Crystals that think
about how they’re growing

David Doty

joint work with Damien Woods, Erik Winfree, Cameron Myhrvold, Joy Hui, Felix Zhou, Peng Yin

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Caltech   Inria Paris   UC Davis   Harvard

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Caltech

Inria Paris

UC Davis

Harvard

Damien Woods

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Erik Winfree

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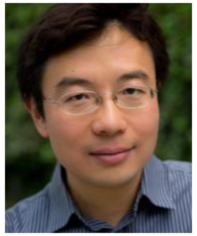
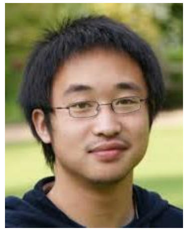
Cameron Myhrvold

Peng Yin



Felix Zhou



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Cody Geary

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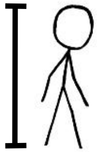
Diverse and robust molecular algorithms using reprogrammable DNA self-assembly.
Damien Woods†, David Doty†, Cameron Myhrvold, Joy Hui, Felix Zhou, Peng Yin, Erik Winfree.
Nature 2019. †*These authors contributed equally*.


Ljubljana Marshes Wheel. 5k years old

Building things


Newgrange, Ireland. 5.2k years old

Building things by hand: use tools! Great for scale of $10^{\pm 2} \times$ 

[slides credit: Damien Woods]

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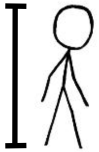
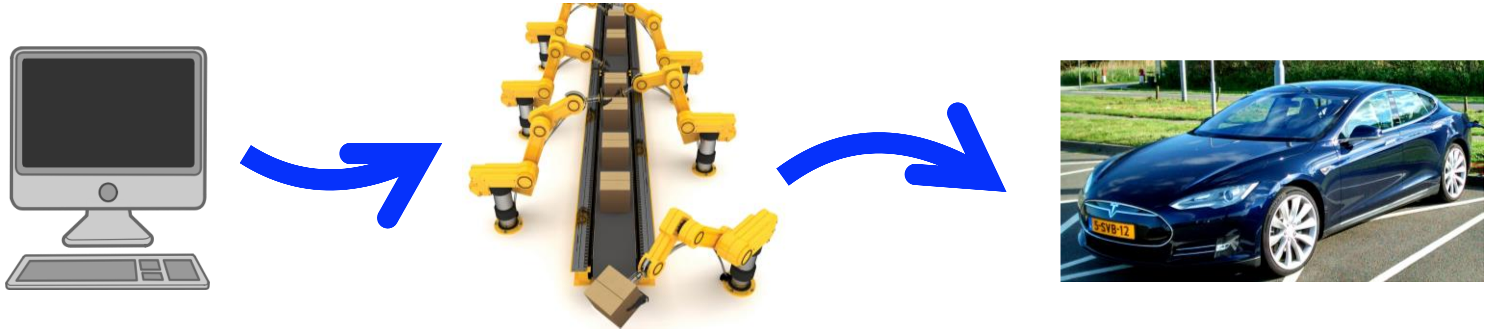
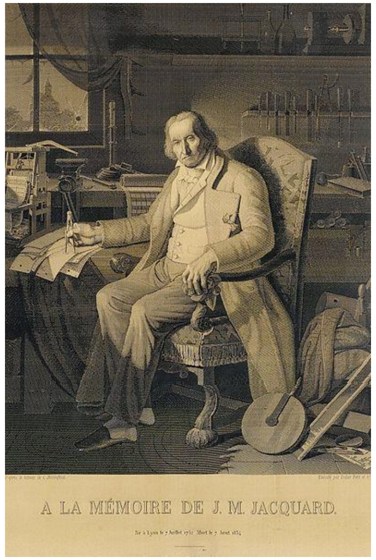
Building things by hand: use tools! Great for scale of $10^{\pm 2}$ × 

Building tools that build things: specify target object with a computer program





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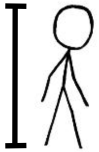
Building things by hand: use tools! Great for scale of $10^{\pm 2}$ × 

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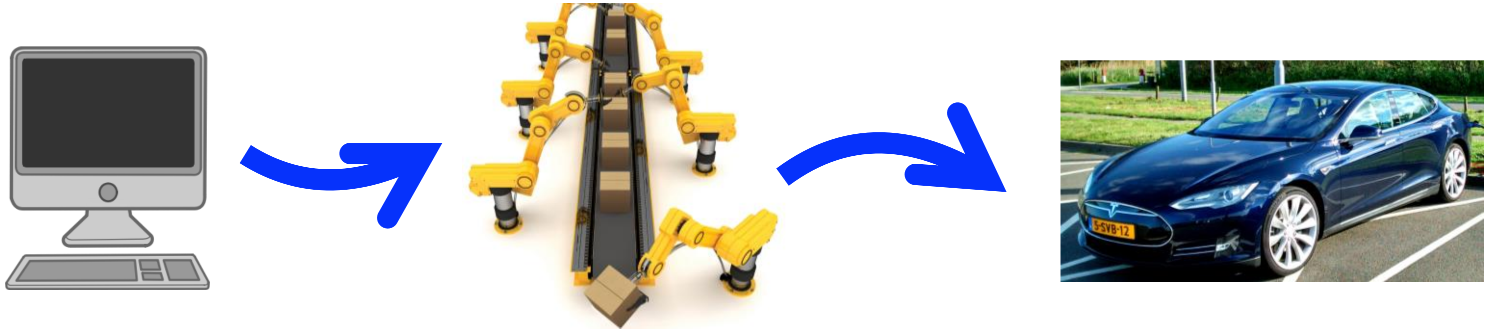
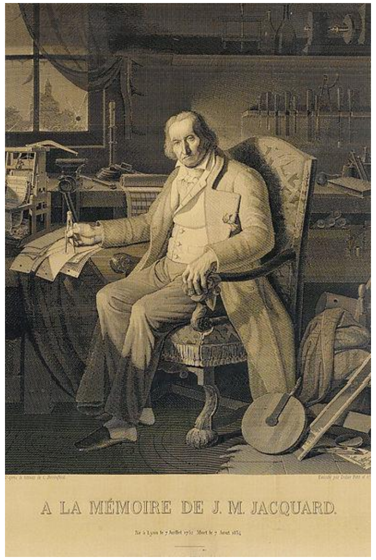
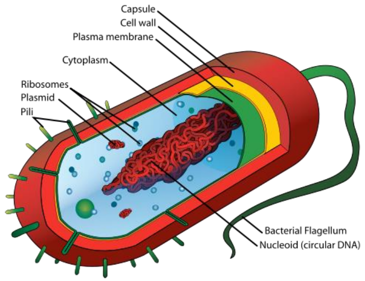




Programming **things to build themselves**: for building in small wet places where our hands or tools can't reach



Mariana Ruiz Villarreal

[slides credit: Damien Woods]

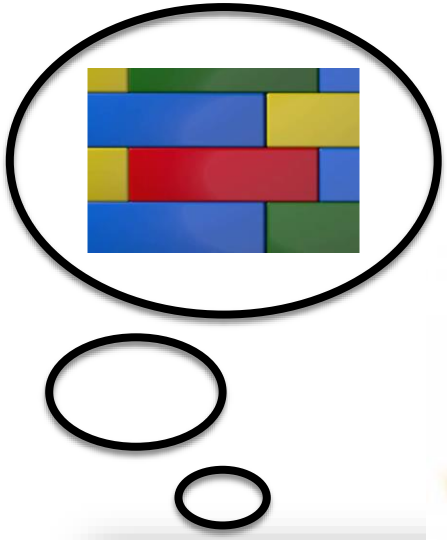
Things that build themselves

I want to stick below blue & yellow and above blue & green

Our topic: self-assembling molecules that compute as they build themselves

[slides credit: Damien Woods]

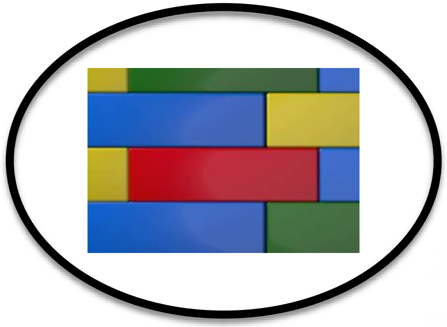
Things that build themselves



Our topic: self-assembling molecules that compute as they build themselves

[slides credit: Damien Woods]

Things that build themselves




Our topic: self-assembling molecules that compute as they build themselves

Hierarchy of abstractions

Bits:	**Boolean circuits compute**
Tiles:	Tile growth implements circuits
DNA:	DNA strands implement tiles

Harmonious arrangement

0

1

1

0

1

1

Harmonious arrangement

0

1

1

0

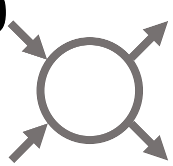
1

1

Harmonious arrangement

0	1
1	1
1	1
0	1
1	0
1	0

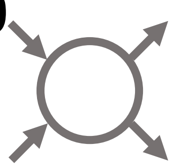
Harmonious arrangement



0	1
1	1
1	1
0	1
1	0
1	0

Harmonious arrangement

0 1



1 0

1

0

1

1

1

1

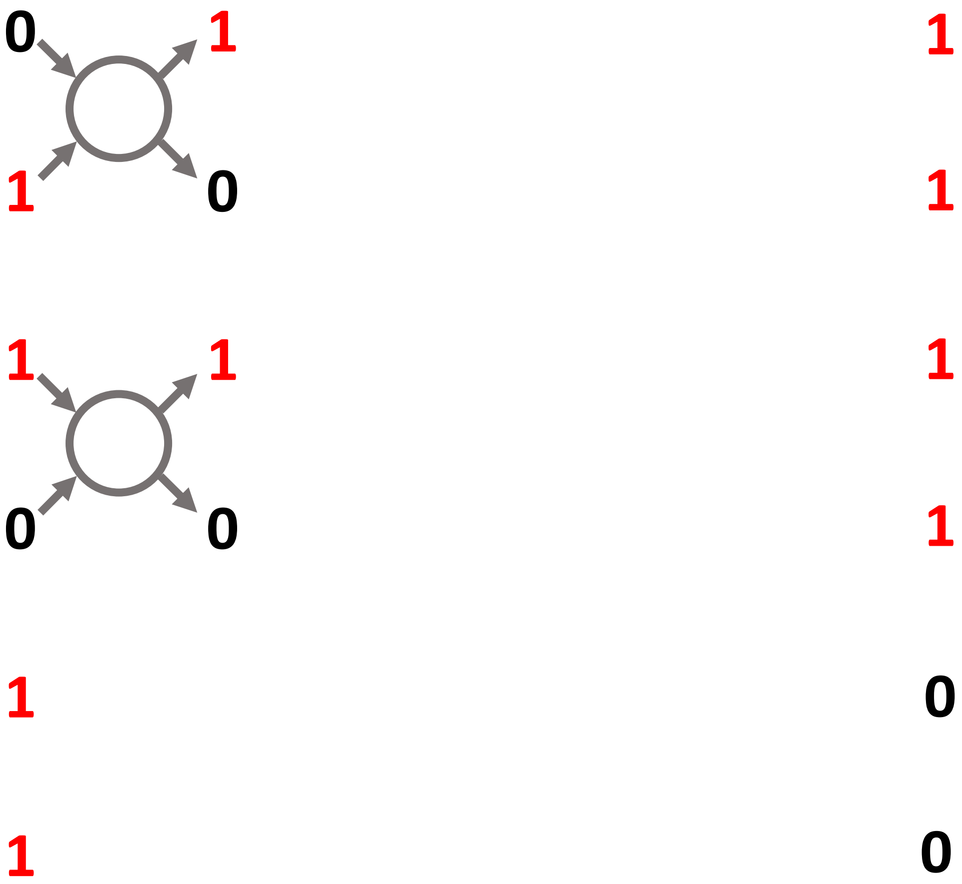
1

1

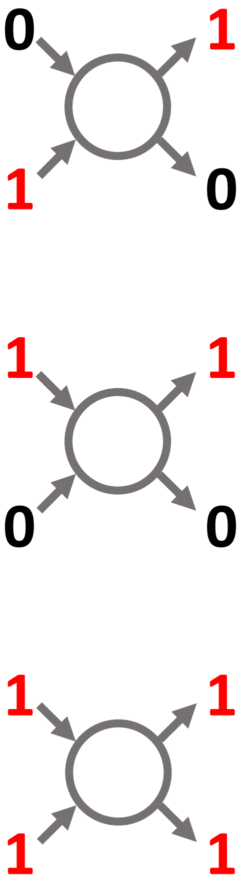
0

0

Harmonious arrangement



Harmonious arrangement



1

1

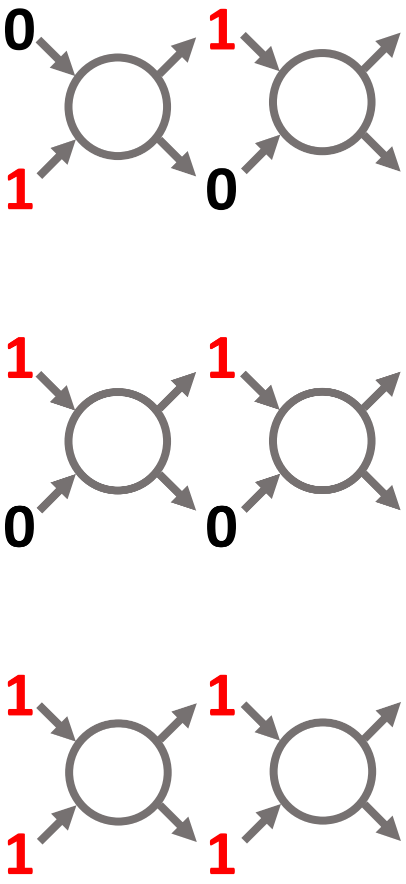
1

1

0

0

Harmonious arrangement



1

1

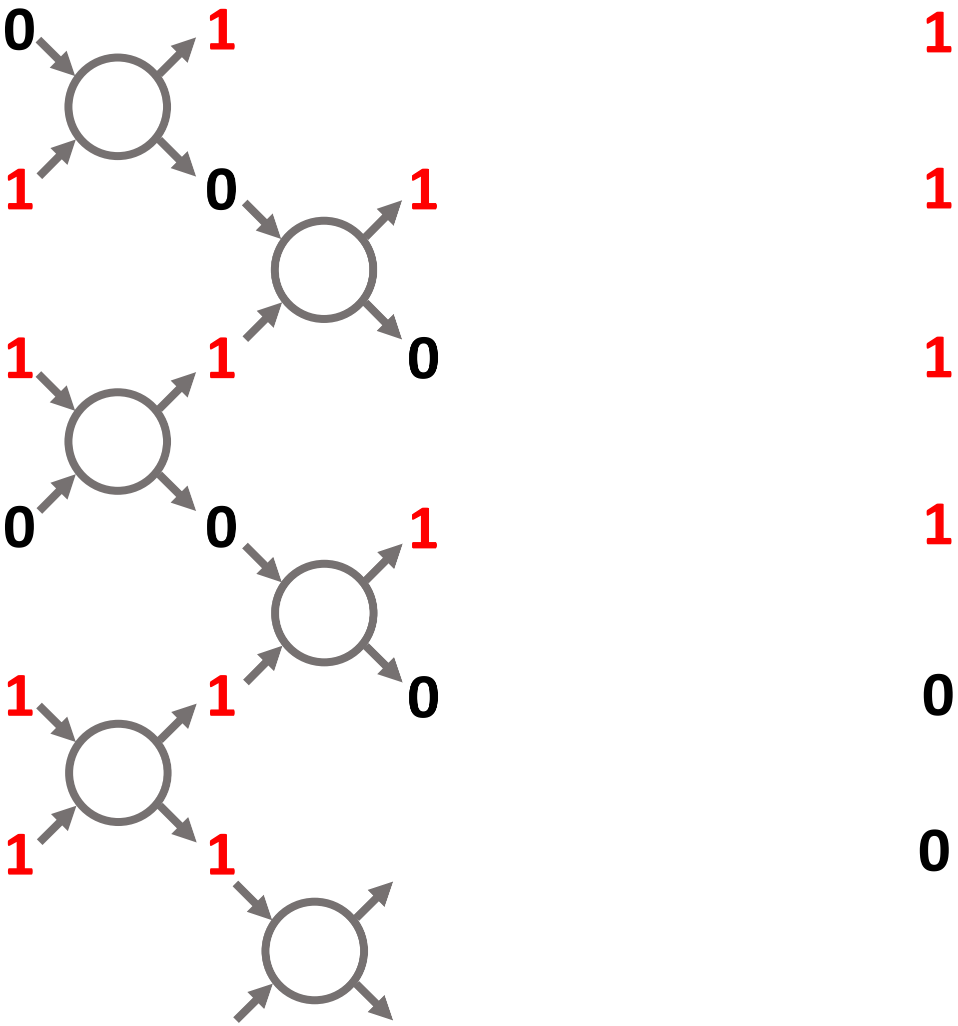
1

1

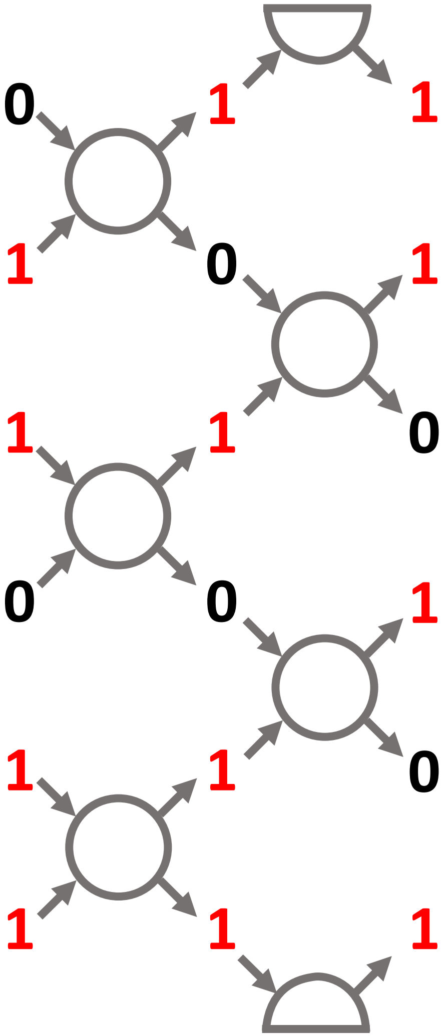
0

0

Harmonious arrangement

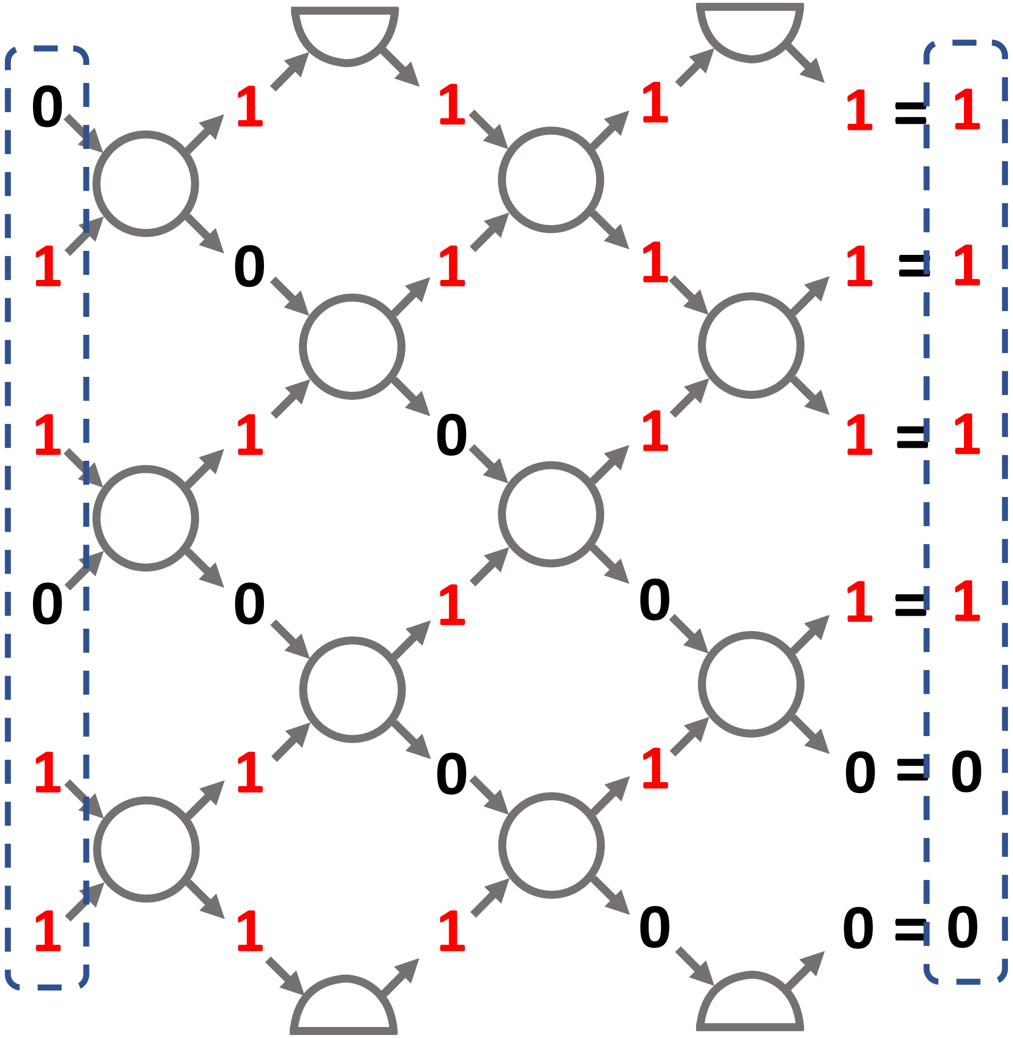


Harmonious arrangement



1
1
1
1
0
0

Harmonious arrangement



a.k.a. sorting

Odd bits

1

0

1

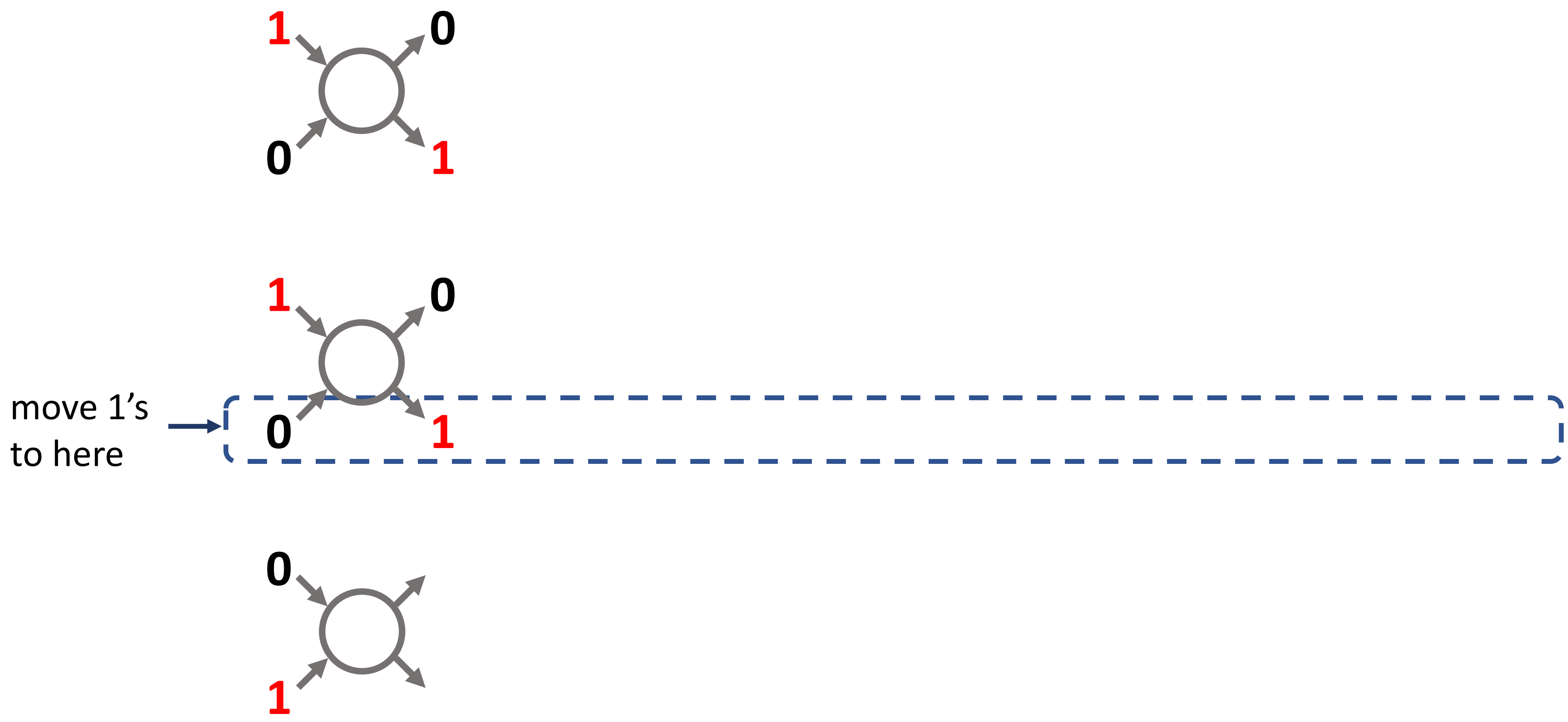
0

0

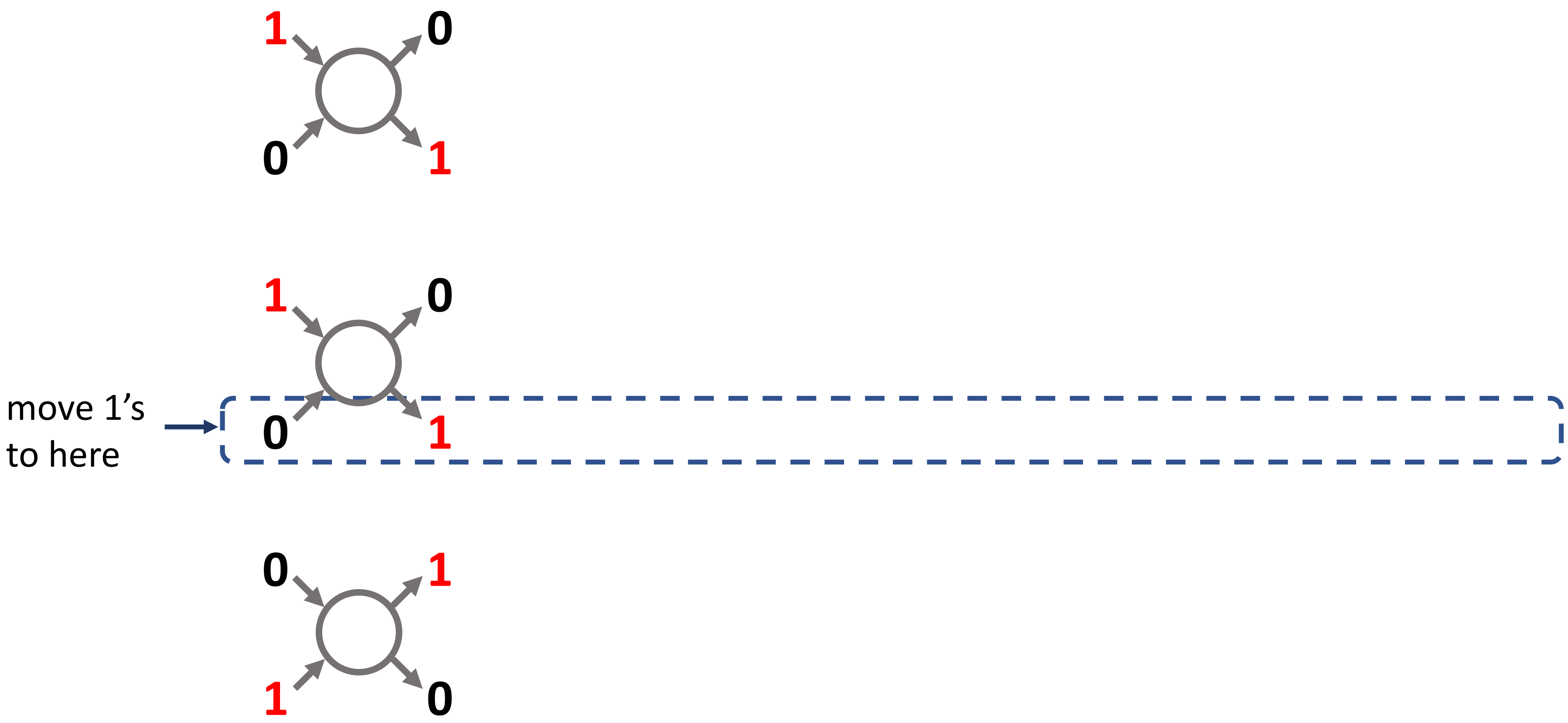
1

Odd bits

Odd bits



Odd bits



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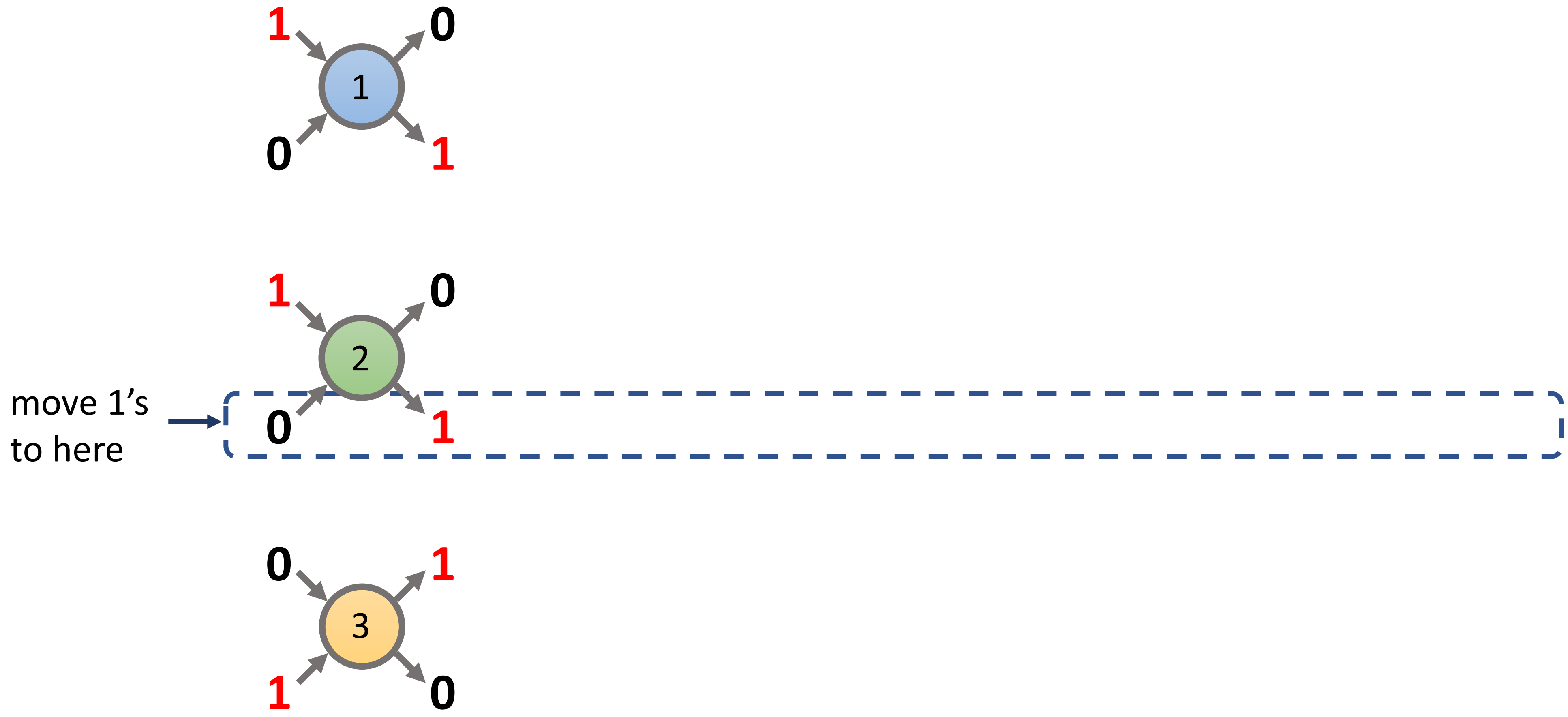

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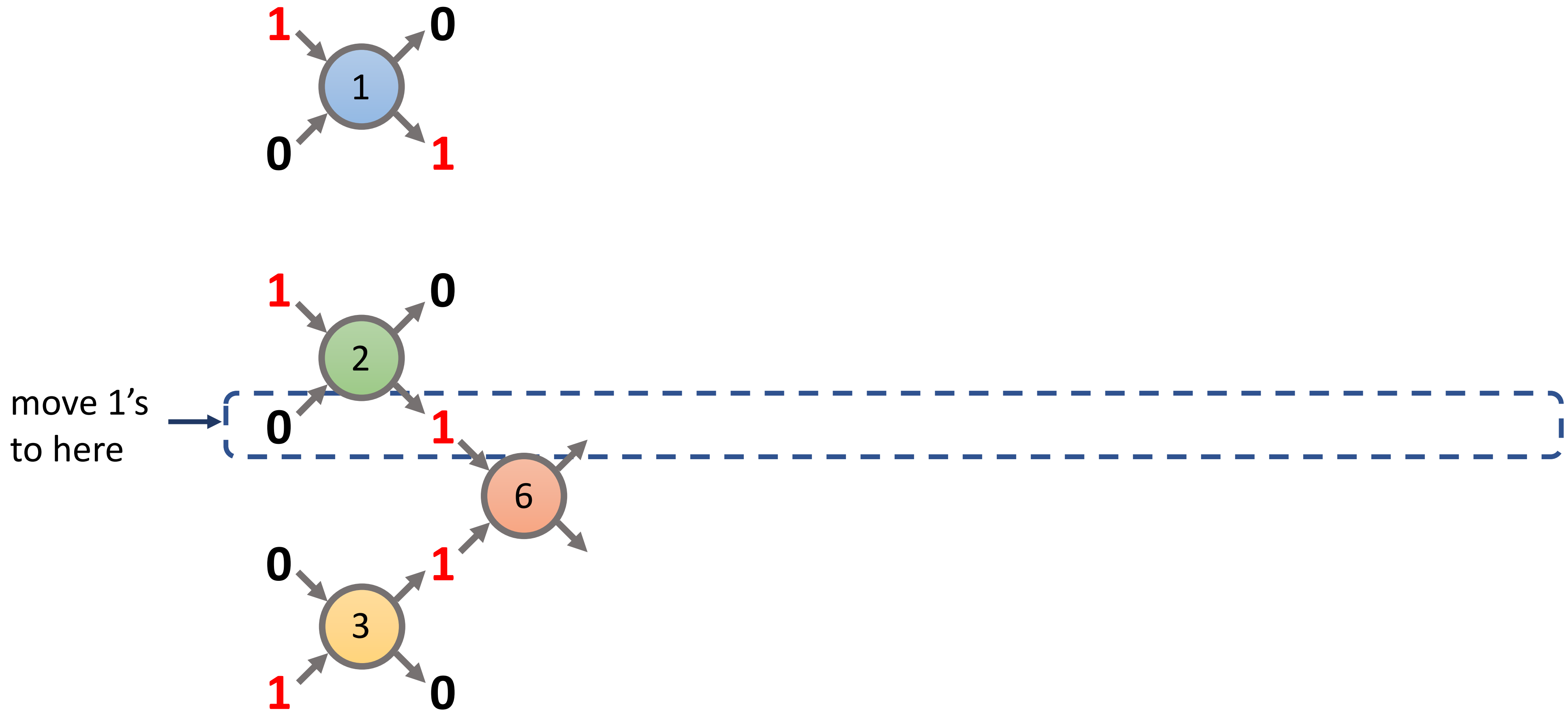
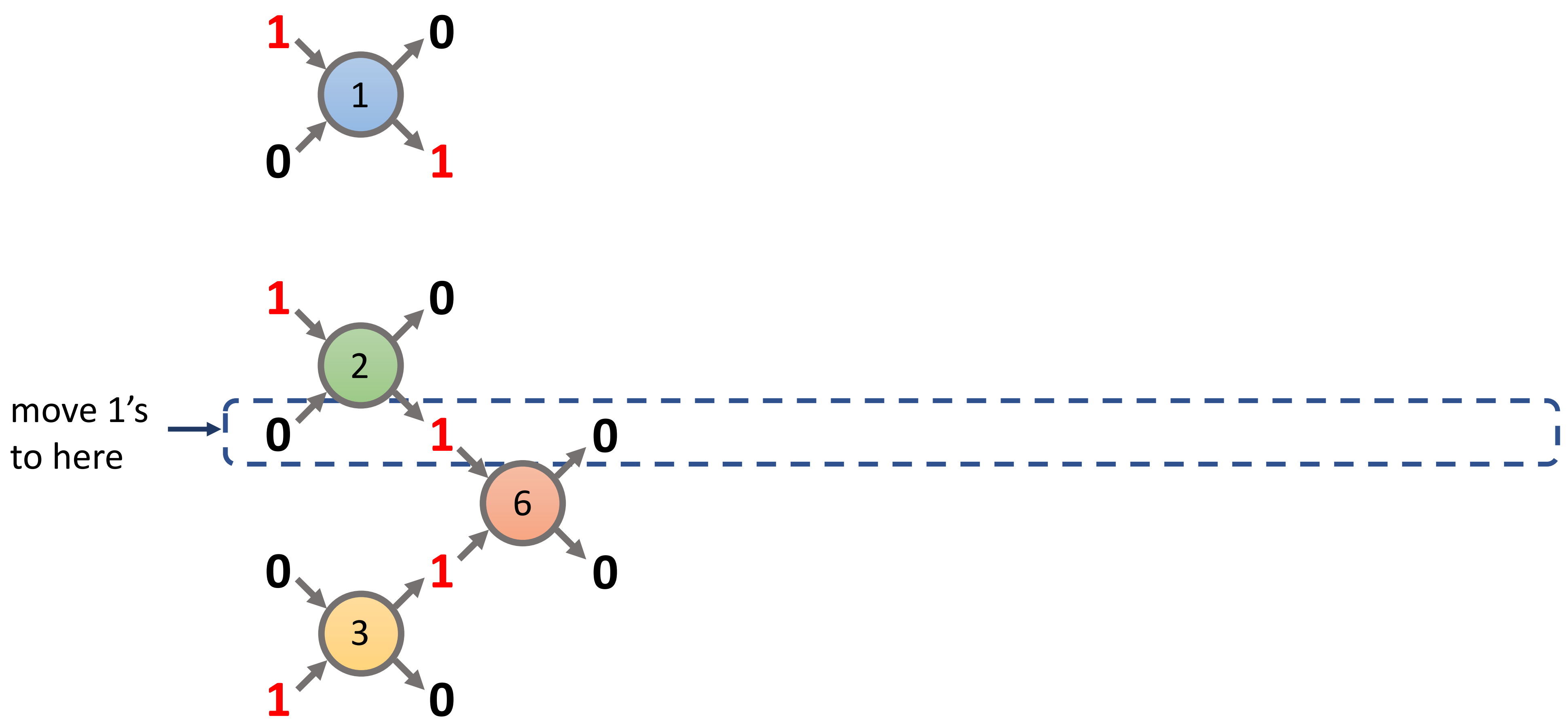
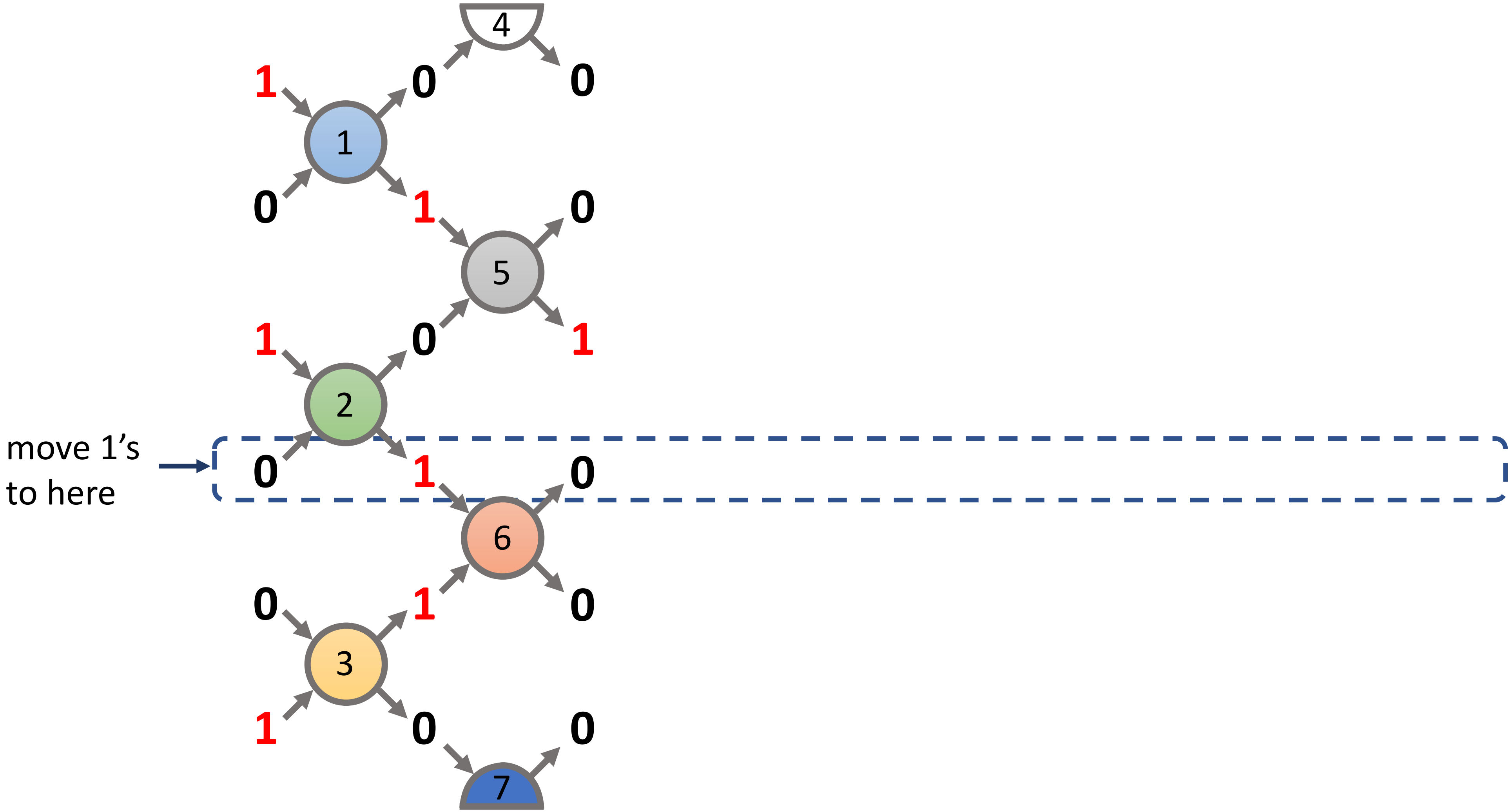


Odd bits

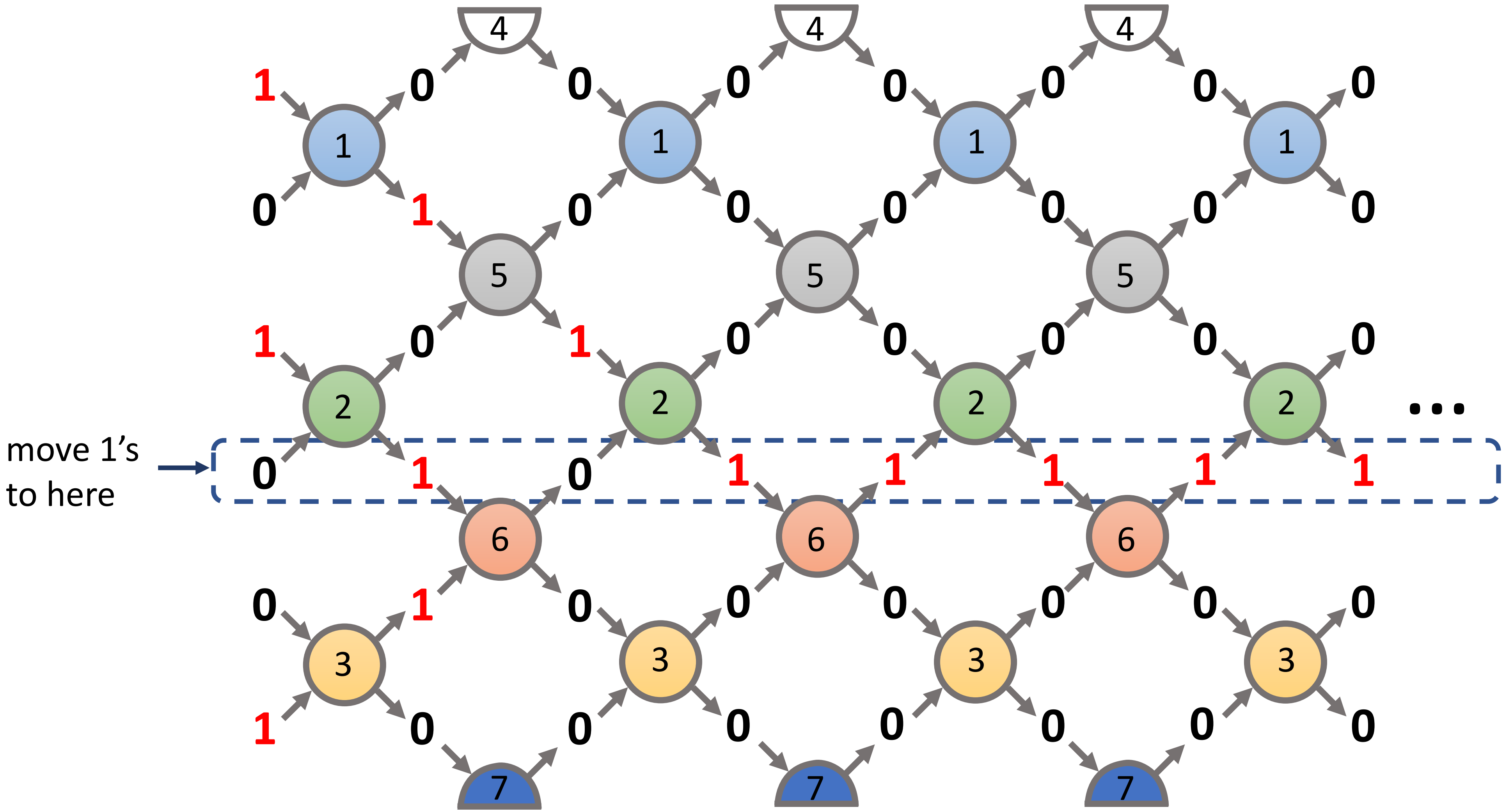


Odd bits



Odd bits

a.k.a. parity



Parity

1

0

1

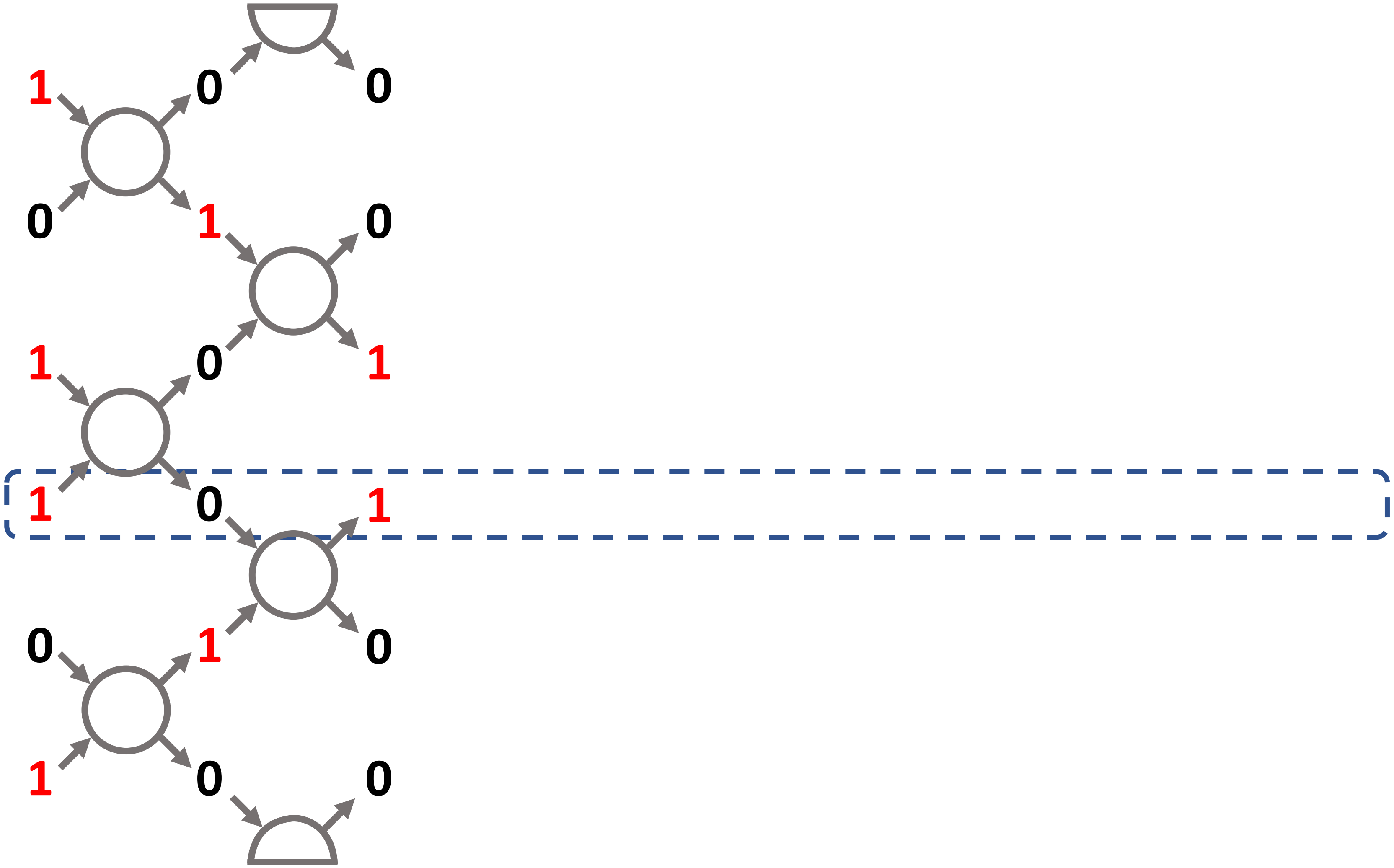
1

0

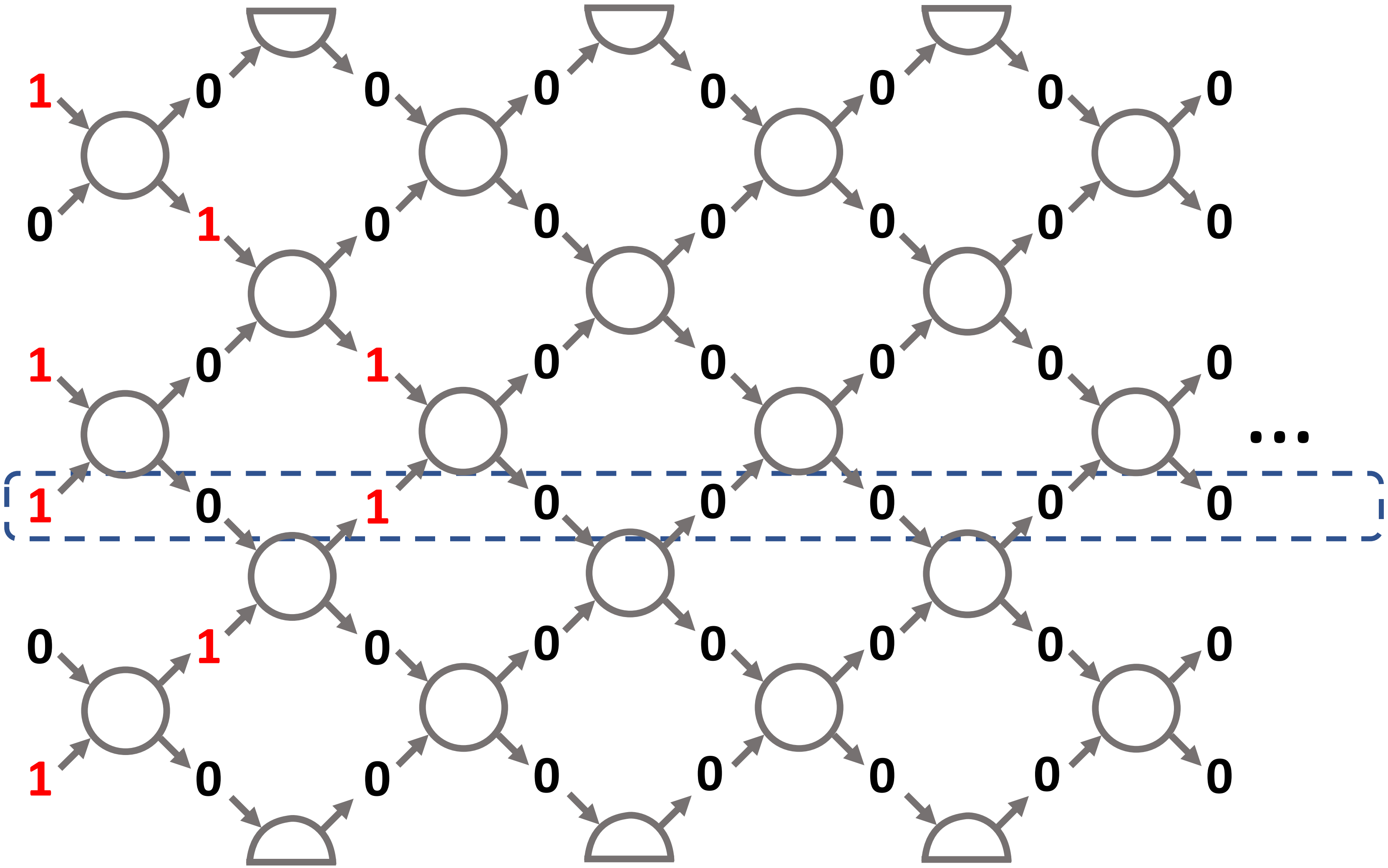
1

Parity

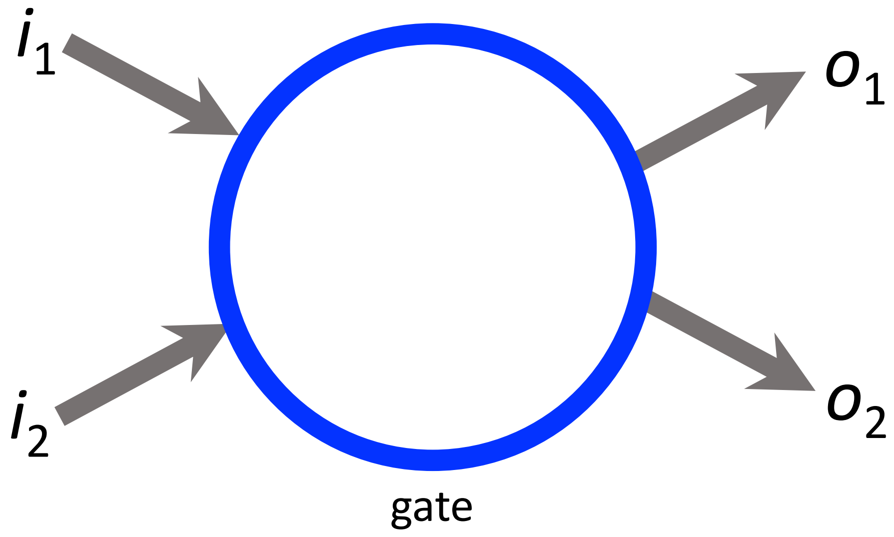
Parity



Parity

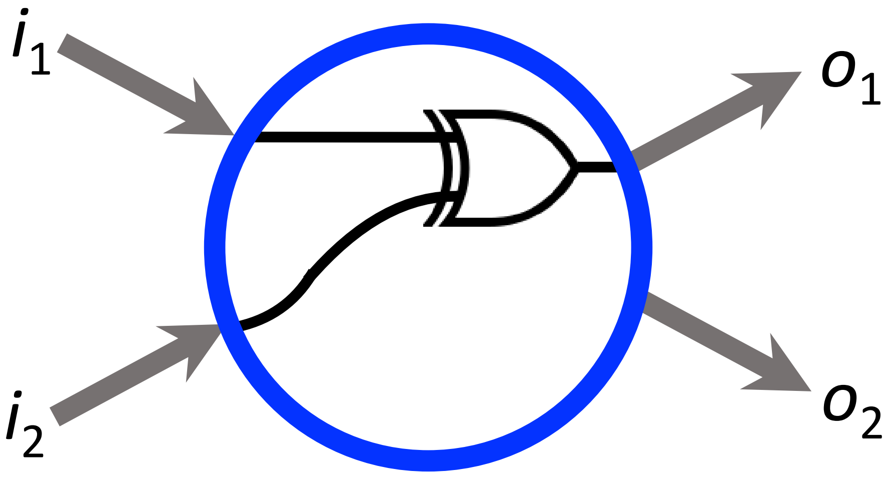


Circuit model



gate: function with two input bits i_1,i_2
and <u>two</u> output bits o_1,o_2

Circuit model

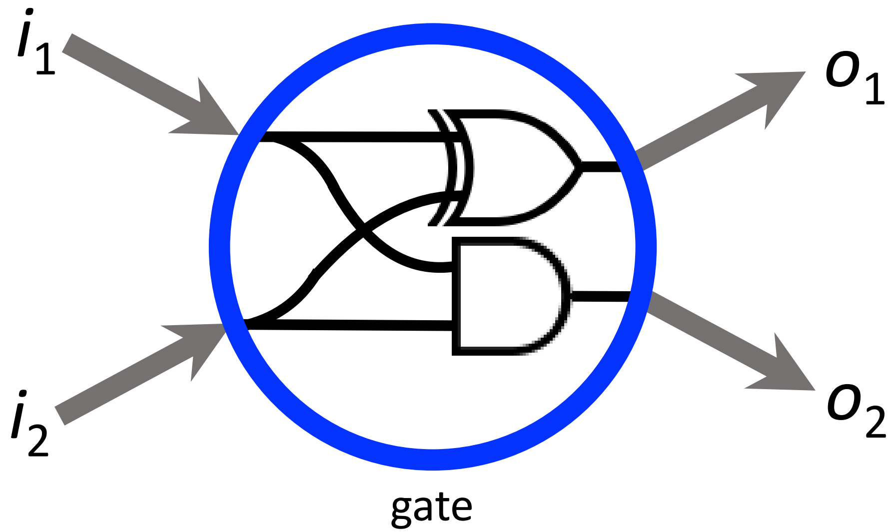


truth table

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

gate: function with two input bits i_1,i_2
and <u>two</u> output bits o_1,o_2

Circuit model



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i_1	i_2	o_1	o_2
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1	1	0	1

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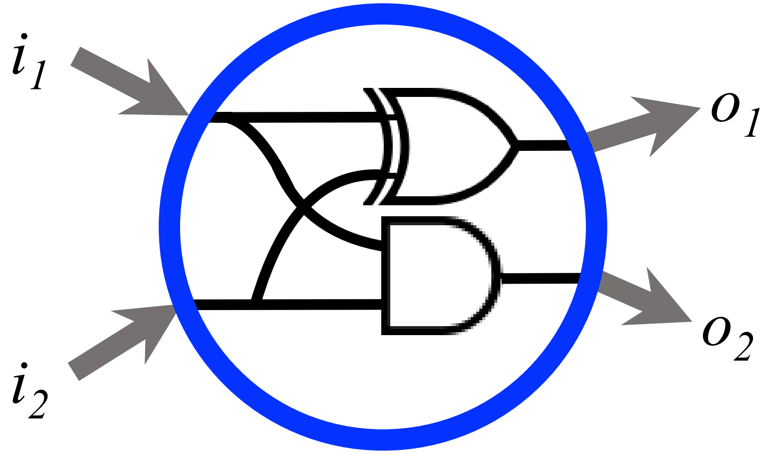
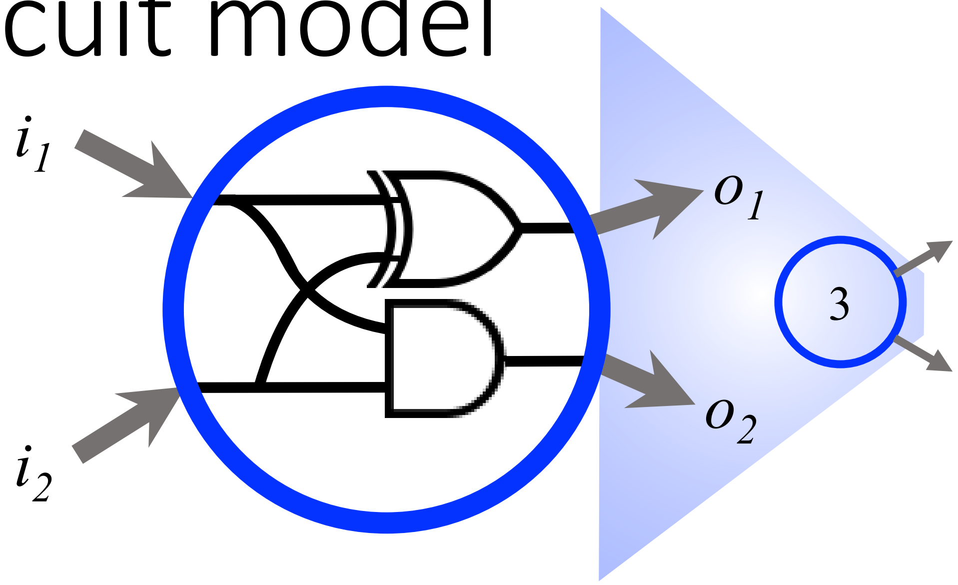
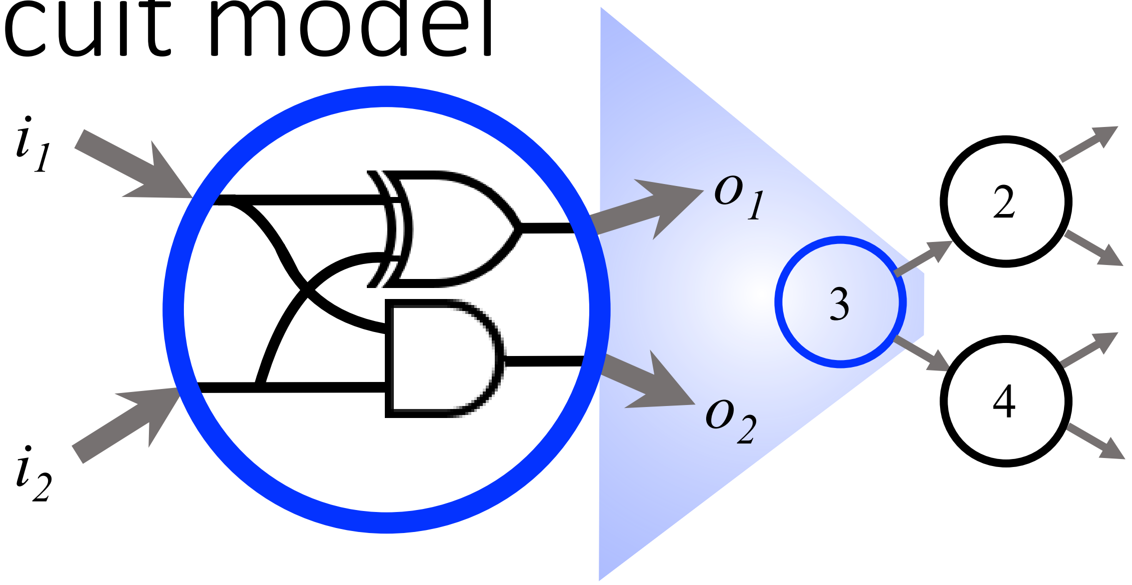


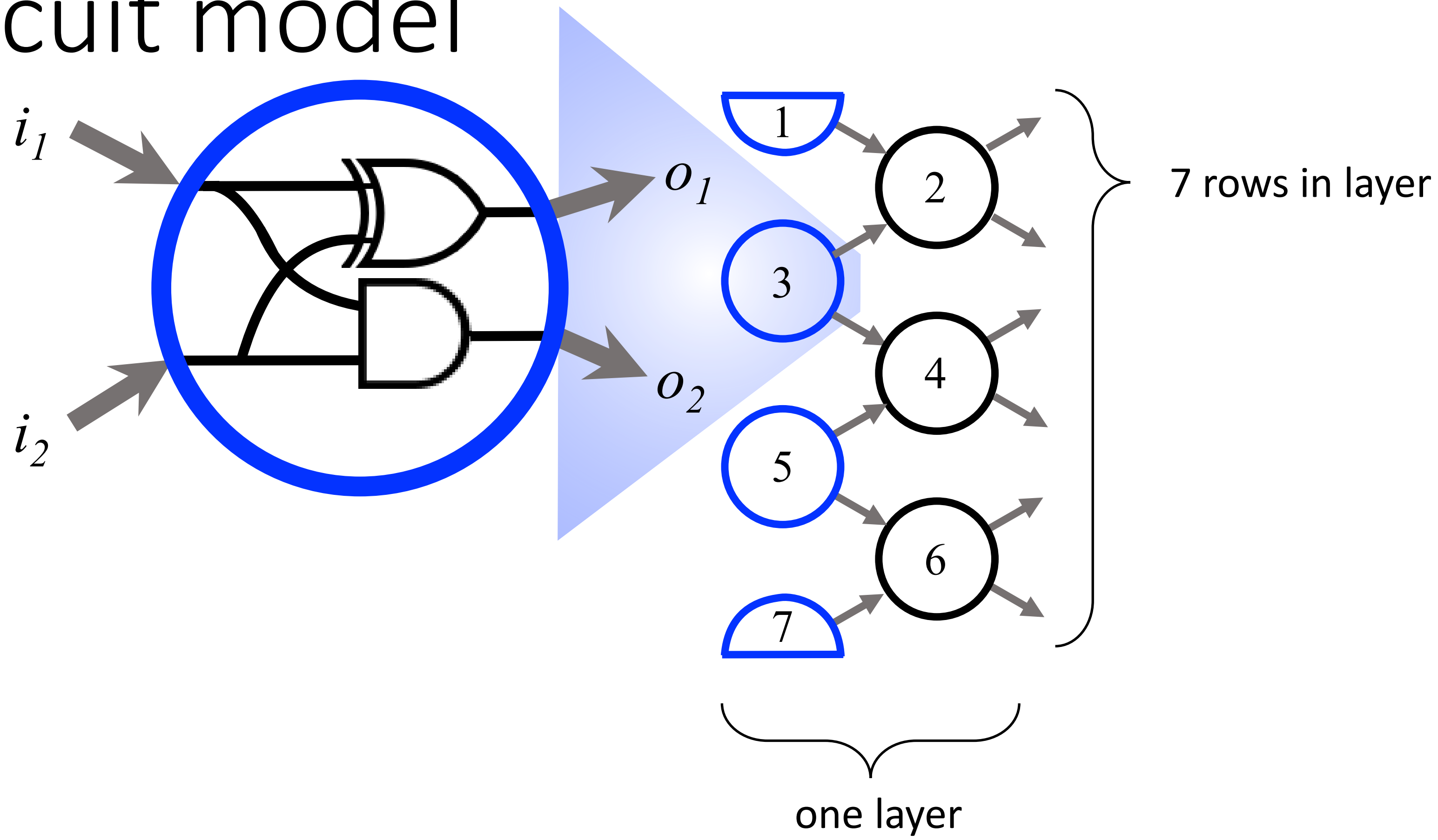
Circuit model



Circuit model



Circuit model



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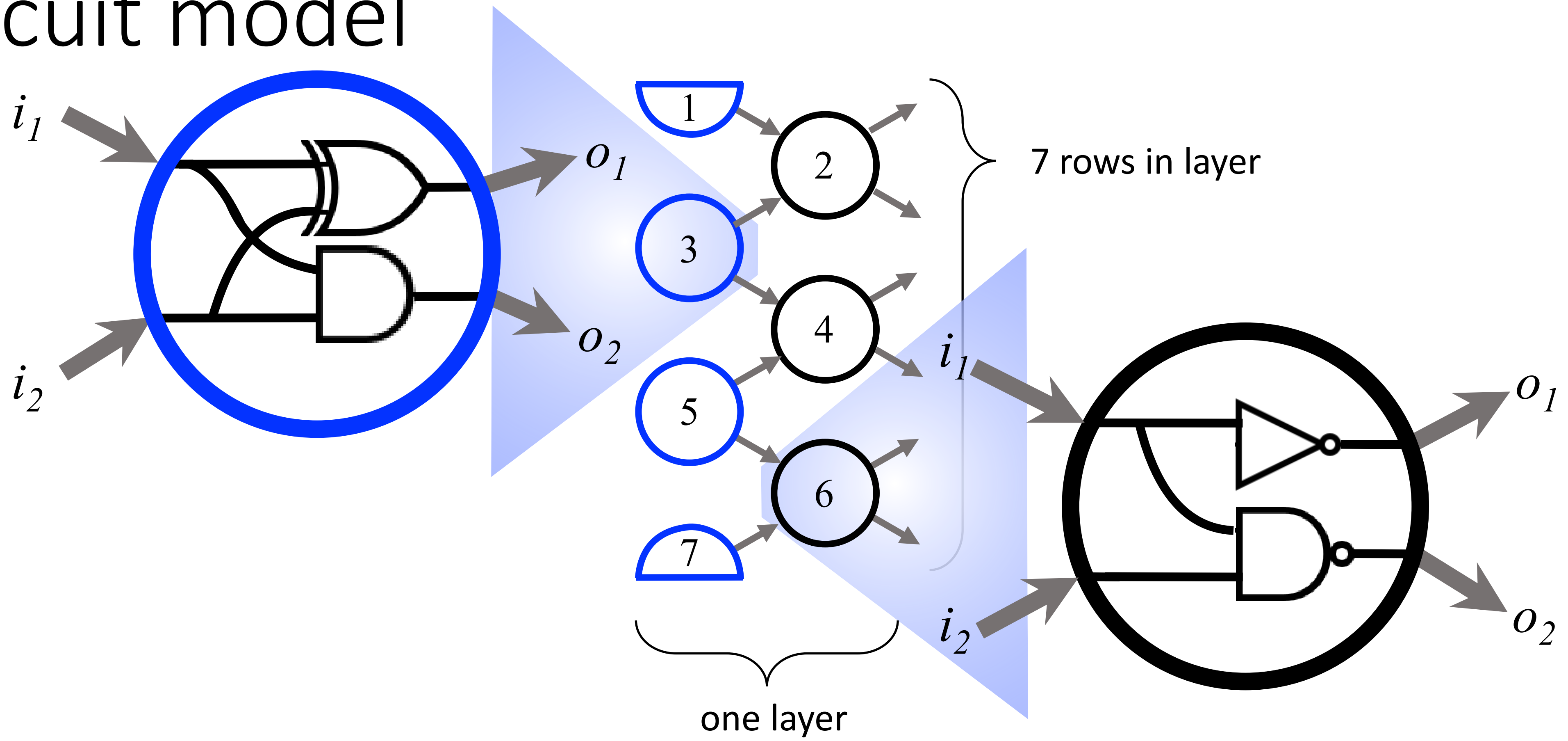
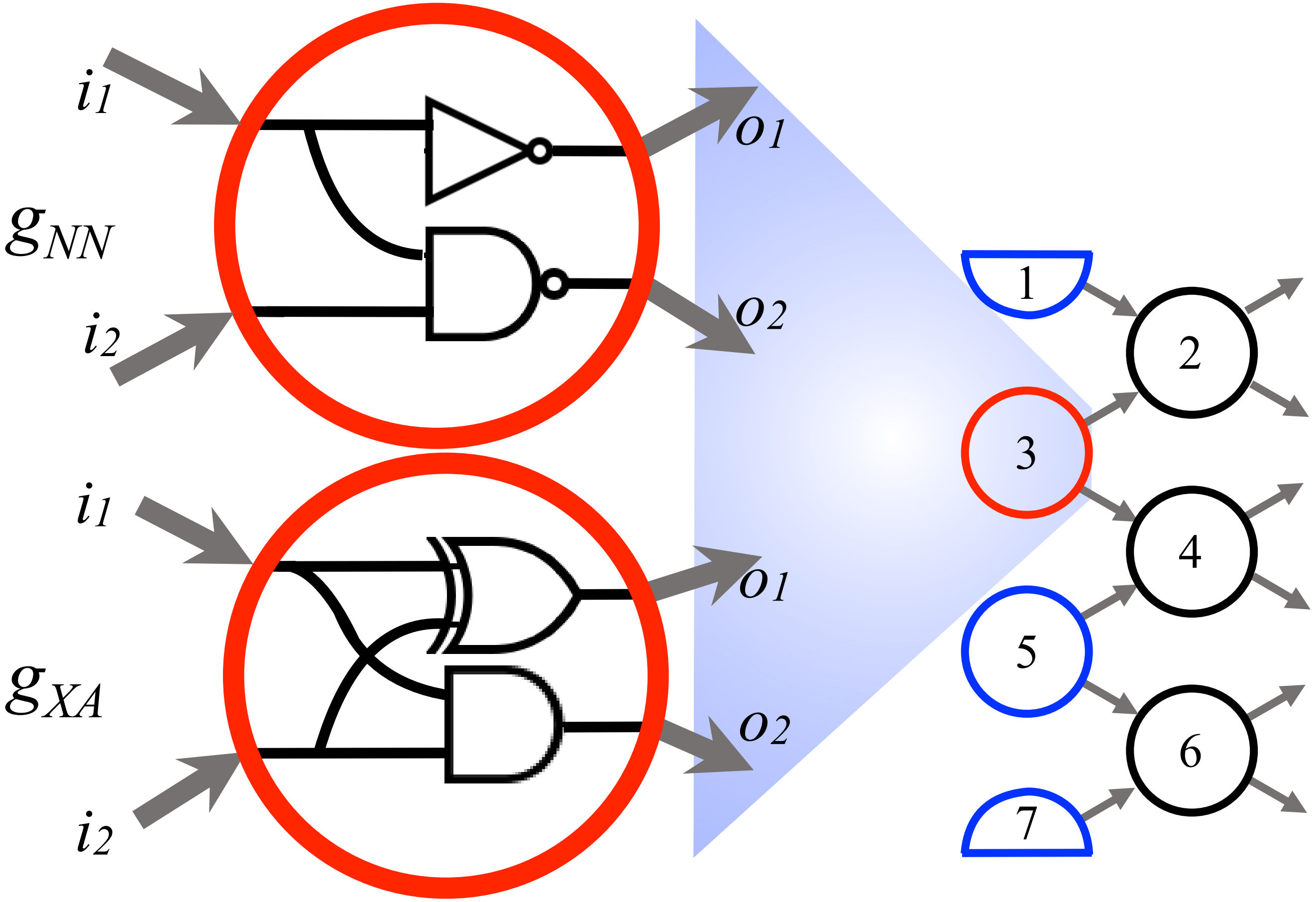


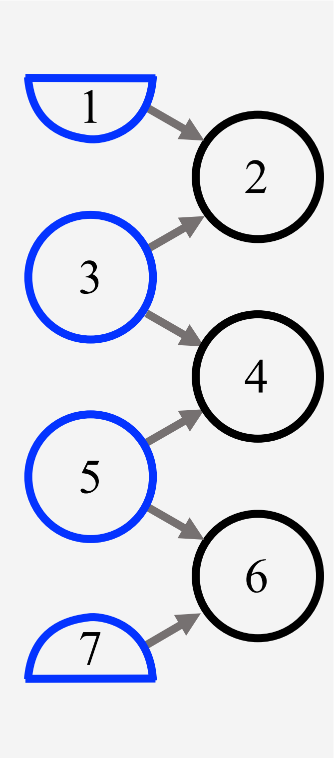
Circuit model



Randomization: Each row may be assigned ≥ 2 gates, with associated probabilities, e.g., $\Pr[g_{NN}] = \Pr[g_{XA}] = ½$

Circuit model

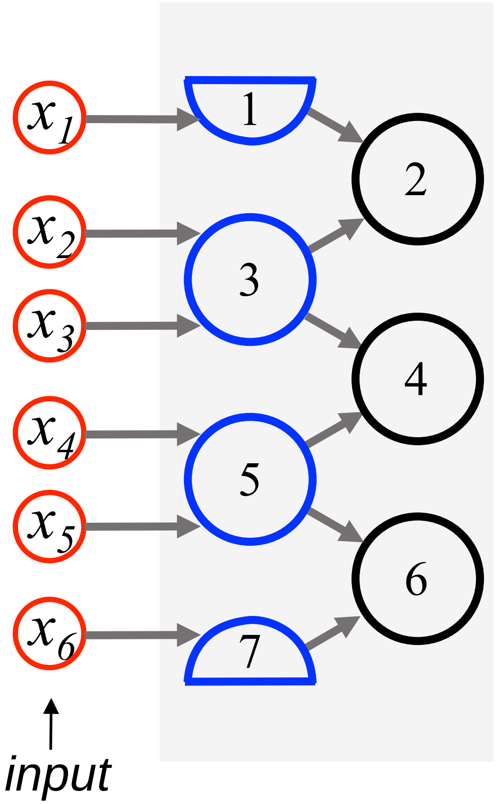
Programmer specifies layer:
gates to go in each row



Circuit model

Programmer specifies layer:
gates to go in each row

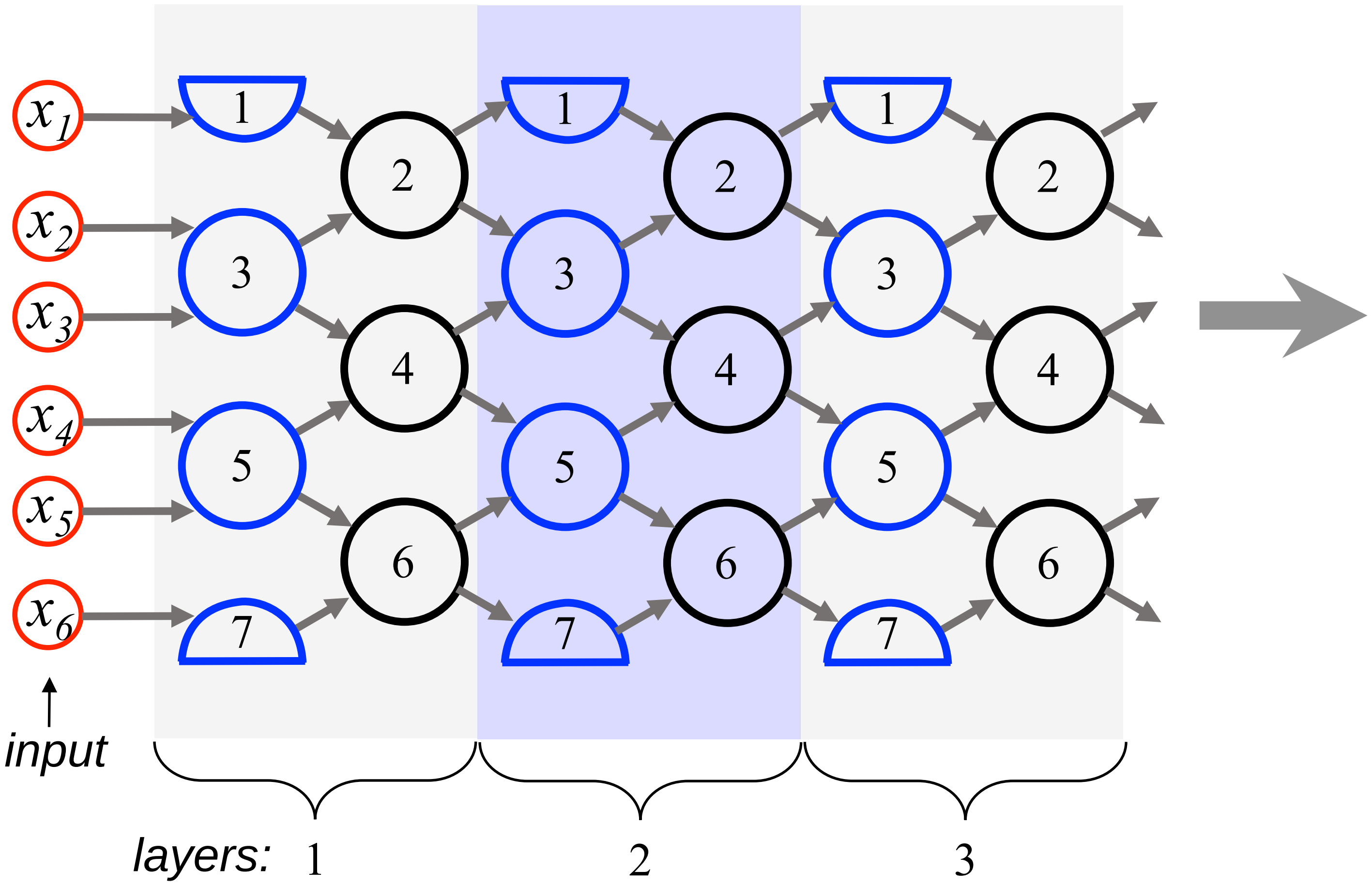
User gives n input bits



Circuit model

Programmer specifies layer: gates to go in each row

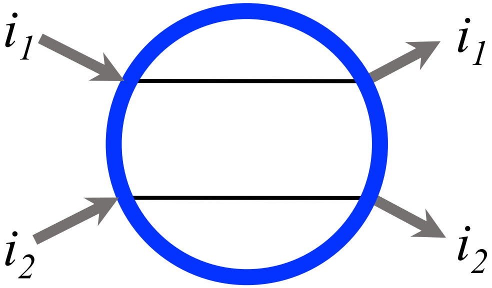
User gives n input bits



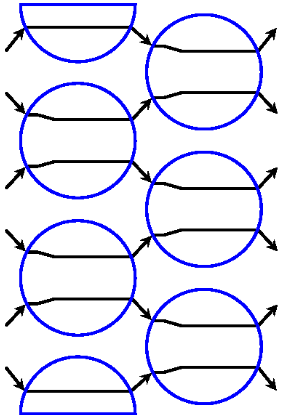
Example circuits with same gate in every row

COPY

COPY gates



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



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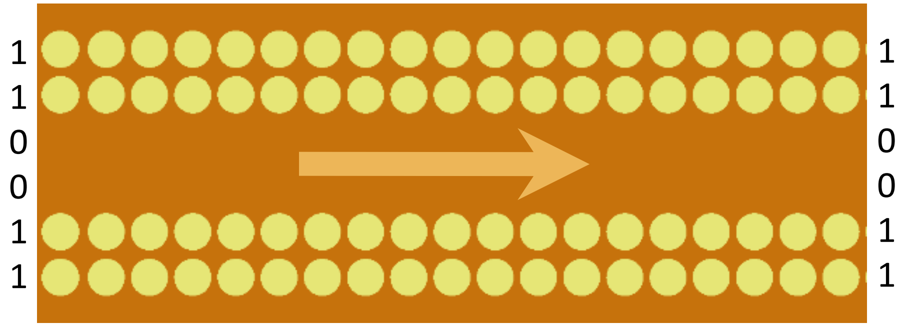

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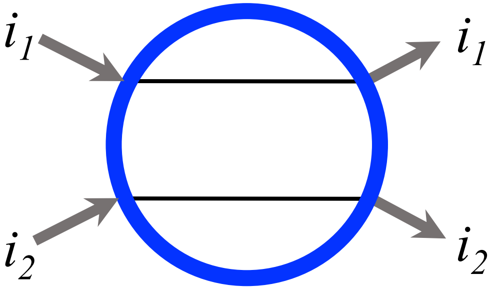
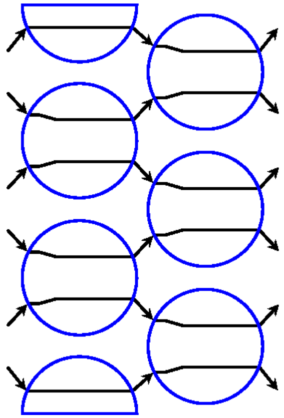


i_1	i_2	o_1	o_2
0	0	0	0
0	1	0	1
1	0	1	0
1	1	1	1



Example circuits with same gate in every row

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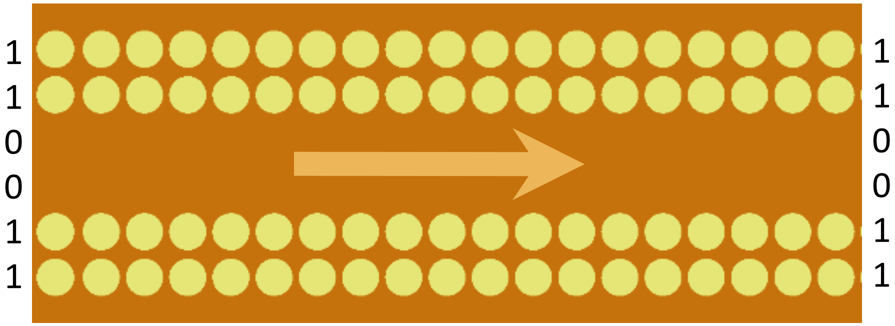
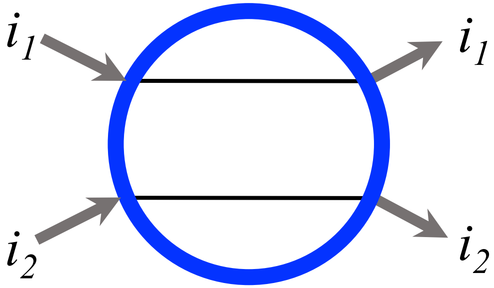
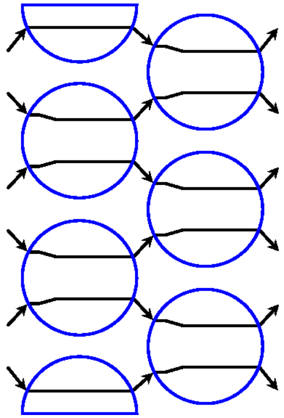


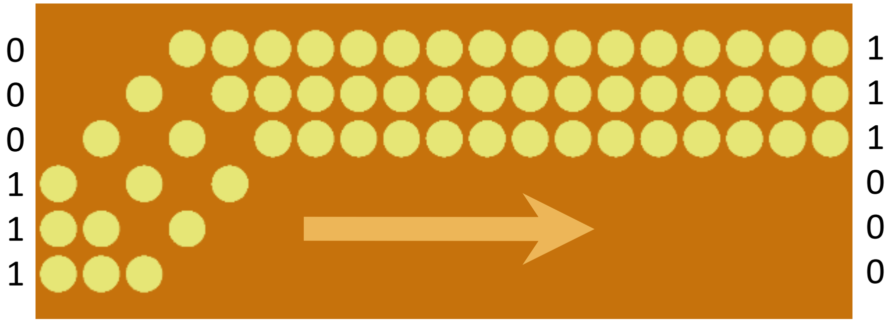
COPY gates



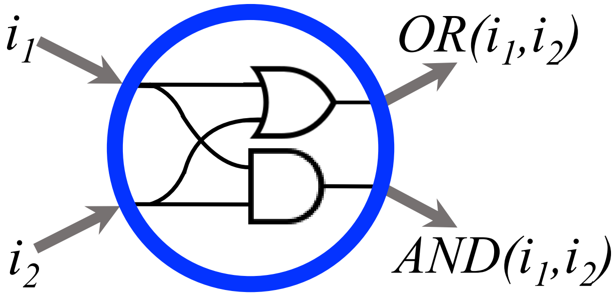
i_1	i_2	o_1	o_2
0	0	0	0
0	1	0	1
1	0	1	0
1	1	1	1



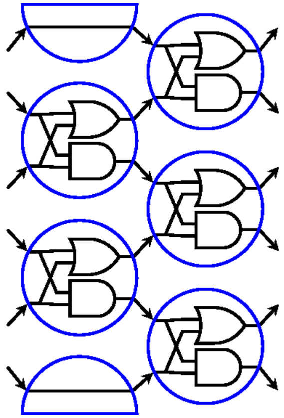
SORTING



SORTING gates

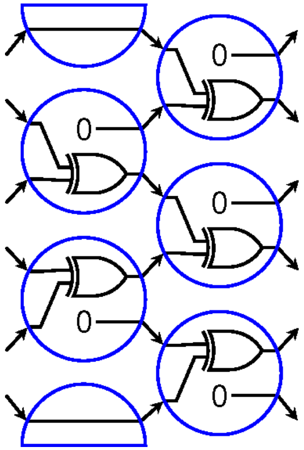


i_1	i_2	o_1	o_2
0	0	0	0
0	1	1	0
1	0	1	0
1	1	1	1



Example circuits with different gates in each row

PARITY



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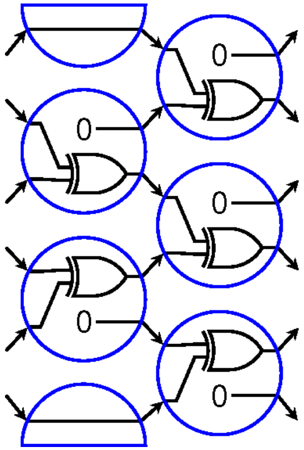

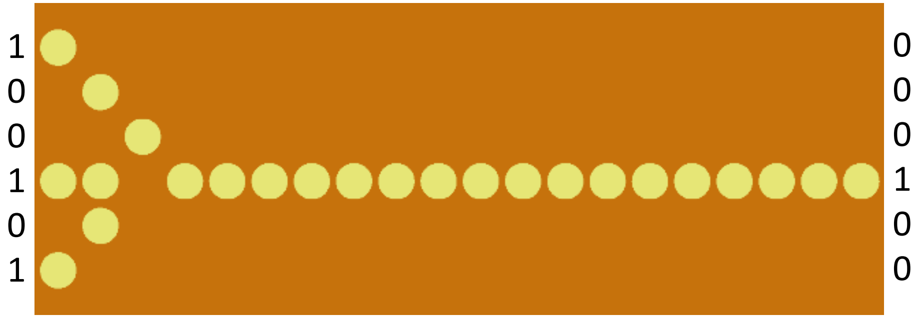

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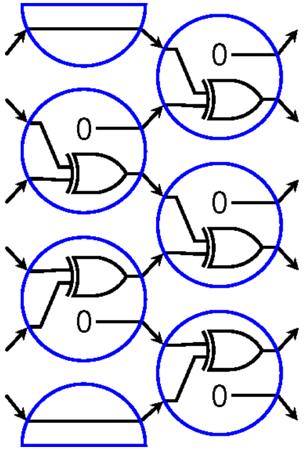
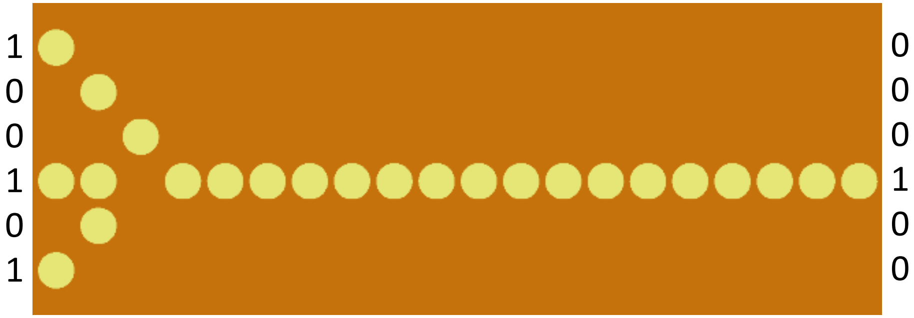
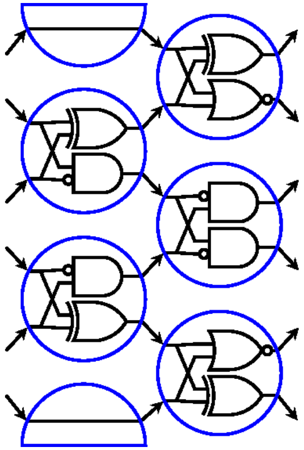
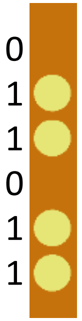




MULTIPLEOF3

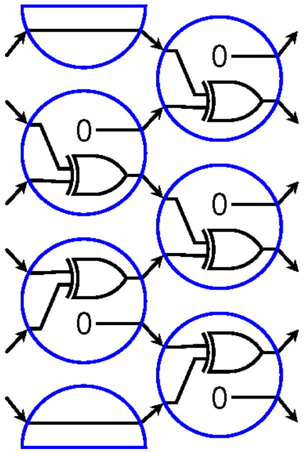
011011_2

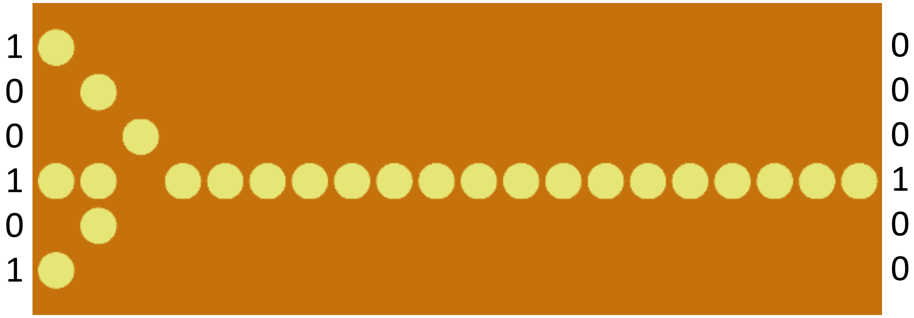




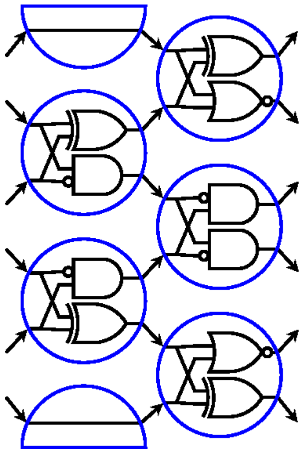
Example circuits with different gates in each row

PARITY

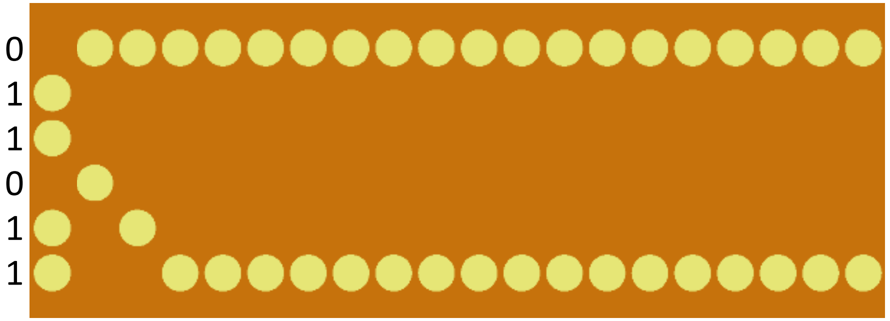




MULTIPLEOF3

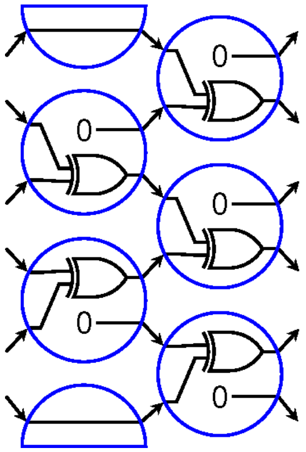


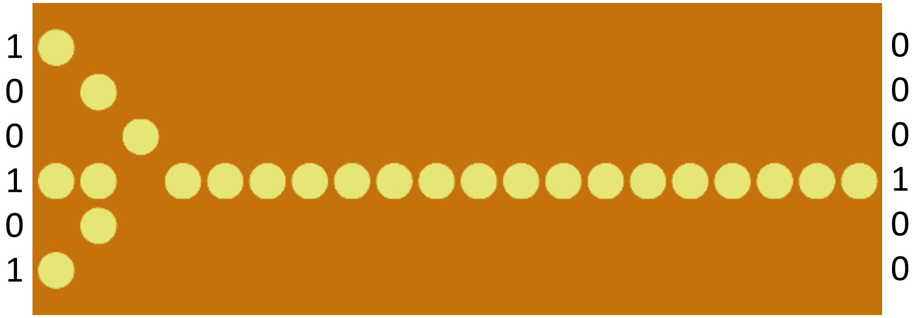
$011011_2 = 27_{10} = 3{\cdot}9$



Example circuits with different gates in each row

PARITY





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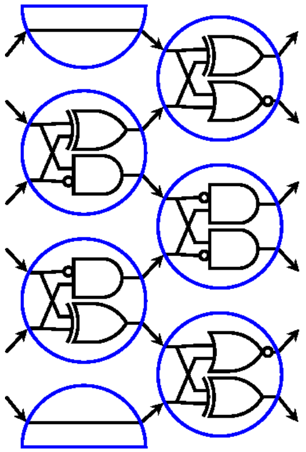
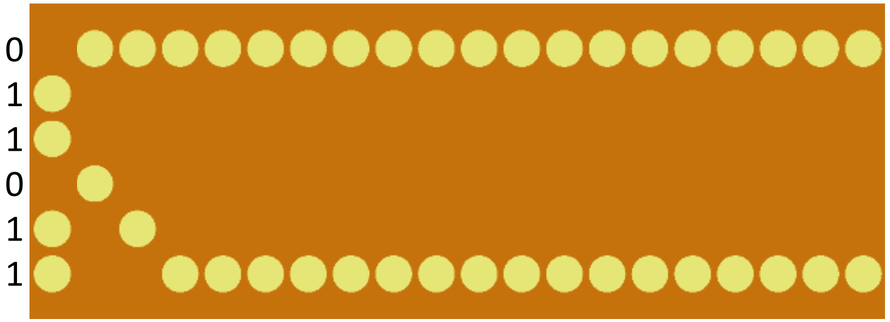
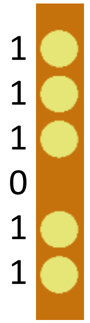


$011011_2 = 27_{10} = 3 \cdot 9$

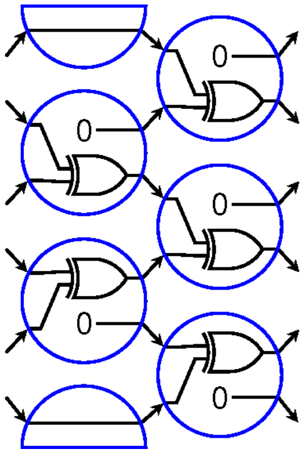


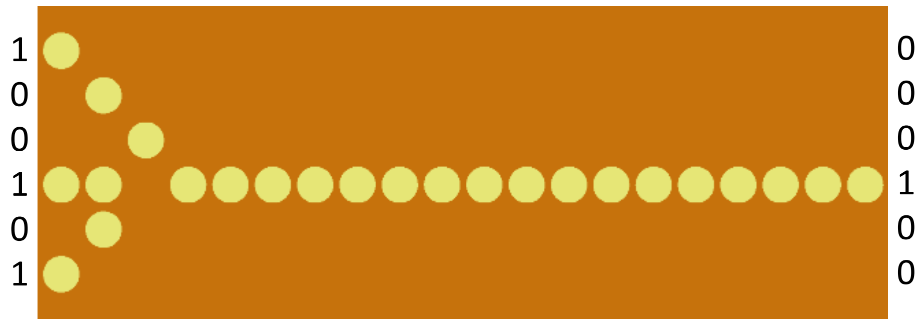
111011_2



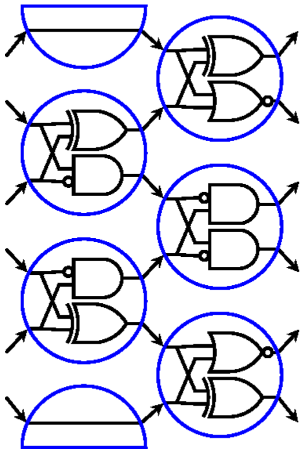
Example circuits with different gates in each row

PARITY

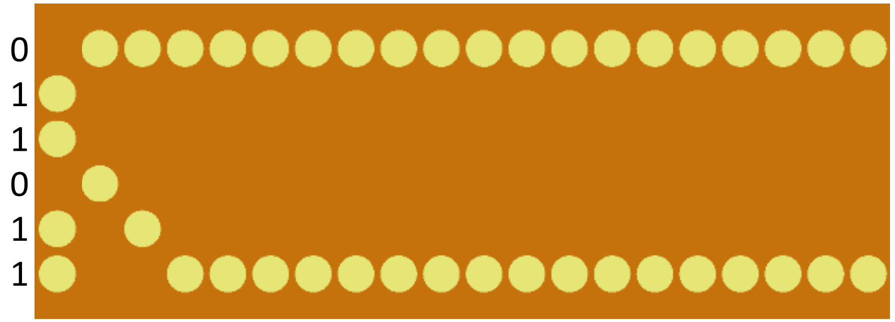




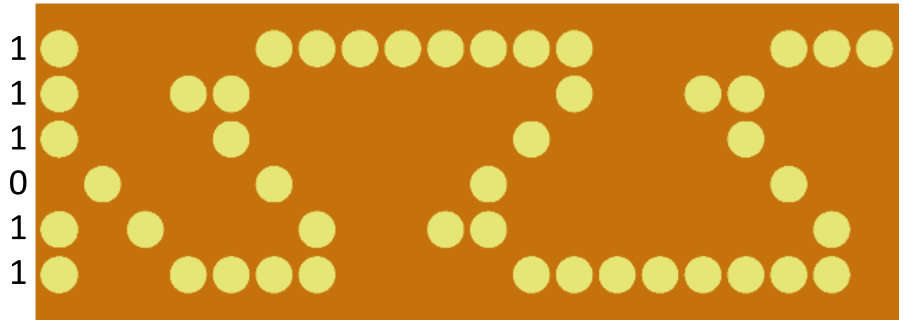
MULTIPLEOF3



$011011_2 = 27_{10} = 3 \cdot 9$

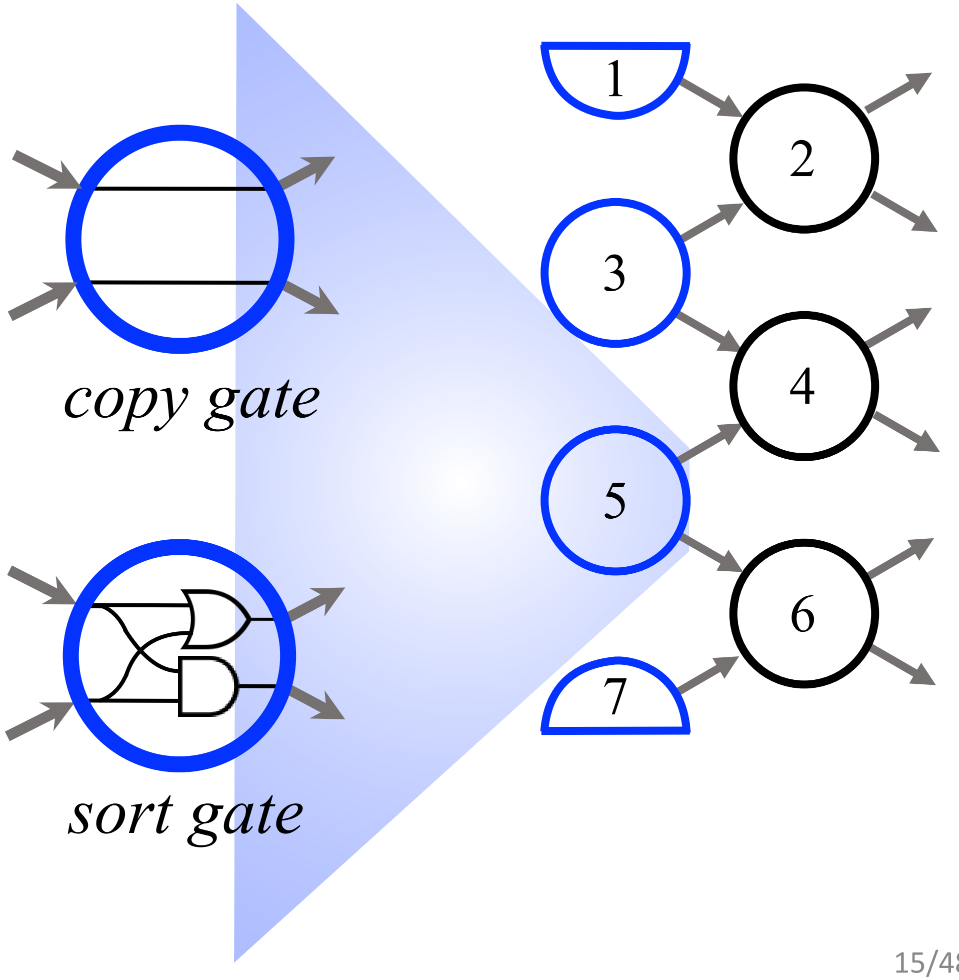


$111011_2 = 59_{10} = 3 \cdot 19 + 2$

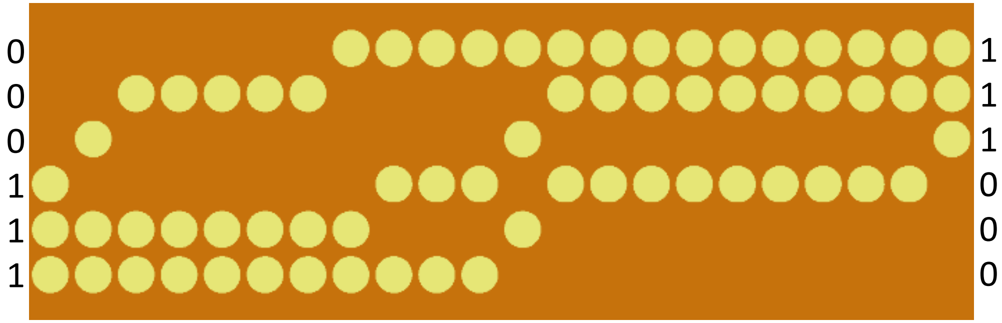


Randomization: "Lazy" sorting

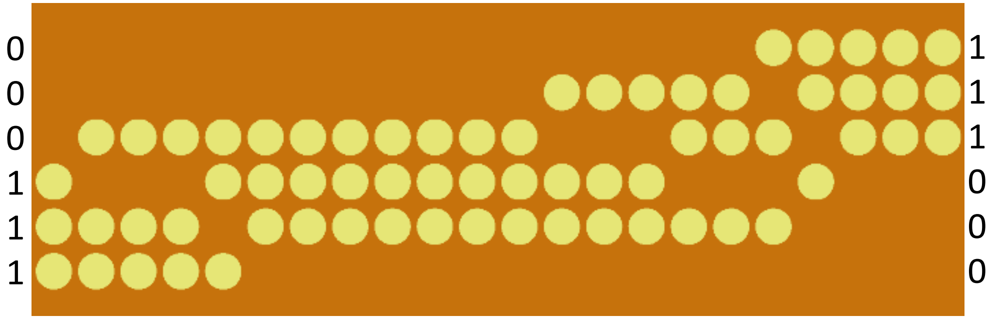
If 1 and 0 out of order, flip a coin to decide whether to swap them.

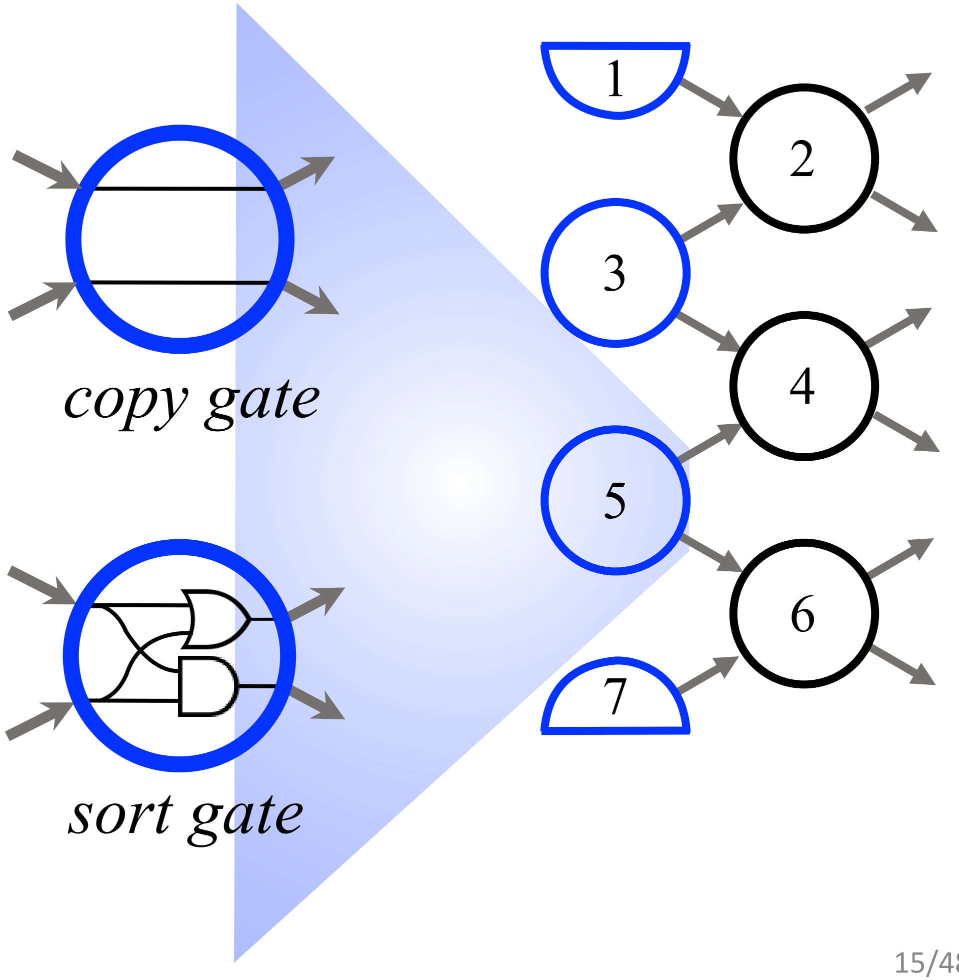


Randomization: "Lazy" sorting



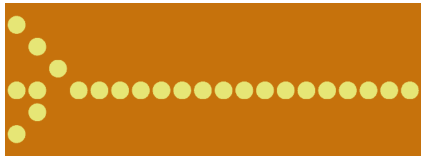
If 1 and 0 out of order, flip a coin to decide whether to swap them.



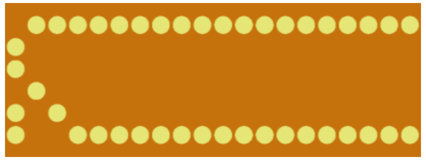


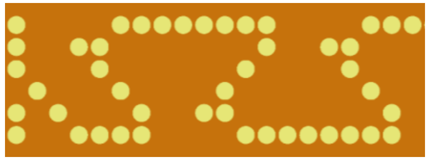
Deterministic circuits

PARITY



MULTIPLEOF3



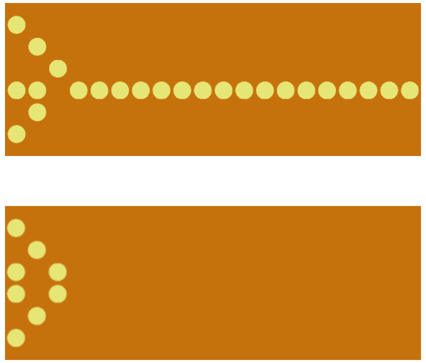


answer yes/no question

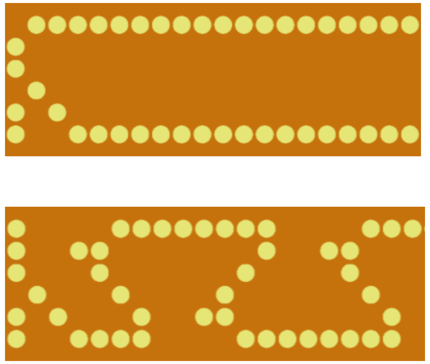
Deterministic circuits

answer yes/no question

PARITY



MULTIPLEOF3



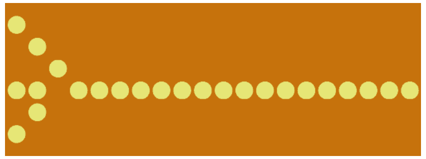
PALINDROME

yes

no

Deterministic circuits

PARITY



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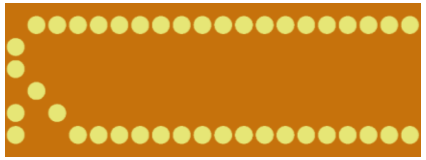
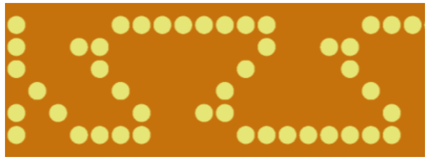


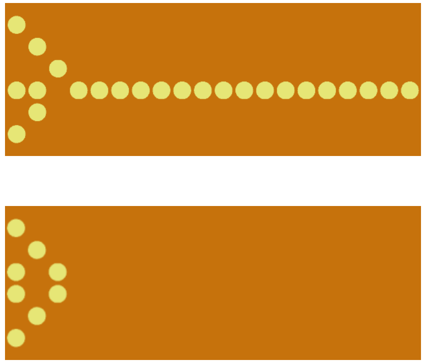


PALINDROME

answer yes/no question

Deterministic circuits

PARITY



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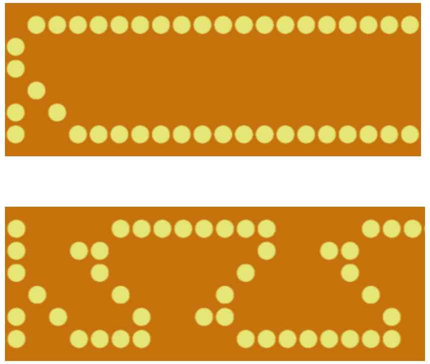
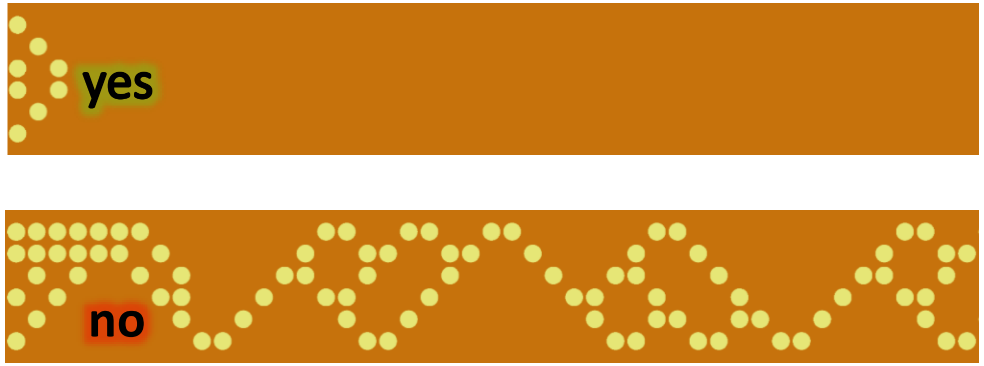


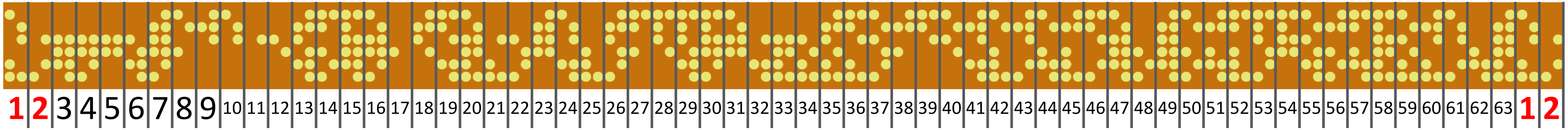
PALINDROME

answer yes/no question



CYCLE63

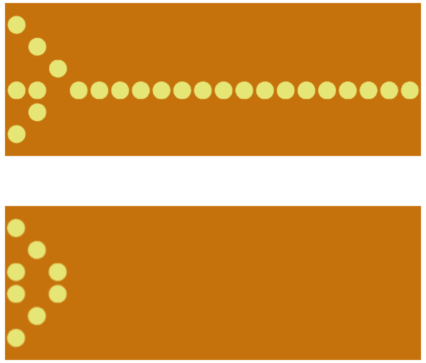
"count" as high as possible



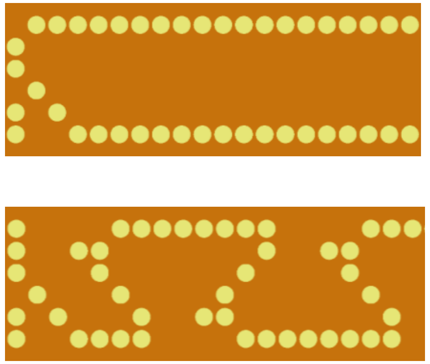
Deterministic circuits

answer yes/no question

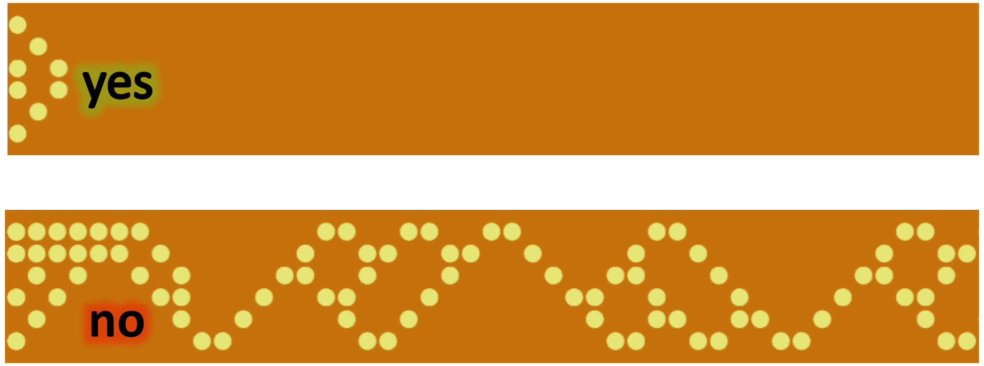
PARITY



MULTIPLEOF3

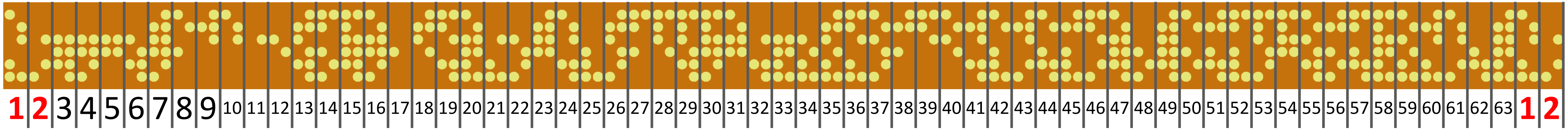


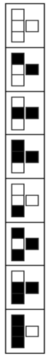
PALINDROME



CYCLE63

"count" as high as possible





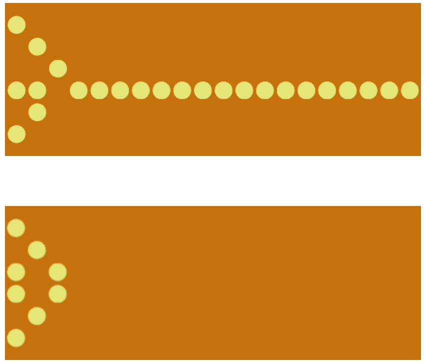
RULE110

simulate cellular automata

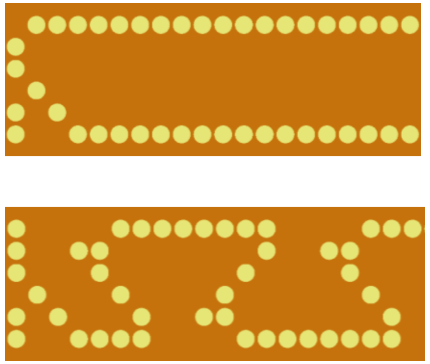
Deterministic circuits

answer yes/no question

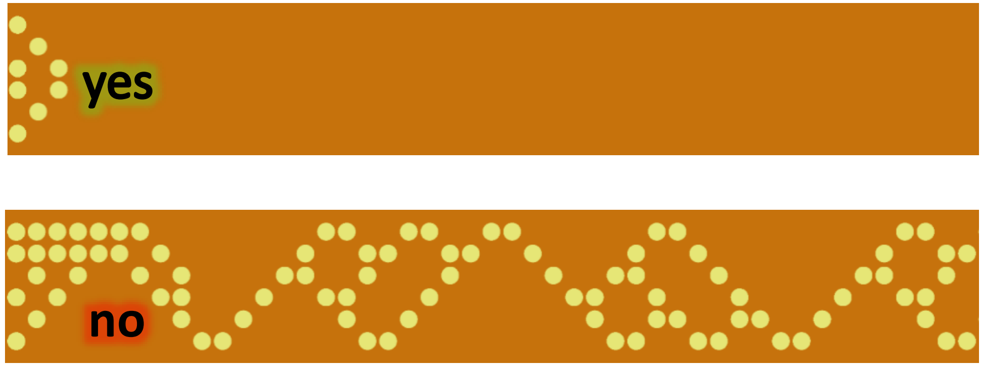
PARITY



MULTIPLEOF3

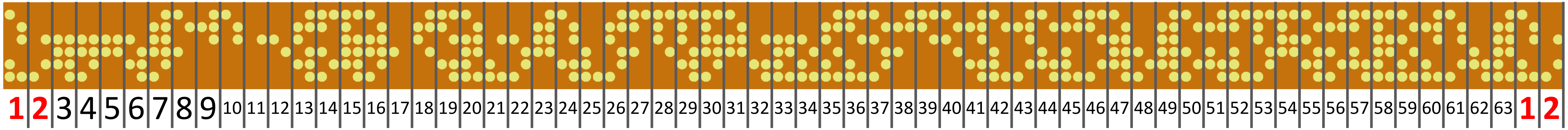


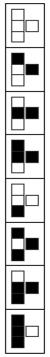
PALINDROME



CYCLE63

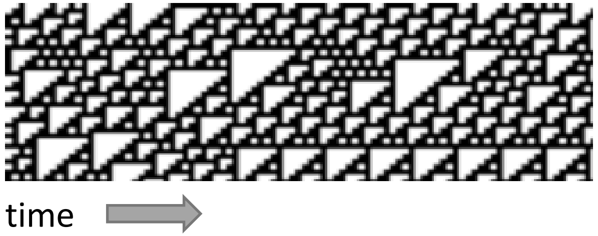
"count" as high as possible





RULE110

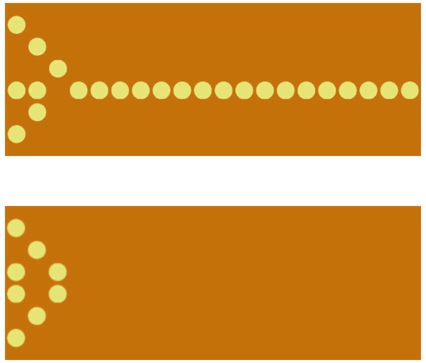
simulate cellular automata



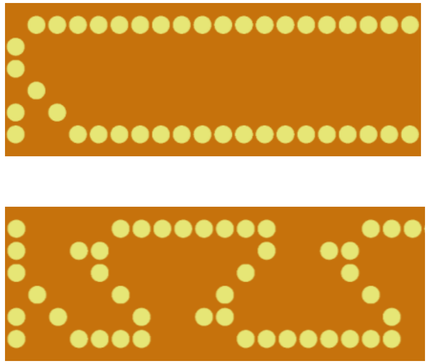
Deterministic circuits

answer yes/no question

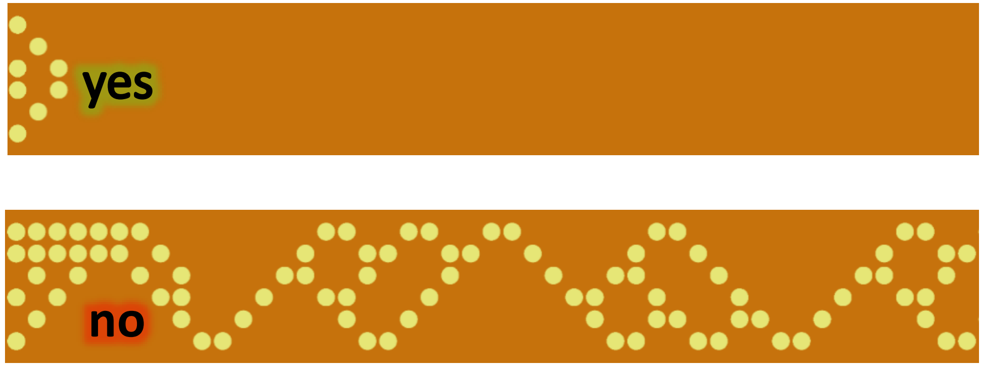
PARITY



MULTIPLEOF3

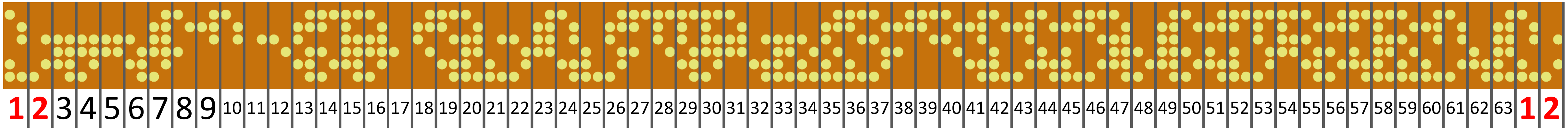


PALINDROME



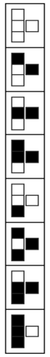
CYCLE63

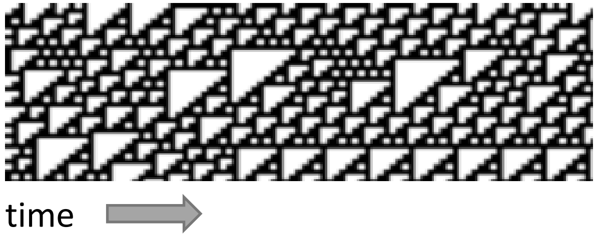
"count" as high as possible

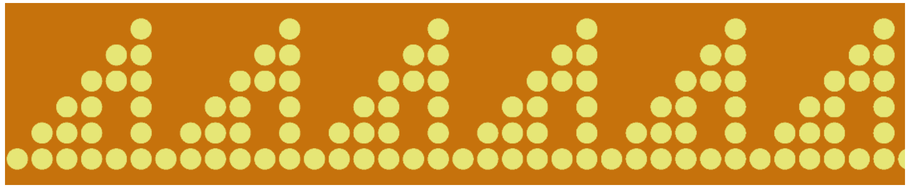


RULE110

simulate cellular automata







Theorem: Rule 110 can efficiently execute any algorithm.

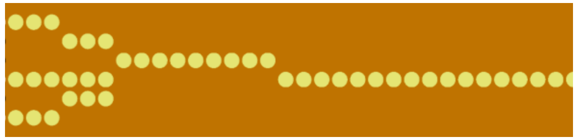
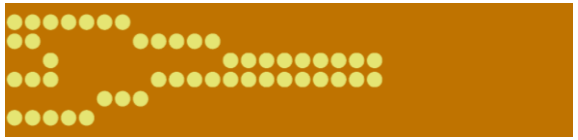
[Cook, Complex Systems 2004]

[Neary, Woods, ICALP 2006]

Randomized circuits

LAZYPARITY

Randomized circuits

LAZYPARITY  

Randomized circuits

LAZYPARITY

RANDOMWALKINGBIT

Randomized circuits

LazyParity

RandomWalkingBit

DiamondsAreForever

Randomized circuits

LAZYPARITY

RANDOMWALKINGBIT

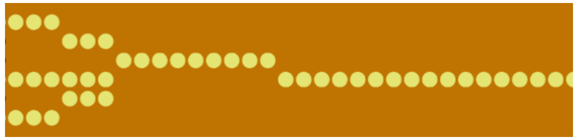
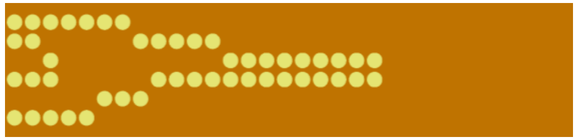
DIAMONDSAREFOREVER

FAIRCOIN

use biased coin to
simulate unbiased coin

Randomized circuits

LazyParity

RandomWalkingBit

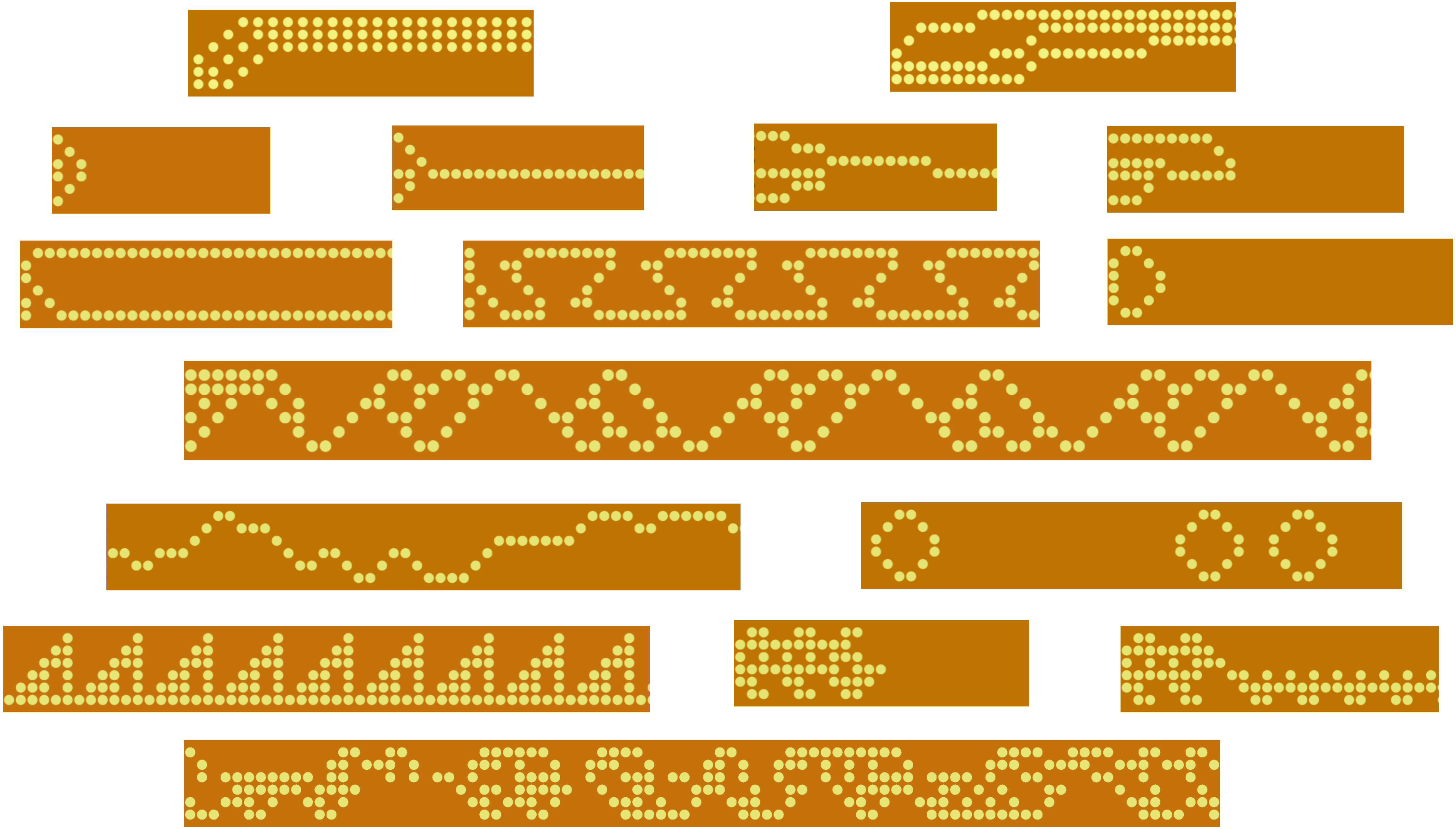
DiamondsAreForever

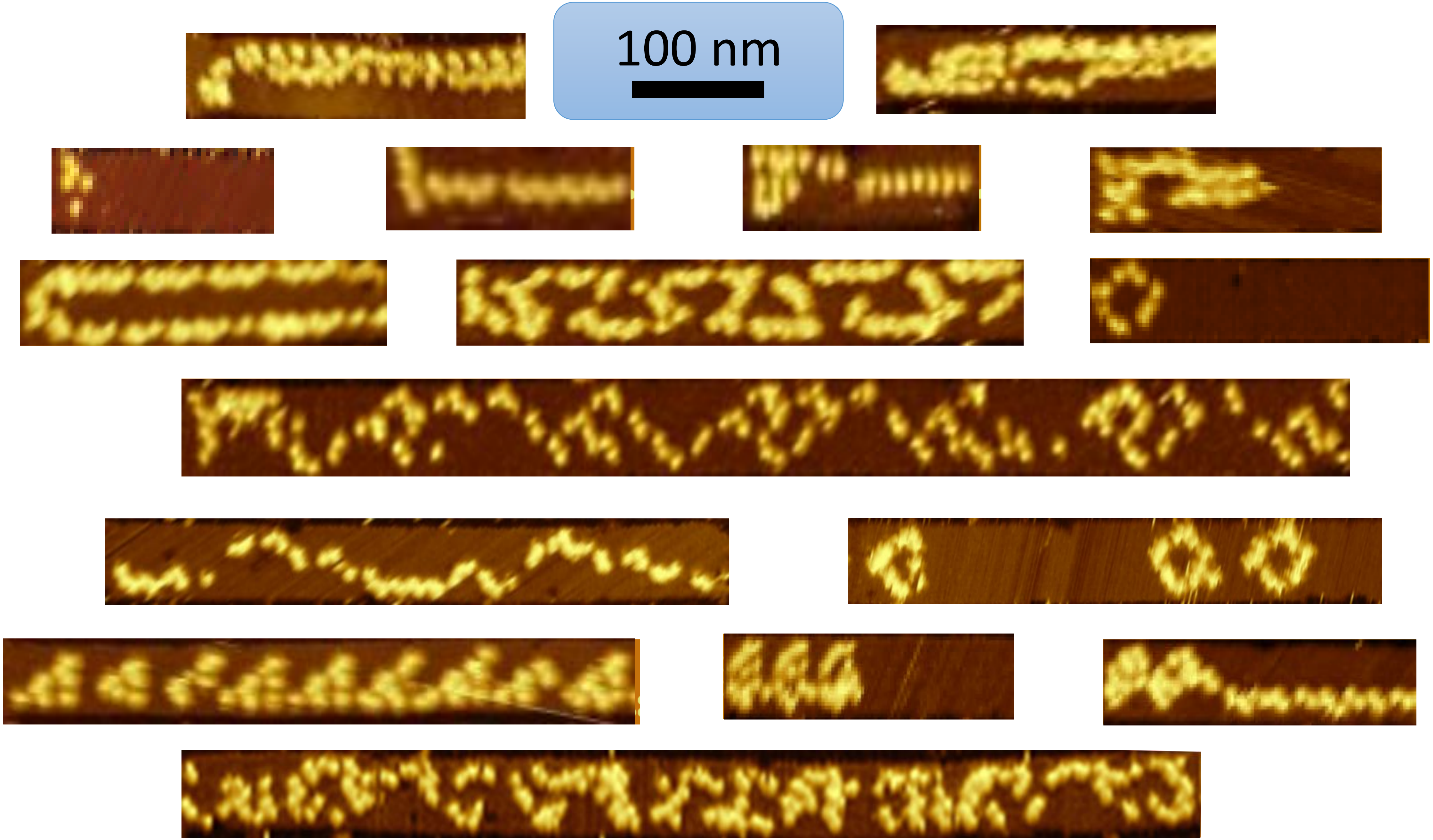
FairCoin

use biased coin to
simulate unbiased coin

Pr [] = Pr [] = ½

for **any** (positive) probabilities for the randomized gate

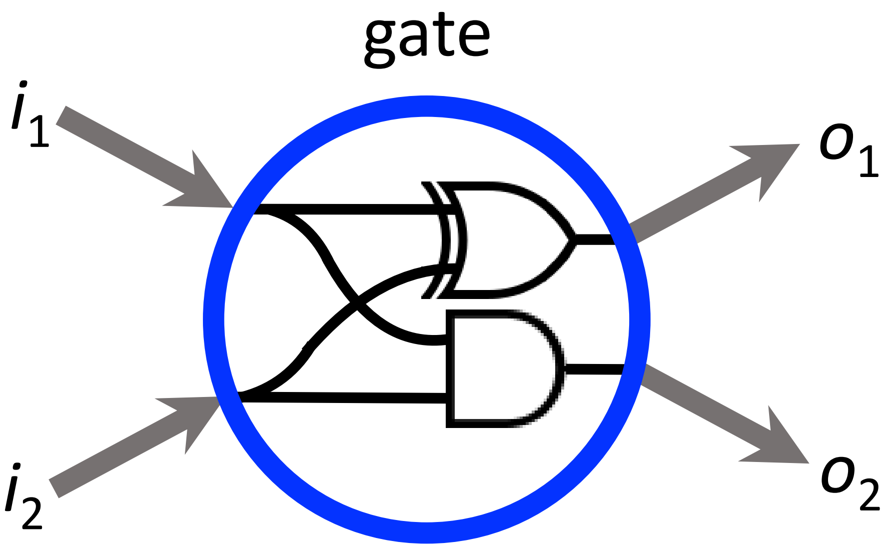



100 nm

Hierarchy of abstractions

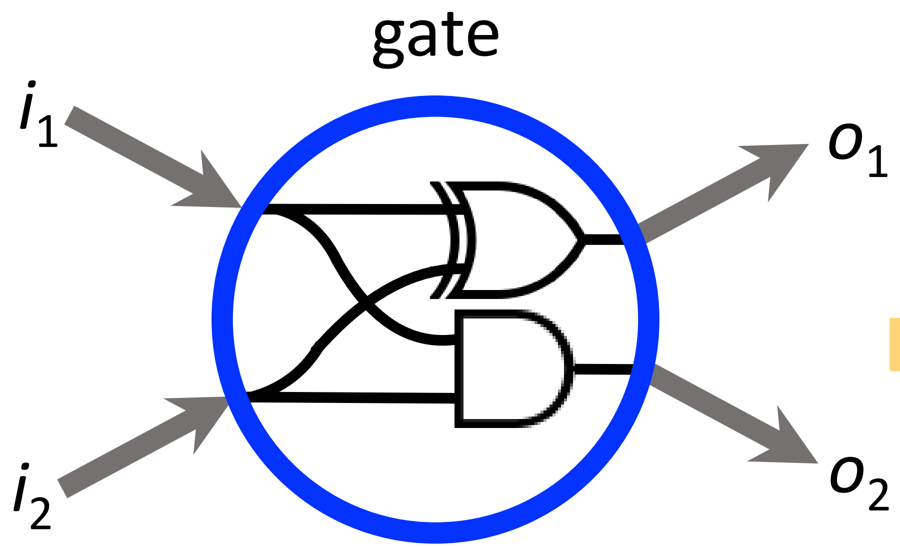
Bits:	Boolean circuits compute
Tiles:	**Tile growth implements circuits**
DNA:	DNA strands implement tiles

Gates → Tiles



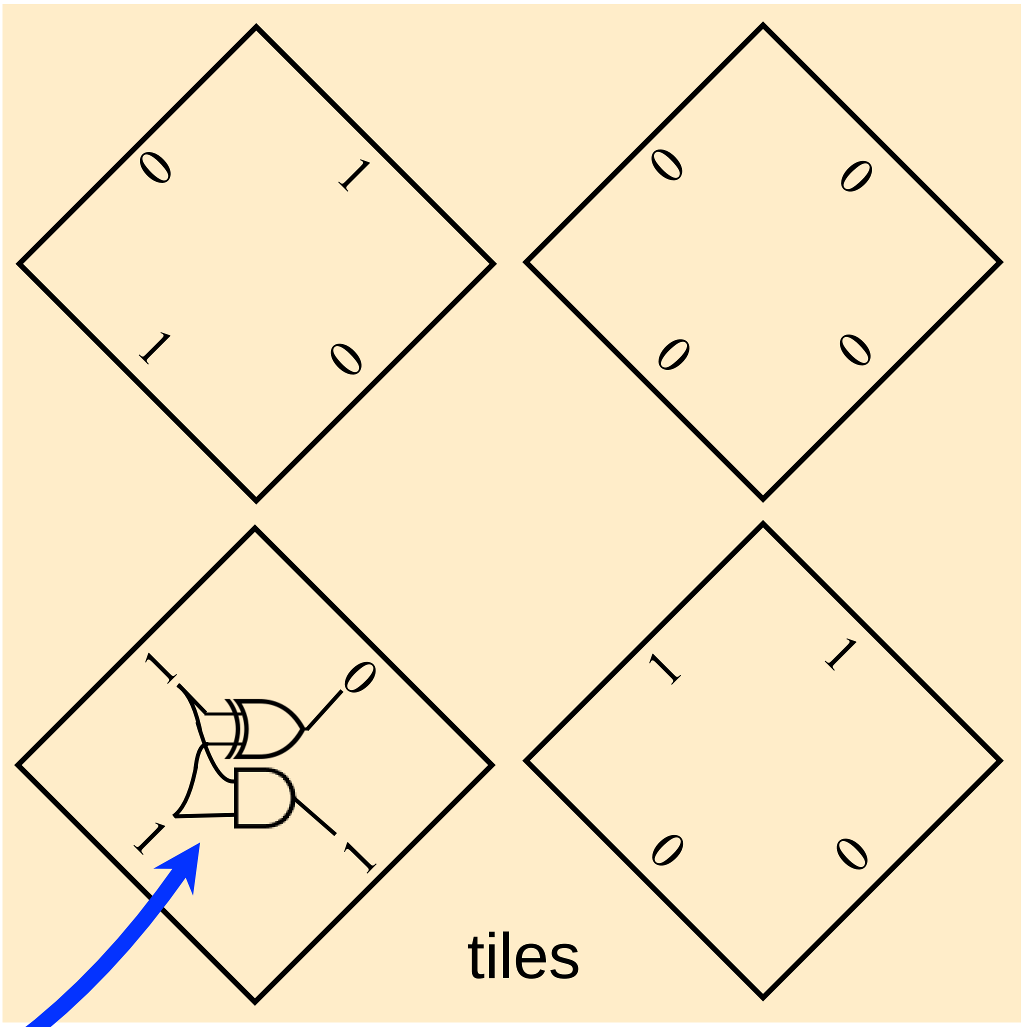
i_1	i_2	o_1	o_2
0	0	0	0
0	1	1	0
1	0	1	0
1	1	0	1

Gates → Tiles

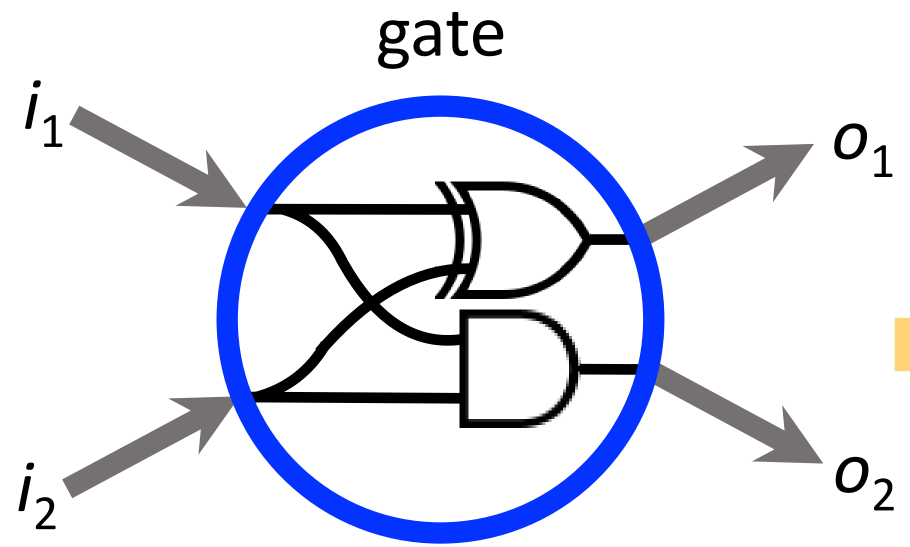


i_1	i_2	o_1	o_2
0	0	0	0
0	1	1	0
1	0	1	0
1	1	0	1

truth table row is encoded by a **tile** with 4 **glues** encoding bits

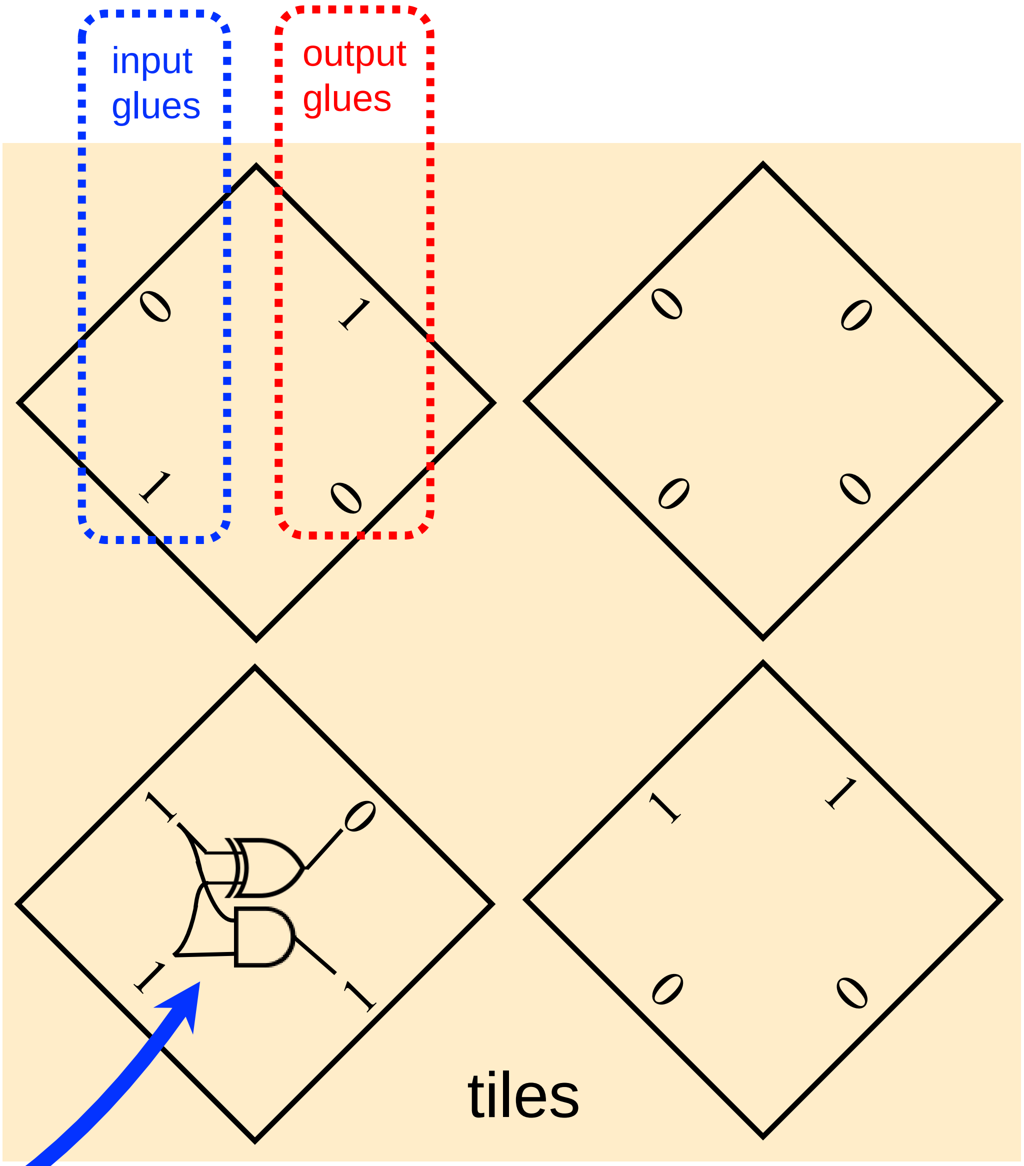


Gates → Tiles

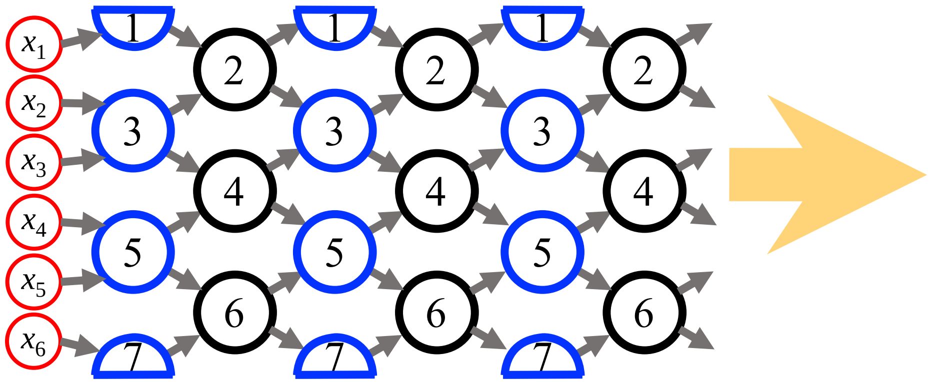


i_1	i_2	o_1	o_2
0	0	0	0
0	1	1	0
1	0	1	0
1	1	0	1

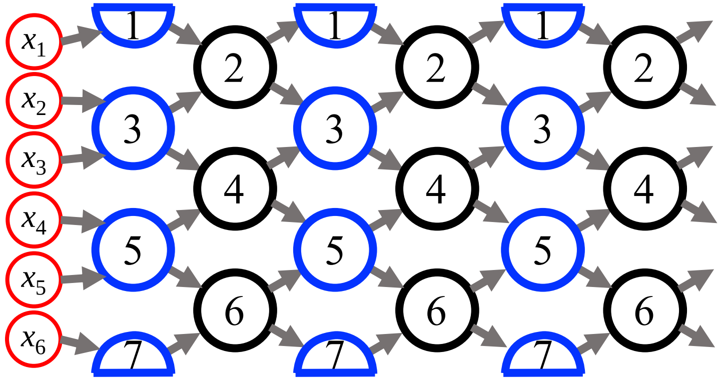
truth table row is encoded by a **tile** with 4 **glues** encoding bits

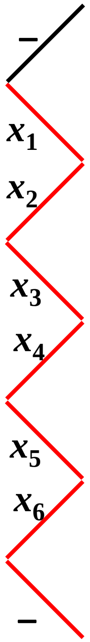


How tiles compute while growing (algorithmic self-assembly)

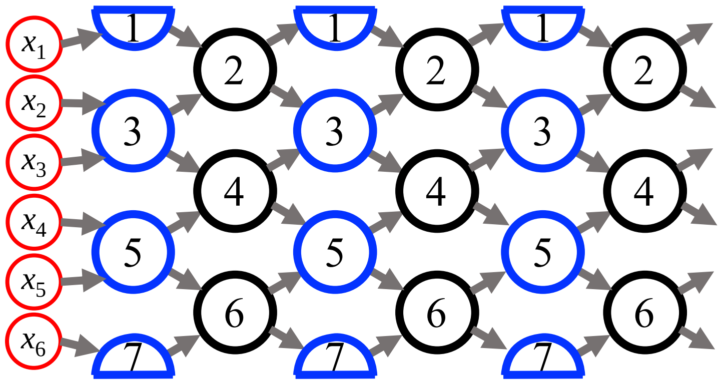


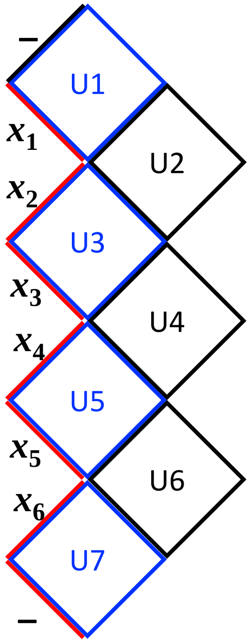
How tiles compute while growing (algorithmic self-assembly)



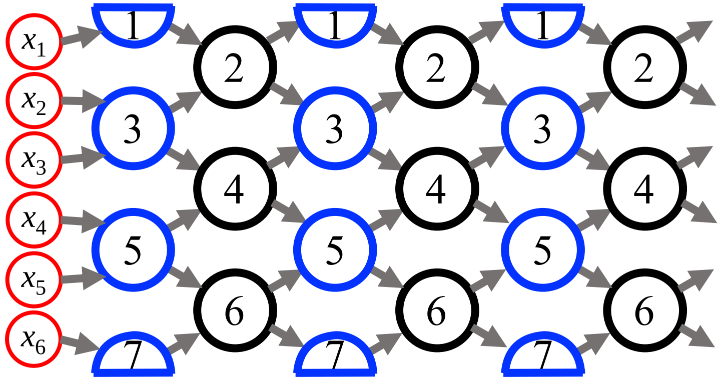


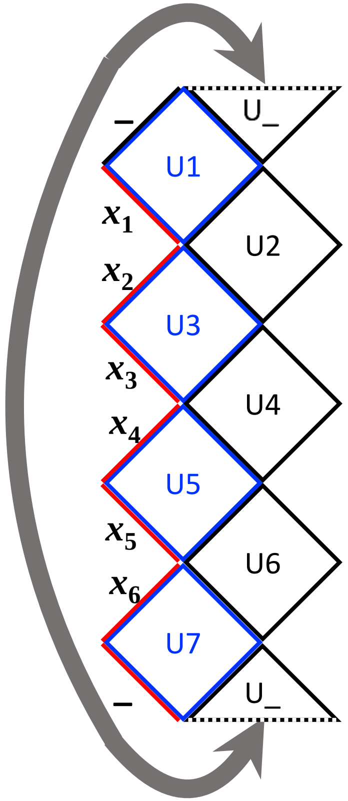
How tiles compute while growing (algorithmic self-assembly)



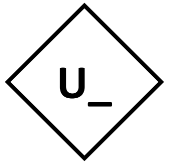


How tiles compute while growing (algorithmic self-assembly)

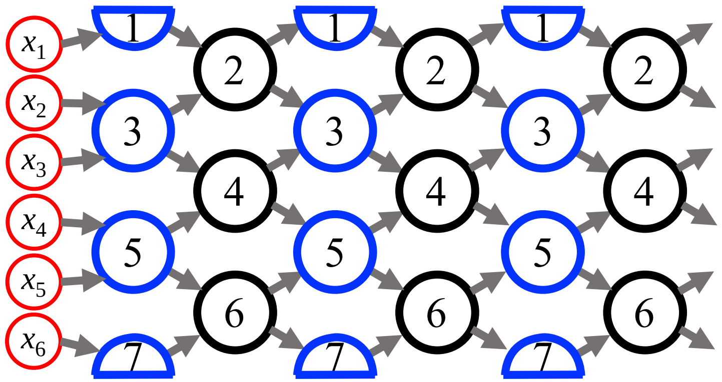


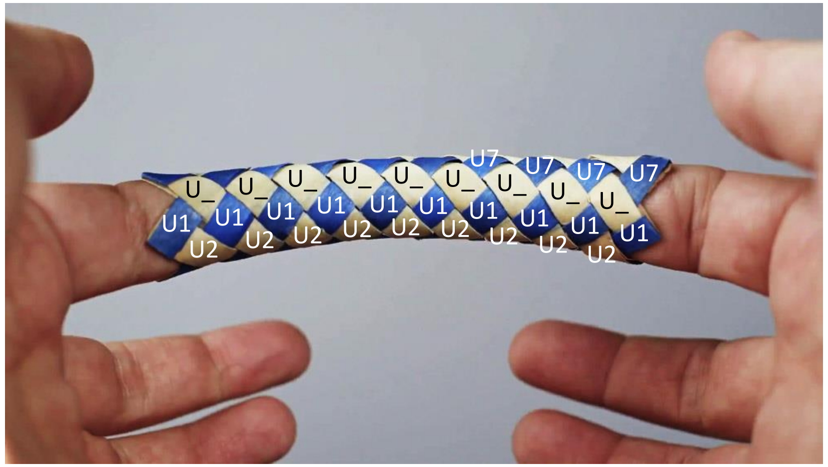


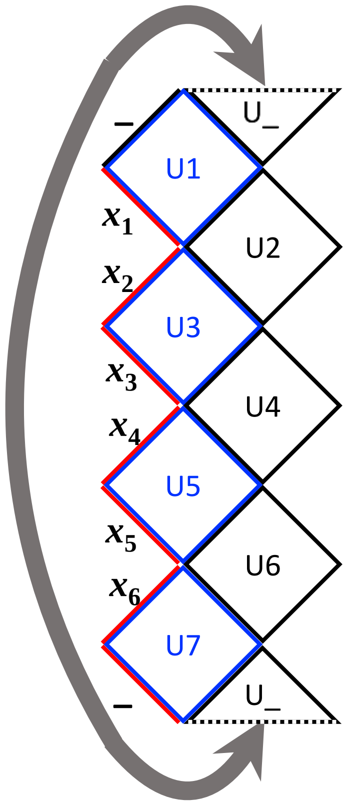
“data-free” tile wraps top to bottom to form a tube



How tiles compute while growing (algorithmic self-assembly)



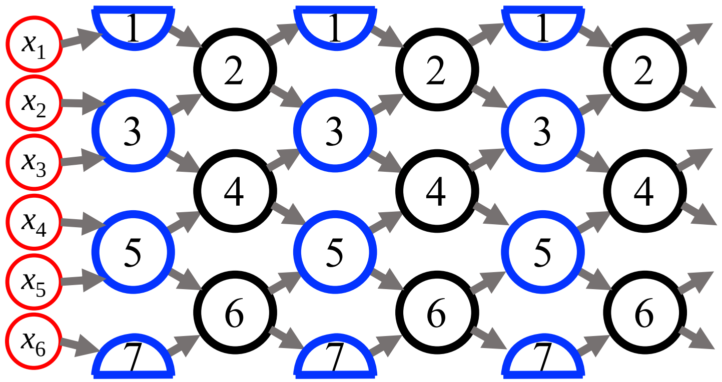


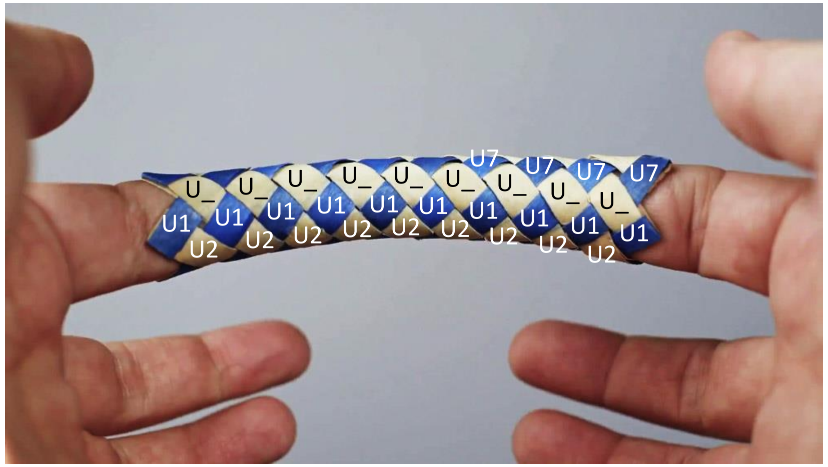


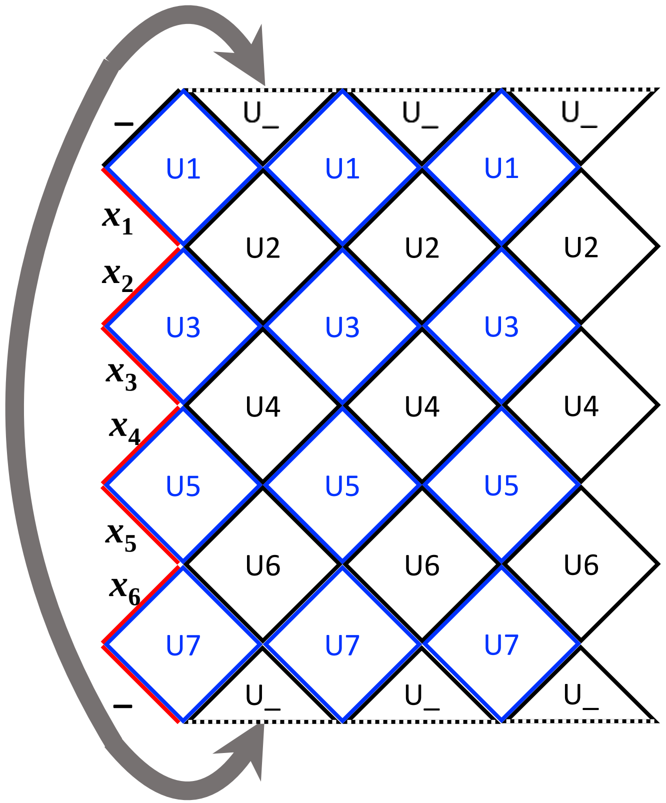
“data-free” tile wraps top to bottom to form a tube

U_

How tiles compute while growing (algorithmic self-assembly)







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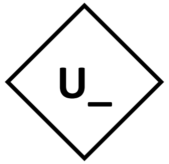

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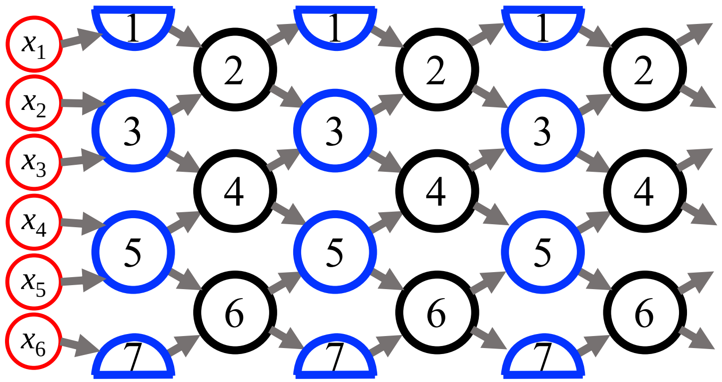

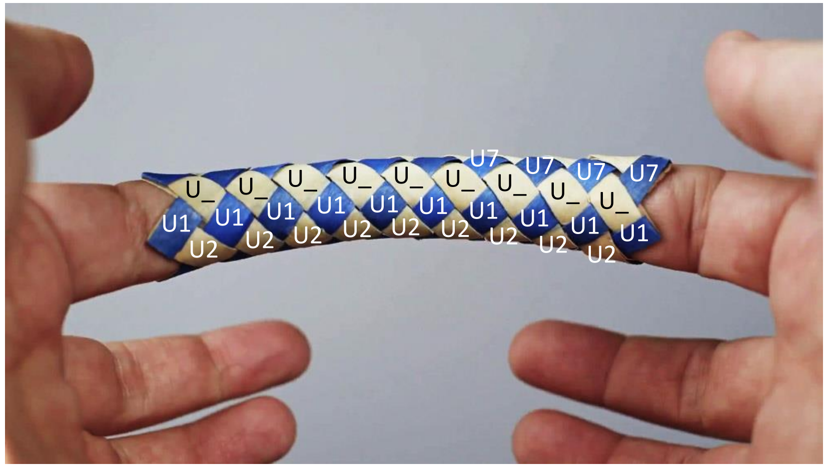

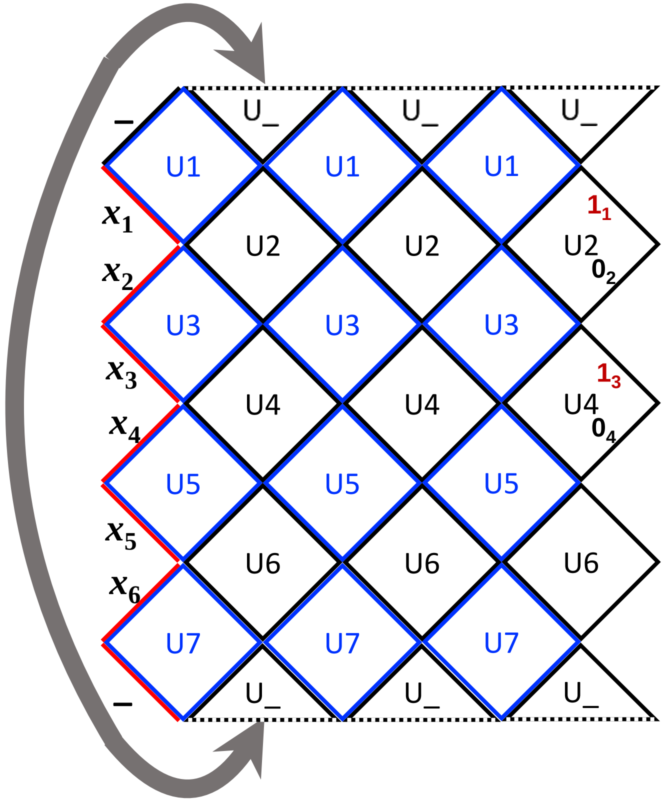

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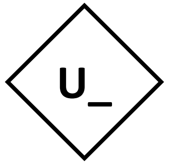

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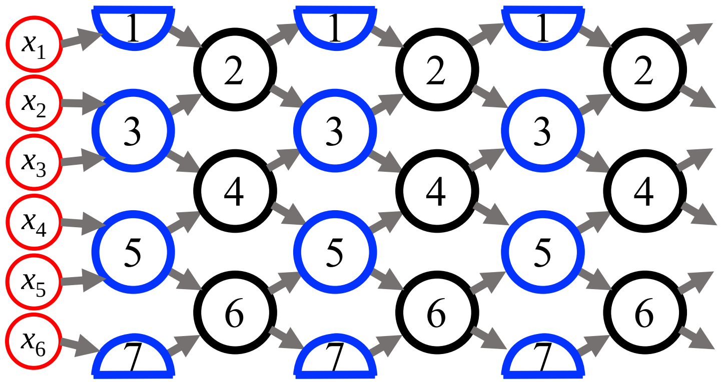

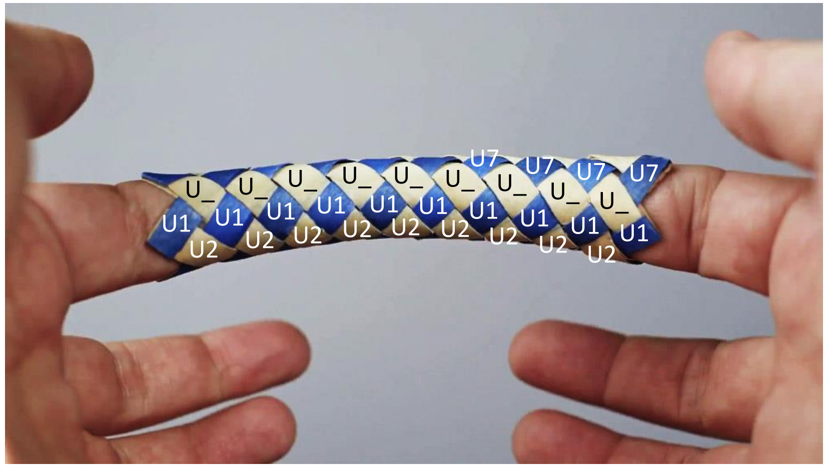

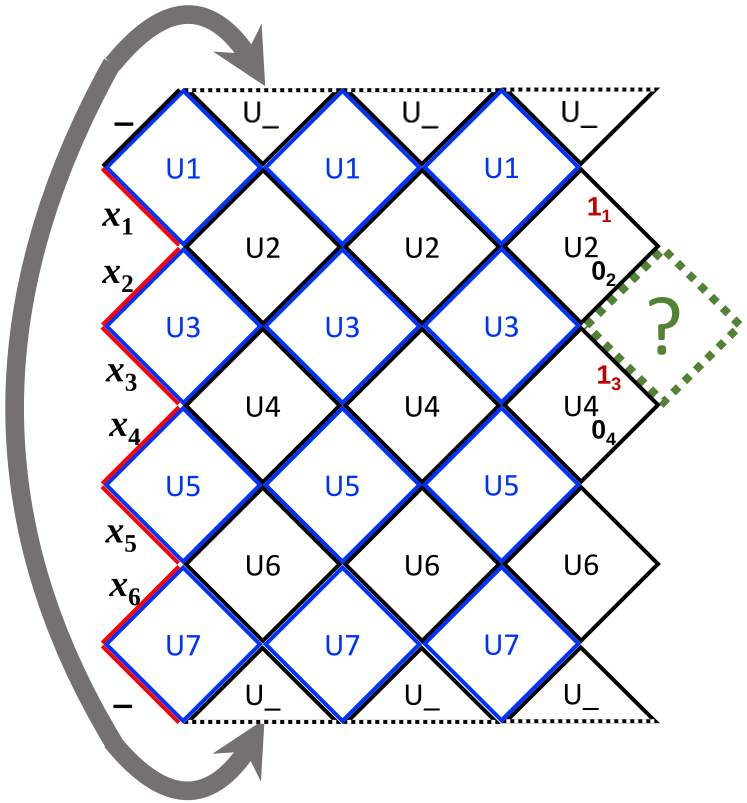

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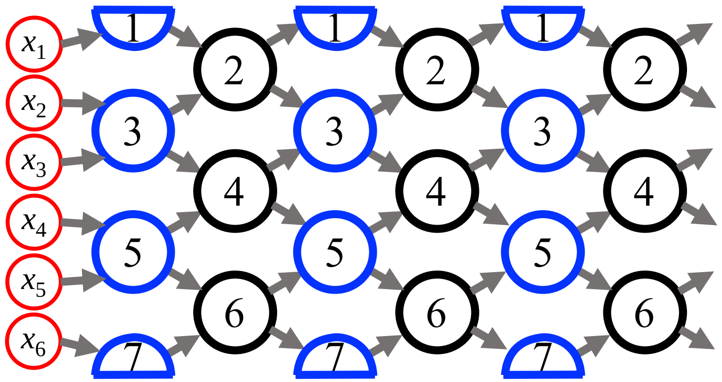

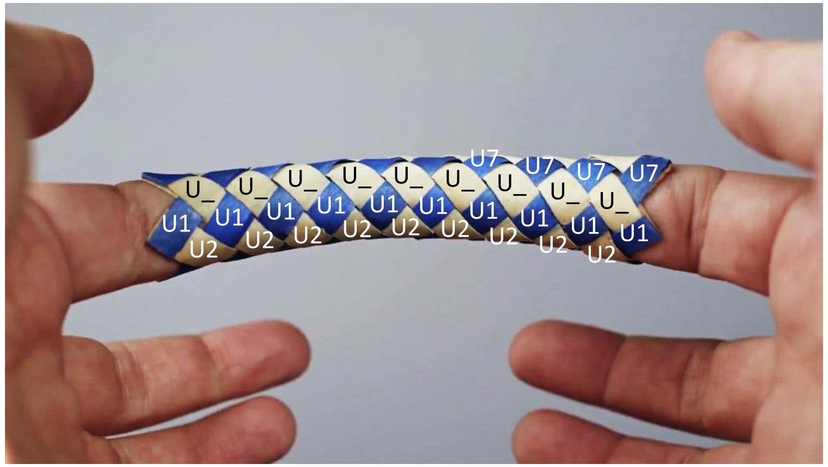

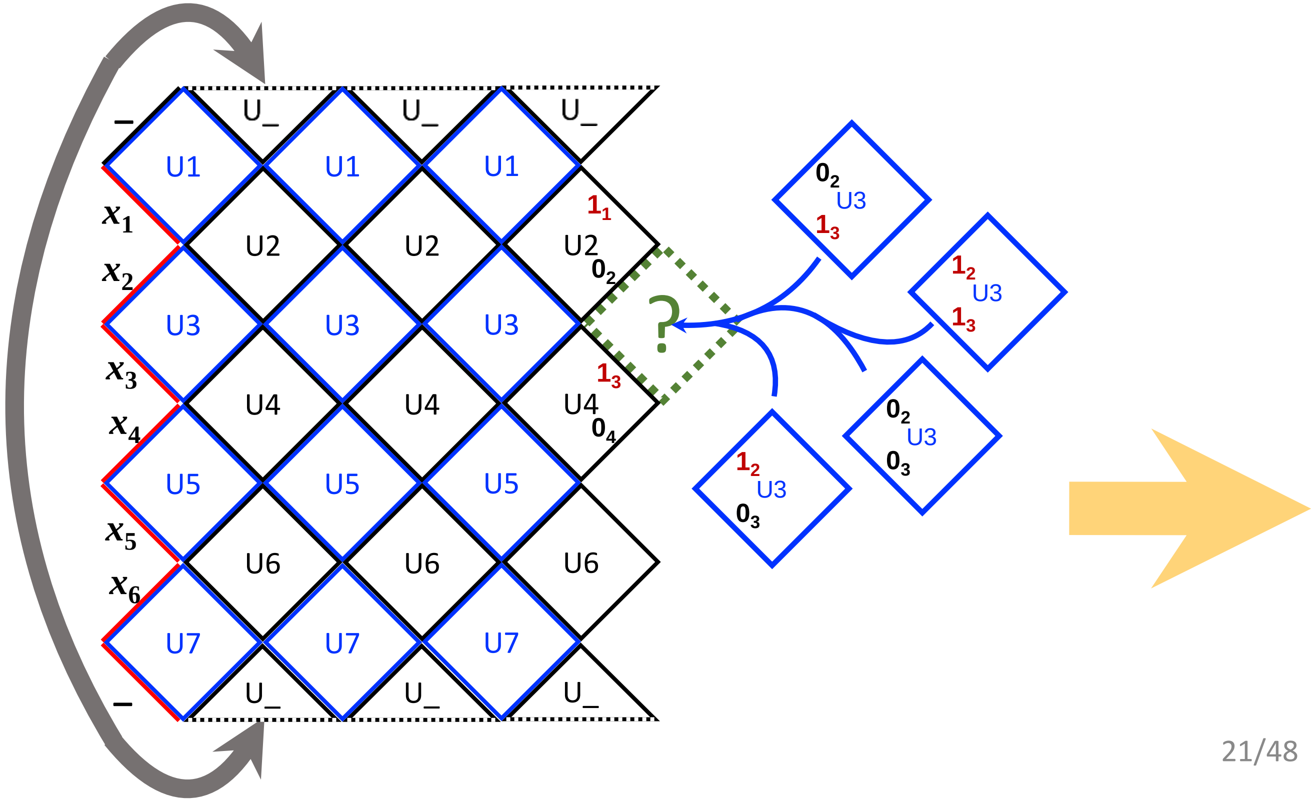

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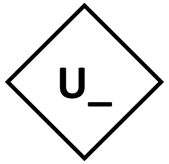
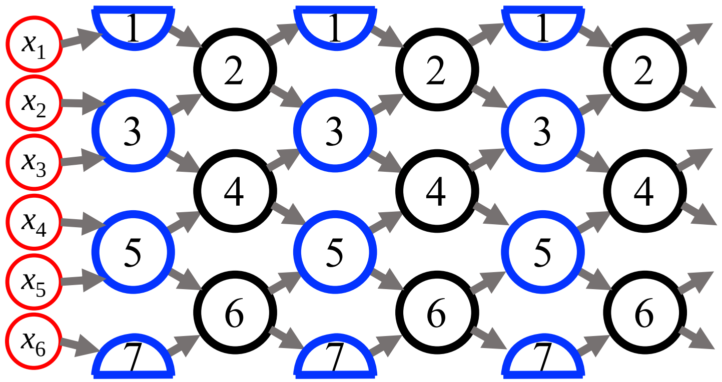
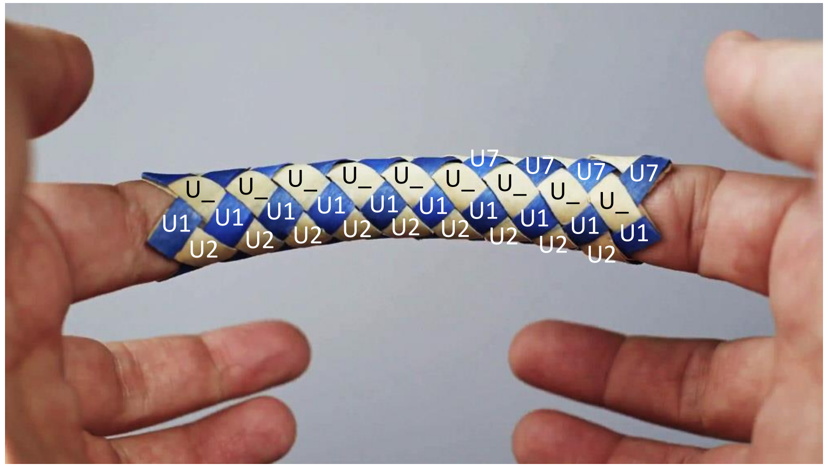
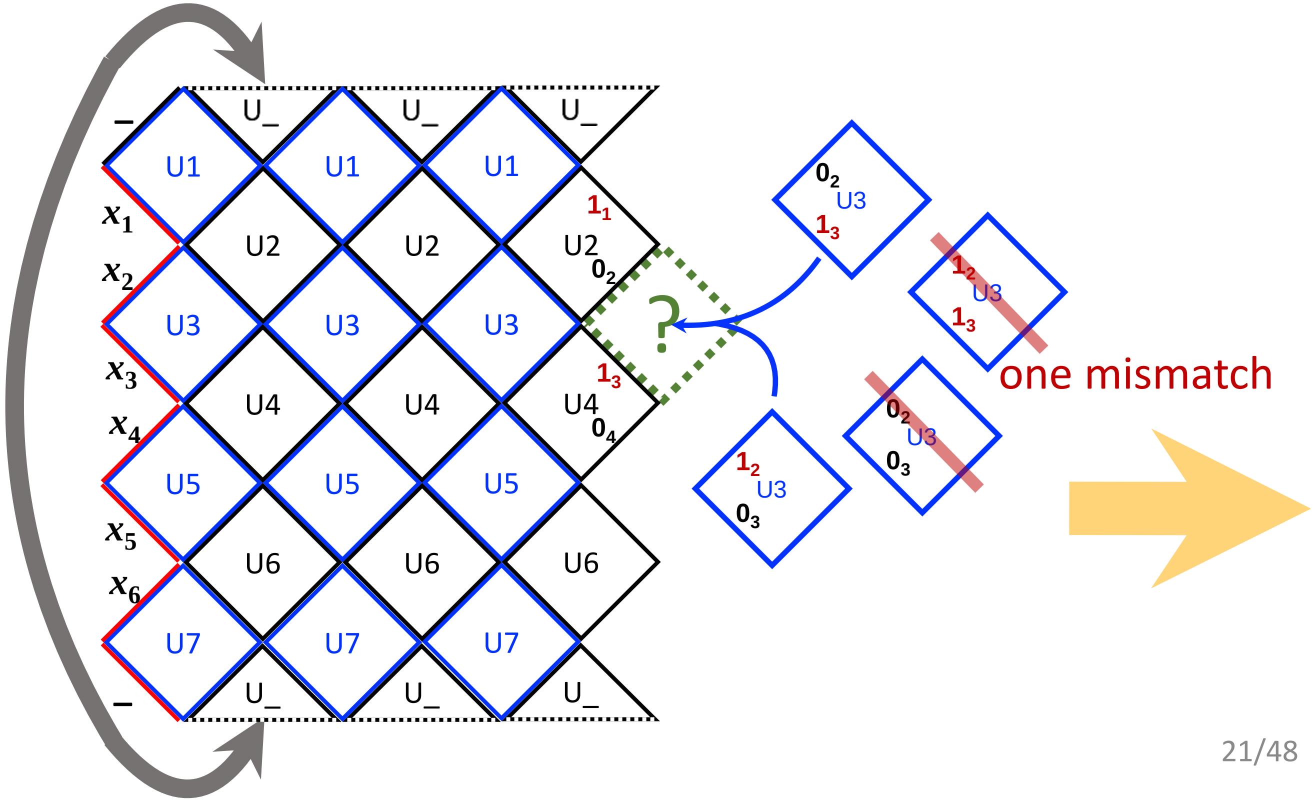


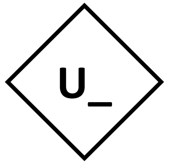
How tiles compute while growing (algorithmic self-assembly)







“data-free” tile wraps top to bottom to form a tube



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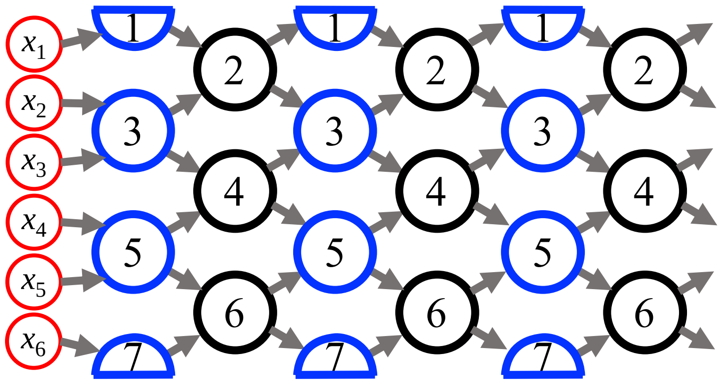

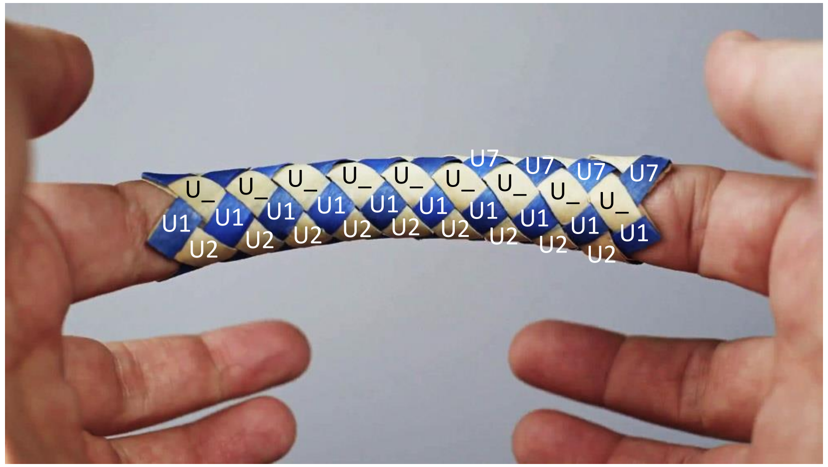

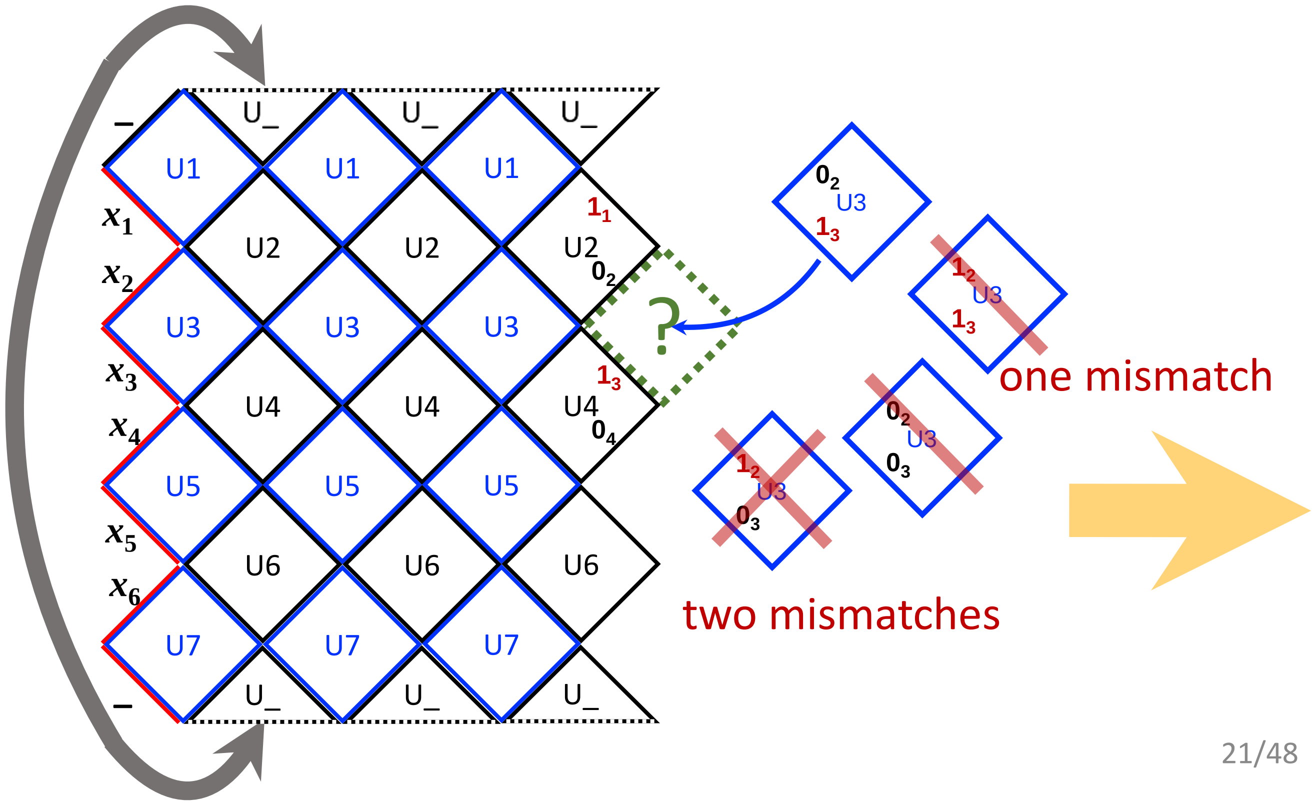

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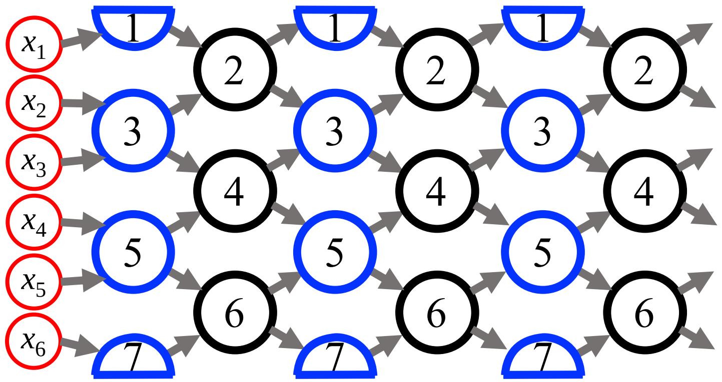

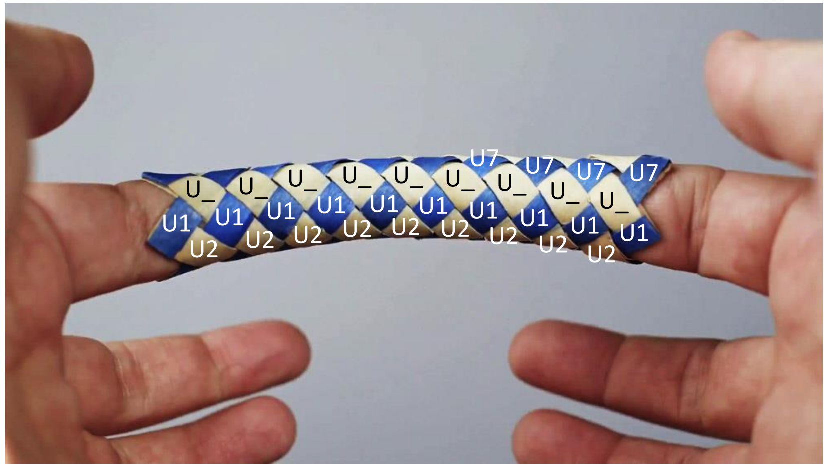

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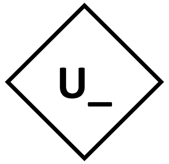
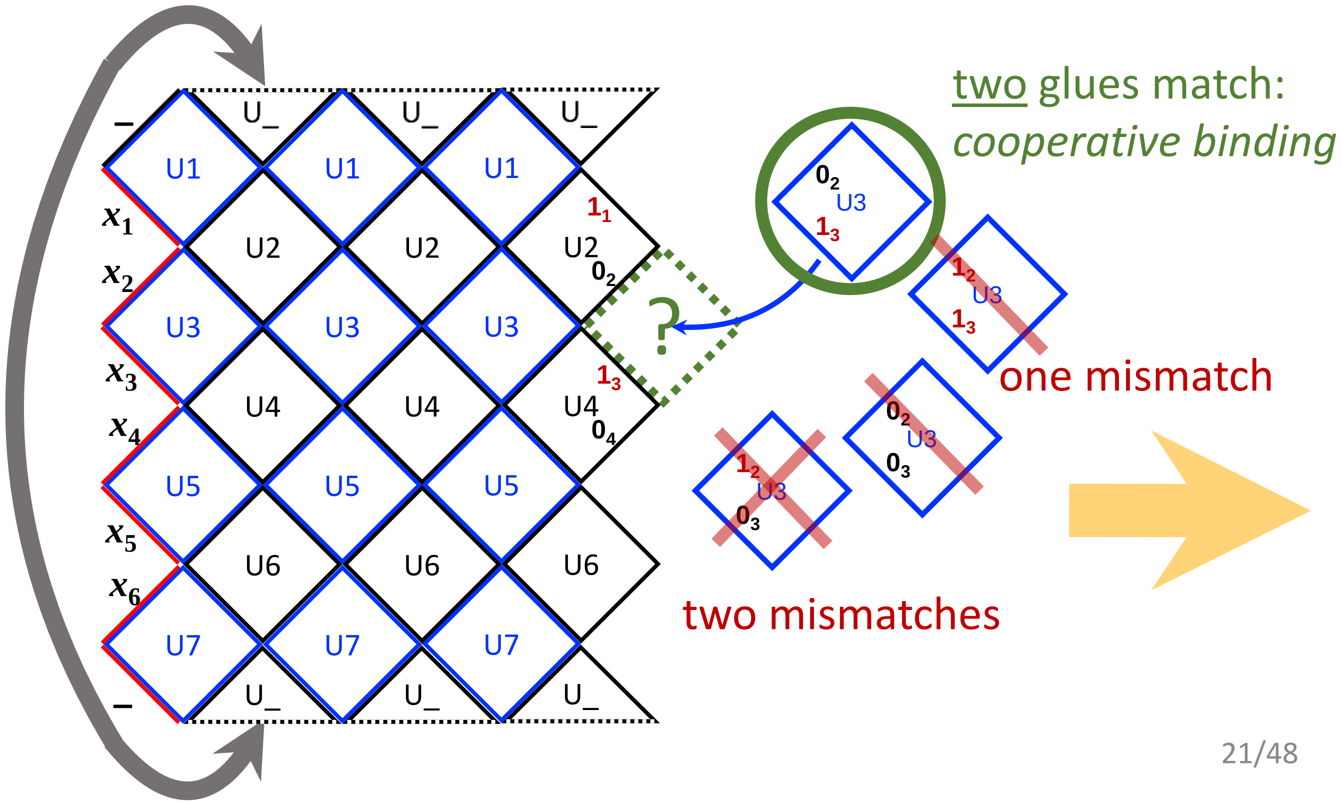
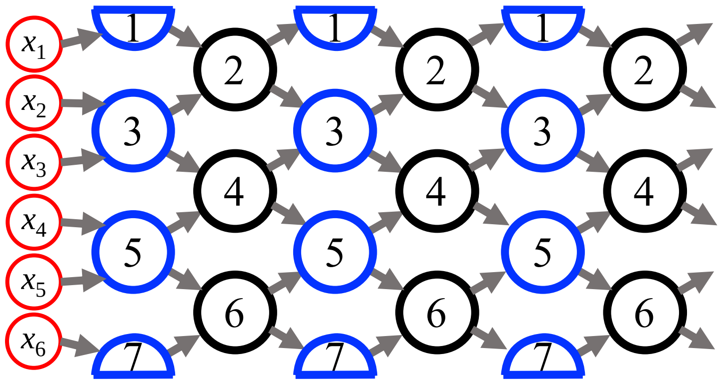
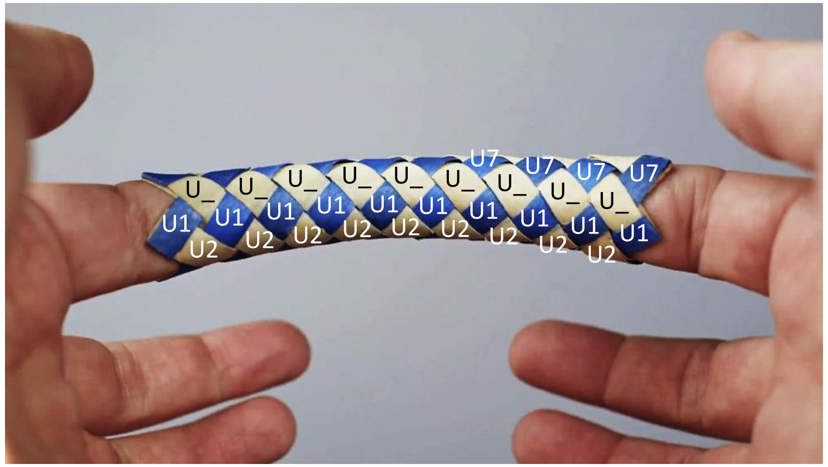
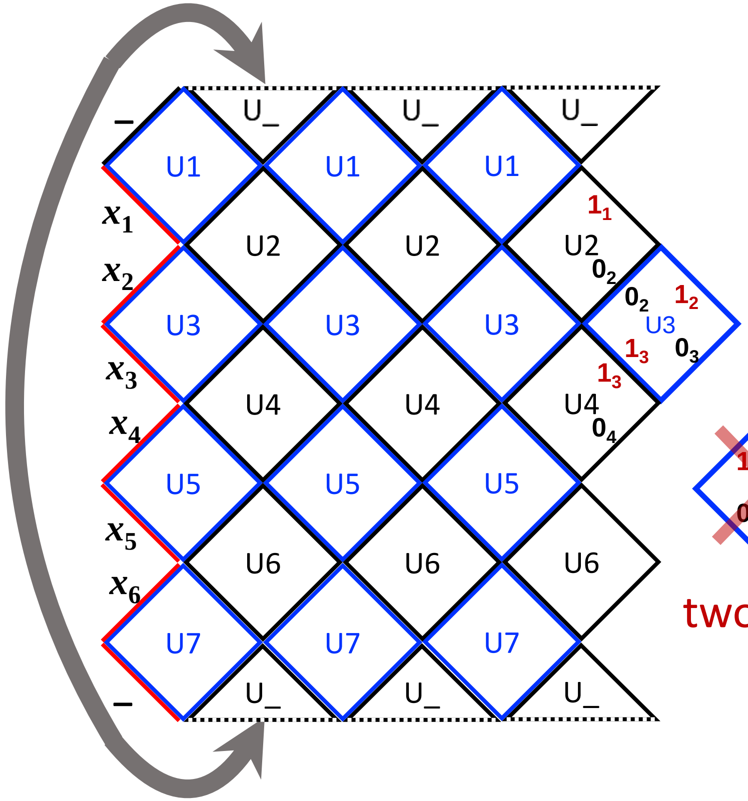




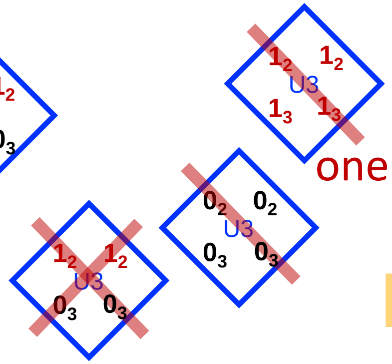
How tiles compute while growing (algorithmic self-assembly)







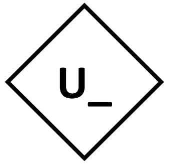
two glues match: *cooperative binding*



one mismatch

two mismatches

“data-free” tile wraps top to bottom to form a tube



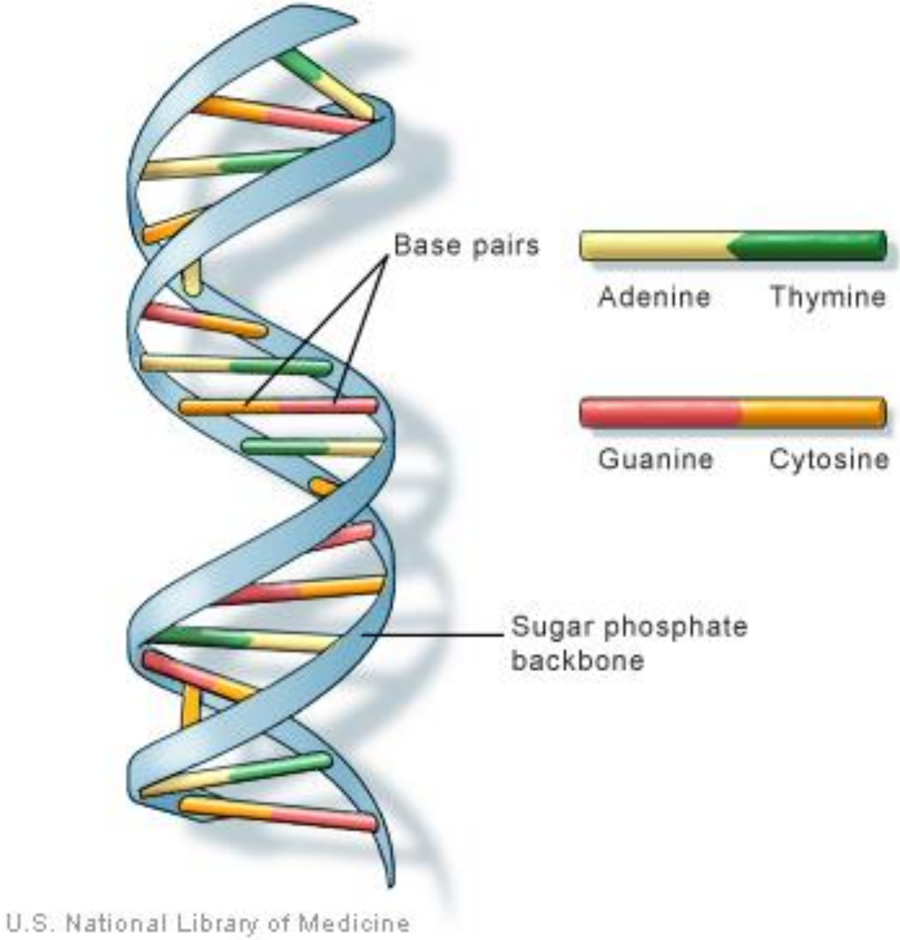
Hierarchy of abstractions

Bits:	Boolean circuits compute
Tiles:	Tile growth implements circuits
DNA:	**DNA strands implement tiles**

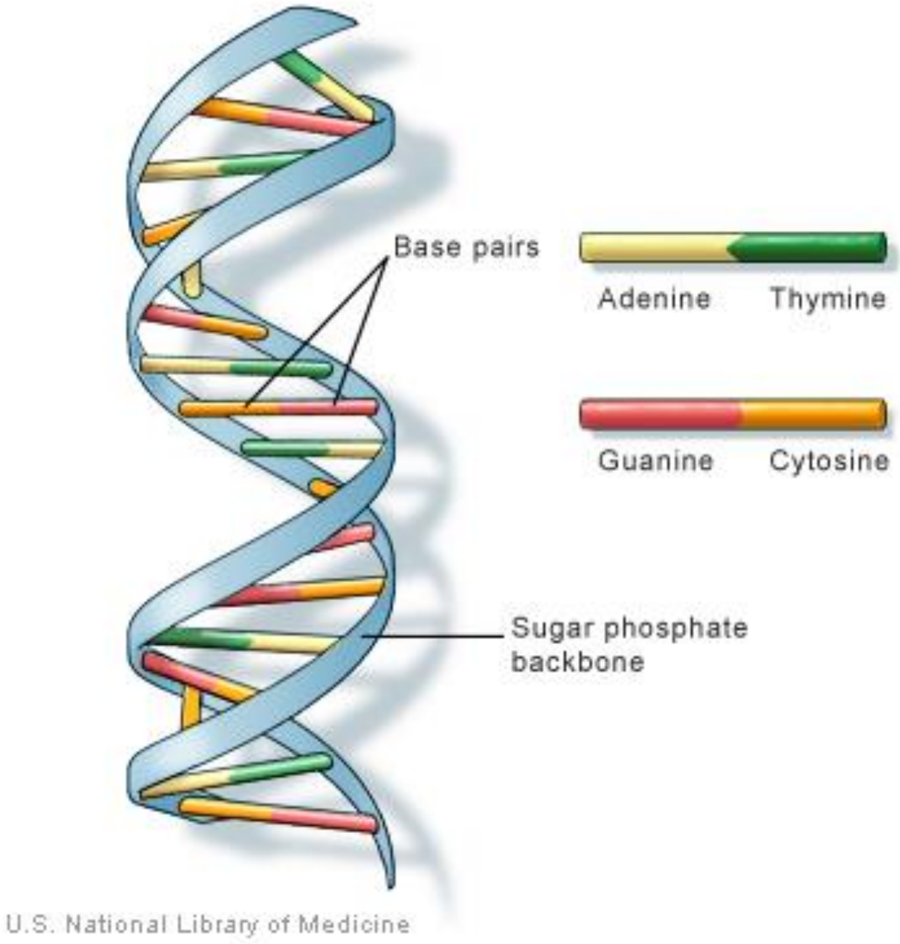
Structural DNA nanotechnology

a.k.a. DNA carpentry

DNA as a building material



DNA as a building material

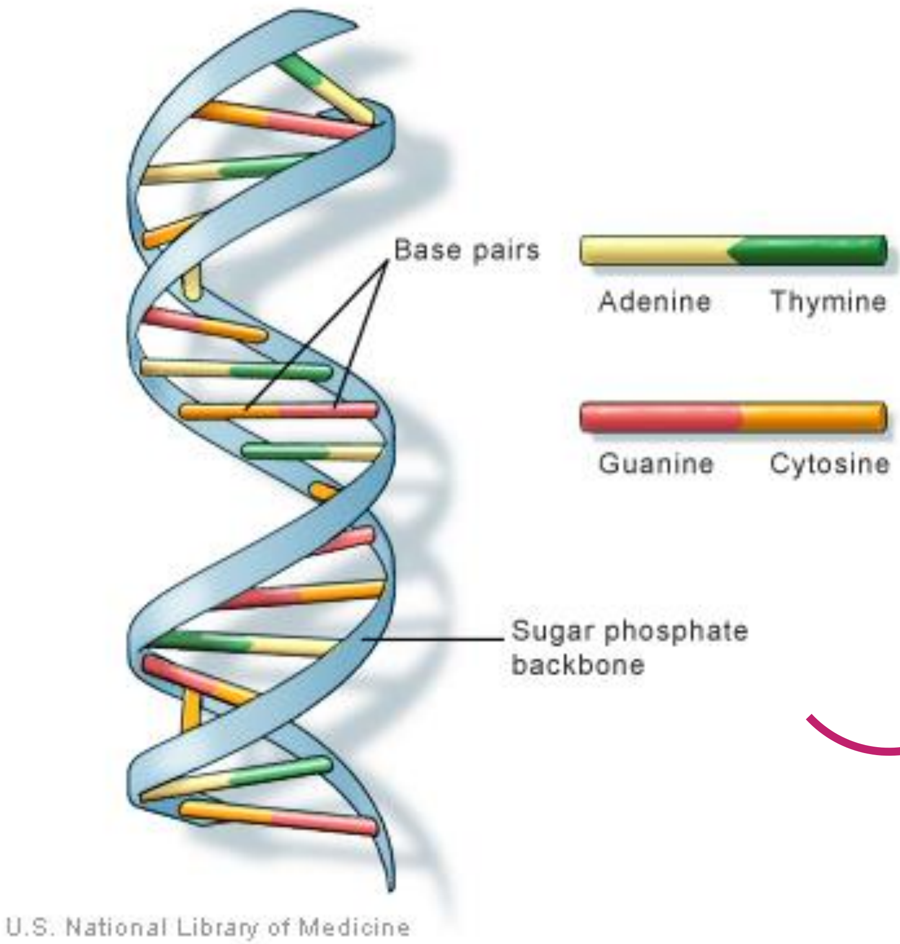


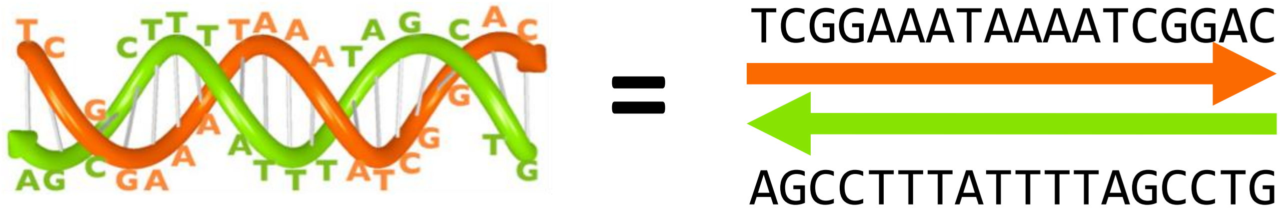
=

TCGGAAATAAAATCGGAC

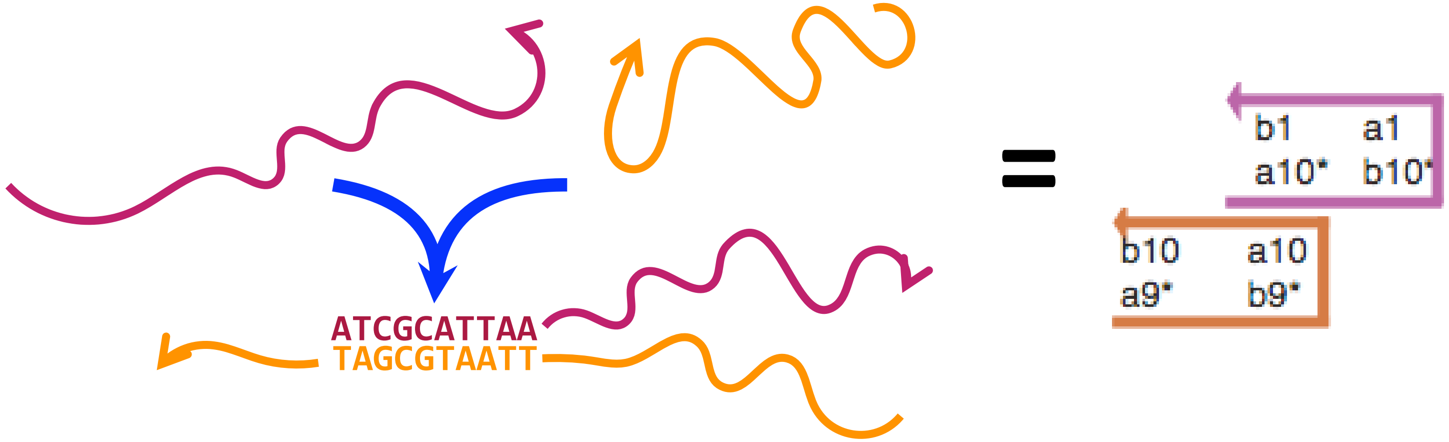
AGCCTTTATTTTAGCCTG

DNA as a building material





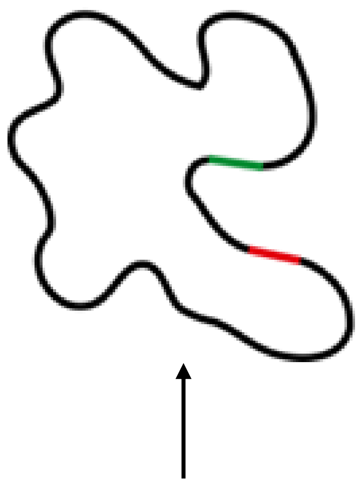
DNA strands can bind even if only part of strands are complementary:



DNA origami

Paul Rothemund
Folding DNA to create nanoscale shapes and patterns
Nature 2006

DNA origami



scaffold DNA strand

(M13mp18 bacteriophage virus)

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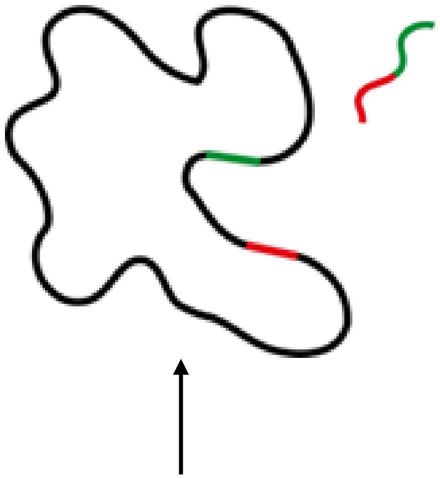
DNA origami



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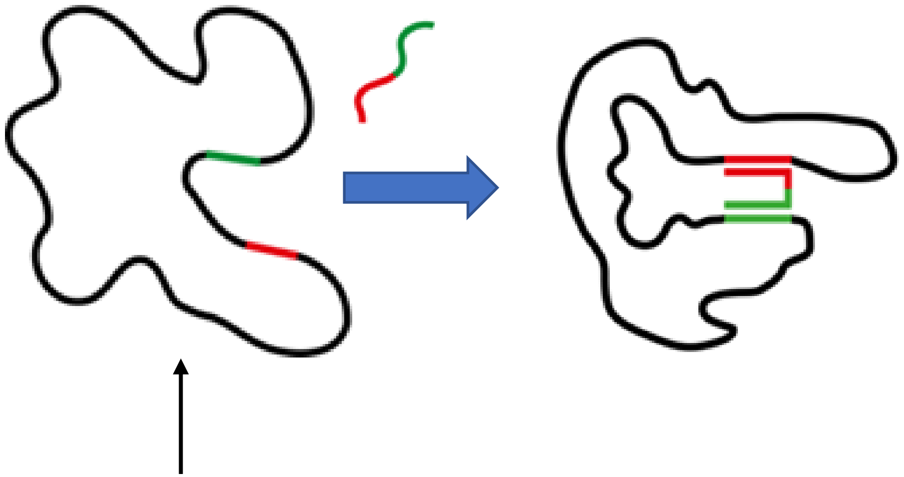

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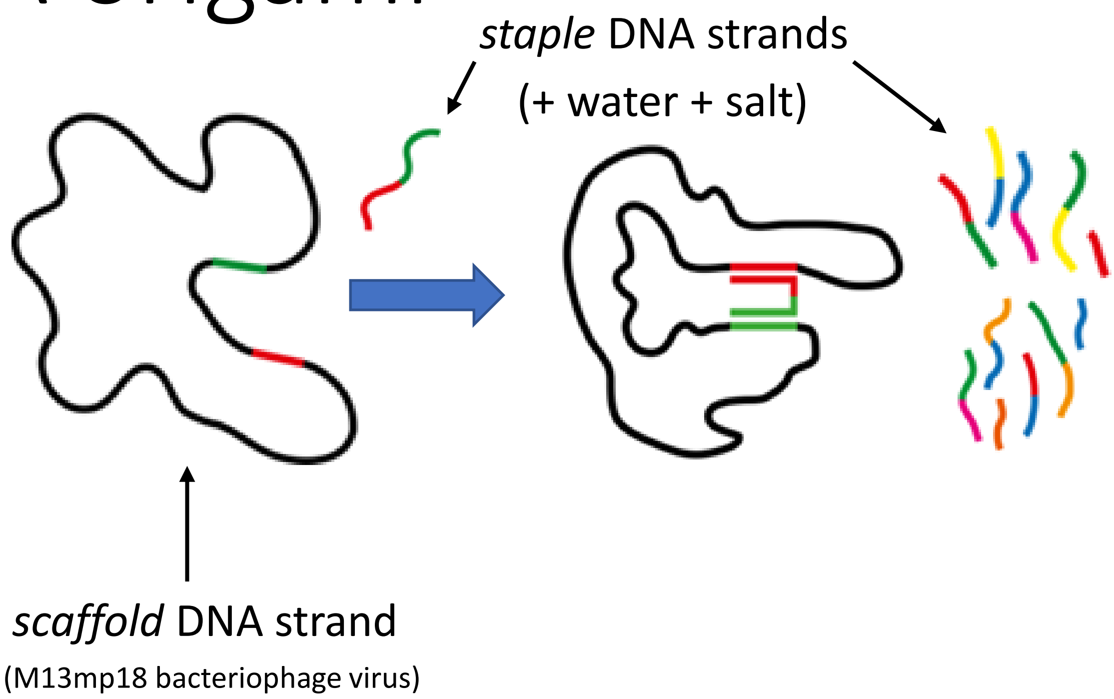

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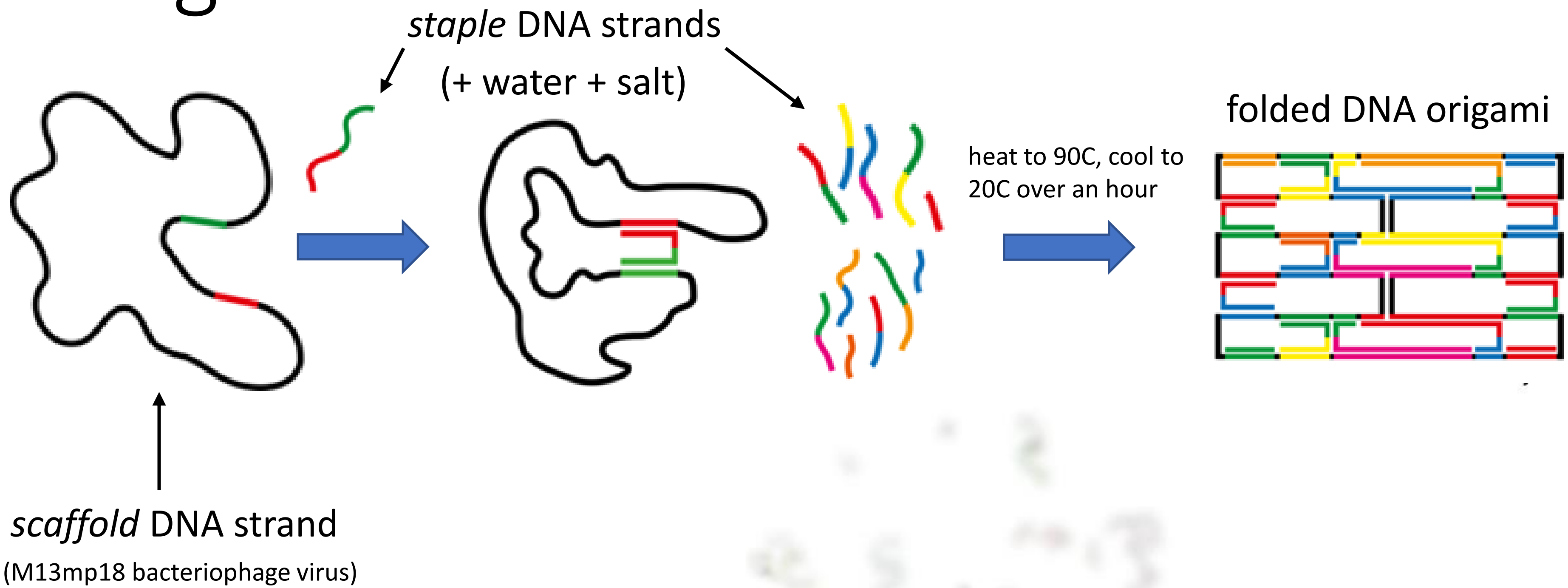
DNA origami



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DNA origami

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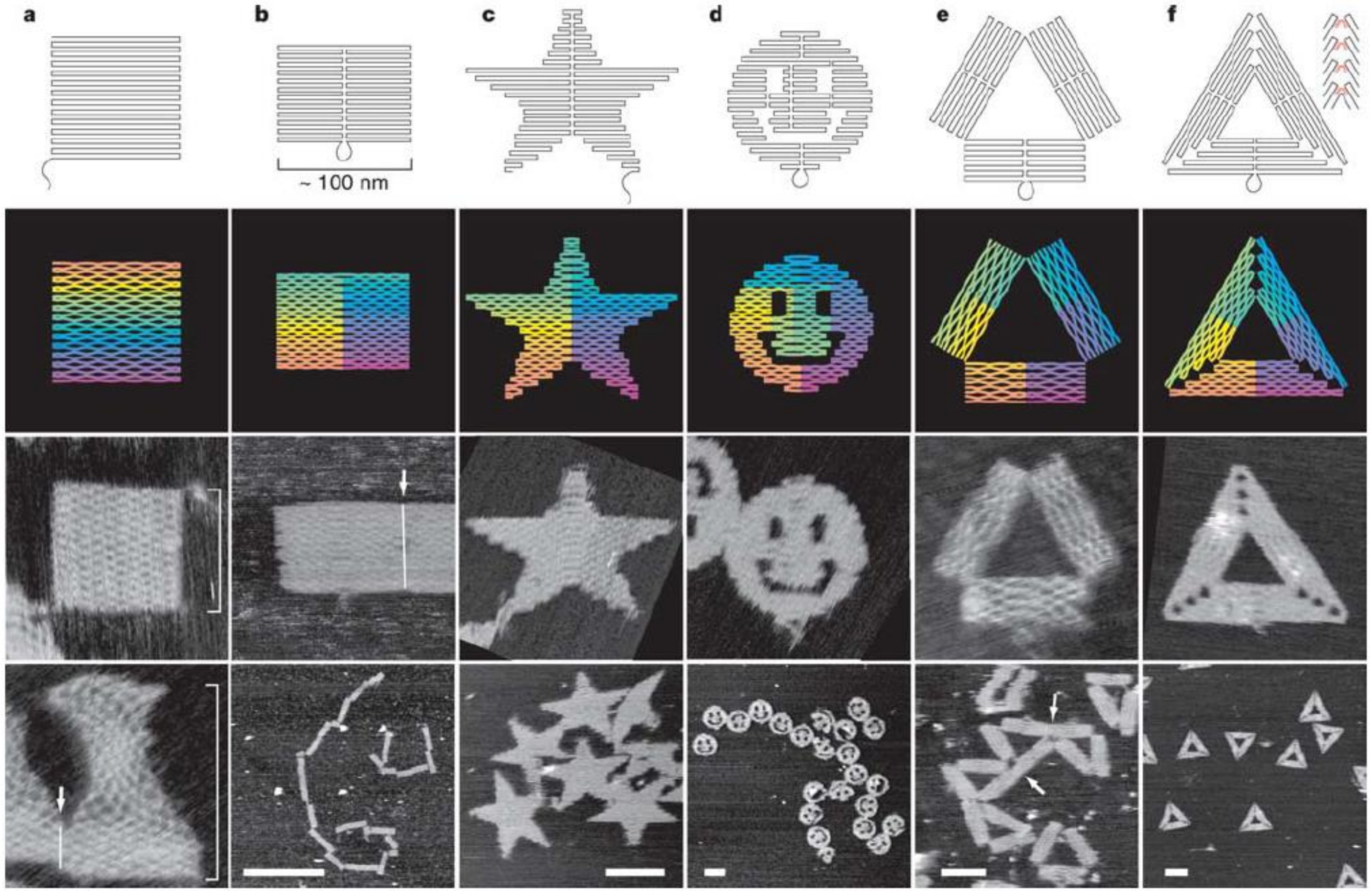
Nature 2006



Atomic force microscope images

100 nm

DNA nanotechnology applications

nonbiological:
- nanoscale resolution surface placement
- X-ray crystallization scaffolding
- molecular motors
- super-resolution imaging
- molecular circuits

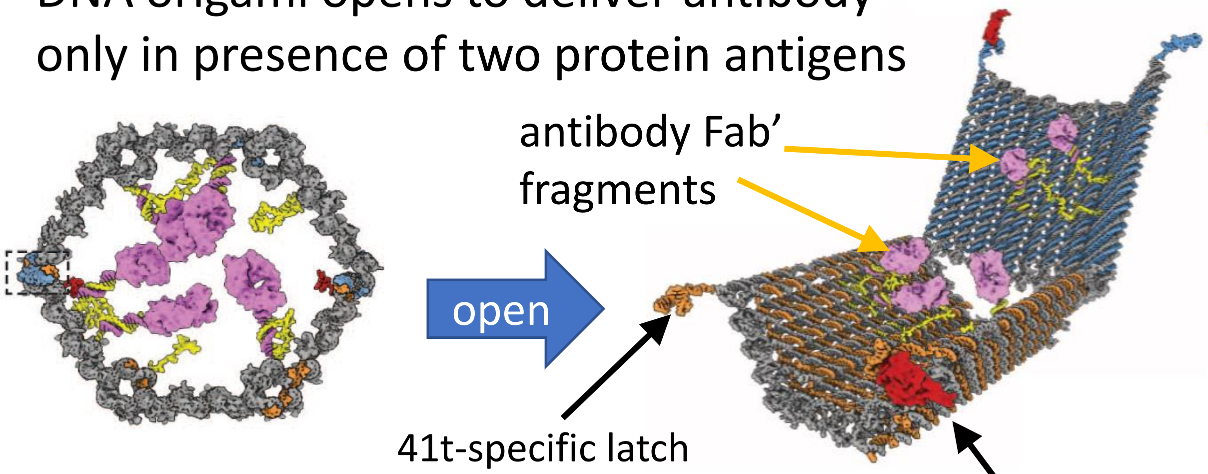
biological:
- smart drugs
- mRNA detection
- cell surface marker detection
- genetically encoded structures

DNA nanotechnology applications

nonbiological:
- nanoscale resolution surface placement
- X-ray crystallization scaffolding
- molecular motors
- super-resolution imaging
- molecular circuits

example

DNA origami opens to deliver antibody only in presence of two protein antigens

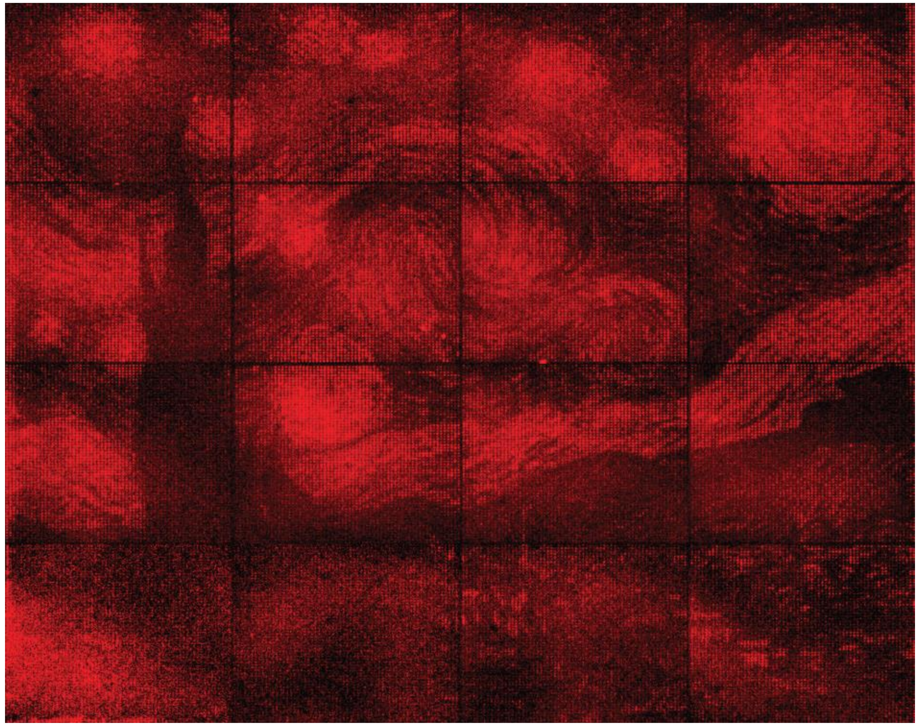


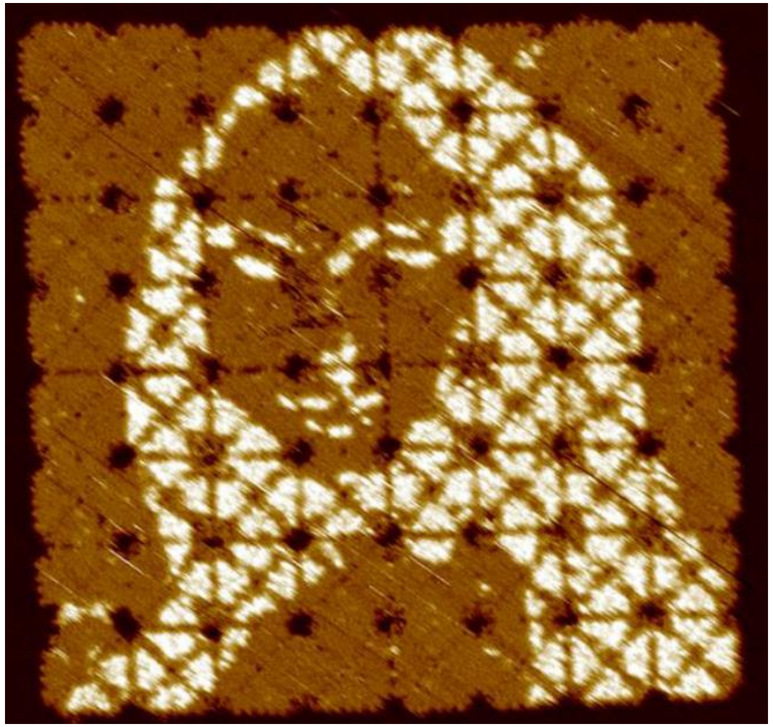
Shawn Douglas, Ido Bachelet, George Church. *A logic-gated nanorobot for targeted transport of molecular payloads*, <u>Science</u> 2012

biological:
- smart drugs
- mRNA detection
- cell surface marker detection
- genetically encoded structures

DNA nanotechnology applications

nonbiological:
- **art**



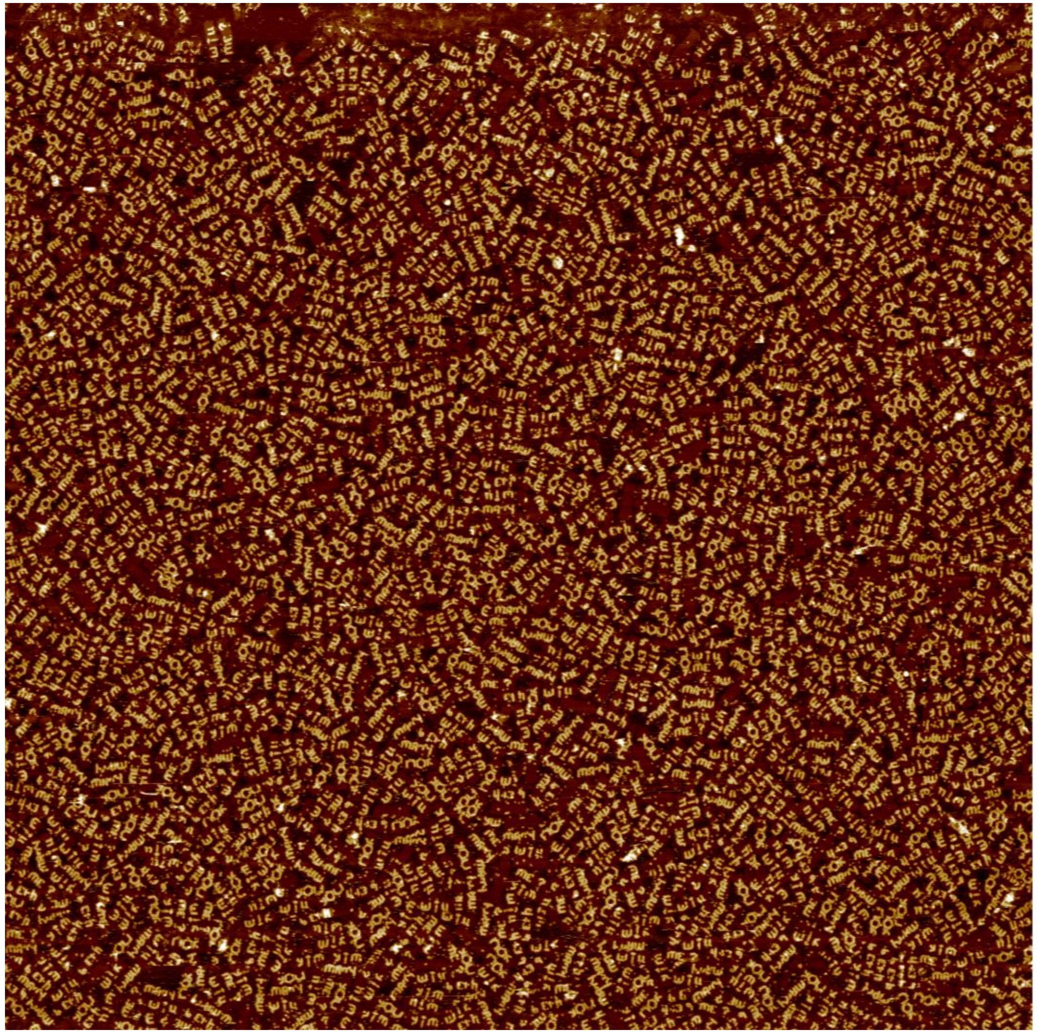


Ashwin Gopinath, Evan Miyazono, Andrei Faraon, Paul Rothemund. *Engineering and mapping nanocavity emission via precision placement of DNA origami*, Nature 2016

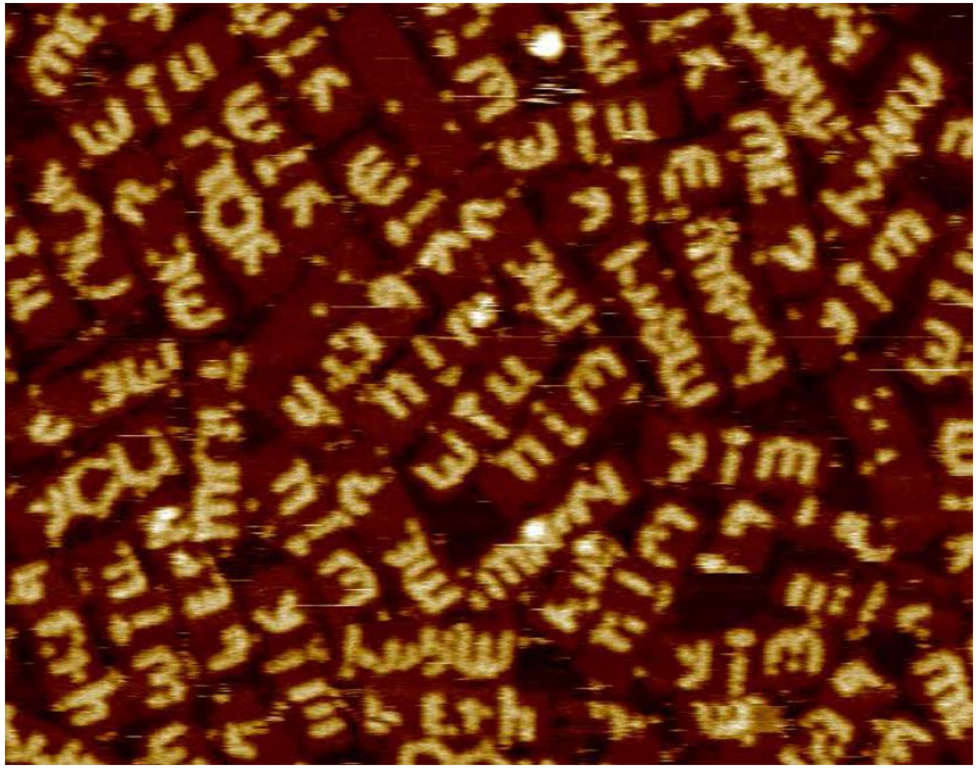
Grigory Tikhomirov, Philip Petersen, and Lulu Qian. *Fractal assembly of micrometre-scale DNA origami arrays with arbitrary patterns*. Nature 2017.

Other applications of DNA nanotechnology

4 μm wide scan

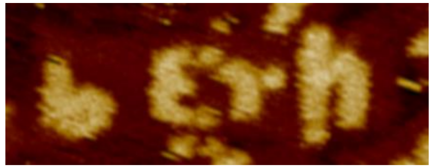


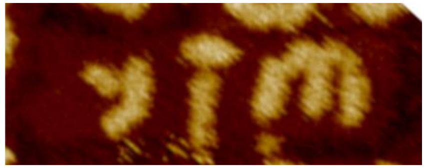
zoom in



A little proposal

100 nm





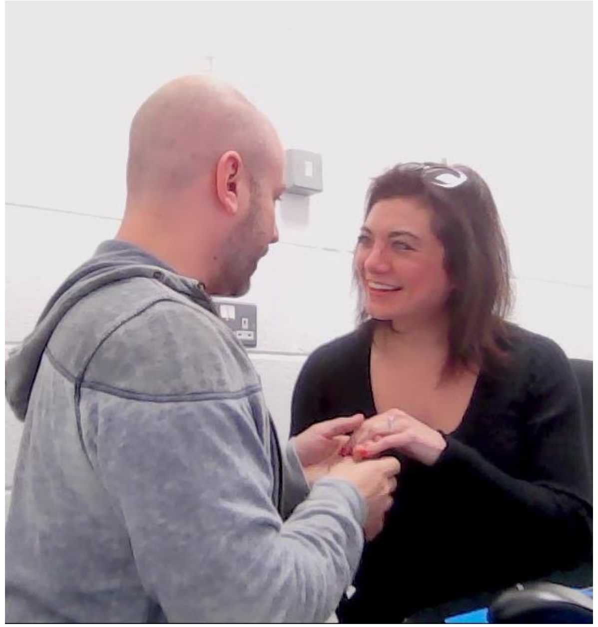
Beth Yim

A little proposal

Beth Yim

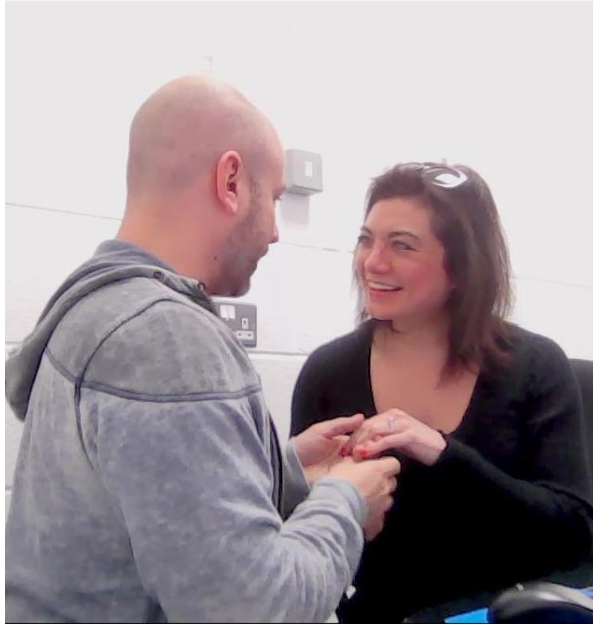
A little proposal

Beth Yim



A little proposal

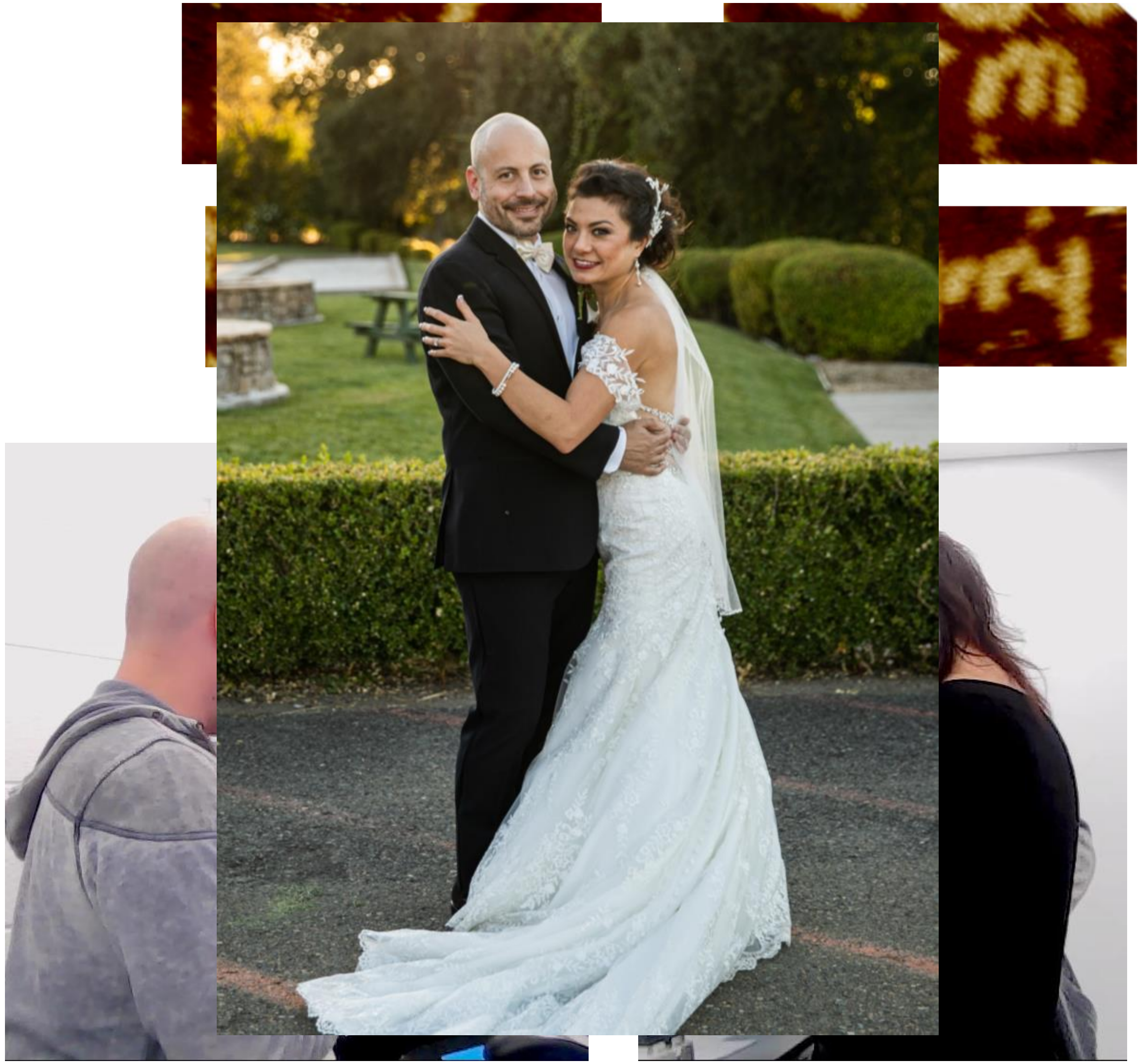
Beth Yim

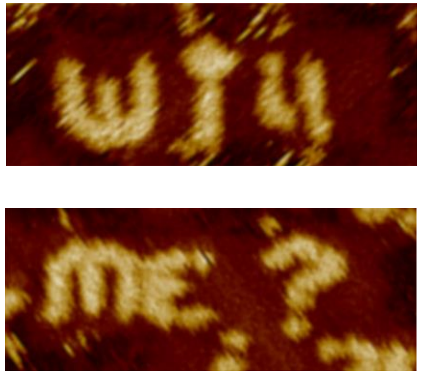


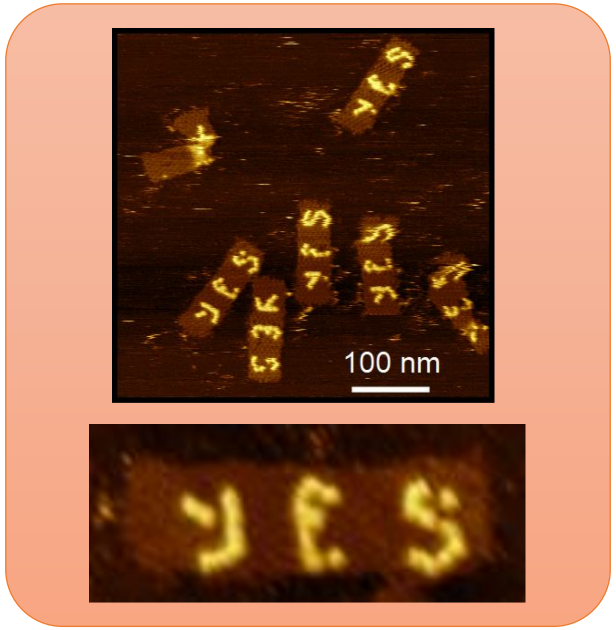
A little proposal and a little reply

100 nm

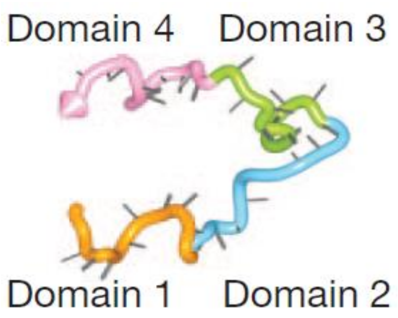
Beth Yim

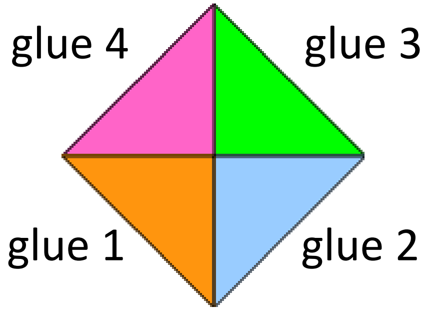


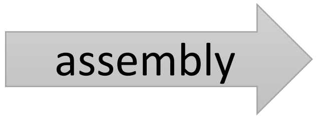


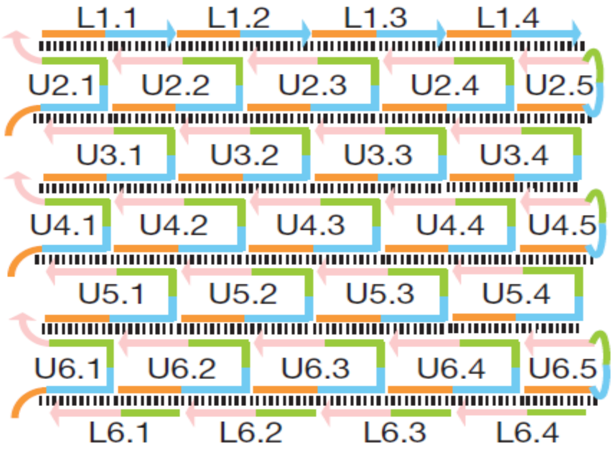


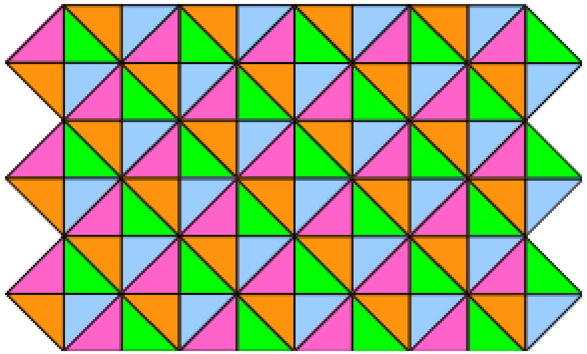
DNA single-stranded tiles





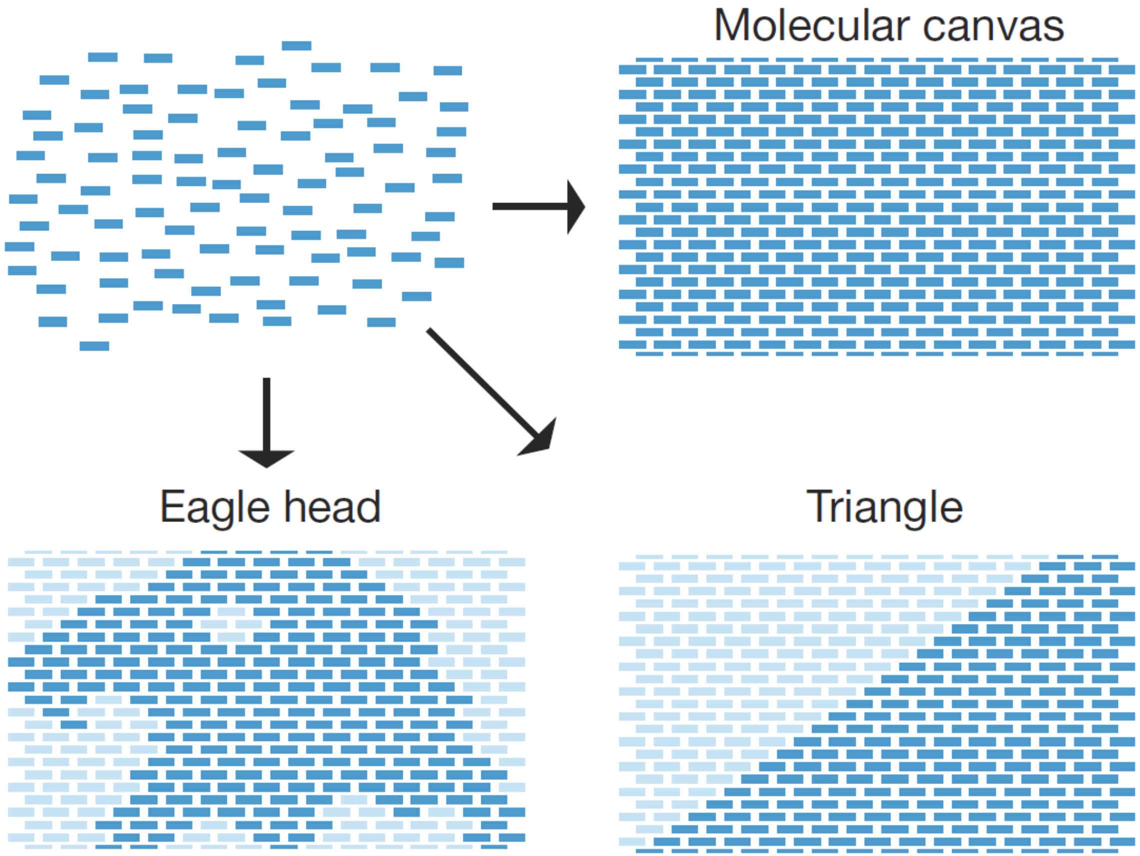






Yin, Hariadi, Sahu, Choi, Park, LaBean, and Reif.
Programming DNA tube circumferences.
Science 2008

Single-stranded tiles for making any shape



Bryan Wei, Mingjie Dai, and Peng Yin.
Complex shapes self-assembled from single-stranded DNA tiles.
Nature 2012.

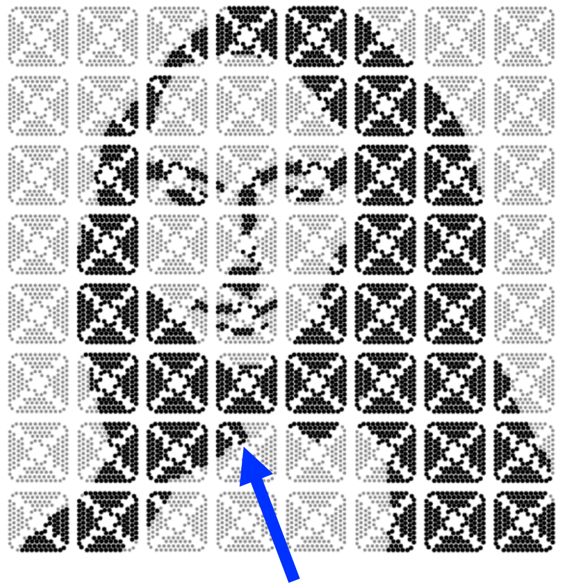
Uniquely addressed self-assembly versus algorithmic

Unique addressing: each DNA "monomer" appears **exactly once** in final structure.

single DNA origami

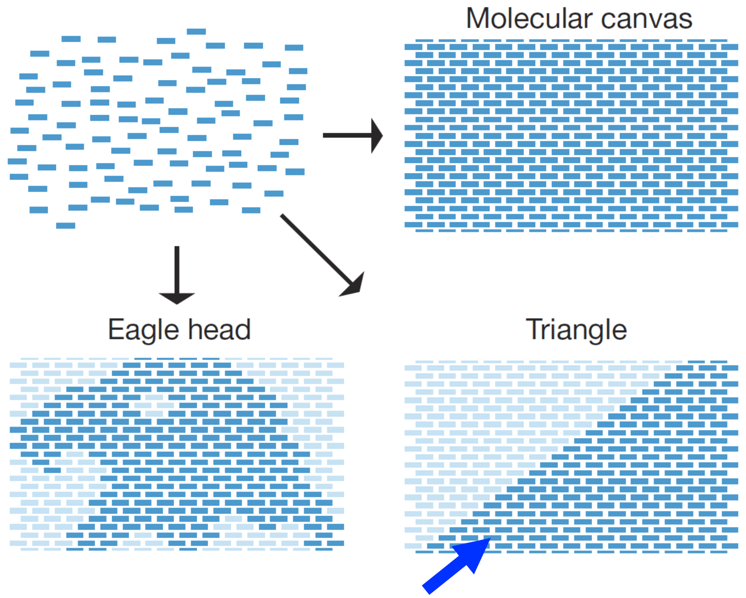
staple strand for position (4,2)

array of many DNA origamis



origami for position (4,2)

uniquely-addressed tiles



tile for position (4,2)

Uniquely addressed self-assembly versus algorithmic

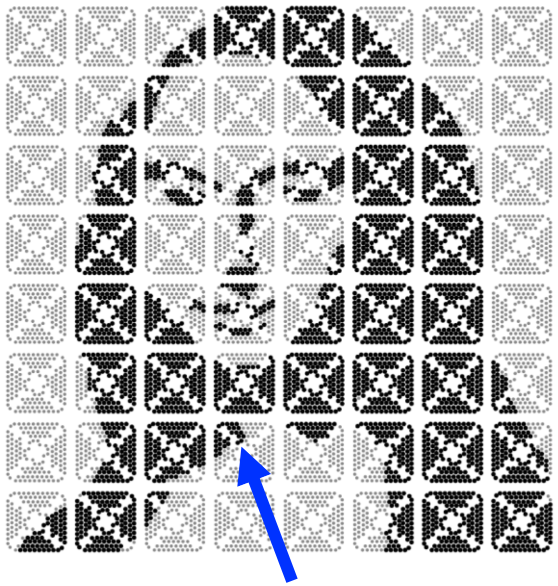
Unique addressing: each DNA “monomer” appears **exactly once** in final structure.

Algorithmic: DNA tiles are **reused** throughout the structure.

single DNA origami

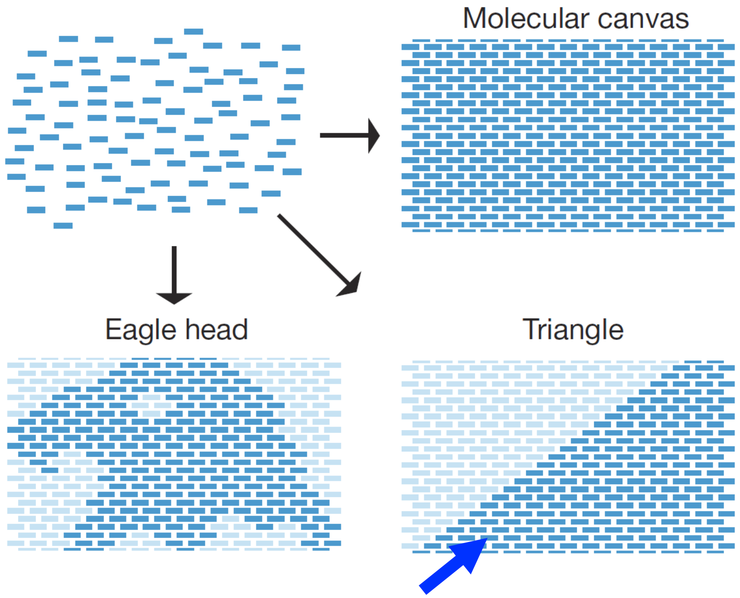
staple strand for position (4,2)

array of many DNA origamis



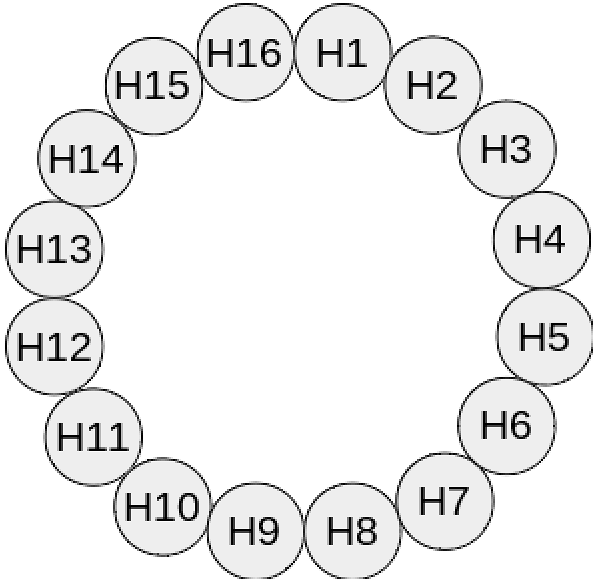
origami for position (4,2)

uniquely-addressed tiles

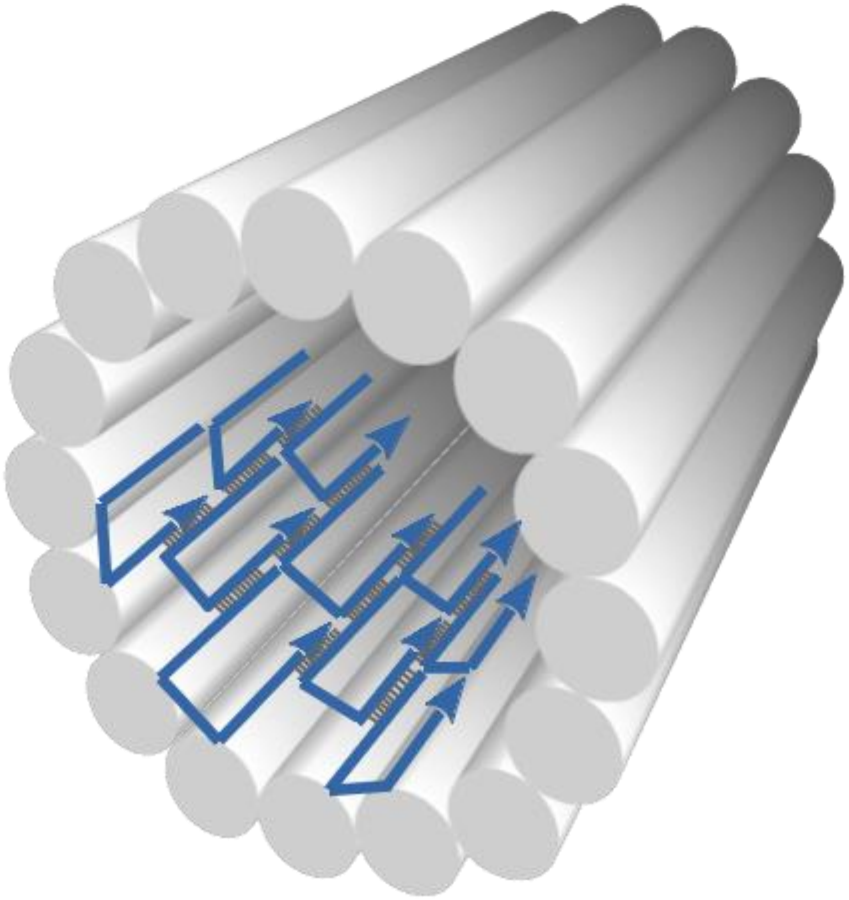


tile for position (4,2)

Single-stranded tile tubes

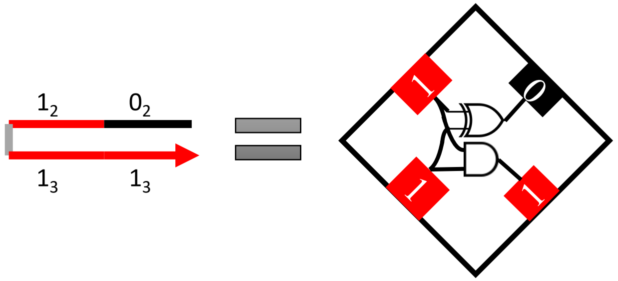


DNA-level diagram of 20-helix tube

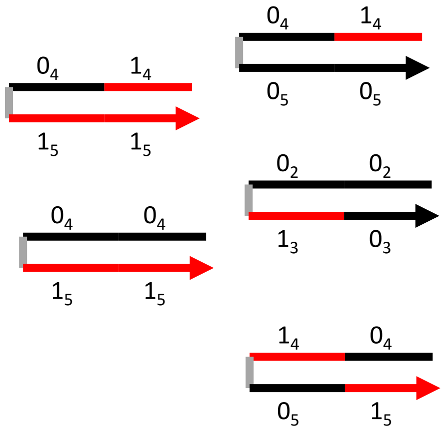


Yin, Hariadi, Sahu, Choi, Park, LaBean, and Reif. *Programming DNA tube circumferences*, Science 2008.

Seeded growth

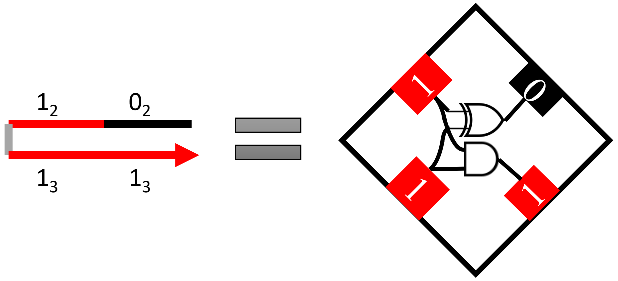


single-stranded tiles
implementing circuit gates

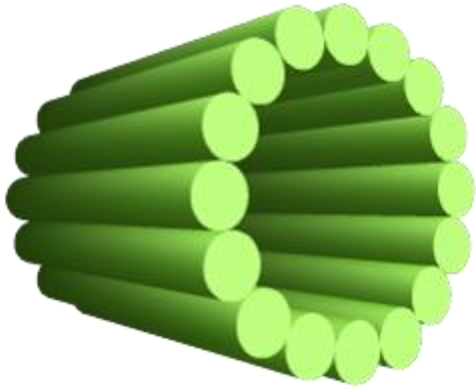


need barrier to <u>nucleation</u>
(tile growth without seed);
[tile]=100 nM;
temperature=50.9° C

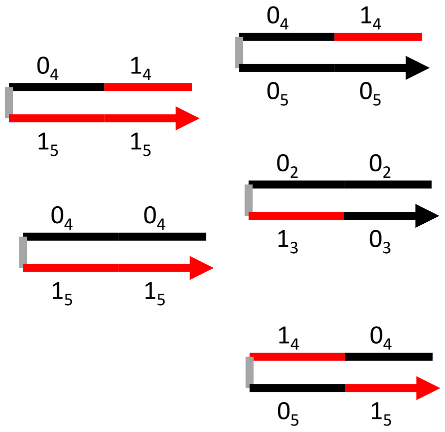
Seeded growth



DNA origami seed



single-stranded tiles
implementing circuit gates



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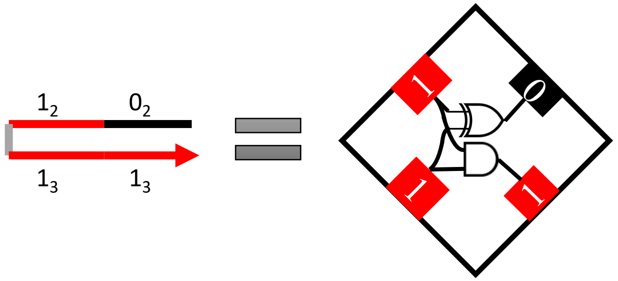
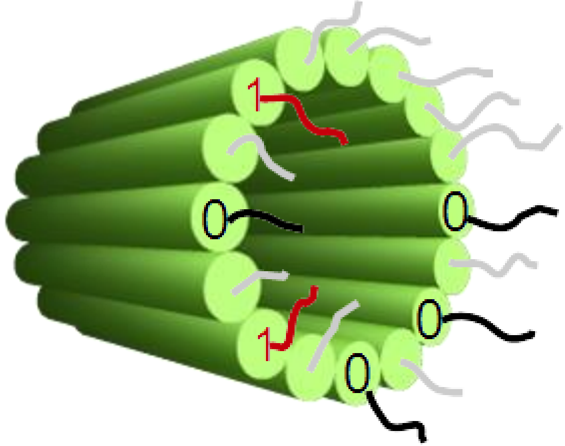
Seeded growth

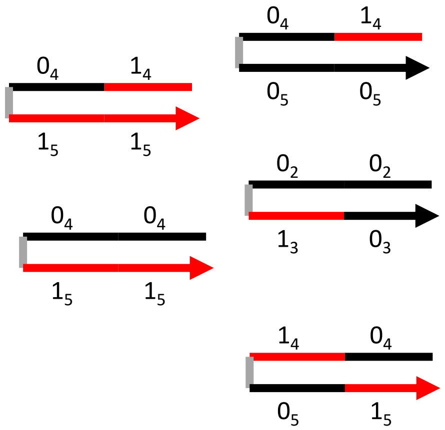


DNA origami seed

single-stranded “input-adapter” extensions encoding 6 input bits



single-stranded tiles implementing circuit gates



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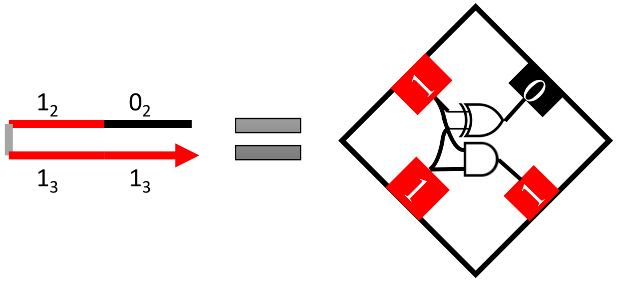
Seeded growth



DNA origami seed

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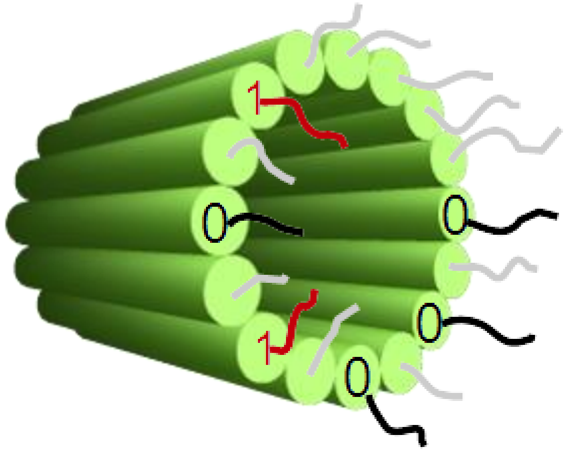
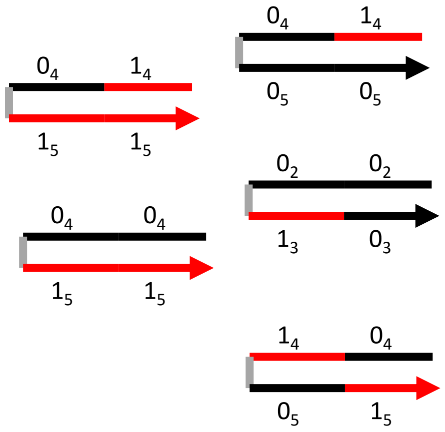
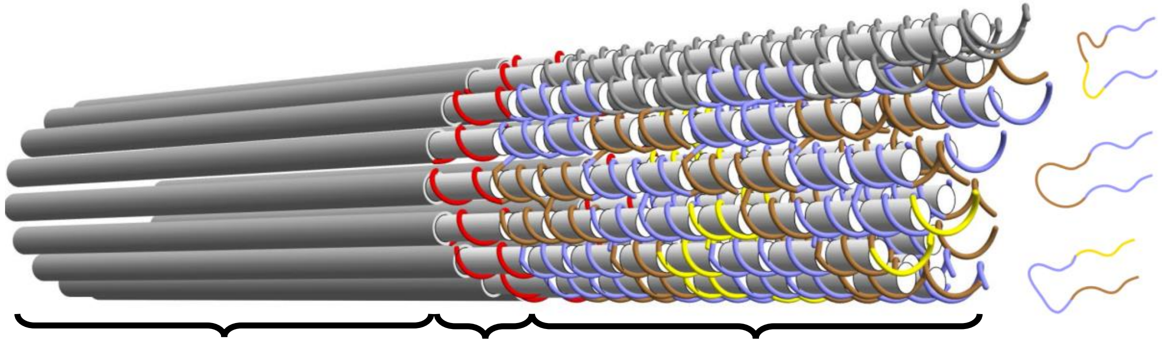


single-stranded tiles
implementing circuit gates



need barrier to <u>nucleation</u>
(tile growth without seed);
[tile]=100 nM;
temperature=50.9° C

hold 8-48 hours

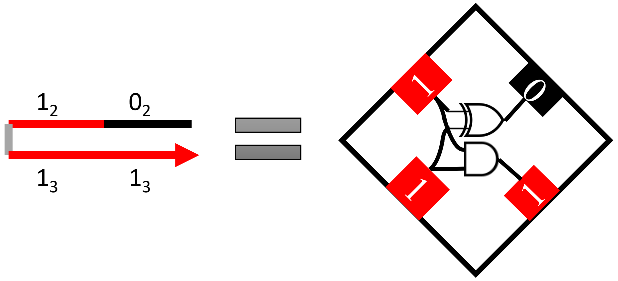


seed

input-
adapters

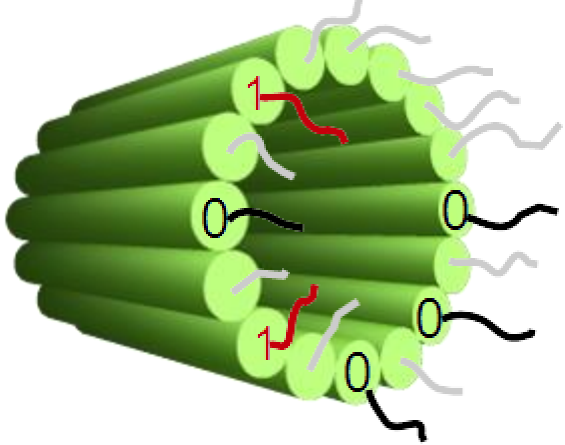
growing
tiles

Seeded growth

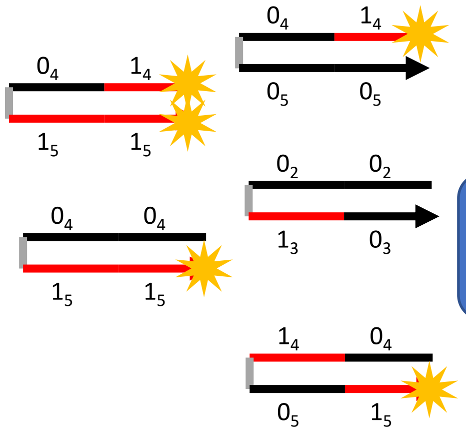


DNA origami seed

single-stranded “input-adapter” extensions encoding 6 input bits



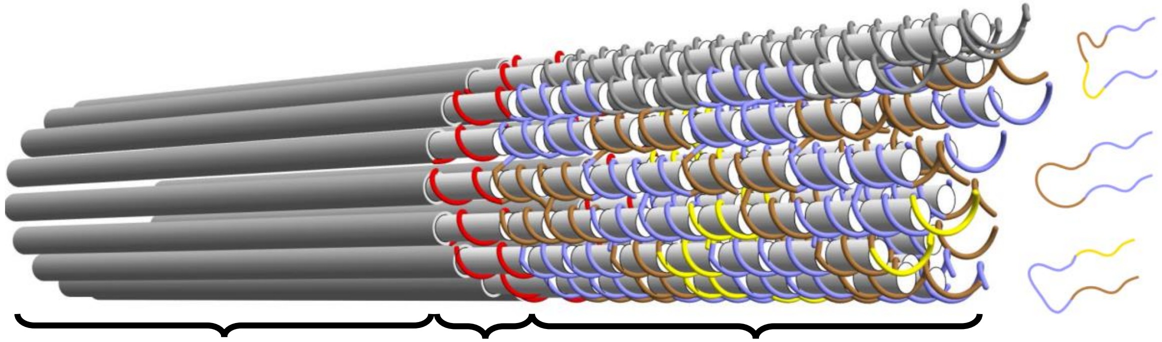
single-stranded tiles implementing circuit gates



biotins where output = 1

need barrier to <u>nucleation</u> (tile growth without seed); [tile]=100 nM; temperature=50.9° C

hold 8-48 hours

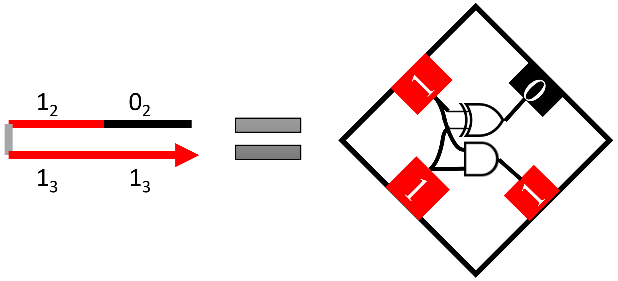


seed

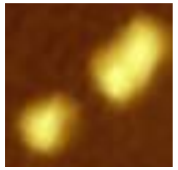
input-adapters

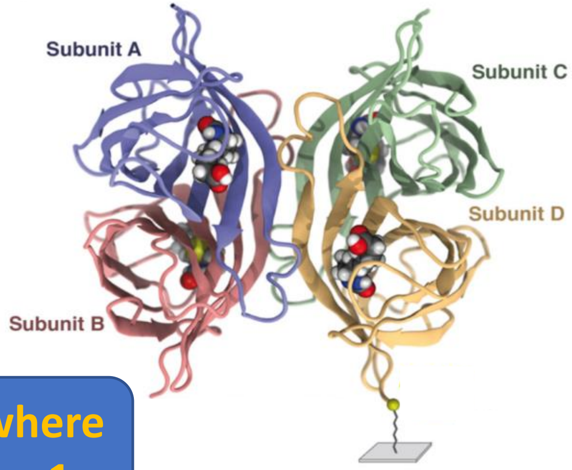
growing tiles

Seeded growth



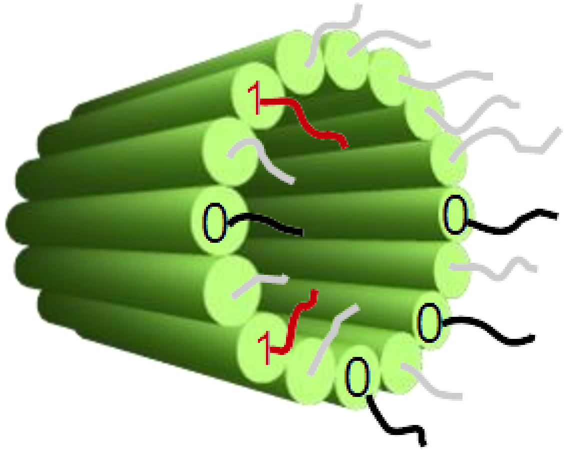
can later add streptavidin (5 nm wide protein) to bind biotins and visualize where the 1's are



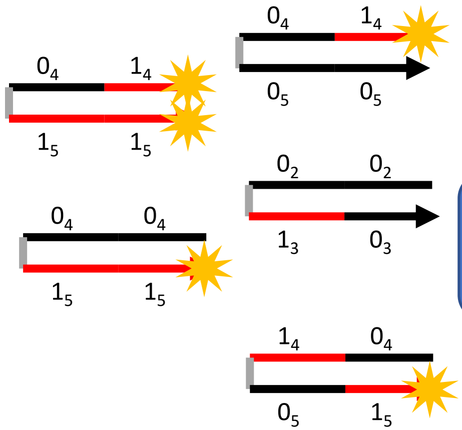


DNA origami seed

single-stranded "input-adapter" extensions encoding 6 input bits



single-stranded tiles implementing circuit gates



biotins where output = 1

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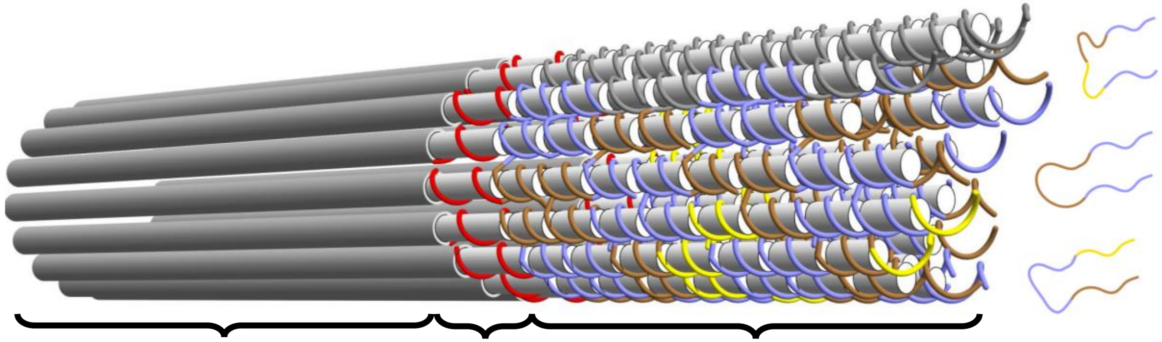
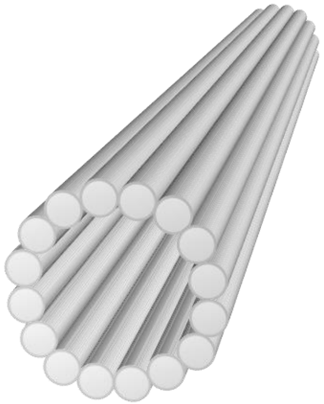
hold 8-48 hours

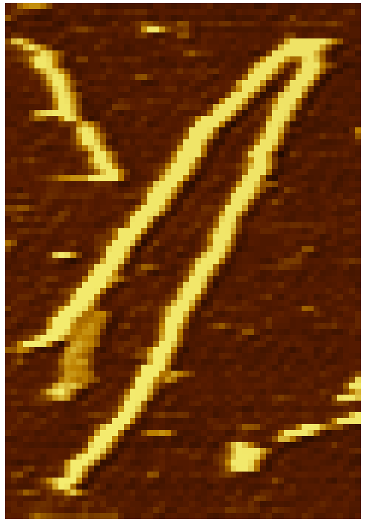


Tubes to ribbons

tube



AFM
image

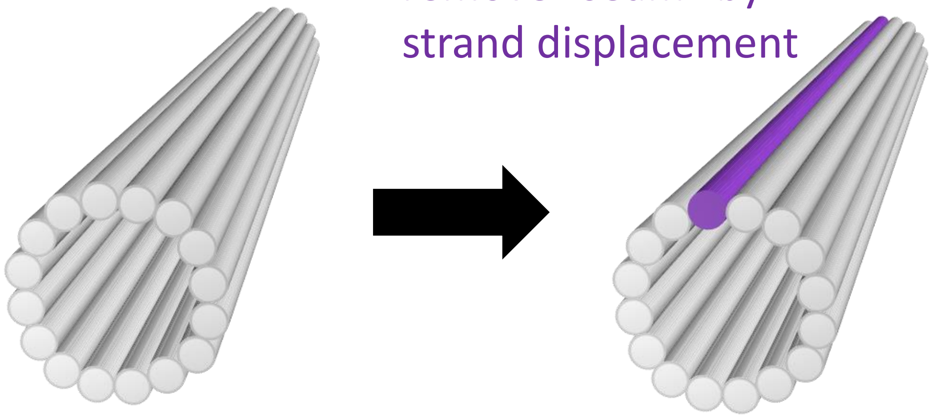


500 nm

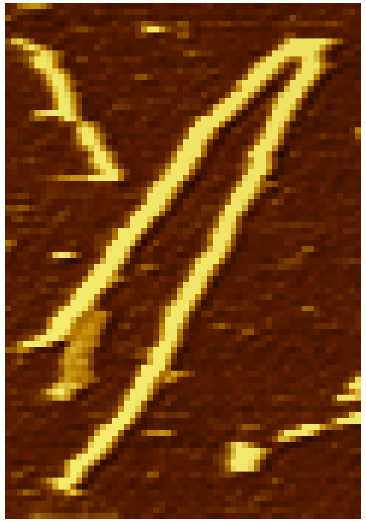
Tubes to ribbons

tube

remove “seam” by strand displacement

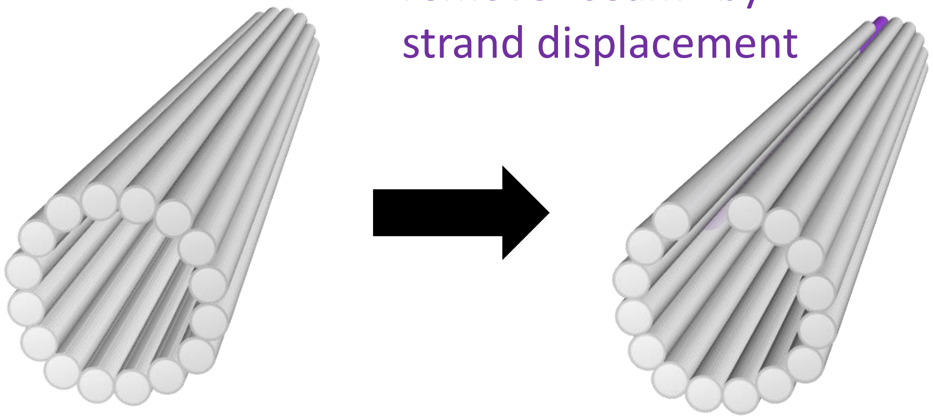


AFM image

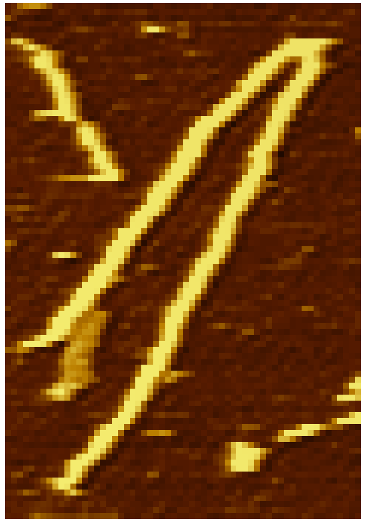


500 nm

Tubes to ribbons

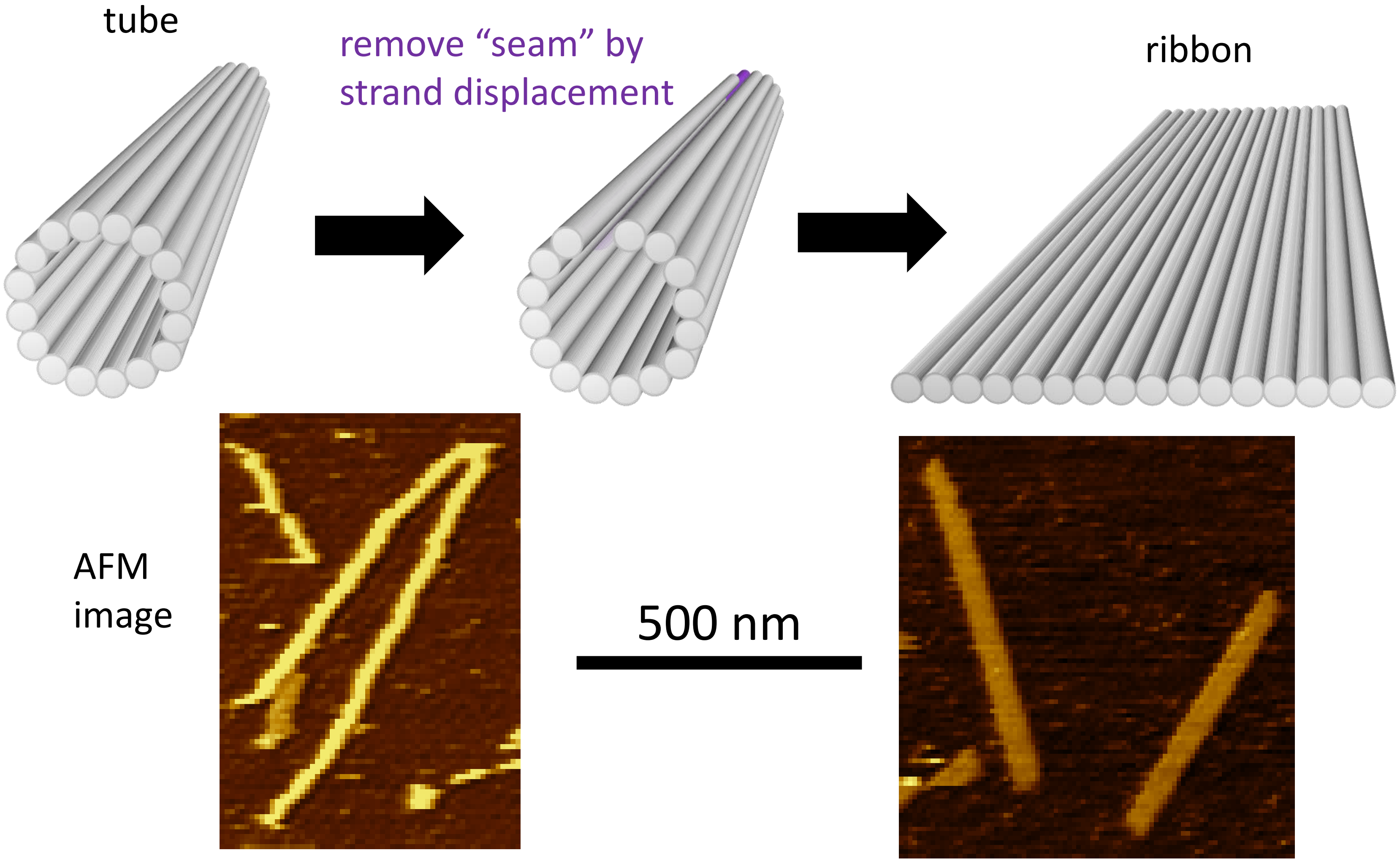


AFM
image

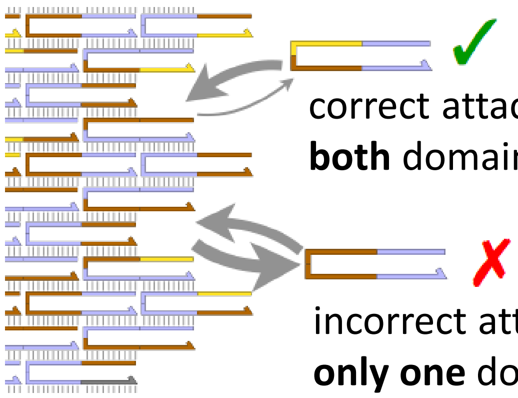


500 nm

Tubes to ribbons



DNA sequence design

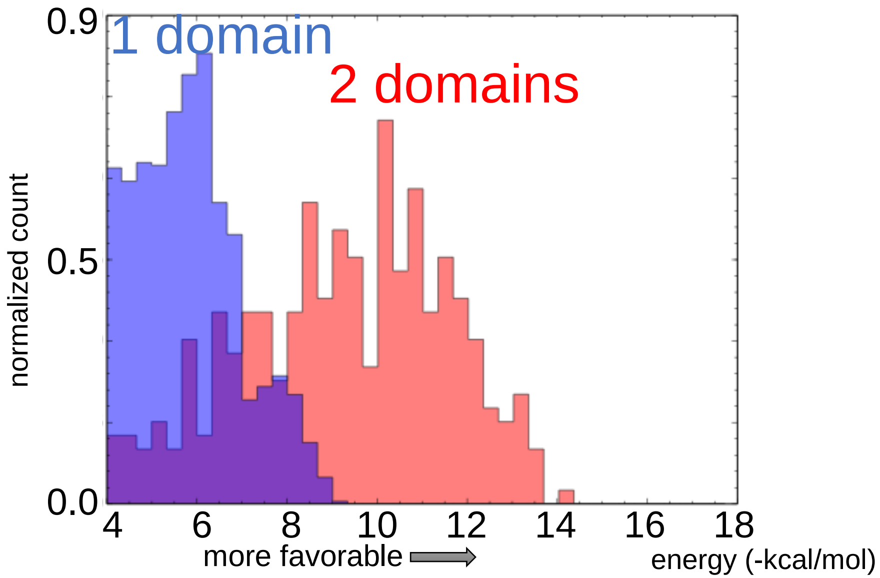


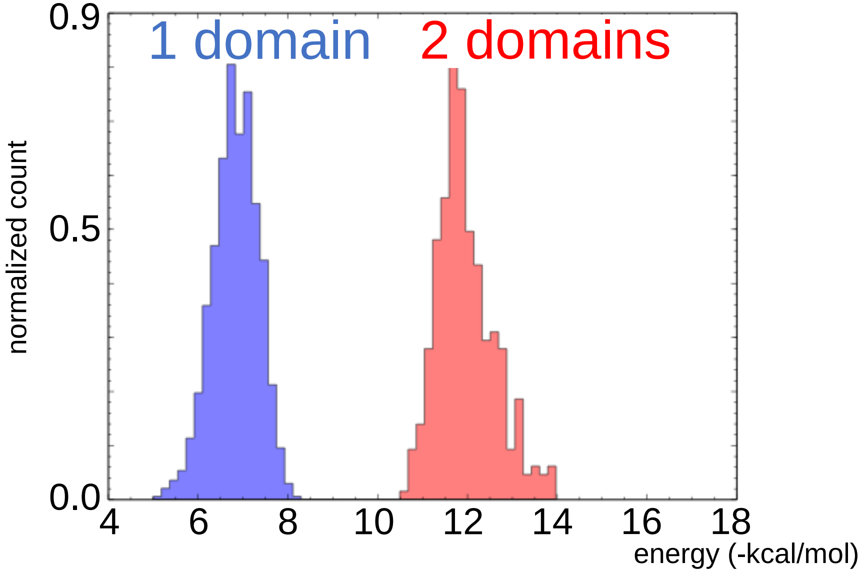
correct attachment:
both domains match

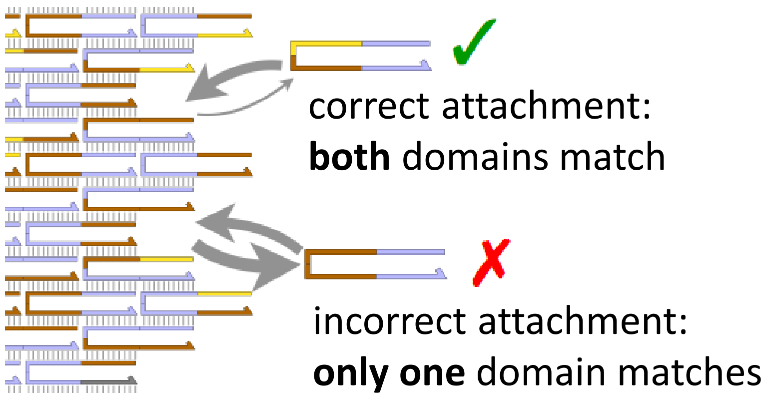
incorrect attachment:
only one domain matches

DNA sequence design

Random sequences vs designed sequences







DNA sequence design

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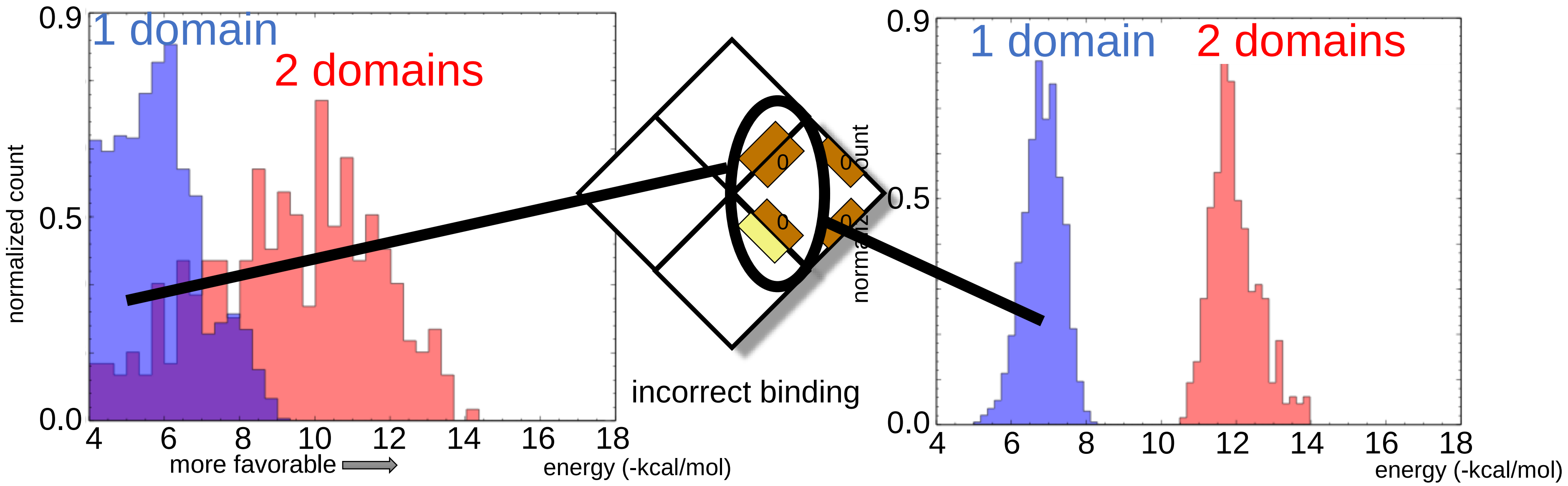

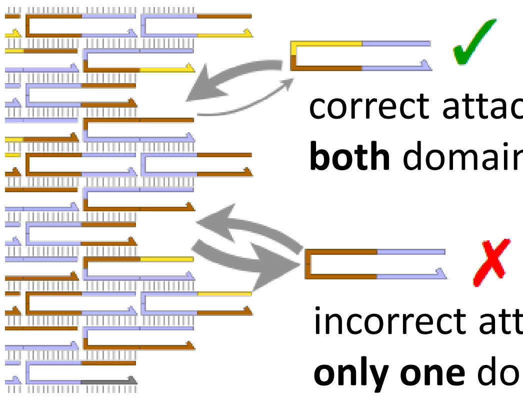

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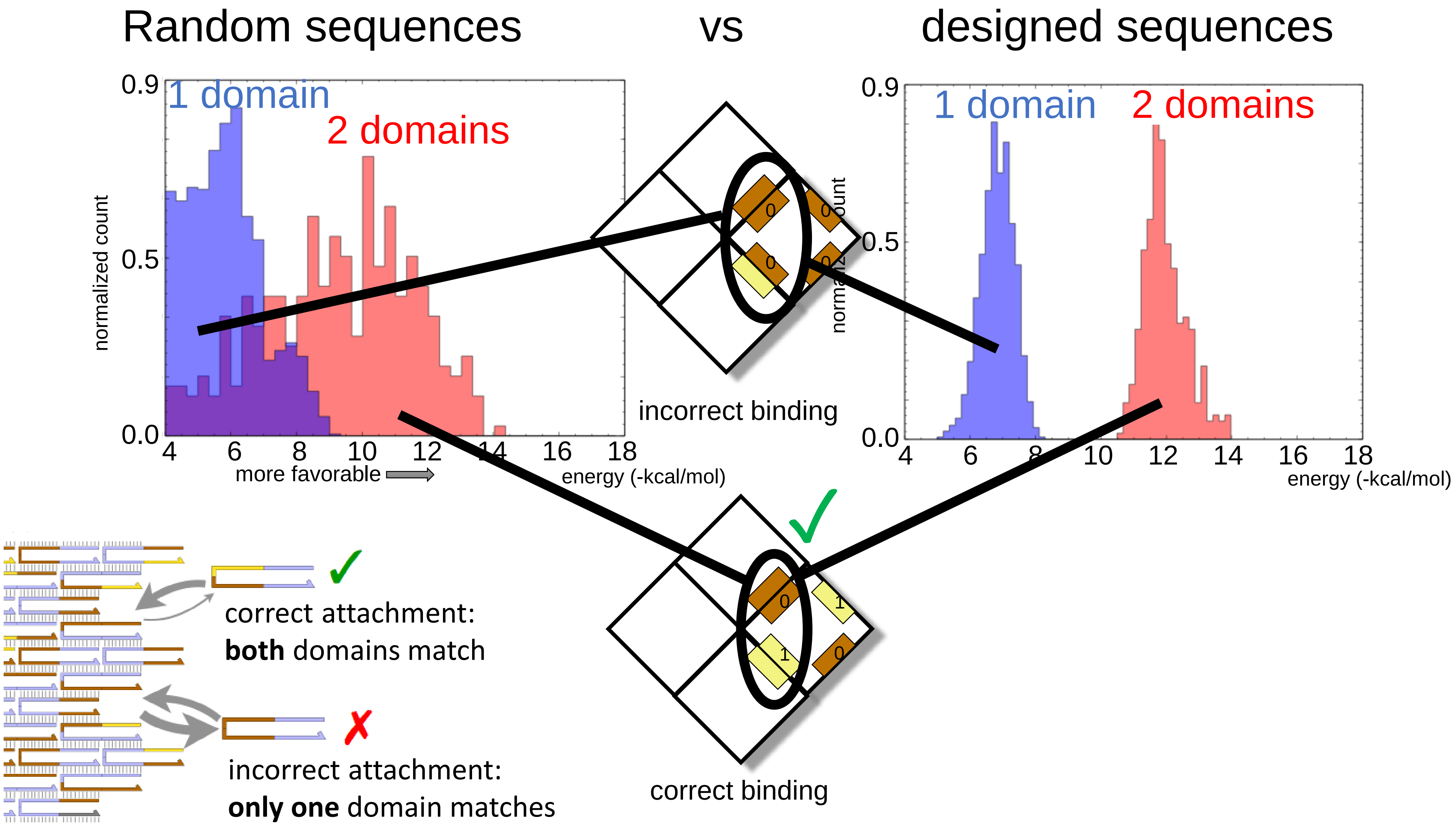
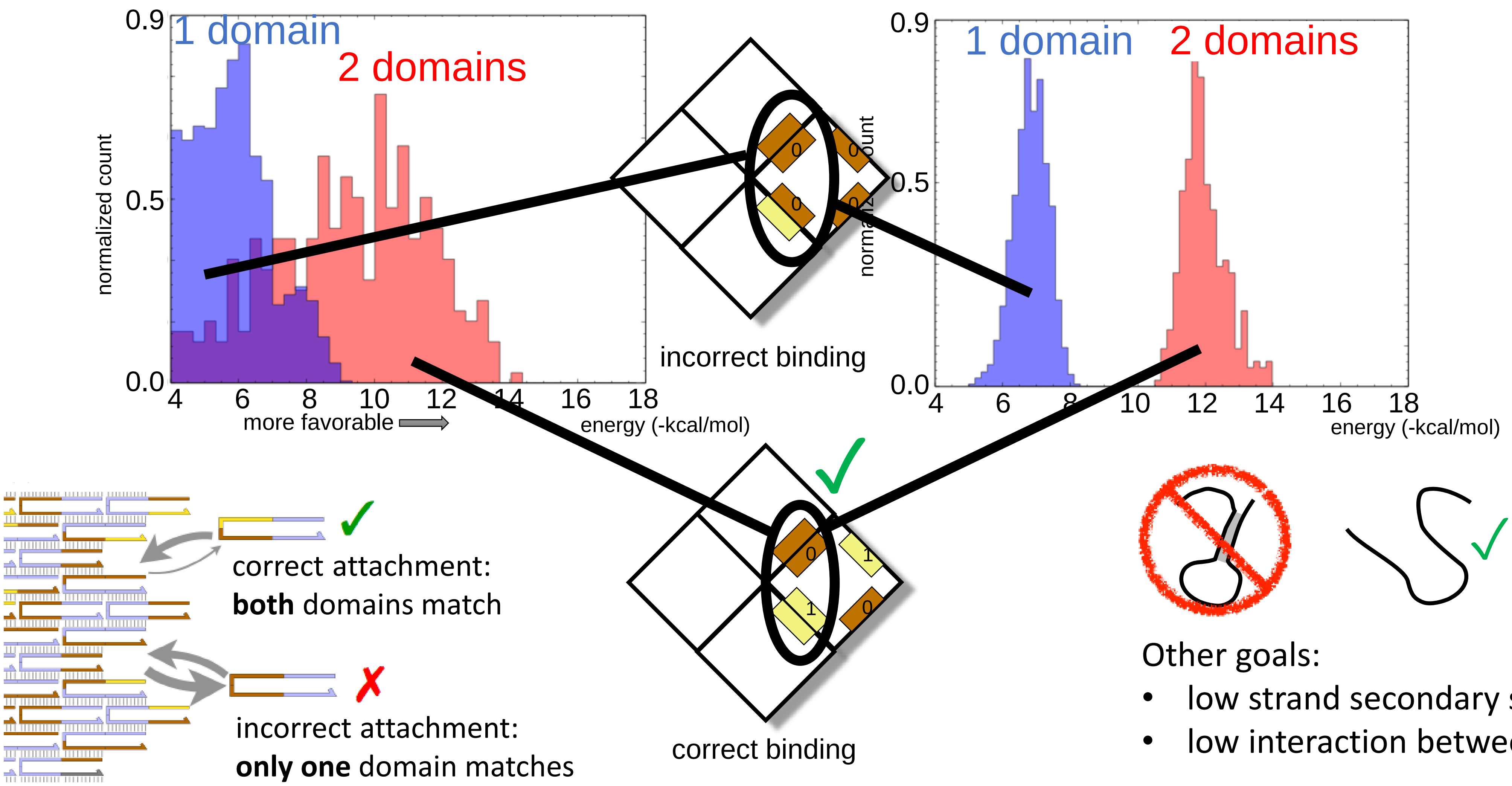


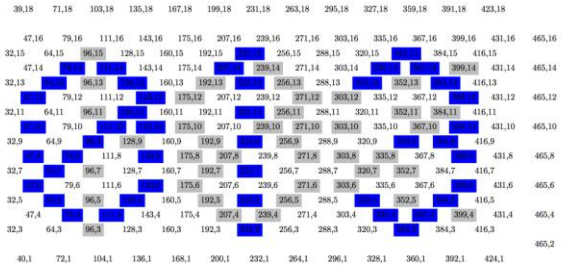
DNA sequence design



Other goals:

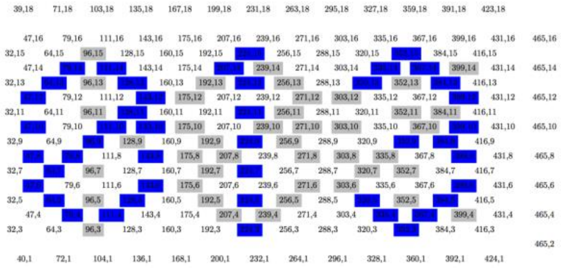
- low strand secondary structure
- low interaction between strands

Bar-coding origami seed for imaging multiple samples at once



some staples of origami seed
have version with a biotin

Bar-coding origami seed for imaging multiple samples at once

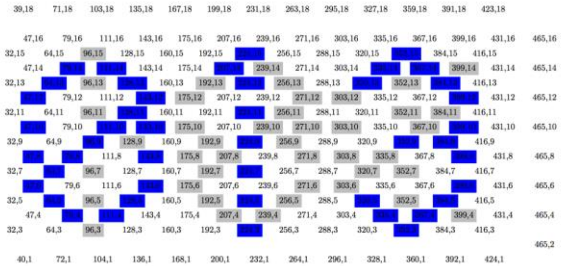


some staples of origami seed have version with a biotin

Generate plate map

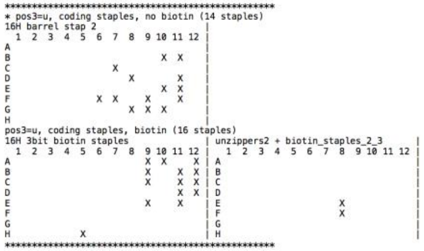
```
**************************************************
* pos3=u, coding staples, no biotin (14 staples)
16H barrel stap 2                    |
  1  2  3  4  5  6  7  8  9 10 11 12 |
A                                    |
B                            X  X    |
C                   X                |
D                      X        X    |
E                            X  X    |
F                X  X     X     X    |
G                      X  X  X       |
H                                    |
pos3=u, coding staples, biotin (16 staples)
16H 3bit biotin staples              | unzippers2 + biotin_staples_2_3     |
  1  2  3  4  5  6  7  8  9 10 11 12 |   1  2  3  4  5  6  7  8  9 10 11 12 |
A                         X  X     X | A                                    |
B                         X     X  X | B                                    |
C                         X     X  X | C                                    |
D                               X  X | D                                    |
E                         X     X    | E                      X             |
F                                    | F                      X             |
G                                    | G                                    |
H             X                      | H                                    |
**************************************************
```

Bar-coding origami seed for imaging multiple samples at once



some staples of origami seed have version with a biotin

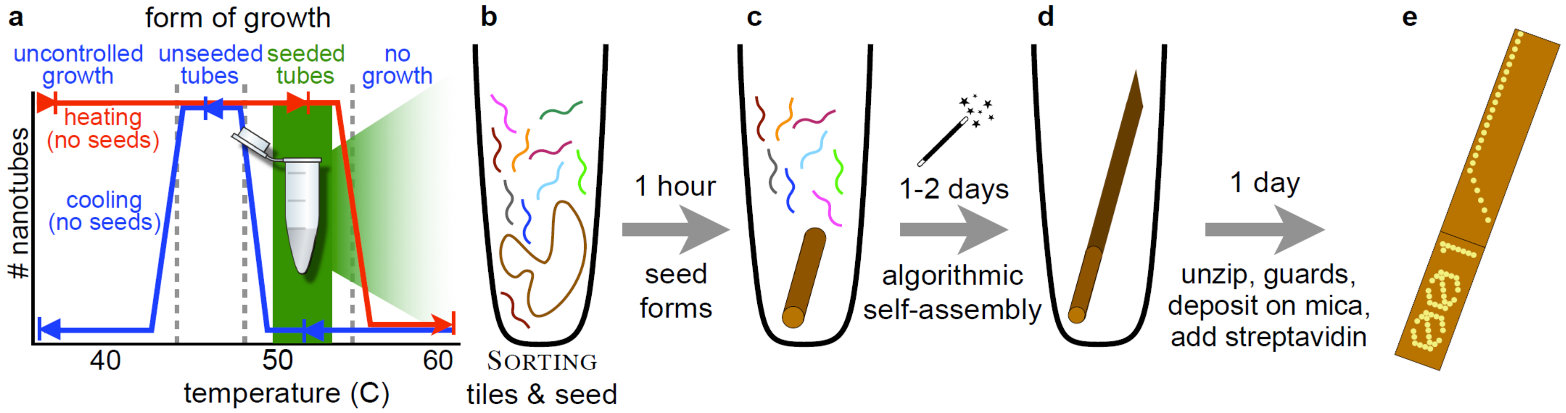
Generate plate map



represents some combination of circuit and input, e.g.,
013 = *"parity circuit, input=011010"*

label with streptavidin

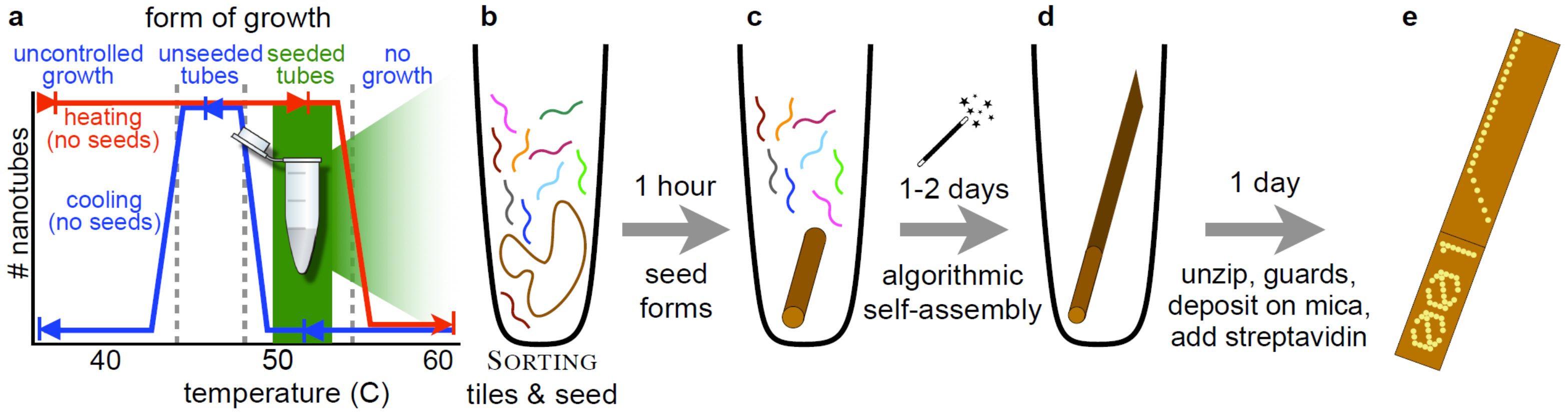
Experimental protocol



To execute circuit γ on input $x \in \{0,1\}^*$:

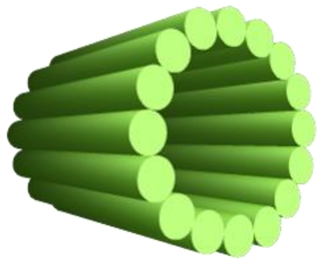
- Mix

Experimental protocol

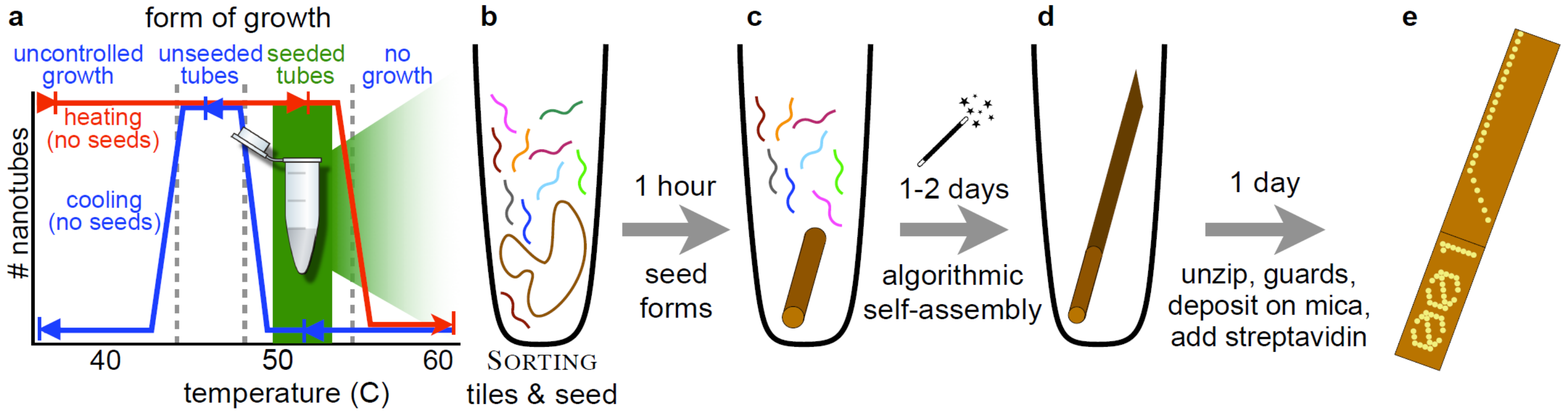


To execute circuit γ on input $x \in \{0,1\}^*$:

- Mix
    - origami seed (bar-coded to identify γ and x)

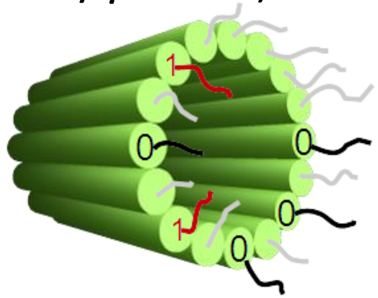


Experimental protocol

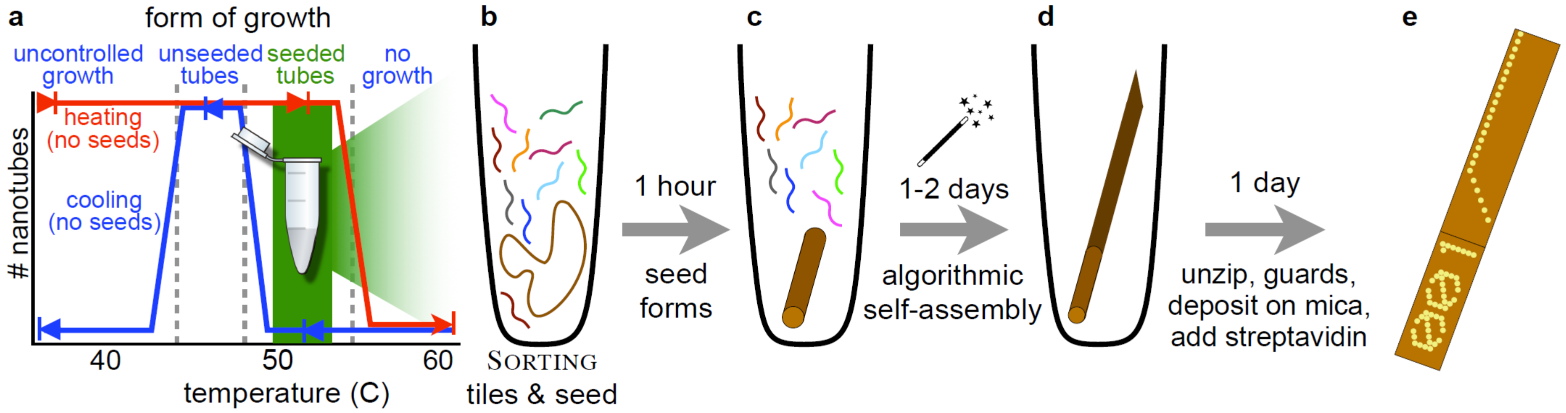


To execute circuit γ on input $x \in \{0,1\}^*$:

- Mix
  - origami seed (bar-coded to identify γ and x)
  - “adapter” strands encoding x

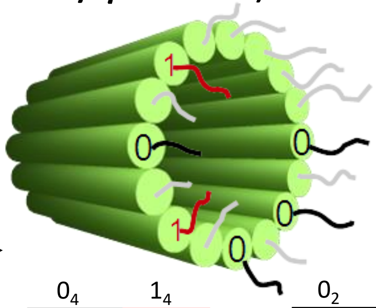


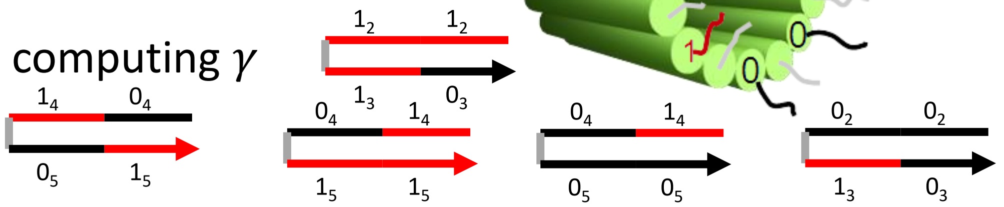
Experimental protocol



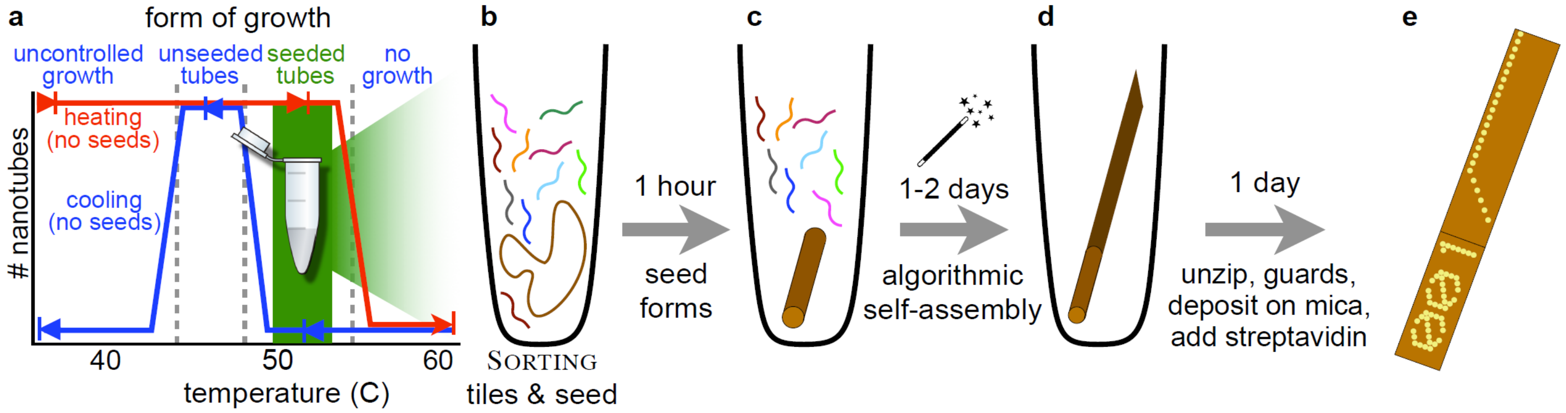
To execute circuit γ on input $x \in \{0,1\}^*$:

- Mix
  - origami seed (bar-coded to identify γ and x)
  - "adapter" strands encoding x
  - tiles computing γ





Experimental protocol



To execute circuit γ on input $x \in \{0,1\}^*$:

- Mix
  - origami seed (bar-coded to identify γ and x)
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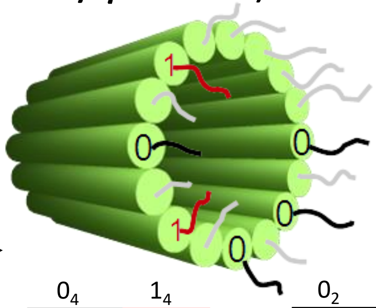
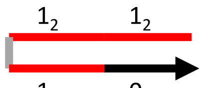
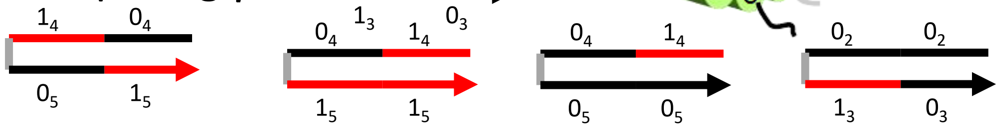
  - tiles computing γ





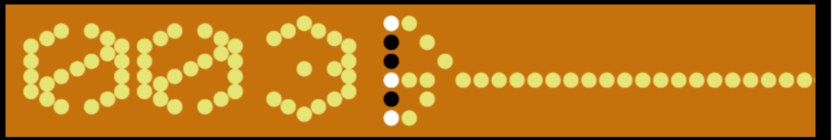


- Anneal 90° C to 50.9° C in 1 hour (*origami seeds form*)
- Hold at 50.9° C for 1-2 days (*tiles grow tubes from seed*)
- Add “unzipper” strands (remove seam to convert tube to ribbon)
- Add “guard” strands (complements of output sticky ends, to deactivate tiles)
- Deposit on mica, buffer wash, add streptavidin, AFM

Results

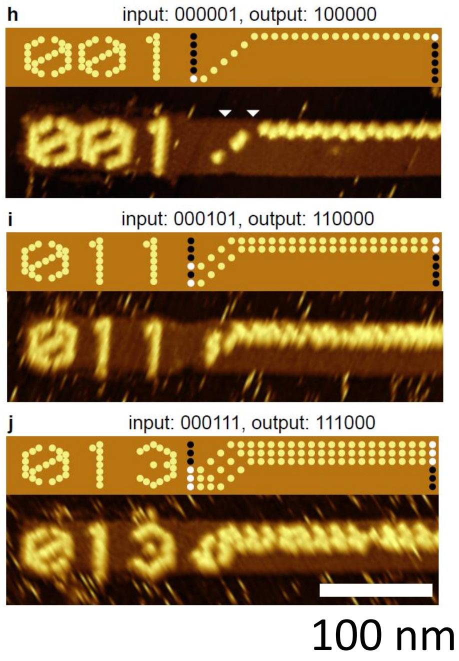
```
def test_parity():
    actual = parity('100101')

    expected =
```

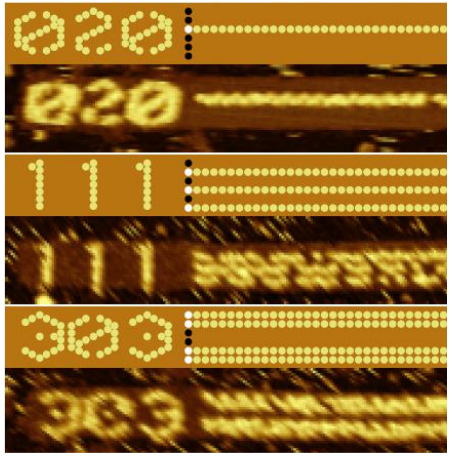


```
    assertEquals(expected, actual)
```

Sorting

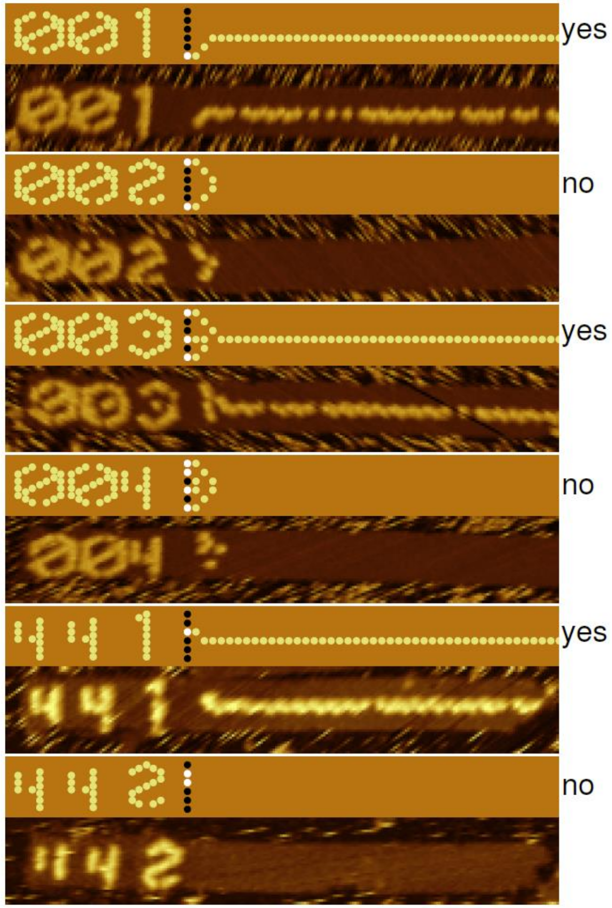


Copy



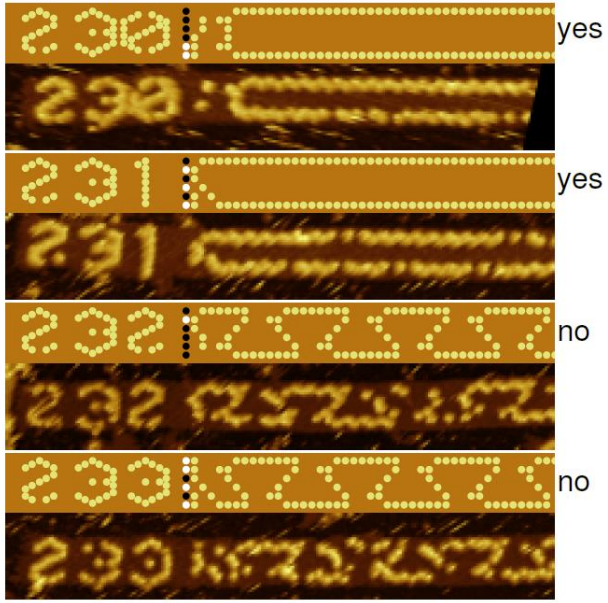
Parity

Is the number of 1's odd?



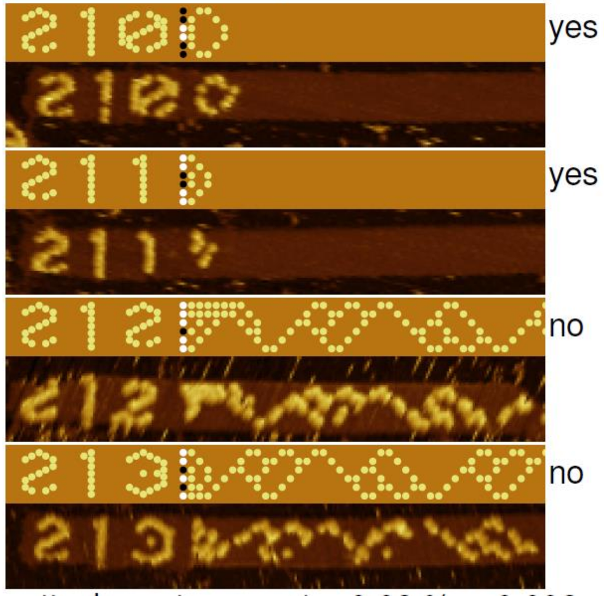
MultipleOf3

Is the input binary number a multiple of 3?



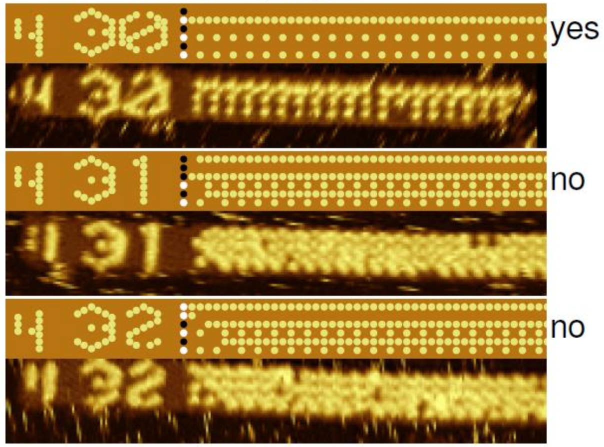
Palindrome

Is the input a palindrome?



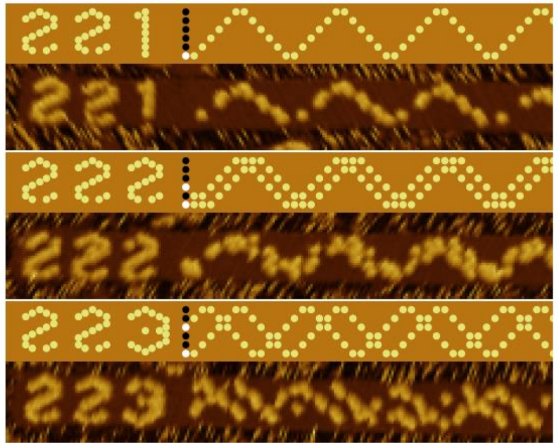
Recognise21

Is the binary input $= 21$?

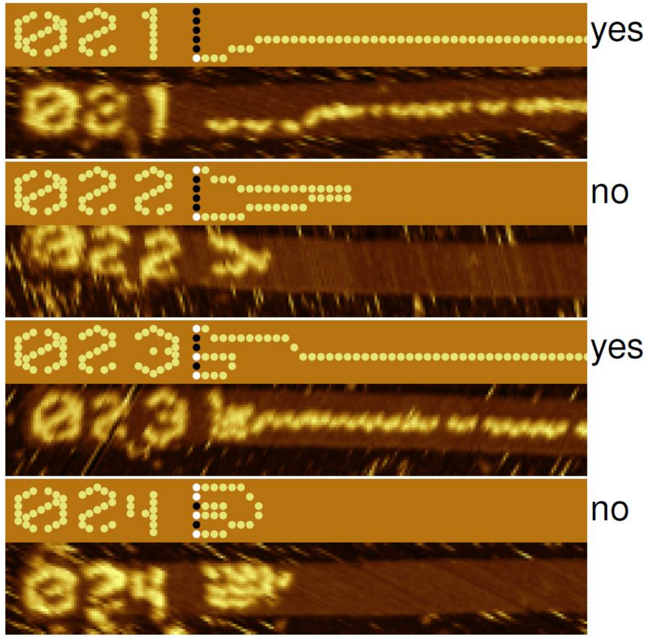


Zig-Zag

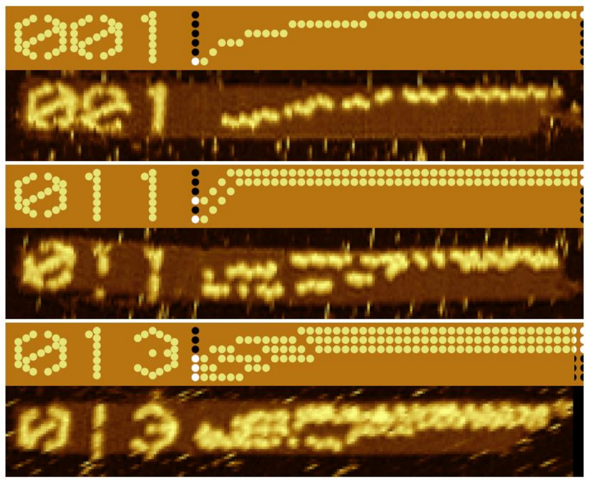
Repeating pattern



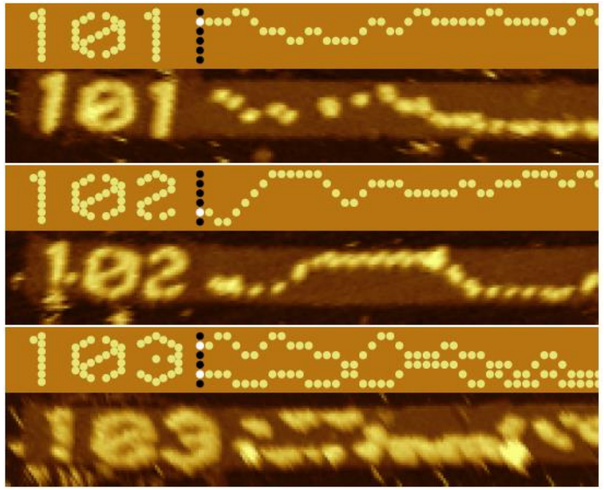
LazyParity



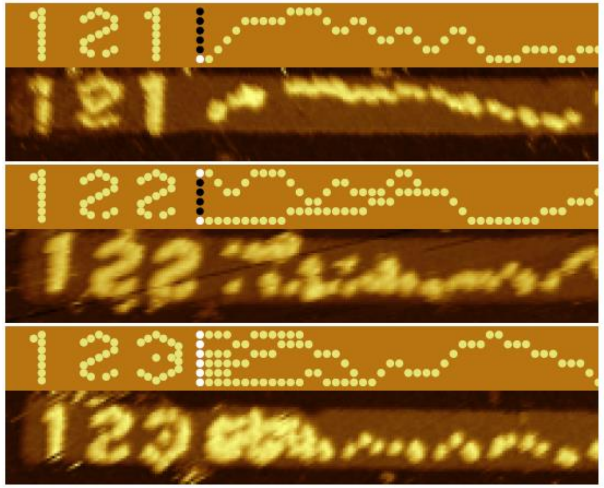
LazySorting



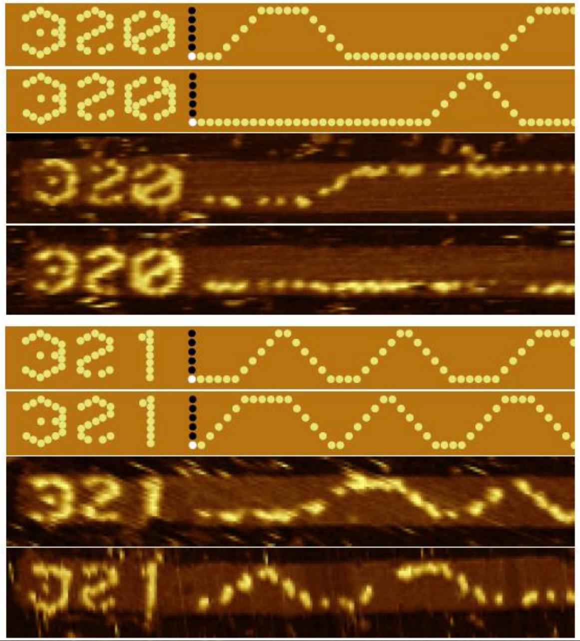
RandomWalkingBit



LeaderElection

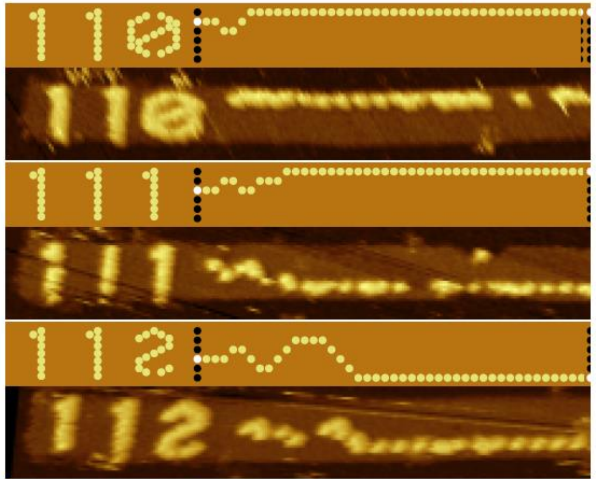


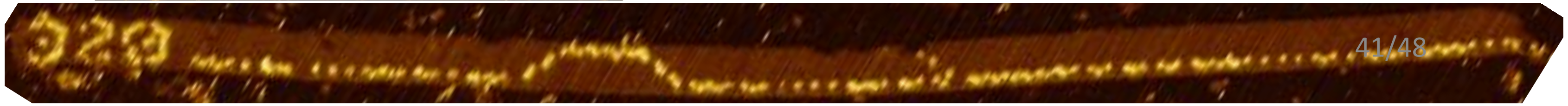
Waves



AbsorbingRandomWalkingBit

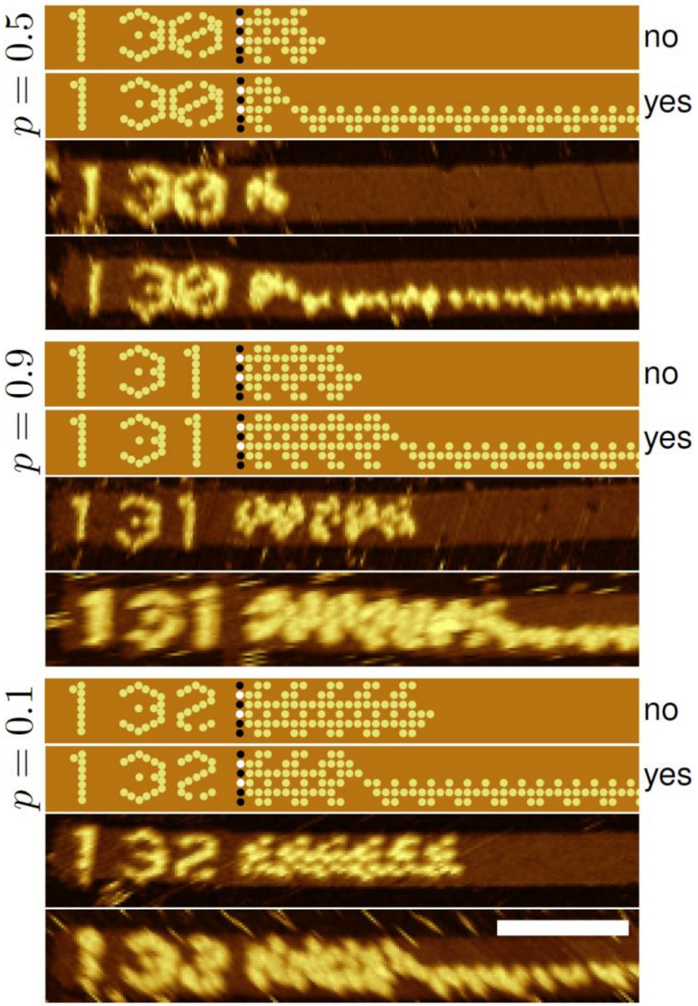
Random walker absorbs to top/bottom

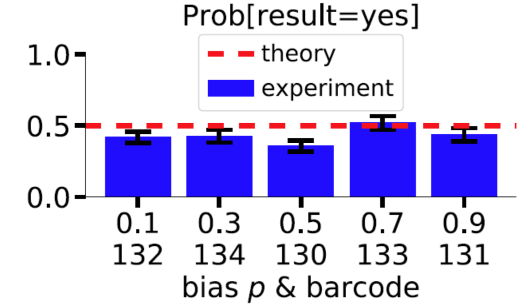


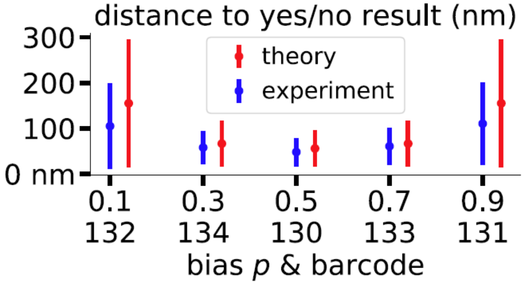


FairCoin

Unbiasing a biased coin

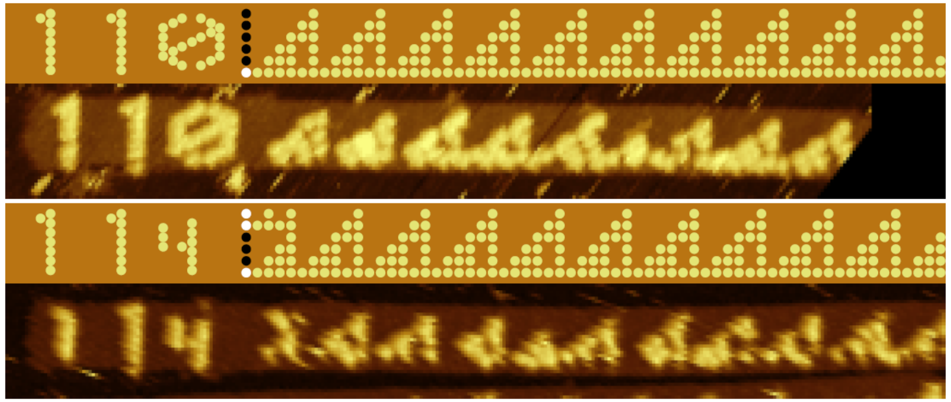






Rule110

Simulation of a cellular automaton



Counting to 63

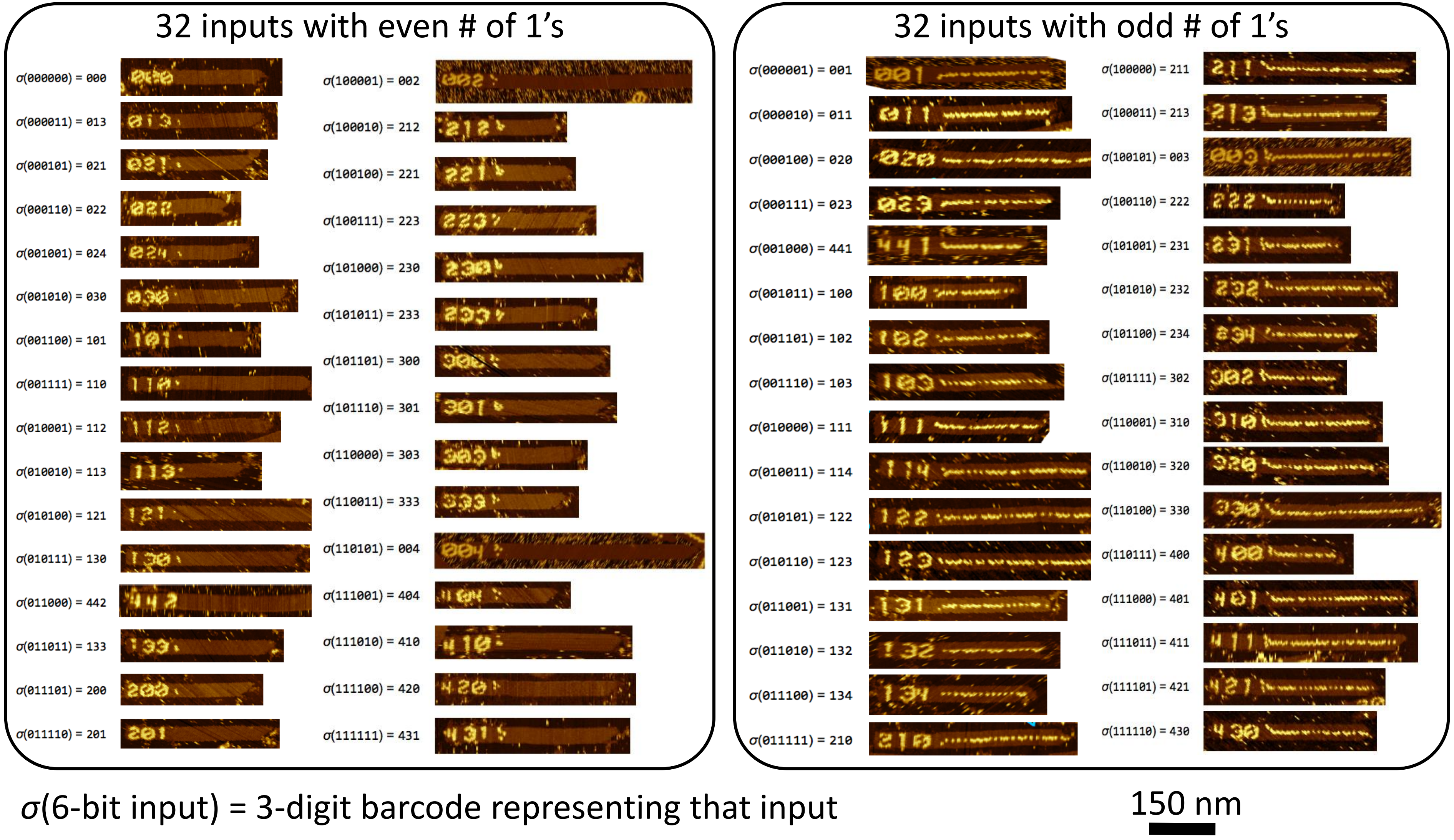
Circuit with 63 distinct strings

Is there a 64-counter?

No!
Proof by Tristan Stérin, Maynooth University
Consequence of following theorem:
No Boolean function computes an odd permutation if some output bit does not depend on all input bits.

Parity tested on all inputs

2^6 = 64 inputs with 6 bits



σ(6-bit input) = 3-digit barcode representing that input

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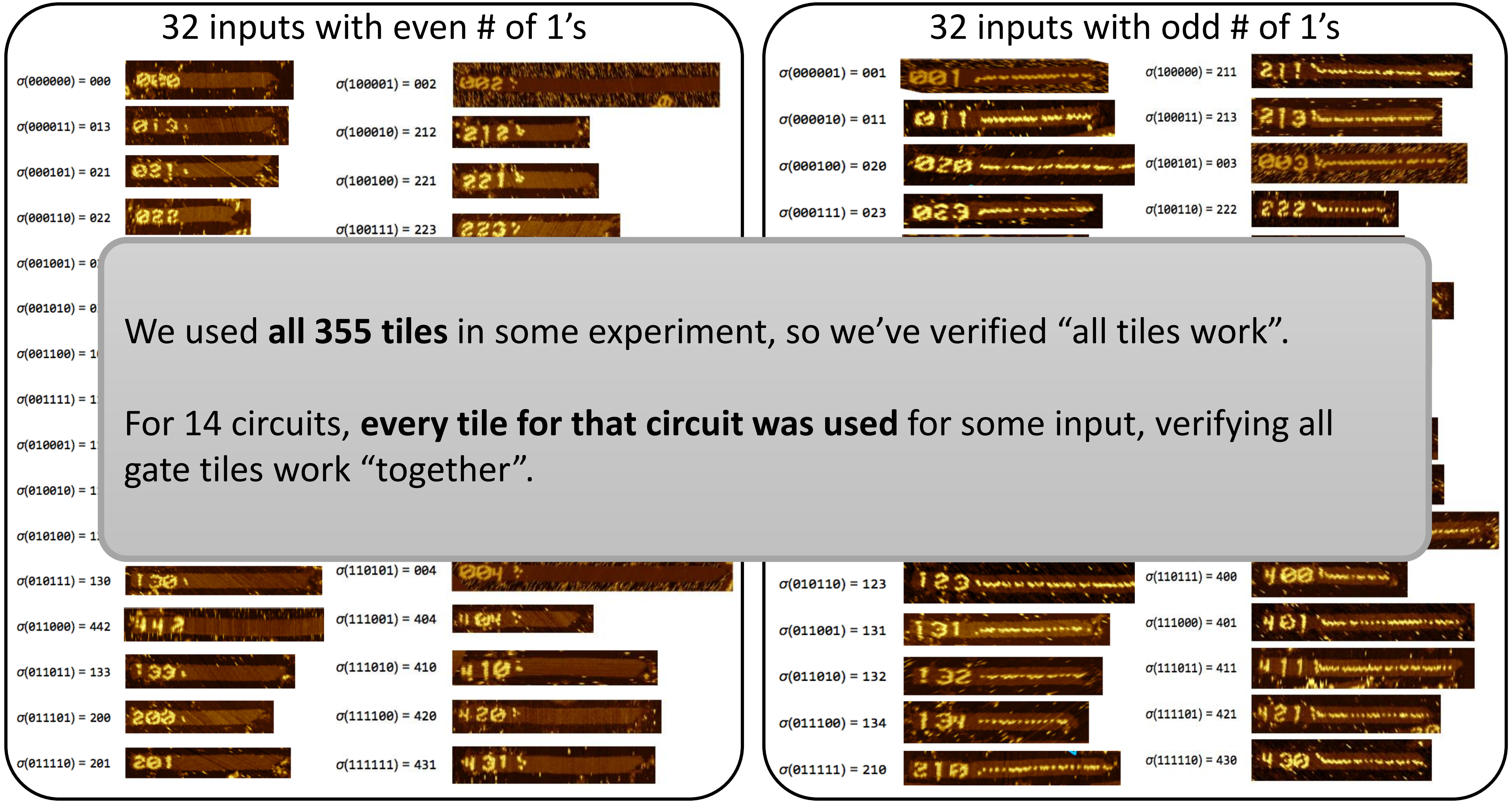


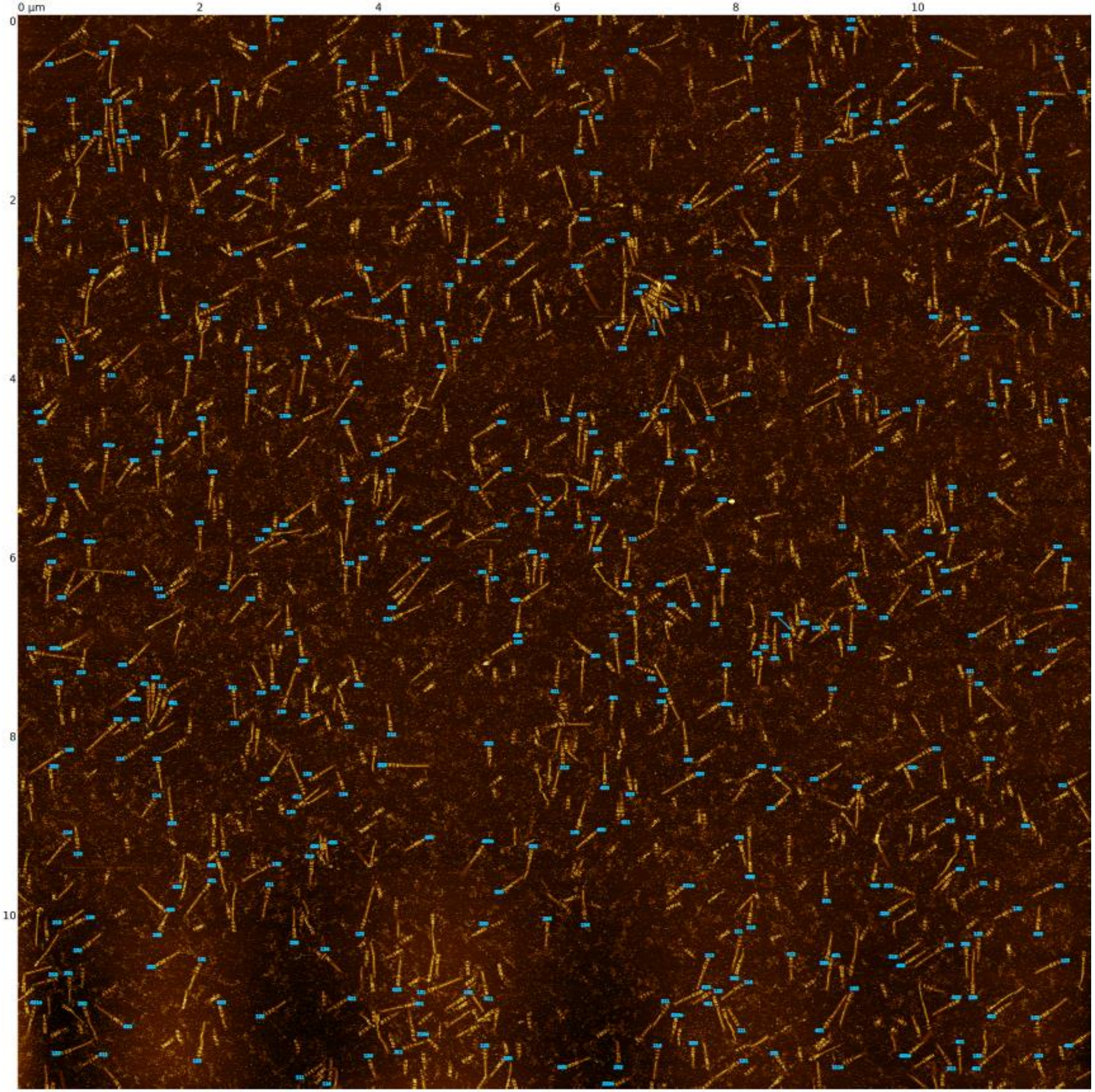
We used **all 355 tiles** in some experiment, so we've verified "all tiles work".

For 14 circuits, **every tile for that circuit was used** for some input, verifying all gate tiles work "together".

σ(6-bit input) = 3-digit barcode representing that input

150 nm

12 µm AFM image of parity ribbons for several inputs whose output is 1



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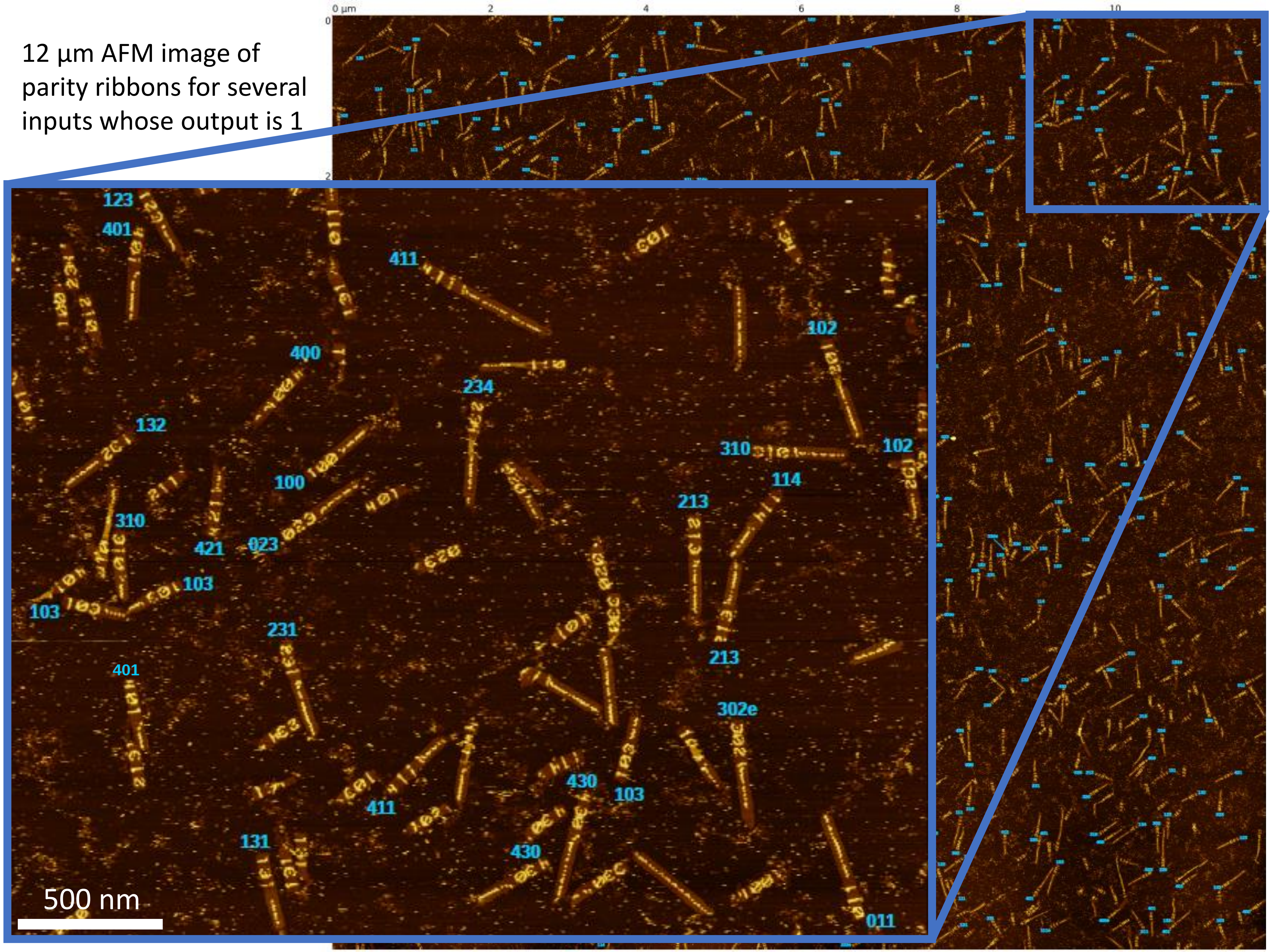

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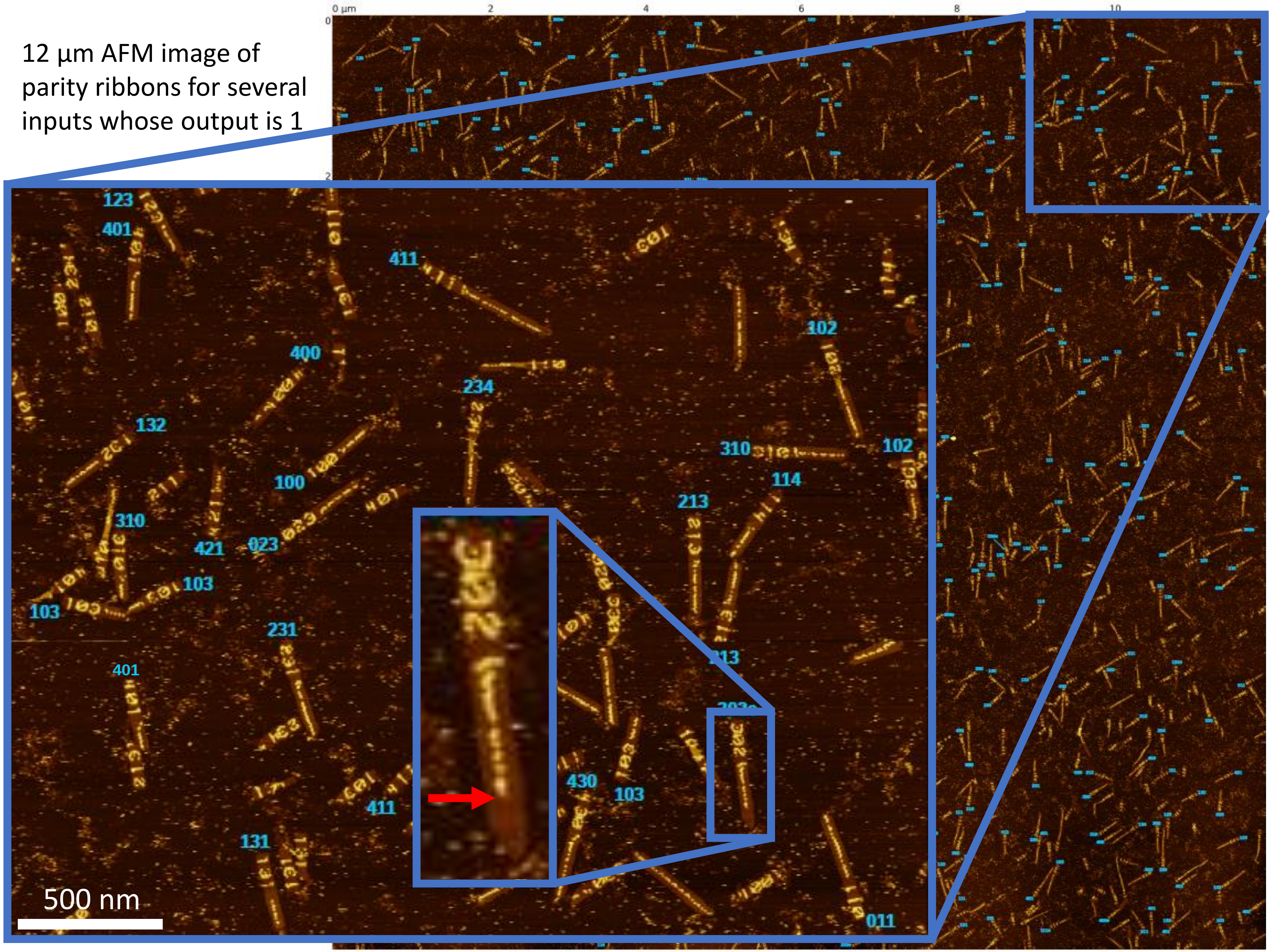

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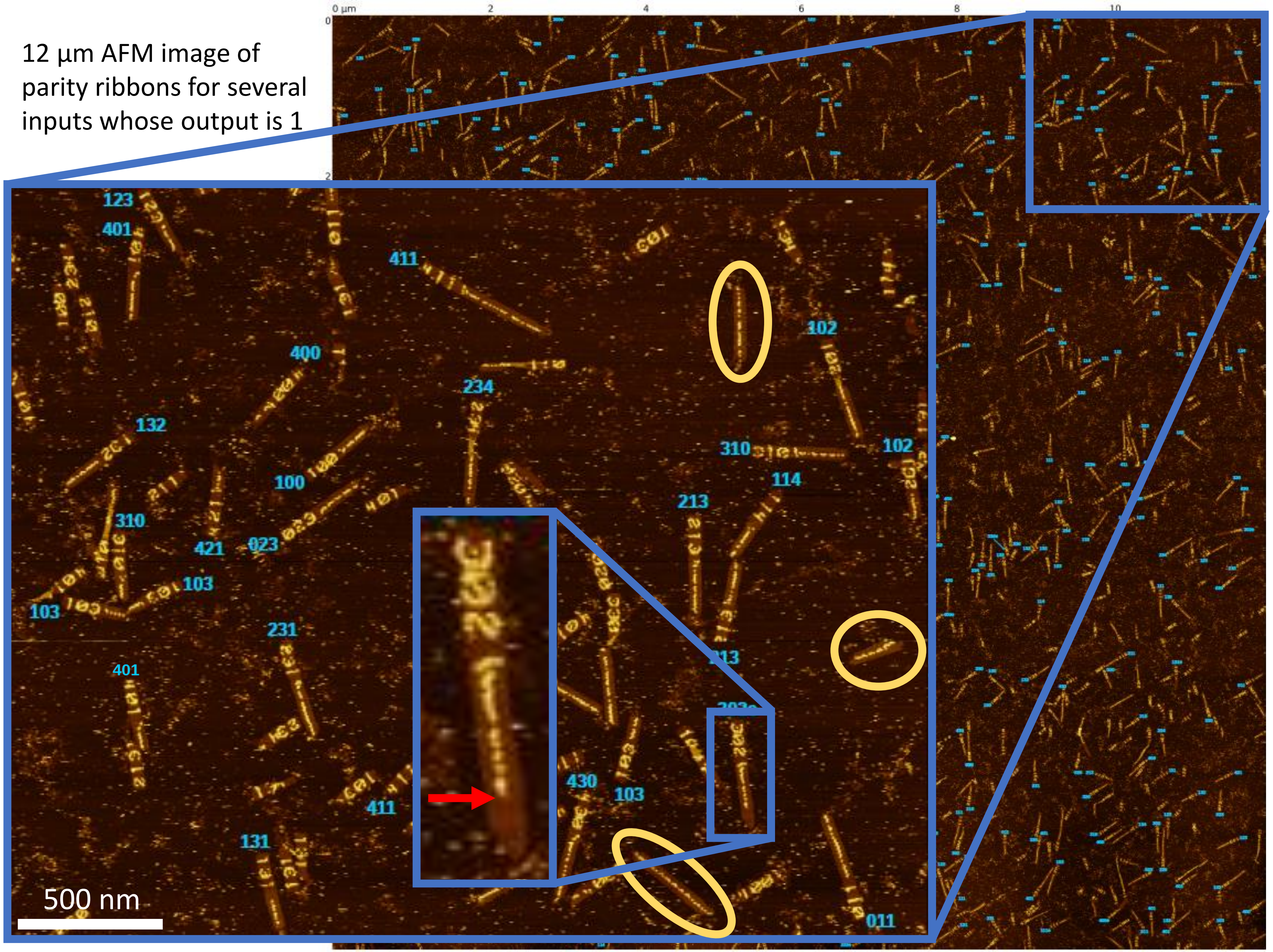

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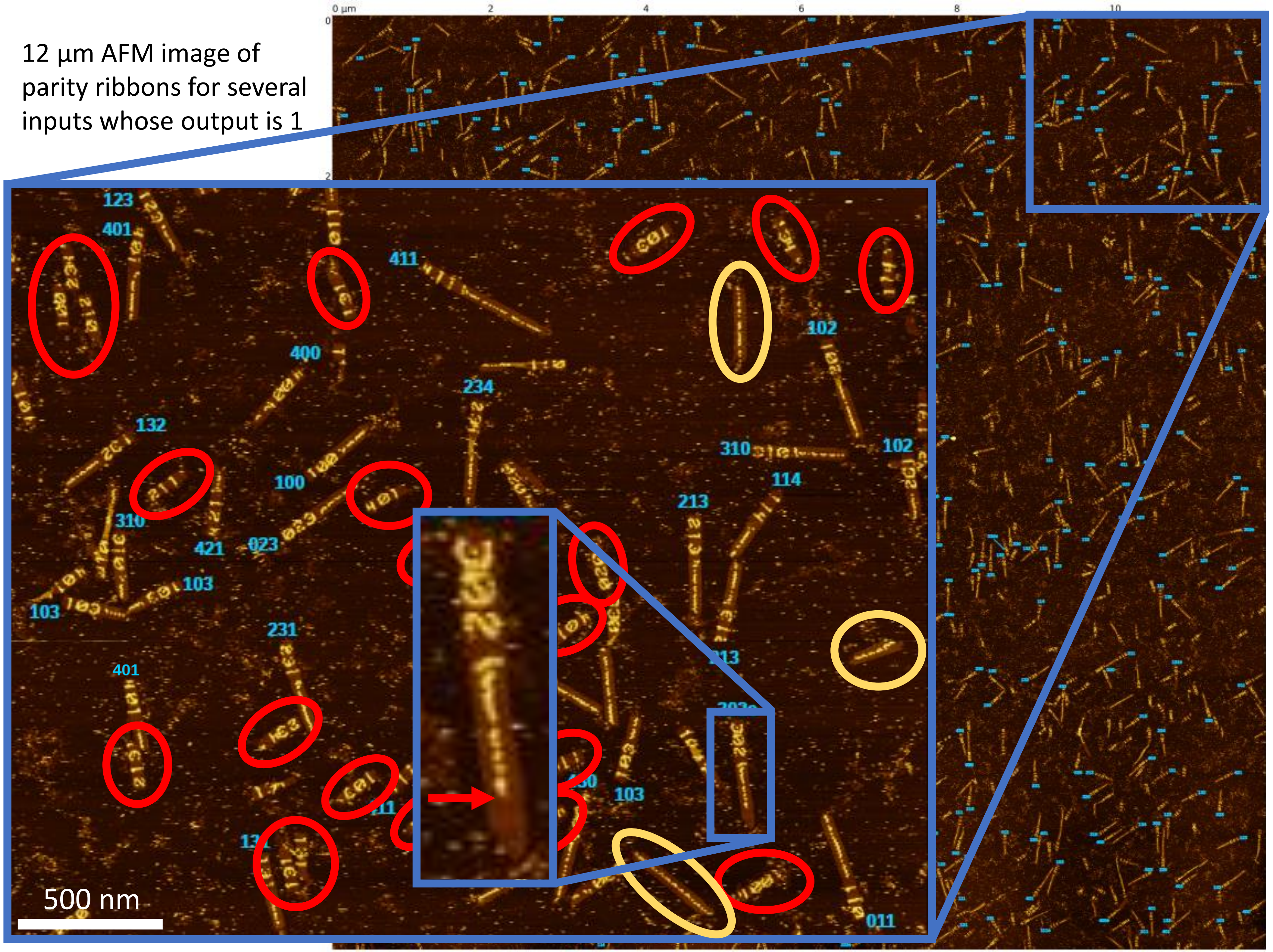

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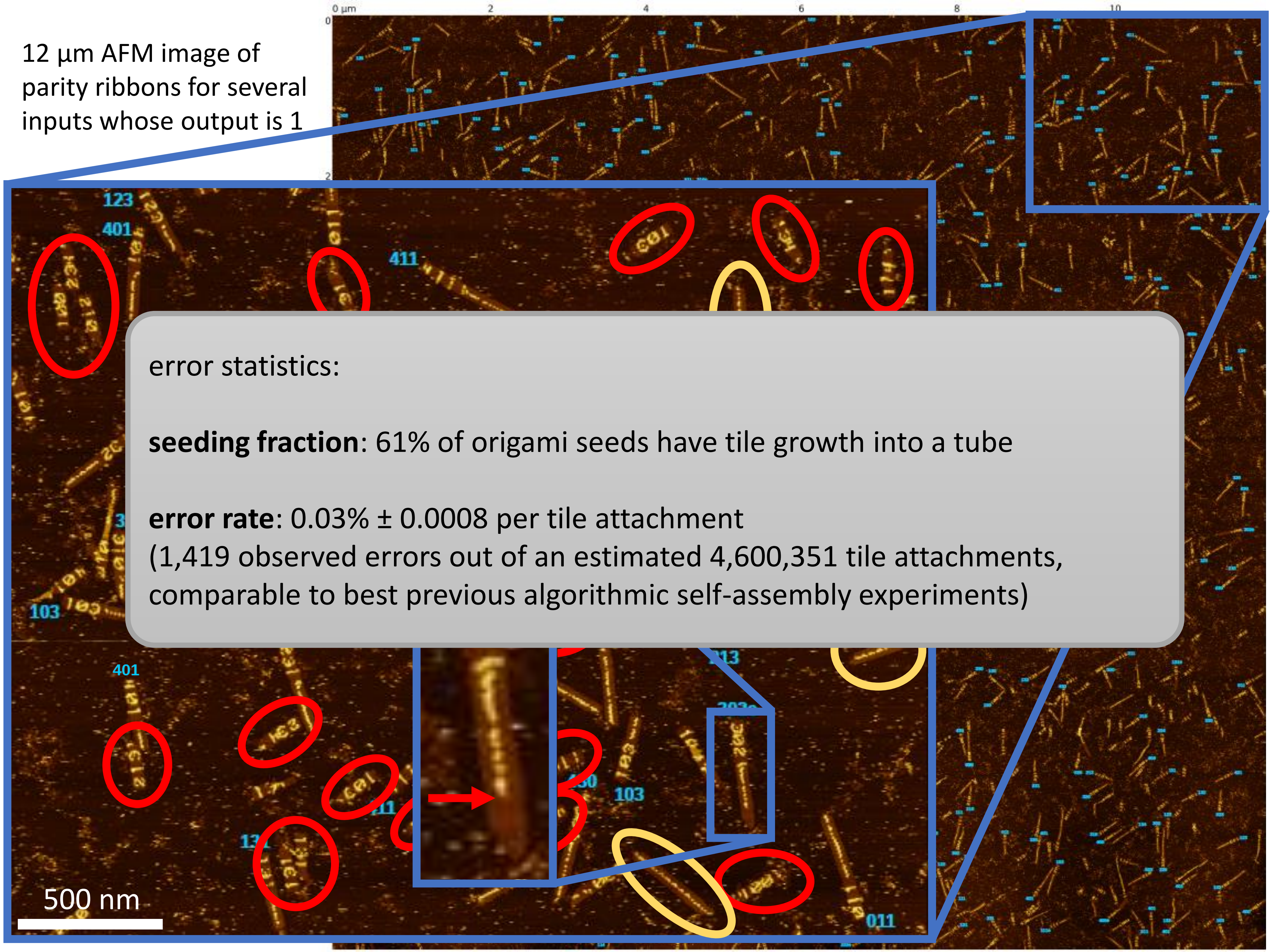

error statistics:

seeding fraction: 61% of origami seeds have tile growth into a tube

error rate: 0.03% ± 0.0008 per tile attachment
(1,419 observed errors out of an estimated 4,600,351 tile attachments, comparable to best previous algorithmic self-assembly experiments)

What did we learn?

A <u>small</u>(ish) library of molecules can be <u>reprogrammed</u> to self-assemble <u>reliably</u> into many complex patterns, by <u>processing information</u> as they grow.

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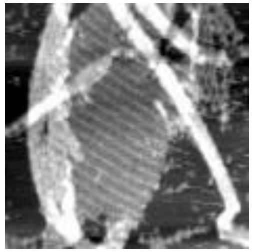
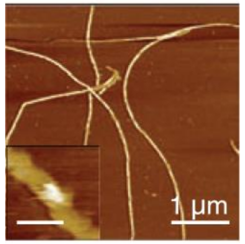
Contrasting with other self-assembly work:

<u>more algorithmic control</u>
than **periodic** self-assembly



2D tile lattices
(Winfree et al.,
Nature 1998)



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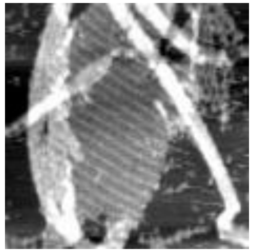

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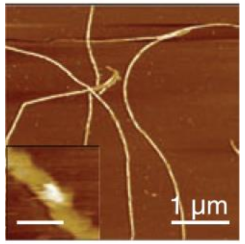

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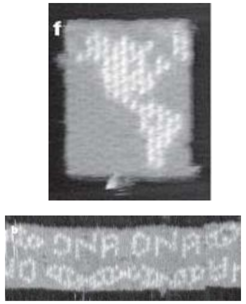
fewer types of DNA strands required than **uniquely-addressed** self-assembly



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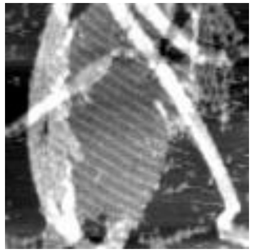

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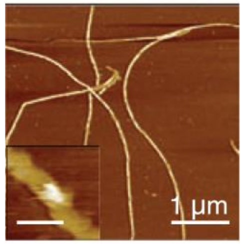

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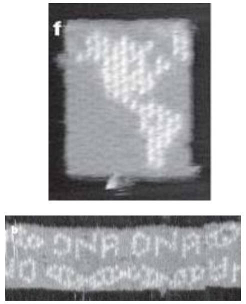
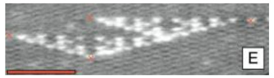


DNA origami (Rothemund, *Nature* 2006)

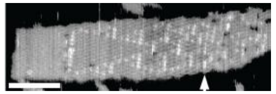
hard-coded tile lattice (Wei et al., *Nature* 2012)

order of magnitude more tile types available than previous **algorithmic** self-assembly

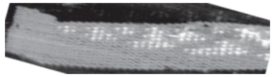
double-crossover tile lattices



(Rothemund et al., *PLoS Bio* 2004)



(Fujibayashi et al., *Nano Letters* 2008)



(Barish et al., *PNAS* 2009)

(Evans, *Ph.D. thesis* 2014)

Next big challenge: Algorithmically control shape

We "drew" interesting patterns on a boring shape (infinite rectangle)

Can we run algorithms to
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[*Complexity of Self-Assembled Shapes*. Soloveichik and Winfree, SIAM Journal on Computing 2007]

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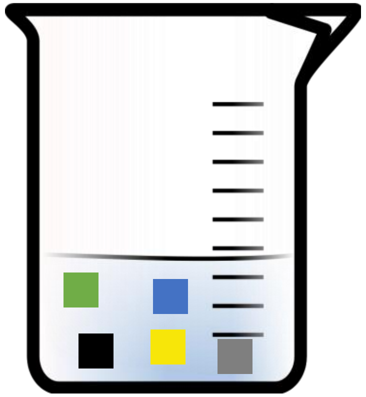

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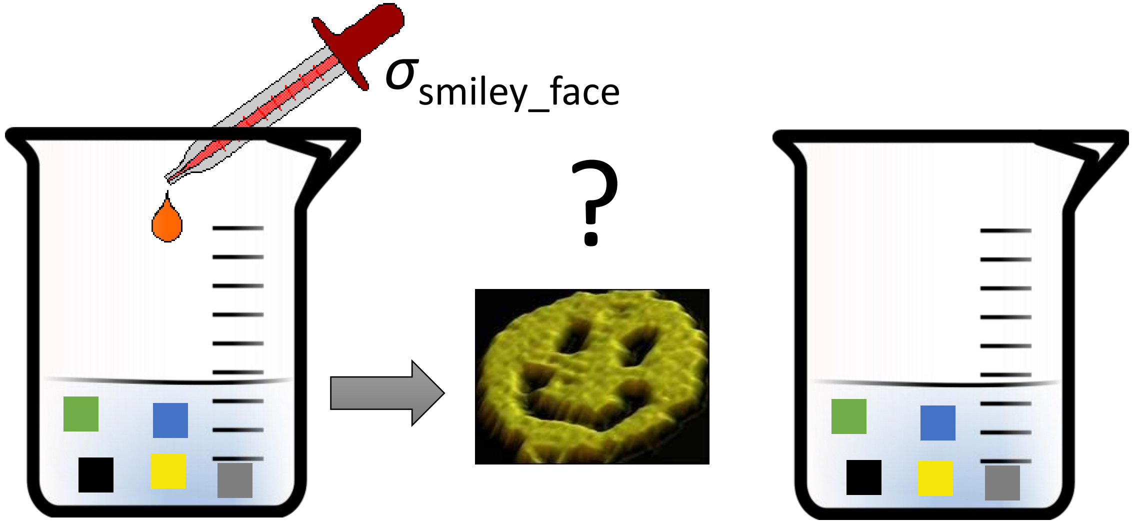

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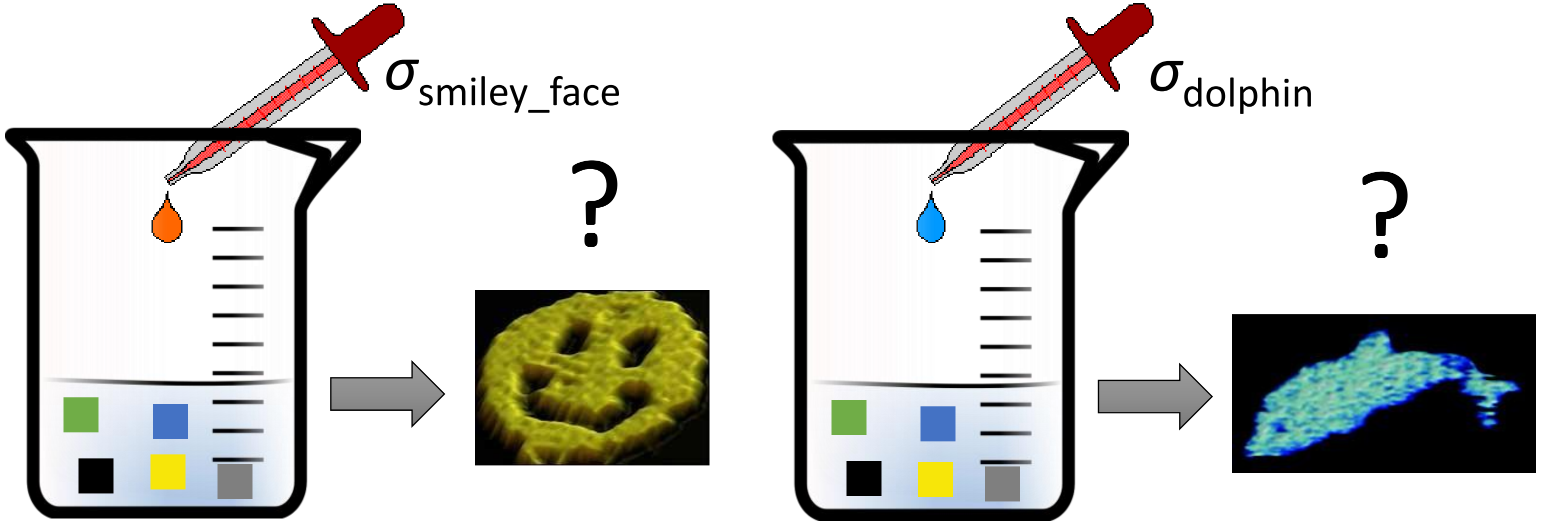

These tiles are universally programmable for building any shape.

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Thank you!