some small steps toward **Artificial Life**

- motility
- metabolism
- self-replication
- evolution

Light Activated Colloidal swimmers

3 generations

Exponential Growth

Doubles every diurnal temperature/light cycle - 24 generations and counting

Growth rate depends on environment - one species takes over system
What I cannot create
I do not understand

Feynman's last board
at Caltech. February 20,
2008 at 5:33 am
Self-Replication, Exponential Growth

Doubles each cycle, 24 cycles >7,000,000 fold increase

Evolutionary Selection
Biology or Physics?
`Living’ Crystals from Light Activated Artificial Surfers

- Flocking - Physics or Biology?
- Diffusive vs Active Colloids
- Light Activated Swimmers/Surfers
- Clustering by Collisions

Jeremie Palacci
Stefano Sacanna
Dave Pine

TPM
Hematite
3-Methacryloxypropyl trimethoxysilane
Two types of particles by magnetism along cube (111)
Segregation in a magnetic field
Manipulation with a magnetic field
Proof that collisions cause clusters/crystals

Field on
Light on
Then Light on
Field on
Light on
No Field
Actually learned something about Non-equilibrium systems:

If things slow down when density increases
   Flux out < Flux in
   density increases more
   ⇒ **Things Flock**

Sounds Trivial but:

   It doesn’t work in equilibrium
   e.g. diffusion
Self-Replication?
We want specificity, control and reversibility in interactions

Specific Interactions with DNA

C/CAA/GTT/ATG/A
G/GTT/CAA/TAC/T
Polystyrene particles, $d=1\mu m$

Neutravidin coated

From Molecular Probes

DNA with biotin end

www.idtdna.com

100 nmole DNA oligo $60.00$
250 nmole DNA oligo $75.00$
1 $\mu$ mole DNA oligo $115.00$

Don’t even have to calculate melting temp

http://www.biophp.org/minitools/melting_temperature/demo.php?primer=TATATATATATA

| PRIMER | 5'–TATATATATATA–3' |
| LENGTH | 12 |
| C+G%  | 0 |
| Molecular weight: | 3722.835 |
| $T_m$ | $24 \, ^{\circ}C$ |
Moreover people have done stuff with it:

Ned Seeman, NYU
The father of DNA nanotechnology
Kavli Prize 2010
“DNA: Not Merely the Secret of Life”
Programmed Assembly of DNA-Functionalized Nanoparticles


Colloids

Valeria T. Milam,† Amy L. Hiddessen,† John C. Crocker,† David J. Graves,† and Daniel A. Hammer†,‡,§ Langmuir 2003, 19, 10317–10323


Marie-Pierre Valignat*, Olivier Theodoly‡, John C. Crocker‡, William B. Russel§, and Paul M. Chaikin*‡ PNAS | March 22, 2005 | vol. 102 | no. 12 | 4225–4229

Now: NYU, Harvard, Penn
0.5 µm radius polystyrene sphere covered with Neutravidin

Number of possible DNA bonds \( \sim 200 \)

\[ N_{tot} \approx 10^4 \text{ DNA/sphere?} \]
From bio - problem is not specific interactions
problem is to prevent non specific interactions
F108: neutral triblock copolymer (Pluronic) PEO-PPO-PEO. $h \sim 15$ nm

PDEGA-b-PAA: amphiphilic charged diblock copolymer. (Rhodia Inc. Cranbury) Poly(diethylene glycol ethylether acrylate)-Poly(acrylic acid)-

- 1K-4K (6 DEGA, 55 AA)
- 3K-12K (18 DEGA, 165 AA)
- 6K-24K (36 DEGA, 330 AA)

$L \sim 20$ nm
Aggregation, reversibility and kinetics
Self-replication?
AUTOMATIC MECHANICAL SELF-REPRODUCTION*

L. S. PENROSE

Perhaps the most remarkable feature of living matter, as opposed to inanimate nature, is the power of self-reproduction. The property is so characteristic that Oparin (1937), perhaps the greatest authority on the origin of life, considers that life can be said to have arisen only after the evolution or emergence of this property. Before self-reproduction began there were conglomerations in the primordial soup, which is supposed to have once existed on the earth, but no life. Crystals, indeed, grow; and each part may be thought of as copying an earlier model. The parts are not differentiated, however, and there is usually no natural division into sections. So Schrödinger (1944) considered life to be an aperiodic crystal, that is to say, one which, by its nature, terminates in space, thus producing discrete organisms.

At this point we may recall another principle, or rule, adumbrated by William Harvey in his phrase 'omne vivum ex ovo', which, in its more modern form, says 'no life except from life'. The reaction of self-reproduction does not arise except from a seed of the same kind. Crystals can be started by a multitude of different kinds of seeds. A living substance, however, must not be able to arise except from its own seed. In extremely unusual circumstances it may arise as a consequence of some event akin to mutation.

There is another fundamental idea, which seems to follow from these principles, and it is genetical. If a change takes place in existing hereditary material, that is to say, a mutation, the changed state is repeated subsequently, not the original pattern.

* A public lecture given at University College London on 14 January 1958. (Drawings executed by A. J. Lee.)

reproducing system, involving a templet, can be made fully automatic.

The deliberate construction of self-reproducing objects is, I believe, a very recent development, less than one year old. It happened that my colleague, Roger Penrose, mentioned that, in his view, self-replication might theoretically be achieved by a set of objects containing magnets whose mutual attractions were altered when they were built up into specified shapes. The idea was sketched in this way. If such pieces were shaken up randomly in a liquid of the same density, or even in a sack or other enclosure, it would be so planned that they would not combine

Fig. 1. Seeded Crystal.
1. Elements in neutral position; they do not link up when agitated horizontally.
2. A neutral element close to a linked pair.
3. The linked pair collects elements from both sides and forms a continuous 'crystalline' chain.
obtaining increased variety was to add similar elements together laterally. In the first models of this type, each unit was multiple, as shown in Fig. 3. Here a three-fold (trimeric) complex has just reproduced.

Fig. 3. Self-reproducing multiple complex.
Three-fold elements of two kinds, one the mirror image of the other, form self-reproducing complexes. There are eight possible alternative objects which can be used as seeds.

Fig. 2. Model to show self-replication, made with two types of unit, A and B.

1. Six units are placed on the track which is then shaken for a period; the units do not link.
2. Two linked units, BA, are now introduced; the shaking is resumed.
3. Now the effect of horizontal shaking is to produce conglomerations.
4. As shaking gradually stops the units separate again, but the old linked pair, BA, remains and a second linked pair has been generated.
5. At stage 2 two differently linked units, AB, are introduced.
7. After separation two new pairs AB are seen to have been generated.
Fig. 7. Exact drawings of working models.
(a) Dimeric unit in neutral phase.
(b) Activated complex which maintains its steady state when fed with neutral units.
(c) Activated complex which reproduces itself when fed with neutral units. The lateral hooks indicate how a chain of such complexes can be constructed.

as with forms described earlier. Fig. 9 indicates how the principle of feeding from semi-crystalline chains of natural elements can be applied to this type of reproduction. Here the synapton is five-fold instead of being two-fold, as in Fig. 8. The arrangement of (+) and (−) tilting could theoretically be extended indefinitely in this manner.

Some people object to these models because, they say, this is not how deoxyribonucleic acid (DNA), the chief component of cell nuclei, replicates itself. The answer is that it is not the intention to show how DNA replicates. The models show how
Basic Replication Scheme

assembly of complementary daughter
Seed

exposure to UV raise T above Tmelt

Tweezer assembly of seeds

Seeds are colloidal particles
Previous generation ‘catalyzes’ ligation of next generation

on seed high conc palindrome
\[ T < T_{\text{palindrome}} \]

in soup low conc. palindrome
\[ T_{\text{palindrome}} < T \]
How can we do this?

Watson - Crick

Transverse Bonds

Palindromic
Longitudinal Bonds

Watson - Crick
Transverse Bonds

For recognition and reversible bonding
New UV activated crosslinker – Cinnamate
Photolithography with Cinnamated DNA

Surface Strand
5'-RSS-50basesBackbone-TTGAGAAATGC*CGTAAGAGTG-3'
Linker Strand
5'-CATCTTCATCC AACTTTTACG*GCATTTCTCAA-3'
Particle Strand
5'-GGATGAAGATG-50basesBackbone-BiotinTEG-3'

High temperature 50°C
Anneal to 25°C
Permanent UV crosslink certain region
Heat up to 50°C and wash out unbound strands
Forming specific binding sites
Photolithography with Cinnamated DNA

DNA pattern decorated with colloids with complementary DNA

DNA pattern decorated with fluorescent complementary DNA

Exposed Pattern

Lang Feng
Melting of ‘NY’

x3 speed
Multi-functionalized surfaces

We can label different regions with whatever we want
Understanding the physics?
Melting Temperature $T_m$ for Watson-Crick pair

- 11 base sequence: CCAAGTTATGA
- 50 mM NaCl
- $C_0 = 1 \, \mu M$

$\Delta G^0 = \Delta H^0 - T \Delta S^0$

$-\Delta H^0 = -77.2 \text{ Kcal/mol}$
$-\Delta S^0 = -227.8 \text{ cal/K.mol}$

$T_m = \frac{\Delta H^0}{\Delta S^0 + R \ln \frac{C_0}{2}} = 29.3^\circ C$

$K = \frac{f}{c_0(1-f)^2} \propto e^{\Delta G_0/kT}$

$f = \frac{\sqrt{4KC_0 + 1} - 1}{2KC_0}$
Quantitatively understanding the DNA mediated interactions

Mean Field Approximation:

\[
Z_s = \left[ 1 + k \exp(-\beta \Delta F_{\text{tether}}) \right]^{N_b}, \text{where } \Delta F_{\text{tether}} = \Delta F_{\text{DNA}} - T\Delta S_p
\]

\[
\Delta F_p = -RT \ln(Z_s - 1)
\]
Thermodynamics

\[ \Delta F_{\text{bead}} = -N_{\text{max}} k_B T \ln \left( 1 + k e^{-\Delta F_{\text{tether}} / k_B T} \right) \]
Problems with Palindromes
Basic Replication Scheme

Assemble daughter
Heat up

Everything seems to work but they don’t come apart completely
Palindromes are made to bind specifically to each other
Palindromes are made to bind specifically to each other. Which means they can also form loops.
Palindromes are made to bind specifically to each other.

Which means they can also form loops.

Which means they can bind non specifically by concatenation.
Topoisomerase I should prove this topological interaction!

Topoisomerase I unknot ssDNA or dsDNA with nicks

Ned’s Simple Bulged 3-Arm Junction Triangle (1996)

Different systems, same idea

Colloids

BTX DNA Tiles

1 µm

40 nm
BTX bent triple crossover motif

(a) Diagram of the bent triple crossover motif with base sequences.

(b) Side View and Cross Section of the motif with detailed sequences:

1. ATGGAGCGAG
2. GCCACGAACATACCTCGGTCT
3. GCTTTGAGGTGACAGTAGG
4. AGATGTCTACACATCC
5. GACTTACATTTGGTA
6. CTGCTACATCGATGCGCAG
7. TTGCTCTTTGGAAATGTCG
8. AGGCAATCTACAGATGCGA
9. CGCTGCTTGAGCAGA

Linker 2: GATGGATCACGGTTGCTG
Linker 6: CTCTCAGCGCCGCTATCA
Linker 9: TATCCGTCTTCCGGTGAGG

Roujie Sha
Tong Wang