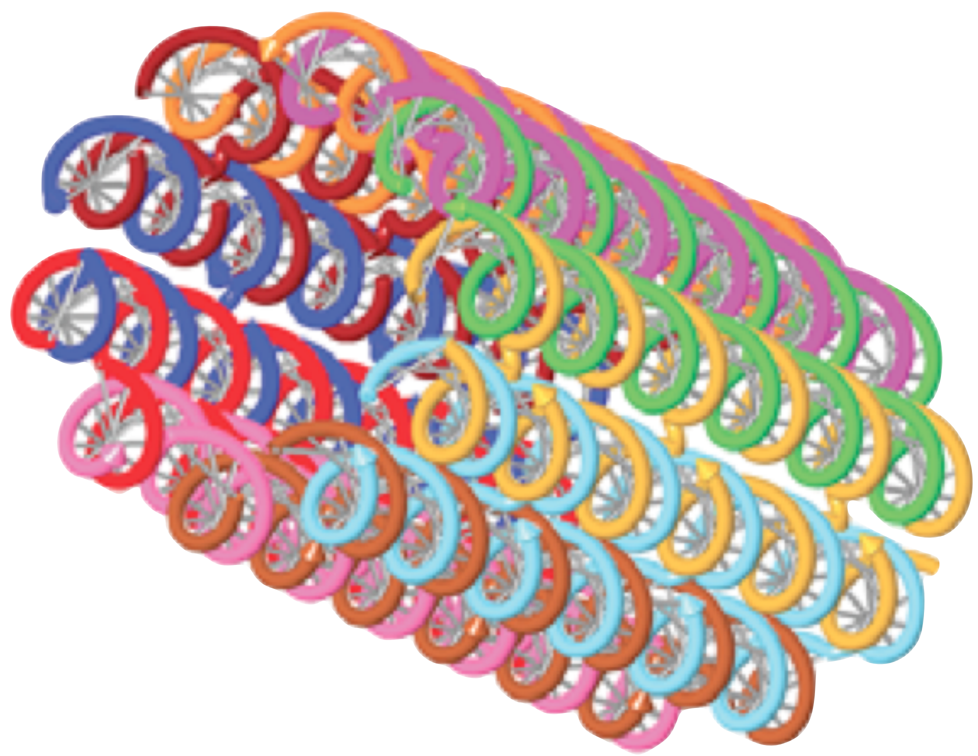
An experimental realization of a universal computer

Nicolas Schabanel
CNRS
LIP & IXXI - ÉNS de Lyon

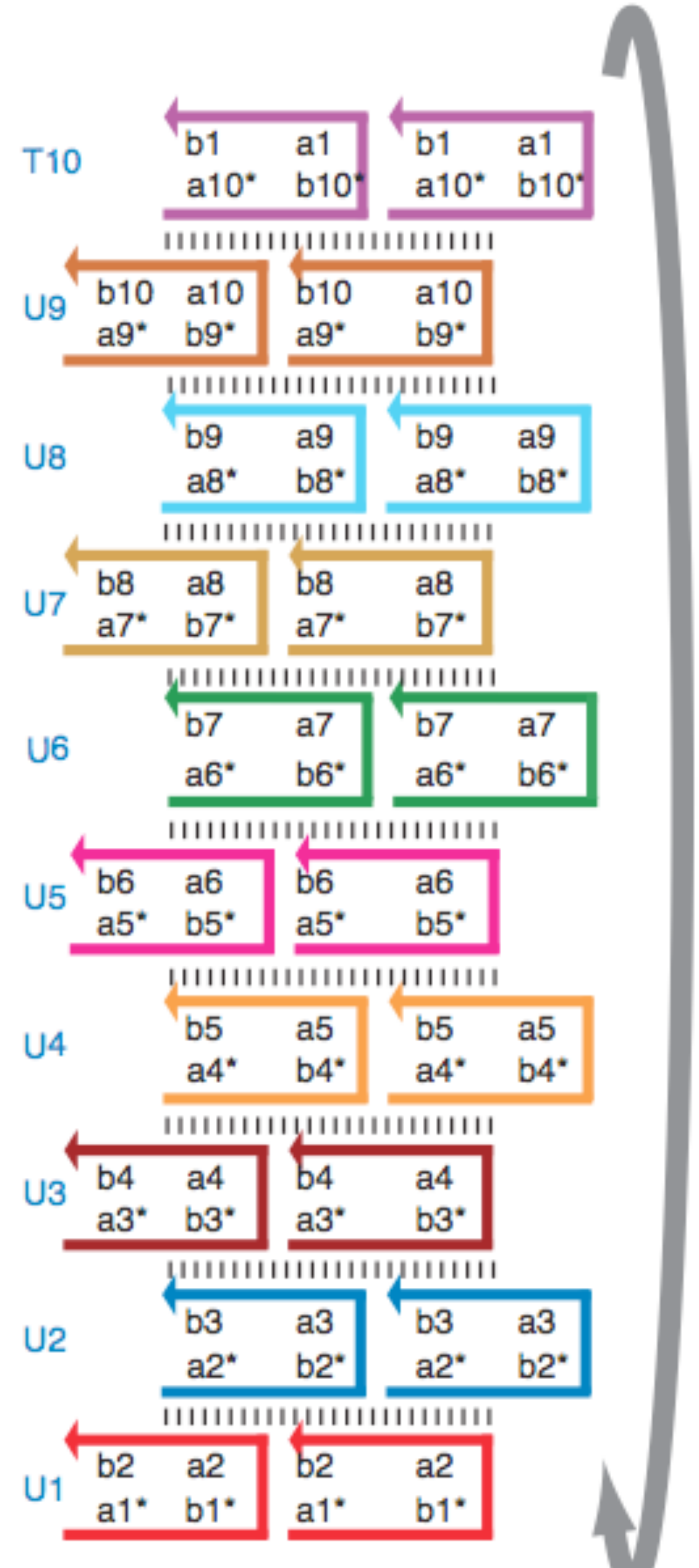
Slides mainly borrowed from Damien Woods et al (Nature 2019)

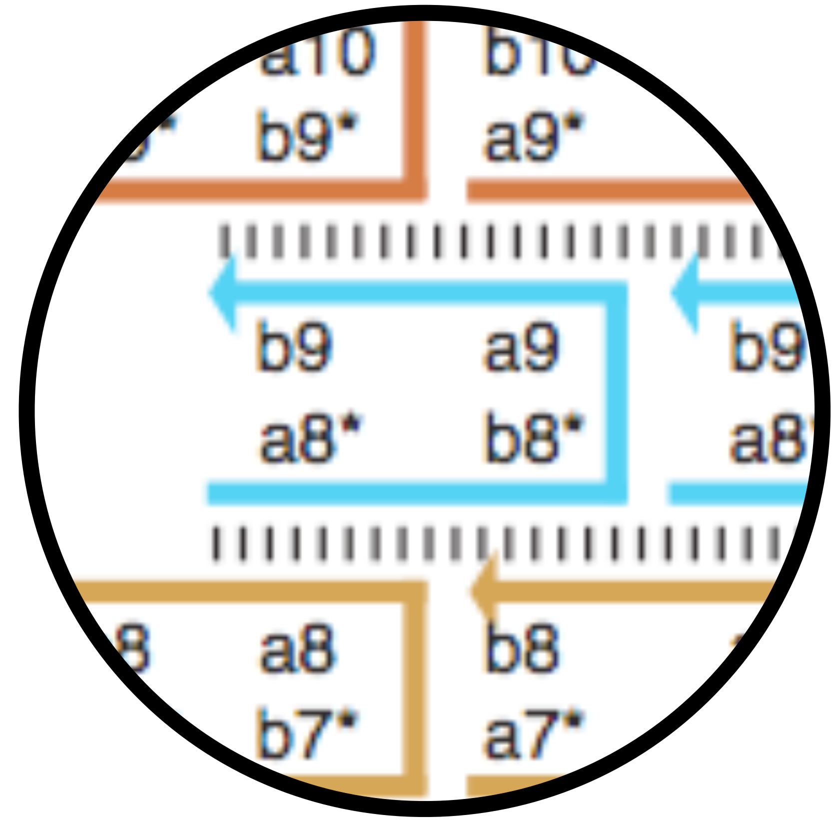
Single Stranded Tiles Nanotubes

Single stranded Nanotubes

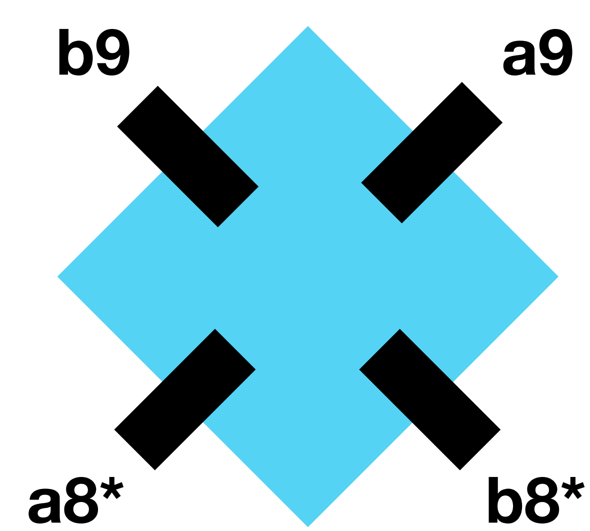


10-helix nanotube schematic,
Yin et al. ’08

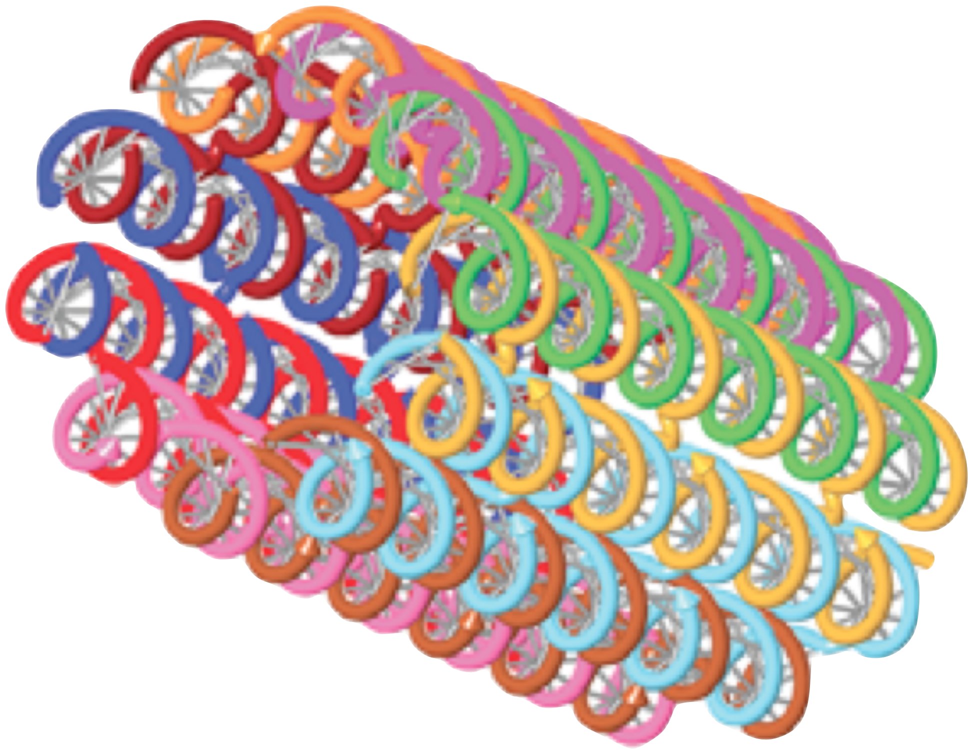




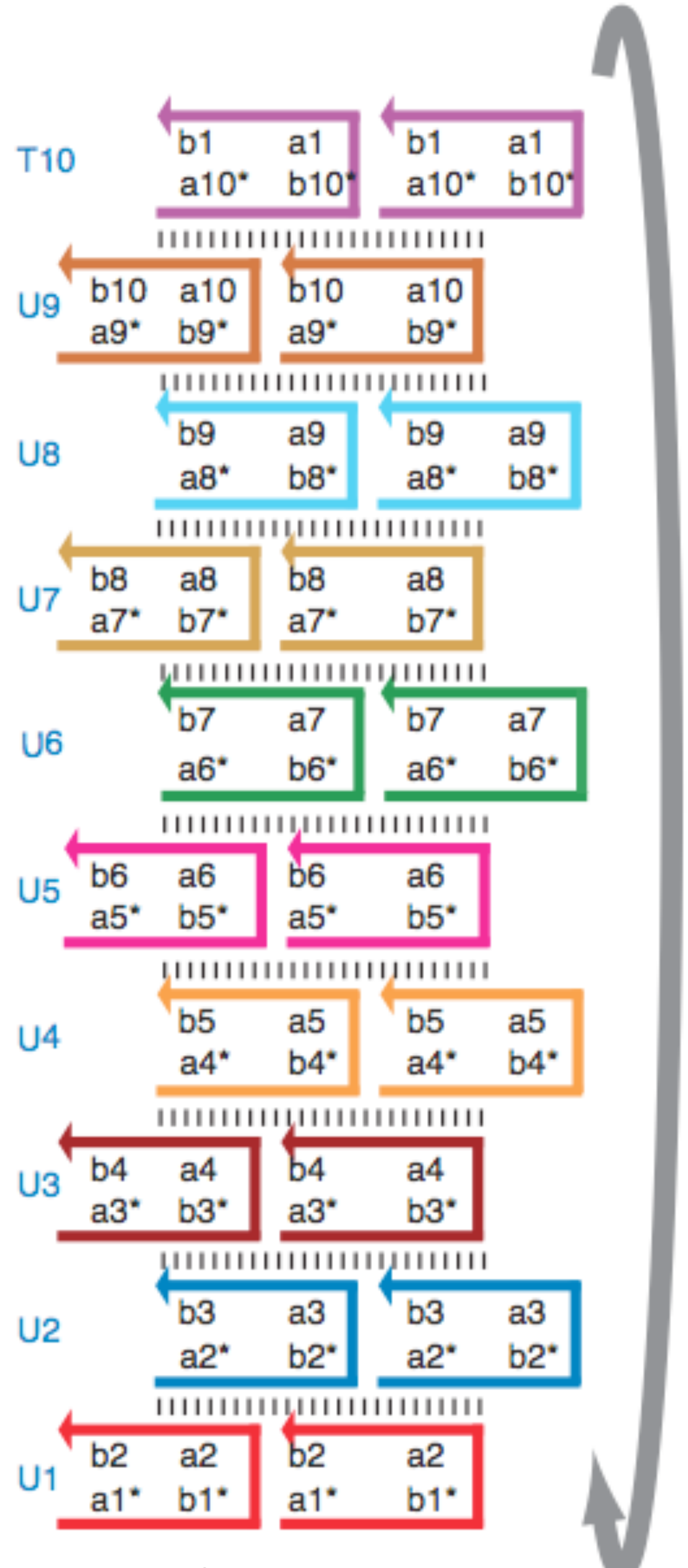
4 domains = 4 glues

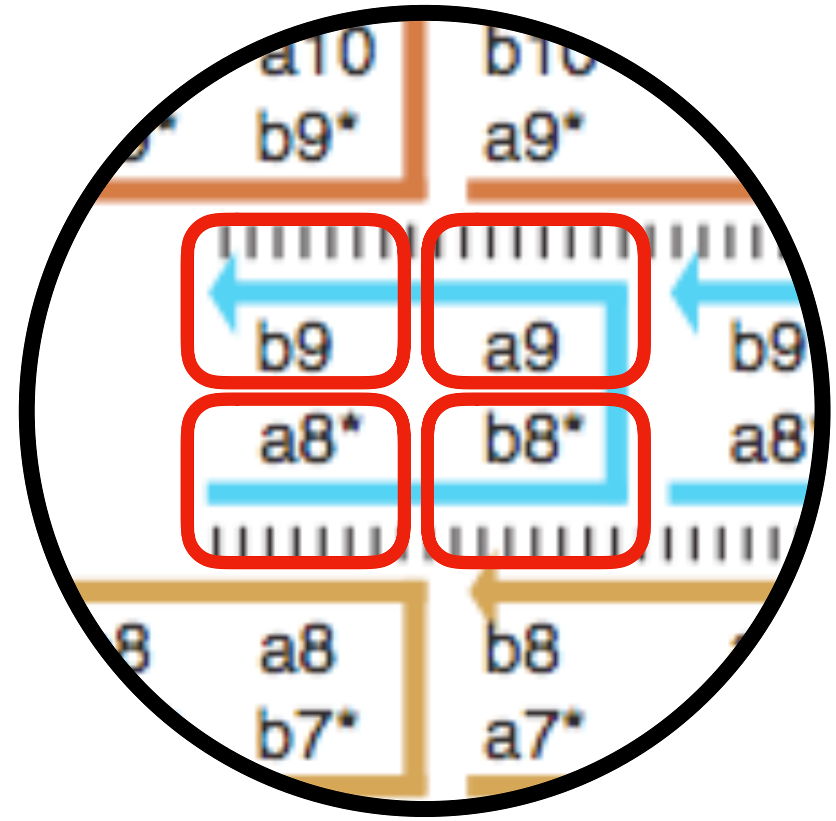


Single stranded Nanotubes

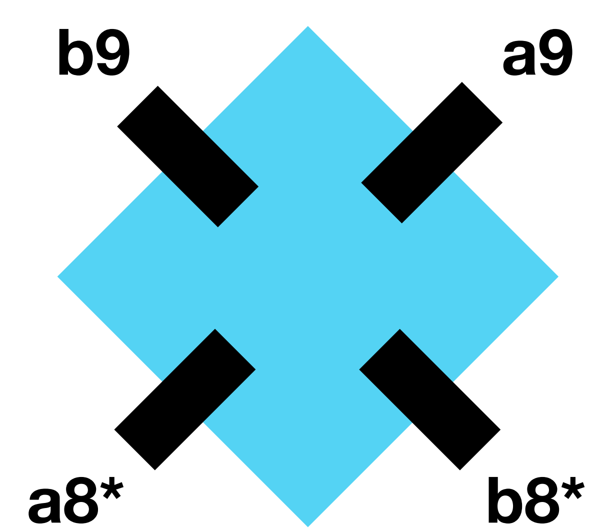


10-helix nanotube schematic,
Yin et al. '08

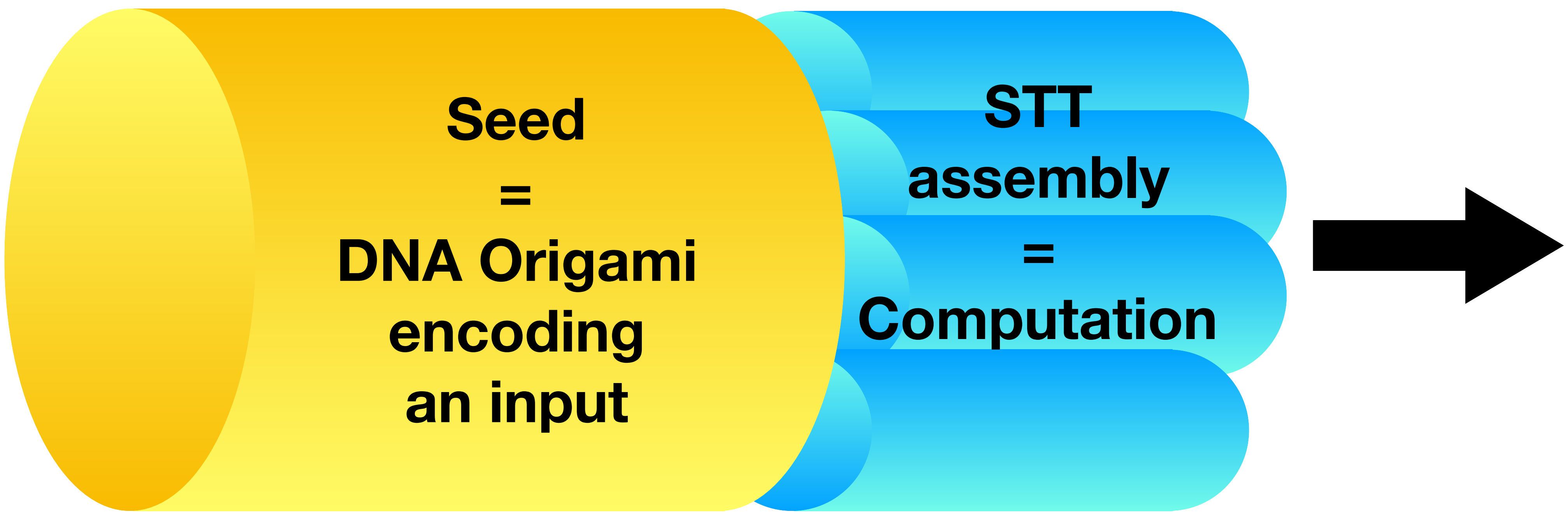


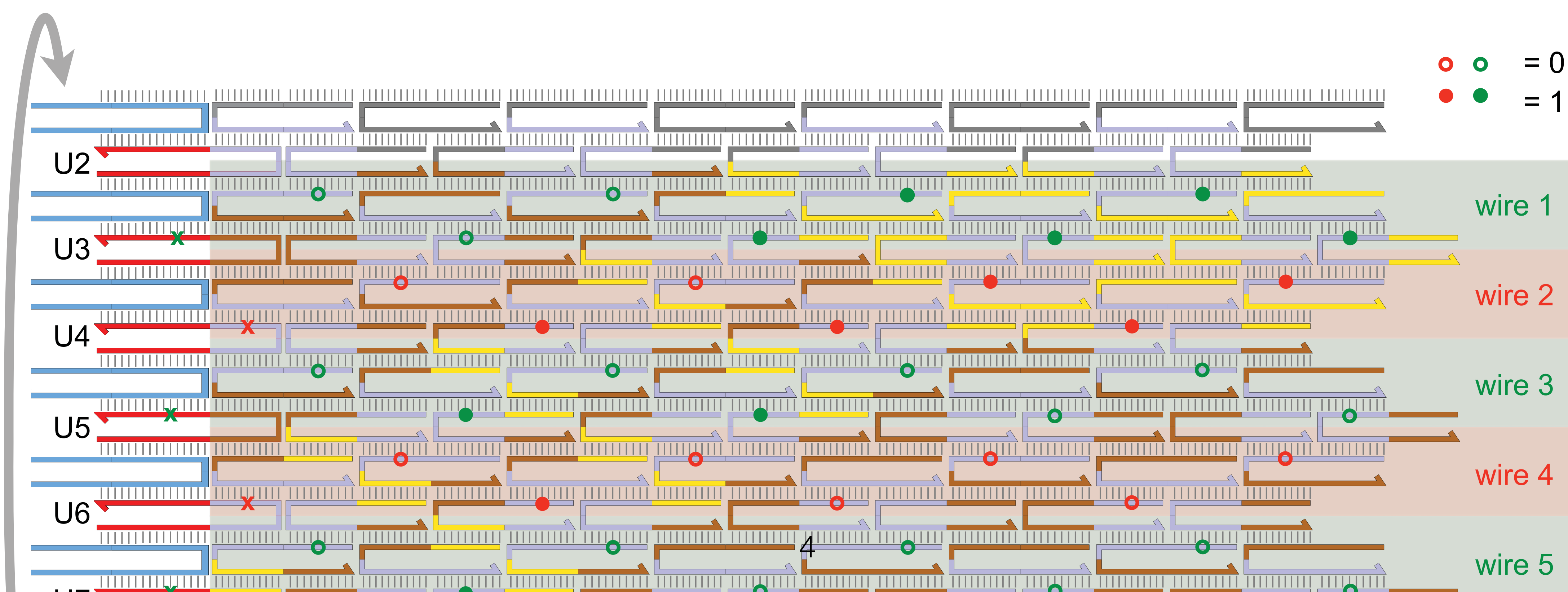


4 domains = 4 glues

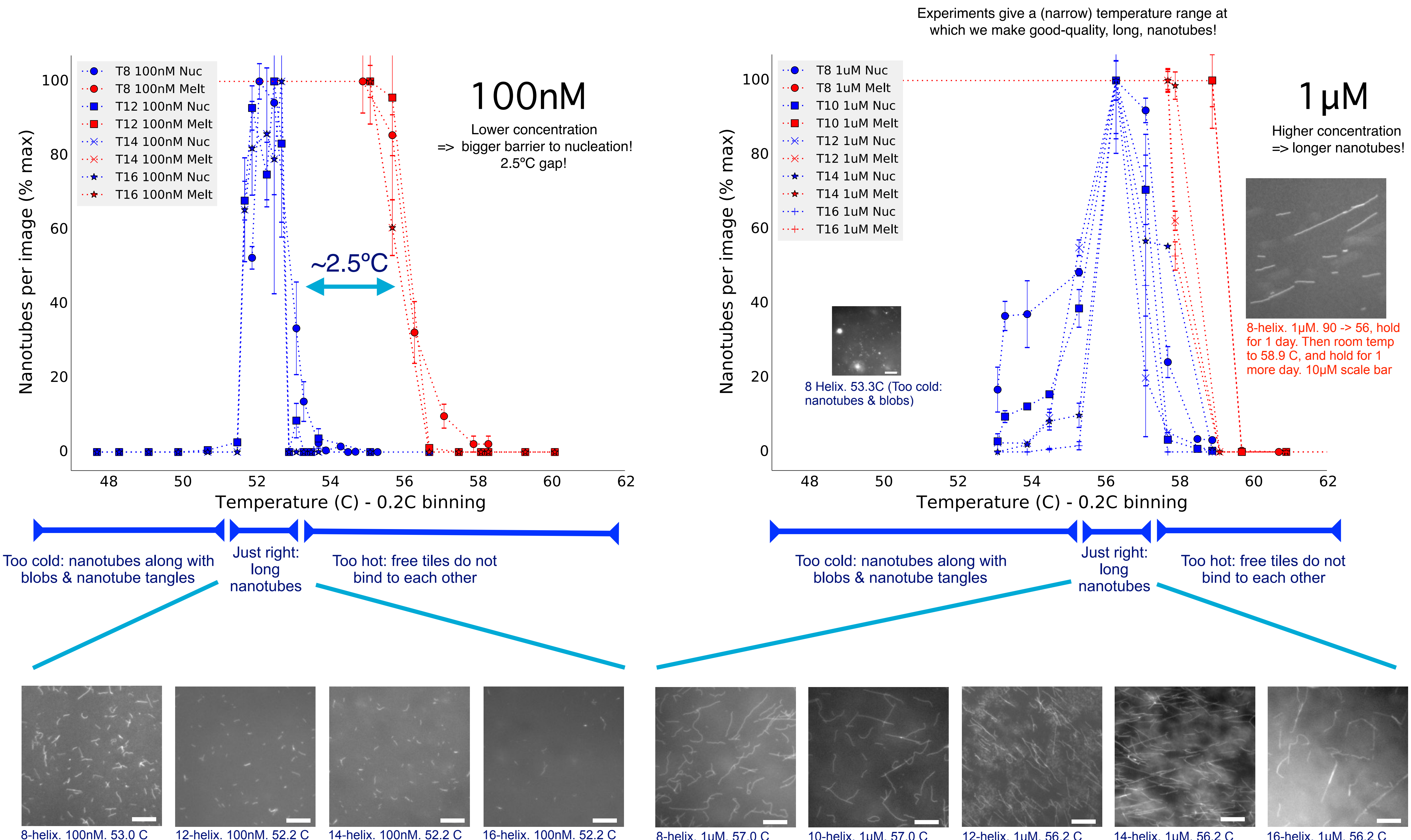


Growing them





Seeded growth: barrier to nucleation at [tile]=100nM



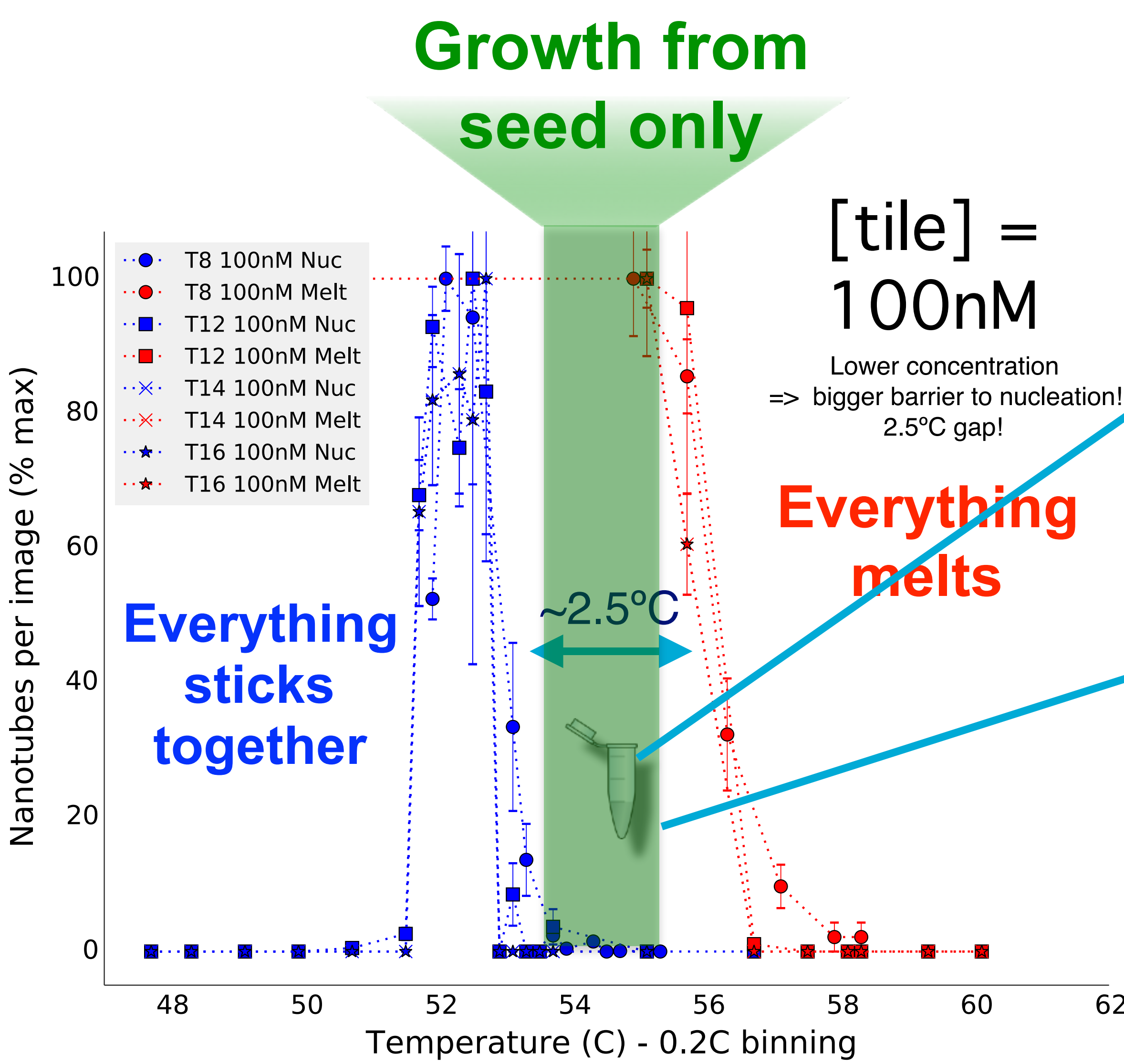
All scale bars 10µm

Each datapoint is a separate ~24 hour temperature hold experiment

Fluorescence microscopy images: cy3 label

Error bars show SEM for *n*=5 experiments for blue, and *n*=2 for red

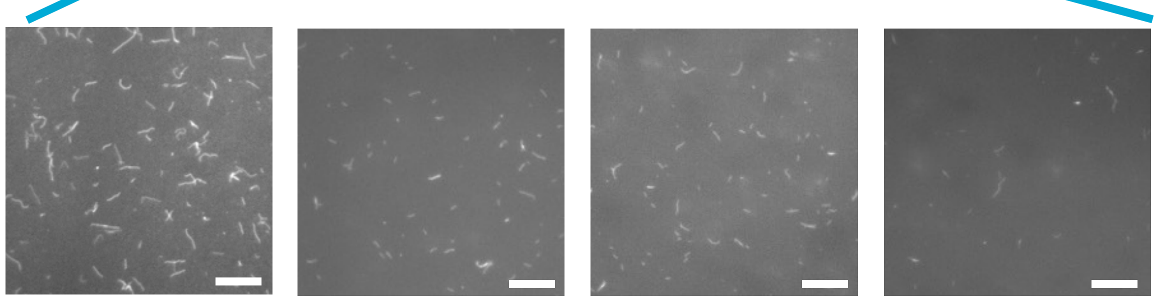
Seeded growth: barrier to nucleation at [tile]=100nM



Too cold: nanotubes along with blobs & nanotube tangles

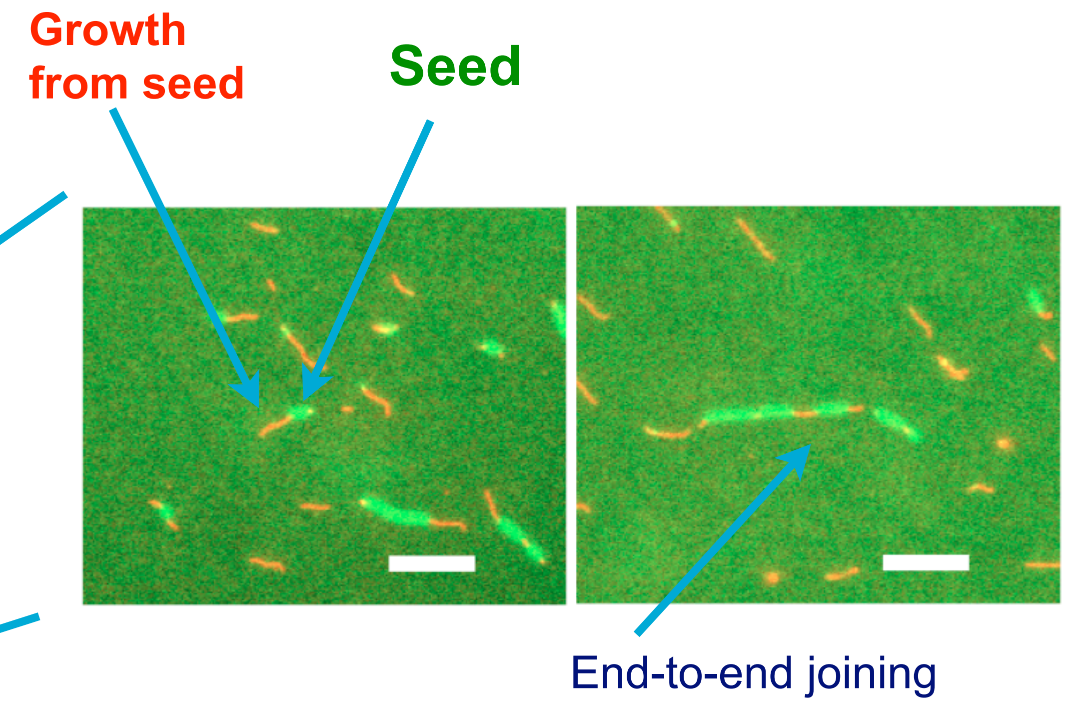
Just right: long nanotubes

Too hot: free tiles do not bind to each other



8-helix. 100nM. 53.0 C | 12-helix. 100nM. 52.2 C | 14-helix. 100nM. 52.2 C | 16-helix. 100nM. 52.2 C

Scale bars 10μm. ~24 hour temperature hold experiments. cy3 label

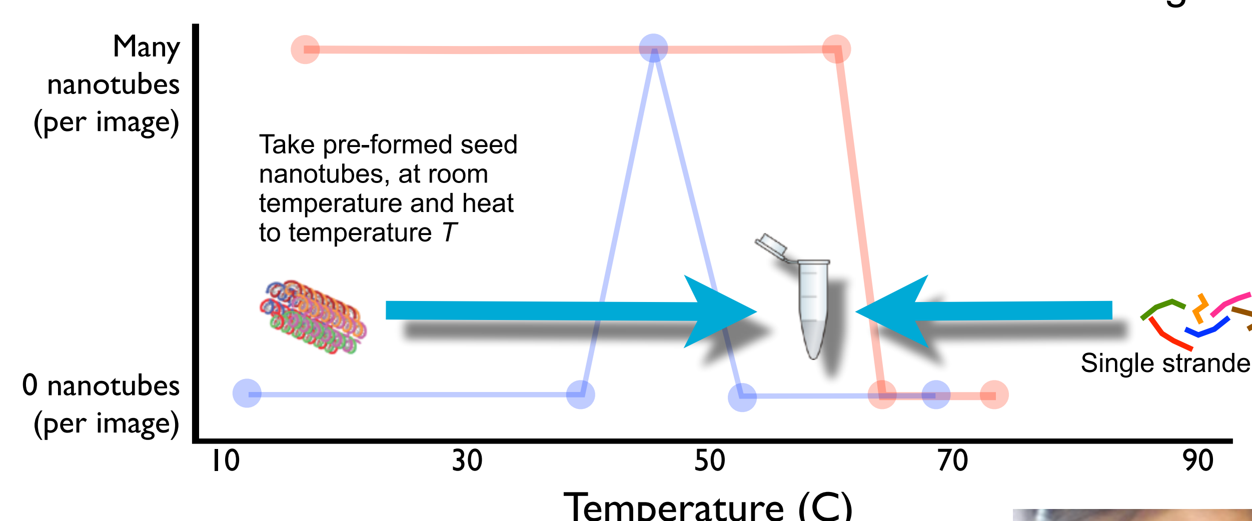


seeds: 8-helix nanotubes, Alexa647 labelled

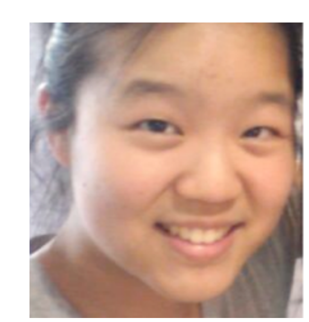
growth from seed: 8-helix tiles, Cy3 labelled

scale bar: 10μm. 100nM tile concentration

Controls: *0* seed nanotubes => 0 nanotubes/image

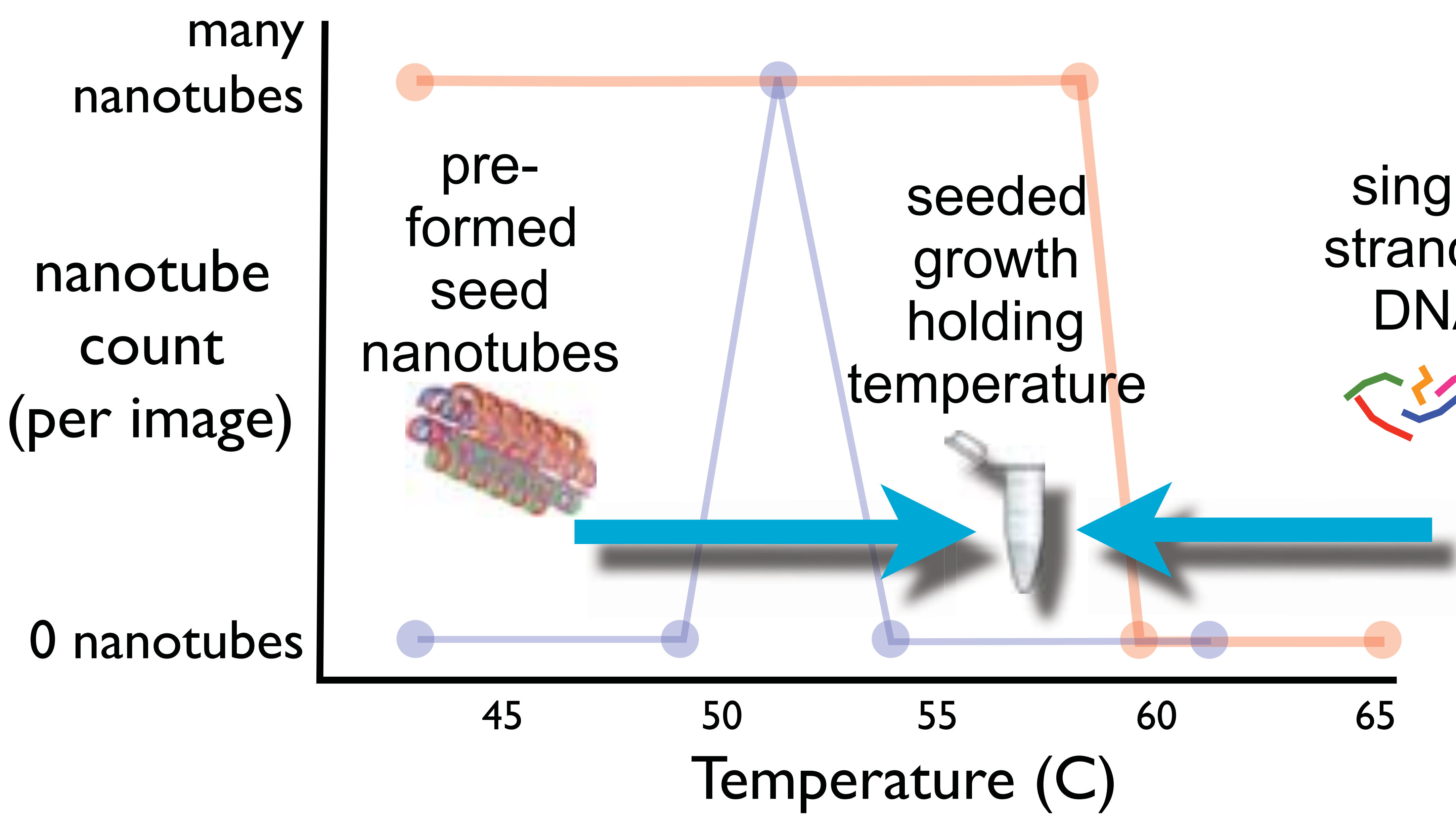


We work at this temperature

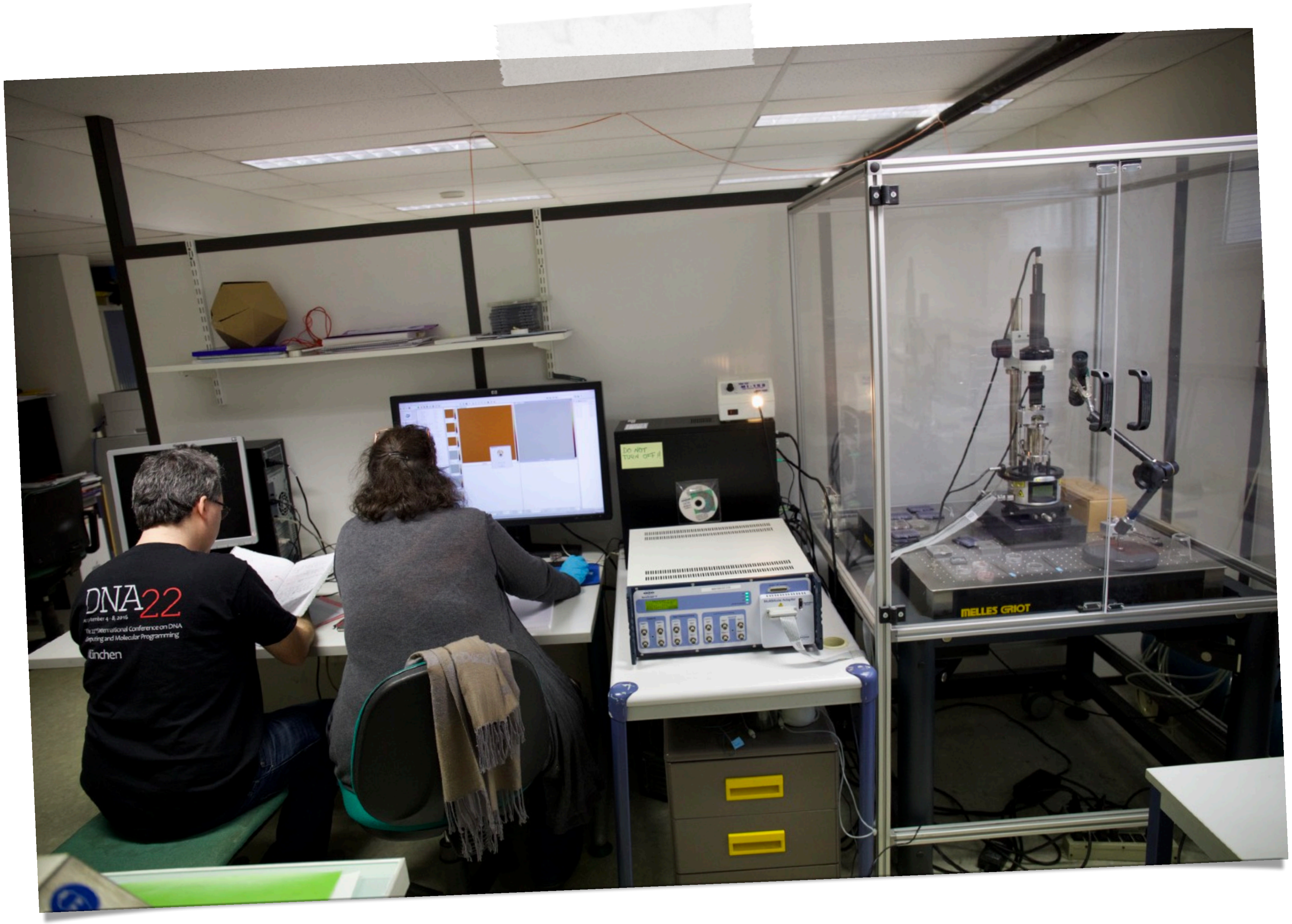


Joy Hui

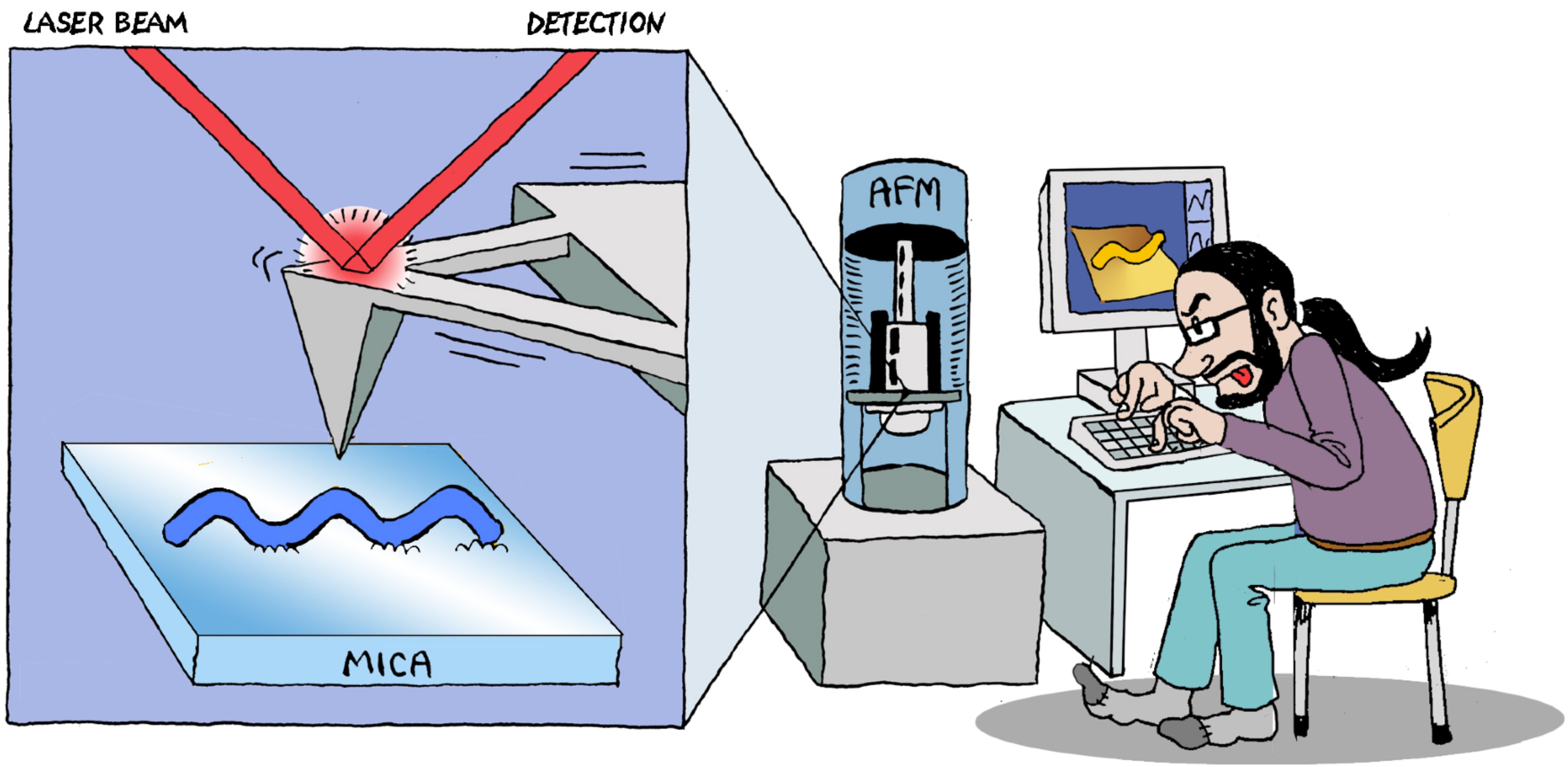
Seeded growth only



Imaging the results



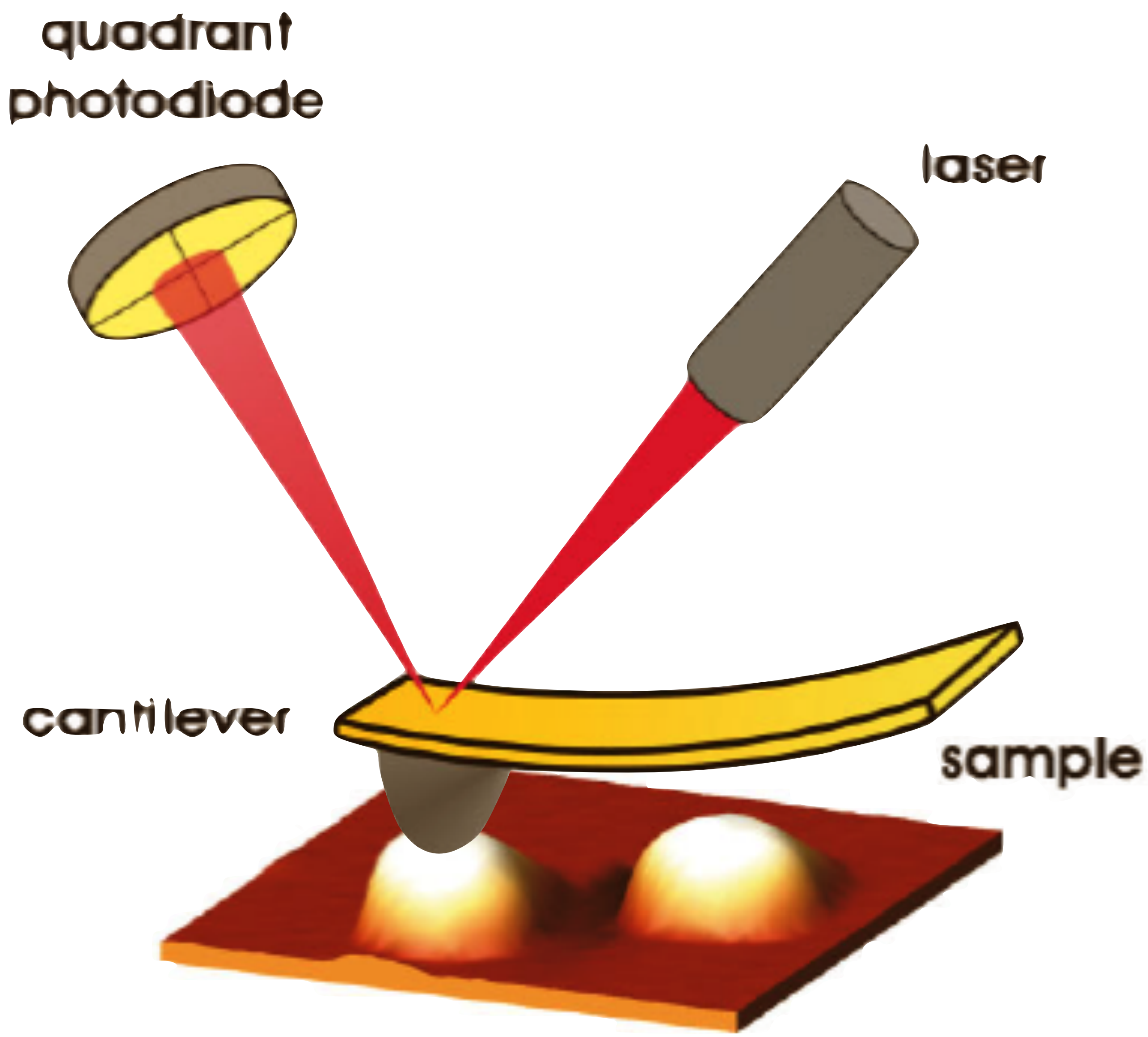
Principle of Atomic Force Microscopy

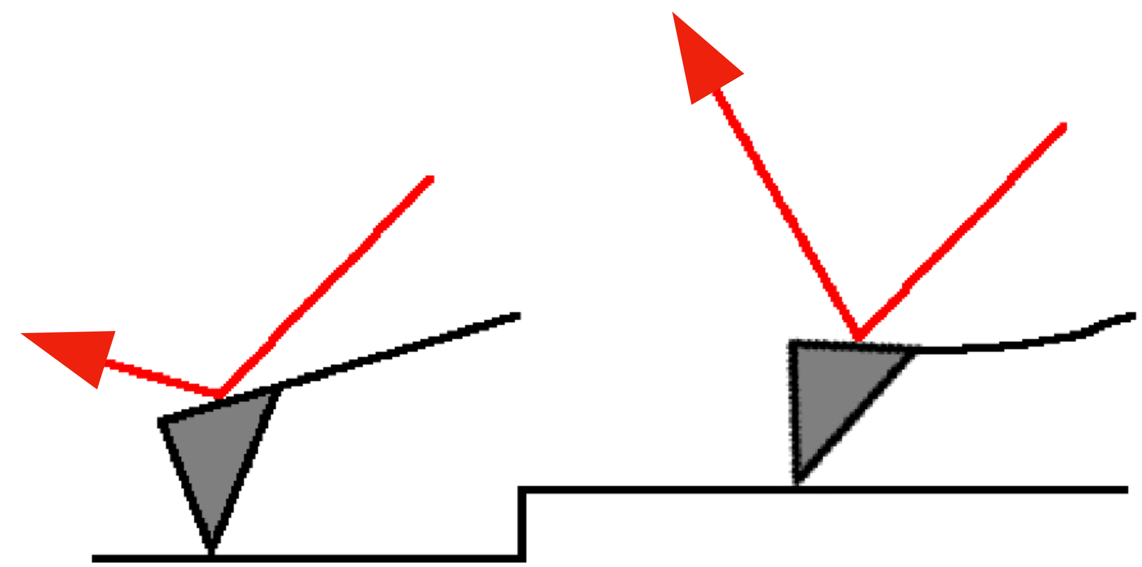


The microscope works by scanning the surface with a sharp probe and gently touching the DNAs that arrange on the mica.

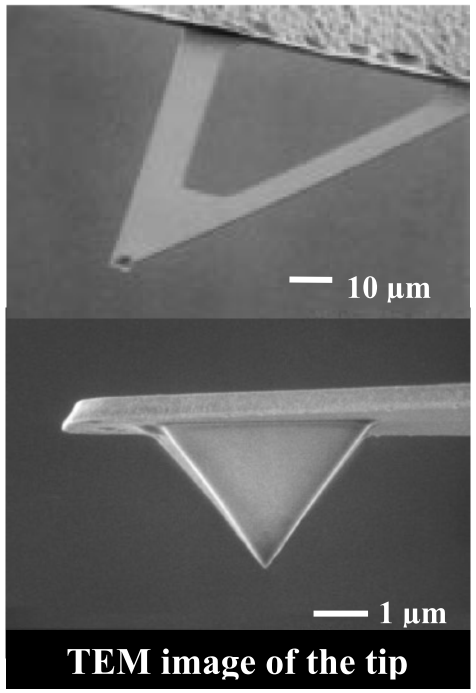
(Artwork: Ebbe Andersen- Slide by Cody Geary)

Laser deflection

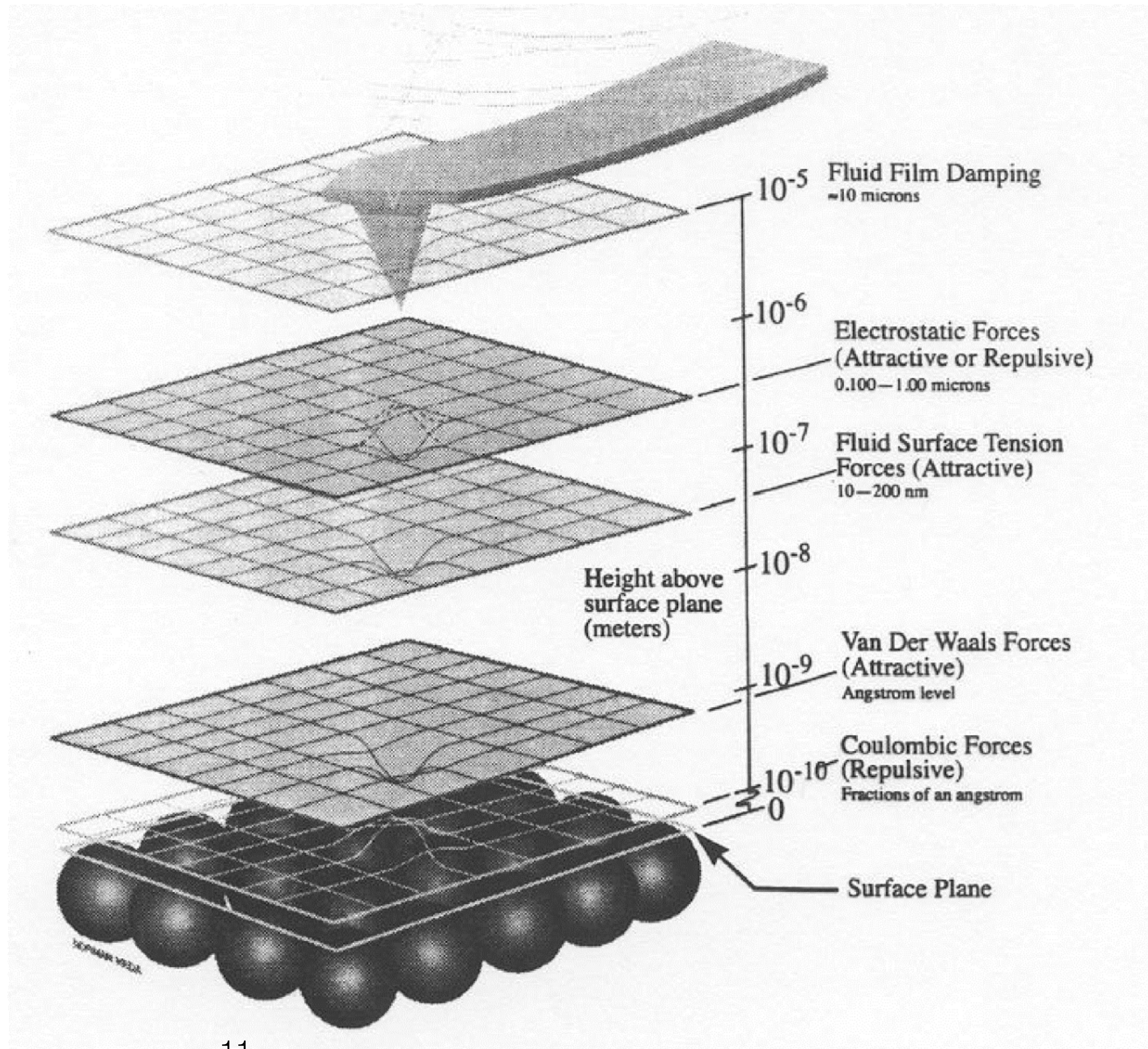




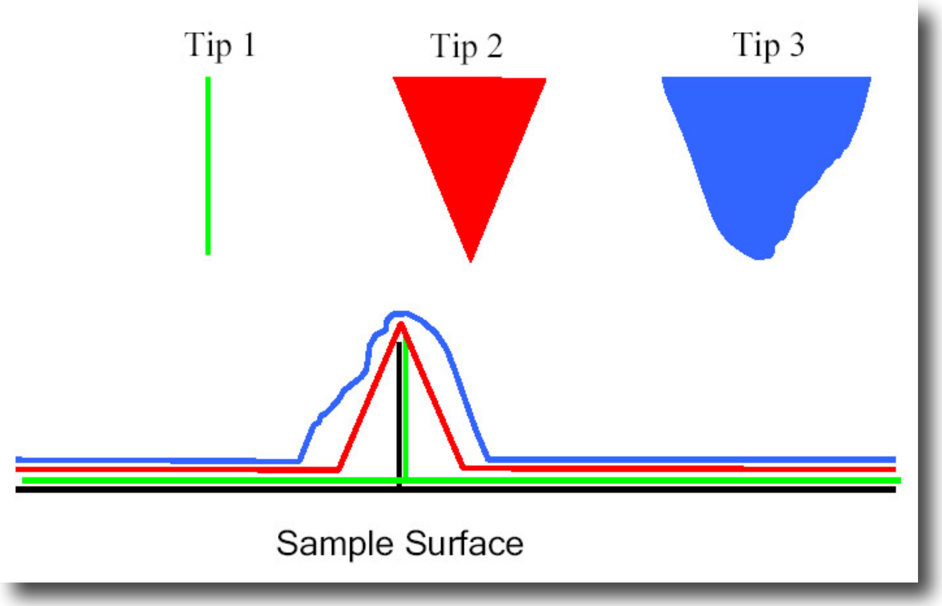
The forces involved in AFM

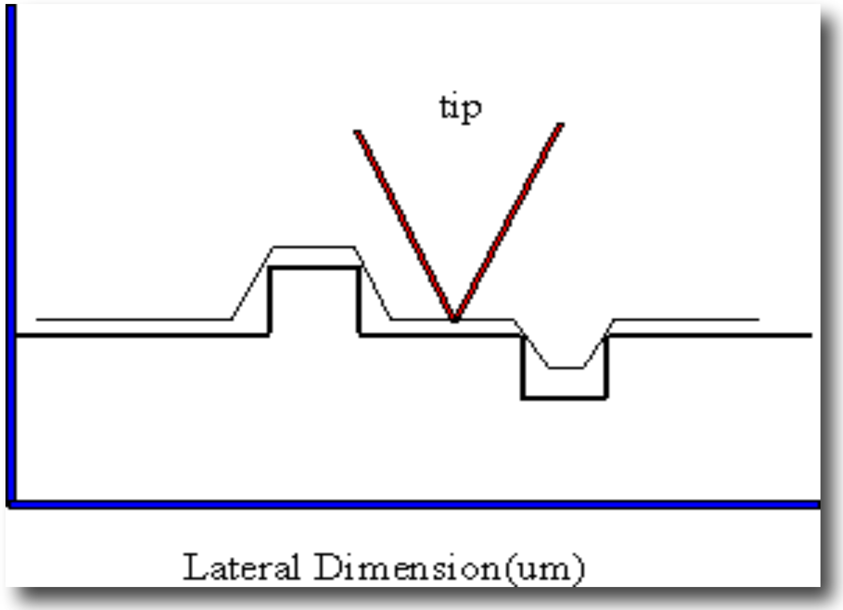


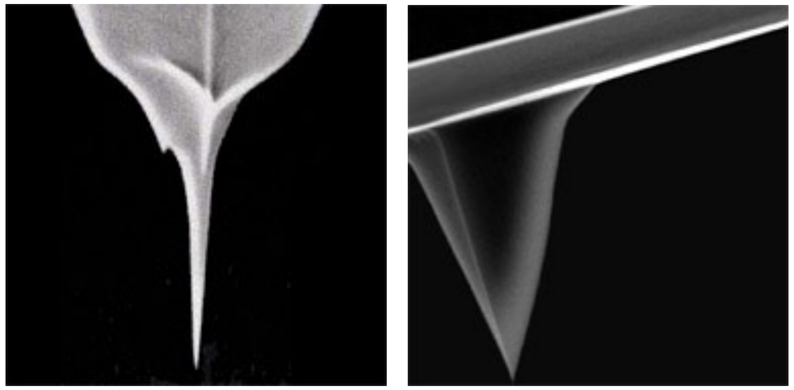
They are interaction forces between the atoms of the end of the tip and the atoms on the sample surface.



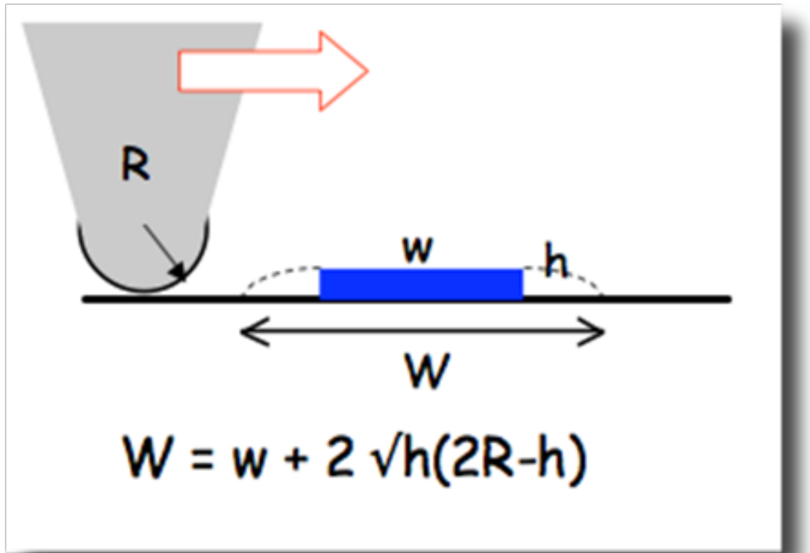
Tip convolution

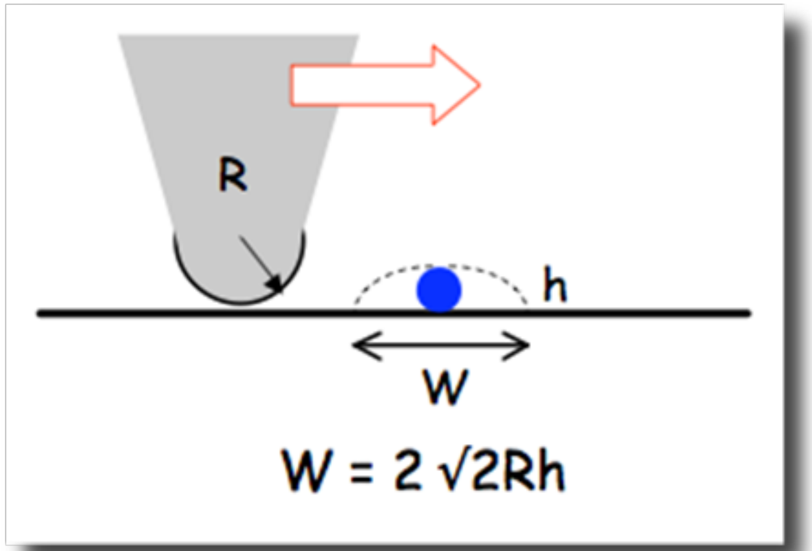






Tip radius 2-20 nm





High resolution imaging

The Chemical Structure of a Molecule Resolved by Atomic Force Microscopy
Leo Gross, *et al.*
Science **325**, 1110 (2009);
DOI: 10.1126/science.1176210

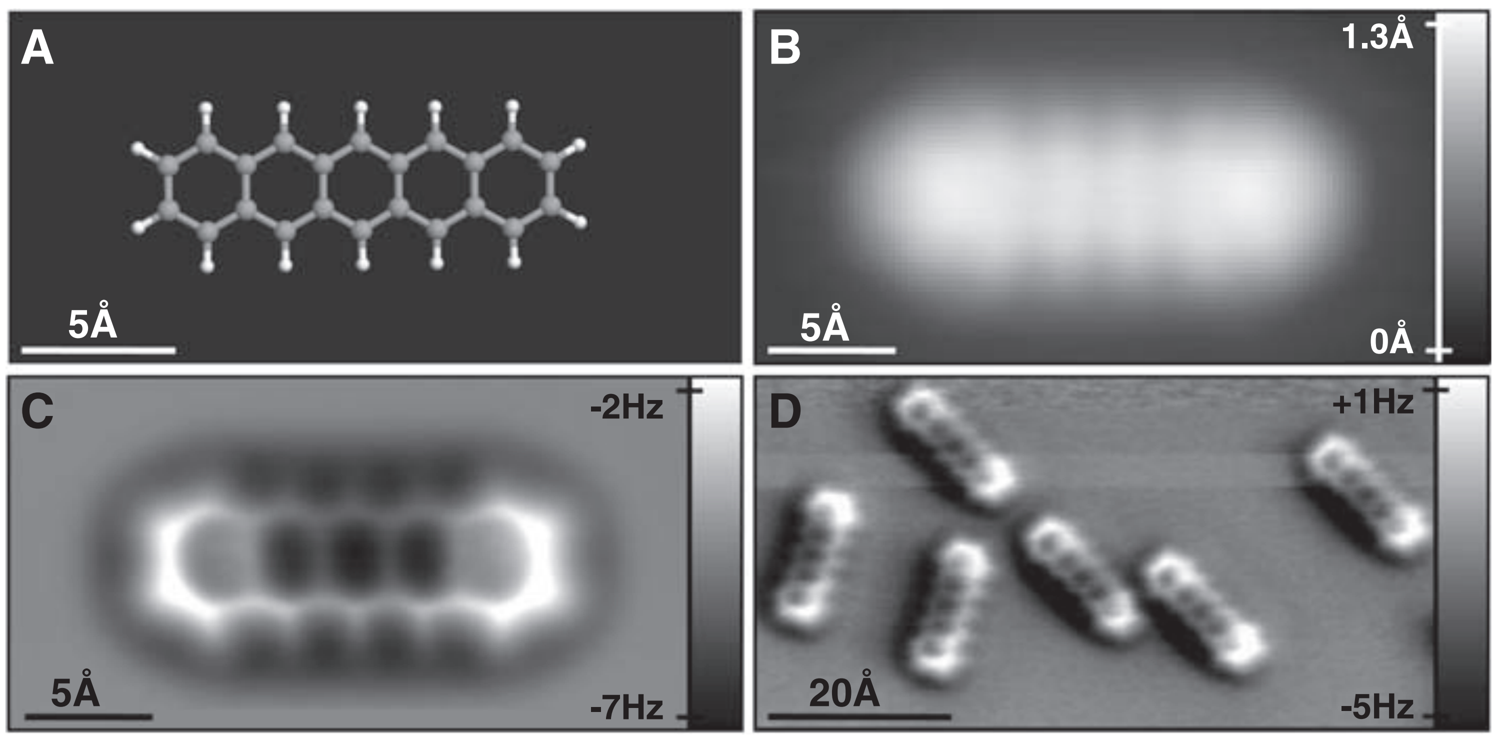
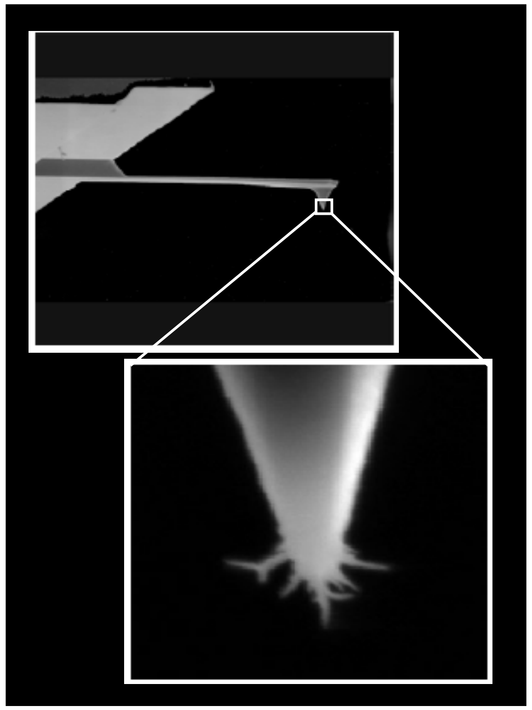
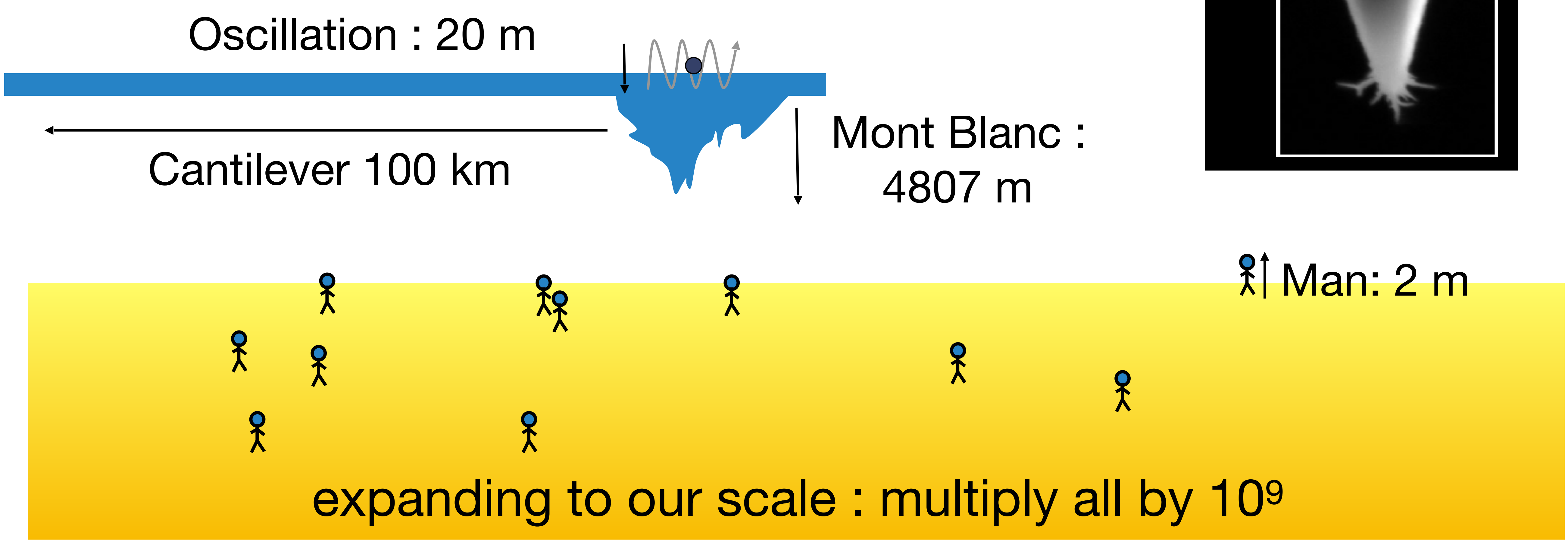


Fig. 1. STM and AFM imaging of pentacene on Cu(111). (**A**) Ball-and-stick model of the pentacene molecule. (**B**) Constant-current STM and (**C** and **D**) constant-height AFM images of pentacene acquired with a CO-modified tip. Imaging parameters are as follows: (B) set point $I = 110$ pA, $V = 170$ mV; (C) tip height $z = -0.1$ Å [with respect to the STM set point above Cu(111)], oscillation amplitude $A = 0.2$ Å; and (D) $z = 0.0$ Å, $A = 0.8$ Å. The asymmetry in the molecular imaging in (D) (showing a "shadow" only on the left side of the molecules) is probably caused by asymmetric adsorption geometry of the CO molecule at the tip apex.

About AFM scale

… how to shake the Mont Blanc over little men heads without crushing them

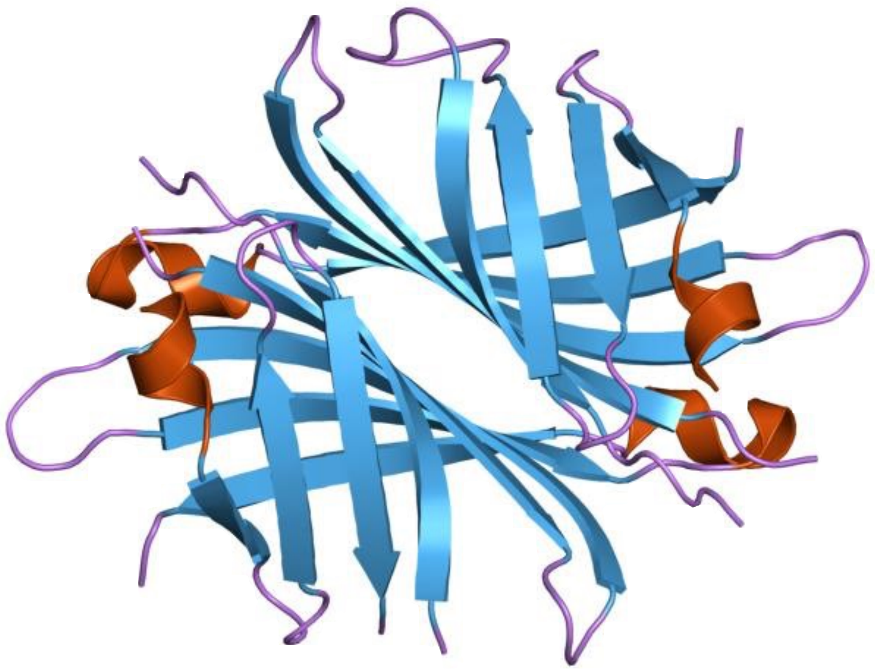




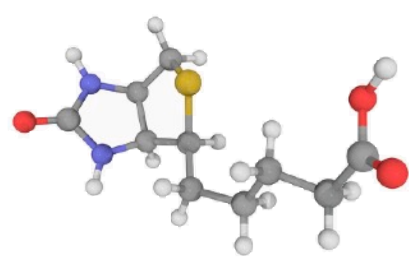
Moskalenko

Marking 0s and 1s

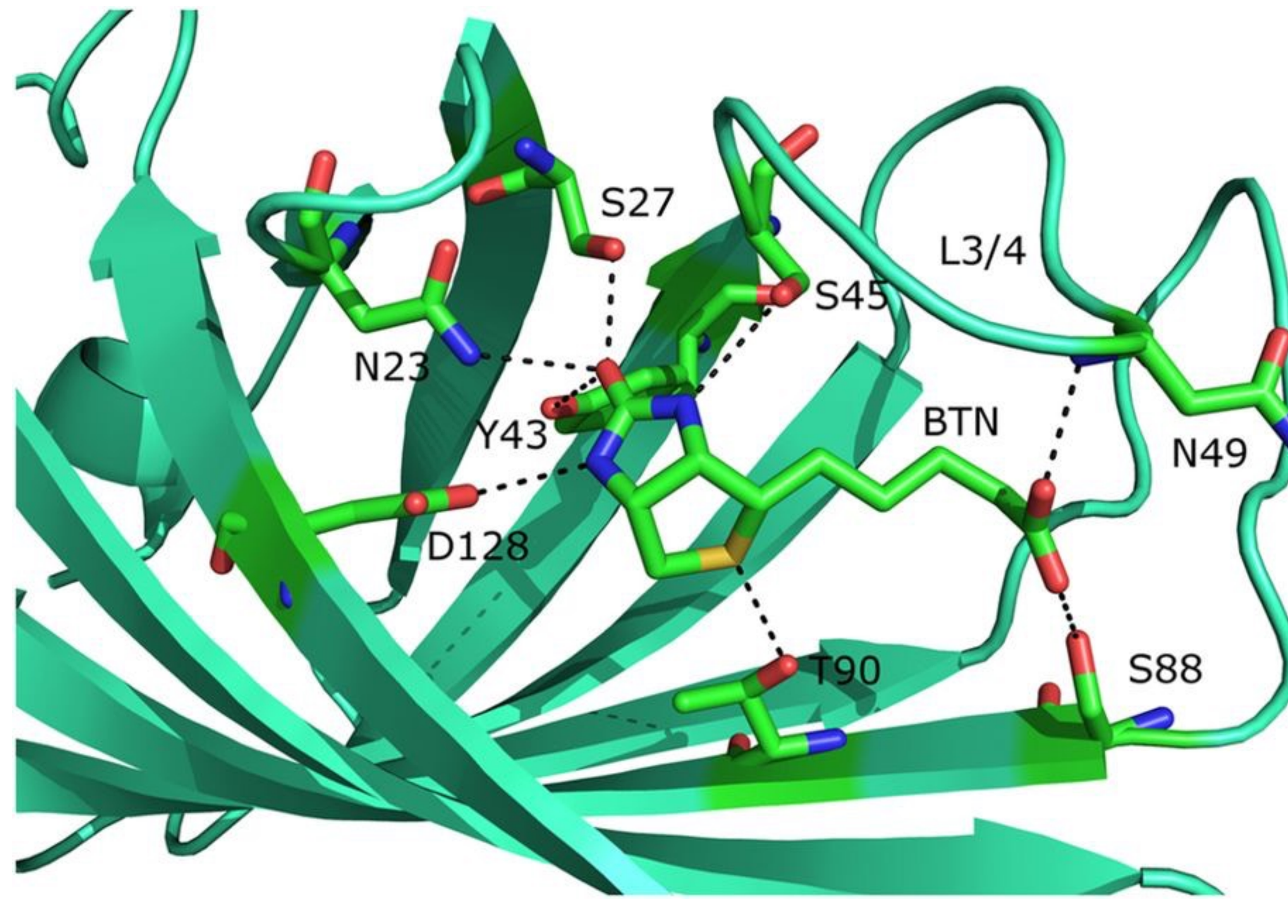
Streptavidin-biotin marker



Streptavidin : a "huge blob"



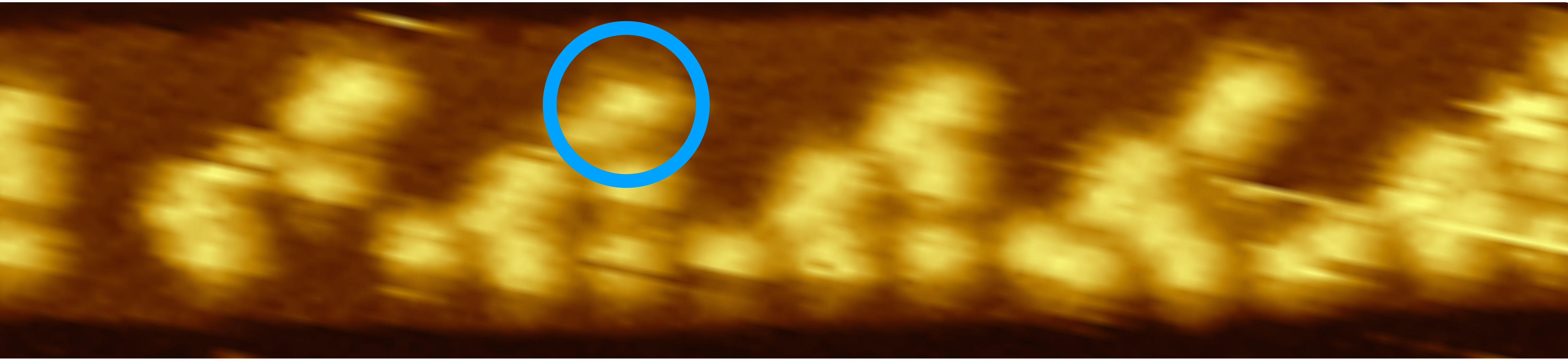
Biotin can easily be attached to DNA strand at order



Together they make one of the <u>strongest</u> non-covalent bond

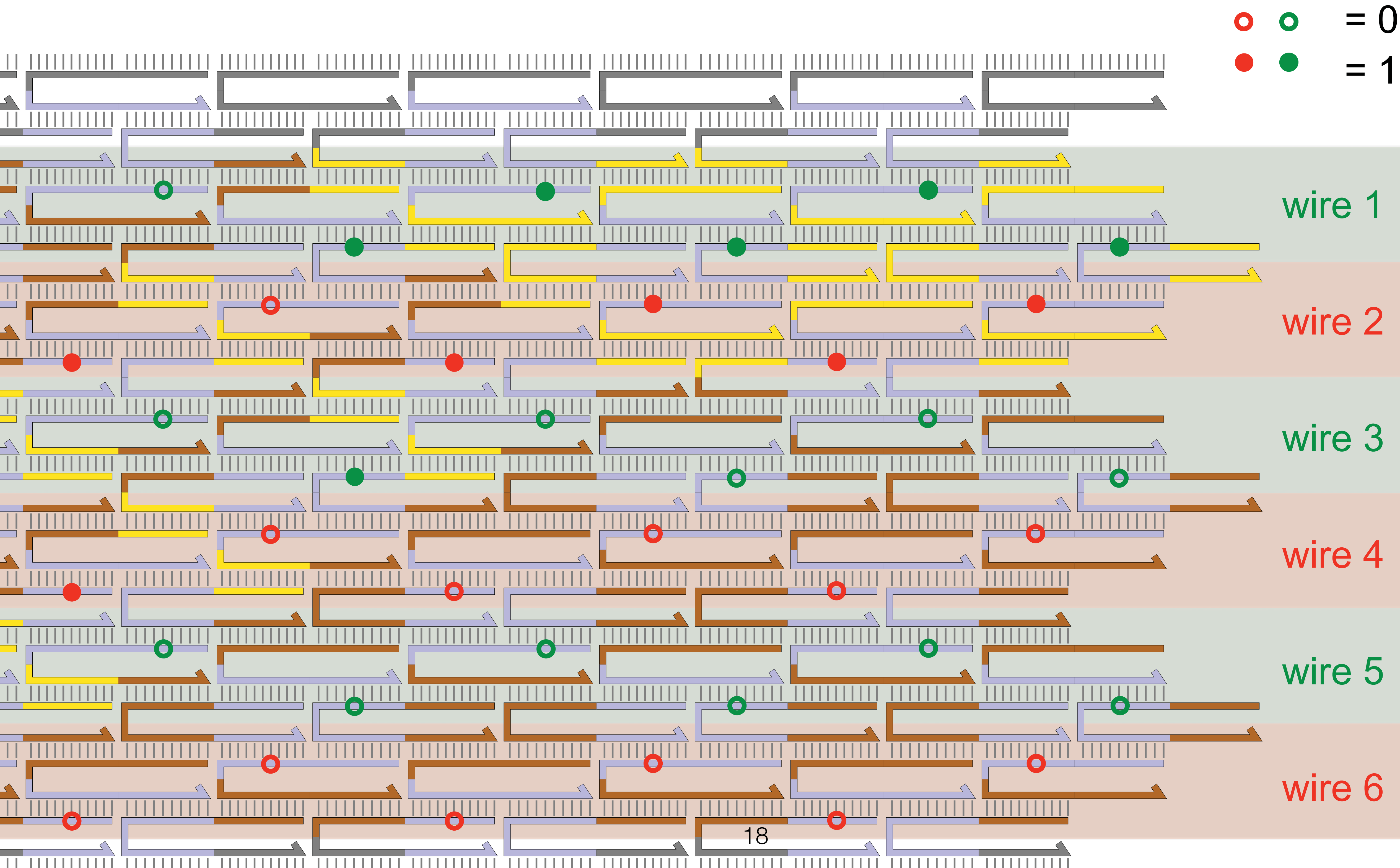
Streptavidin-biotin marks

We can order single DNA strand with biotin attached
(the tiles encoding a 1!)



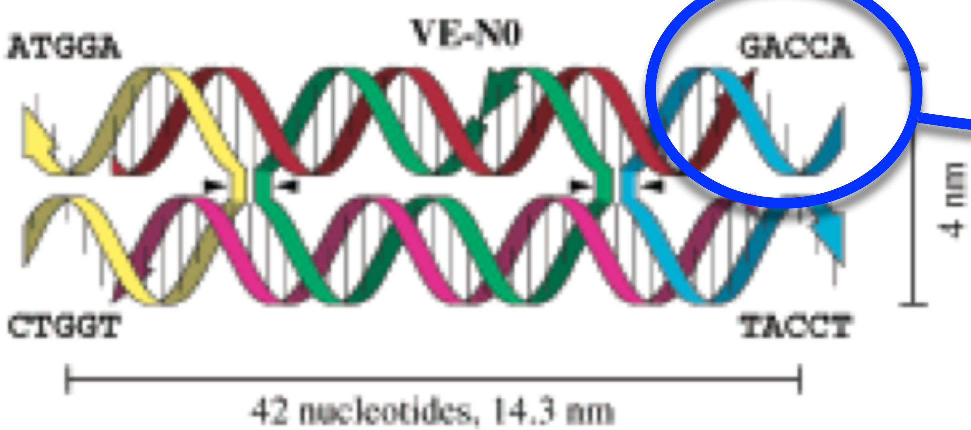
When added to the solution while imaging,
Streptavidin attaches to biotin,
marking the corresponding single stranded tiles

Streptavidin-biotin marks



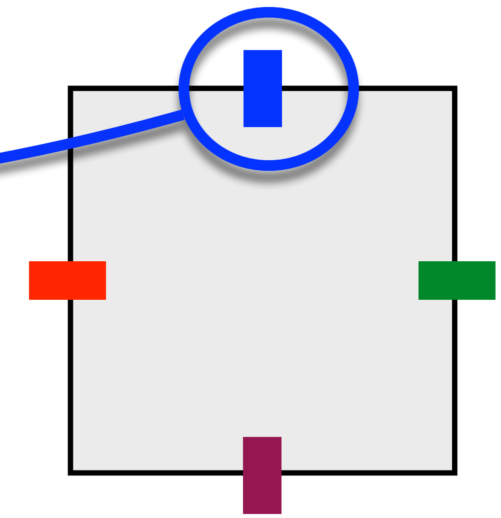
kTAM model for algorithmic assembly

Algorithmic self-assembly

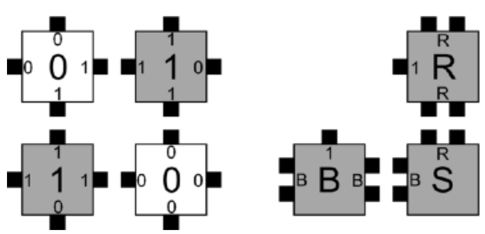


=

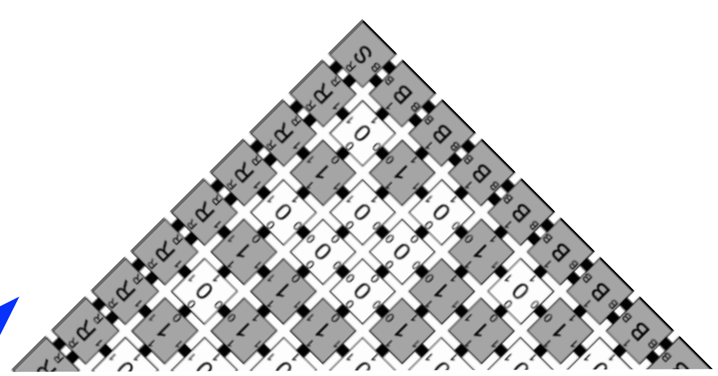
Winfree. 1998.
PhD Thesis



Erik Winfree had the idea that a growing lattice of DNA tiles could run a computer program, like Wang tiles or a CA

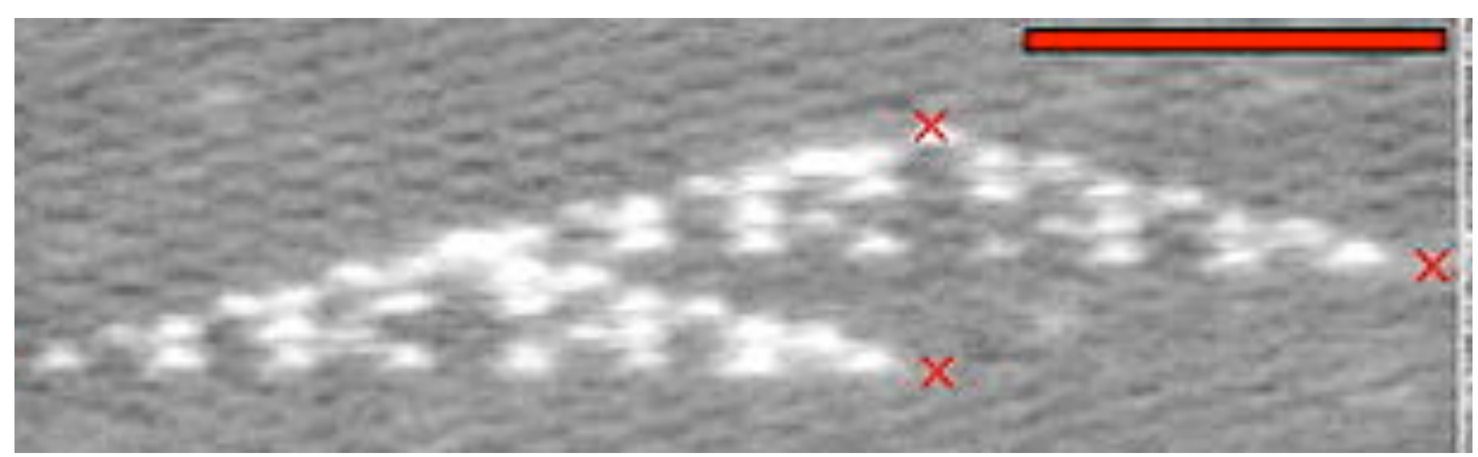


tiles = program



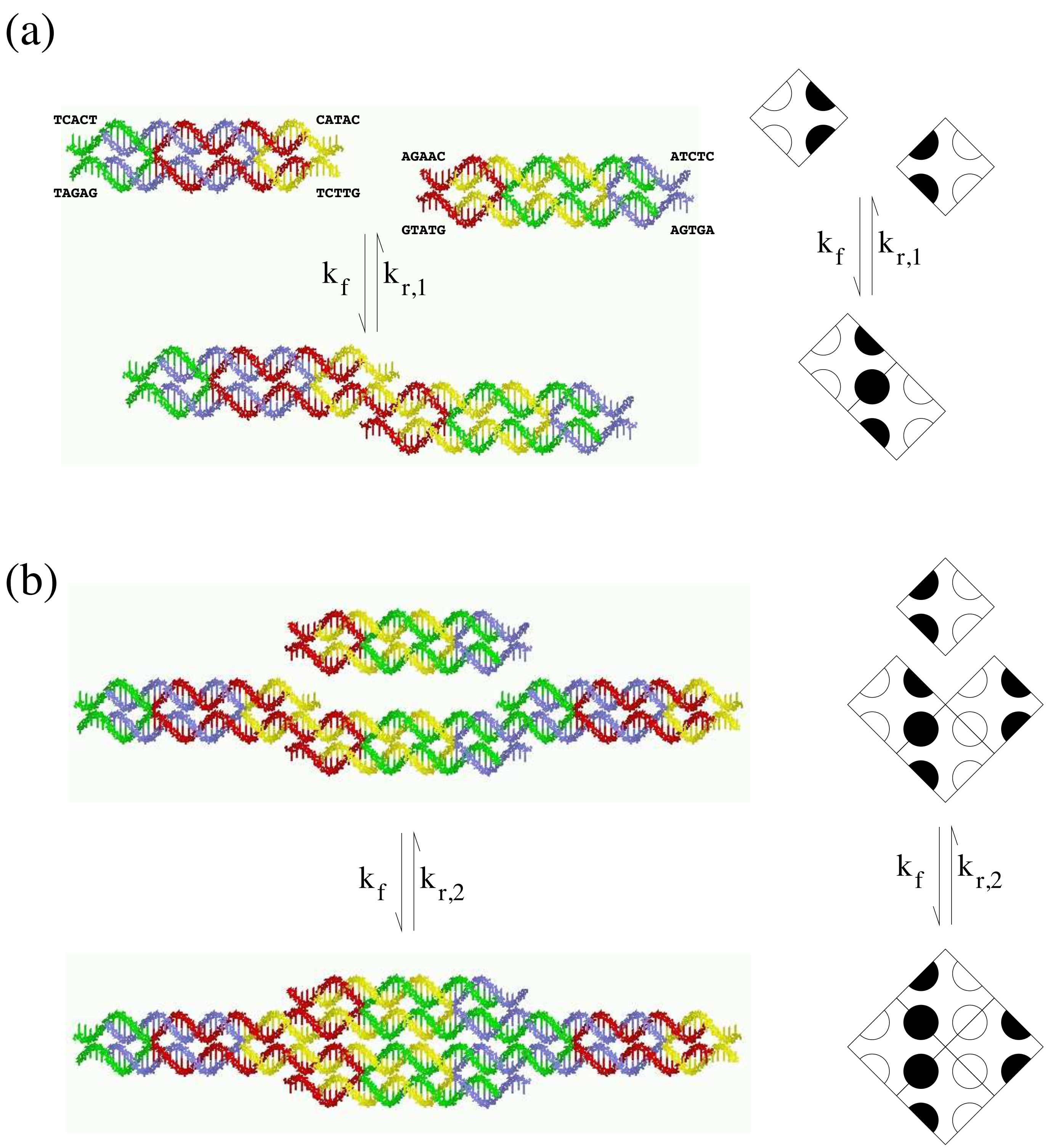
crystal growth = program execution

self-assembly.net



Rothemund, Papadakis, Winfree 2004

Thermodynamical model



Attachement rate

=

$$\boldsymbol{k_f} \cdot [\ \boldsymbol{Strand}\ ]$$

$$=$$

$$\boldsymbol{k_f} \cdot \mathbf{e}^{-\boldsymbol{Gmc}}$$

(mainly entropy)

Detachment rate

=

$$\boldsymbol{k_f} \cdot \mathbf{e}^{-(\boldsymbol{b} \cdot \boldsymbol{Gse})}$$

where b is the number of bonds

and $G_{se} = \Delta G / RT$

the bonding unit energy in RT units

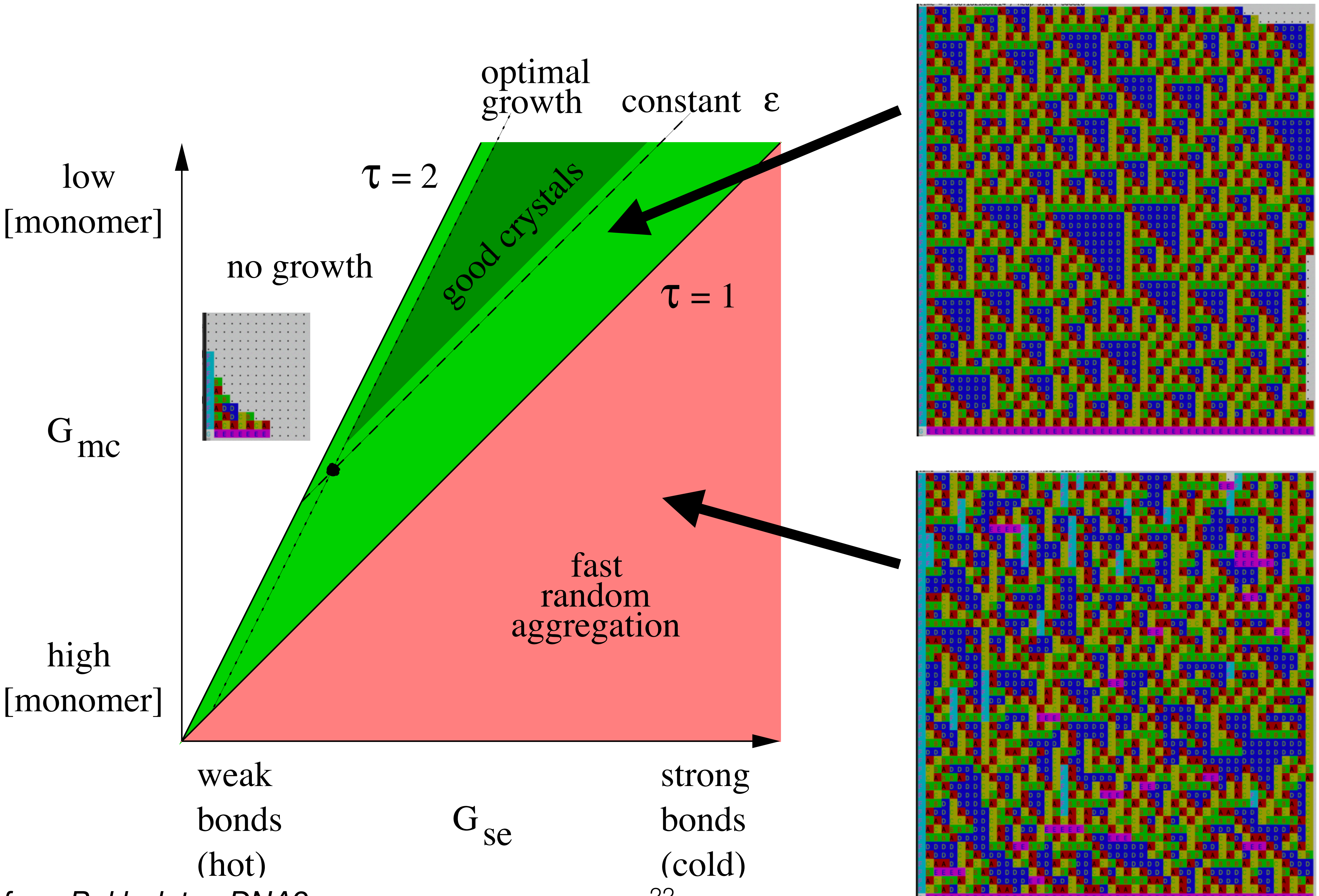
(mix of entropy and enthalpy)

mc = **m**onomer **c**oncentration

se = **s**ticky **e**nd bond strength

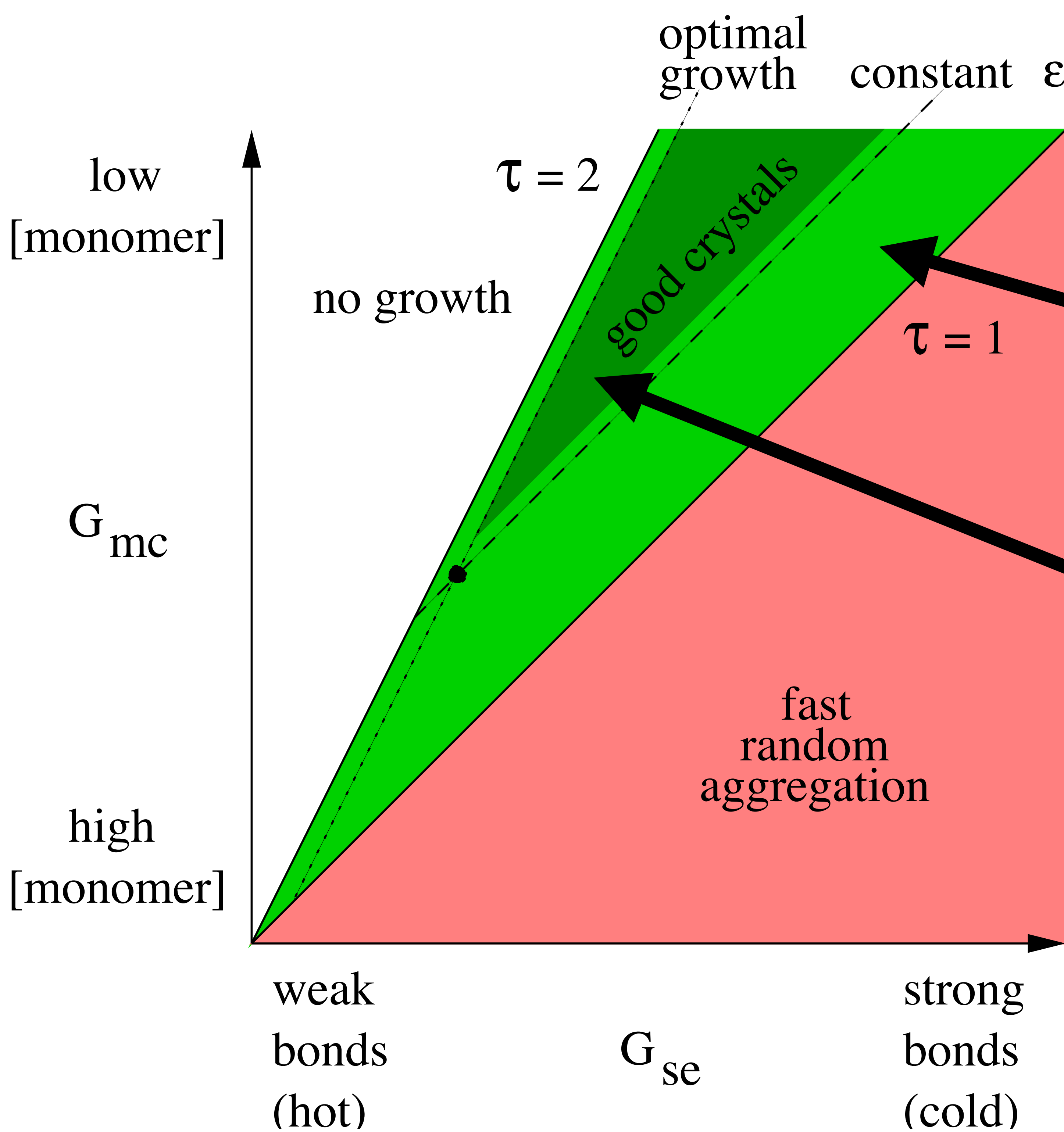
Winfree, Bekbolatov DNA9

V



Winfree, Bekbolatov DNA9

Simulations



$G_{se} < G_{mc} < 2G_{se}$

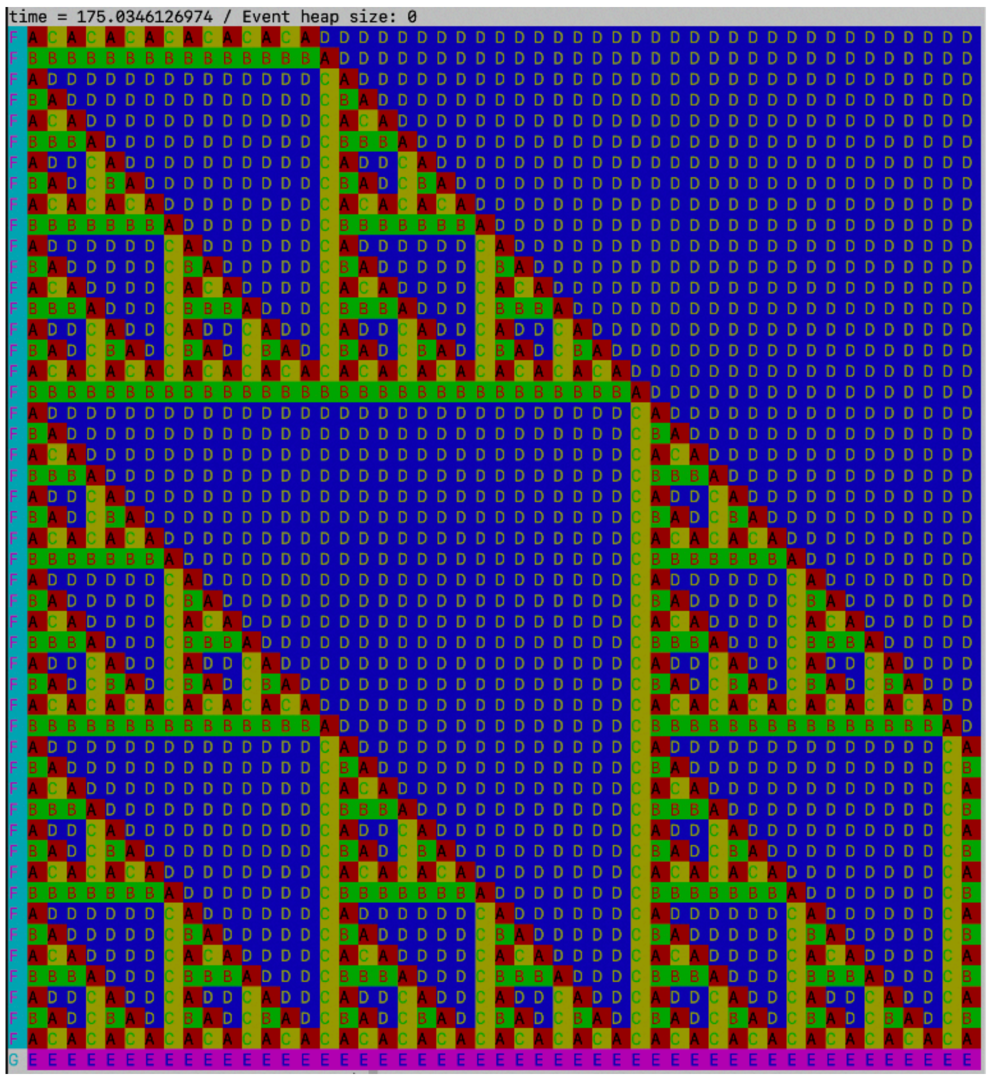
Fastest when

$G_{mc} \sim 2G_{se} - \varepsilon$

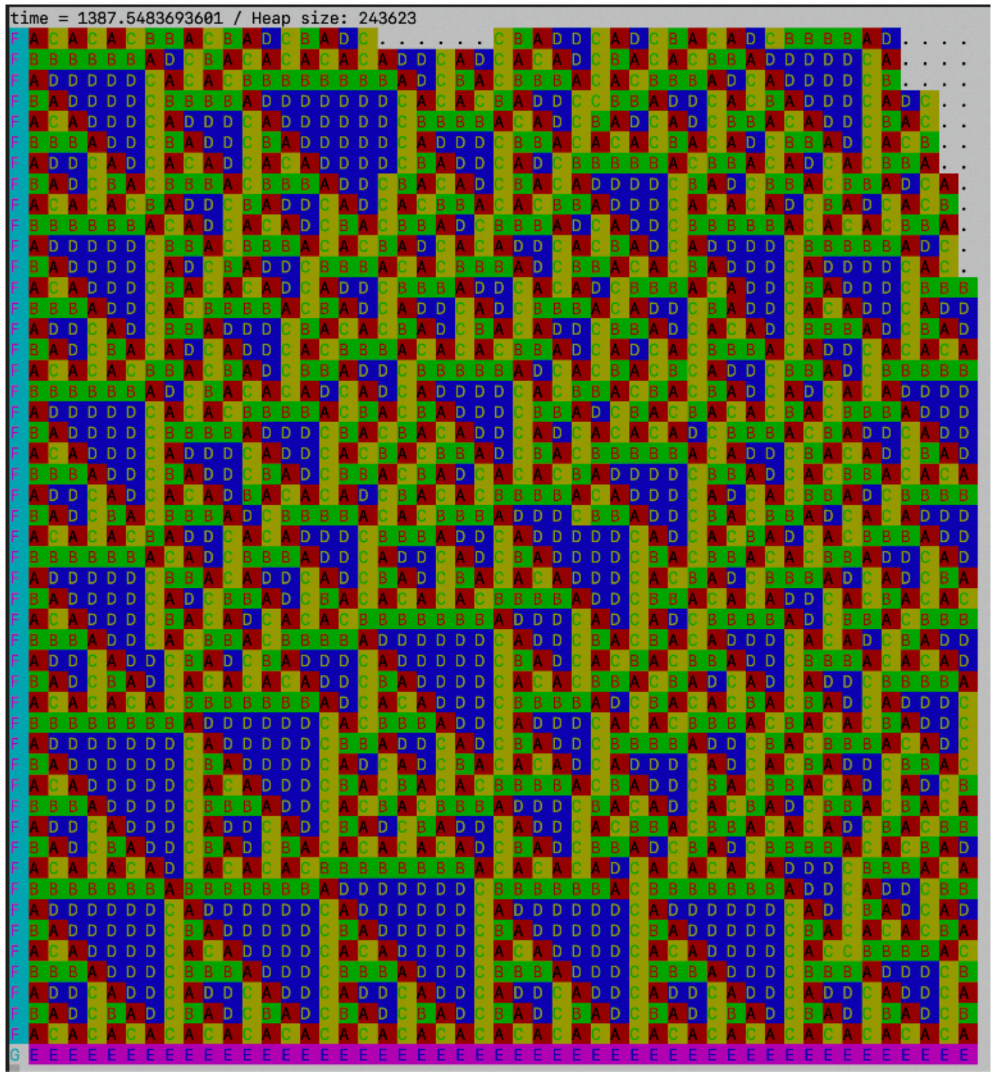
Sweet spot

Winfree, Bekbolatov DNA9

Minimzing errors

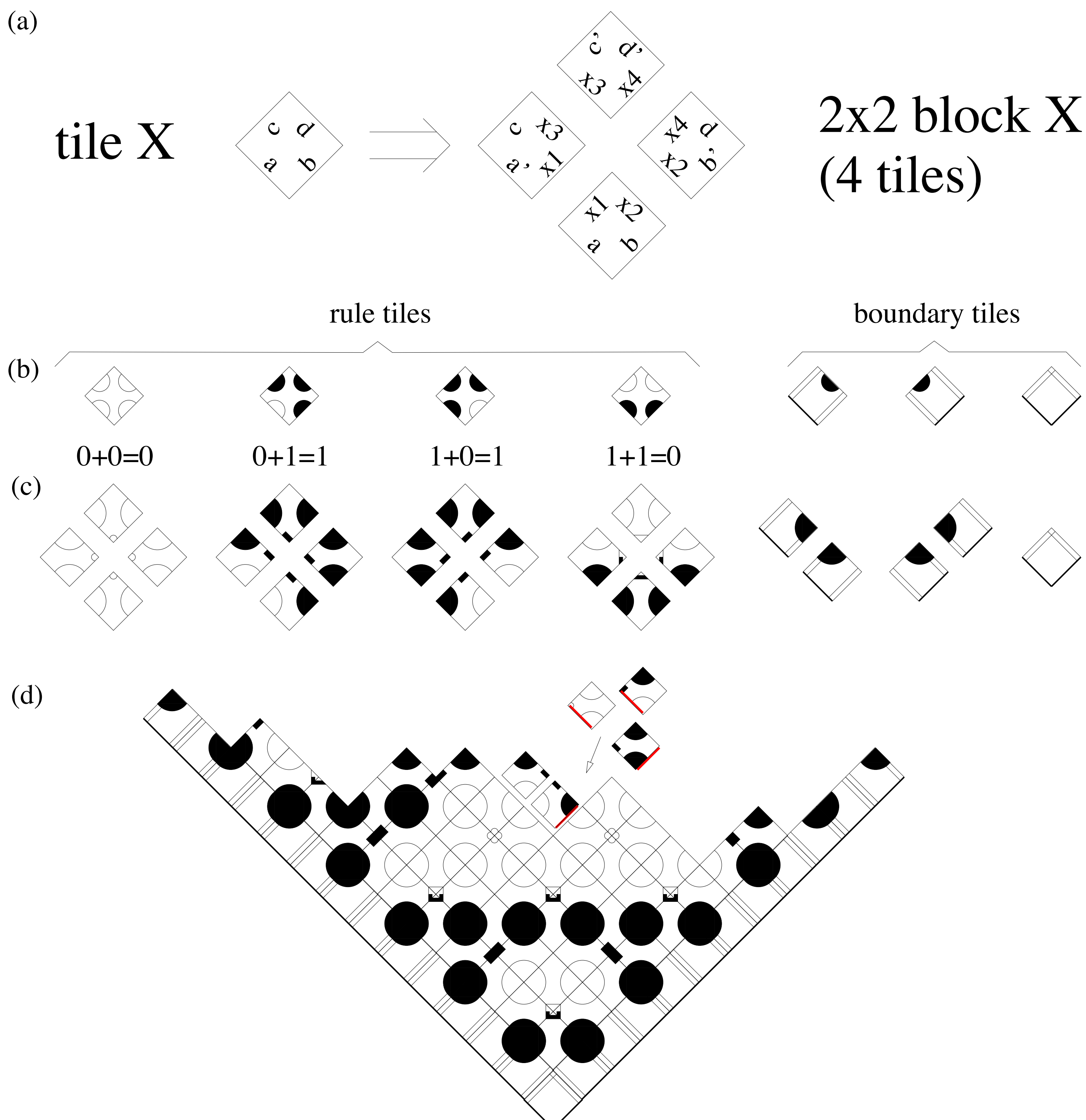


Desired



Obtained

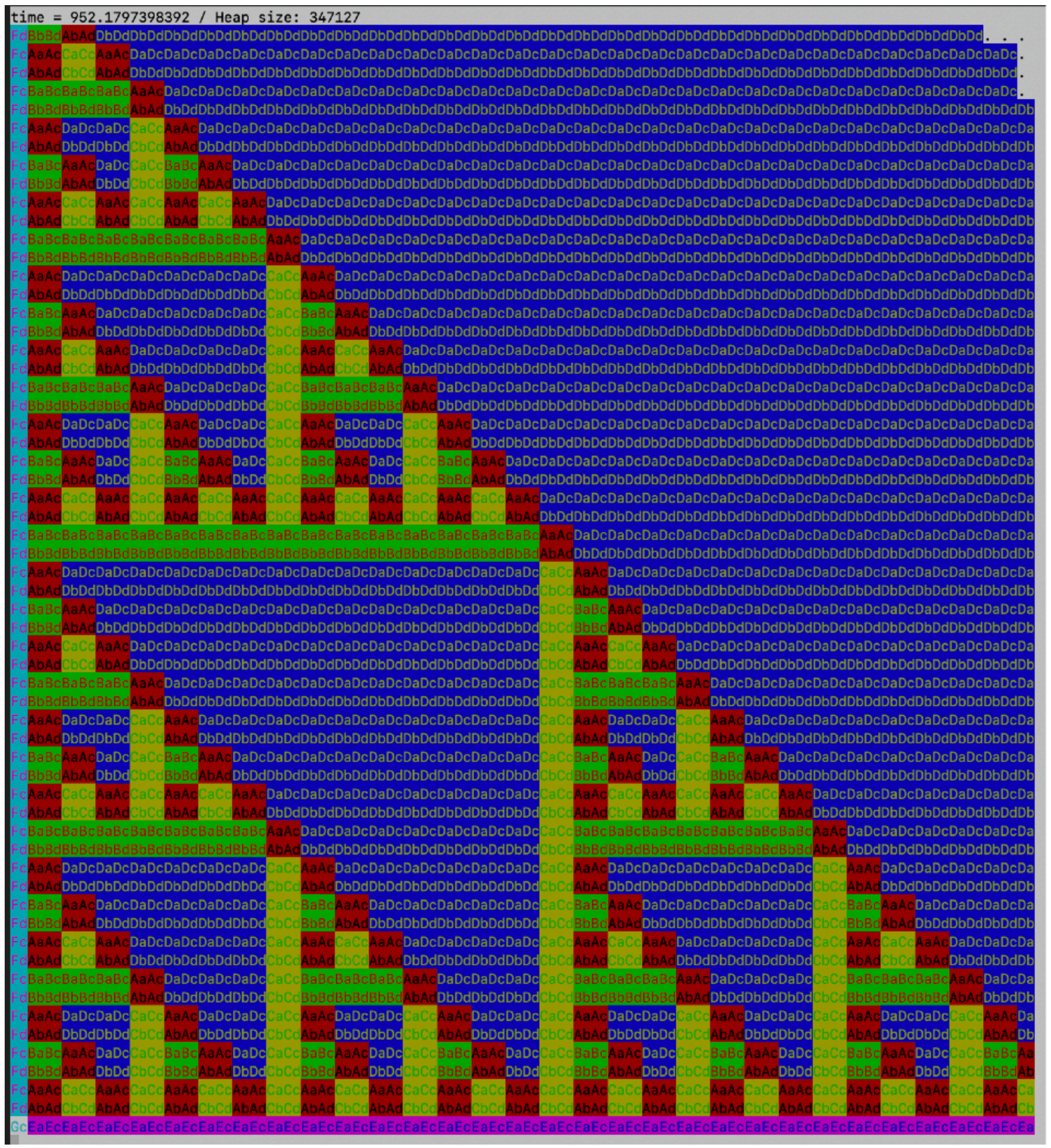
Proofreading tiles



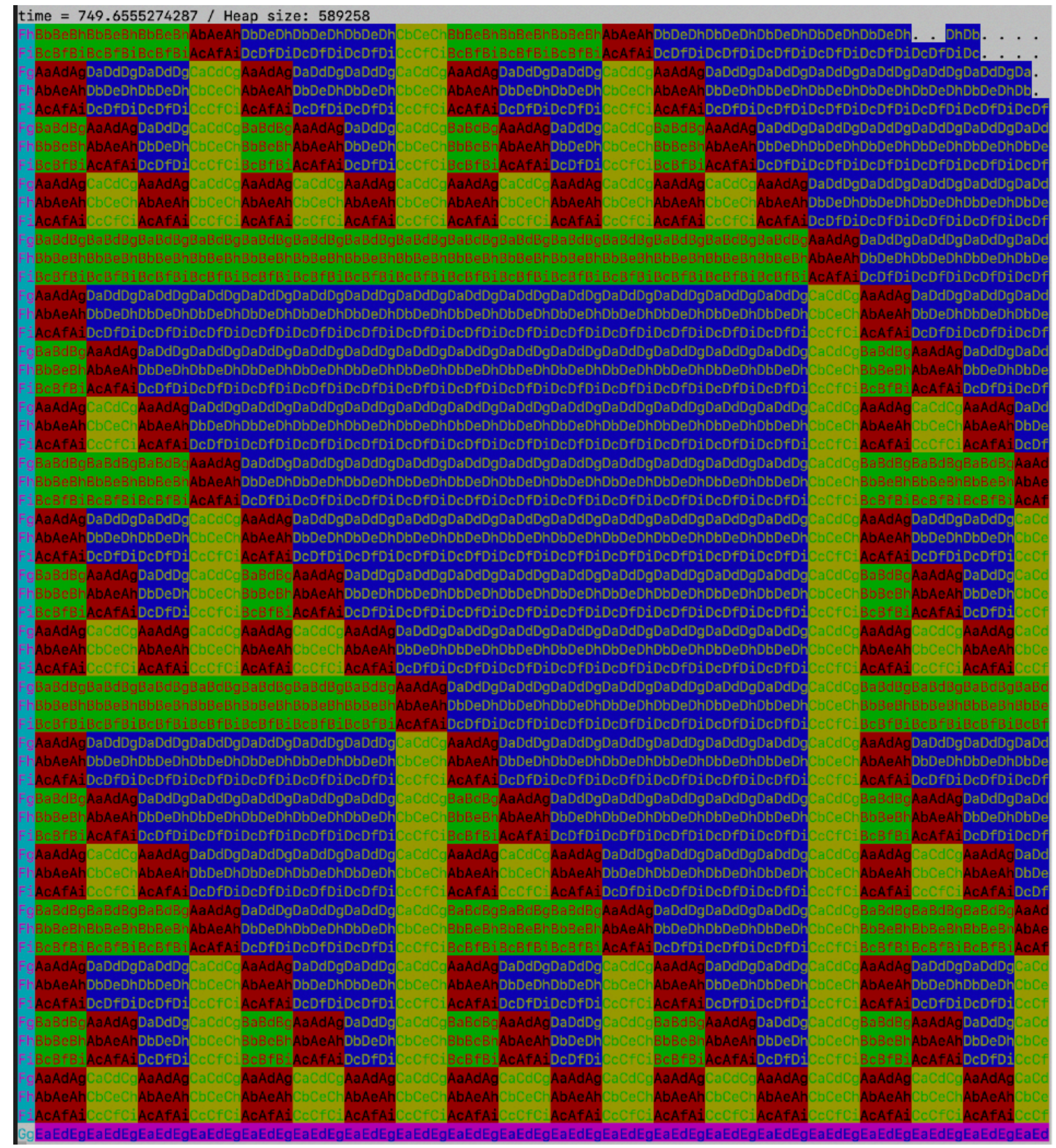
- Cut every tile into k x k tiles
- Now, you need to ***make an other error*** to compensate for an error
- The error rate is squared for $k = 2$!

Winfree, Bekbolatov DNA9

Proofreading tiles

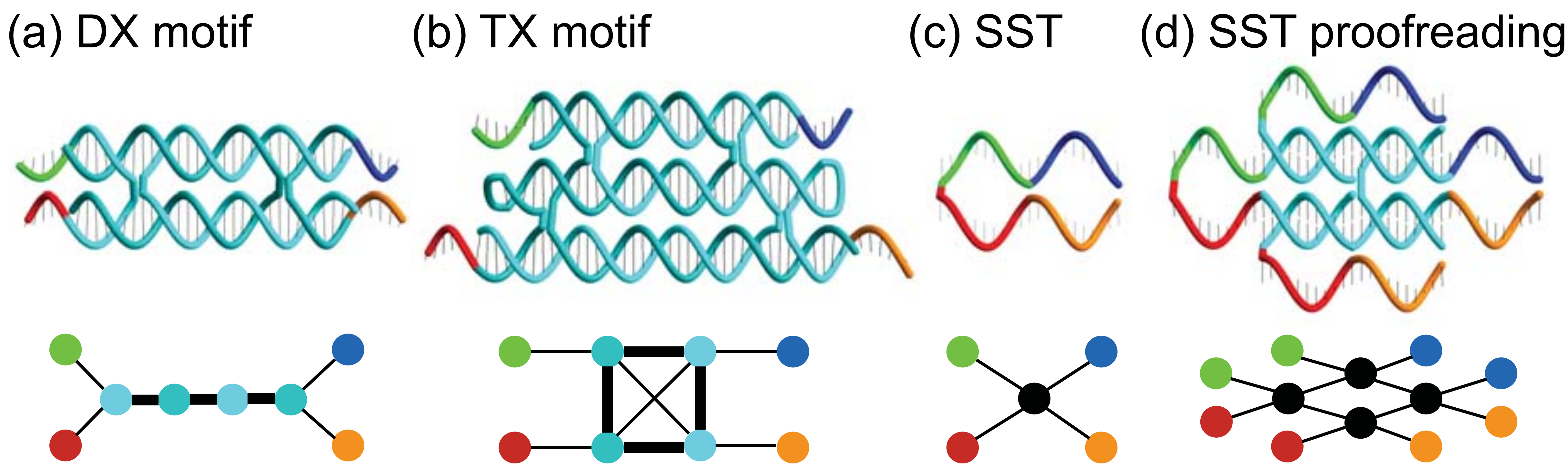


$k = 2$



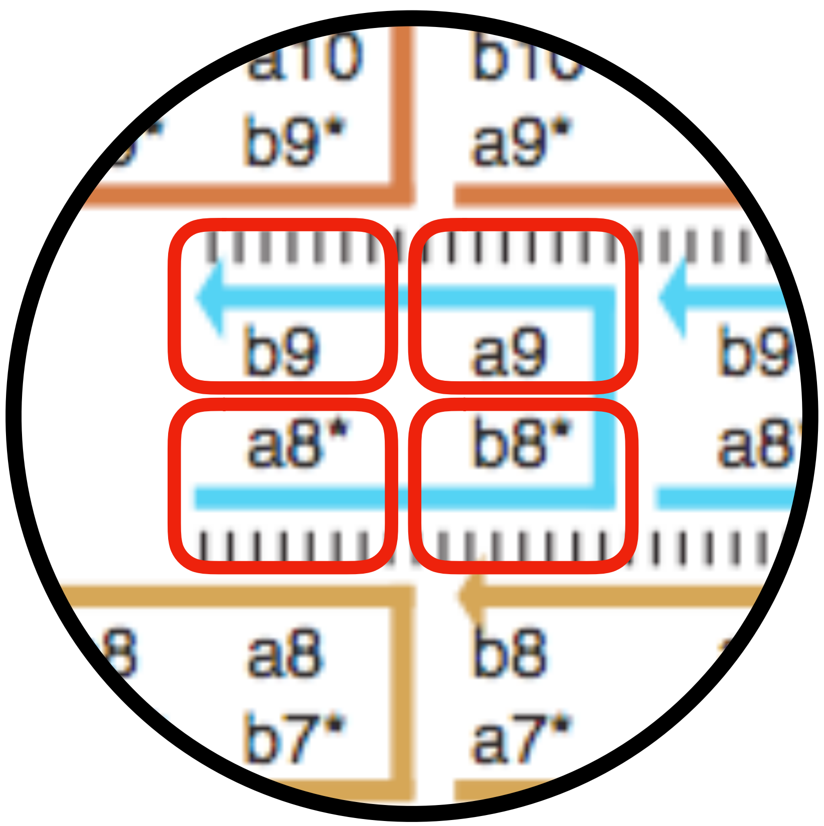
$k = 3$

Proofreading tiles compared to other tiles



Implementing boolean circuits

Tile as gates



4 domains = 4 glues

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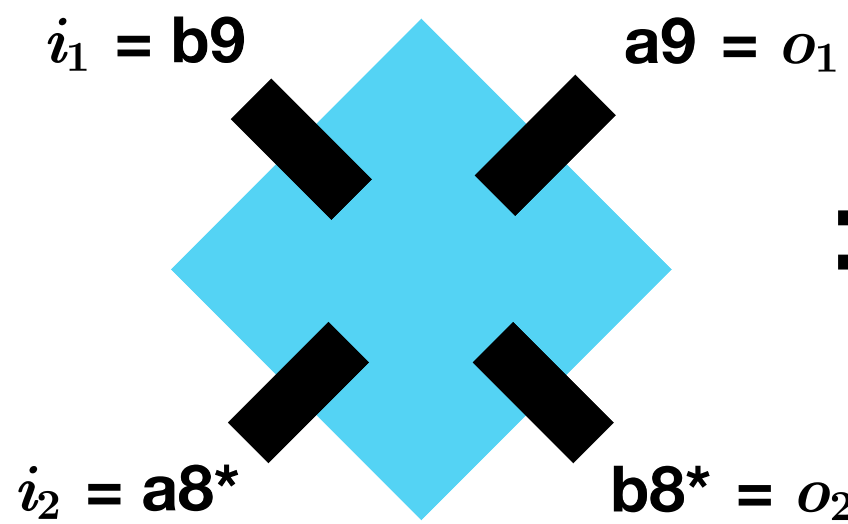

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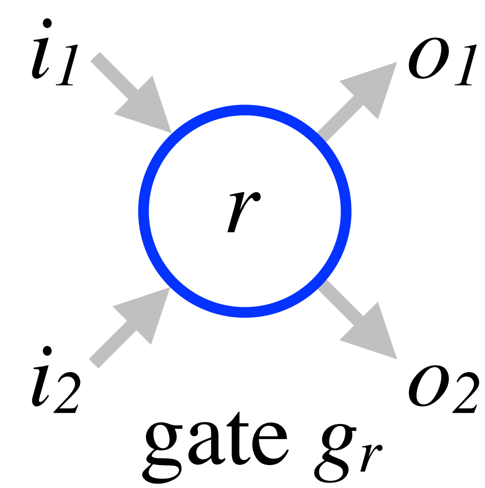
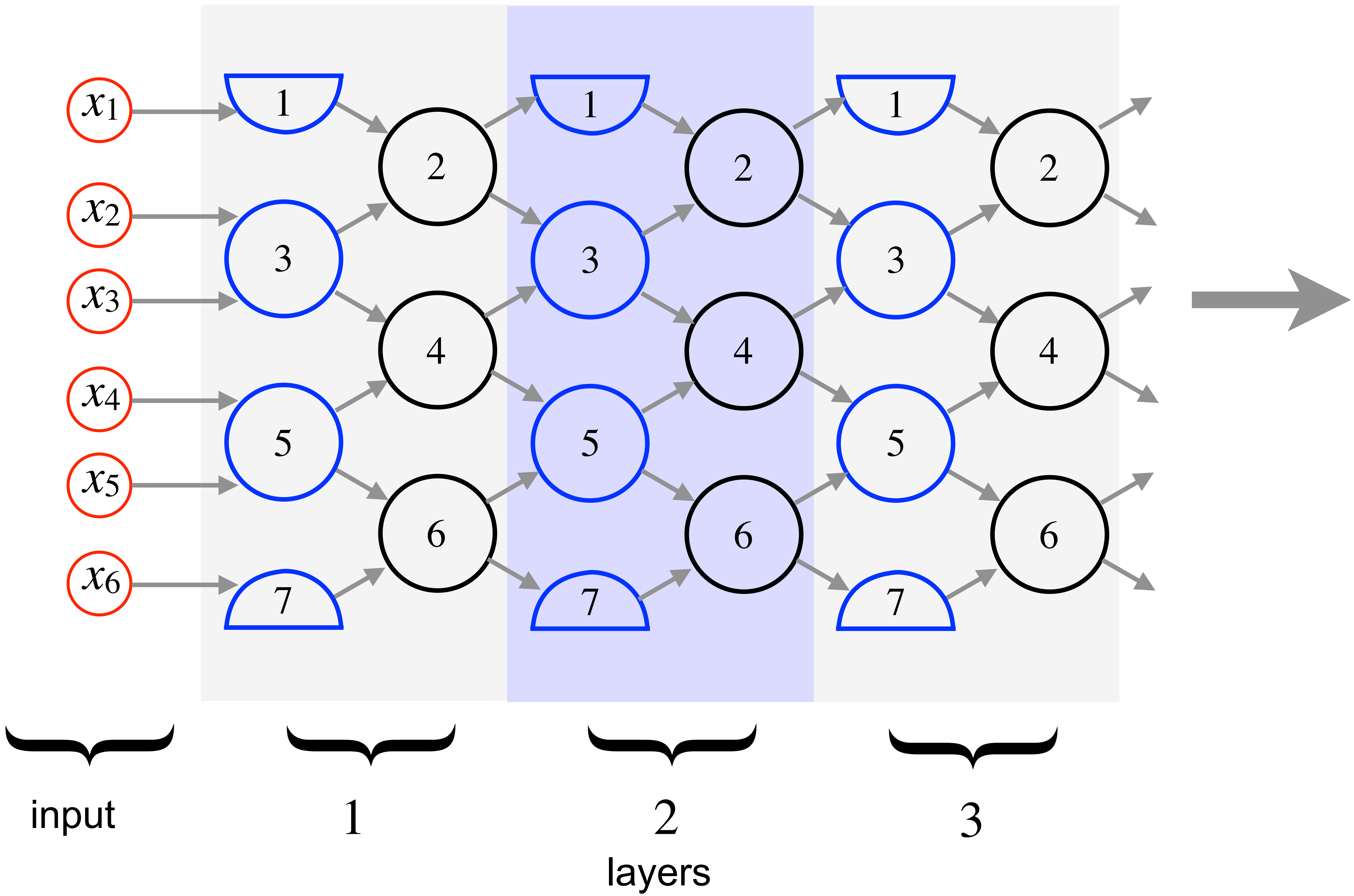
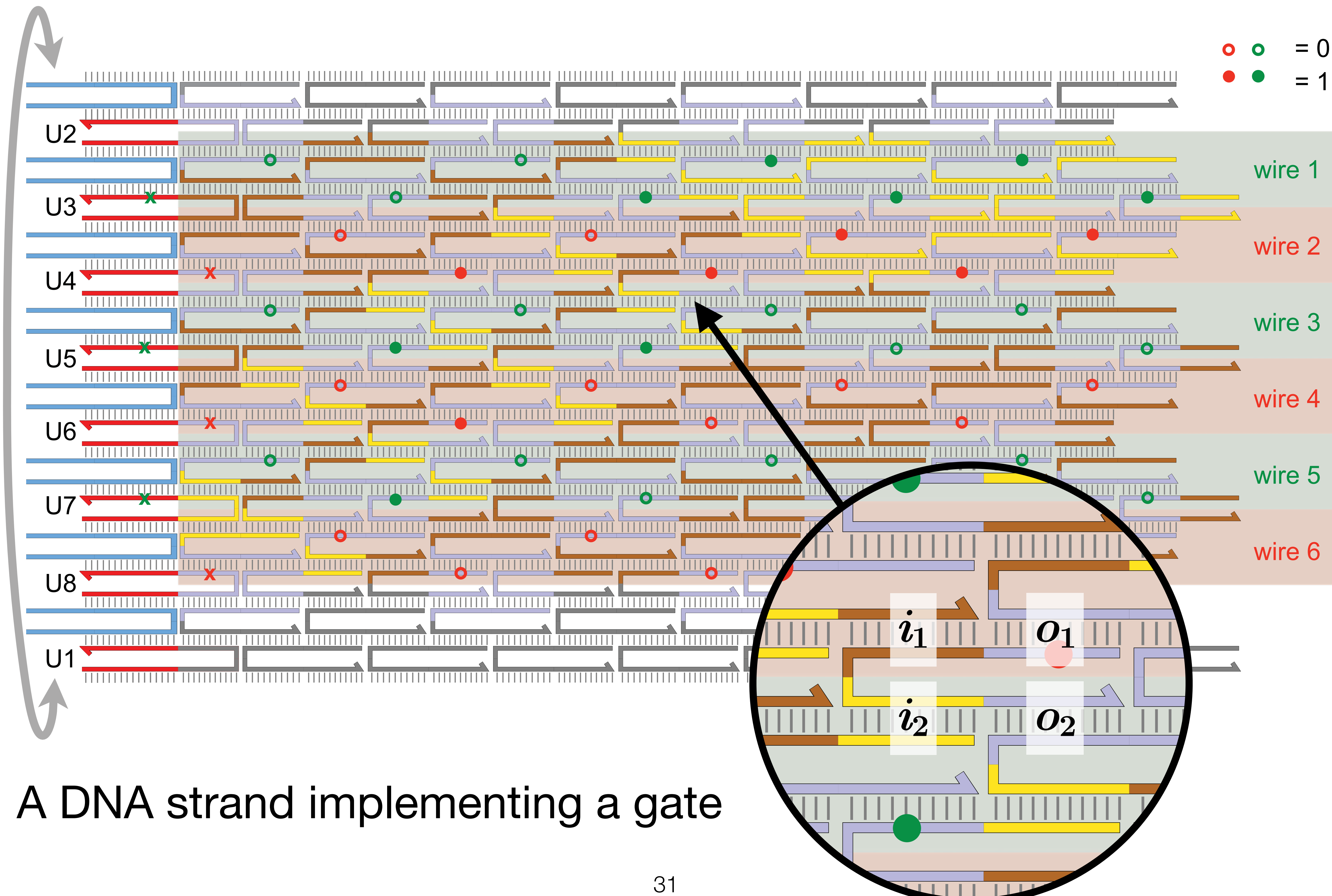


Tiles assembly is a rewriting system

DNA nanotube circuit model

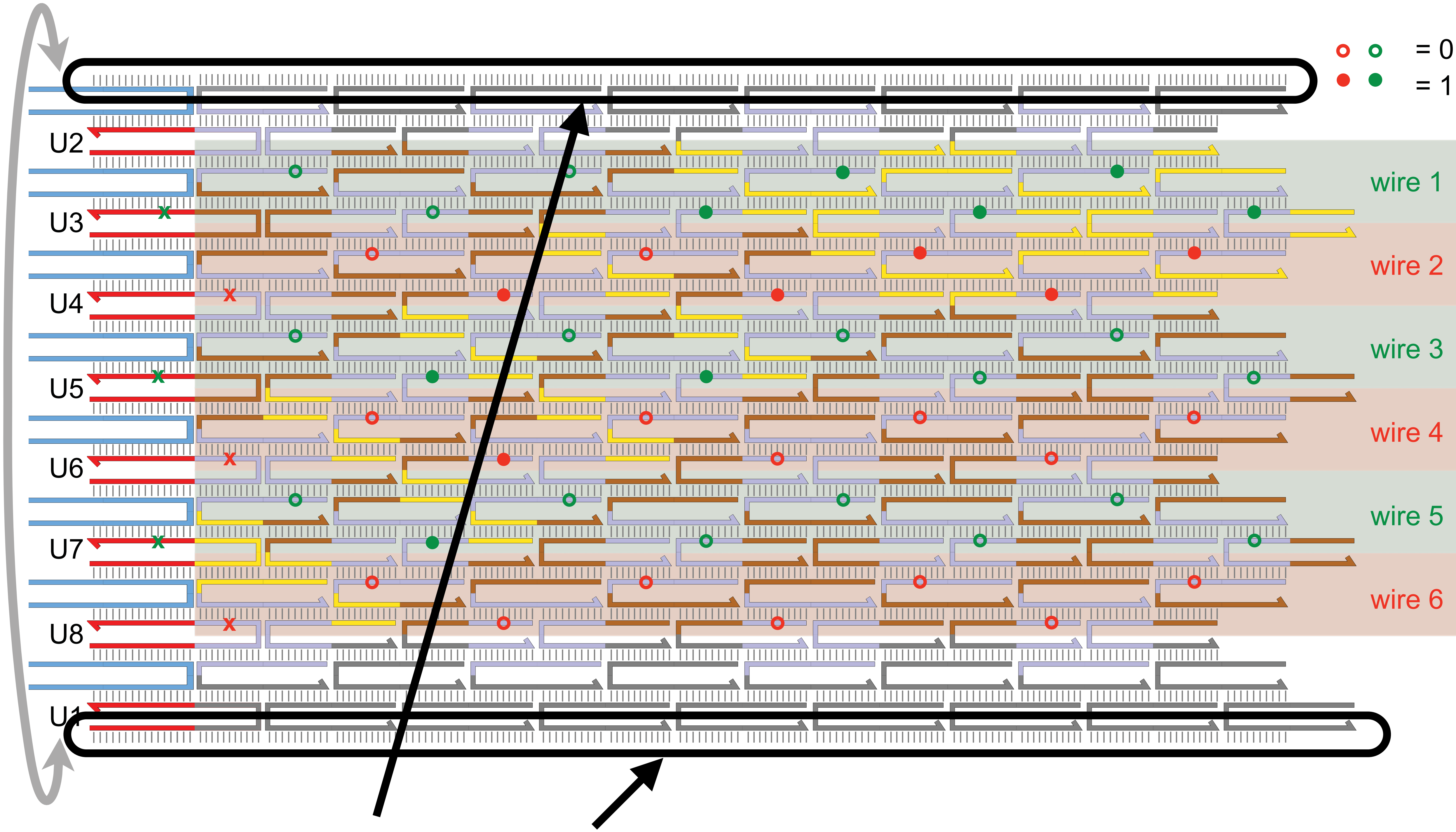


DNA nanotube circuit model



A DNA strand implementing a gate

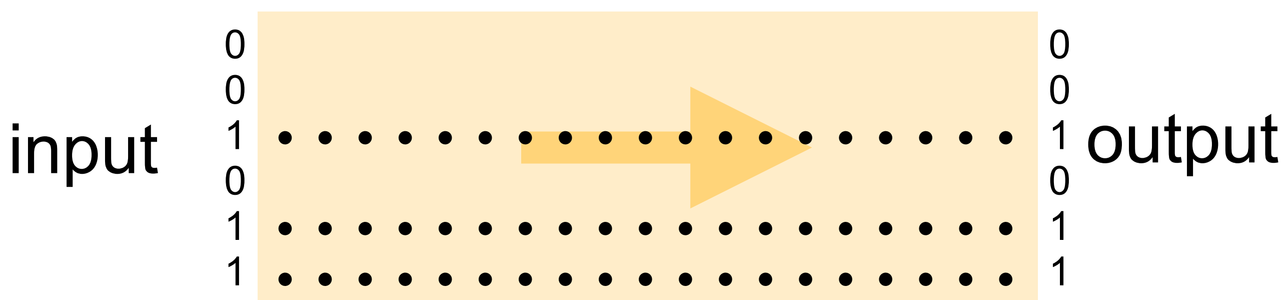
DNA nanotube circuit model



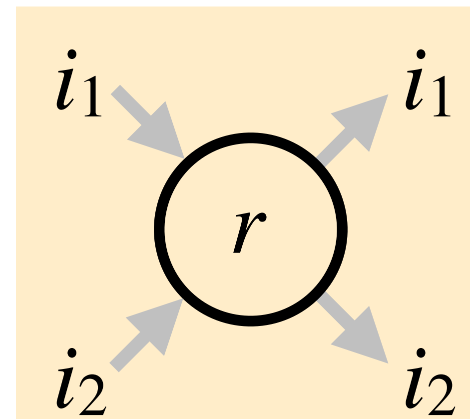
The *seam* which can be *unzipped* to flatten the assembly for imaging

Example nanotube circuits

- ***n*-bit copying**: n+1 copy gates



6-bit copying circuit



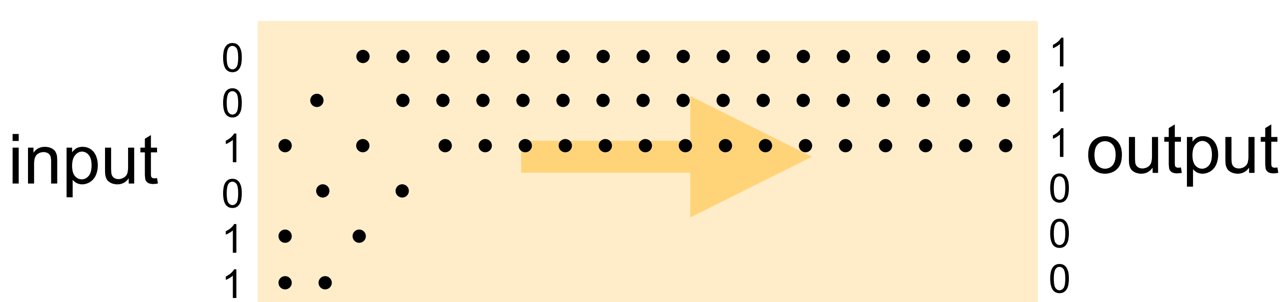
copy gate

$i_1, i_2 \in \{0,1\}$

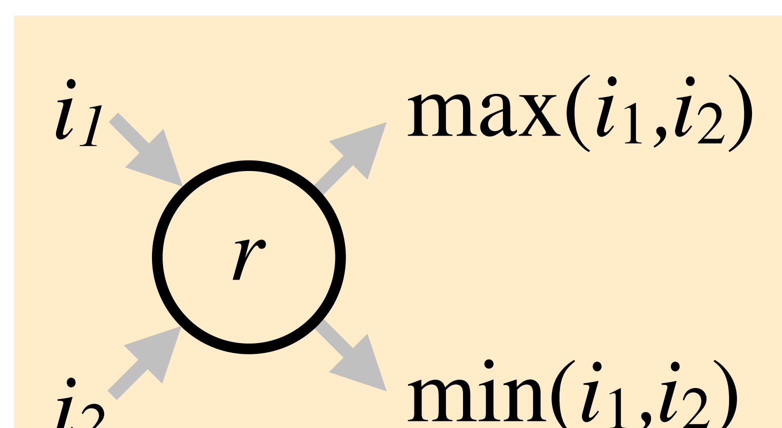
i_1	i_2	o_1	o_2
0	0	0	0
0	1	0	1
1	0	1	0
1	1	1	1

copy gate truth table

- ***n*-bit binary sorting:** n+1 sort gates



6-bit sorting circuit



sort gate

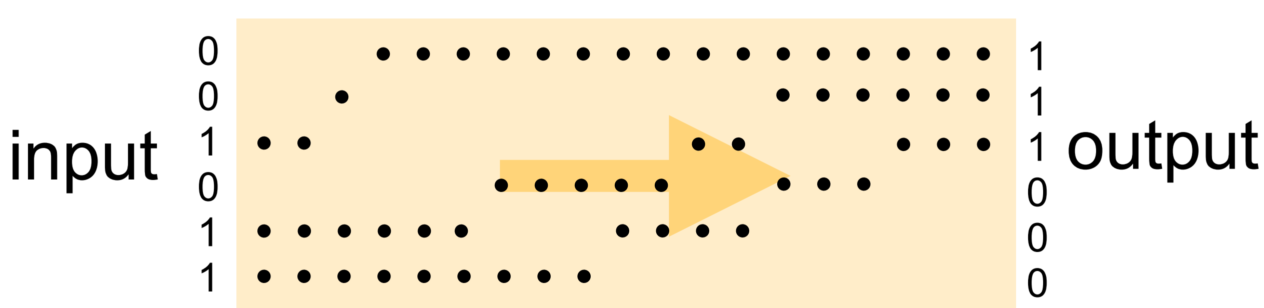
i_1	i_2	o_1	o_2
0	0	0	0
0	1	1	0
1	0	1	0
1	1	1	1

sort gate truth table

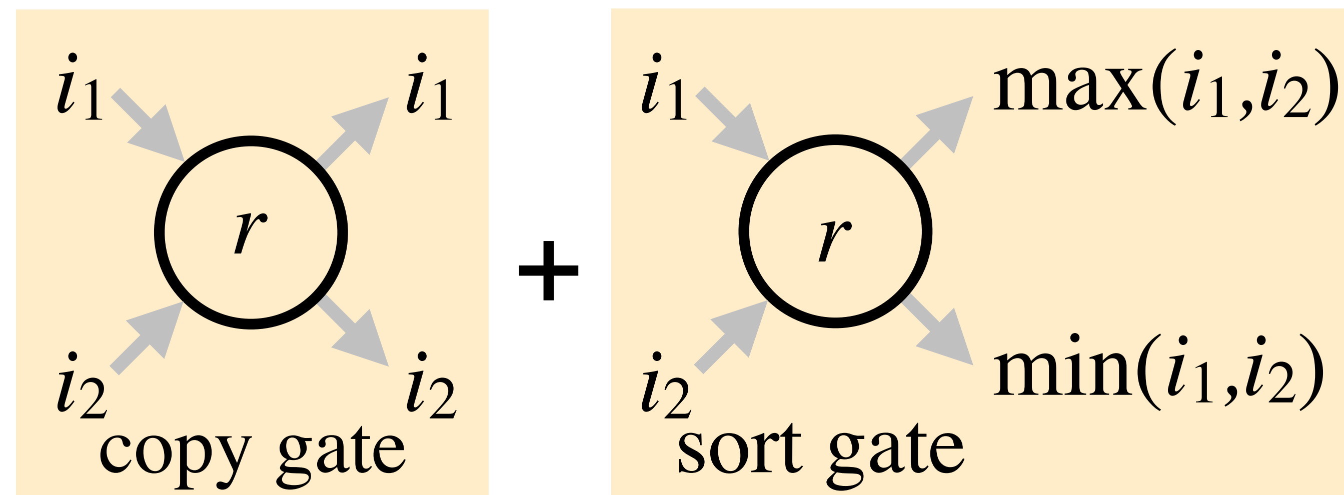
Note that 2 gates are single input, single output

Example nanotube circuits

- **Lazy sorting**! Take the union of the copy gate set and the sort gate set. Copying fights to slow down the sorting process, but assuming a fair execution, sorting will eventually win.



6-bit slow randomised sorting

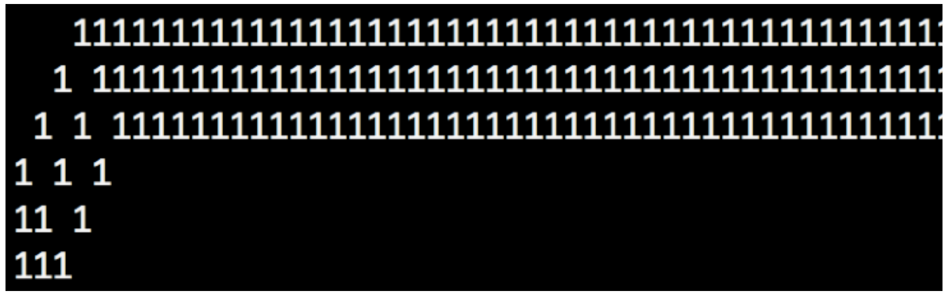


- Since, in any given circuit, each gate “knows” its row number *r*, we will also write circuits (programs) that exploit this feature, do something that is interesting *and* (more importantly) provably impossible without that feature

Circuits

sorting

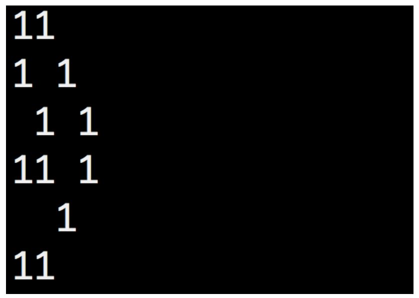
0
0
0
1
1
1



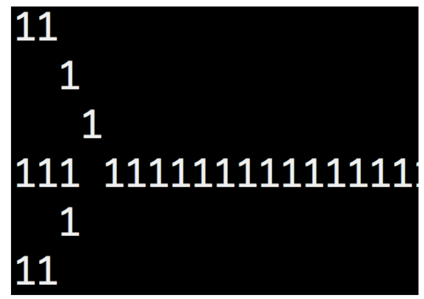
Function computation

parity

1
1
0
1
0
1



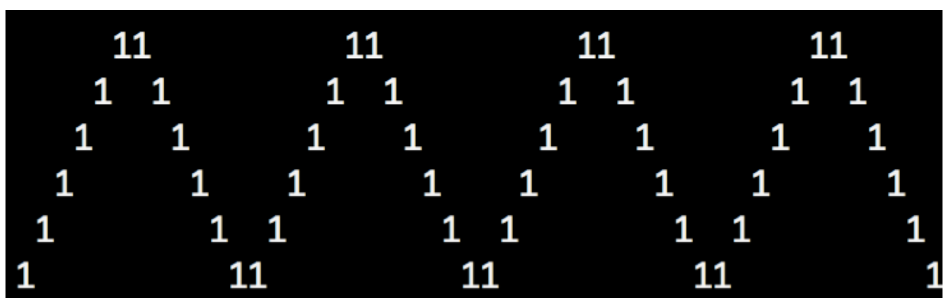
1
0
0
1
0
1



Solving a “hard” decision problem

zig-zag

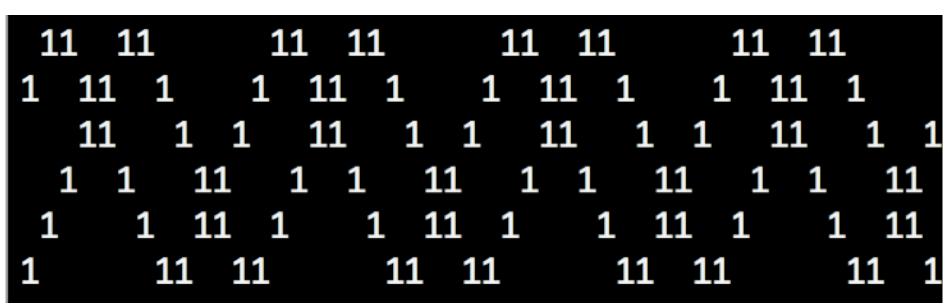
0
0
0
0
0
1



Glider: A common cellular automata primitive

zig-zag

0
1
0
0
0
1



Pattern: DNA

long repeat

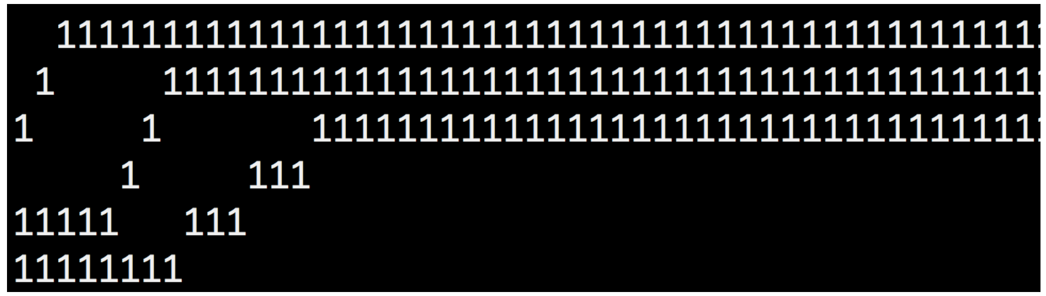
Behaviour: 63 layers to see the same thing twice!

Rule 110

Circuits: randomised

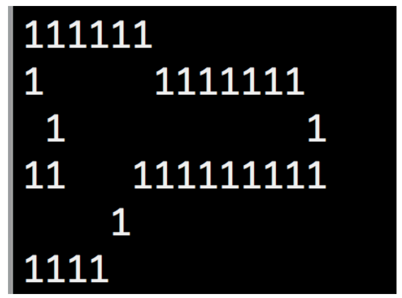
lazy sorting

0 0 1 0 1 1

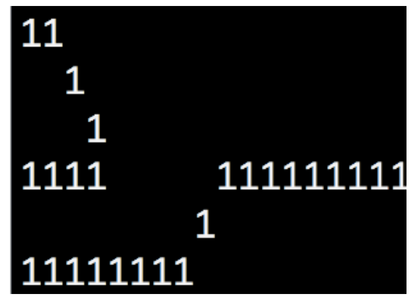


lazy parity to-the-middle

1 1 0 1 0 1

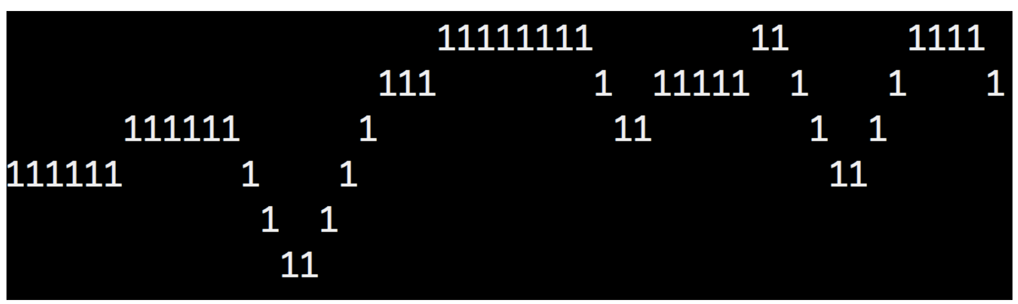


1 0 0 1 0 1



random walking bit

0 0 0 1 0 0

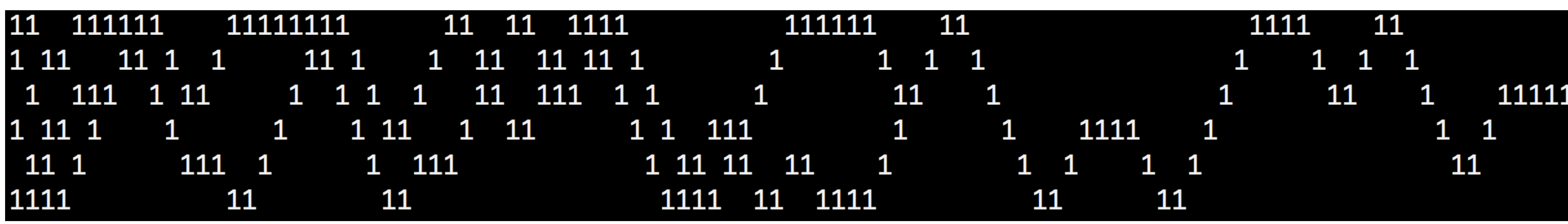


Also, rand walk, absorbing at edge

leader election

under randomised bit walking

1 1 0 1 0 1



problem studied in cellular automata, distributed computing, networks, CRNs

fair coin

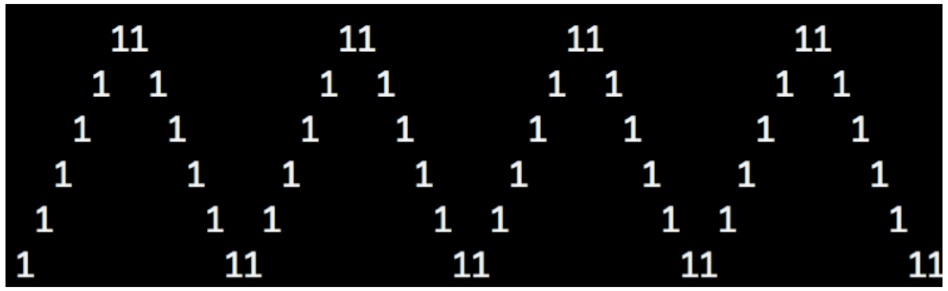
Randomised programs may be a useful tool to calculate energetics of tile binding, or groups of tiles binding, from AFM data

A nice method to assess the quality of our sequence design

Circuits

zig-zag

0
0
0
0
0
1



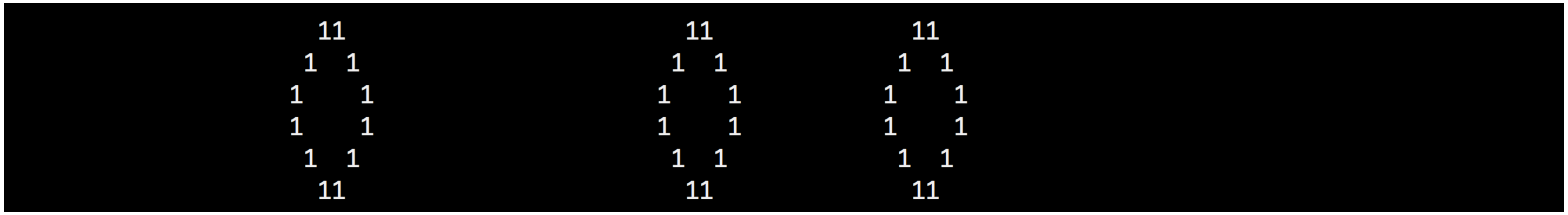
Glider: A common cellular automata primitive

Pattern: Monotone / horizontally connected

Nonmontonic widely-spaced patterns are provably impossible in the deterministic circuit model

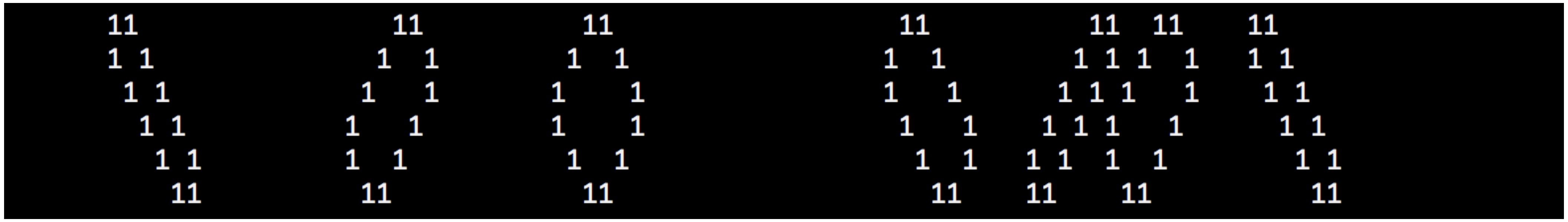
Diamonds are forever

0
0
0
0
0
0



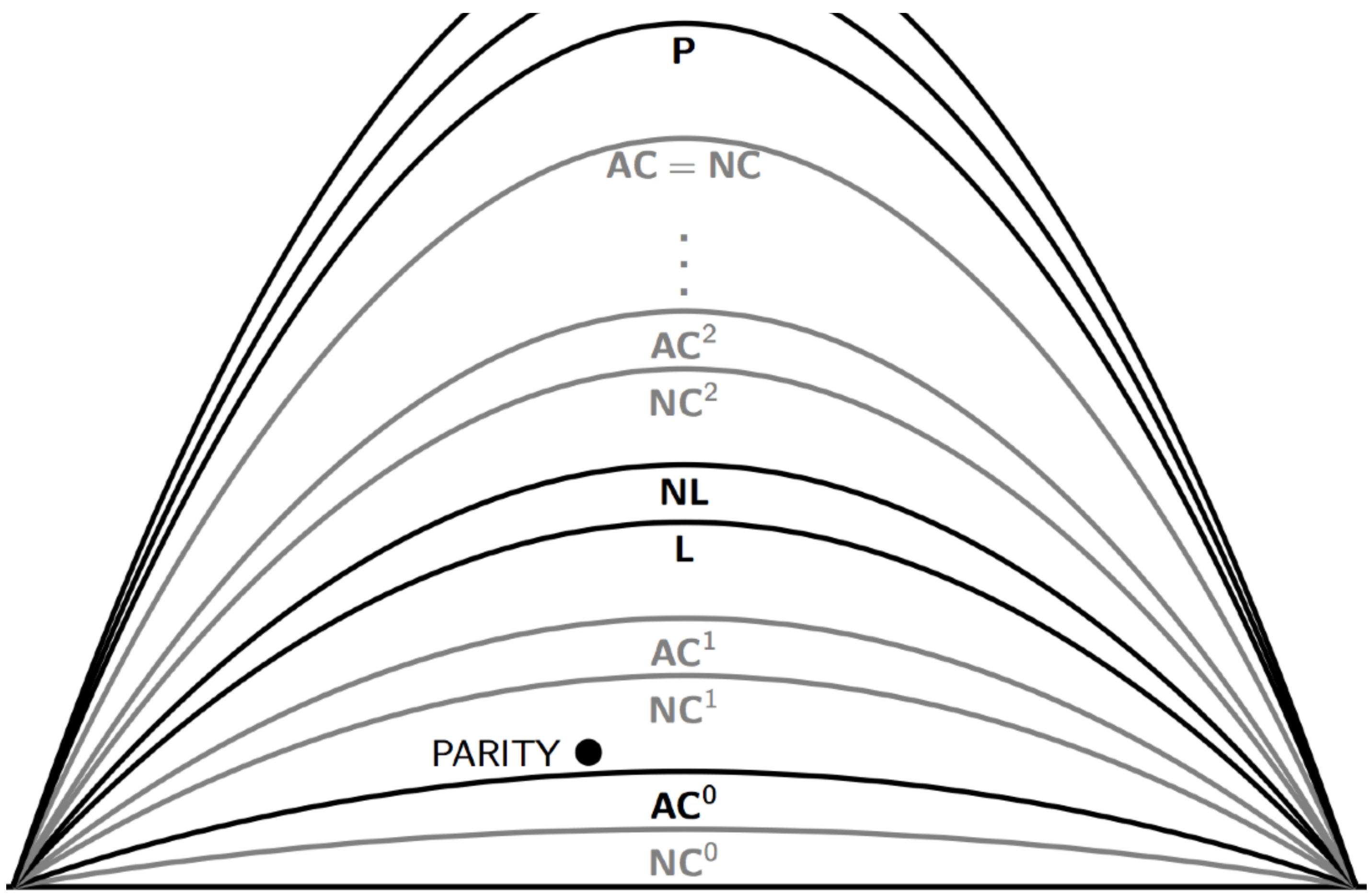
Blowing bubbles

0
0
0
0
0
0



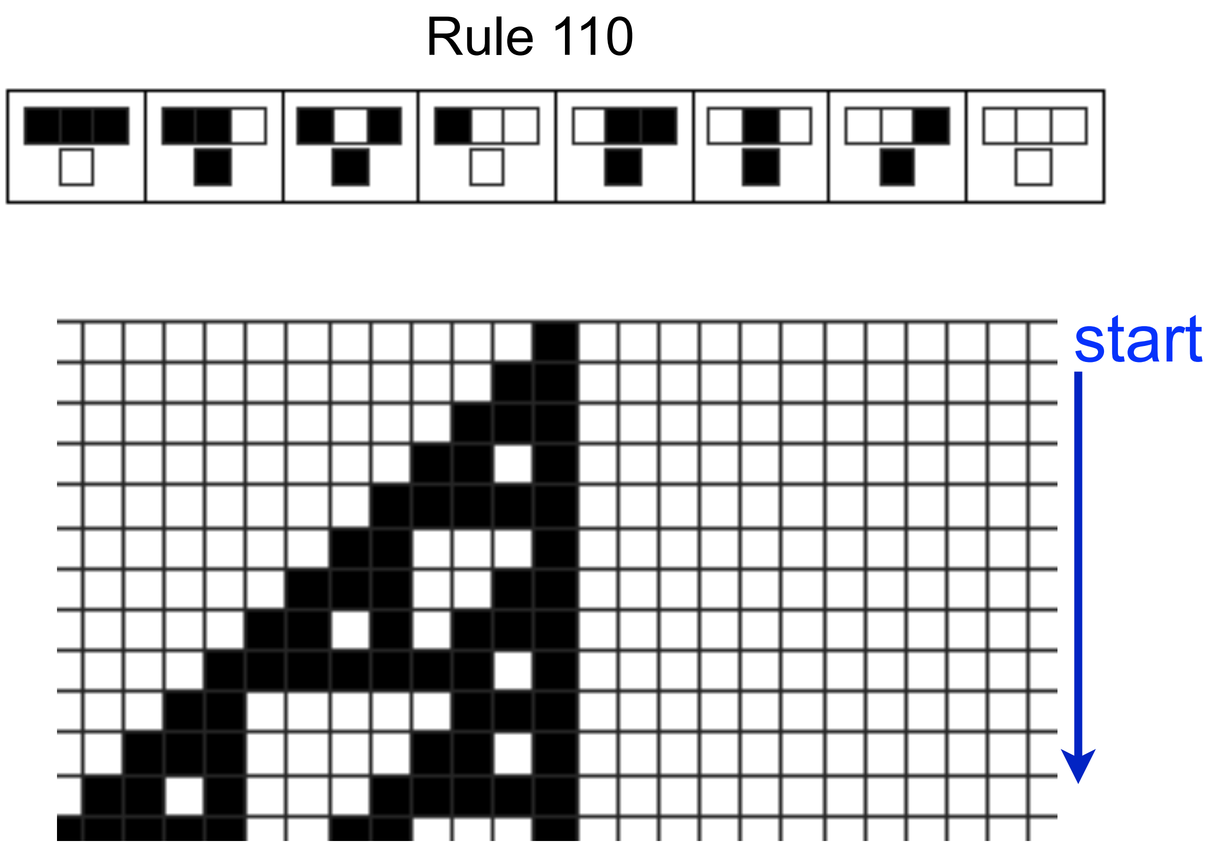
Computational power of DNA
(DNA = DNA nanotube algorithms)

- What is the computational power of our circuit model?
- With *n* input bits, depth-2 layer, and poly(n) depth circuit, what can be solved?
  - No more than P (proof: simulate poly(n) depth circuit in polynomial time on a Turing machine)
  - We've seen already that the model can solve SORTING, PARITY both of which are outside AC^0

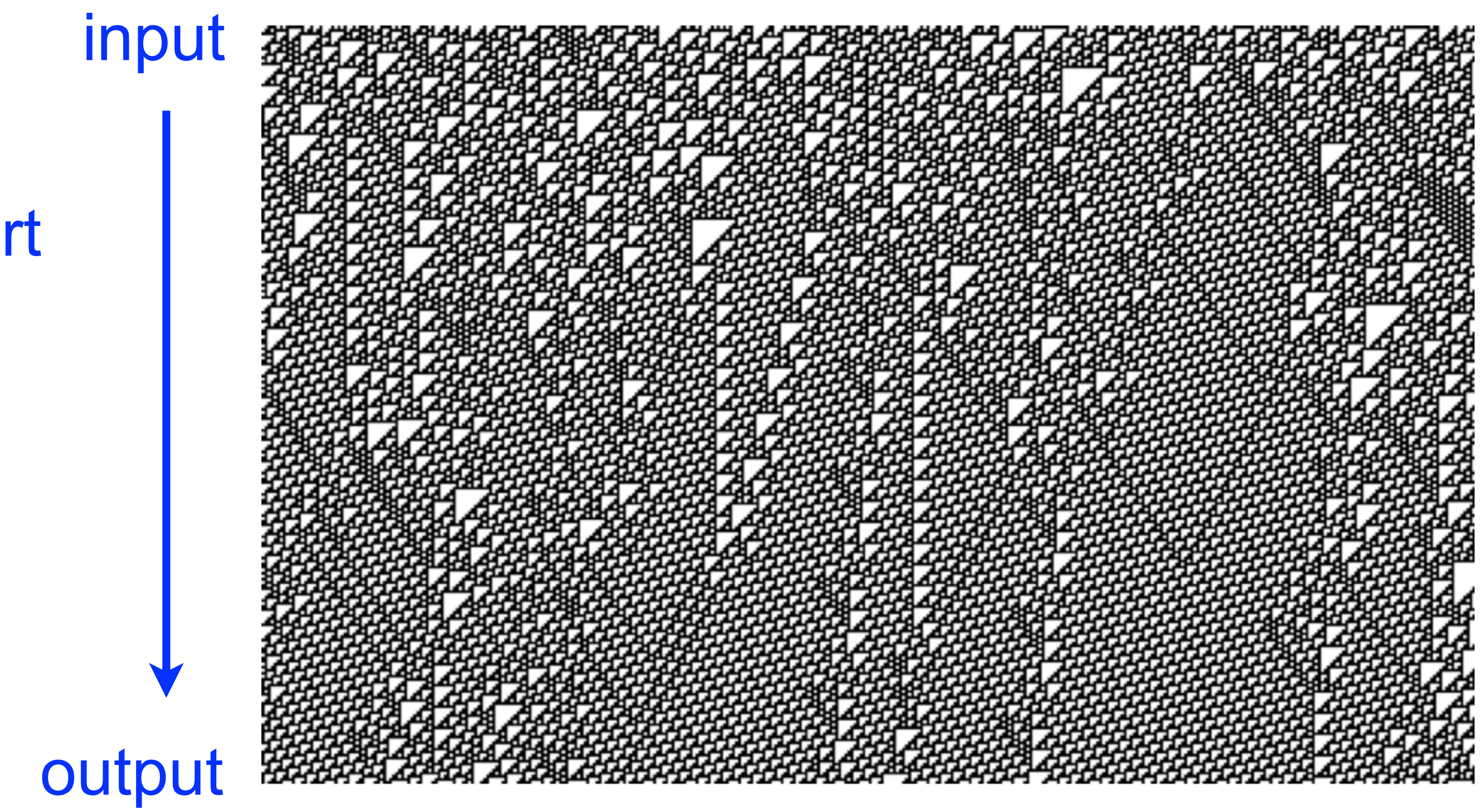


?

Rule 110



https://automatas.wordpress.com/2008/11/10/rule-110/



- **Theorem:** Rule 110 is an **efficient** and **general purpose** computer

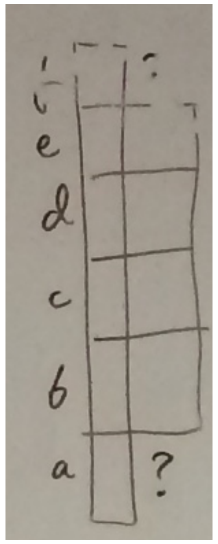
Neary, Woods. ICALP 2006

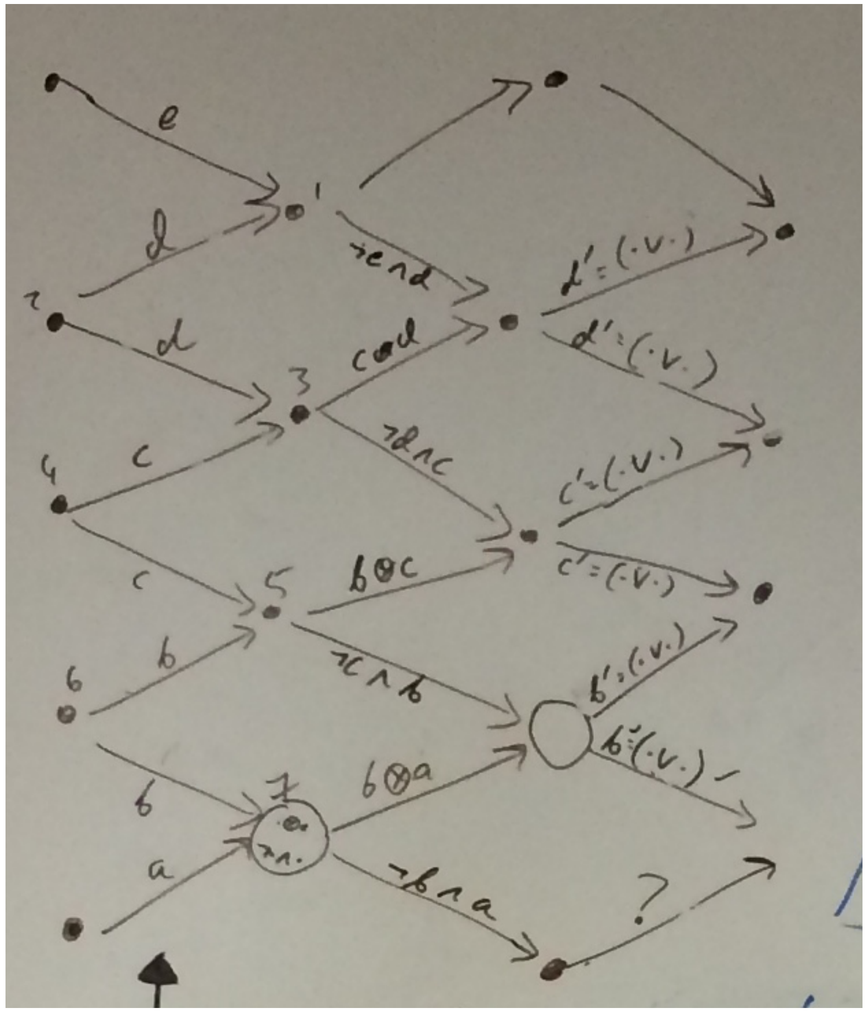
Cook. Complex Systems. 15:1-40 2004

Computational power of DNA
(DNA = DNA nanotube algorithms)

- What is the computational power of our circuit model?
- With *n* input bits, depth-2 layer, and poly(n) depth circuit, what can be solved?
  - No more than P. Proof: simulate poly(n) depth circuit in polynomial time on a Turing machine
  - All of P: Proof: simulate Rule 110

$$
\begin{array}{ll}
\quad\ \ c\ b\ a & \quad\ \ c\ b\ a \\
F(0,0,0)=0 & F(1,0,0)=0 \\
F(0,0,1)=1 & F(1,0,1)=1 \\
F(0,1,0)=1 & F(1,1,0)=1 \\
F(0,1,1)=1 & F(1,1,1)=0
\end{array}
$$





Computational power of DNA (DNA = DNA nanotube algorithms)

- What is the computational power of our circuit model?
- With *n* input bits, depth-2 layer, and poly(n) depth circuit, what can be solved?
  - Answer: Exactly P, via Rule 110 simulation

T. Neary, D. Woods. P-completeness of cellular automaton Rule 110. ICALP 2006. Springer LNCS 4051(1):132-143
Cook, M.: Universality in elementary cellular automata. Complex Systems 15 (2004) 1–40