some small steps toward **Artificial Life**

life?

- ✔motility
- ✔metabolism

Light Activated
Colloidal sw
scienc

- ✔self-replication

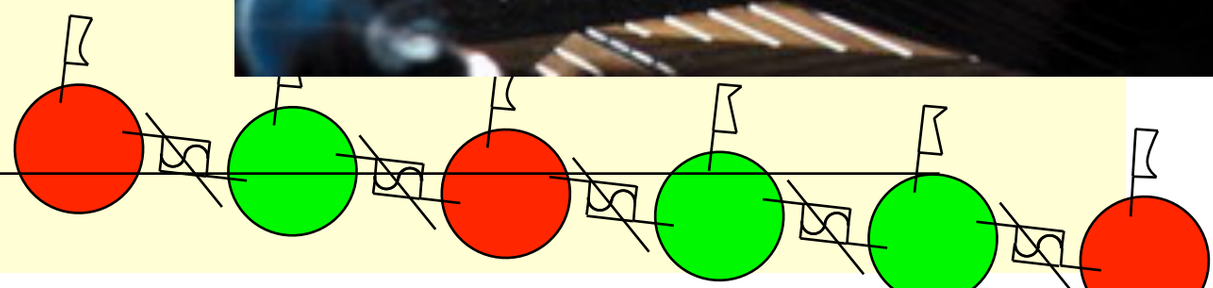
3 generations na

Exponential Gro
Doubles ever
cycle - 24 g

- ✔evolution

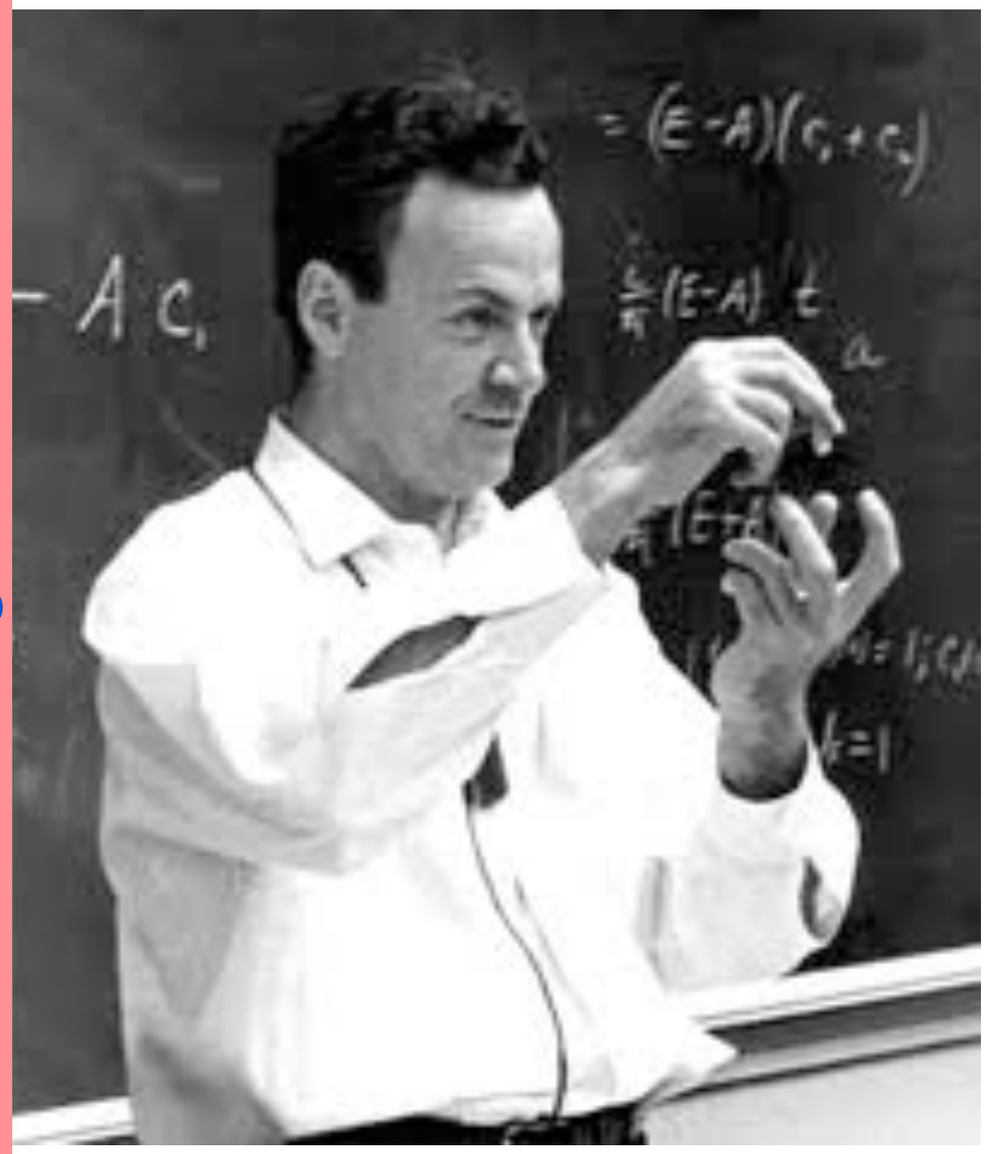
Growth rate depends on environment
one species takes over system

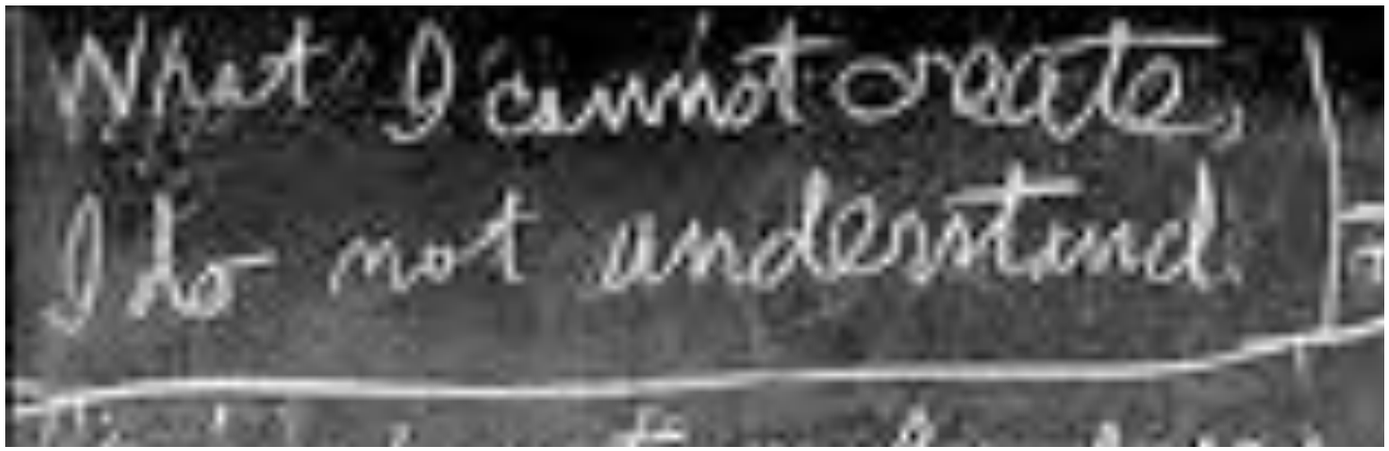

Sean Young in Blade Runner

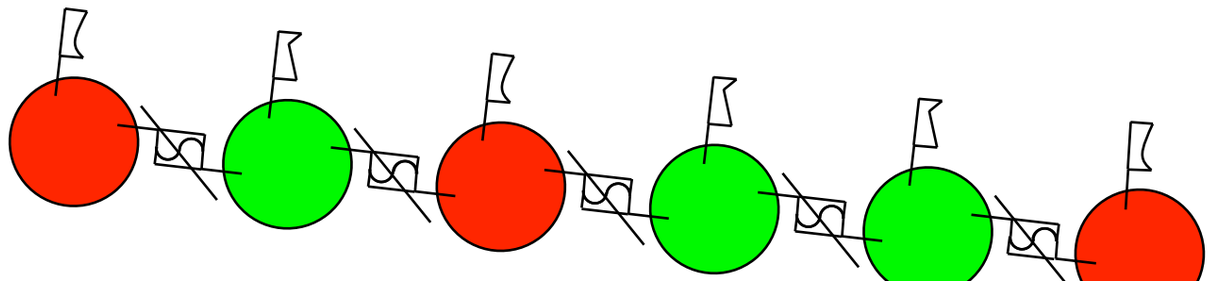


What I cannot create
I do not understand

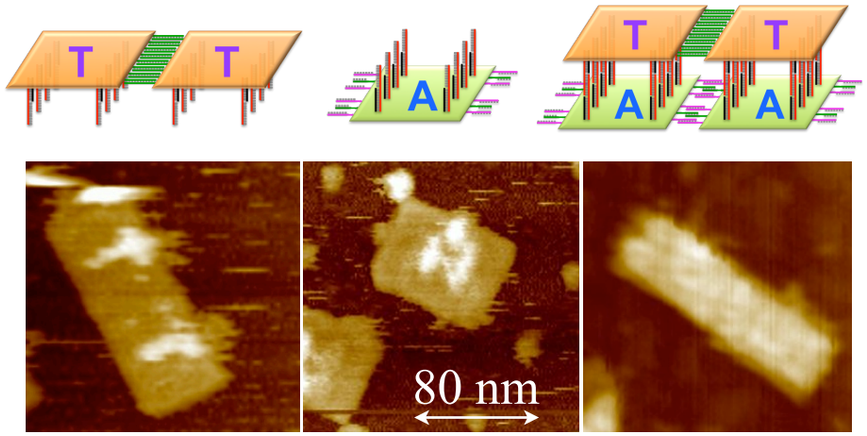
Feynman's last board
at Caltech. February 20,
2008 at 5:33 am

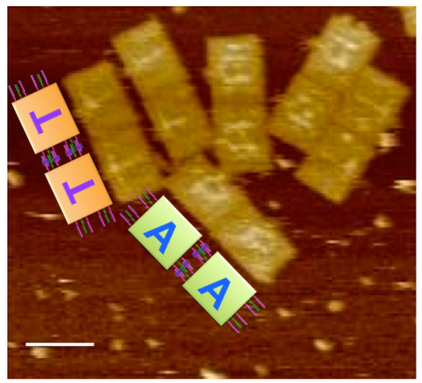


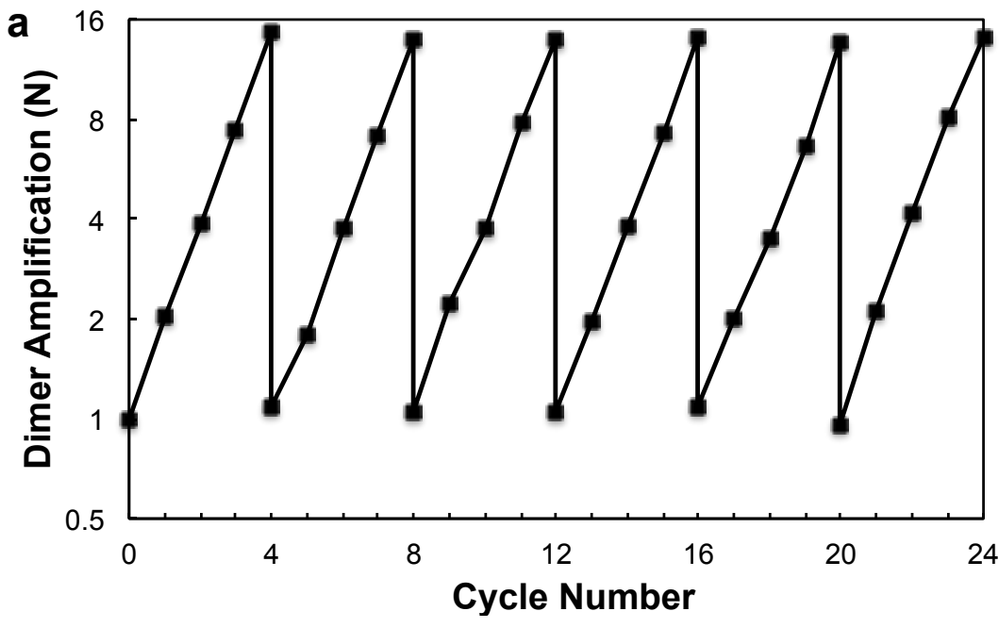




Self-Replication, Exponential Growth

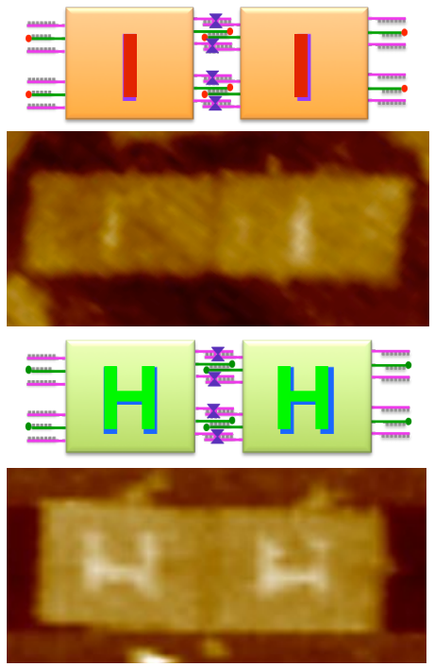


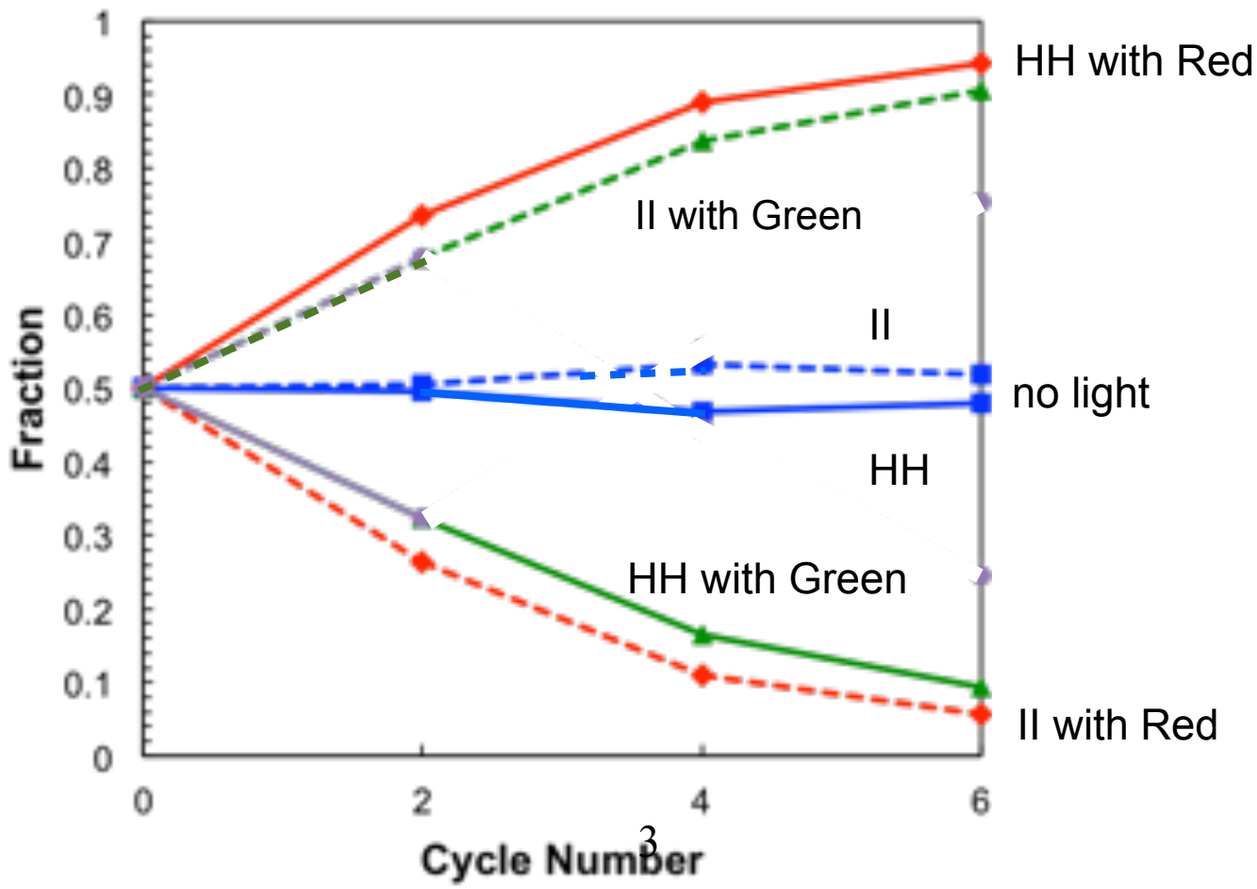




Doubles each cycle, 24 cycles
>**7,000,000** fold increase

Evolutionary Selection





Biology or Physics?

From Vicsek's webpage

`Living' Crystals from Light Activated Artificial Surfers

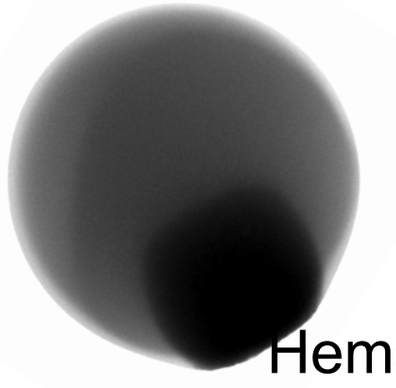
- Flocking - Physics or Biology?
- Diffusive vs Active Colloids
- Light Activated Swimmers/Surfers
- Clustering by Collisions

Jeremie Palacci

Stefano Sacanna

Dave Pine

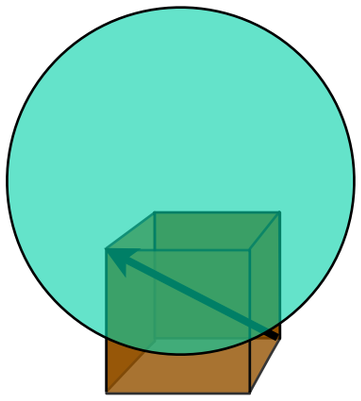
TPM

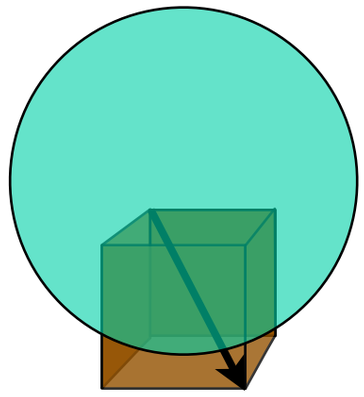


Hematite

3-Methacryloxypropyl trimethoxysilane

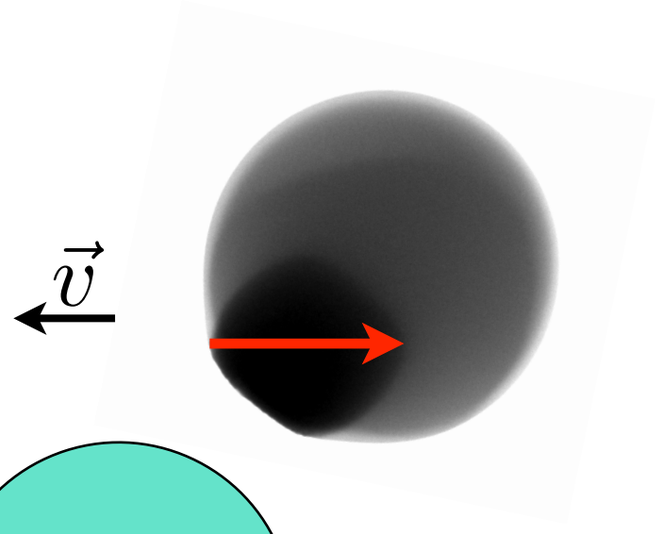
Two types of particles by magnetism along cube (111)

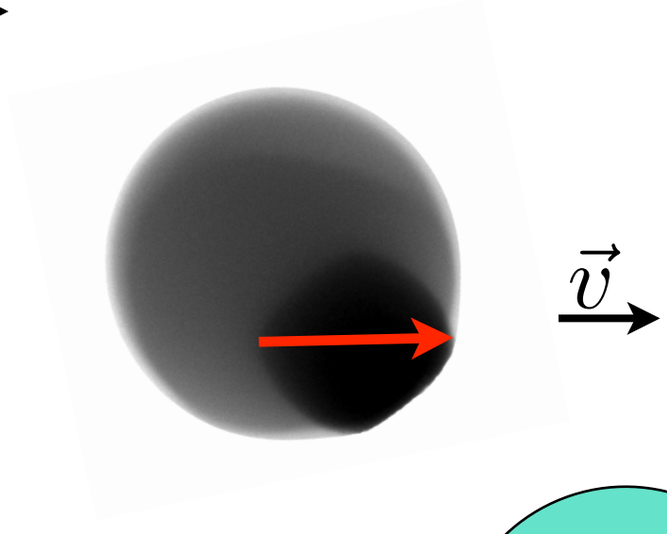


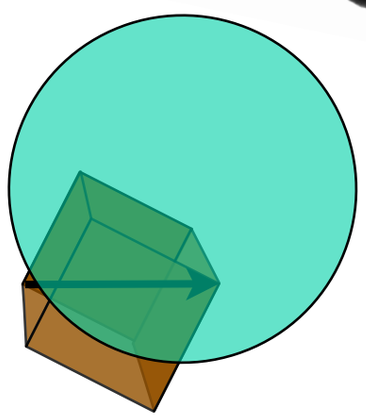


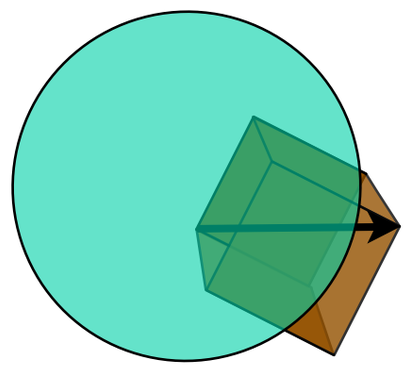
In field

B →

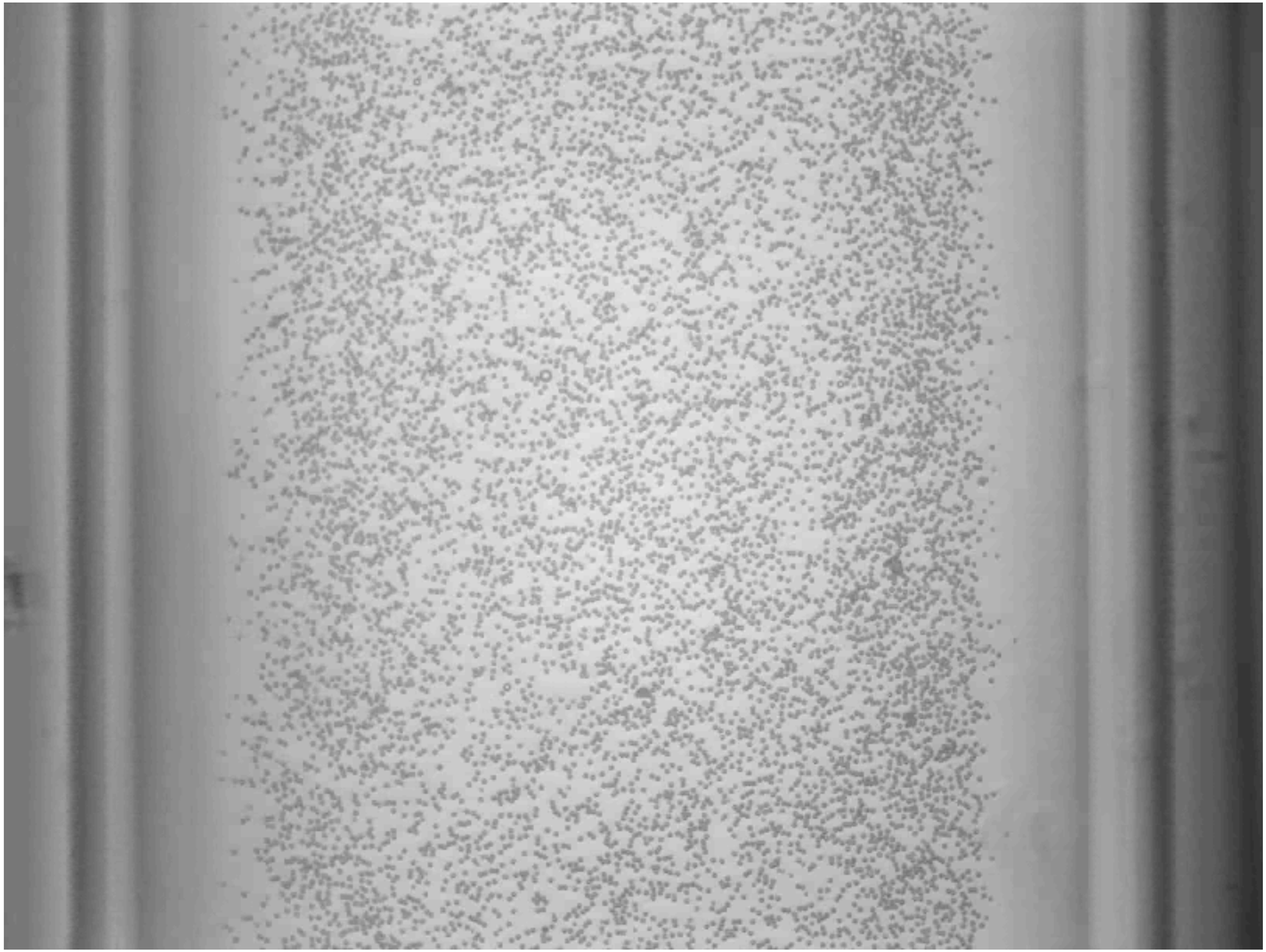




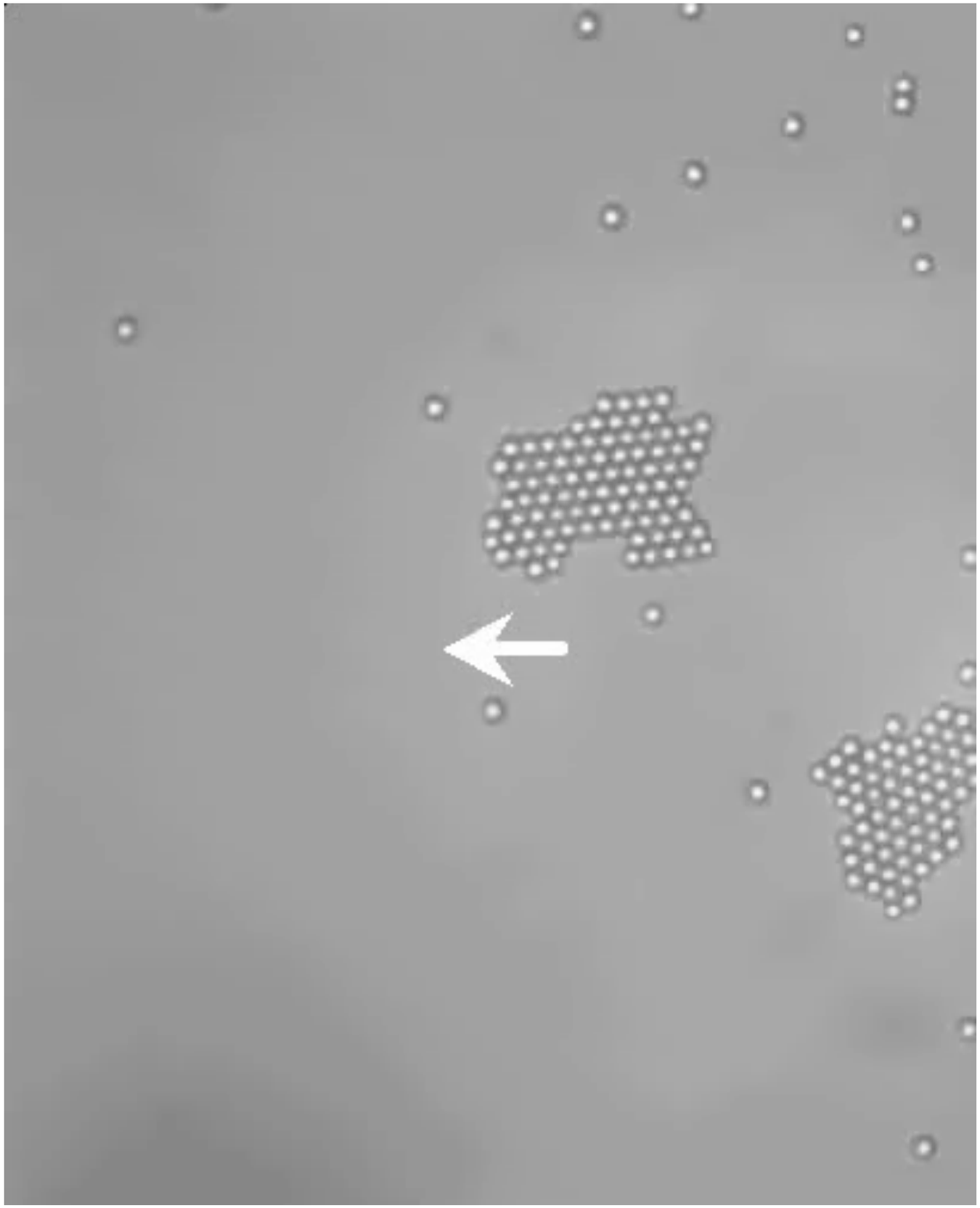




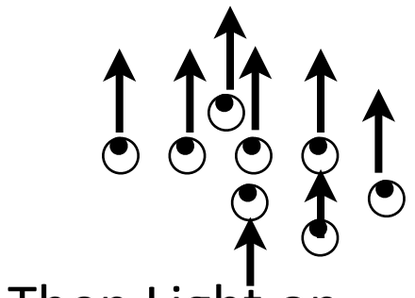
Segregation in a magnetic field

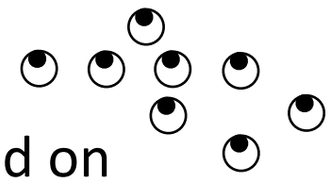


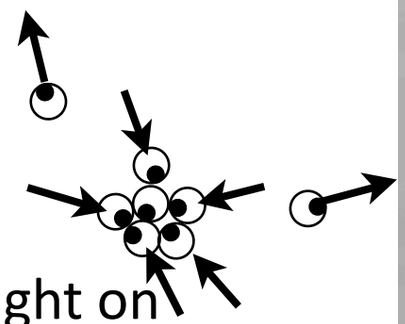
Manipulation with a magnetic field

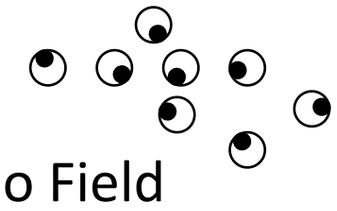


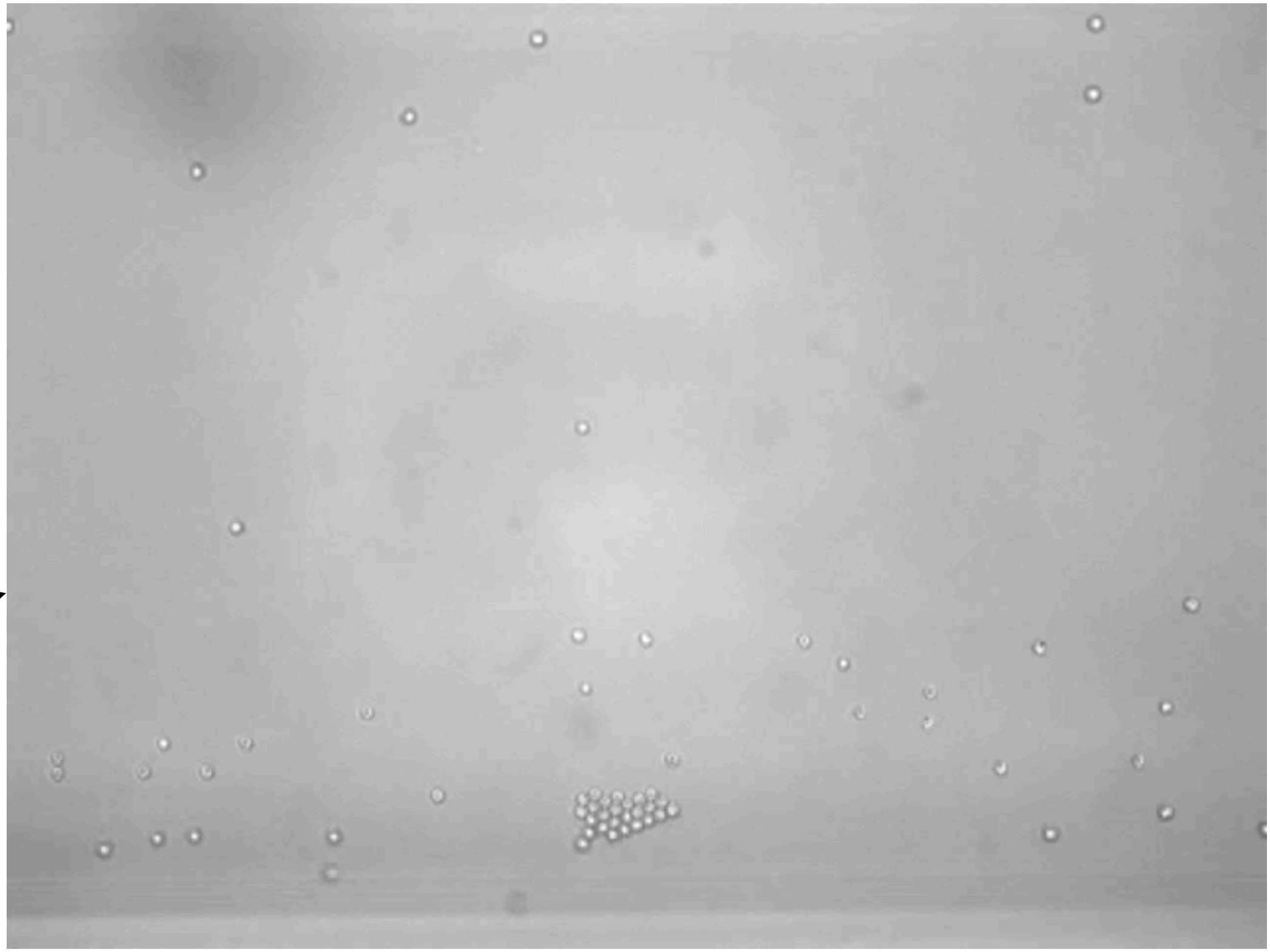
Proof that collisions cause clusters/crystals











Actually learned something about Non-equilibrium systems:

If things slow down when density increases

Flux out < Flux in

density increases more

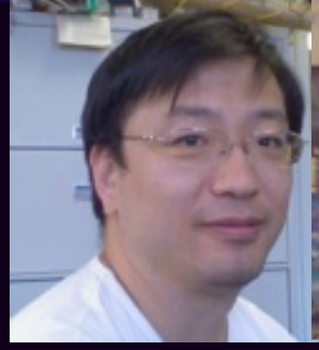
⇒ **Things Flock**

Sounds Trivial but:

It does’t work in equilibrium

e.g. diffusion

Self-Replication?



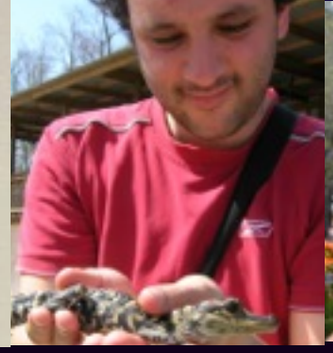
Tong Wang

Ruojie Sha

Minfeng Li

William Irvine

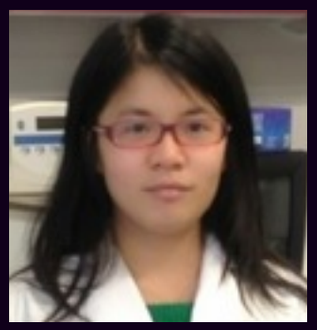
Stefano Sacanna



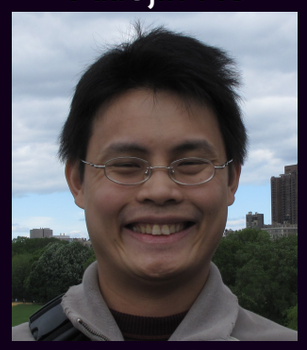
Remi Dreyfus

Mirjam Leunissen

Corinna Maas



Xiaojin He



Kunta Wu

Joy Romulus

Lang Feng

Ned

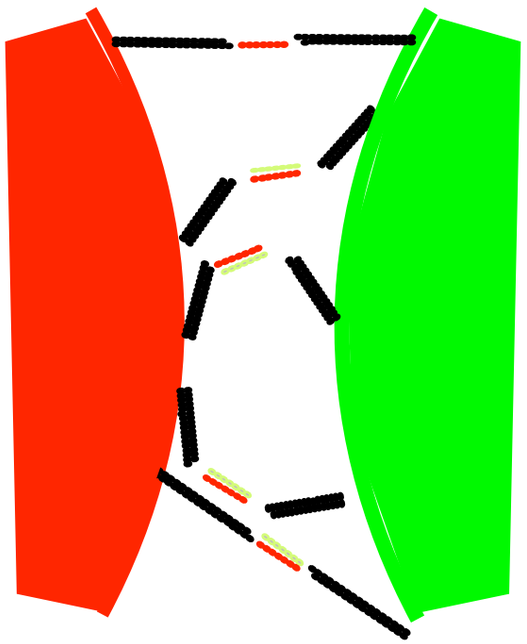
Pine

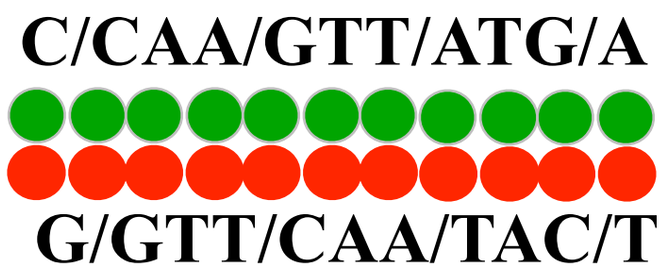
Grierstein

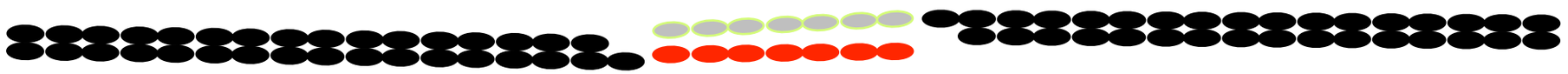
Marcus Weck

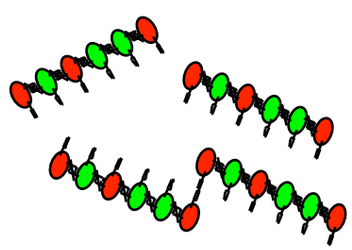
We want specificity, control and reversibility in interactions

Specific Interactions with DNA



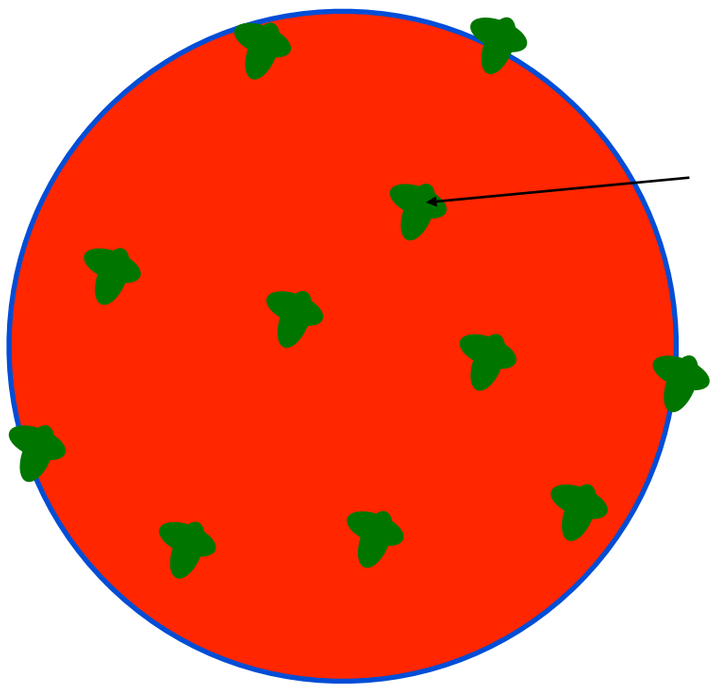






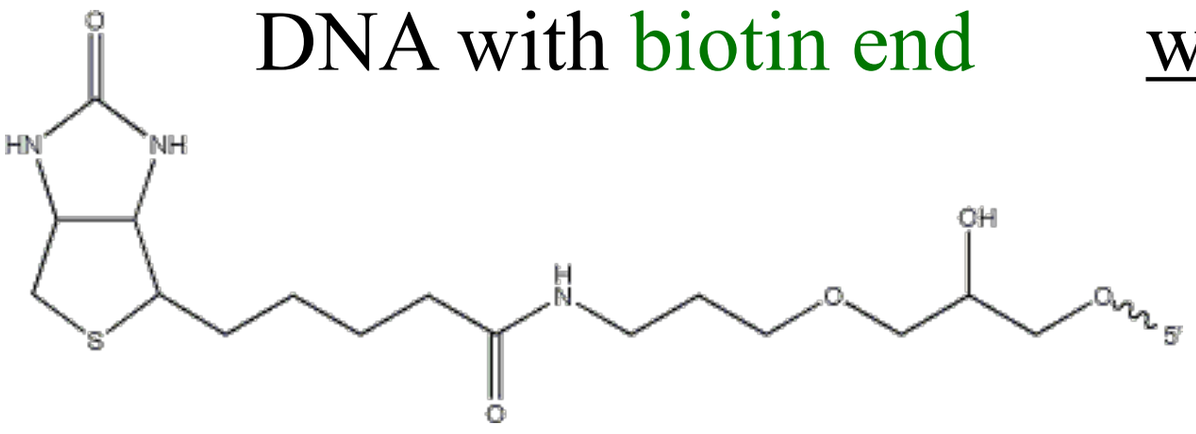
Why Use DNA?

Because it's "easy", it's been done, and it works
-- you can buy everything you need



Polystyrene particles, d=1μm
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 μmole DNA oligo	$115.00

Don't even have to calculate melting temp

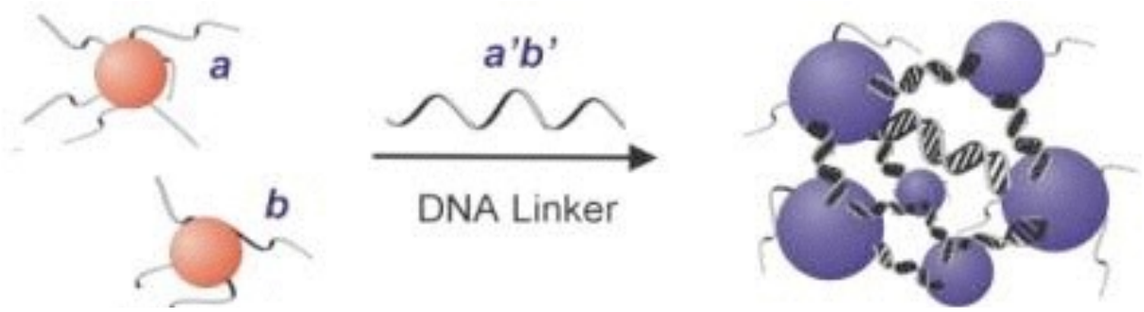
http://www.biophp.org/minitools/melting_temperature/demo.php?primer=TATATATATATA

PRIMER	5'-TATATATATATA-3'
LENGTH	12
C+G%	0
Molecular weight:	3722.835
Tm	24 °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

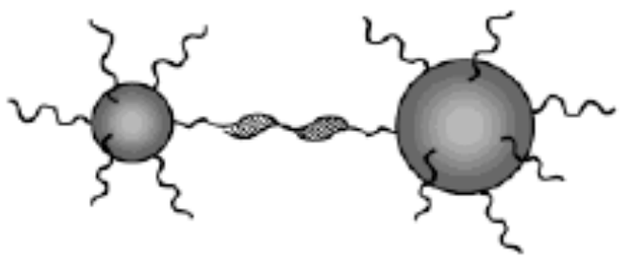


-Mirkin, C. A.; Letsinger, R. L.; Mucic, R. C.; Storhoff, J. J. *Nature* **1996**, *382*, 607

-S. Y. Park, A. K. R. Lytton-Jean, B. Lee, S. Weigand3, G. C. Schatz & C. A. Mirkin, Nature 451, 553 (2008), DNA-programmable nanoparticle crystallization

-Nykypanchuk, D., Maye, M. M., van der Lelie, D. & Gang, O. DNA-guided crystallization of colloidal nanoparticles. Nature 451,549552 2008)..

Colloids

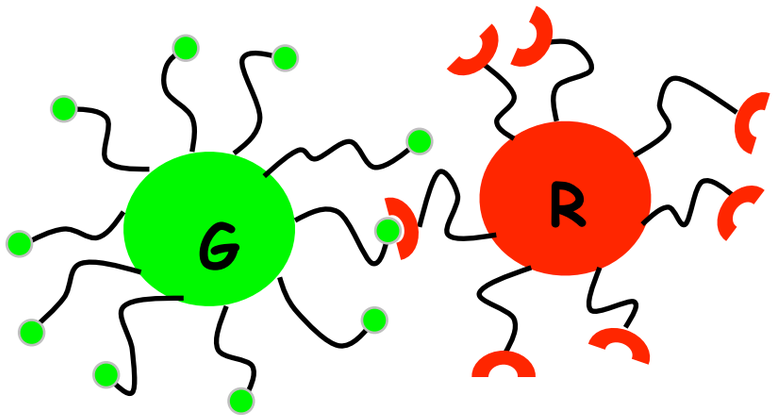


Valeria T. Milam,[†,‡] Amy L. Hiddessen,[†,‡] John C. Crocker,[†,] David J. Graves,[†] and Daniel A. Hammer*[,†,‡,§]
Langmuir **2003**, *19*, 10317−10323

Phillip H. Rogers,[†] Eric Michel,[‡] Carl A. Bauer,[†] Stephen Vanderet,[†] Daniel Hansen,[†] Bradley K. Roberts,[§,∥] Antoine Calvez,[†] Jackson B. Crews,[†] Kwok O. Lau.[§] Alistair Wood.[†] David J. Pine.[‡,⊥] and Peter V. Schwartz*[,†]
Langmuir **2005**, *21*, 5562−5569

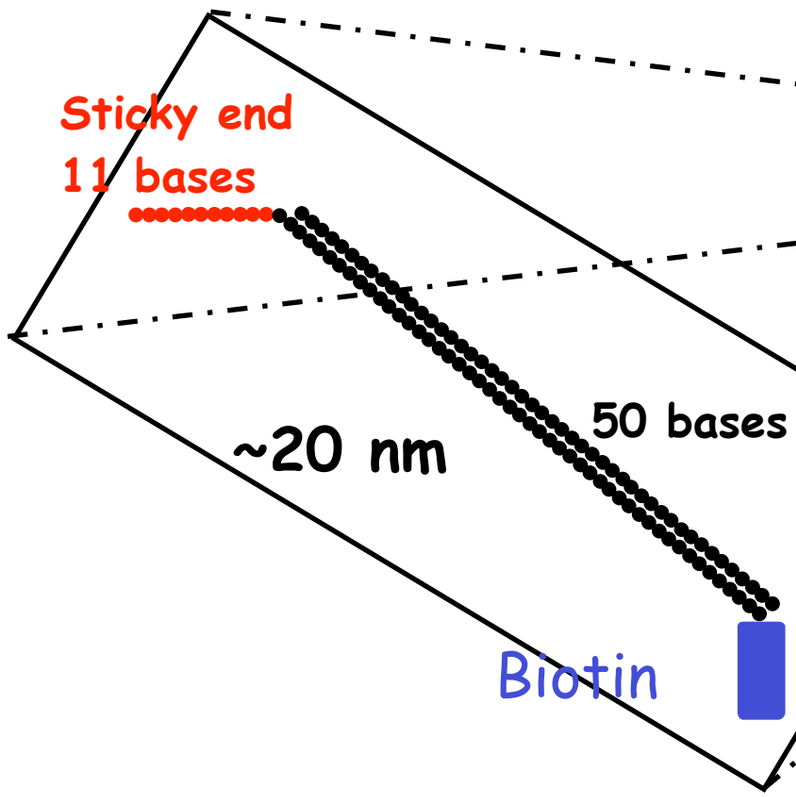
Marie-Pierre Valignat*, Olivier Theodoly†, John C. Crocker‡, William B. Russel§, and Paul M. Chaikin*¶
PNAS | March 22, 2005 | vol. 102 | no. 12 | 4225–4229

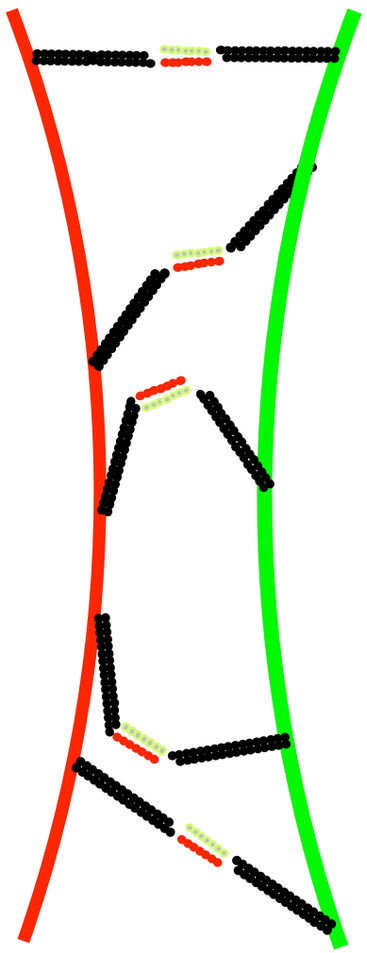
Now: NYU, Harvard, Penn



$N_{tot} \approx 10^4$ DNA/sphere?

20 nm





0.5 μm radius polystyrene s
covered with Neutravidin

Number of possible DNA bonds ~ 200

Easy - but doesn’t work!

not always specific

not always reversible

From bio - problem is not specific interactions

problem is to prevent non specific interactions

Stabilization

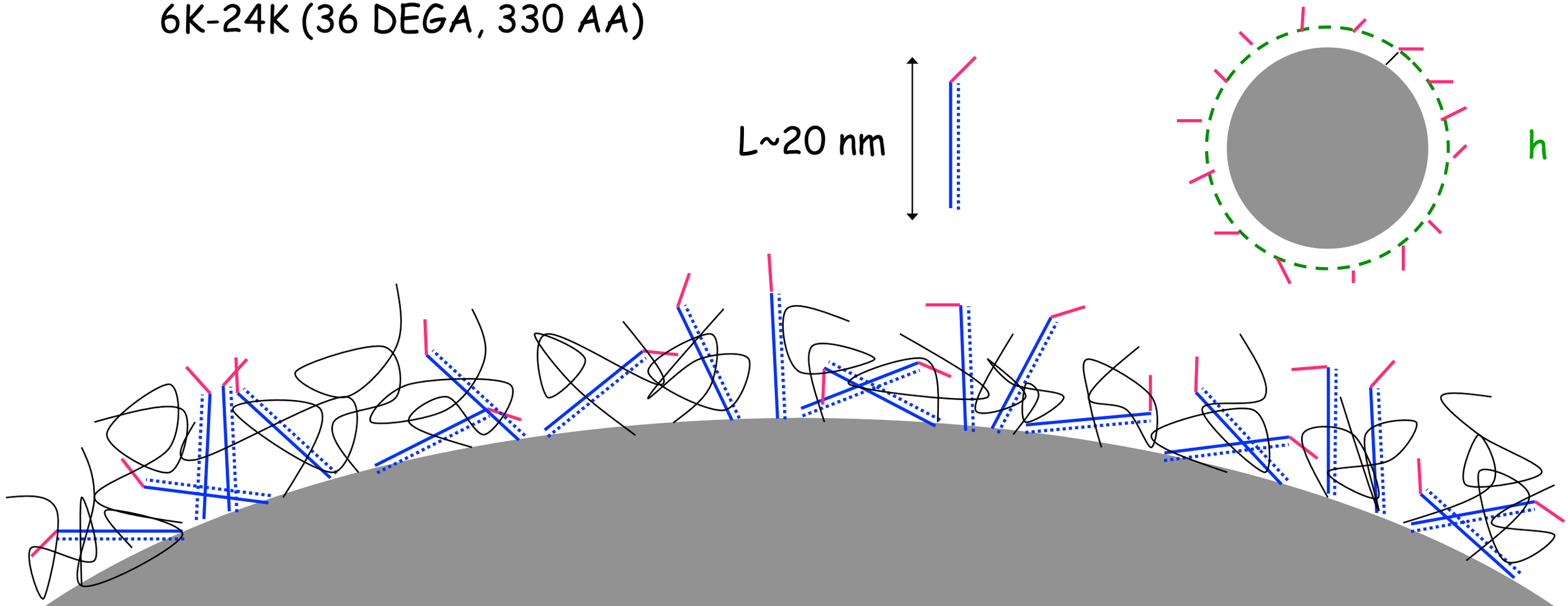
-F108 : neutral triblock copolymer (Pluronic) PEO-PPO-PEO. h ~ 15 nm

-PDEGA-b-PAA : amphiphillic charged diblock copolymer. (Rhodia Inc. Cranbury)Poly(diethyleneglycol ethylether acrylate)-Poly(acrylic acid)-

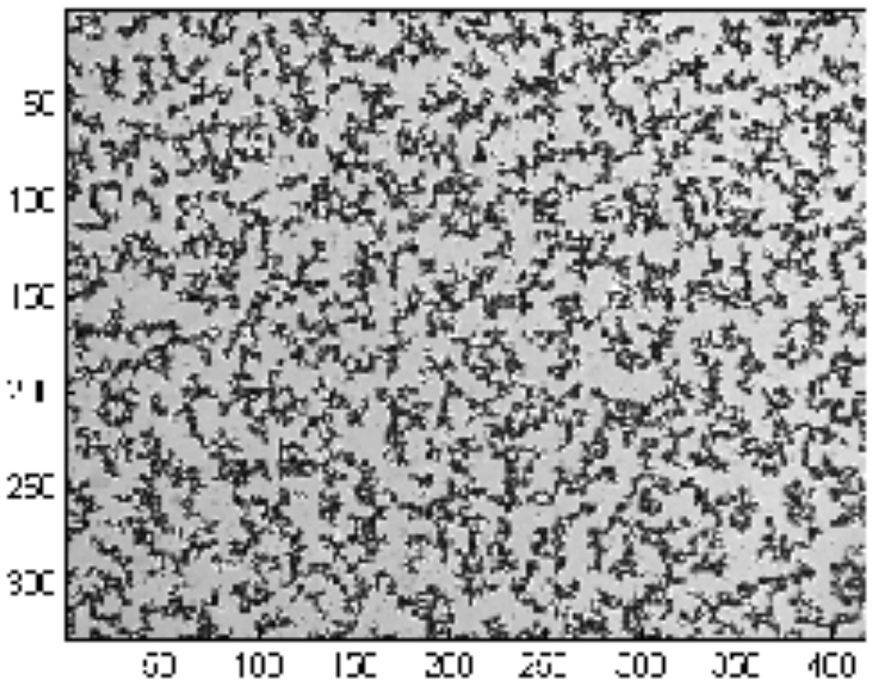
1K-4K (6 DEGA, 55 AA)

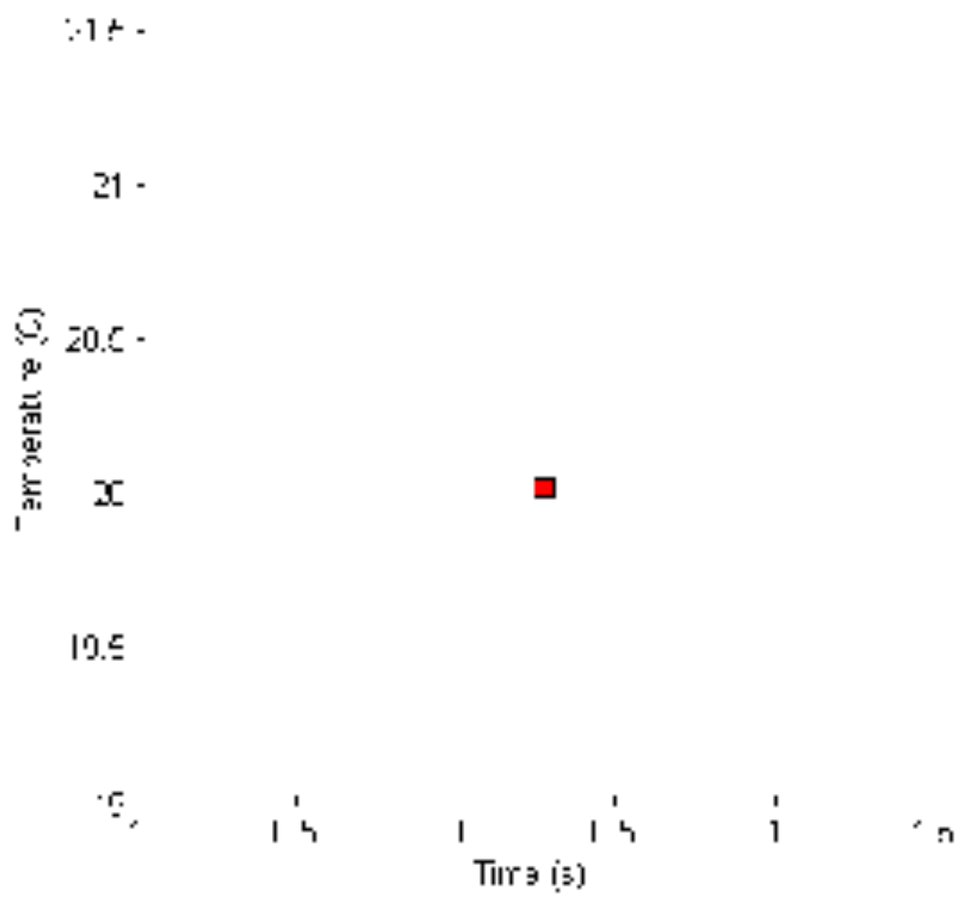
3K-12K (18 DEGA, 165 AA)

6K-24K (36 DEGA, 330 AA)



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 (1957), 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

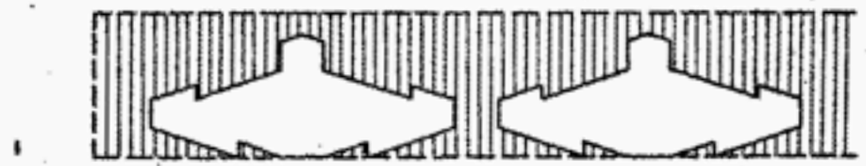


Fig. 1. Seeded Crystal.

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.

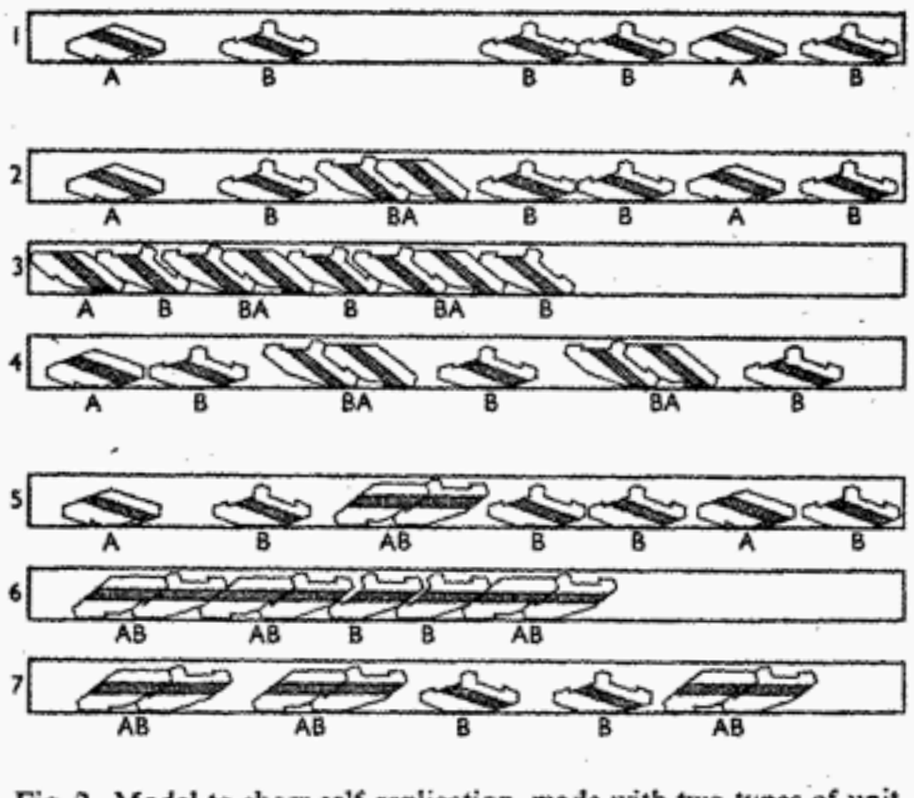
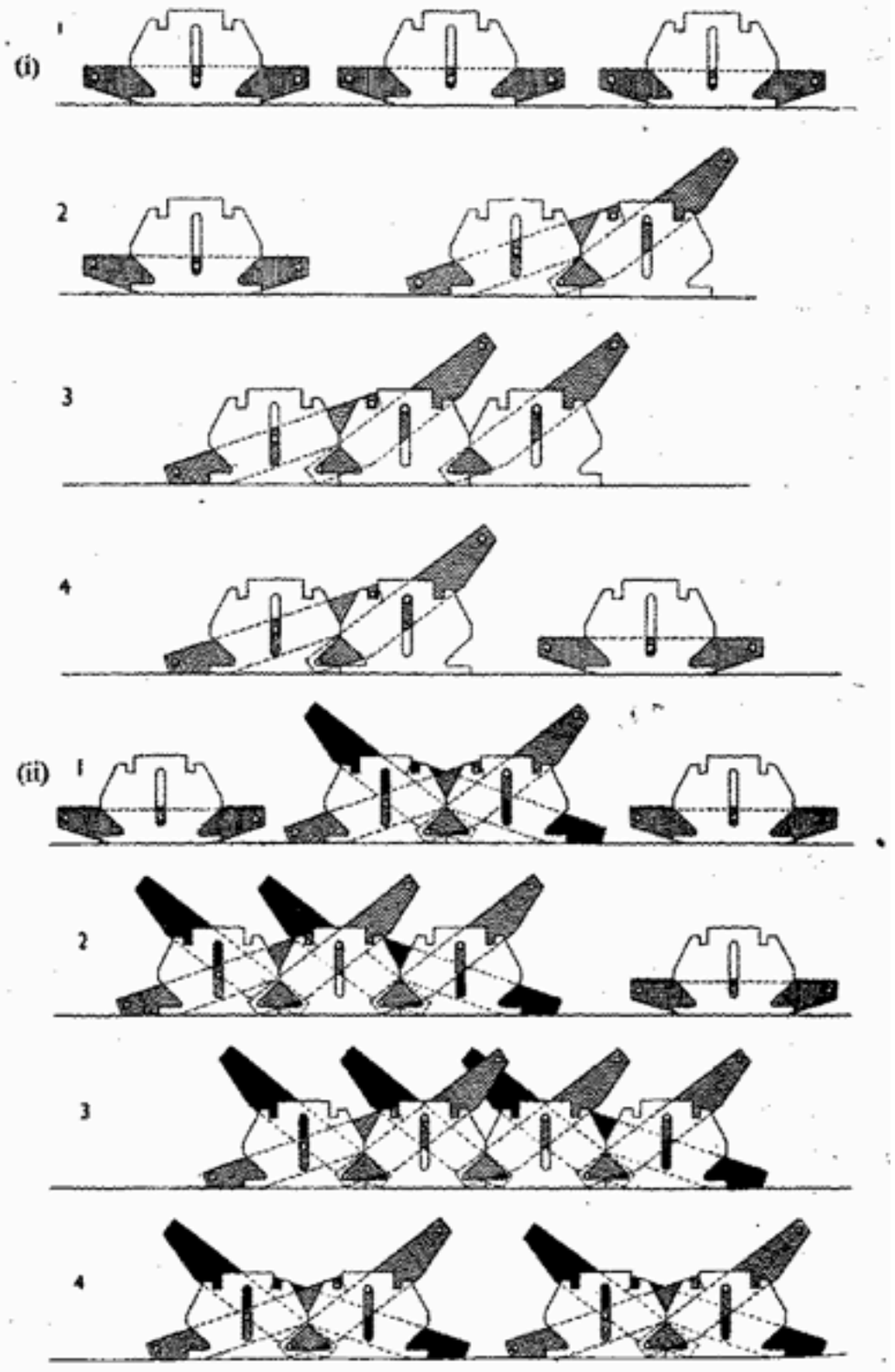


Fig. 2. Model to show self-replication, made with two types of unit, A and B.

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.
6. Conglomeration produced by horizontal shaking.
7. After separation two new pairs AB are seen to have been generated.

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.



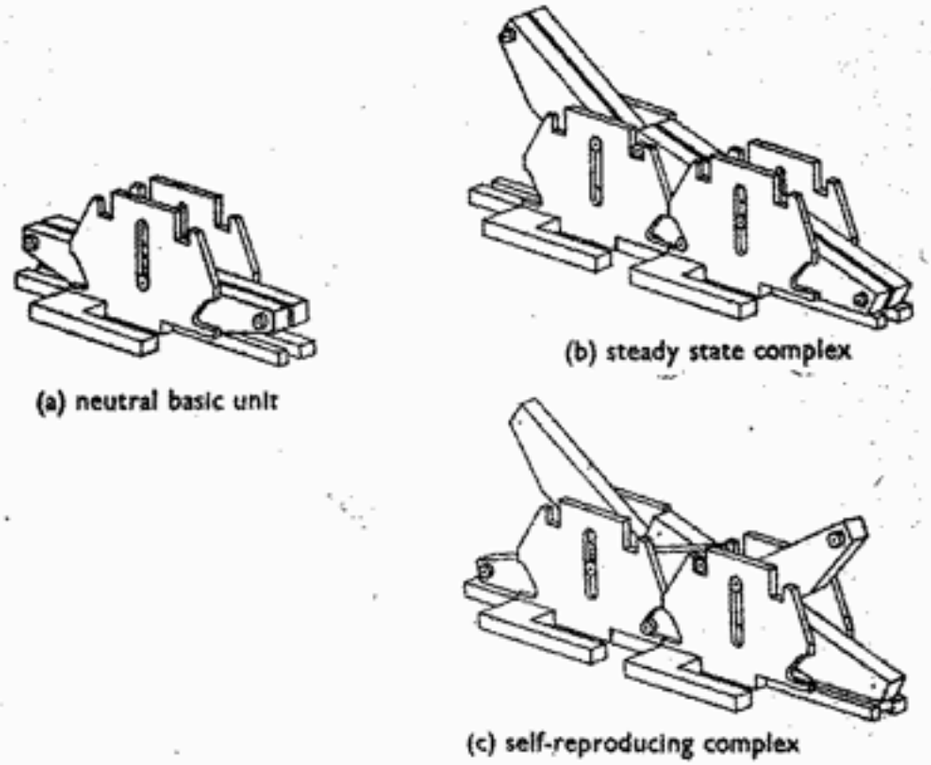


Fig. 7. Exact drawings of working models.
(a) Dimeric unit in neutral phase.
(b) Activated complex which maintains its steady state when fed with neutral units.
(c) Activated complex which reproduces itself when fed with neutral units. The lateral hooks indicate how a chain of such complexes can be constructed.

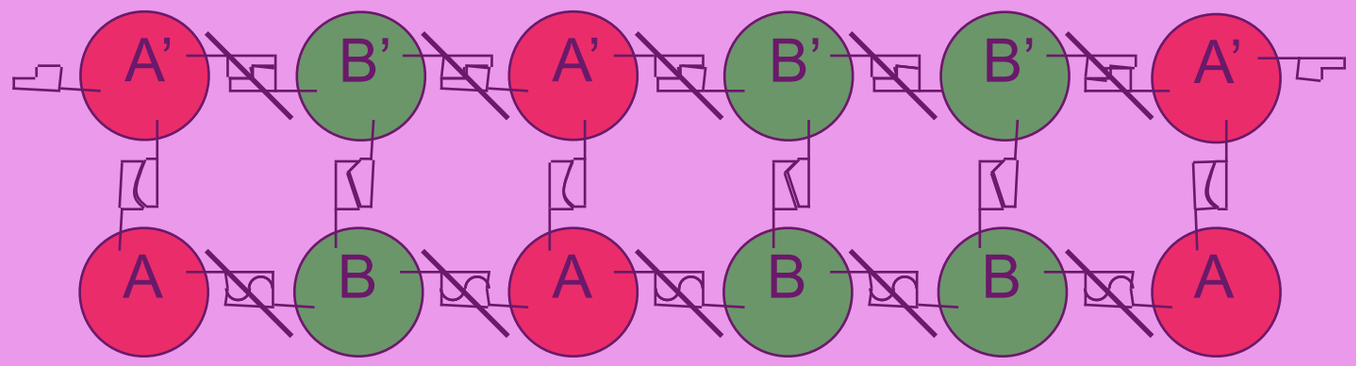
as with forms described earlier. Fig. 9 indicates how the principle of feeding from semi-crystalline chains of natural elements can be applied to this type of reproduction. Here the synapton is five-fold instead of being two-fold, as in Fig.8. The arrangement of (+) and (−) tilting could theoretically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

Some people object to these models because, they say, this is not how desoxyribosenucleic 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

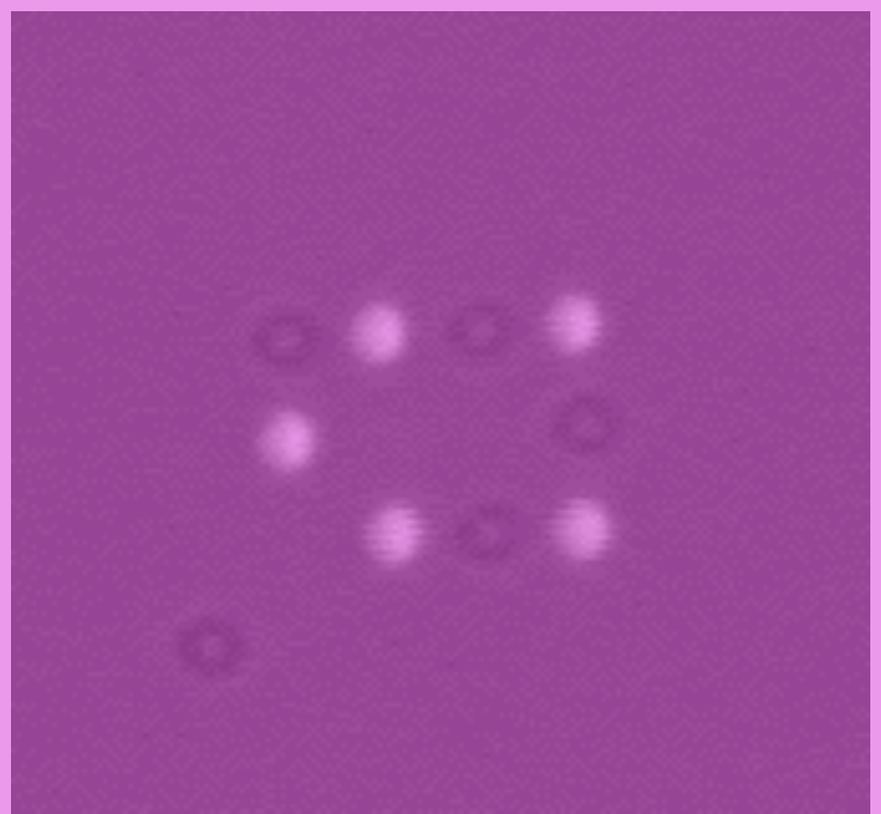
Seed



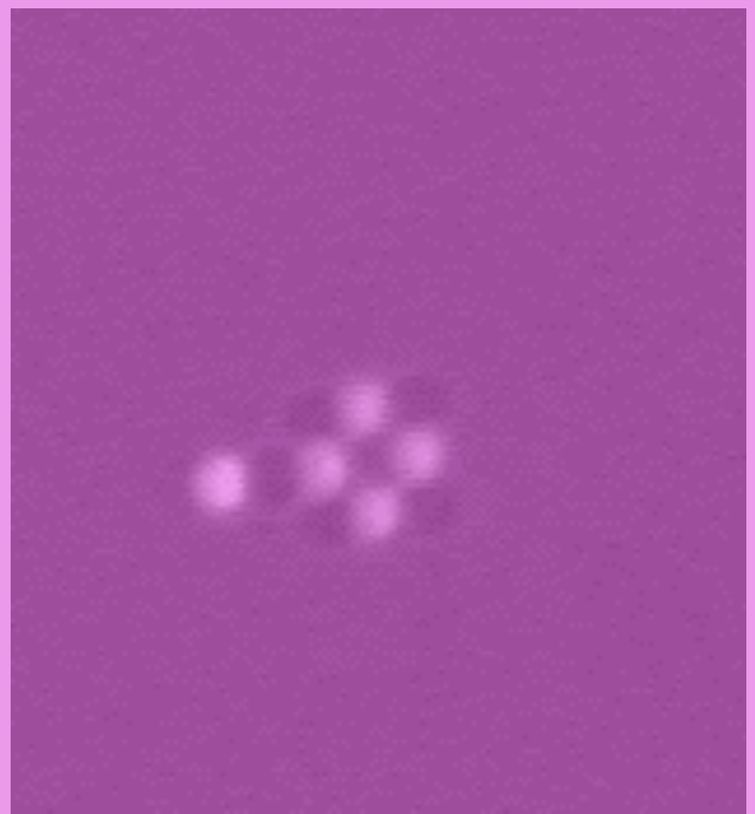
exposure to UV

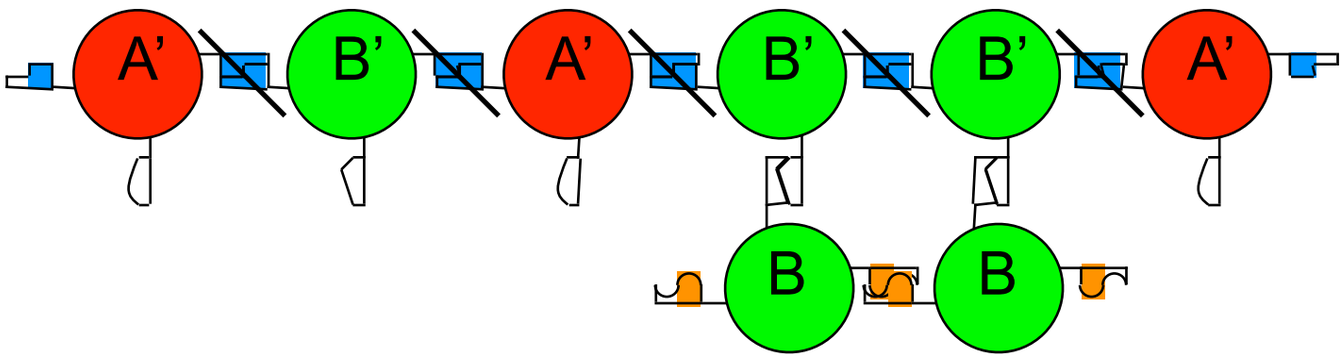
raise T
above Tmelt

Tweezer assembly of seeds



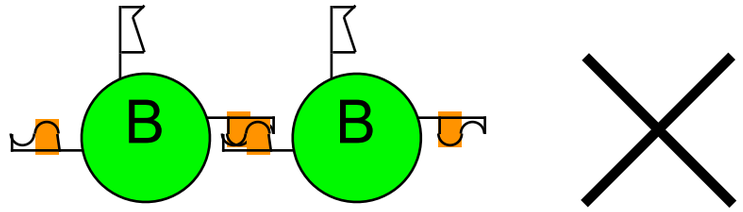
Seeds are colloidal particles





on seed high conc palindrome

$T < T_{palindrome}$



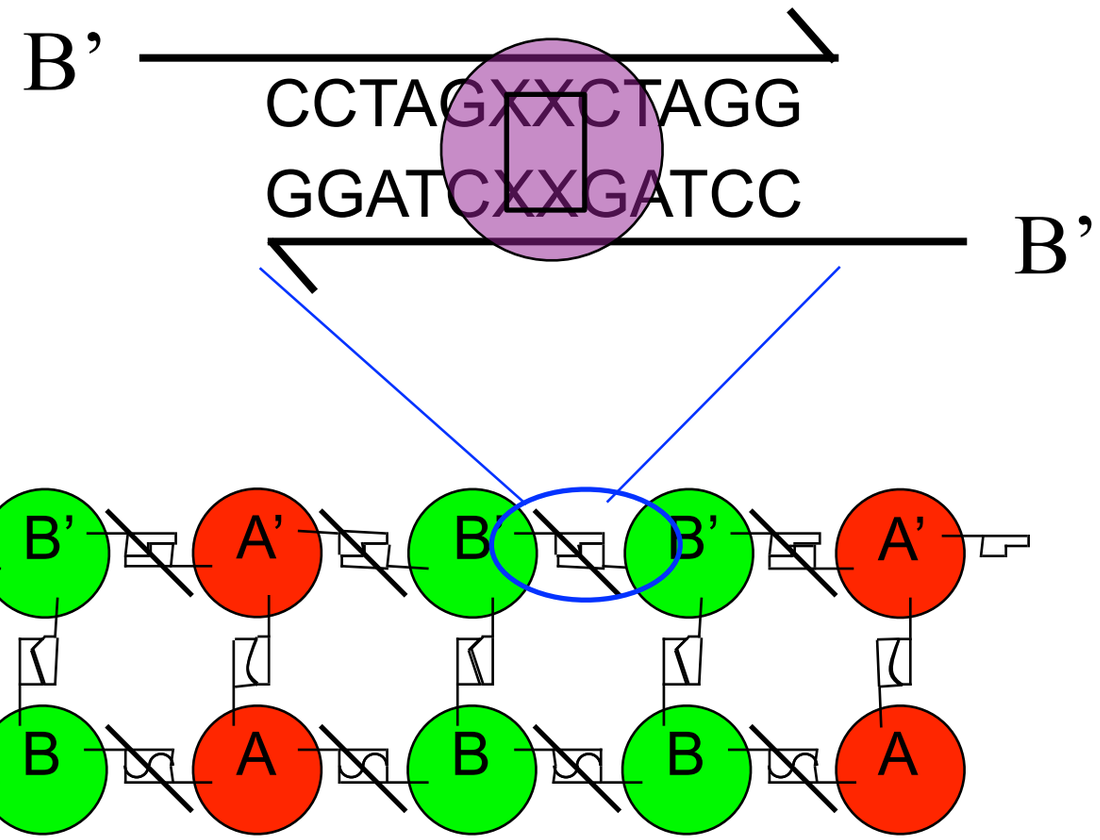
in soup low conc. palindrome

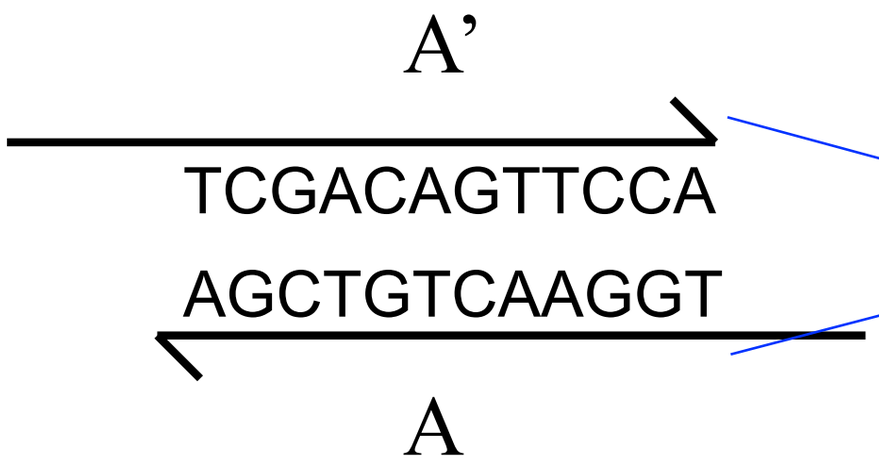
$T_{palindrome} < T$

Previous generation ‘catalyzes’ ligation of next generation

How can we do this?

Palindromic
Longitudinal Bonds

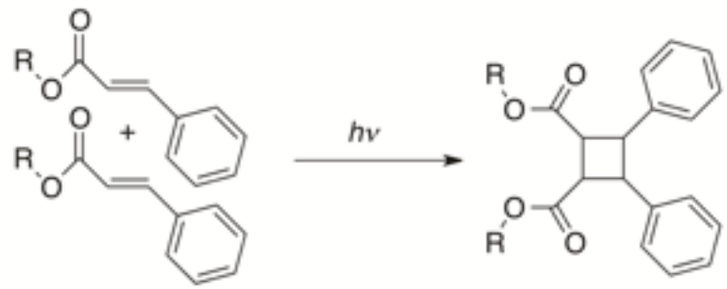




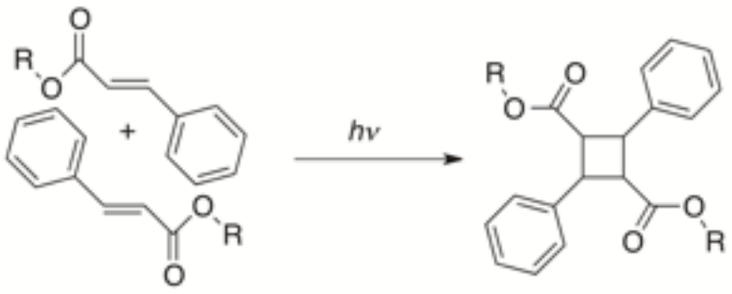
Watson - Crick
Transverse Bonds

New UV activated crosslinker – Cinnamate

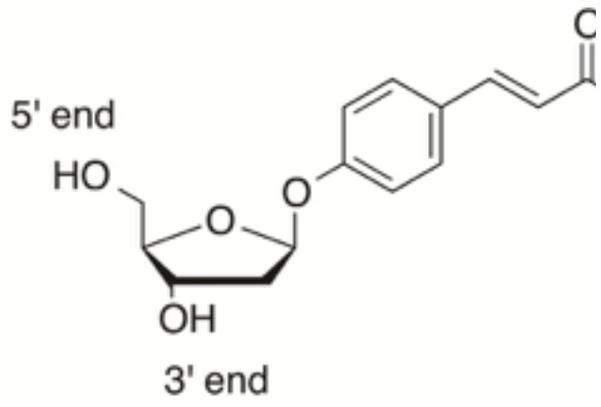
Head to head cycloaddition:



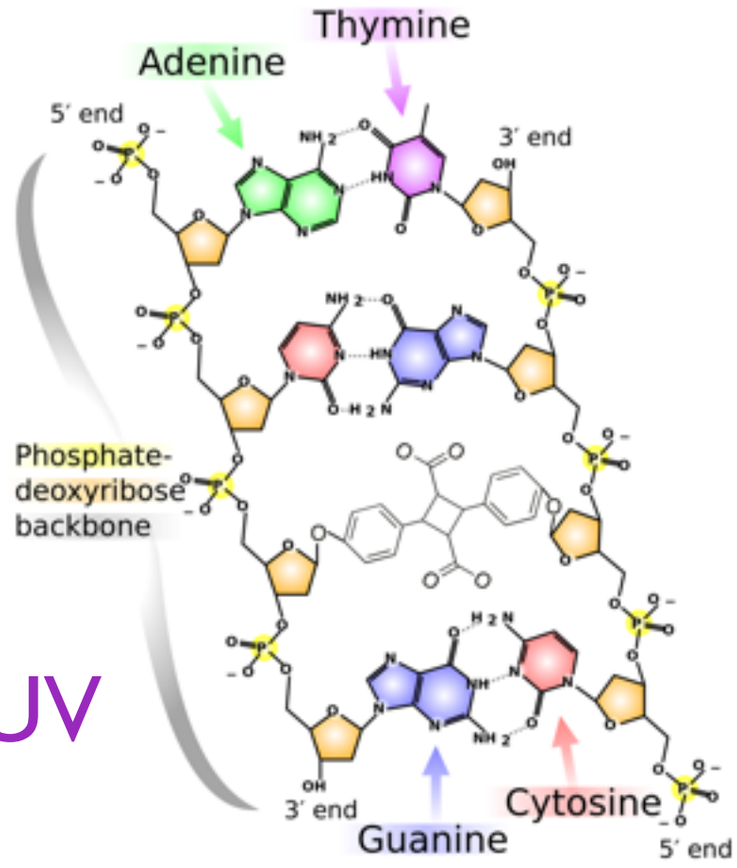
Head to tail cycloaddition:



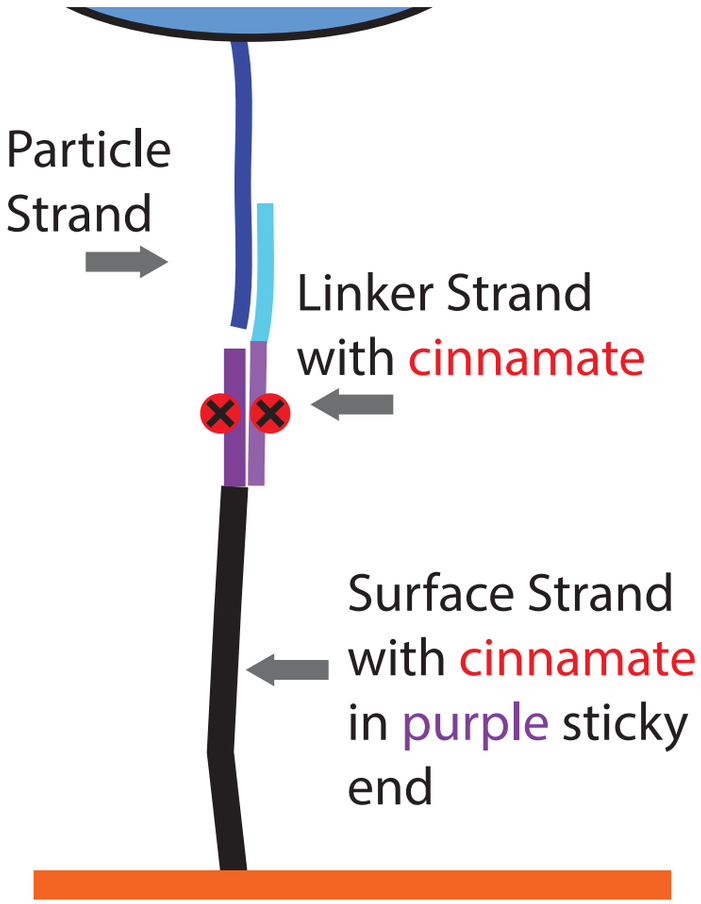
Weck Group



UV



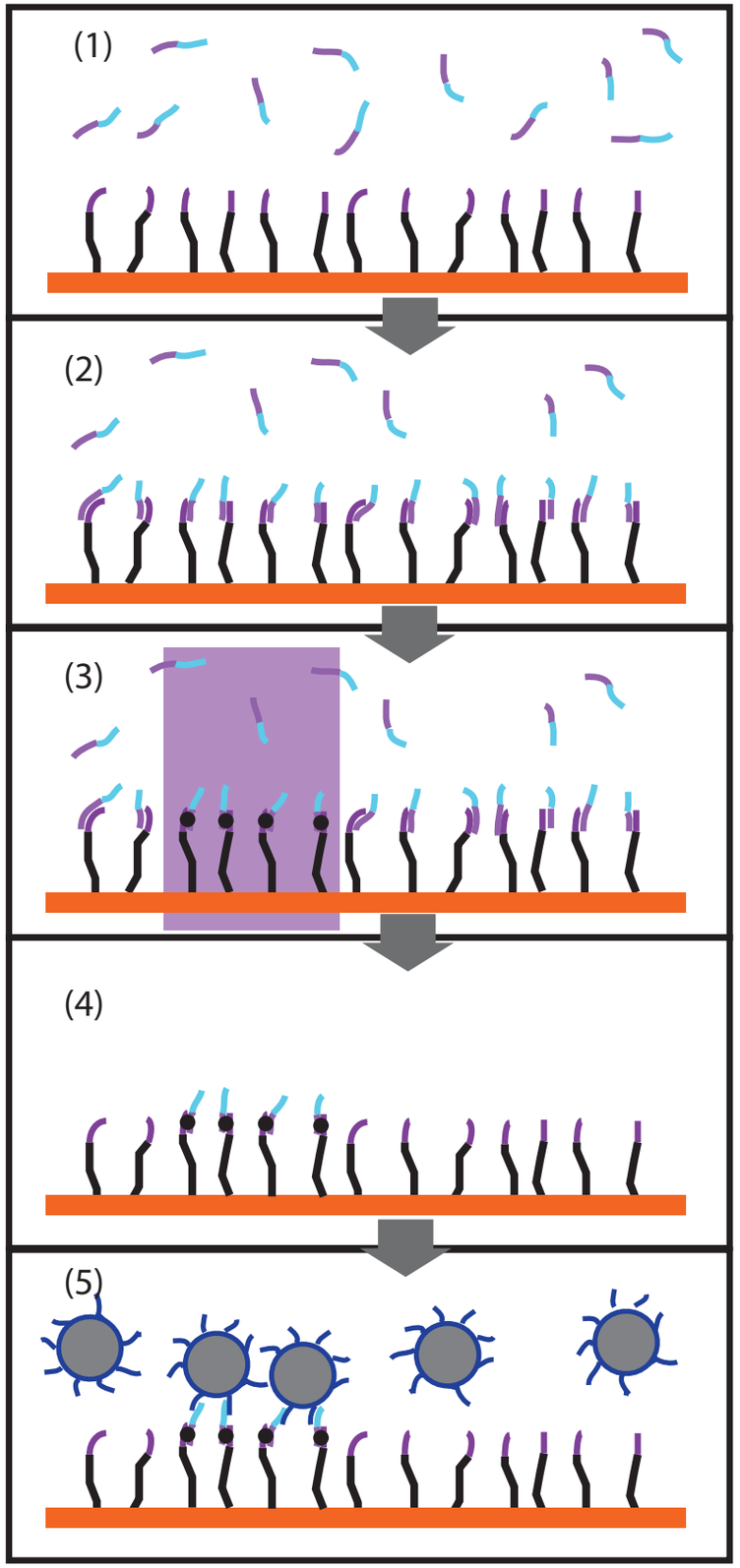
Photolithography with Cinnamated DNA



Surface strand
5'-RSS-50basesBackbone-TTGAGAAATGC*CGTAAAGAGTT-3'

Linker Strand
5'-CATCTTCATCC AACTCTTTACG*GCATTTCTCAA-3'

particle strand
5'-GGATGAAGATG-50basesBackbone-BiotinTEG-3'



High temperature 50°C

Anneal to 25°C

Permanent UV crosslink certain region

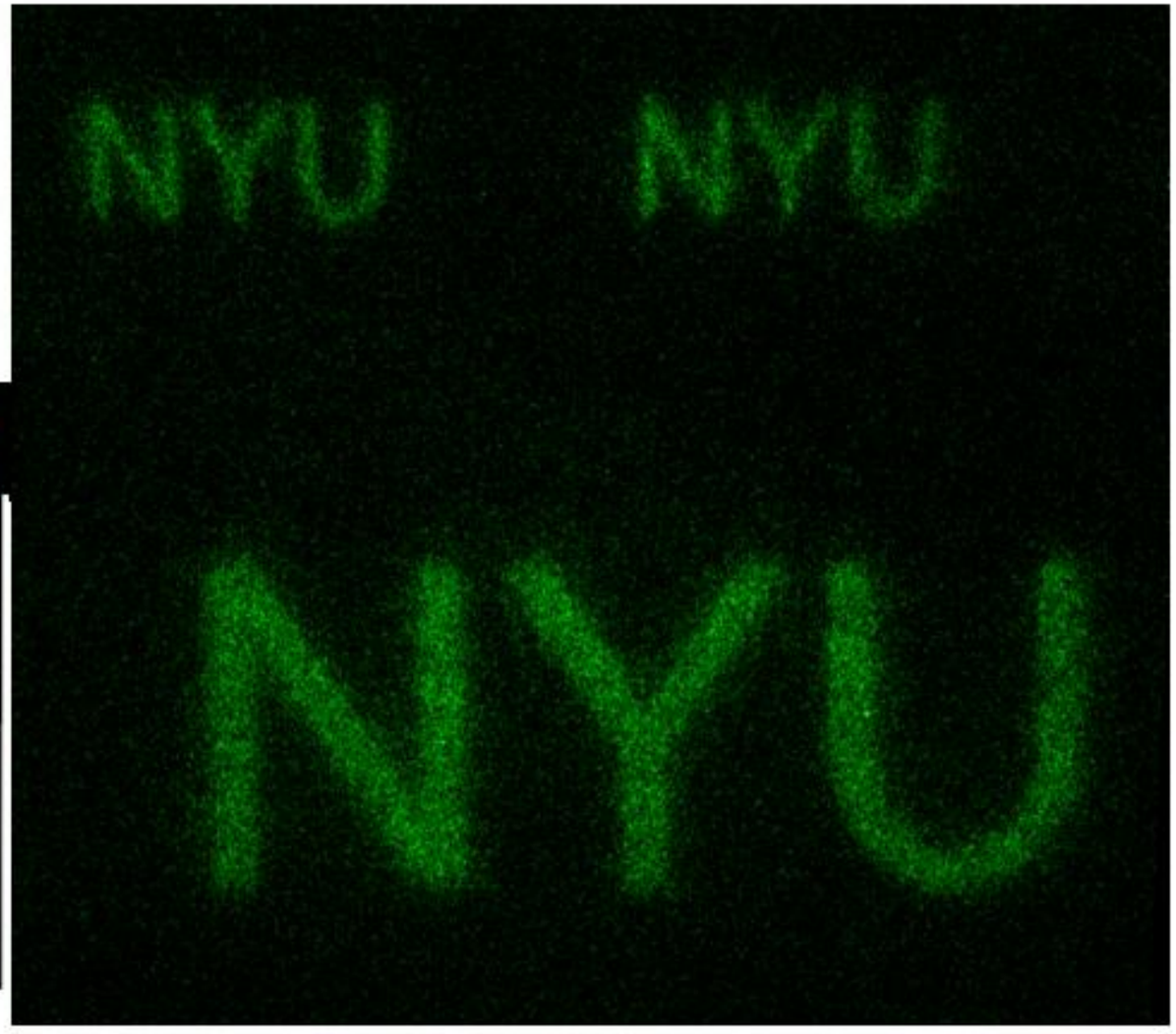
Heat up to 50°C and wash out unbound strands

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

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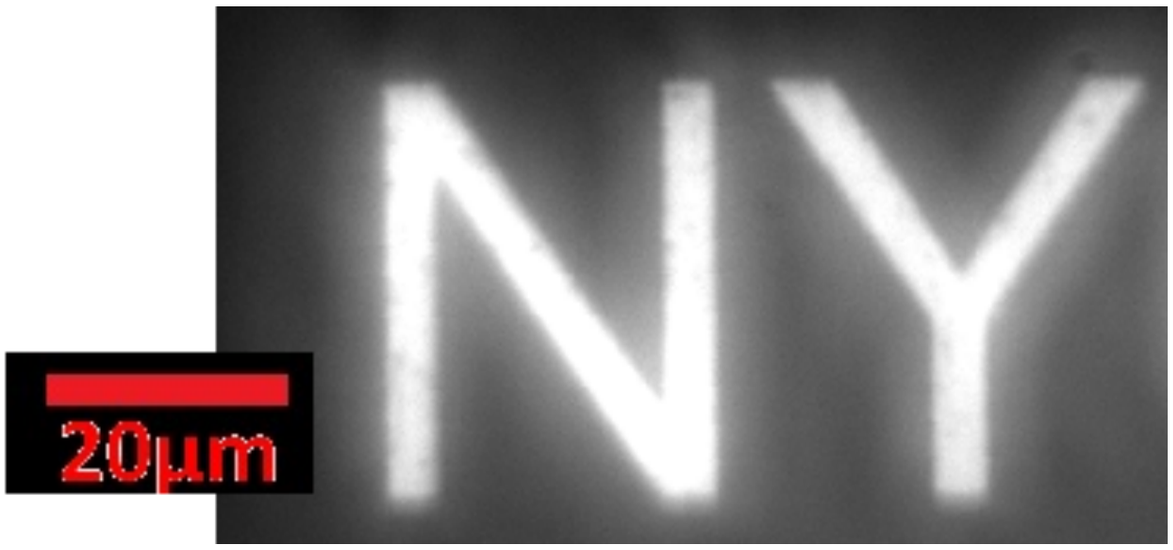
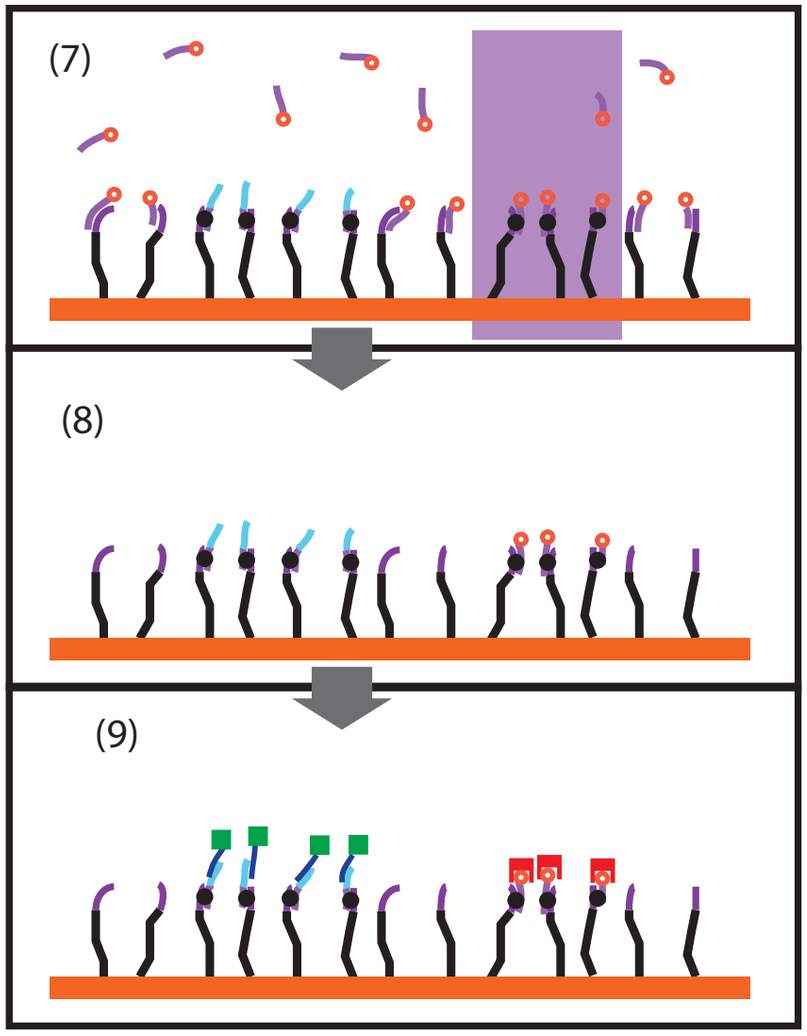
Melting of ‘NY’

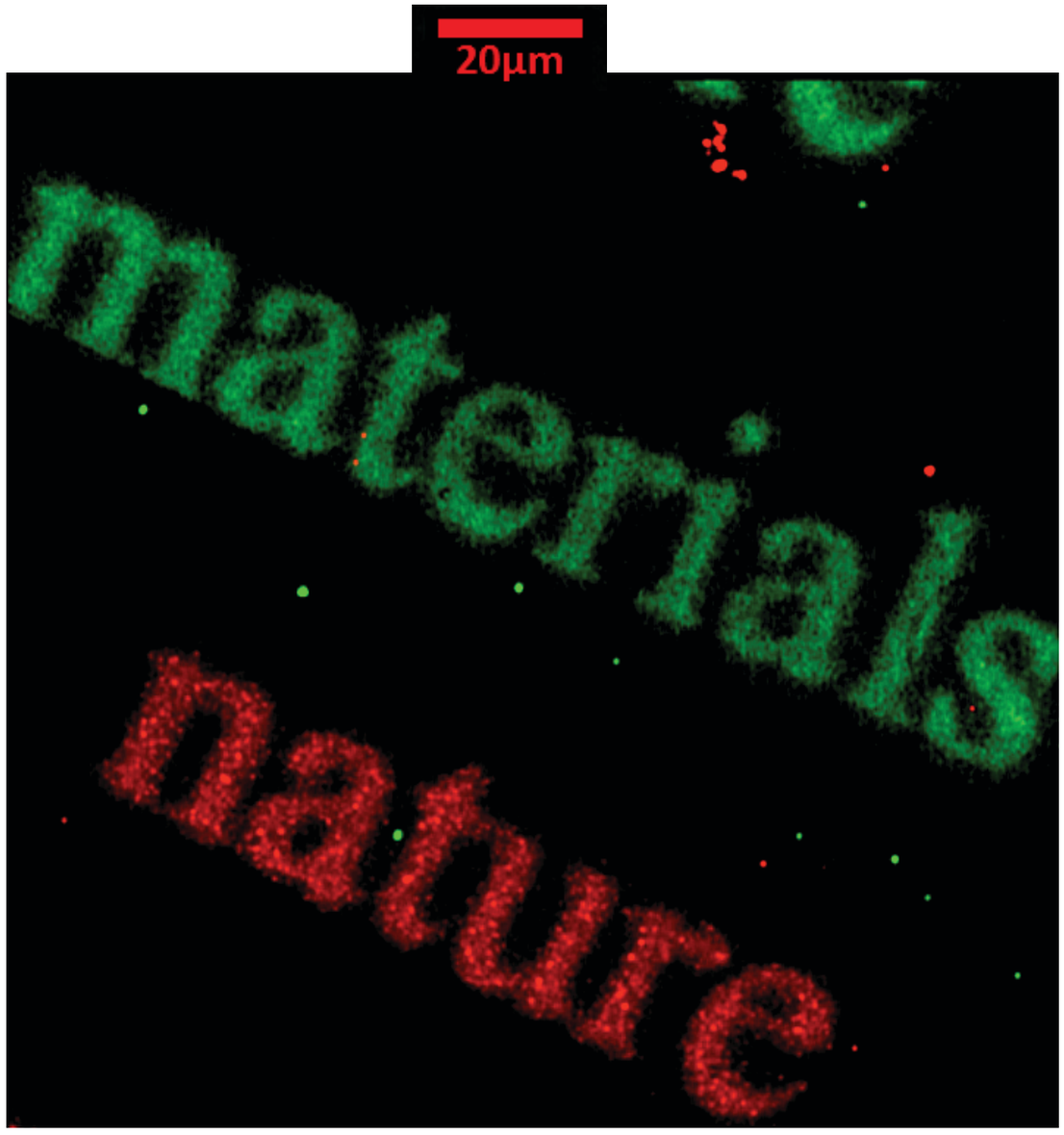


x3 speed

Multi-functionalized surfaces

We can label different regions with whatever we want





Understanding the physics?

Melting Temperature T_m for Watson-Crick pair

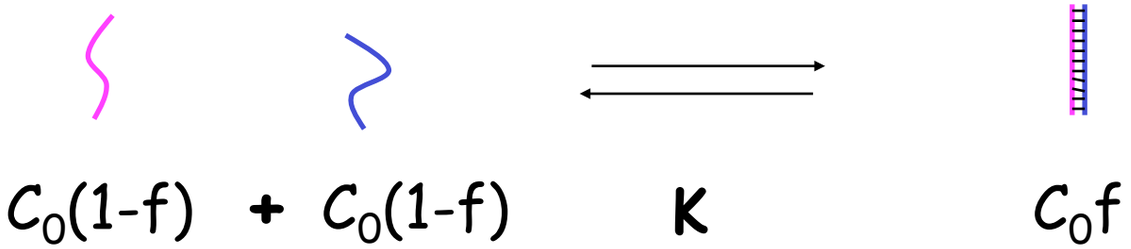
- 11 base Sequence: CCAAGTTATGA
- 50 mM NaCl
- C_0 = 1 μM

f=1/2

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

-ΔH° = -77.2 Kcal/mol
-ΔS° = -227.8 cal/K.mol

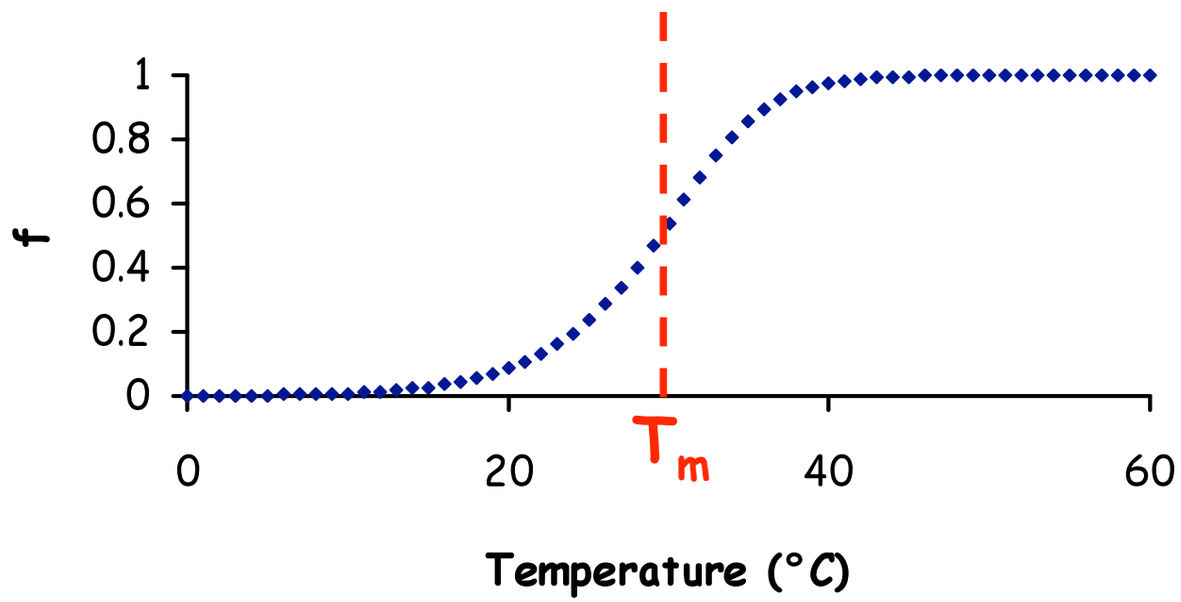
$$T_m = \frac{\Delta H^\circ}{\Delta S^\circ + R \ln \frac{c_0}{2}} = 29.3^\circ C$$



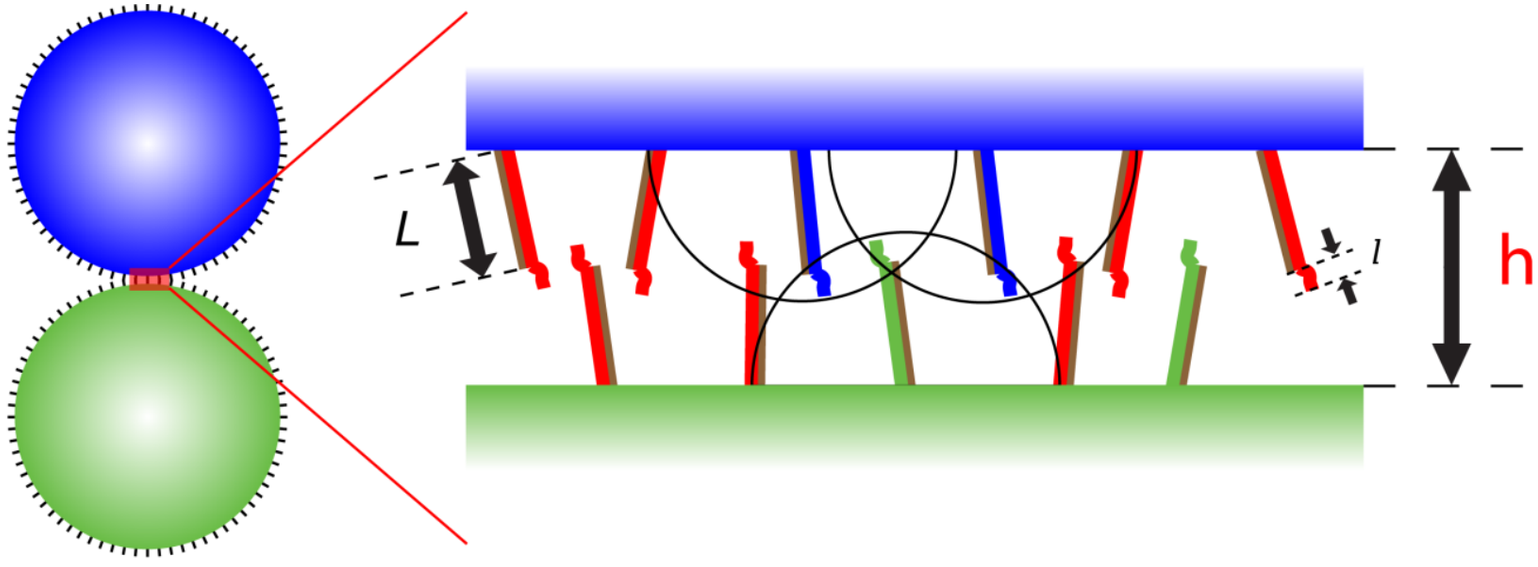
$$K = \frac{f}{c_0(1-f)^2} \propto e^{\Delta G_0 / kT}$$

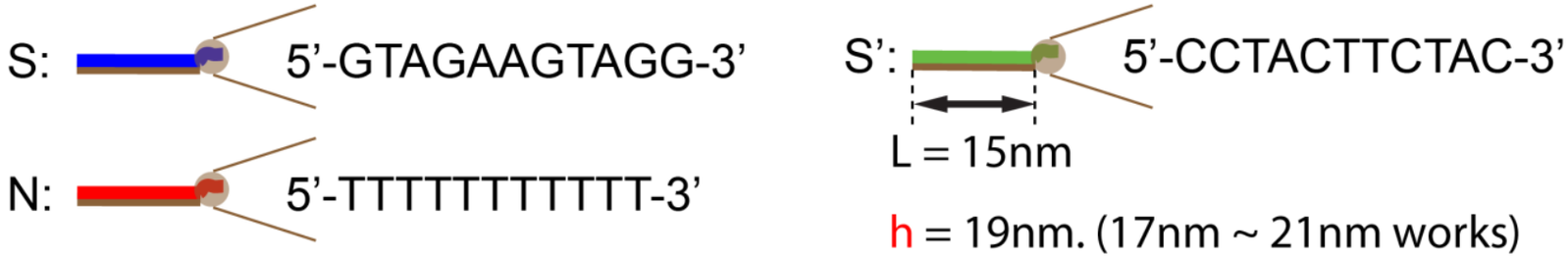
$$f = \frac{\sqrt{4KC_0 + 1} - 1}{2KC_0}$$

DNA Single strand fraction versus temperature



Quantitatively understanding the DNA mediated interactions





Mean Field Approximation:

$$\boxed{Z_s = [1 + k\,\exp(-\beta\,\Delta F_{\text{tether}})]^{N_b}},\ \text{where}\ \ \Delta F_{\text{tether}} = \Delta F^{\circ}_{\text{DNA}} - \text{T}\Delta\text{S}_{\text{p}}$$

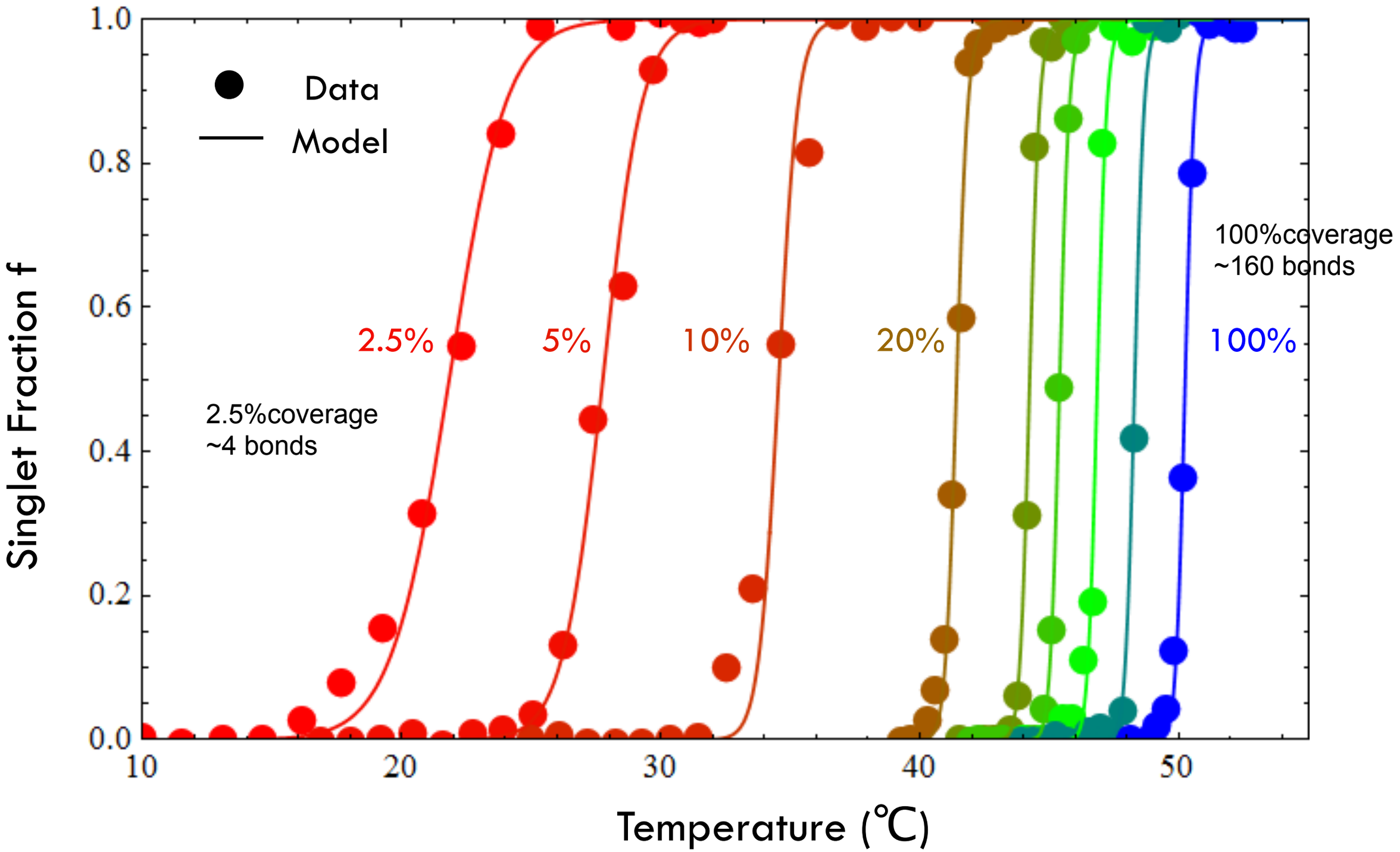
$$\Delta F_p = -RT\,\ln(Z_s - 1)$$

PRL 102, 048301 (2009)
Soft Matter 5, 2422 (2009)

Remi Dreyfus | Mirjam Leunissen | Kun-Ta Wu | Lang Feng

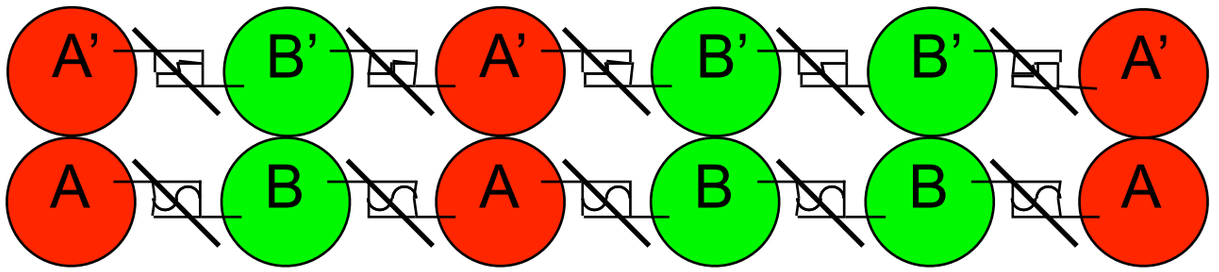
Thermodynamics

$$\Delta F_{bead} = -N_{max} k_B T ln(1 + k e^{-\Delta F_{tether}/k_B T})$$

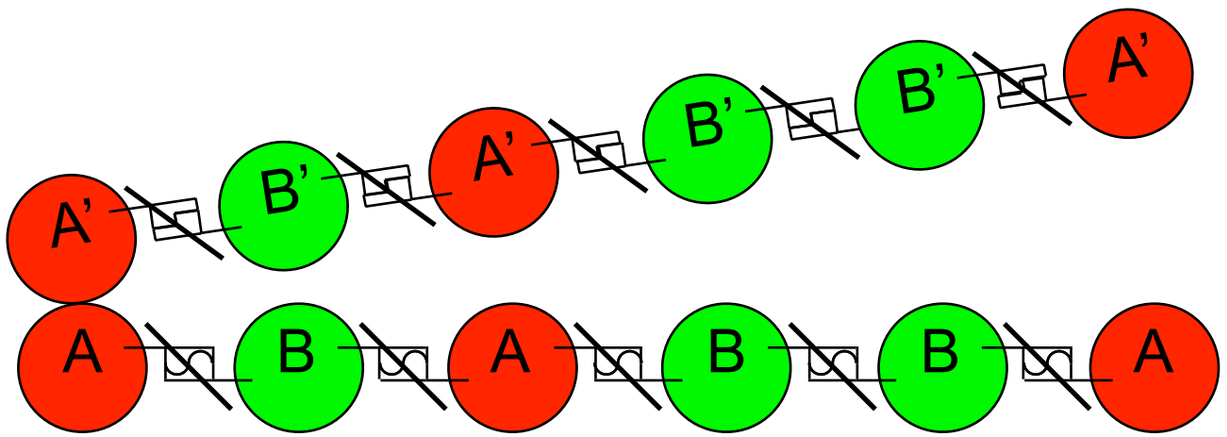


Problems with Palindromes

Basic Replication Scheme



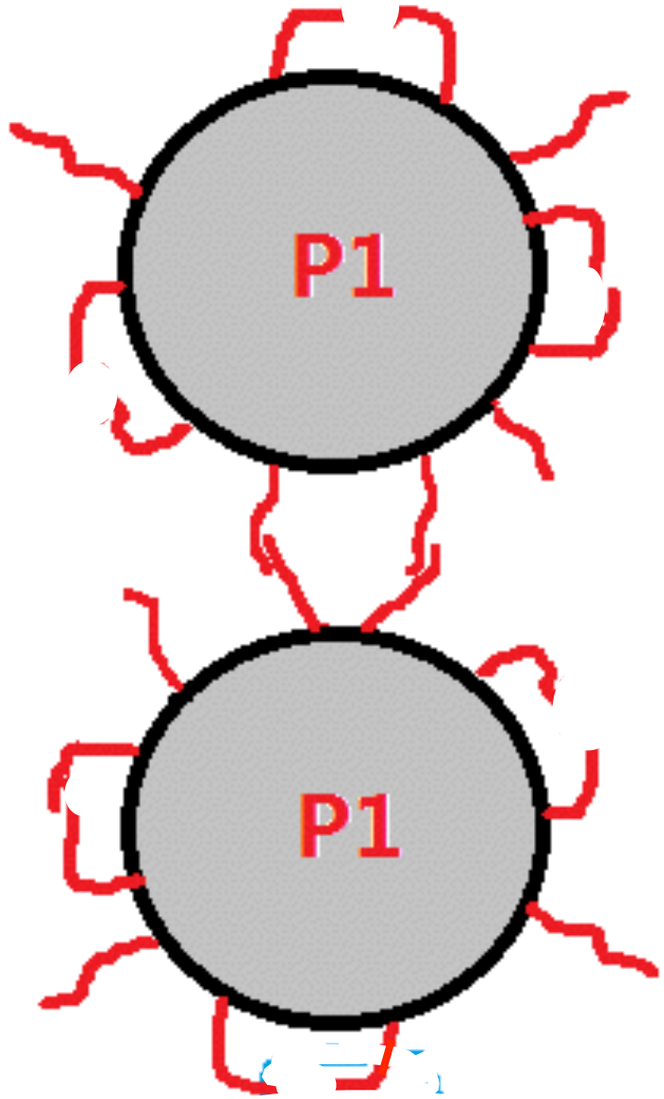
Assemble daughter



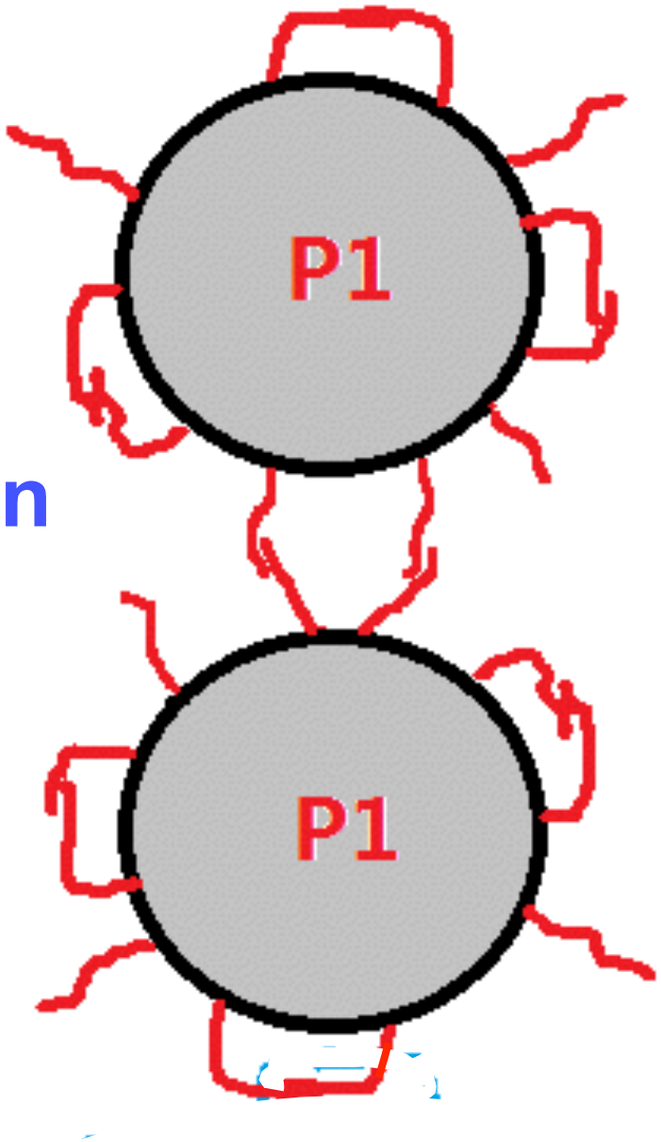
Heat up

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

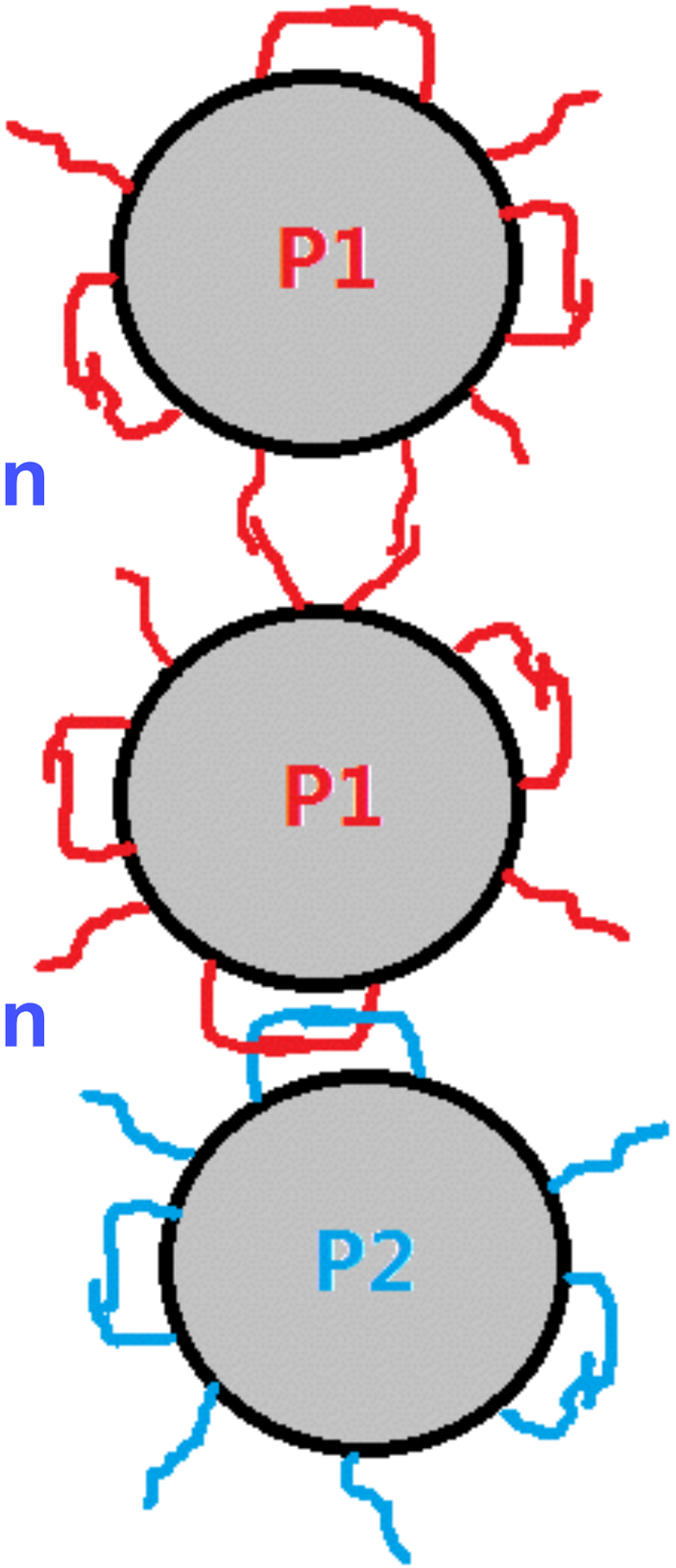


Which means they can also form loops

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



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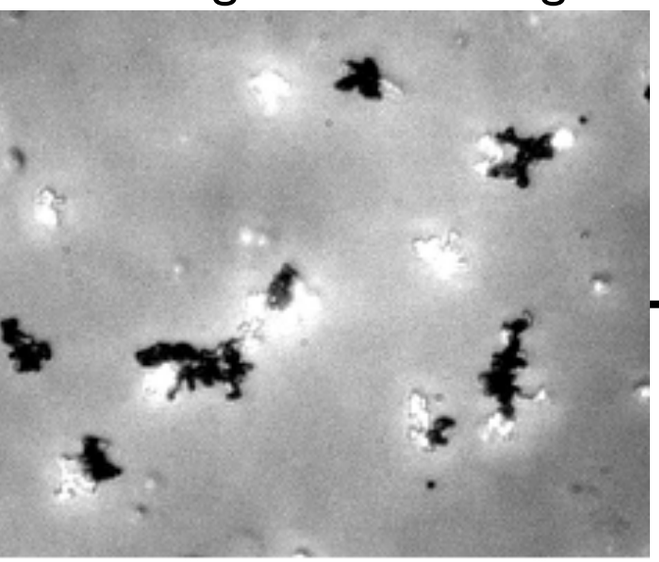
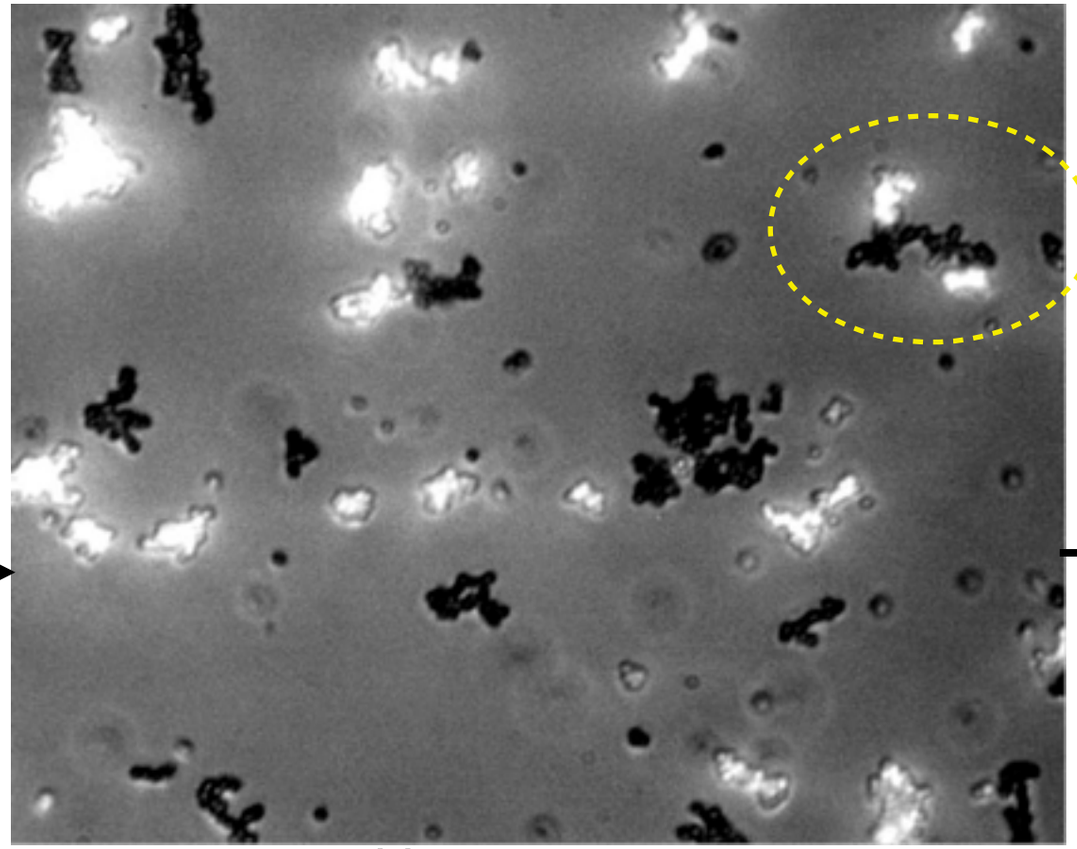
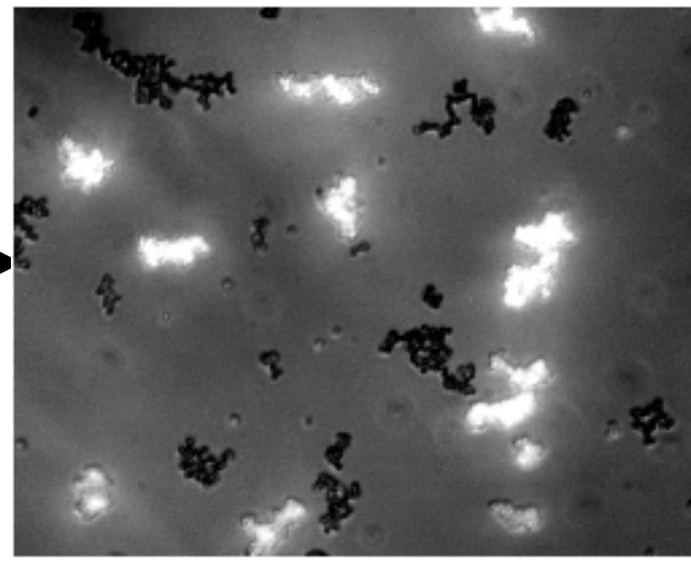
entanglement binding

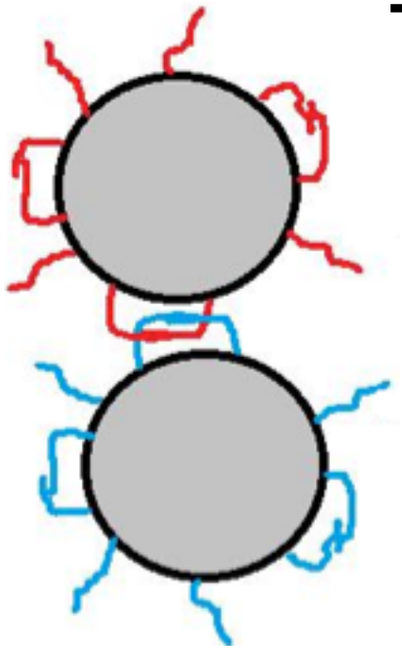




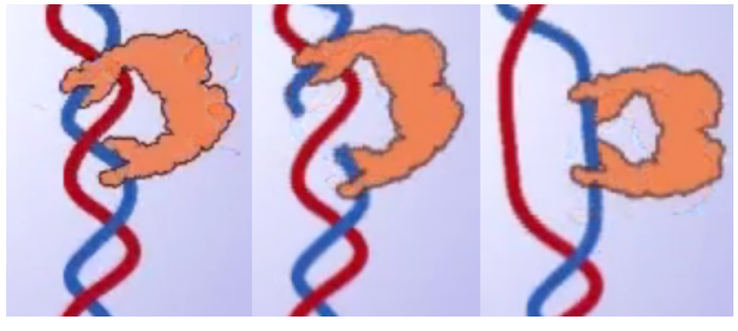
adding topoisomerase

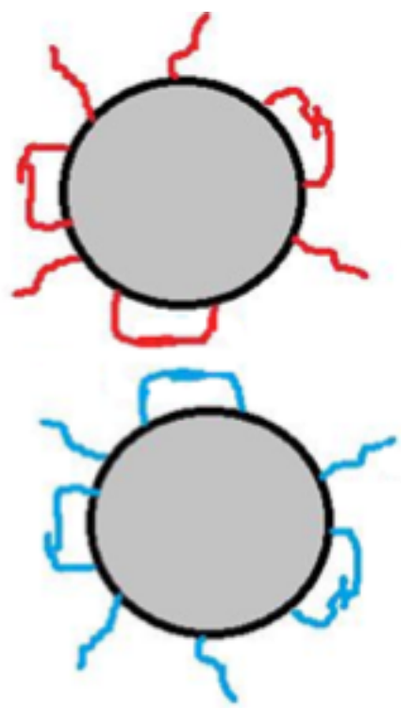


Topoisomerase I should prove this topological interaction!



Topoisomerase I unknot ssDNA or dsDNA with nicks

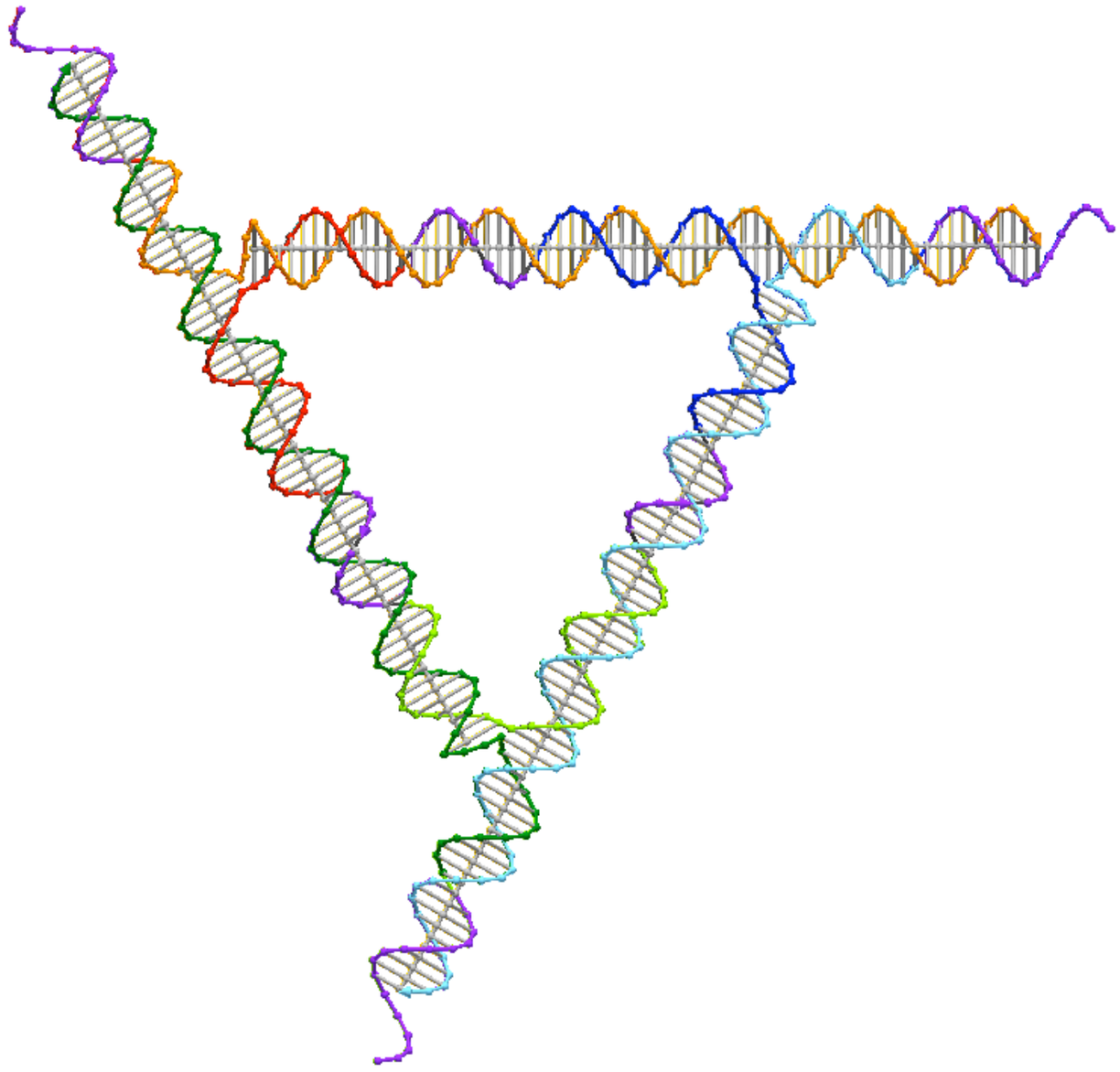




Phys. Rev. Lett. 109 , 188301, (2012)

DNA Tiles

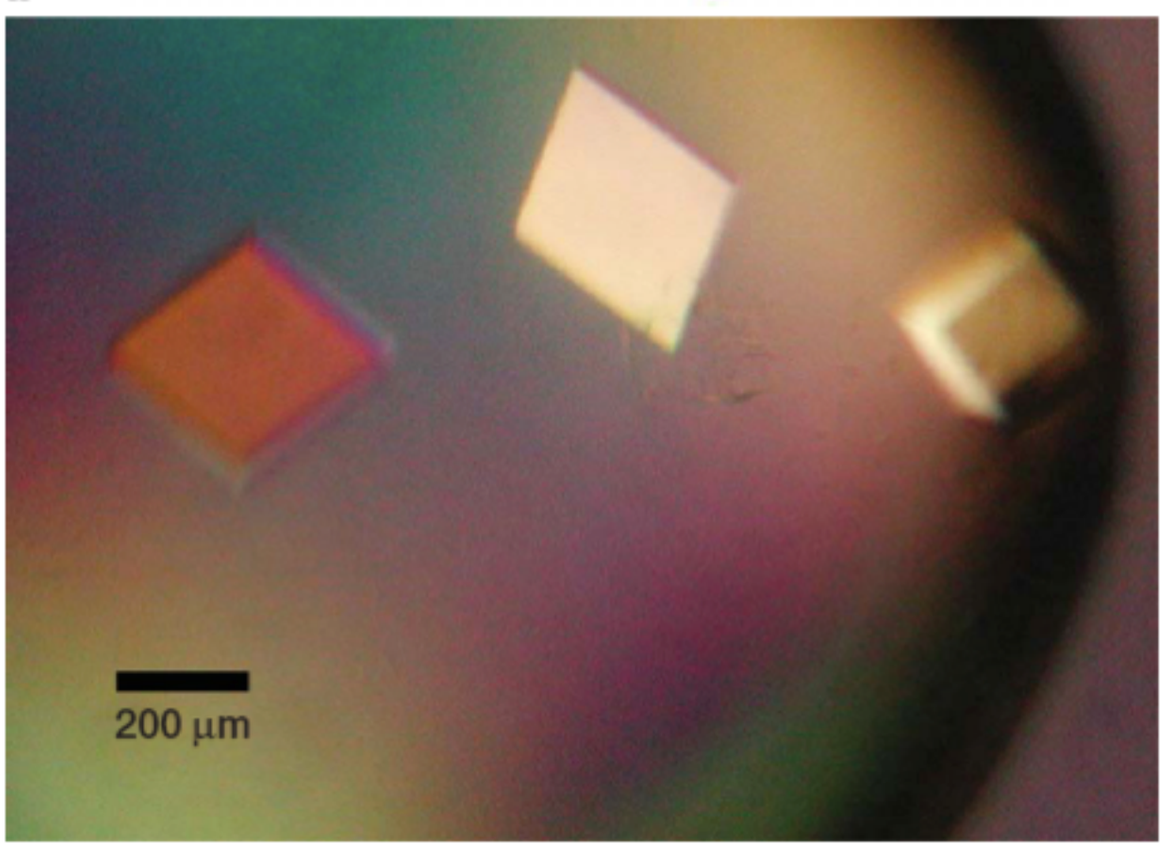
Ned's Simple Bulged 3-Arm Junction Triangle (1996)



J. Qi, X. Li, X. Yang & N.C. Seeman,
J. Am. Chem. Soc., **118**, 6121-6130 (1996).

a

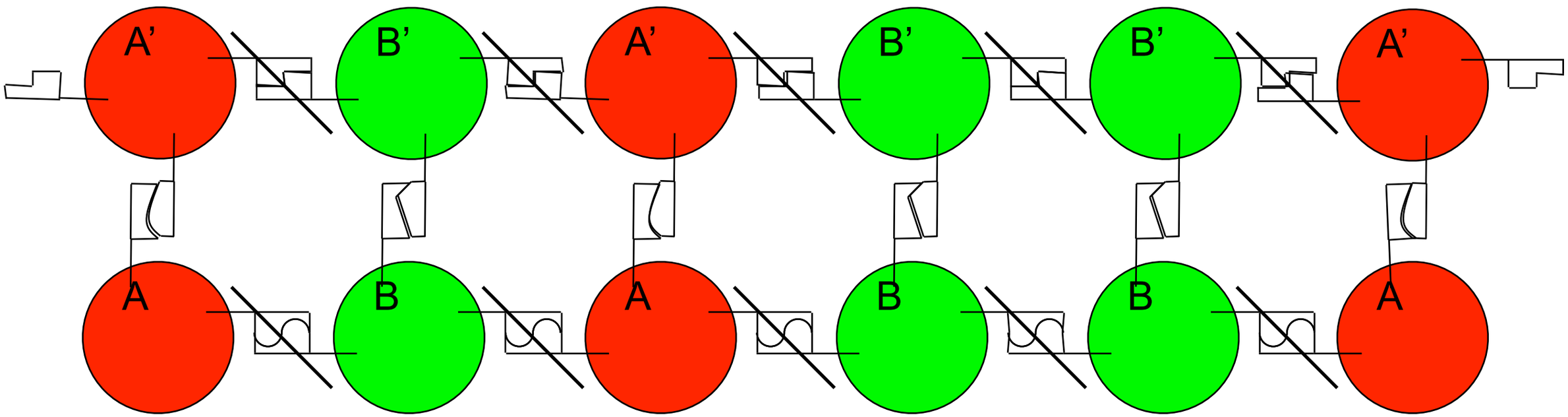
b



Jianping Zheng, Jens J. Birktoft, Yi Chen, Tong Wang, Ruojie Sha, Pamela E. Constantinou, Stephan L. Ginell, Chengde Ma
& Nadrian C. Seeman
Nature 3 September 2009

Different systems, same idea

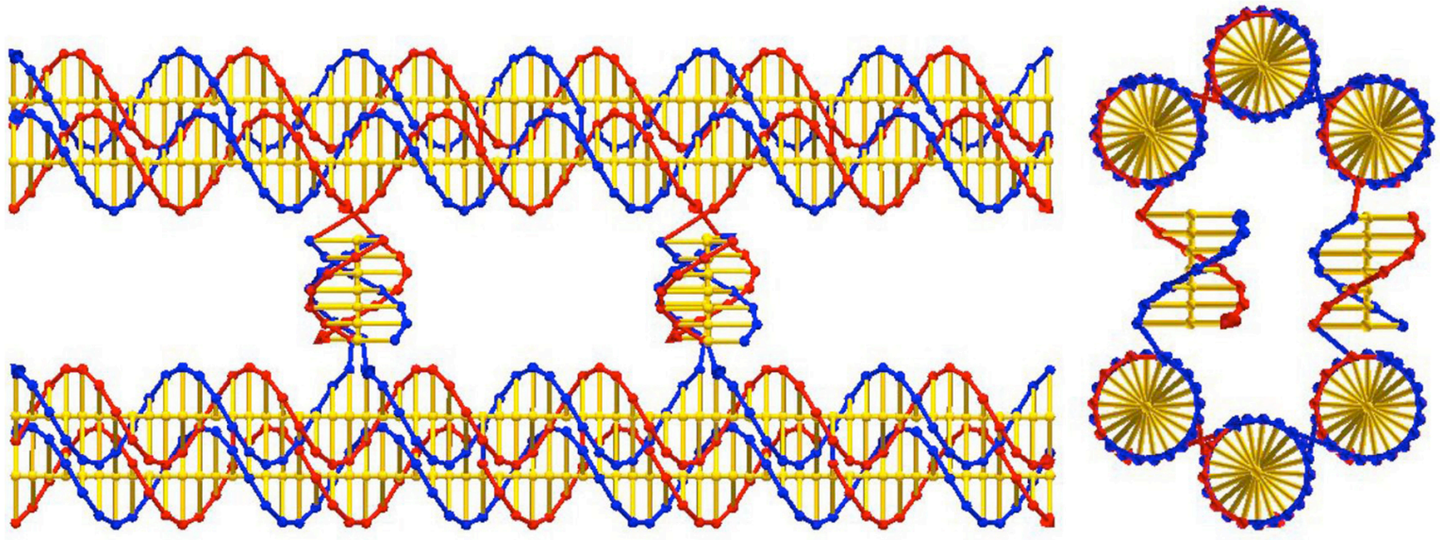
Colloids



BTX DNA Tiles

BTX
bent triple
crossover
motif

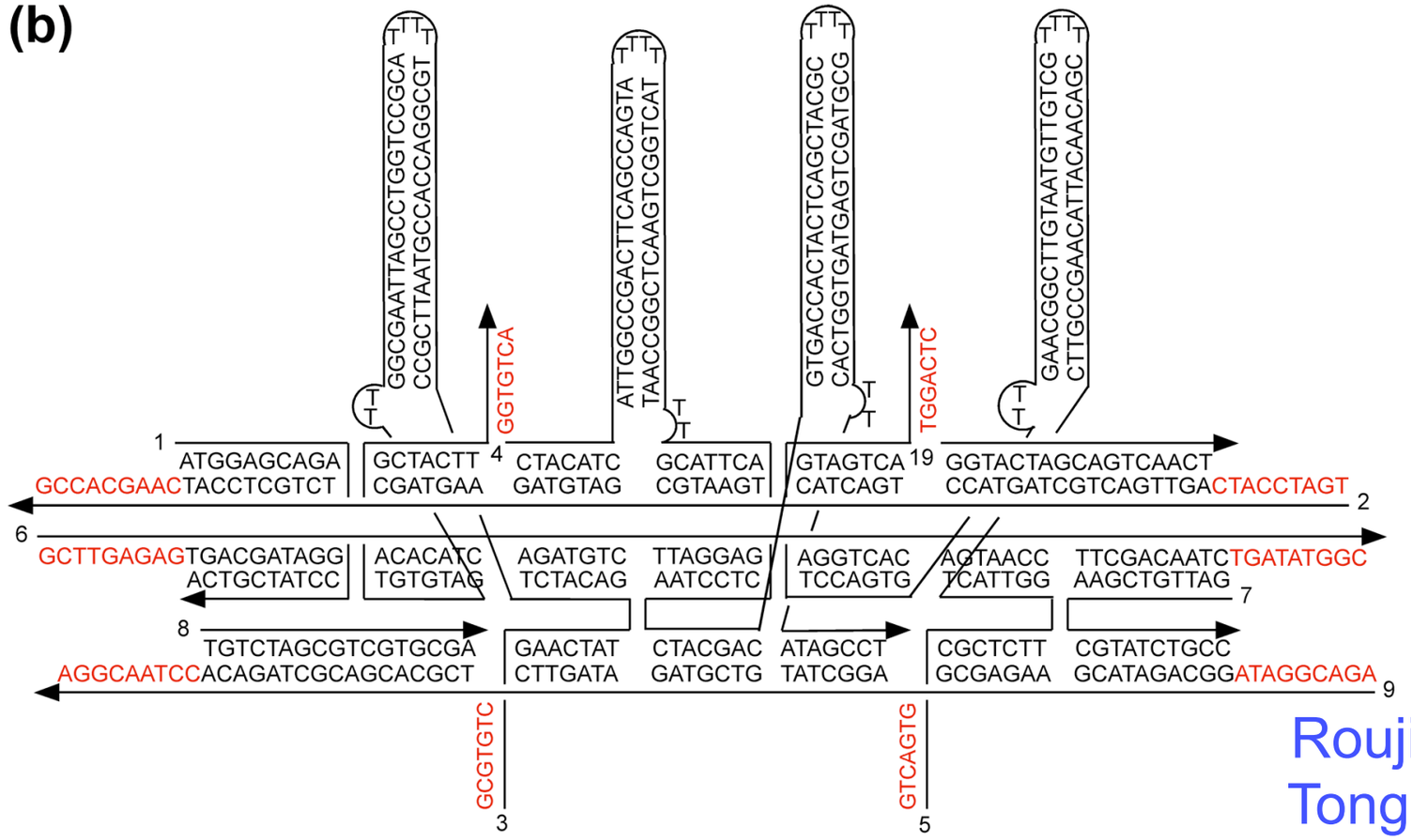
(a)



Side View

Cross Section

(b)



Roujie Sha
Tong Wang