Algorithmic self-assembly with DNA tiles

David Doty (University of California, Davis)

Algorithmic Foundations of Programmable Matter

Dagstuhl, August 2018

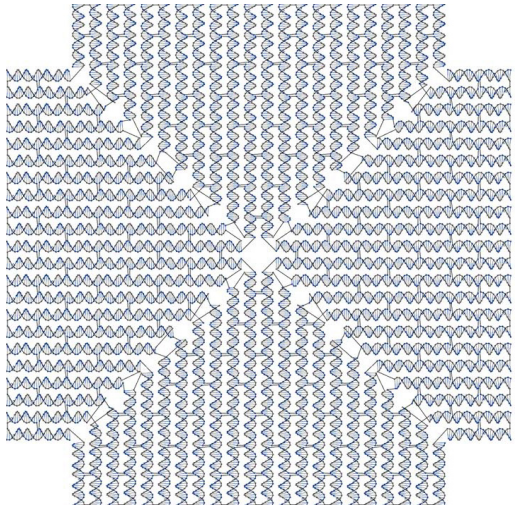
SCHLOSS DAGSTUHL
Leibniz-Zentrum für Informatik

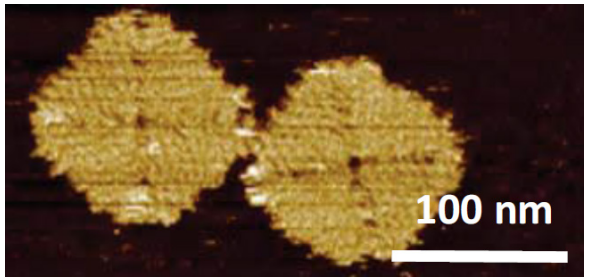
DNA tile self-assembly

DNA tile self-assembly

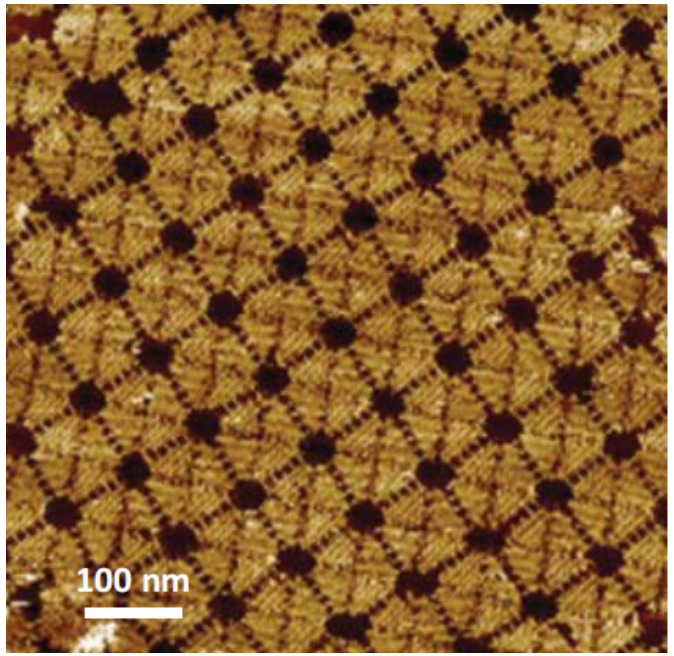
monomers (“tiles” made from DNA) bind into a crystal lattice

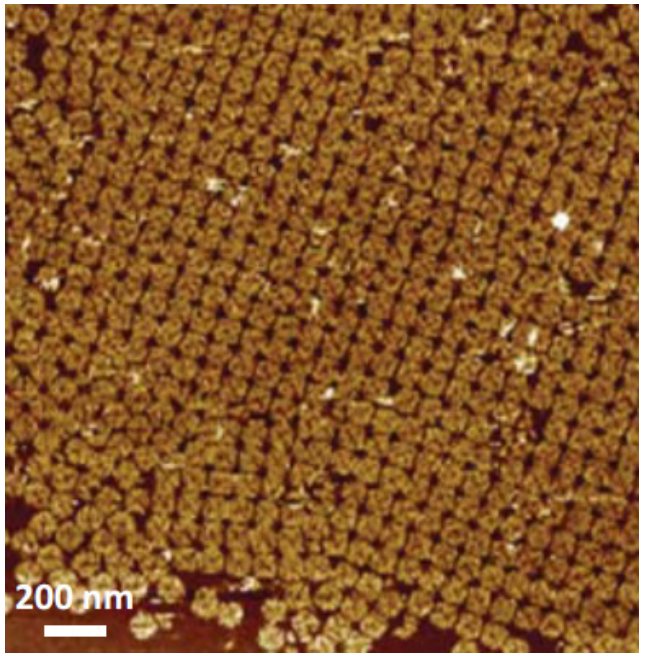
tile





lattice

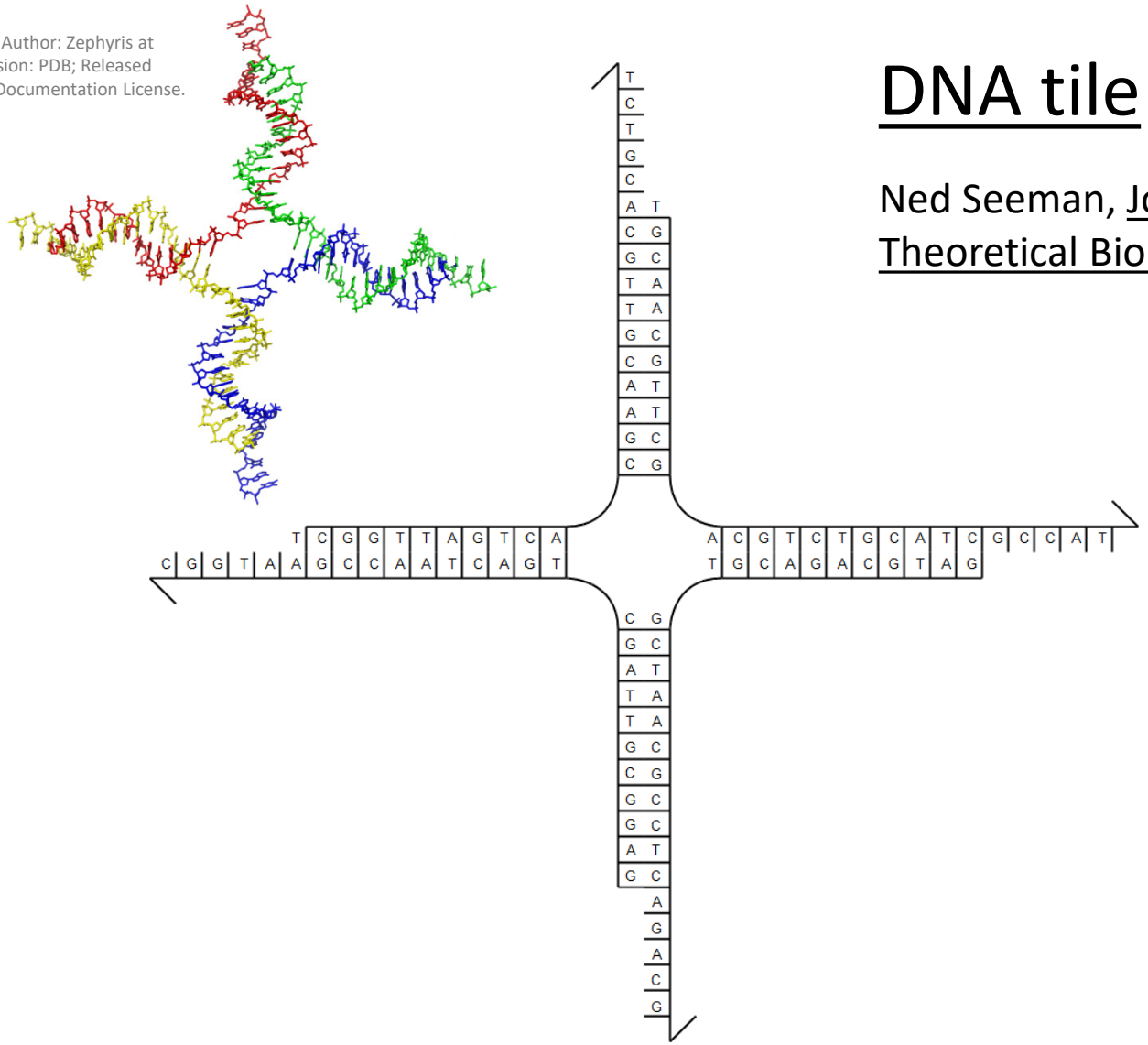




Source: *Programmable disorder in random DNA tilings*. Tikhomirov, Petersen, Qian, Nature Nanotechnology 2017

Practice of DNA tile self-assembly

Source:en.wikipedia; Author: Zephyris at en.wikipedia; Permission: PDB; Released under the GNU Free Documentation License.



DNA tile

Ned Seeman, Journal of Theoretical Biology 1982

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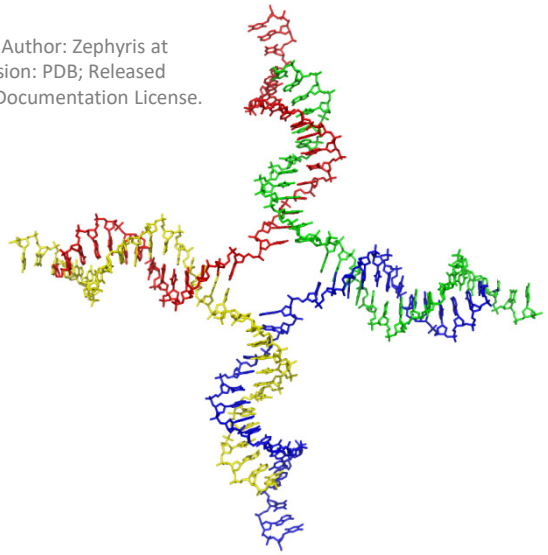

DNA tile

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sticky end

Practice of DNA tile self-assembly

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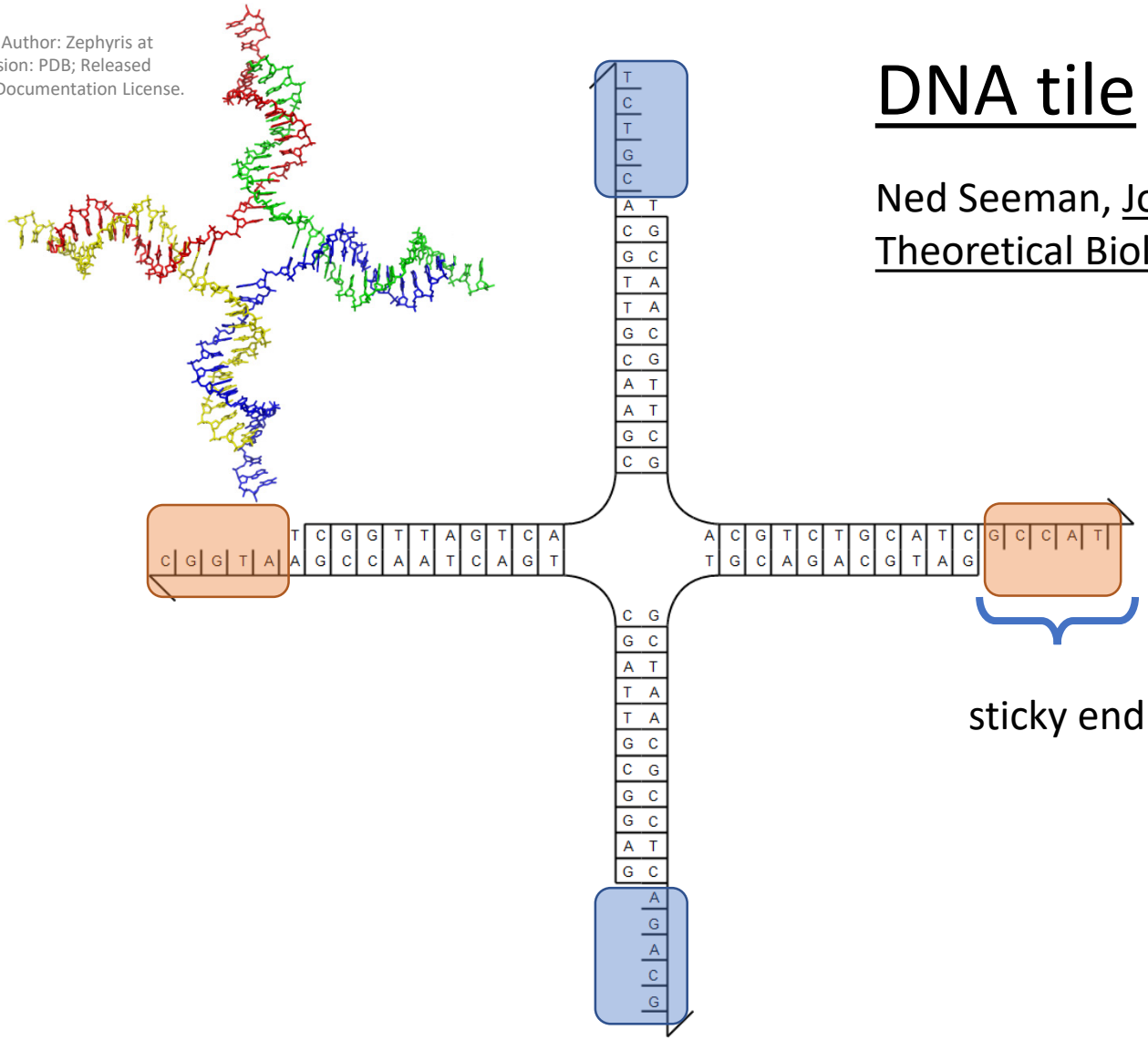


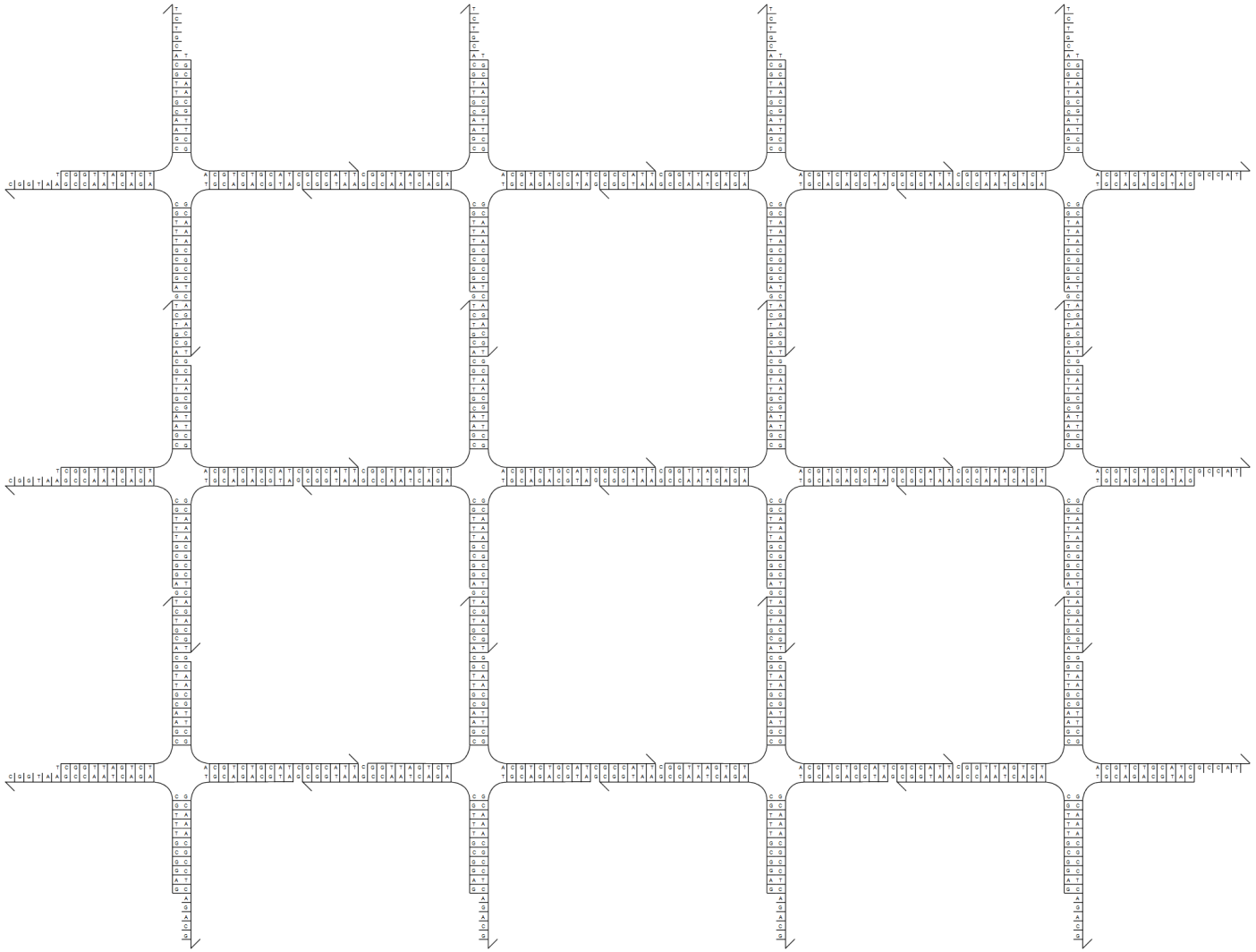
DNA tile

Ned Seeman, Journal of Theoretical Biology 1982

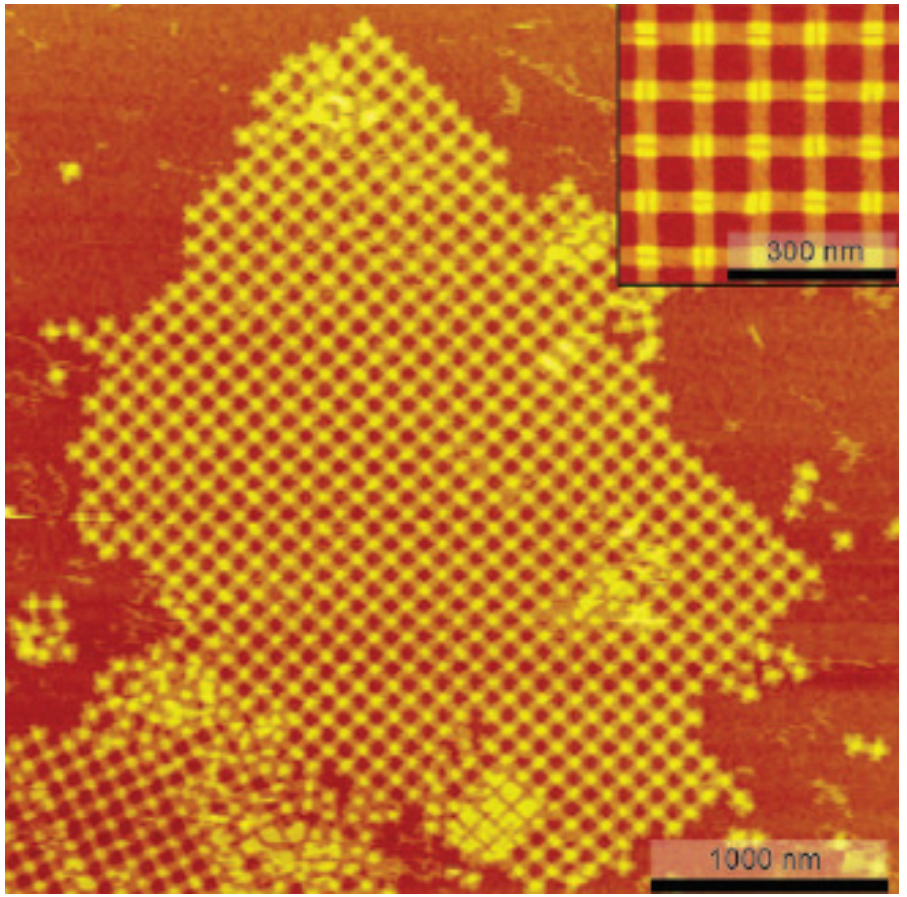
sticky end

Practice of DNA tile self-assembly

Place many copies of DNA tile in solution…



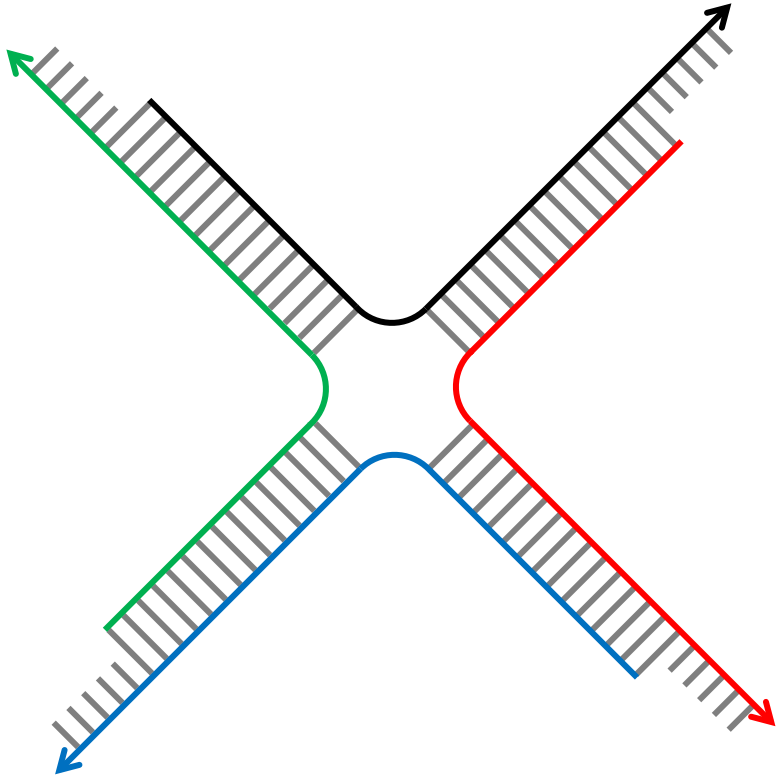
(not the same tile motif in this image)



Liu, Zhong, Wang, Seeman, Angewandte Chemie 2011

Practice of DNA tile self-assembly

What really happens in practice to Holliday junction (“base stacking”)



Practice of DNA tile self-assembly

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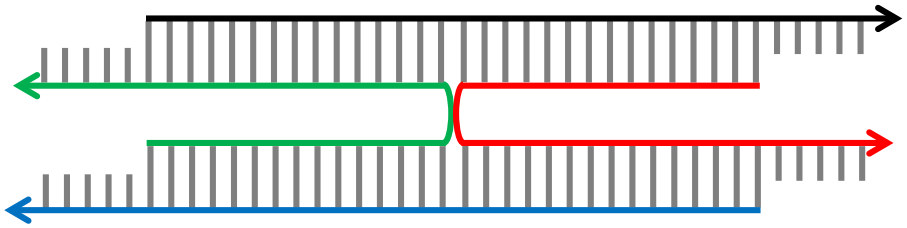

Practice of DNA tile self-assembly

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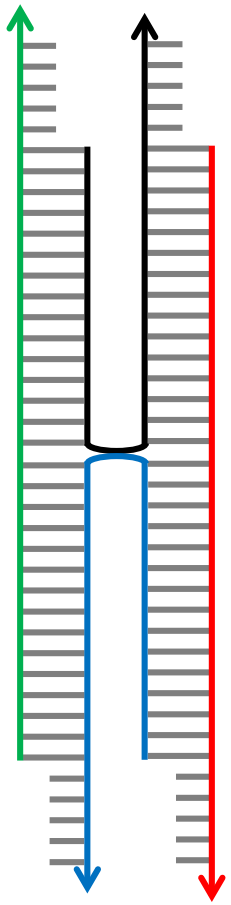

Practice of DNA tile self-assembly

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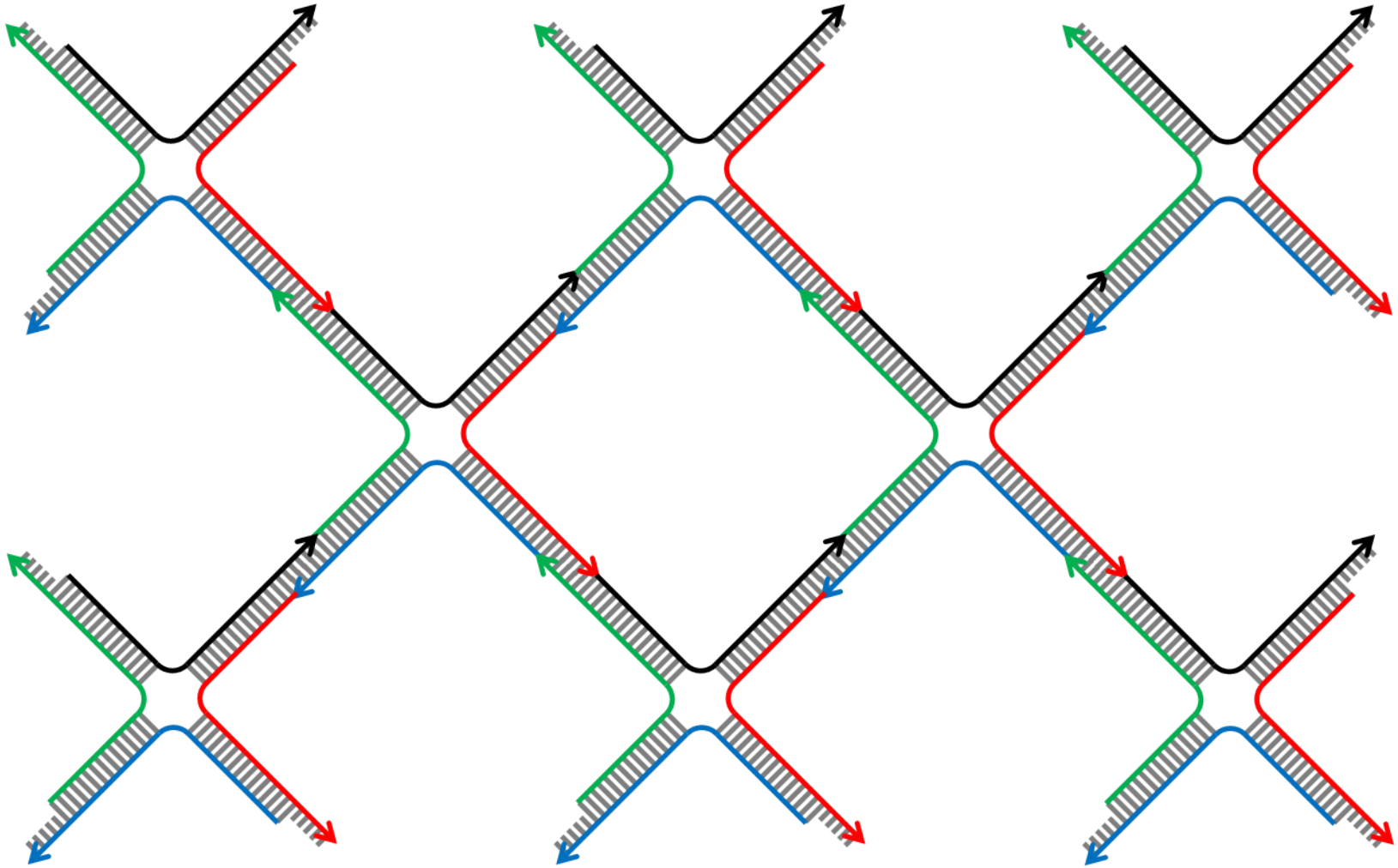

Practice of DNA tile self-assembly

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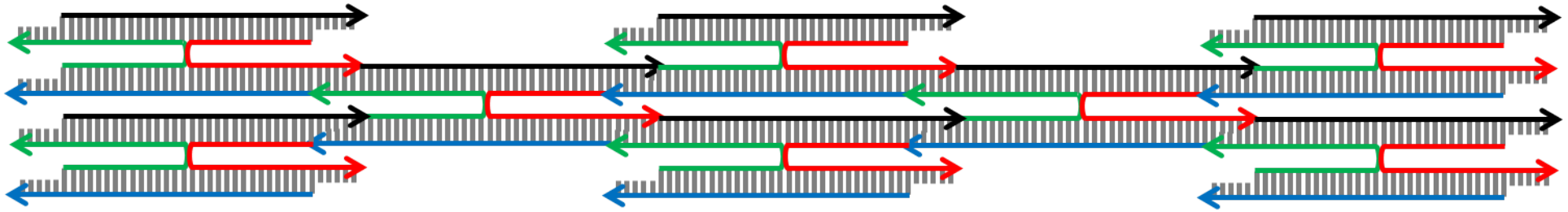
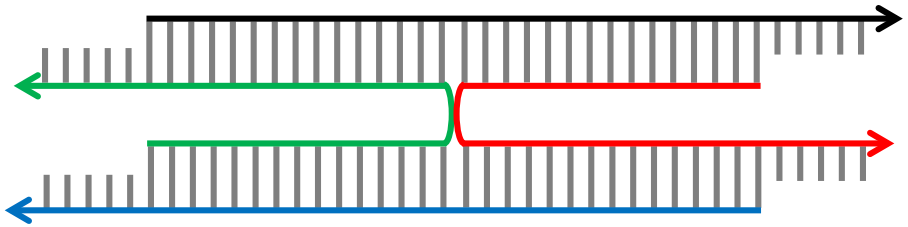
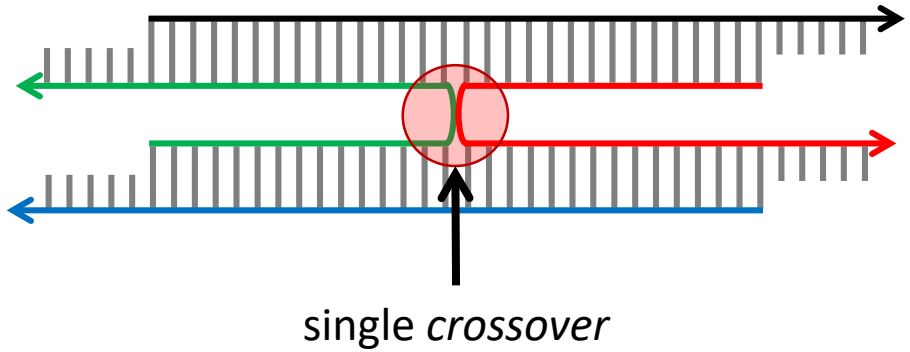


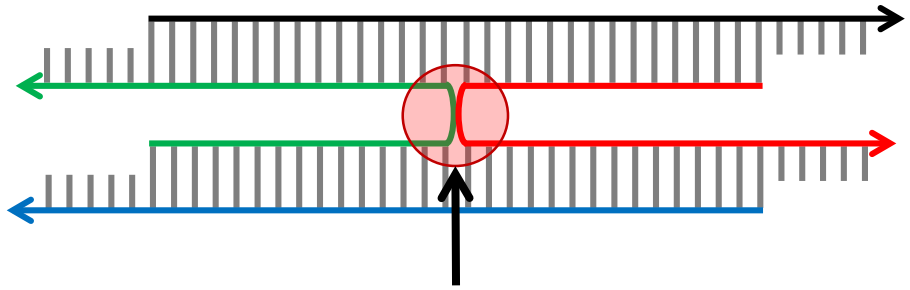
Practice of DNA tile self-assembly



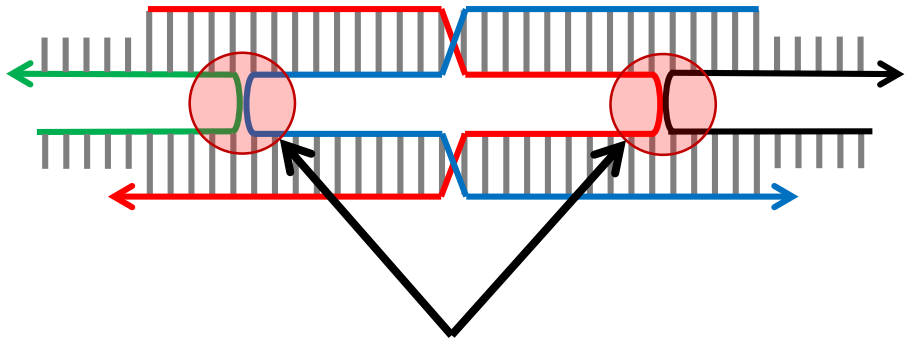
Practice of DNA tile self-assembly



Practice of DNA tile self-assembly



single *crossover*



double crossover

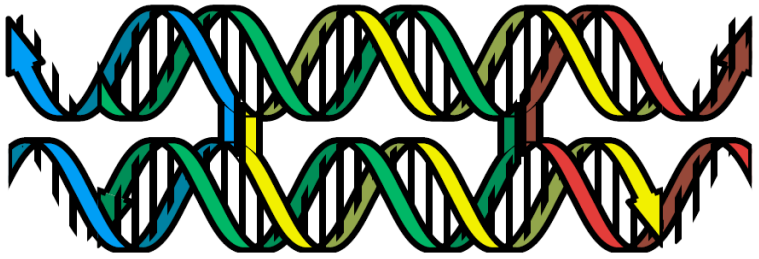
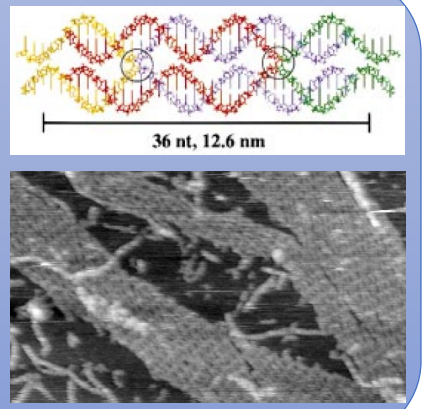


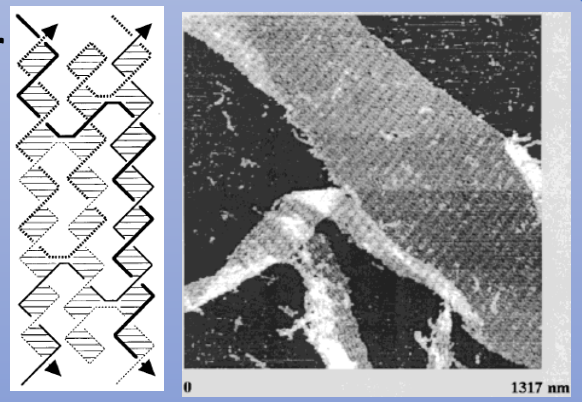
Figure from Schulman, Winfree, *PNAS* 2009

Practice of DNA tile self-assembly

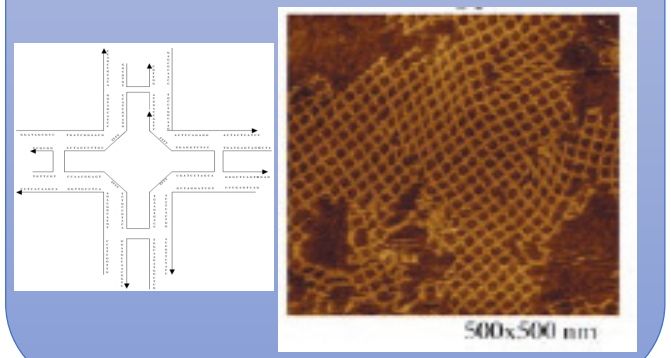
double-crossover tile (Winfree, Liu, Wenzler, Seeman, *Nature* 1998)



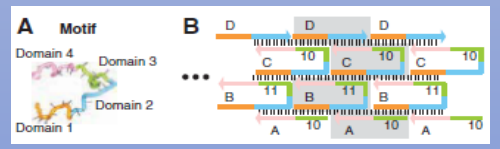
triple-crossover tile (LaBean, Yan, Kopatsch, Liu, Winfree, Reif, Seeman, *JACS* 2000)



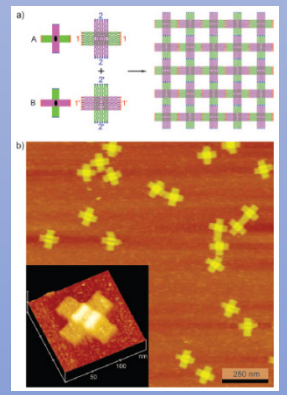
4x4 tile (Yan, Park, Finkelstein, Reif, LaBean, *Science* 2003)

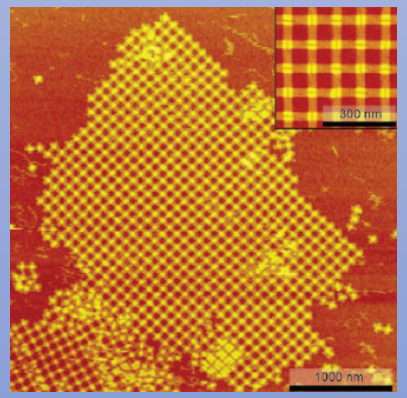


single-stranded tile (Yin, Hariadi, Sahu, Choi, Park, LaBean, Reif, *Science* 2008)

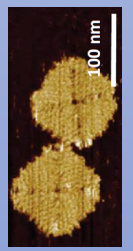


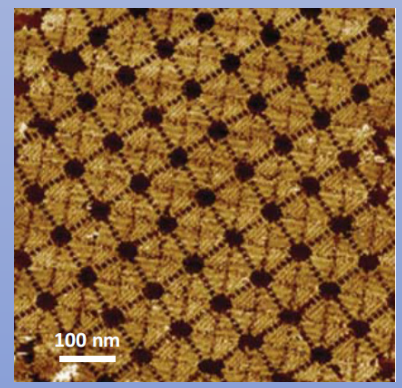
DNA origami tile (Liu, Zhong, Wang, Seeman, *Angewandte Chemie* 2011)





Tikhomirov, Petersen, Qian, Nature Nanotechnology 2017



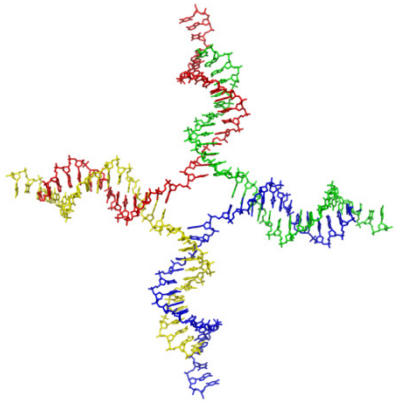


Theory of *algorithmic* self-assembly

What if…
… there is more than one tile type?
… some sticky ends are “weak”?

Erik Winfree

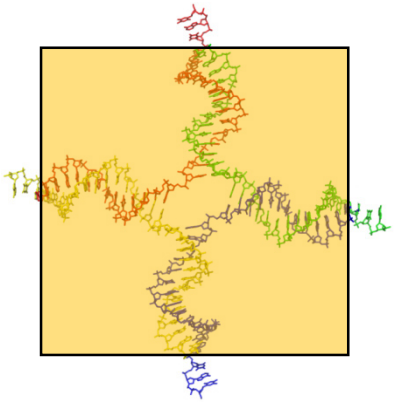
Abstract Tile Assembly Model



Erik Winfree, Ph.D. thesis,
Caltech 1998

Abstract Tile Assembly Model

- **tile type** = unit square



Erik Winfree, Ph.D. thesis,
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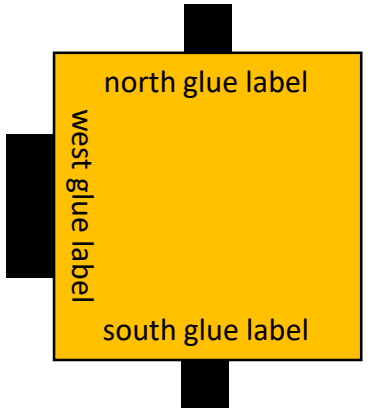
Abstract Tile Assembly Model

- **tile type** = unit square

- each side has a **glue** with a **label** and **strength** (0, 1, or 2)



strength 0

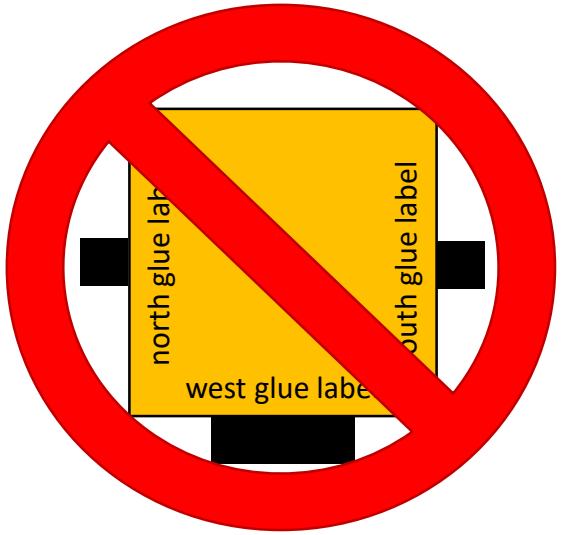
strength 1 (weak)

strength 2 (strong)

Erik Winfree, Ph.D. thesis, Caltech 1998

Abstract Tile Assembly Model

- **tile type** = unit square
- each side has a **glue** with a **label** and **strength** (0, 1, or 2)
- tiles cannot rotate



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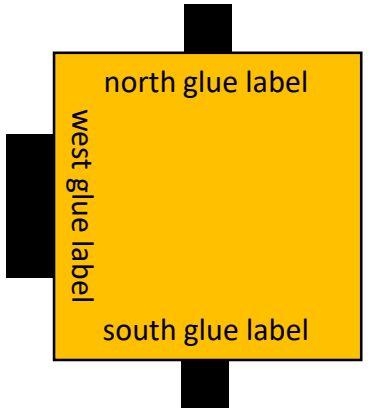

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- finitely many tile **types**
- infinitely many **tiles**: copies of each type

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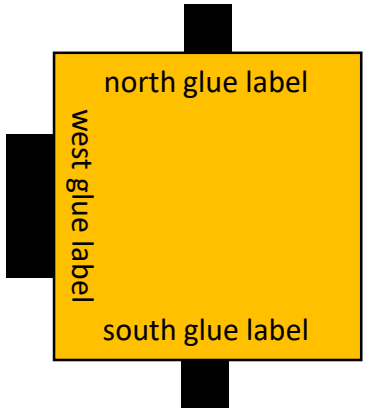

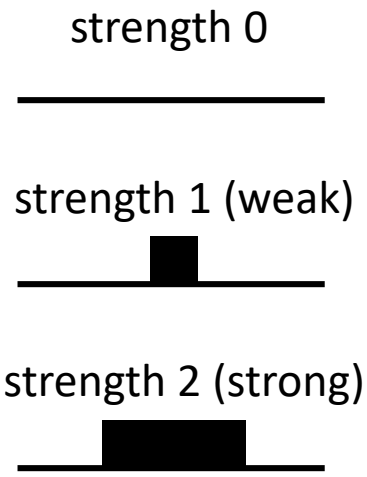

- finitely many tile **types**
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- assembly starts as a single copy of a special **seed** tile

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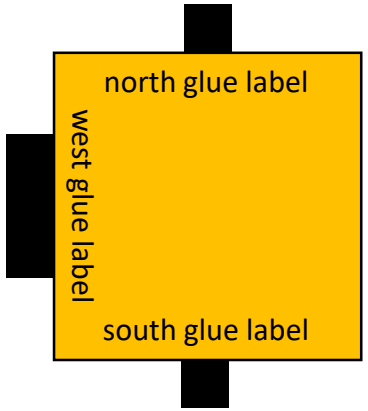
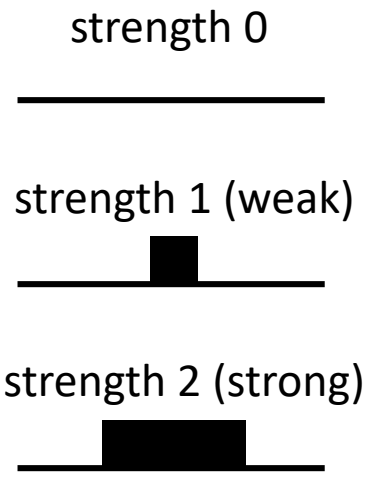
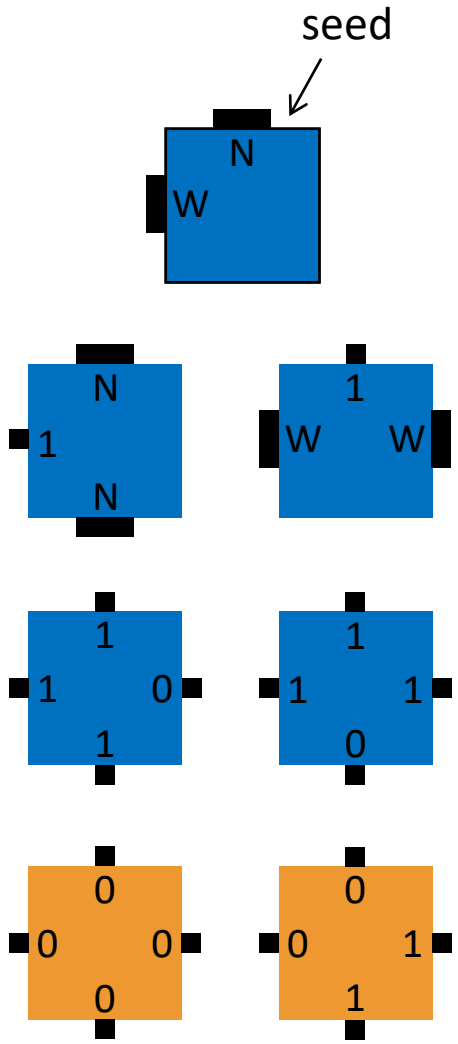




- finitely many tile **types**
- infinitely many **tiles**: copies of each type
- assembly starts as a single copy of a special **seed** tile
- tile can bind to the assembly if total binding strength ≥ 2 (two weak glues or one strong glue)

Erik Winfree, Ph.D. thesis, Caltech 1998

Example tile set



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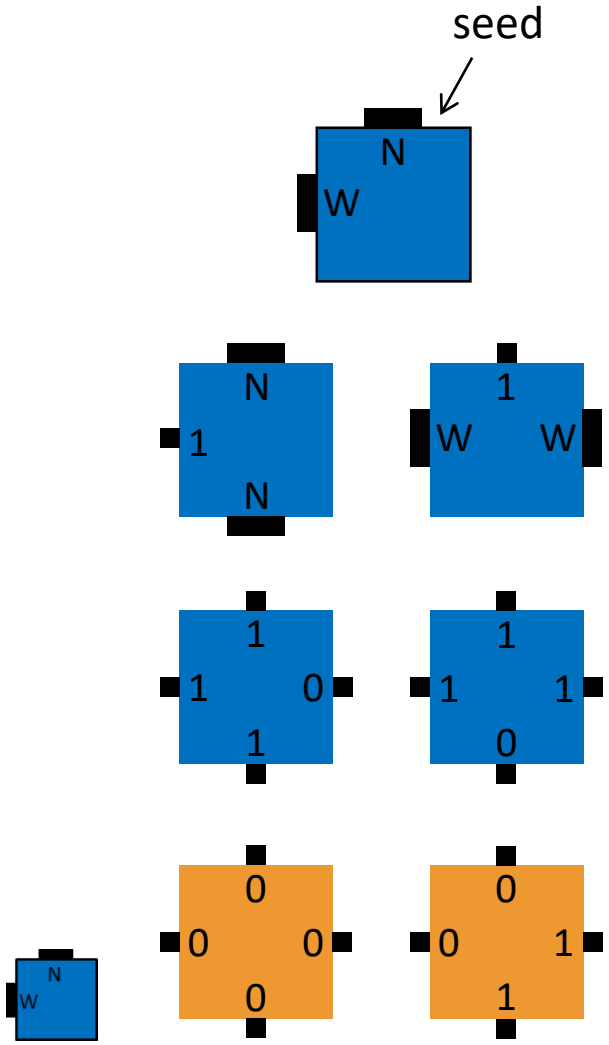

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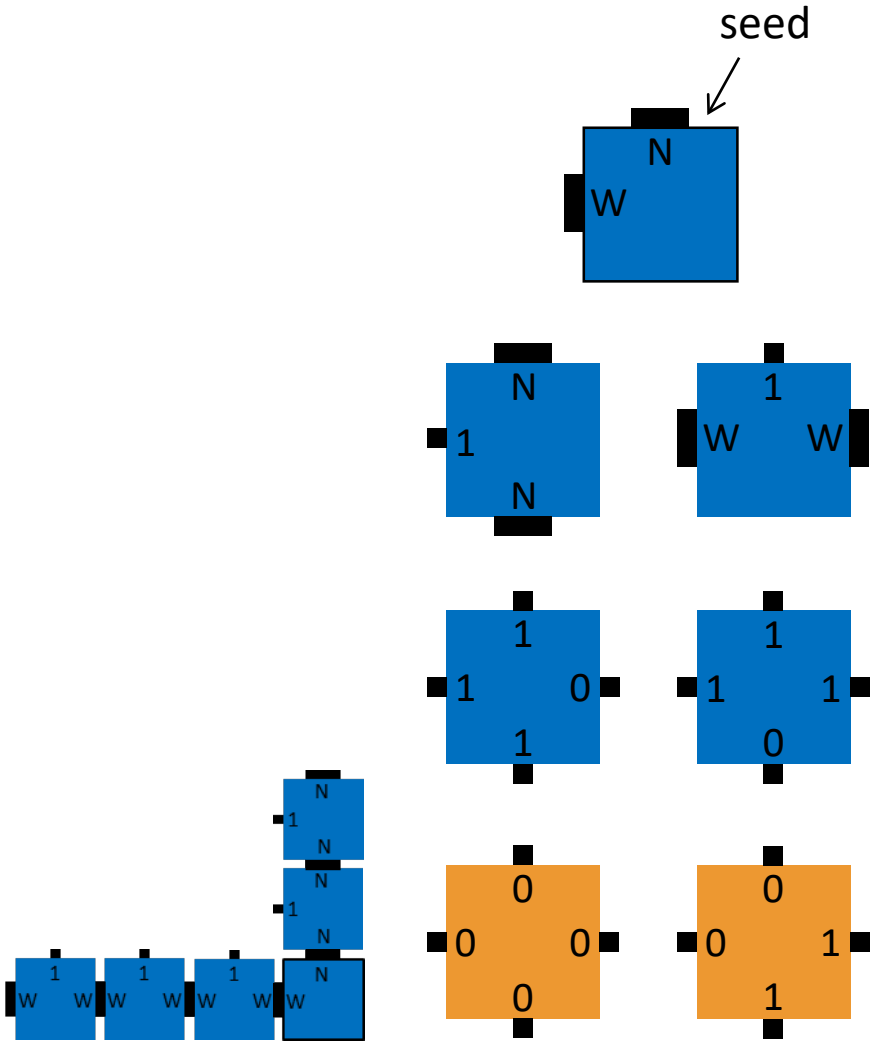

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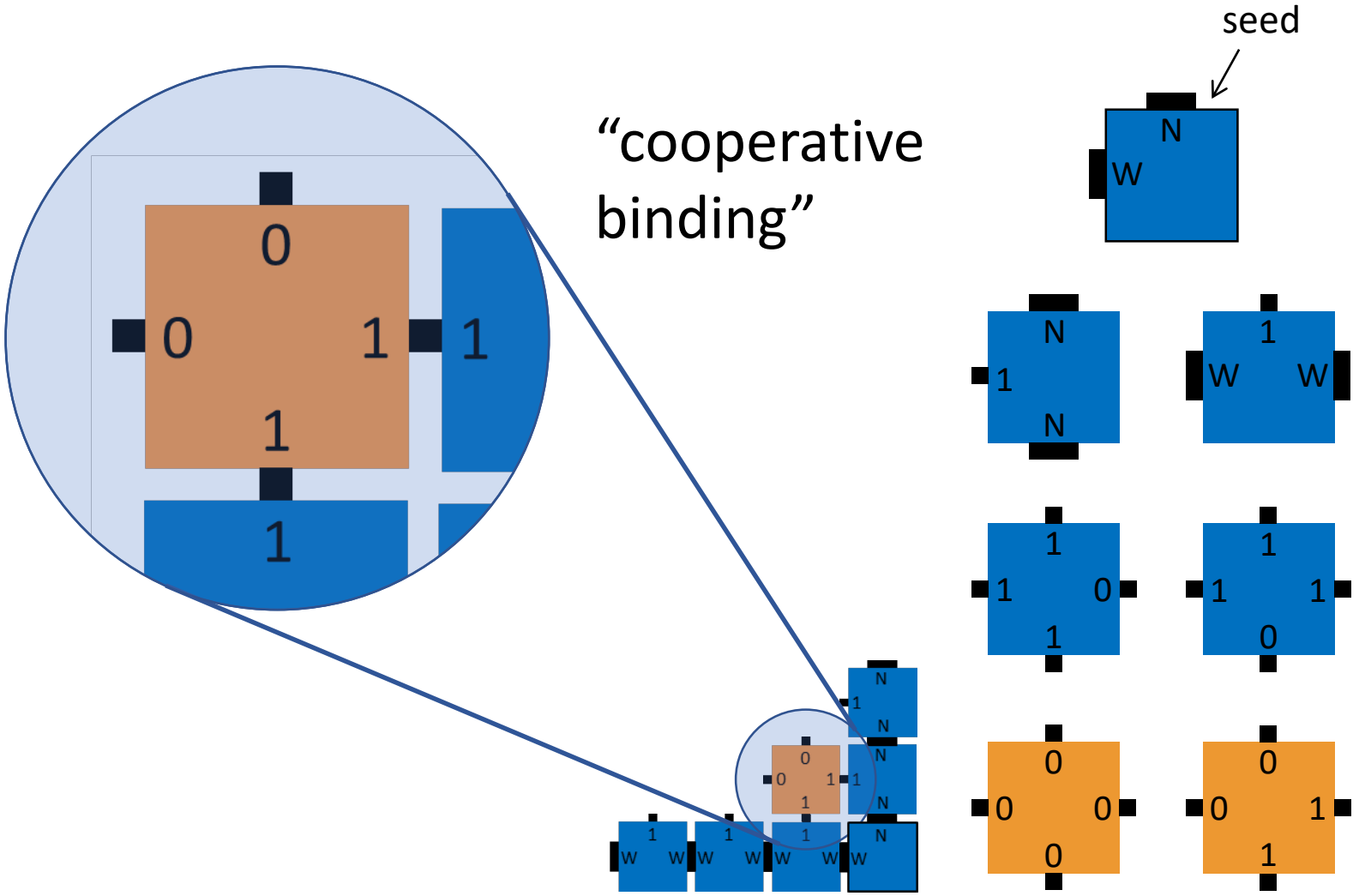

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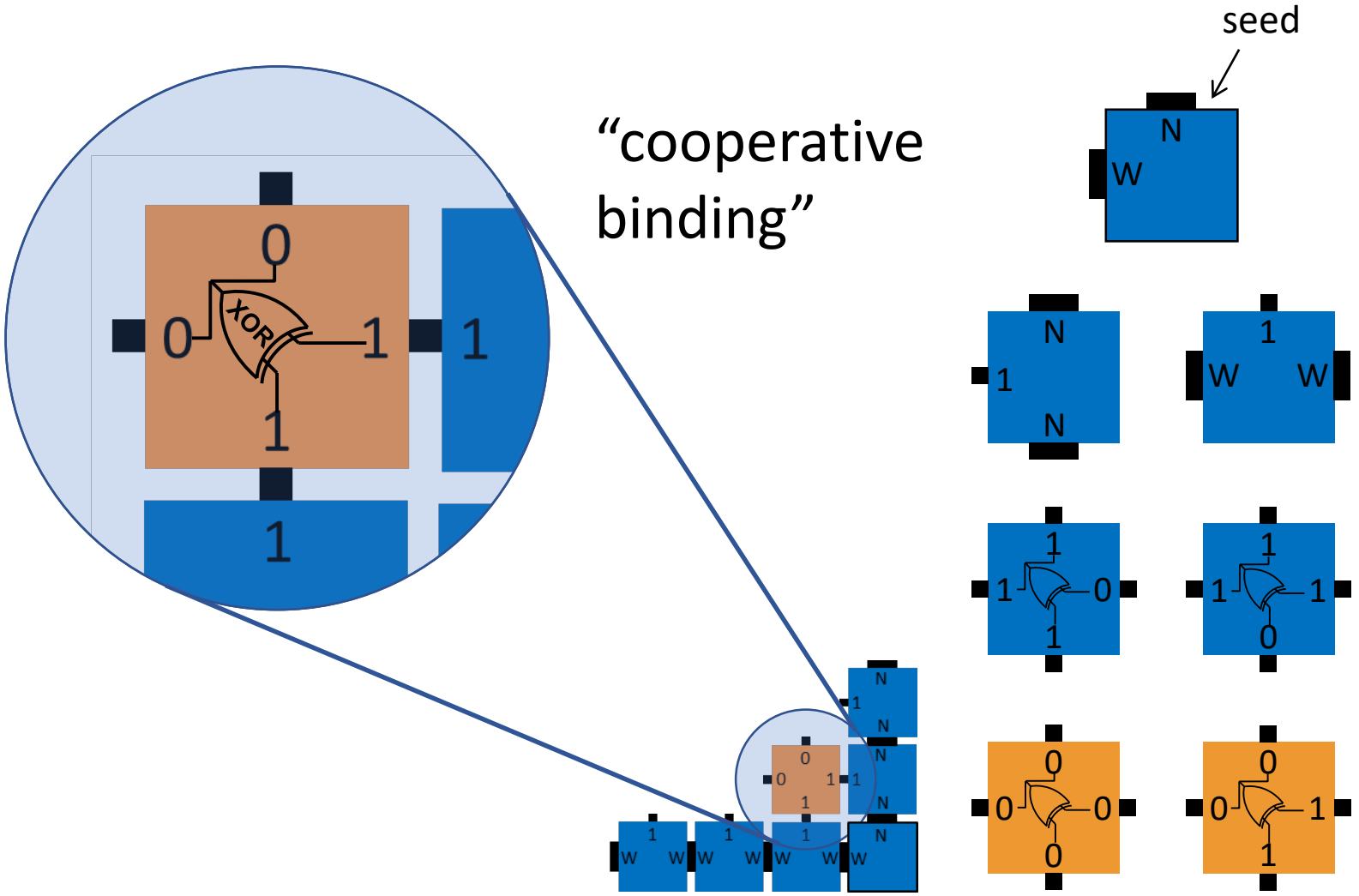

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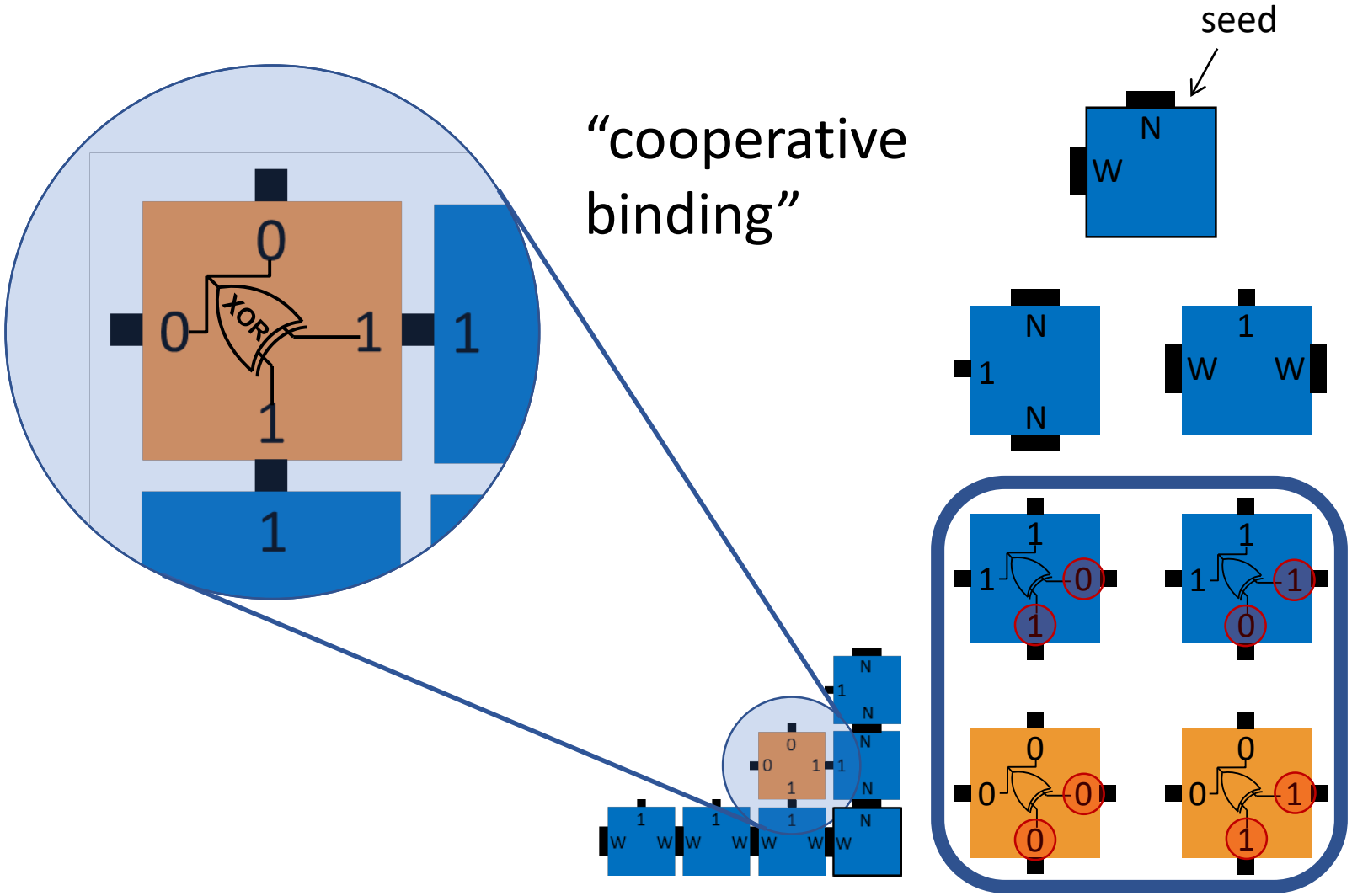

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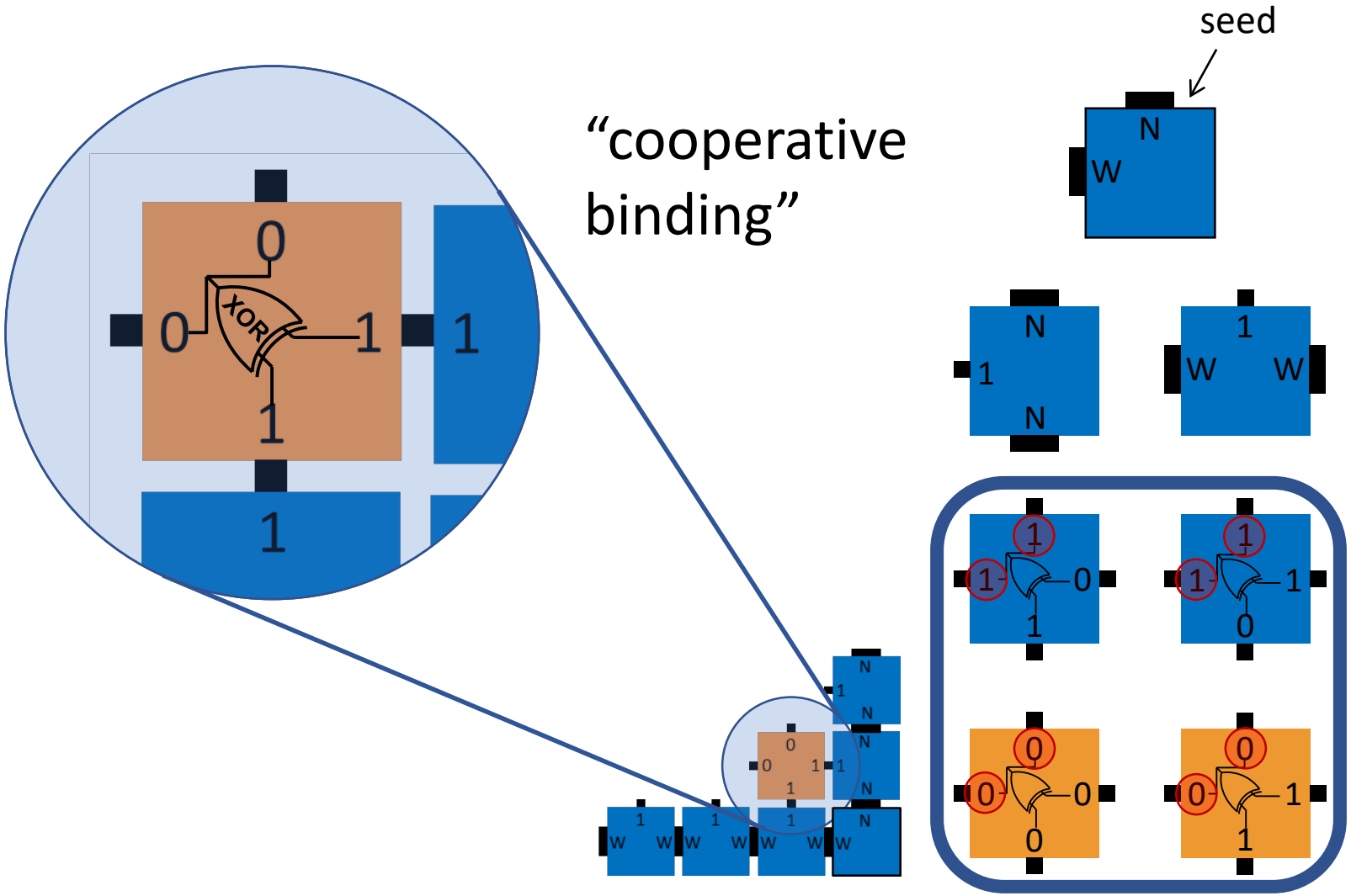

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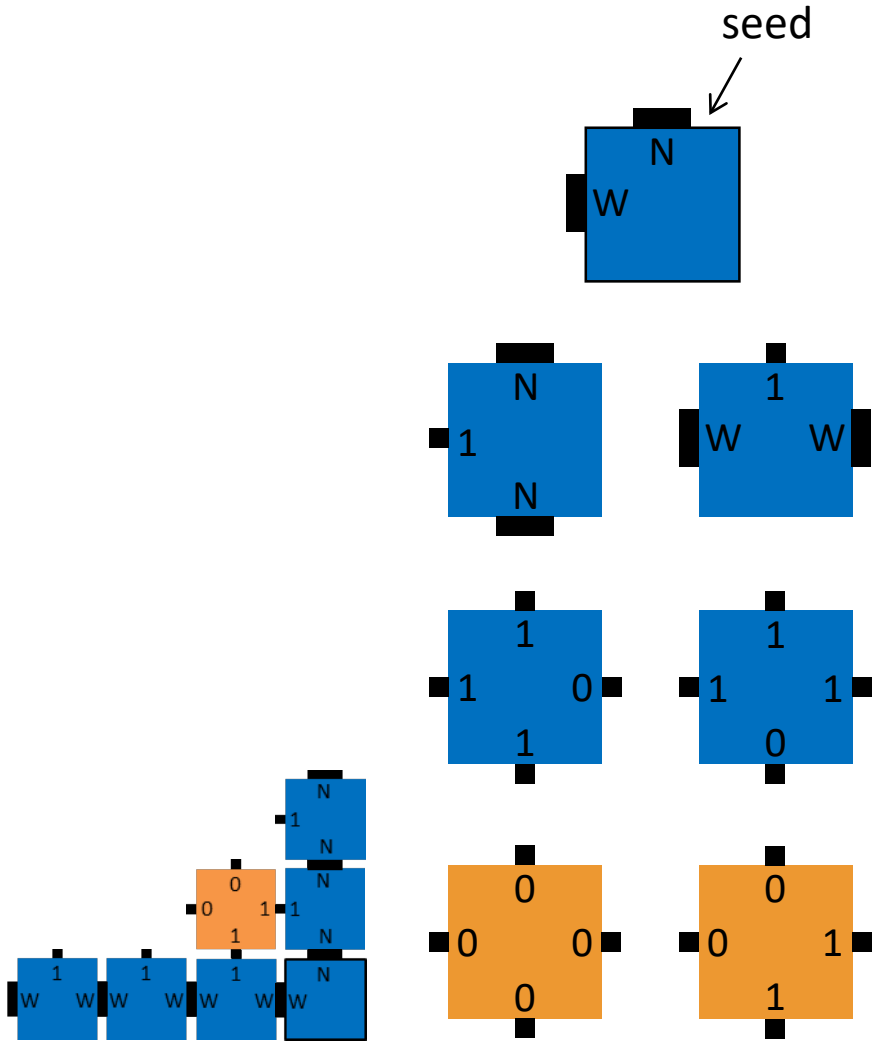

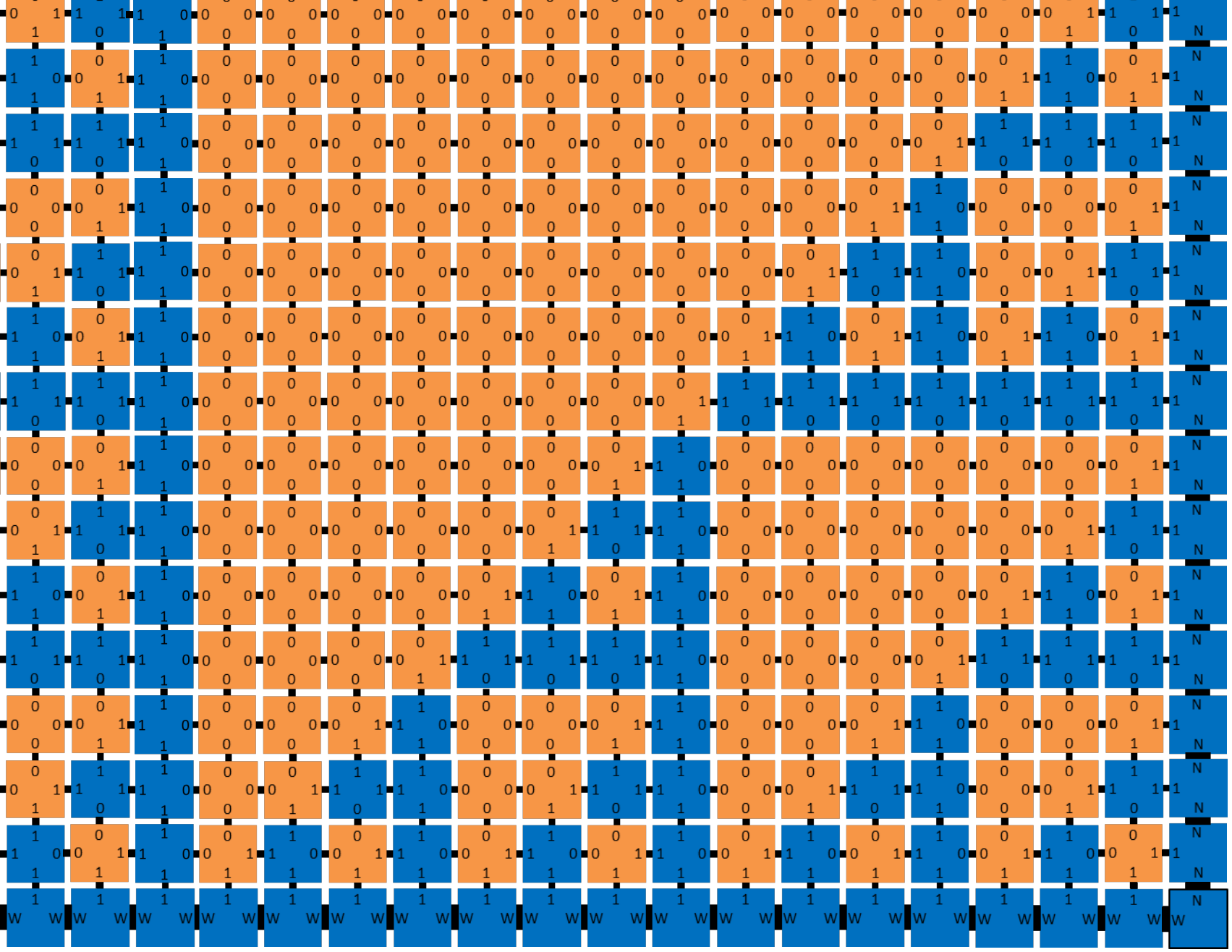

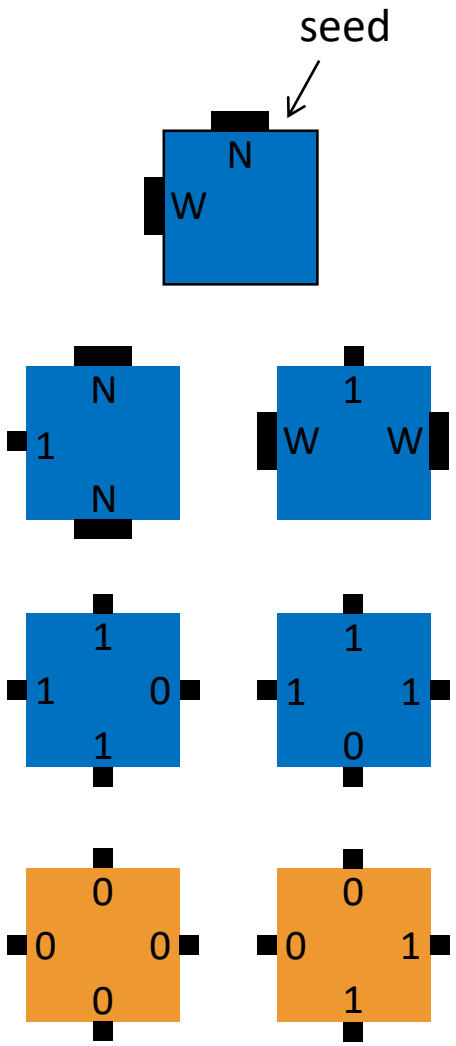
seed
N
W
N
1
N
1
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1
1
0
1
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0
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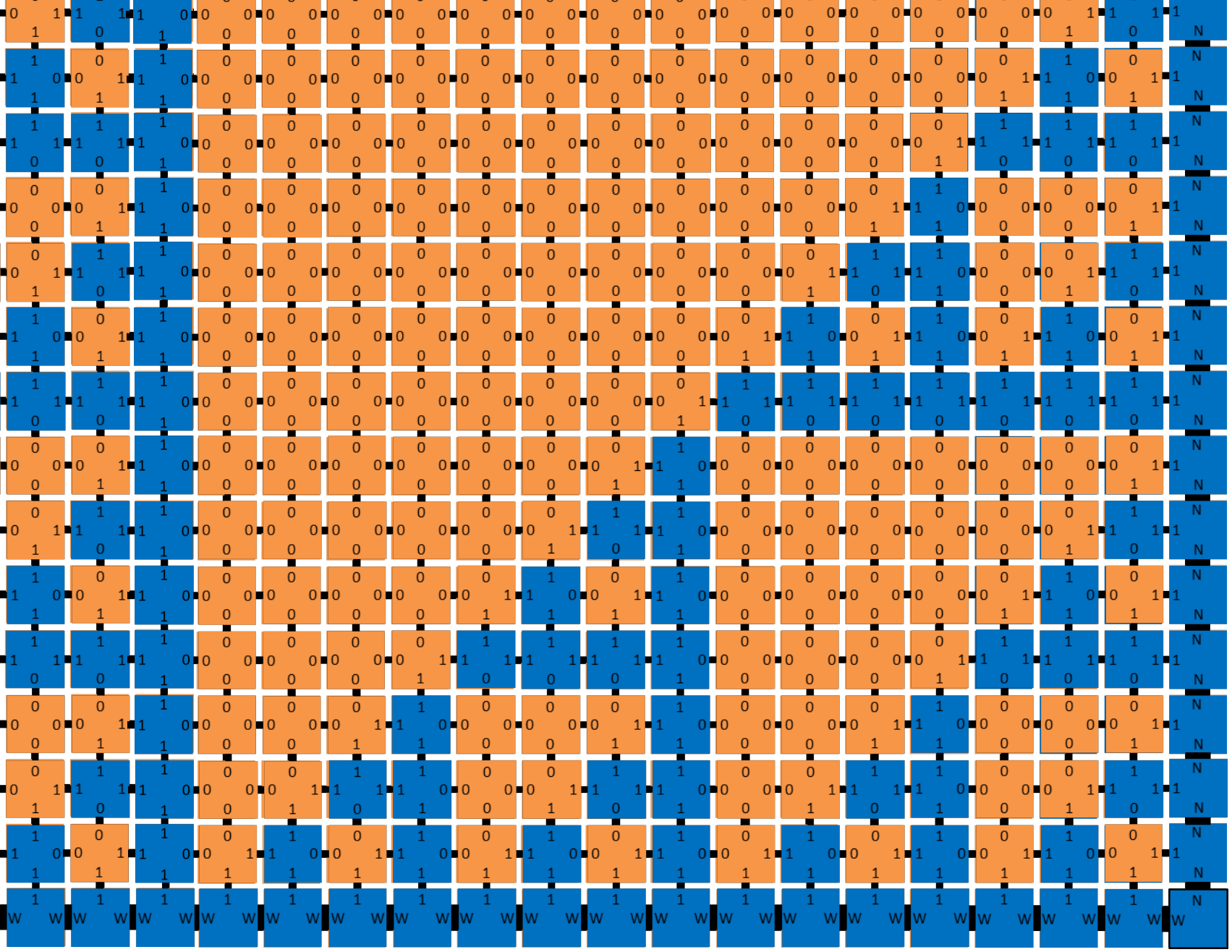
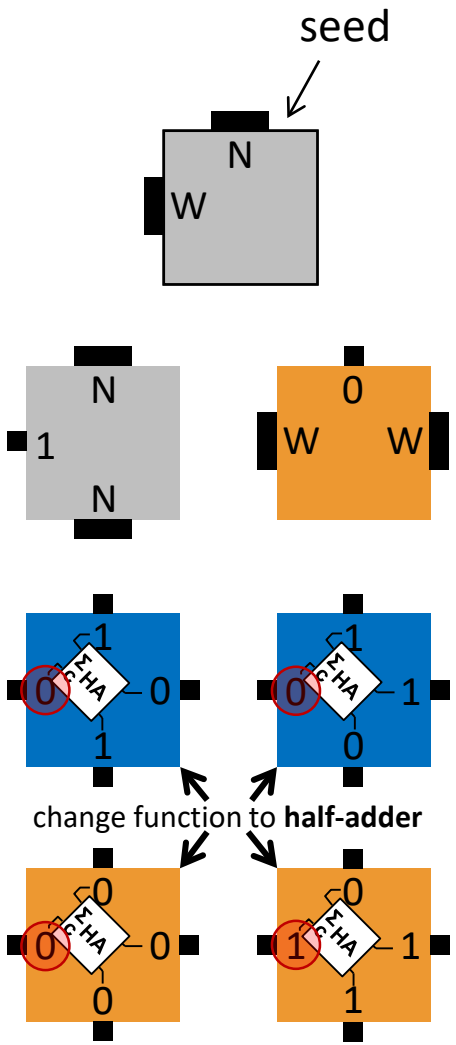
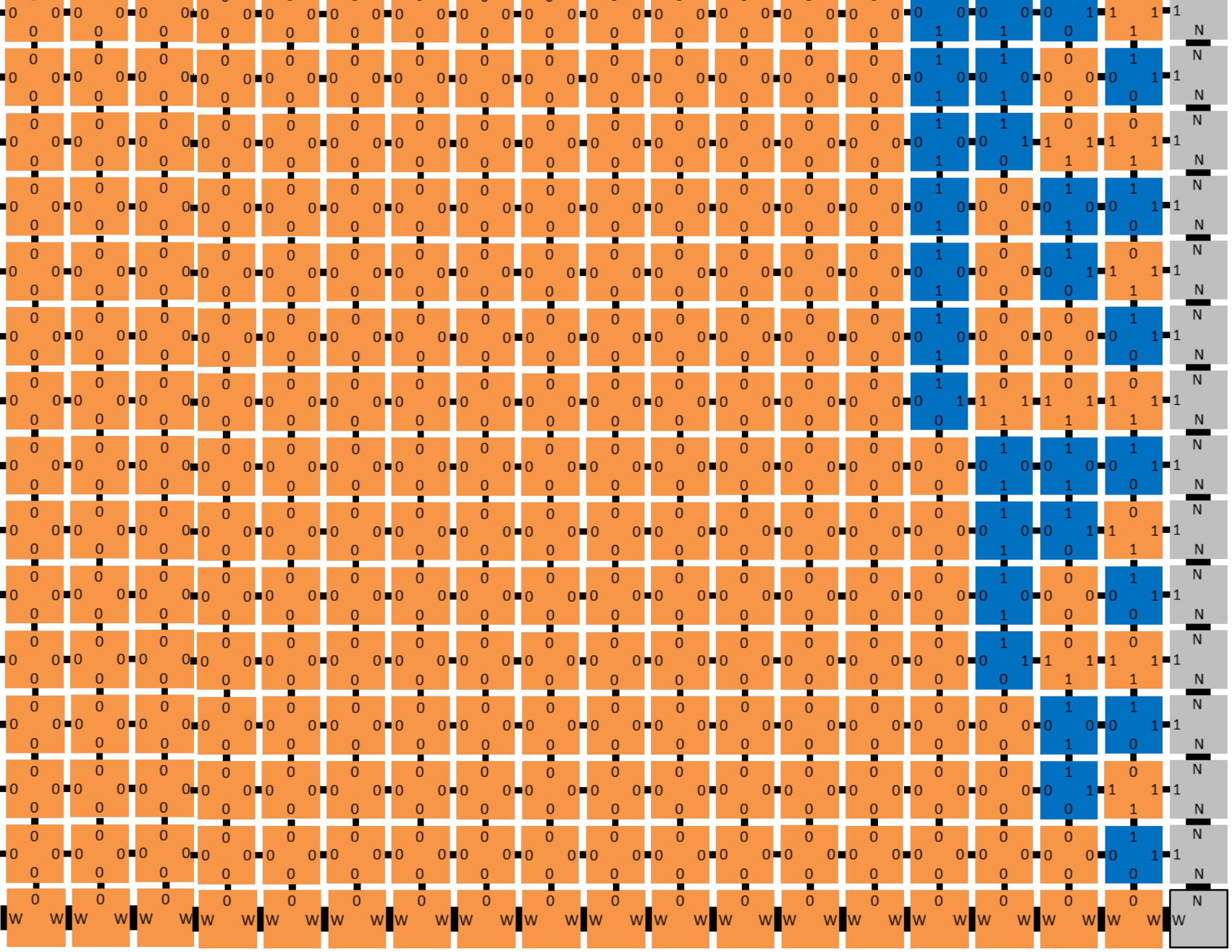
1




seed
N
W
N
1
N
0
W
W
1
0
0
1
change function to **half-adder**
0
0
0
0
1
1
0
1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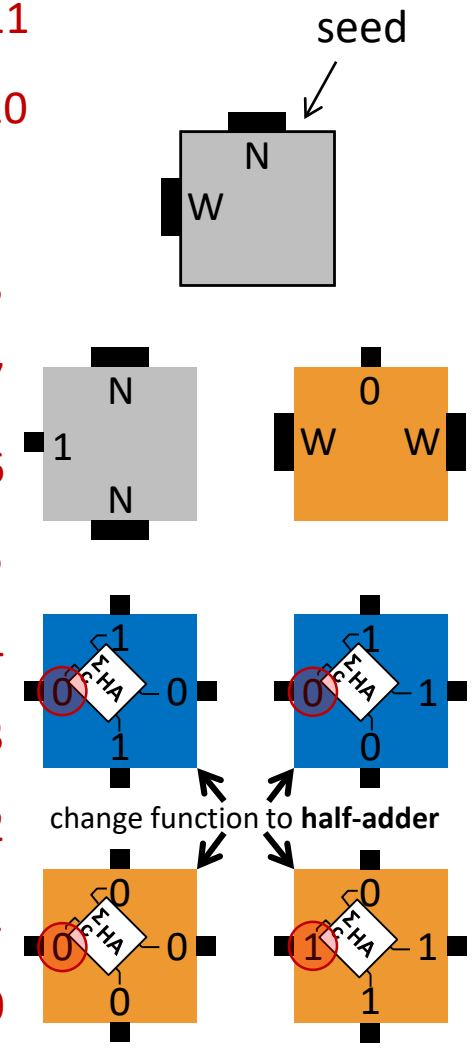
seed
N
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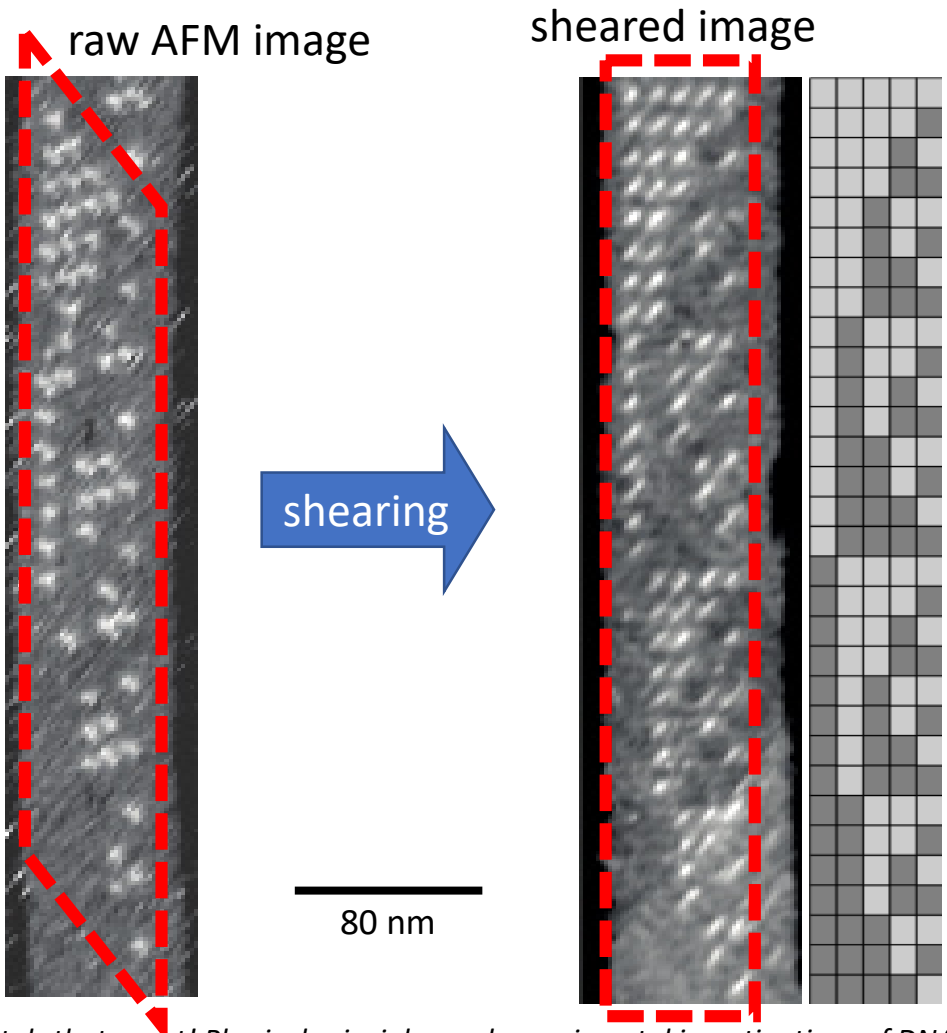
1
N
0
W
W
1
0
0
1
1
0
change function to **half-adder**
0
0
0
0
1
1
1
0

Algorithmic self-assembly in action



[*Crystals that count! Physical principles and experimental investigations of DNA tile self-assembly*, Constantine Evans, Ph.D. thesis, Caltech, 2014]

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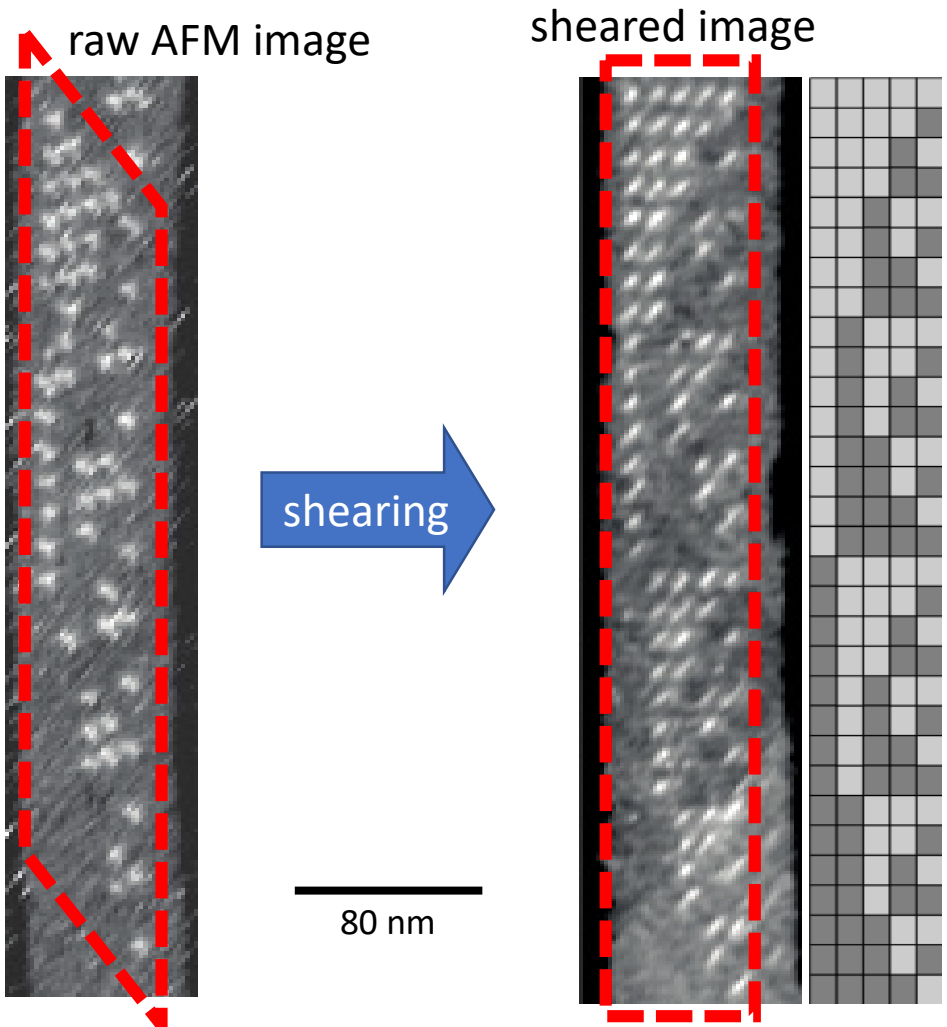

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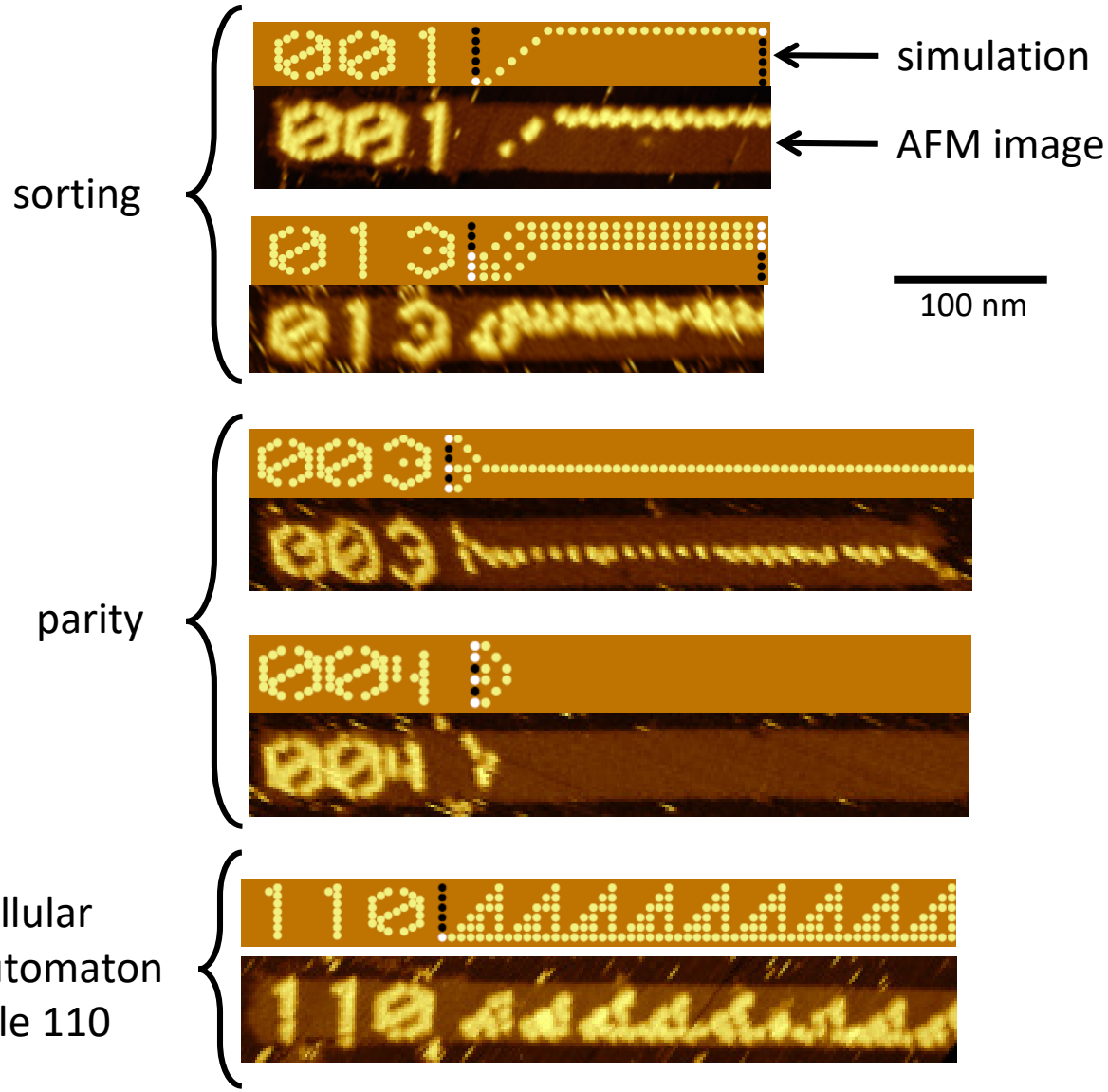
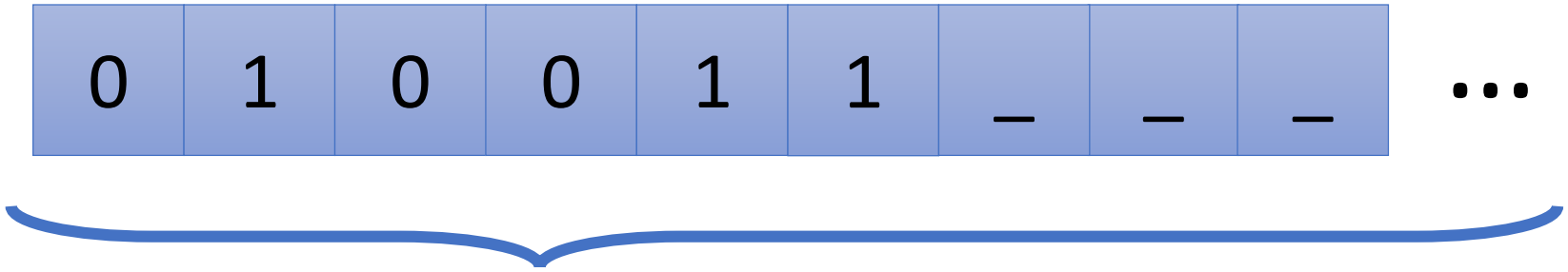


[*Diverse and robust molecular algorithms using reprogrammable DNA self-assembly*. Woods, Doty, Myhrvold, Hui, Wu, Yin, Winfree, submitted]

How computationally powerful are self-assembling tiles?

Turing machines

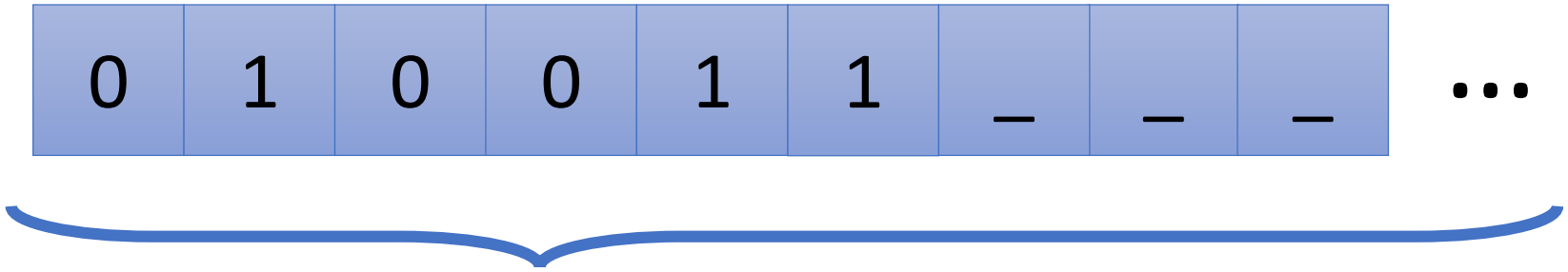
Turing machines



tape ≈ memory

Turing machines

state ≈ line of code



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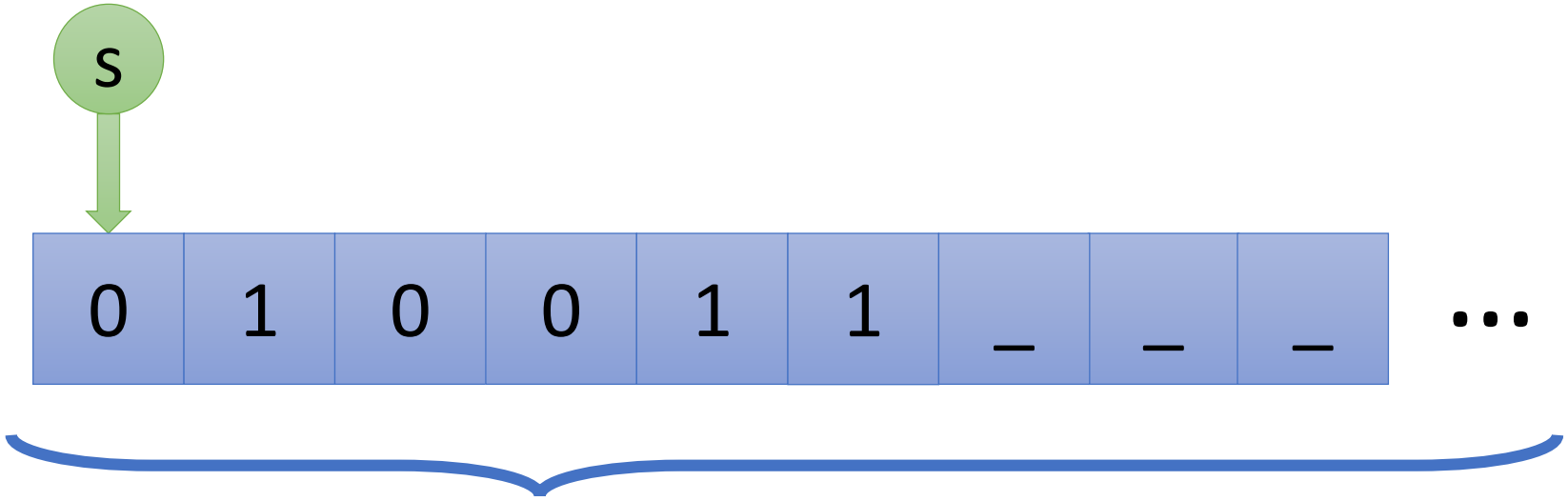

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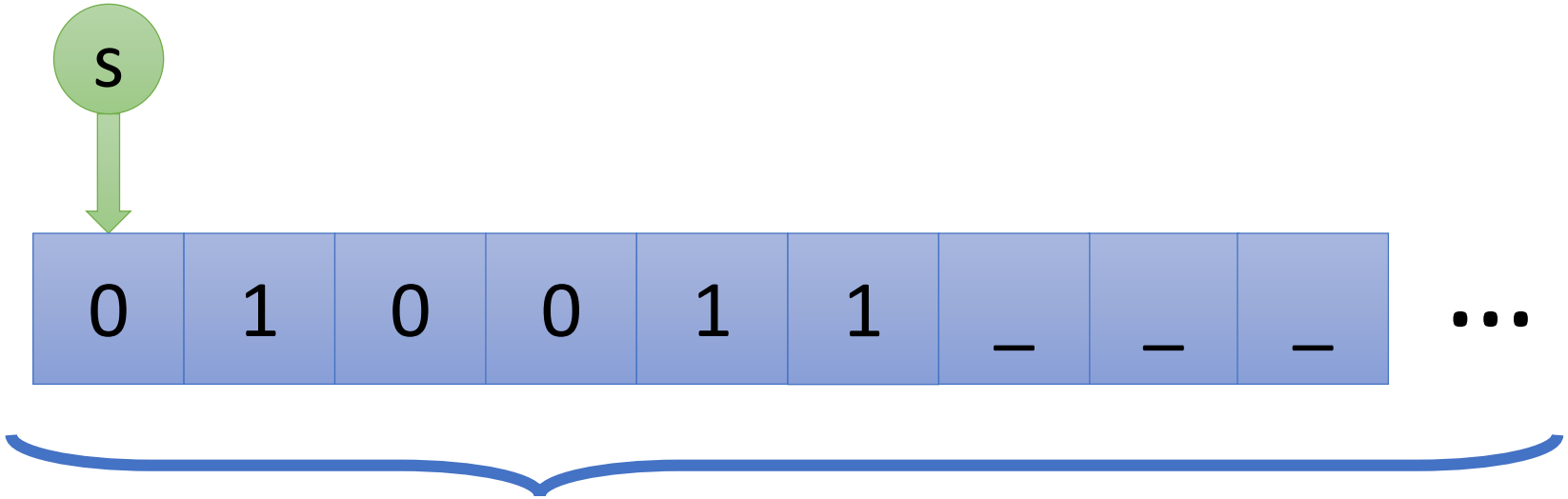

transitions
(instructions)

tape ≈ memory

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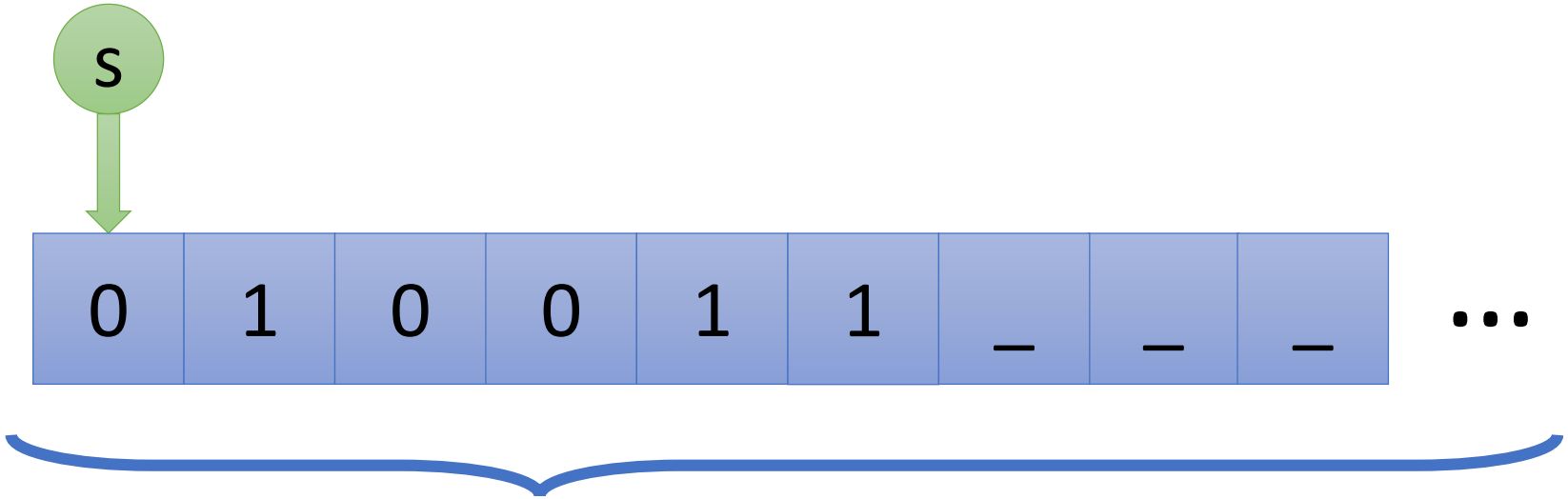
current state



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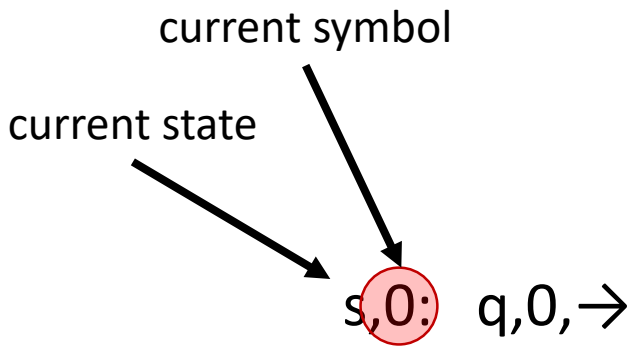

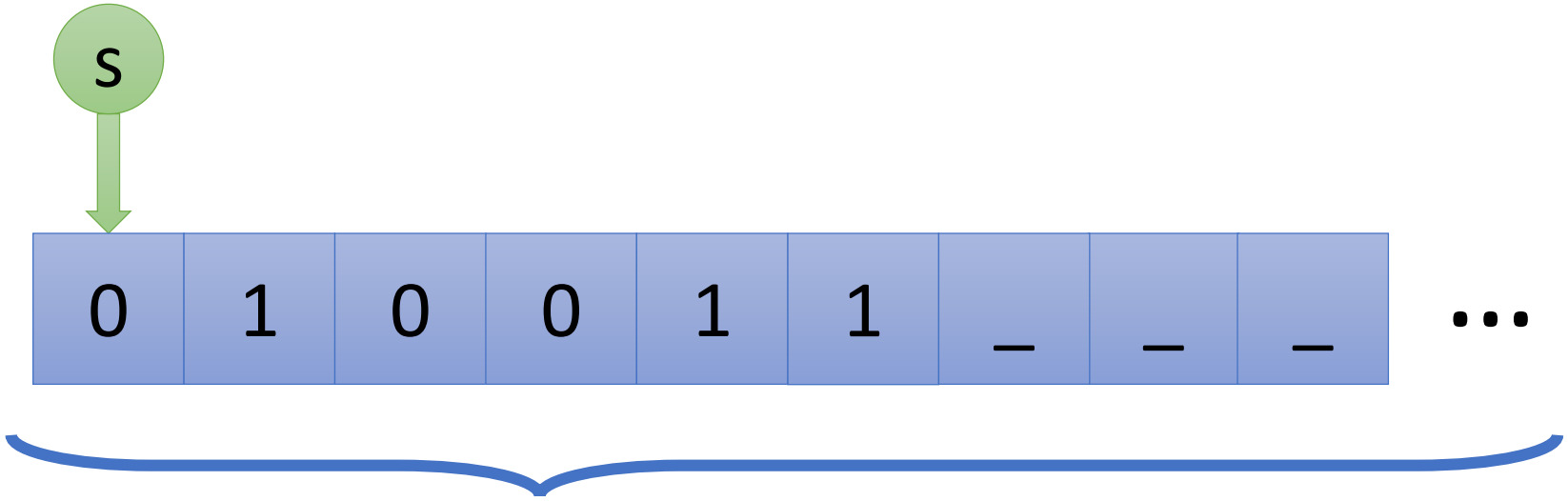

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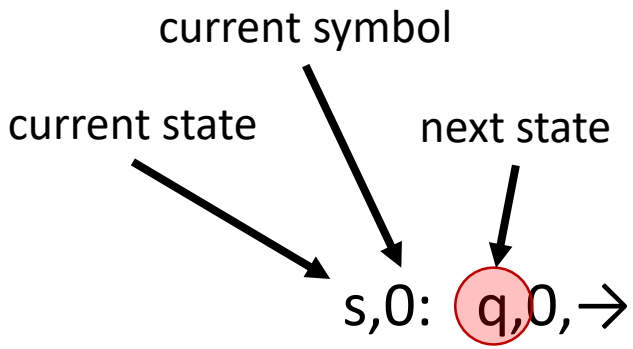

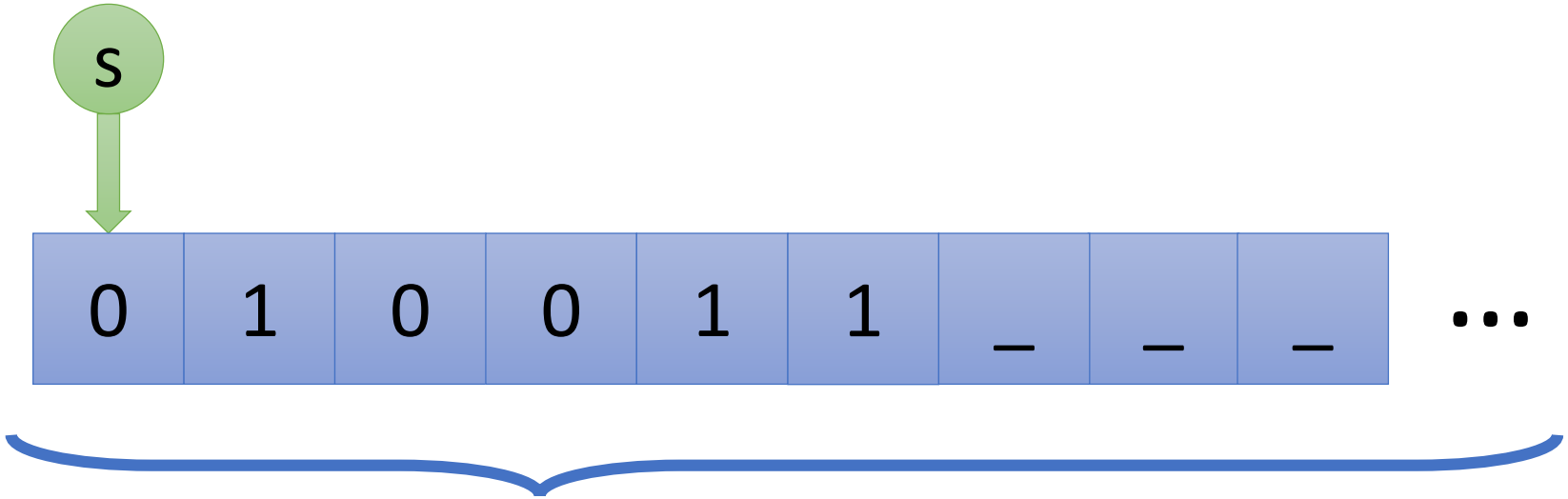

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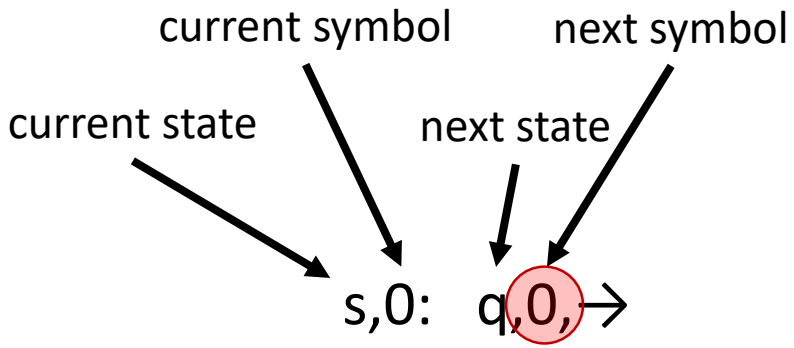

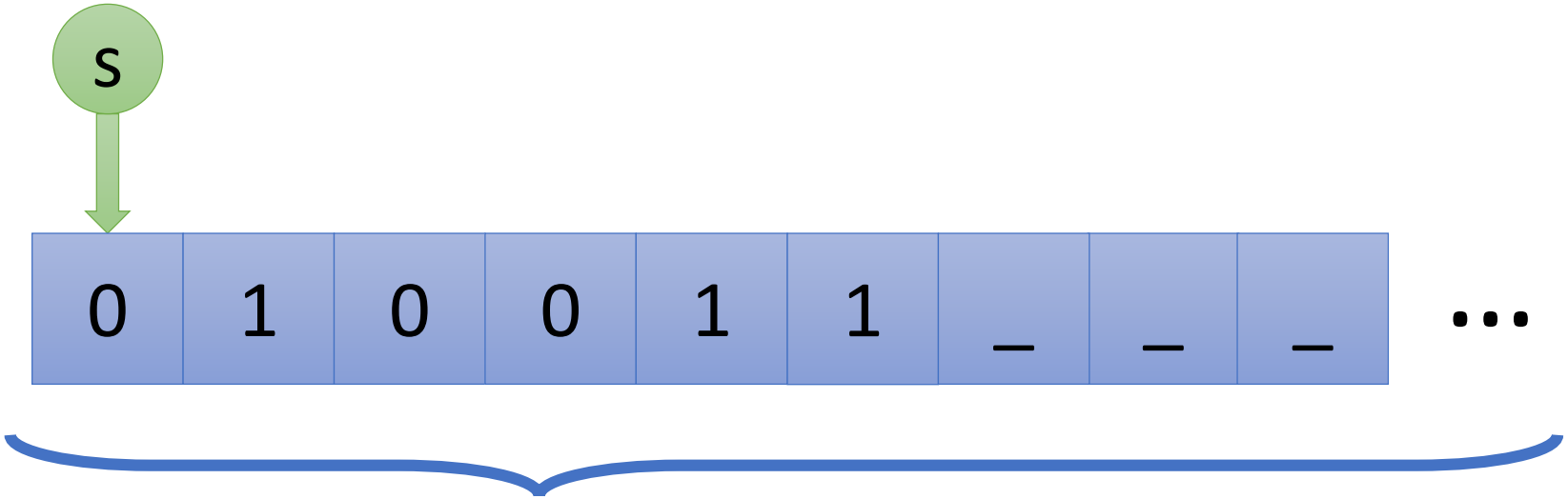

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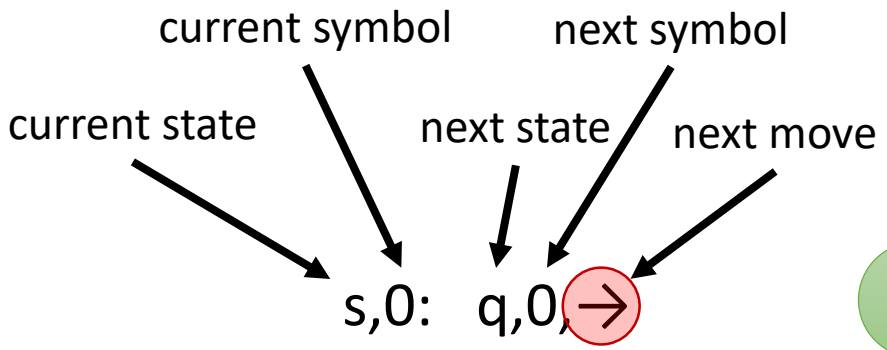

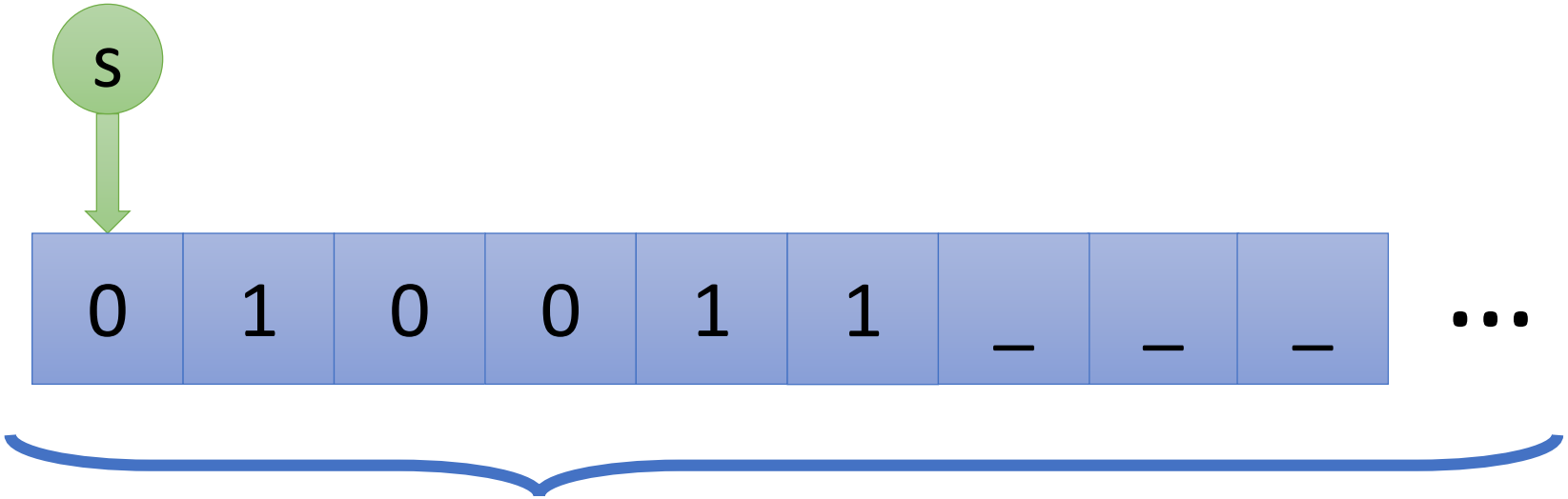

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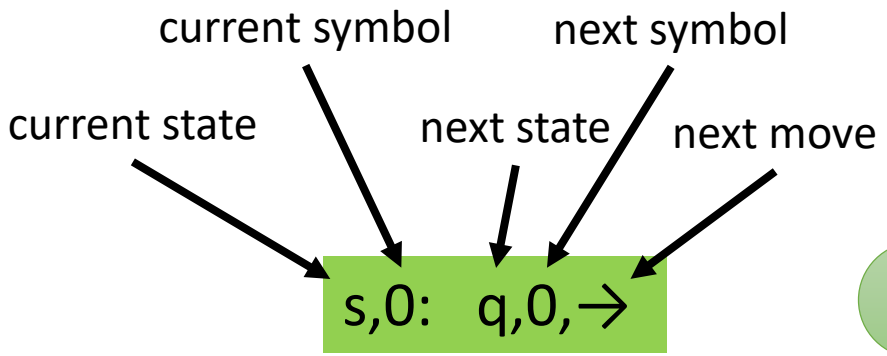

q,0: t,1,←

q,1: s,0,→

t,0: u,1,→

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transitions
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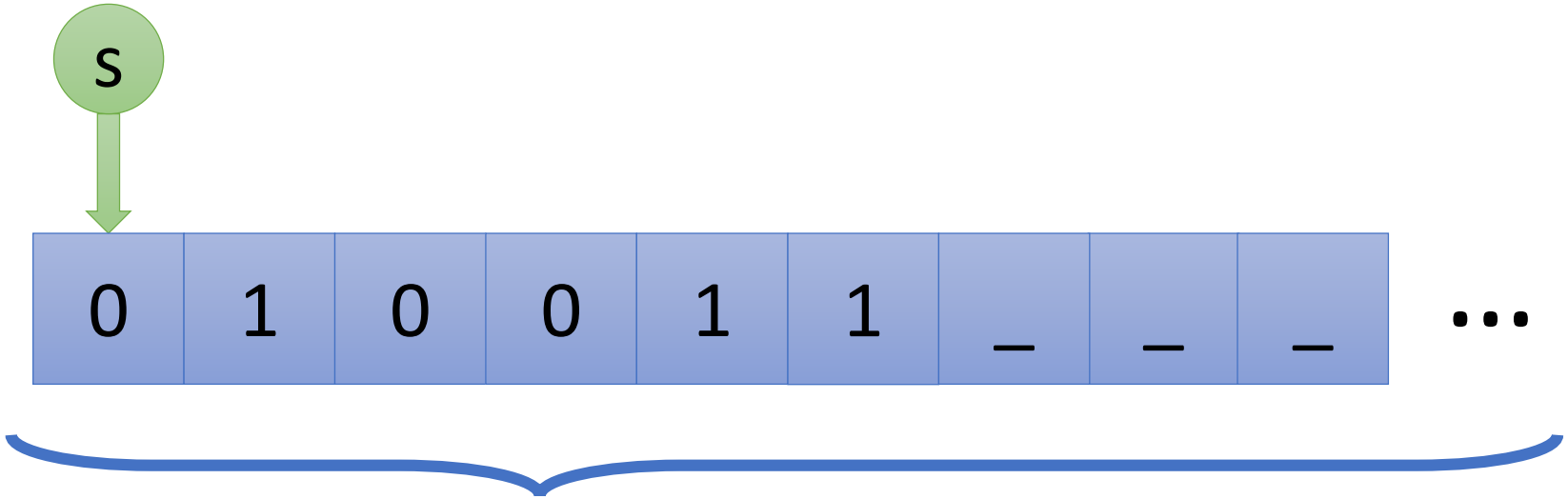

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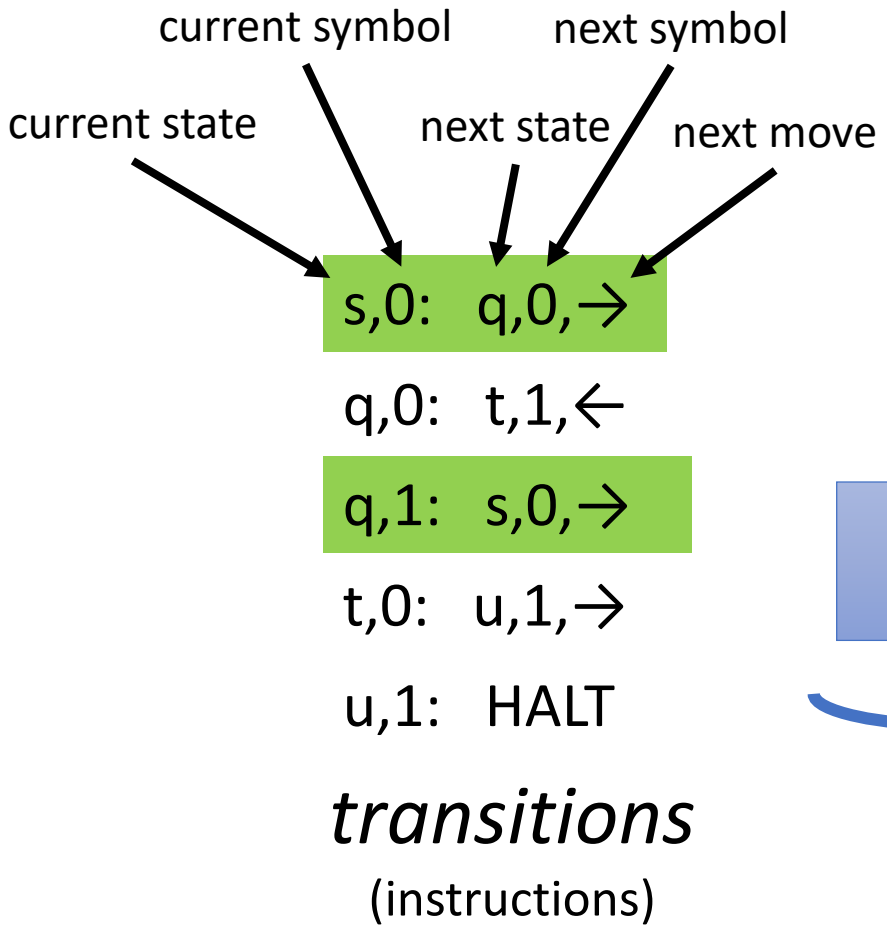

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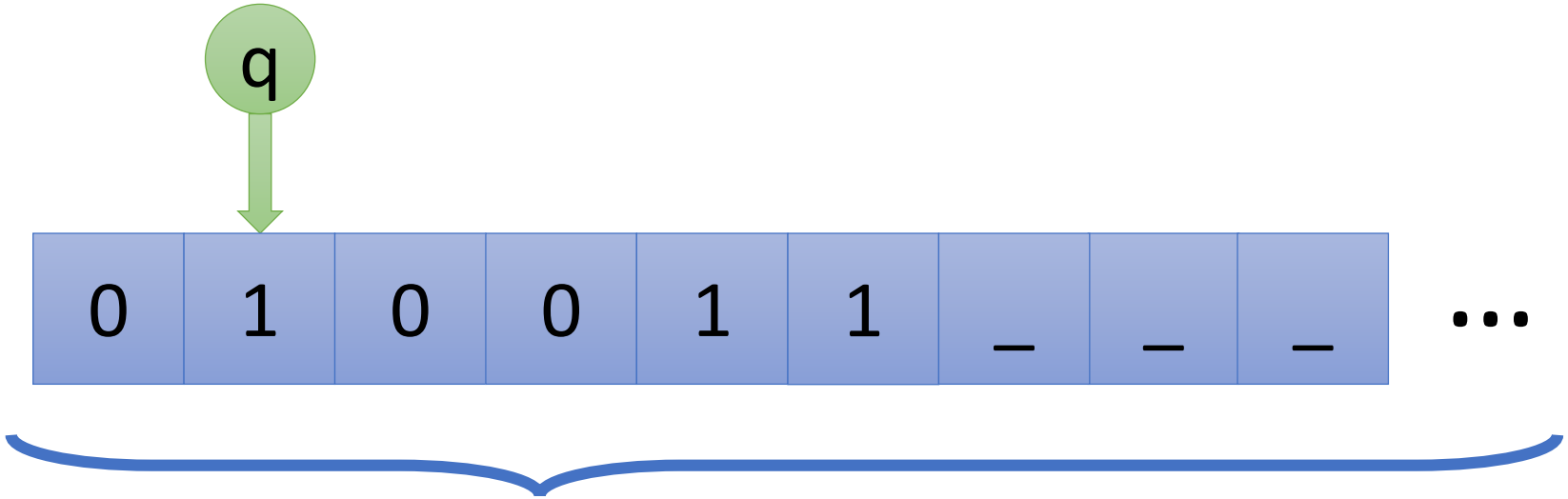

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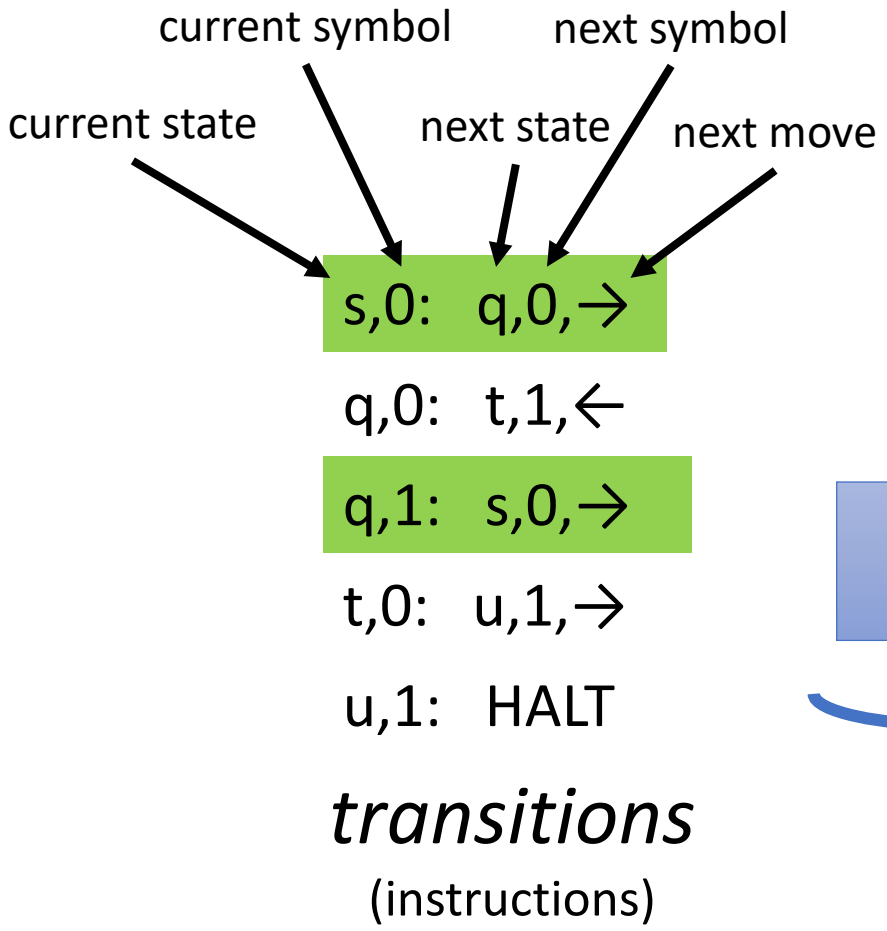
Turing machines



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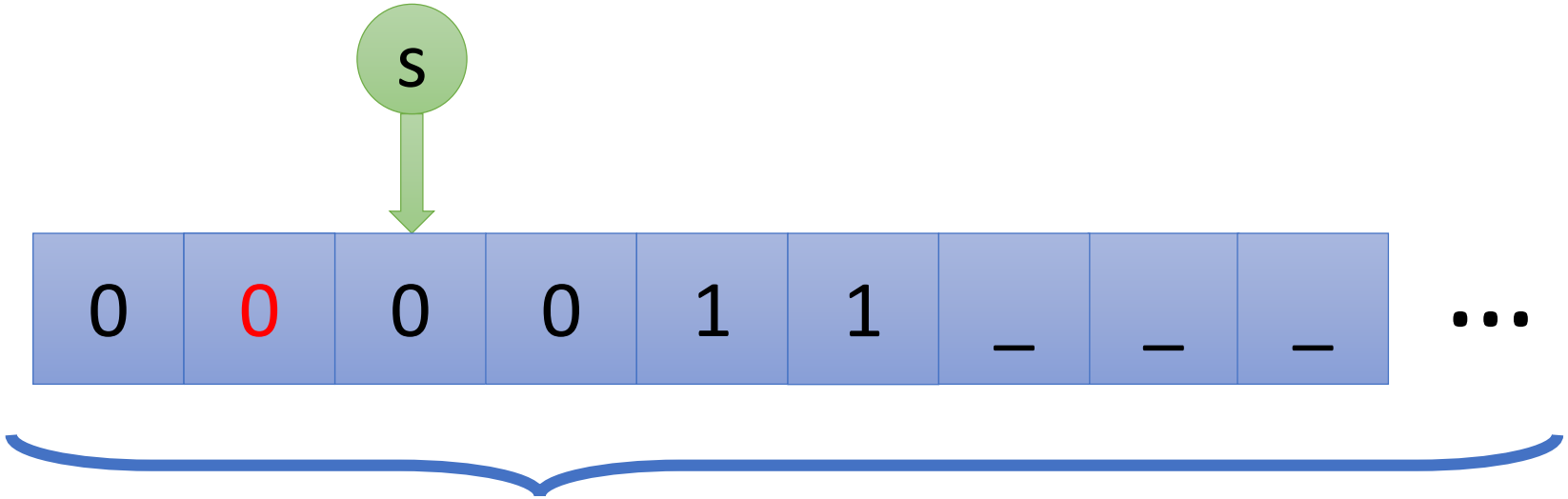

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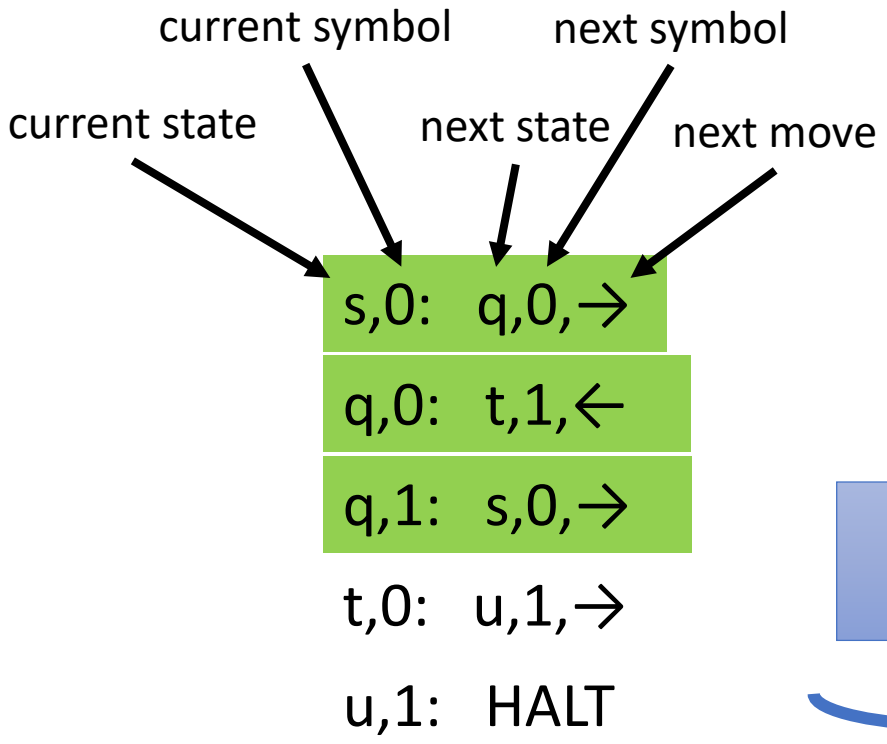

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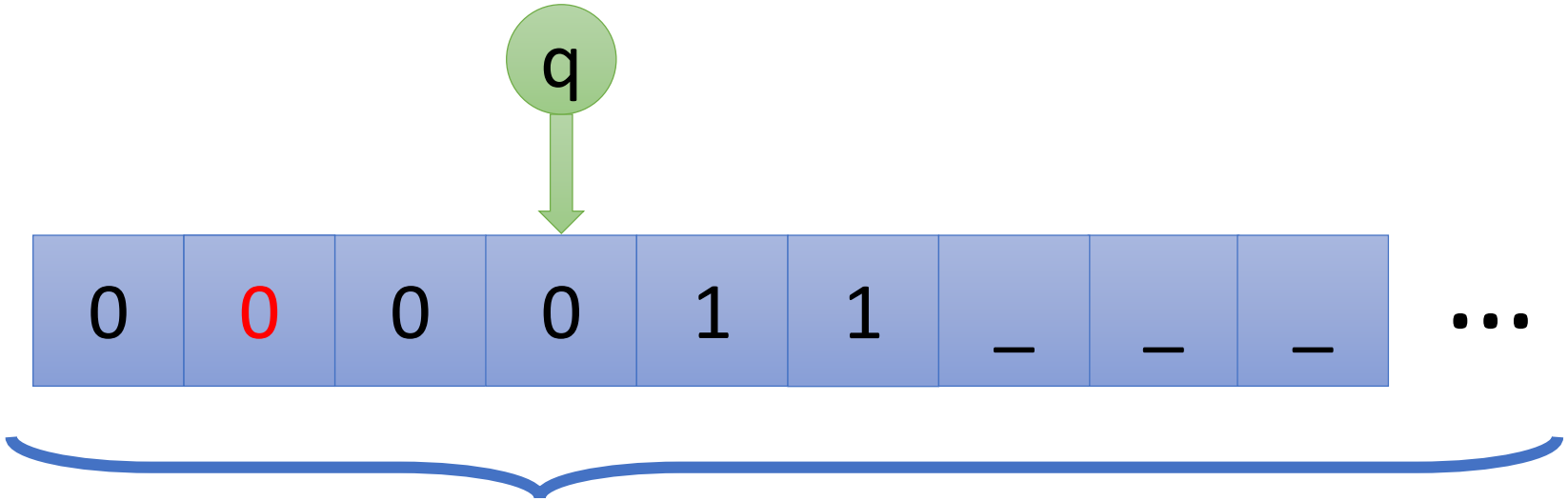

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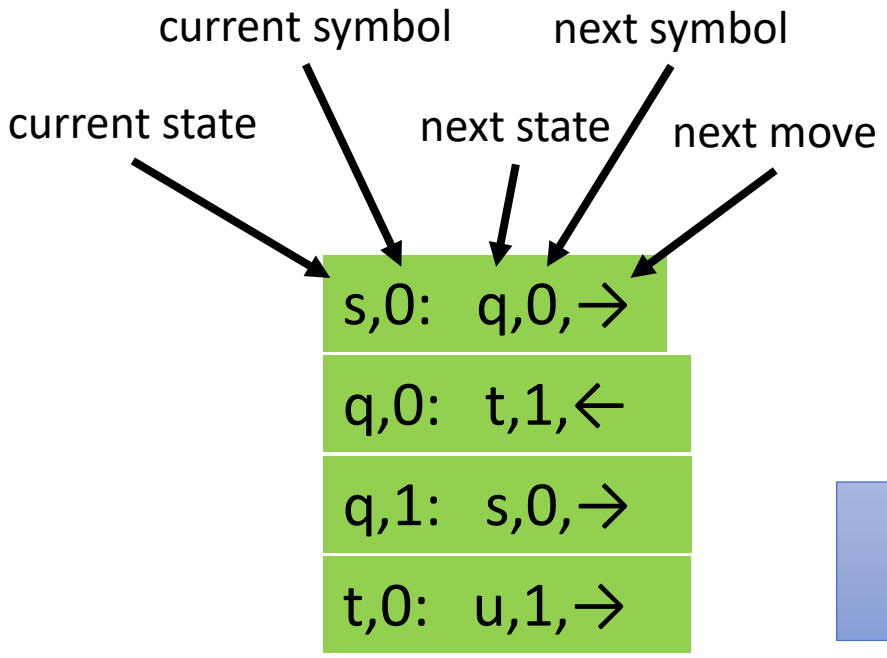

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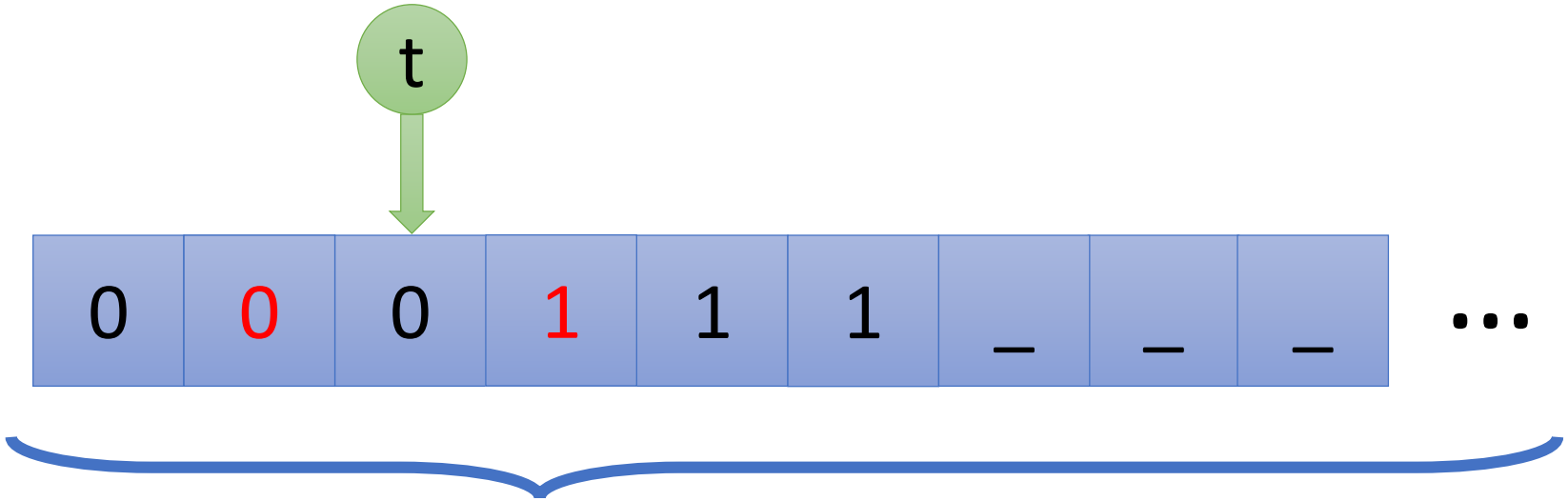

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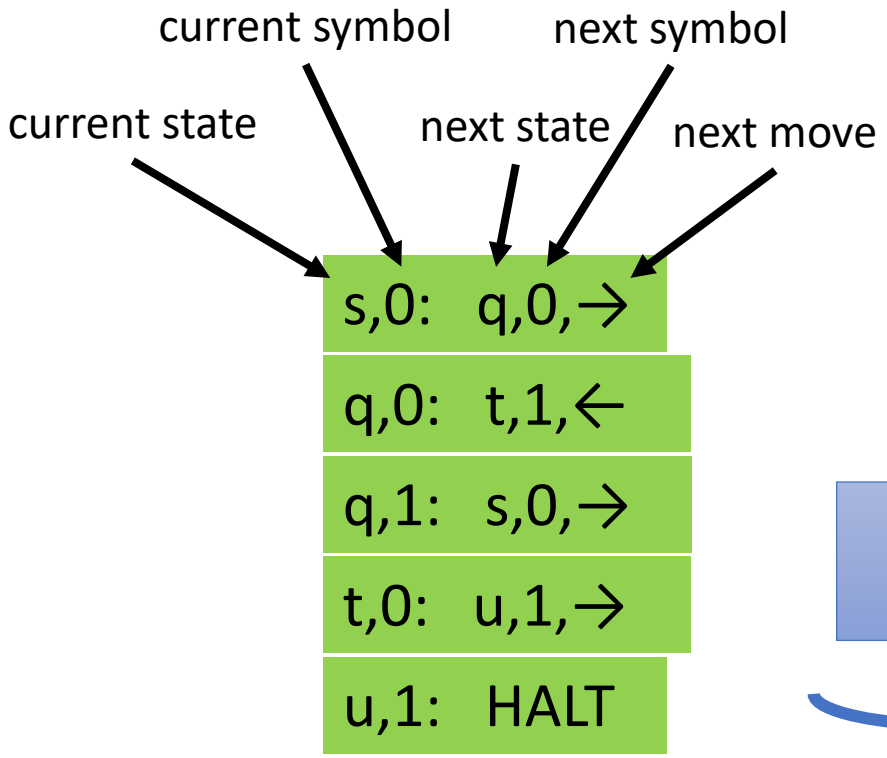

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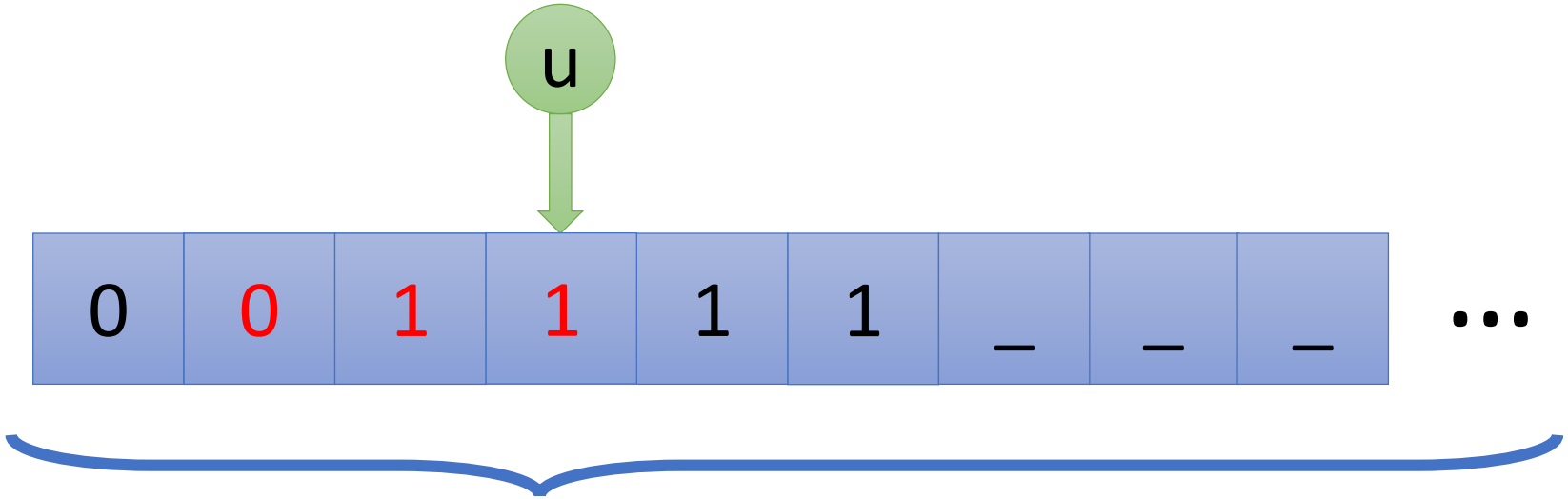

tape ≈ memory

Tile assembly is Turing-universal

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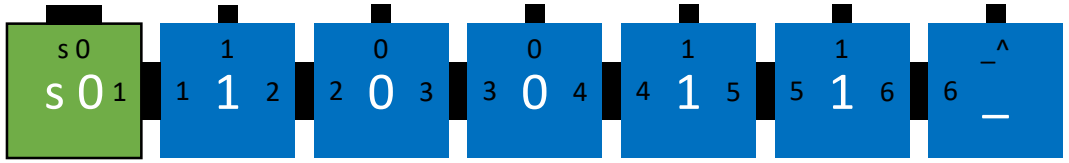

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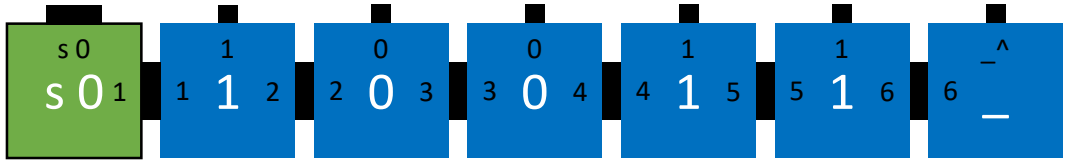

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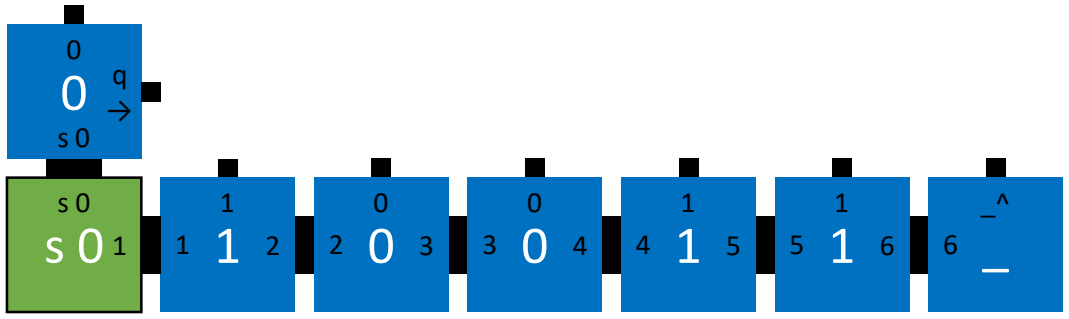

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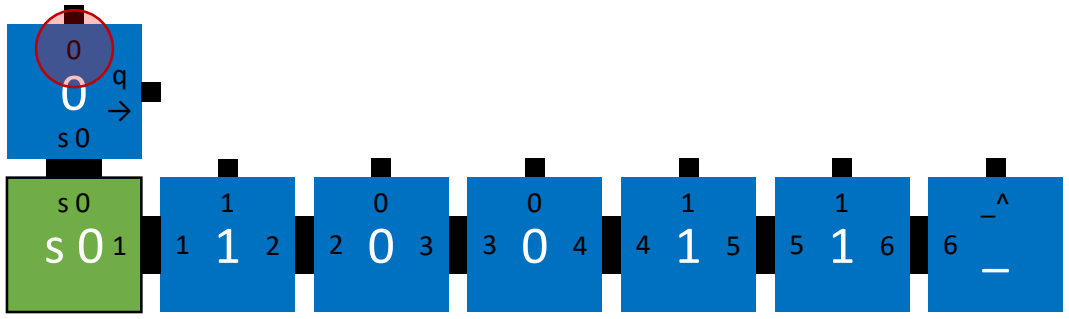

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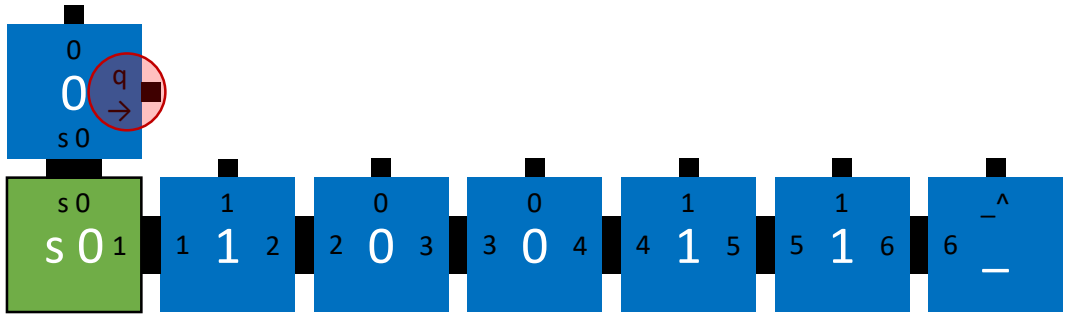

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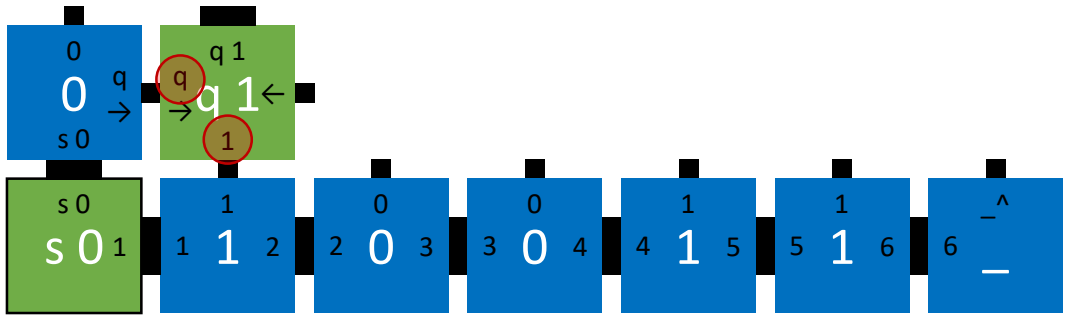

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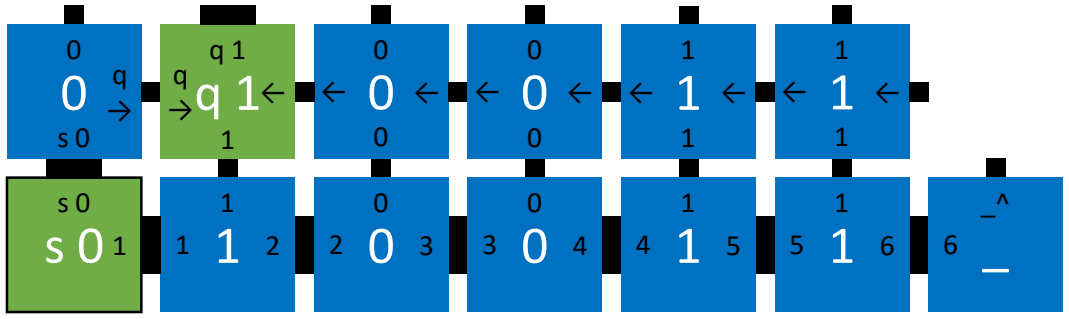

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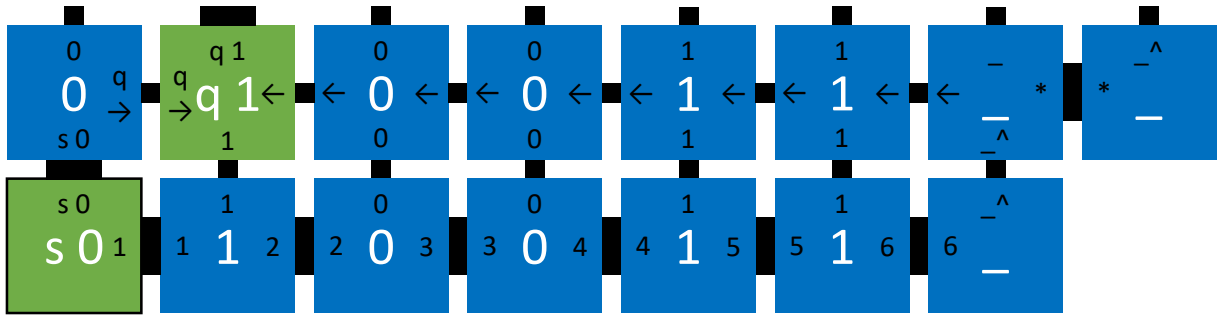

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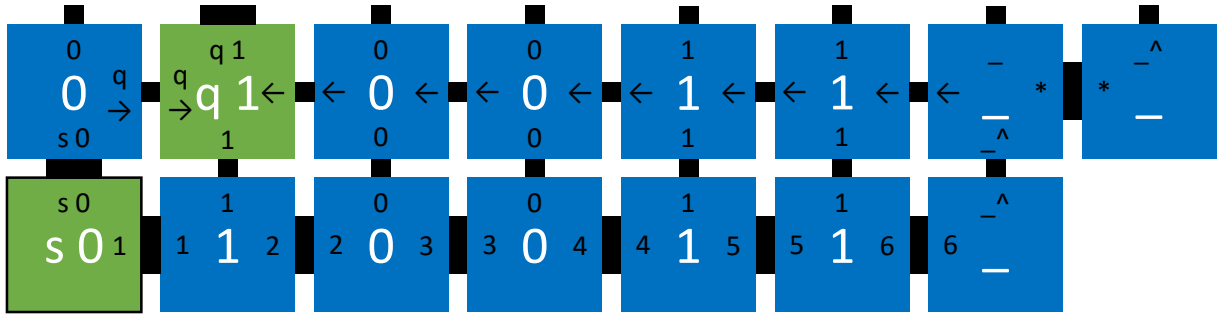

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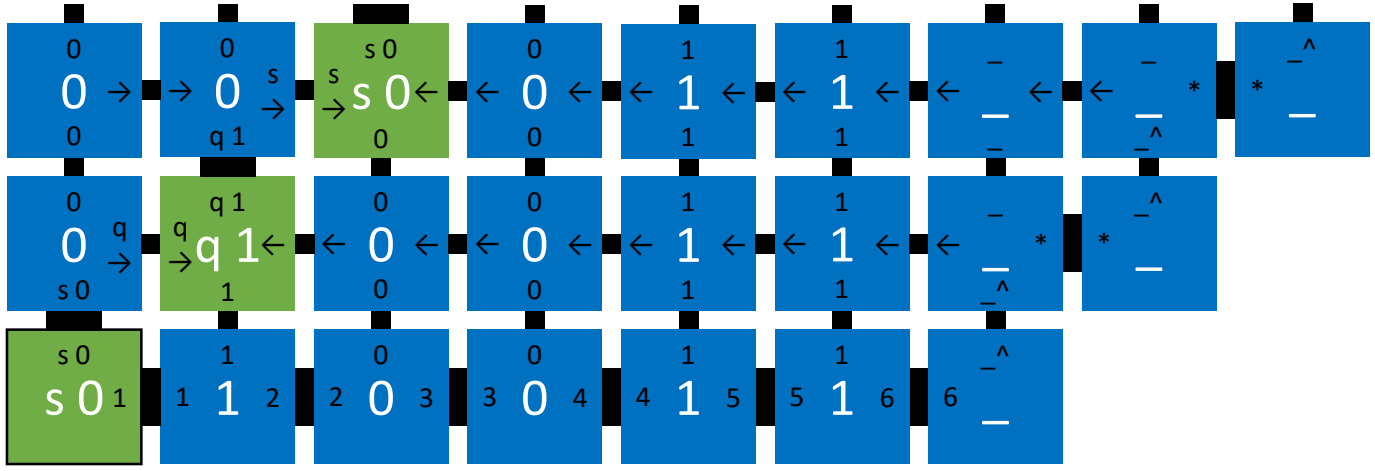

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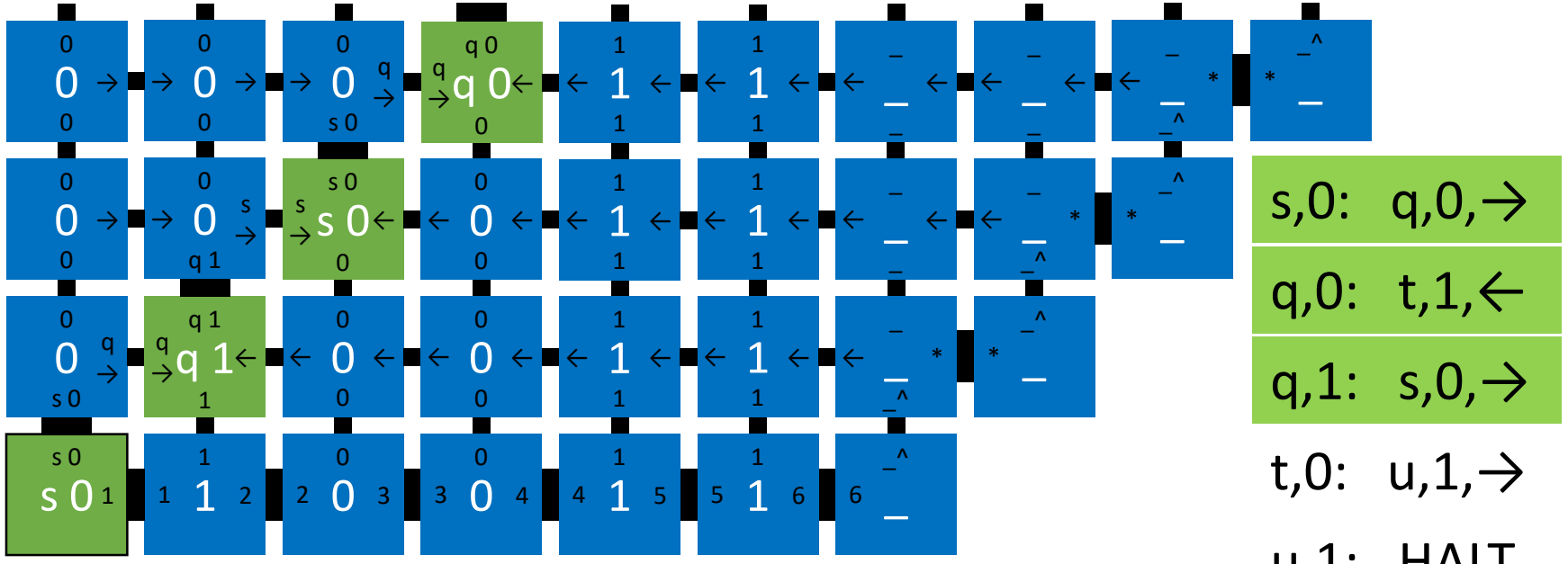

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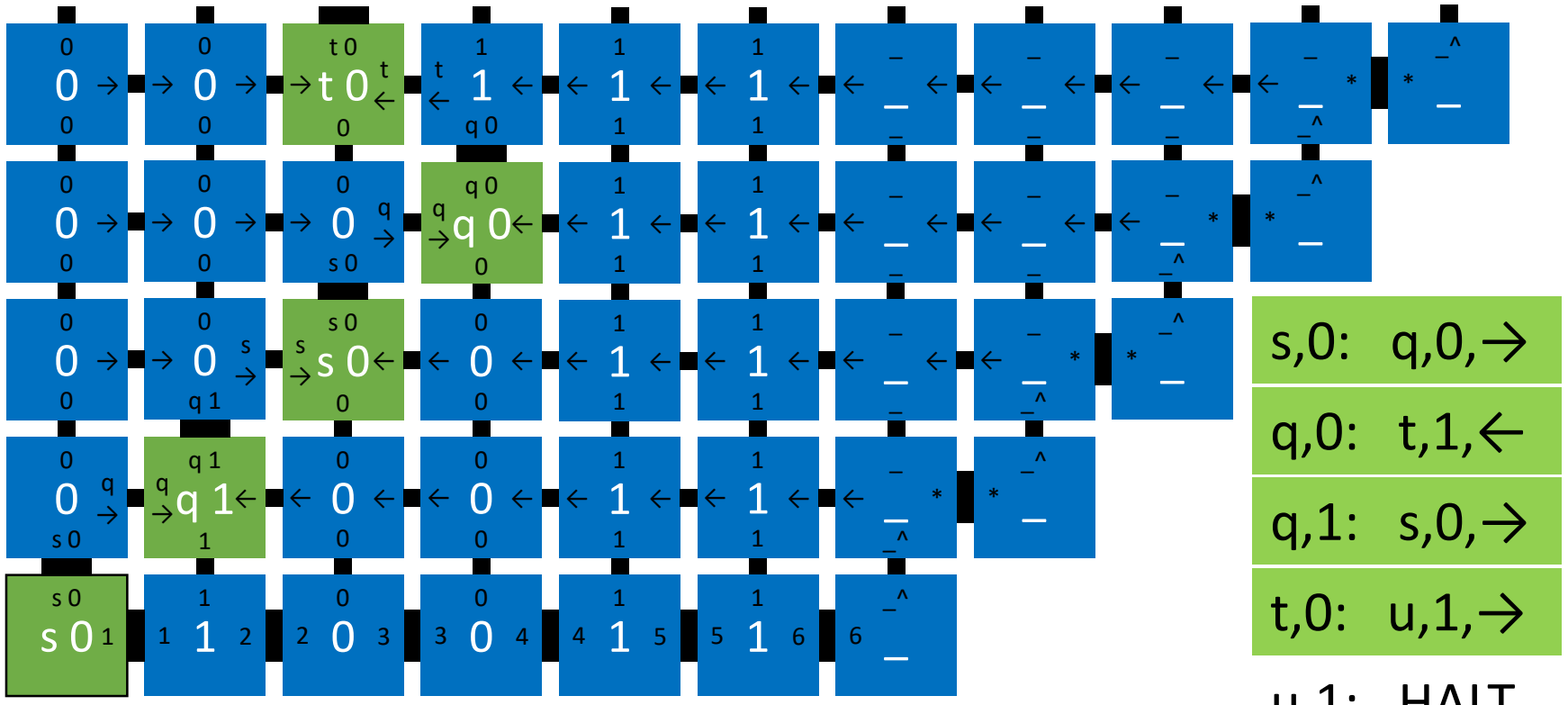

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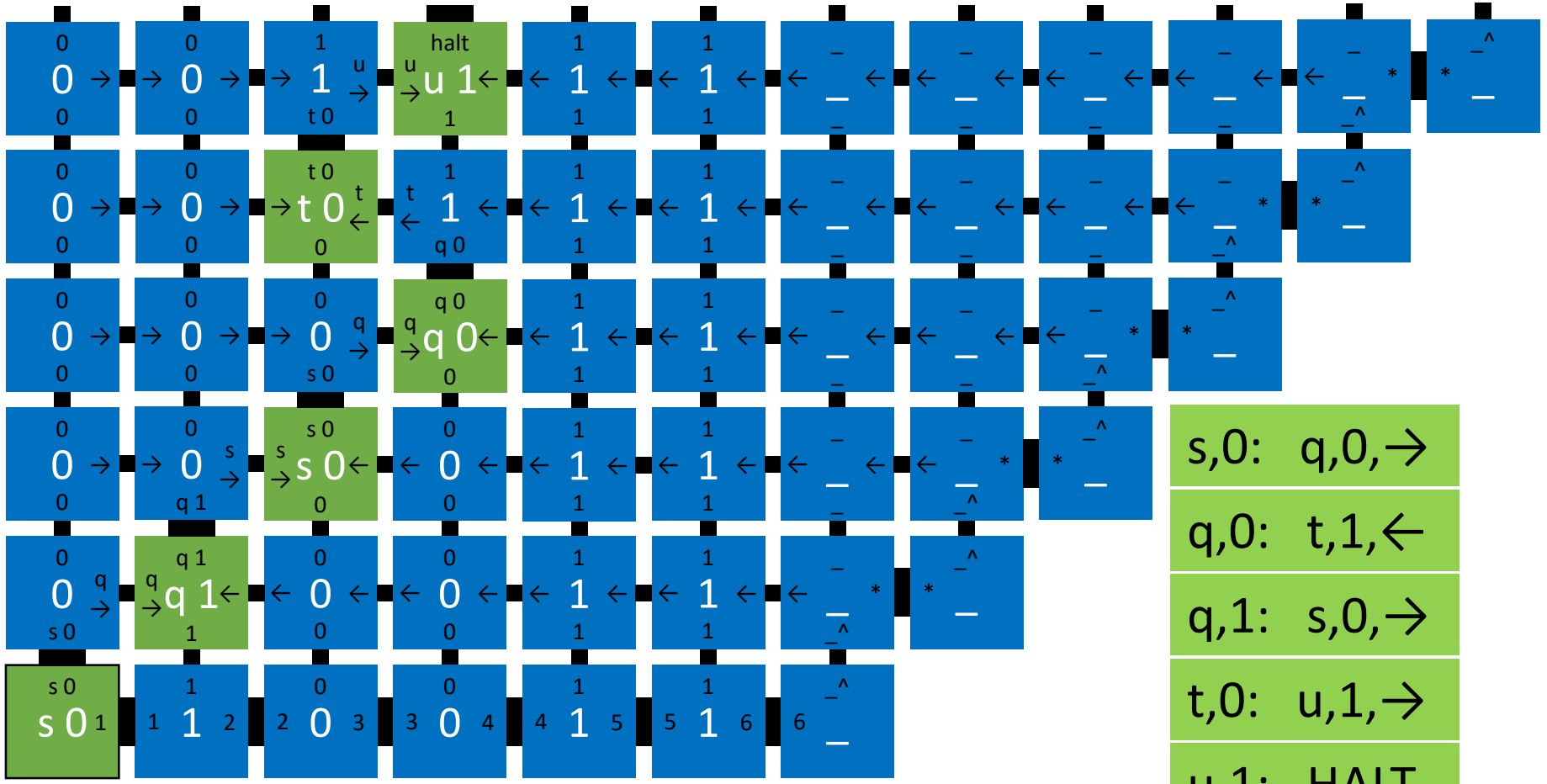

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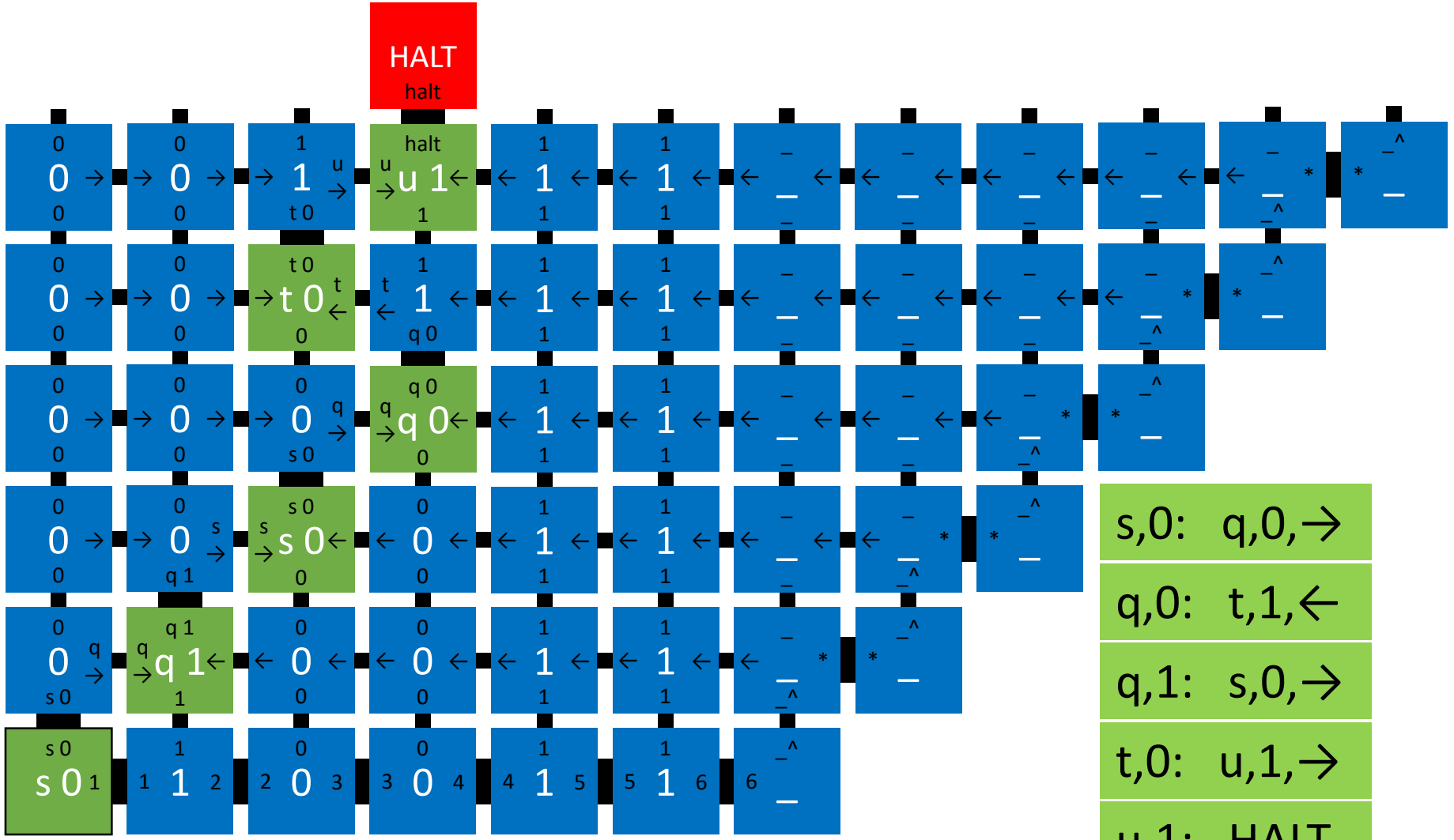

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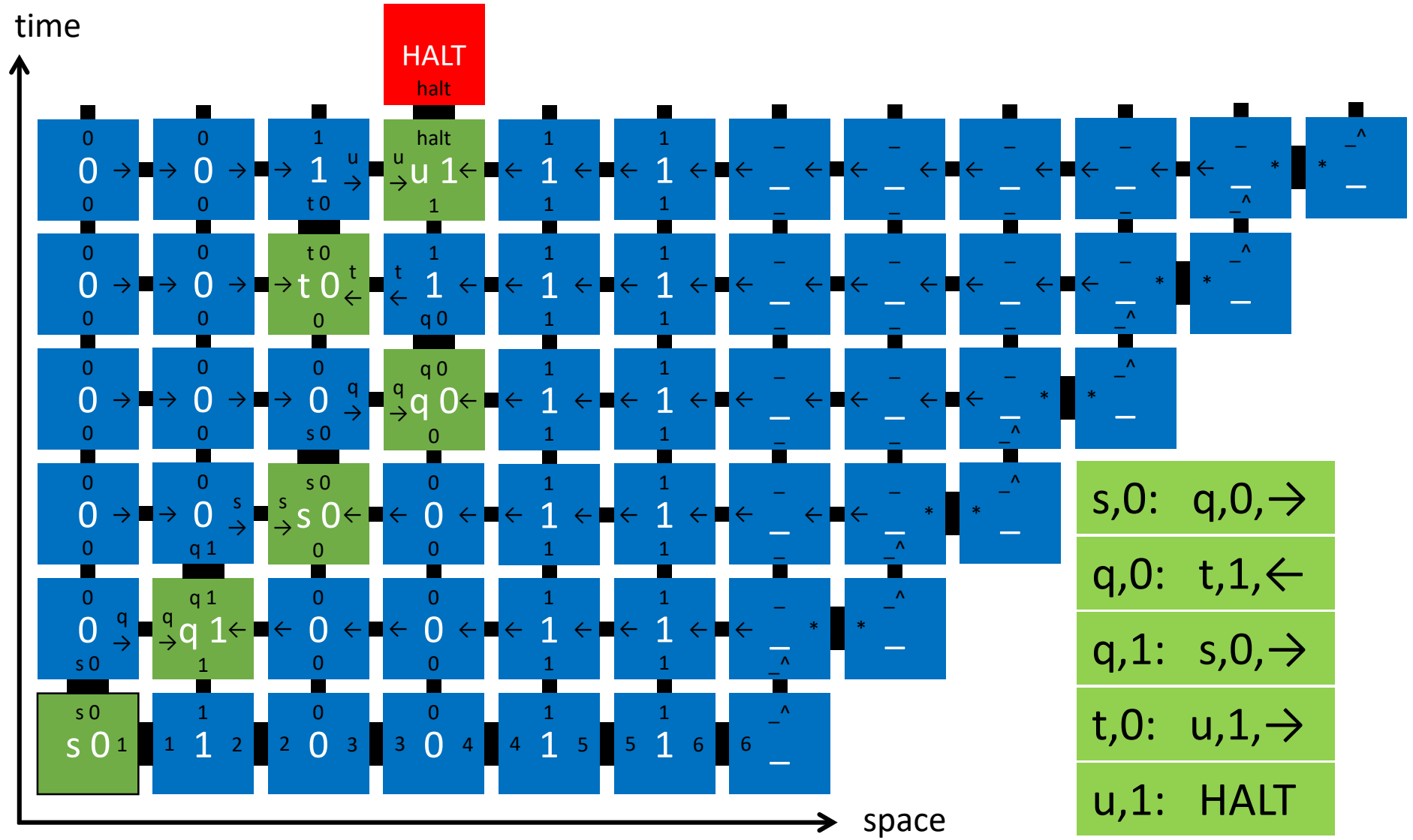
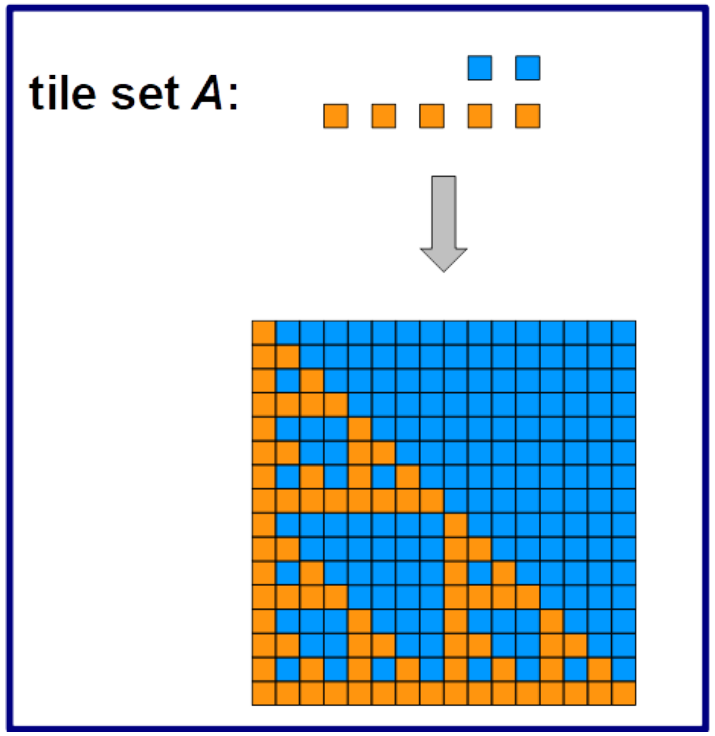
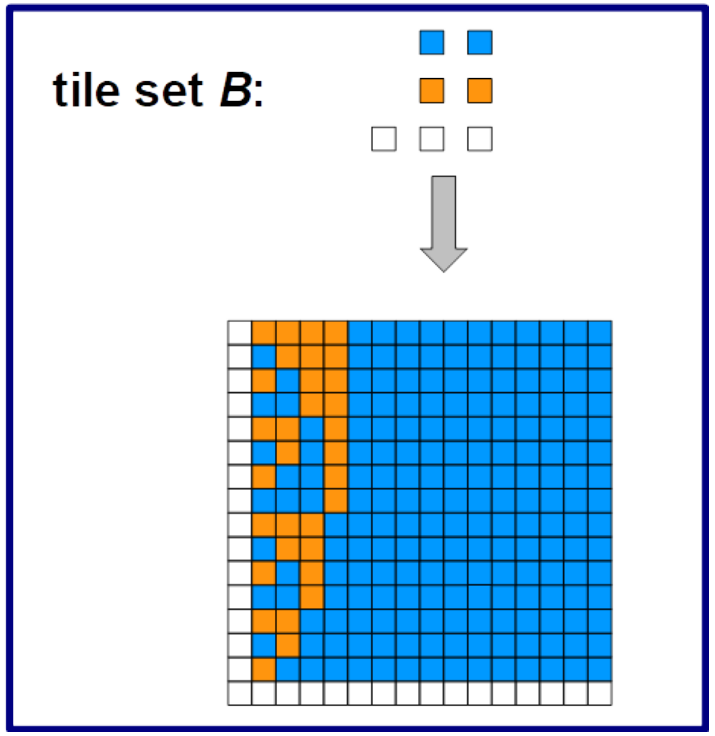


Putting the *algorithm* in *algorithmic* self-assembly

- set of tile types is like a program
- shape it creates, or pattern it paints, is like the output of the program





Putting the *algorithm* in *algorithmic* self-assembly

How is a set of tile types **not** like a program?

Putting the *algorithm* in *algorithmic* self-assembly

How is a set of tile types **not** like a program?

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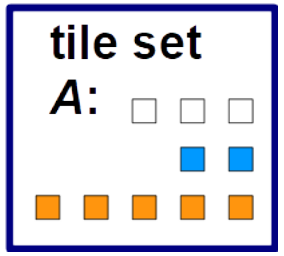

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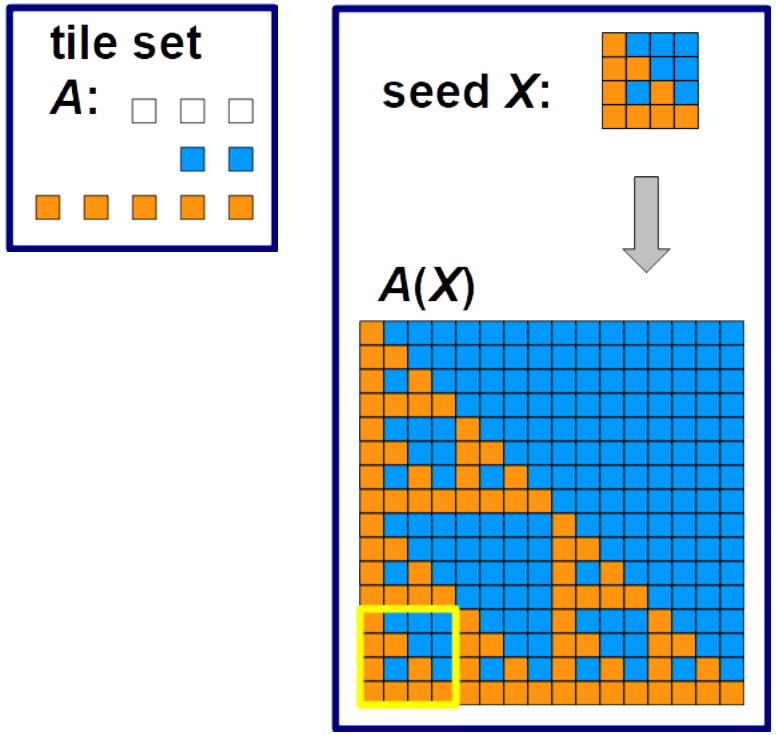

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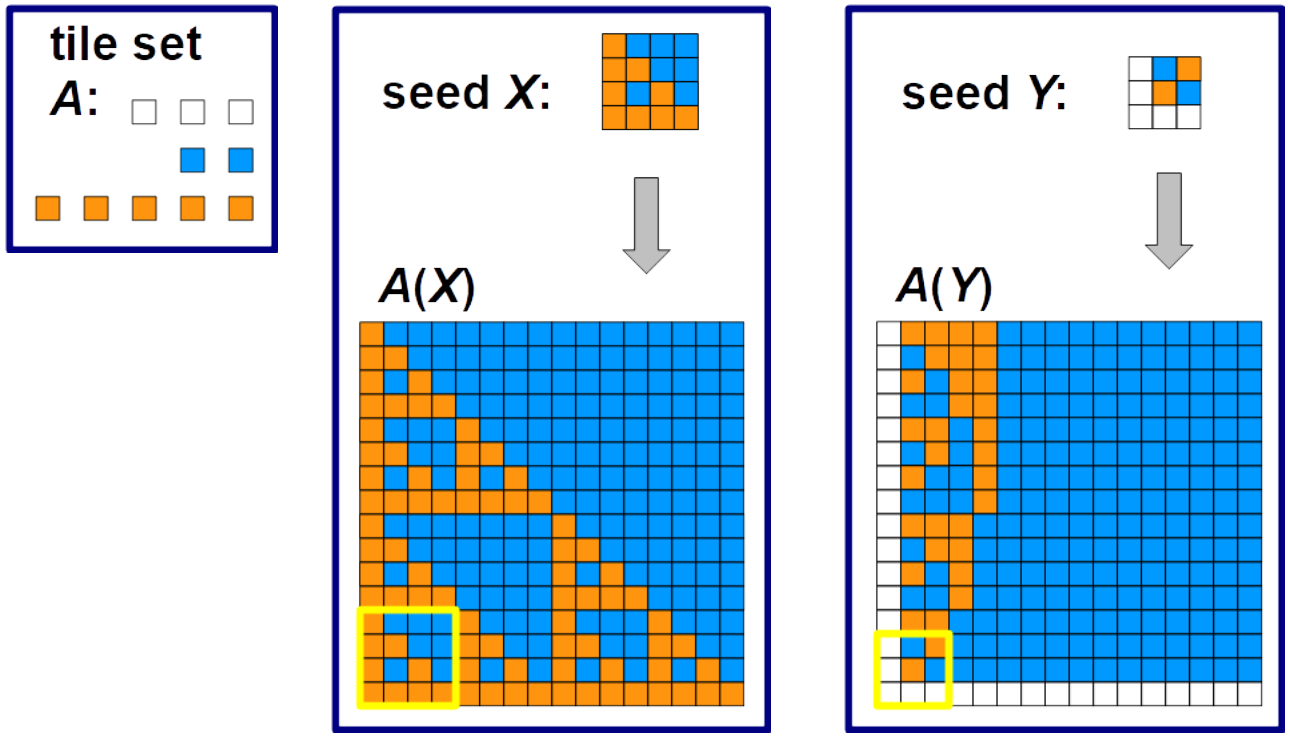

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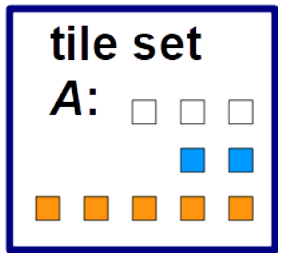

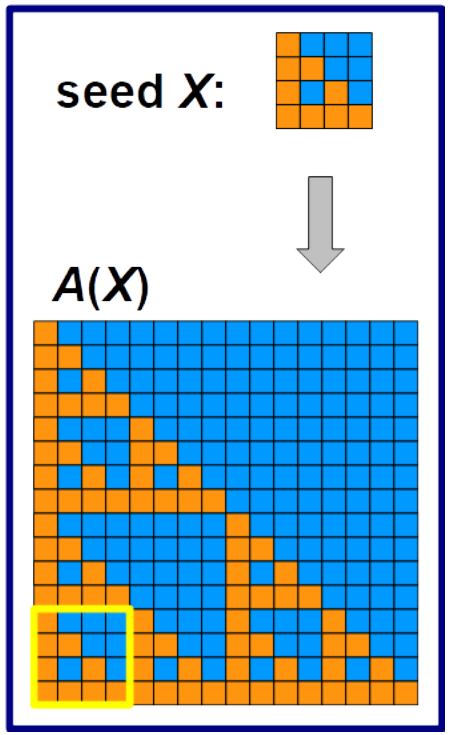

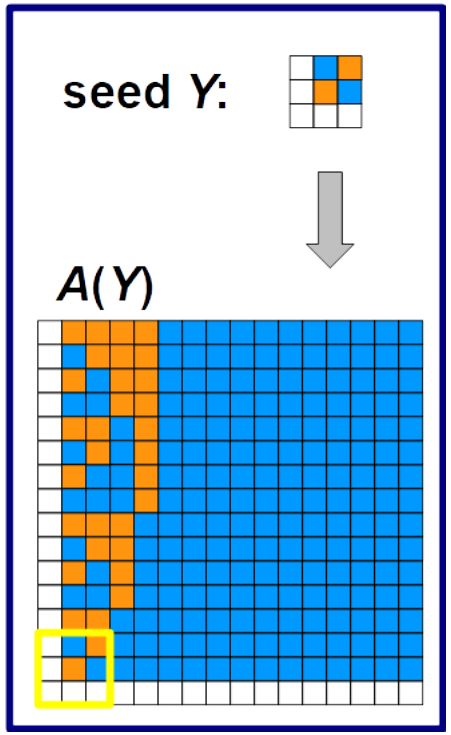

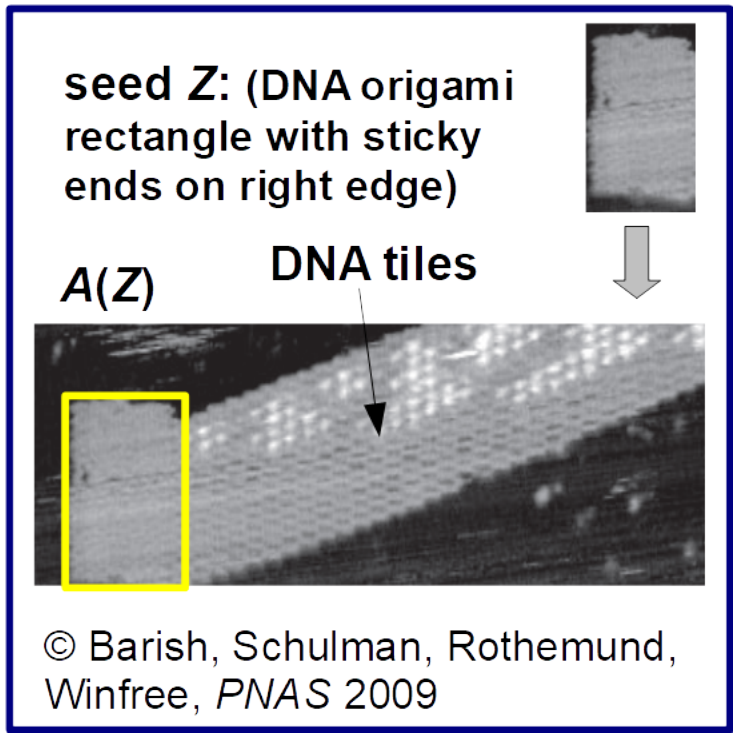

Calculating parity of 6-bit string: 1 algorithm, 2^6 inputs

seed encoding **1**0**0**1**0**1

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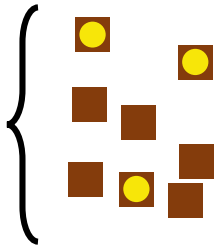
single set of tiles computing parity



seed encoding **11**0**1**0**1**

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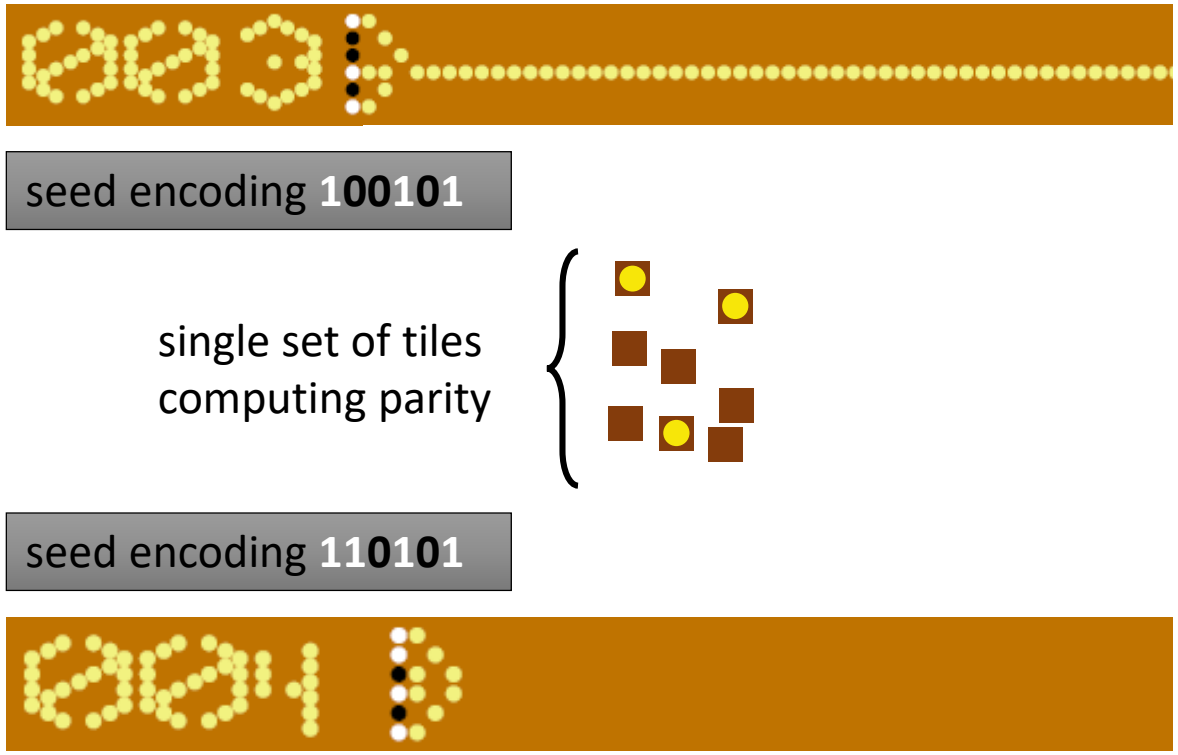

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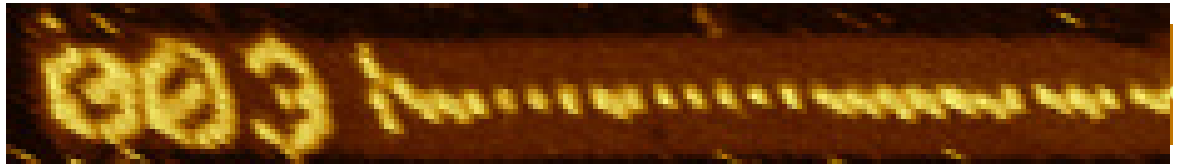

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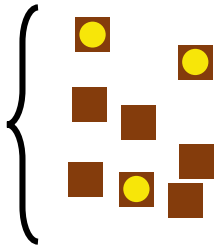
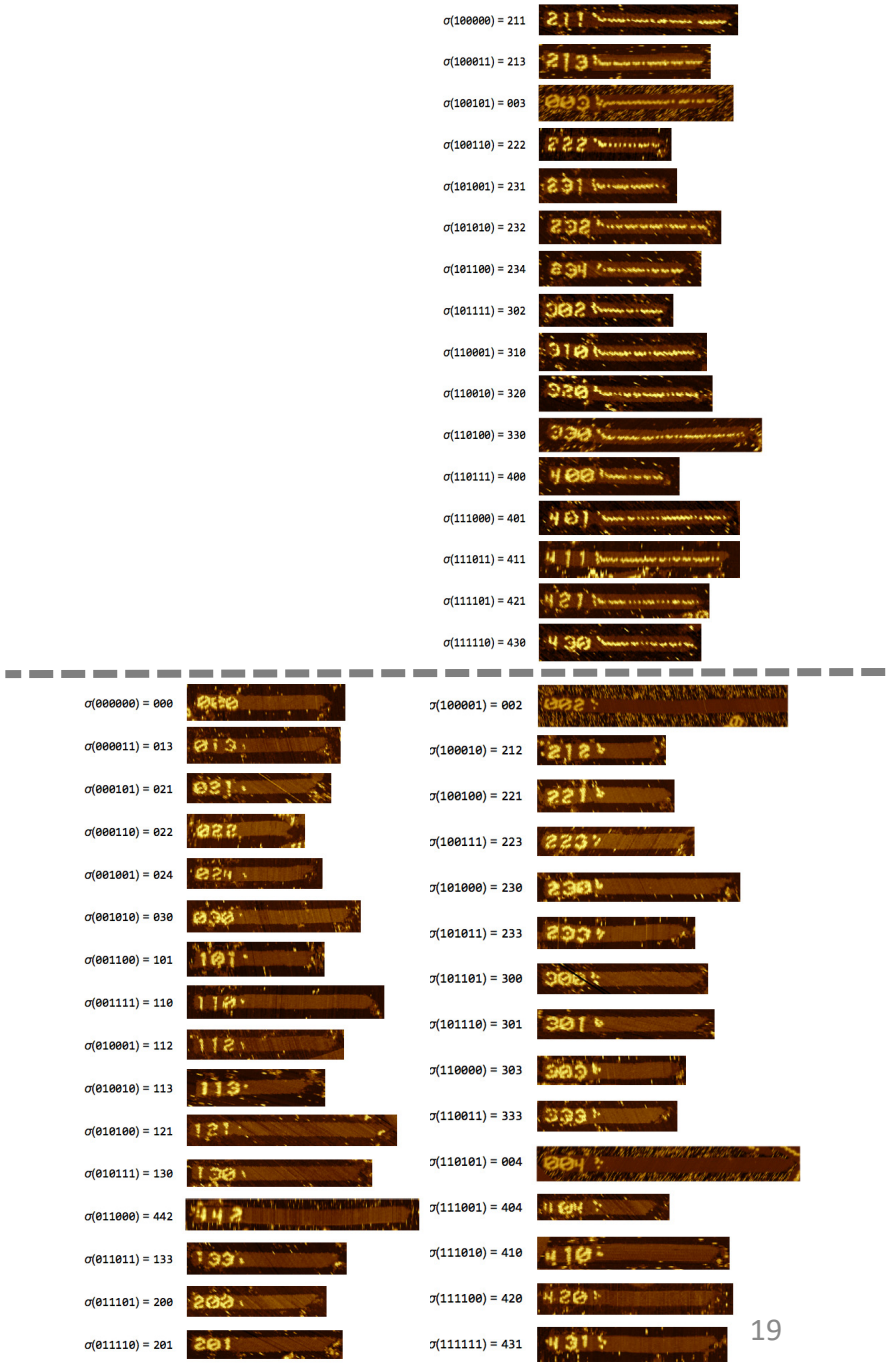


seed encoding **1**10**1**0**1**

[*Iterated Boolean circuit computation via a programmable DNA tile array*. Woods, Doty, Myhrvold, Hui, Wu, Yin, Winfree, submitted]

2^6 seeds:



So tiles can compute… what’s that good for?

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Theorem: There is a single set T of tile types, so that, for any finite shape S, from an appropriately chosen seed σ_S "encoding" S, T self-assembles S.

[*Complexity of Self-Assembled Shapes*. Soloveichik and Winfree, SIAM Journal on Computing 2007]

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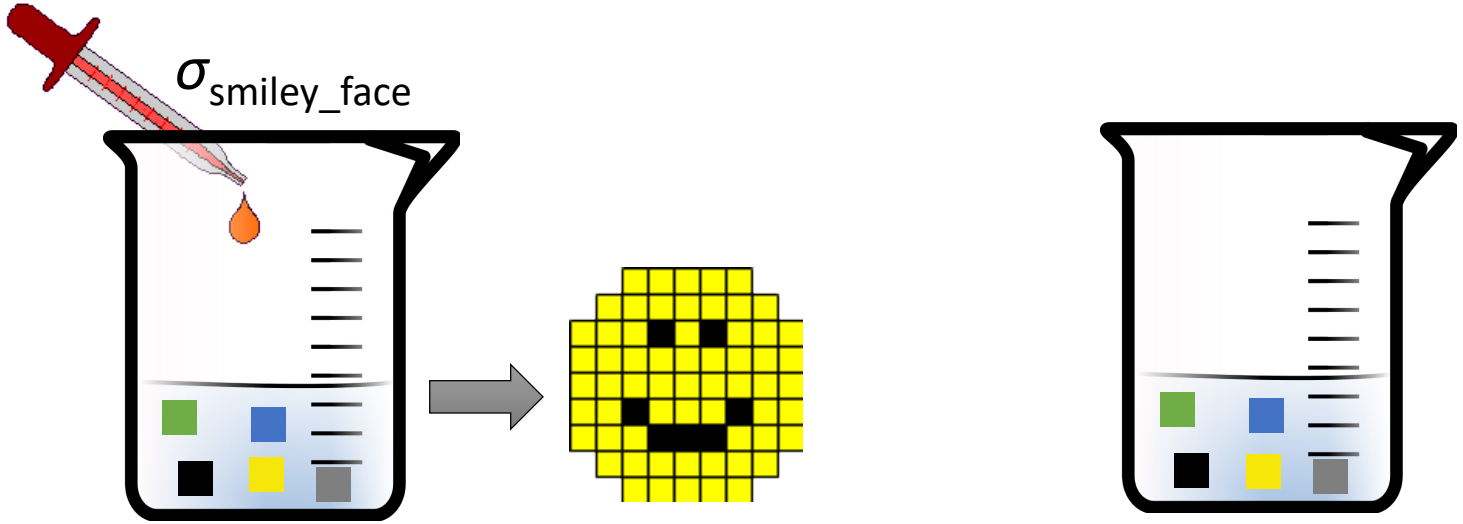

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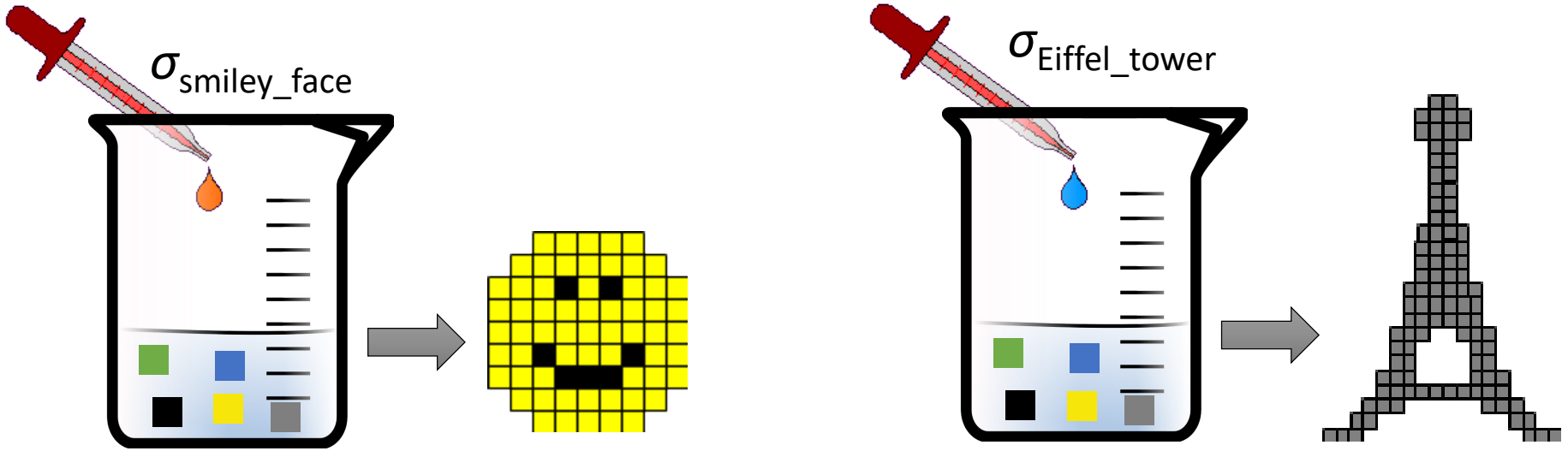

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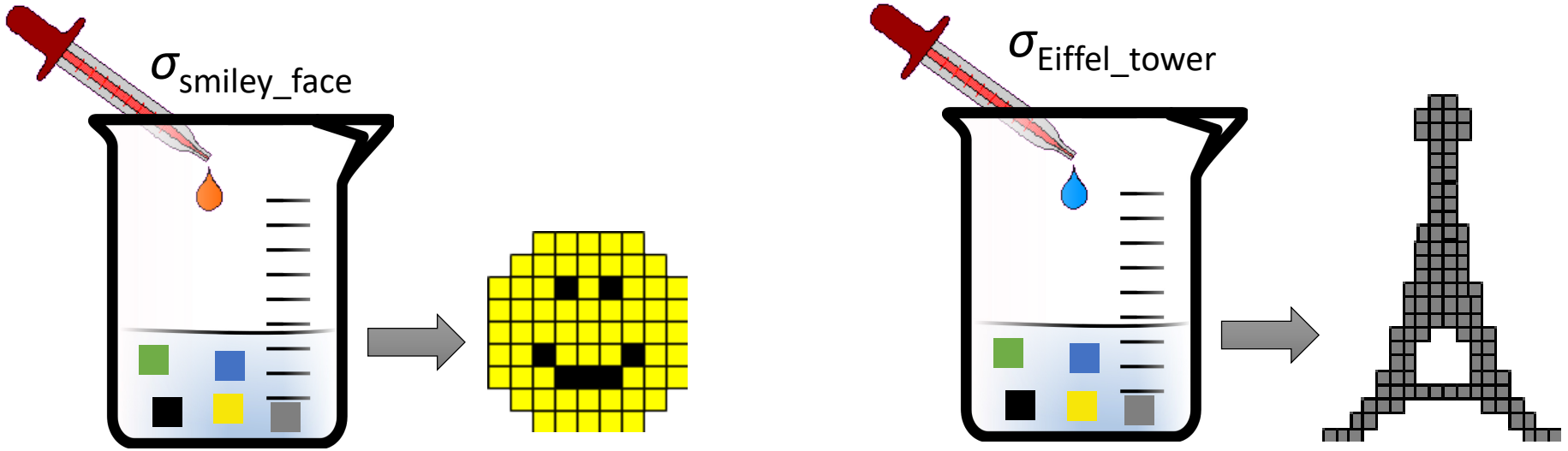

These tiles are universally programmable for building any shape.

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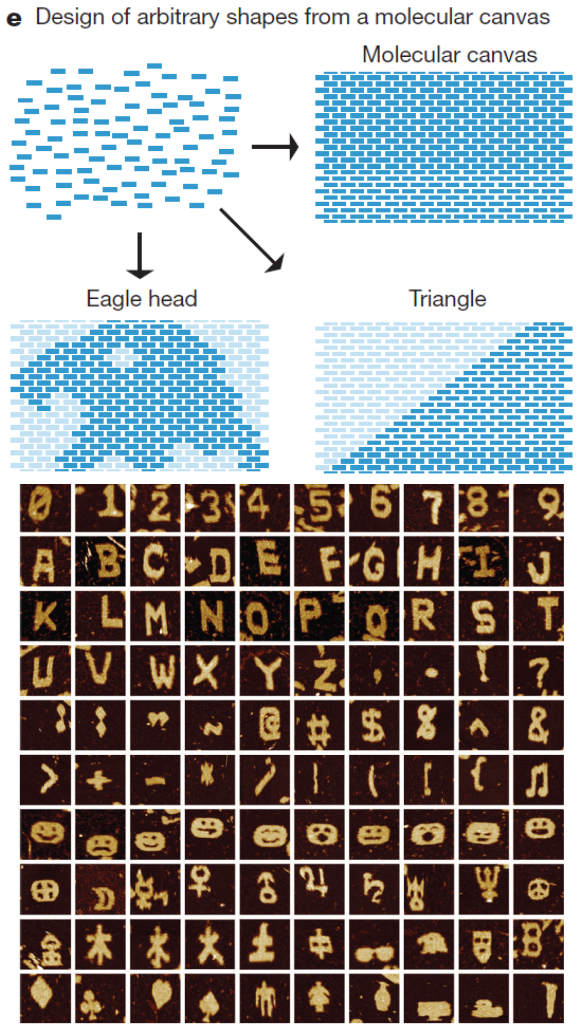
Open problems

Theory of programmable barriers to nucleation in tile self-assembly

Experimental tile self-assembly



Wei, Dai, Yin, *Nature* 2012

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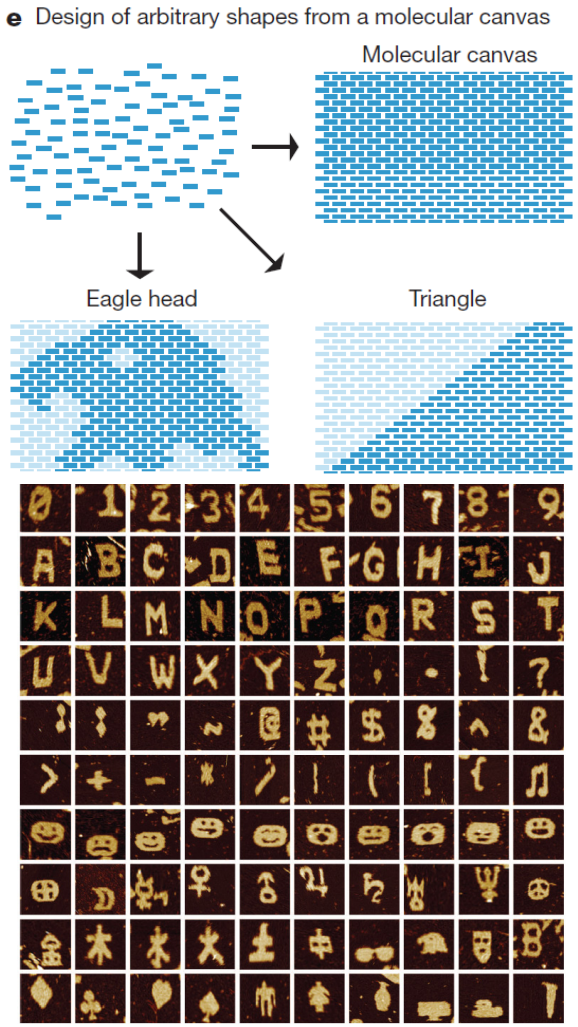

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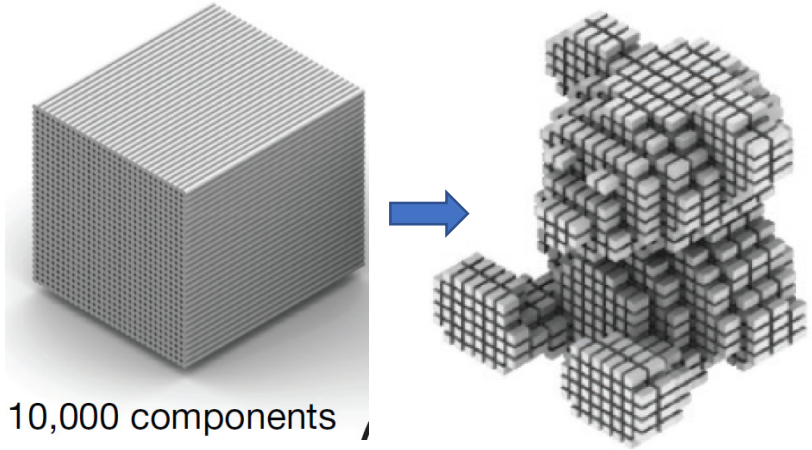

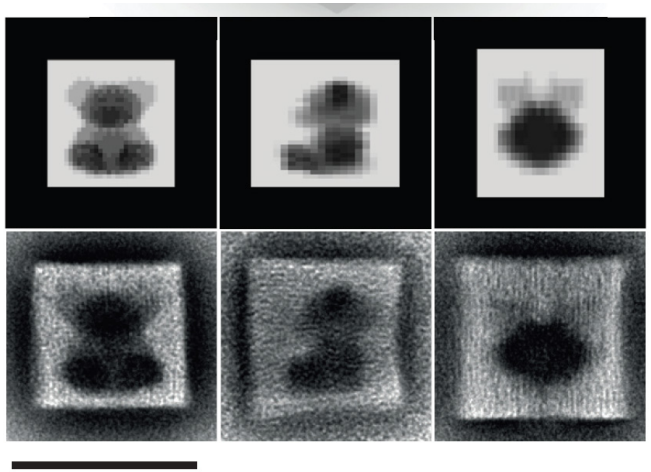

Ong *et al*, *Nature* 2017

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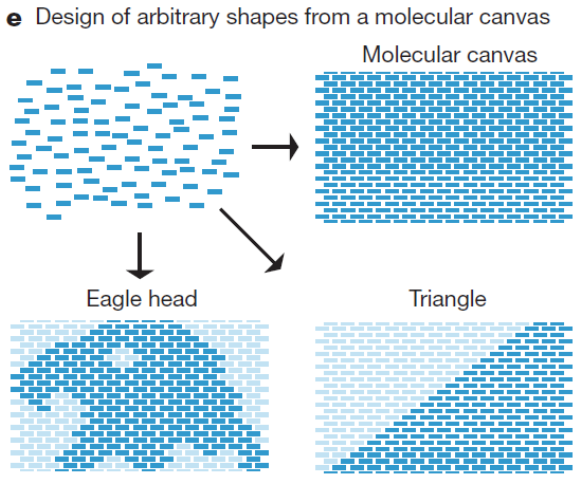

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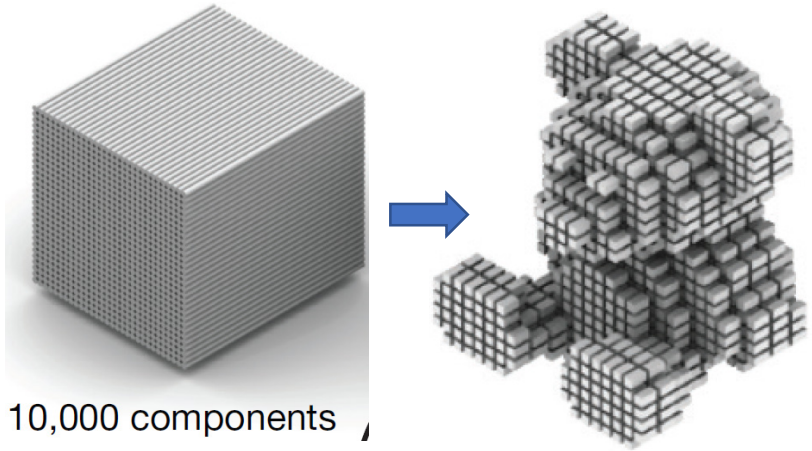
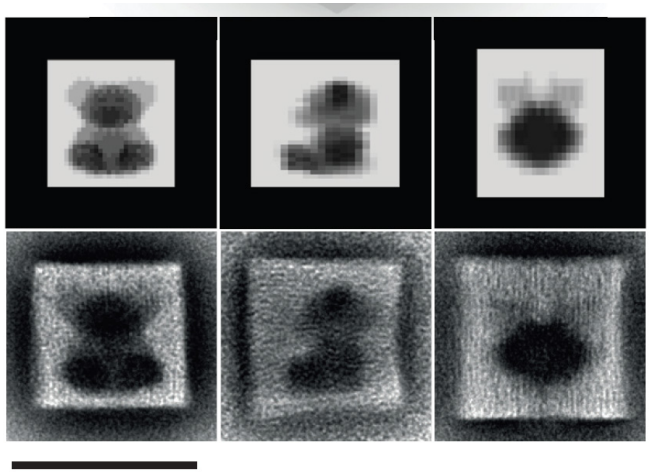
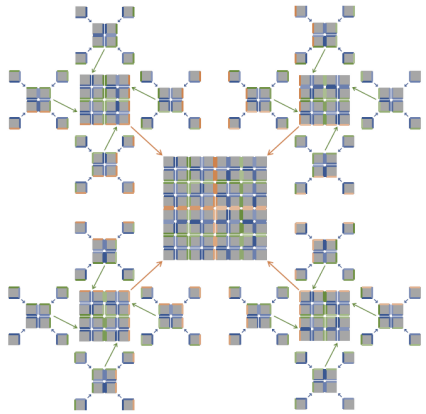
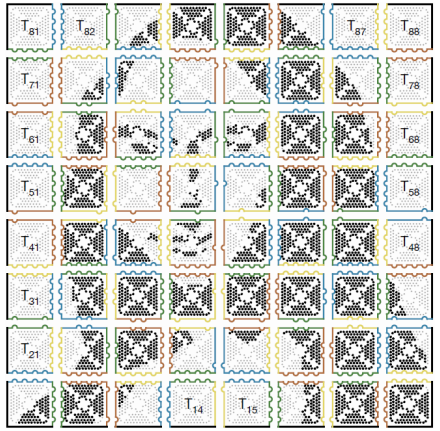
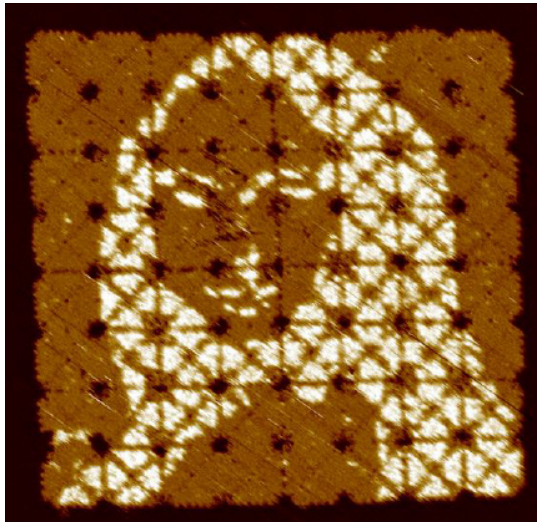




Ong *et al*, *Nature* 2017







Tikhomirov, Peterson, Qlan, *Nature* 2017

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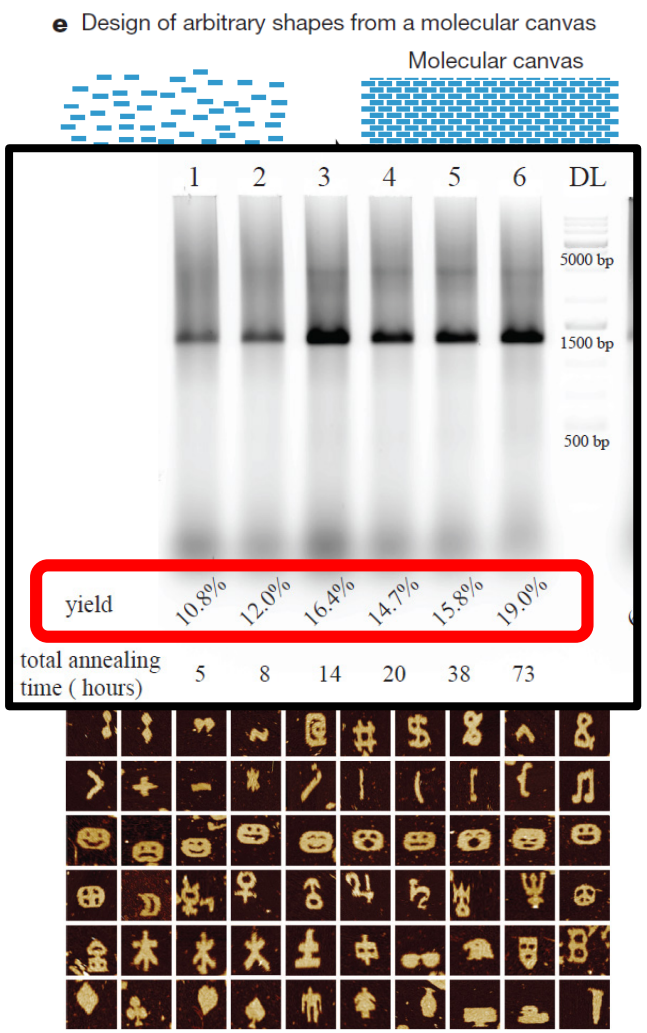

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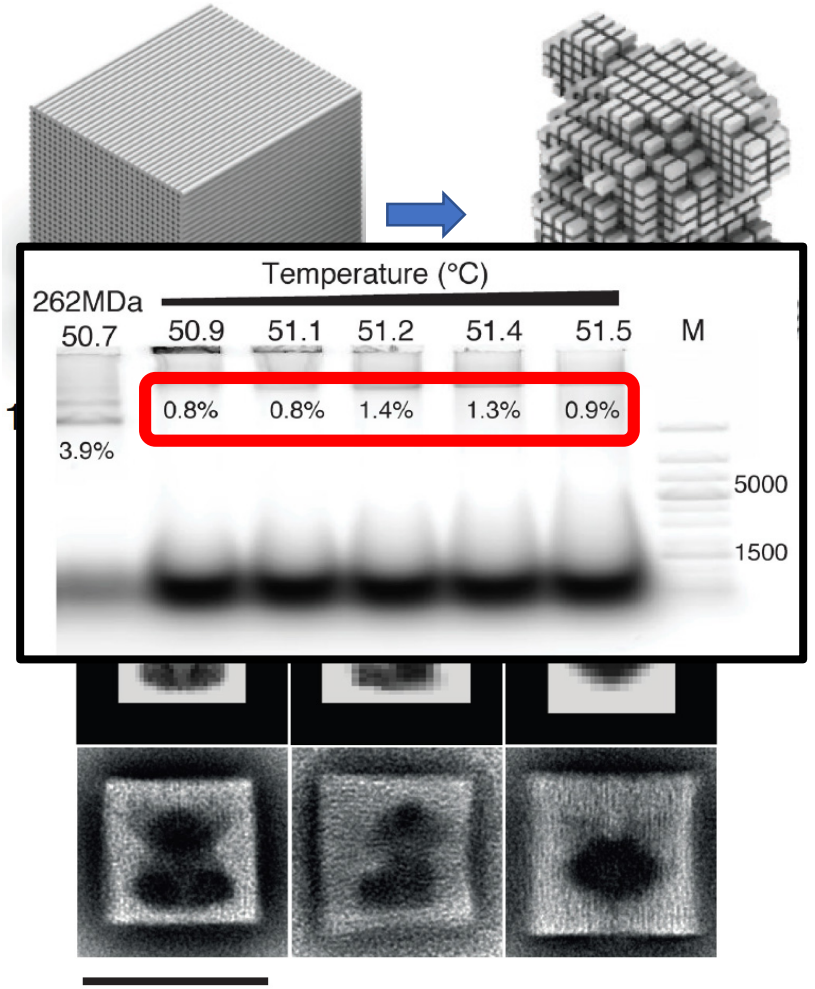

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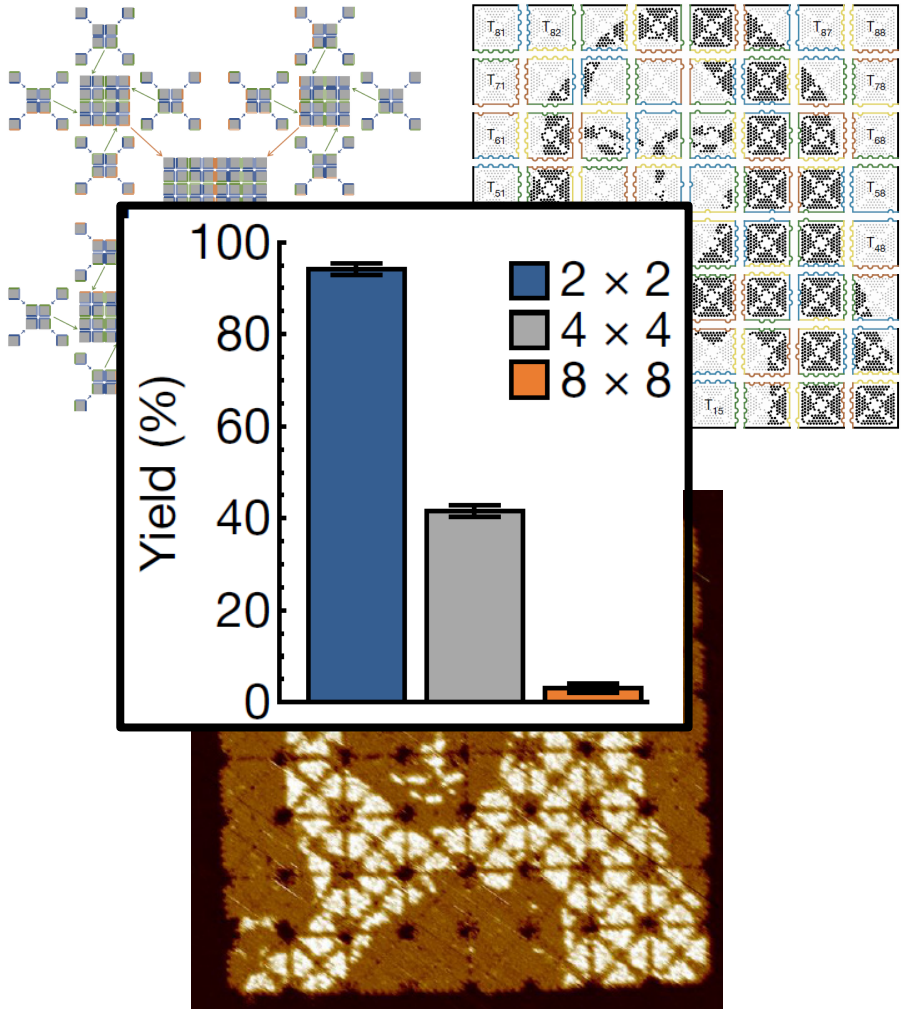

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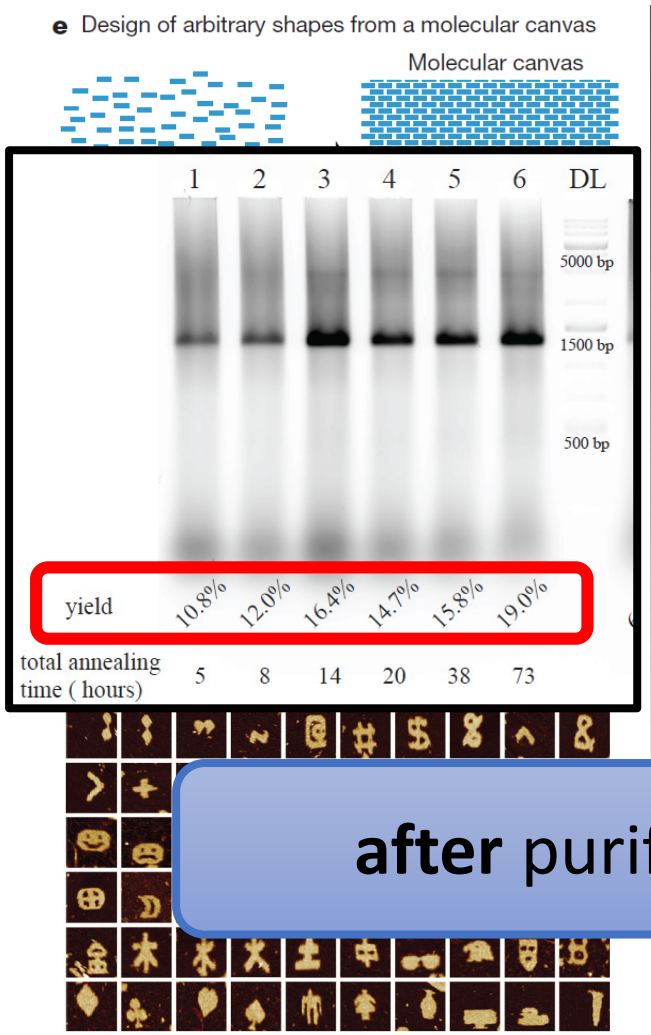

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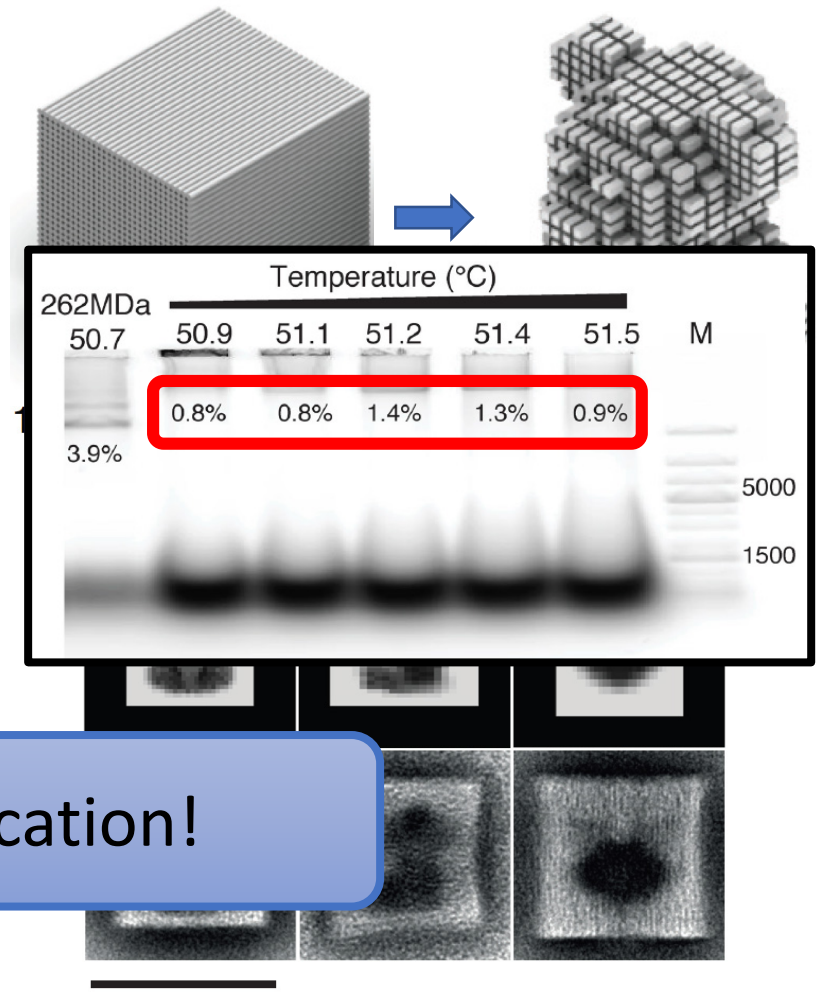
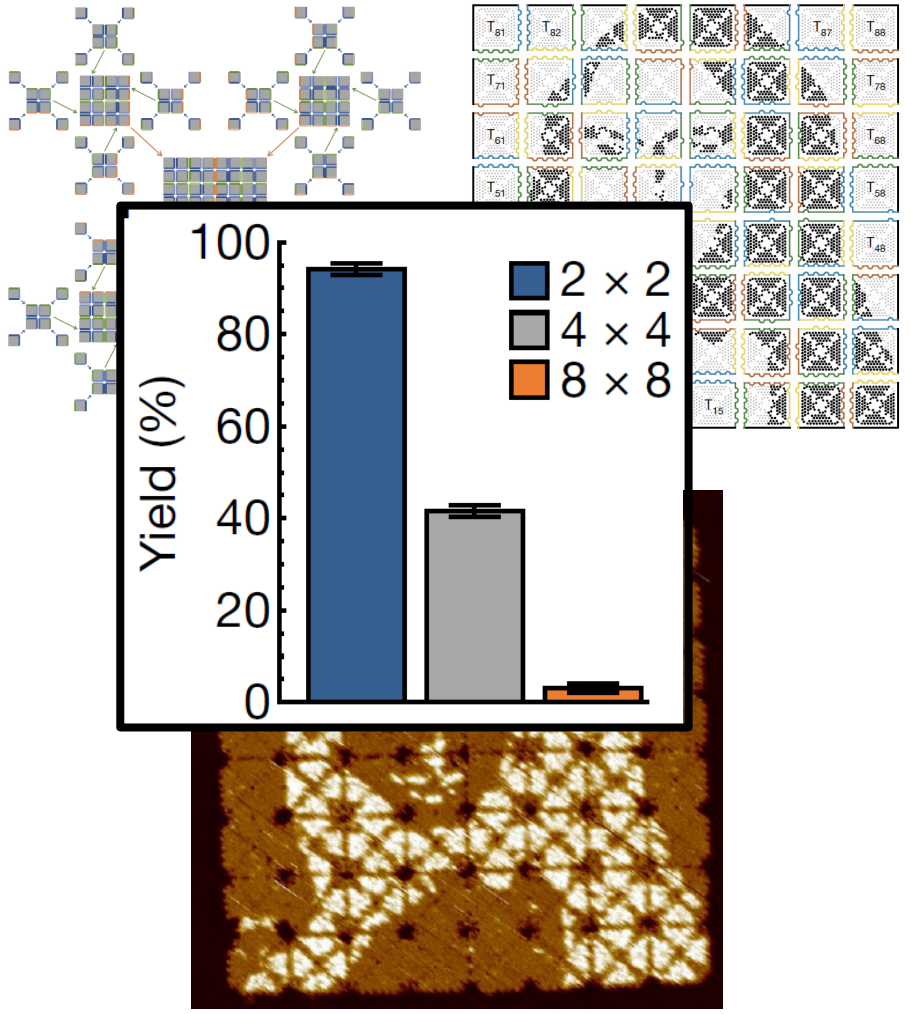


Ong *et al*, *Nature* 2017



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after purification!

Secret to higher yields: Control of nucleation

Schulman, Winfree, *SICOMP* 2009

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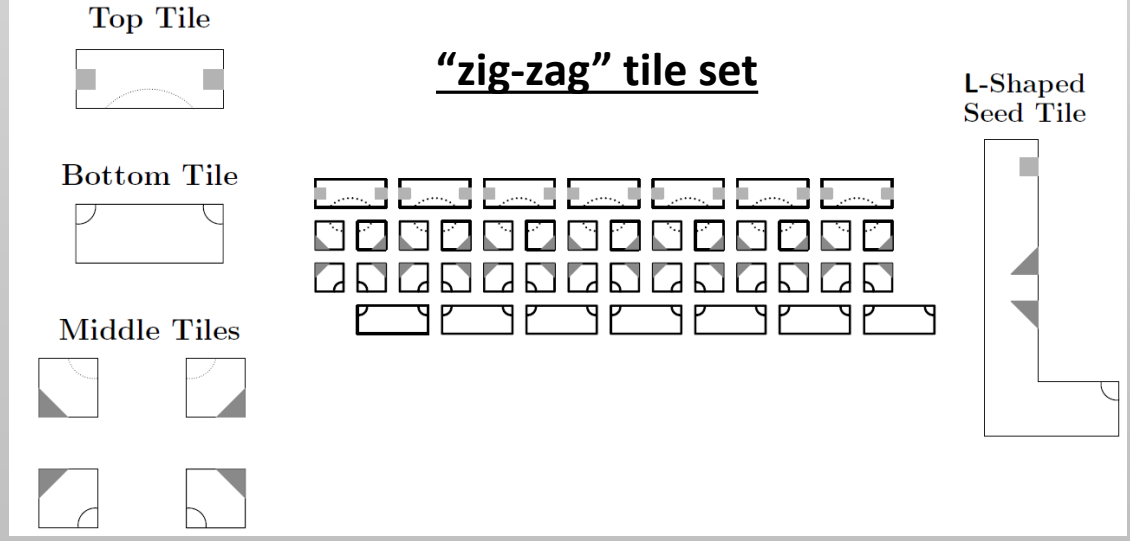

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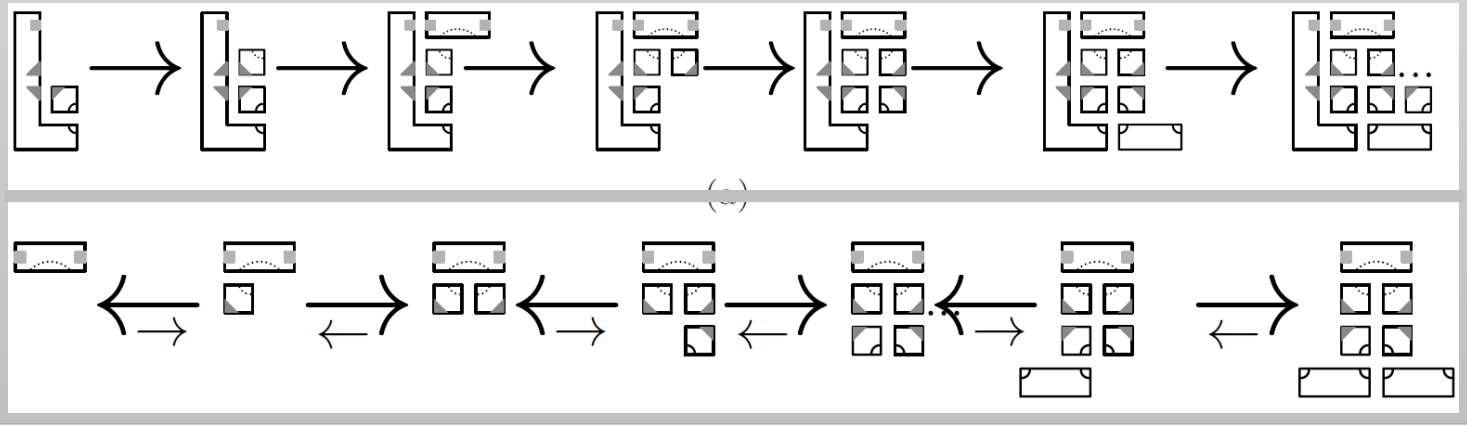

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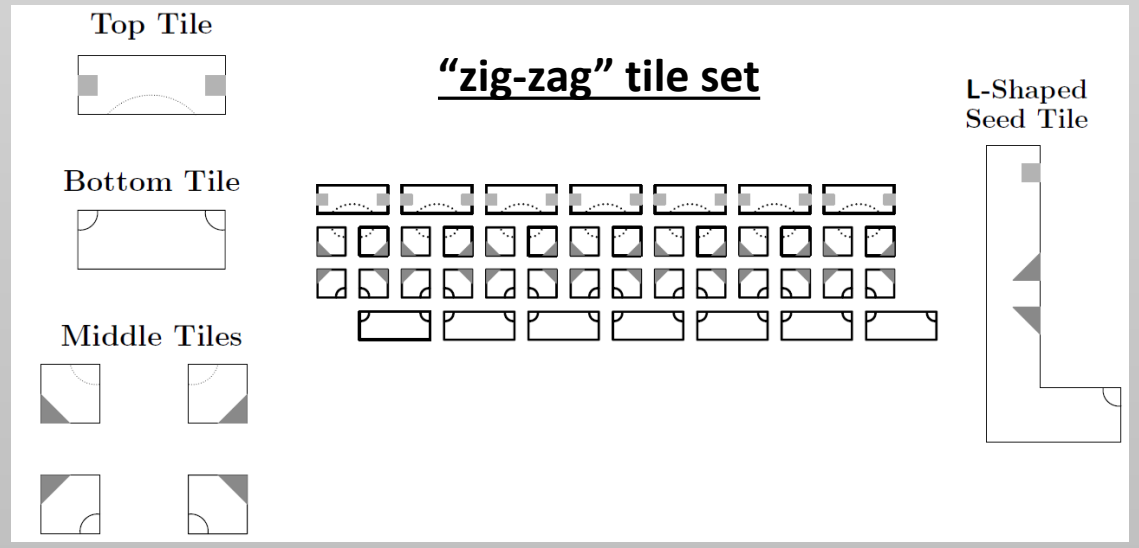

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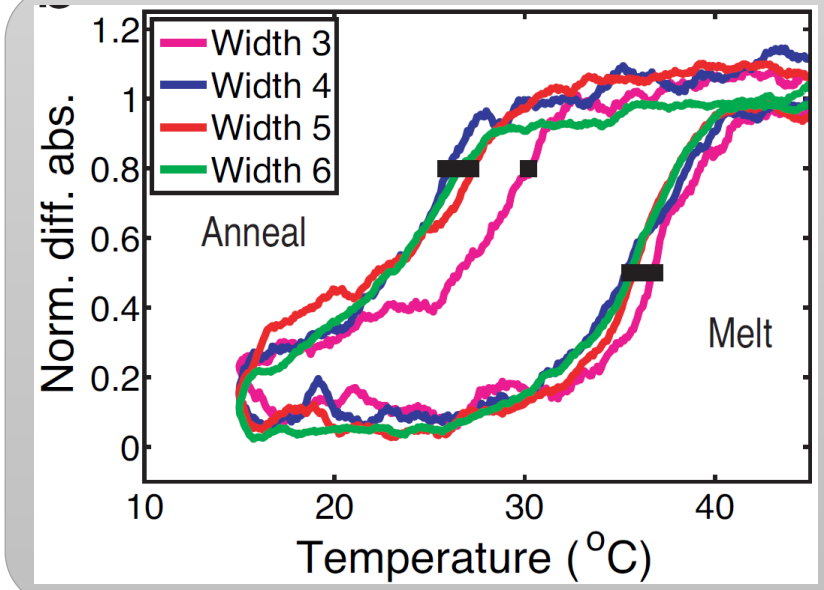

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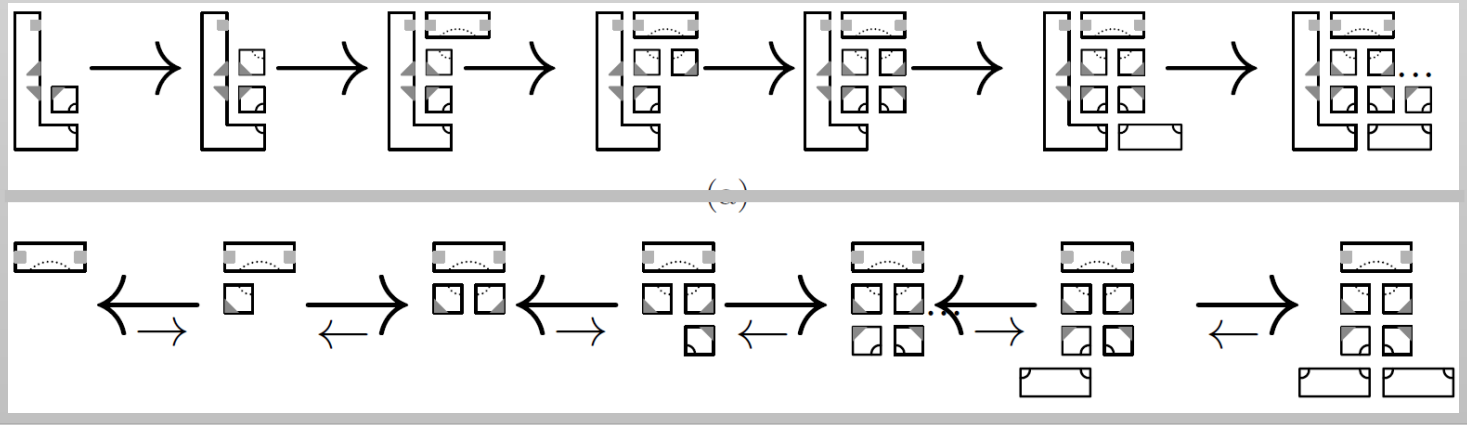

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- **Goal:** Develop general scheme for self-assembling shapes with programmable kinetic barriers to nucleation. (even “hard-coded” would be interesting given low yields of experimental results)

Thank you!

Questions?