The Materials Requirements for The Origin of Life

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Inspiration

- Richard Jones, Steve Scott, Steve Armes & Ramin Golestanian
- Colin Crook, Jon Howse, Beppe Battaglia, Paul Topham, Adam Blanazs, Joshua Swann, Andy Parnell, ...........
- Alberts .......................... & Watson (Molecular Biology of the Cell)
A vesicle made from block copolymers - a 100nm bag made from a 3nm thick rubber membrane.
What is nanotechnology?

• Not a single technology, but an underlying philosophy.
• Aim: to achieve superior material properties and functionality by control of matter on the atomic and molecular scale.
• What is now described as nanotechnology comes in different varieties........
Why go small? Surface matter

Surfaces are proportionately more important for finely divided matter...

...properties depending on surfaces
- reactivity,
  catalysis, etc.
- are enhanced for nanomaterials.

e.g. socks with embedded nanoparticles
Why go small? Quantum matter

When physical dimensions approach the length-scales associated with quantum objects - like electrons - properties change.

Vials containing quantum dots showing size dependent fluorescence under UV illumination.
Why go small?
Soft matter

Exploits strong surface forces and ubiquitous Brownian motion

Design principles:
• Self-assembly
• Molecular shape change
• Environmentally responsive materials

e.g. self-assembled structures from block copolymers

Beppe Battaglia
Two ways of thinking about soft nanotechnology

• What nanoscale constructs and devices can we make from the synthetic ingredients of soft matter science? (polymers, amphiphiles, block copolymers, brushes, colloids etc)?

• What features of living cells can we emulate using synthetic components?
Some features of living cells

- Containment
- Source of free energy
- Adaption to the environment
- Molecular logic

Controlled traffic
- in....... ...
- and out

Replication

Far from equilibrium

Resulting in:
- Change of the cell’s activity
- Change to the environment
- Movement to a new environment
Two Observations

• Cell Biology is nanotechnology that works!

• To understand the mechanisms of Cell Biology We need ideas from soft matter + complexity
Staying far from equilibrium needs a constant energy supply
The 2nd Law of Thermodynamics: disorder in the Universe tends to increase.

“T pump heat – therefore I am”
Iron ore was laid down

Evolutionary timeline

Reducing Atmosphere → Iron ore was laid down → Oxidising Atmosphere

OXYGEN LEVELS IN ATMOSPHERE (%)

TIME (BILLIONS OF YEARS)

- formation of the earth
- formation of oceans and continents
- first living cells
- first photosynthetic cells
- first water-splitting photosynthesis releases O₂
- origin of eucaryotic photosynthetic cells
- aerobic respiration becomes widespread
- first multicellular plants and animals
- present day
Primordial Ponds & Labs

Stanley Miller & Harold Urey 1950s
NASA: dried up ponds on Titan

Solution and rerystallisation are important!
The small molecules of life.....

...make the larger units of life...
through the polymers of life

4 nucleotides ACGT

4 nucleotides ACGU

20 amino acids
DNA encodes the information in every cell today.
DNA can make a copy of itself ….
...and DNA can be transcribed into many copies of mRNA
…..and mRNA makes protein in the Ribosome

Figure 1-10a. Molecular Biology of the Cell, Fifth Edition (© Garland Science 2008)
These polymers make each other in an autocatalytic cycle that needs a constant source of energy.
Which came first.........
The Polymers of Life

DNA synthesis (replication)

RNA synthesis (transcription)

protein synthesis (translation)

amino acids

DNA

RNA

PROTEIN

Can be very stable

Less stable

& mildly catalytic

Unstable in water

& highly catalytic

So which came first?

Figure 1-4  Molecular Biology of the Cell, Fifth Edition (© Garland Science 2008)
Enzymes

Proteins act as catalysts....
(make reactions go faster)

...but they are unstable in dilute solution
The “Marmite” problem

\[ \text{HOO}	ext{C-}	ext{R}	ext{-NH}_2 + \text{HOOC-}	ext{R’-NH}_2 \rightleftharpoons \text{HOO}	ext{C-}	ext{R}	ext{-NHOC-}	ext{R’-NH}_2 + \text{H}_2\text{O} \]

amino acid \hspace{10em} \text{protein and water}

Proteins are unstable in lots of water and equilibrium favours short peptides.
A pond of small molecule soup that dries up and rehydrates

• Sugars
• Fatty acids
• Amino acids
• Nucleic acids

Needs another step to generate “life”
A catalytic surface......
Mud & clay template RNA formation
…..and a crust of fatty acids that make membranes…..

Figure 10-7  Molecular Biology of the Cell (© Garland Science 2008)
…..which wrap up to make bags

from the crust on the edge of a pond

Called vesicles or liposomes

Figure 10-8  Molecular Biology of the Cell (© Garland Science 2008)
RNA in a bag has an improved chance to replicate and keep the protein catalysts it makes.

With the high concentration inside, solving the “Marmite” problem.
Complex chemical systems can develop in an environment that is far from equilibrium.

RNA adsorbed on a clay platelet encapsulated in a fatty acid vesicle is more efficient at catalysing RNA synthesis.

Experimental Models of Primitive Cellular Compartments: Encapsulation, Growth, and Division
Martin M. Hanczyc, et al.
Science 302, 618 (2003);
DOI: 10.1126/science.1089904
Membranes permitted life to develop in the first cell with diversification & competition.
Measuring membrane properties

3 nm

4 nm

10 nm

20 nm

\[ \frac{k_e}{K_A} \times 10^{10} \, m^2 \]

\[ d \, (nm) \]

The earth as an energy source

Figure 1-15  *Molecular Biology of the Cell*, Fifth Edition (© Garland Science 2008)
Iron sulfide: the first membrane?

- Uses geothermal energy
- Spontaneously generates a proton gradient across a membrane

EV Koonin1 and W Martin
TRENDS in Genetics 212005
How do we get to photosynthesis?

Extremophiles or bags of clay met sunshine

$\text{H}_2\text{S}$ splitting came first .......

and then $\text{H}_2\text{O}$
Light as an energy source

Anabaena cylindrica a phototrophic bacteria which specialises in photosynthesis and nitrogen fixation.
Photosynthesis transformed the environment enabling aerobic bacteria to evolve.
Mycoplasma genitalium

Only 477 genes versus 6,300 for a yeast cell & 24,000 for me
Procaryotes reproduce by binary fission

- Procaryotic cells are structurally simple
- Bag of soup – and it’s hungry
- Bacteria - survival of the fastest
- Division in 20 minutes
- Genome replication in 40 minutes
- 7 billion cells in less than 12 hours
- The mass of the earth in 2 days!
Aerobic scavengers occupy many ecological niches.

Escherichia coli

Vibrio cholerae

Figure 1-18a  Molecular Biology of the Cell, Fifth Edition (© Garland Science 2008)
The development of a nucleus means more membrane surface area.
......for proteins......
......which control the traffic in & out!


Figure 1-13b Molecular Biology of the Cell, Fifth Edition (© Garland Science 2008)
Followed by girders, ropes and motors.
That lead to shape change motility and......

......armour plating
• Simon Foster (MBB) and Jamie Hobbs (Physics)
• 20nm wide “ropes” of peptidoglycan wound helically to produce 50nm cables.
• Wall is 2 cables thick
• Inner intact cable is stress bearing (cylindrical pressure vessel)
Eucaryotes: the 1st predators
Didinium: a carnivorous protazoan
Phagocytosis: a white blood cell eats a red one
Symbiosis leads to mitochondria?

- Anaerobic pre-eucaryotic cell
- Internal membranes
- Early aerobic eucaryotic cell with mitochondria with a double membrane
- Cellular membrane
- Aerobic procaryotic cell
- Membrane derived from eucaryotic cell
Mitochondria: The source of ATP and the power station of cell biology

Protein catalysts trapped in a membrane

Figure 1-33  Molecular Biology of the Cell, Fifth Edition (©Garland Science 2008)
Early plant cells make their own food
Plants made the transition from hunting to farming
Sunshine, water and CO$_2$ feed all life on earth!

plants & algae  

metabolites  

everything else
Cell biology is soft nanotechnology

Biology uses Brownian motion, self-assembly & responsiveness to make complex, functional nanomachines and structures...

Nanotechnology should look to biology for inspiration.

T4 bacteriophage infecting E.coli
So which company has the biggest nanotechnology patent portfolio? Why?
Biological nanotechnology is soft nanotechnology

The characteristic length scale of cell biology is the nanoscale...

...so the nanoscale is the right scale for intervening in biology

David S. Goodsell

Nanomedicine
A molecular delivery device we might be able to make

- Self-assembled polymersome membrane
- Flagellum powered by molecular motor
- Surface patterned with receptors
- Ligands
- Site recognition by ligand-receptor interaction

100 nm
Synthetic self assembly

monomers: styrene, dienes, acrylates, oxirans, siloxanes
synthesis: mainly living anionic polymerisation $M_w/M_n \approx 105$

amphiphiles

hydrophilic

hydrophobic

AB diblock

ABA triblock

ABC triblock

ABC star block

$AB_n$ comb

$(AB)_n$ multiblock
Amphiphilic polymers self-assemble in water just like lipids.
Vesicle formation by film rehydration recreates that crusty pool in the lab!

Spontaneous generation of vesicles from a polymer film formed by evaporation

Beppe Battaglia
Polymer Vesicles

(1) Photos et al. J. Control. Release 2003, 90, 323
(2) Smart et al. under review
(4) Battaglia et al. Langmuir 2006, 22, 4910
**Vesicle Size**

- **Electroformation**
- Rehydration
- Rehydration + Extrusion
- Rehydration + Sonication
- 2000 mesh
- 1000 mesh
- Electroformation

**Graph:**
- **Particle Number**
- **Diameter in nm**

- **Sonication**
- **Extrusion**

- **Images:**
  - 50 µm
  - 1 µm
Monodisperse Vesicles of $E_{16}B_{22}$

Formation of patches of $E_nB_m$  

Water absorption & microphase separation  

Further water absorption & formation of lamellae  

Expansion & unbinding of external bilayer  

Detachment  

Surface minimisation, closure and vesicle formation.

$L = 19 \, \mu m$  

$L^2 = 4\pi \ r^2$  

d$_{MAX} = 10.72 \, \mu m$
Patches on a Surface

1. Au evaporated onto Silicon wafer

2. Formation of Perfluorinated SAM
   \[ \text{CF}_3(\text{CF}_2)_7-\text{CH}_2-\text{CH}_2-\text{SH} \]

3. UV lithography TEM grid mask (244 nm laser)
   1000 mesh and 2000 mesh (lines/inch)

4. Formation of patterned SAM using hydrophilic thiol
   \[ \text{HO}-(\text{CH}_2)_{11}-\text{SH} \]

A patterned hydrophilic, fluorophilic surface
Putting Polymer on the Patches

5. Spin-coat vesicle forming polymer + Rhodamine dye solution

6. Spontaneous dewetting
Optical Microscopy – Reflection – Differential Interference Image
SEM of lamellar patches
Confocal Fluorescence Microscopy
Howse, Jones, Battaglia, Ducker, Leggett, Ryan
Templated Formation of Giant Polymer Vesicles with Controlled Size Distributions
Propulsion at the cellular level

- Wiggly Tails
- Myosin Crawlers
- Chemically propelled (not heat engines!)

**bacteria** driven by rotating flagella

synthetic sperm = vesicle + propulsion
Muscles: Molecular Motors

A molecular device to translate chemical energy into mechanical work

MASSIVE UNIT CELL $\sim 10^5 \text{ nm}^3$

Images courtesy of John Squires
Polyelectrolyte response

Polybase:
• Poly(di-ethylamino methacrylate) PDEA:
  – swells in acid
  – contracts in base.

Polyacid:
• Poly(methacrylic acid) PMAA:
  – swells in base
  – contracts in acid.
Triblock microstructure

PMMA-PMAA-PMMA

100 kg/mol triblocks with ~ 0.15 glassy ends give liquid-like spheres and not bcc grains
Synthetic muscle

Self assembled from block copolymers

Generates force by serial addition of molecular motion

Howse, Topham, Armes, Jones & Ryan
NanoLetters 2005
Synthetic Muscle

pH change causes a 3 nm shape change which is seen by SAXS

The connected molecules integrate (over $10^5$) this nanoscale action up to the macroscale
Work = force*distance
Power = work/time
Power = force*velocity
Power = F * (dl/dt)

\[ P_{\text{MAX}} = 20 \text{ mW kg}^{-1} \]

\[ \sim 200 \text{ erg s}^{-1} \text{ g}^{-1} \]

Maximum power immediately after change in pH
How does it compare?

**Science 95, 288 (2000)**

**Table 1.** Engines. The performance of various cellular engines is compared with thermal energy ($kT$) and an automobile engine. Calculations for the specific power are based on the molecular weight of the smallest unit of the engine. Thus, molecular motors and polymerization-based engines are more powerful than the cellular structures in which they are found; for example, compare myosin to striated muscle.

<table>
<thead>
<tr>
<th>Engine</th>
<th>Velocity ($\mu$m s$^{-1}$)</th>
<th>Force (dynes)</th>
<th>Specific power (erg s$^{-1}$ g$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$kT$ (thermal energy)</td>
<td>–</td>
<td>$4 \times 10^{-7}$</td>
<td></td>
</tr>
<tr>
<td>Actin polymerization (40)</td>
<td>1</td>
<td>$1 \times 10^{-6}$</td>
<td>$1 \times 10^9$</td>
</tr>
<tr>
<td>Microtubule polymerization (49)</td>
<td>0.02</td>
<td>$4 \times 10^{-7}$</td>
<td>$5 \times 10^6$</td>
</tr>
<tr>
<td>Myosin II (55)</td>
<td>4</td>
<td>$1 \times 10^{-6}$</td>
<td>$2 \times 10^6$</td>
</tr>
<tr>
<td>Kinesin (56)</td>
<td>1</td>
<td>$6 \times 10^{-7}$</td>
<td>$7 \times 10^7$</td>
</tr>
<tr>
<td>Vorticellid spasmoneme (4)</td>
<td>$8 \times 10^4$</td>
<td>$1 \times 10^{-3}$</td>
<td>$4 \times 10^7$</td>
</tr>
<tr>
<td>Typical passenger car engine (57)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Striated muscle (57)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacterial flagellar motor (58, 59)</td>
<td>100 Hz</td>
<td>$4.5 \times 10^{-11}$ dyn cm</td>
<td>$1 \times 10^6$</td>
</tr>
<tr>
<td>Thyone acrosomal reaction (60)</td>
<td>6–9</td>
<td>$5 \times 10^{-4}$</td>
<td>$1 \times 10^5$</td>
</tr>
<tr>
<td>Limulus acrosome reaction</td>
<td>10</td>
<td>$1 \times 10^{-6}$</td>
<td>$1 \times 10^4$</td>
</tr>
<tr>
<td>Eukaryotic flagellum (57)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mitotic spindle (57)</td>
<td>2</td>
<td>$1 \times 10^{-5}$</td>
<td></td>
</tr>
</tbody>
</table>

**Triblock gel in pH oscillator**  
$2 \text{ \mu m.s}^{-1}$  
$2 \times 10^{-11}$  
$2 \times 10^2$
Even I’m good for 15 W/kg!

$1.5 \times 10^5 \text{ erg/s/g}$
How can we improve?

- Nature’s method
- Bundles of fibres
- Reduce diffusion distance
- $t_D \sim 1/x^2$
- Increase power (energy/time)

Wang, Topham, Armes, & Ryan
Advance Materials 2007
Bipolymeric Strip

Solvent evaporation

microphase separation

pH 3

pH 7

= trajectory marker

1 mm

Howse, Topham, Armes, Jones & Ryan Macromolecules 2007
Bipolymeric Strip

\[ t_{\text{final}} = 36 \text{ minutes} \]

\[ t = 0 \text{ minutes} \]
Bipolymeric Strip
We can build all the bits!

But how do we put them together?
An Alternative is Reaction-Driven Propulsion

\[ 2 \text{H}_2\text{O}_2 \rightarrow 2 \text{H}_2\text{O} + \text{O}_2 \]

Golestanian et al PRL 94, 220801(2005)
Janus Particle Preparation

Polystyrene beads in isopropanol (diameter 162 microns)

80,000 particles per cm²

Jon Howse
Janus Particles

Control:
1.62 µm diameter Polystyrene

55 Å layer of Platinum evaporated onto surface

AFM

Pt thickness ~5.5 nm

SEM
Control Particle Behaviour 0%

x5 particle traces x=y=100 microns, t=25 sec

5 microns
Blank

Pt coated Janus particle

H₂O

10% H₂O₂

Each trace: 127 x 127 µm, 25 sec
Increasing Hydrogen Peroxide Concentration

Control

Platinum coated
Long-time behaviour

At short times, propelled with velocity $v$.

Direction of particle randomised by Brownian motion after $\tau_R$

Random walk with step-size $v \tau_R$
Propulsion versus Brownian Motion

\[ \Delta L^2 = 4D \Delta t + \frac{V^2 \tau_R^2}{2} \left( \frac{2\Delta t}{\tau_R} + e^{-2\Delta t/\tau_R} - 1 \right) \]

\[ \Delta L^2 = 4D \Delta t + V^2 \Delta t^2 \quad (t \ll \tau_R) \]

\[ \Delta L^2 = \left(4D + V^2 \tau_R\right) \Delta t - \frac{V^2 \tau_R^2}{2} \quad (t > \tau_R) \]

From the particle track we can extract \( D \), \( V \) and \( \tau \)

\( D \) - diffusion coefficient
\( V \) - velocity
\( \tau_R \) - rotational diffusion coefficient
More complex particles

- Possible combinations from pairs of particles
Make different trajectories
Stack of trajectories as a function of v/w – 25 seconds duration (doublets 20, 16, 19, 14, 11, Control 4)
Quantitative analysis and fitting of experimental MSD data

<table>
<thead>
<tr>
<th>Mean Velocity</th>
<th>StDev</th>
<th>w from rate of chaw fit</th>
<th>tR fit</th>
<th>Time</th>
<th>D</th>
<th>tR</th>
<th>v</th>
<th>w</th>
<th>Fit Duration</th>
<th>Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.637759957</td>
<td>0.7575</td>
<td>1.065785308</td>
<td>1.08222</td>
<td>22.83105</td>
<td>5</td>
<td>0.155902</td>
<td>15.60715</td>
<td>1.292295</td>
<td>1.070696</td>
<td>10</td>
</tr>
<tr>
<td>1.08222</td>
<td>16.42036</td>
<td></td>
<td></td>
<td></td>
<td>10</td>
<td>0.157906</td>
<td>16.42969</td>
<td>1.287352</td>
<td>1.068462</td>
<td>20</td>
</tr>
<tr>
<td>0.163406</td>
<td>17.58908</td>
<td></td>
<td></td>
<td></td>
<td>40</td>
<td>0.157906</td>
<td>16.42969</td>
<td>1.287352</td>
<td>1.068462</td>
<td>20</td>
</tr>
</tbody>
</table>

ΔL²/µm² vs Δt / sec

Δθ²/µm² vs Δt / sec

D = 0.16092
v = 1.283626
tR = 17.21504
w = 1.069808
What we can and can’t do!

• Things we can do
  • Self-assembly (to some extent)
  • Simple design rules
  • Encapsulation
  • Exploiting conformation change

• Things we can’t do
  • Evolutionary design
  • Molecular computing
  • Understand systems driven far from equilibrium
A viable medical nanobot?

Beppe Battaglia
Thanks

• The experimentalists
  Jon Howse, Paul Topham
  Colin Crook, Beppe Battaglia
  Andy Parnell, Joshua Swann,
  Adam Blanazs

• Richard Jones
• Steve Armes
• Ramin Golestanian
To Discover And Understand.