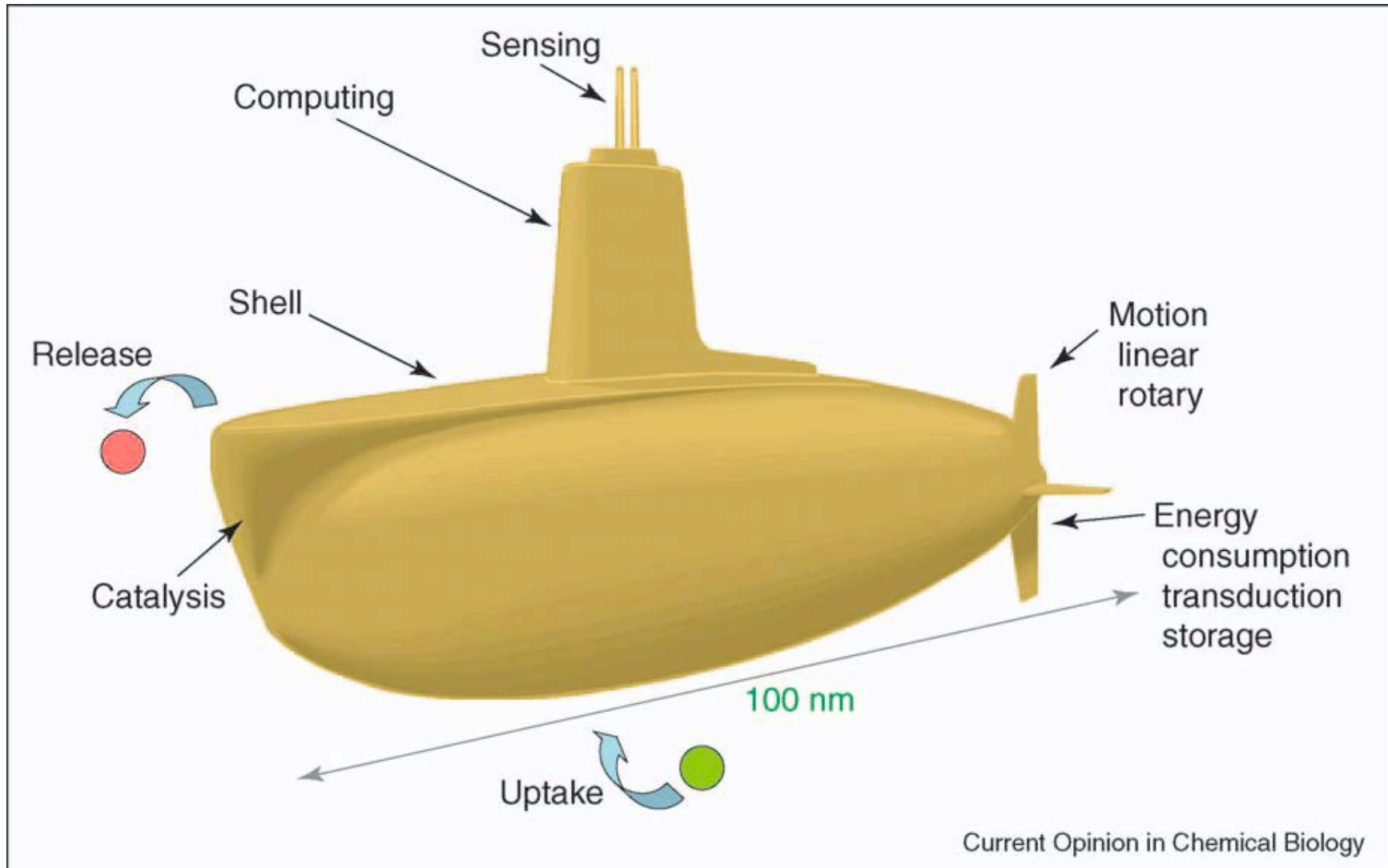


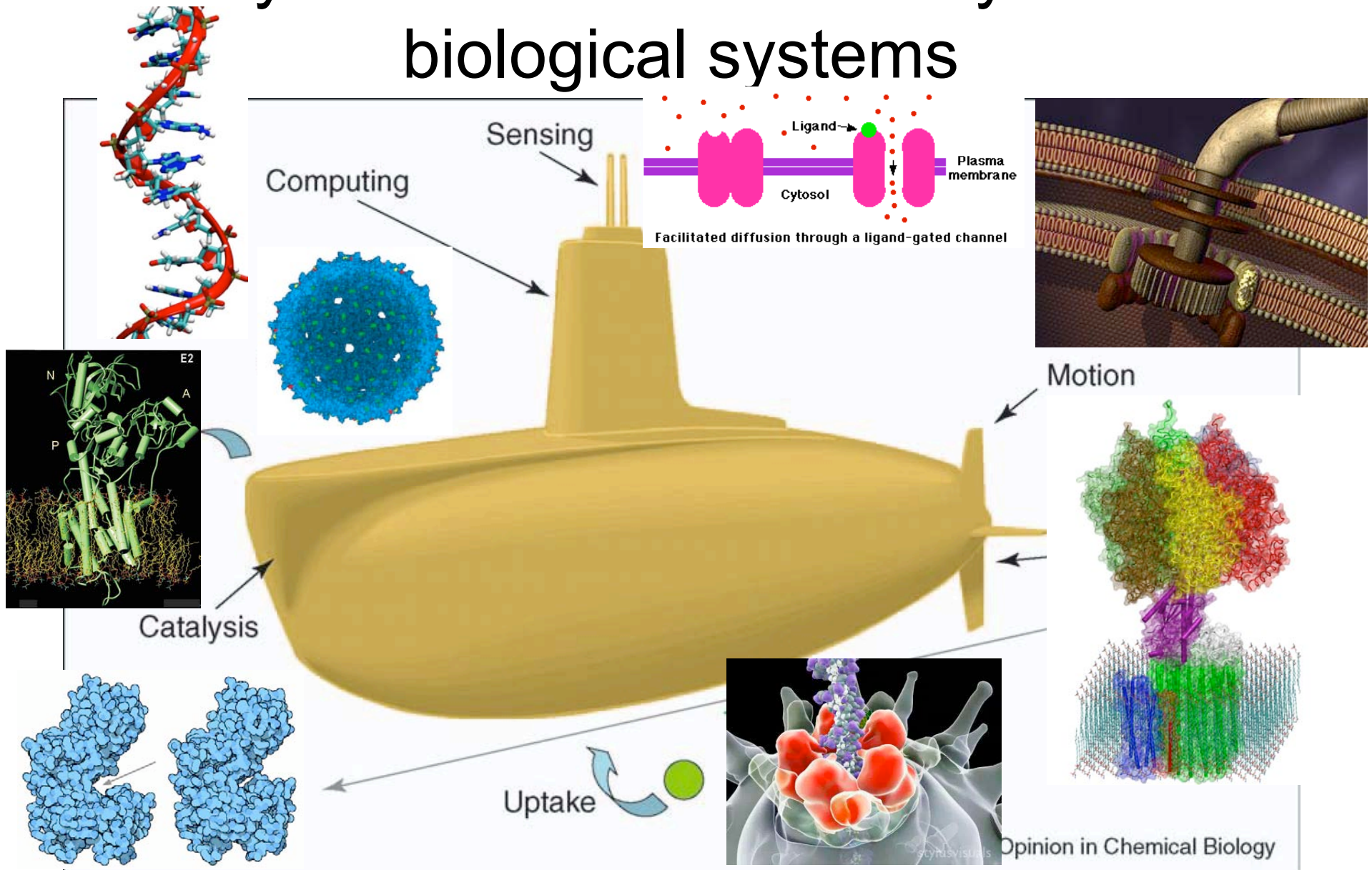
Lecture 20: Biomolecular machines in man-made devices

Nanorobots

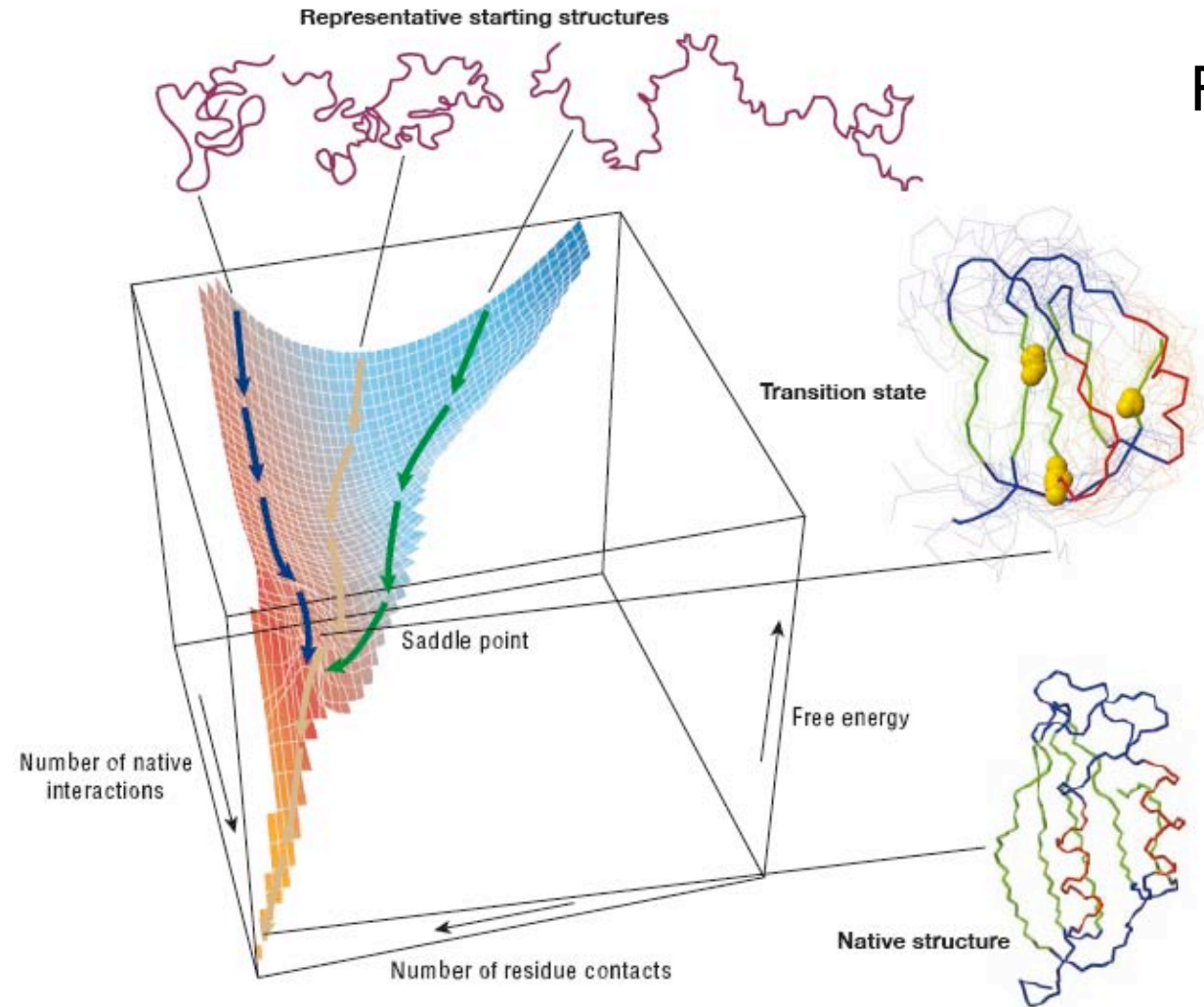


Yann Astier, Hagan Bayley and Stefan Howorka

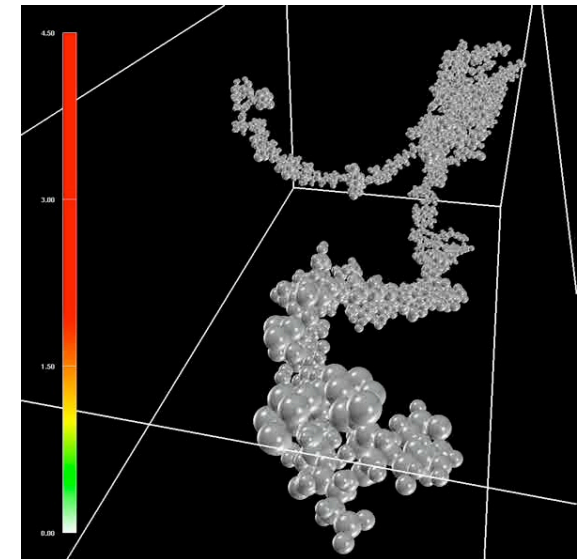
Many functional units already exist in biological systems



Proteins always fold into the same 3D structure

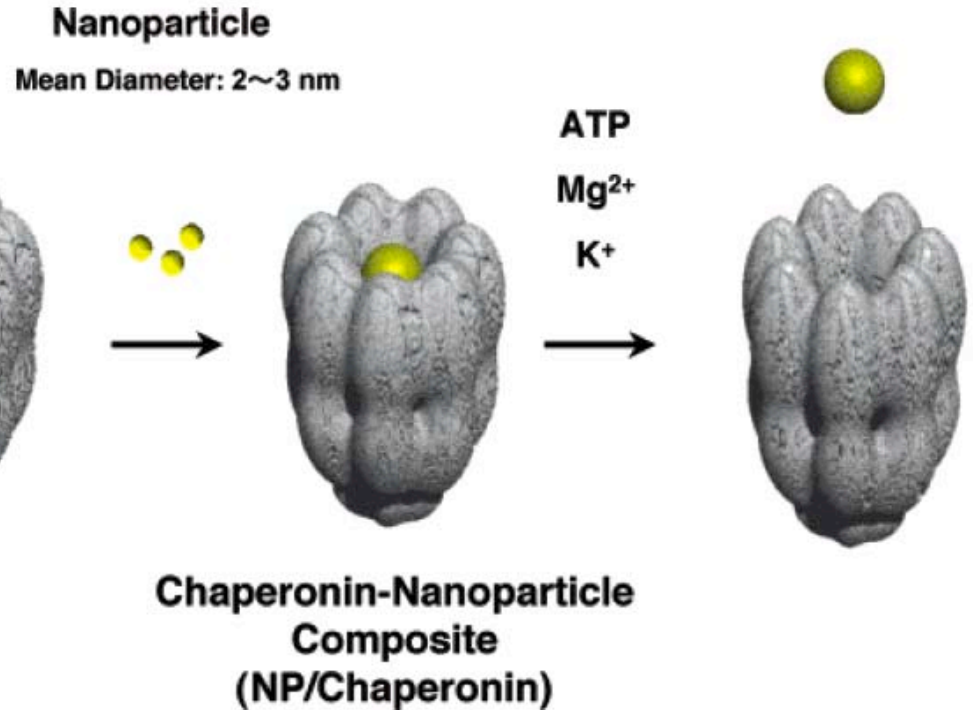
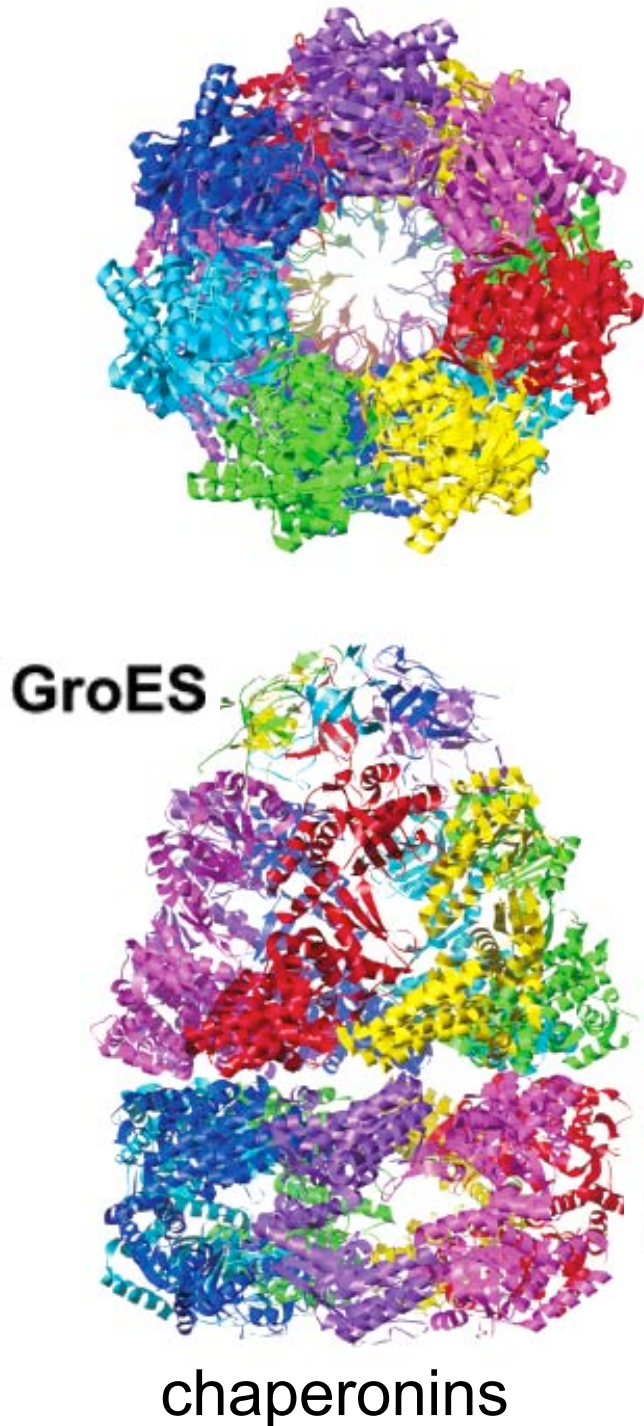


Free-energy funnel



Nano-containers

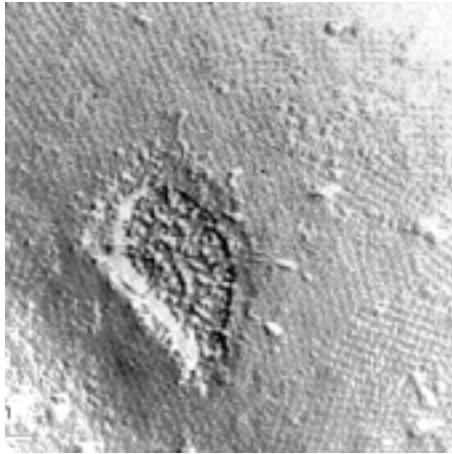
cadmium sulfide (CdS) nanodots



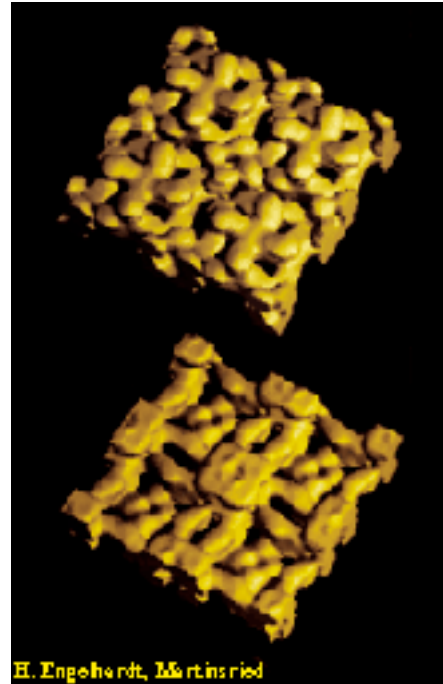
Mg²⁺ and ATP trigger release

Increased stability from 2h to 1 year

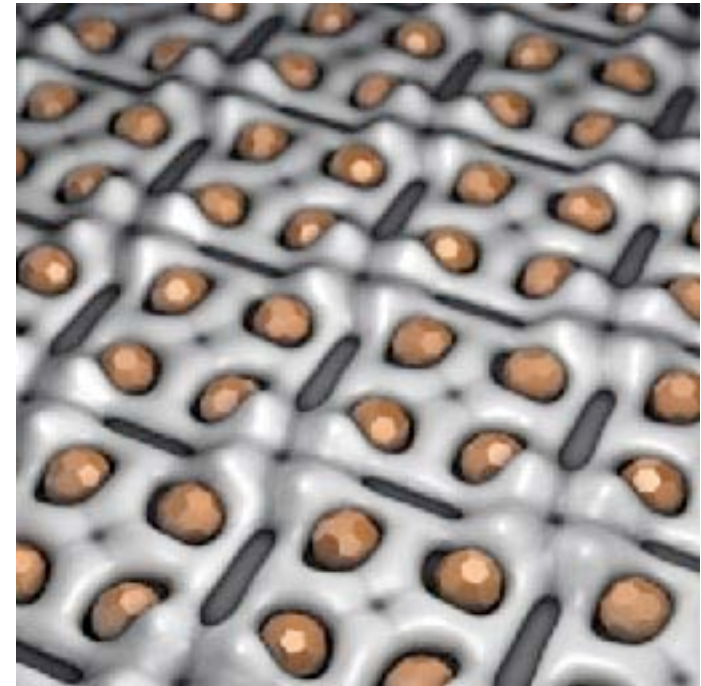
Self-assembled scaffolds



S-layer: Outermost component of the cell wall most of archaea.

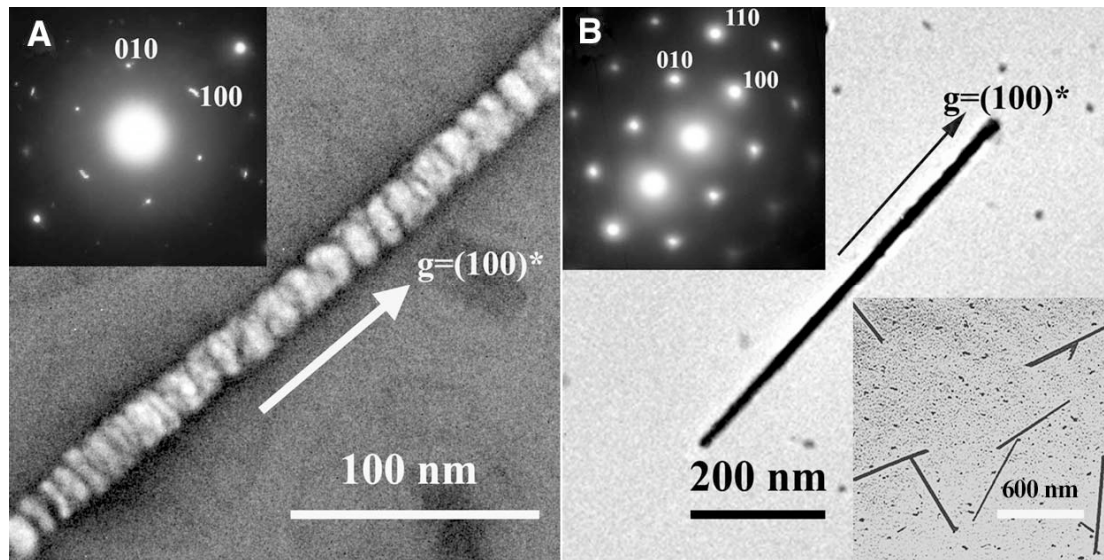


Natural two-dimensional protein crystals



Pd nanoclusters located at the S-layer protein (50-80 Pd atom).

Many S-layers are molecular sieves with pores of about 2 to 4 nm in size

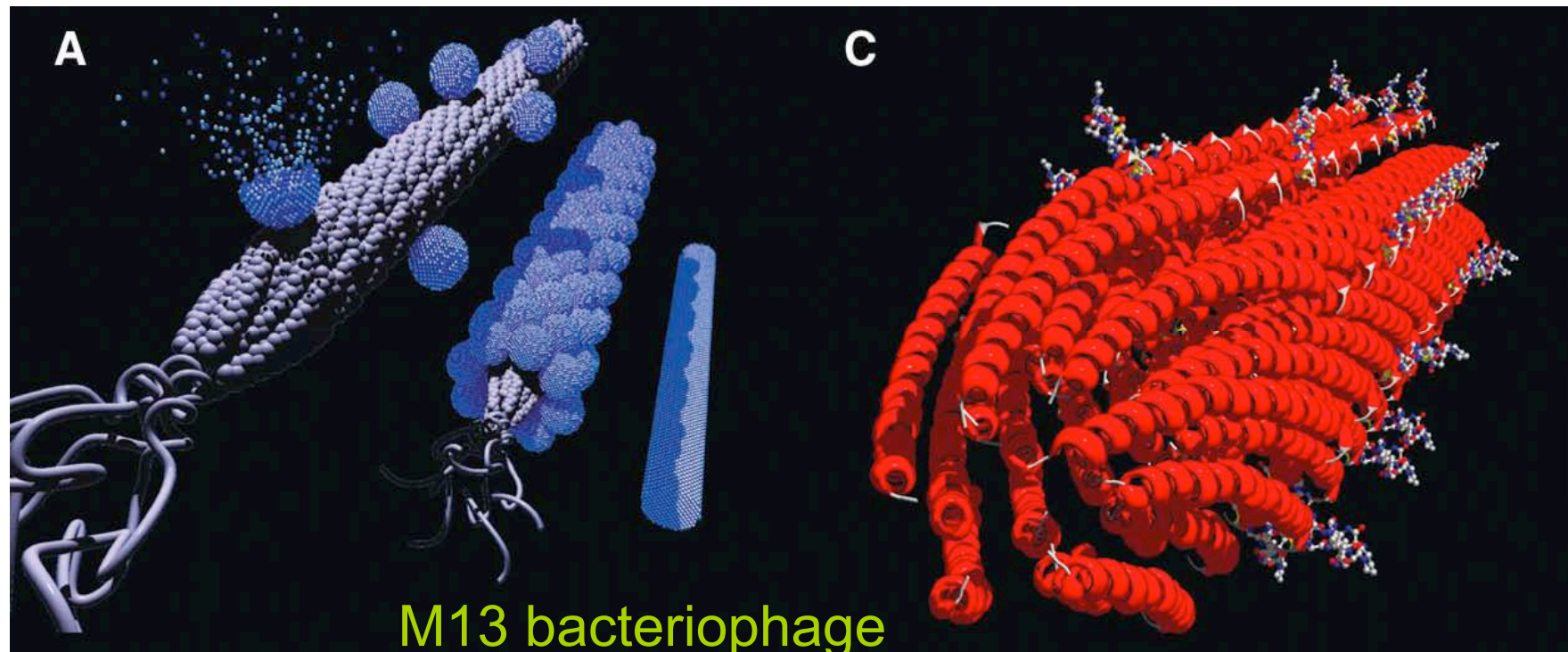


before

after

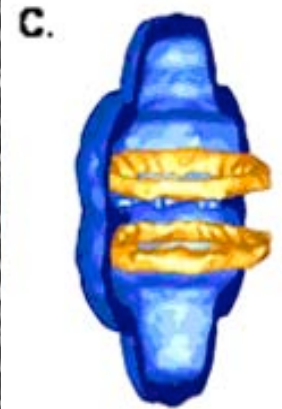
Virus-directed self-assembly

ZnS, CdS semiconductor and CoPt, FePt magnetic nanowires



M13 bacteriophage

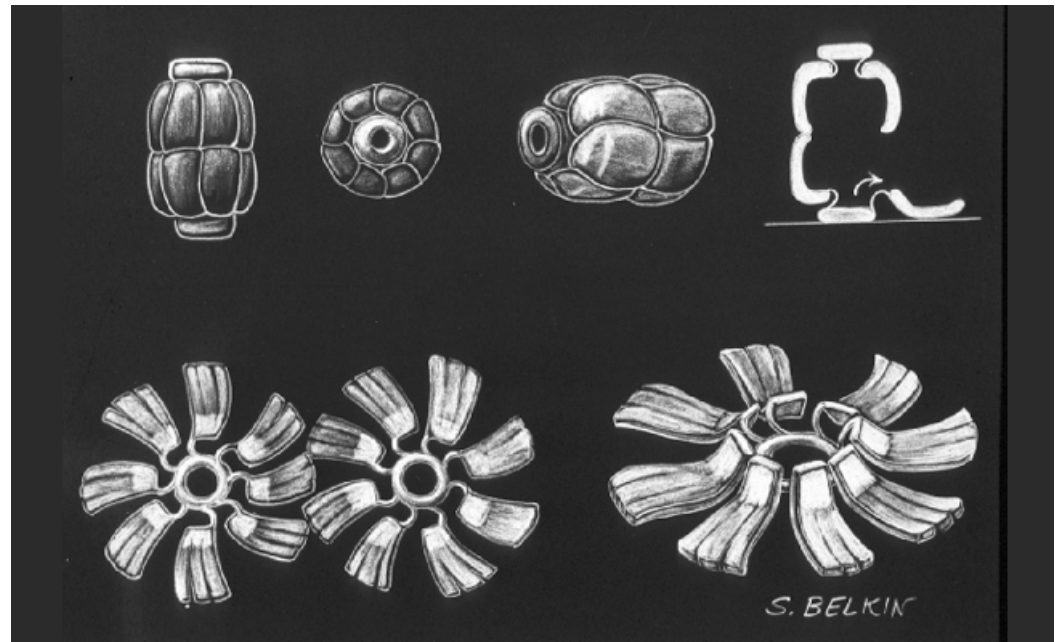
Biological nano-vaults

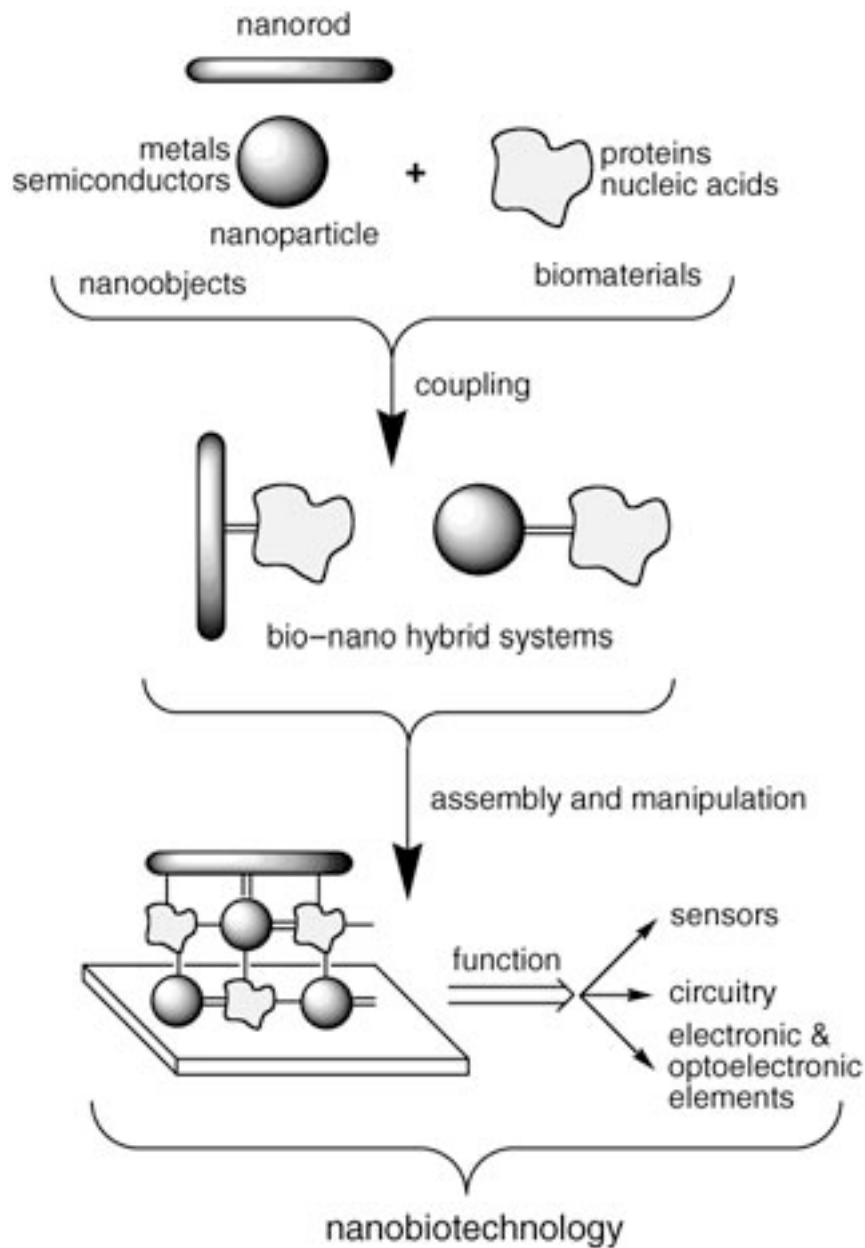


hollow, barrel-like
structures 42 x 75 nm

Biological function:
unknown!

Leonard Rome
www.vaults.arc.ucla.edu

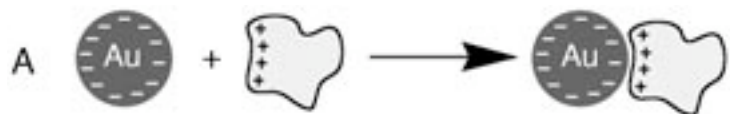




Hybrid systems

Protein components provide:

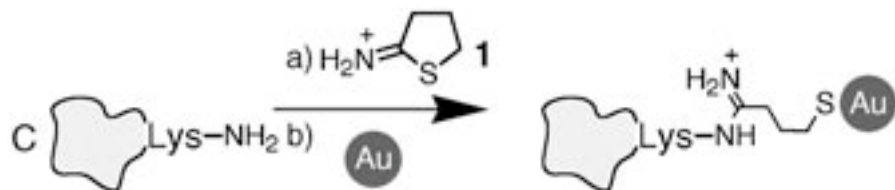
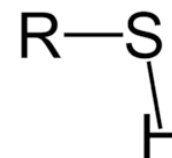
- recognition and self-assembly
- multiple binding
- can be genetically engineered
- catalytic activity can shape biocomponents



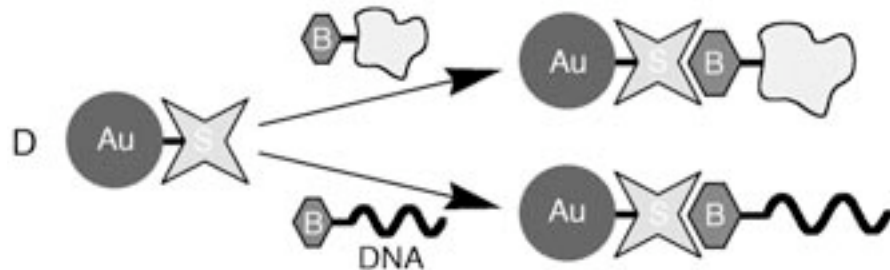
Electrostatic adsorption (can span multiple layers). Proteins can denature.



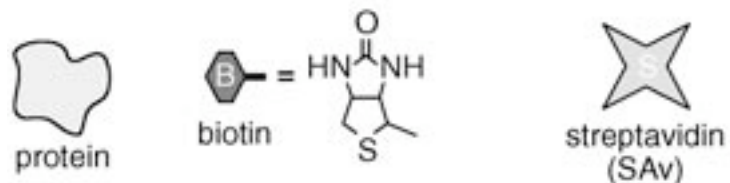
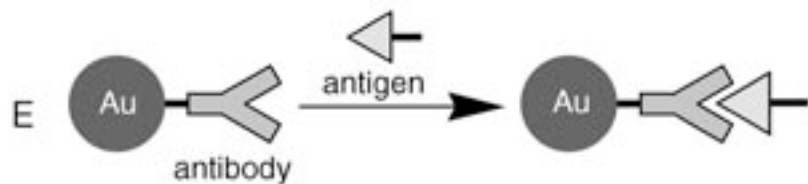
Covalent binding (thiol, bifunctional linkers)



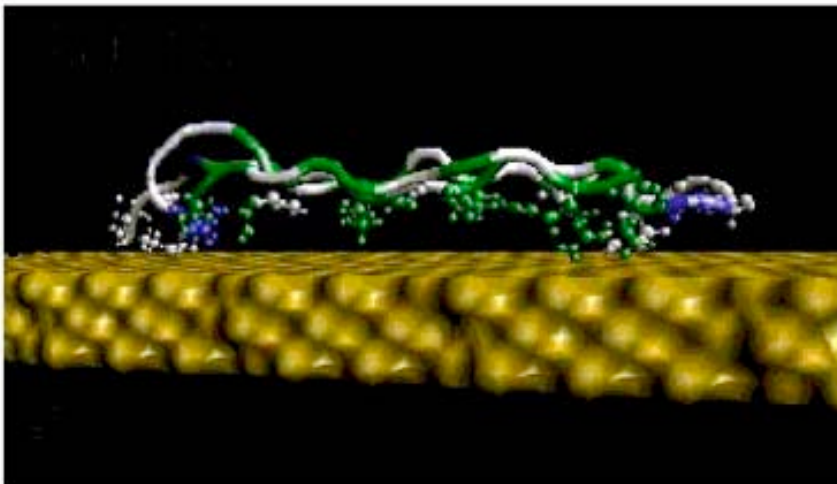
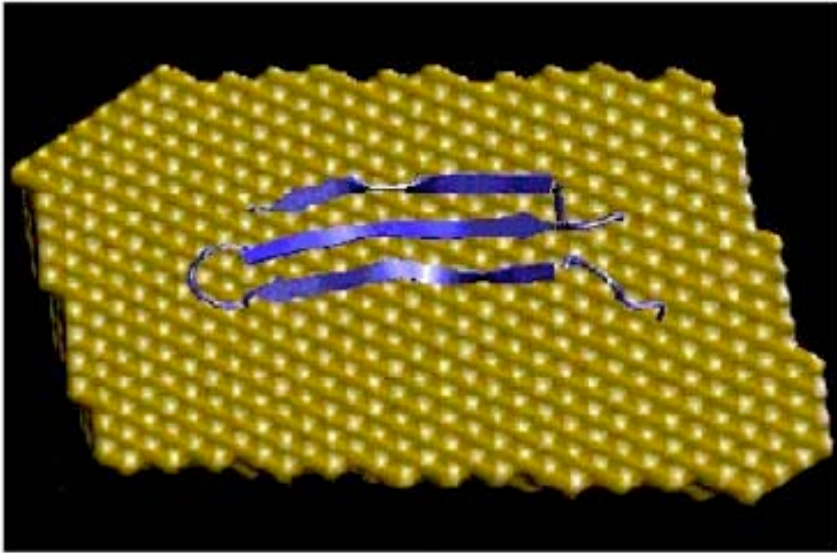
Specific affinity interactions



Assembly of hybrid systems



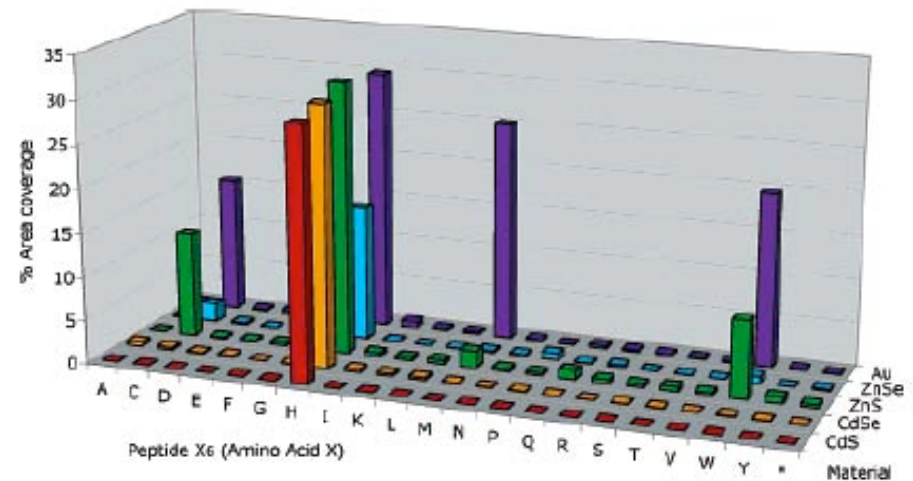
Metal binding proteins



Gold binding protein

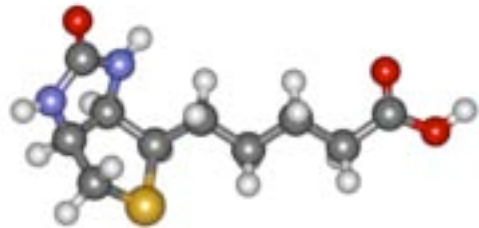
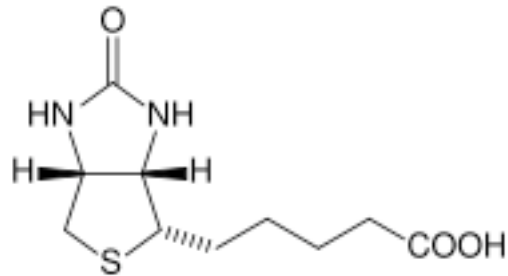
General form: XHXHXHX

High affinity: His-Ni

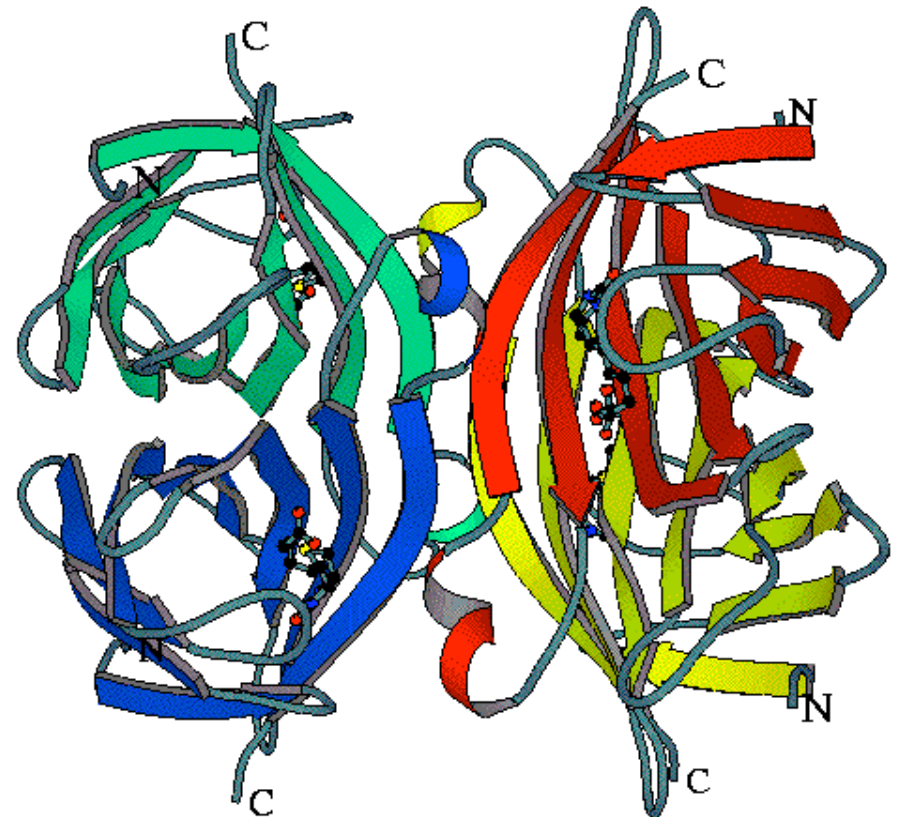


Short peptides can bind specific lattice faces of crystalline silicon!

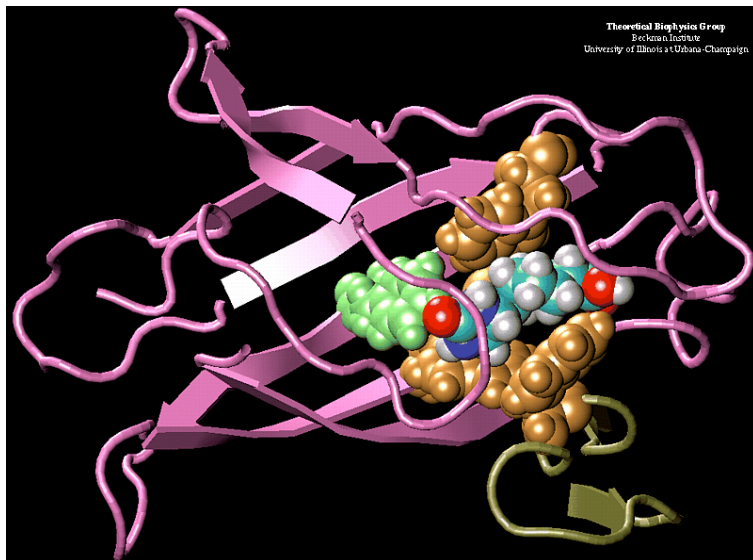
Biotin-streptavidin



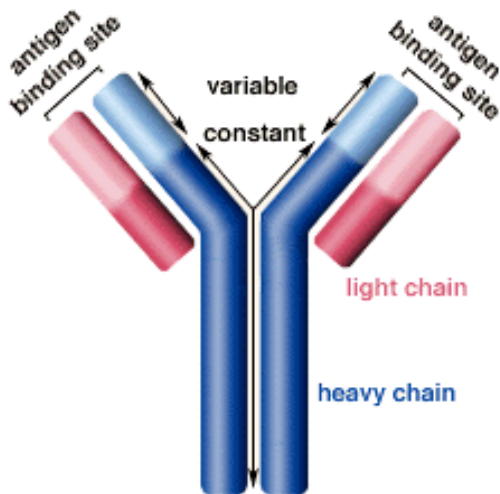
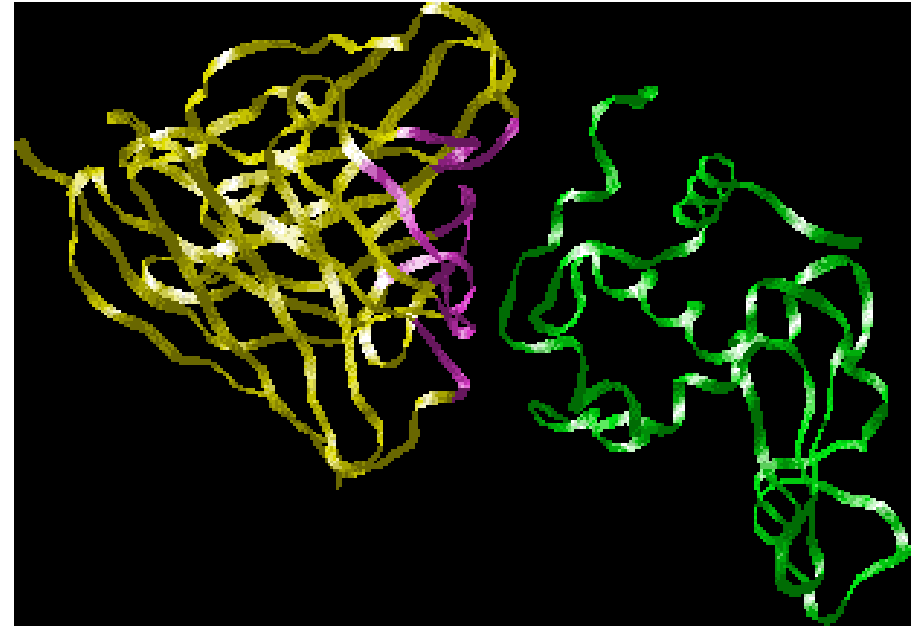
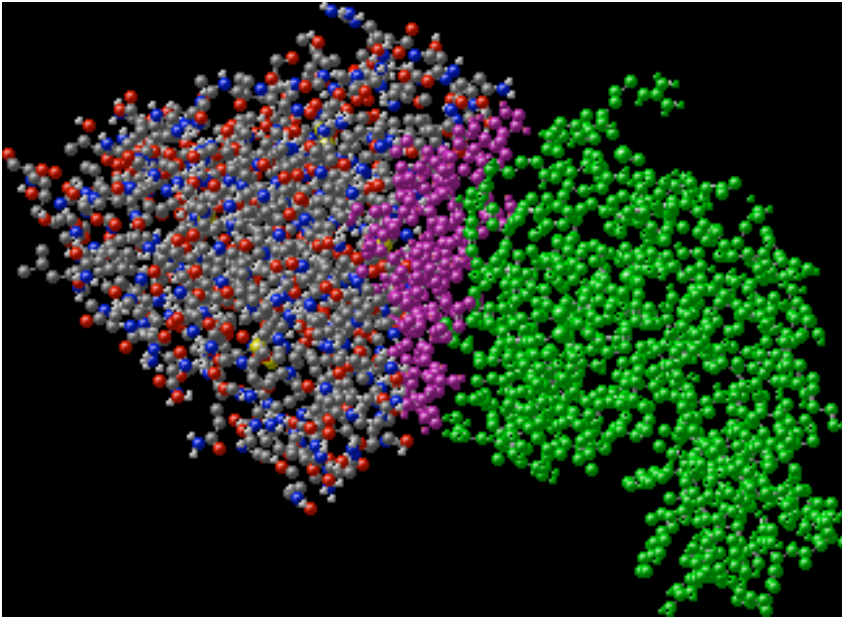
Biotin (vitamin H)



Streptavidin
(tetrameric protein)

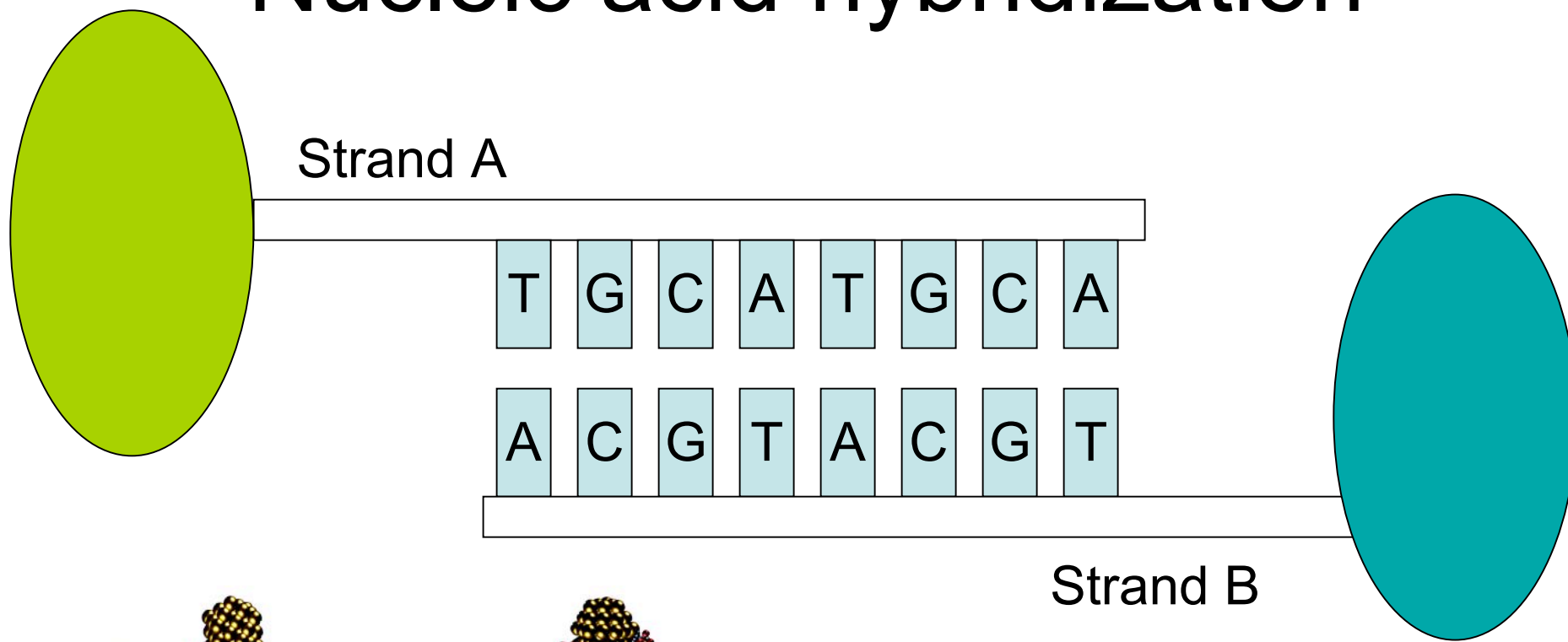


Antibody-antigen



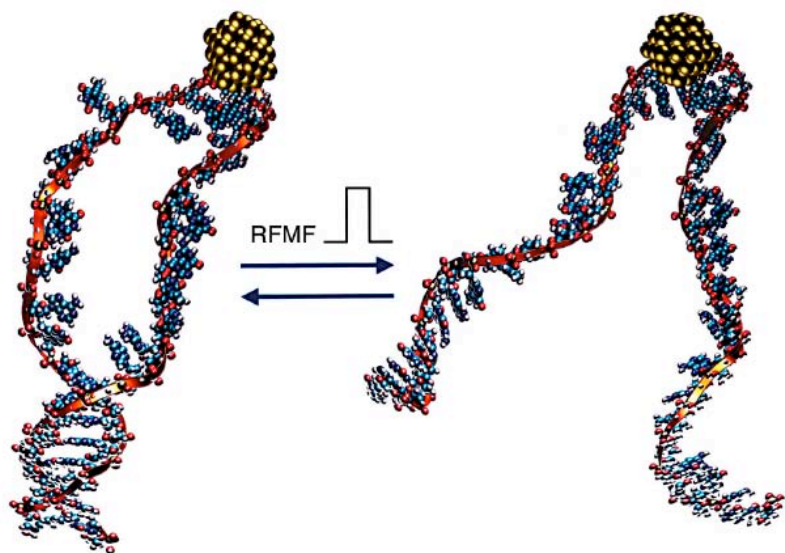
Antibodies are immune system-related proteins called immunoglobulins.

Nucleic acid hybridization



Strand B

Gold nanocluster

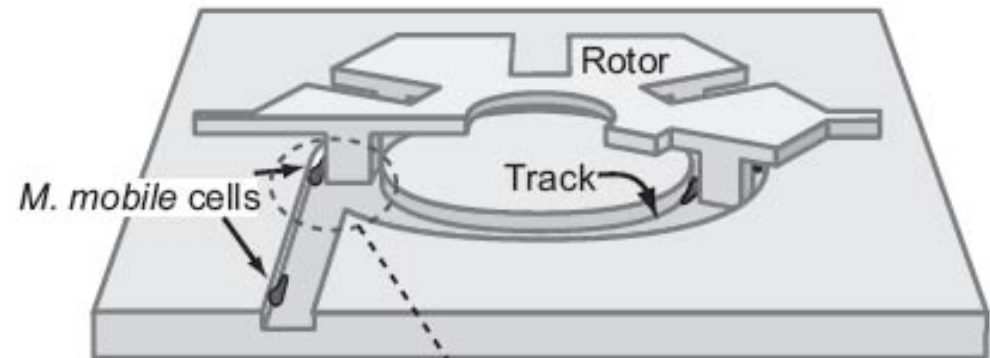


Bacteria-powered motor

Mycoplasma mobile:

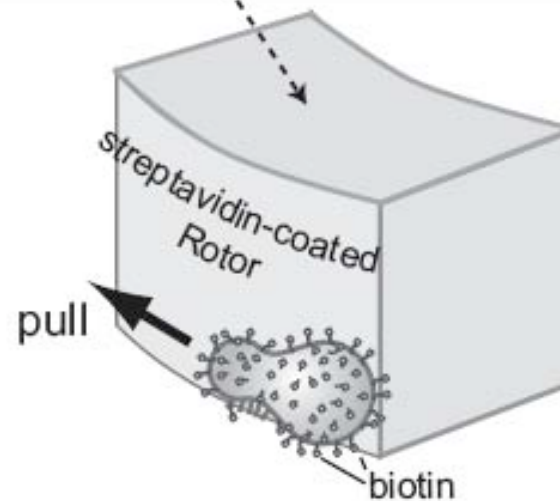
about $1\mu\text{m}$ in length

glides continuously $2\text{-}5\mu\text{m}/\text{second}$

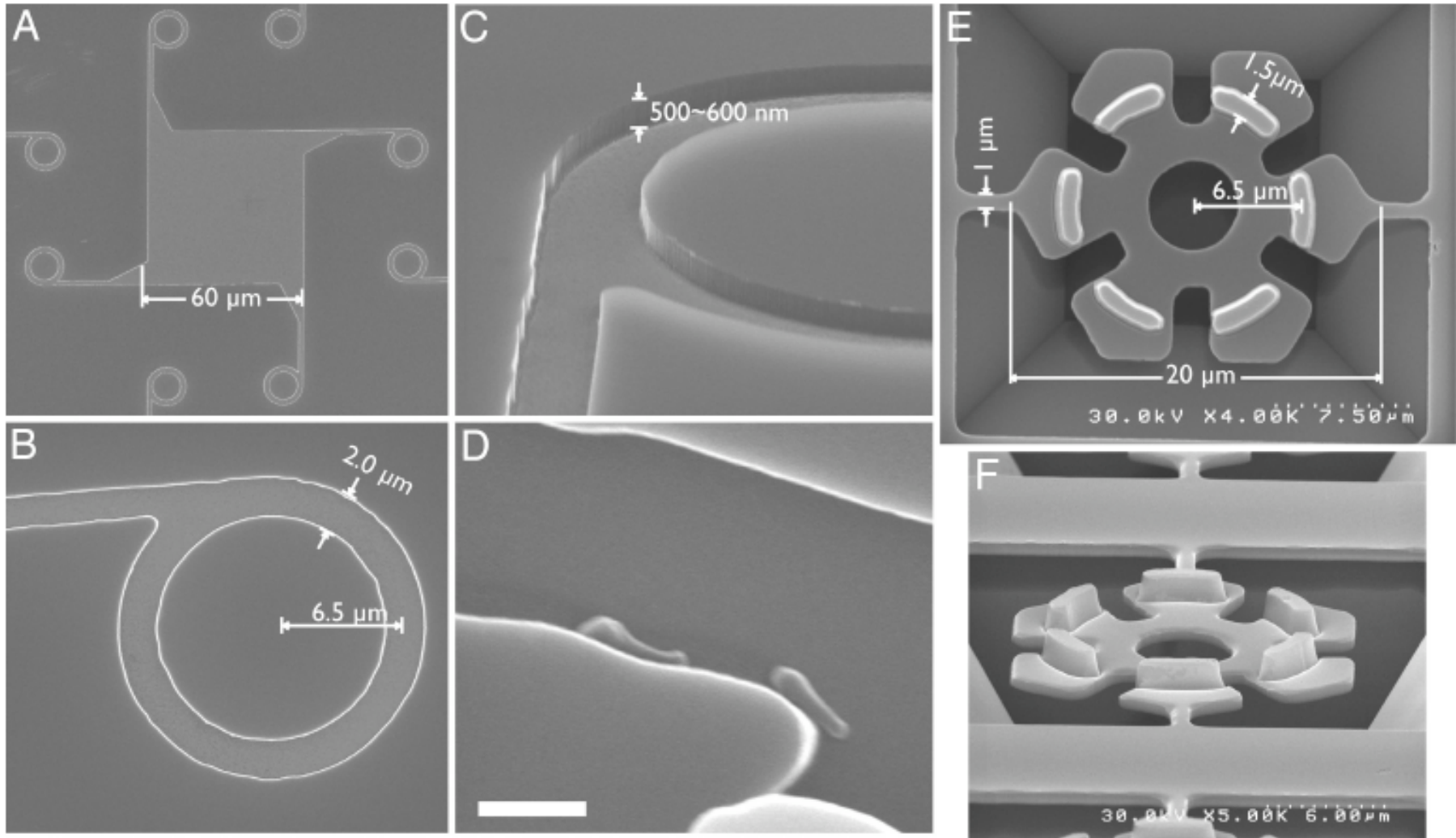


microrotary motor

PNAS103:13618



Bacteria-powered motor

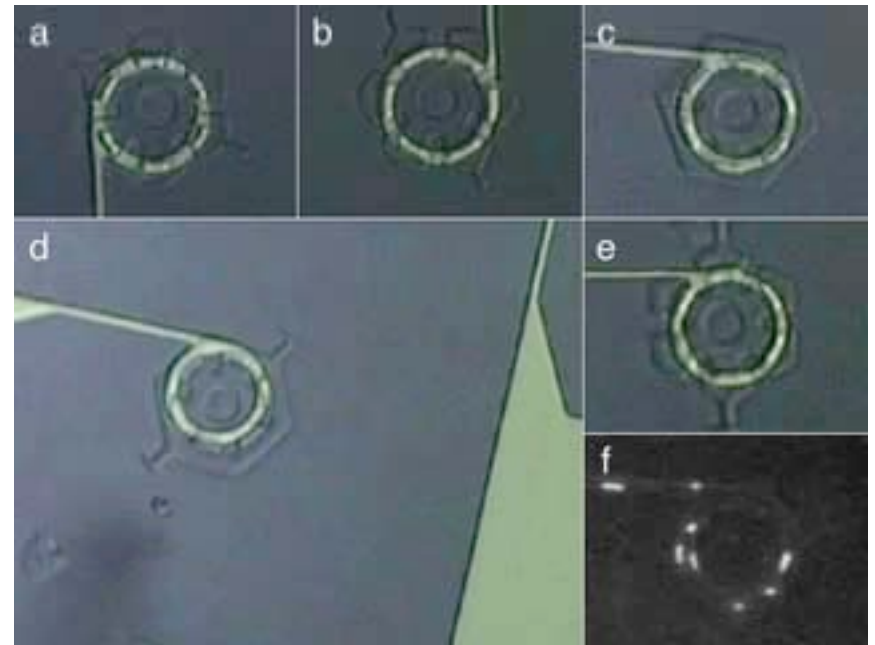


Trenches are covered with sialic acid-rich proteins

Bacteria-powered motor

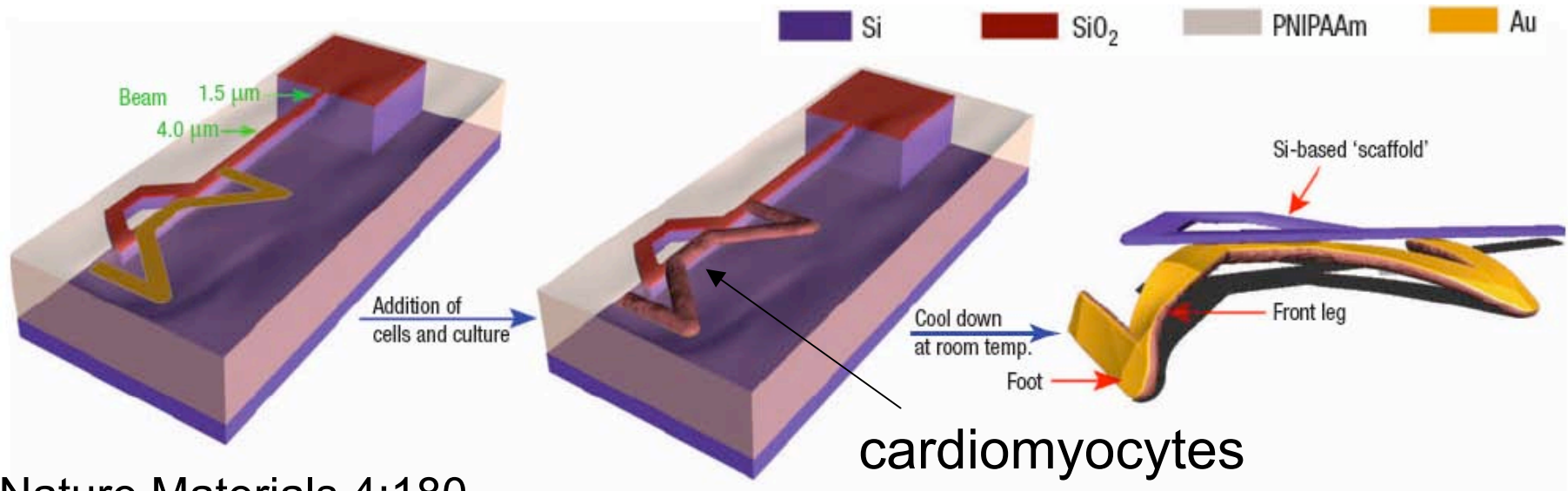


Rotation speed: 2 rpm
Torque: 180 nN nm
(1000 times smaller than MEMS)

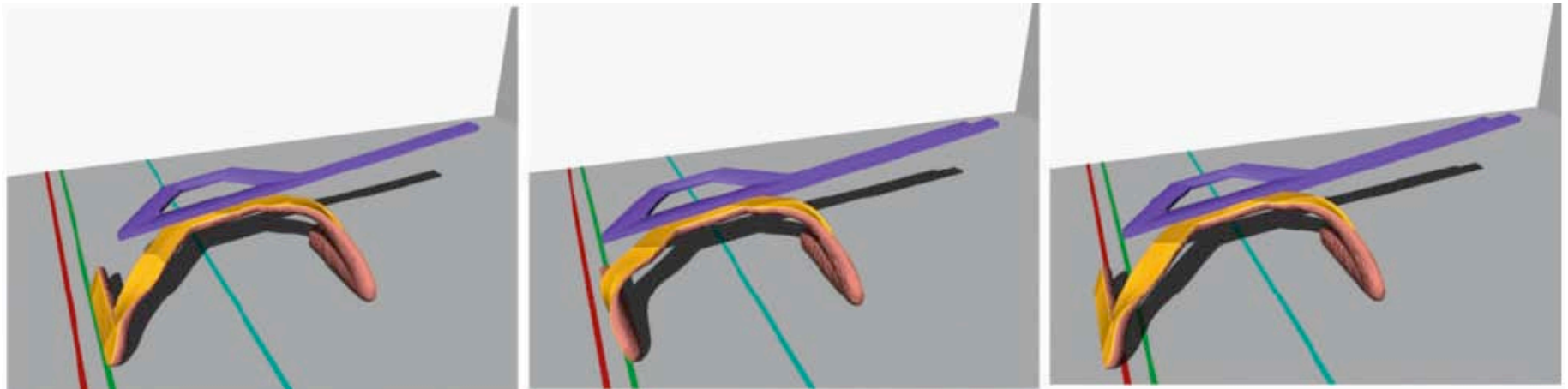


- Assembled in liquid
- Can reverse direction
- Driven by the motion of a few cells

Muscle powered walker



Nature Materials 4:180



138 μm long, 40 μm wide, and 20 nm/300 nm (Cr/Au) thick.

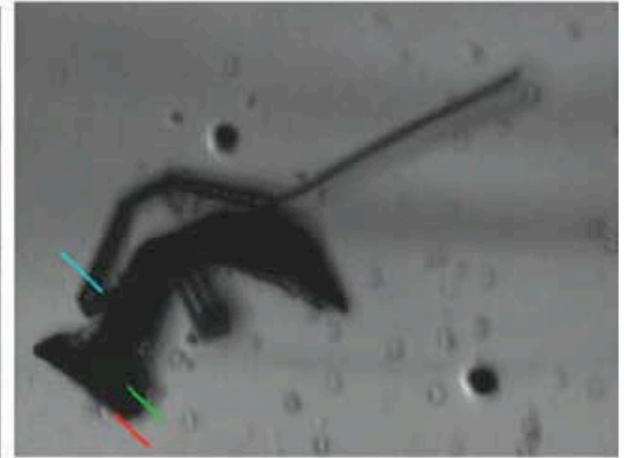
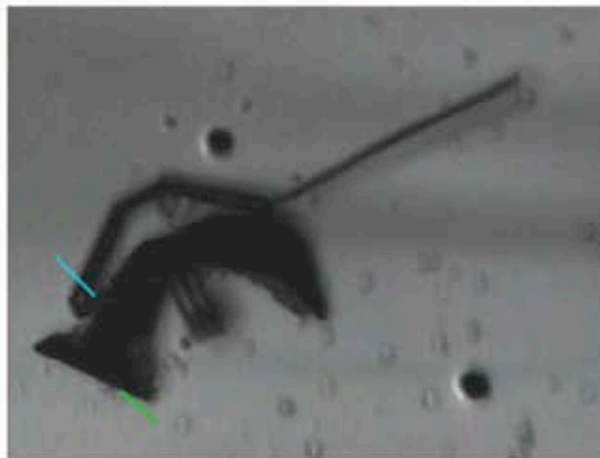
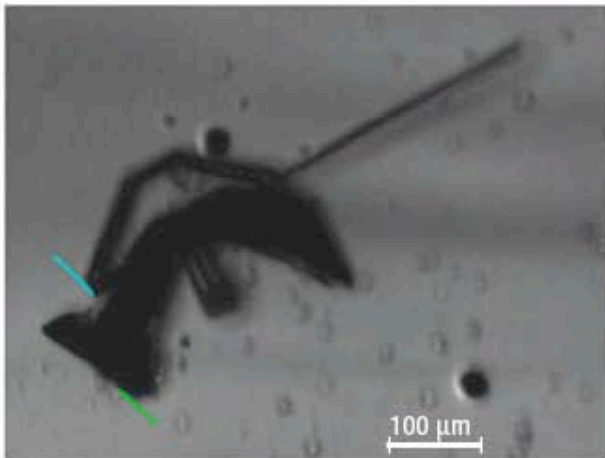
Muscle powered walker



average stepsize: $25 \mu\text{m}$

step frequency: 1.8 Hz

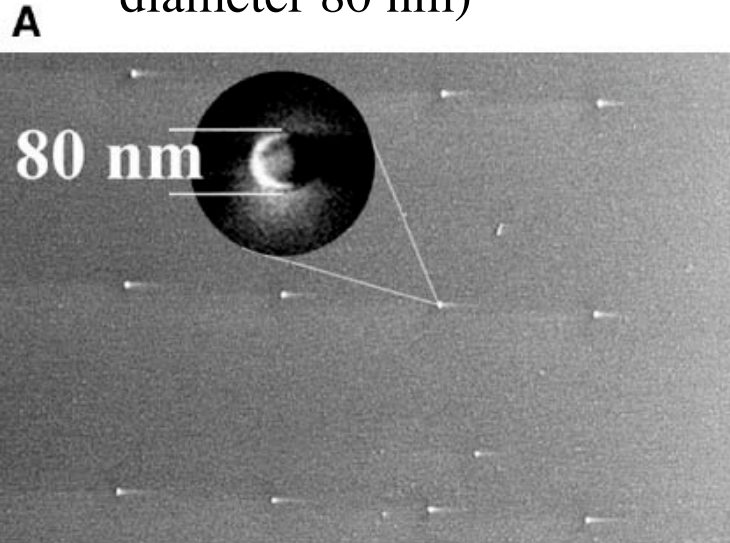
maximum speed: $38 \mu\text{m s}^{-1}$



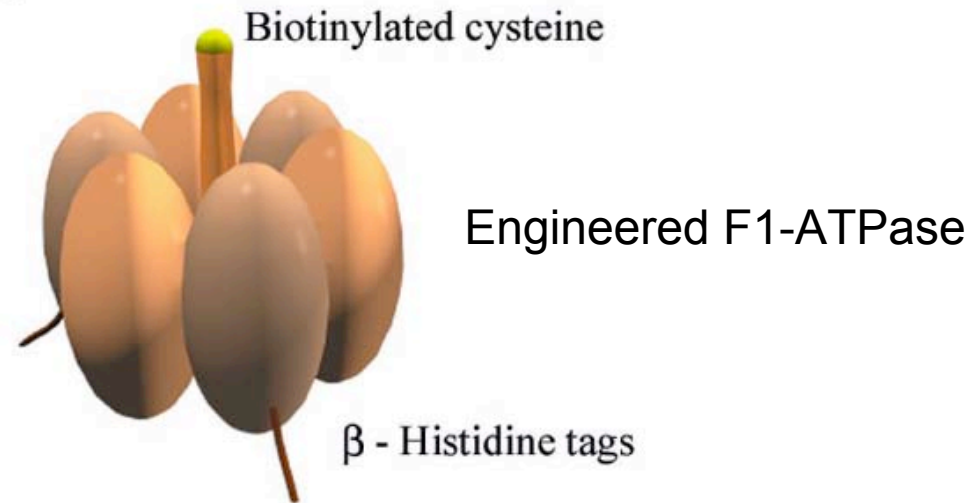
Nature Materials 4:180

F1-ATPase propeller

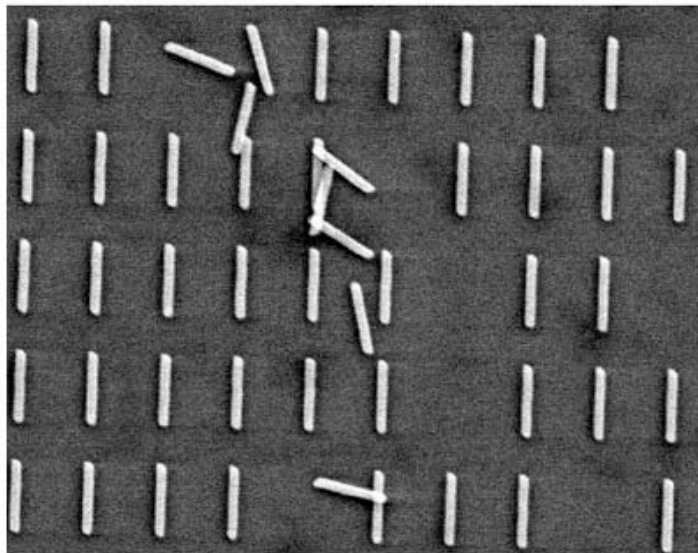
Ni post (height 200 nm,
diameter 80 nm)



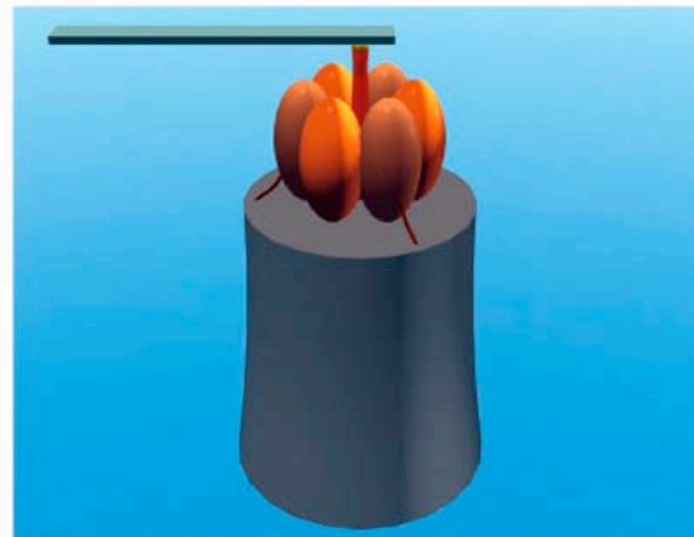
B



C



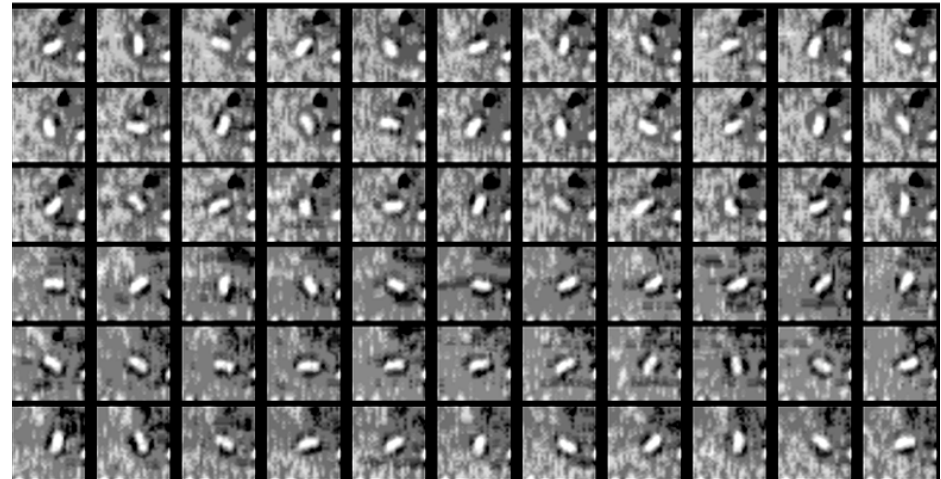
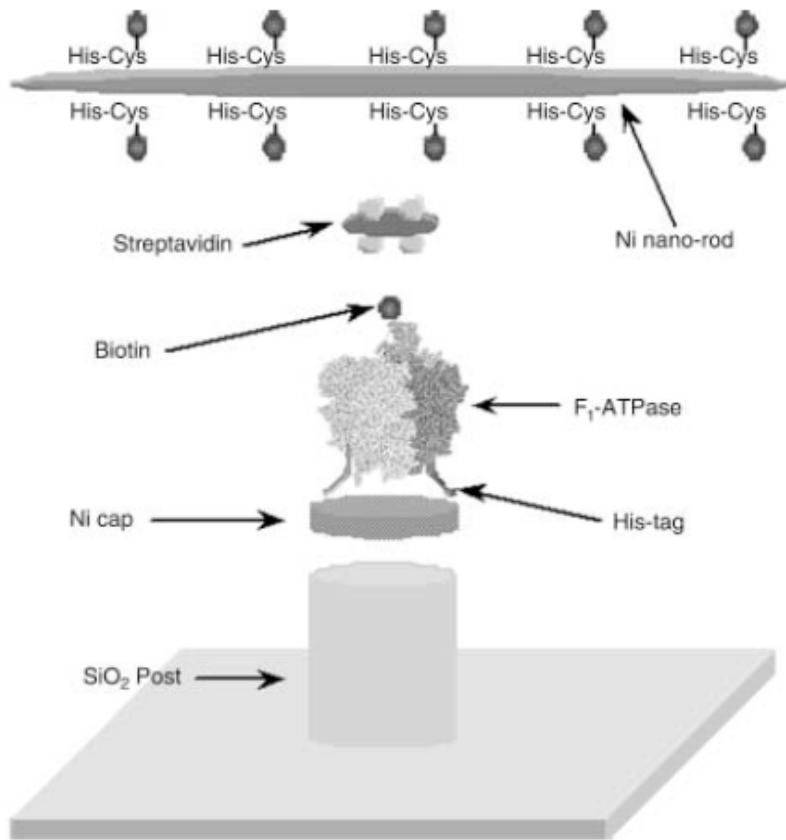
D



Nano-propeller

nanopropeller (length 750 to 1400 nm, diameter 150 nm).

F1-ATPase propeller



5 out of 400 propellers work

Speed: 0.74 to 8.3 revolutions
per second

Total torque: 20 pN nm

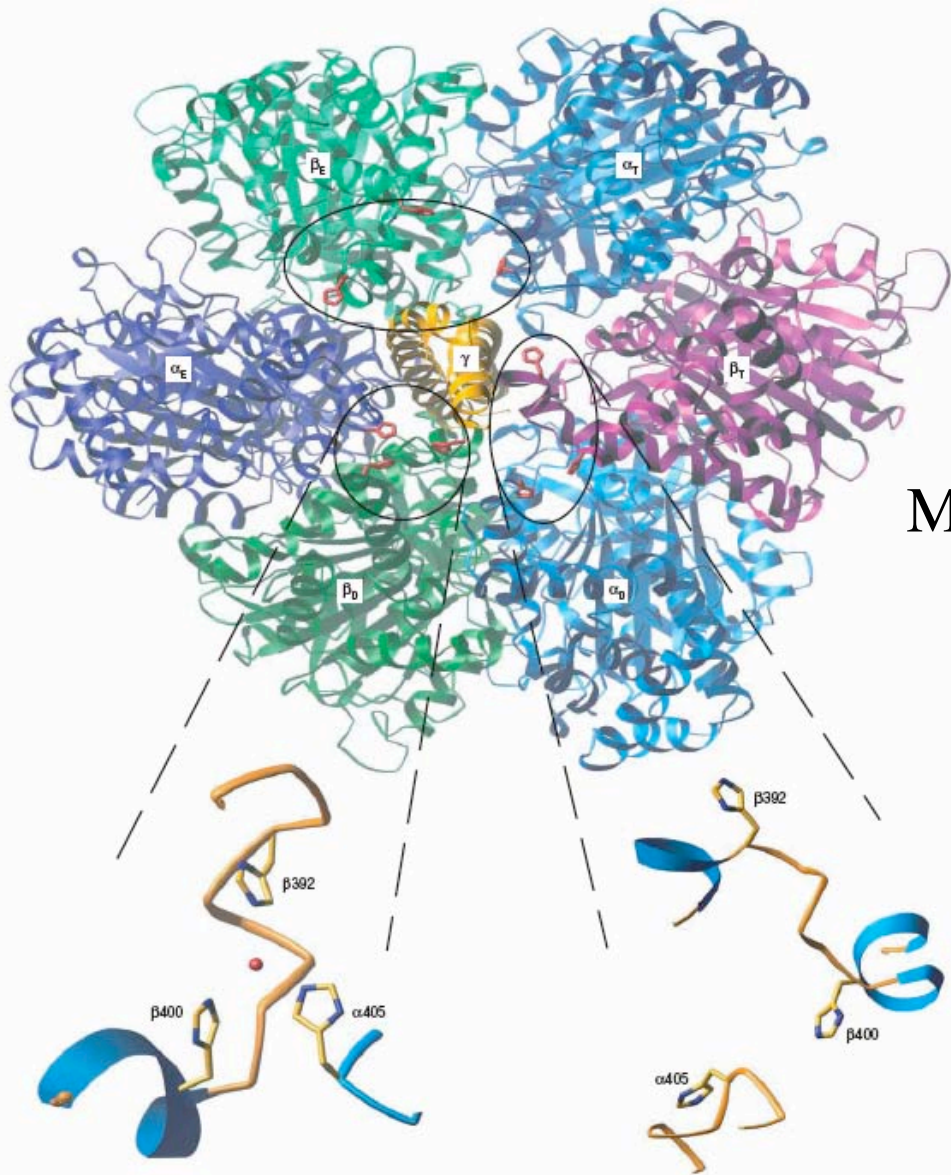
Efficiency: 50 to 80%



Assembly recipe:

1. Add biotinylated F₁-ATPase, wait 30 min (to bind Ni), wash with buffer
2. Add streptavidin, incubate for 15 minutes (cystein bond), wash
3. Add peptide-labeled nanopropellers, wait 30 min (for streptavidin/biotin)

F1-ATPase propeller

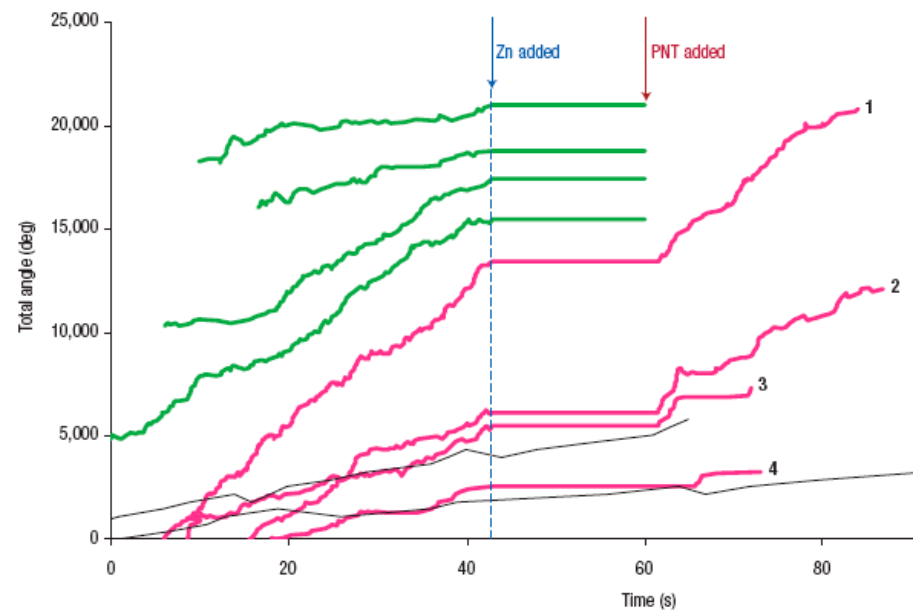


Zn²⁺ binding site

Nature materials 1:173

Zn²⁺ inhibits conformational cycle

Metal chelator (PNT) sequesters Zn²⁺



Rotation is chemically regulated
(in the presence of ATP and Mg²⁺)

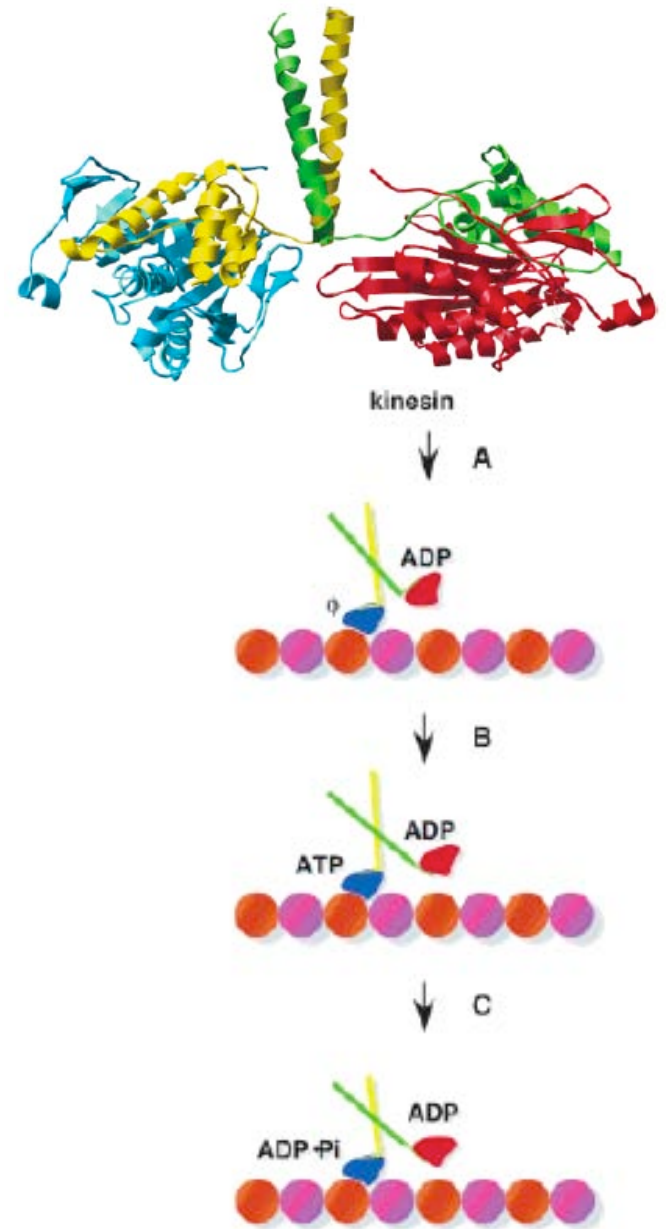
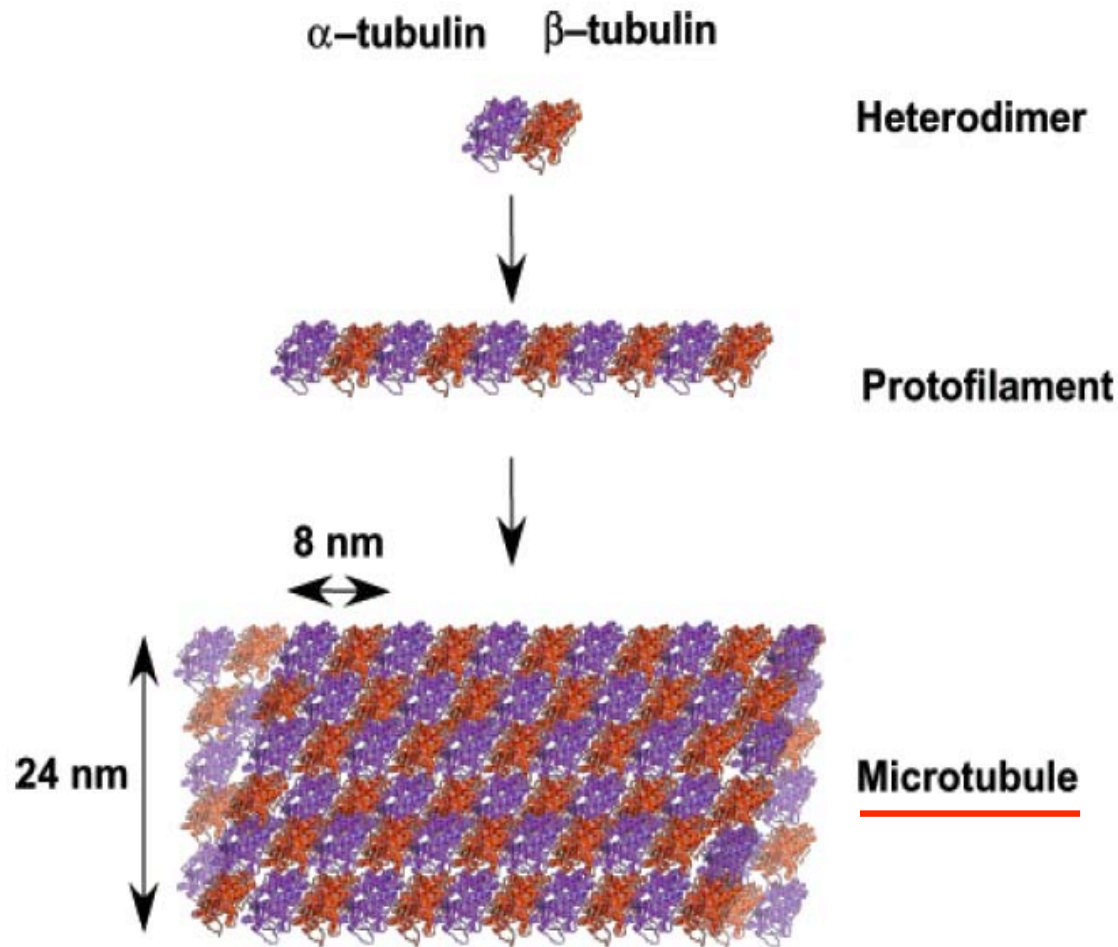
Produce ATP via applying electric potential

- Dimroth, EMBO J., 17, 5887

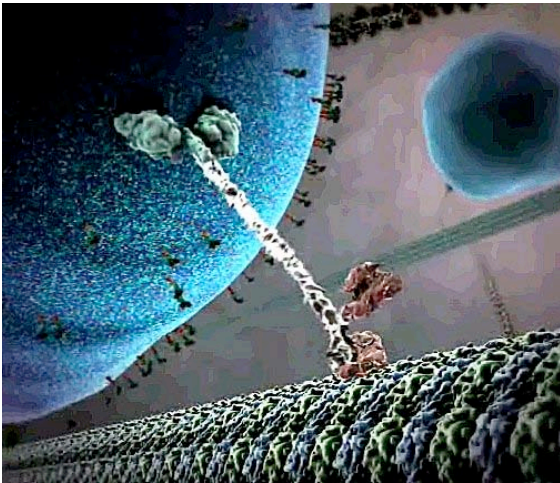
Produce ATP by rotating magnetic bead

- Itoh, Nature 2004, 427, 465

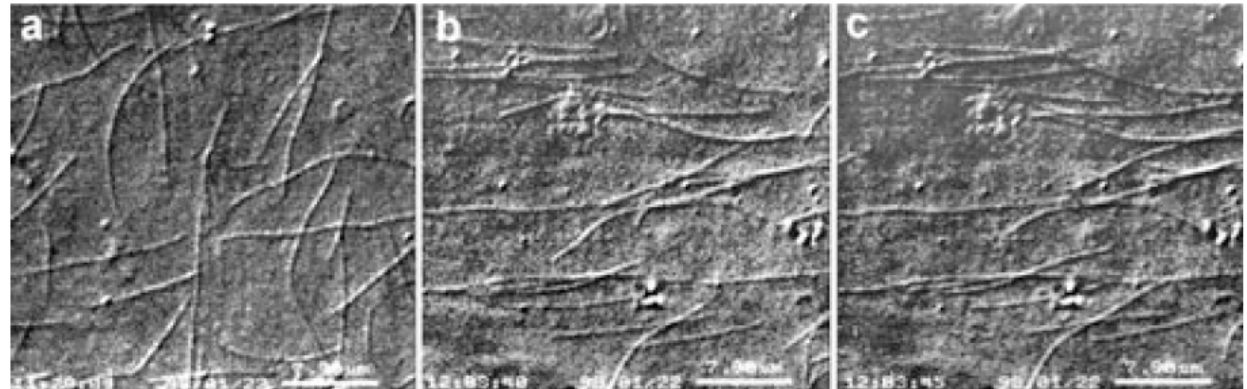
Molecular tracks



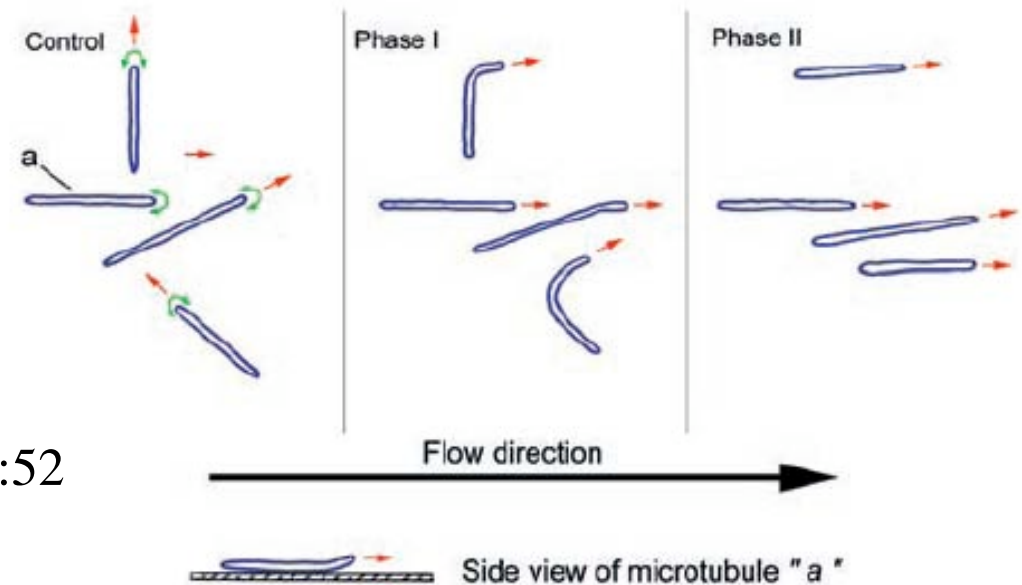
Aligning Microtubule



Unidirectional transport requires proper orientation of microtubules



Flow field aligns microtubules.



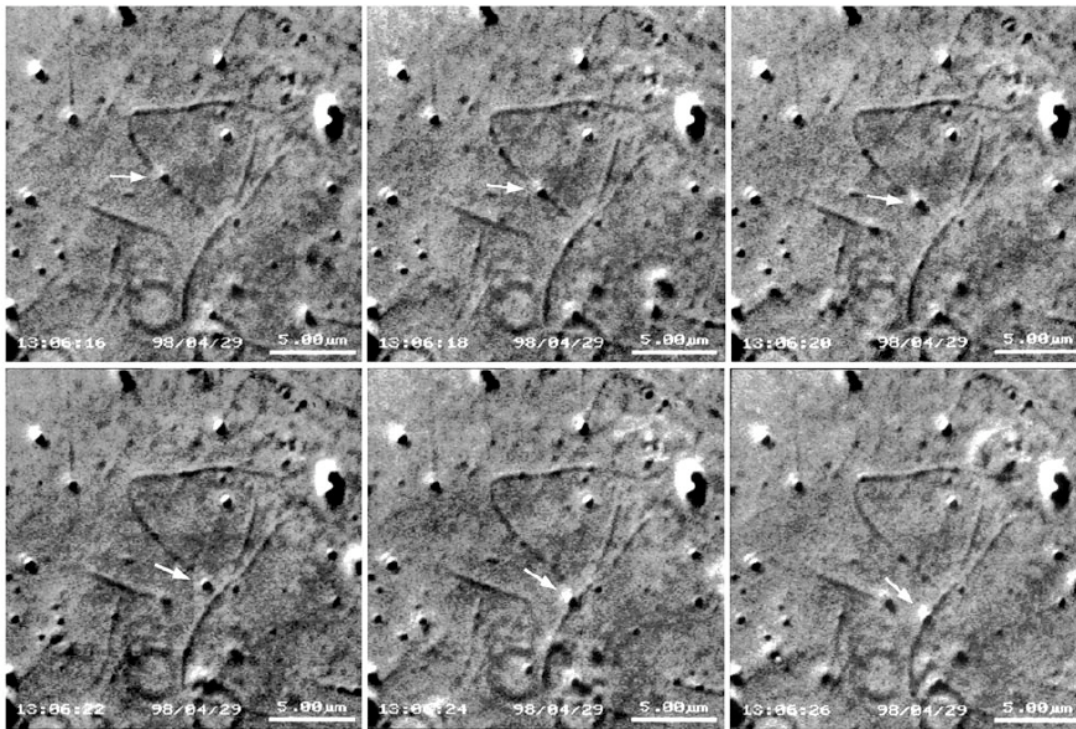
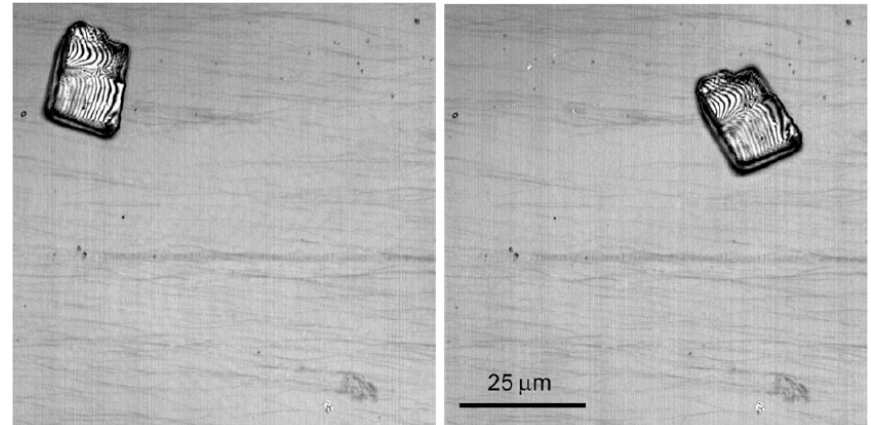
Nanotechnology 11:52

To gain proper orientation, microtubules were mechanically forces to glide in the same direction

Microtubular carper

Flow-oriented microtubules were immobilized.

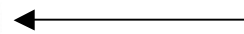
Beads were coated with kinesin.



Glass particle



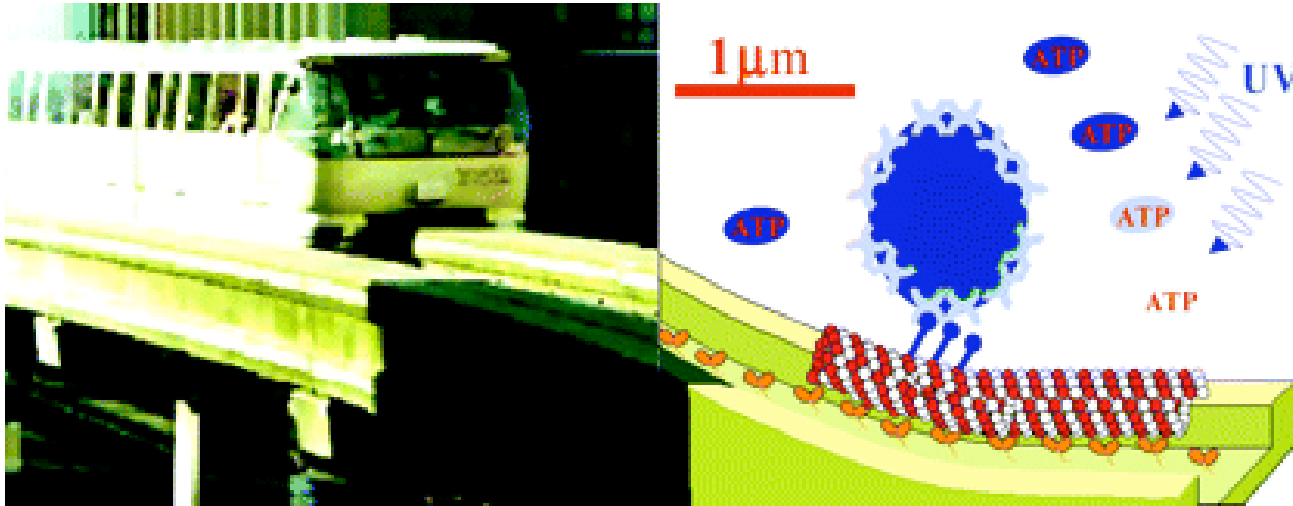
Cross-microtubule transport



Macroscopic transport was observed (mm)

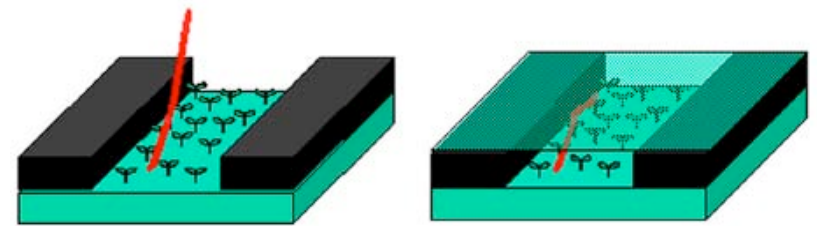
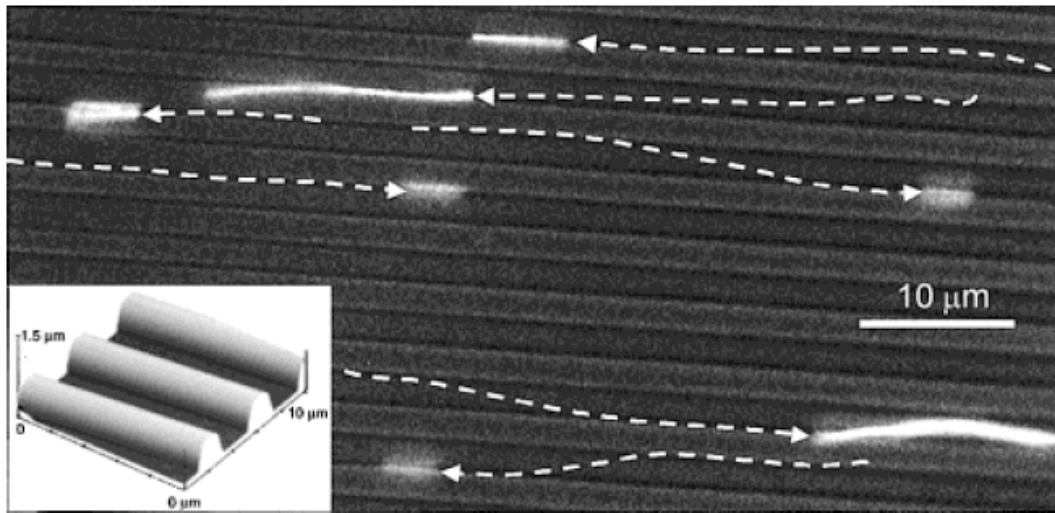
Nanotechnology 12:238

Molecular Shuttles



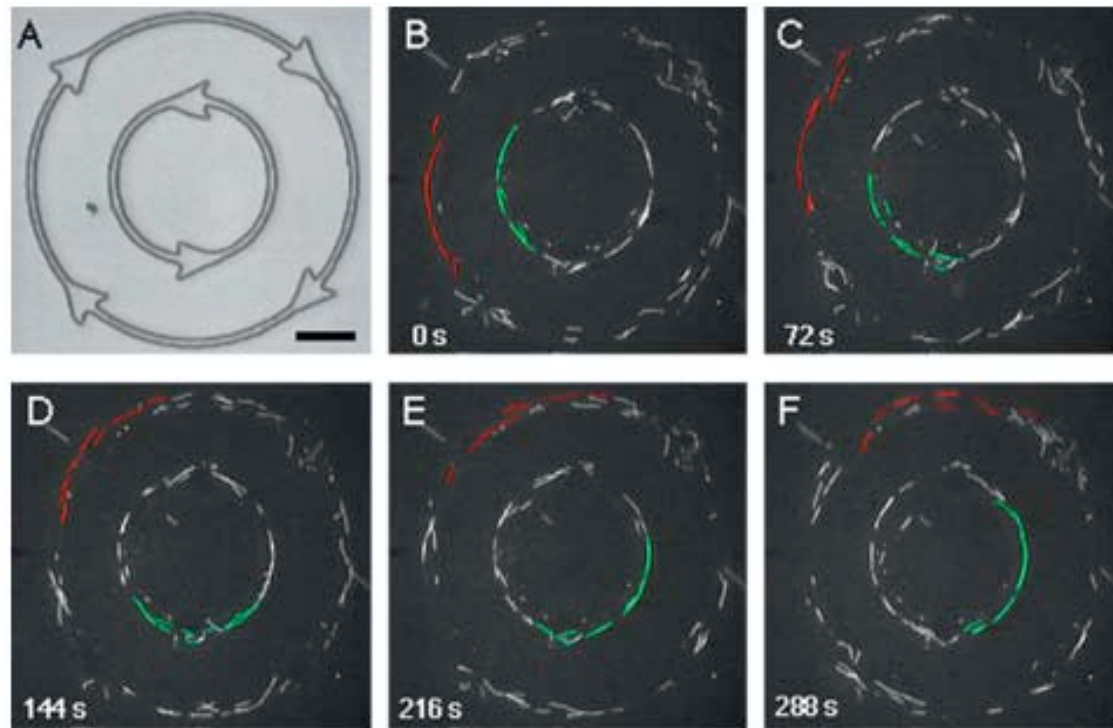
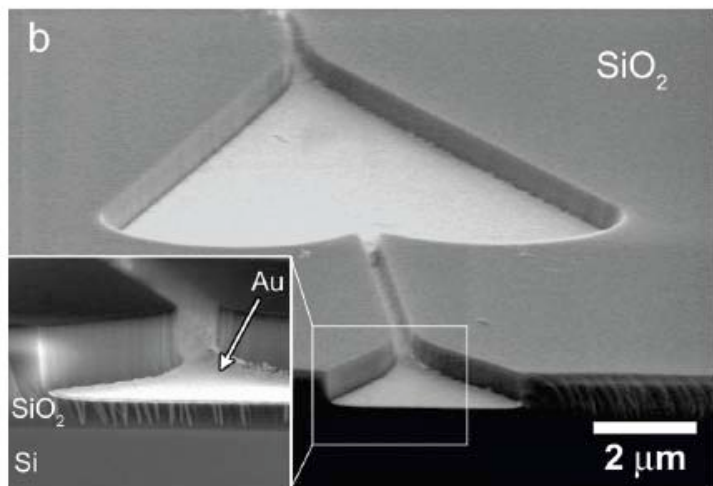
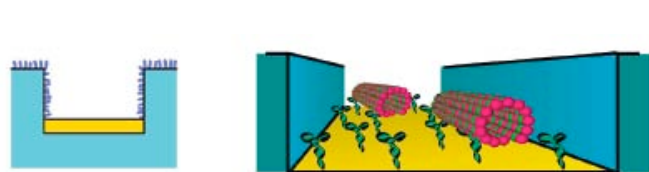
Inverted system

Transport is directed through microfabricated tracks

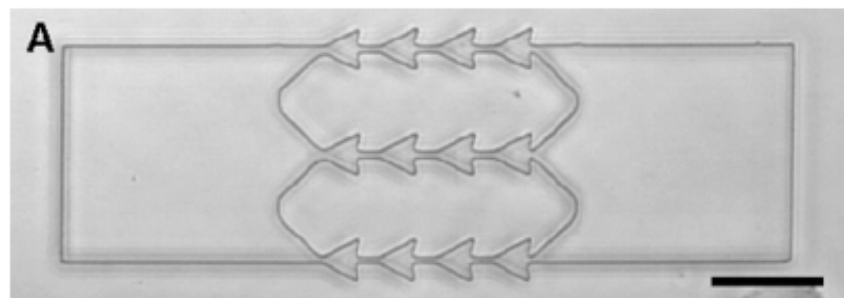


Closed channel setup

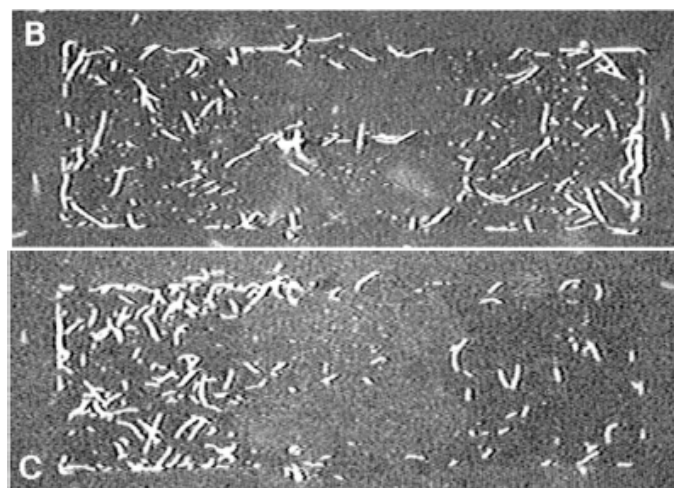
Transport rectification



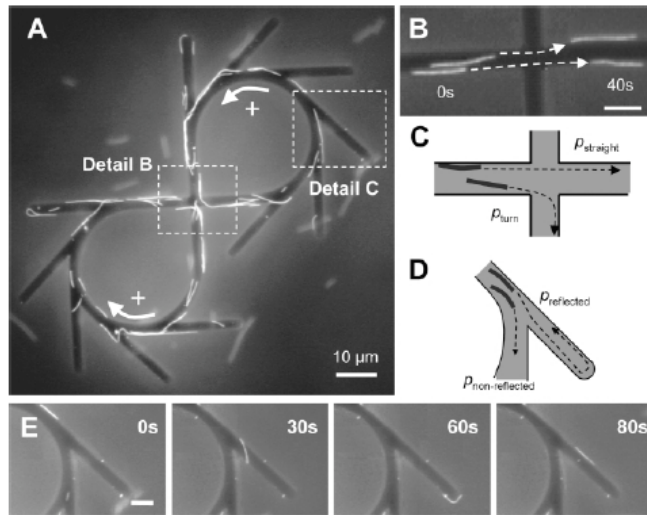
Nano Letters 5:1117



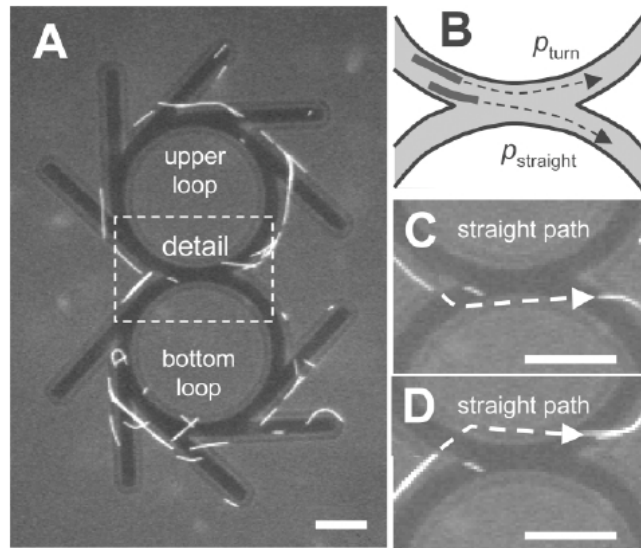
Biophys. J. 81:1551



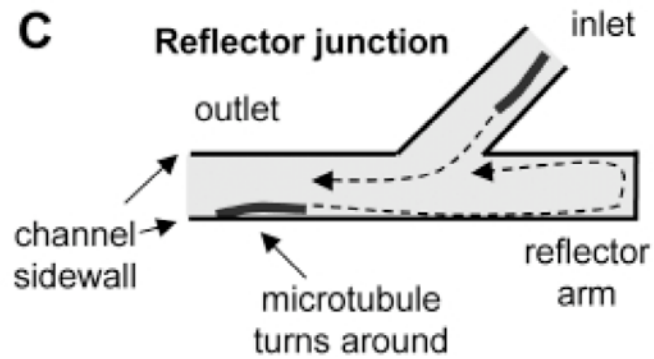
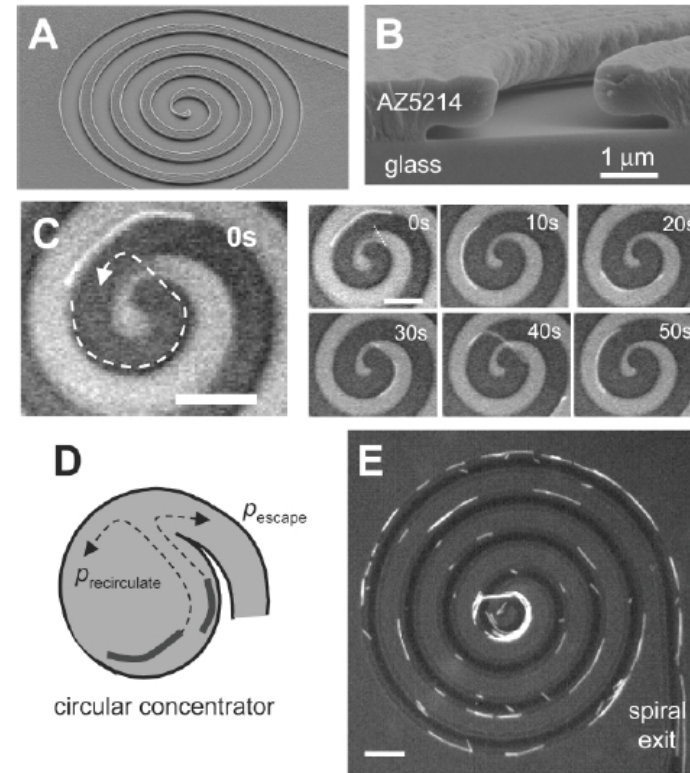
Motor-protein roundabouts



Crossing junctions



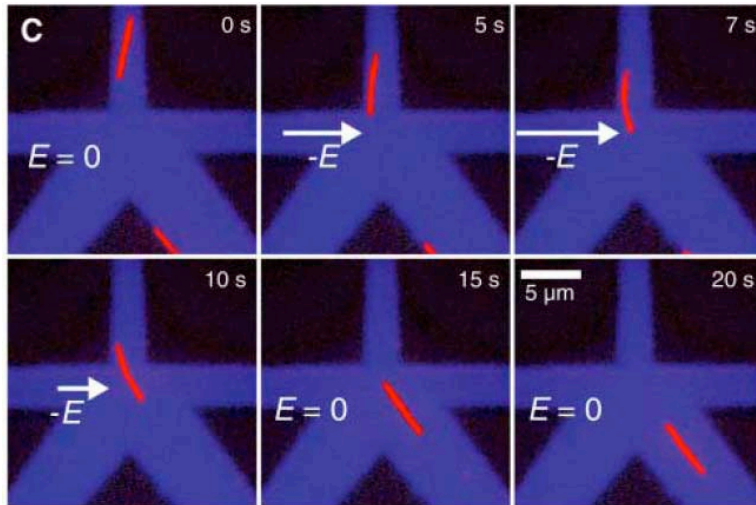
Scale bar: 10 μm



Unidirectional motion

Steering transport

Electric field:

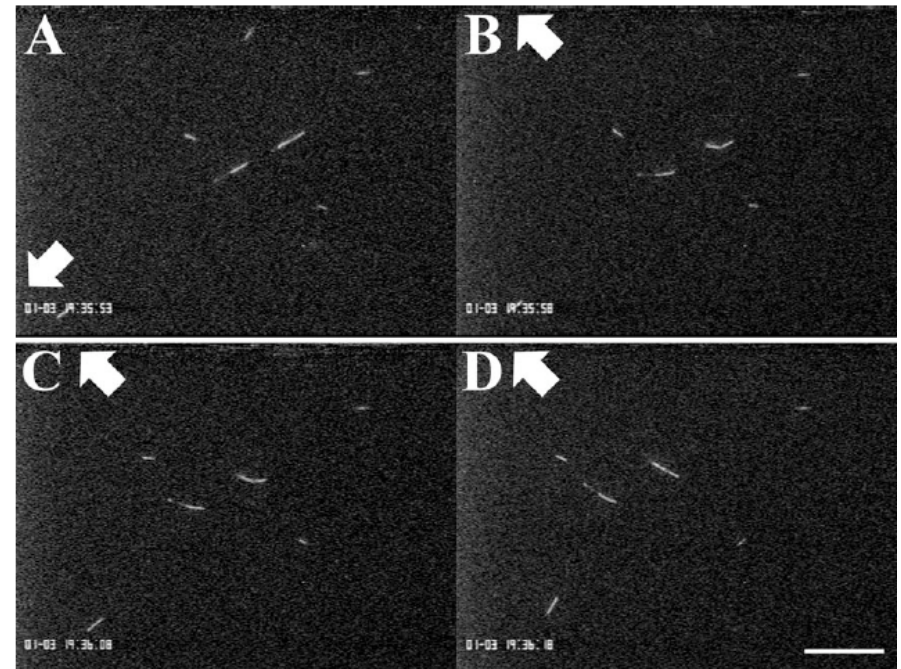
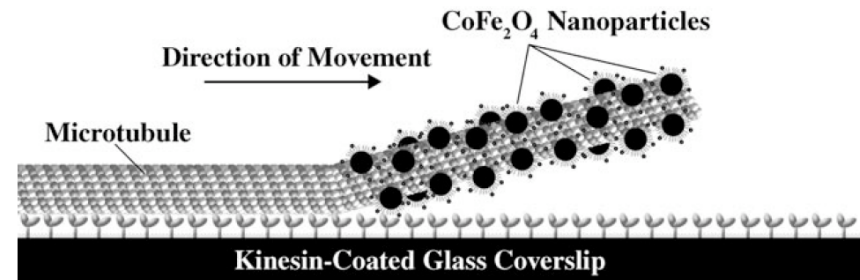


"Molecular sorting of green and red labelled microtubules"

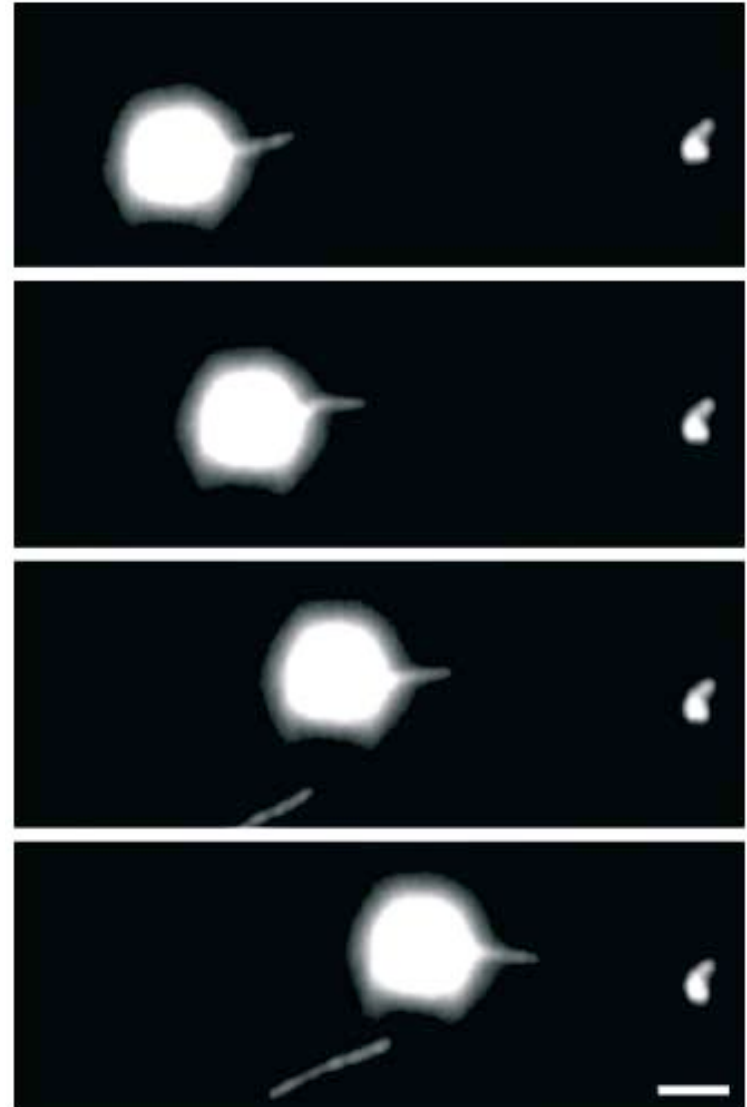
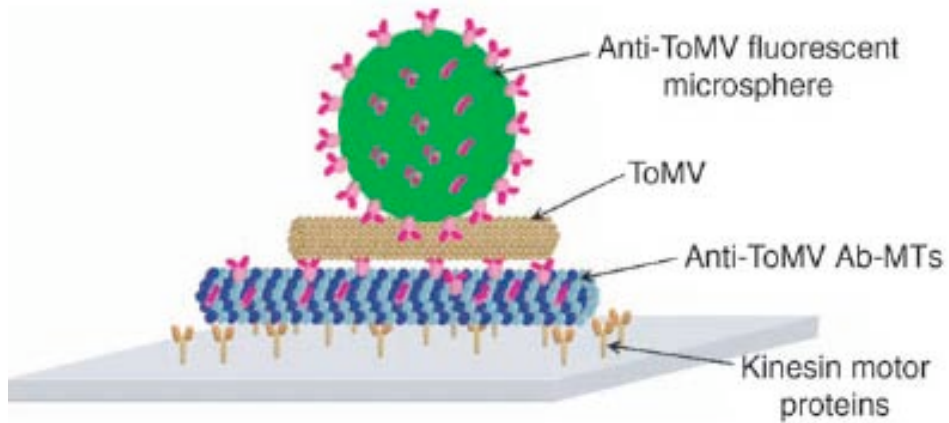
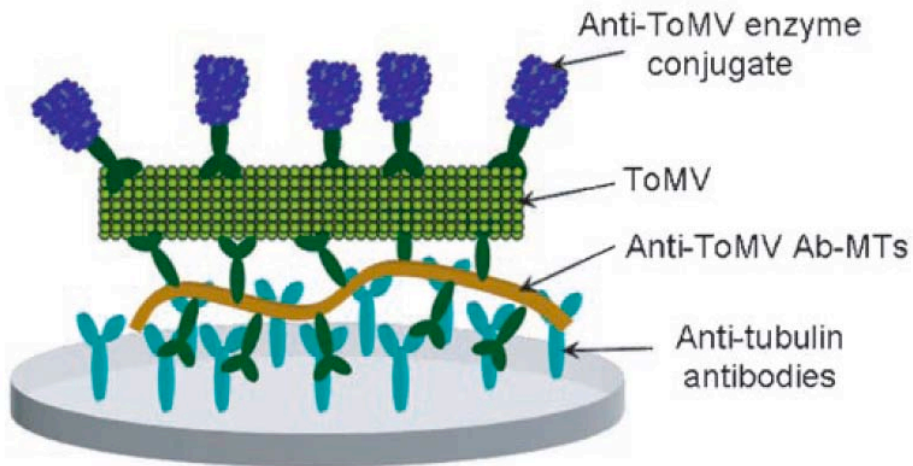
M.G.L. van den Heuvel et.al
Kavli Institute of Nanoscience, Delft

15 x accelerated

Magnetic field:



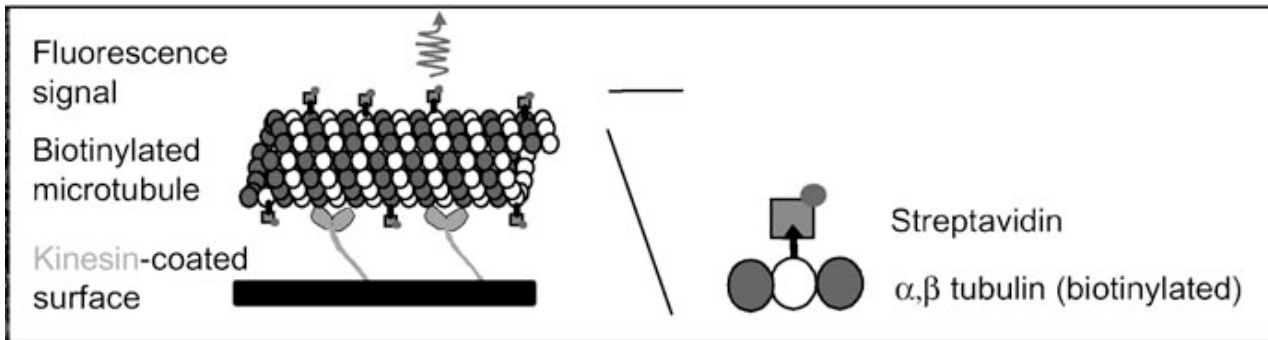
Transporting viruses



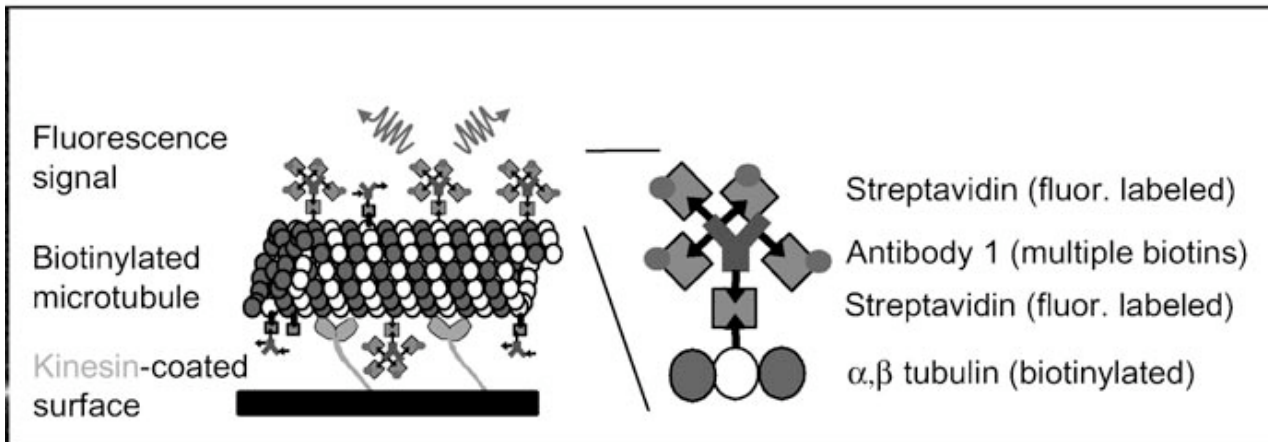
Time: 5s

1 μ m

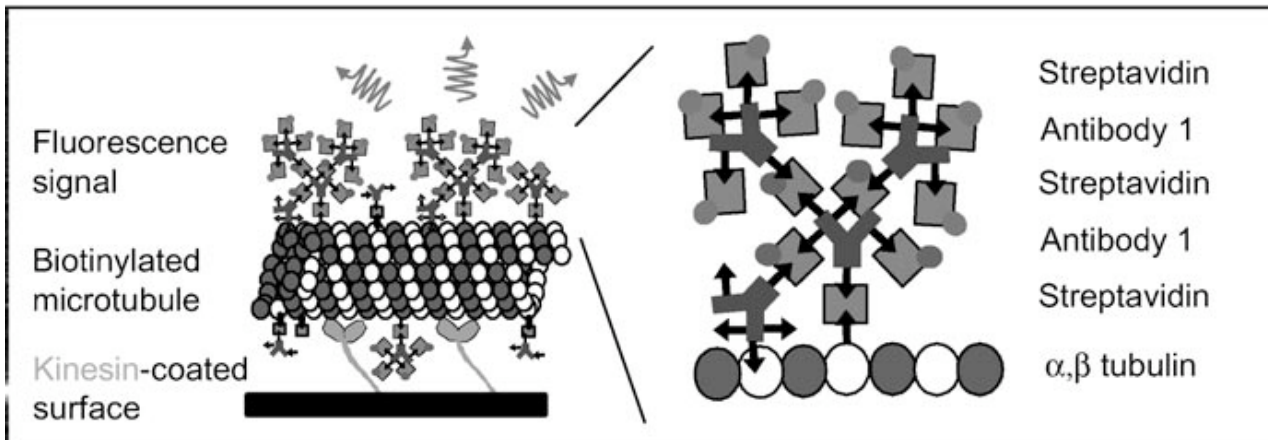
Active transport sensors



selective capture of proteins;
subsequent detection of the capture event

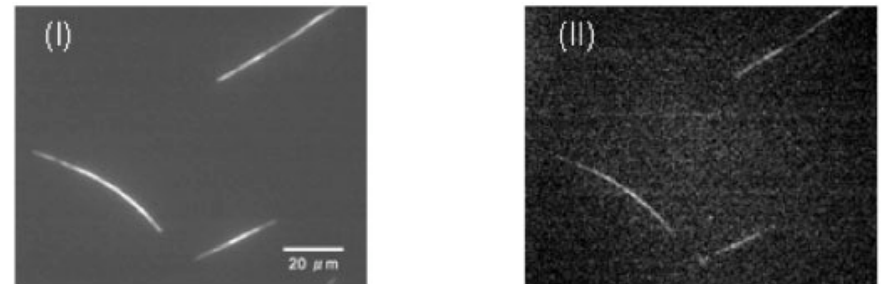
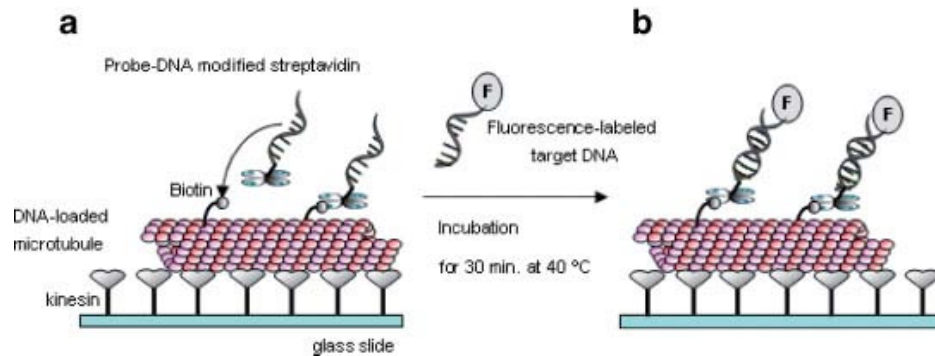


analytes of different types can be

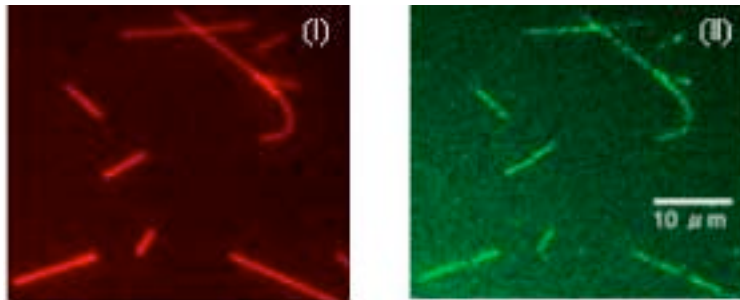


transported to the sight of detection assay

Selective DNA transport

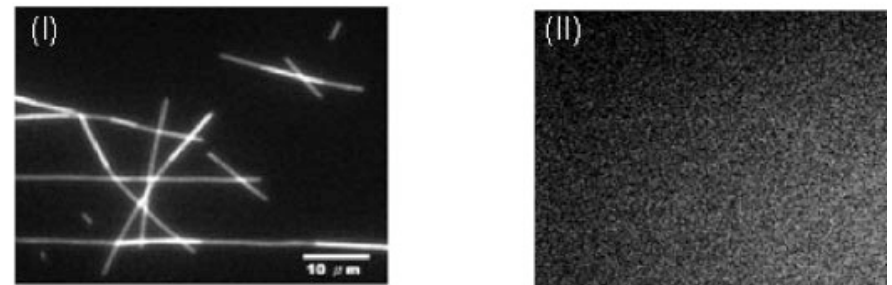


Fully matched DNA

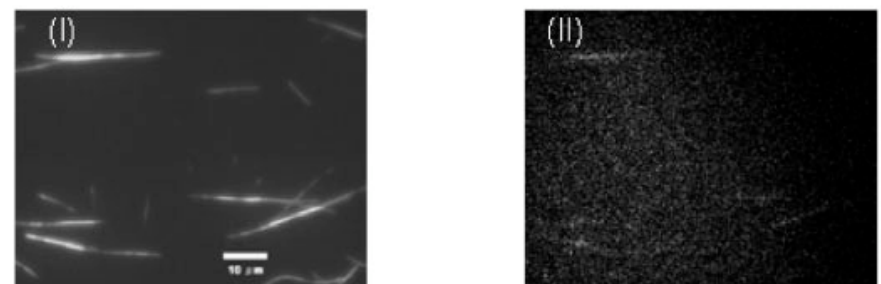


Fluorescence from MT and DNA

Can be used to concentrate DNA and DNA-associated proteins

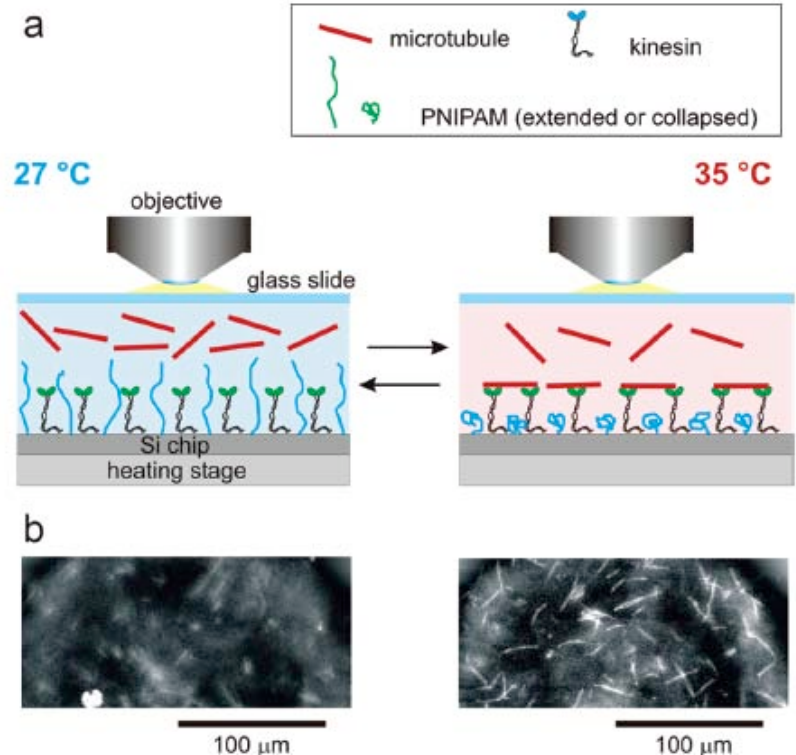
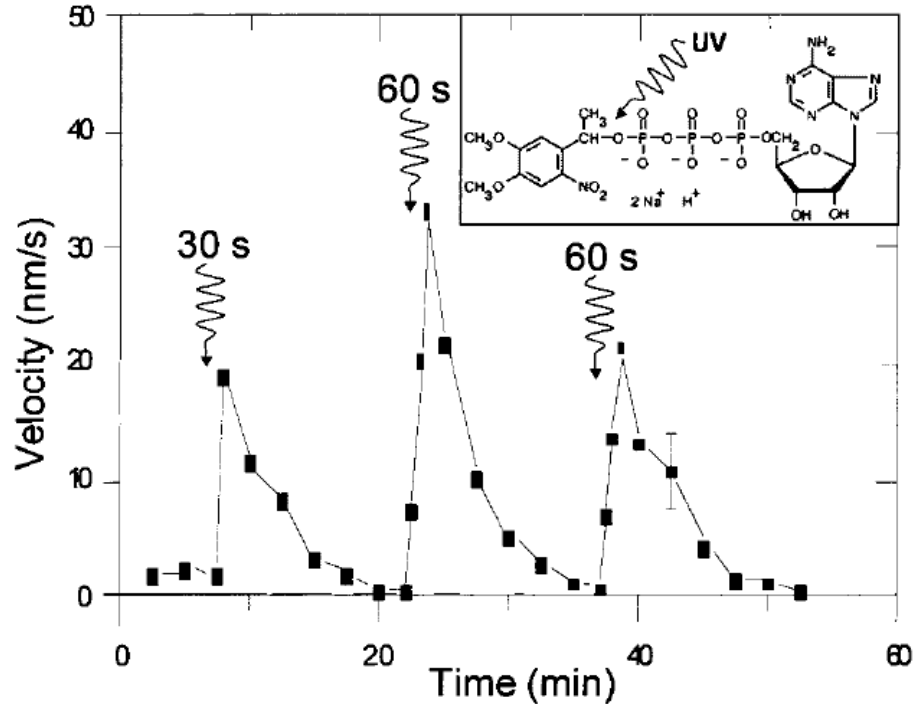


Unmatched DNA (Same GC contents)

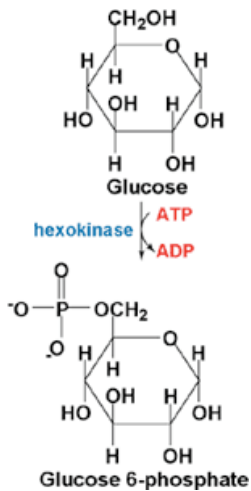
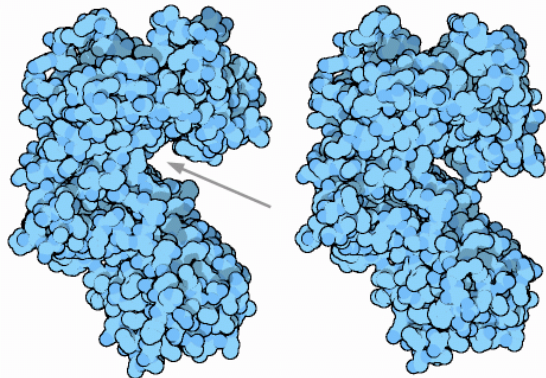


SNP

Transport control

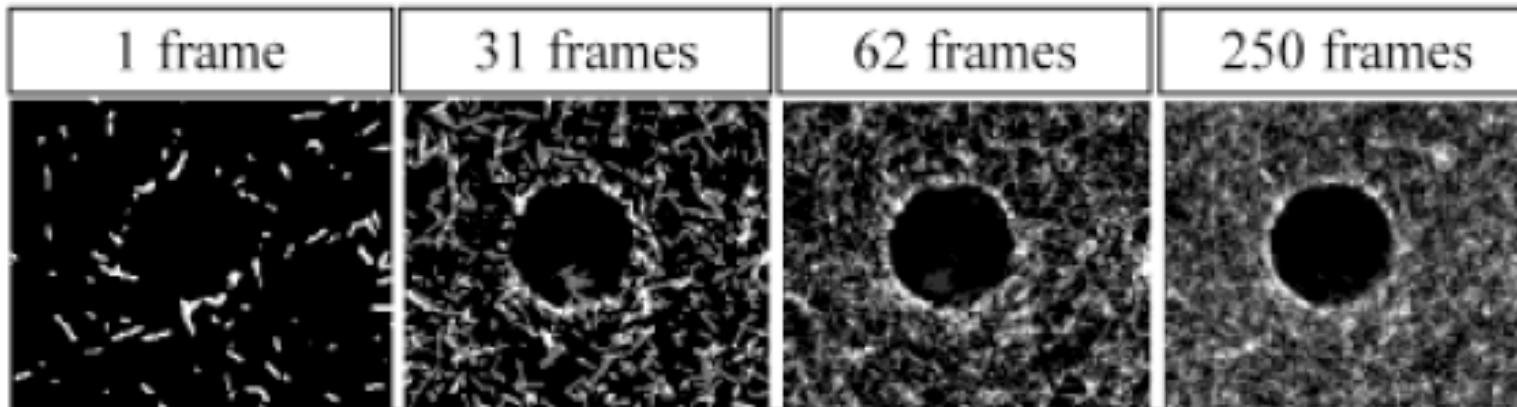
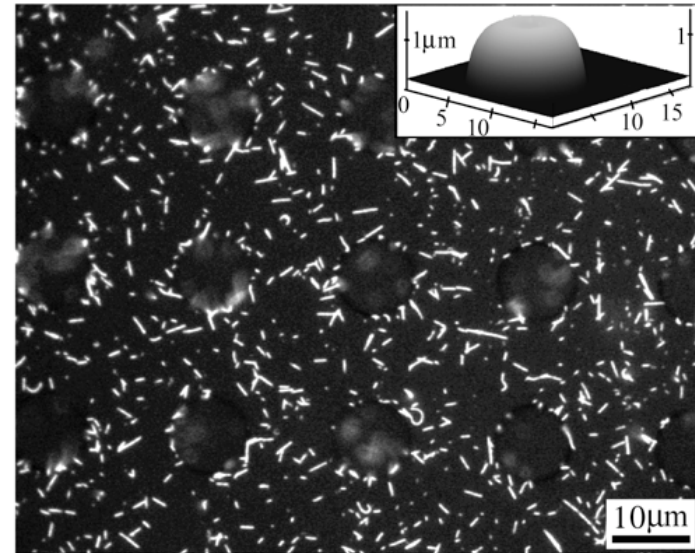
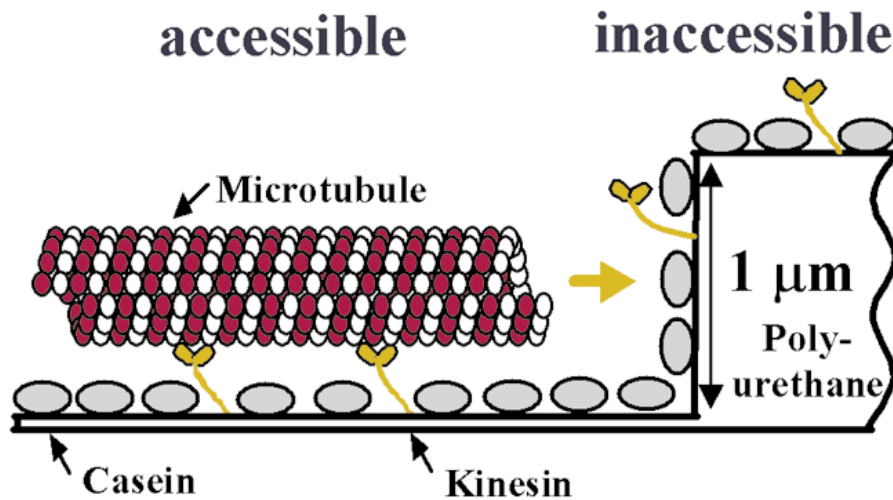


UV light + enzyme



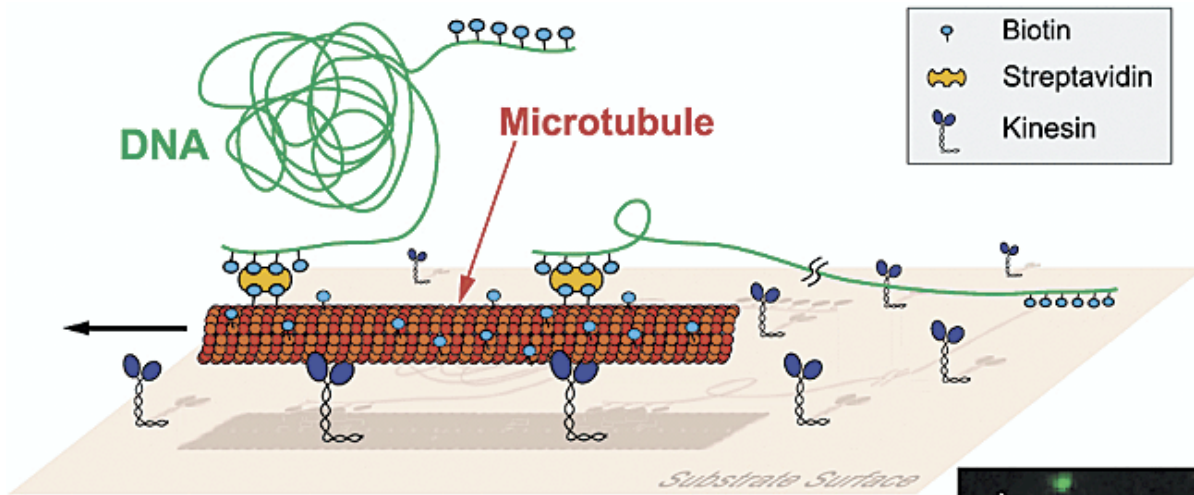
Thermal collapse of a polymer brush

Surface imaging with walkers



Nano Letters 2002, 2, 113

superimposed images
reveal surface topography

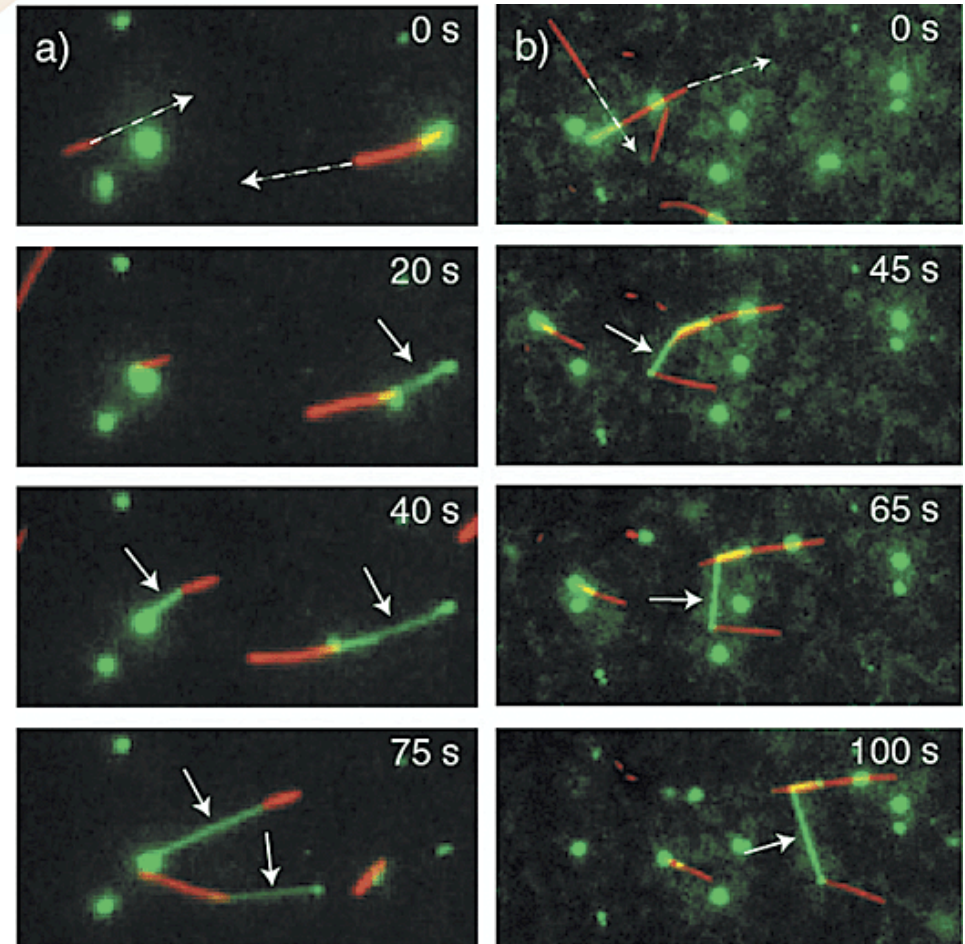


Stretching DNA

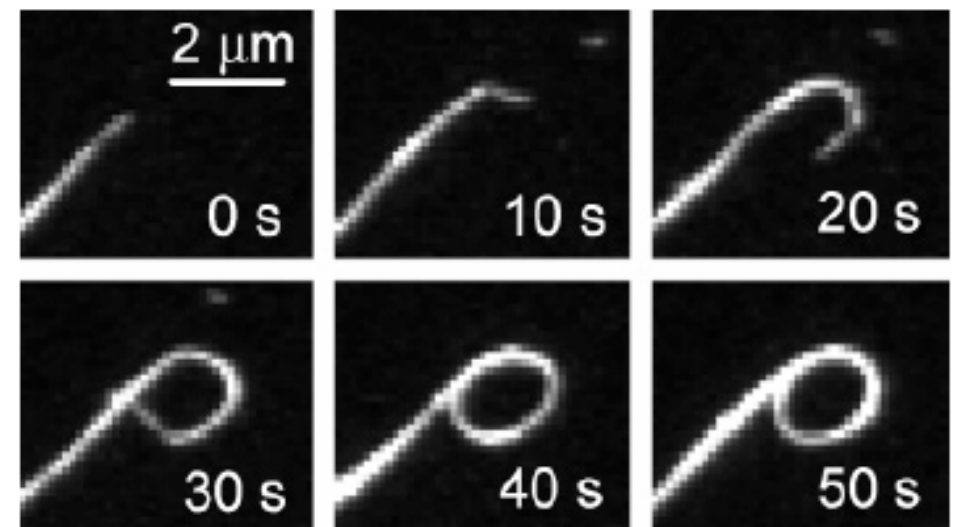
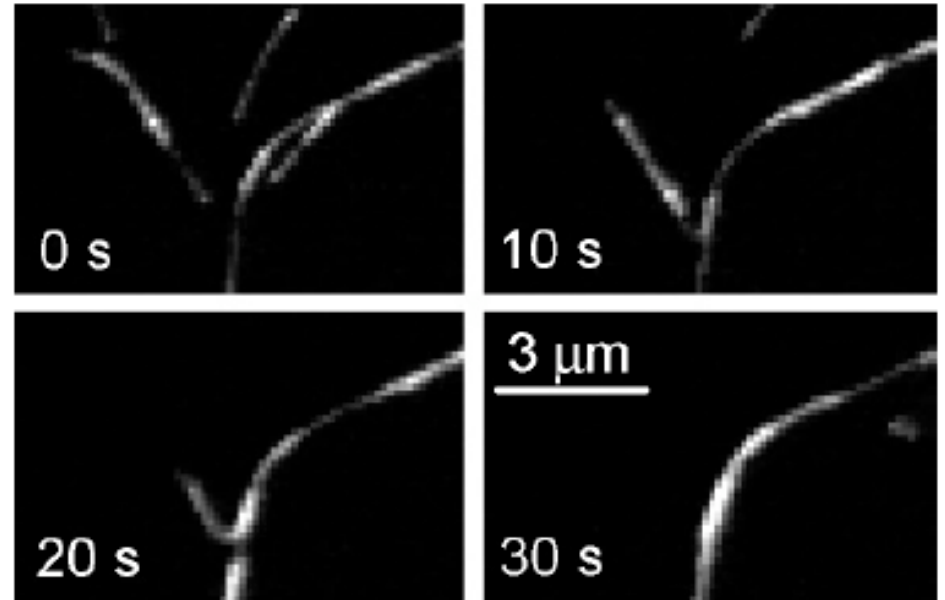
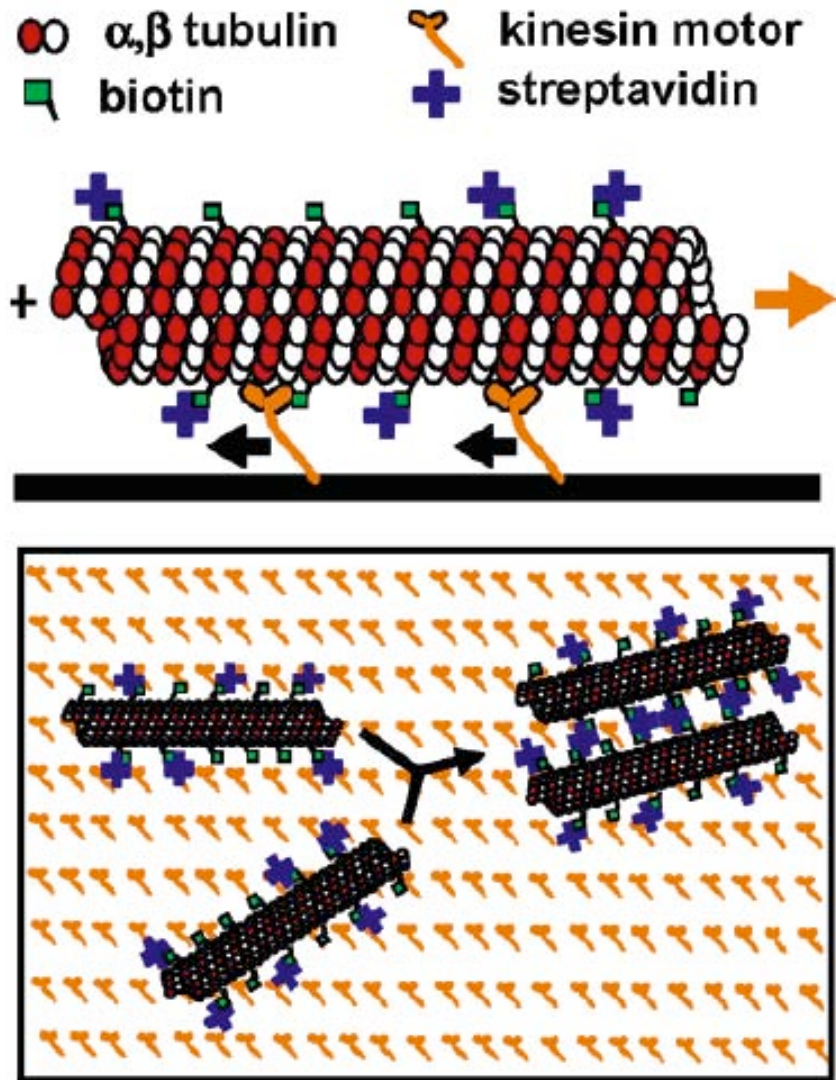
ATP-driven transport of microtubules stretches DNA

Can be used as templates for nanowire circuits

Nano Letters 2003, 3, 1251

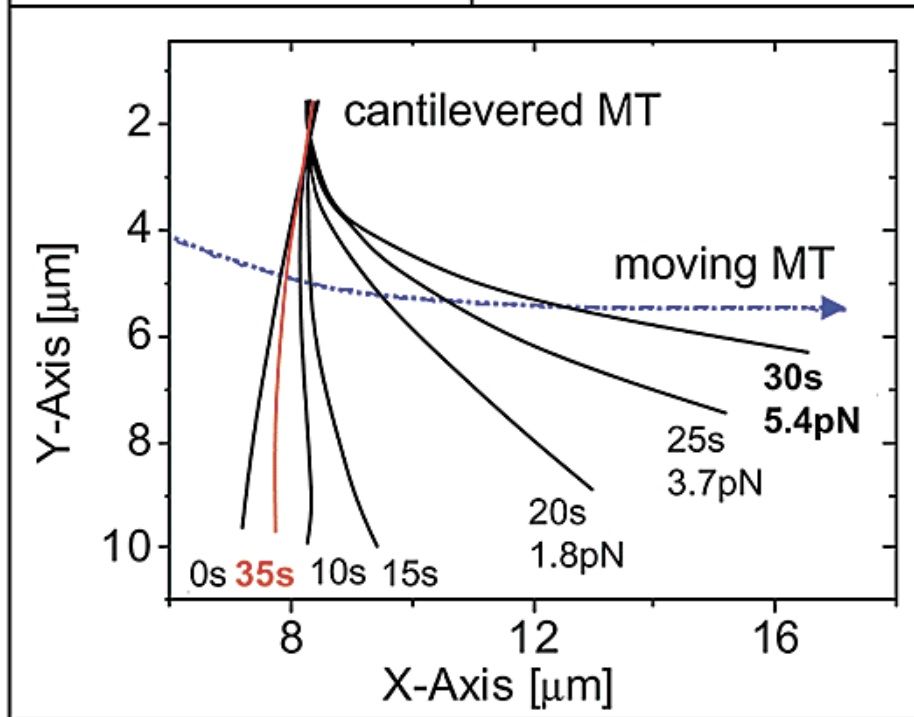
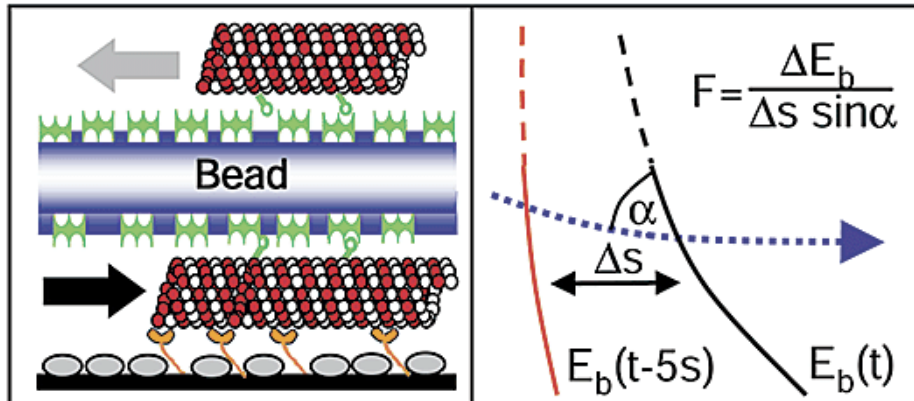


Active transport self-assembly

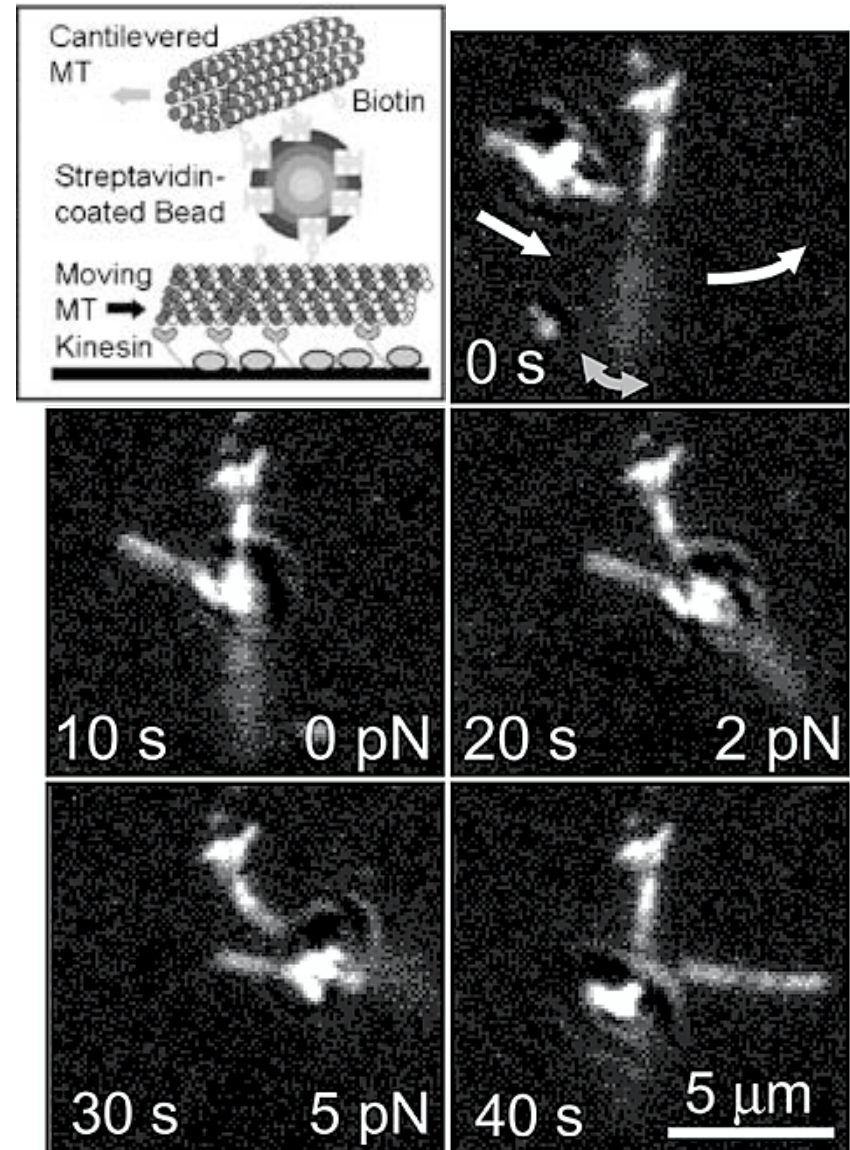


Nano Lett. 5:629

Pico-Newton force sensor

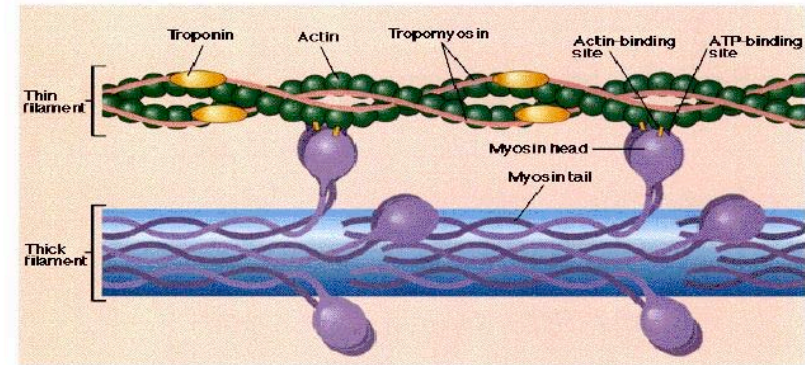


Nano Letters 2002, 2, 1113

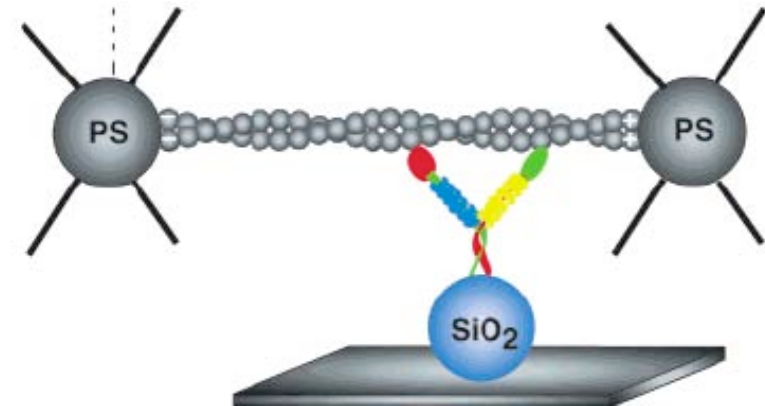
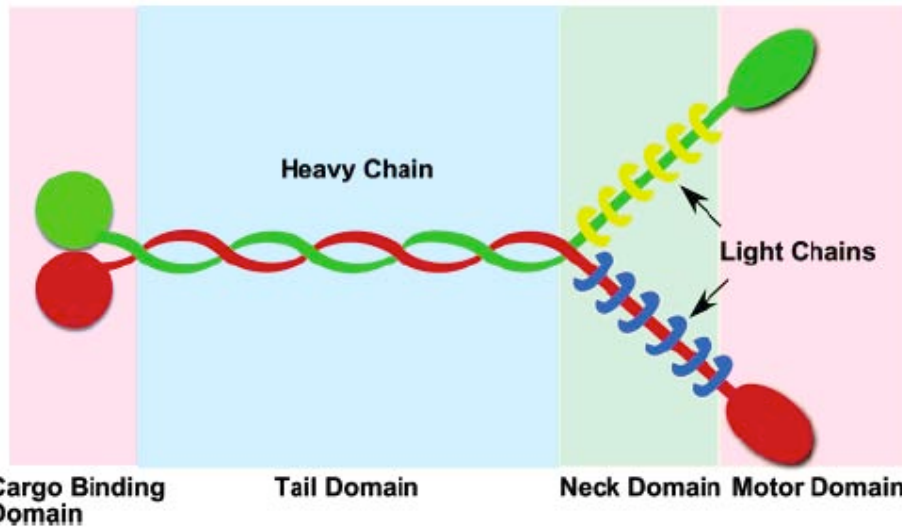
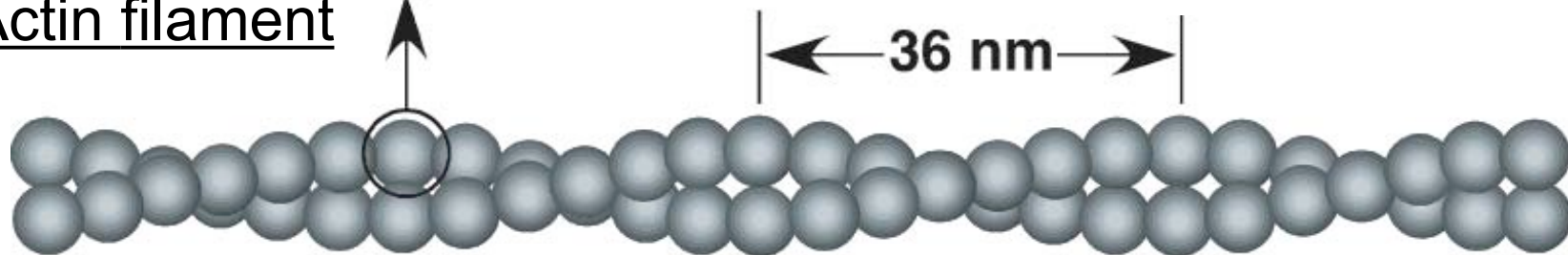


Load rate: 1pN/s

Molecular tracks



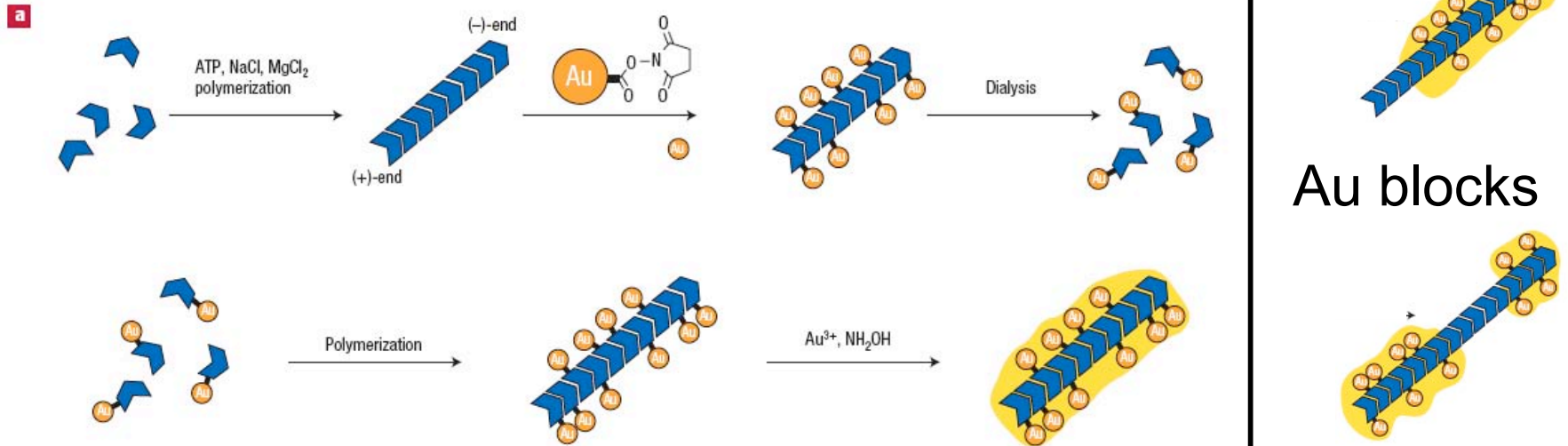
Actin filament



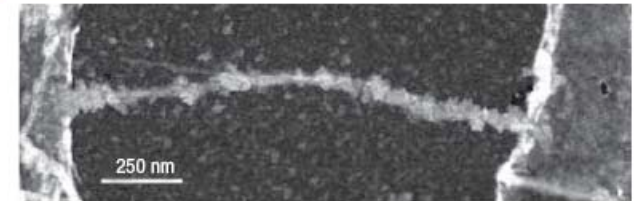
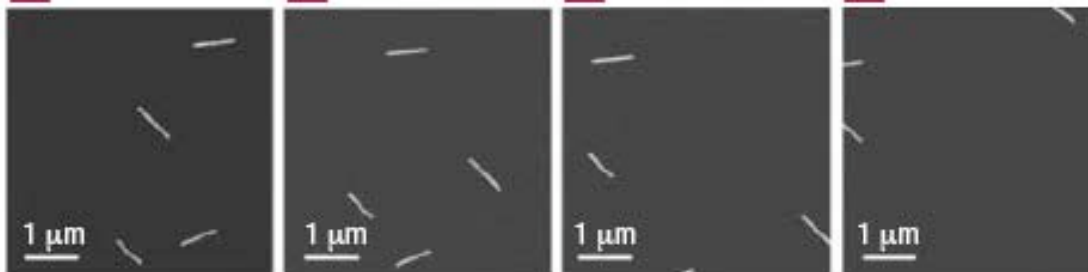
Myosin V

Speed: 10 $\mu\text{m/s}$

Gold nanowire assembly



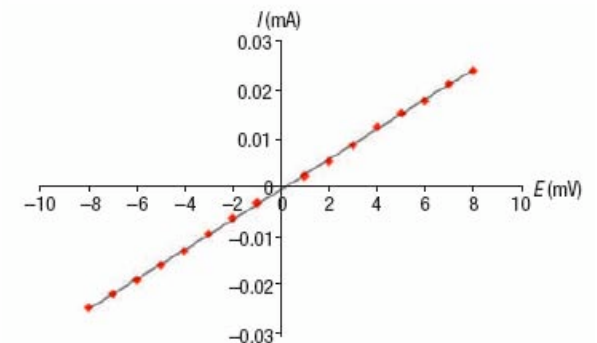
Assembly of gold nanowires



Gold nanowires can move on a myosin-coated surface!

Speed: 250nm/s

Nature Mat.3:692



Actin shuttles

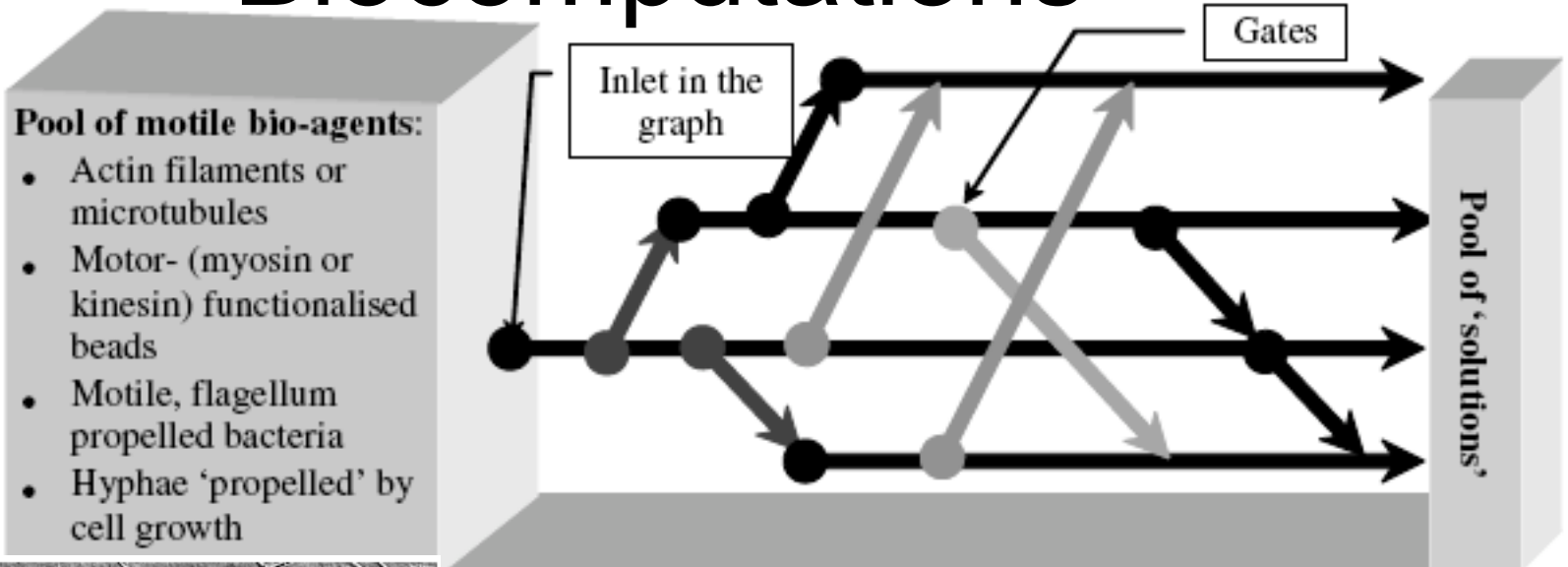


High precision gliding

Active filament is guided through
fabricated structure

Nanotechnology 16:710

Biocomputations



- Network of channels confining the movement of bio-agents**
- 2D (xy) network – interconnected channels
 - 3D (xyz) network – channels connected at different levels
 - 4D (xyzt) network – gates open and close

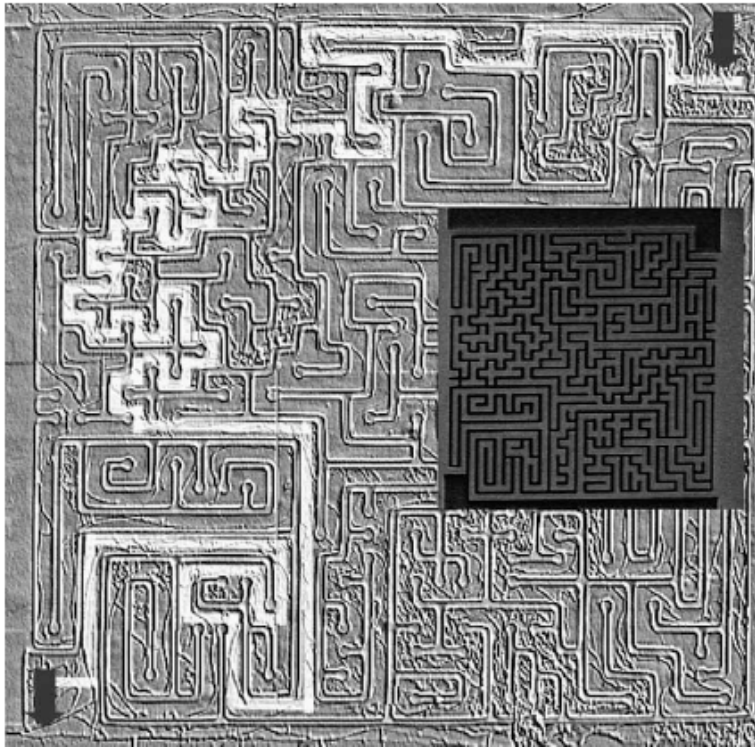
Large maze solved (in 3 days)
by fungal filaments.

Realistic problem:

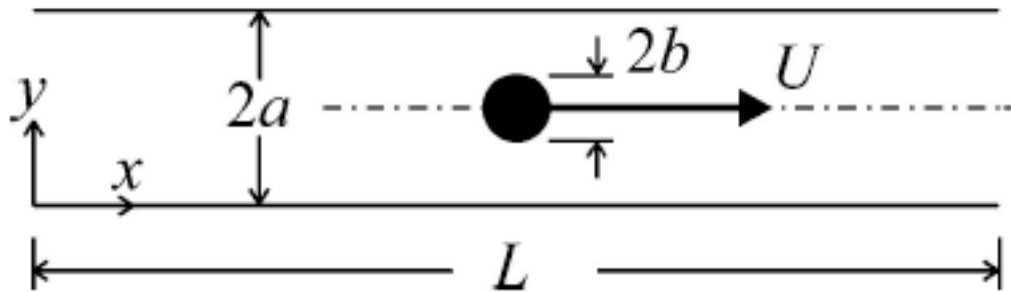
30x30cm² side with 0.5μm
feature size

5 μm/s speed: 16 h to solve

Microelectronic Engineering 83:1582

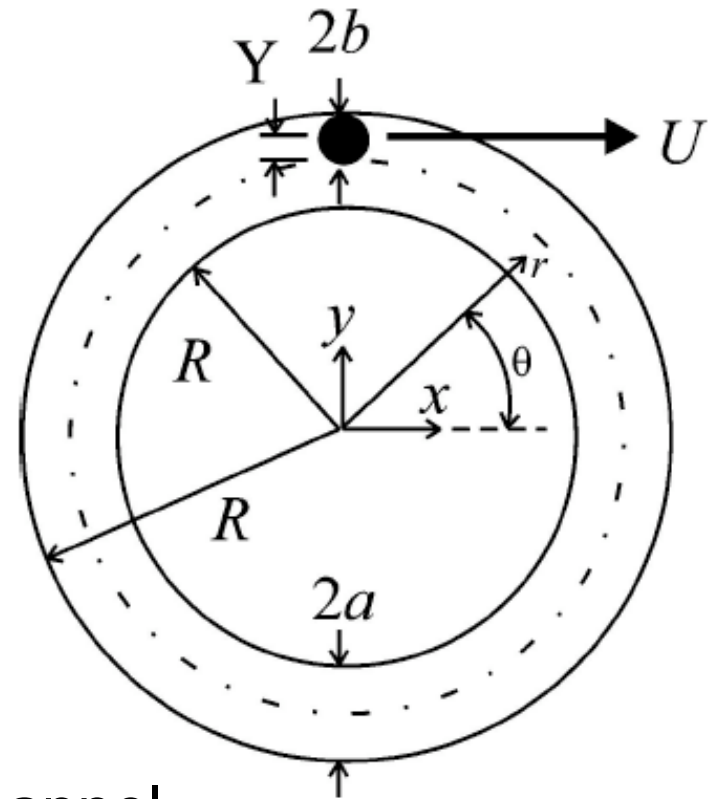


Biomotor-driven fluid pump



Straight channel

Bead is moved by a kinesin motor



Circular channel

Will they make their way?

