*Summer School on Soft Matter Self-Assembly, 2015, June 28-July 7*

# Lecture 3: DNA-coated colloids

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# You can build anything with Lego

Big Ben


different functionalities

Sagrada Familia

different structures

Red Square

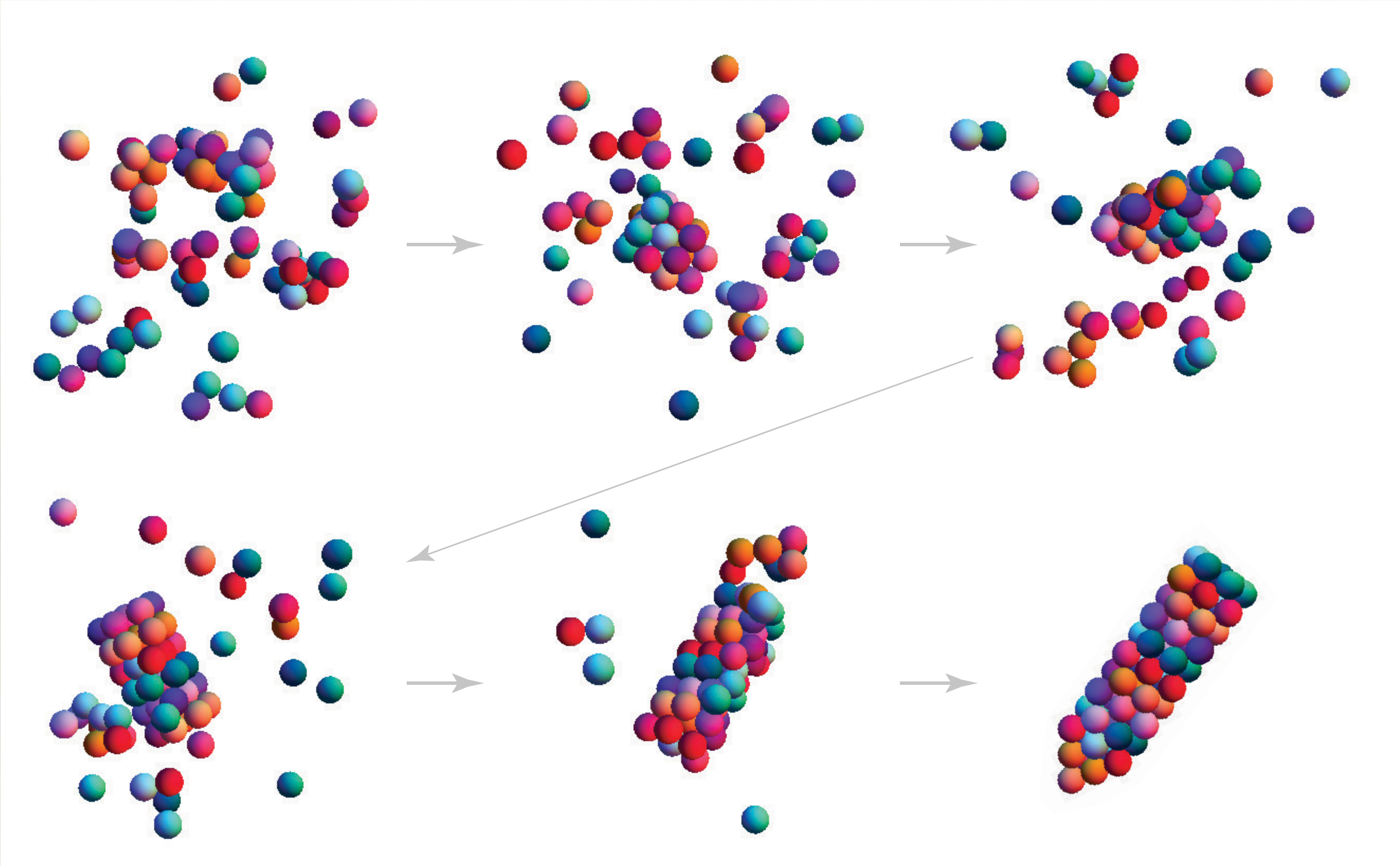
multiple materials

Developing colloidal Lego

# Building "Big Ben" with colloids

Assembly of 69-particle "Big Ben" (computer simulation)

Each color particle signifies a different set of pairwise interactions



Zeravcic, Manoharan, & Brenner, PNAS **111**, 15918–15923 (2014)

Need one specific pairwise interaction per contact (3-12 per particle)

In principle, this can be done using DNA coatings

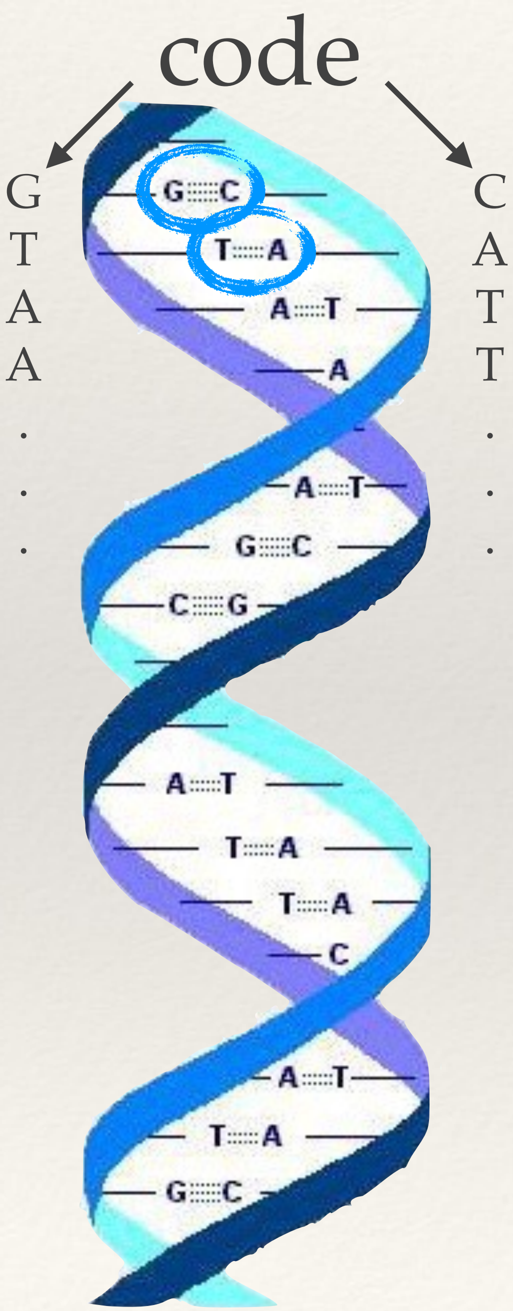
# A New Materials Science…

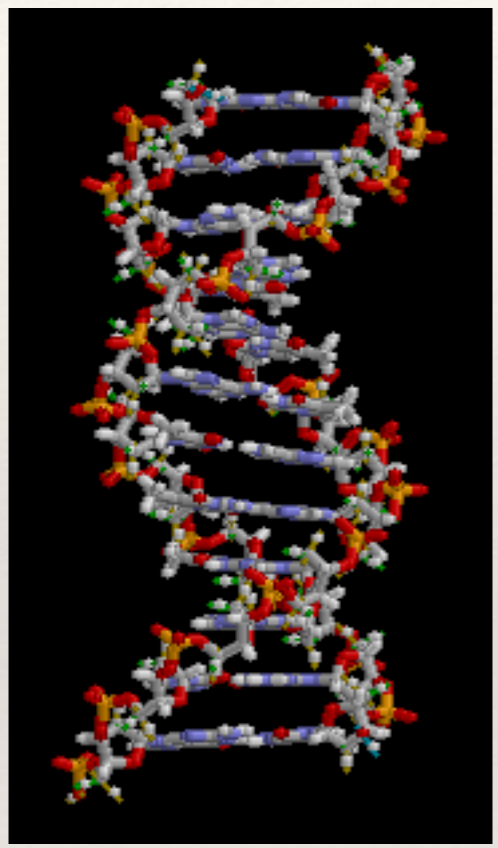
based on colloids with DNA coatings for programmable self-assembly

- DNA as glue that provides programmable specific interactions between colloids
- Colloidal particles are the majority components that determine the material properties:
  - **colloidal materials**: polymers, inorganics, metals, semiconductors,…)
  - DNA coating is much smaller than particle size (glue shouldn't occupy much volume)
- Colloids must anneal to achieve lowest free energy state
- Need directional interactions for greatest programmability
  - (next lecture on patchy particles will focus on directional interactions)

# DNA: “the secret of life”

—James Watson



DNA is a polymer consisting of

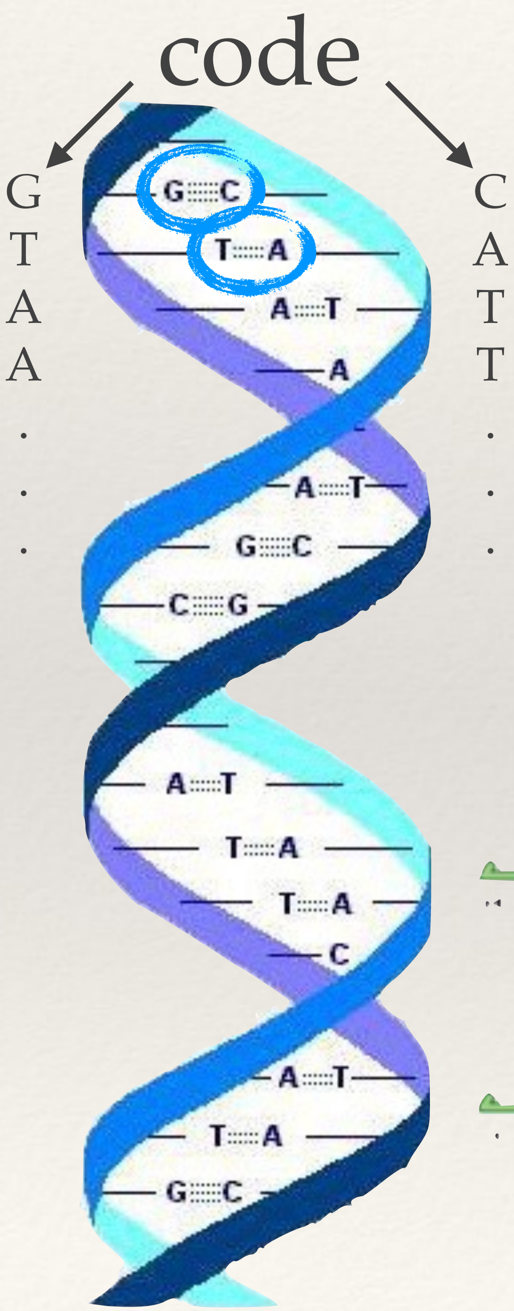
- the genetic code: a sequence of bases adenine (A), cytosine (C), guanine (G) and thymine (T)
- T pairs with A (2 hydrogen bonds)
  G pairs with C (3 hydrogen bonds)
- 2 single strands of DNA bind when they have complementary sequences of the A, C, G, & T bases.

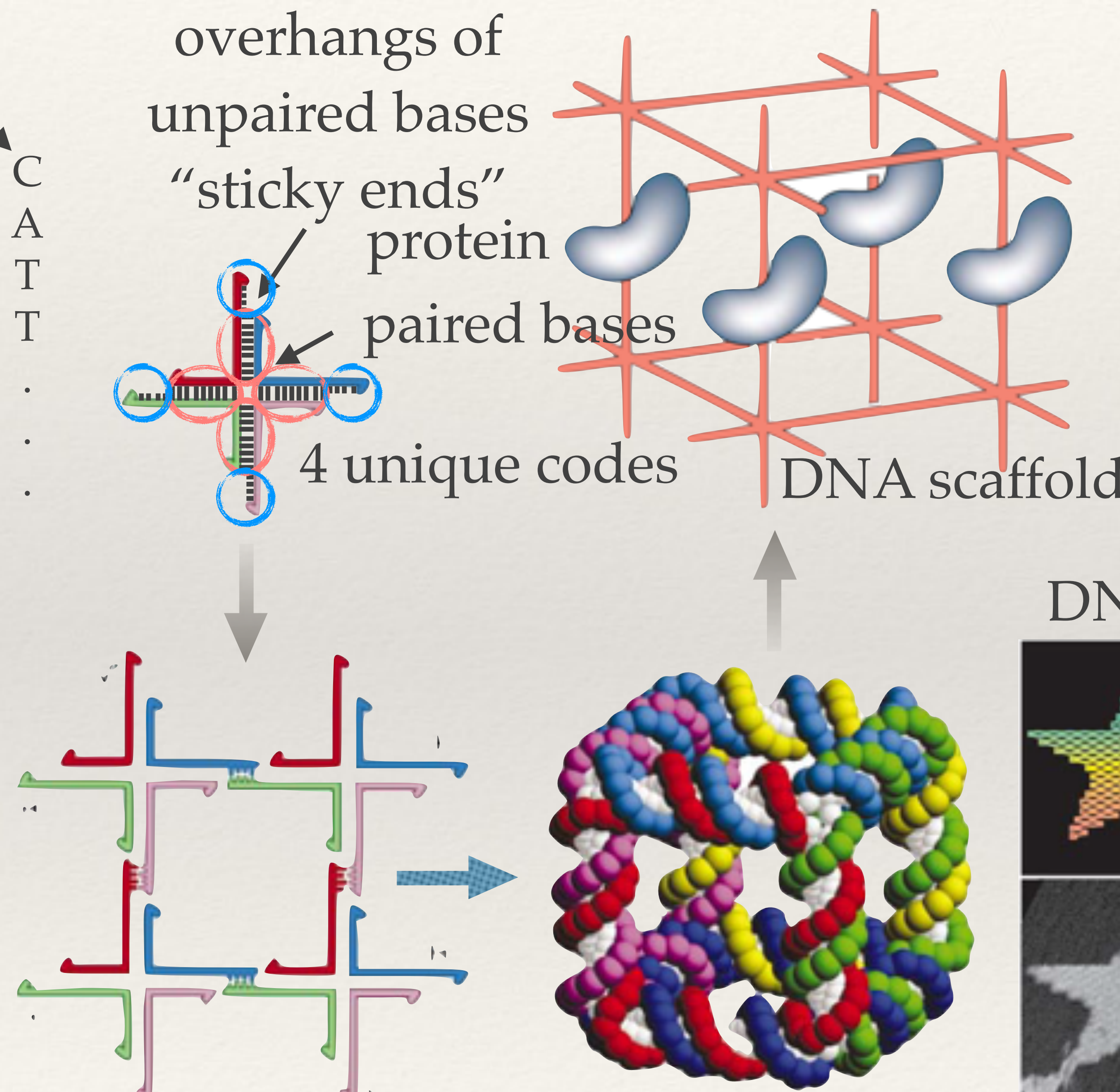
DNA movie from Wikipedia article on DNA

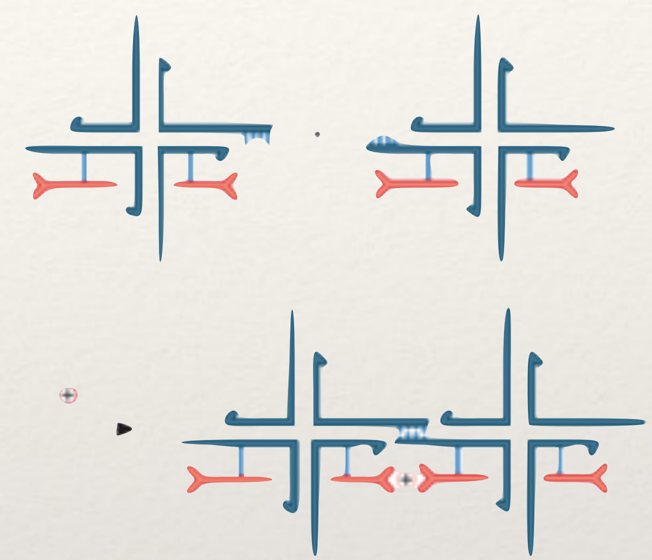
# DNA: “Not merely the secret of life”

—Ned Seeman

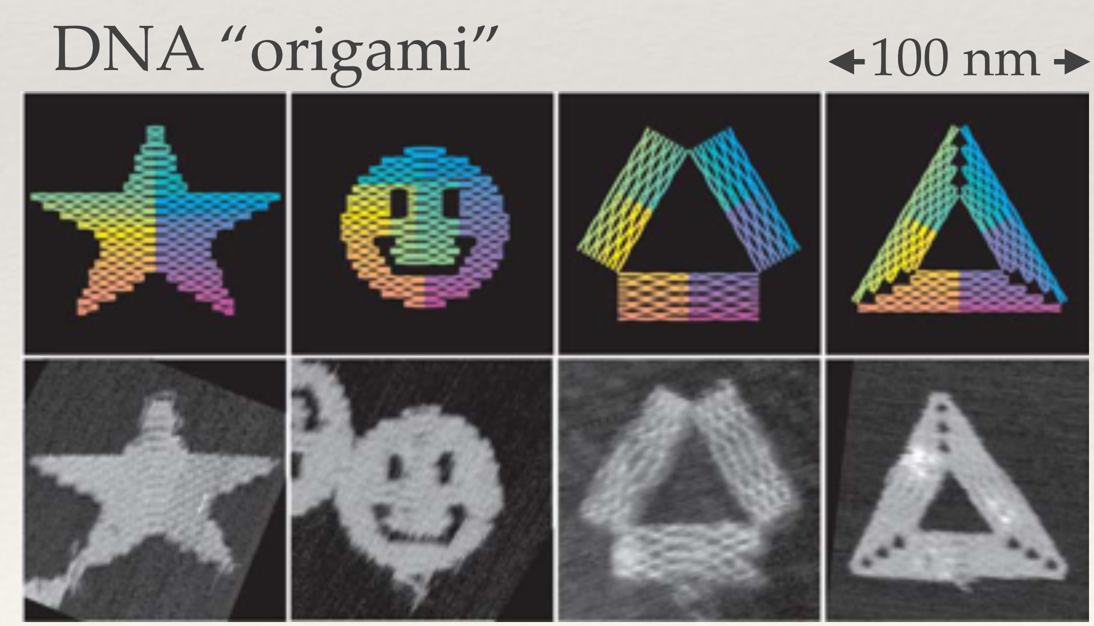
## DNA nanotechnology



Seeman, Nature **421**, 427-431 (2003)

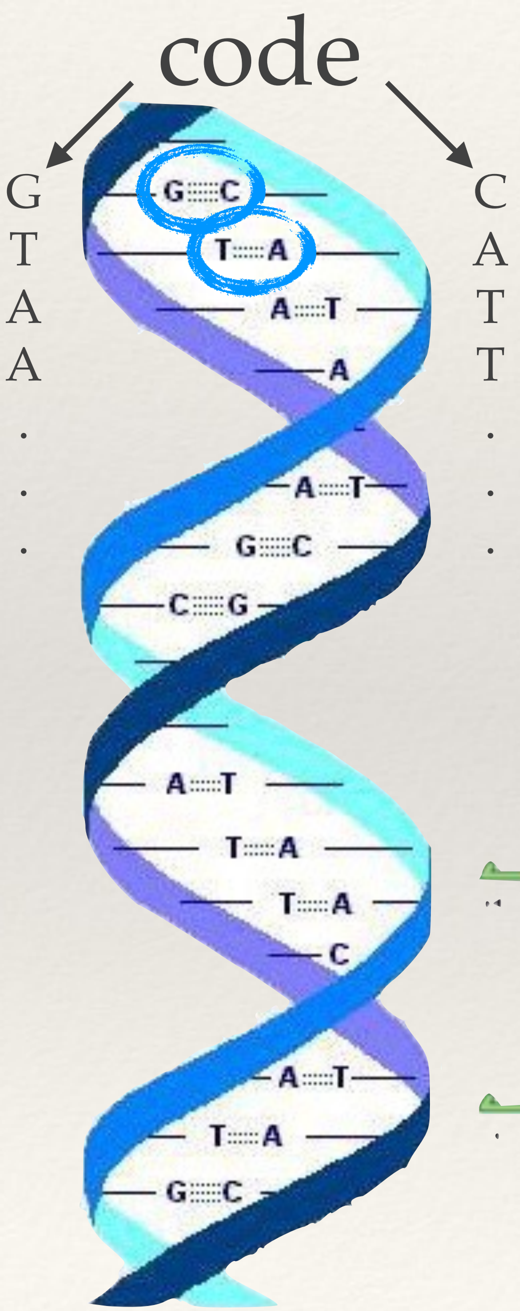


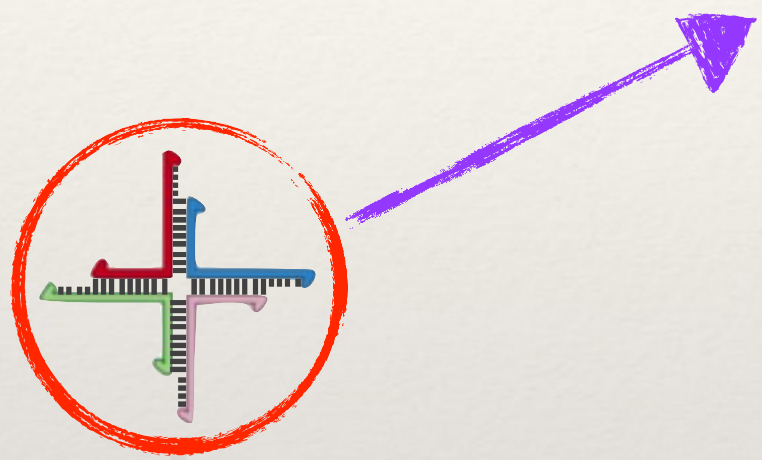

Rothemund, Nature **440**, 297-302 (2006)

# DNA: “Not merely the secret of life”

—Ned Seeman

<u>DNA nanotechnology</u>

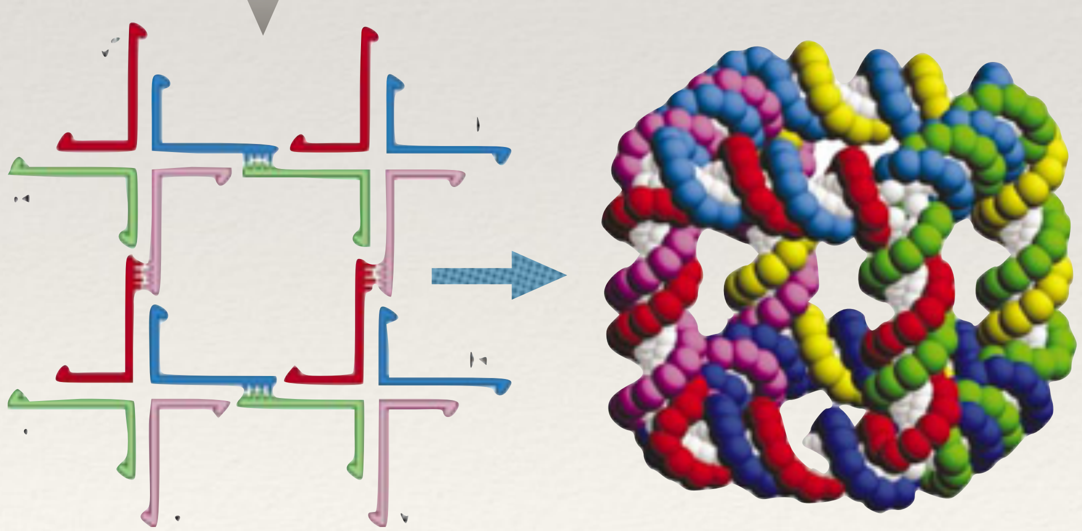


ssDNA overhangs (4 “flavors”: G-C, T-A)

- 4 different sticky ends
- 4 different base-pair sequences

⇛ can stick to 4 different things



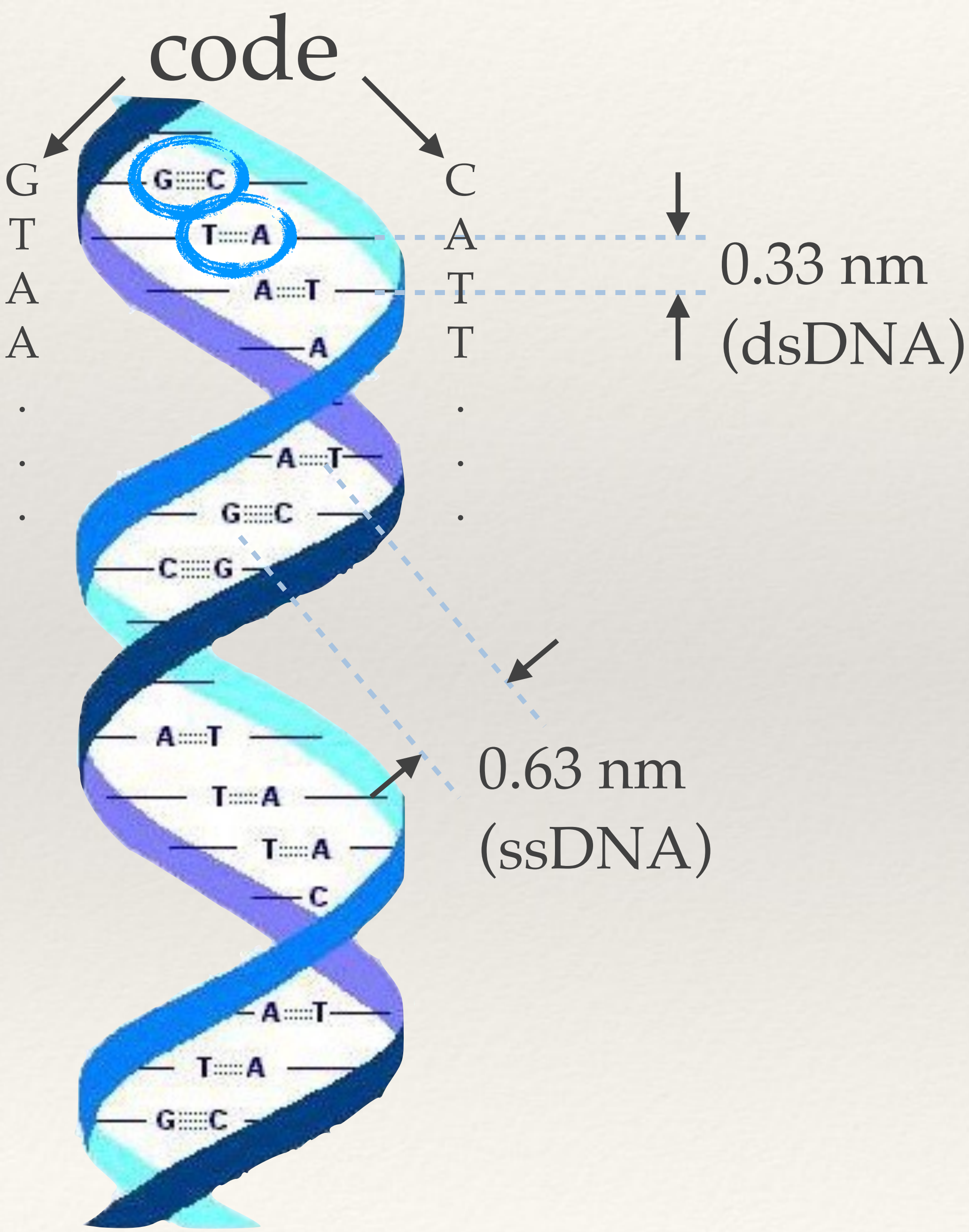
Seeman, Nature **421**, 427-431 (2003)

We are interesting in DNA as a programmable glue used to bind together colloidal particles made from different materials

# “Not merely DNA: the secret of life”

—Ned Seeman

DNA nanotechnology



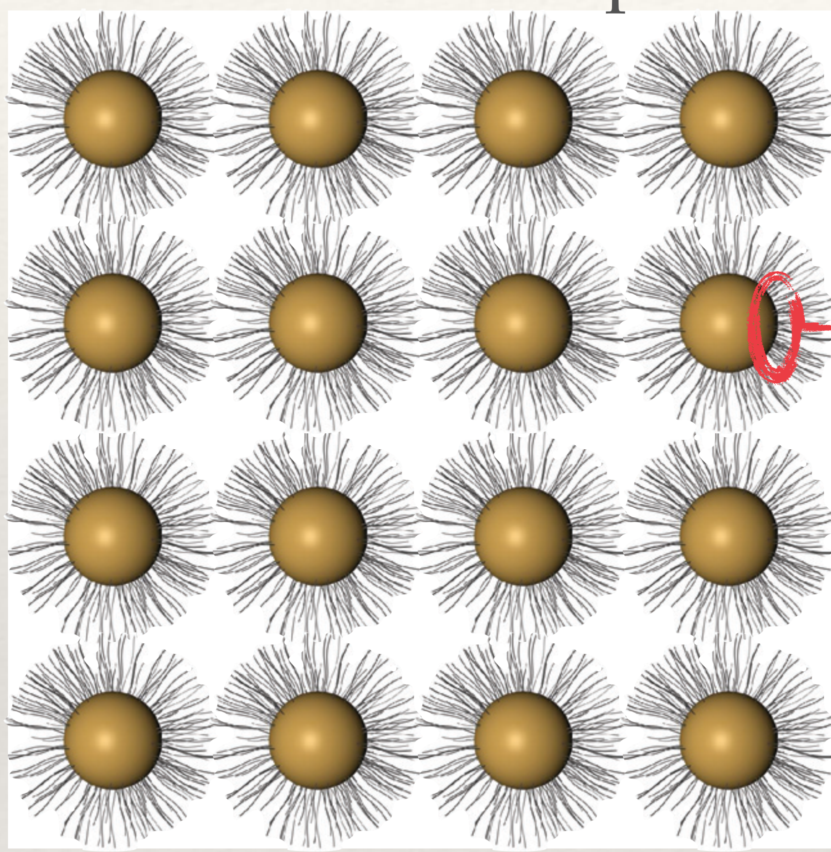

## DNA physical properties

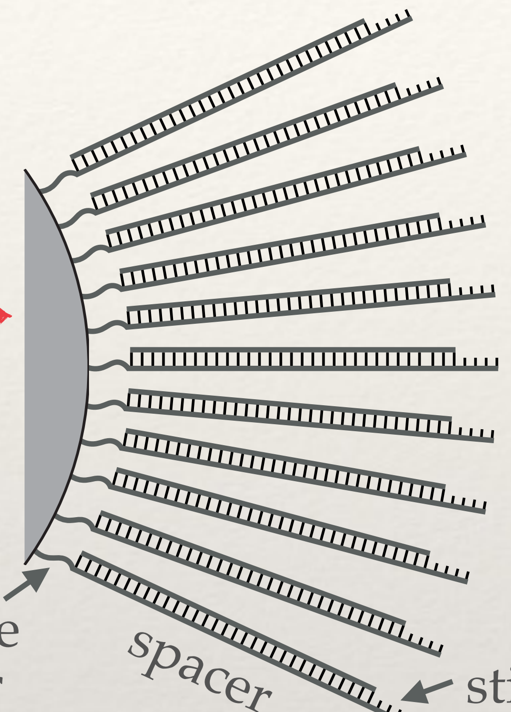
- **highly charged**. Need to add salt (~100 mM NaCl) to screen electrostatic repulsion of strands so that they can hybridize (bind)
- **DNA is stiff** (depends on salt conc)
  - dsDNA ~50 nm
  - ssDNA ~2.5 nm
- **Can buy** any sequence on internet (next-day delivery)

# DNA-coated (gold) nanoparticles

~40 nm

nanoparticle crystal

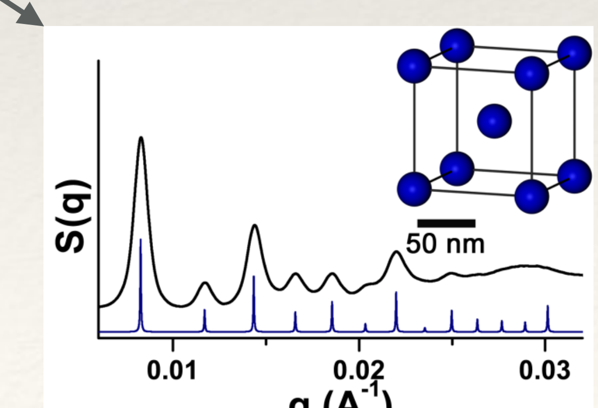





Sample is mostly $H_2O$ + DNA
>98% $H_2O$ + DNA by volume
< 2% particles

particle diameter ~ 20 nm
DNA length ~ 20 nm

x-rays




**too small to see directly**
(use x-rays)


Mirkin *et al.*,.Nature **382**, 607–609 (1996).

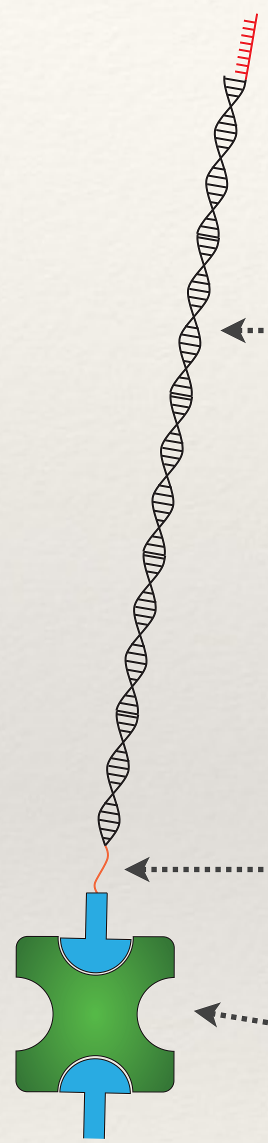
Alivisatos *et al.*, Nature **382**, 609–611 (1996)

Gang *et al.*, Nature **451**, 549–552 (2008)

MacFarlane *et al.*, Science **334**, 204-208 (2011)

# DNA-coated colloids

## are different



single-stranded "sticky" ends
~10 bases

double-stranded DNA
(50 bases ≃ 20 nm)
(persistence length ~50 nm)

flexible PEG linker strand

biotin-streptavidin-biotin link

surfactant brush
(PEO-PPO-PEO, Pluronic F127)


**Sample is mostly particles**

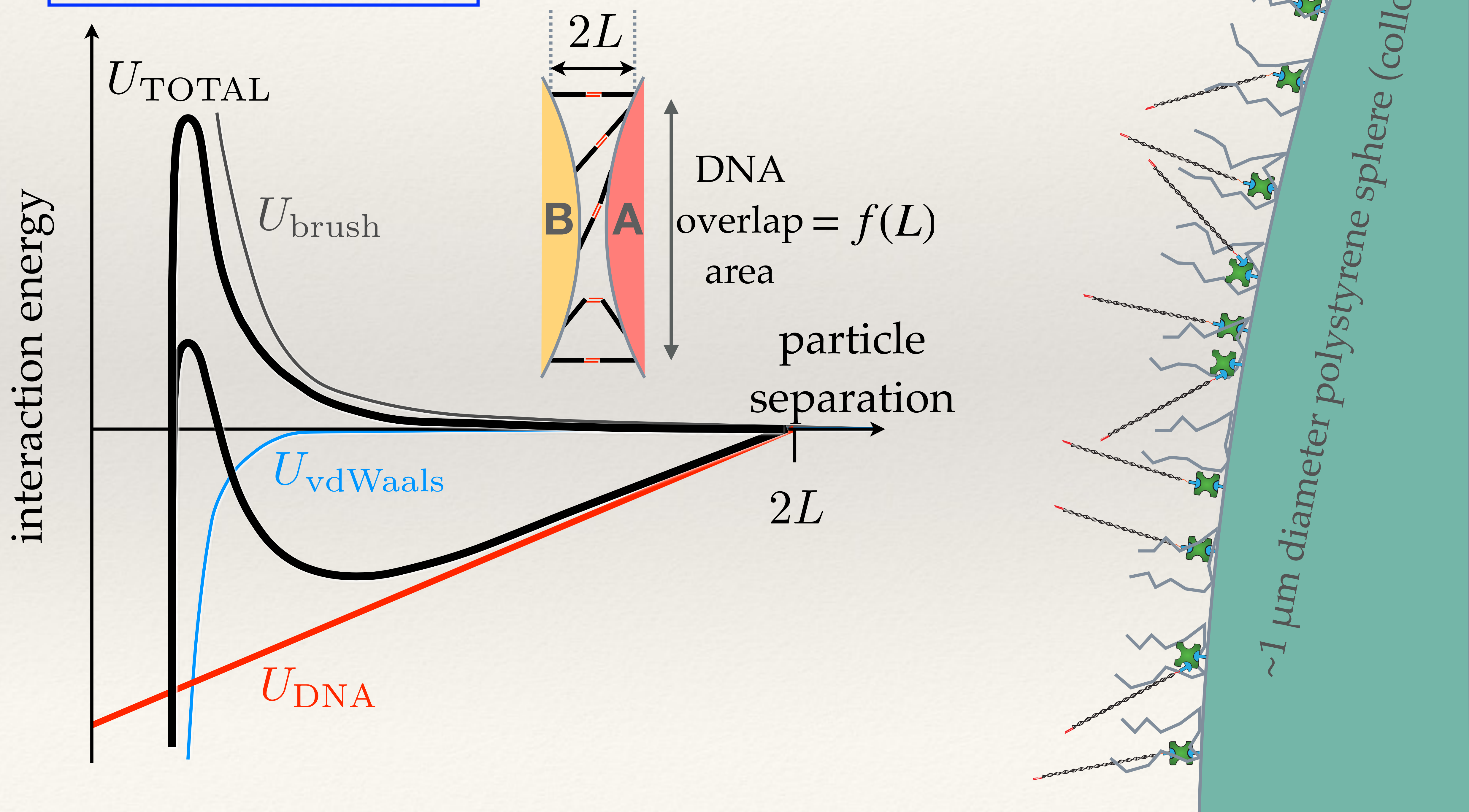
~ 5% DNA by volume

~70% particles

# Colloid pair interaction with coating

## of short dsDNA with ssDNA sticky ends

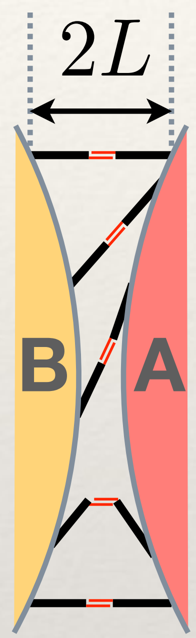
$$\Delta F \approx -k_B T \langle N_{bonds} \rangle$$

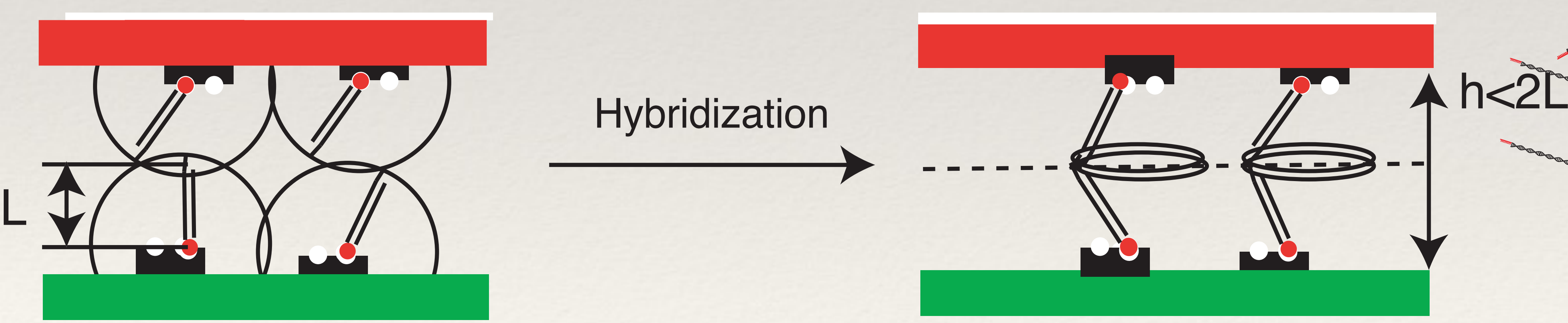


# Entropy loss due to binding

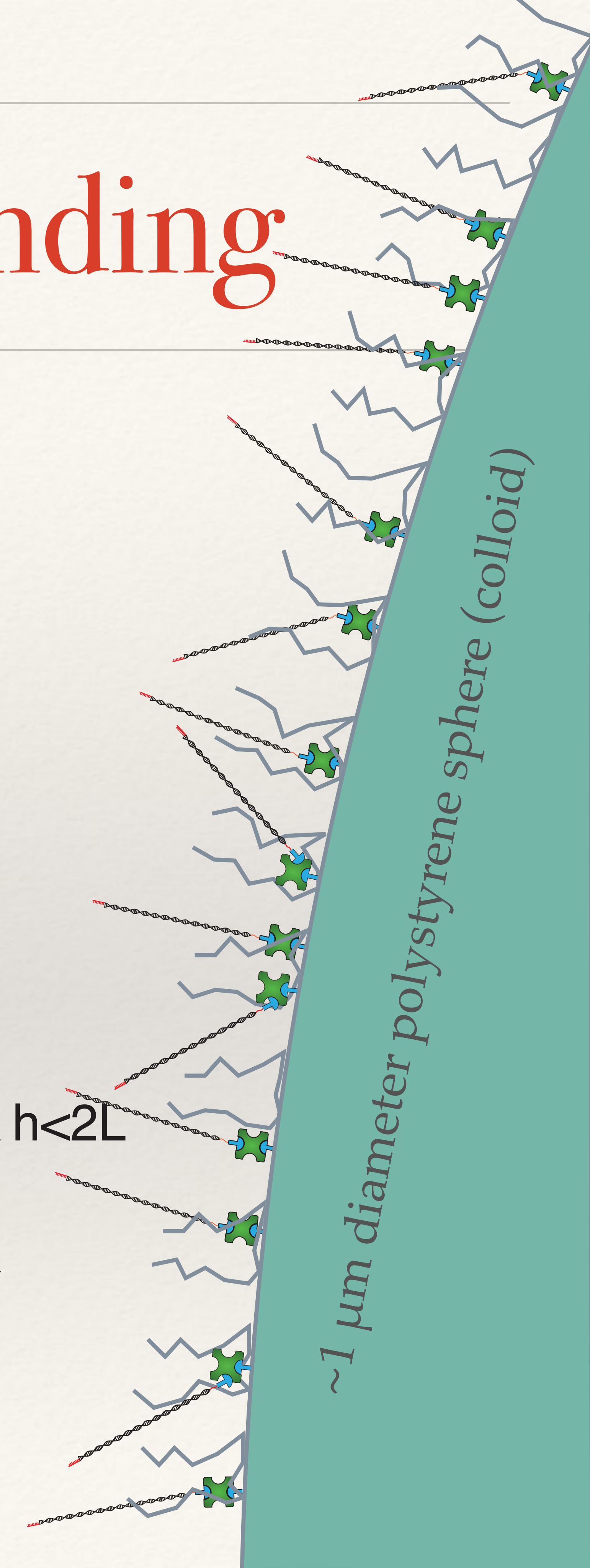
$$\Delta F \approx -k_B T \langle N_{bonds} \rangle$$

- From geometry, about 100 DNA strands are close enough to bind, depending on coverage
- From thermodynamics, only a fraction bind

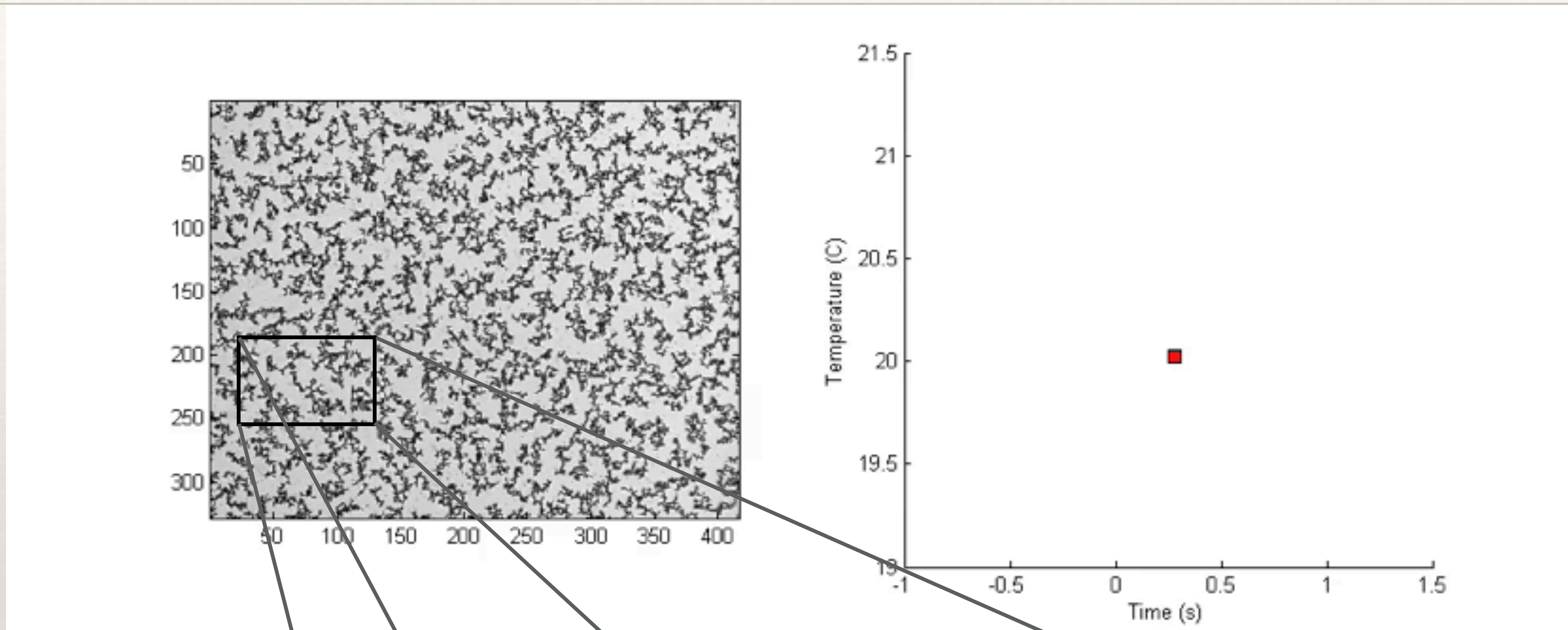


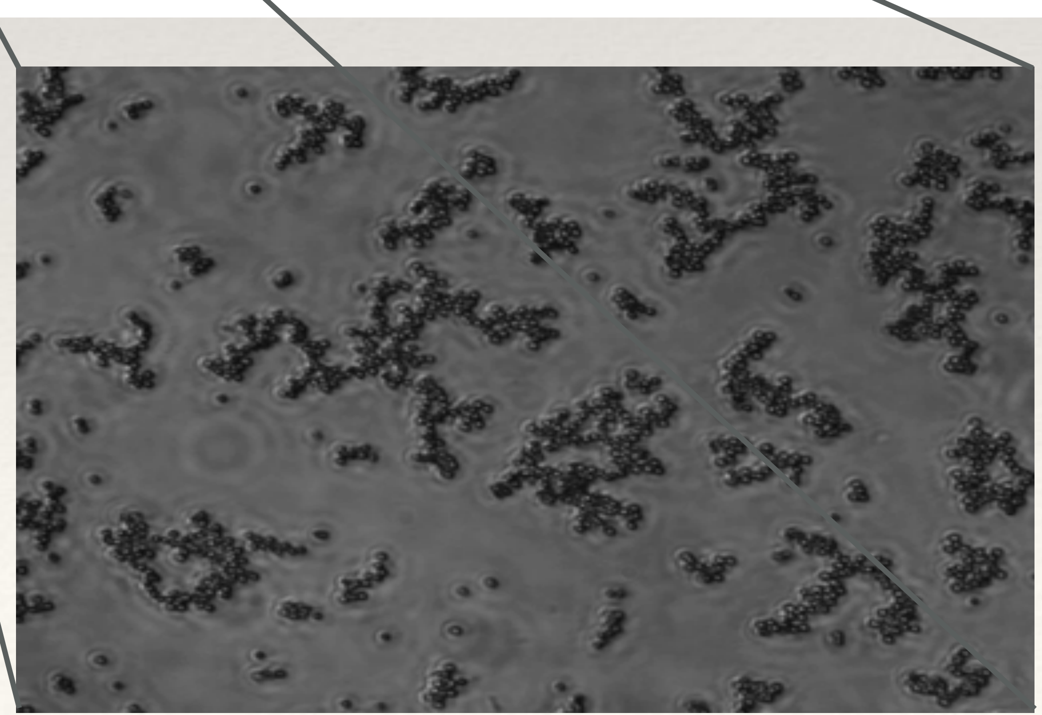




some entropy loss of tethered ssDNA upon binding



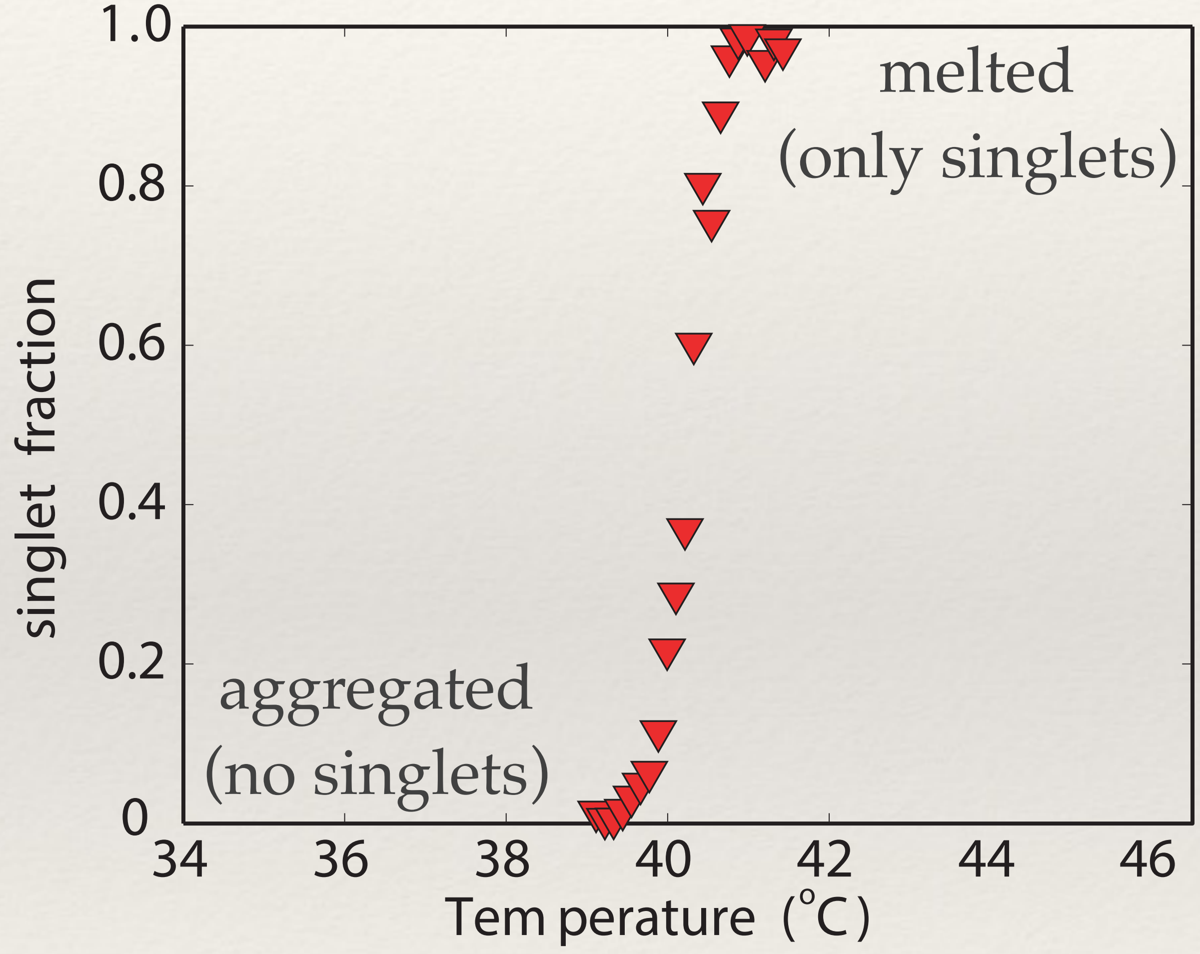
# Thermally reversible aggregation!



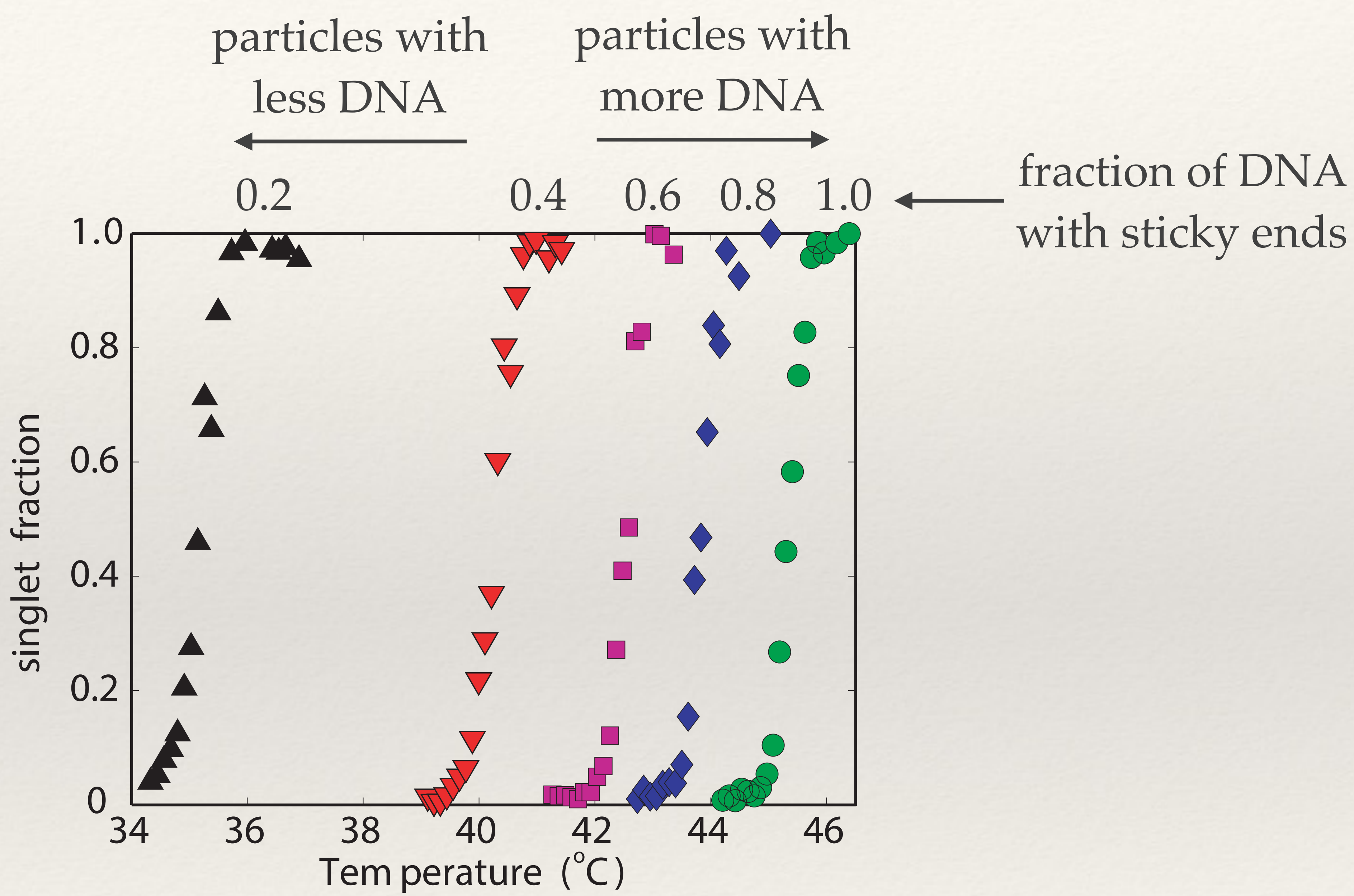
Can avoid non-specific and irreversible binding by coating particles with plutonic surfactant (PEO-PPO-PEO) triblocks

# Melting curves for DNA-coated colloids



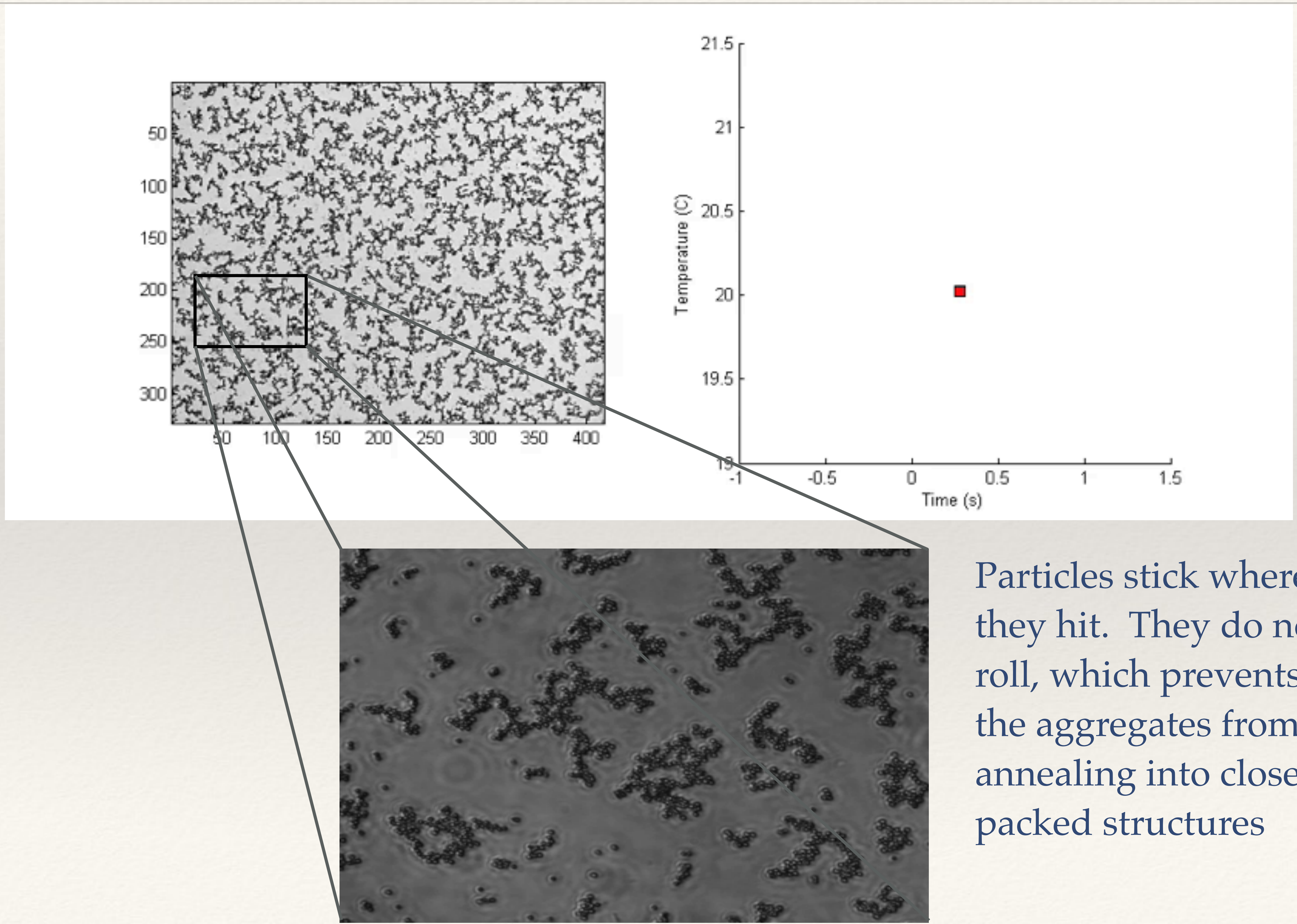

Dreyfus *et al*., Phys. Rev. E **81**, 041404 (2010)

# Melting curves for DNA-coated colloids




Dreyfus *et al*., Phys. Rev. E **81**, 041404 (2010)

# Fractal aggregation, no crystals!

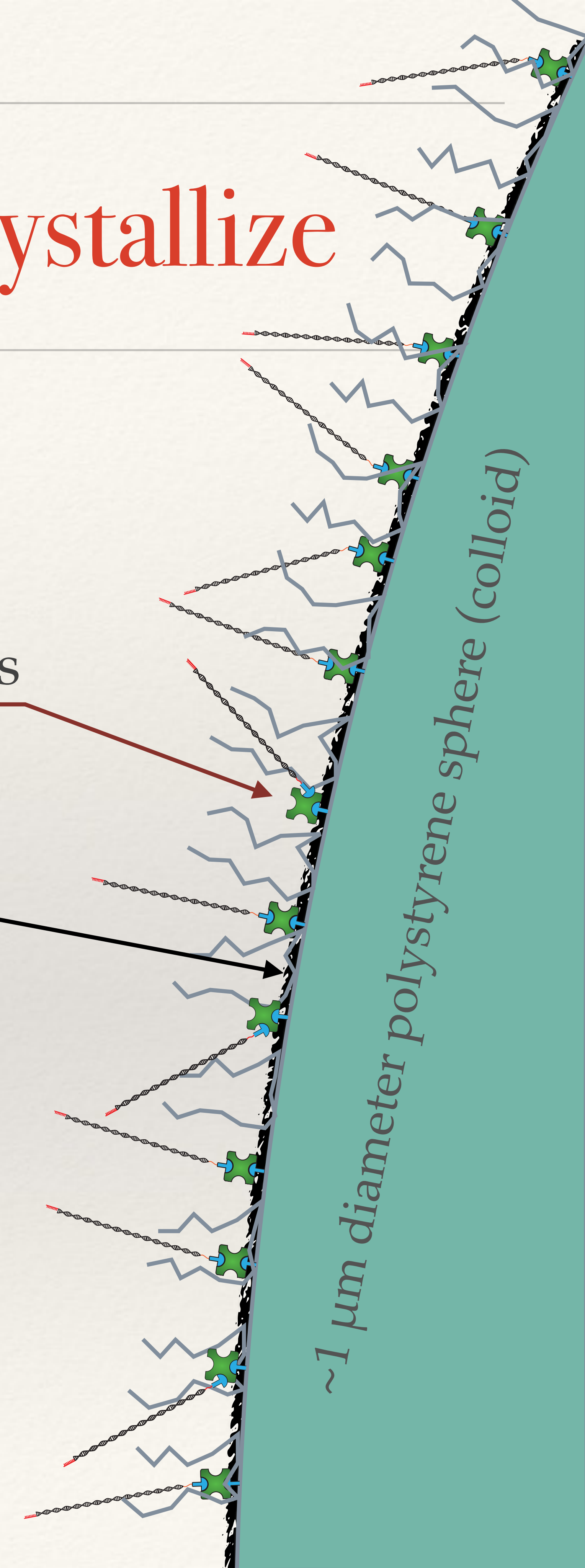



Particles stick where they hit. They do not roll, which prevents the aggregates from annealing into close-packed structures

# DNA-coated colloids don't crystallize

## Why?

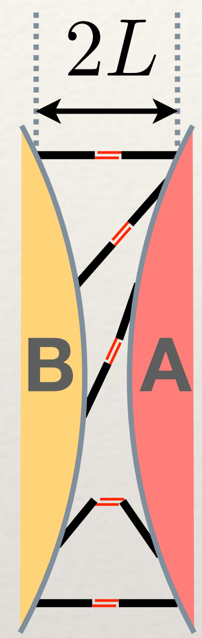
- Colloidal surface roughness
  - large streptavidin linker with multiple binding sites
  - intrinsic surface roughness
- Low areal DNA coverage
  - bulky streptavidin linker limits areal density
    - ≲ 18,000 DNA/1-μm-diameter particle (13 nm between grafting points)
  - poor (low) yield of DNA linking reaction
- Double-stranded DNA



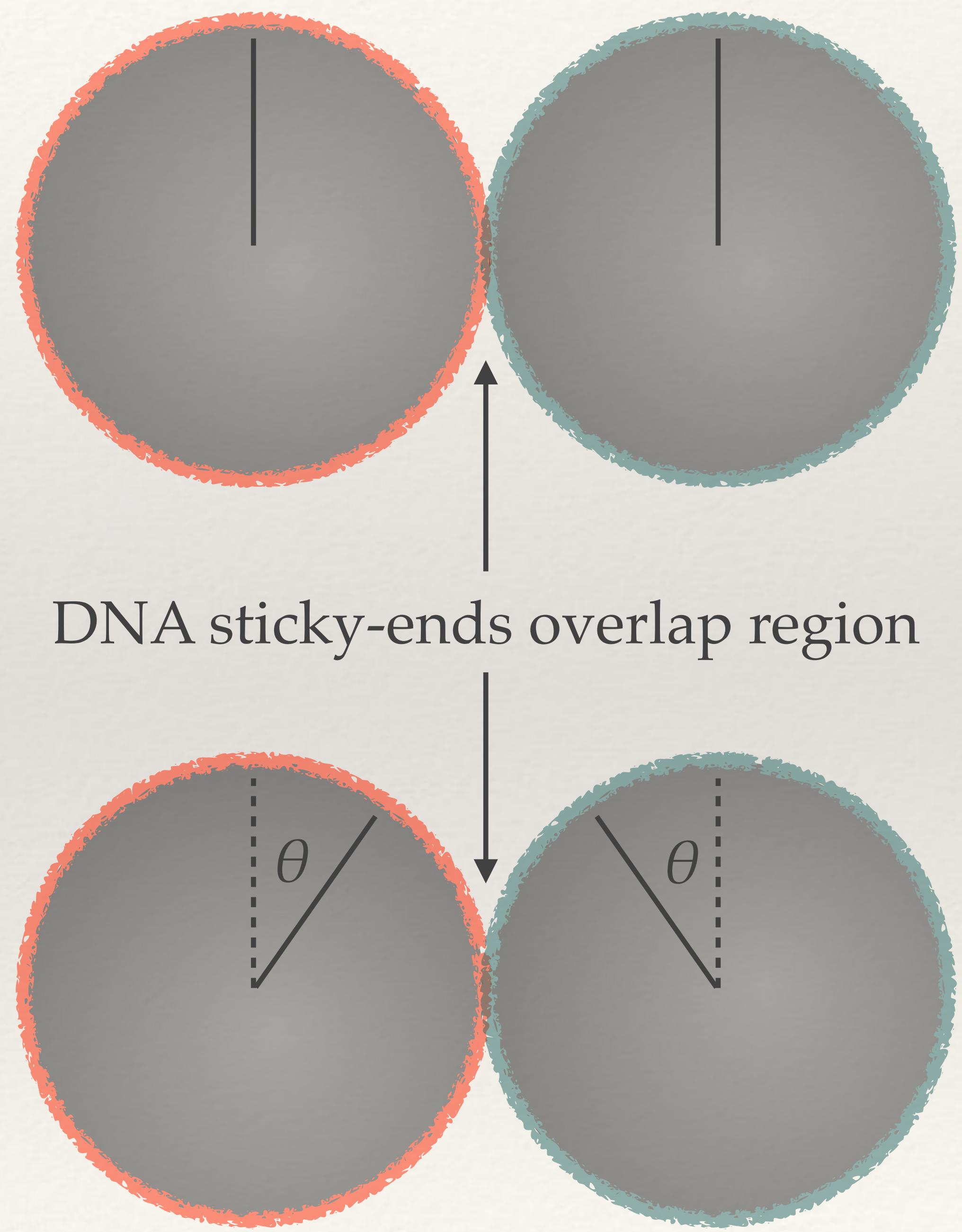
# Why is roughness a problem?

$$\Delta F \approx -k_B T \langle N_{bonds} \rangle$$

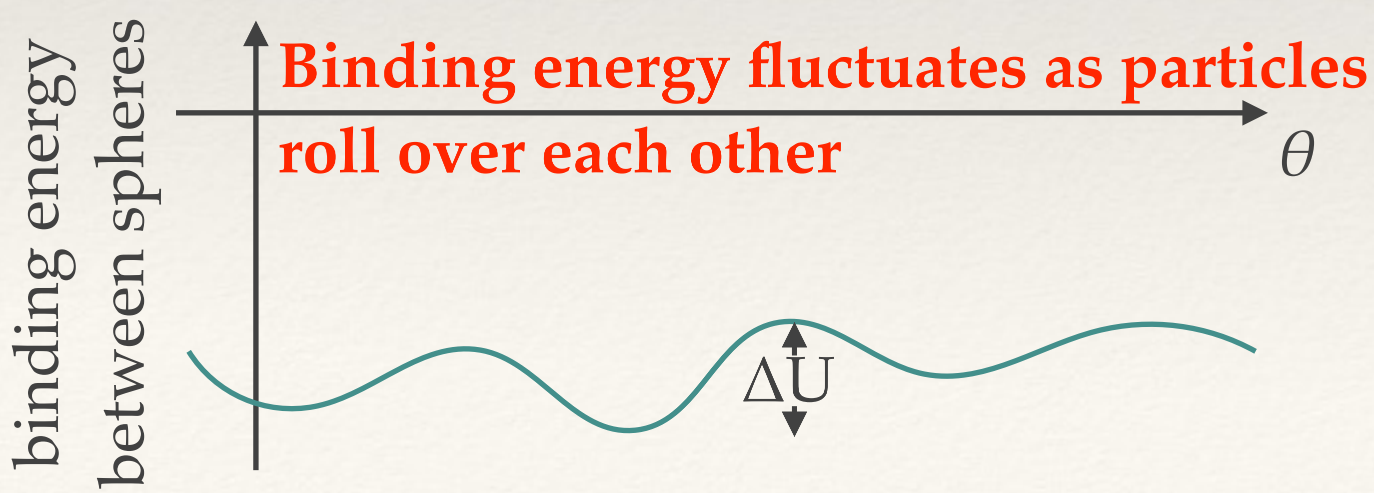
- From geometry, about 100 DNA strands are close enough to bind, depending on coverage
- From thermodynamics, only a fraction bind




This number fluctuates as spheres roll on each other




⇛



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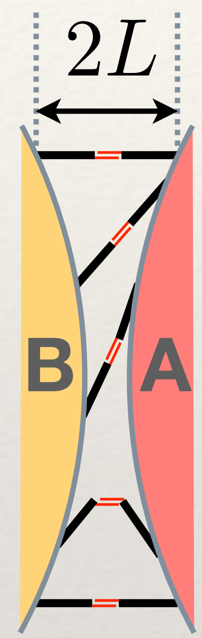


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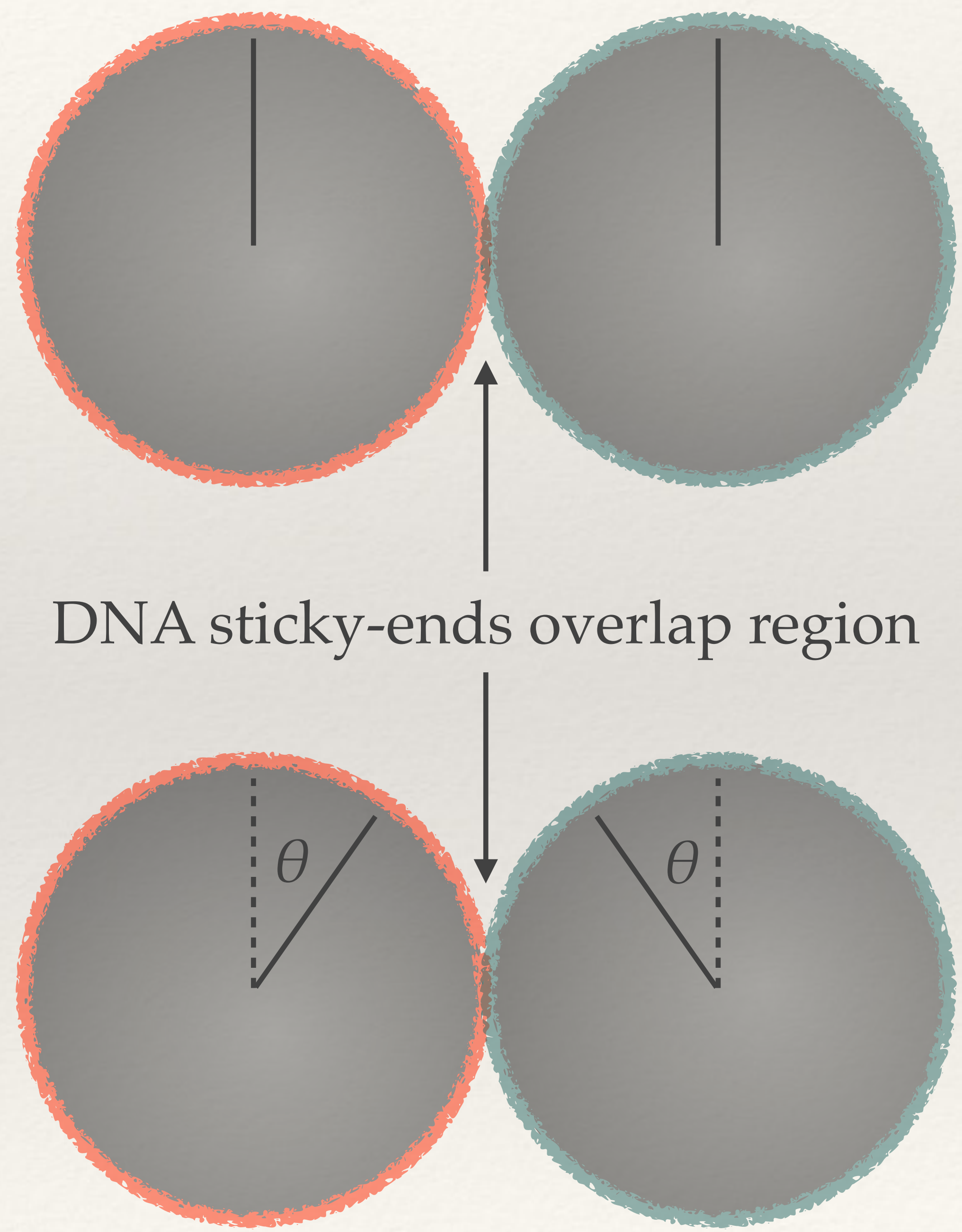
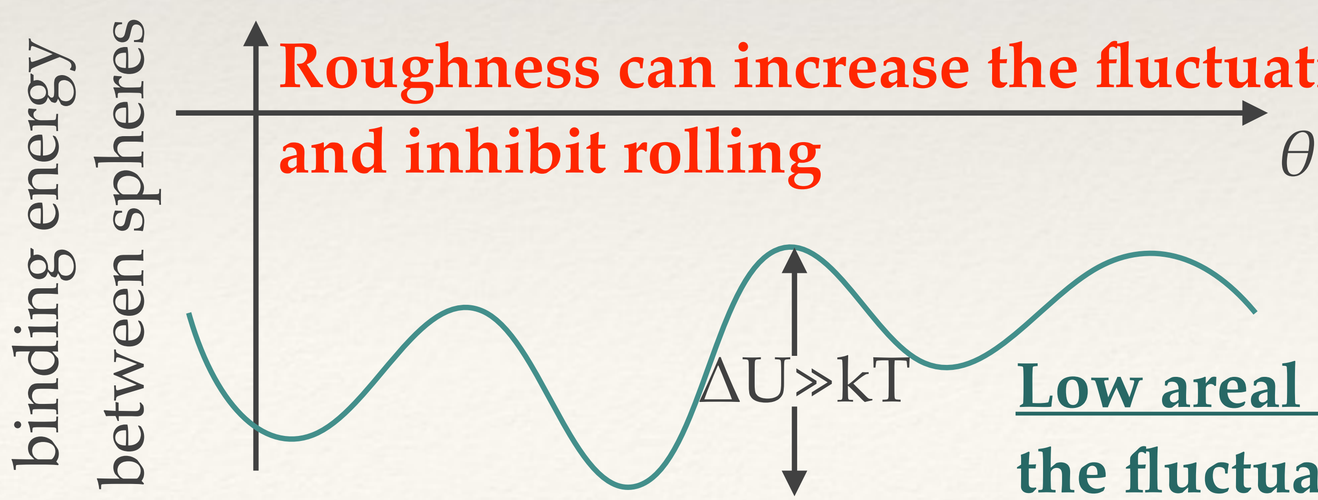



**Roughness can increase the fluctuations and inhibit rolling**




**<u>Low areal density of DNA</u> can also increase the fluctuations and inhibit rolling**

# Why is roughness a problem?

$$\Delta F \approx -k_B T \langle N_{bonds} \rangle$$

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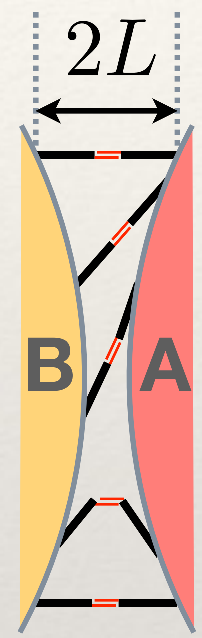
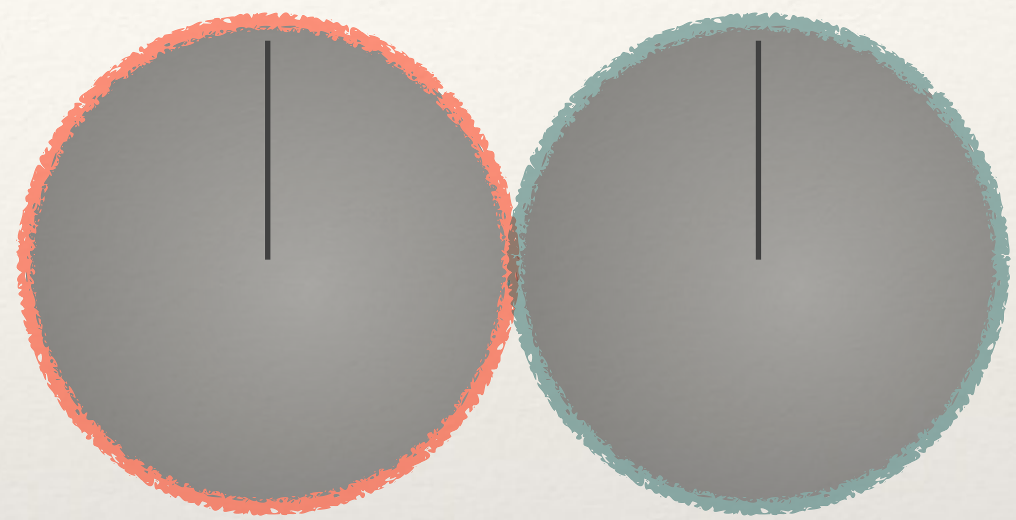
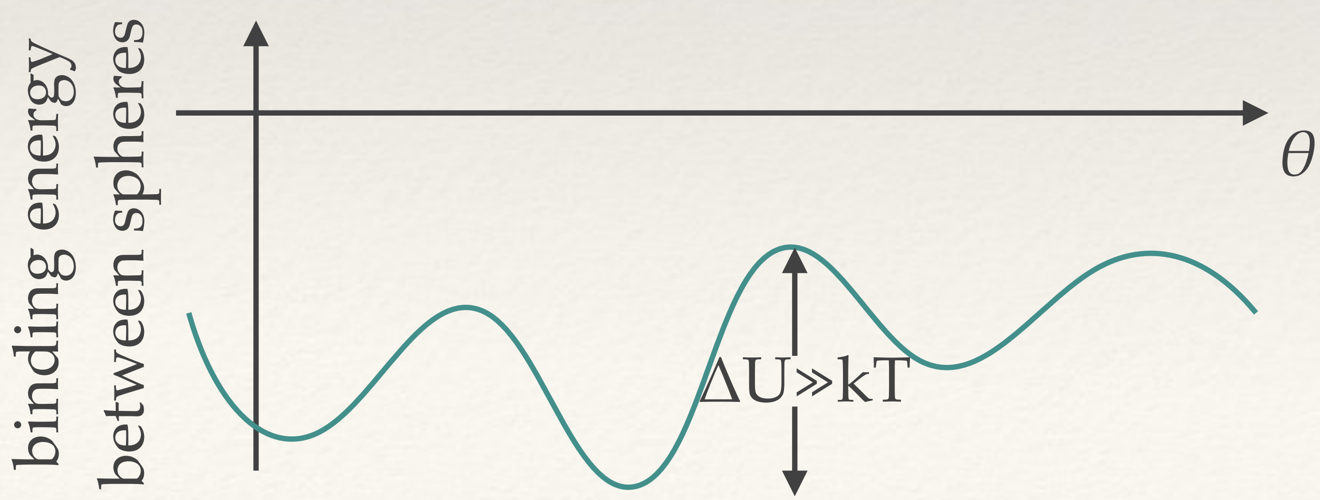
- From thermodynamics, only a fraction bind



This number fluctuates as spheres roll on each other




Need better DNA coating

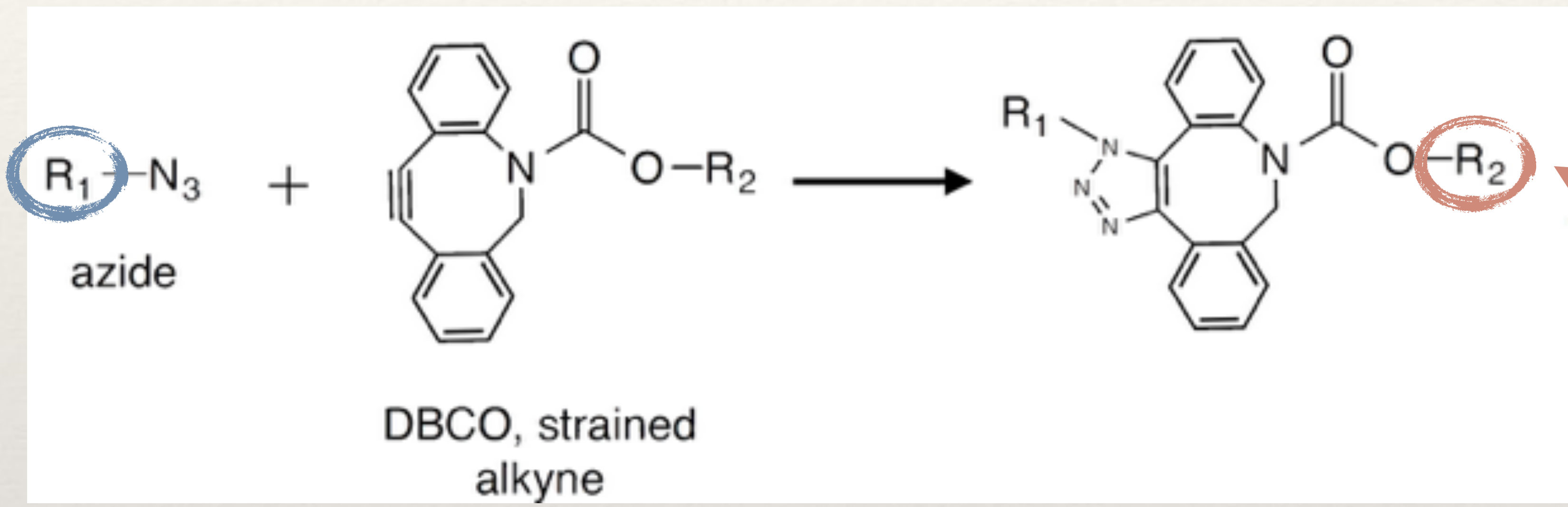
- smooth surfaces
- high density DNA coating

⇛ abandon streptavidin-biotin linkage

# Different chemistry to attach DNA

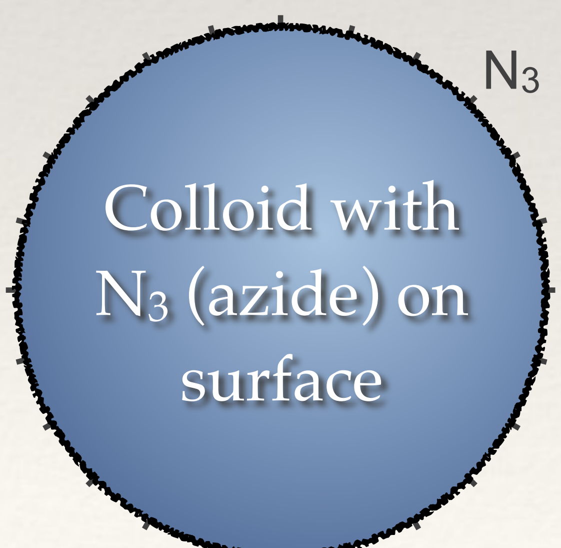
SPAAC: Strain-Promoted Azide-Alkyne Cycloaddition

Agard, Prescher, & Bertozzi, JACS **126**, 15046-15047 (2004)




colloid

DNA




**P: DBCO-T50-CGCG**

**A: DBCO-T20-Cy3-T30—GCAG**

**B: DBCO-T20-Cy5-T30—CTGC**

# Different chemistry to attach DNA

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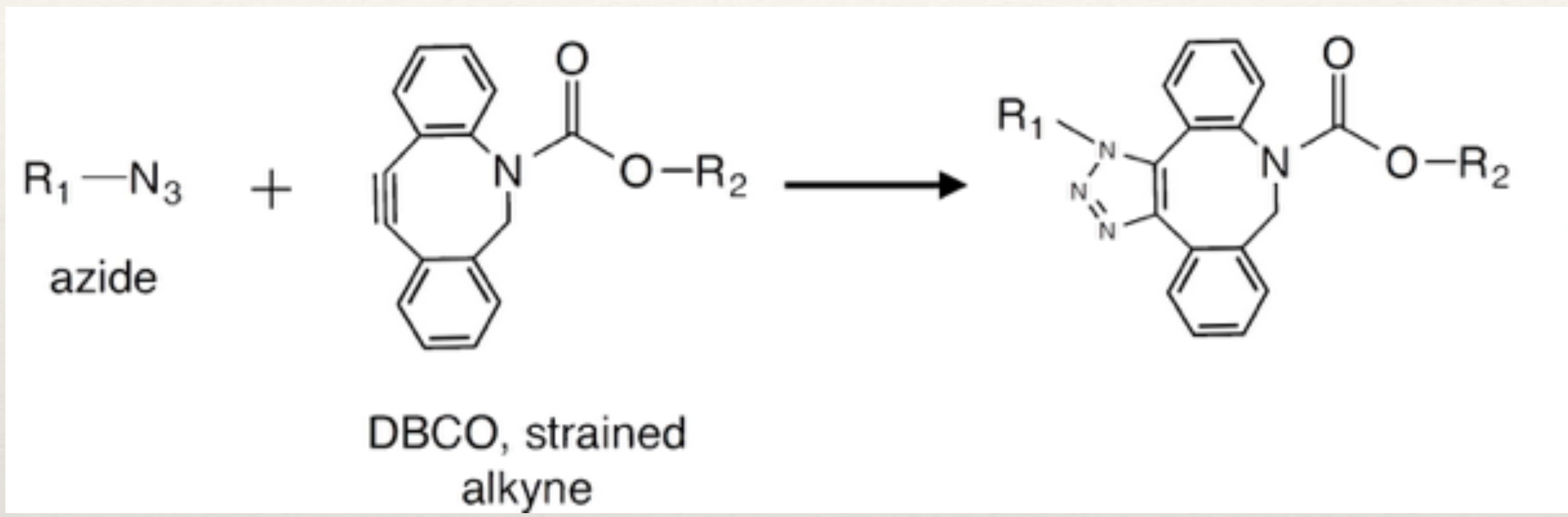
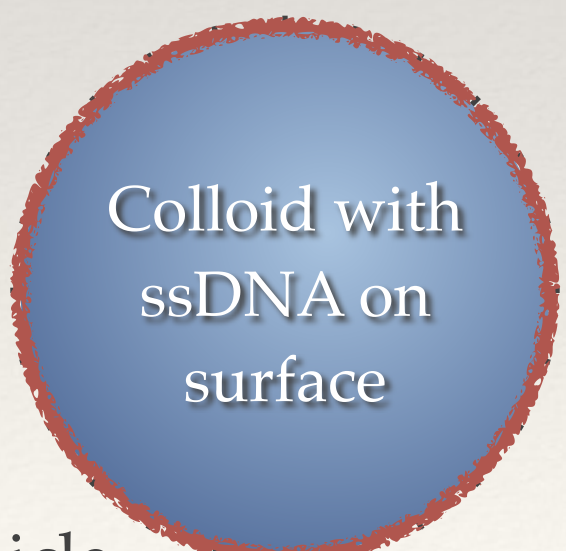



covalent bond (small)




P: DBCO-T50-CGCG

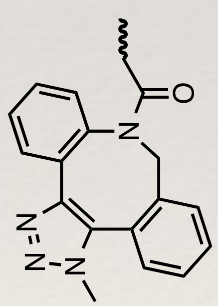
A: DBCO-T20-Cy3-T30—GCAG

B: DBCO-T20-Cy5-T30—CTGC

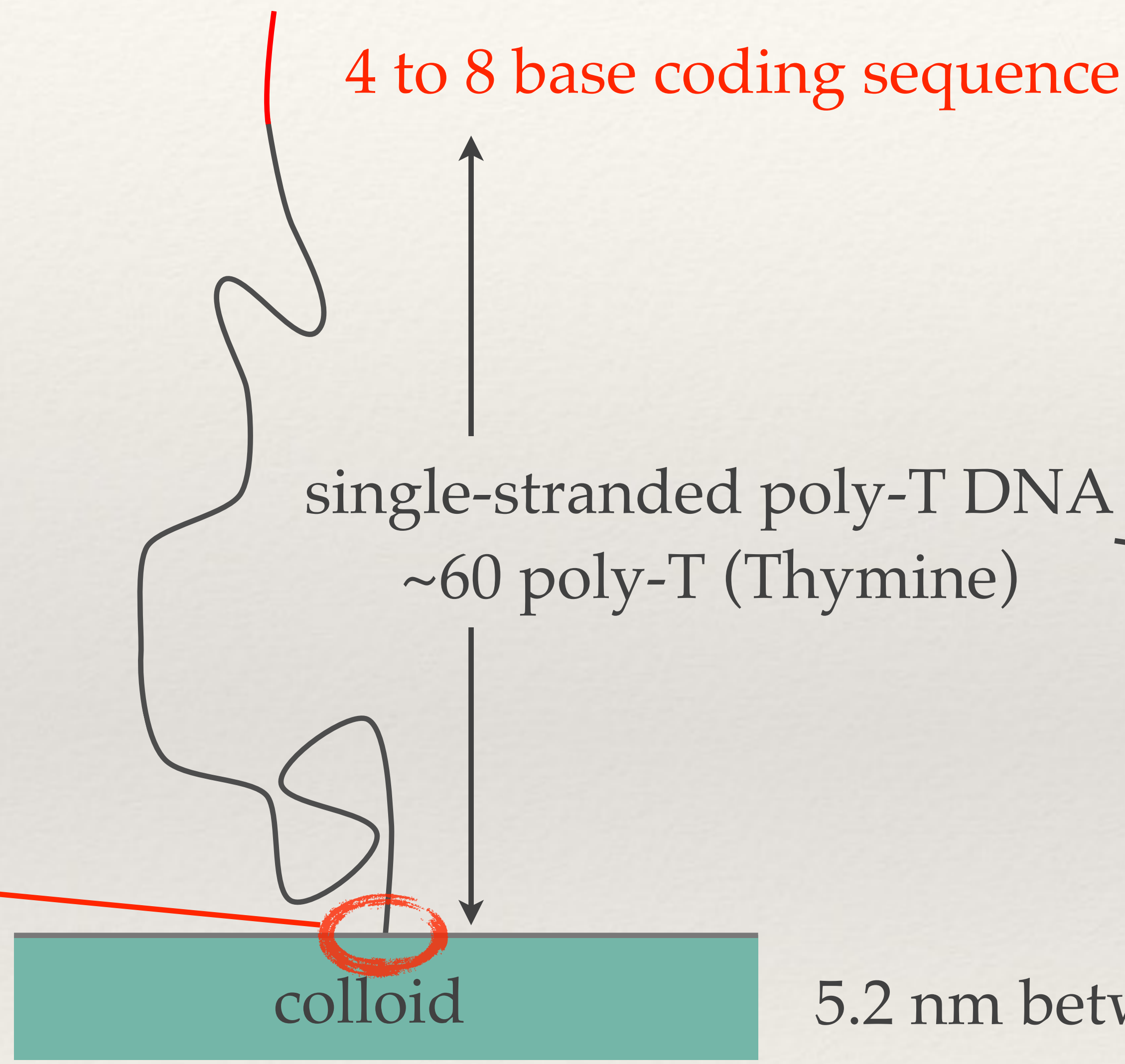
$10^5$-$10^6$ DNAs per micron size particle

(6-150 times greater than previously achieved)

# Improved DNA-coated colloids



covalent DCBO linkage of ssDNA to colloid

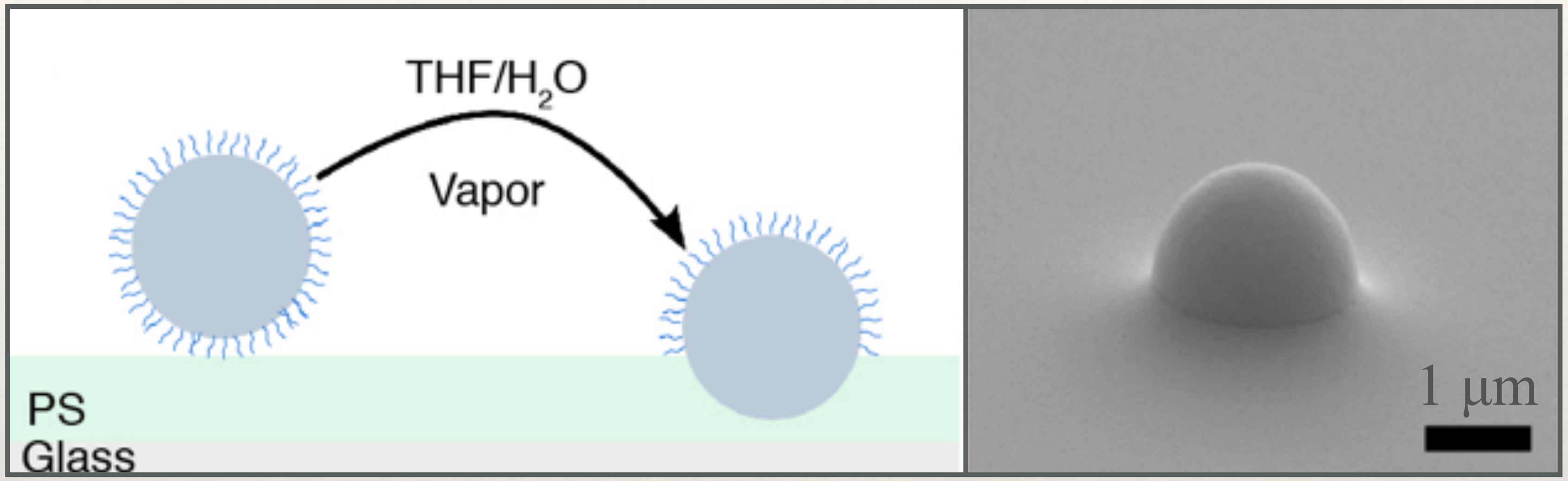


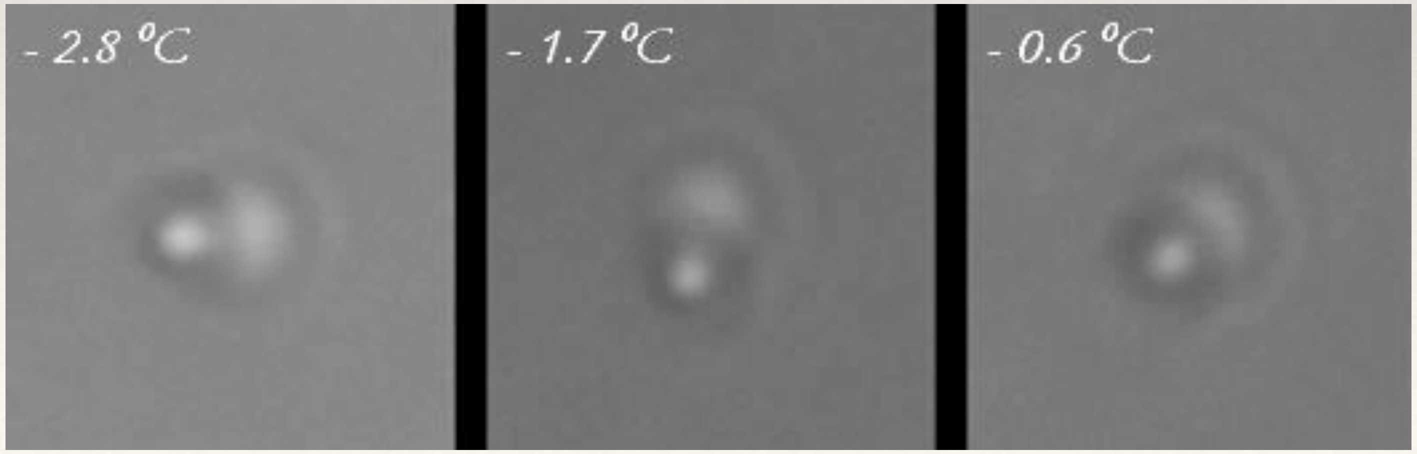

5.2 nm between grafts


**~120,000 ssDNA / 1-µm-diameter particle**

(compared to 6,000 (23 nm) - 18,000 (13 nm) obtained previously)

# DNA-coated colloids that stick and roll

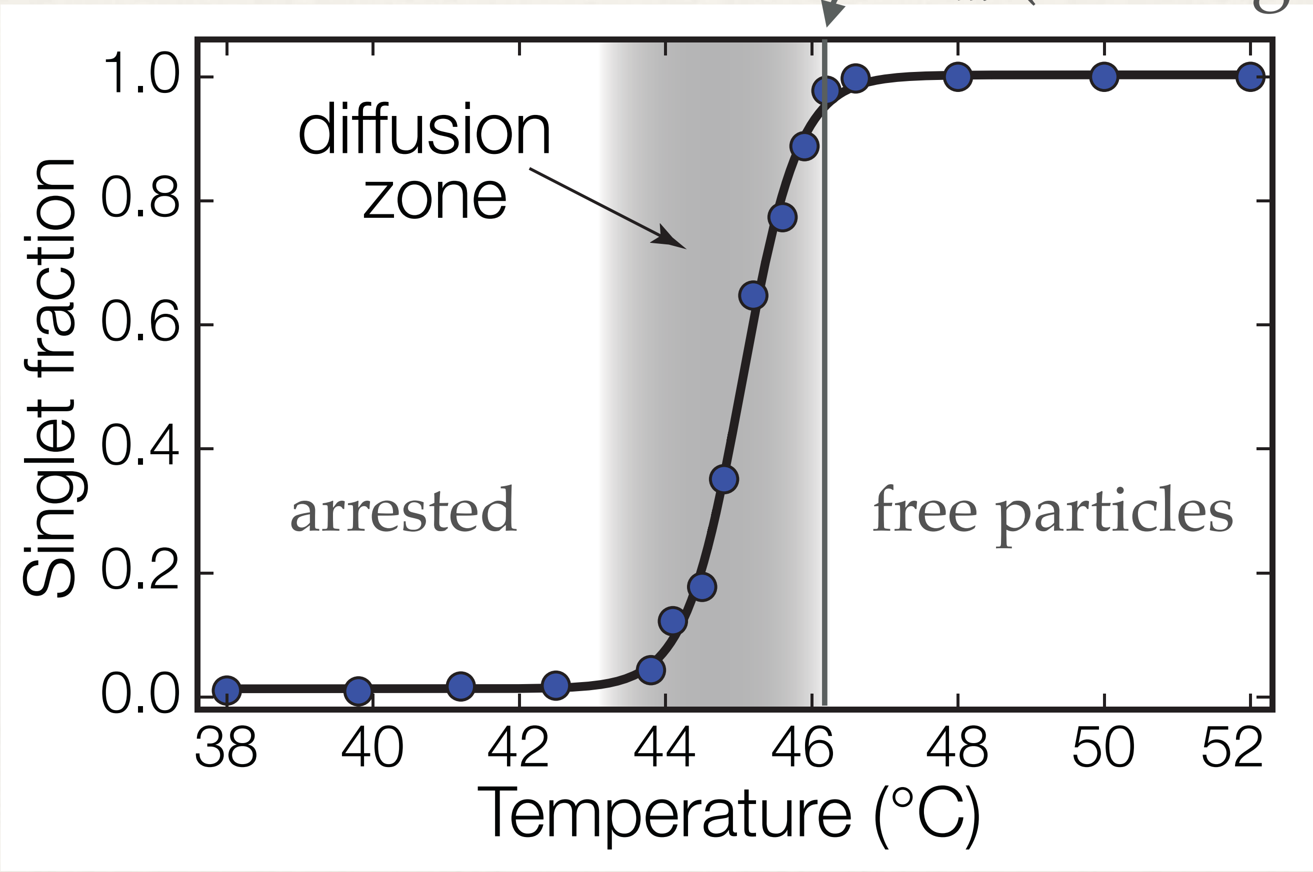


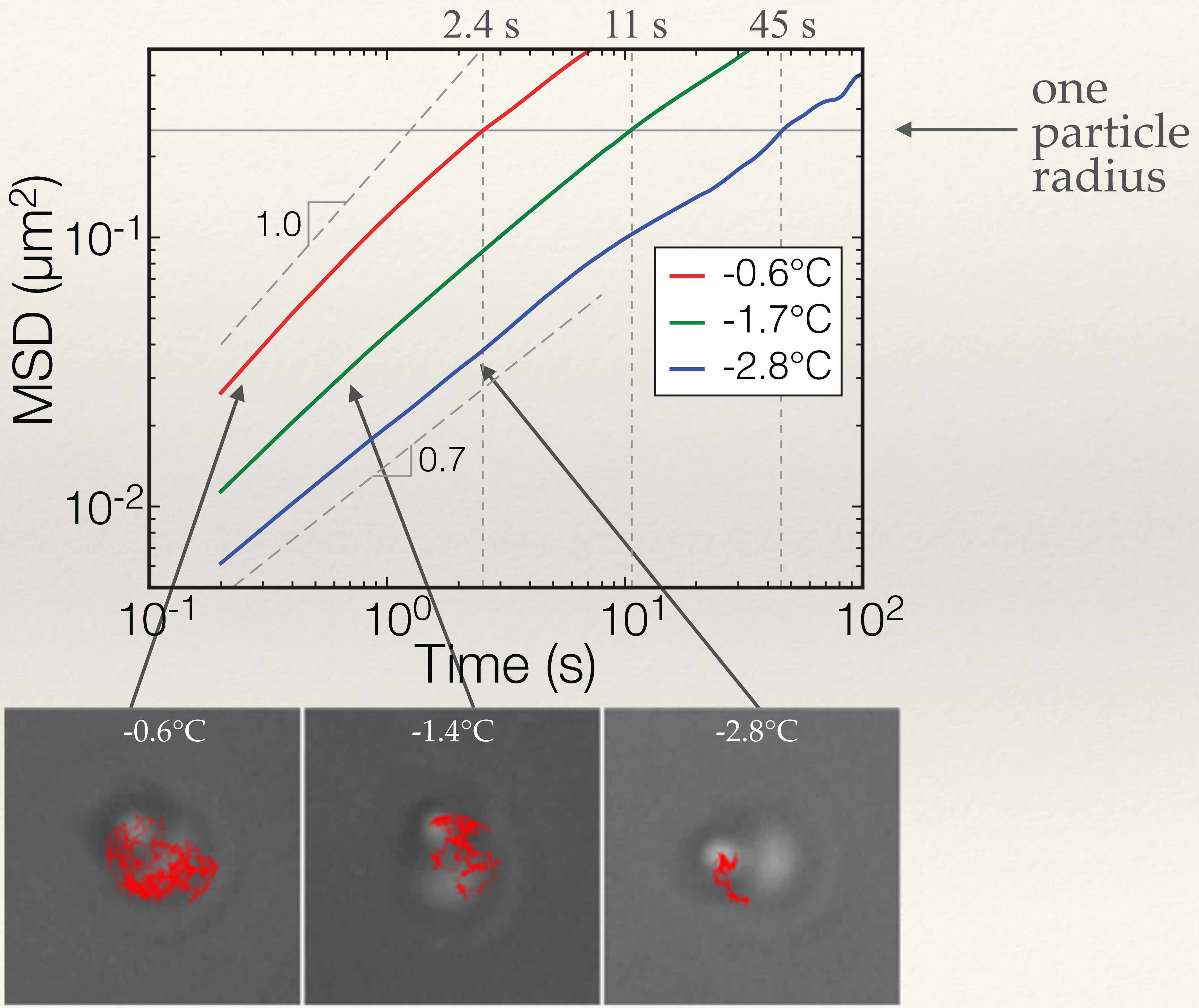
# Melting curves for DNA-coated particles

Measure fraction of singlets (unaggregated particles) as a function of temperature

$T_m$ (melting temperature)

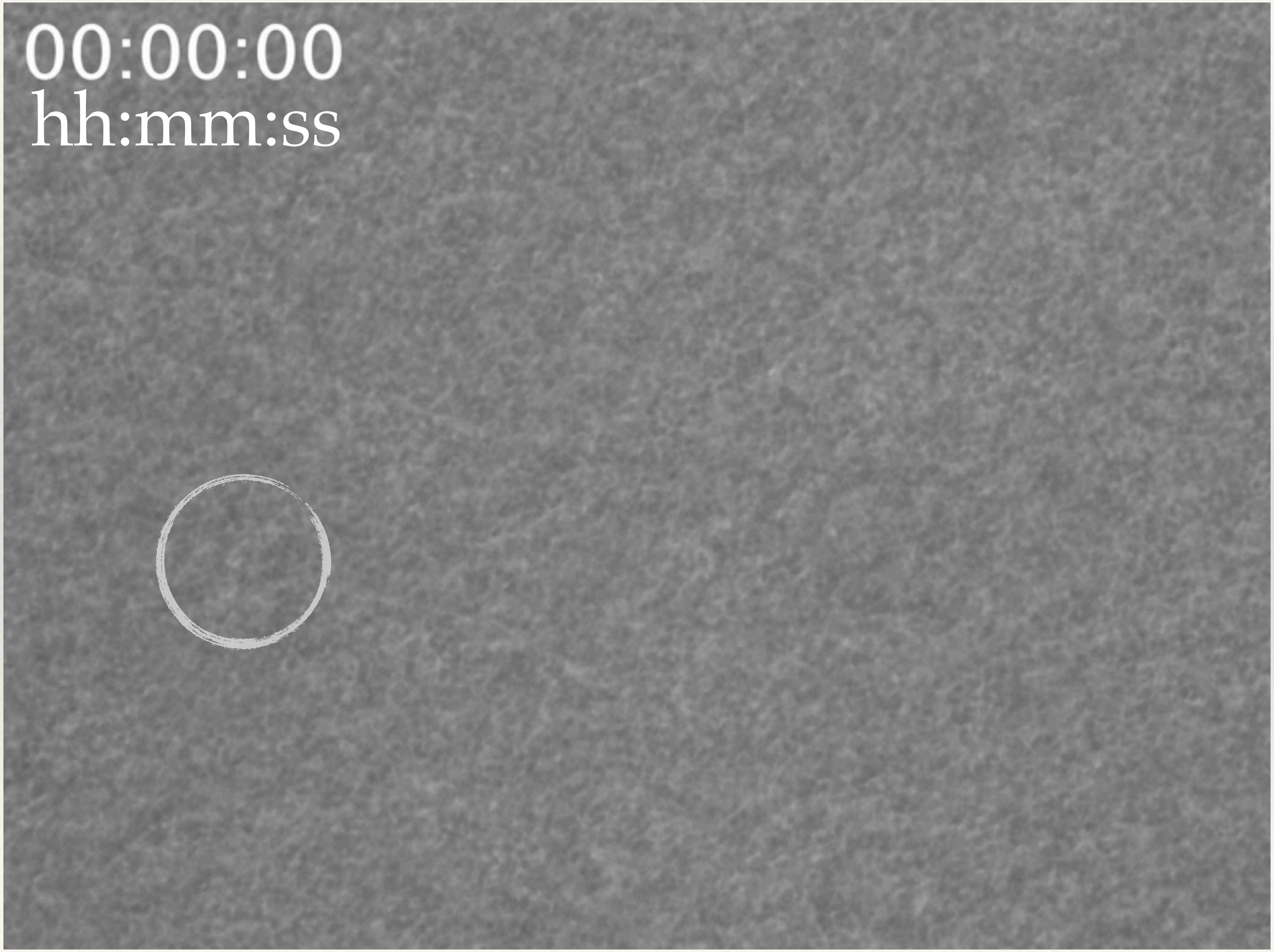


# DNA-coated particles that roll and diffuse

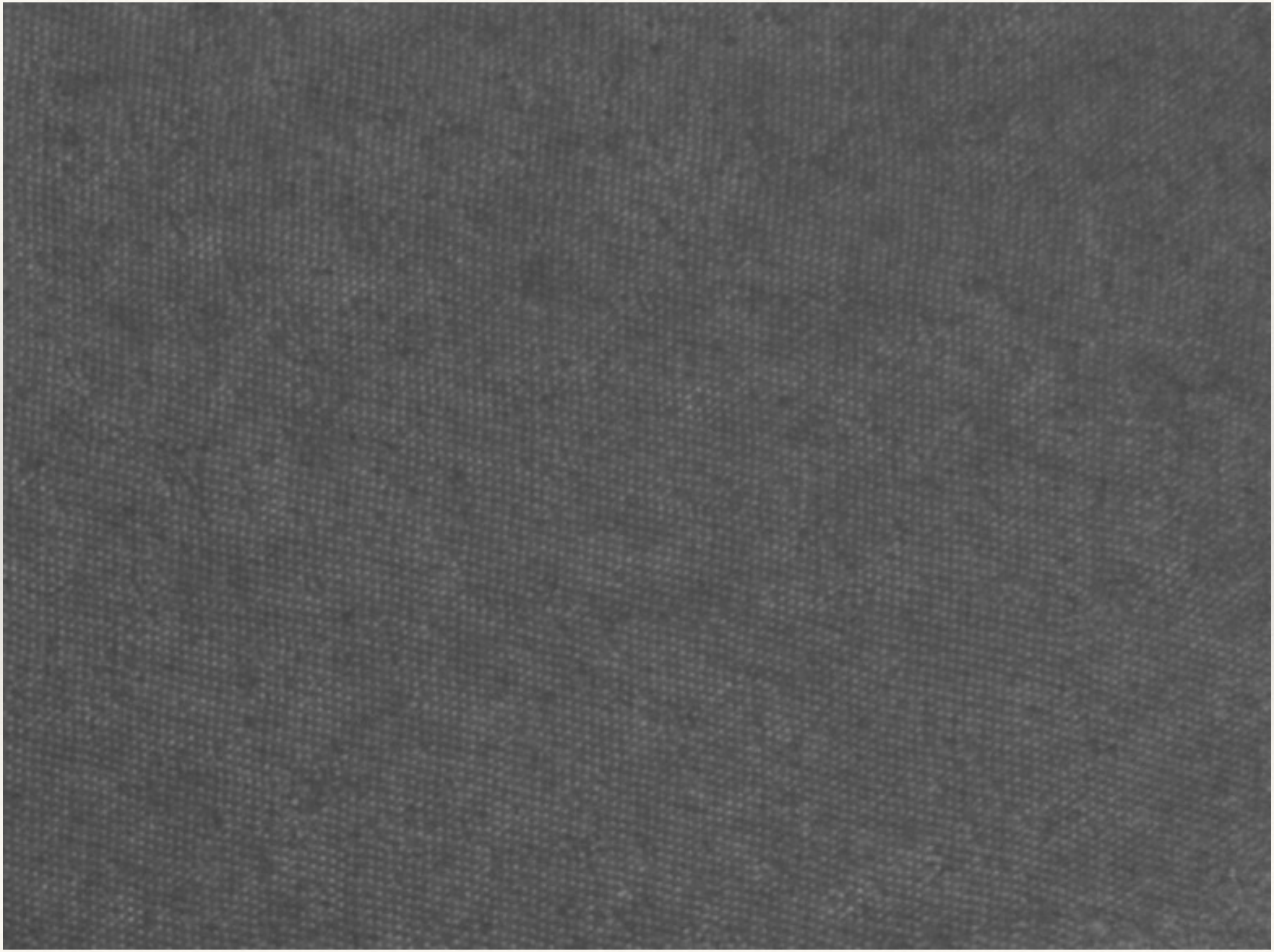


# DNA-coated colloids that stick and roll

$T$-$T_m$=-0.6

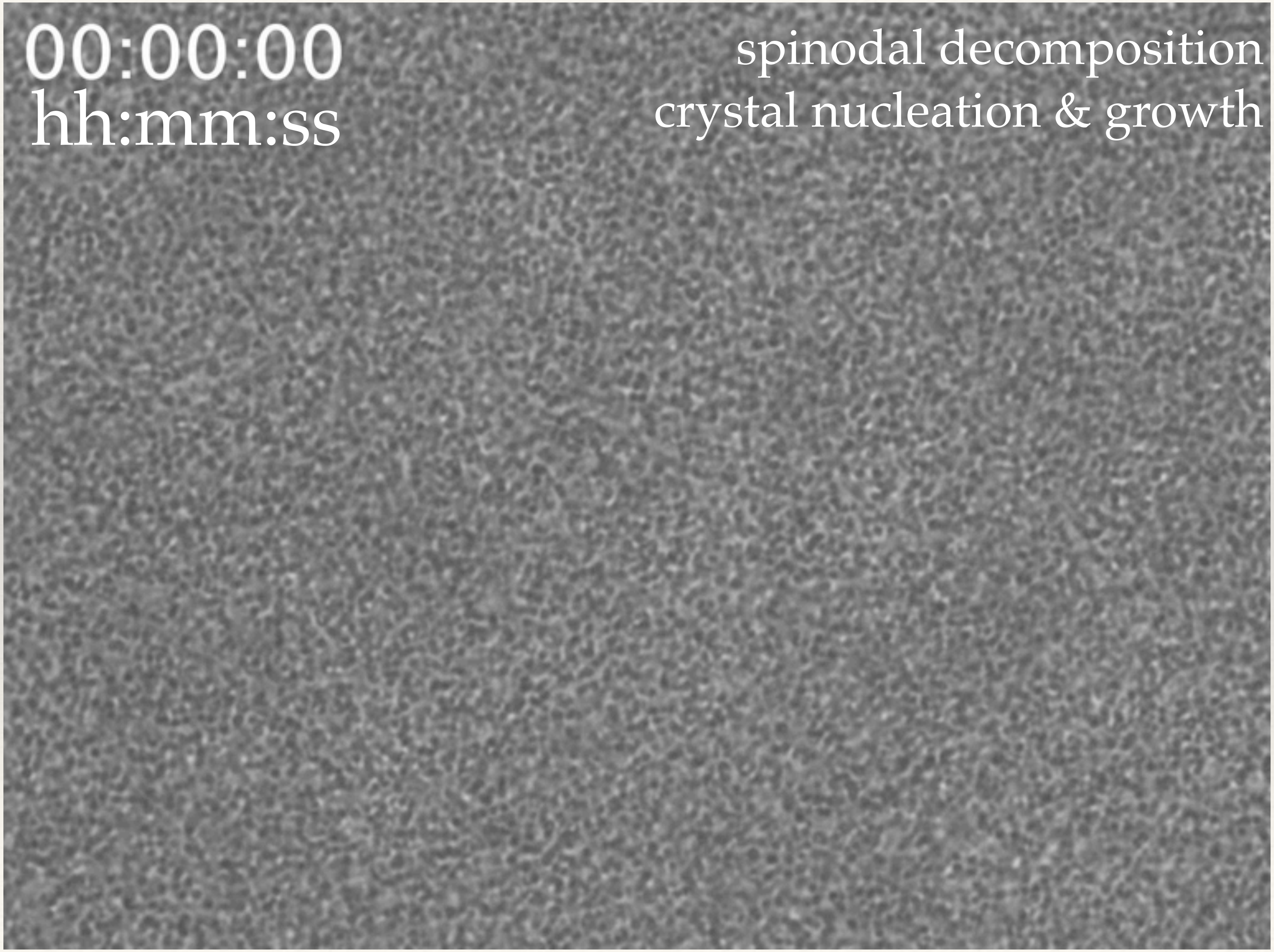


# Single crystal of 1-μm spheres



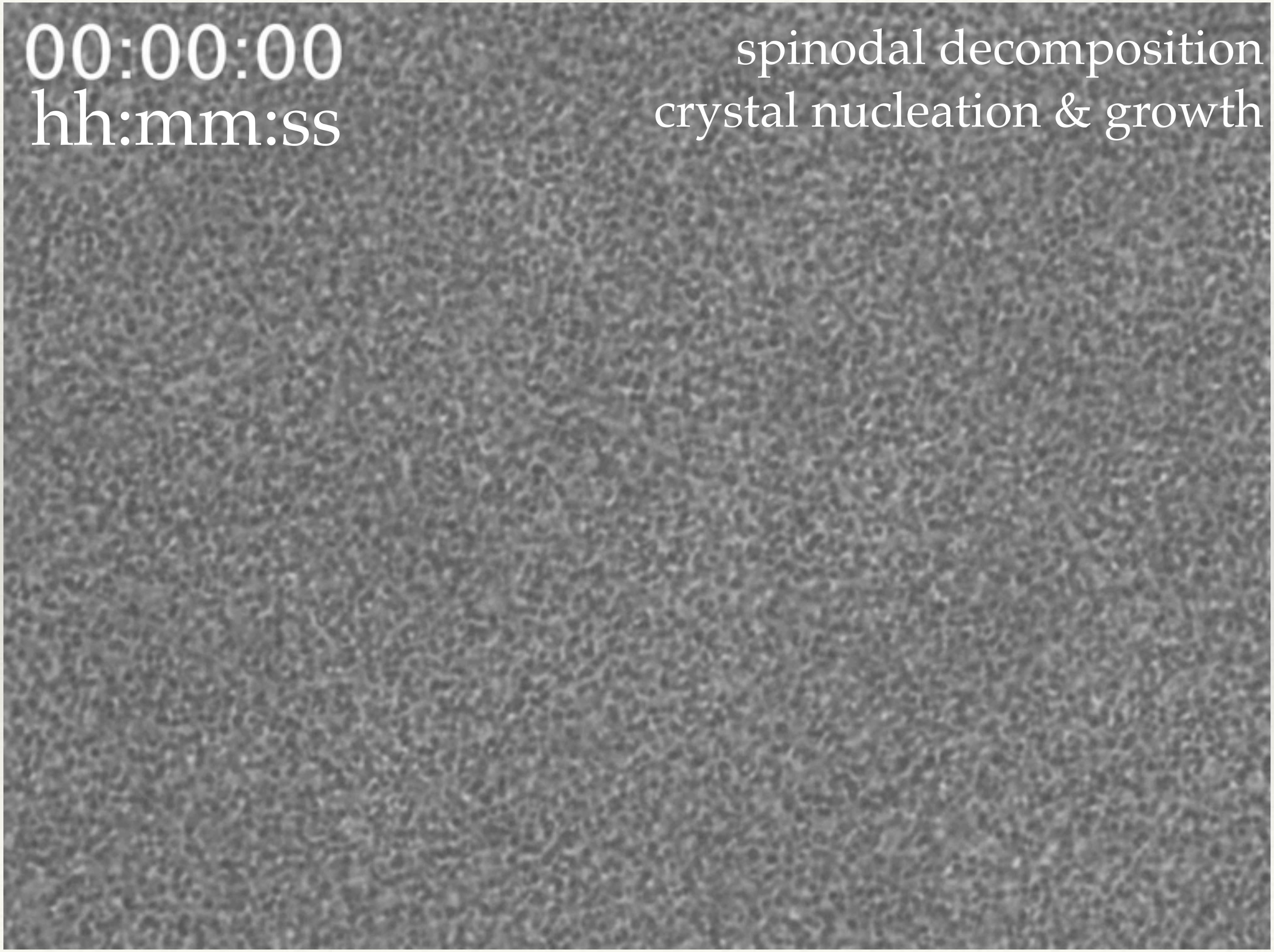
# Deep quench

$T\text{-}T_m$=-2.8

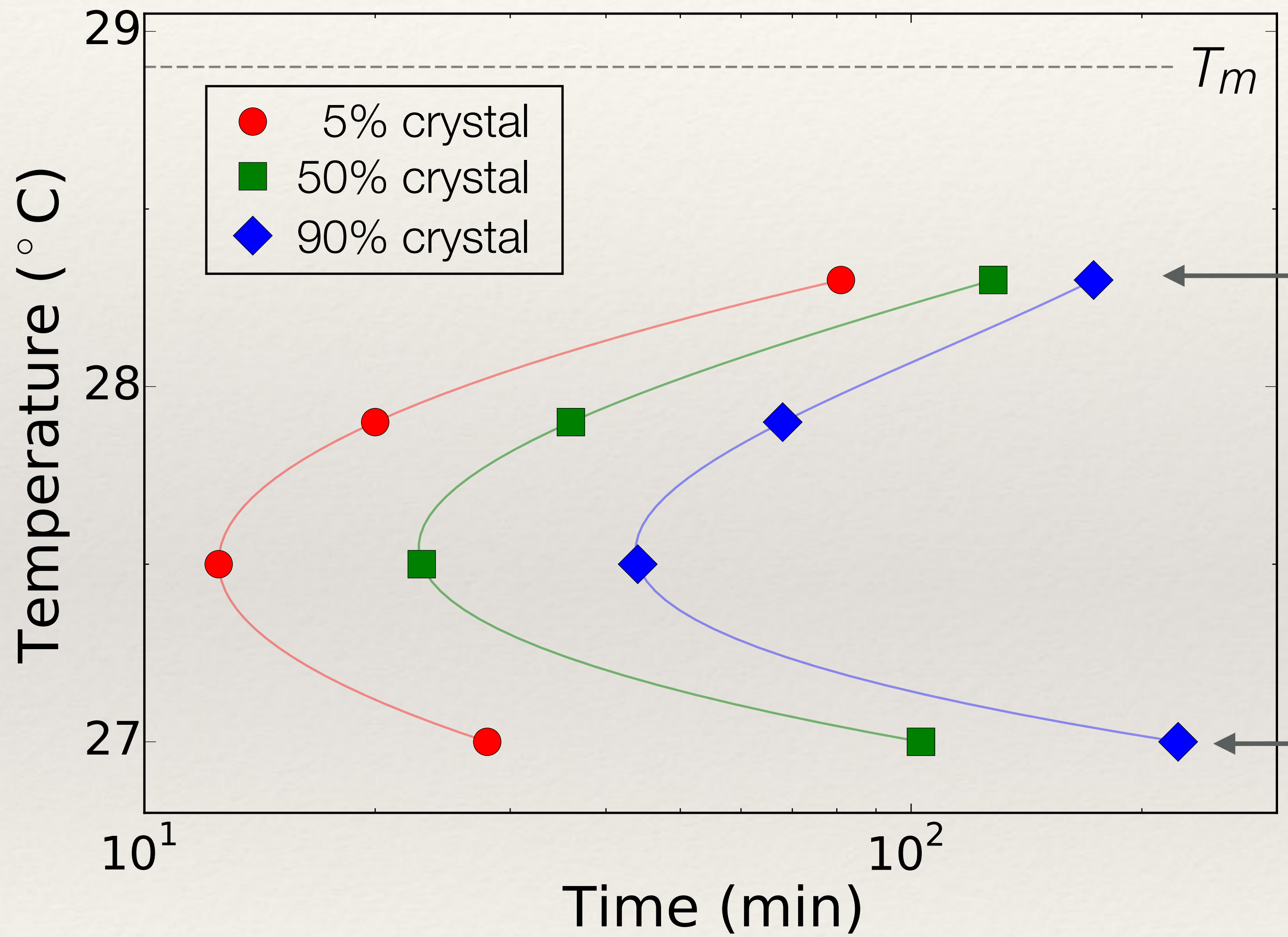


# Deep quench

$T$-$T_m$=-2.8



# Time to crystallize

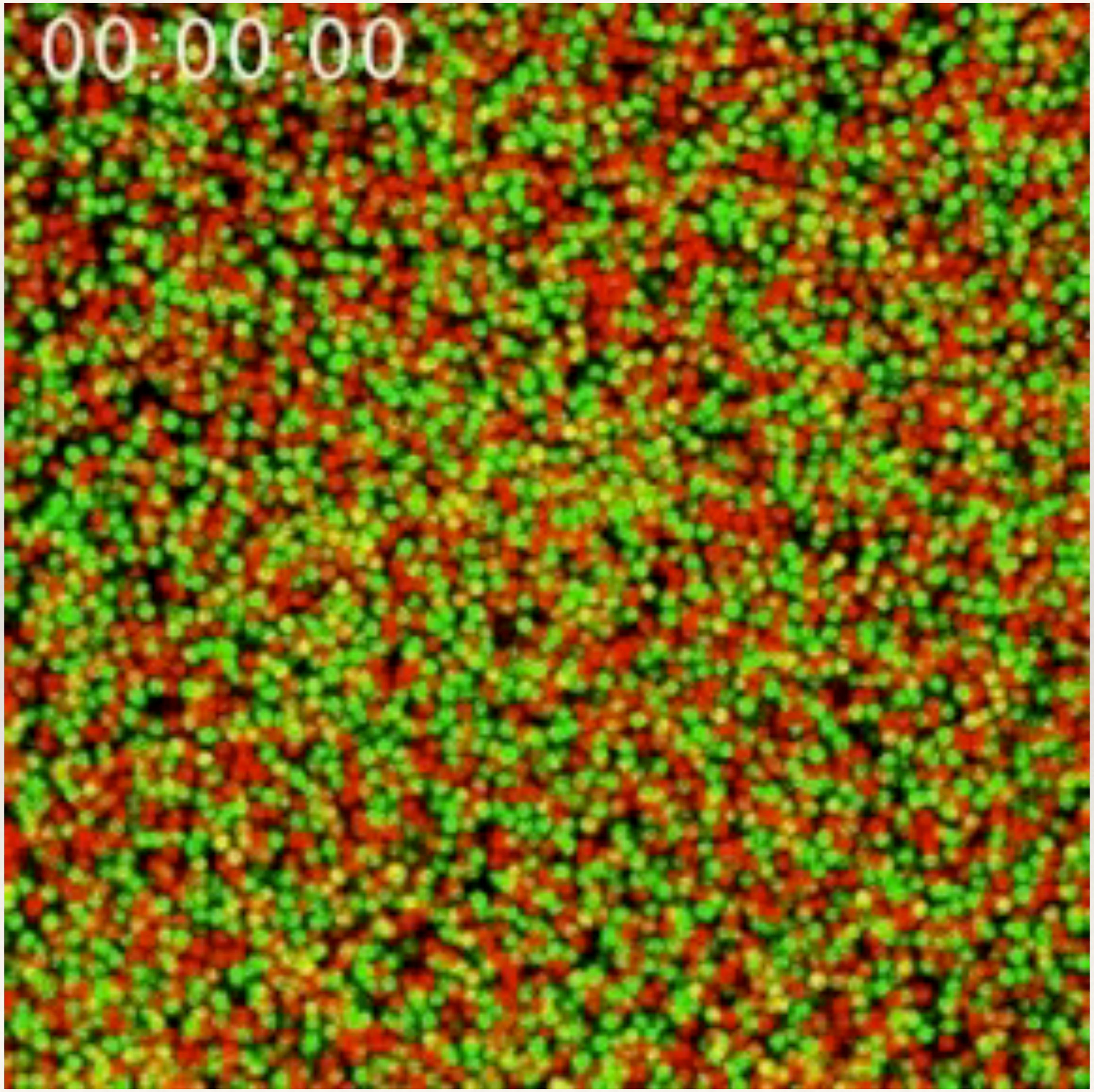



long time for nucleation
(shallow quench)

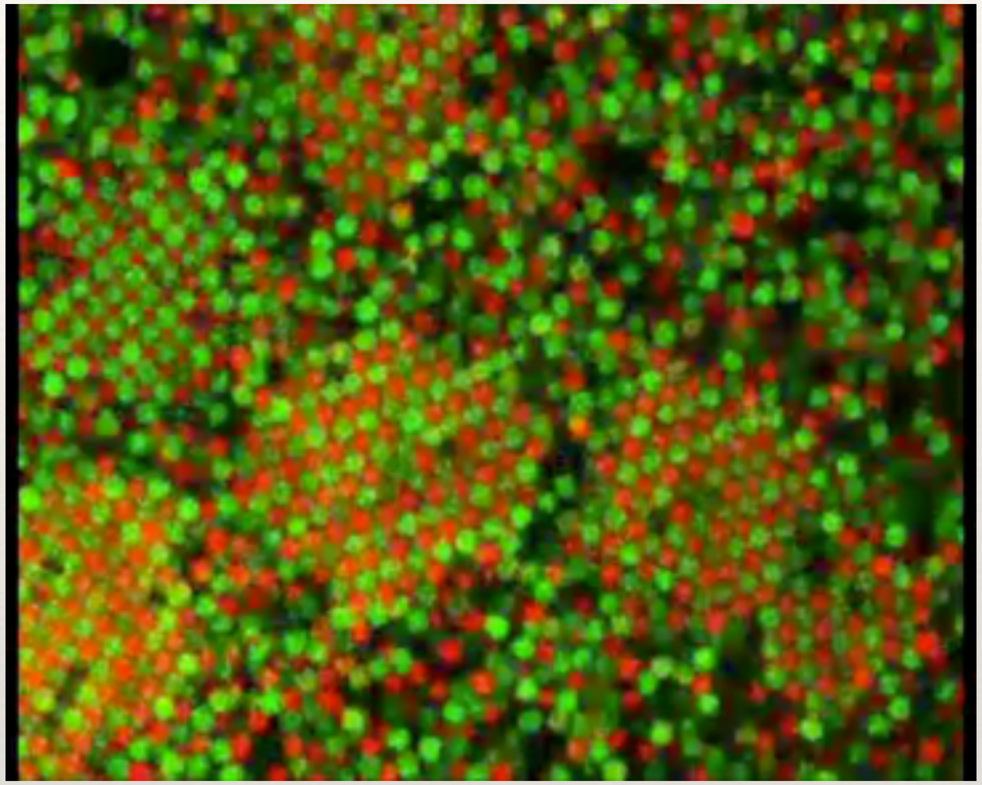
long time for diffusion
(deep quench)

# AB crystal (CsCl structure)

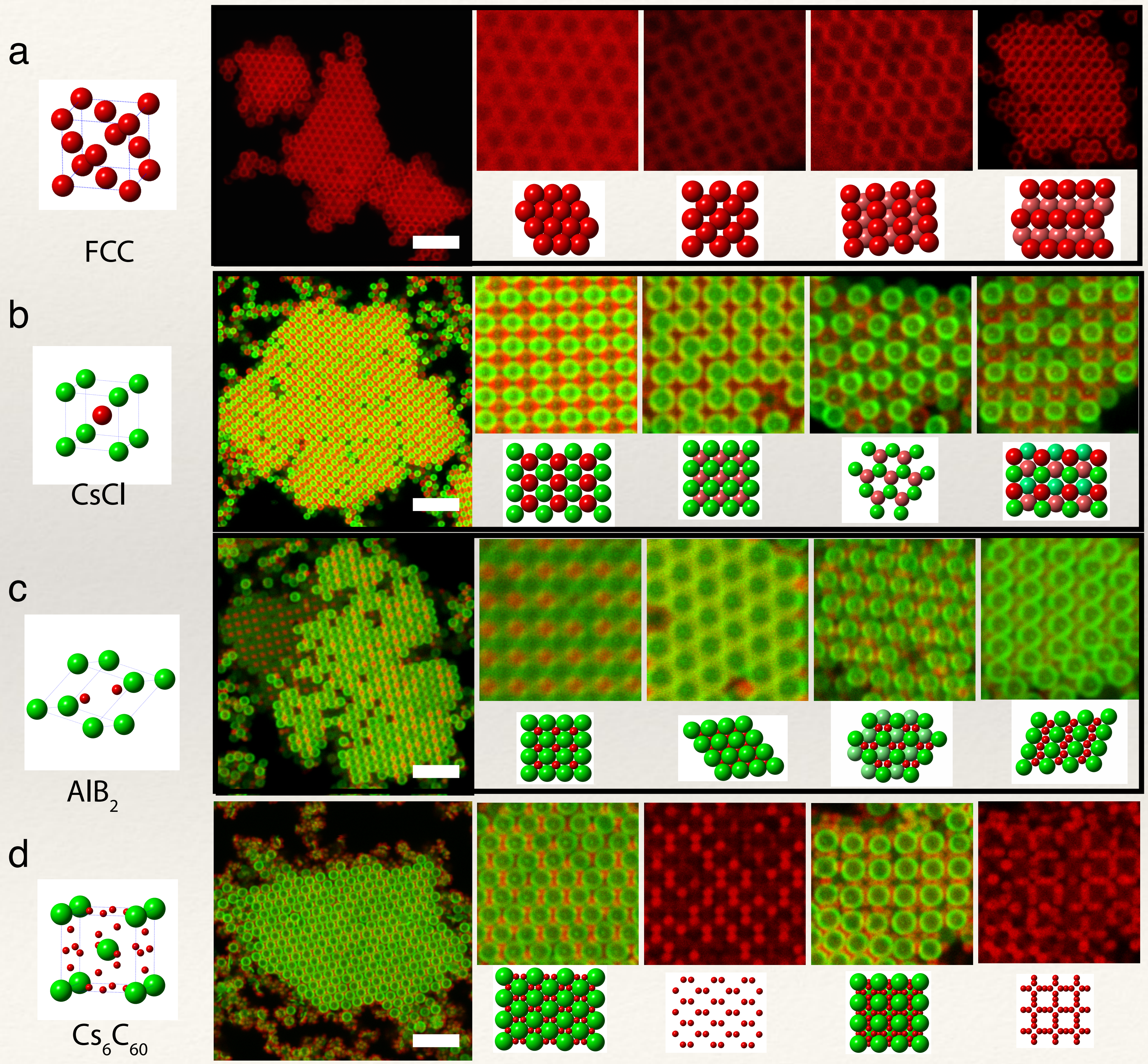
spinodal decomposition and crystal growth




formation of antisite defect



# Different crystal structures



# Materials we have coated with DNA

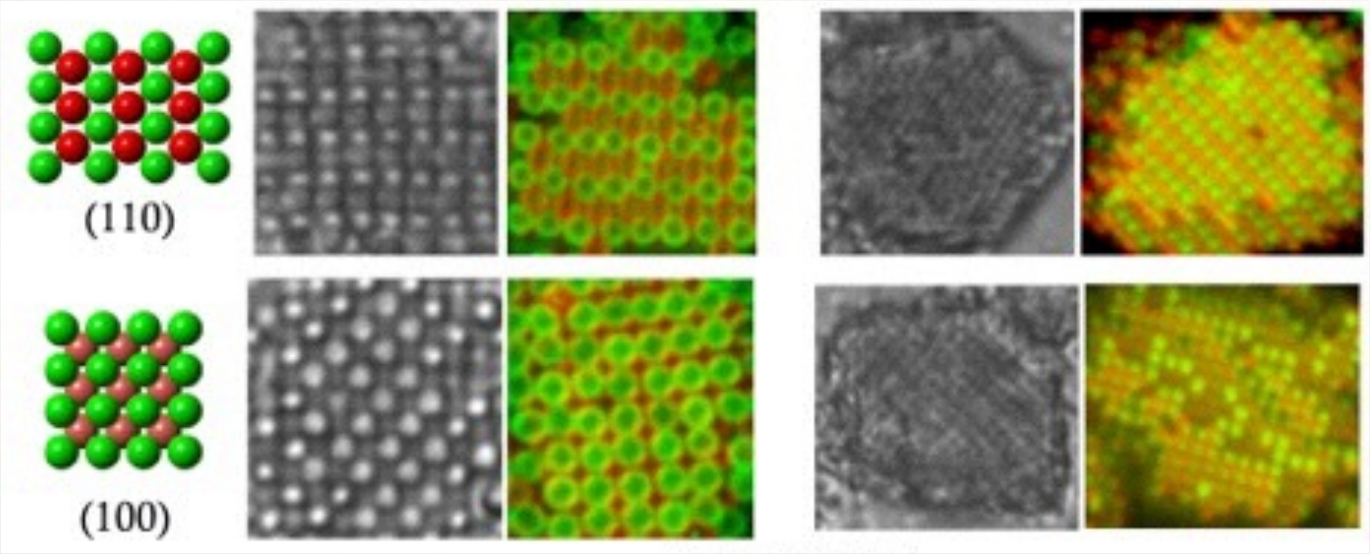
- polystyrene improved (functional !) DNA coatings
- polymethylmethacrylate (PMMA) new
- silica ($SiO_2$) new
- titania ($TiO_2$) new
- 3-methacryloxypropyl trimethoxysilane (TPM) new
- poly(pentafluoropropylmethacrylate) (PPFPMA) new
  (low-refractive index for confocal imaging in water)

*i.e.* everything we have tried

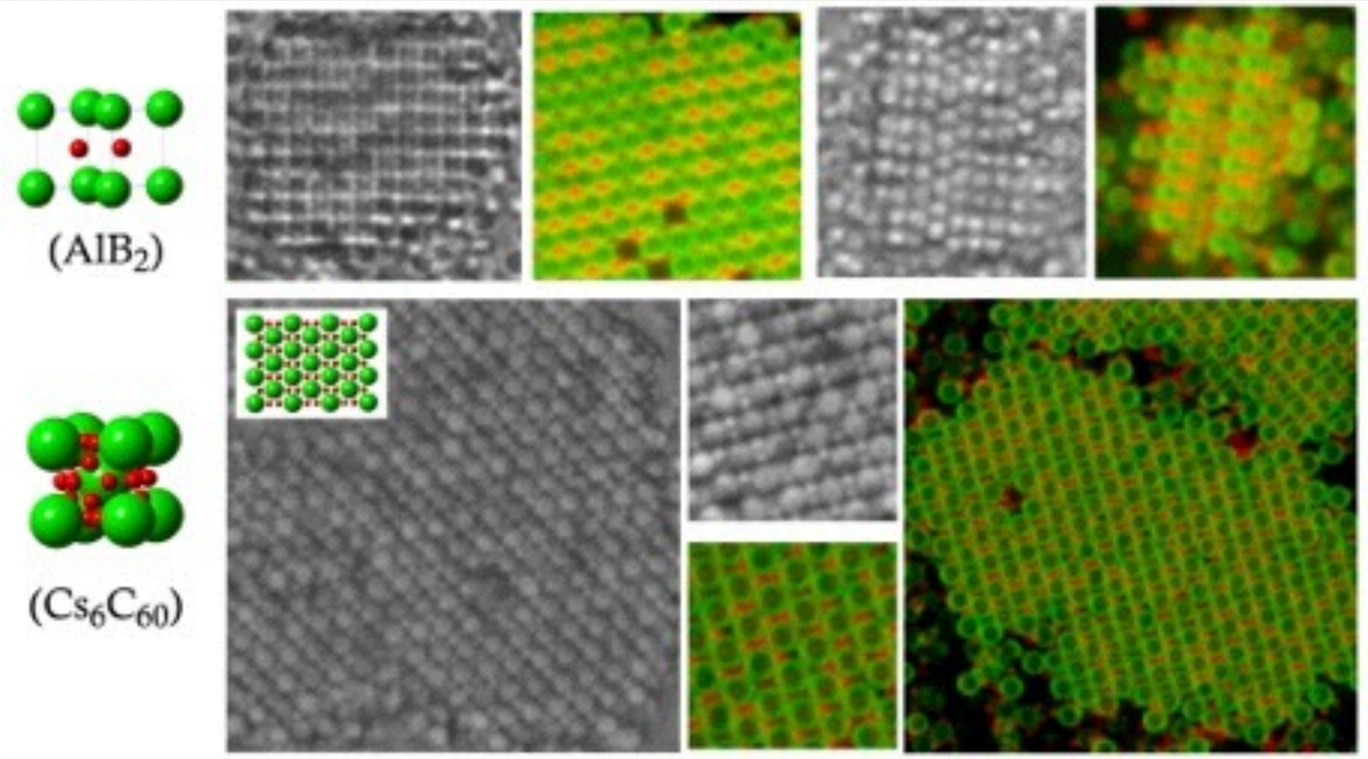
method for grafting DNA onto colloids is versatile

# Sublattices from different materials

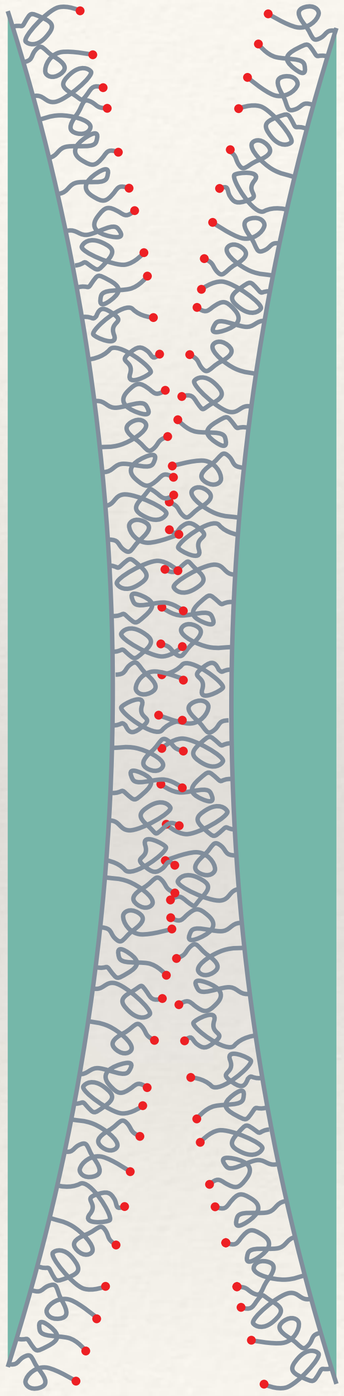
PS & silica                PS & TPM




TPM & PMMA

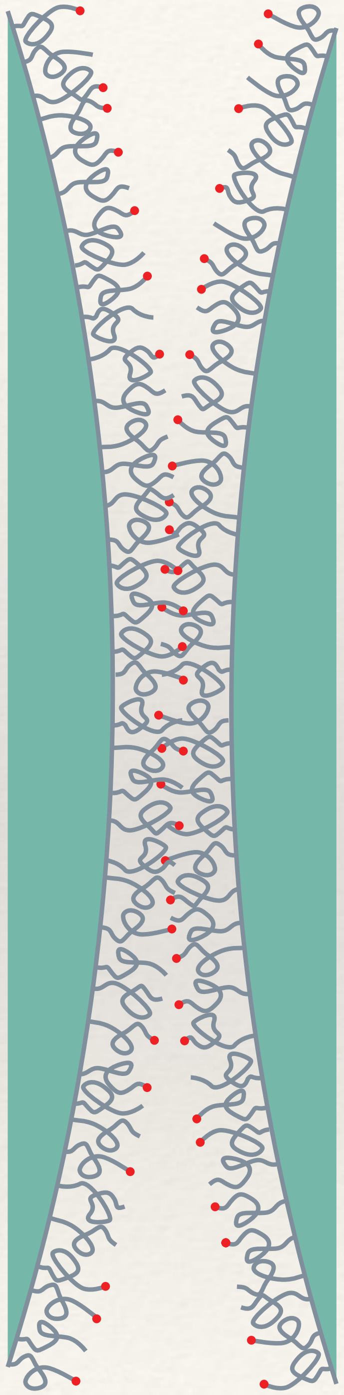


# Colloidal crystallization & density of DNA sticky ends



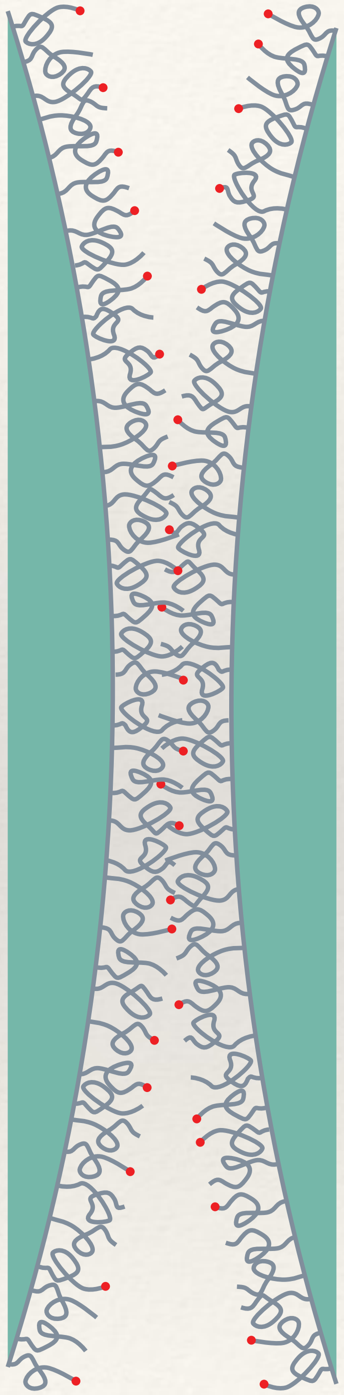
As the density of stick ends …

# Colloidal crystallization & density of DNA sticky ends



As the density of stick ends decreases, …

# Colloidal crystallization & density of DNA sticky ends



As the density of stick ends decreases, a sticky can find only one sticky end on the other particle that is within its lateral reach.

⇛ It has only one possible partner on the other particle

⇛ Bound particles can no longer roll over each and crystallization is suppressed

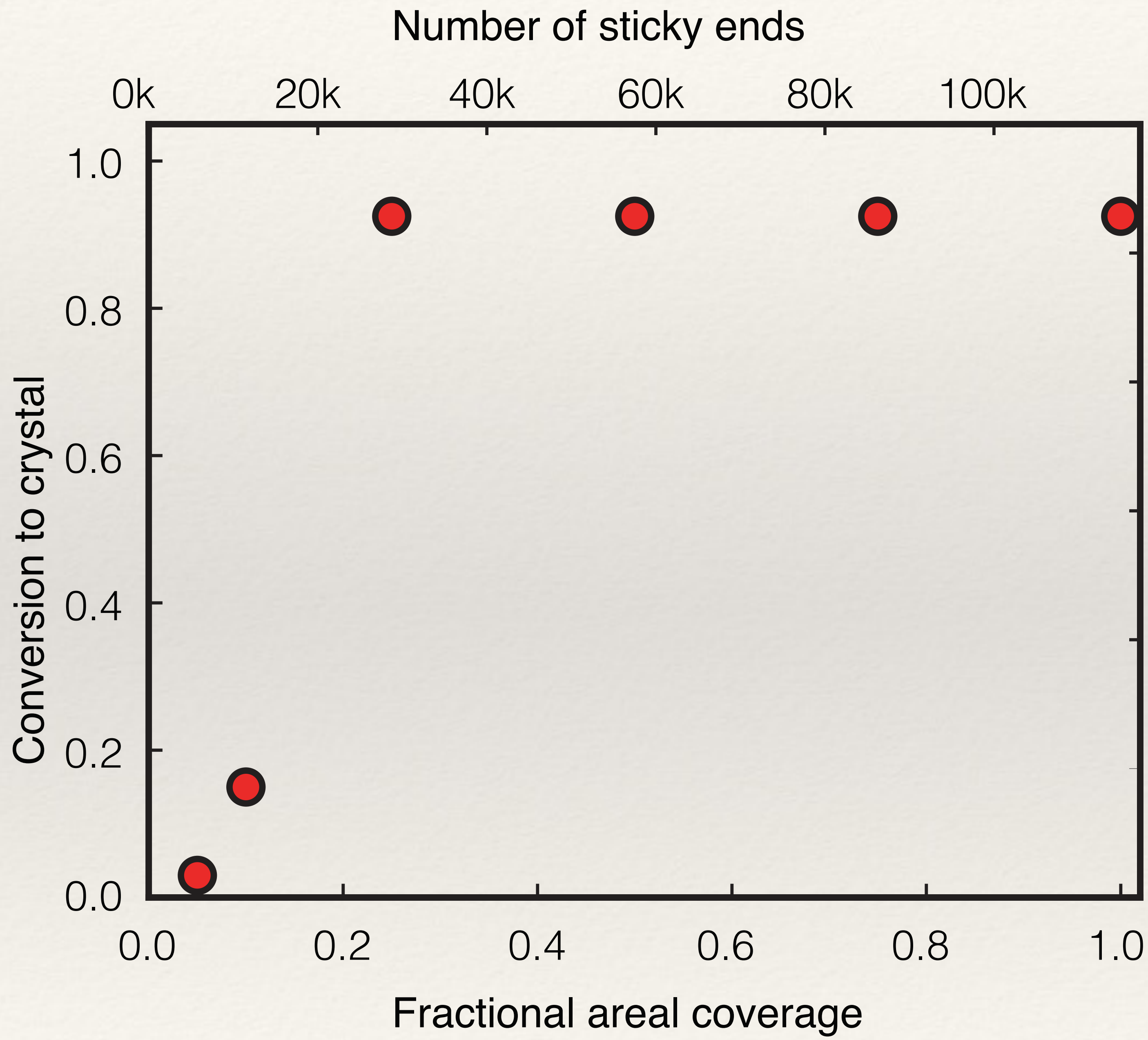
Lateral reach

$$R \simeq \sqrt{2L_pL} = 14\text{ nm}$$

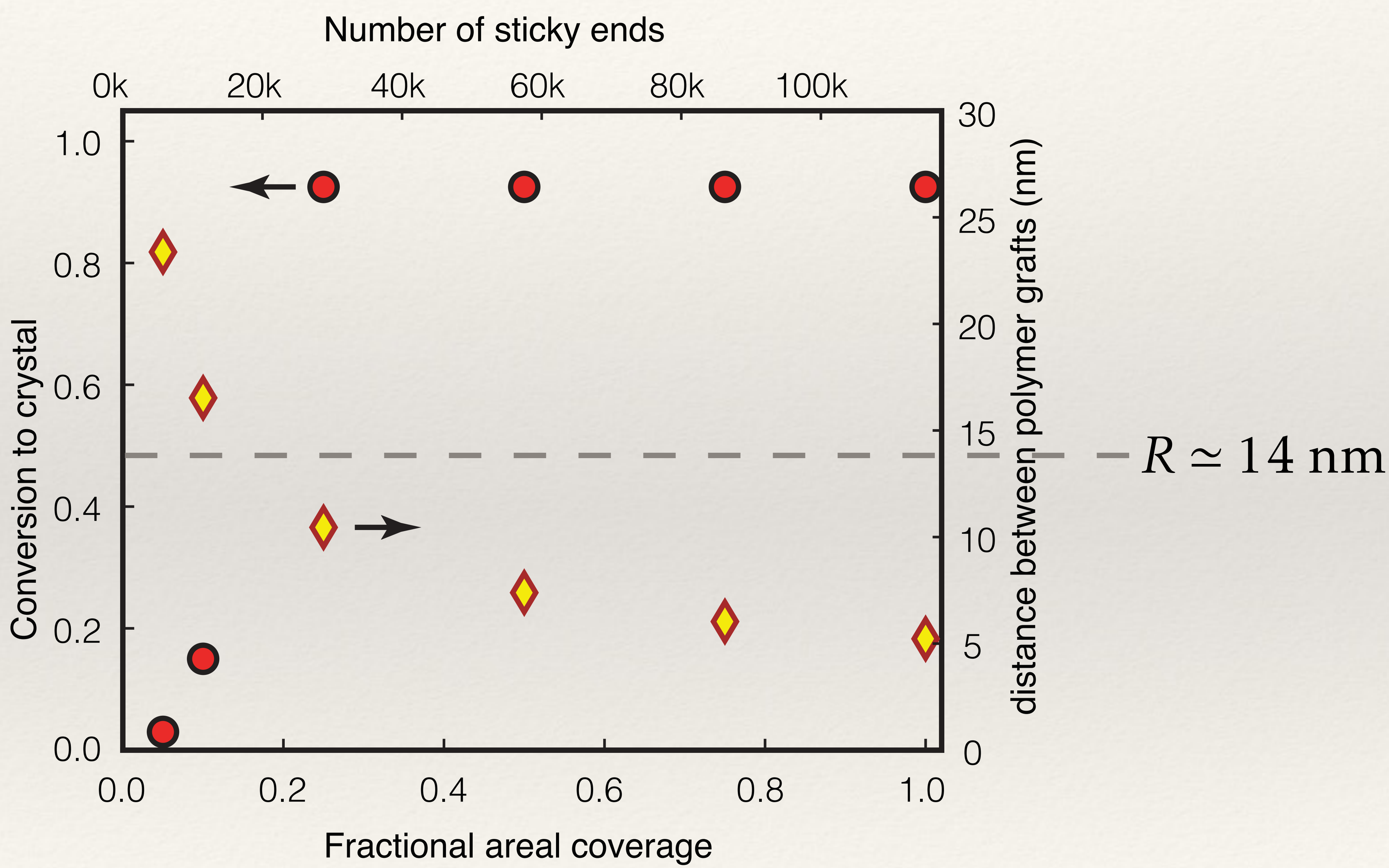
$L_p = 2.5$ nm (persistence length)

$L = 38$ nm (contour length)

# Crystal formation *vs* sticker density

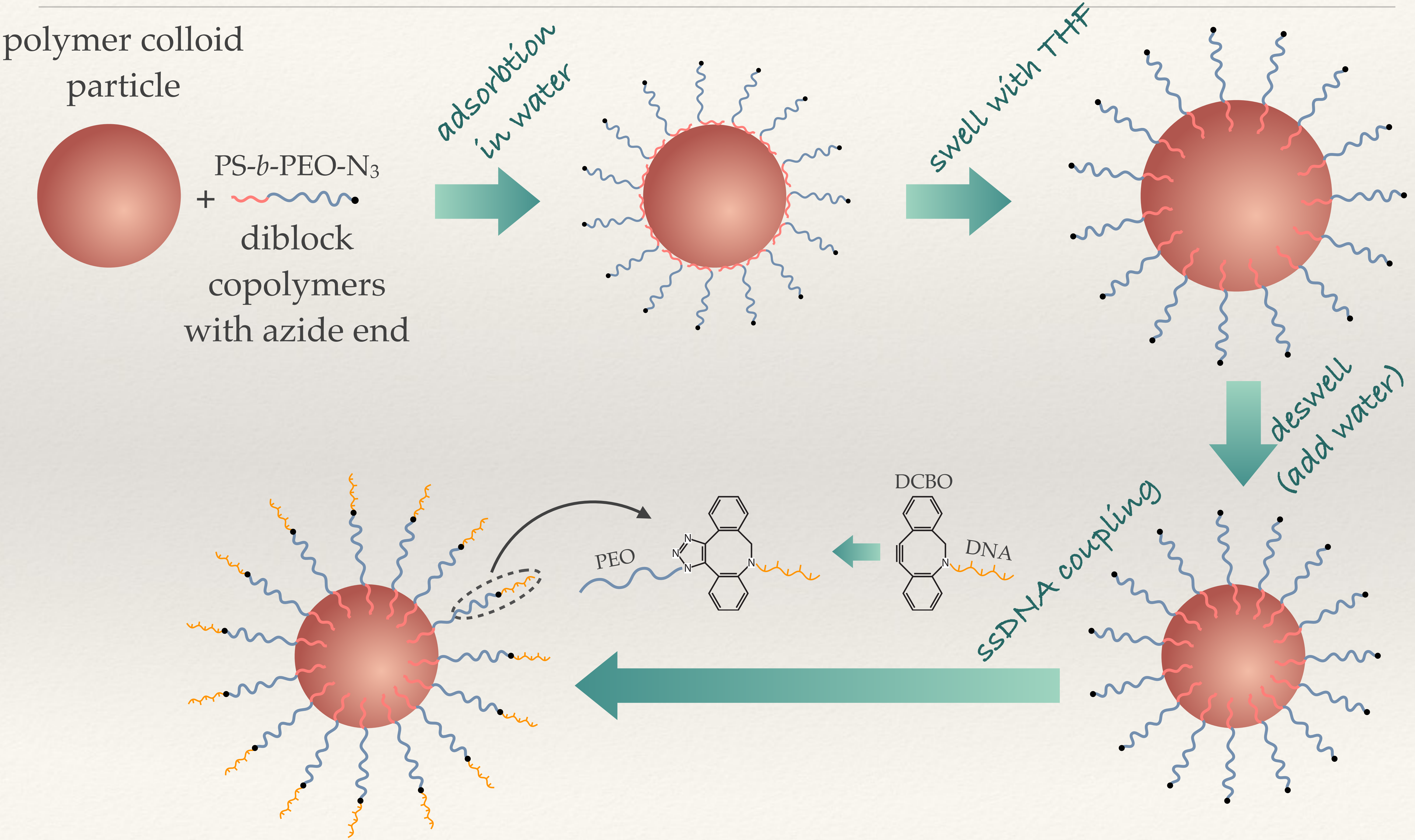


# Areal coverage & crystallization



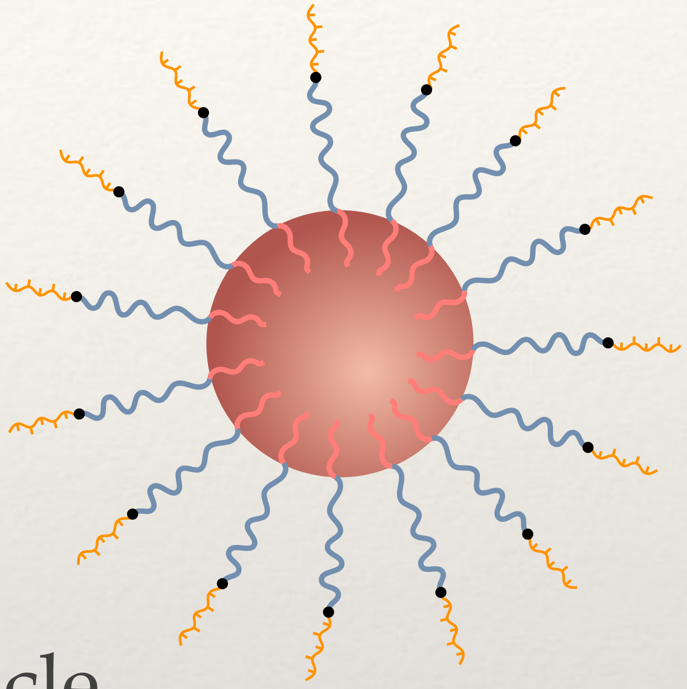
# Swelling-Deswelling method

Another way to attach DNA to polymer colloids (polystyrene, PMMA)



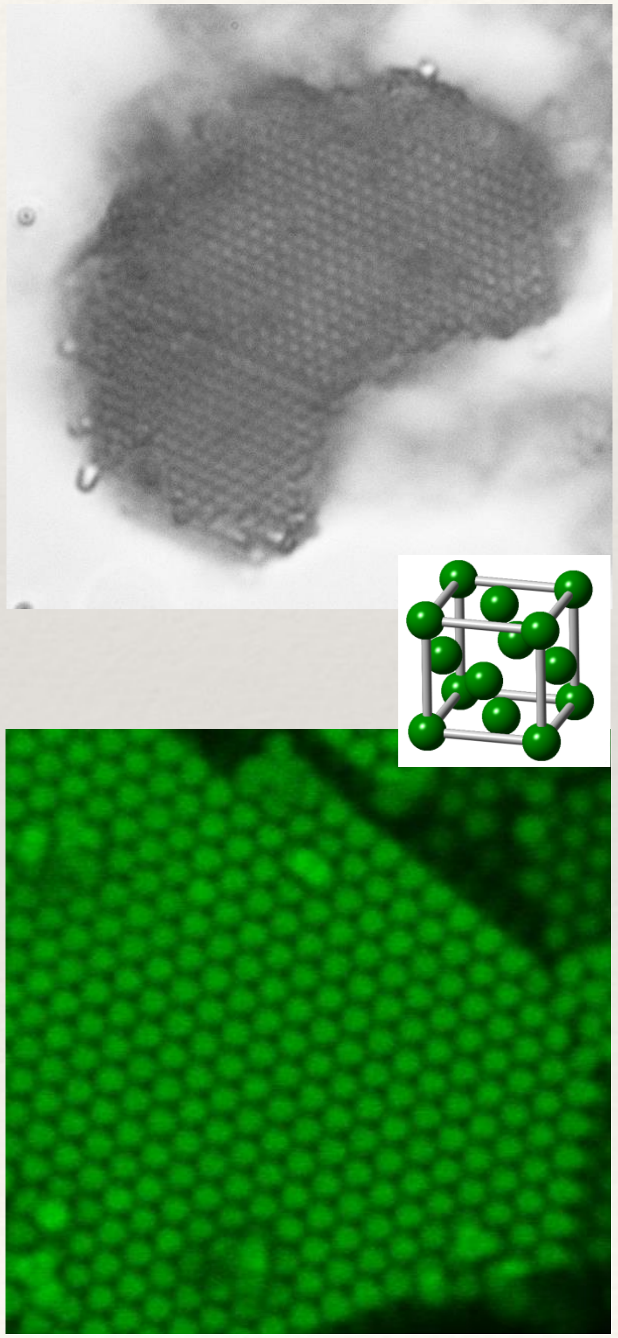
# Swelling-Deswelling method

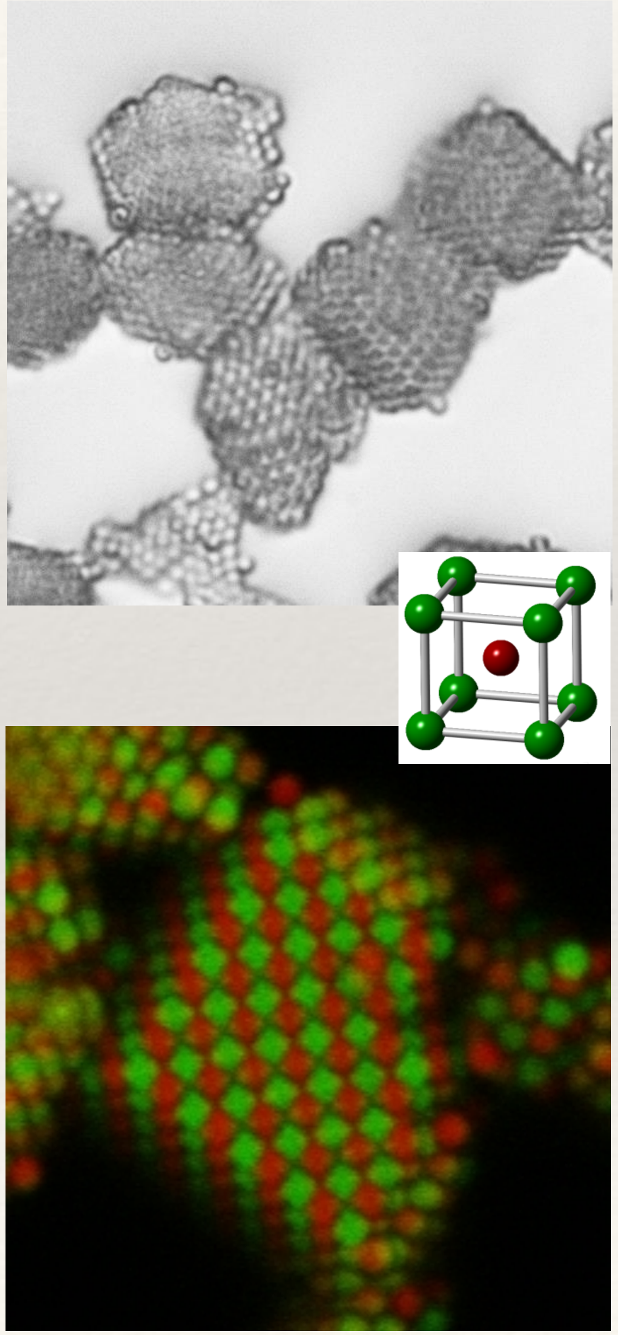
Another way to attach DNA to polymer colloids (polystyrene, PMMA)



- PS block is physically trapped inside particle
- PEO spacer forms a (stretched) polymer brush
- ssDNA coding block; no other DNA in brush
- 200,000 to 1,000,000 ssDNA / 1-µm-diameter particle
  - 3.7 nm to 1.8 nm between ssDNA grafts
- limited to (polymer) particles that can be swollen & deswollen

# These particles crystallize too





# Next lecture …

Patchy colloids with DNA

(or diamonds are a boy's best friend)

*Summer School on Soft Matter Self-Assembly, 2015, June 28-July 7*

# Lecture 4: Patchy colloids with DNA


David Pine

Department of Physics

Dept of Chemical & Biomolecular Eng

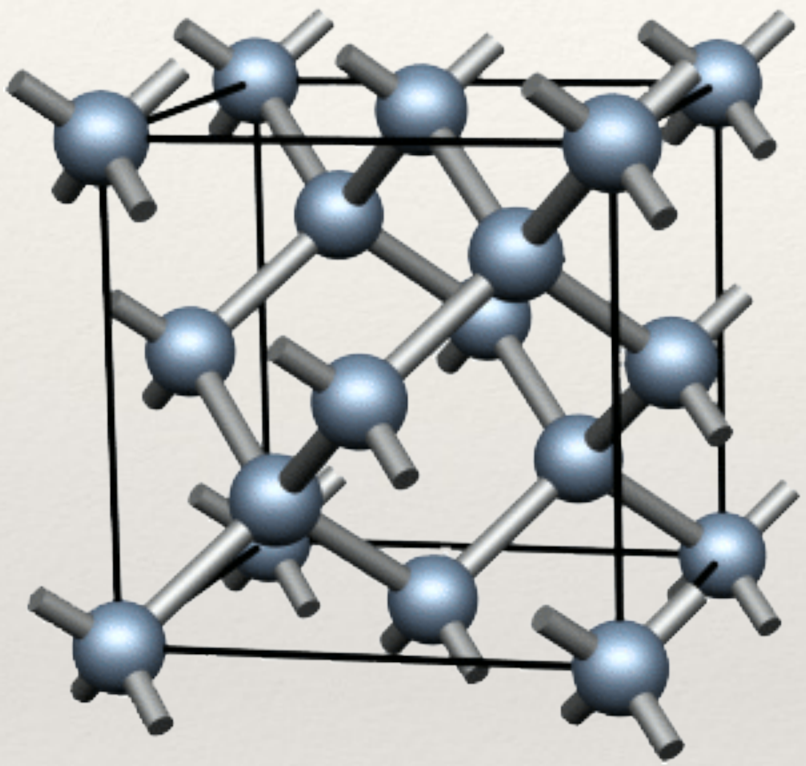
New York University

NYU

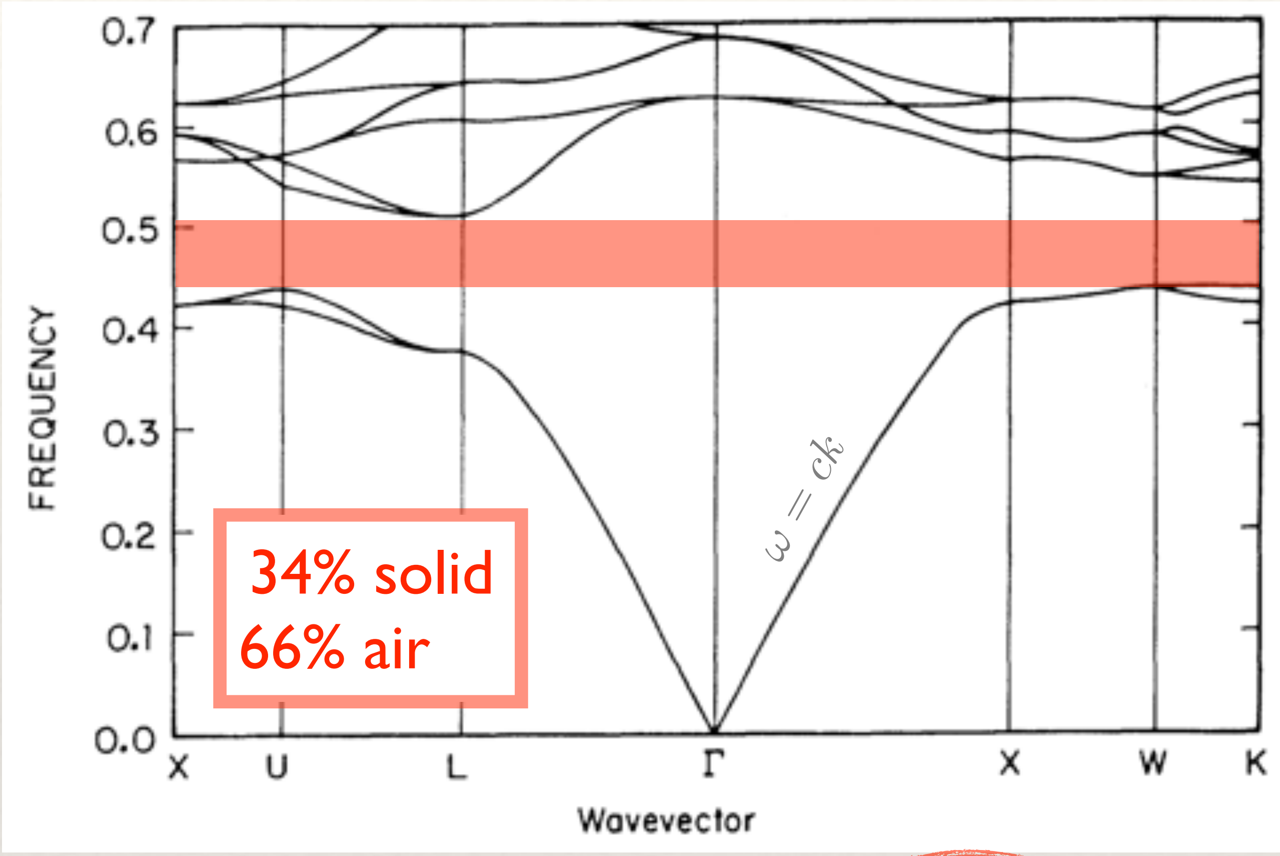

*International School of Physics "Enrico Fermi" in Varenna, Italy*

# A Challenge: Make this

diamond lattice



photonic band gap



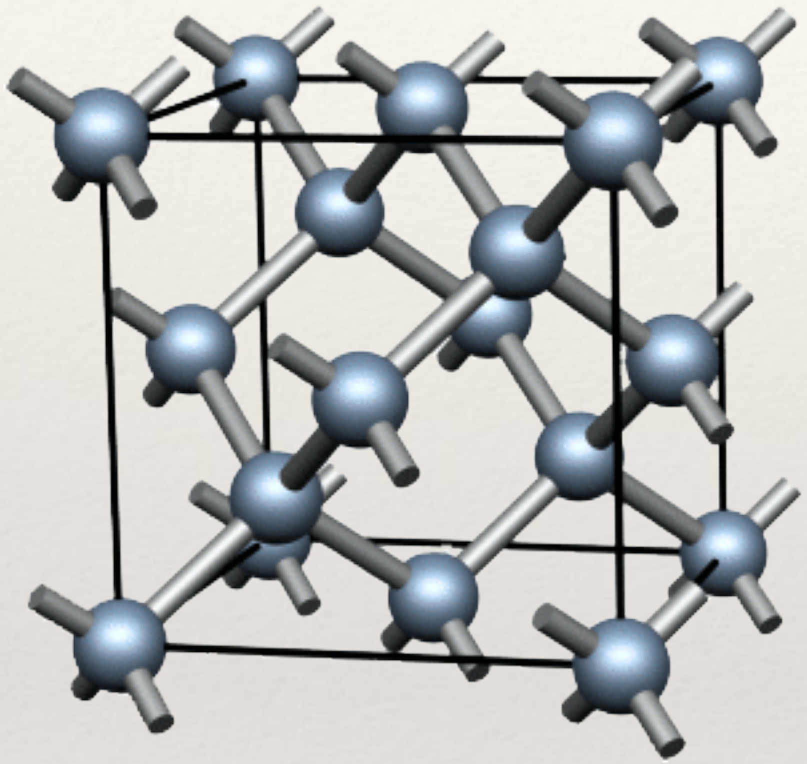

Ho, Chan, Soukoulis, PRL **65**, 3152 (1990)

25 years

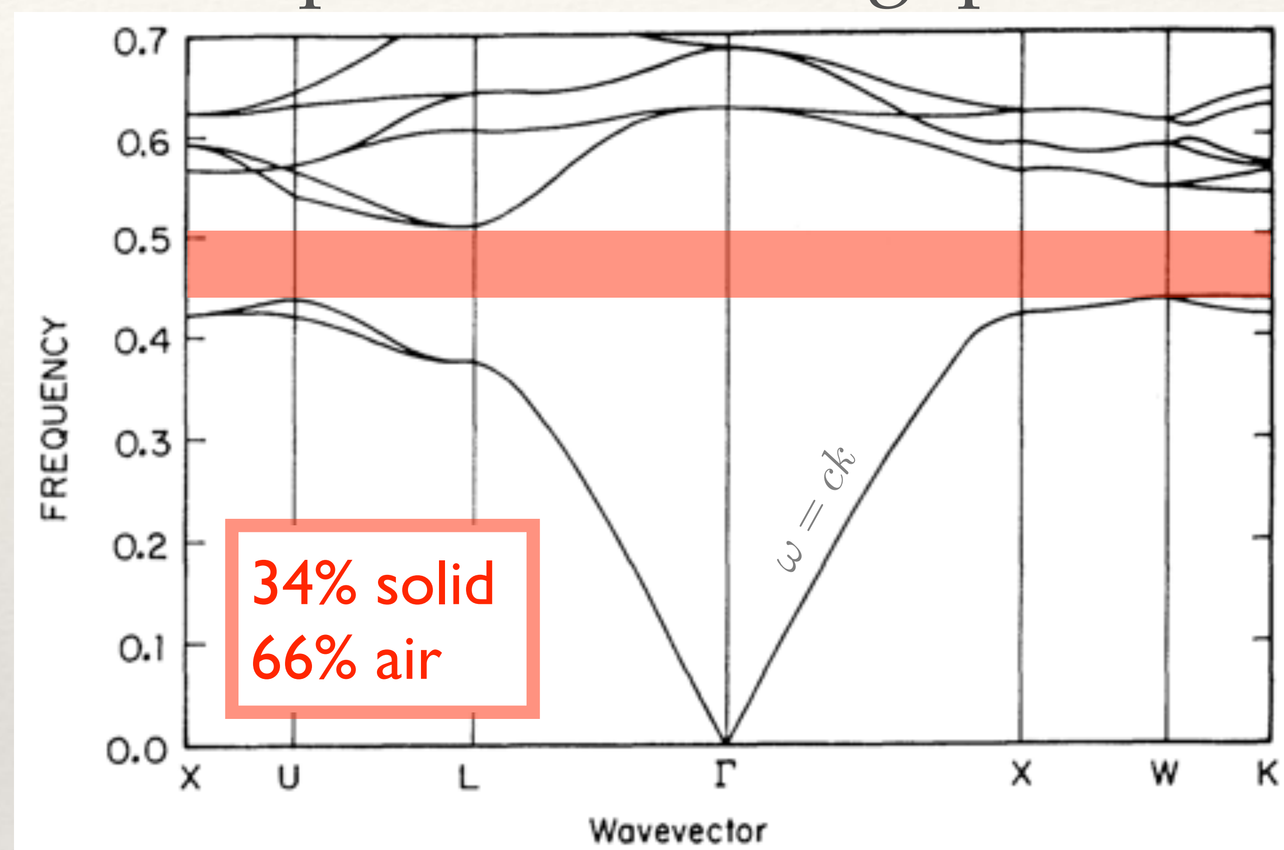
...so what's the problem ?

# A Challenge: Make this

diamond lattice



photonic band gap



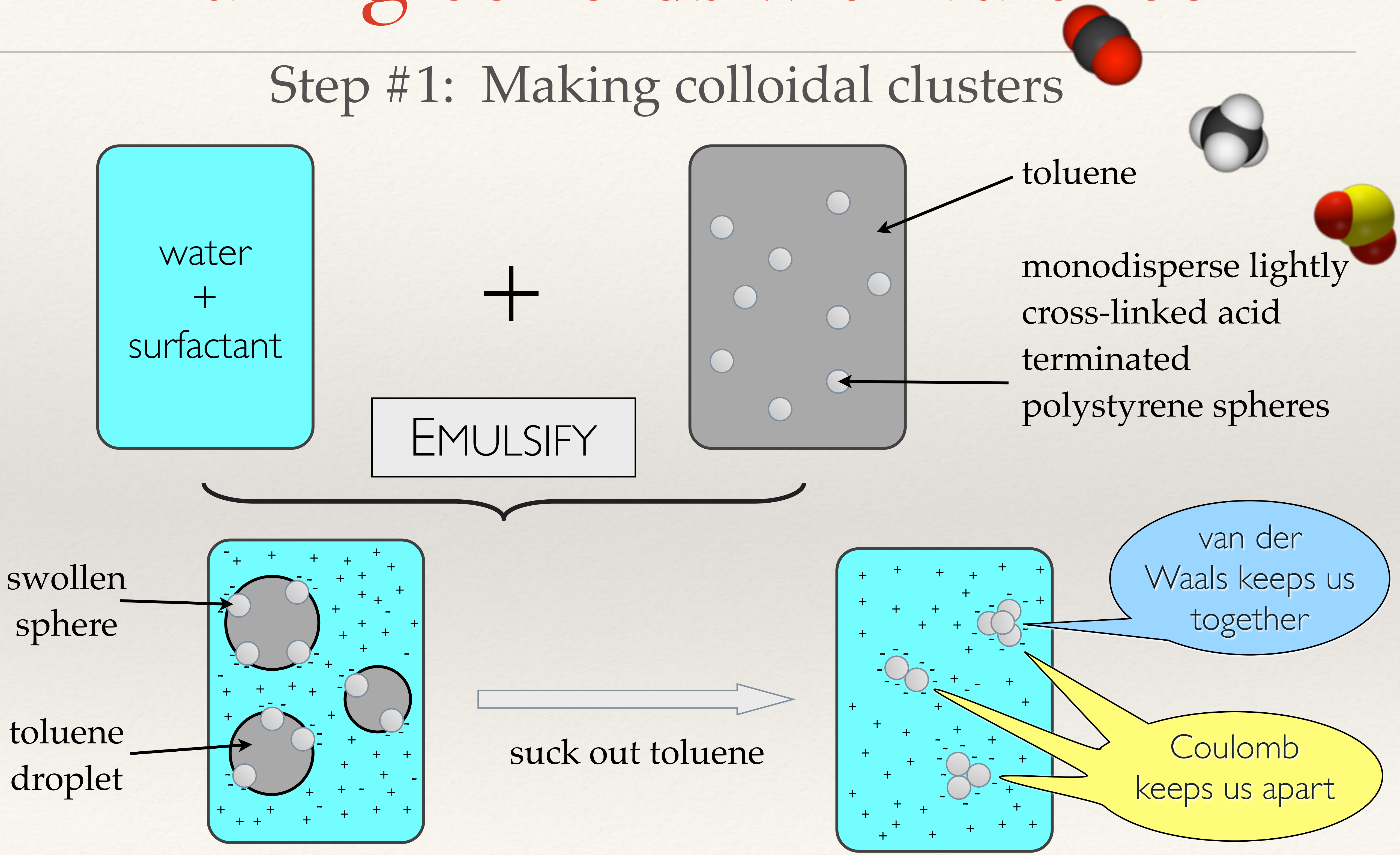

Ho, Chan, Soukoulis, PRL **65**, 3152 (1990)

We need colloids with directional interactions (valence)

$CO_2$ $CH_4$ $H_2O$

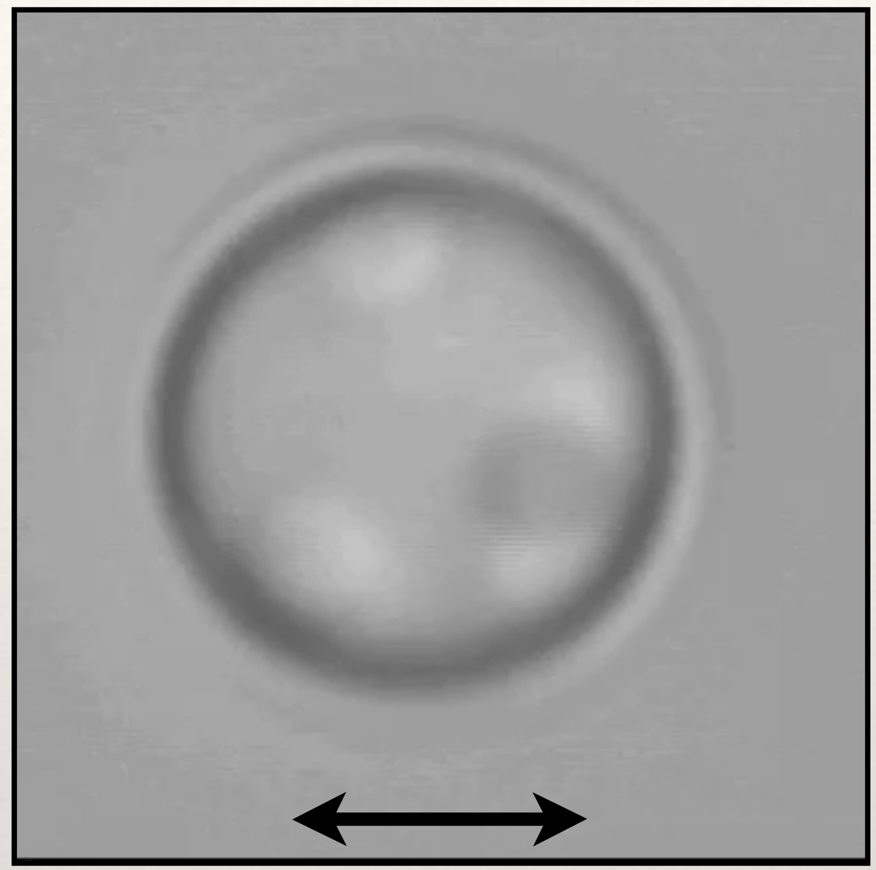
# Making colloids with valence

## Step #1:  Making colloidal clusters

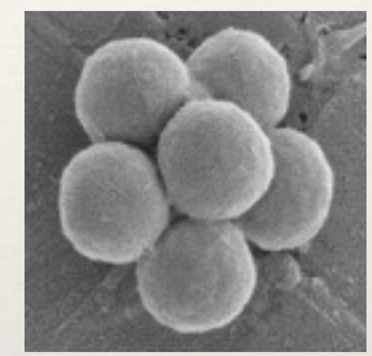


# Cluster formation

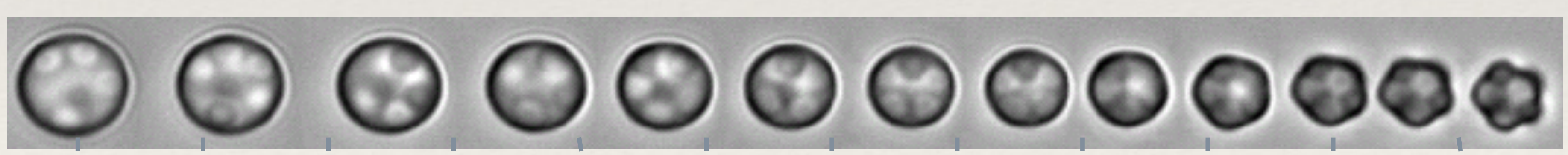
particles are confined
to droplet surface,
not the interior



$2\ \mu m$



capillary force
pulls spheres
towards center



0 secs 2 4 6 8 10 12 14 16 18 20 22

particles move at surface

particles touch and jam

droplet deforms

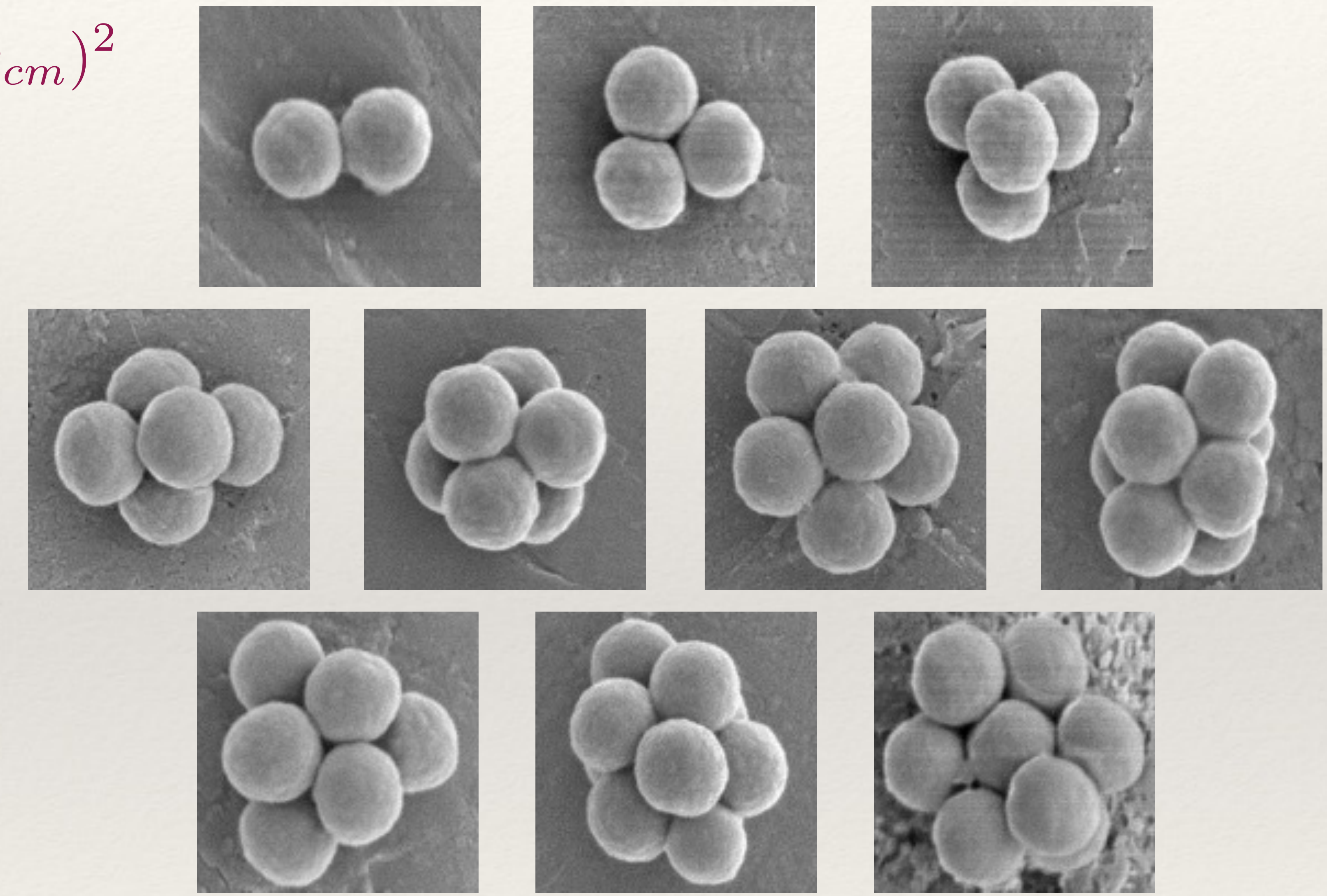
Rearrangement

drying

# First 11 minimal-moment clusters

$$M_2 = \sum_{0}^{n} (\mathbf{r} - \mathbf{r}_{cm})^2$$

John Conway*
(Princeton)



Calculated by John Conway, Neil Sloane et al

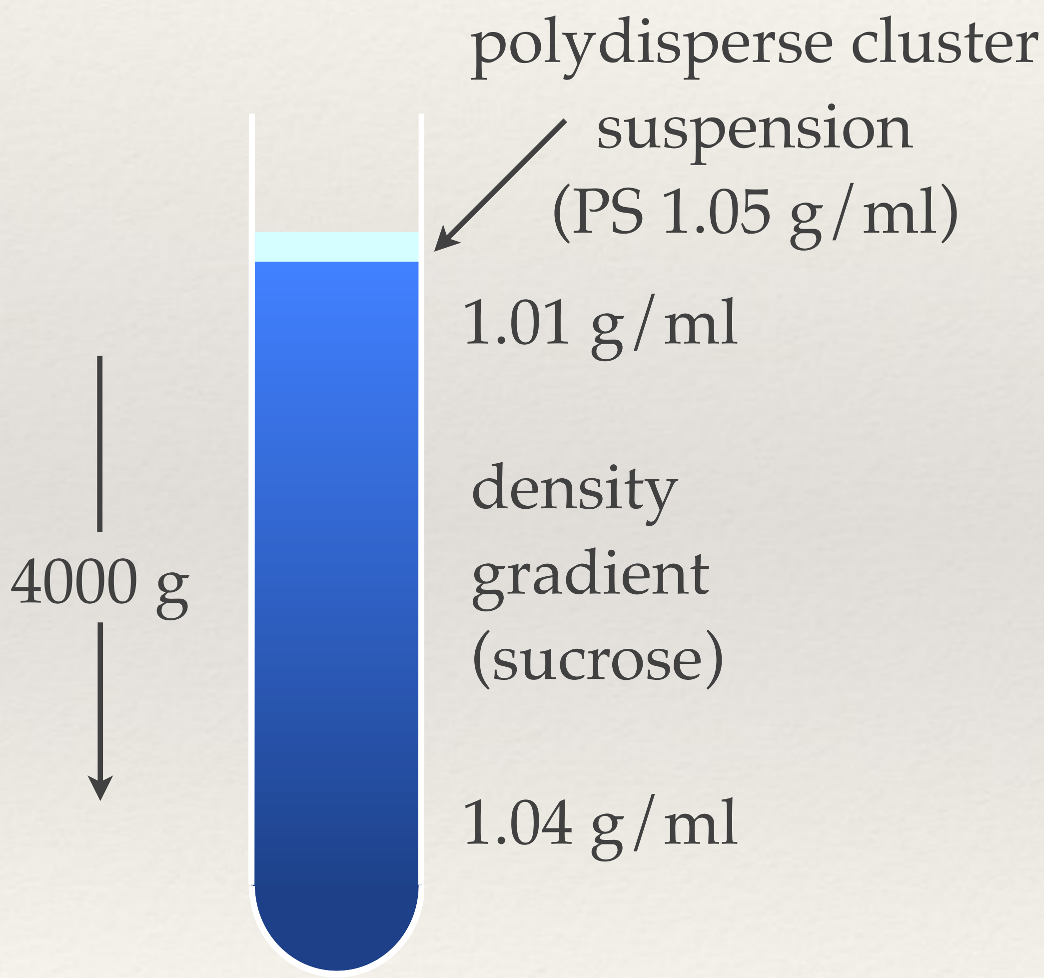
Assembled & measured by Vinny Manoharan

* Conway, Sloane, et al. Discrete Comp. Geom. **14**, 237 (1995)

Manoharan *et al*. Science **301**, 483 (2003)

# Separating clusters

density gradient centrifugation




$$\Delta m g = 6\pi\eta R_{hyd} v_{sed}$$

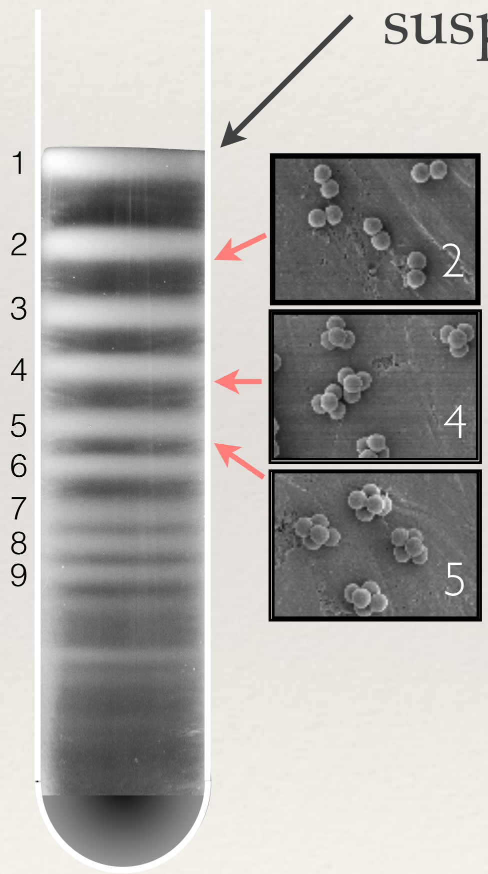
$$\Rightarrow \; v_{sed} = \frac{\Delta\rho}{\eta} R_{hyd}^2 g$$

It's a race

Clusters with large hydrodynamic radius sediment faster

# Separating clusters

polydisperse cluster suspension




$$\Delta m g = 6\pi\eta R_{hyd} v_{sed}$$

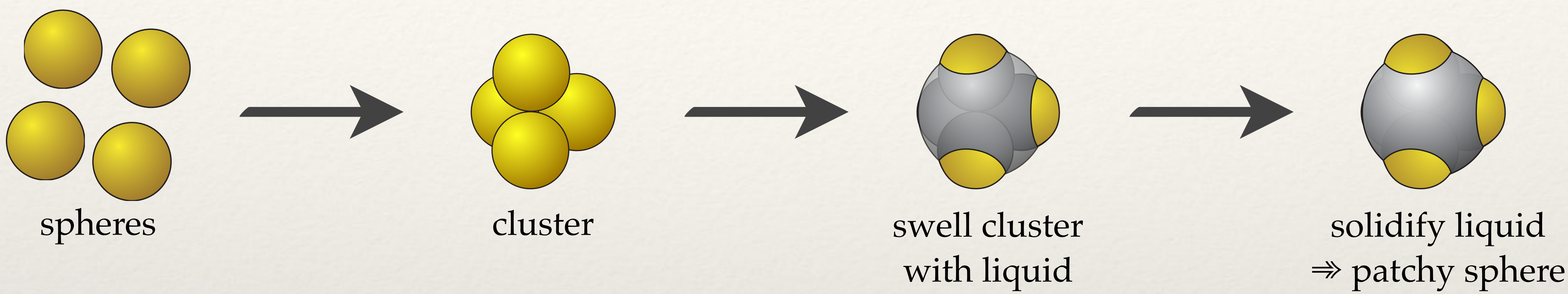
$$\Rightarrow \; v_{sed} = \frac{\Delta\rho}{\eta} R_{hyd}^2 g$$

It's a race

Clusters with large hydrodynamic radius sediment faster

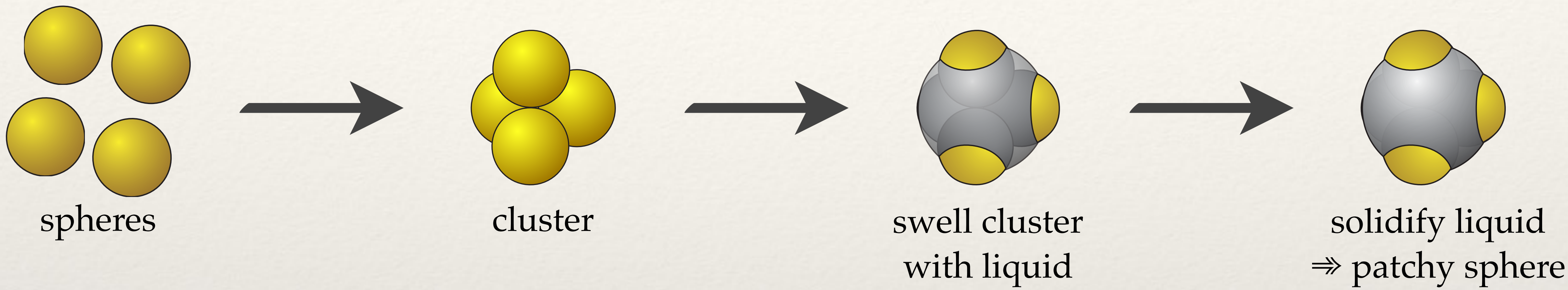
# Making patchy particles

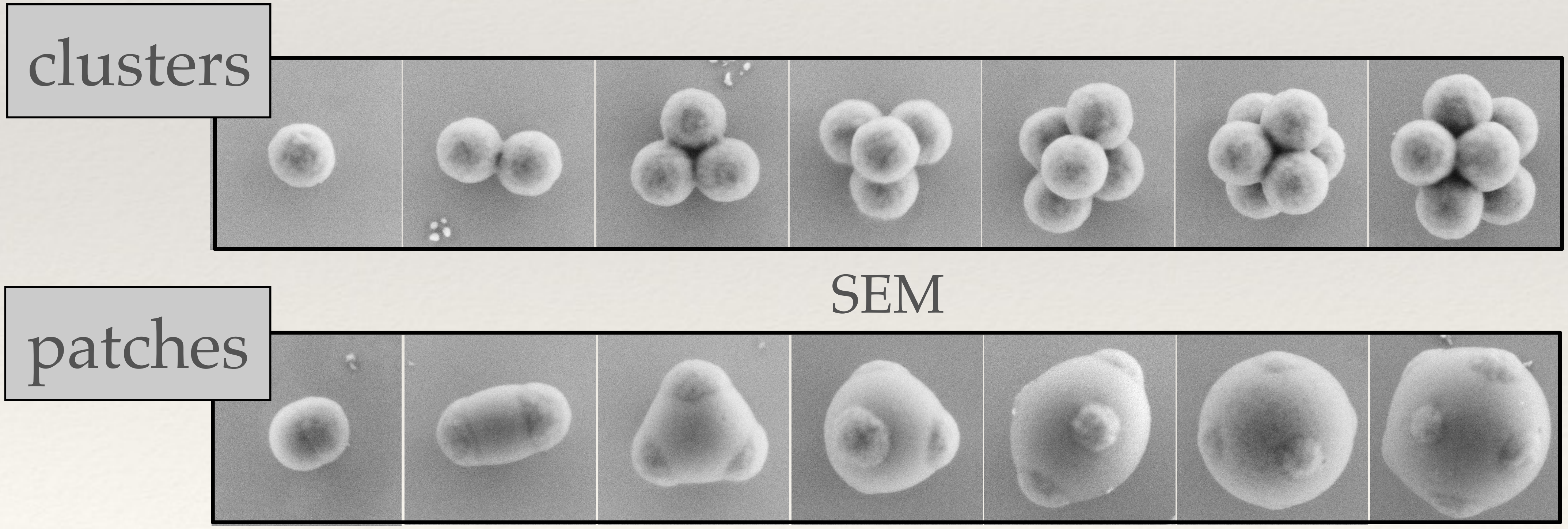
## Step #2: Making patches



# Making patchy particles

## Step #2: Making patches

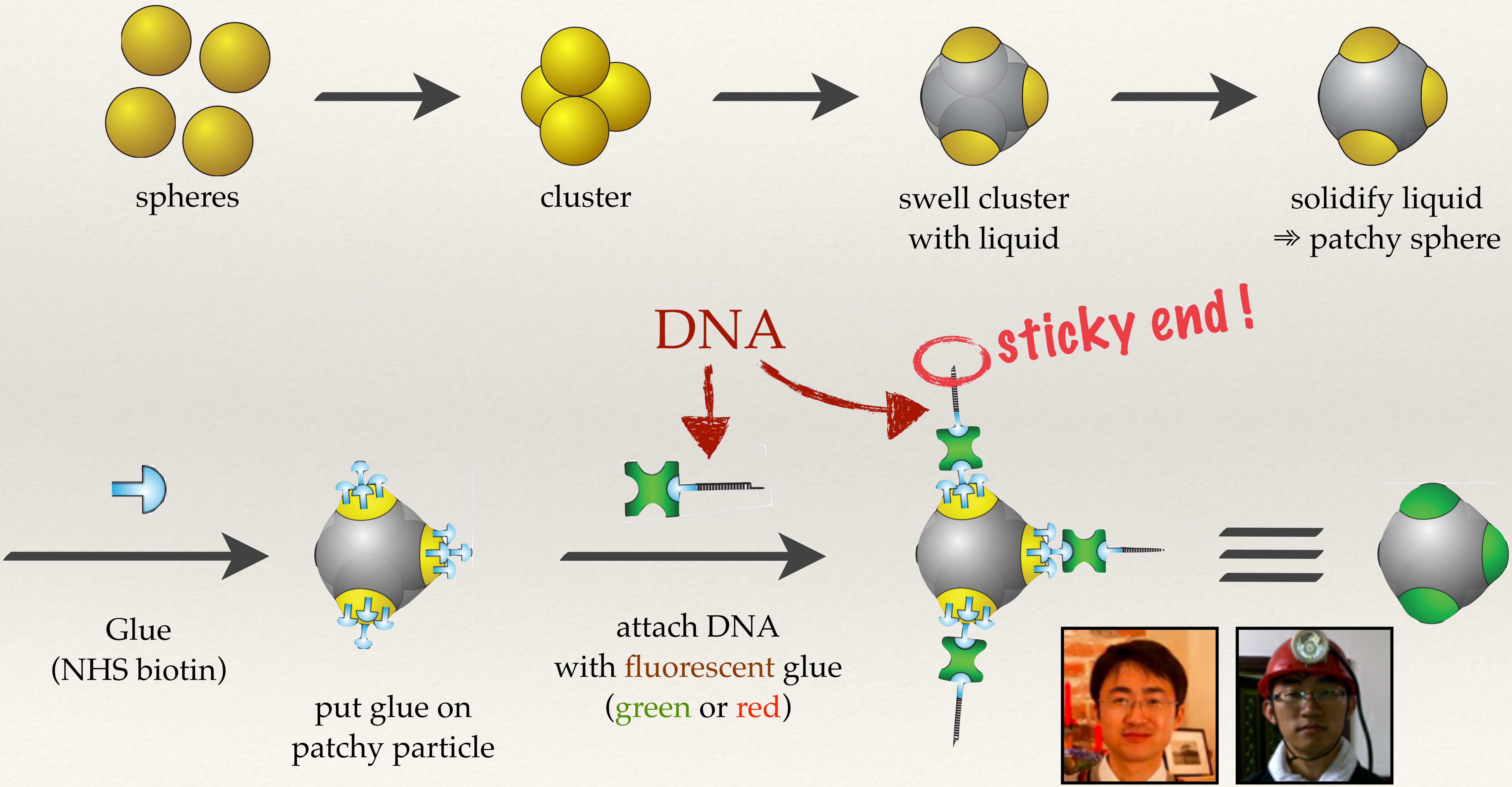



sphere diameter = 0.85 μm

# Making patchy particles

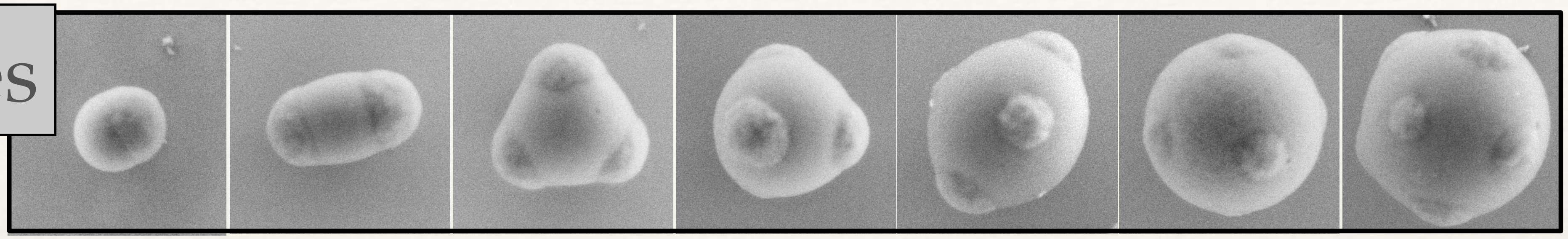
## Step #2: Making patches



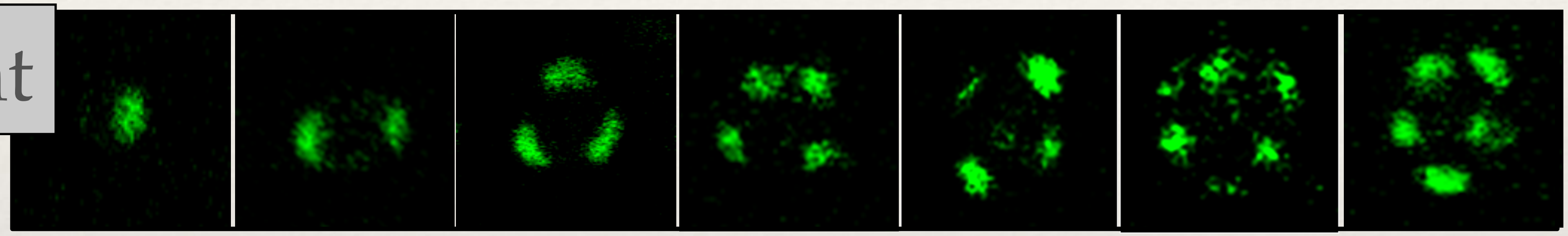

Wang, Wang *et al.*
Nature **491**, 51–55 (2012)

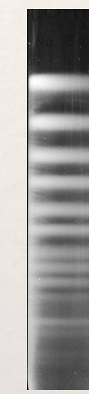
# Functionalizing patchy particles

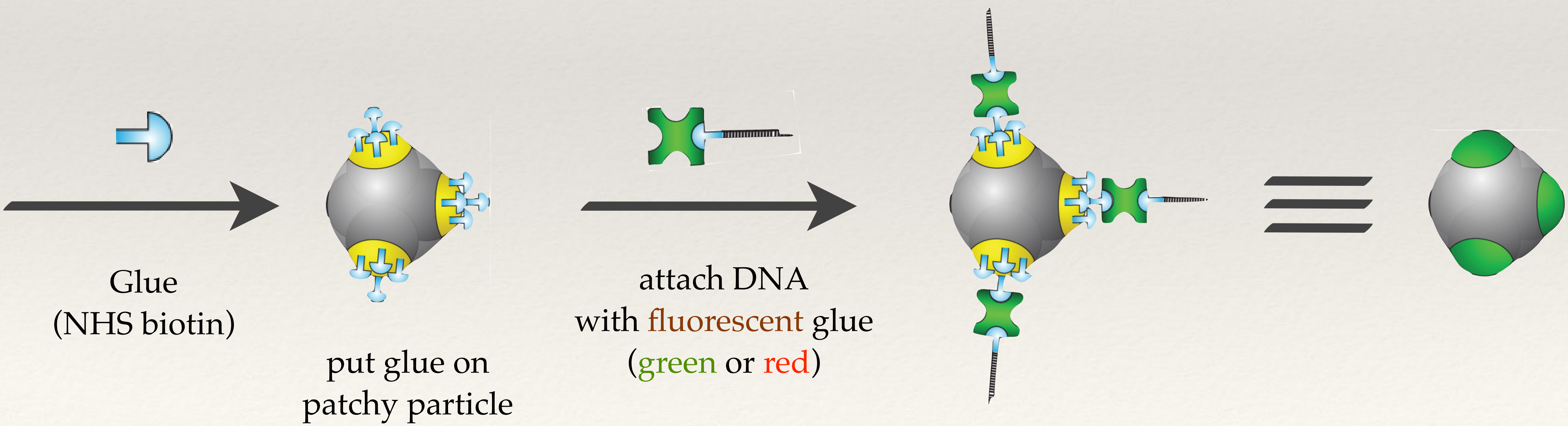
patches



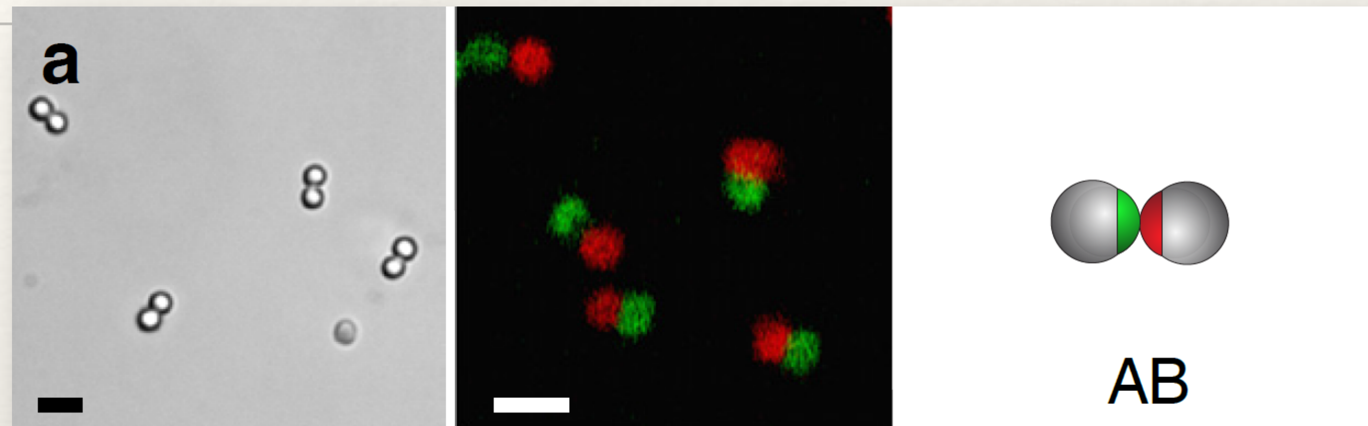
fluorescent



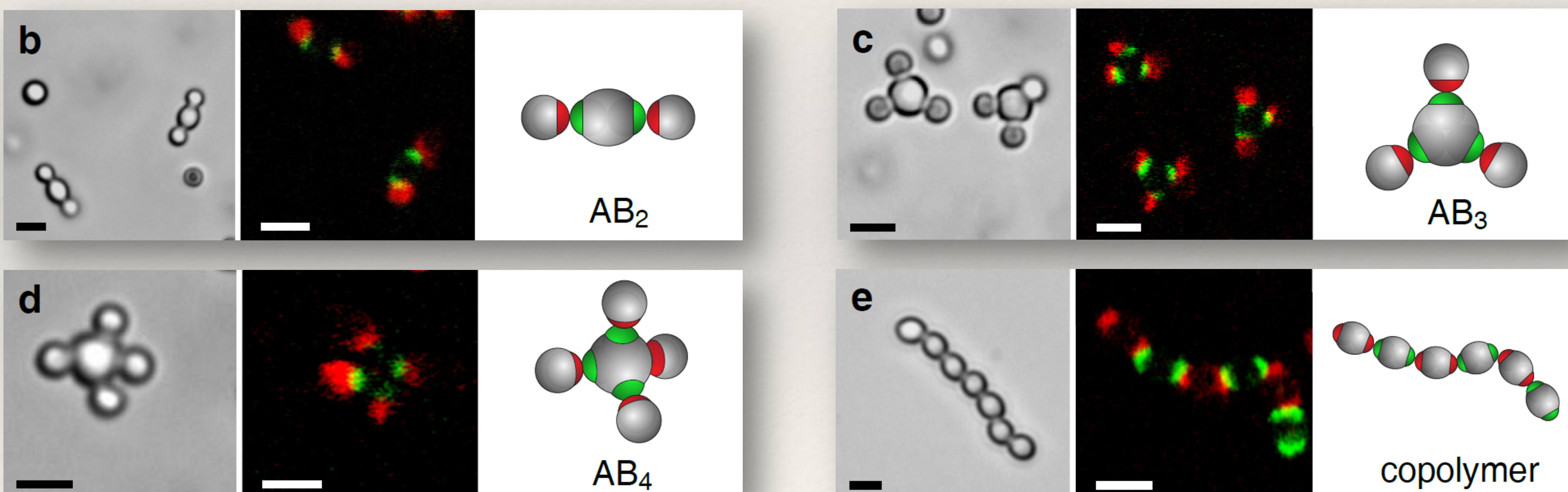




# Specific bonding: colloidal molecules




DNA sticky ends on patches [red-green] bind together)

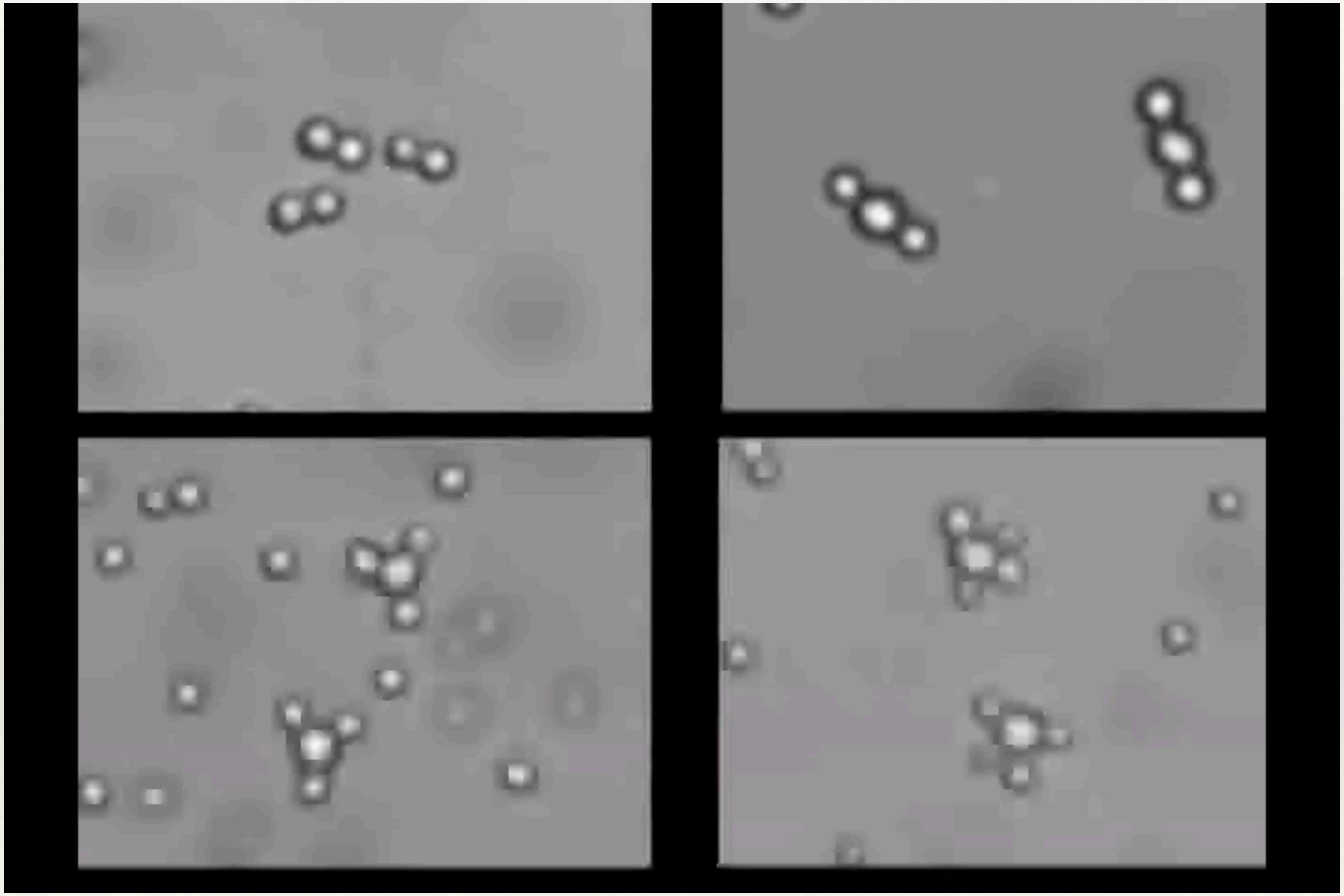



Directional interactions

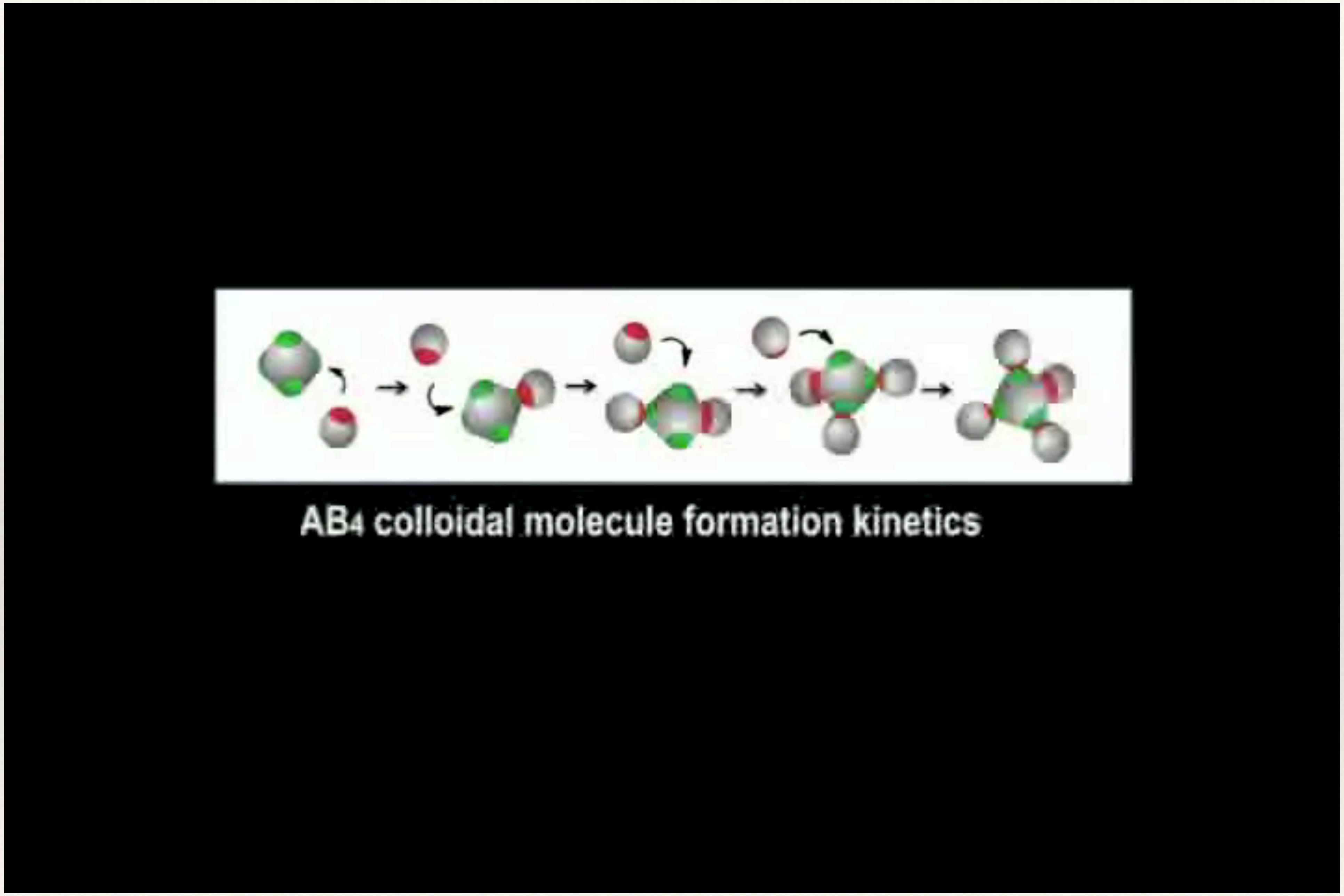
Programmable glue

Wang *et al.*, Nature **491**, 51-55 (2012)

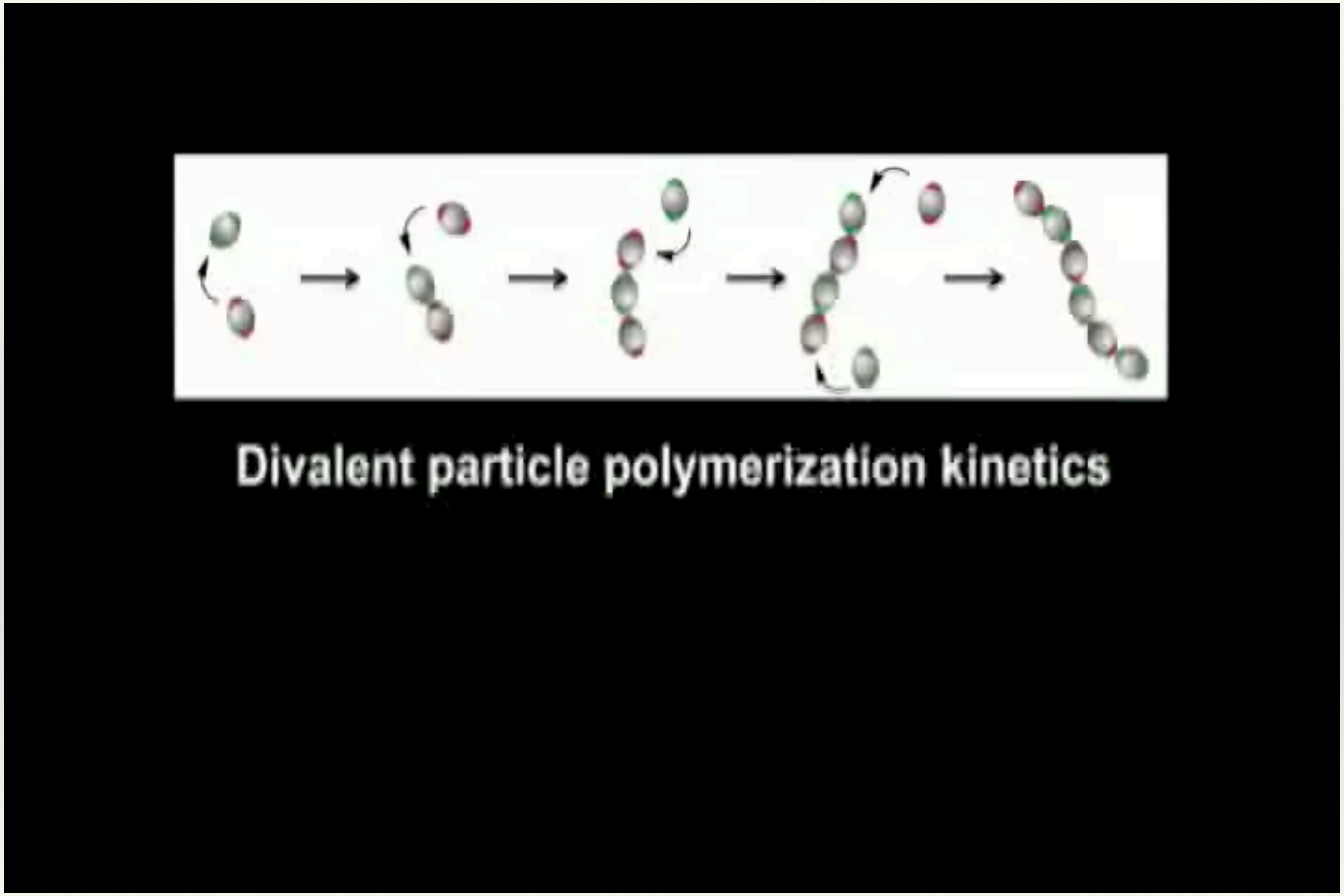
# Colloidal molecules



# $AB_4$ formation kinetics

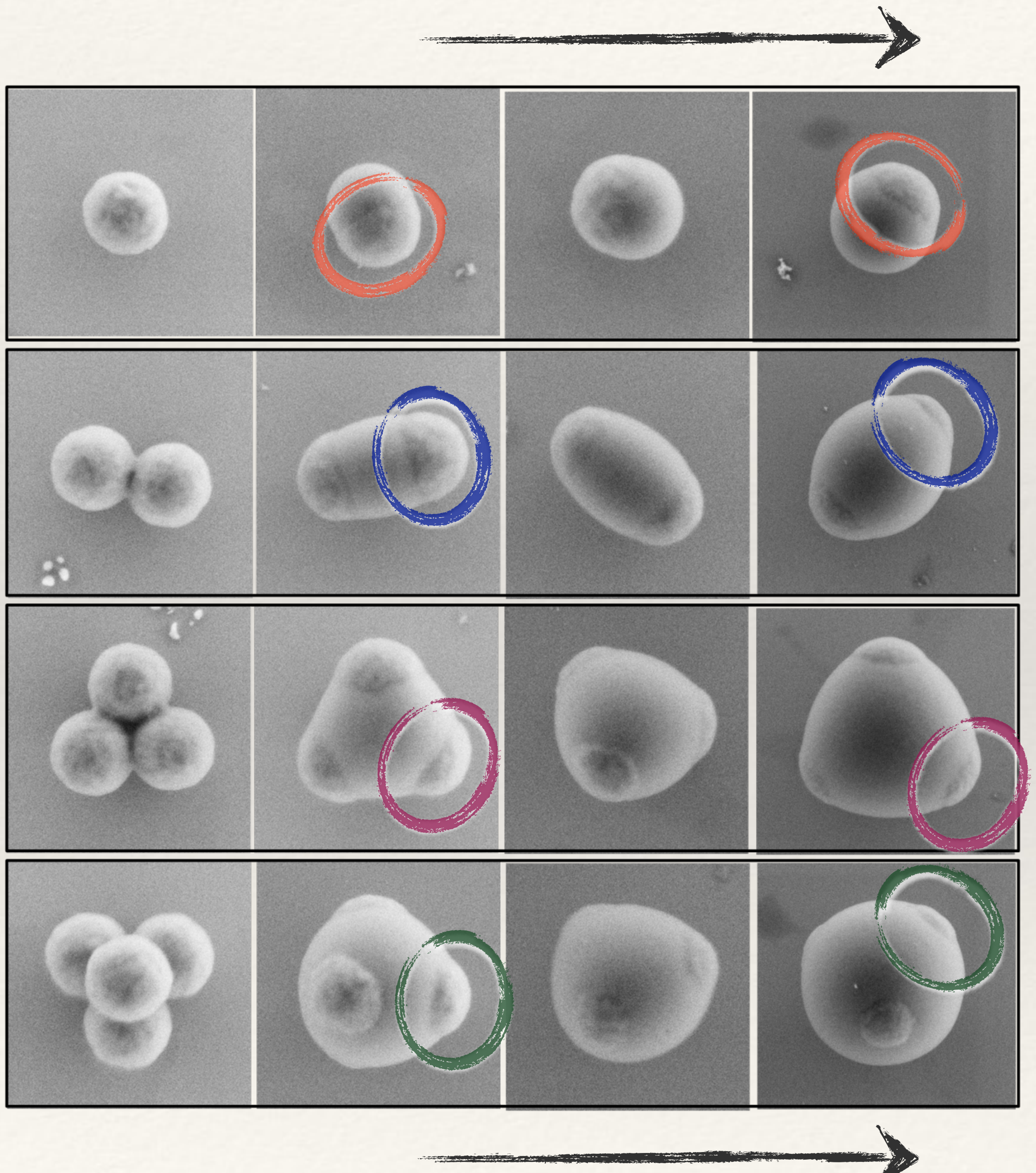


# Colloidal polymerization kinetics



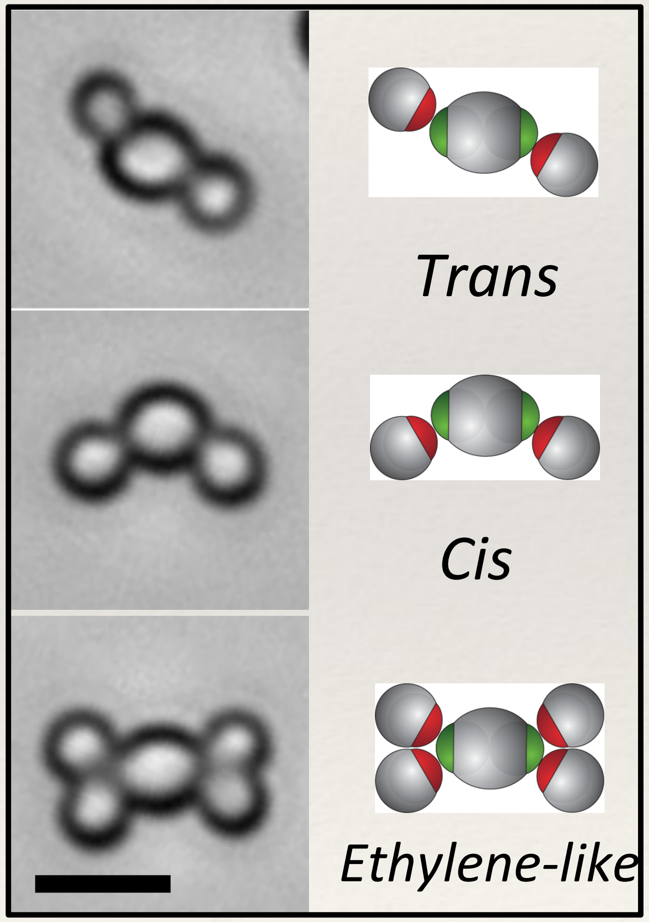
# Controlling patch size

decreasing patch size



decreasing patch size

Linking with complementary particles




big patches

# Skyfall released

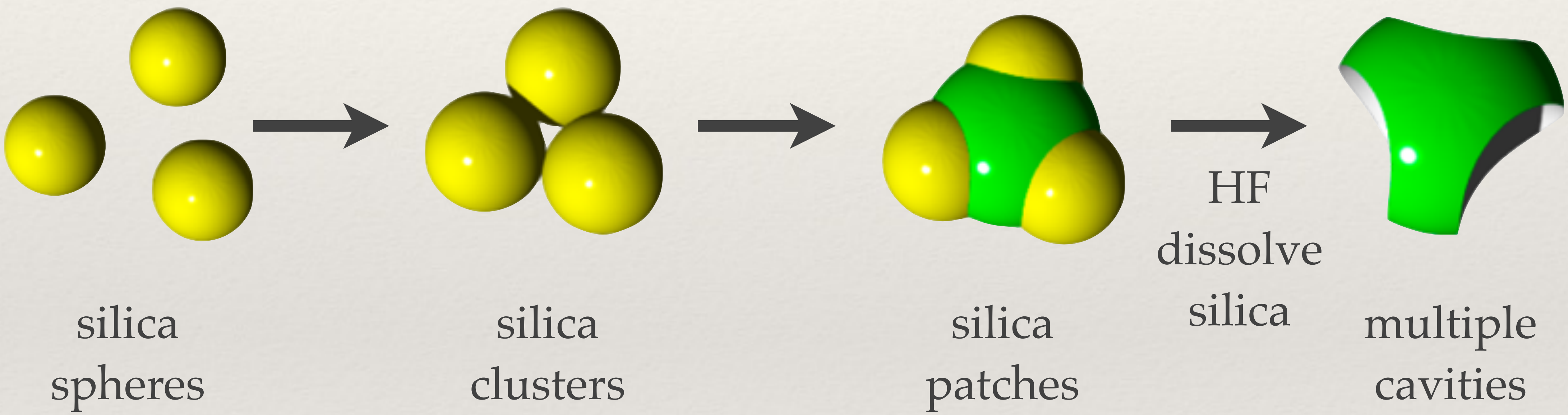
UK: 26 October 2012

1 November 2012

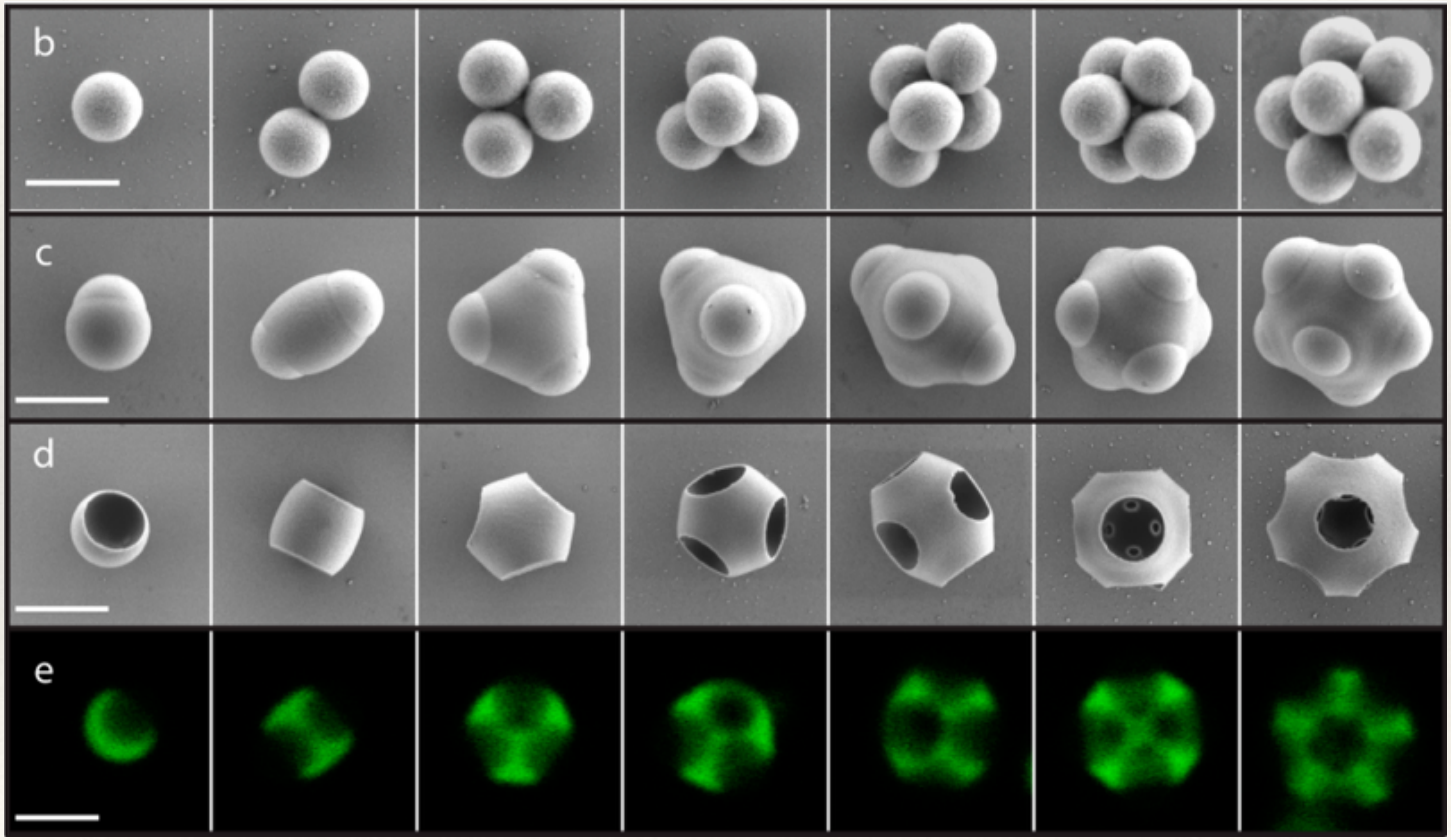


USA: 8 November 2012

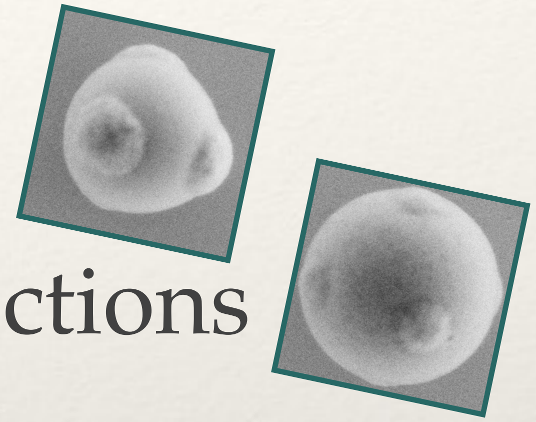
# Three dimensional lock & key



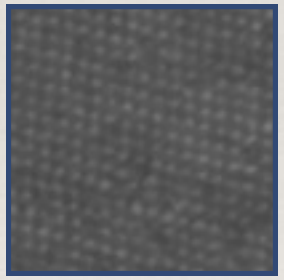
# Three dimensional lock & key



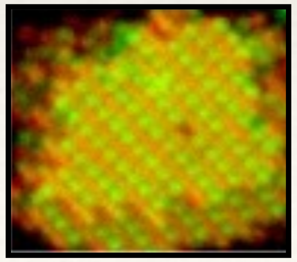
# Enabling technologies



- Colloidal clusters
- Patchy colloids with fully 3-d directional interactions
- thin DNA coatings that bind and anneal (*i.e.* diffuse, roll)
  - very ***high areal density*** ⇛ multiple-flavor particles
  - large single crystals that easily form

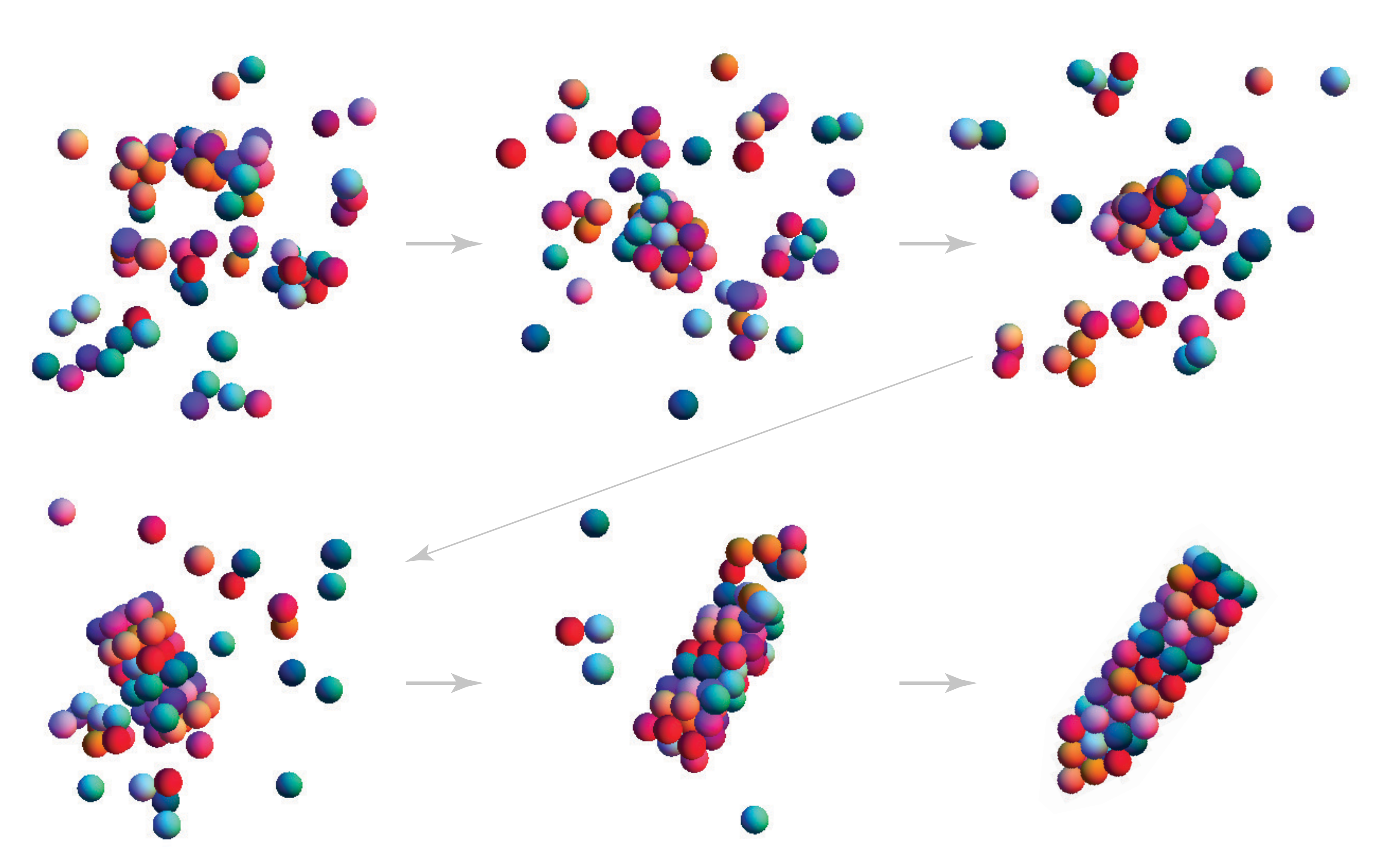


- DNA-coated colloids made from multiple materials
  - titania, silica, polystyrene, PMMA, *etc.*



# Building "Big Ben" with colloids

Assembly of 69-particle "Big Ben" (computer simulation)



Zeravcic, Manoharan, & Brenner, PNAS **111**, 15918–15923 (2014)

Different particles can be different materials
⇛ can assemble complex micro-structured materials

# A New Materials Science…

## …based on DNA colloid coatings for programmable self-assembly

- DNA as glue that provides programmable specific interactions between colloids
- Colloidal particles are the majority components and they determine the material properties:
  - colloidal materials: metals, polymers, inorganics, semiconductors,…)
  - DNA coating is much smaller than particle size (glue doesn't occupy much volume)
- Colloids that anneal to achieve lowest free energy state
- Directional interactions for greatest programmability

# Collaborators & Support


Yufeng Wang
Étienne Ducrot
Myung-Goo Lee
Andy Hollingsworth
Rémy Dreyfus
Daniela Kraft
Yu Wang
Xiaolong Zheng
Marcus Weck
Paul Chaikin
Lang Feng
Mirjam Leunissen
Joon Suk Oh
Gi-Ra Yi
Vinny Manoharan
Mark Elsesser
Dana R Breed