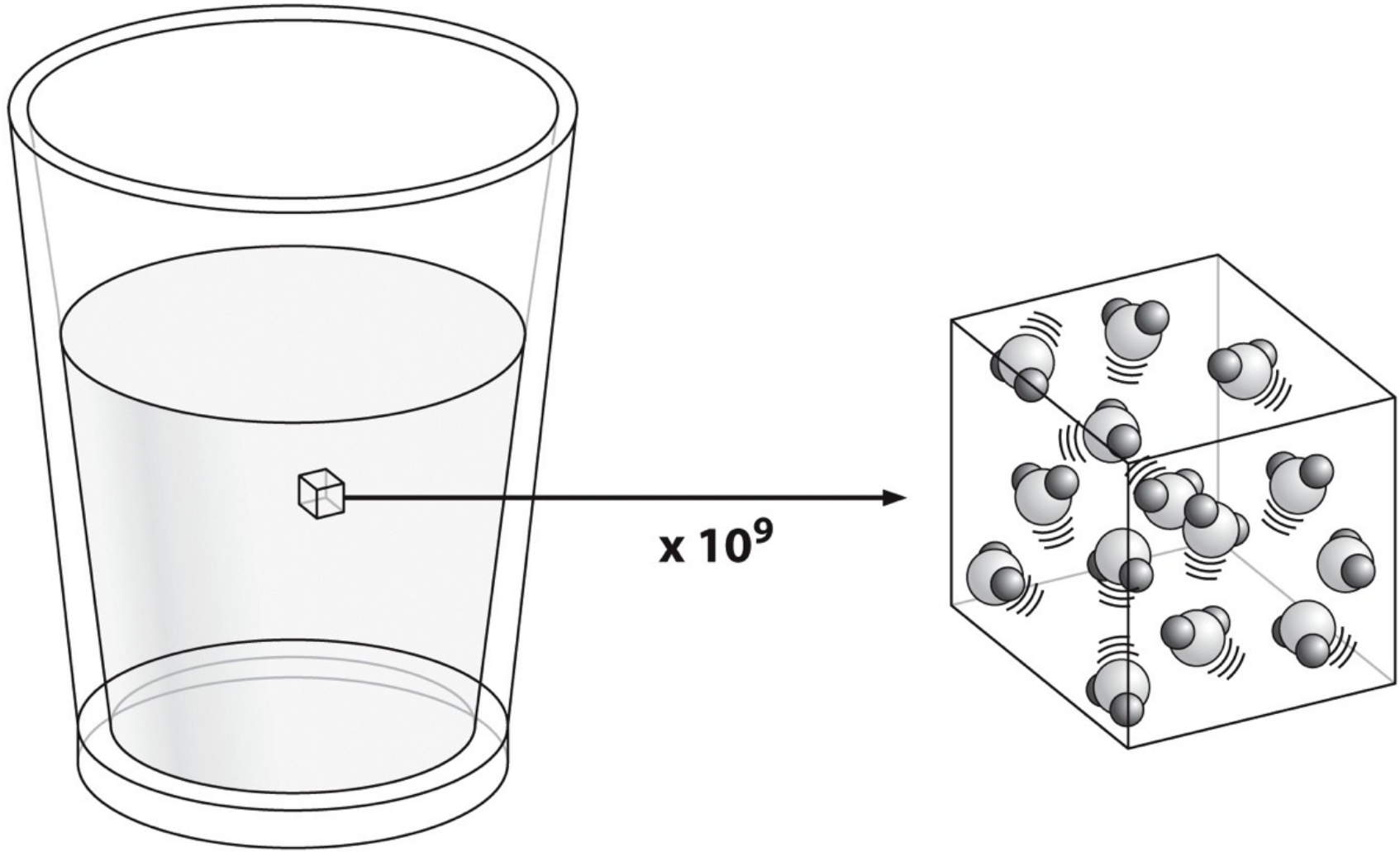


Figure 12.1 Physical Biology of the Cell (© Garland Science 2009)

What survives coarsegraining?

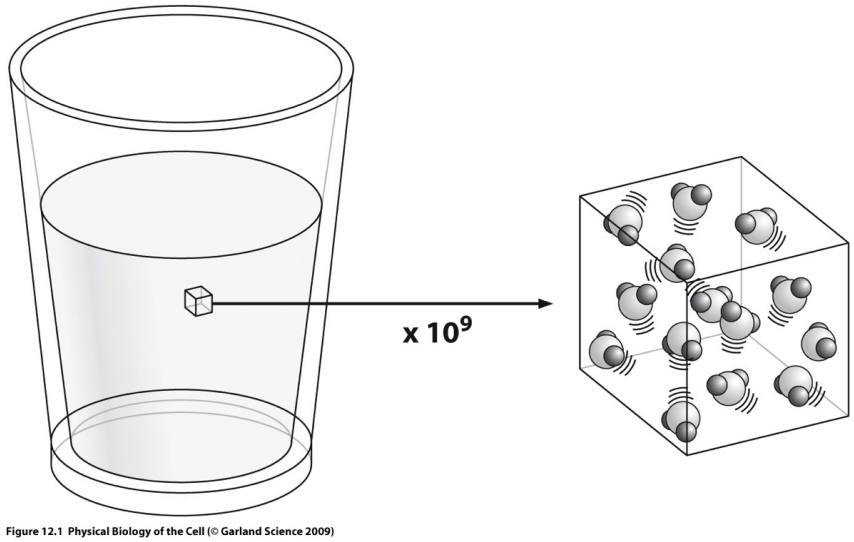


Figure 12.1 Physical Biology of the Cell (© Garland Science 2009)

- Slow variables (hydrodynamic modes) *vs.* fast variables (atomic motions)
- Slow variables represent modes which decay ever more slowly as their wavelength increases
- Uniform space variations of slow variables cost no energy, relaxation time is infinite
- Conservation Laws and Broken symmetries

Equations of Motion

$$\begin{aligned}
\frac{\partial \epsilon}{\partial t} &= -\nabla \cdot j^{\epsilon} \\
\frac{\partial \rho}{\partial t} &= -\nabla \cdot g \\
\frac{\partial \mathbf{g}_i}{\partial t} &= -\nabla_j \pi_{ij}
\end{aligned}$$

The current j^{ϵ} is the energy current and π_{ij} is the momentum current tensor, related to the stress tensor.

Conserved momentum density acts as a current for another conserved density, the mass (equivalently, number) density
Write currents j^ϵ and π_{ij} in terms of the hydrodynamic fields ρ, ϵ and $\mathbf{g}$.

Constitutive relations

Close to thermal equilibrium, rules for constructing such constitutive relations

Very generally, these rules indicate

$$\frac{\partial \Phi_\mu(\mathbf{x},t)}{\partial t} = V_\mu(\mathbf{x}) - \Gamma_{\mu\nu}\frac{\delta \mathcal{H}}{\delta \Phi_\nu(\mathbf{x})}$$

$V_\mu(\mathbf{x})$ is the non-dissipative or streaming velocity.

Second term induces dissipation.

All neglected microscopic degrees of freedom give rise to the dissipative terms

$\Gamma_{\mu\nu}$ is called the dissipative tensor

Note that $\Phi_\mu(\mathbf{x}, t)$ can only couple to $\frac{\delta\mathcal{H}}{\delta\Phi_\nu(\mathbf{x})}$ if these terms possess different signs under time-reversal.

Also, (Onsager), $\Gamma_{\mu\nu}$ must be a symmetric tensor at zero magnetic field.

Also, contribution from broken symmetry variables

Conserved fields are always hydrodynamical.

But broken symmetry variables also share the same property that making very long wavelength distortions in the broken symmetry field cost vanishingly small energy as the wavelength tends to infinity.

Identifying the broken-symmetry variables not always straightforward (e.g. superfluids)

Hydrodynamic description of fluids with internal order must account for additional modes arising out of the fact that the ordering represents a broken symmetry.

For small deviations fom equilibrium, derive an equation for entropy generation and casts it in terms of the product of a flux and a force.

Such fluxes vanish at thermodynamic equilibrium.

Close to equilibrium, it is reasonable to expect that fluxes should have a smooth expansion in terms of forces.

For example, for the simple fluid without dissipation, we have

$$\begin{aligned} \mathbf{g} &= \rho \mathbf{v} \\ \pi_{ij} &= p\delta_{ij} + v_j g_i = -\sigma_{ij} + \rho v_i v_j \\ \mathbf{j}^{\epsilon} &= (\epsilon + p)\mathbf{v} = \left(\epsilon_0 + p + \frac{\rho v^2}{2}\right) \end{aligned}$$

The mass conservation equation is just

$$\frac{\partial \rho}{\partial t} = -\nabla \cdot (\rho \mathbf{v}),$$

while the momentum conservation equation is

$$\frac{\partial \mathbf{g}_i}{\partial t} = \frac{\partial \rho \mathbf{v}_i}{\partial t} = -\nabla_j \pi_{ij} = -\nabla_i p - \nabla_j (\rho v_i v_j)$$

This is Eulers equation, usually written as

$$\frac{\partial \mathbf{v}}{\partial t} + (\mathbf{v} \cdot \nabla)\mathbf{v} = \frac{-1}{\rho} \nabla p$$

The dissipative contribution to the stress tensor is accounted for by adding a term $\sigma^{'}_{ij}$ to the stress tensor

$$\pi_{ij} = p\delta_{ij} + \rho v_i v_j - \sigma^{'}_{ij}$$

Dissipation can only arise from velocity gradients, since any constant term added to the velocity can be removed via a Galilean transformation.
The dissipative coefficient coupling the stress tensor to the velocity gradient is a fourth rank tensor

$$\sigma^{'}_{ij} = \eta_{ijkl}\nabla_k v_l$$

However, symmetry requires that

$$\sigma^{'}_{ij} = \eta(\nabla_i v_j + \nabla_j v_i - \frac{2}{3}\delta_{ij}\nabla\cdot\mathbf{v}) + \zeta\delta_{ij}\nabla\cdot\mathbf{v}$$

This gives the Navier-Stokes equations, with incompressibility

$$\frac{\partial \rho}{\partial t} = 0 = -\nabla \cdot (\rho \mathbf{v}) = -\nabla \cdot \mathbf{v}$$

Thus

$$\rho \frac{\partial \mathbf{v}}{\partial t} + \rho(\mathbf{v} \cdot \nabla)\mathbf{v} = -\nabla p + \eta \nabla^2 \mathbf{v}$$

along with the constraint $\nabla \cdot \mathbf{v} = 0$.

For a nematic fluid, need equation of motion for the director $\mathbf{n}$ (or for the $\mathbf{Q}_{\alpha\beta}$ tensor) in addition to equations for the conservation of matter, momentum and energy.

Distortions of configurations of the nematic order parameter field also contribute to stress tensor

Director is aligned with the local molecular field in equilibrium; Distortions away from molecular field direction must relax to minimize the free energy. The local molecular field in the equal Frank constant approximation as

$$h_i = K\nabla^2 n_i$$

Director does not change under rigid translations at constant velocity. Leading coupling of $\mathbf{n}$ to $\mathbf{v}$ must involve gradients of $\mathbf{n}$.

$$\frac{\partial n_i}{\partial t} - \lambda_{ijk}\nabla_j v_k + X_i^{'} = 0$$

where $X^{'}$ is the dissipative part of the current.

Dissipative part can be written as

$$X_i^{'} = \delta_{ij}^T \frac{1}{\gamma} h_j$$

where γ is a dissipative coefficient. Projector isolates components of the fluctuation in plane perpendicular to the molecular field direction. Constraint $\mathbf{n} \cdot \partial \mathbf{n}/\partial t = 0$ implies only two independent components of the tensor λ_{ijk}, thus

$$\lambda_{ijk} = \frac{1}{2}\lambda(\delta_{ij}^T n_k + \delta_{ik}^T n_j) + \frac{1}{2}\lambda_2(\delta_{ij}^T n_k - \delta_{ik}^T n_j)$$

where

$$\delta_{ij}^T = \delta_{ij} - n_i n_j$$

Under a rigid rotation

$$\frac{\partial n_i}{\partial t} = \omega \times \mathbf{n} = \frac{1}{2}(\nabla \times \mathbf{v}) \times \mathbf{n}$$

so coefficient λ_2 of the antisymmetric part must be -1.

Final equation of motion for the director

$$\partial_t n_i + \mathbf{v}\cdot\nabla n_i + \omega_{ij} n_j = \delta^T_{ij}\left(\lambda u_{ij} n_j + \frac{h_i}{\gamma}\right)$$

The coupling of $\mathbf{n}$ to $\mathbf{v}$ leads to an additional term in the reactive (non-dissipative) part of the stress tensor.

$$\sigma^R_{ij} = -p\delta_{ij} + \lambda_{kji} h_k$$

where p is the normal fluid pressure and λ_{kji} follows from the definitions above.

All dissipative coefficients tensorial in character. Two thermal conductivity coefficients

$$\kappa_{ij} = \kappa_{\parallel} n_i n_j + \kappa_{\perp}\delta^T_{ij}$$

and five viscosities

$$\begin{aligned}
\sigma'_{ij} \;=\; & 2\nu_2 A_{ij} + 2(\nu_3-\nu_2)[A_{ik}n_k n_l + A_{jk} n_i n_k] \\
& -(\nu_4-\nu_2)\delta_{ij}A_{kk} - 2(\nu_1+\nu_2-2\nu_3) n_i n_j n_k n_l A_{kl} \\
& +(\nu_5-\nu_4+\nu_2)[\delta_{ij} n_k n_l A_{kl} + n_i n_j A_{kk}]
\end{aligned}$$

These equations, representing the response close to equilibrium of the nematic fluid, must be supplemented with additional terms for the modeling of the active fluid.

How does one construct such terms?

The theory of active gels

Broadly equivalent to theories for active fluids (Ramaswamy, Simha, Rao, Hatwalne . . .).

Specifically motivated for sub-cellular elasticity, cell crawling

Kruse, Julicher, Prost, Joanny. . .)

Starting point: Cytoskeletal gels are viscoelastic materials. Deform: at short times get elastic response

$$\sigma = G\gamma$$

where σ is the shear stress, G is the shear modulus and γ the strain.
At long times, get fluid or viscous response

$$\sigma = \eta\dot{\gamma}$$

Characteristic time of viscoelastic relaxation is then

$$\tau = \frac{\eta}{G}$$

Maxwell model, spring and dashpot in series

$$\dot{\gamma} = \frac{\dot{\sigma}}{G} + \frac{\sigma}{\eta}$$

Or

$$\sigma + \tau\dot{\sigma} = \eta\dot{\gamma}$$

Suppose suddenly shear at constant rate $\dot{\gamma}$.

$$\sigma(t) = \eta\dot{\gamma}\left[1 - \exp\left(-t/\tau\right)\right]$$

Passive gel: Viscoelasticity via a Maxwell model

Deviatoric stress $\sigma_{\alpha\beta}$ related to the strain rate tensor $v_{\alpha\beta} = \frac{1}{2}\left(\partial_\alpha v_\beta + \partial_\beta v_\alpha\right)$ where v_α is the velocity field in the gel, via

$$\frac{\partial \sigma_{\alpha\beta}}{\partial t} + \frac{\sigma_{\alpha\beta}}{\tau} = 2E v_{\alpha\beta}$$

Add convective term, term representing the effects of local rotation of the fluid: Convected Maxwell model.
Polar order in active gels described by a free-energy-like expression from theory of polar nematic liquid crystals.

$$\begin{aligned}\mathcal{F} &= \int d\mathbf{r}[\frac{K_1}{2}(\nabla\cdot\mathbf{p})^2 + \frac{K_2}{2}(\mathbf{p}\cdot(\nabla\times\mathbf{p}))^2 + \frac{K_3}{2}(\mathbf{p}\times(\nabla\times\mathbf{p}))^2 \\ &+ k\nabla\cdot\mathbf{p} - \frac{h_\parallel^0}{2}\mathbf{p}^2]\end{aligned}$$

Active gel

Hydrodynamic theory of active gels (Julicher, Kruse, Prost, Joanny ..) identifies, along classical lines, fluxes and forces.

Hydrodynamic description contains phenomenological parameters, called Onsager coefficients.

Fluxes are mechanical stress, $\sigma_{\alpha\beta}$ rate of change of polar order (the polarization) $\dot{\mathbf{P}}$ and the rate of consumption of ATP per unit volume r.

Force conjugate to the ATP consumption rate is the chemical potential difference $\Delta\mu$ between ATP and the products of ATP hydrolysis. Force conjugate to changes in the polarization is the field $\mathbf{h}$.

The force conjugate to the stress tensor is the velocity gradient tensor $\partial_\alpha u_\beta$. Expand into traceless symmetric, pure trace and antisymmetric parts.

Construct equations of motion for the deviatoric stress, using the convected Maxwell model

Equation must couple mechanical stress and the polarization field. Also include a term coupling activity to the stress.

$$\begin{aligned} 2\eta u_{\alpha\beta} &= \left((1+\tau\frac{D}{Dt}\right)[\sigma_{\alpha\beta}+\zeta\Delta\mu q_{\alpha\beta}+\tau A_{\alpha\beta} \\ &- \frac{\nu}{2}(p_\alpha h_\beta + p_\beta h_\alpha - \frac{2}{3}h_\gamma p_\gamma \delta_{\alpha\beta})] \end{aligned}$$

Co-rotational derivative is

$$\frac{D}{Dt}\sigma_{\alpha\beta} = \left(\frac{\partial}{\partial t} + v_\gamma \frac{\partial}{\partial r_\gamma}\right)\sigma_{\alpha\beta} + \left[\omega_{\alpha\gamma}\sigma_{\gamma\beta} + \omega_{\beta\gamma}\sigma_{\gamma\alpha}\right],$$

Tensor $A_{\alpha\beta}$ (geometrical non-linearities): $q_{\alpha\beta} = \frac{1}{2}(p_\alpha p_\beta - -\frac{1}{3}p^2\delta_{\alpha\beta})$.

The antisymmetric part of the stress tensor leads to torques on the fluid and is obtainable from

$$\sigma^a_{\alpha\beta} = \frac{1}{2}\left(p_\alpha h_\beta - p_\beta h_\alpha\right)$$

Viscoelastic relaxation time is τ, ν_1 describes the coupling between mechanical stresses and the polarization field, ζ is the coefficient of active stress generation, acting to couple activity to the stress.

The second flux, defined from the rate of change of polarization is given by

$$\dot{\mathbf{P}} = \frac{D\mathbf{P}}{Dt}$$

where, as earlier,

$$\frac{D}{Dt}p_\alpha = \left(\frac{\partial}{\partial t} + v_\gamma \frac{\partial}{\partial r_\gamma}\right) p_\alpha + \omega_{\alpha\beta} p_\beta$$

The Onsager relation for the polarization is

$$\frac{D}{Dt}p_\alpha = \frac{1}{\gamma_1}h_\alpha + \lambda_1 p_\alpha \Delta\mu - \nu_1 v_{\alpha\beta}p_\beta - \bar{\nu}_1 v_{\beta\beta}p_\alpha$$

Several phenomenological parameters, such as the rotational viscosity γ_1 which characterizes dissipation from the rotation of the polarization as well as the constants ν_1 and $\bar{\nu}_1$.

Equation for the rate of consumption of ATP. This takes the form

$$r = \Lambda\Delta\mu + \zeta p_\alpha p_\beta v_{\alpha\beta} + \bar{\zeta} v_{\alpha\alpha} + \lambda_1 p_\alpha h_\alpha$$

These are simple but generic equations representing the basic symmetries of the problem.

Interesting consequences: an active polar gel can exhibit spontaneous motion as well as defects in the polar ordering which are dynamic in character

These ideas have been applied to the study of the motion of the cell lamellipodium and to the organization of microtubules by molecular motors.

The generality of these equations follow from the fact that they are motivated principally by symmetry considerations.

But they make a large number of assumptions and there are many coefficients which appear to be largely undetermined

How can one "derive" such equations?

The importance of the field of active matter is that it can suggest ideas for describing the unusual mechanical properties of living systems, while providing a largely self-consistent framework for calculations.

Must calculate and benchmark more against experimental data from biology to understand the limitations and the power of such approaches.