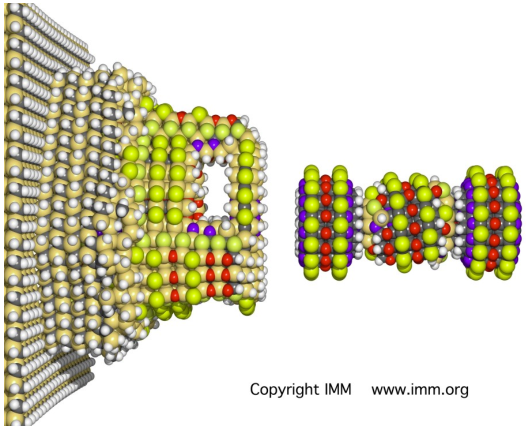
From Fantastic Voyage to Soft Machines: two decades of nanotechnology visions *(and some real achievements)*

Richard Jones

University of Sheffield

Three visions of nanotechnology…

1. Drexler's mechanical vision



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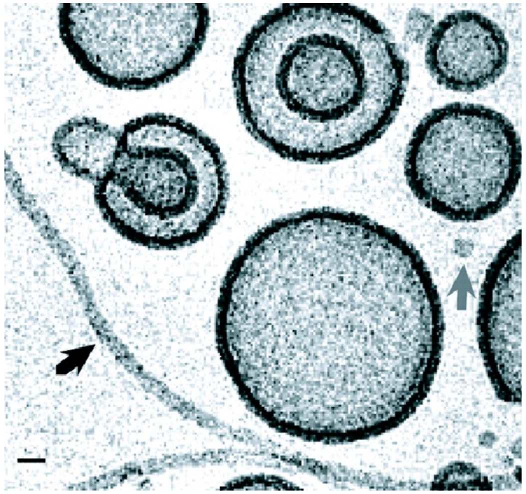
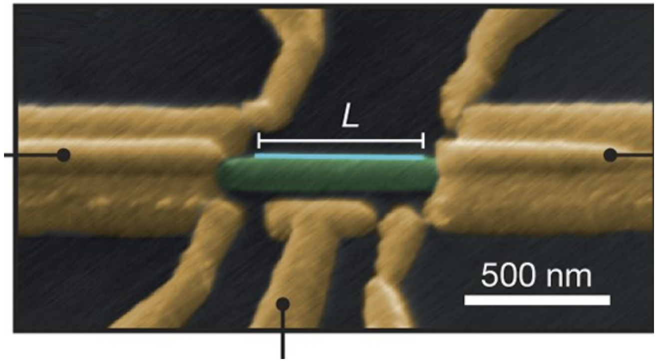
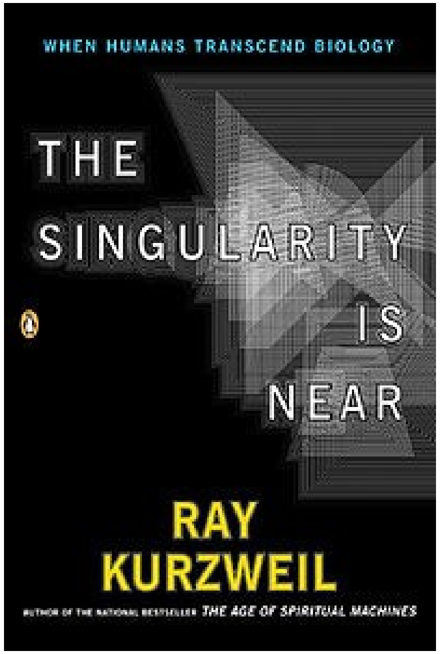


2. Biological/ soft machines

3. Quantum nanodevices

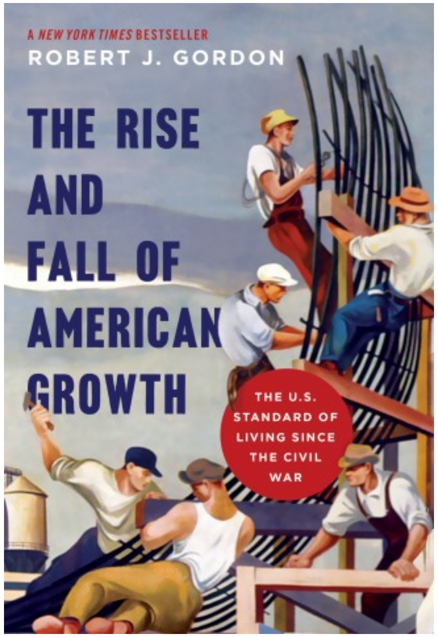


… and two narratives about technological progress



Accelerating change…

…or innovation stagnation?



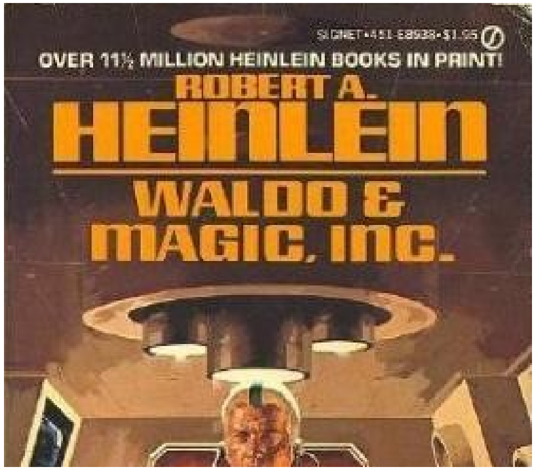
Who invented nanotechnology?

Richard
Feynman
(1918-1988)

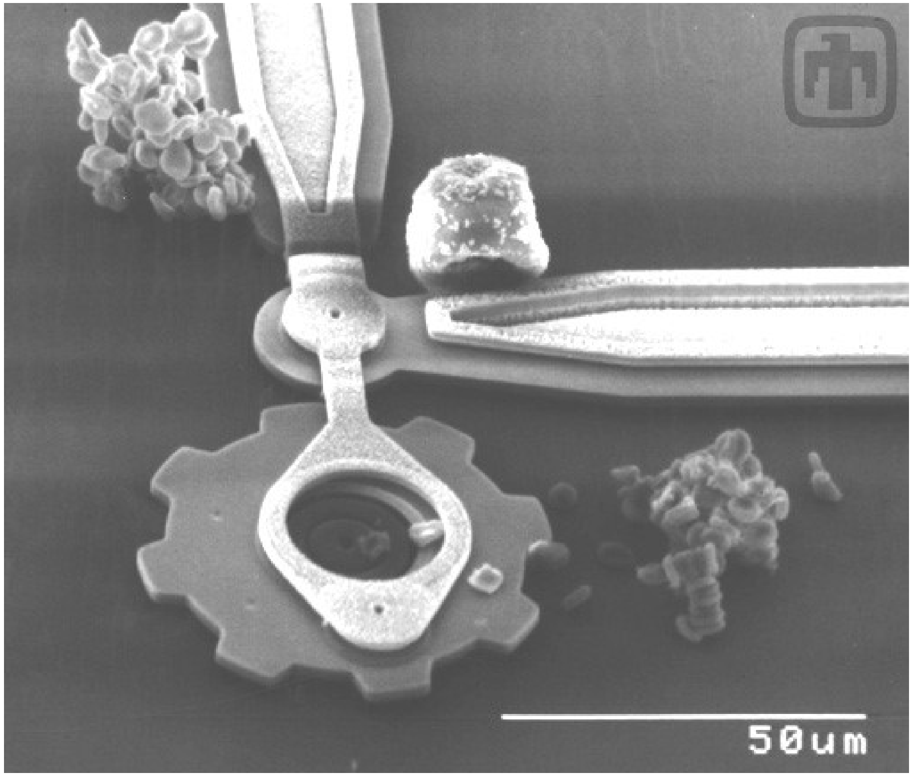
Theoretical
Physicist, Nobel
Laureate

*"There's Plenty
of Room at the
Bottom"* - 1959

Robert Heinlein?

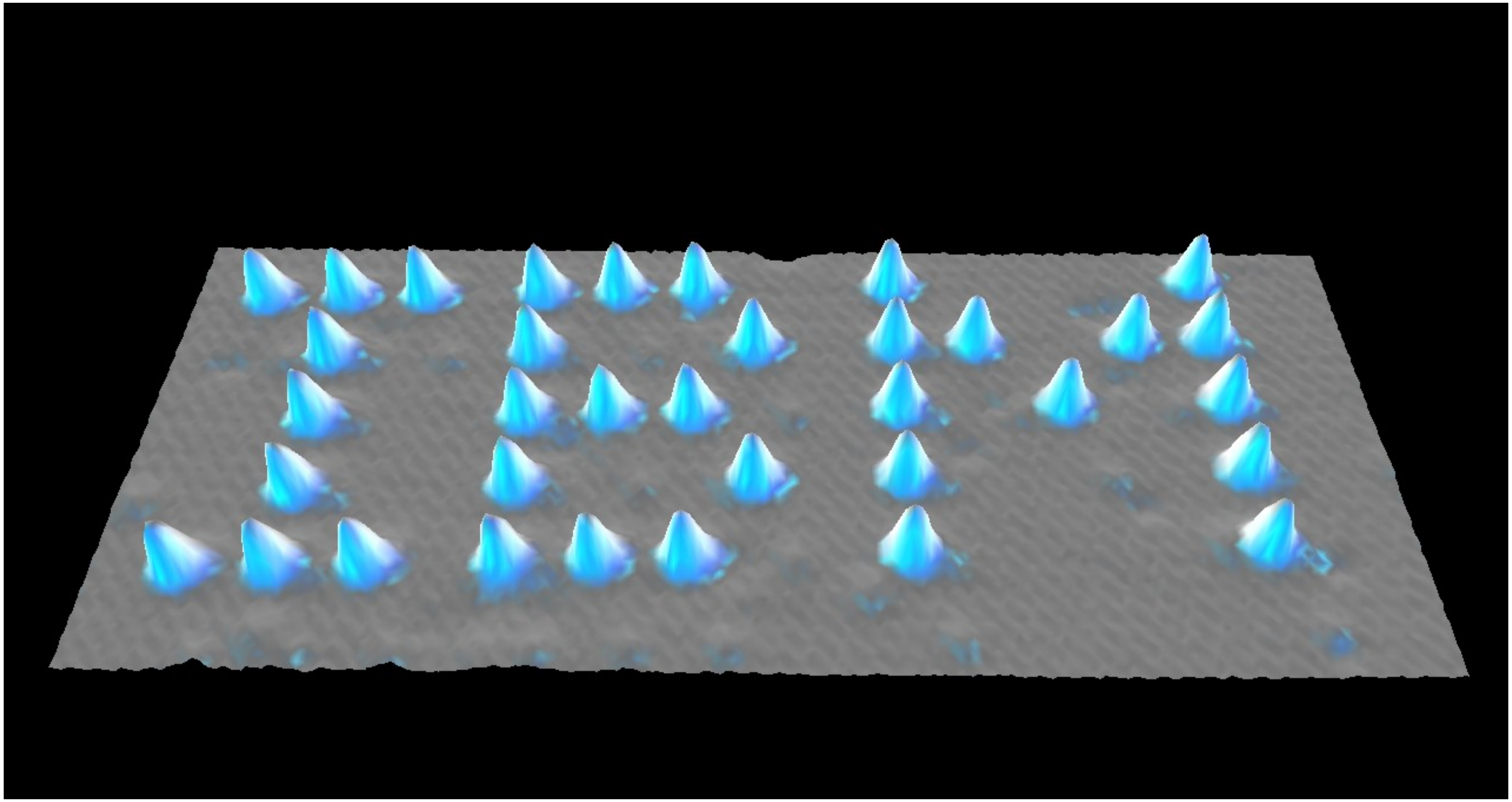


Norio Taniguchi?



Coined the term “nanotechnology” in 1974

Don Eigler?

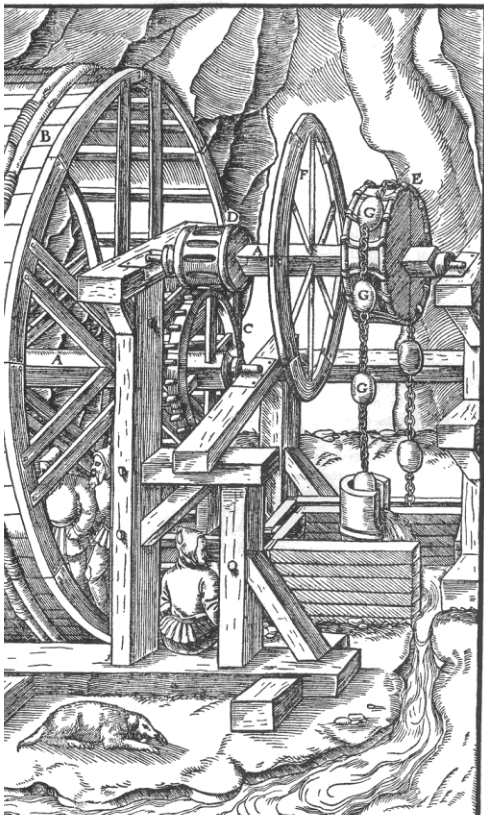


1994 – used the STM (invented by Binnig & Rohrer) to rearrange atoms

“Engines of Creation”

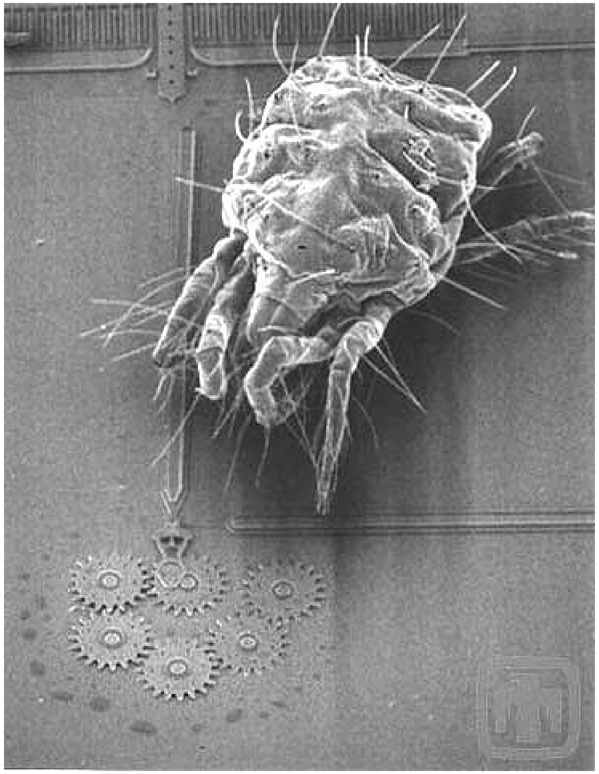
K. Eric Drexler 1986

The history of technology : increasing precision and miniaturisation



Medieval macro-engineering
Late medieval mine pump, Agricola

19th century precision engineering
Babbage difference engine, 1832

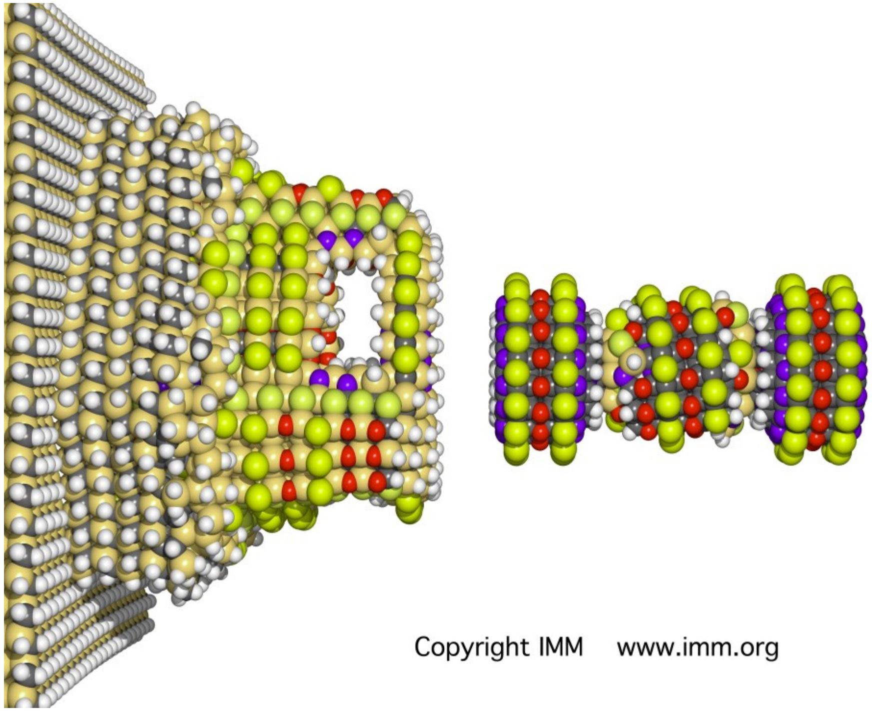


Modern micro-engineering
MEMS device, Sandia

Where next?

Nanotechnology as "the principles of mechanical engineering applied to chemistry"

Ideas developed by K.Eric Drexler



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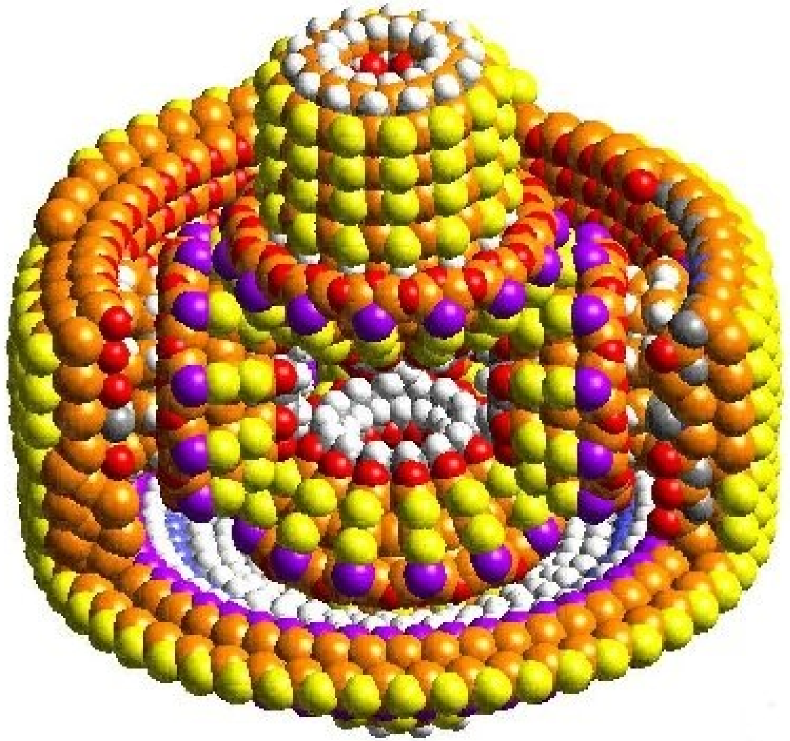

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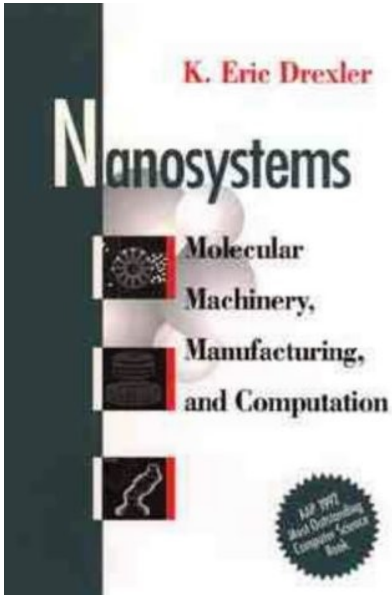
Computer graphics and simulation

Technical objections to Drexler’s vision

Drexler’ s *Nanosystems:*

More research required

Josh Hall: “Noone has ever found a significant error in the technical argument. Drexler’s detractors in the political argument don’t even talk about it.”



K. Eric Drexler

Nanosystems

Molecular Machinery, Manufacturing, and Computation

- Friction
- Uncontrolled mechanosynthesis
- Thermodynamic and kinetic stability of nanostructures
- Tolerance
- Implementation path
- Low level mechanosynthesis steps

“If x doesn’t work, we’ll just try y”, versus an ever-tightening design space.

“Any material you like, as long as it’s diamond”

- *Nanosystems* and subsequent MNT work concentrate on diamond
  - Strong and stiff (though not quite as stiff as graphite)
  - H-terminated C (111) is stable wrt surface reconstruction
- Potential disadvantages
  - Not actually the thermodynamic ground state (depends on size and shape - clusters can reconstruct to diamond-filled fullerene onions)
  - Non-ideal electronic properties. Many designs in *Nanosystems* explicitly demand other materials (e.g. electrostatic motor).

How to make a nanobot

Not like this!

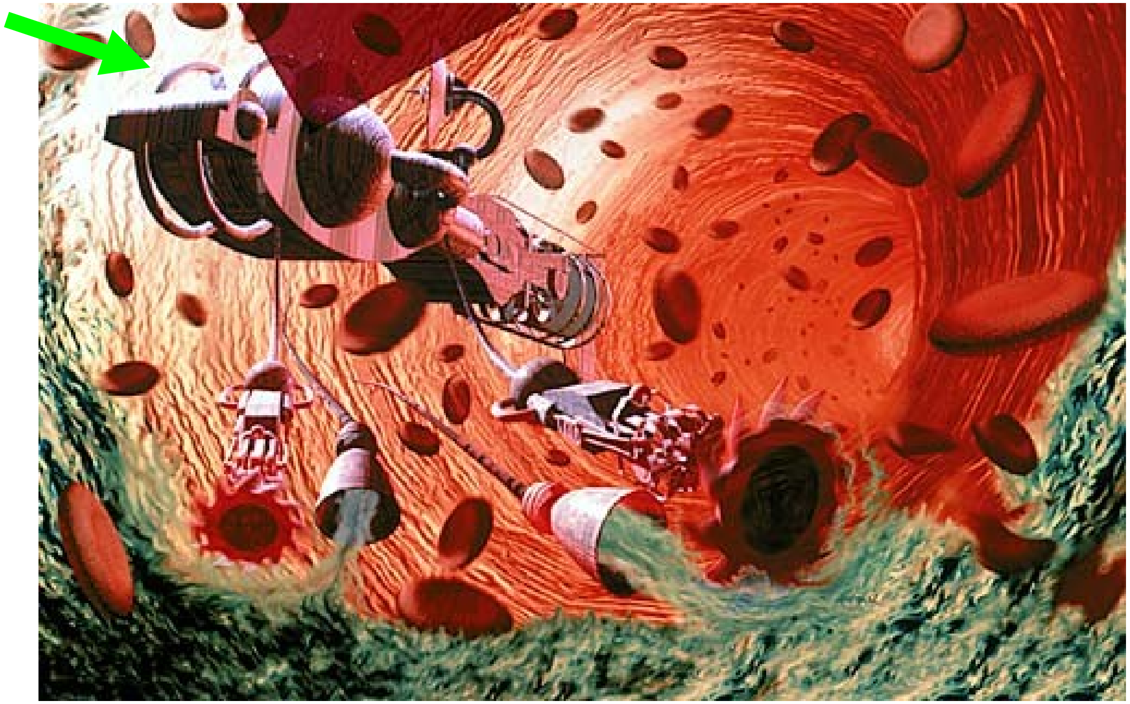
“Nanobot Computers of the Future”

Microsoft Encarta on-line encyclopedia

What’s wrong with this nanobot?

Physics looks different when you're small...

Viscosity dominates - how do we move it around?



At the nanoscale, water is gooey and viscous

Characteristics of flow are determined by the Reynolds number:

$$\frac{\text{Density} \times \text{velocity} \times \text{size}}{\text{viscosity}}$$

- If we (or a dolphin) were shrunk to the nanoscale water would feel like the most viscous treacle…

Physics looks different when you're small...

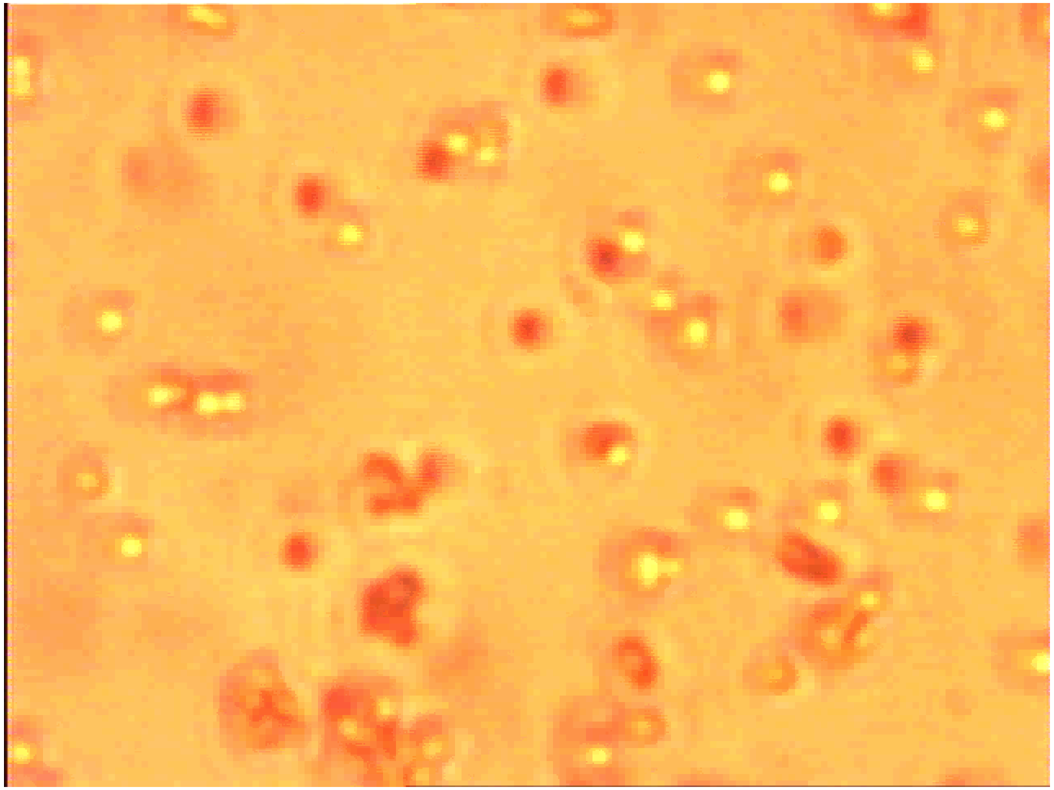
Viscosity dominates - how do we move it around?

Buffetted by constant Brownian motion - how can we make anything rigid enough?

At the nanoscale, everything is continually shaken around

- *Brownian motion* - random jostling by colliding water molecules.
- The smaller you are, the more important this is:

  Velocity $\propto \sqrt{(kT)}/\ (\text{size})^{3/2}$
- Causes internal flexing as well as motion



Sub-micron polymer particles in water

Physics looks different when you're small...

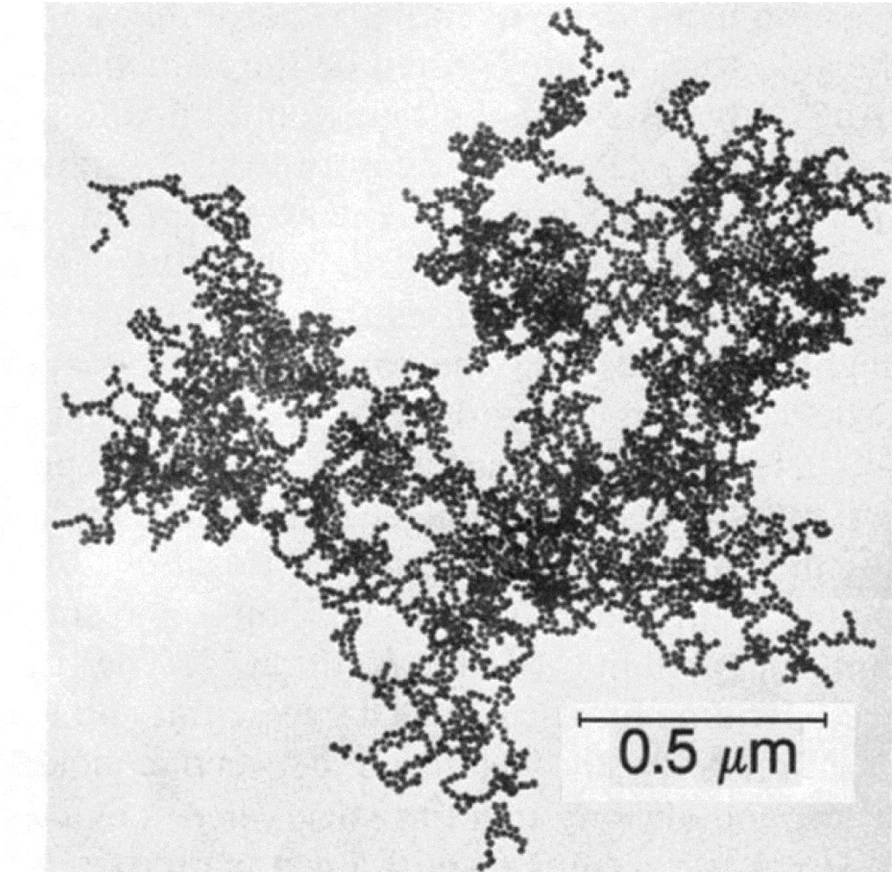
Viscosity dominates - how do we move it around?

Strong surface forces between neighbours - how do we stop them sticking together?

Buffetted by constant Brownian motion - how can we make anything rigid enough?

At the nanoscale, everything is sticky

- Strong surface forces make nanoscale objects tend to stick to each other
- Proteins are particularly sticky, hence biocompatibility difficulties



TEM image of aggregated gold nanoparticles

Physics looks different when you're small...

Viscosity dominates - how do we move it around?

Strong surface forces between neighbours - how do we stop them sticking together?

Surfaces rapidly fouled by adsorbed proteins - how can we make it biocompatible?

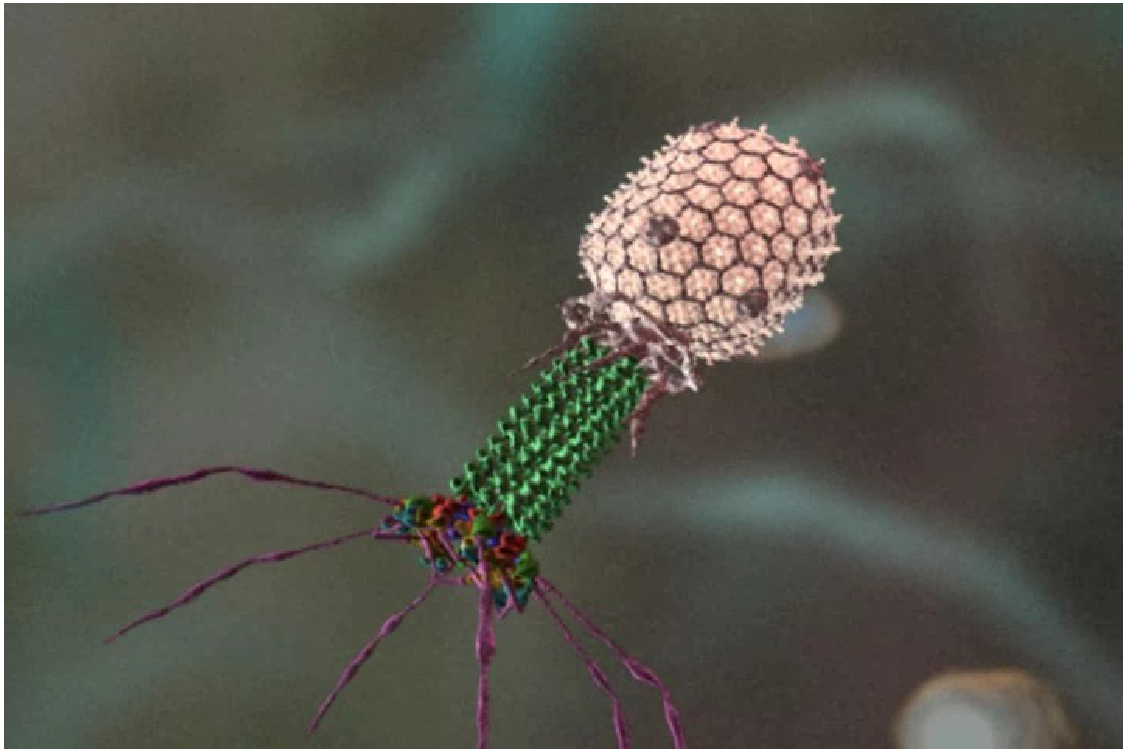
Buffetted by constant Brownian motion - how can we make anything rigid enough?

How can we make one?
How can we make 10 trillion?

Is it impossible to make nanoscale machines?

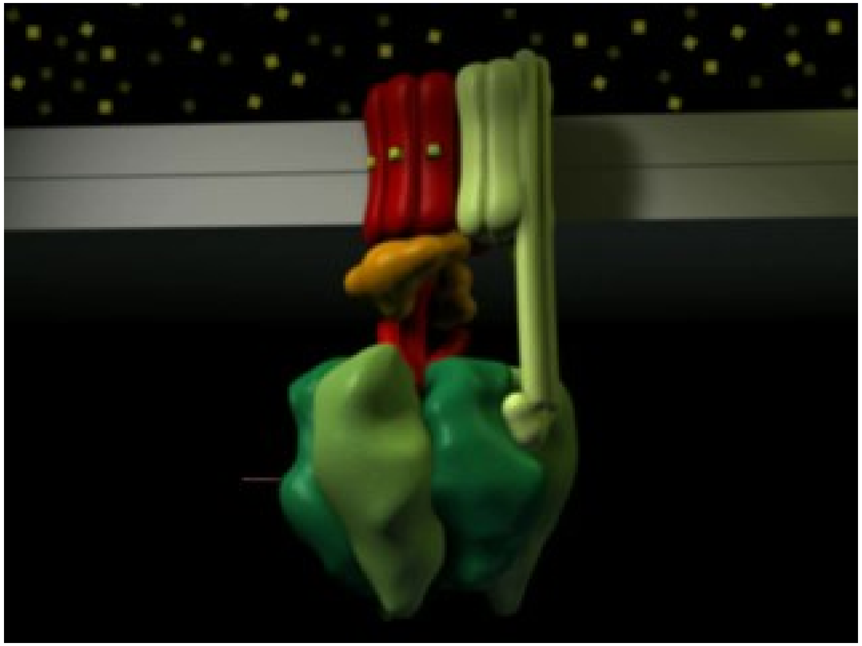
Is it impossible to make nanoscale machines?

No - cell biology is full of them!



T4 bacteriophage infecting E.Coli: Leiman et al., Cell *118* , pp. 419–429 Rossman group, Purdue U.

Biology is astonishingly efficient at the nanoscale!



ATP-synthase
a sophisticated nanomachine that almost all living things share…

Creates ATP, life’s fuel.
>95% efficient.

Animation: Molecular Biology of the Cell
Alberts et el.

Biology is nanotechnology that works!

- Design principles quite different from macro-engineering
- Exploits the different physics at the nanoscale
- Scaled down macro-engineering won’t work better that biology - don’t worry about grey goo!

Why is biological nanotechnology so effective?

- Design principles quite different from macro-engineering
- Exploits the different physics at the nanoscale:

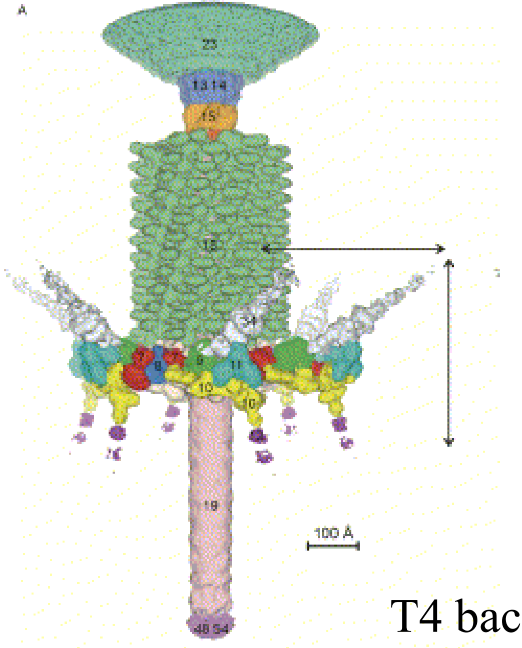
  Surface forces + Brownian motion
  = **self-assembly**

  Brownian motion + lack of stiffness
  = **conformational transitions**

  Weak binding + Brownian motion
  = **chemical computing**
- Can we copy these design principles?

Surface forces + Brownian motion = self-assembly

- Complex structures in nature are made by self-assembly



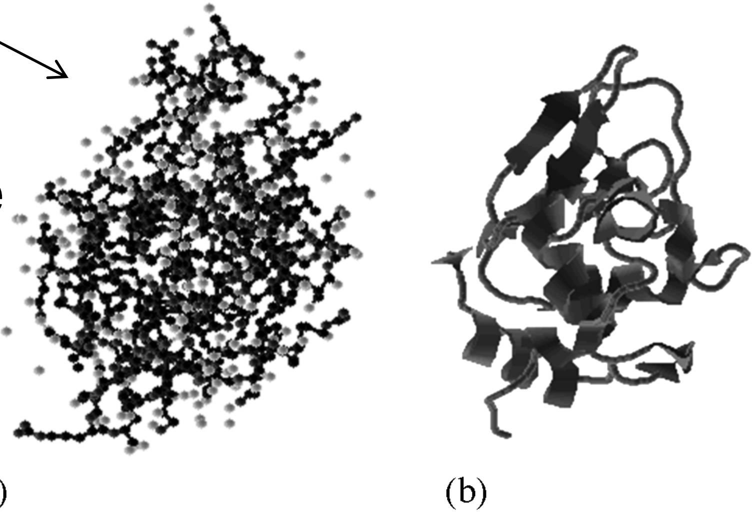
T4 bacteriophage
Rossler, Purdue

Information flow in protein self-assembly

```
1 mlgkndpmcl vlvllgltal lgicqggtgc ygsvsridtt gascrtakpe glsycgvras
61 rtiaerdlgs mnkykvlikr vgealciepa viagiisres hagkilkngw gdrgngfglm
121 qvdkryhkie gtwngeahir qgtrilidmv kkiqrkfprw trdqqlkggi saynagvgnv
181 rsyermdigt lhddysndvv araqyfkqhg y
```

One 1-d sequence

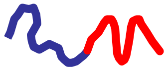
One 3d structure


(a) (b)

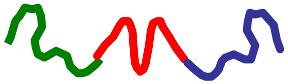
Synthetic self assembly

monomers : styrene, dienes, acrylates, oxirans, siloxanes

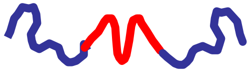
synthesis : mainly living anionic polymerisation $M_w/M_n \approx 1.05$



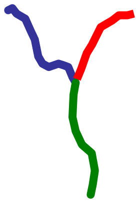
AB diblock



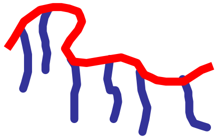
ABC triblock



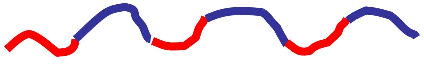
ABA triblock



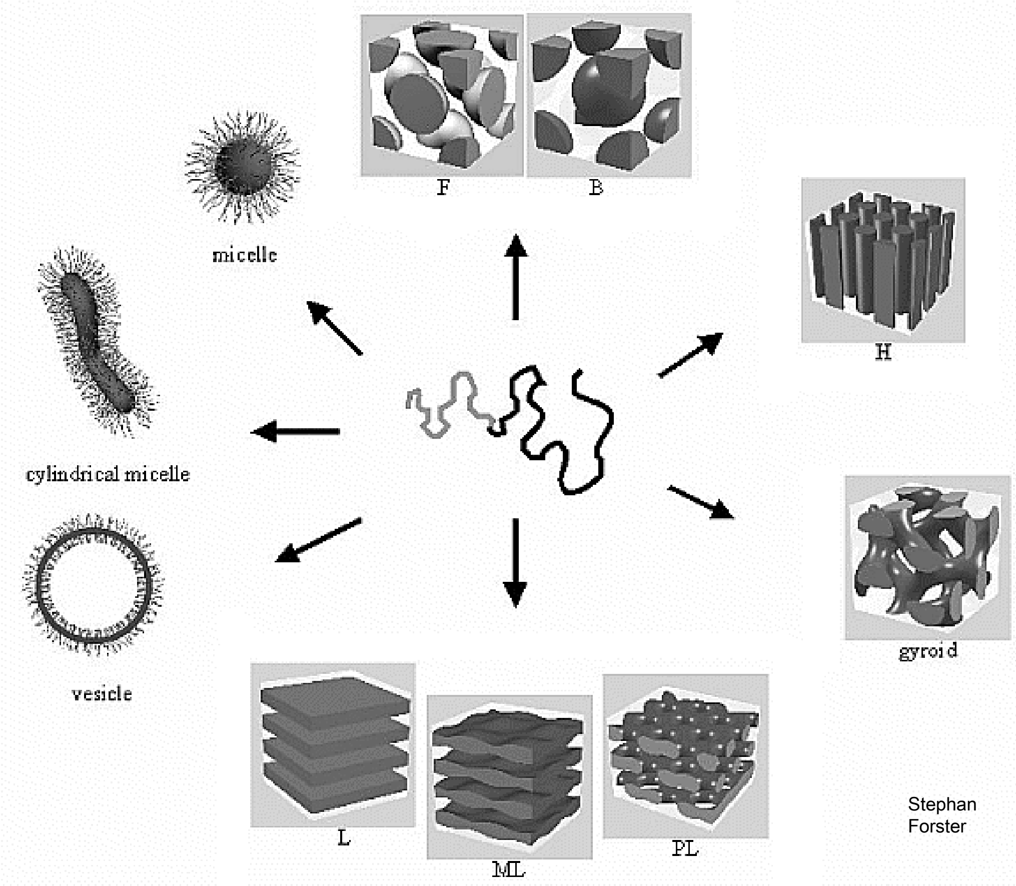
ABC star block



AB_n comb

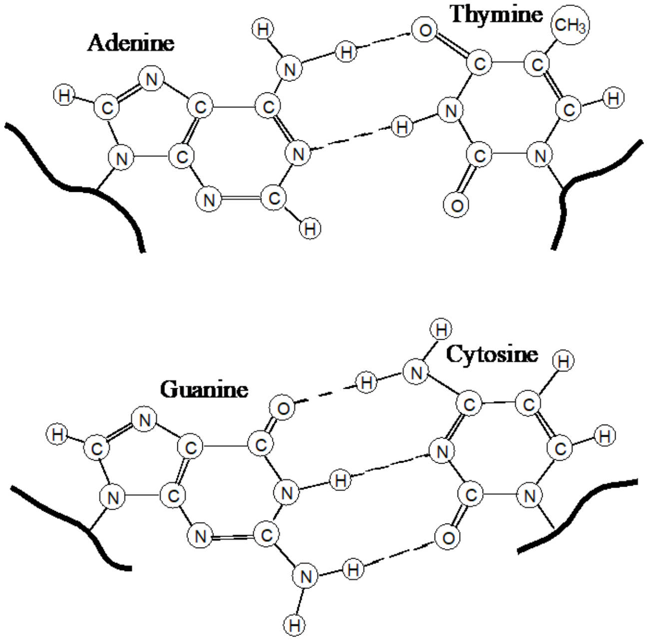


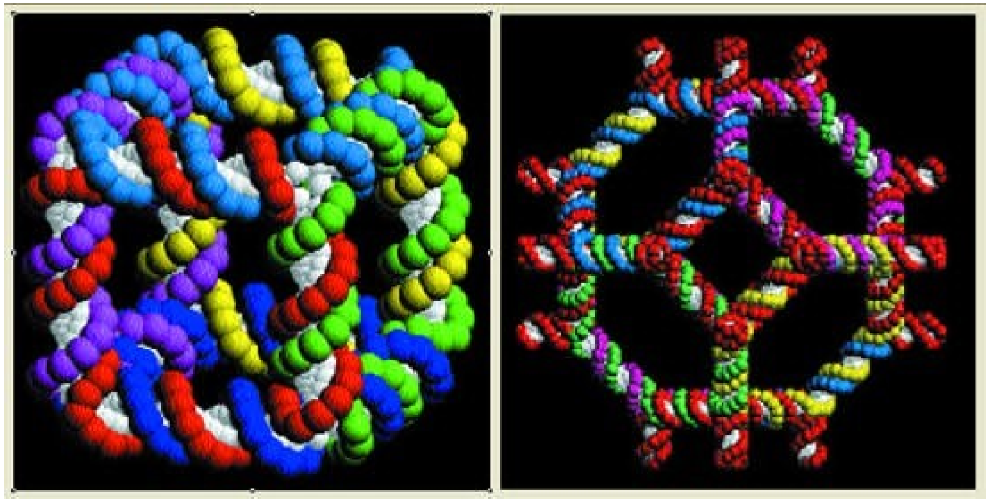
$(AB)_n$ multiblock



Stephan Forster

Synthetic self-assembly - DNA



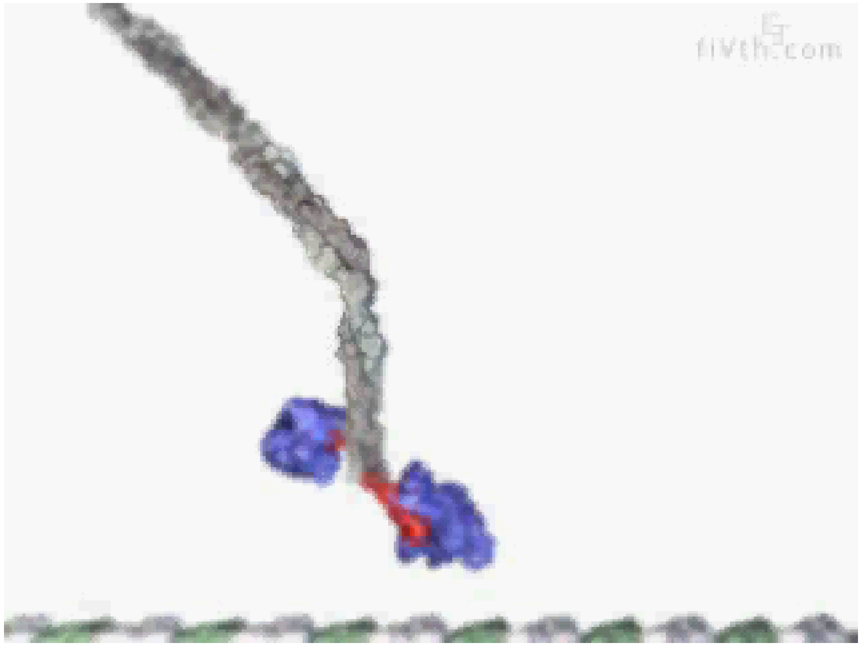


Simplicity of base-pair interaction allows precise design of sequences that self-assemble into complex 3-d structures

e.g. Seeman, Rothemund, Turberfield

Brownian motion + lack of stiffness = conformational transitions

- Motor proteins change shape in response to changes in the environment
- This is how our muscles work



Simulation of the motor protein kinesin
Vale & Milligan, Science **288** 88 (2000)

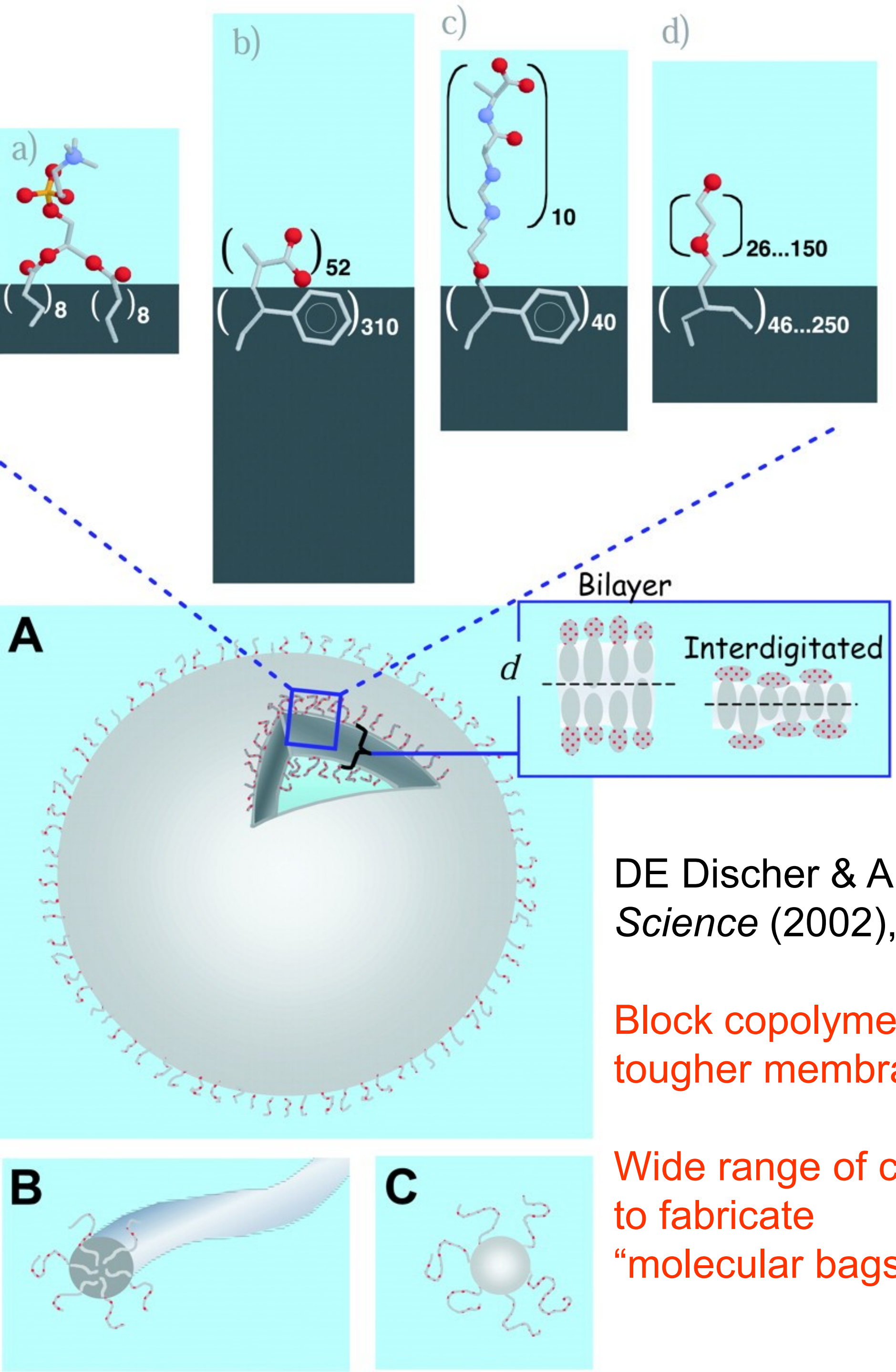
What would a realistic medical nanobot look like?

Certainly not like the popular vision!

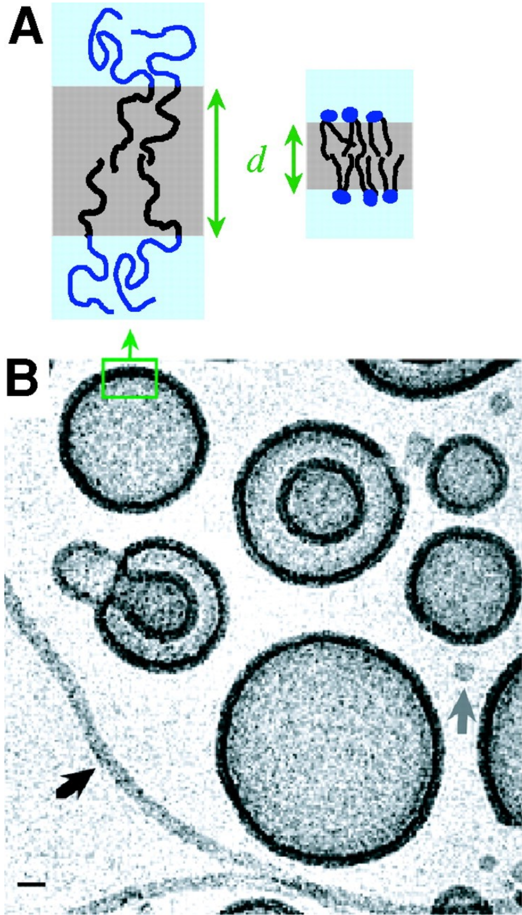
E. Coli bacteria

- More likely to be bio-inspired
- Early prototypes - drug delivery devices like stealth liposomes
- How could we power and steer a more advanced version?

Self-assembled vesicles & polymersomes



Block copolymers

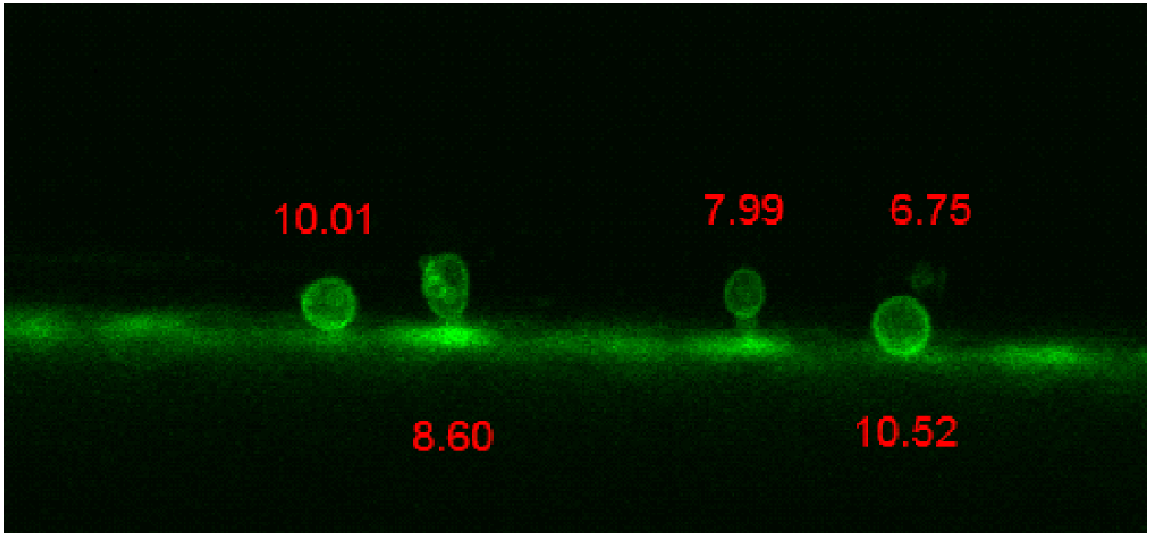


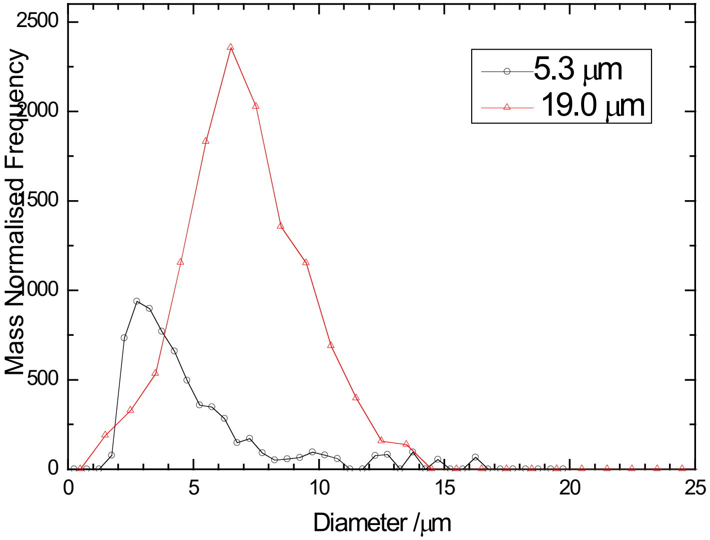
DE Discher & A Eisenberg,
Science (2002), **297**, 967-973.

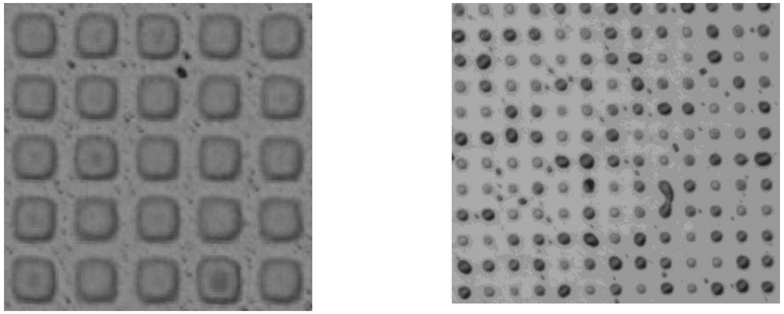
Block copolymers make thicker & tougher membranes than lipids

Wide range of chemistry available to fabricate
“molecular bags”

Vesicles with a narrow size distribution determined by the size of surface patterning







Howse, Jones, Battaglia, Ducker, Leggett, Ryan
Templated Formation of Giant Polymer Vesicles with Controlled Size Distributions
Nature Materials

Some new therapies will not be possible without nanotechnology

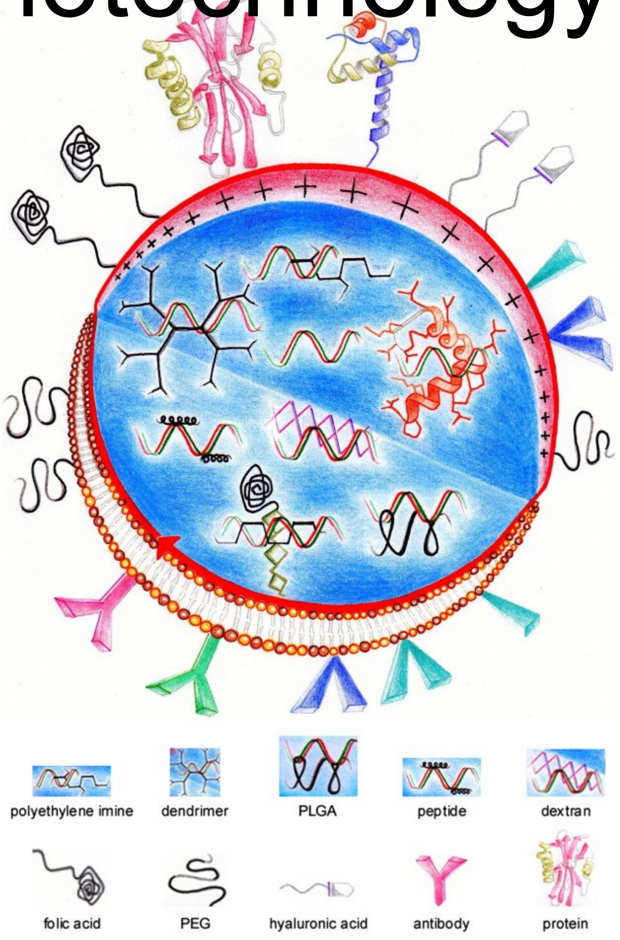
siRNA – only possible with sophisticated delivery devices

FDA News Release

FDA approves first-of-its kind targeted RNA-based therapy to treat a rare disease

First treatment for the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adult patients

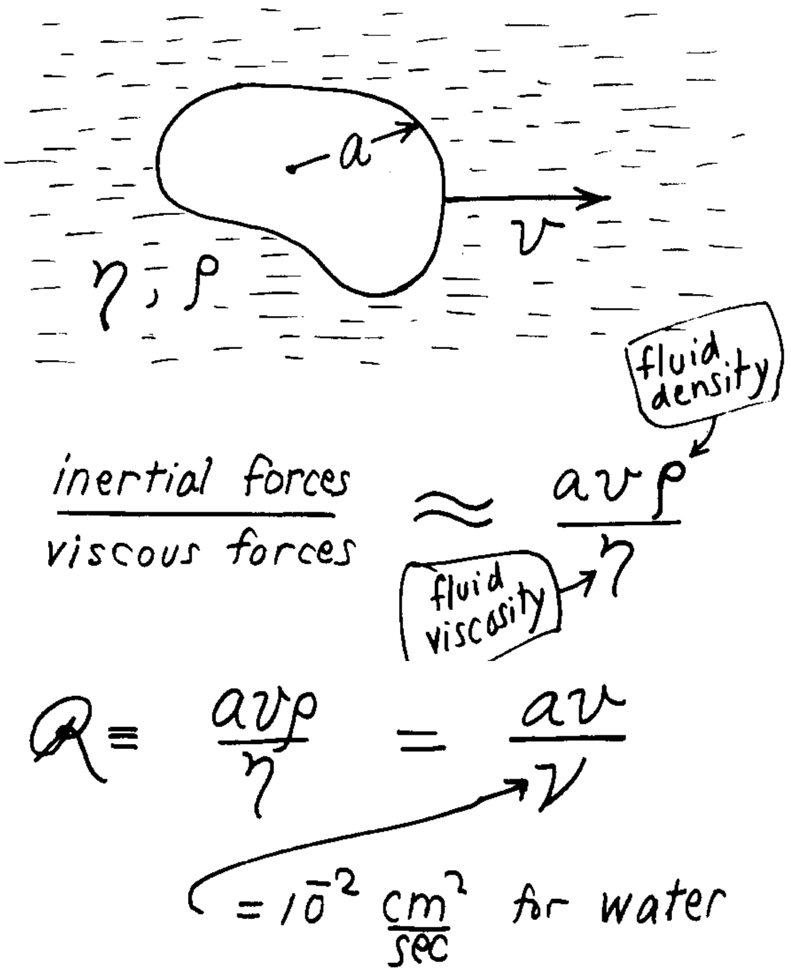
For Immediate Release August 10, 2018

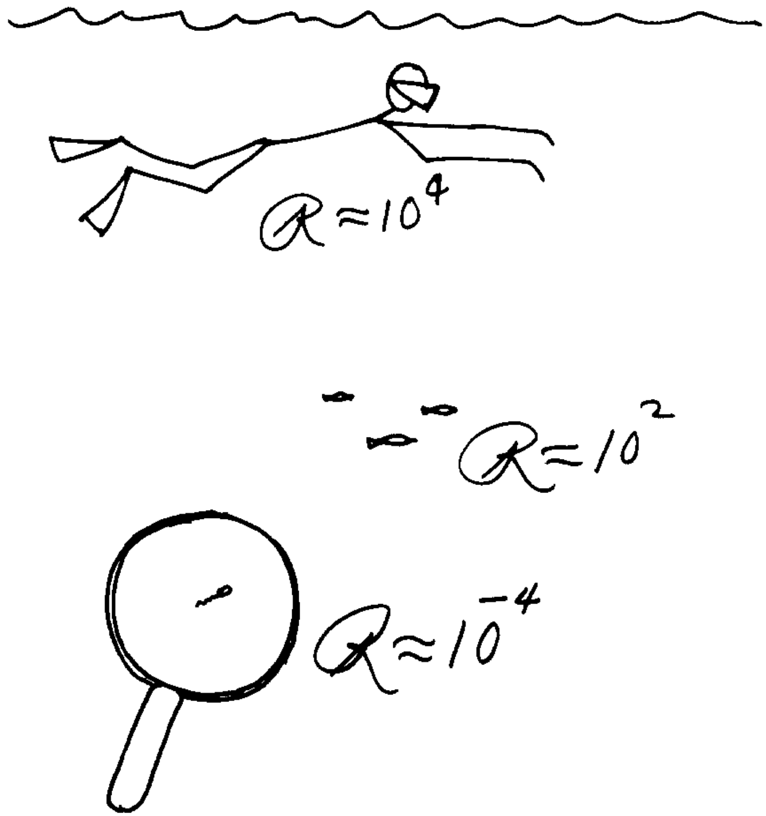


Lorenzer et al
https://doi.org/10.1016/j.jconrel.2015.02.003

Moving around

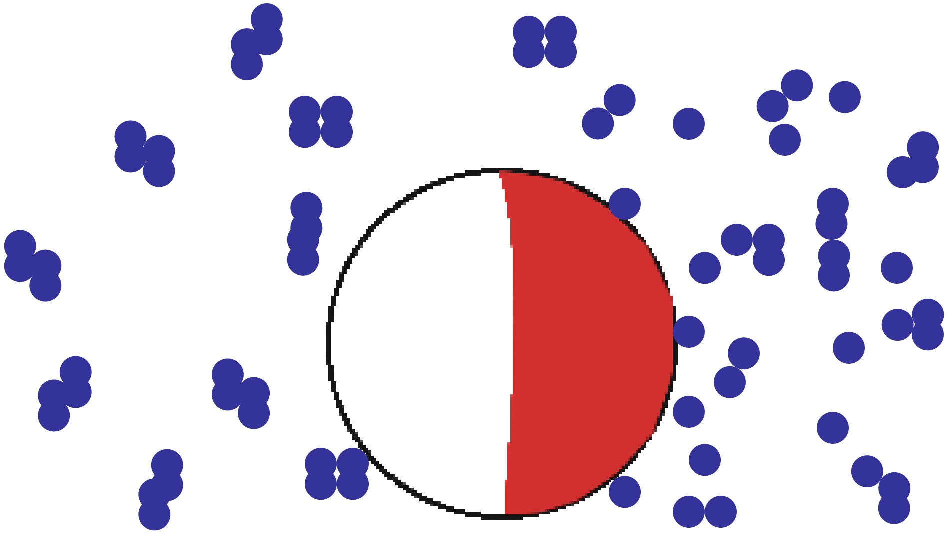
Different strategies needed for low Reynolds number





From EM Purcell – Life at Low Reynolds Number
American Journal of Physics (1977) **45** 3-11

One way of propelling a nanobot



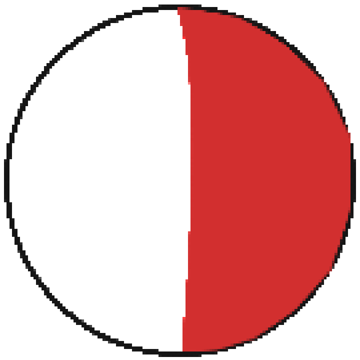
Chemical reaction produces
more products than
reactants

← Osmotic pressure gradient

Particle with one half
coated with catalyst

Ramin Golestanian

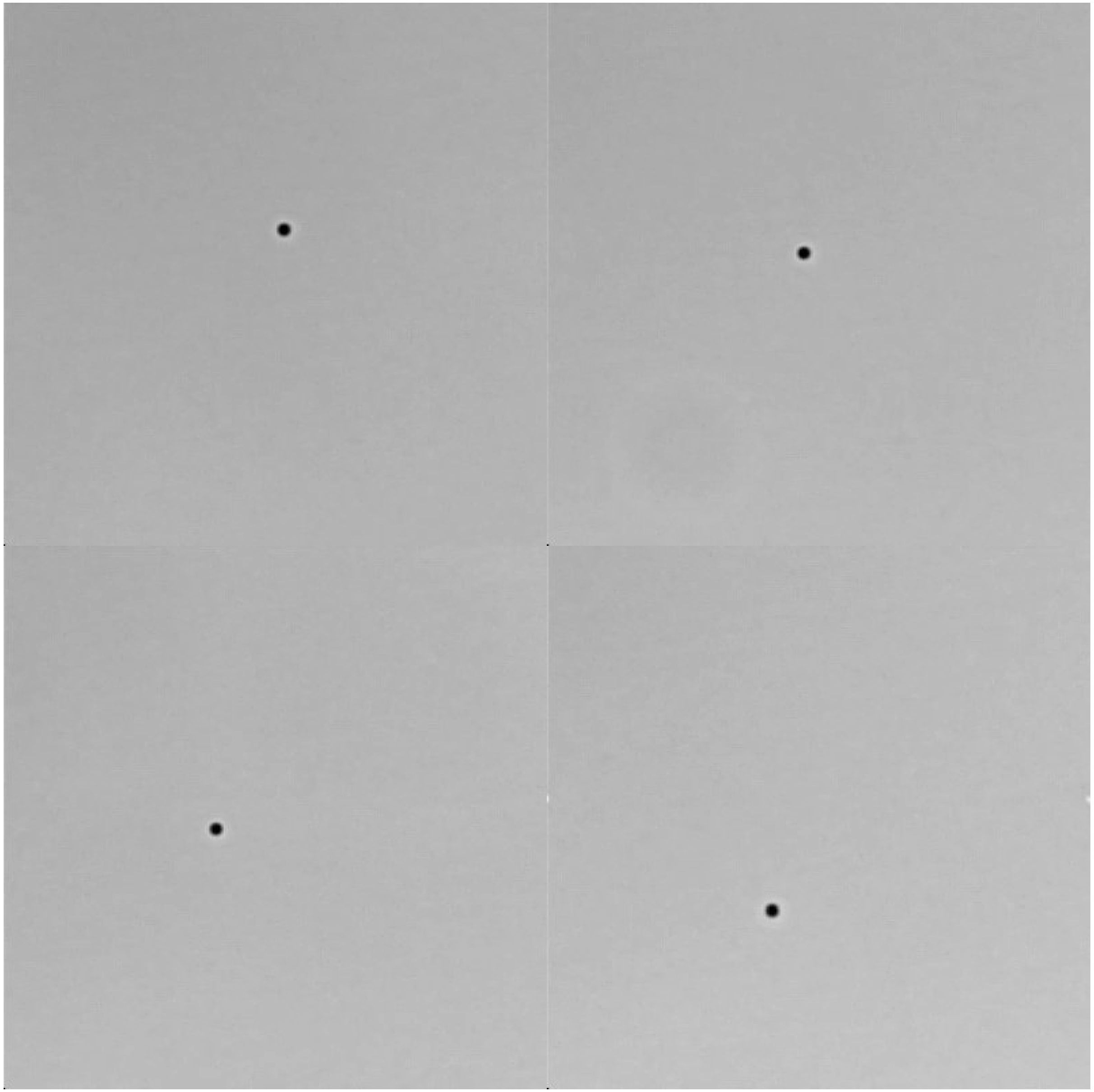
Self-motile particles



$$2\,H_2O_2 \rightarrow 2\,H_2O + O_2$$

Micron sized polystyrene sphere half coated with platinum

Jon Howse + RALJ

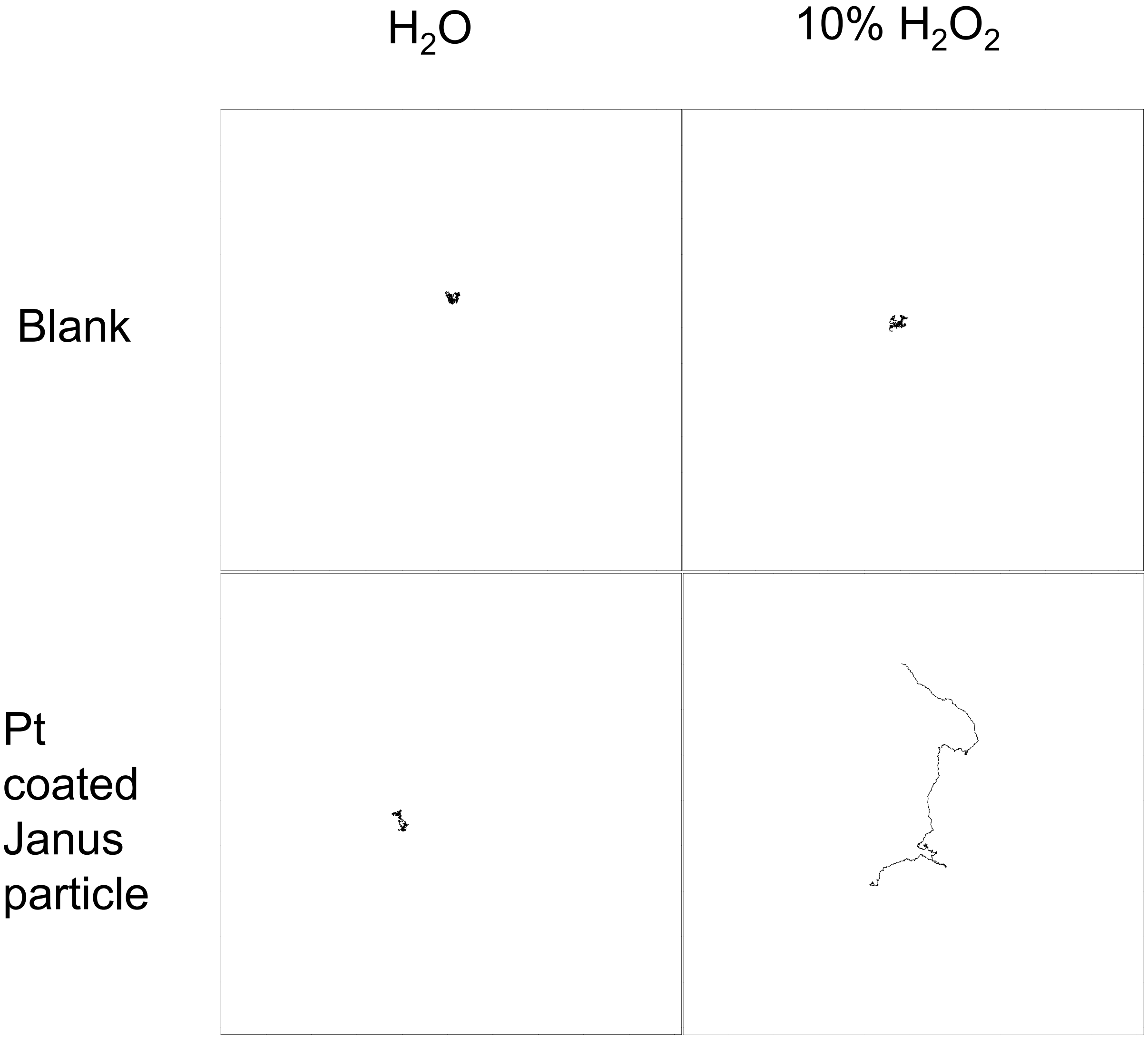


No Pt
No H_2O_2

No Pt
H_2O_2

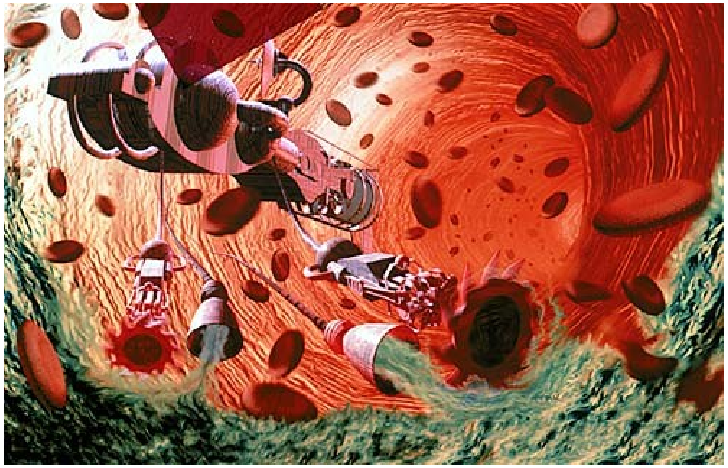
Pt
No H_2O_2

Pt
H_2O_2



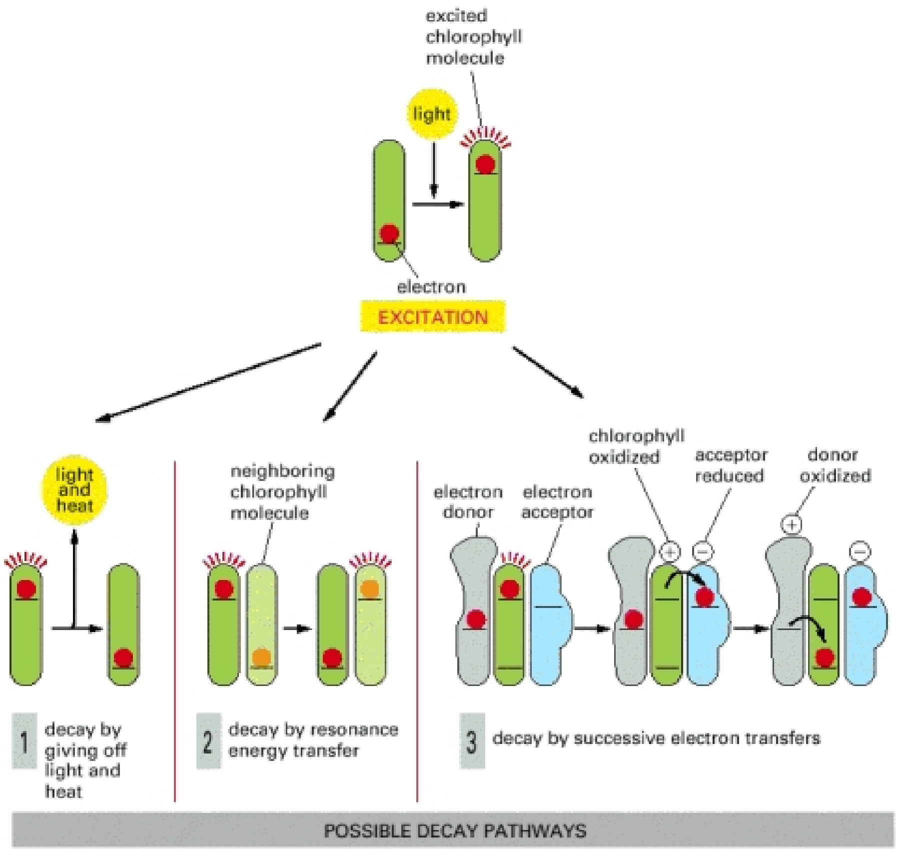
Each trace ; 127 x 127 µm, 25 sec

A real nanobot



Assembly from external blueprint	Self-assembly, out-of equilibrium pattern formation
Hard materials, mechanical paradigm	Soft materials, responsiveness and shape change
Separation of hardware and software	Coupling of hardware and software
Design	Evolution

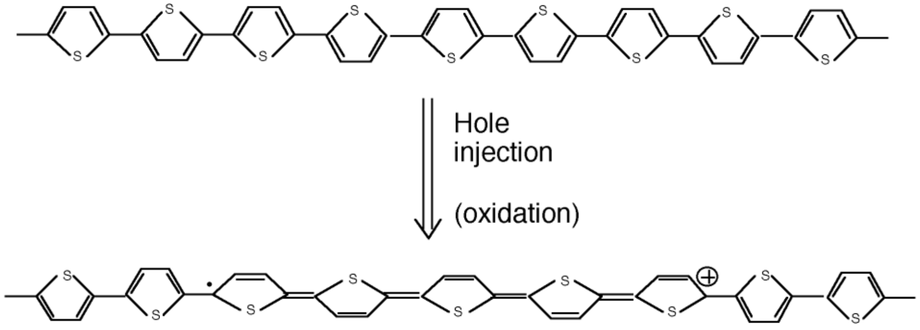
Photosynthesis



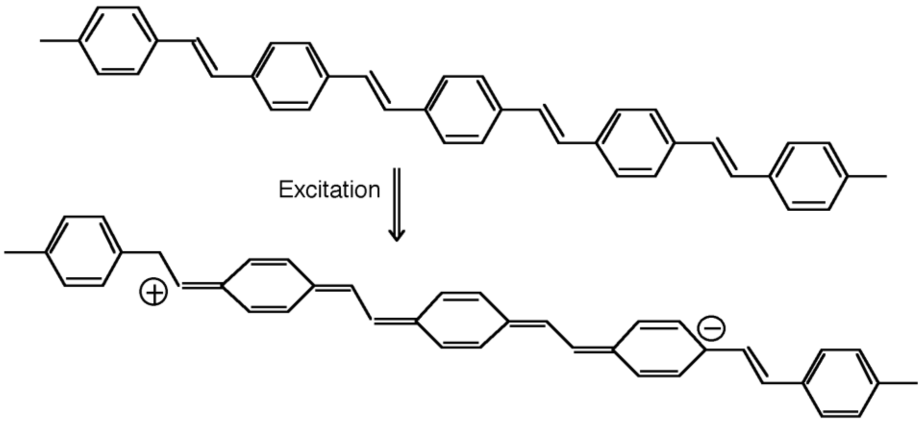
- Biology is quite effective at harvesting solar energy.
- Is there anything we can learn from how photosynthesis works?
- Starting point is the absorption of photons by dye molecules to produce excitons

Molecular Biology of the Cell. 4th edition. Alberts B, Johnson A, Lewis J, et al.New York: Garland Science; 2002.
http://www.ncbi.nlm.nih.gov/books/NBK26819/#A2576

Excitonic materials vs inorganic semiconductors?

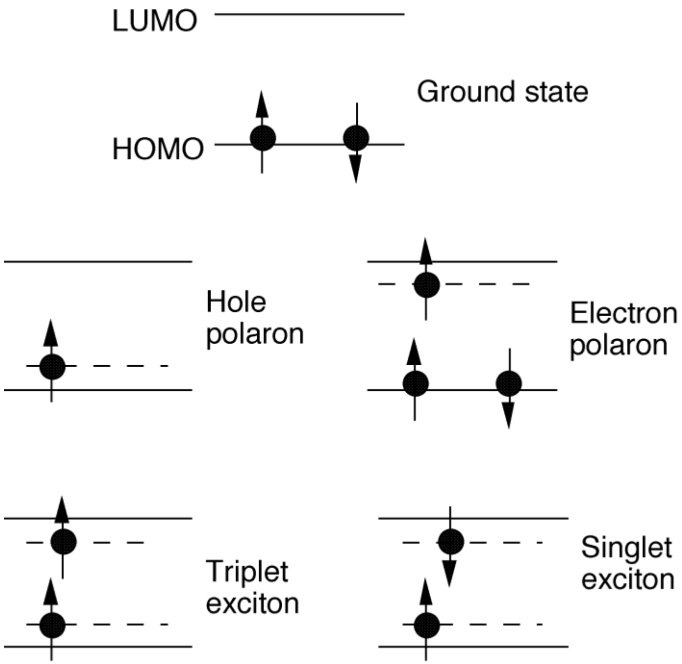


A hole in polythiophene



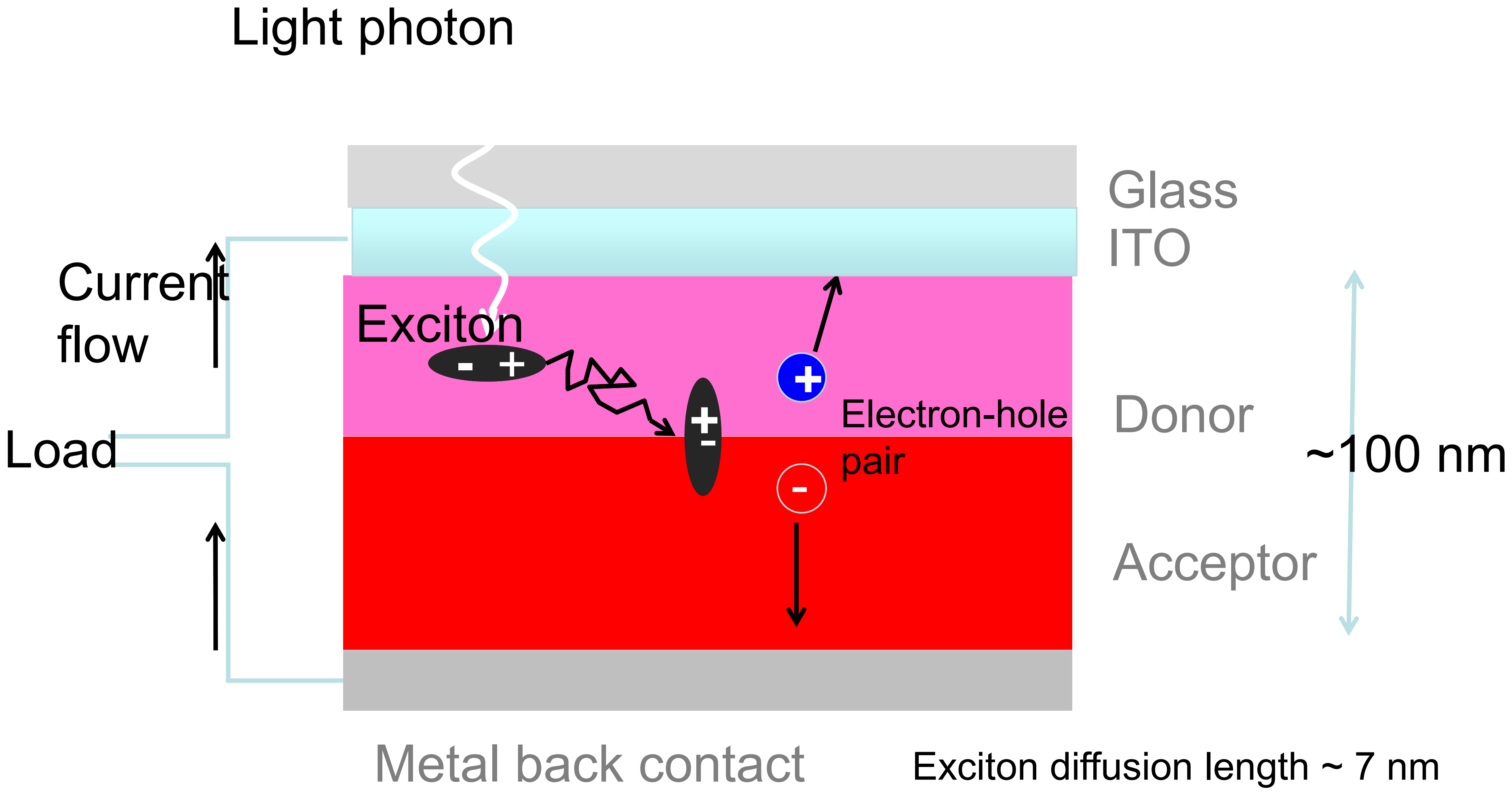
An electron-hole pair (exciton) in PPV

Strong coupling between charge states and molecular conformation



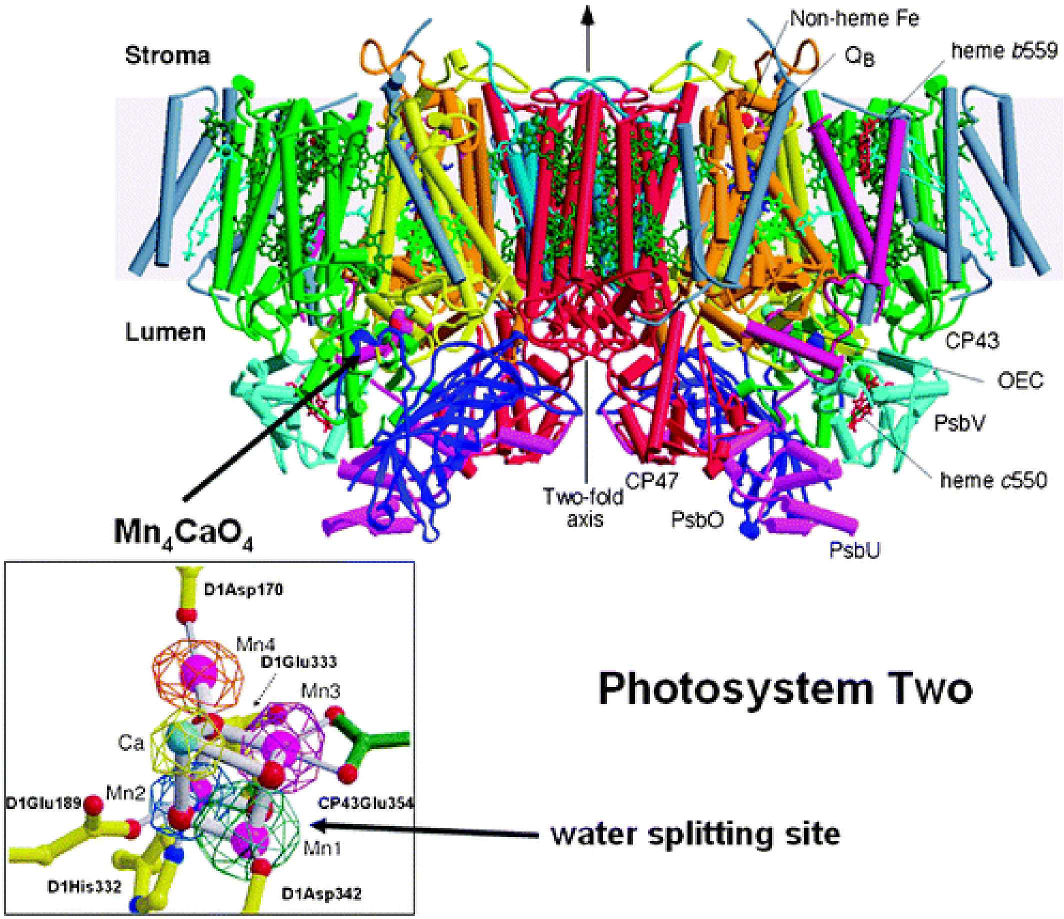
Energy level diagrams for semiconducting polymers

A bilayer organic solar cell



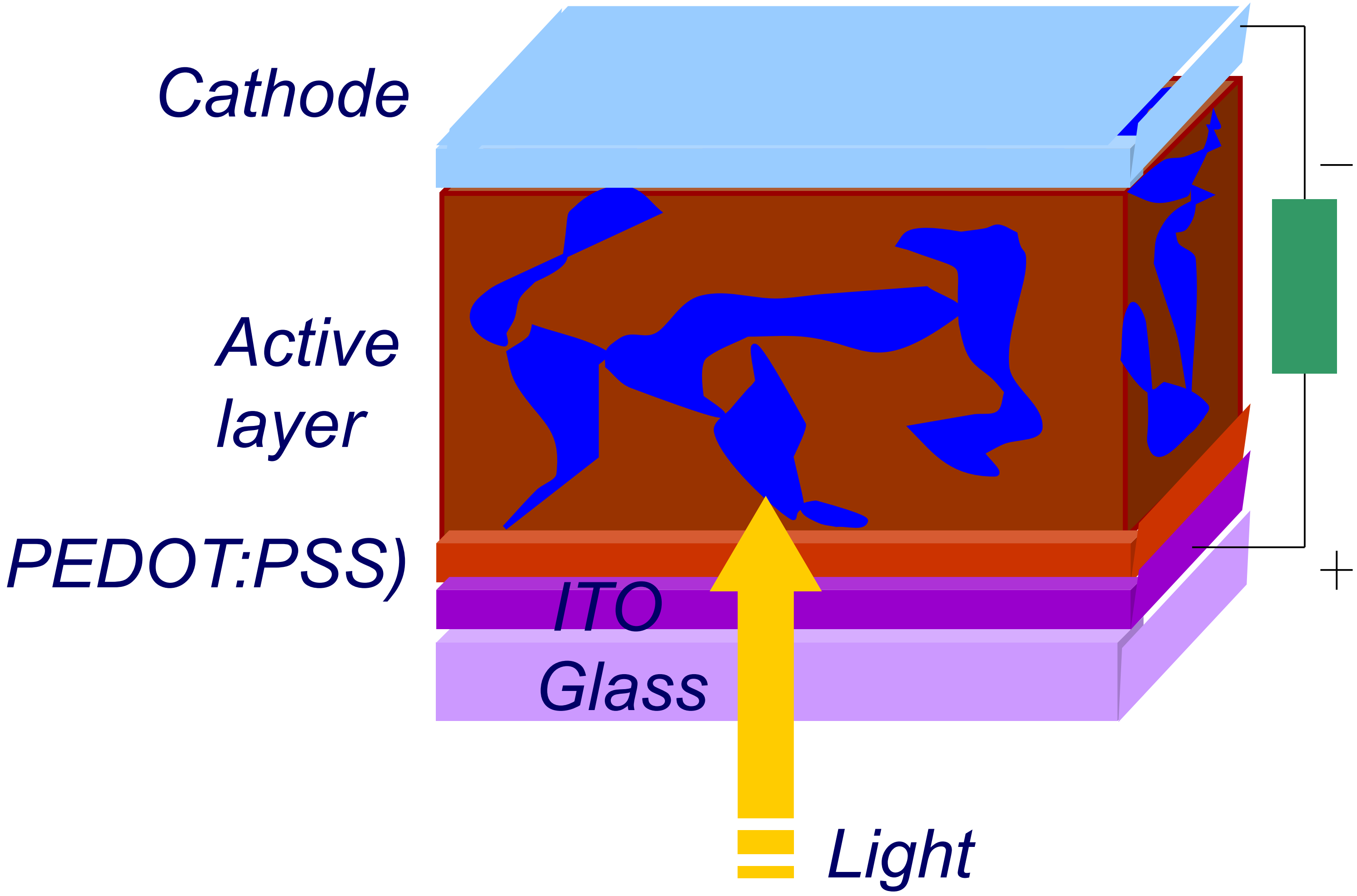
Exciton diffusion length ~ 7 nm
Hence low efficiency

Photosynthetic centres have very precise nanostructures to direct the charge to where its needed



A self-assembled complex of protein molecules and dyes

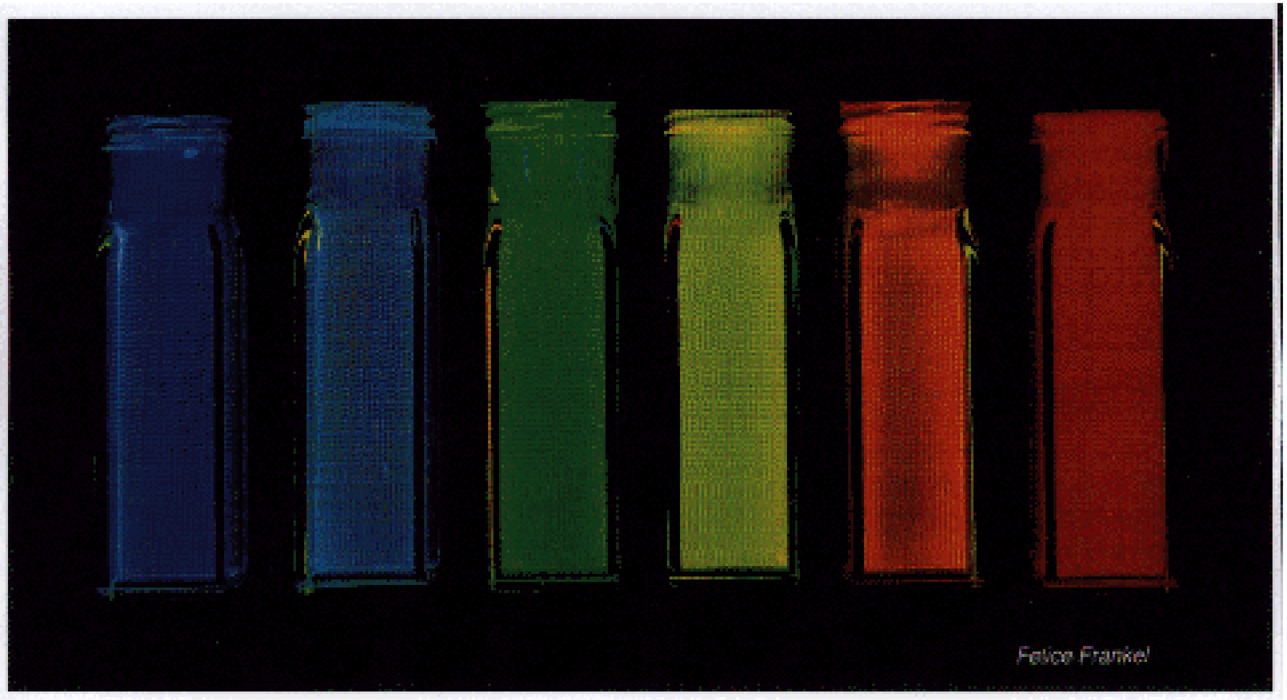
Bulk heterojunction PVs as crude self-assembled systems to optimise charge separation and transport



The quantum domain

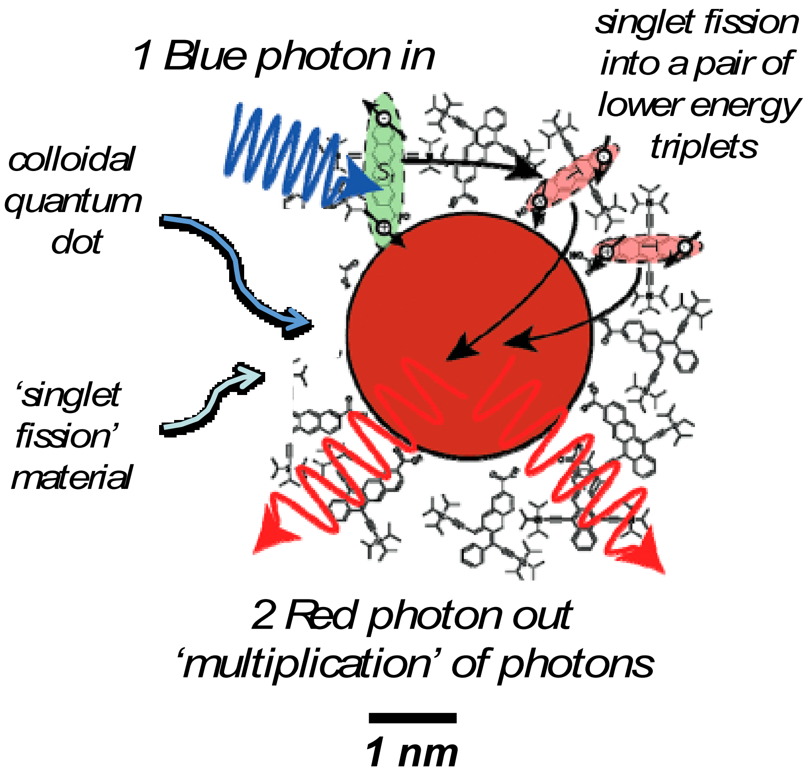
- Drexler’s conception of nanotechnology is entirely classical – not quantum – in character
- The physics of “Soft Machines” is largely classical statistical mechanics
- Yet early discussions of the potential of nanotechnology focused on the quantum mechanical character of the very small
- *“Below about 50 nm something that scientists call the quantum size effect kicks in: quantum mechanics takes over from classical mechanics”* (ETC Group, The Big Down, 2003)

Size effects in semiconductor nanoparticles



Quantum confinement means that bandgaps depend on size in semiconductor nanoparticles

Combining organic semiconductors with inorganic quantum dots



100% efficient down-conversion through singlet fission in composite nanoparticles

Akshay Rao, Neil Greenham, Richard Friend – structural characterisation by Mike Weir + RALJ

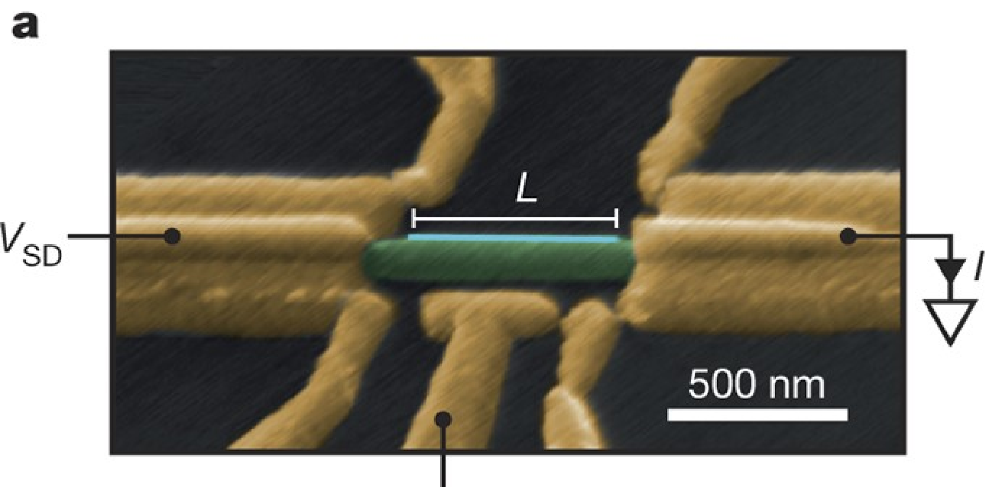
Real quantum magic arises from *coherence* and *entanglement*

- Currently a live debate about how important quantum coherence is for photosynthesis and excitonic solar cells
- But the real prize for controlling coherence and entanglement is for quantum information and quantum computing

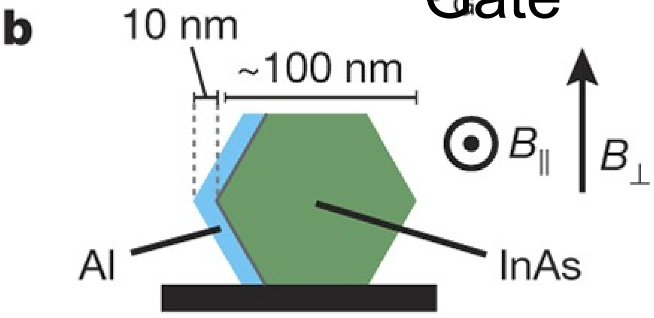
Majorana modes for noise tolerant quantum computing?

"Majorana modes" form at each end of the nanowire

The two Majorana modes are quantum entangled to form a single quantum state, which is protected against disturbance from noise in the environment.

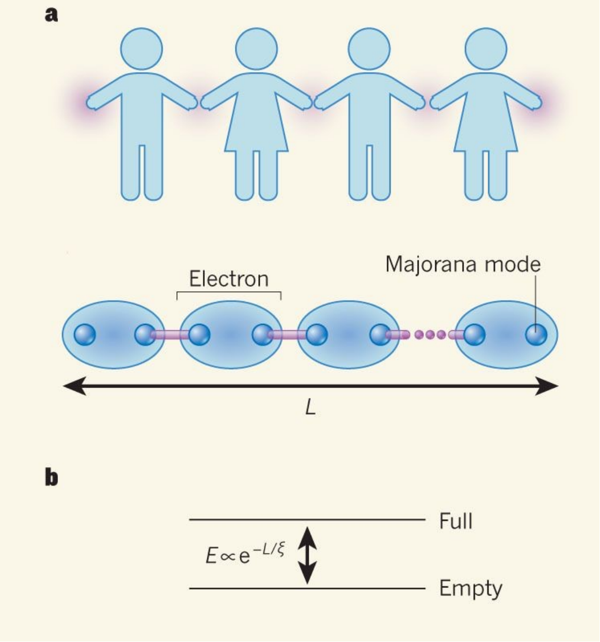


Gate



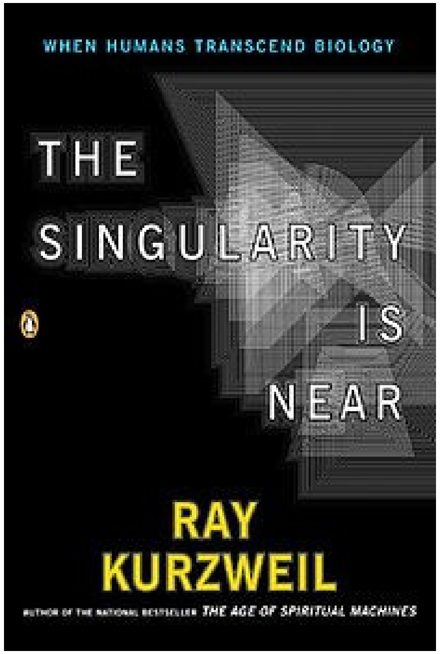
Semiconducting indium arsenide nanowire

Superconducting aluminium shell

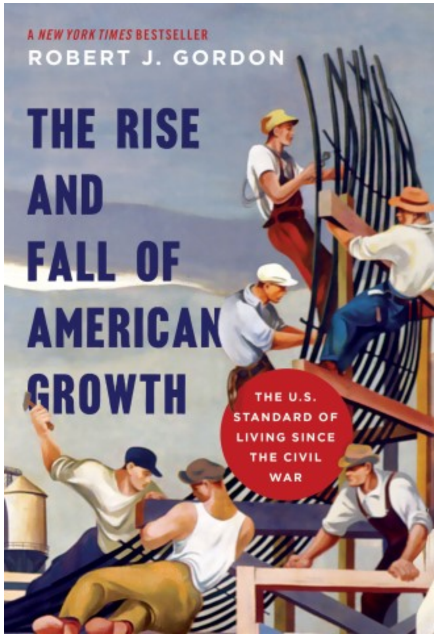


S M Albrecht *et al.* *Nature* **531**, 206–209 (2016)

Accelerating change – or innovation stagnation?



- Technological innovation is accelerating



- Technological innovation is slowing down

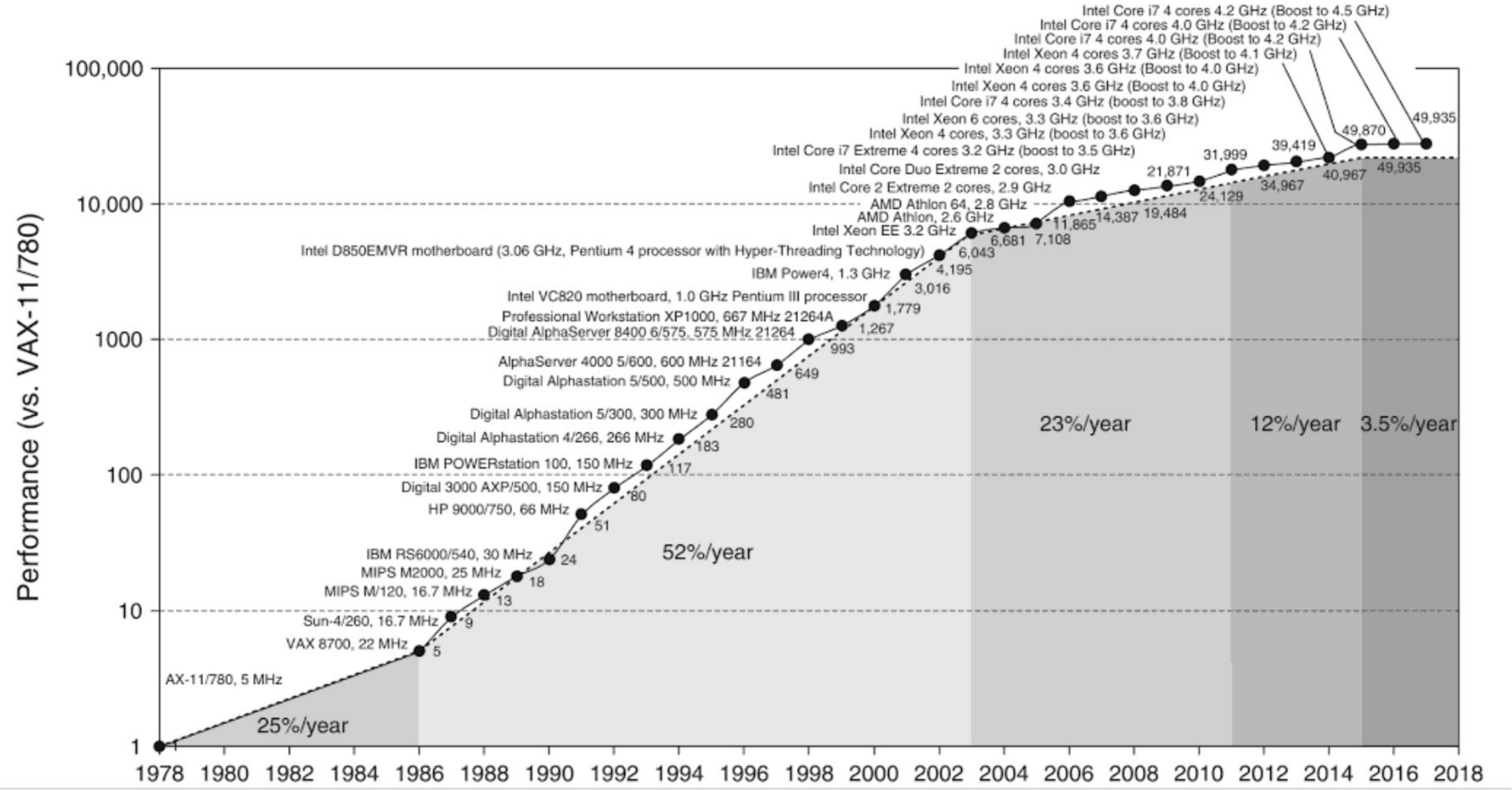
The economic facts on the ground

US Labor productivity, all business

If there was a "new economy", it was less dynamic than the postwar decades
And since the global financial crisis, productivity growth lowest in living memory

Diminishing returns in technological innovation?

End of exponential growth in microprocessor performance

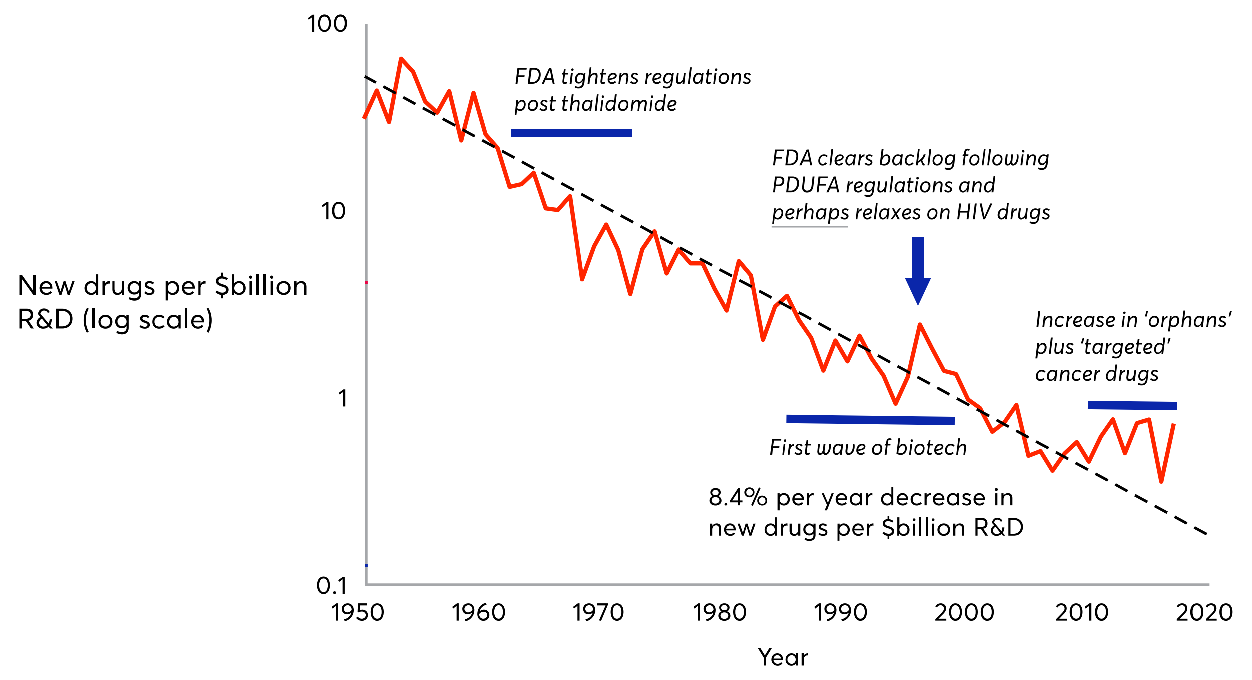


From Computer Architecture: A Quantitative Approach (6th edn) by John Hennessy & David Patterson

Diminishing returns in technological innovation?

Erooms’ law – exponentially falling R&D productivity in the pharma/biotech industry

Figure 3.1. Eroom’s law: the number of new molecules approved by the US Food and Drug Administration (pharma and biotech) per US$bn global R&D spending.



FDA tightens regulations post thalidomide

FDA clears backlog following PDUFA regulations and perhaps relaxes on HIV drugs

Increase in ‘orphans’ plus ‘targeted’ cancer drugs

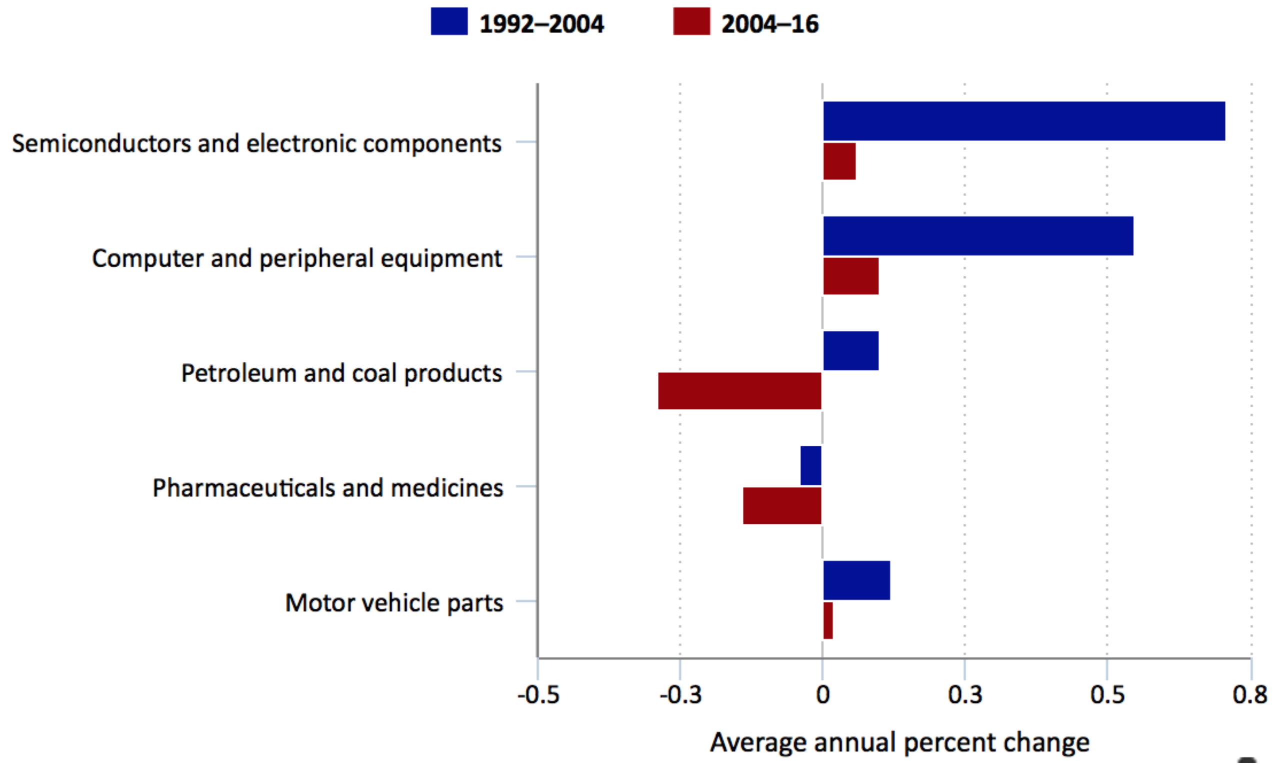
First wave of biotech

8.4% per year decrease in new drugs per $billion R&D

Source: Plot after Scannell et al. (2012),[63] with additional post-2012 data.[64]

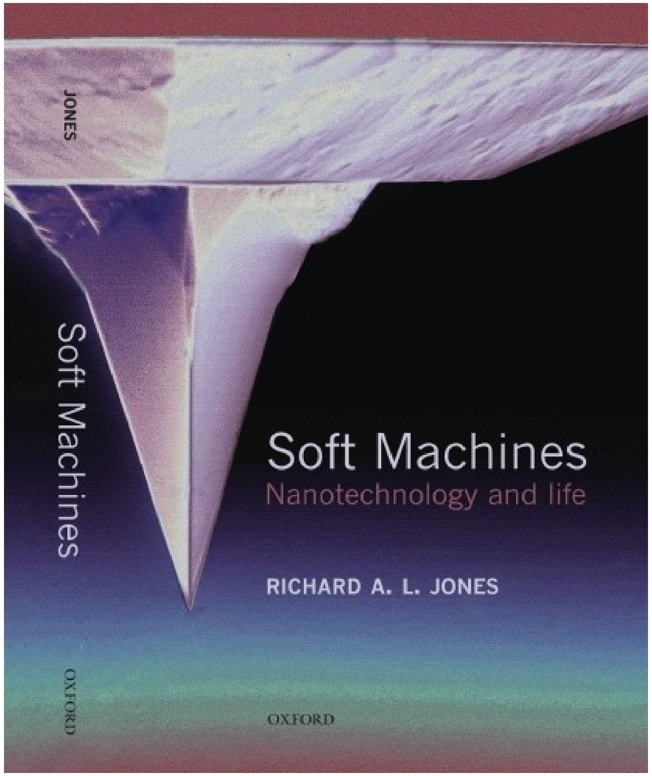
Semiconductors, computers and pharmaceuticals are in the top 5 contributors to the US productivity slowdown

Figure 3. Contributions to manufacturing sector multifactor productivity growth by industries with the largest relative declines in contributions from 1992–2004 to 2004–16



https://www.bls.gov/opub/mlr/2018/article/multifactor-productivity-slowdown-in-us-manufacturing.htm

Soft Machines: 14 years on



- Published 2004: since then:
- Drexlerian nanotechnology –
  - essentially no progress
- Soft Machines:
  - self-assemby, DNA nanotech, artificial molecular motors & active matter
- Quantum nanotech:
  - fantastic physics, it may even lead to practical quantum computing
- Economic impact
  - Still to materialise at scale.