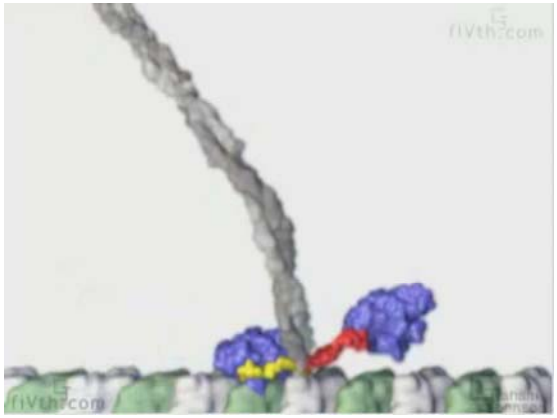
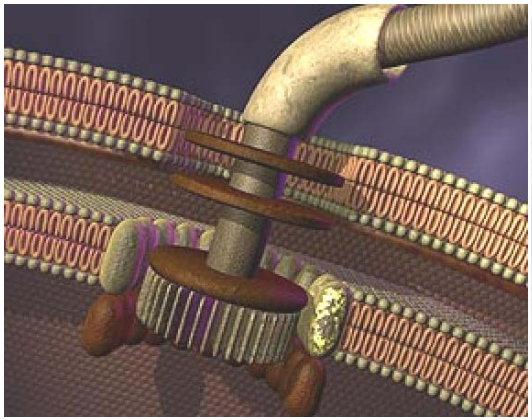
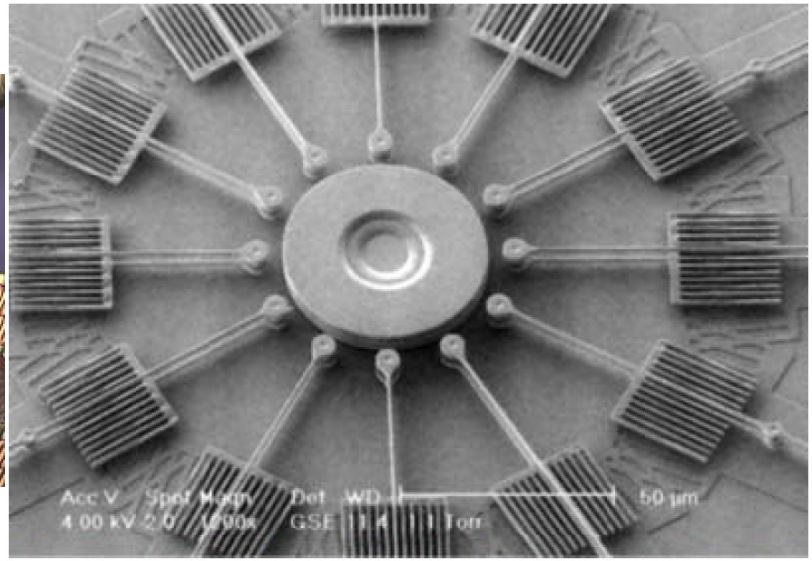
Biological Machines, Cell Mechanics and Nanotechnology Part III







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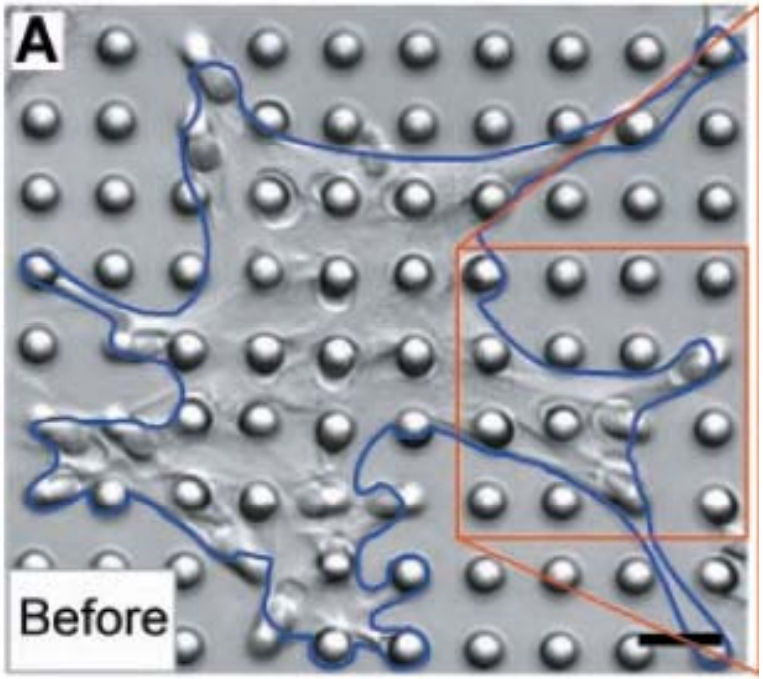
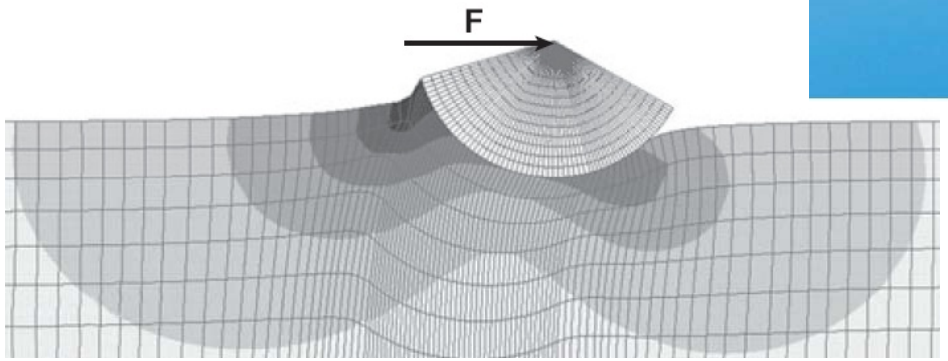
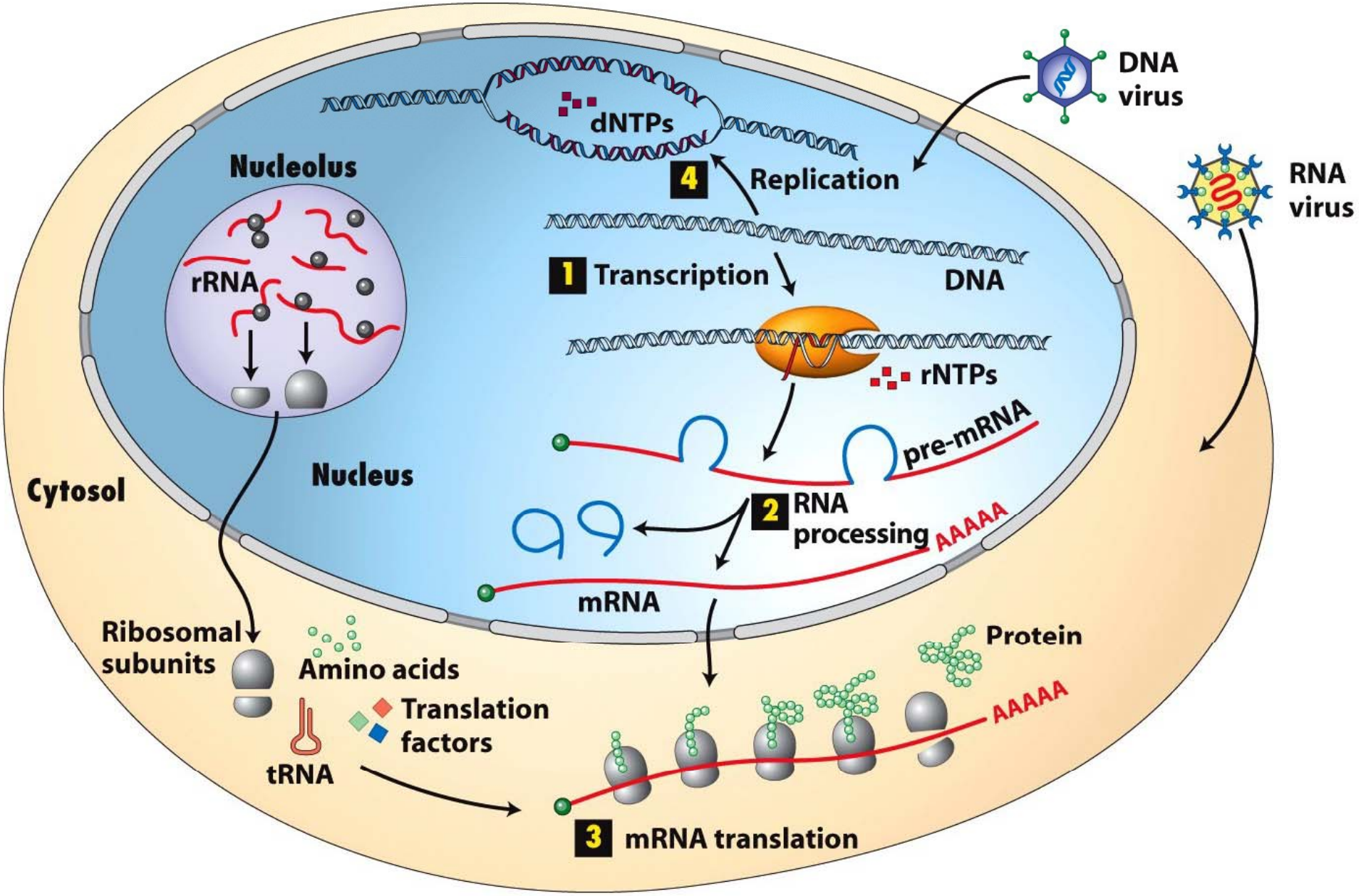
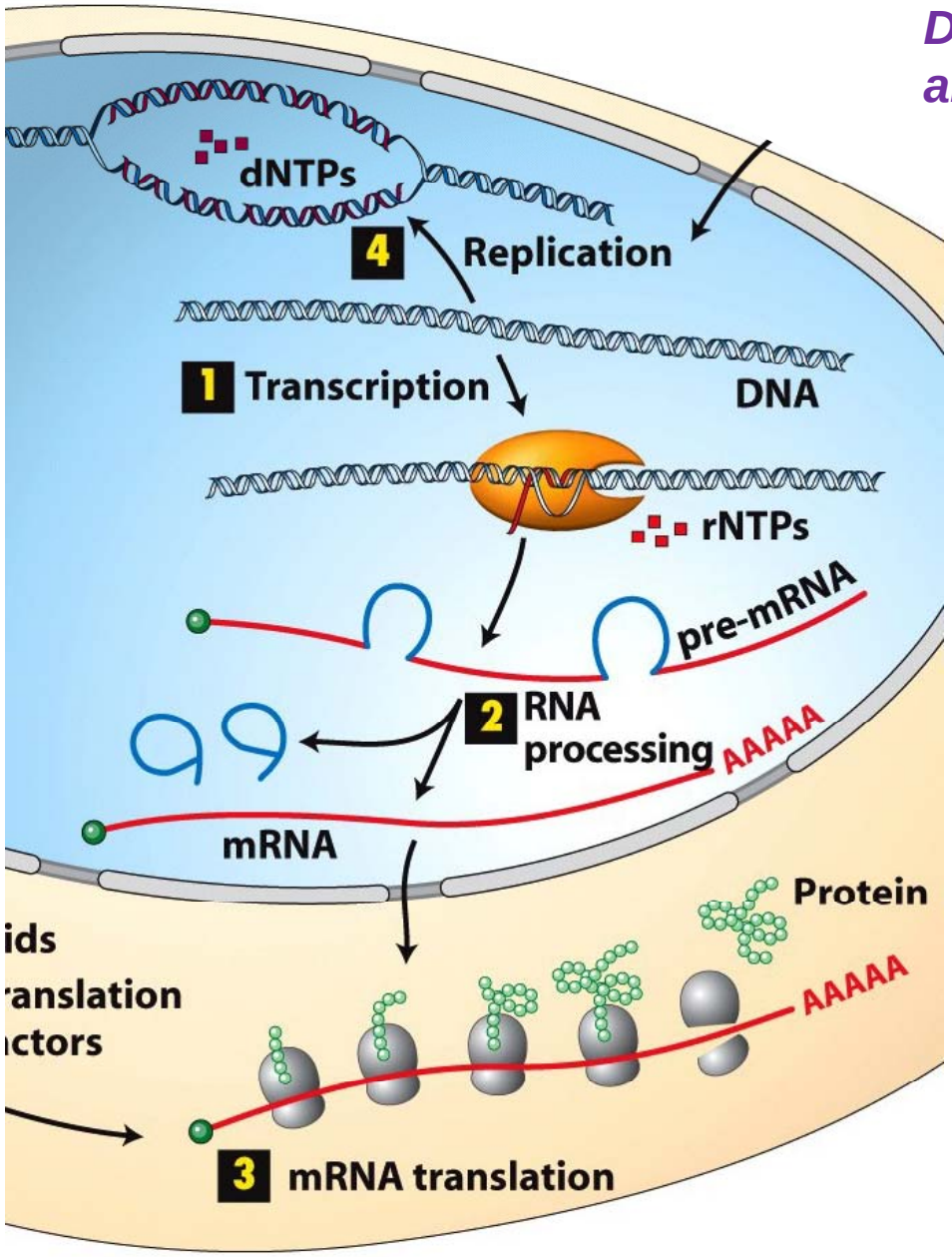




The protein nano-factory



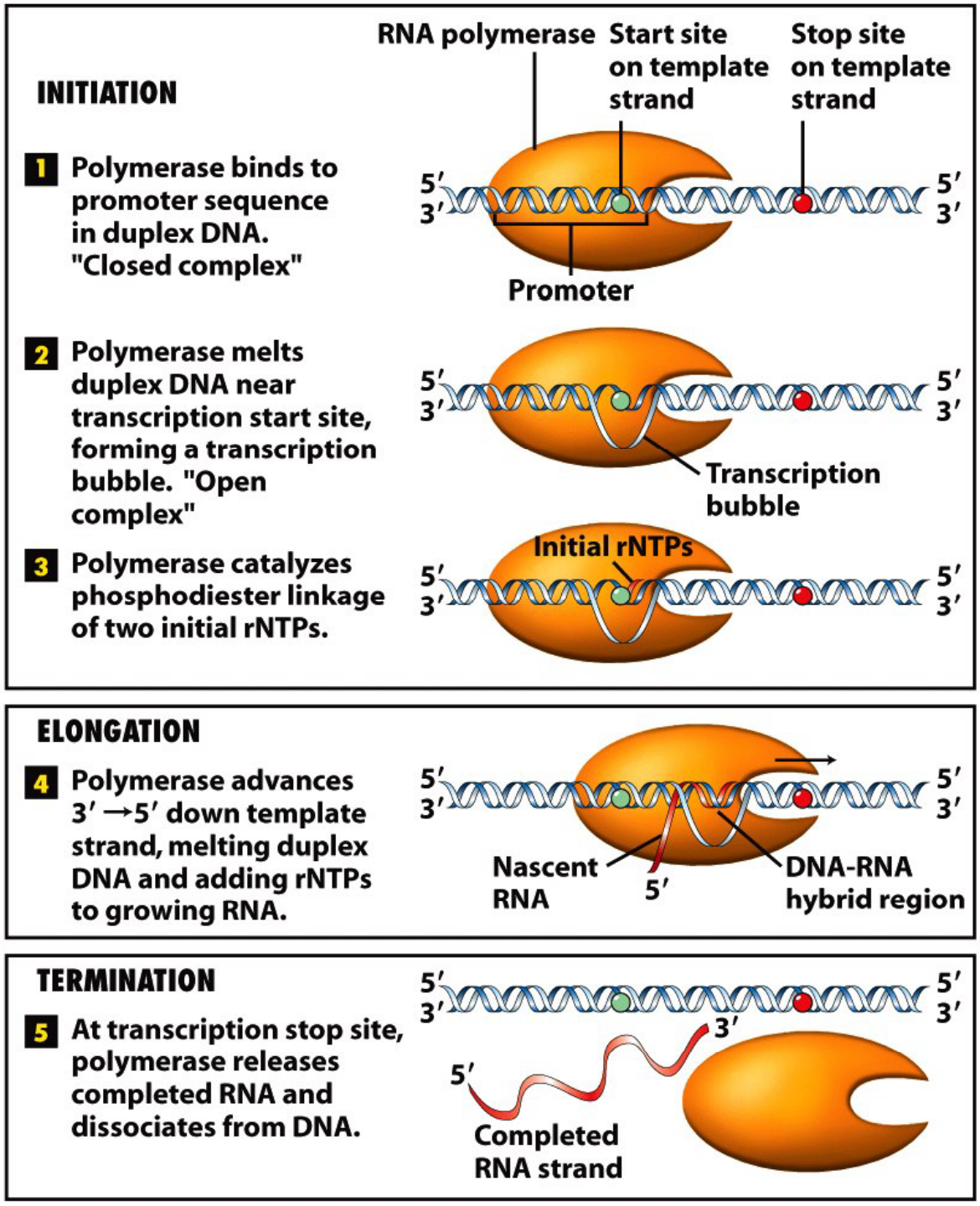
DNA and RNA polymerases are important biological machines



DNA polymerase and RNA polymerase are molecular motors that walk on DNA

DNA polymerases (and helicases) are biological motors that function in DNA replication (and repair)

RNA polymerase make a copy of DNA (transcription) and from this copy (**mRNA**) proteins are designed in the cell (translation)

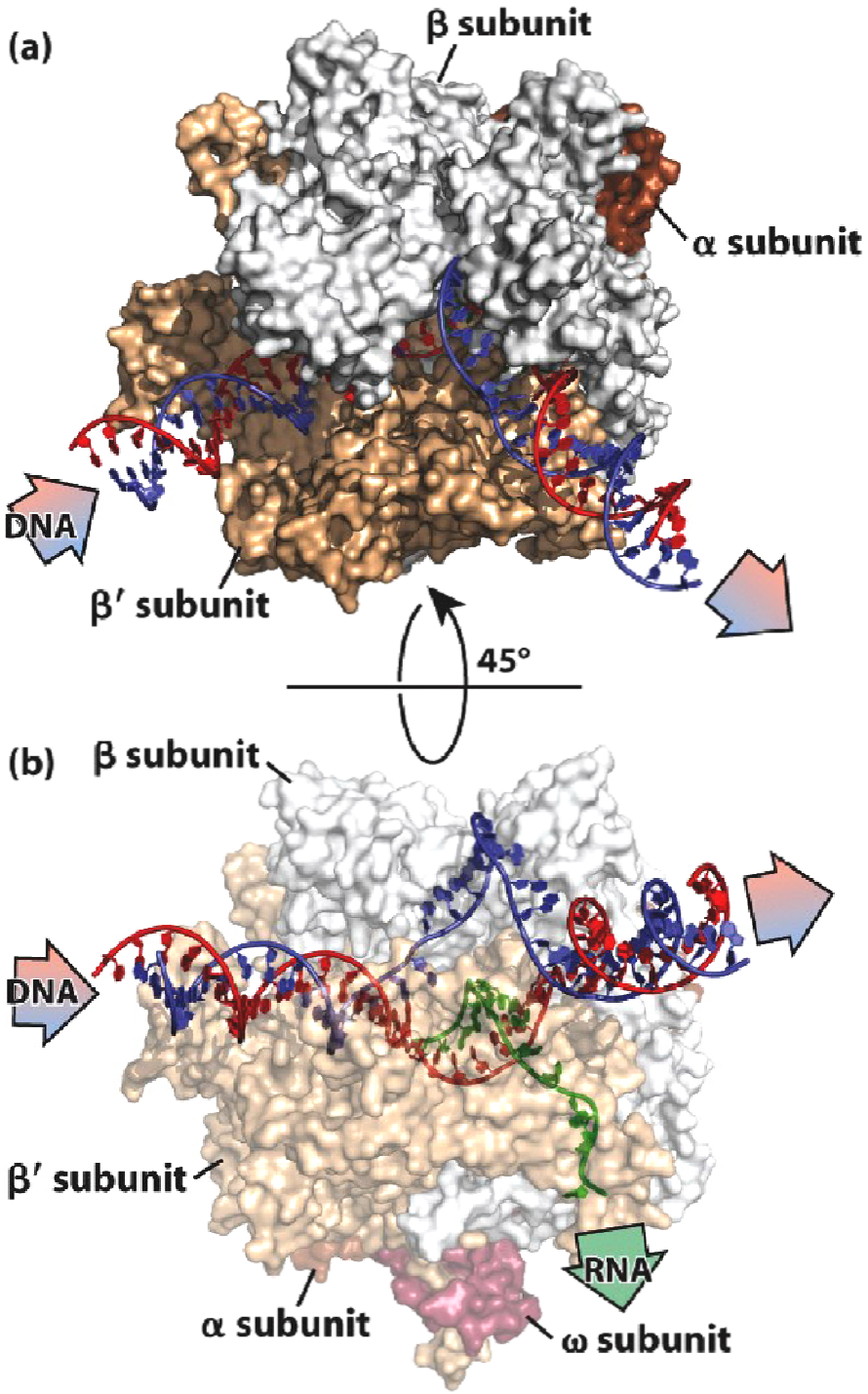


Transcription is powered by a complicated molecular machine:
The **RNA polymerase**

RNA polymerase is a **copy machine**:
It moves along the (double stranded) **DNA** and makes an exact (single stranded) copy (= **mRNA**)

3 steps:

1) Complicated **initiation** step
2) **Elongation** (3' -> 5')
3) **Termination** (RNA released)

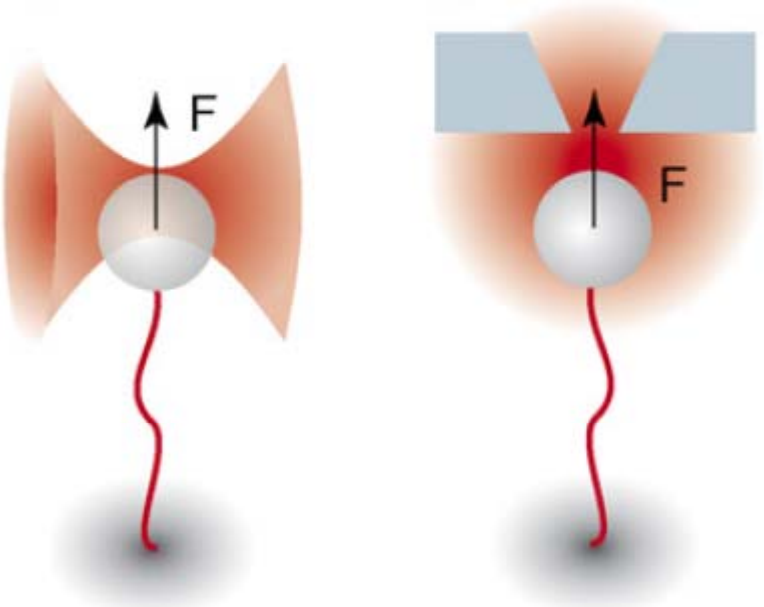


The RNA polymerase is a macromolecular machine with a difficult design

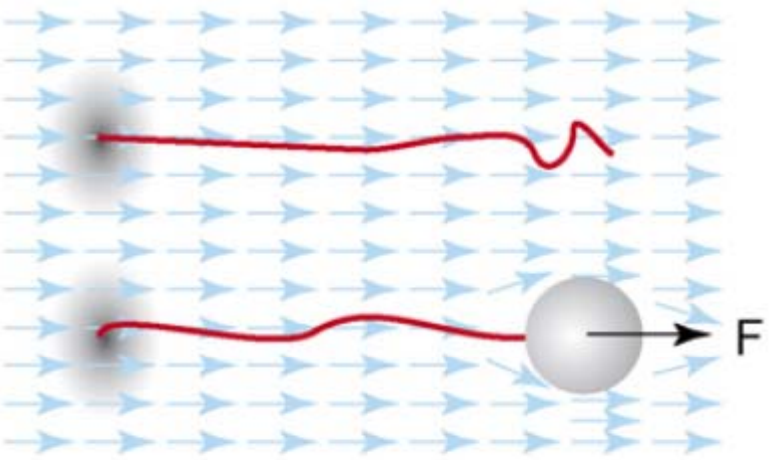
Example from your reading material!

• DNA is clamped between two subunits and then the **double helix** is **opened**
• Then a **copy** from a single DNA strand is **made** into a single strand RNA

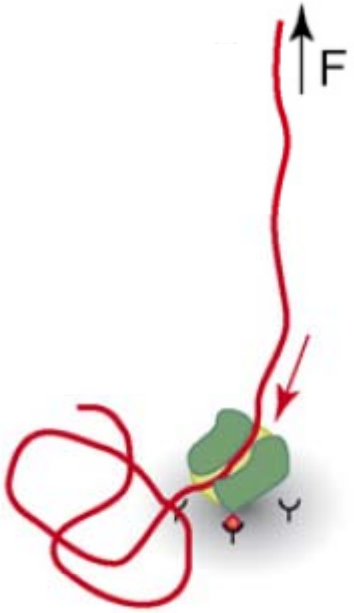
Single molecule methods to study DNA/RNA motors



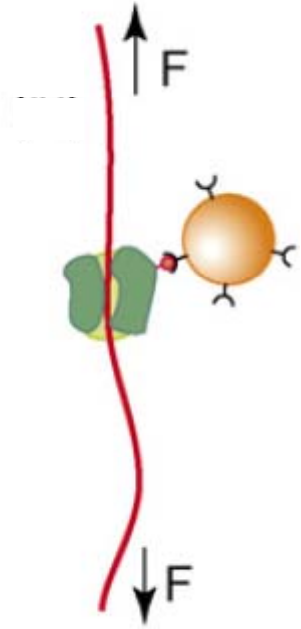
DNA or RNA is <u>first stretched by a bead</u> using **optical traps**, **magnetic beads** or **hydrodynamic flow**



Seidel and Dekker, 2007, Curr. Opin. Struct. Biol.

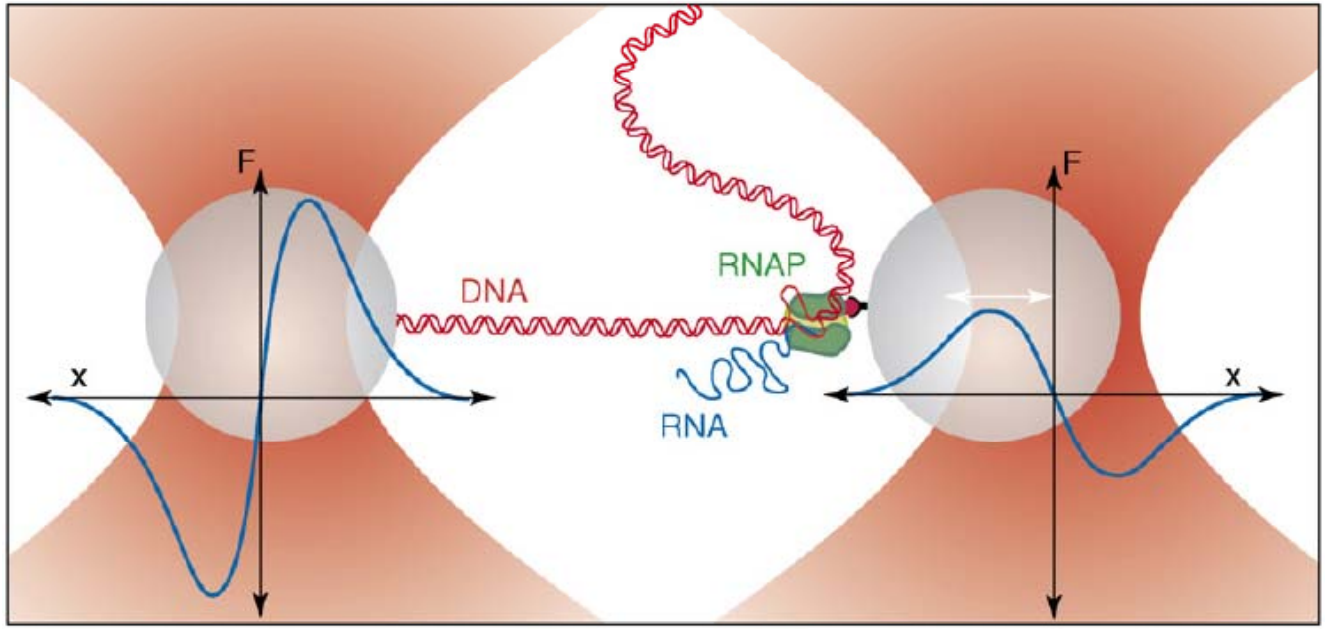


Immobilized DNA/RNA motor <u>shortens or lengthens</u> the DNA/RNA that can be detected by <u>bead displacements</u>

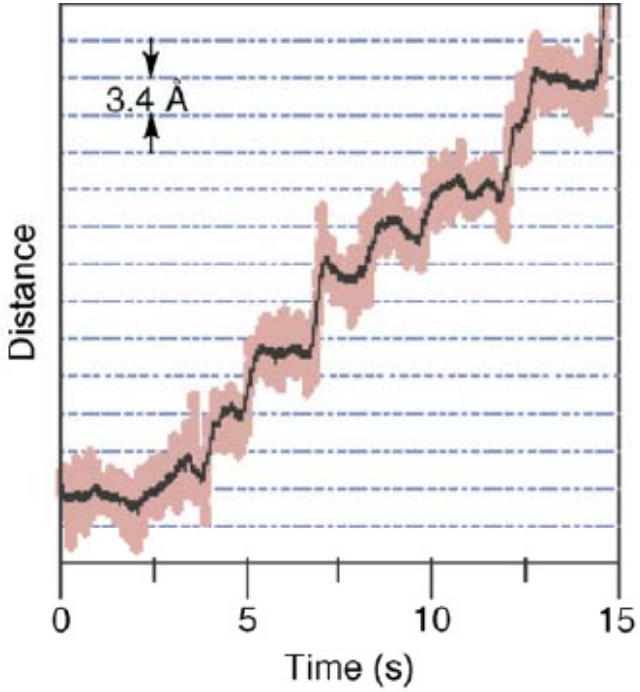


Direct motor movement on stretched DNA/RNA can be detected by <u>attaching a fluorescently labeled bead</u>

Detection of single base pair stepping by *E. coli* RNA polymerase (RNAP)



Two optical traps:
- One holds the DNA with **strong force**, the other holds the RNAP with **weak force**
- If RNAP moves, the attached bead is displaced (to the right)



Recorded single base pair steps of RNAP

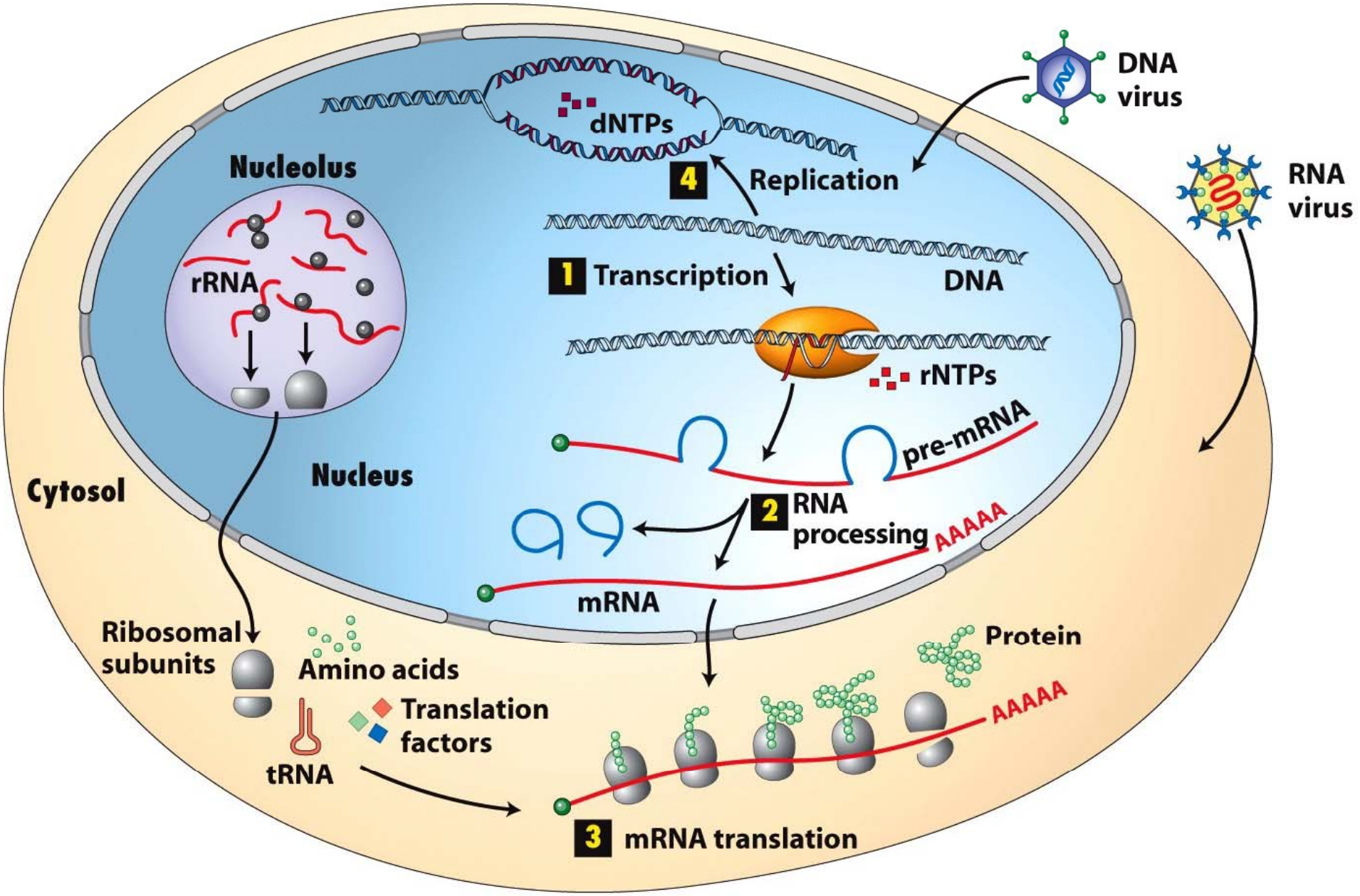
Single molecule methods to study DNA/RNA motors

Properties of nucleic acid motors characterized using single-molecule techniques during the past two years[a].

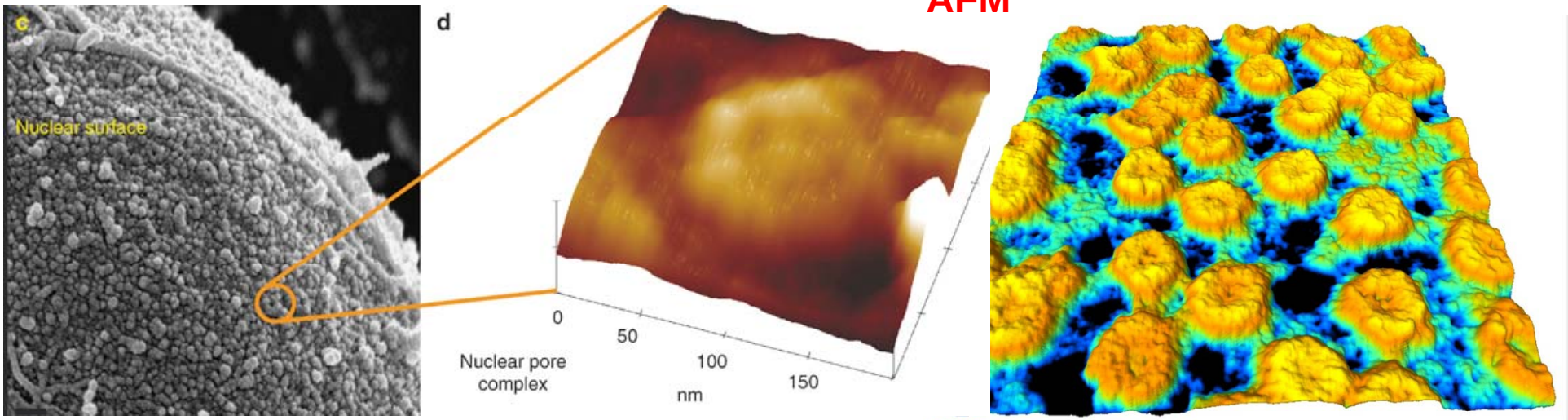
Name	Type	Function	No. catalytic subunits	Velocity (bp s^{-1})[b]	Force (pN)[c]	Processivity (bp)[d]	Step size (bp)
E. coli RNA polymerase	RNA polymerase	Transcription	1	16	25	Several kbp	1
T7 RNA polymerase	RNA polymerase	Transcription	1	130	16	>1000	1
FtsK	dsDNA translocase	Chromosome segregation	6	5000	40	>5000	2 or 13
Φ29 portal motor	dsDNA translocase	Viral packaging	5	100	57	15 000	NN
RuvAB	dsDNA translocase	Migrates Holliday junctions	6	43	25	4000	NN
HCV NS3 RNA helicase	RNA helicase	HCV replication	1 or 2	50	NN	18	11
*Eco*R124I	dsDNA translocase	Type I restriction enzyme	1	550	>5	5000	1–2
RSC complex	dsDNA translocase	Chromatin remodeling	1	350	>2	400	12
Rad54	dsDNA translocase	Homologous recombination	NN	300	NN	12 000	NN
RecBCD	DNA helicase	dsDNA break processing	2	520	8	30 000	<6 or 23
B. subtilis DNA uptake	ssDNA translocase	Horizontal gene transfer	NN	80	45	>10 000	NN
T7 replisome	DNA replicase	DNA unwinding and synthesis	6 and 1	160	NN	17 000	NA

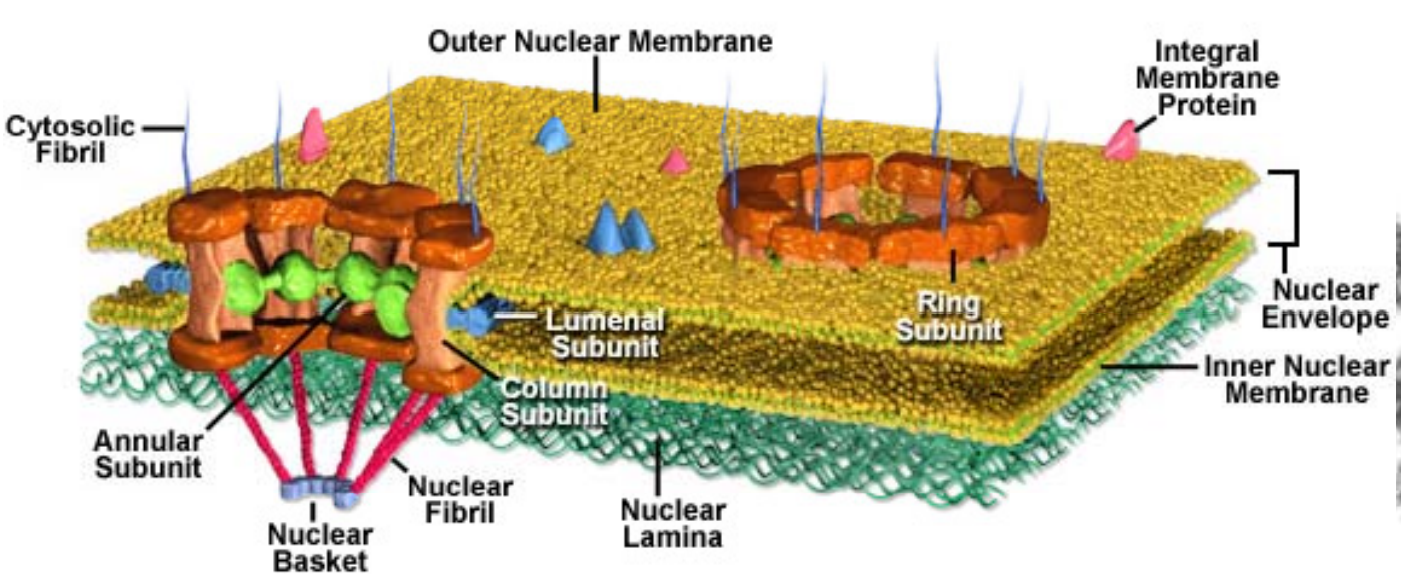
Seidel and Dekker, 2007, Curr. Opin. Struct. Biol.

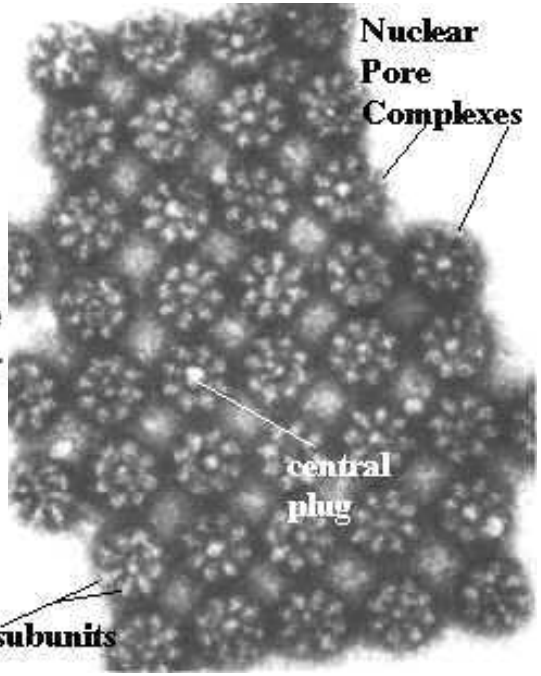
The nuclear pore: the smallest filter in the world



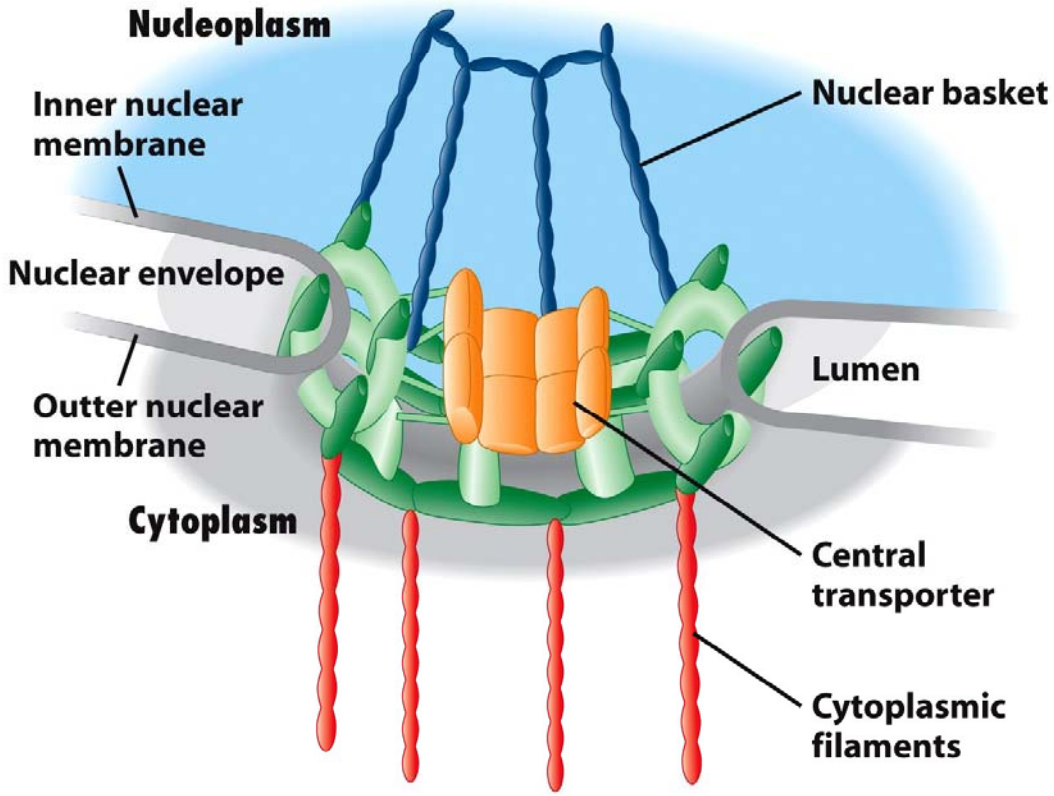
The nuclear pore: a molecular nano-filter

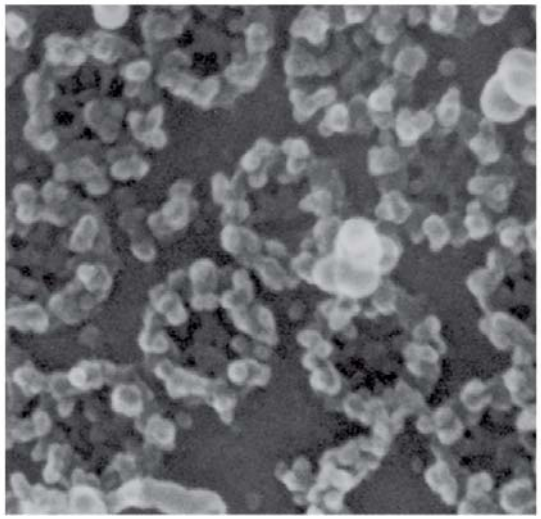


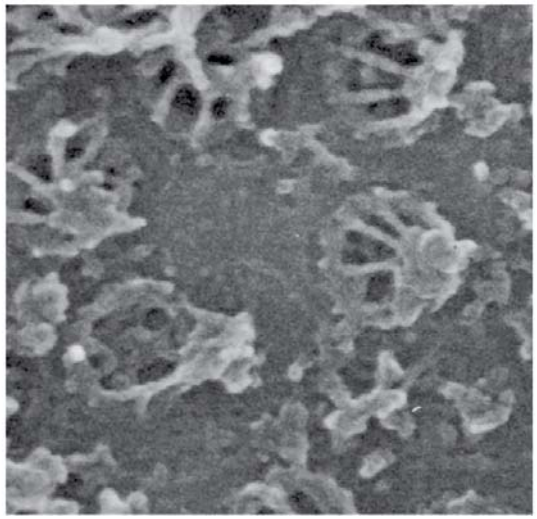




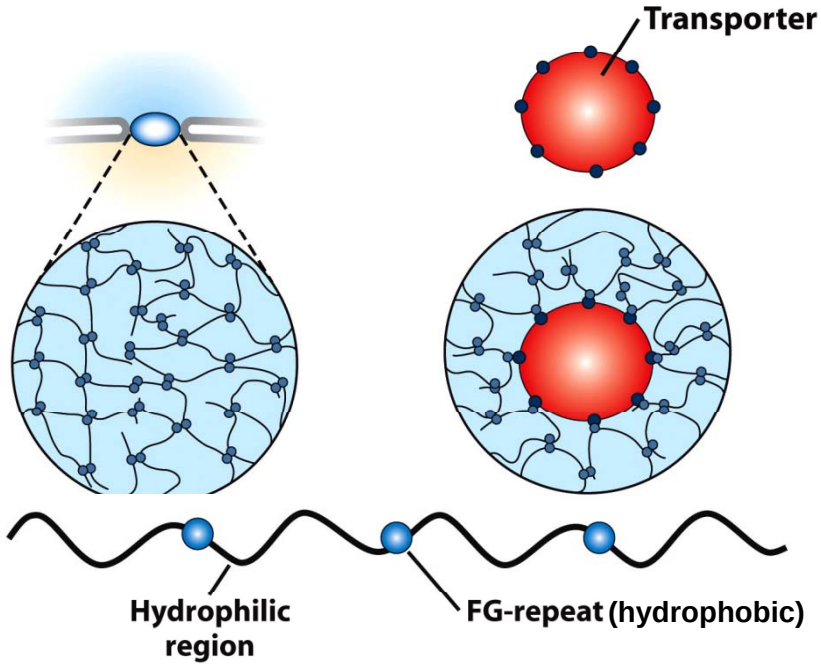
The nuclear pore: a molecular nano-filter



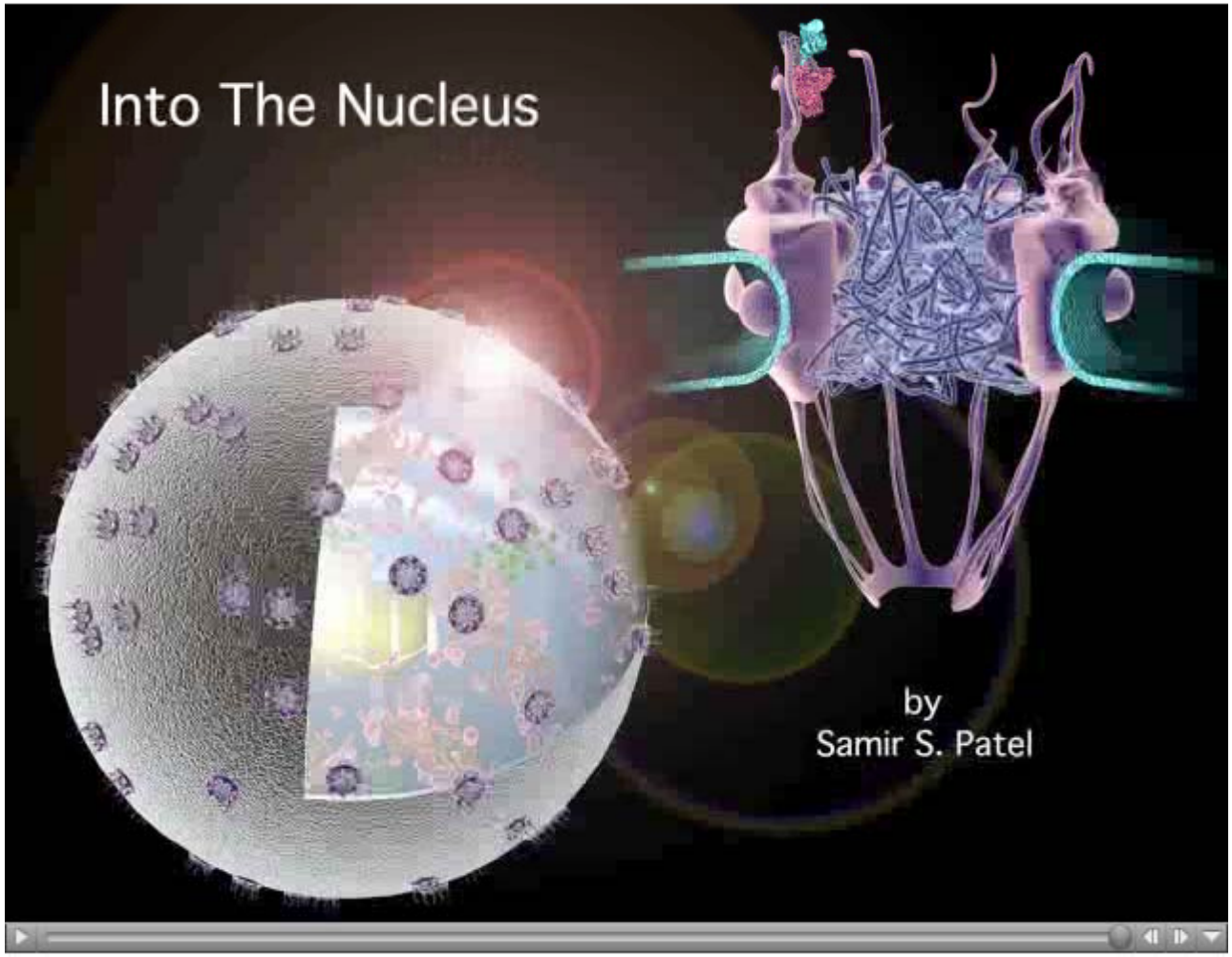




How the **nano-sieve** works:



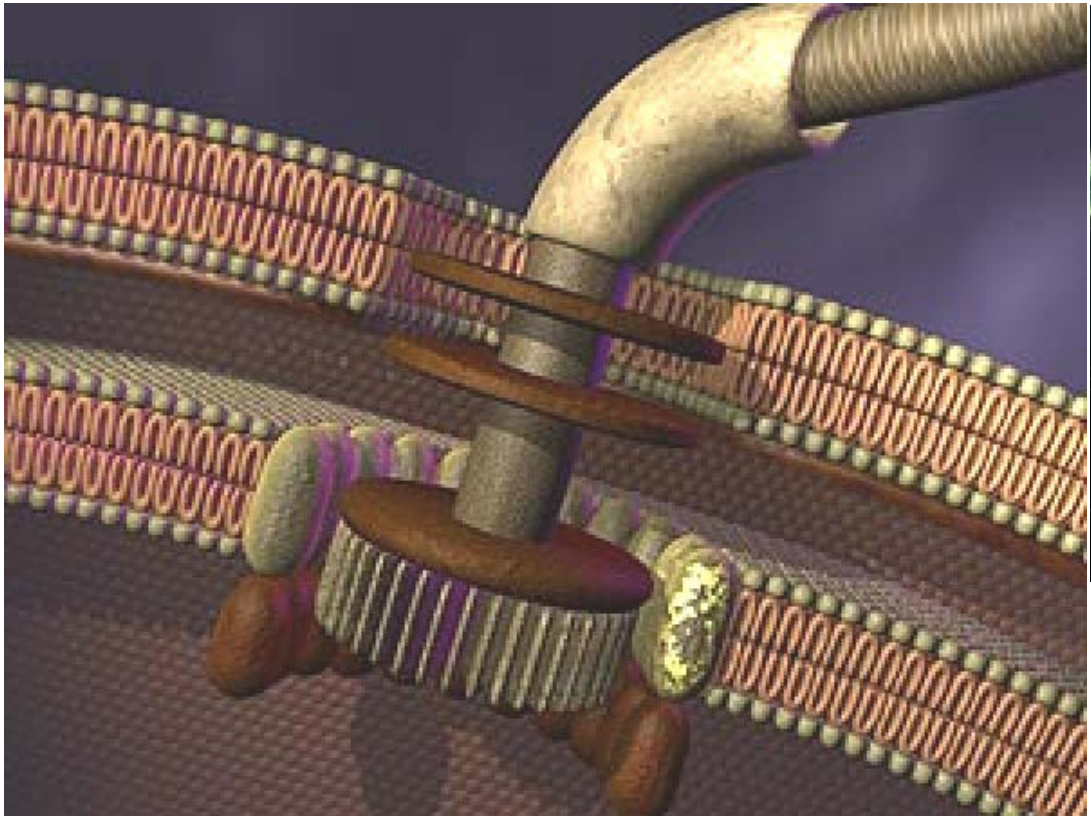
- The nuclear pore complex (**NPC**) is a complicated structure containing about 30 different proteins (nucleoporins)
- The **central channel** is filled with **filamentous hydrophilic polypeptides**
- The polypeptides contain **hydrophobic regions** (**FG-repeats** = Phenylalanine/Glycin)
- These structures are able to constantly and rapidly re-arrange **acting as a sieve** for small molecules
- A nuclear transporter can interact with the FG-repeats shuttling other molecules

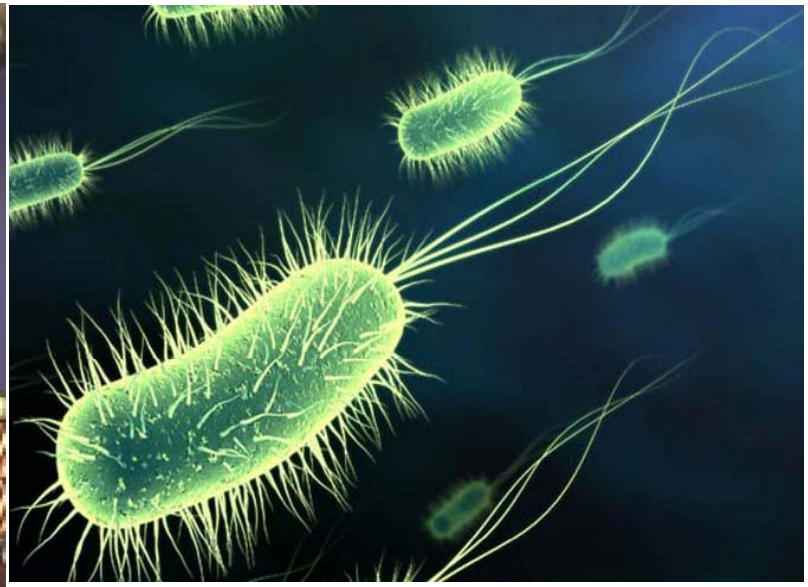


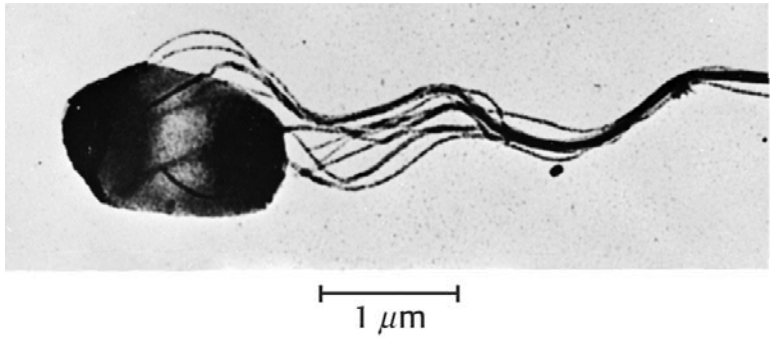
Animation
IntoTheNucleus.mov

http://sspatel.googlepages.com/nuclearporecomplex2

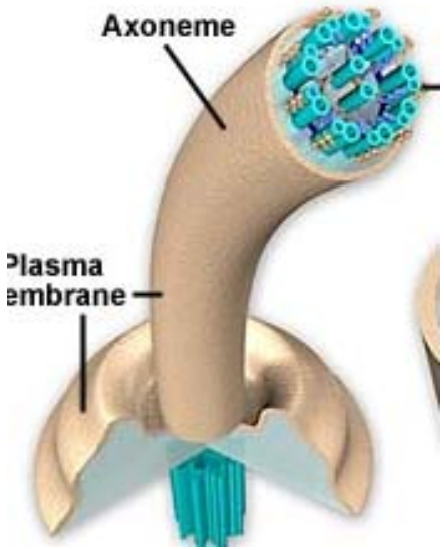
The bacterial flagellum motor

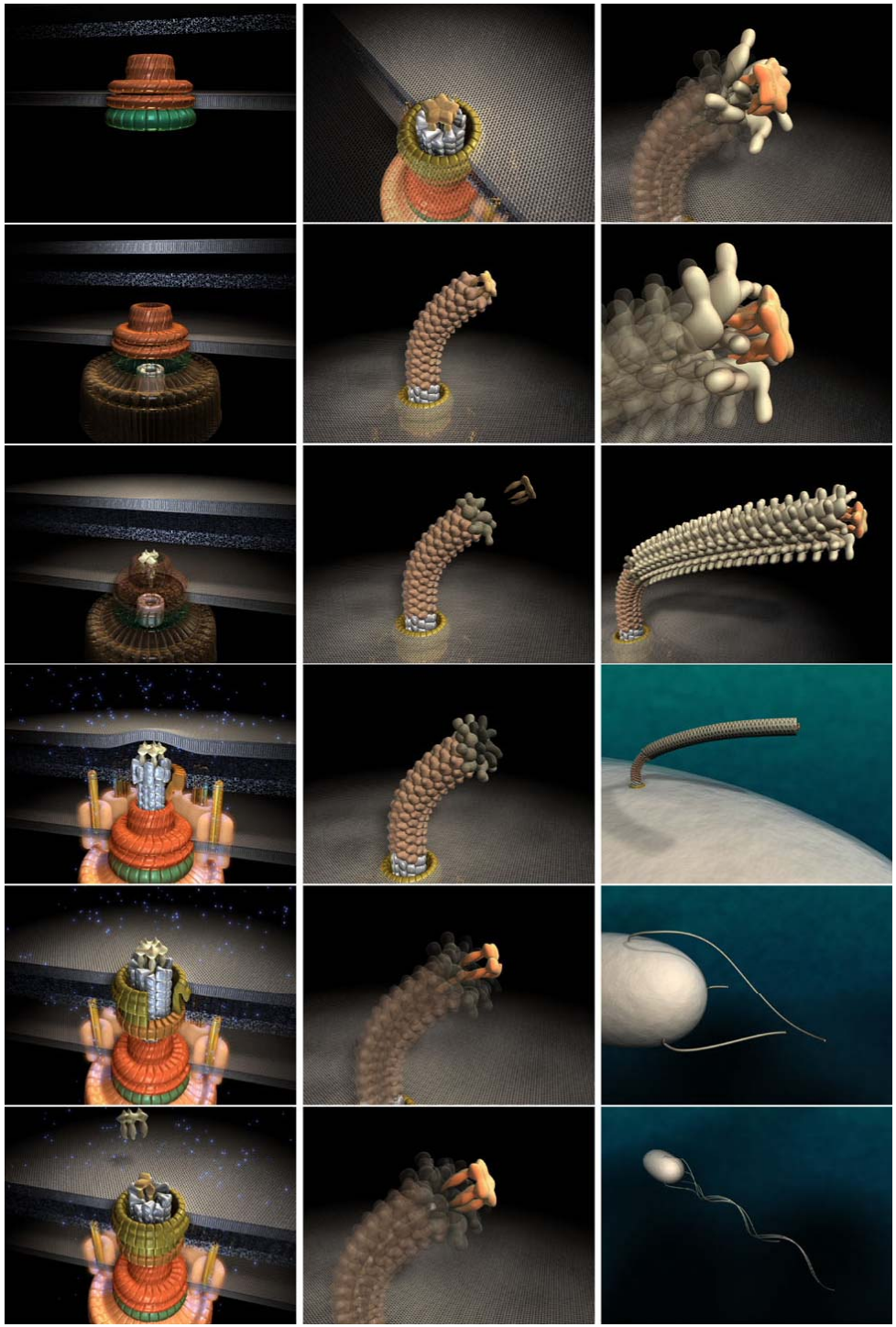






Not a flagella as found
in other (non-bacterial) cells
(**not** made of microtubules)



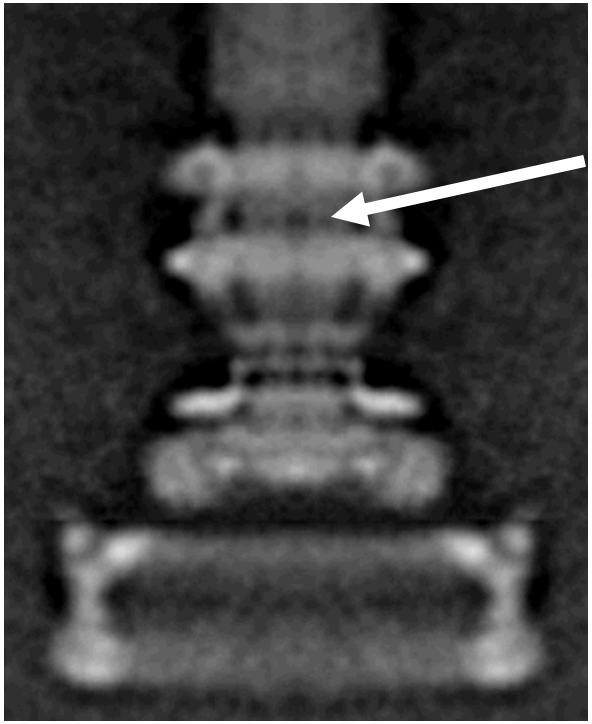


The bacterial flagellum motor

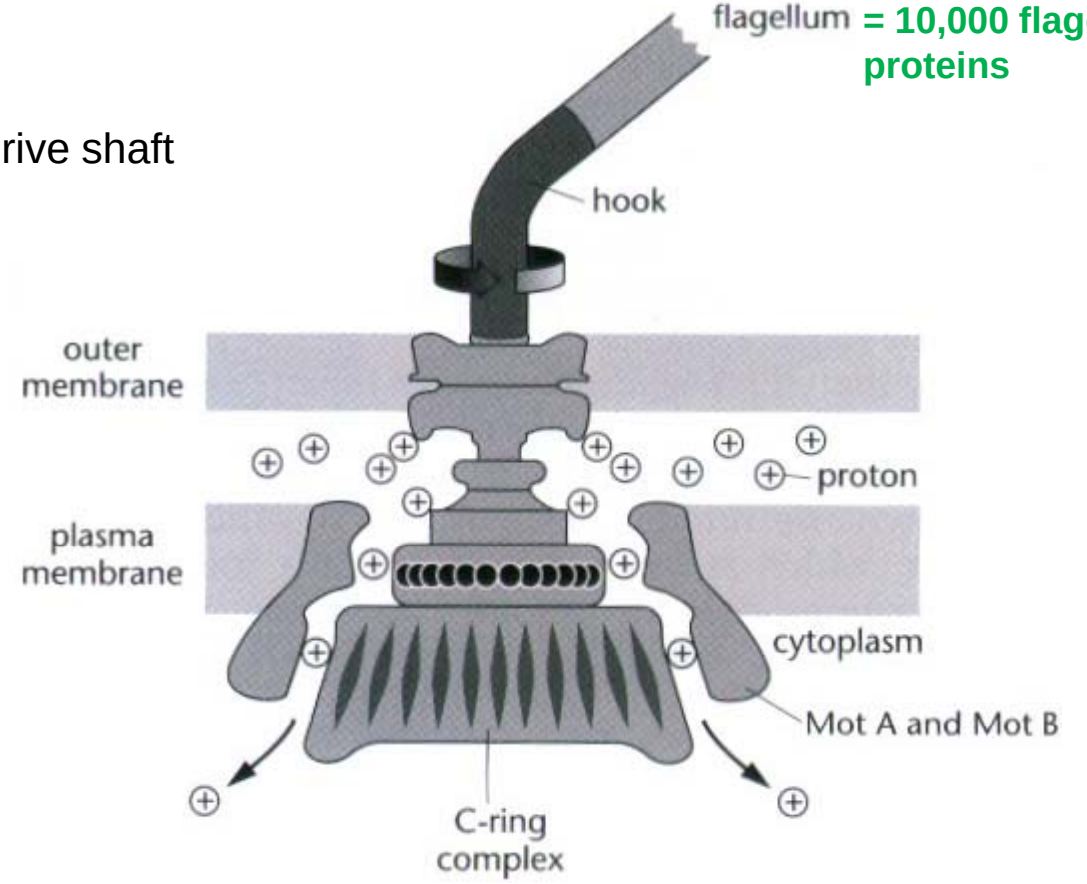
Example from your reading material!

- Motor composed of **20 proteins**
- **40 genes** needed to make the motor and its flagellum
- **8 torque** (turning) **generators** driven by proton motion force (no ATP required)
- **1200 protons** needed per turn
- **100 revolutions** per second
- **18,000 RPM** (300 Hz)
- Directional reverse within 1/10 of second
- Efficiency: < 5%
- Power output: 10^{-15} Watt (2-3 more efficient than ATP motors)

A proton gradient drives the motor like water drives a turbine



Low-dosage EM and
image-averaging techniques

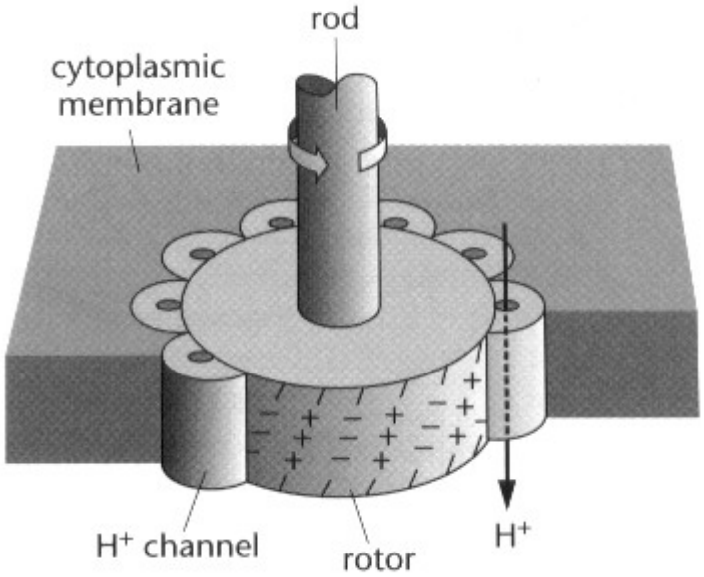


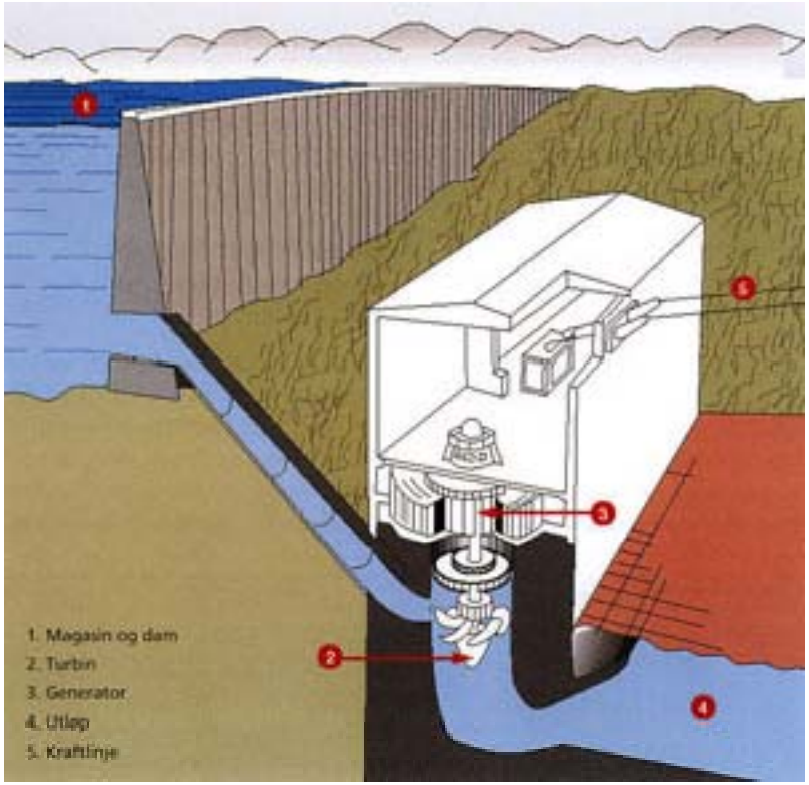
- **Drive shaft** passes thru <u>two rings</u> in the <u>outer membrane</u>. The rings act as bearings. Not involved in force generation
- **C-ring** (cytoplasmic ring) is important for <u>force production</u> and directional reversal
- **MotA** and **MotB** rings form the **proton channels**

Howard, Mechanics of Motor Proteins, 1st Ed.

Electrostatic model of the flagellum motor

Rotor-stator (motor) interaction generates the torque (turning):





A water-flow driven turbine

Alternating charges on the rotor might be used to **drive the motor**:

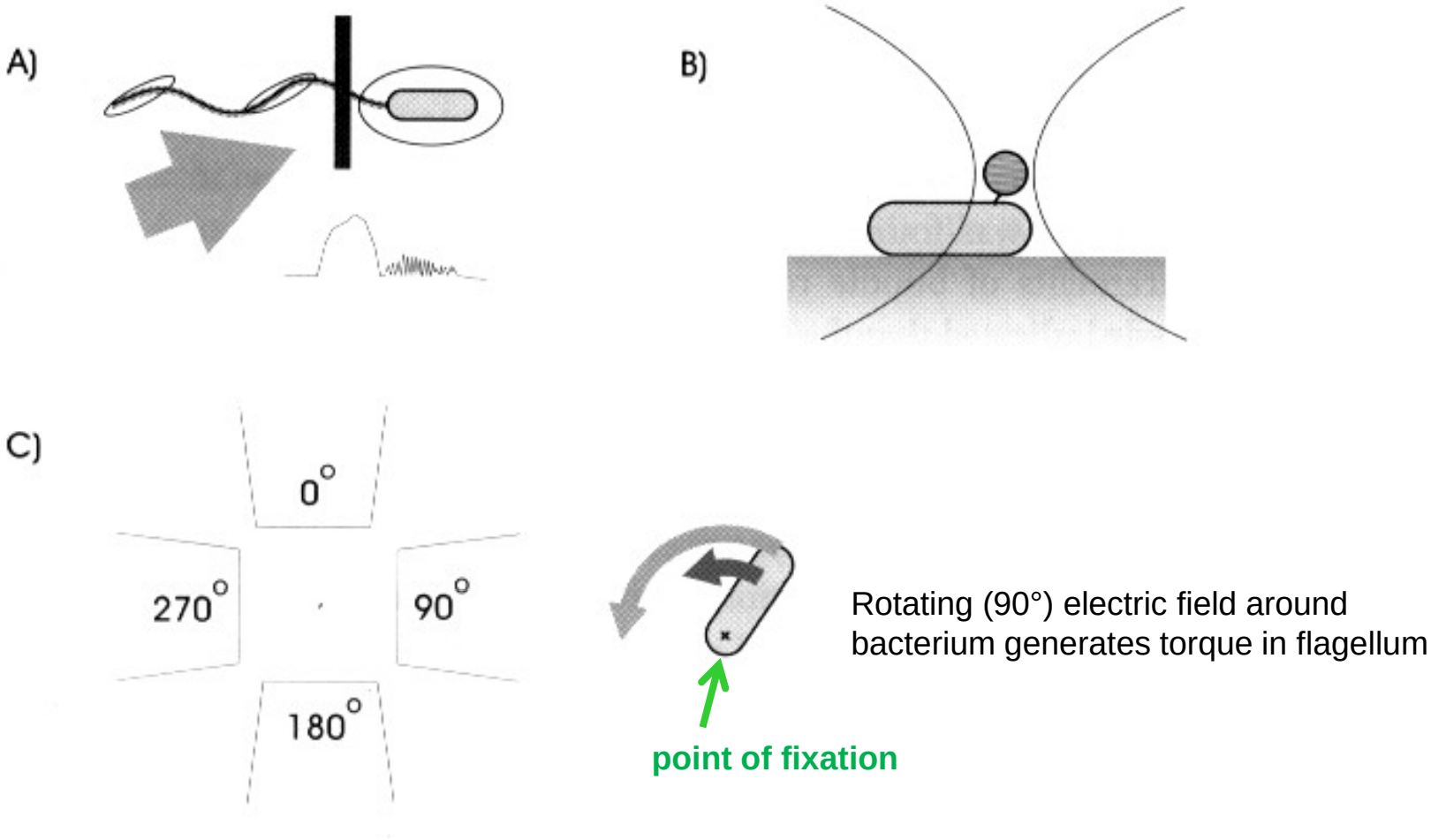
- The lines of charges on the rotor are tilted with respect to the channels
- As **positive protons** move thru the channels, they **attract negative charges** on the rotor
- These electrostatic attraction forces might turn the motor

Howard, Mechanics of Motor Proteins, 1st Ed.

Torque-speed relationships

Methods to measure rotation of single motors:

A) Laser illumination: flagellum illuminatied by a laser thru a small slit (dark bar)
B) Polystrene beads: beads attached to flagellum and deflection monitored by laser
C) Oscillating voltage: fixed cells are exposed to an oscillating (90°) voltage field

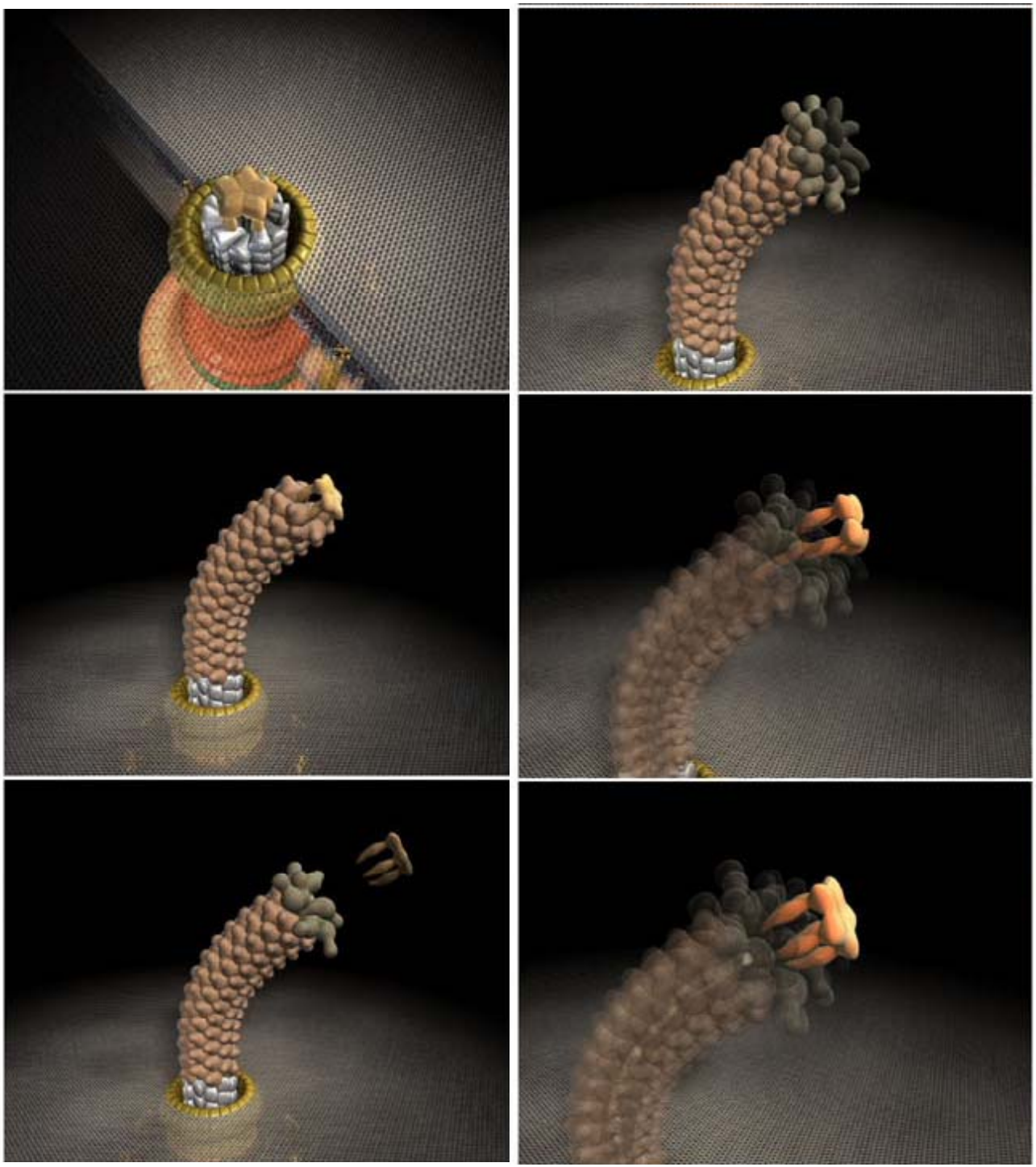


Rotating (90°) electric field around bacterium generates torque in flagellum

Schliwa, Molecular Motors, 1st Ed.

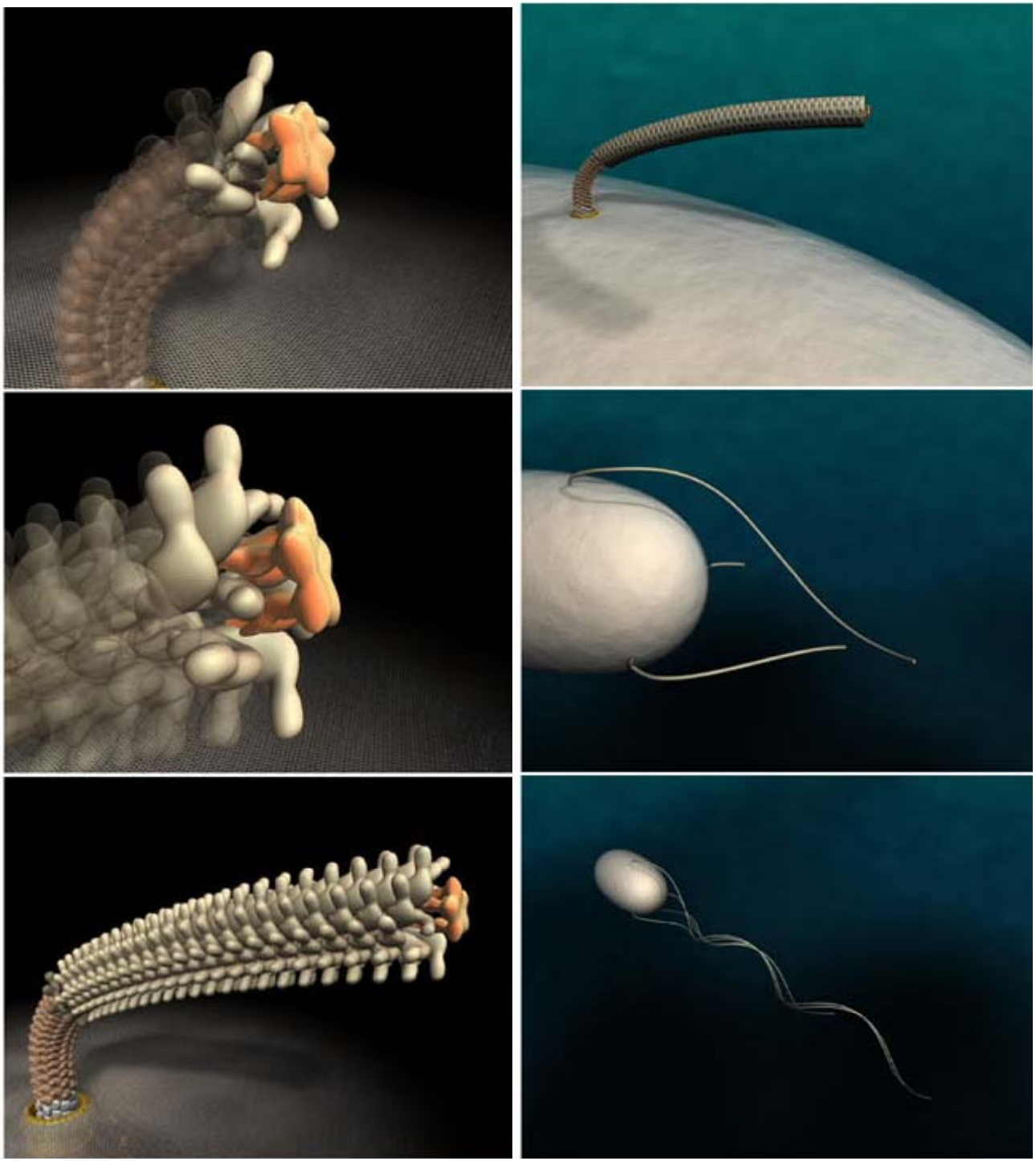
- Flagellum motor made of **20 different proteins**
- It spans across three layers of membranes: **outer membrane**, **peptidoglycan layer** and **cytoplasmic membrane**
- It consists of various components, such as a rotor, **stators**, a drive shaft, a **plug socket**, a rotation-switch regulator, and so on.

OM
PL
CM



• Rotary motor embedded at the base of a **helical filament**

• A short segment (55 nm) connects the motor and the helical propeller = **hook** (universal joint)



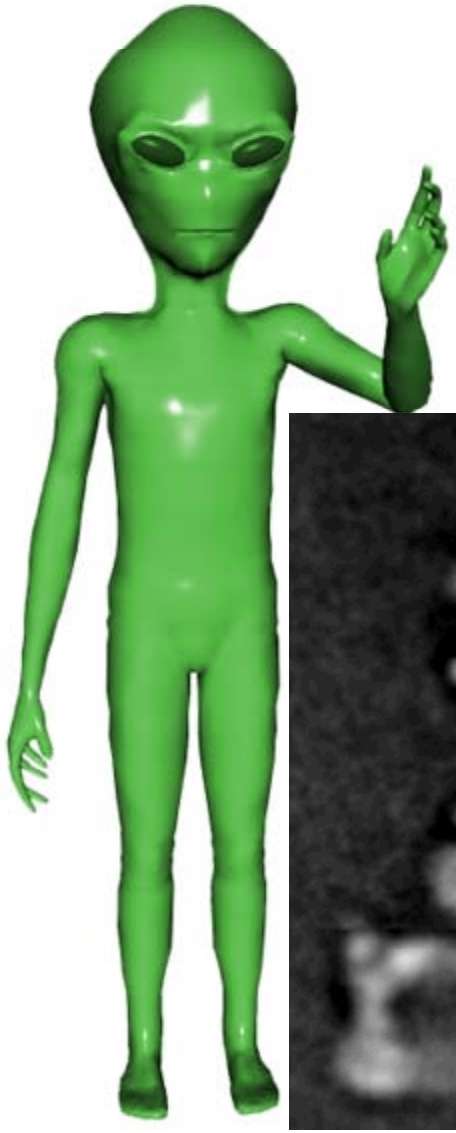
• **Flagellin** molecules (synthesized in the cytoplasm) transported to the end of the filament through the channel
• Flagellin binding is coordinated by a **rotating cap** (always preparing only one flagellin binding site)
• Cap movements looks like climbing up the helical stairs step by step.

Movie
bacterial_motor.wmv

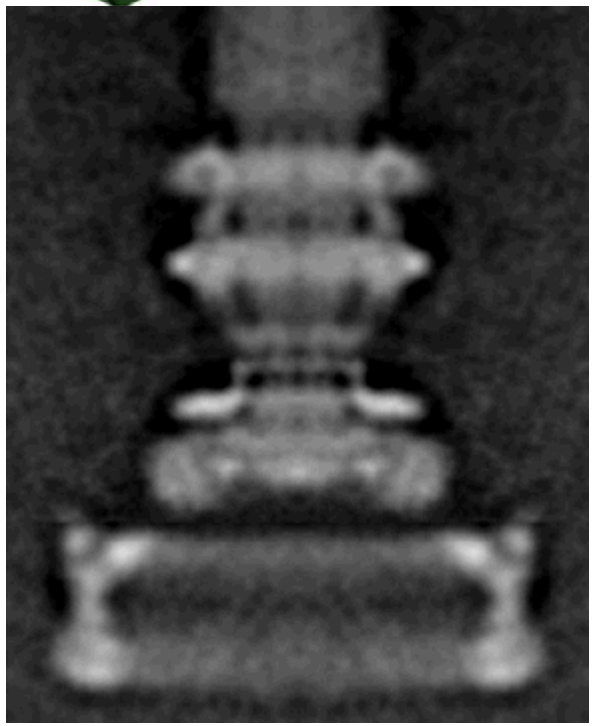
18:42

The bacterial flagella motor: Evolution or Intelligent design?

Intelligent design (ID) is the concept that some aspects of the natural universe are better explained by an **intelligent cause** rather than by an undirected process such as **natural selection**



- "The bacterial flagellum is an **irreducible** complex system" (a minimal, not reducible system)
- "This **complexity** could not have arisen through gradual variation or natural selection"
- "This system is so complex that it can only function when all of their components are present" (could not evolve from a simpler assembly which would be fully functionary)



nature REVIEWS MICROBIOLOGY

PERSPECTIVES

SCIENCE AND SOCIETY

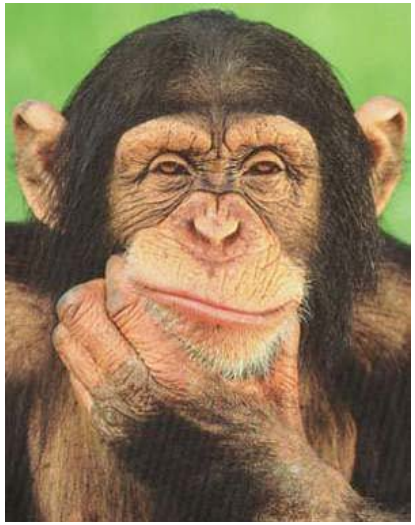
From *The Origin of Species* to the origin of bacterial flagella

Mark J. Pallen and Nicholas J. Matzke

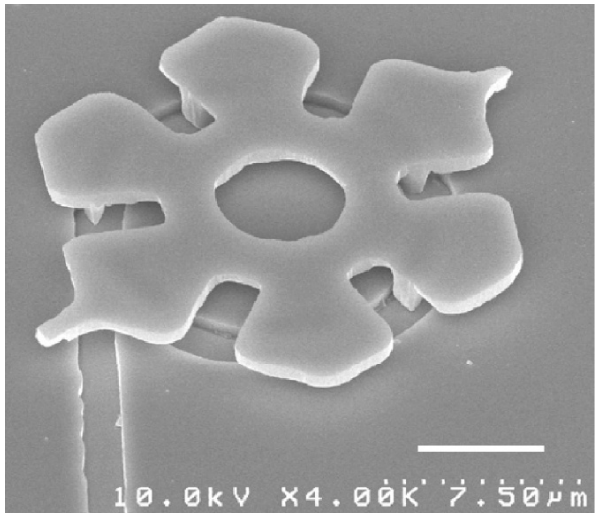
Protein	Location	Function	Indispensable?	Homologies*
FlgA	P ring	Chaperone?	Absent from Gram-positive bacteria	CpaB‡
FlgBCFG	Rod	Transmission shaft	Yes	FlgBCEFGK§
FlgD	Hook	Hook cap	Yes	
FlgE	Hook	Universal joint	Yes	FlgBCEFGK
FlgH	L ring	Bushing	Absent from Gram-positive bacteria	None yet known
FlgI	P ring	Bushing	Absent from Gram-positive bacteria	None yet known
FlgJ	Rod	Rod cap; muramidase	FlgJ N-terminal domain absent from some systems	None yet known
FlgK	Hook–filament junction	Hook-associated protein 1	Yes	FlgBCEFGK§
FlgL	Hook–filament junction	Hook-associated protein 3	Yes	FliC§
FlgM	Cytoplasm and exterior	Anti-σ factor	Absent from *Caulobacter*	None yet known
FlgN	Cytoplasm	Chaperone	Undetectable in some systems	None yet known
FlhA	T3SS apparatus	Protein export	Yes	LcrD/YscV‖
FlhB	T3SS apparatus	Protein export	Yes	YscU‖
FlhDC	Cytoplasm	Transcriptional regulator	Absent from many systems	Other activators‡
FlhE	Unknown	Unknown	Mutant retains full motility	
FliA	Cytoplasm	σ factor	Absent from *Caulobacter*	RpoD, RpoH, RpoS‖
FliB	Cytoplasm	N-methylase	Absent from *Escherichia coli*	
FliC	Filament	Flagellin	Yes	FlgL§, EspA¶
FliD	Filament	Filament cap; hook-associated protein 2	Absent from *Caulobacter*	None yet known
FliE	Rod/basal body	MS ring–rod junction	Yes	None yet known
FliF	T3SS apparatus	Protein export	Yes	YscJ§
FliG	Peripheral	Motor	Yes	MgtE¶
FliH	T3SS apparatus	Regulates FliI	Mutant retains some motility	YscL*, AtpFH¶
FliI	T3SS apparatus	ATPase for protein export	Yes	YscN‖, AtpD‖, Rho‖
FliJ	Cytoplasm	Chaperone	Undetectable in some systems	YscO¶
FliK	Hook/basal body	Controls hook length	Yes	YscP¶
FliL	Basal body	Unknown	Mutant retains full motility	None yet known
FliM	T3SS apparatus	Protein export	Yes	FliN‡, YscQ‡
FliN	T3SS apparatus	Protein export	Yes	FliM‡, YscQ‡
FliO	T3SS apparatus	Protein export	Undetectable in some systems	None
FliP	T3SS apparatus	Protein export	Yes	YscR‖
FliQ	T3SS apparatus	Protein export	Yes	YscS‖
FliR	T3SS apparatus	Protein export	Yes	YscT‖
FliS	Cytoplasm	FliC chaperone	Absent from *Caulobacter*	None yet known
FliT	Cytoplasm	FliD chaperone	Absent from many systems	None yet known
FliZ	Cytoplasm	Regulator	Absent from many systems	None yet known
MotA	Inner membrane	Motor	Yes	ExbB‡, TolQ‡
MotB	Inner membrane	Motor	Yes	ExbD‡, TolR‡, OmpA‡

- Only 50% of components are really necessary (=> indispensable)
- There is not "*the*" bacterial flagellum: thousands (if not millions) different bacterial flagellum systems exist
- Some are **redundant** and non-function and used for functions others than motility
- Several proteins have sequence homology indicating a **common ancestor**
- The flagellum evolved starting from just two proteins (e.g., **proto-flagellin**)
- Similarities between flagellar and non-flagellar systems exist
- Proto-flagellum could **easily arose** from pre-existing modules as the ATPase, polymerized filaments, ion-channels and domains of the chemotaxis apparatus

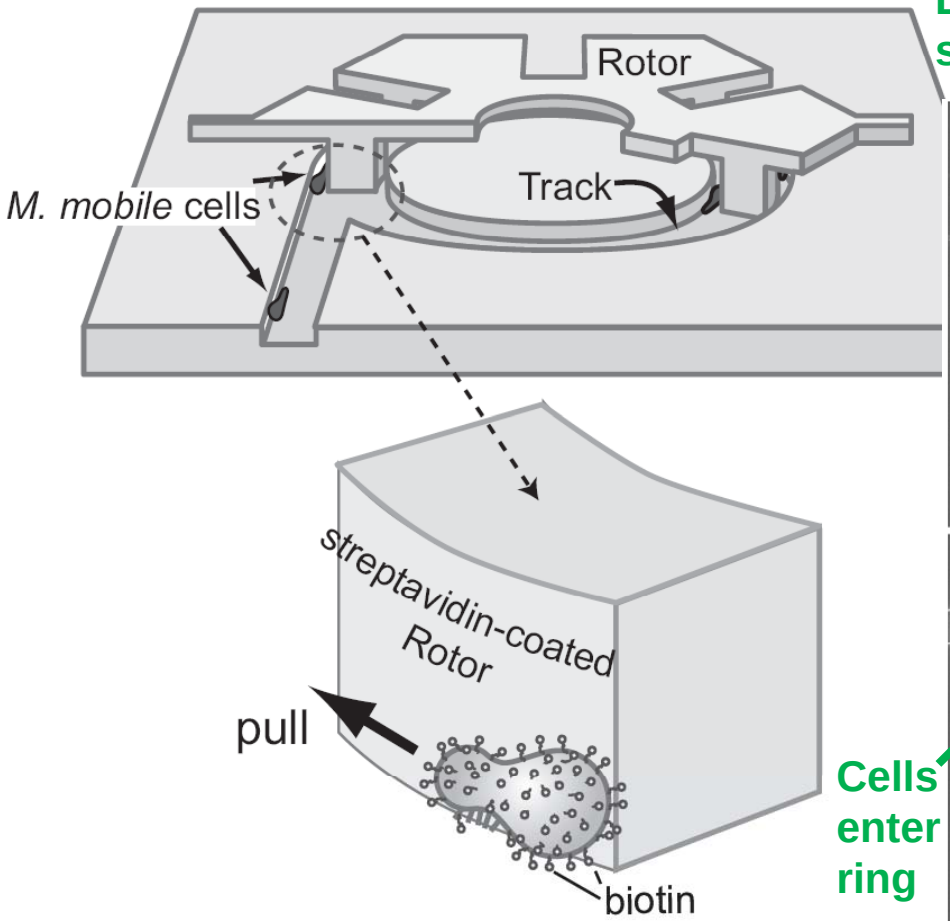
The bacterial flagella motor: Evolution or Intelligent design?



A nano-biomachine powered by highly motile bacteria

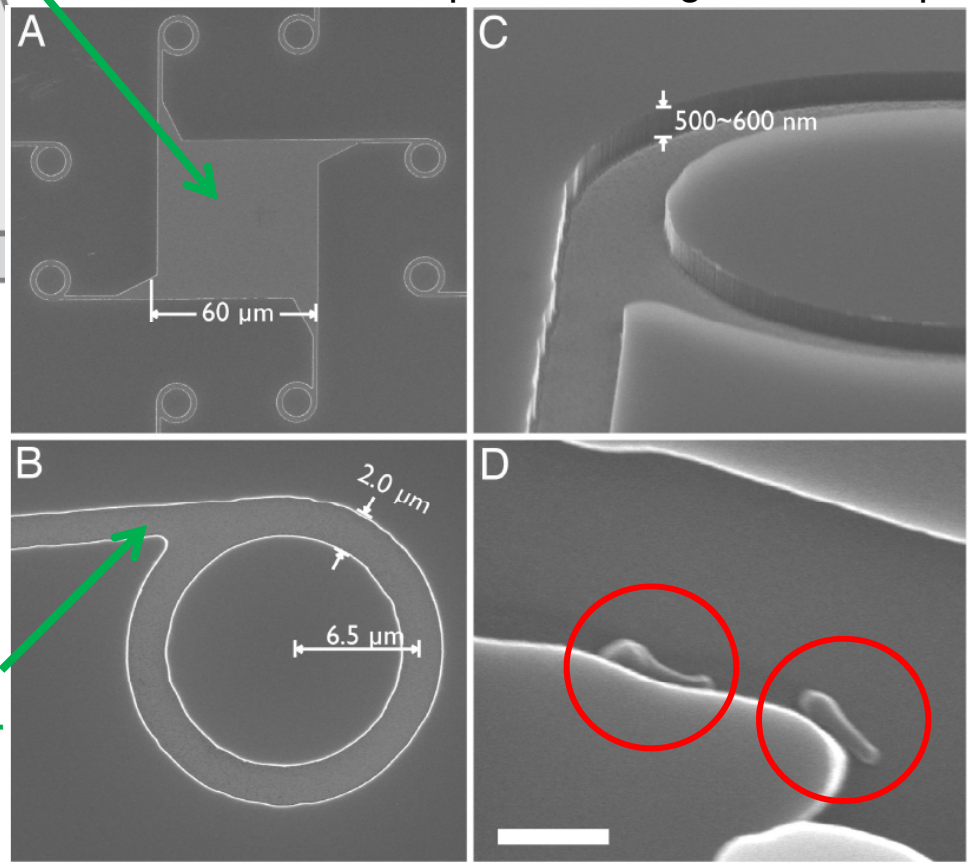


- Highly motile **gliding bacteria** *Mycoplasma mobile* pulled on a micro-rotor fueled by glucose
- How it works:
  - ➢ Floating of cells into the circular track
  - ➢ Glycoprotein coating on track-bottom helps bacteria attachment
  - ➢ Restricting **biotin-labeled bacteria** movements to streptavidin-coated rotor



Drop bacteria solution here

Rotor placed in ring in a 2nd step



Cells enter ring

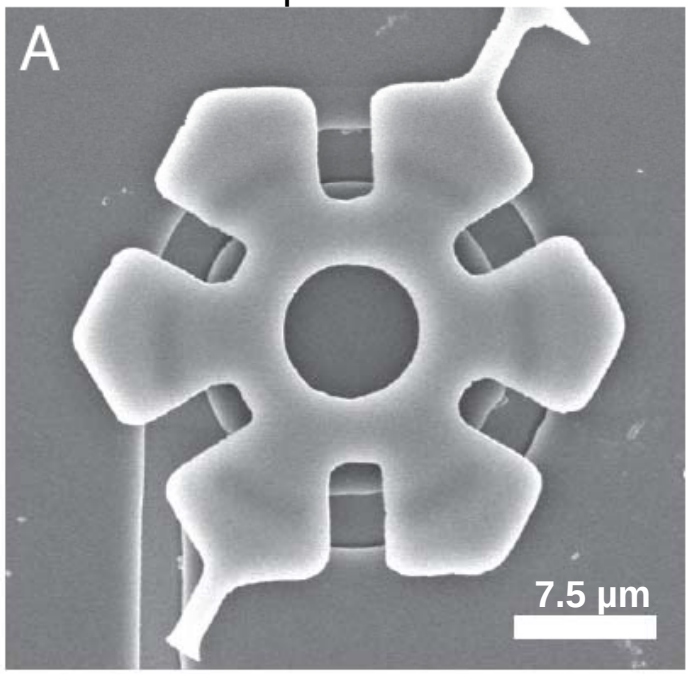
A nano-biomachine powered by highly motile bacteria

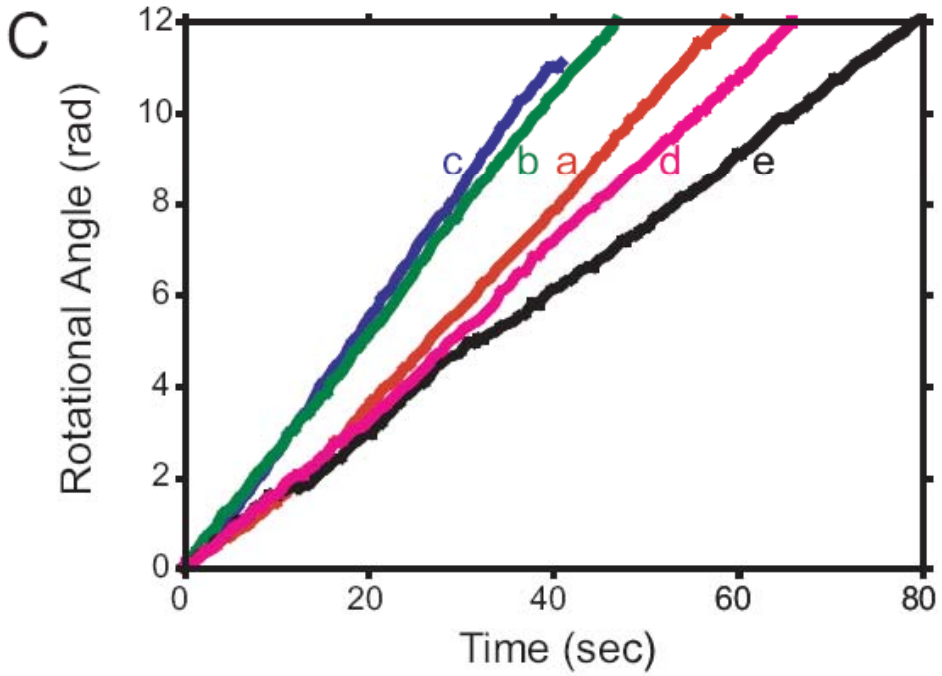
Example from your reading material!

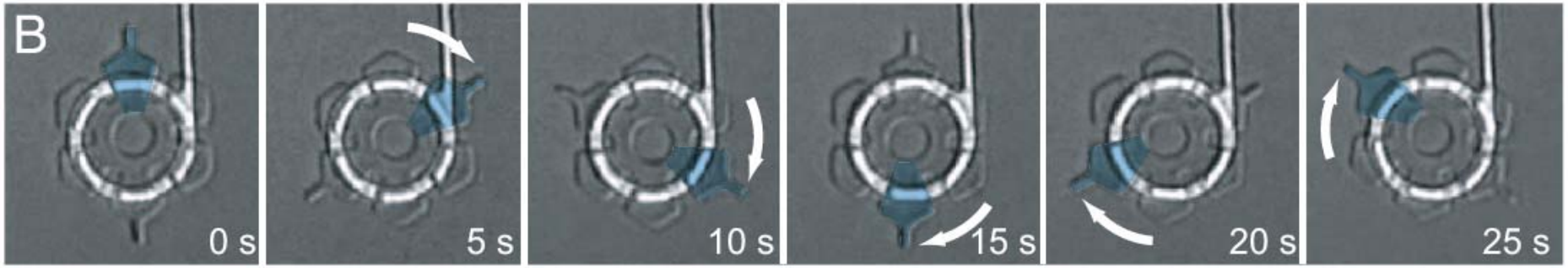
Speed: 3 rpm
Torque: 2-5 x 10^{-16} N·m
Stall force: 27 pN

Movie
bacteria powered microrotor.mov

Movie
bacteria powered microrotor_B.mov







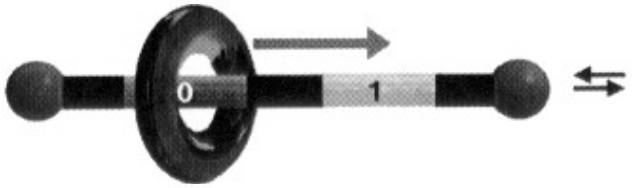
Synthetic molecular motors

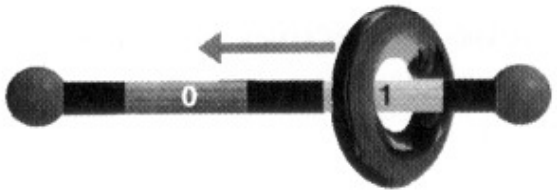
Biological motors offer great inspiration for the design of **artificial motors** to achieve controlled movement at the molecular level

Rotaxane systems:

• A **macrocylce** (*train*) can travel along a **molecular chain** (*rail*) between two *stations* (0,1)

• *Train's* position depend on the electron composition of the *stations* and *train*





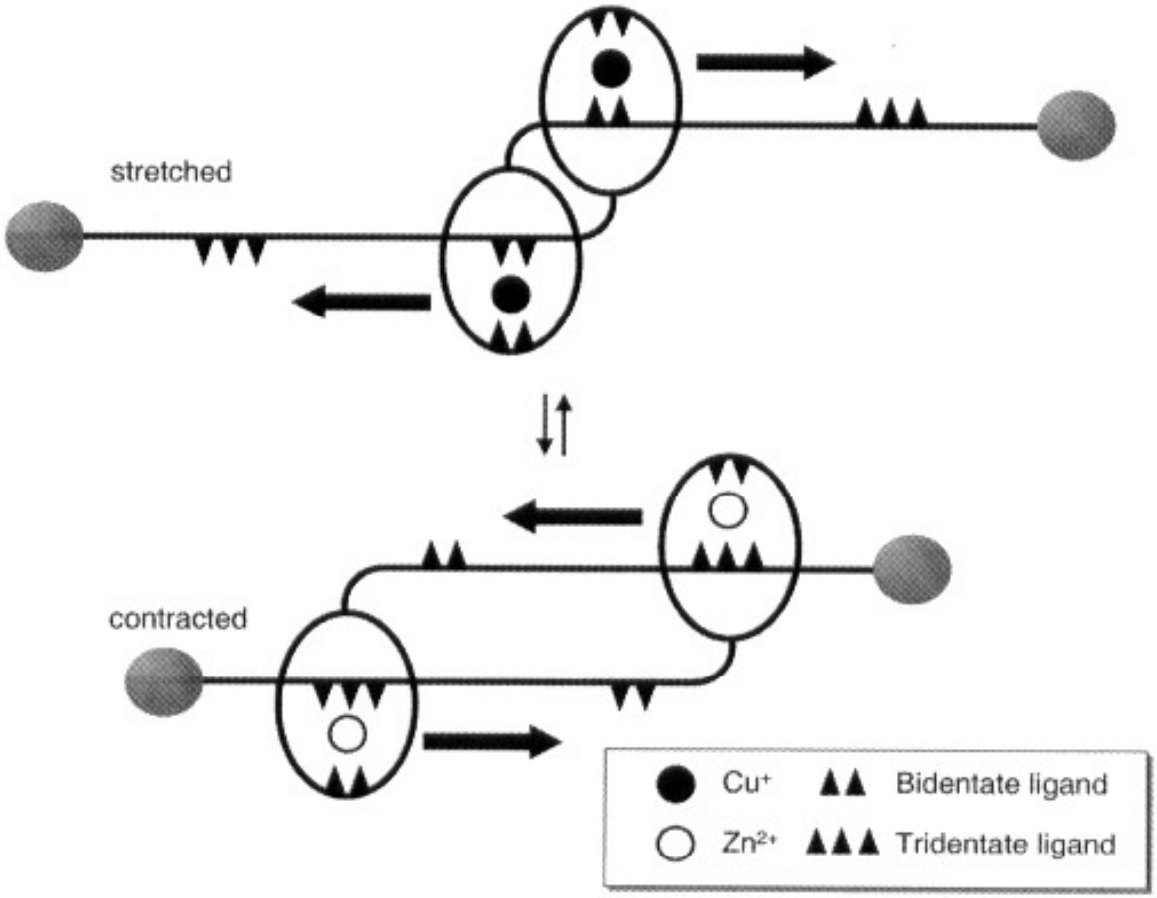
• Translocation of train can be achieved by redox or acid/base stimuli as well as photochemically

• Translocation is initiated by **protonation of station 0** making the interaction between **train and station repulsive** (train moves to station 1 as a result)

• After deprotonation the system relax back to its initial state (train back to station 0)

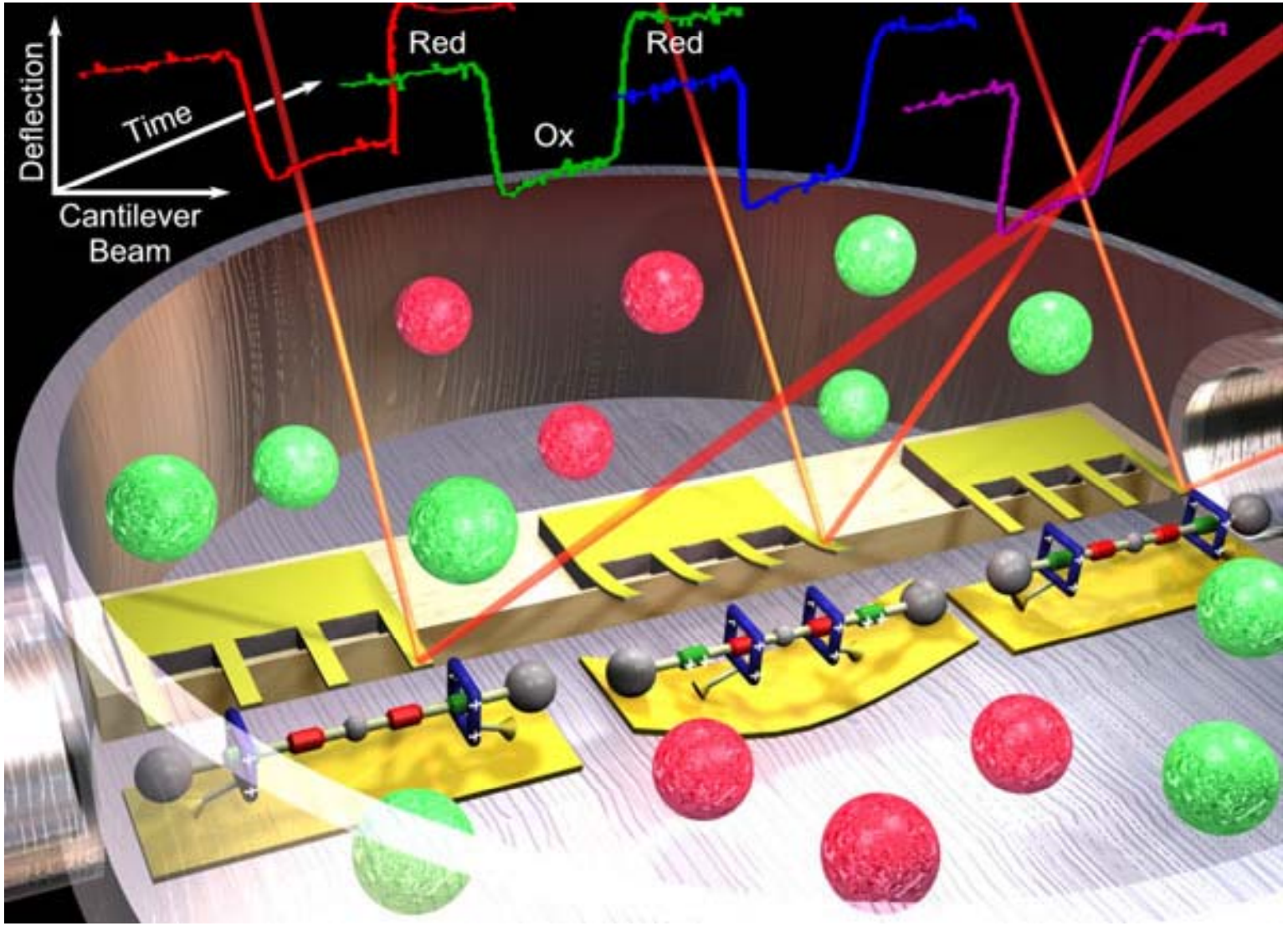
Synthetic molecular muscle

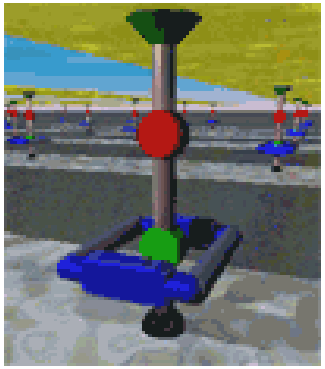
- Two linear **intertwined rotaxane** units can <u>contract and stretch like a muscle</u>
- In the presence of Cu^{+} the conformation is **stretched**
- In the presence of Zn^{2+} the configuration is **contracted**



Molecular muscles

NEMS (Nanoelectromechanical systems) device based on rotaxane coated AFM cantilevers: redox-driven contraction/relaxation of rotaxanes results in a measureable deflection of the laserbeam

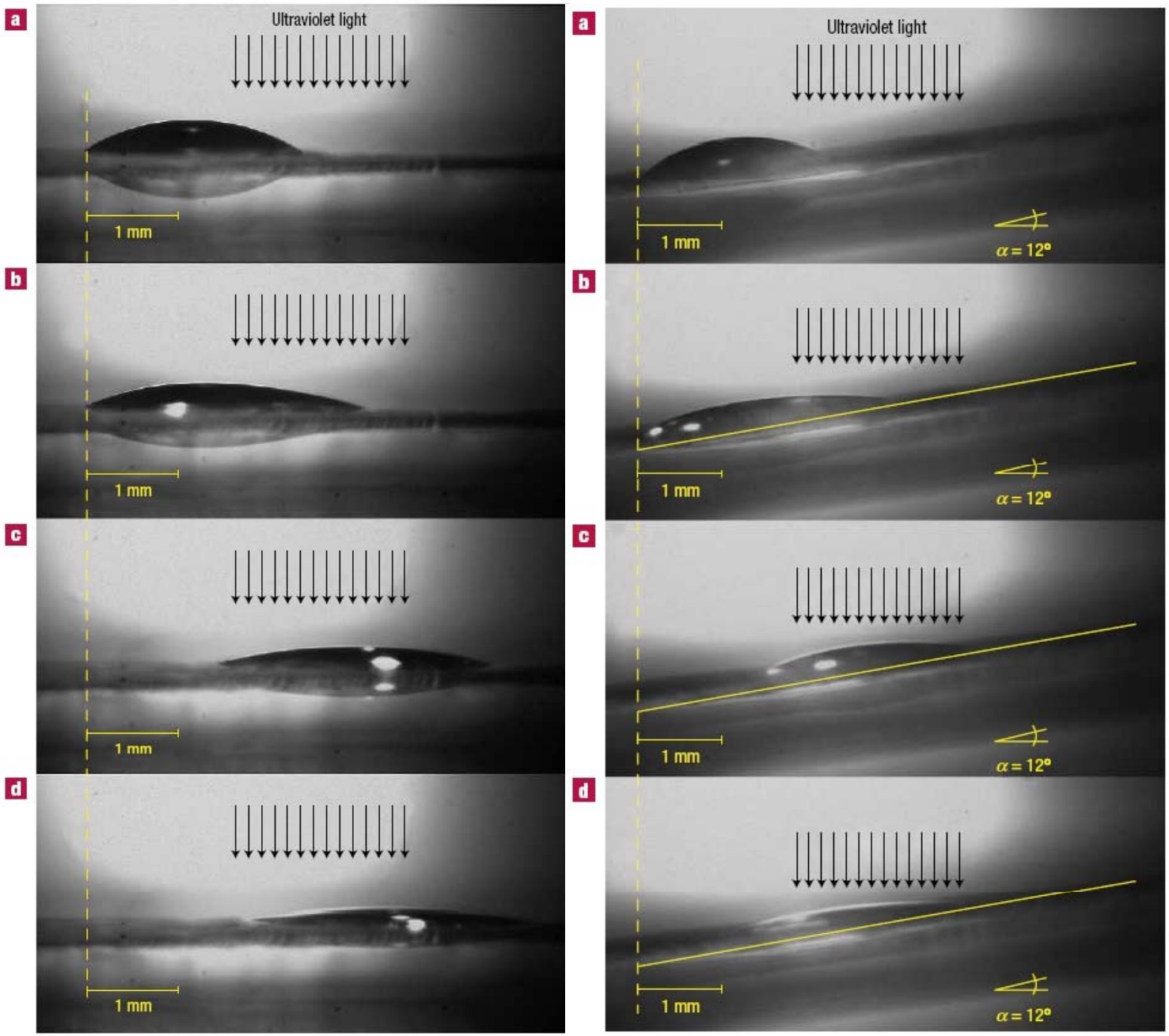




Reducing agent

Oxidizing agent

“Magic” movement of a liquid drop driven by rotaxanes



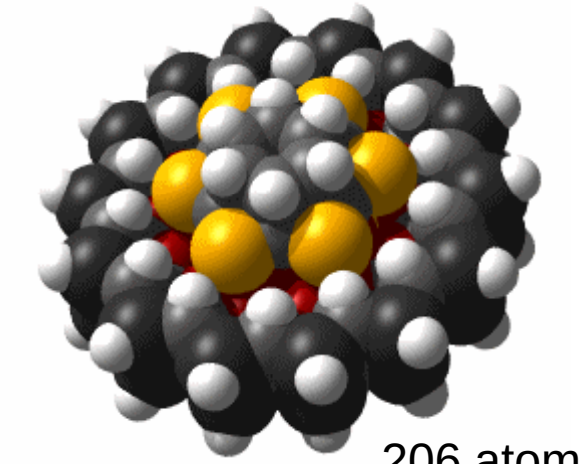
A monolayer of rotaxanes (turned on and off by UV-light) was able to move a liquid drop (1.25 µl) on a steep surface

Berná et al., Nat. Mater., 2005

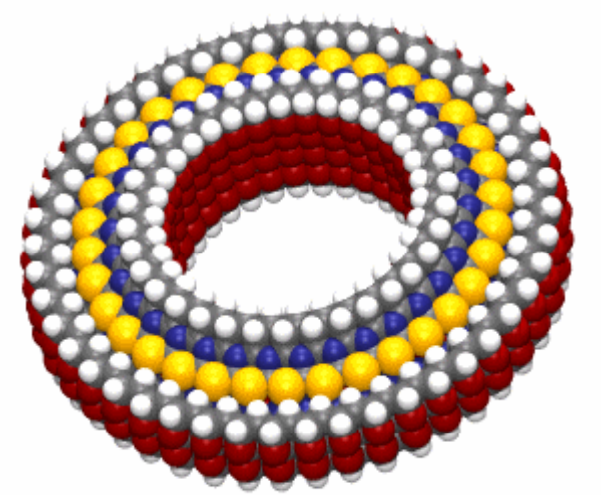
Computer models of non-biological nano-machines

- Many **macroscopic machines** can be reduced to the nano-level
- Some might work even better (no friction, no wearing/tiring) some might be impossible to design based on their complexity (e.g., atomic power plant)
- Examples of current modeled nano-constructions are:
    - Nano Bearing
    - Nano Gear
    - Nano Filter
    - Nano Pump
    - Nano Electromotor/ Nano Car
    - Nano Computer (simple I/O)
- A nano-bearing does not need any bearingballs or lubricants
- It works based on **strong** covalent bonds and **weak** "van der Waals" repulsive forces
- **Simulations** are based on reliable software tools already used by Chemists for many years

Nano-bearings



206 atoms



2,808 atoms

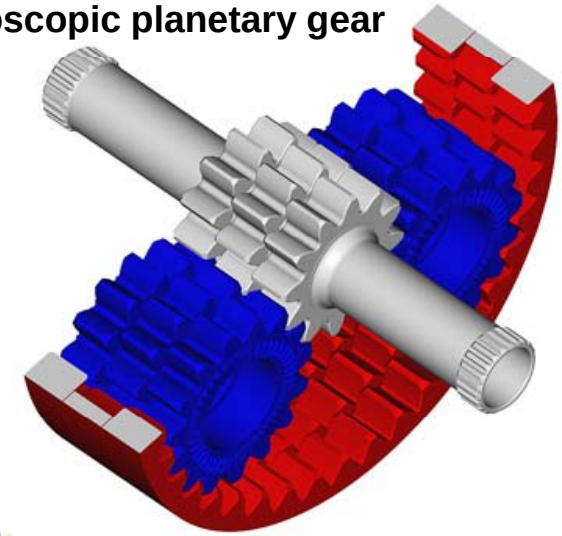
Macroscopic bearing with bearing balls embedded in lubricant

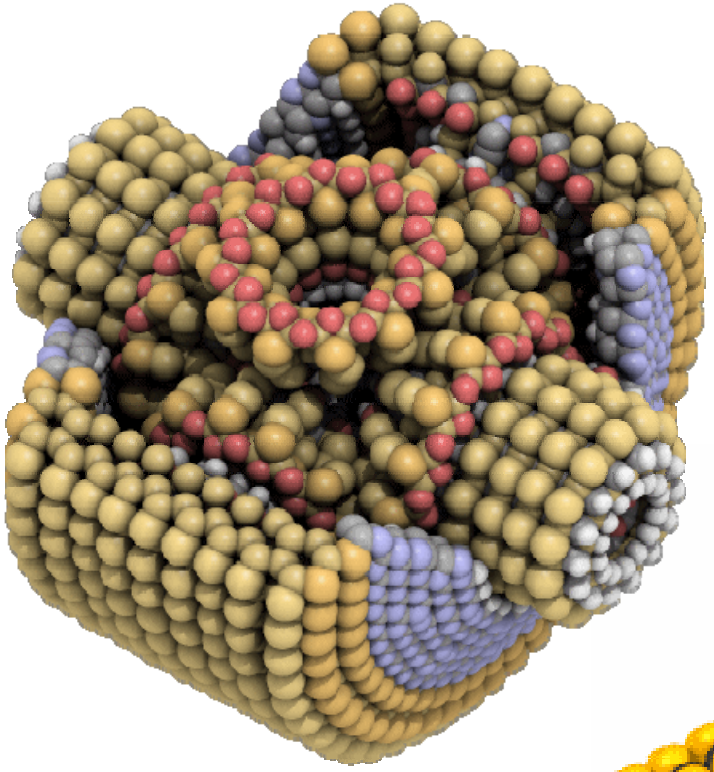
http://www.e-drexler.com/

Computer models of non-biological nano-machines

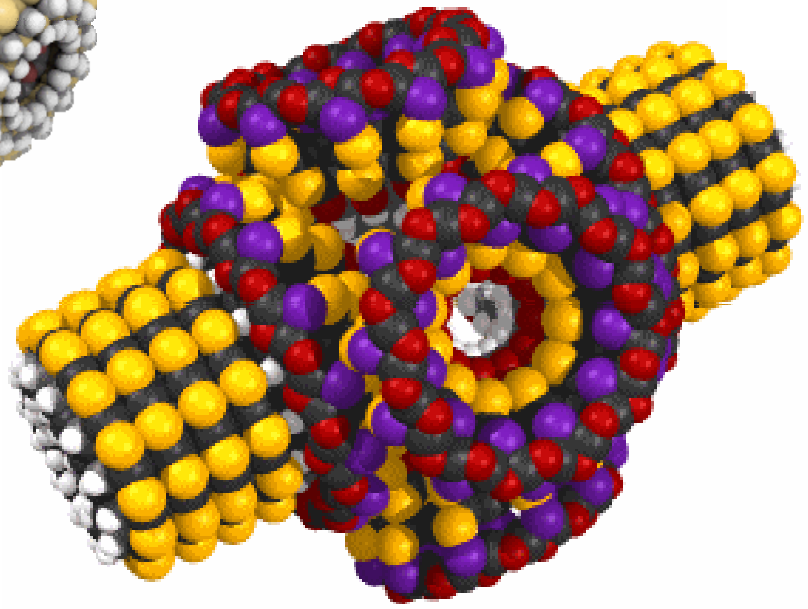
- Planetary gearing is a gear system that consists of one or more outer gears, or **planet gears**, revolving about a central, or **sun gear**
- Planetary gears **convert shaft power** from one angular frequency to another

Macroscopic planetary gear





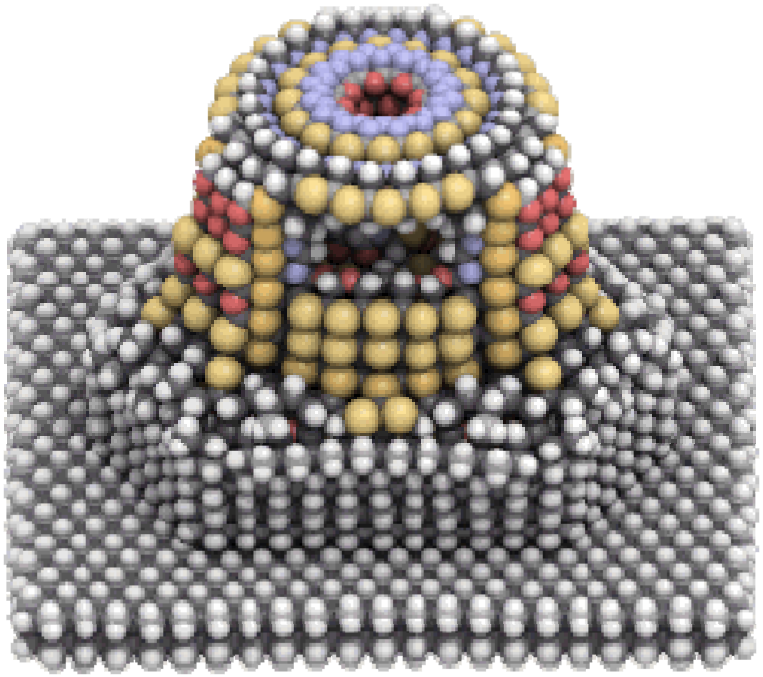
Nano planetary gear

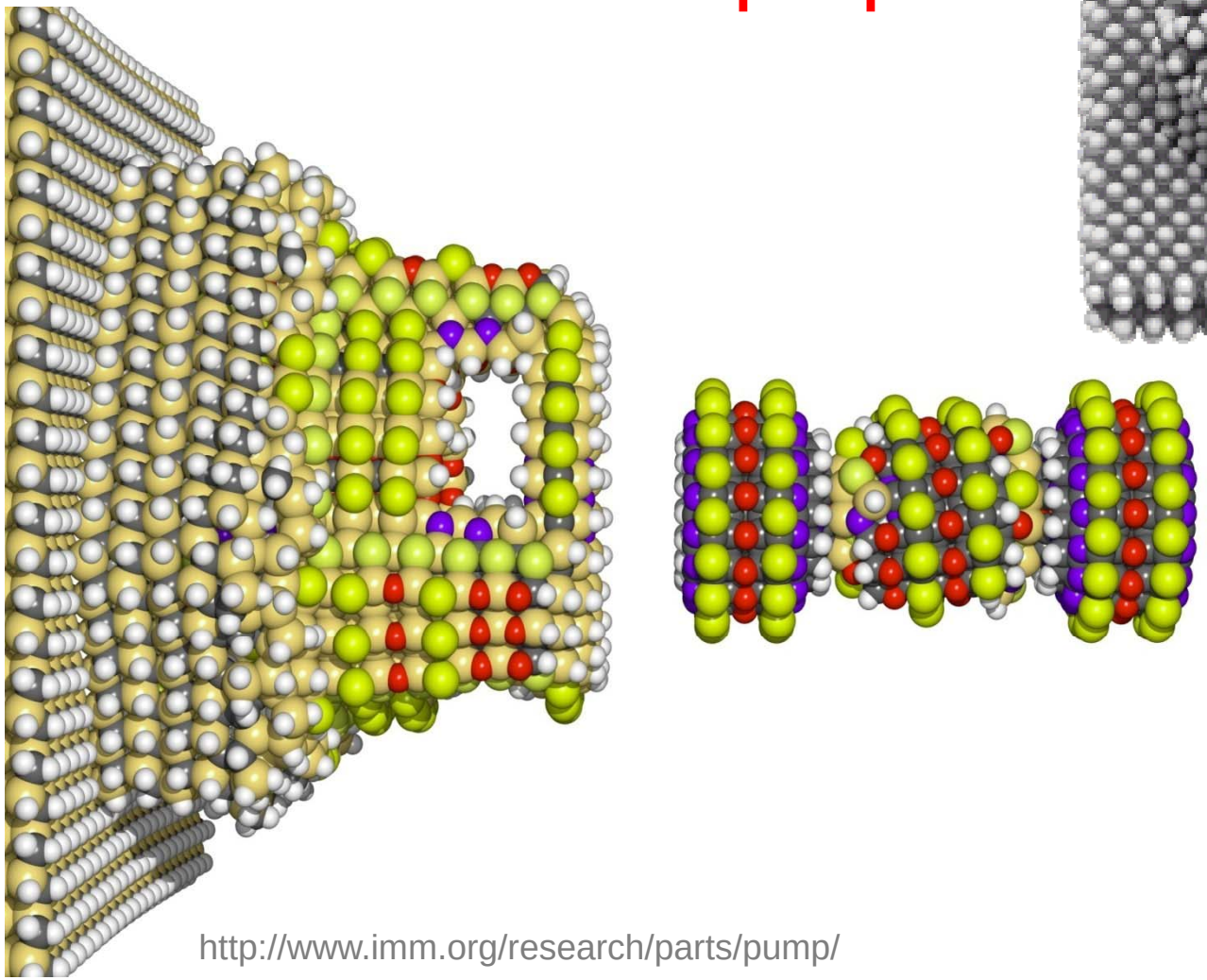


http://nanoengineer-1.com/

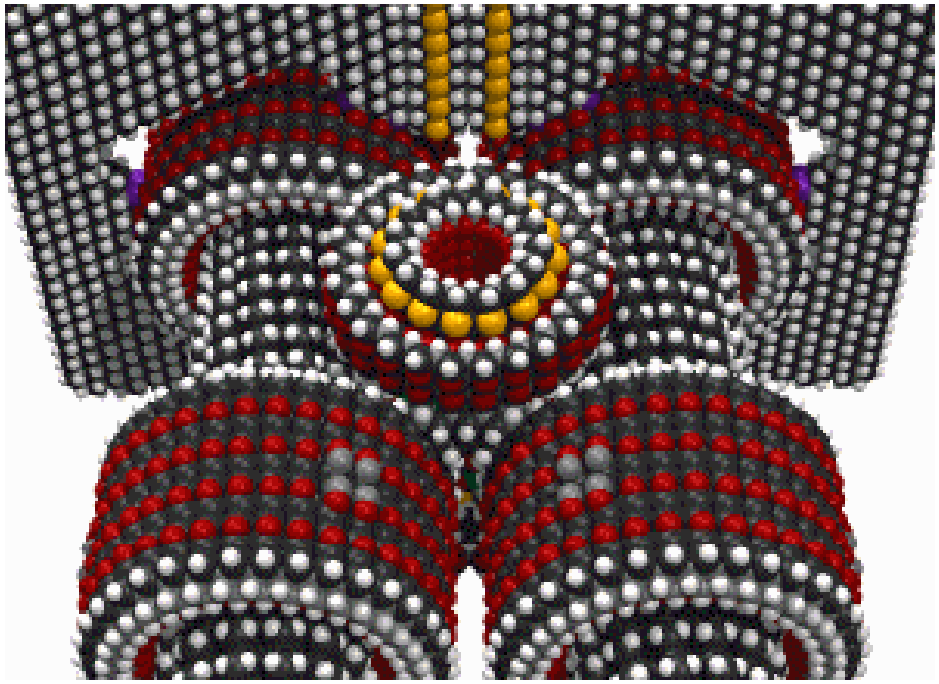
Computer models of non-biological nano-machines

Nano-pump



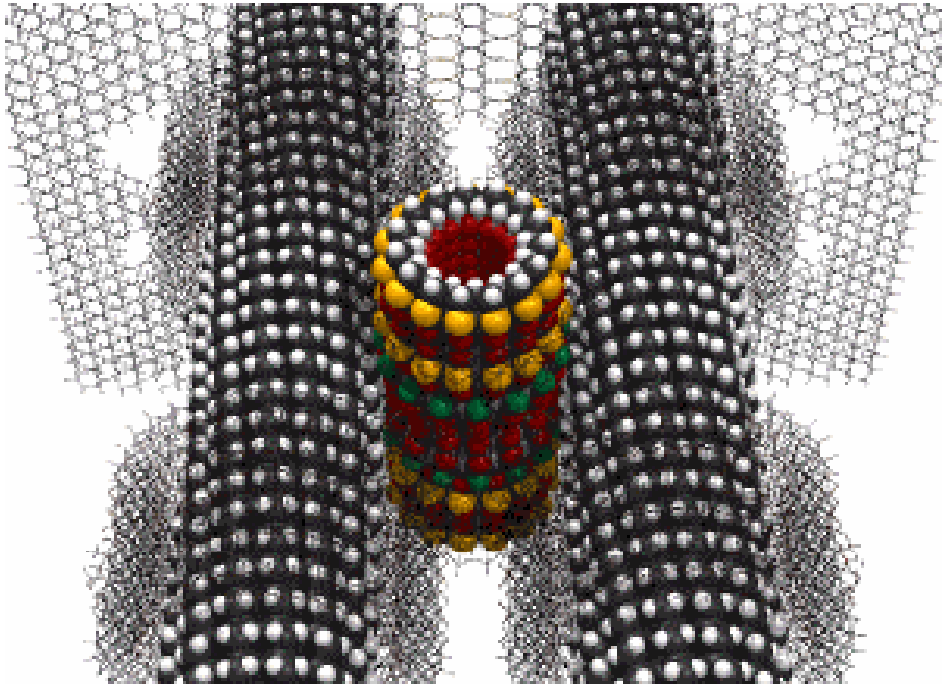


http://www.imm.org/research/parts/pump/

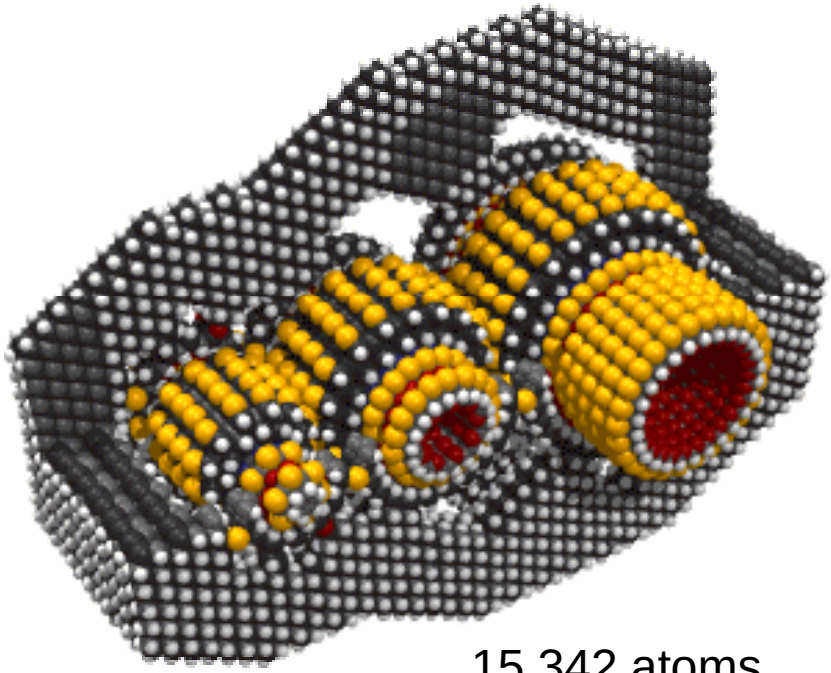


Complex nano-machines

- **Nano-worm drive** assembly containing 11 components made from 25,374 atoms
- Simulations **took 340 hours** to complete (on a regular desk-top computer)



Nano speed gear reducer

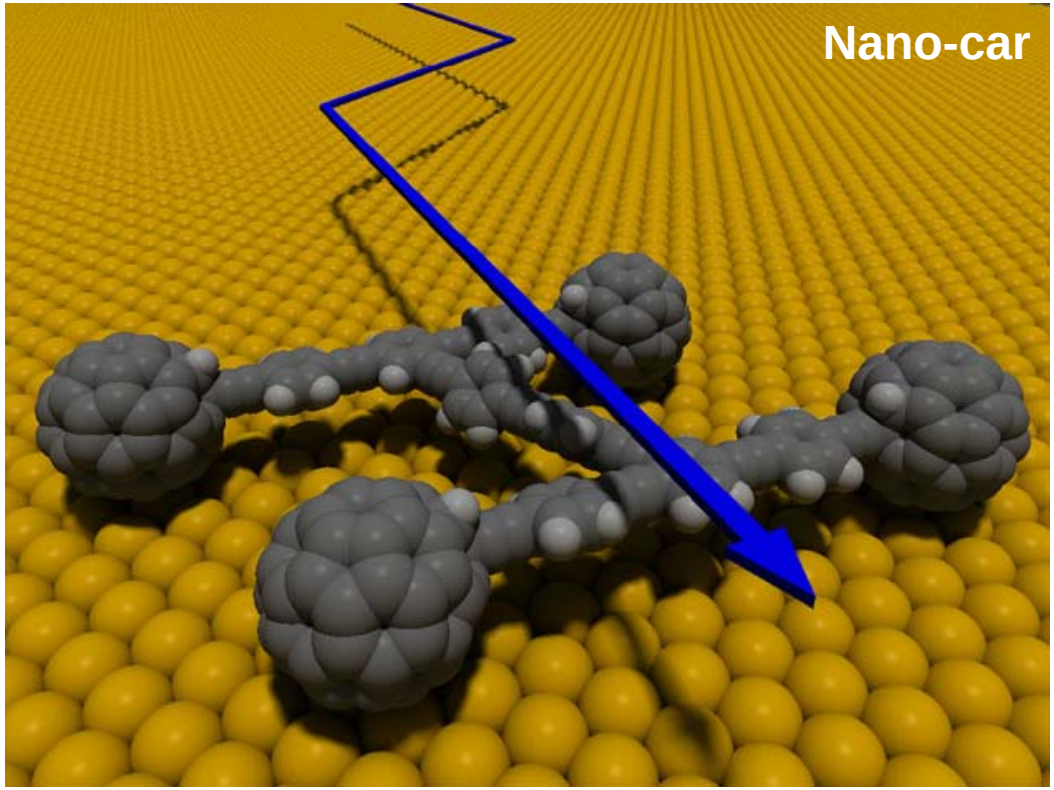


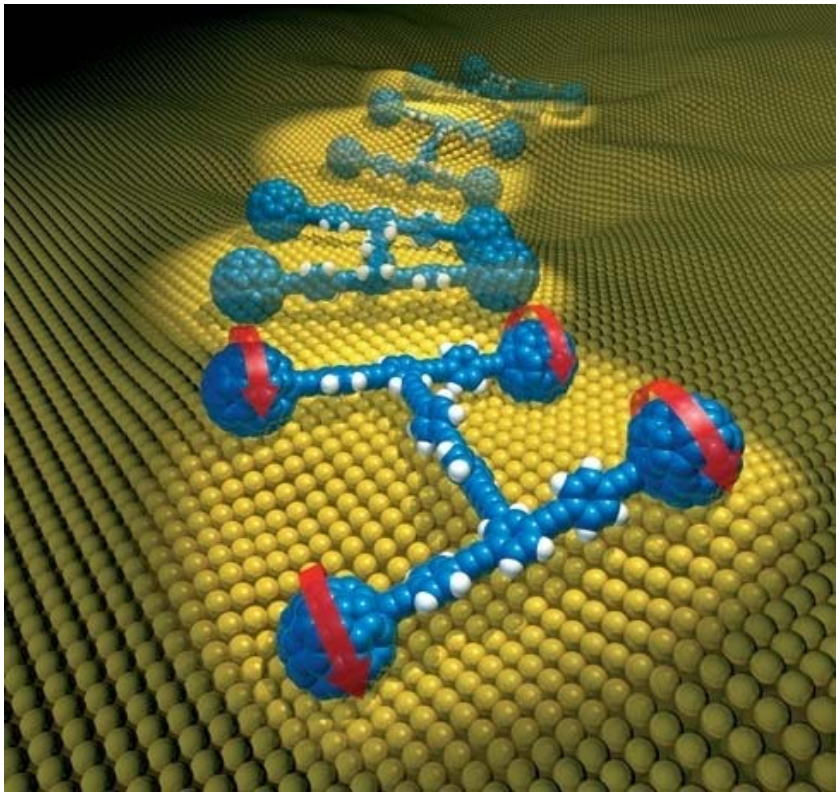
15,342 atoms

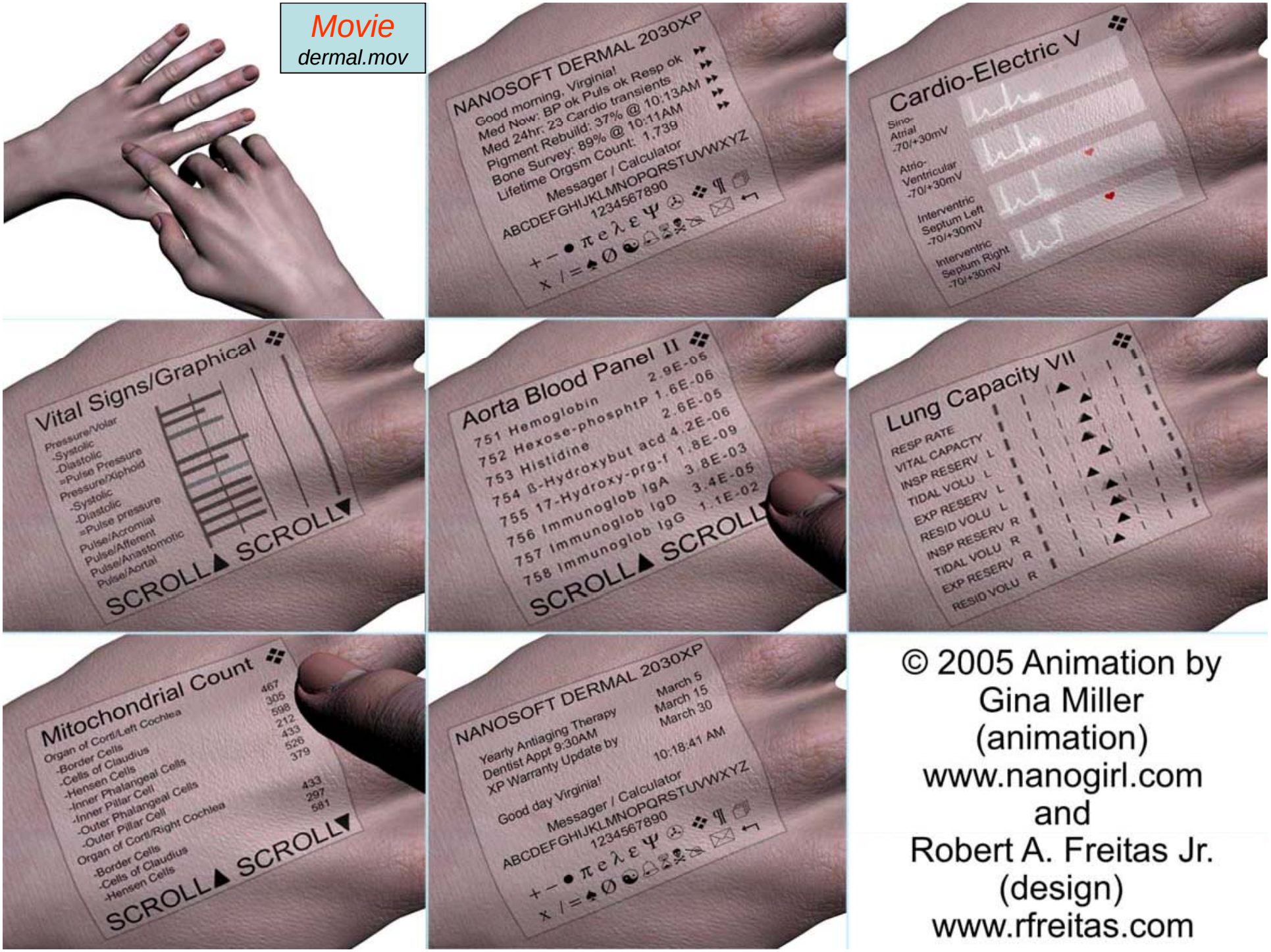
http://www.e-drexler.com/

Applications, open questions and critique

• It's **only a matter of time** before nanotechnology (combined with MEMS and optofluidics) can result in the fabrication of **neuroprosthetic devices**, **artificial retina** etc.
• Very far from now perhaps a brain implant using biological molecules to store data can back-up human memories (which might otherwise be lost due to ageing or degenerative diseases)
• It might be feasible to think of atom-by-atom manufacturing of such components in **nanofactories**
• However: The two machines containing about 25,000 atoms, are the most complex simulations ever created and they haven't even been built yet!
• By comparison: An **ion channel** (one of nature's sophisticated nanomachines) can have a molecular mass approaching 1MD (Mega Dalton), and contains **millions of atoms**

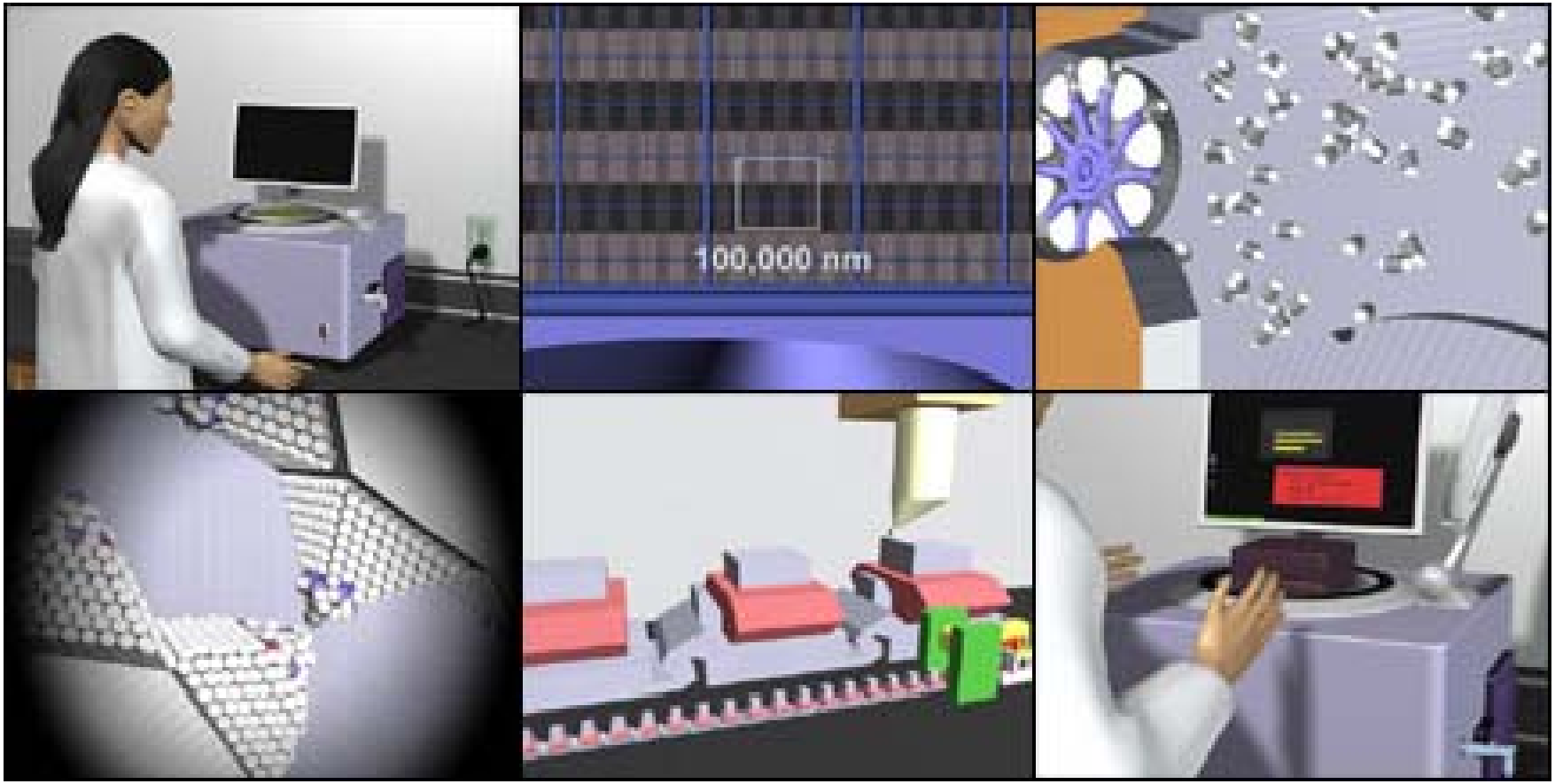






Nano Factory

Movie
NanoFactory.mov



http://www.e-drexler.com/

What is nature, what is life, what is a machine?

• Since **we are composed of units** that can be dissect into parts, modules, domains, proteins and atoms the question might arose: **Is life artificial?**
• Protein motors, intercellular sensors, membrane channels, protein scaffolds etc. leads to an **mechanistic** **understanding of the cell** (contrary to **vitalist** view)
• However: **Less fruitful** doing biological research is to pull organisms apart and inspecting them piece by piece (**reductionism**)

• A distinction between natural and artificial goes back at least to **Aristotle** and **Plato** but this distinction **is becoming increasingly irrelevant**: living organisms look more and more like machines, and machines look more and more like living organisms
• The **natural/artificial distinction** is highly discussed in religion, genetic engineering, food production, virtual realities, computer intelligence, medicine etc.
=> here "natural" is mostly considered beneficial, safe, reliable and trustworthy while "artificial" is basically considered imperfect, immoral, unhealthy, damaging and dangerous

Raymond Kurzweil's vision

- **Inventor and futurist**: optical character recognition (OCR), text-to-speech and speech recognition technology and electronic keyboard instruments
- **Author** of several books on artificial intelligence (AI), transhumanism, **the technological singularity**, and futurism
- Receiving many awards in including 15 (!) honorary doctoral degrees
- He made many **future (technology) predictions** while many of them became surprisingly reality

The technological singularity (predicted 2005):

2010-2020

- $1000 computers have **same processing power as human brains**
- Computers become smaller and increasingly integrated into everyday life (clothes, furniture...)
- **Glasses** that beam images onto our retinas to a **produce virtual reality (VR)**
- VR glasses have built-in computers with "virtual assistant" programs that can help us with various daily tasks ("**augmented reality**")

2020-2030

- Computers less than 100 nm big
- **Nanomachines** are **used for medical purposes** ("brainscans")
- Nanobots capable of entering the bloodstream to "feed" cells and extract their waste (we don't need to eat anymore)
- Nanotech-based manufacturing everywhere
- **Virtual reality** will be of such a high-quality that it will be **indistinguishable from real reality**
- A computer is a "Strong A.I." (artificial intelligence) and can think like a human

Kurzweil's prediction of a technological singularity

2030-2040

- **Mind uploading** becomes possible: "Copy and paste" a complete human's mind
- Nanomachines in brain control incoming and outgoing signals (can also block internal signals)
    - As a result, **truly full-immersion virtual reality** can be generated
    - Better cognitive, emotional, memory and sensory capabilities
    - Directly interfaing with computers
    - "Telepathically" communicate with other
- "Human body 2.0" consists of a nanotechnological system of nourishment and circulation: **no need for many internal organs**
- "Human body 3.0": Improved skeleton and **can alter its shape and external appearance**

2045-

The singularity

- Technological singularity = artificial intelligences beat human beings as the smartest and most capable life forms on the Earth
- Technological development is taken over by the machines
- Machines enter into an **uncontrolled reaction of self-improvement cycles**
- From this point, **technological advancement is explosive**

Kurzweil’s prediction of a technological singularity

• The **elimination of humanity** by violent machines is **unlikely** because it is difficult to say who is (an enhanced) human and who is machine (A.I.) anyway
• A.I.s **convert more and more** of the Earth's **matter into engineered**, **computational substrate** to support even more A.I.s. **until the whole Earth is one, gigantic computer**
• At this point, the only possible way to increase the number of machines any further is to begin **converting all of the matter in the universe into similar massive computers**
• This is called the **"wake up of the universe”**: all "dumb" matter (stones, dust, gases, etc.) is converted into intelligent matter

2099

• Planet-sized computers exist

2199

• Process of “wake-up of the universe” is completed
• Physical control over the whole universe: **clearing the laws of physics possible**, therefore time, space and interdimensional travel possible

http://en.wikipedia.org/wiki/Ray_Kurzweil

The critiques

Douglas R. Hofstadter (Author of popular book “Goedel, Escher, Bach”):
• "It’s as if you took a lot of **very good food** and some **dog excrement** and **mix it all** up so that you can't possibly figure out what's good or bad”.
• “It's an intimate **mixture of rubbish and good ideas**, and it's very hard to distinguish between the two, because these are smart people; they're not stupid."

Bill Joy (Cofounder of Sun Microsystems): Agrees with Kurzweil's timeline of future progress, but believes that technologies such as A.I., nanotechnology and advanced biotechnology **will create a dark, pessimistic, harmful and depressing (dystopian) world**

Integrating single cells into stable tissues

3 principles act to form a tissue from single cells:

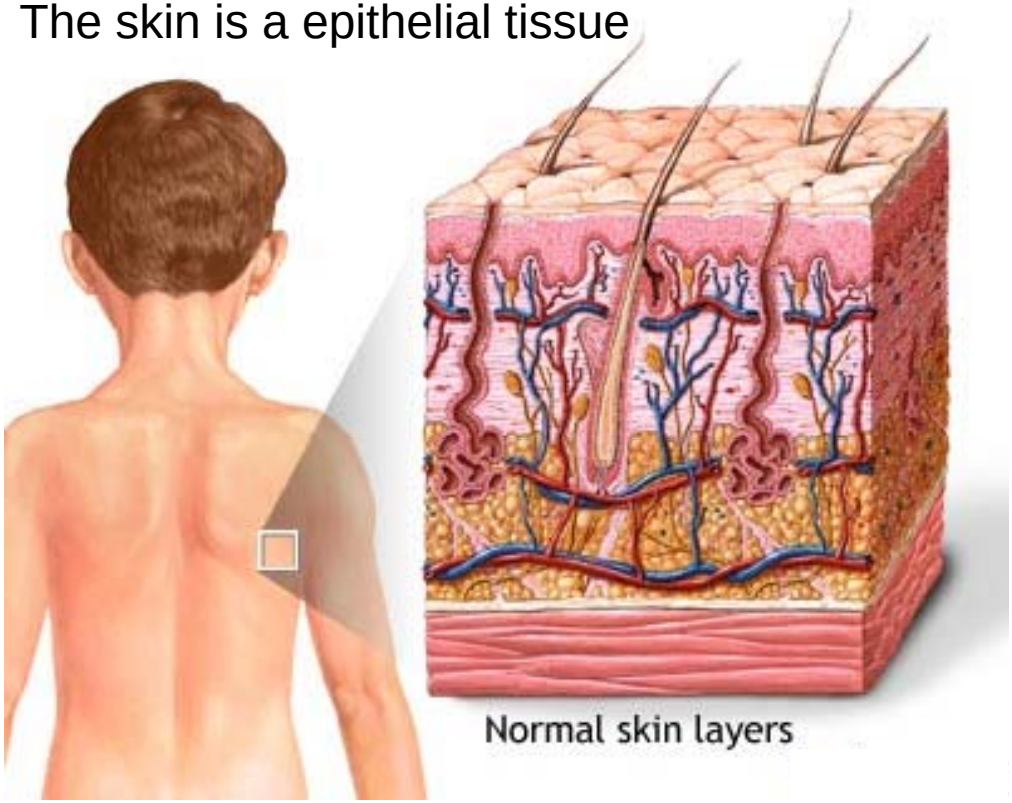
1) **Cytoskeleton** not only acts to stabilize single cells but also helps to **connect a cell to a neighbor cell**

2) Specialized (polymeric) proteins make **cell-cell contacts** (cell adhesion molecules, **CAM**)

3) An matrix outside the cell (extracellular matrix, **ECM**) acts as a **fibrous filling material** and to glue cells to each other

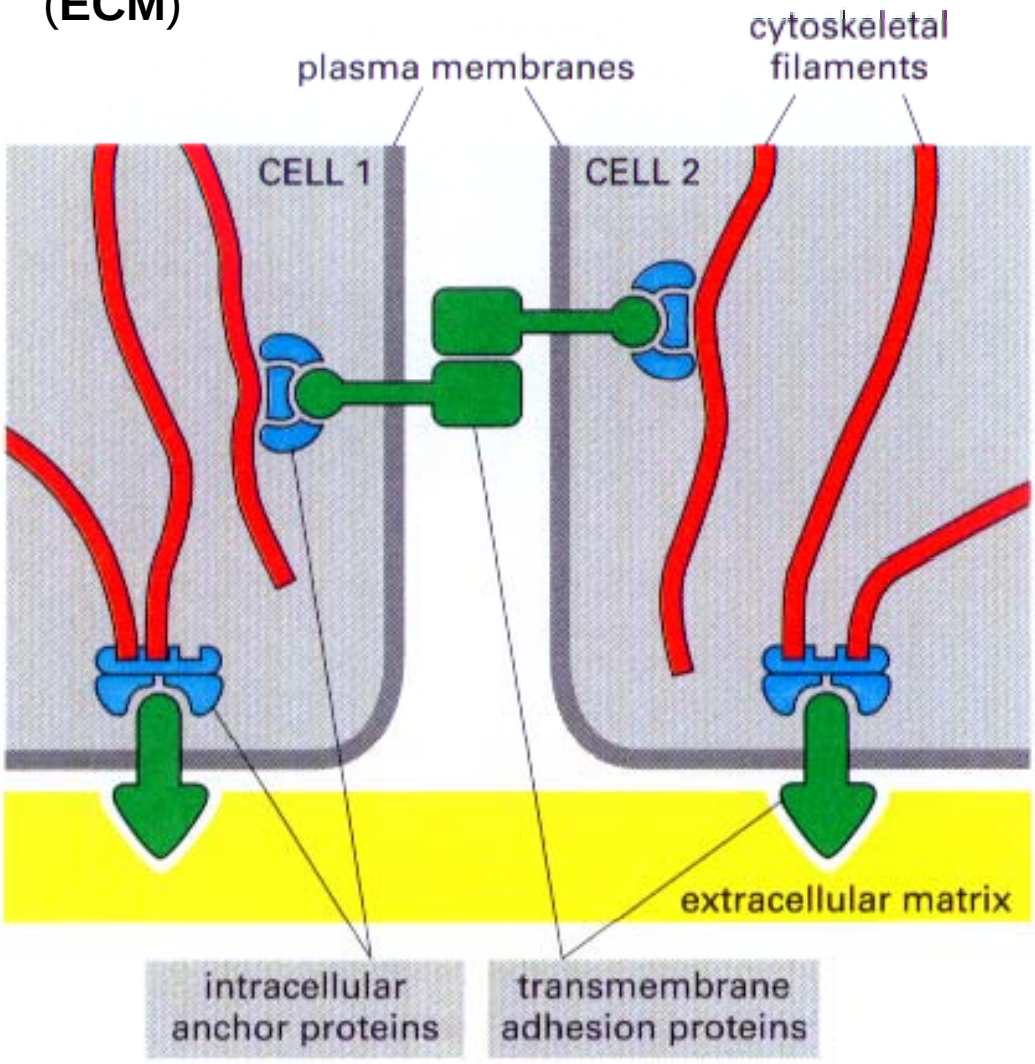
Single cells need to be stick together in a tissue as bricks in a wall

The skin is a epithelial tissue

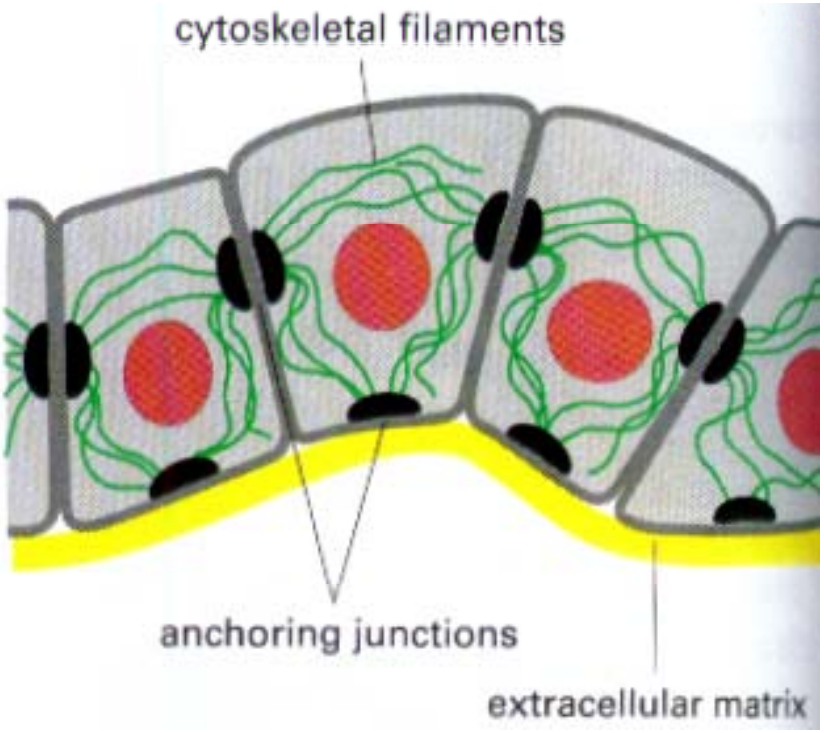


Integrating single cells into stable tissues

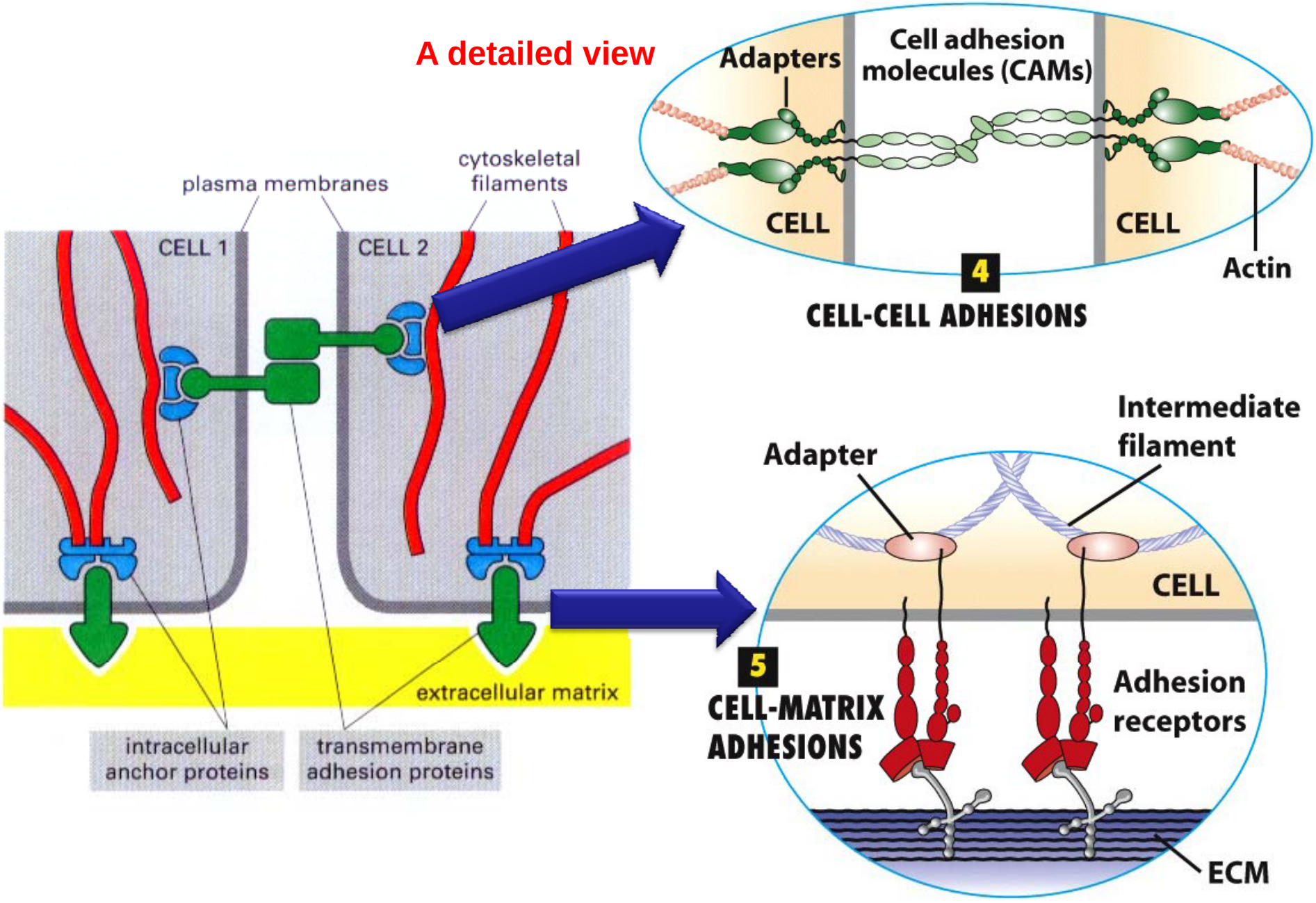
- **Intracellular anchor proteins** connect the **cytoskeleton** to **transmembrane adhesion proteins** (**CAM**s)
- **Transmembrane adhesion proteins** are embedded in the **extracellular matrix** (**ECM**)



Cytoskeletal filaments are connected to the anchoring junctions

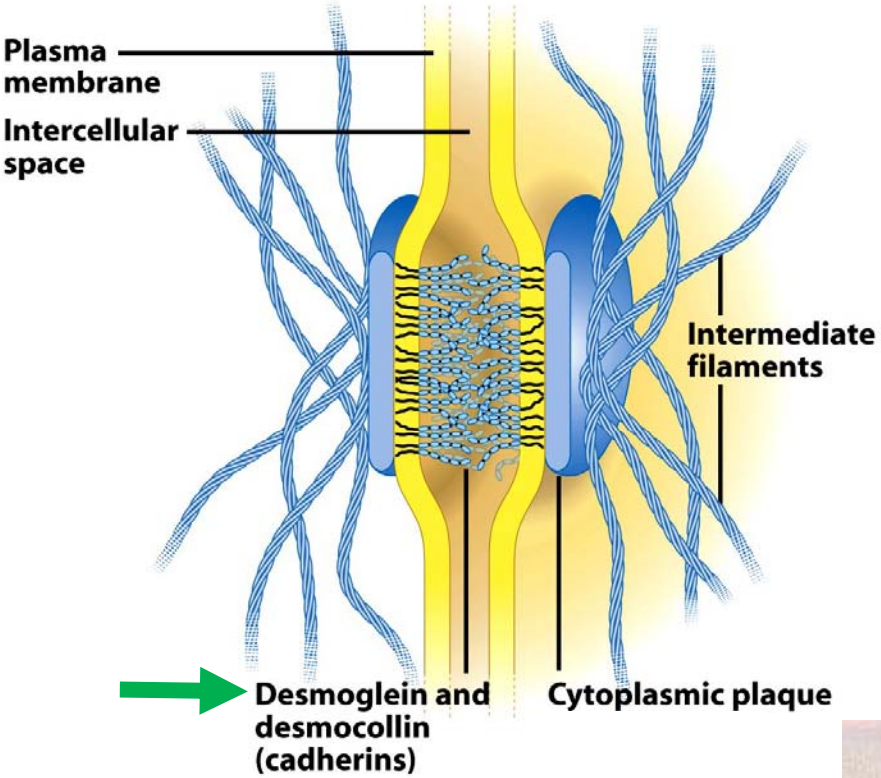


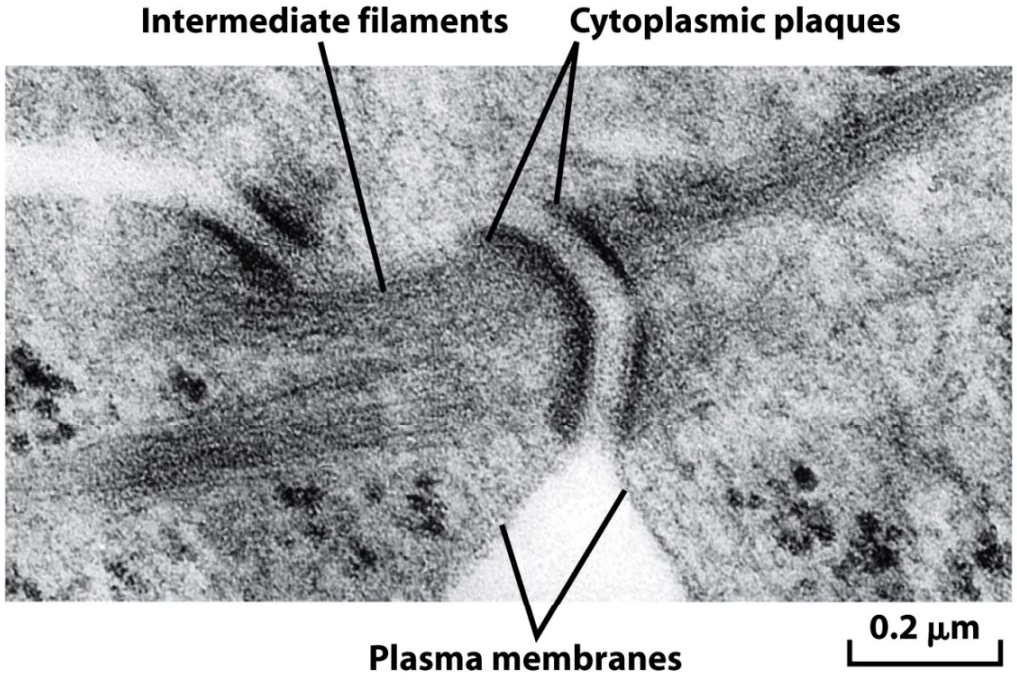
Integrating single cells into stable tissues



Desmosomes are button-like structures connecting two cells

Thick intermediate filament bundles connected to electron dense structures can be seen in EM of **two keratinocytes** (skin cells) firmly connected to each other

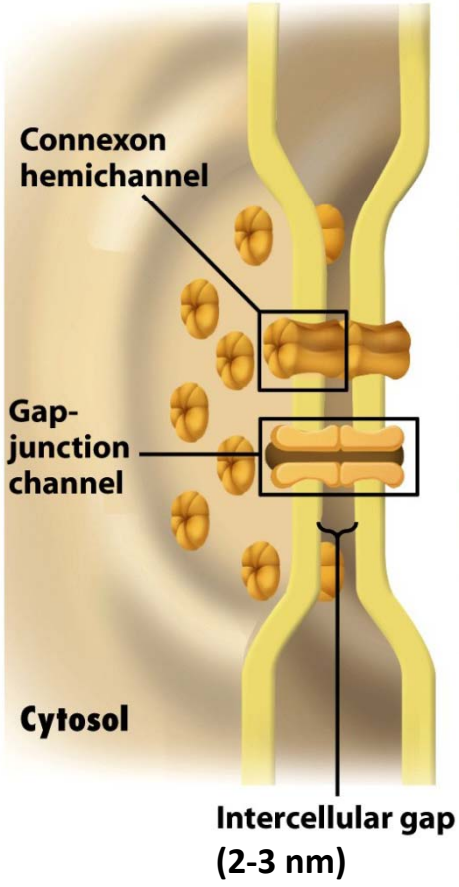


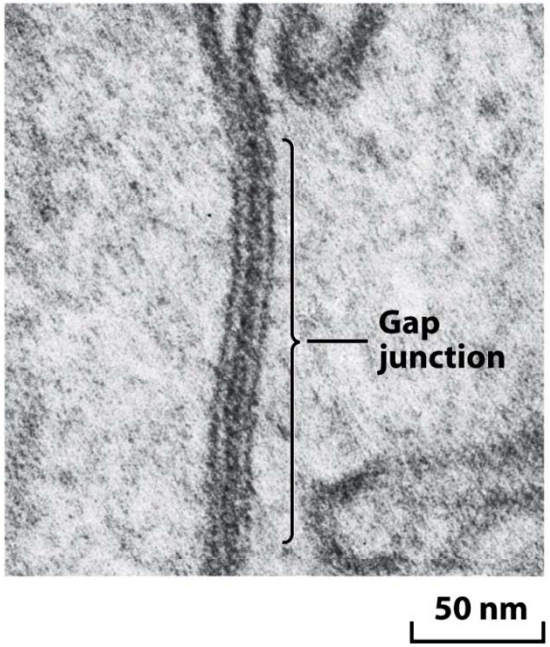


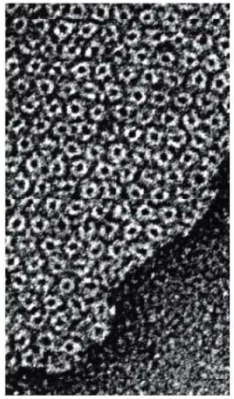
In the skin disease ***pemphigus vulgaris*** the protein **desmoglein** is non-functional, resulting in severe skin blistering

Gap junctions are 2-3 nm wide “food-channels” between 2 cells

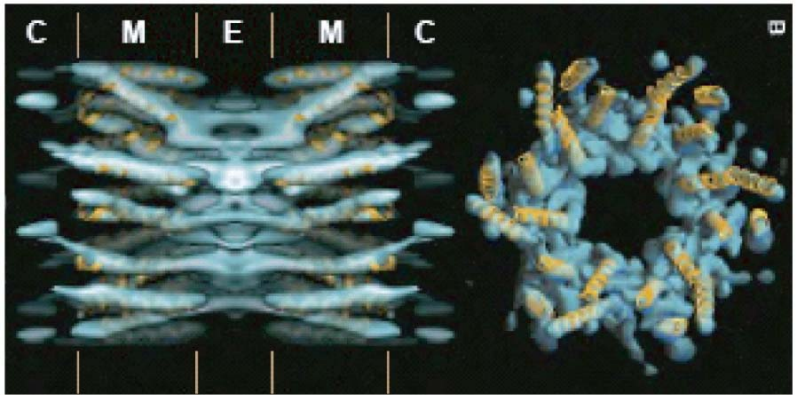
Gap junctions form a channel system for the exchange of small metabolites (as ions, sugars, vitamins, ATP etc.) between two cells







The gap junction channels is formed by the hexagonal protein **connexin**



Atomic structure of gap junctions

C = cytosol, M = membrane bilayer
E = extracellular gap

Cell junctions are crucial for tension and mechanical stability of tissues

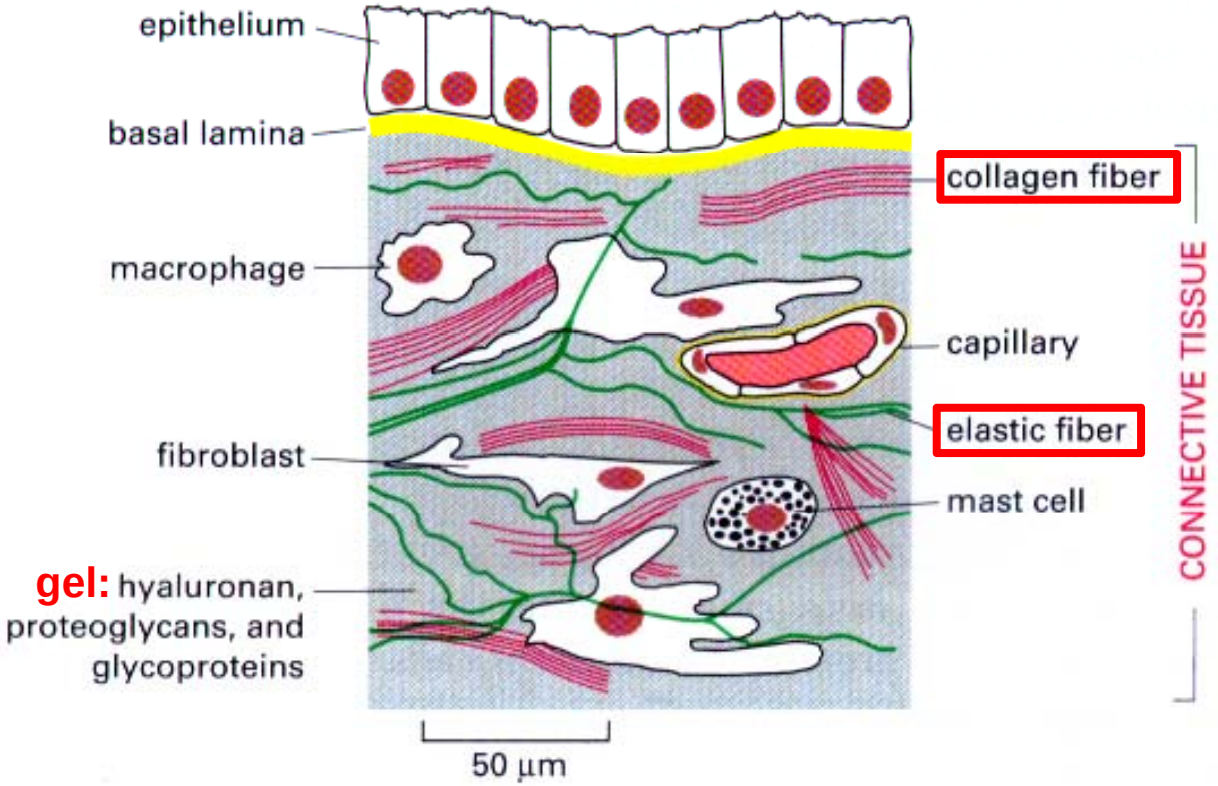
Since cell **junctions** integrate a cell's cytoskeleton and at the same time strongly connect to neighboring cells, shape, rigidity and cell strength are largely increased

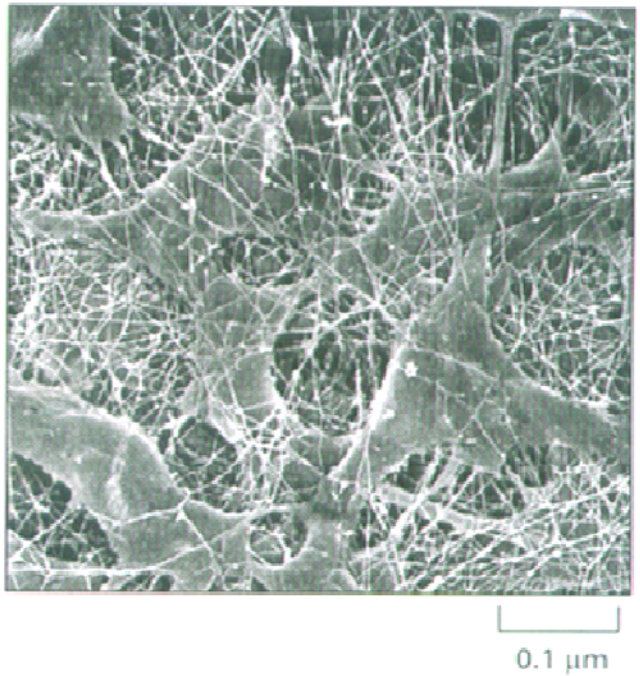
Functions of cell junctions

JUNCTION	ADHESION TYPE	CYTOSKELETAL ATTACHMENT	FUNCTION
Anchoring junctions			
1. Adherens junctions	Cell-cell	Actin filaments	Shape, tension, signaling
2. Desmosomes	Cell-cell	Intermediate filaments	Strength, durability, signaling
3. Hemidesmosomes	Cell-matrix	Intermediate filaments	Shape, rigidity, signaling
Tight junctions	Cell-cell	Actin filaments	Controlling solute flow, signaling
Gap junctions	Cell-cell	Possible indirect connections to cytoskeleton through adapters to other junctions	Communication; small-molecule transport between cells

ECM (extracellular matrix)

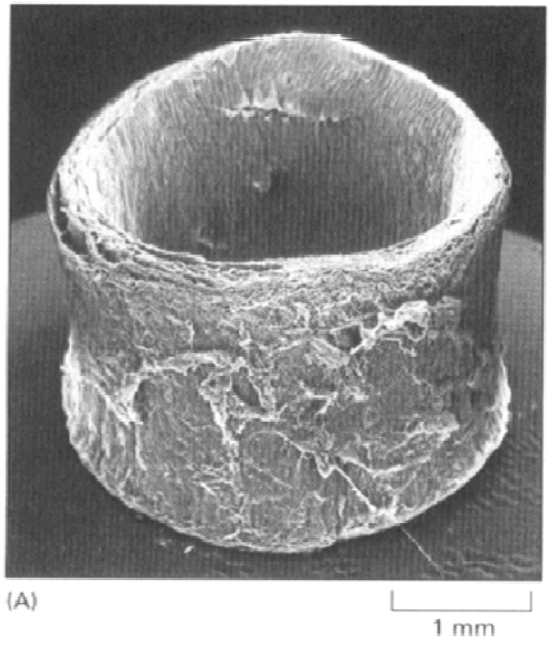
- Extracellular matrix (**ECM**) is the tissue below an epithelium (single cell layer)
- ECM contains **many highly elastic fibers** but also the cells that secrete these fibers
- These fibers and cells are embedded in a gel (**hyaluronan** and **proteoglycans**)



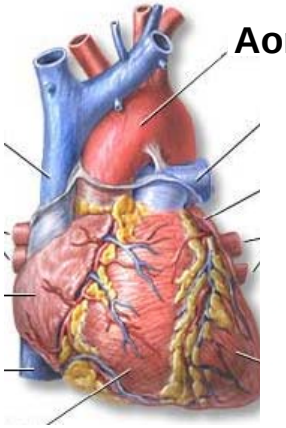


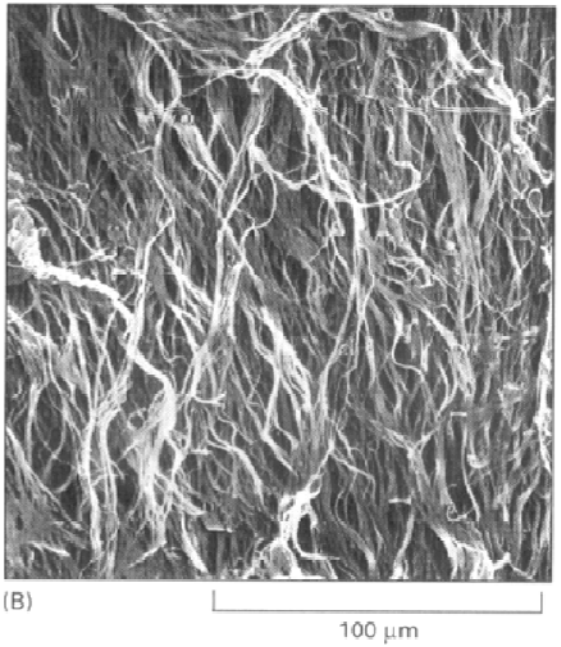
Fibroblasts embedded in the ECM

ECM contains stiff/non-elastic and highly elastic fibers



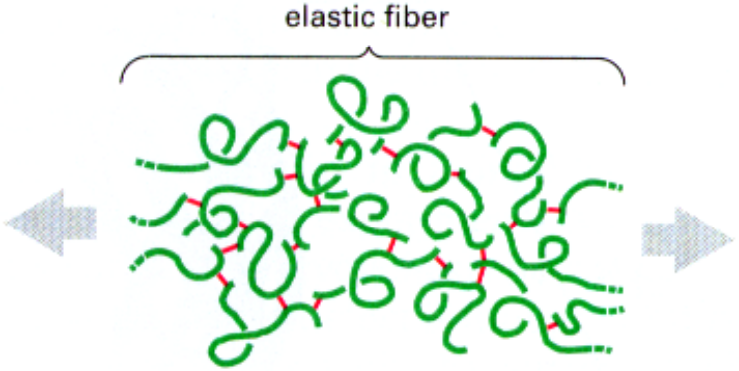
Highly elastic aorta need to resist strong and alternating blood pressure

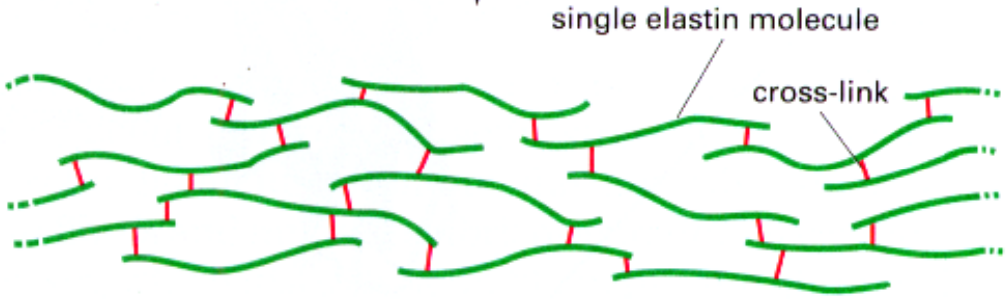


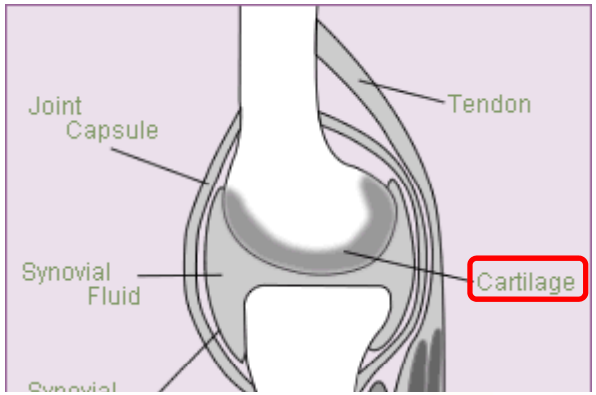


Elastic fiber (**elastin**) in the outer layer of the aorta

- **Elastin** molecules are highly cross-liked by covalent bonds
- An elastin assembly can stretch and relax like a **rubber-band**

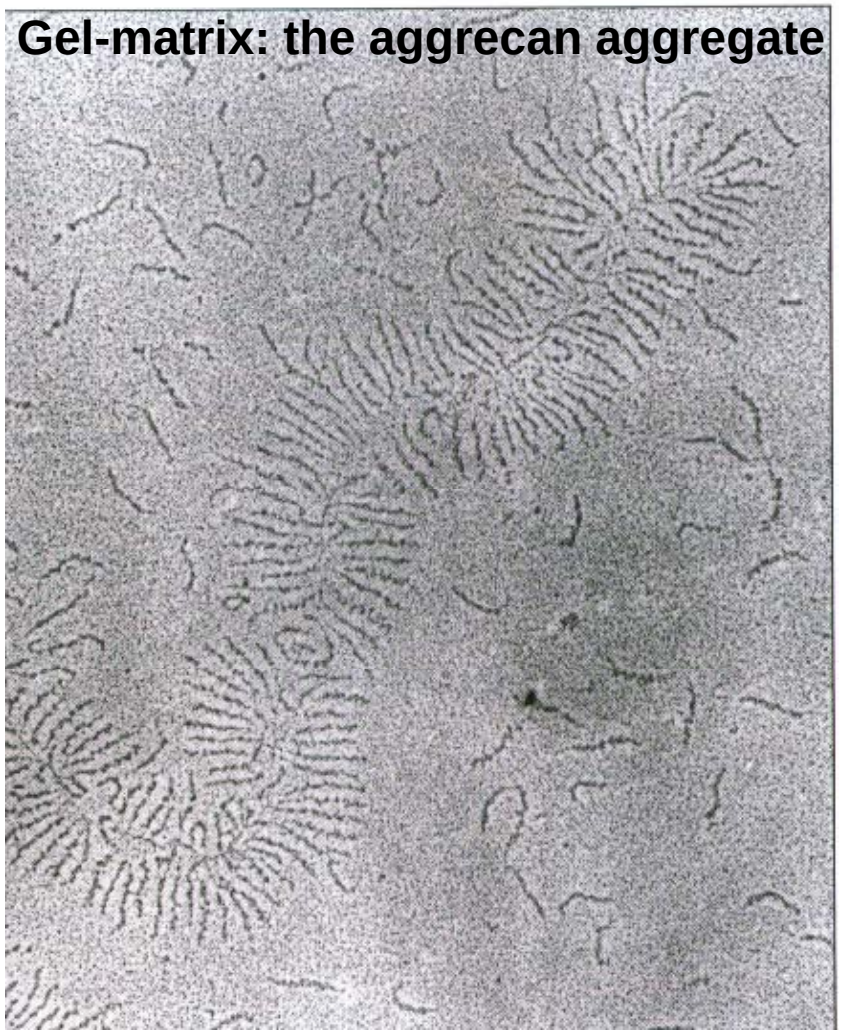


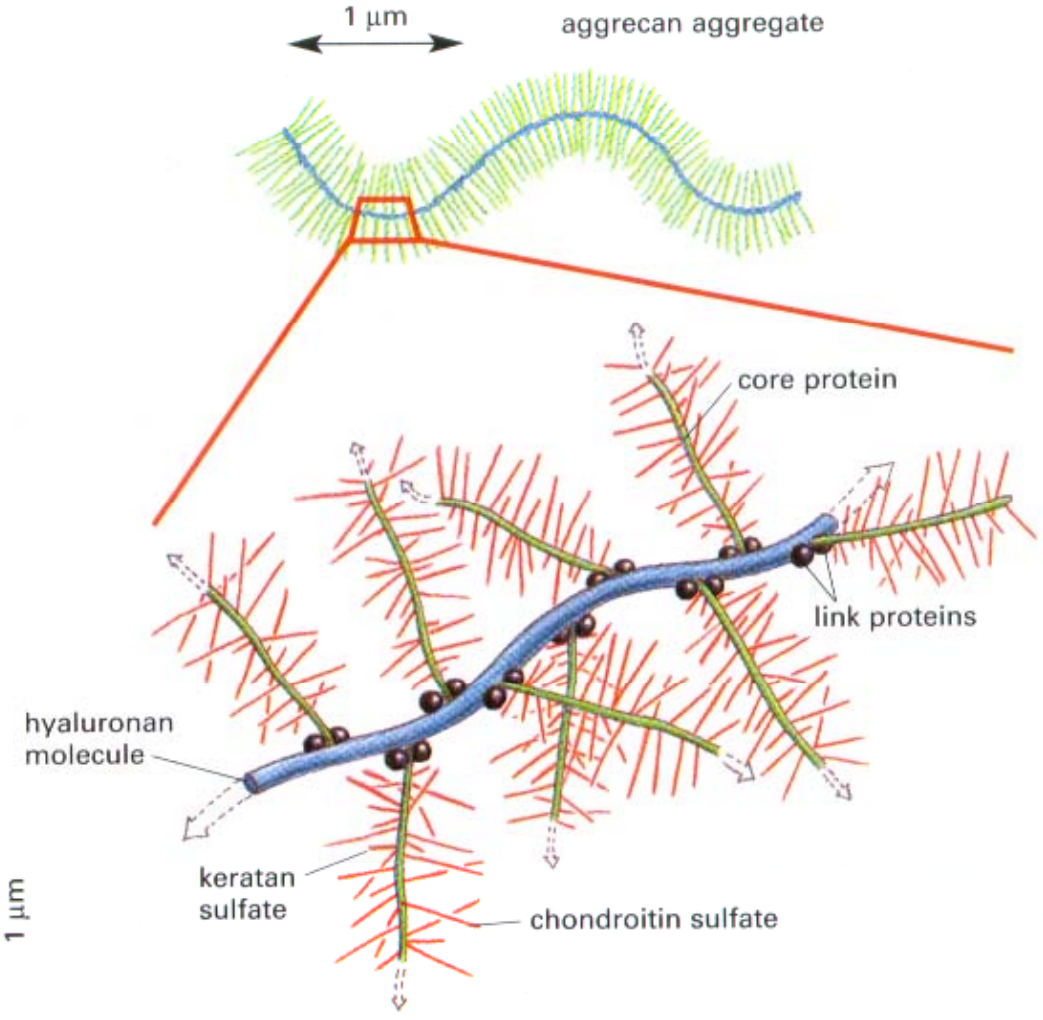




Hyaluronan resists compression and gives cartilage its gel-like properties

- Major component of cartilage is the **aggrecan aggregate**: huge molecule (MW 2 x 10^8) with a size of a bacterium
- Up to 100 **aggrecan** molecules are connected to a **hyaluronan** backbone

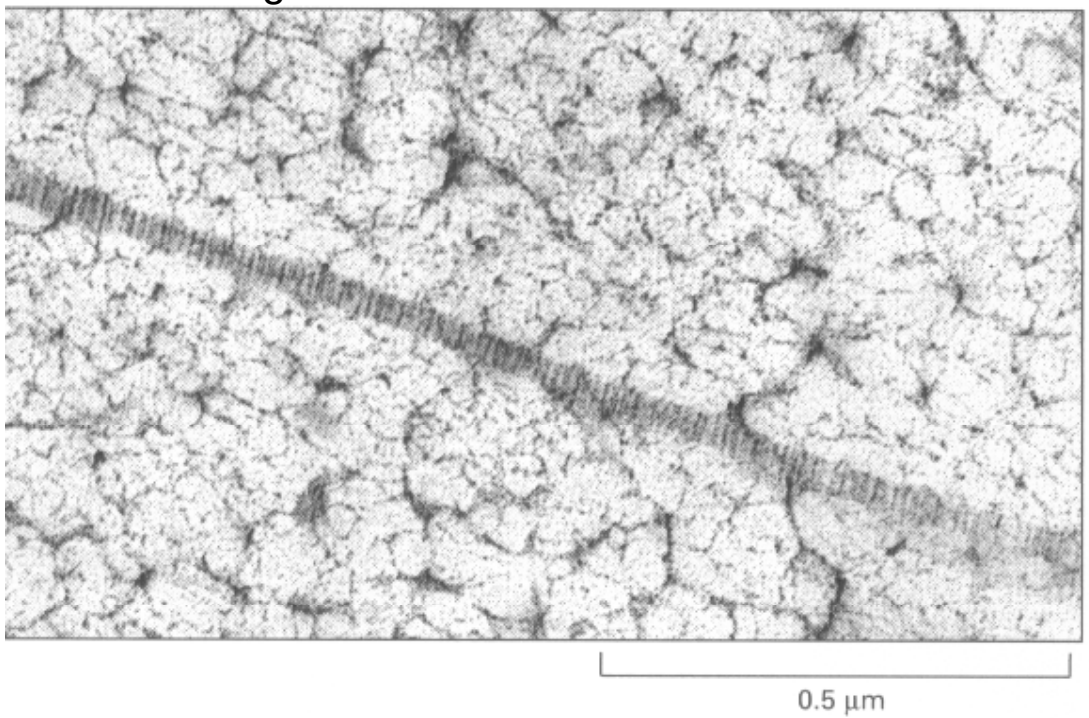




Collagens are elastic fibers found in skin and bone

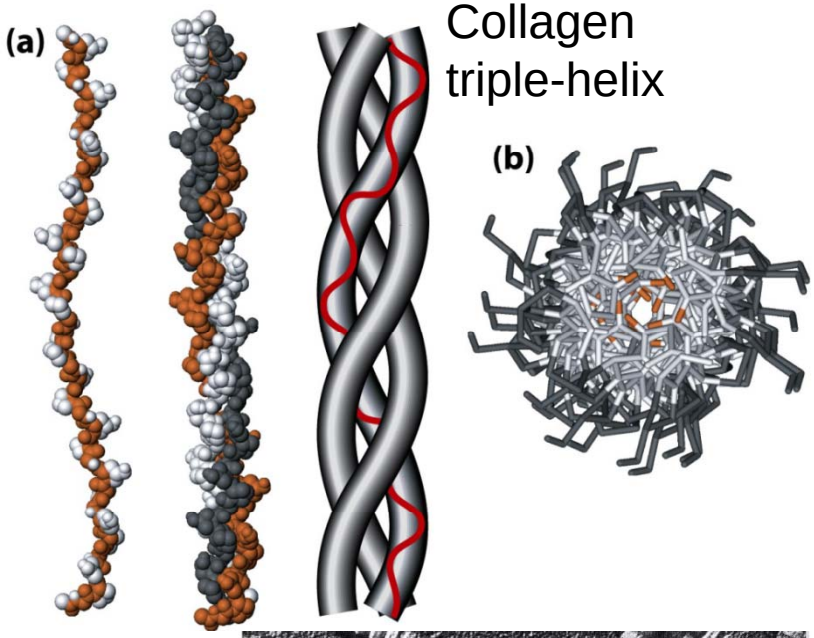
Collagens are complex molecules embedded in the ECM

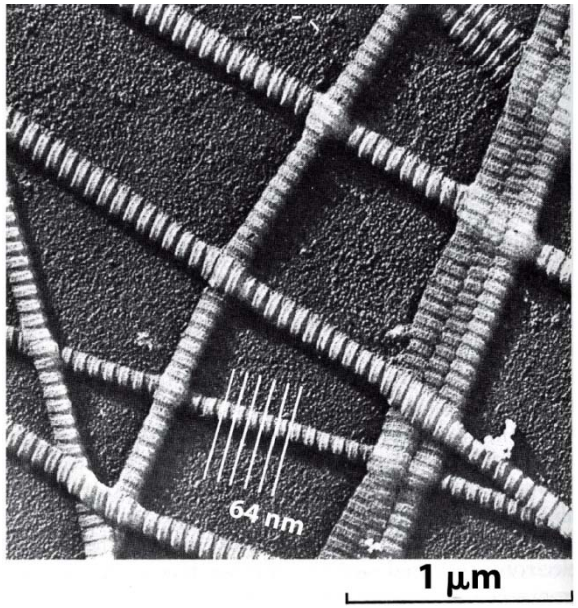
EM of cartilage



A **single collagen fiber** in the gel-forming matrix of <u>cartilage</u>

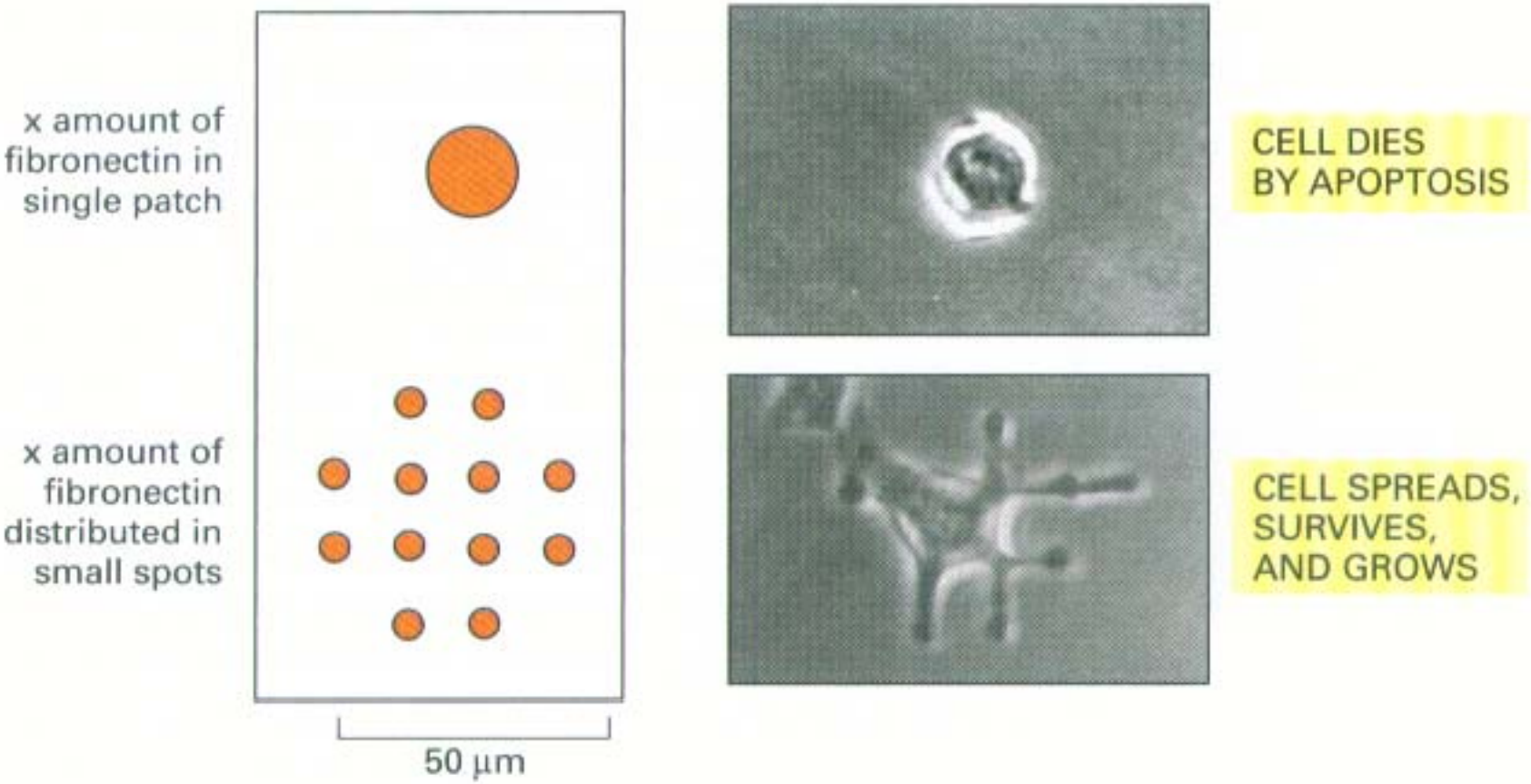
Collagen triple-helix





Cell contact with the ECM (e.g., fibronectin) is important for cell growth (proliferation) and cell survival

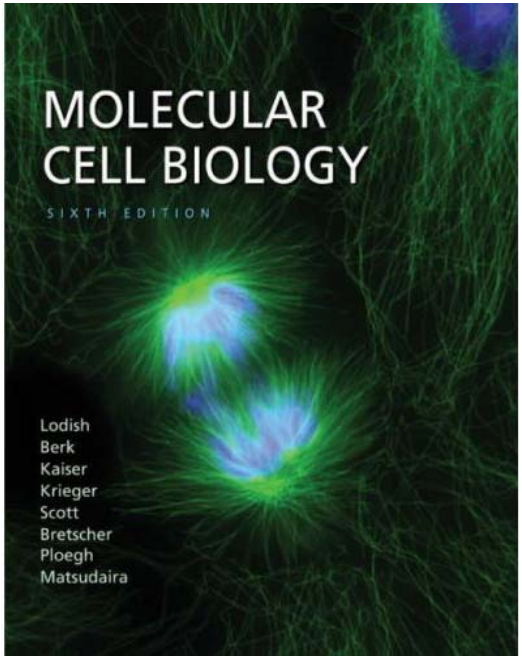
If a cell cannot spread on a <u>larger space</u> on the substrate it will eventually die:



The **spreading** of ECM proteins on a surface is <u>more important</u> than the **concentration** of these proteins (in a smaller area)

Literature

Molecular Cell Biology 6th Edition
by Harvey Lodish etc.



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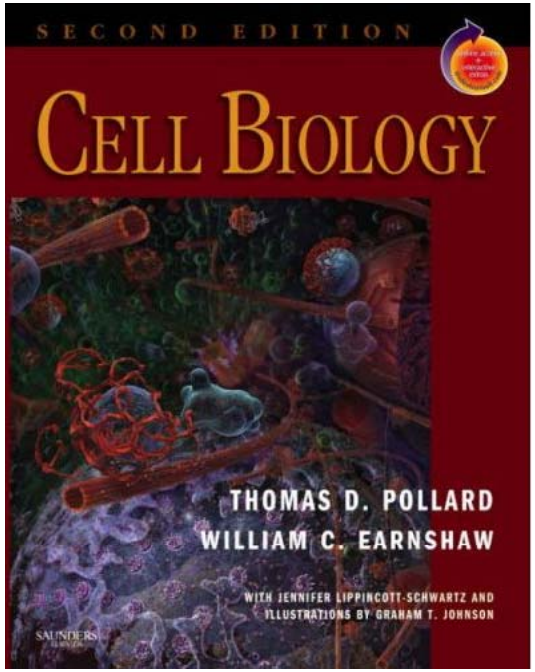
by Thomas D. Pollard etc.



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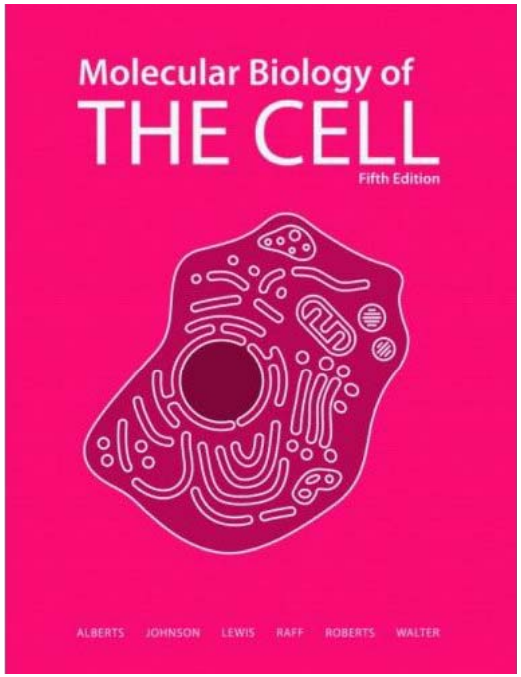

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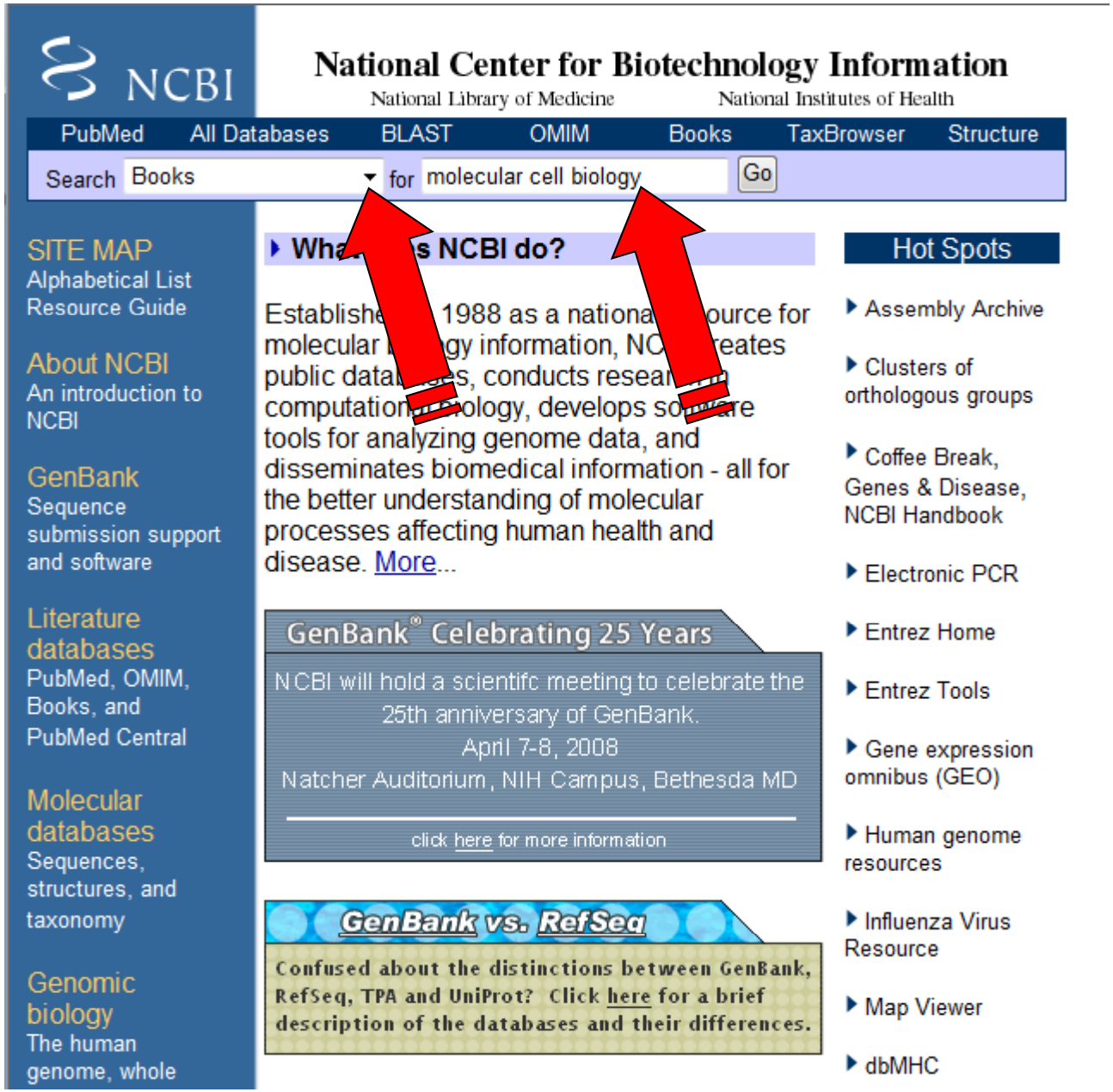

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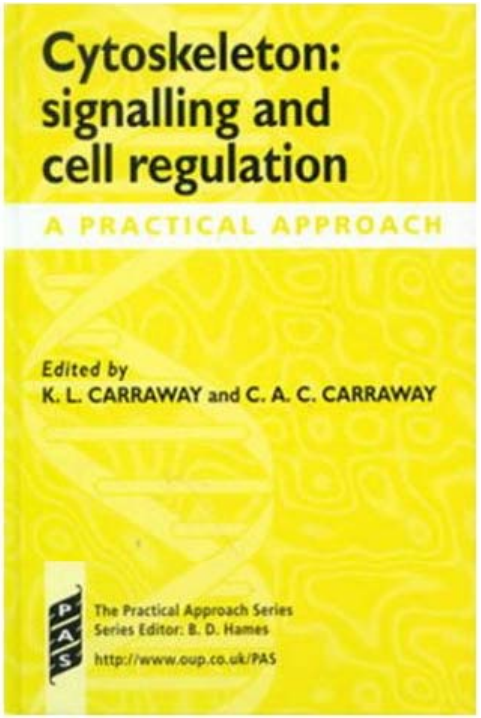

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Cytoskeleton Methods and Protocols
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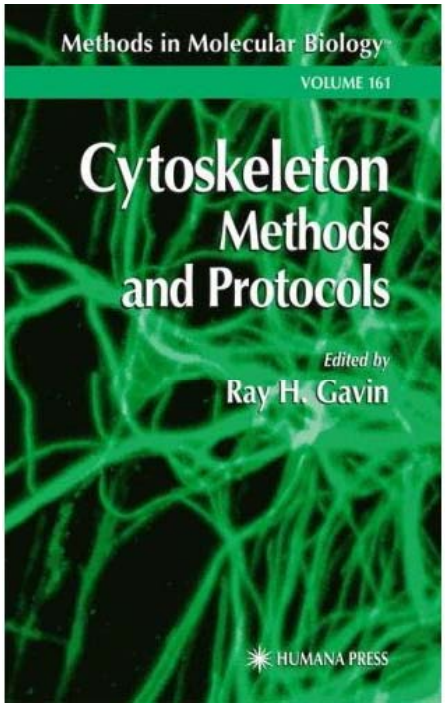

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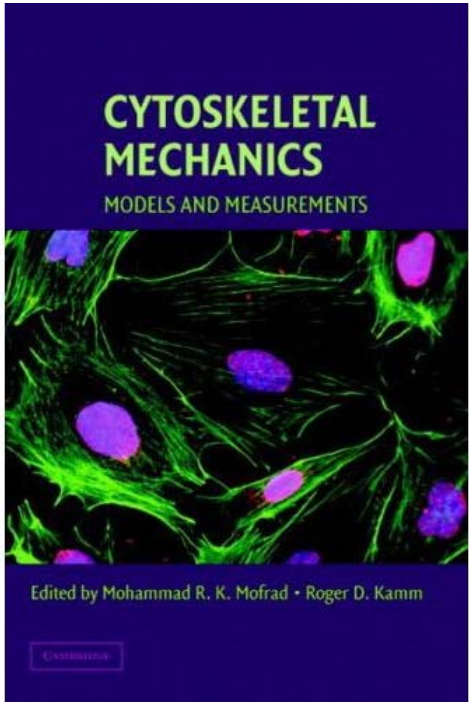

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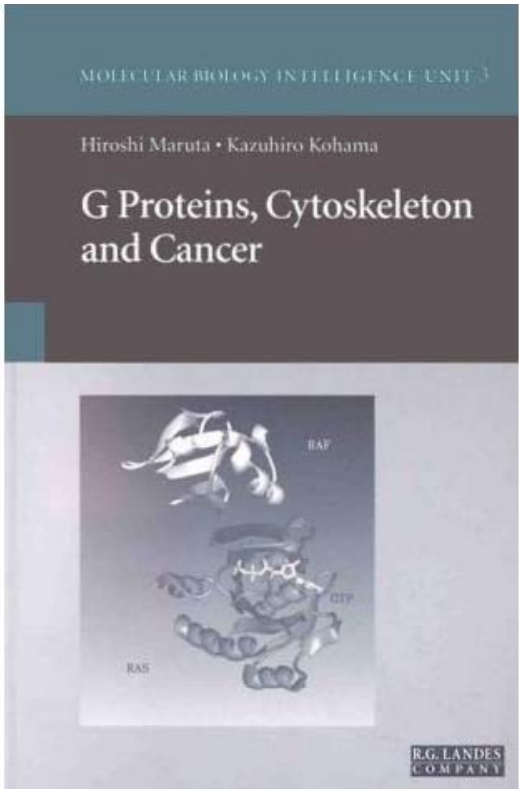

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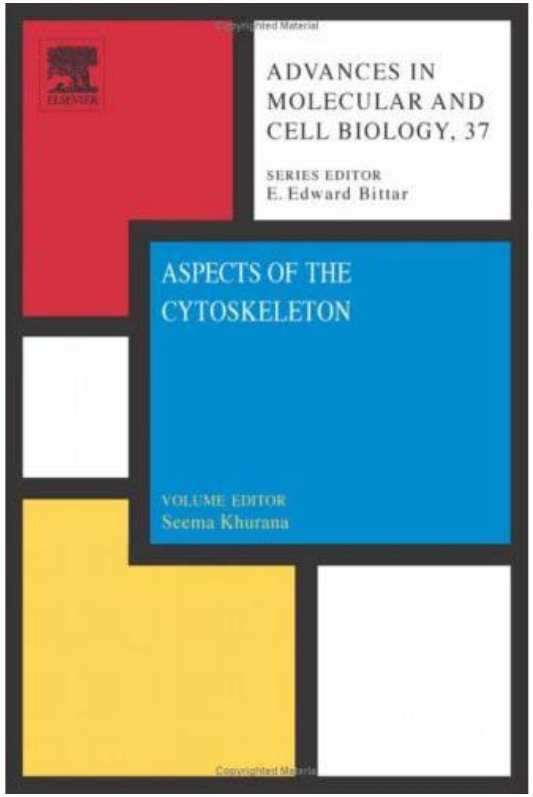

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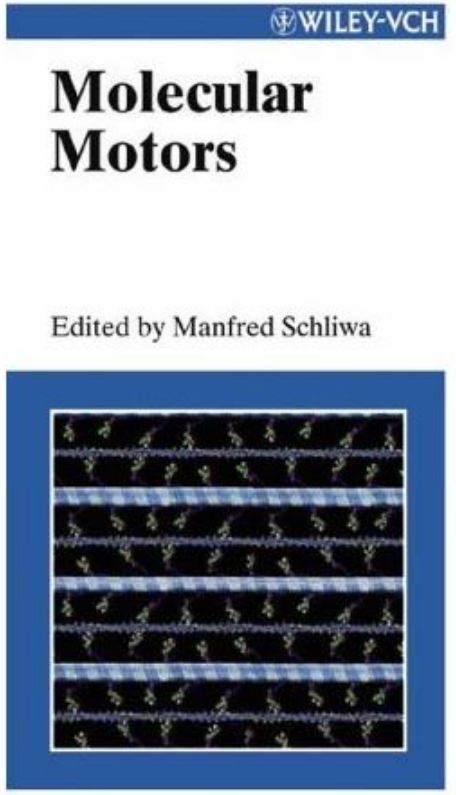

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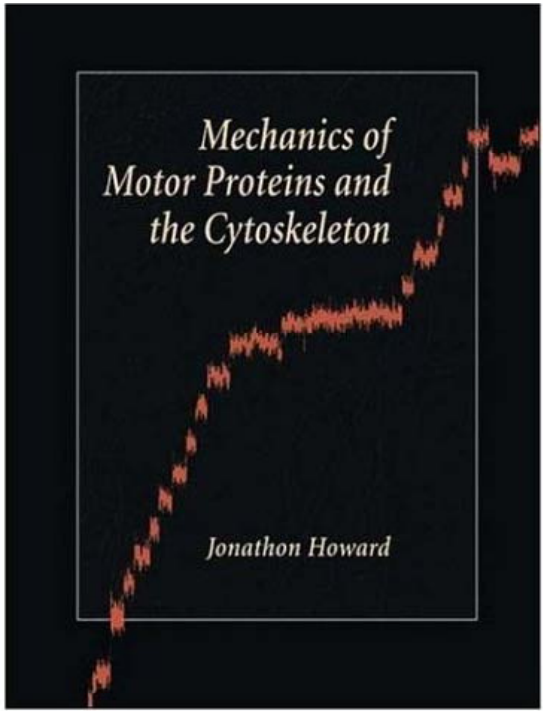

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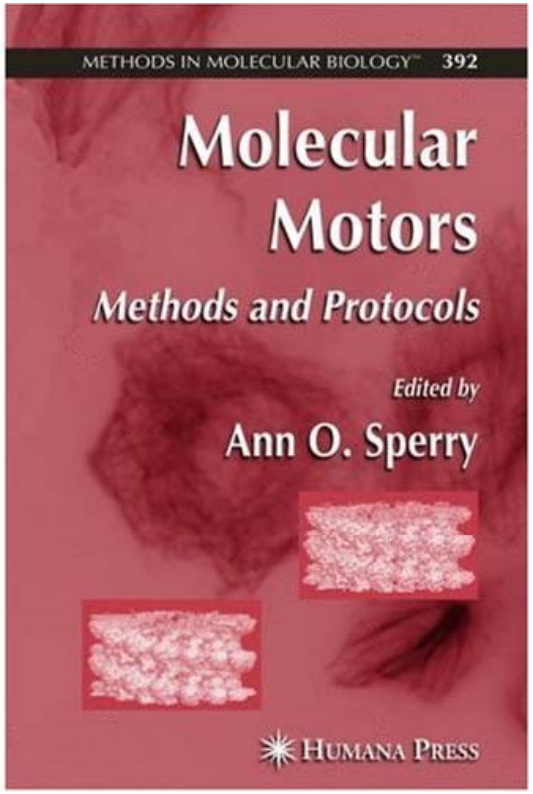

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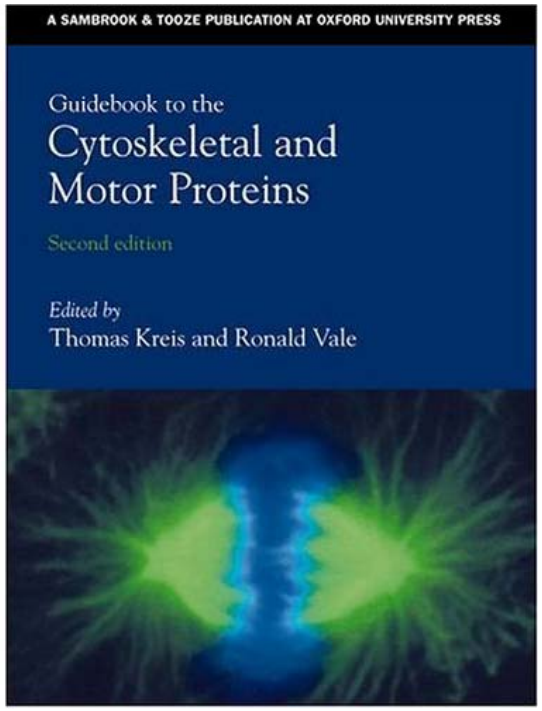

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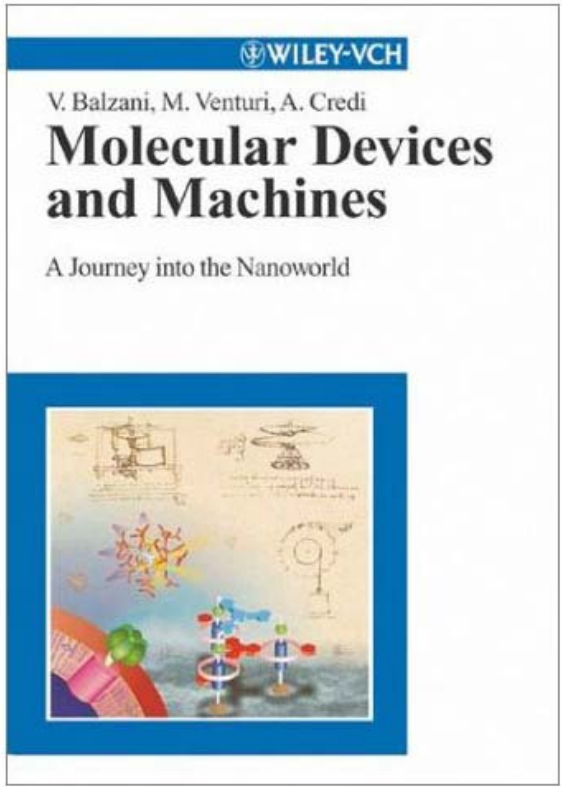

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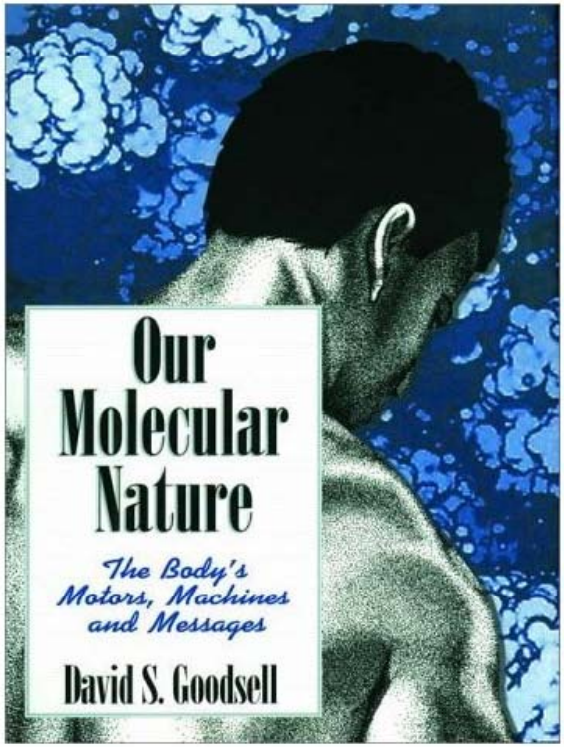

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Molecular Machines
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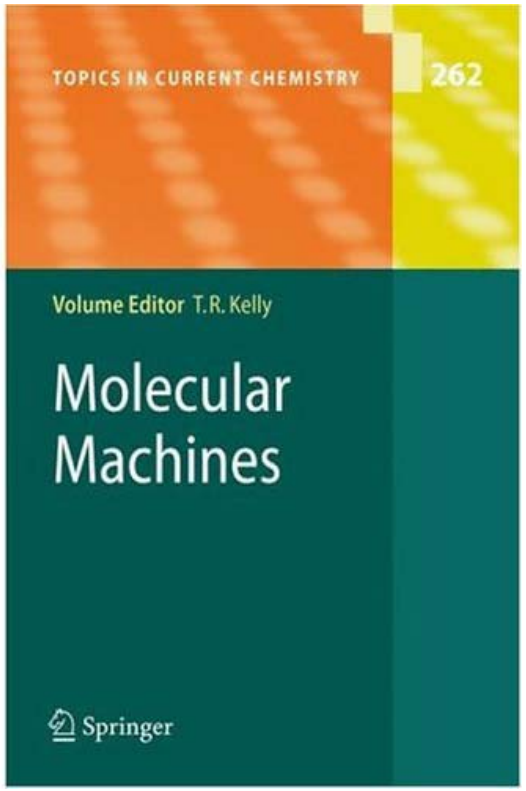

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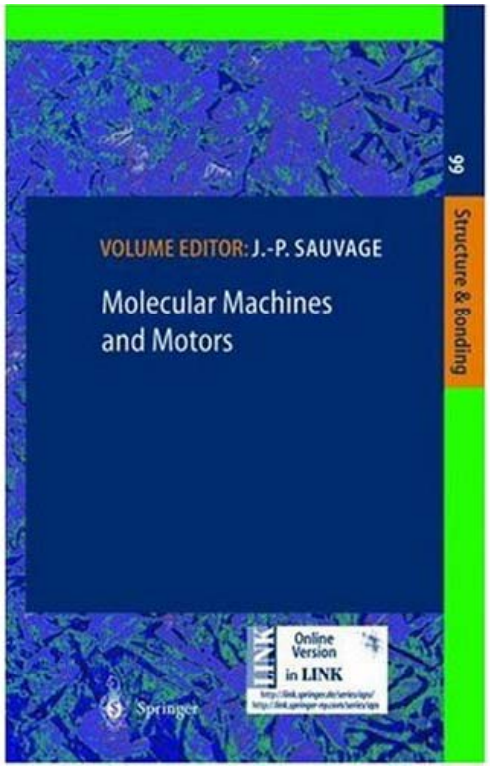

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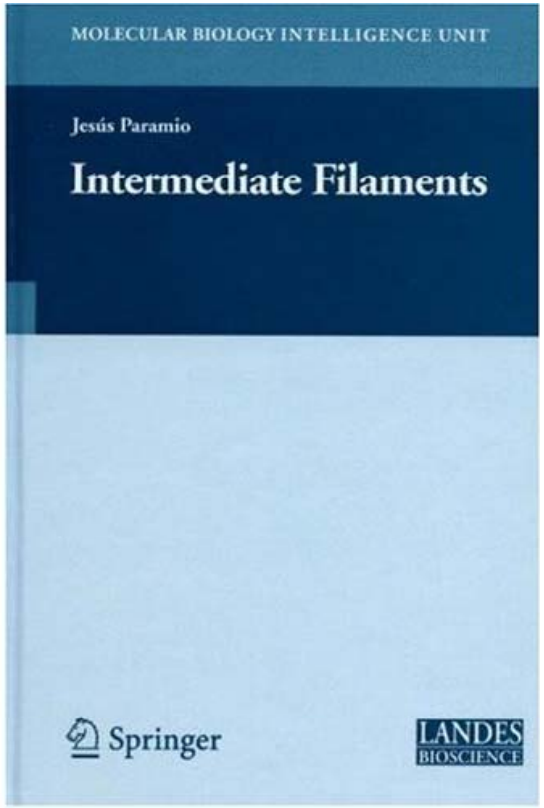

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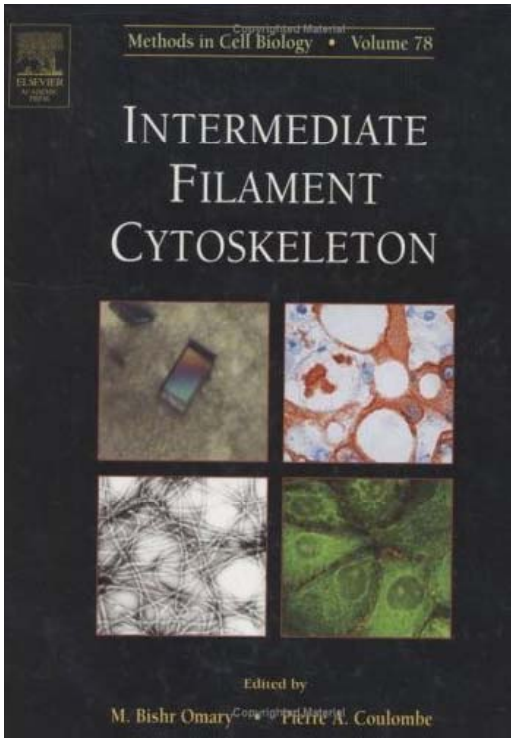

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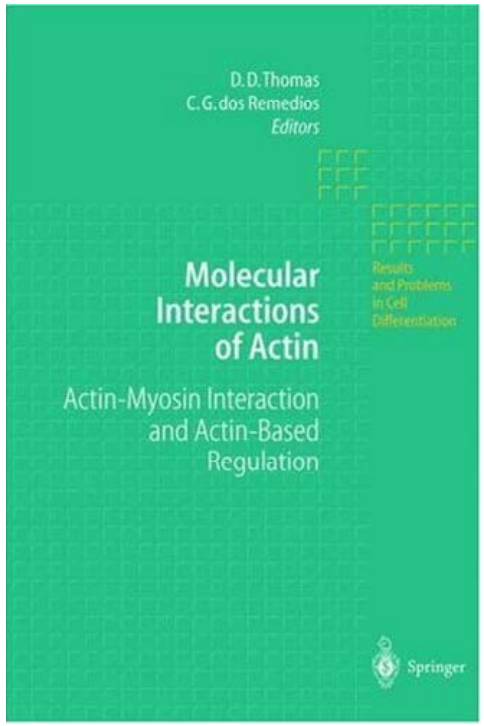

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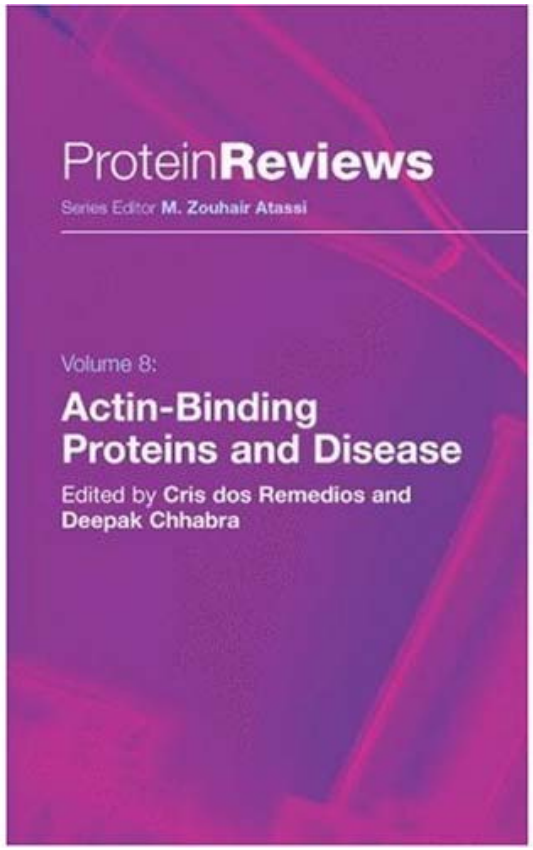

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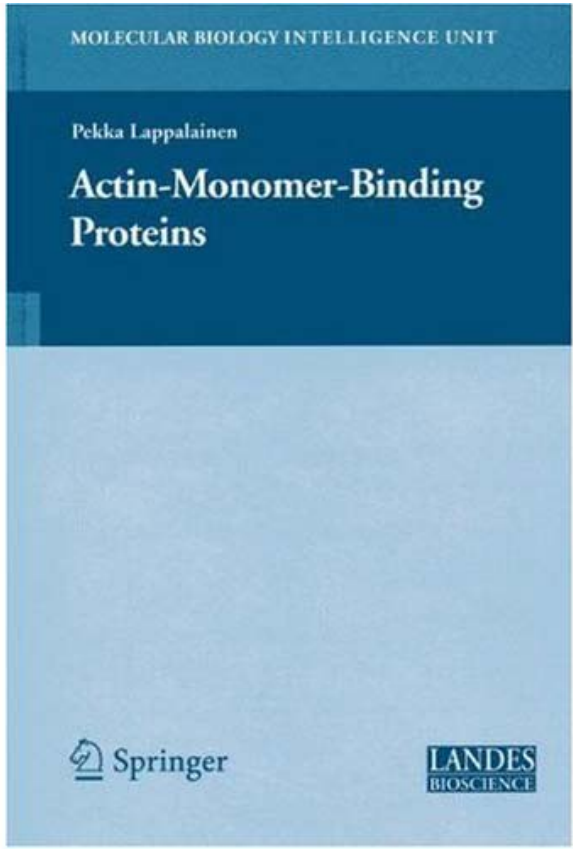

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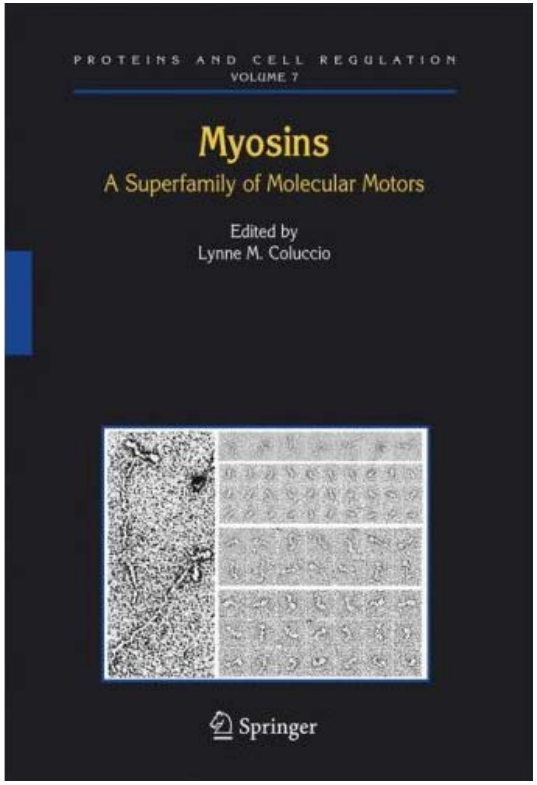

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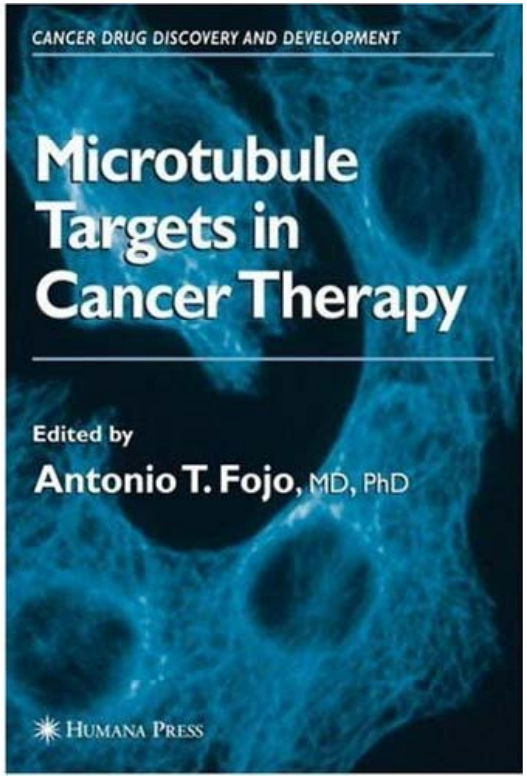

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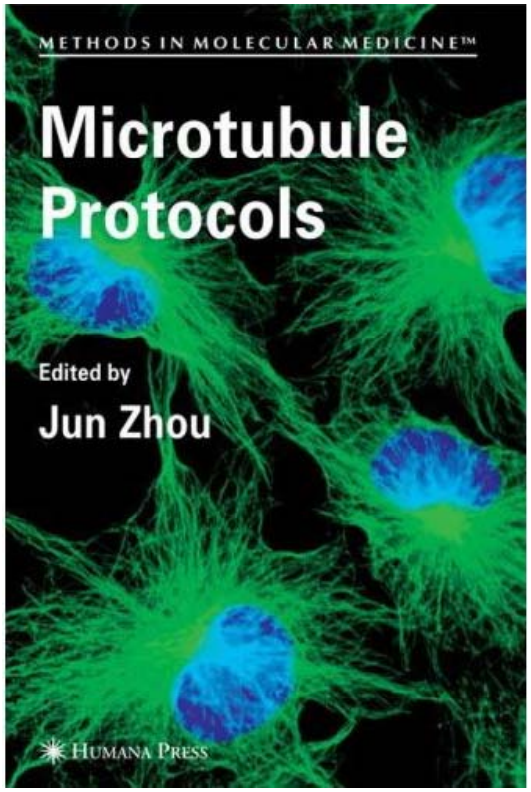

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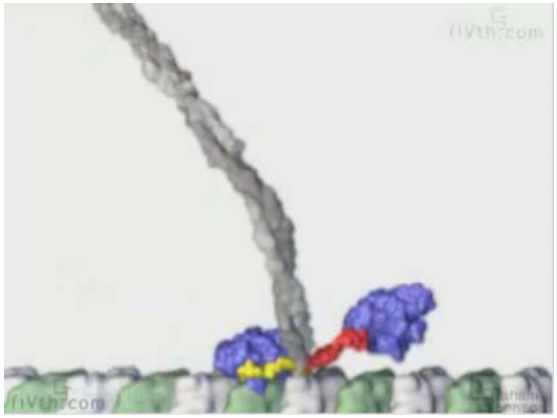

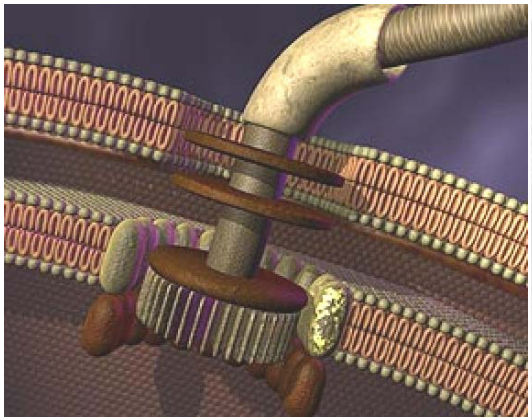

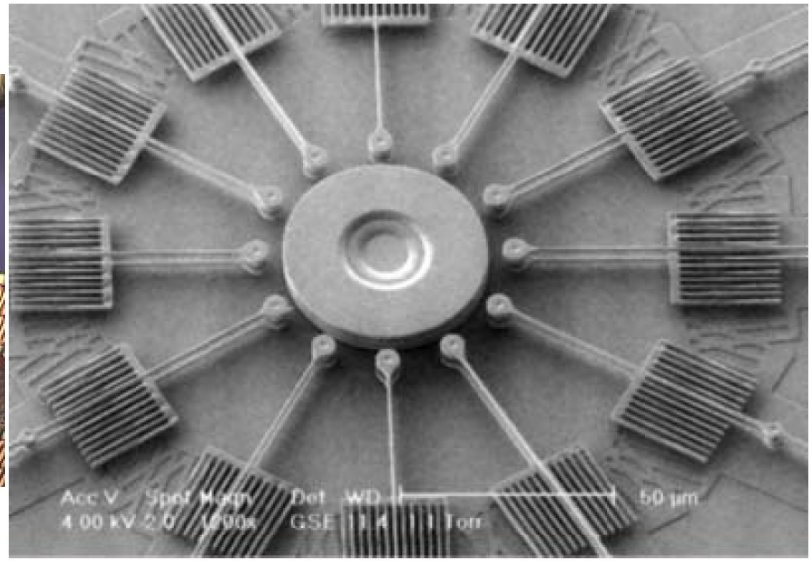

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