# kinetic Tile Assembly Model

# kinetic Tile Assembly Model (kTAM)

differences with aTAM:

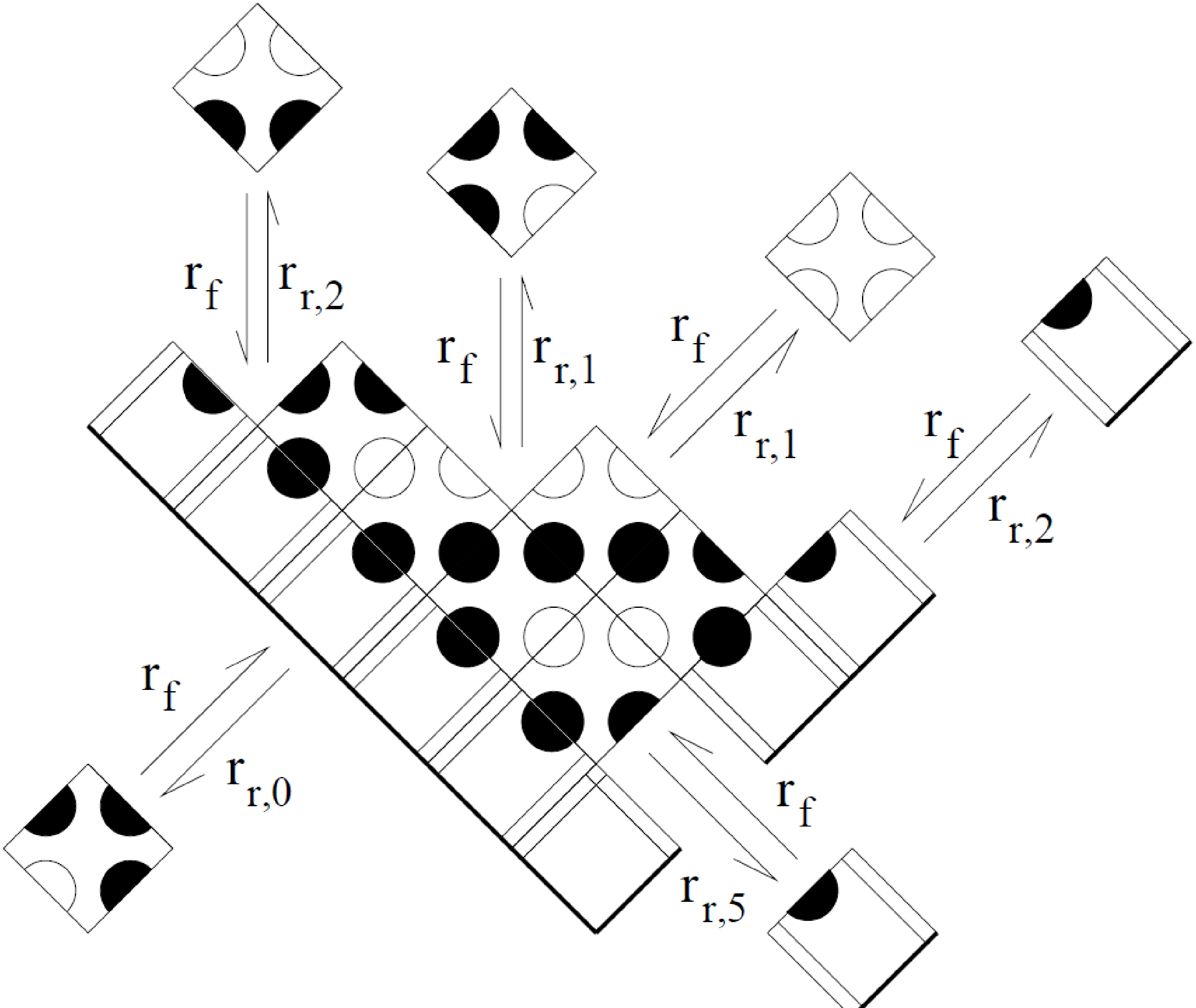
- tiles can attach by any positive strength glue
- tiles fall off, more quickly if bound weakly

| | |
|---|---|
| $r_f \sim e^{-G_{mc}}$ | forward rate |
| $r_r \sim e^{-b \cdot G_{se}}$ | reverse rate |
| $e^{-G_{mc}}$ | tile concentration |
| $b$ | # sticky ends bound |
| $G_{se}$ | strength of 1 sticky end |

optimal growth when **forward rate just barely larger than reverse rate**, i.e., when

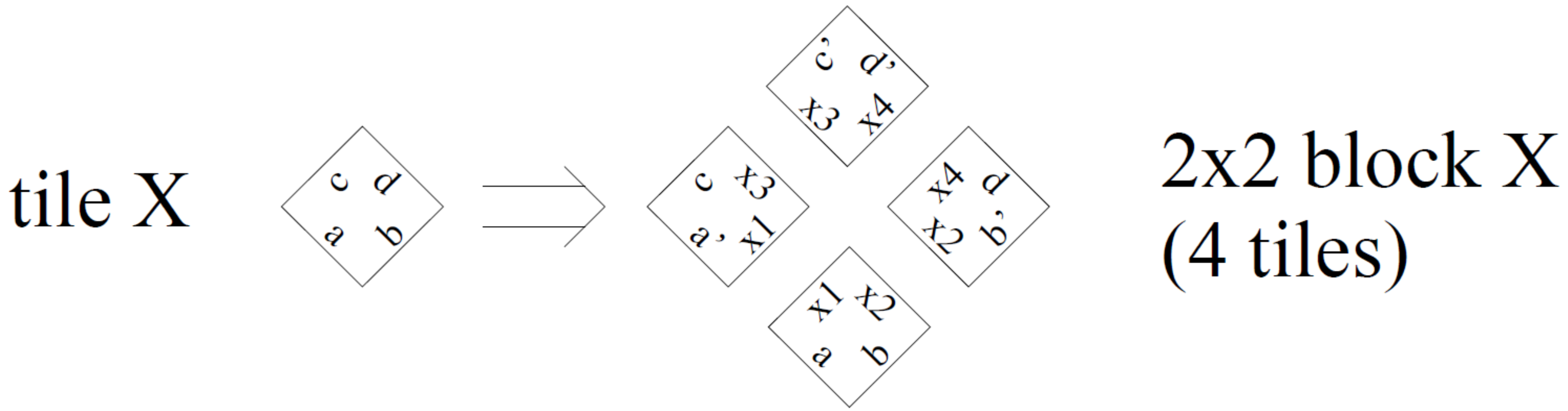
$$G_{mc} \approx 2 \cdot G_{se}$$

# kTAM



# Proofreading: Error-correction in the kTAM

**Definition**: error = attachment by single strength 1 glue



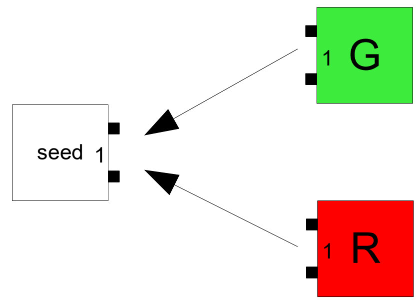

glues internal to block are all unique

errors must occur in multiples of 2

*k* x *k* proofreading roughly turns error rate of ε into $\varepsilon^k$

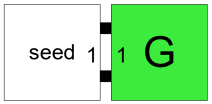
# Concentration programming

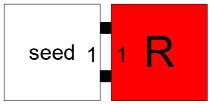
# Nondeterministic binding




concentration 11

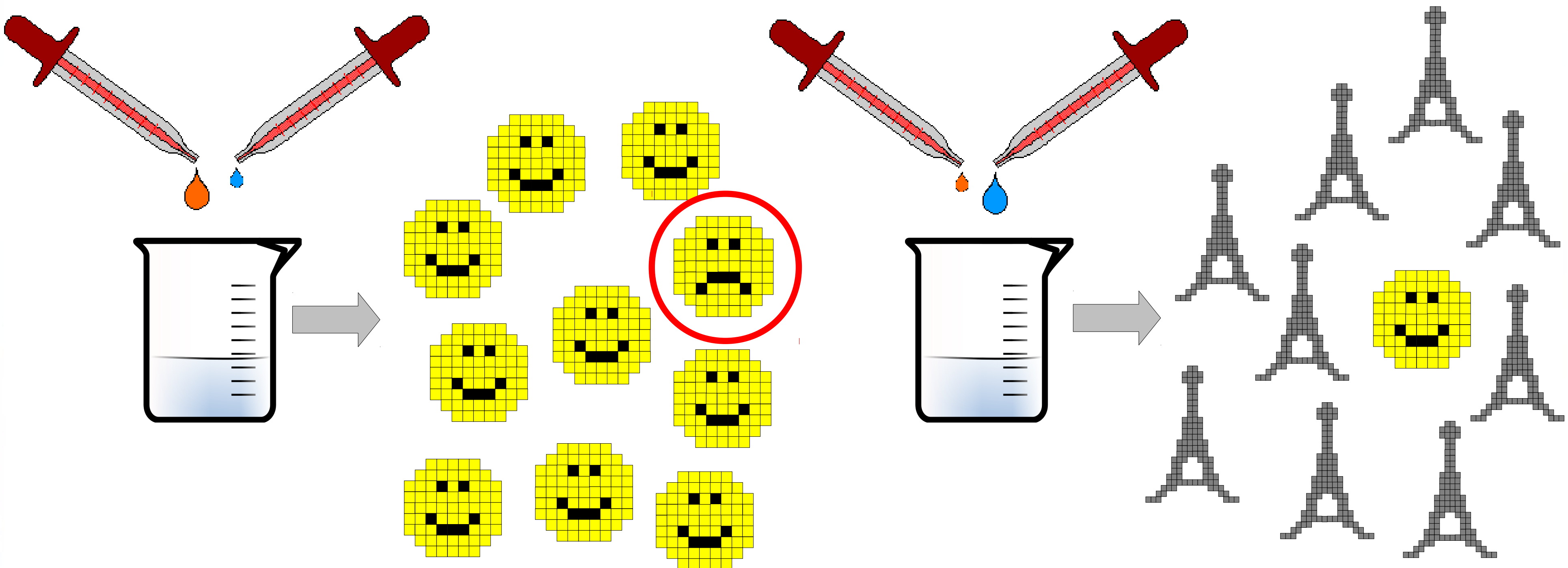
concentration 1

Pr[   ] = 11/12

Pr[   ] = 1/12

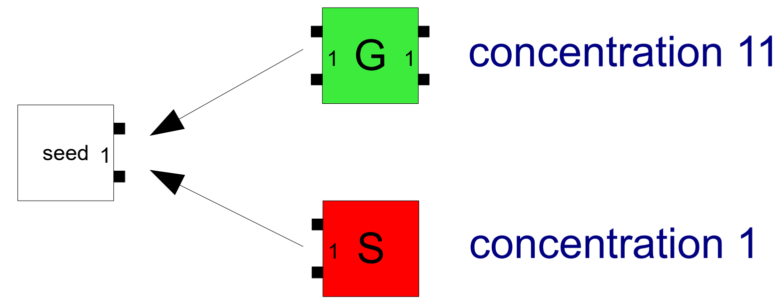
# Concentration programming of universal self-assembling molecules

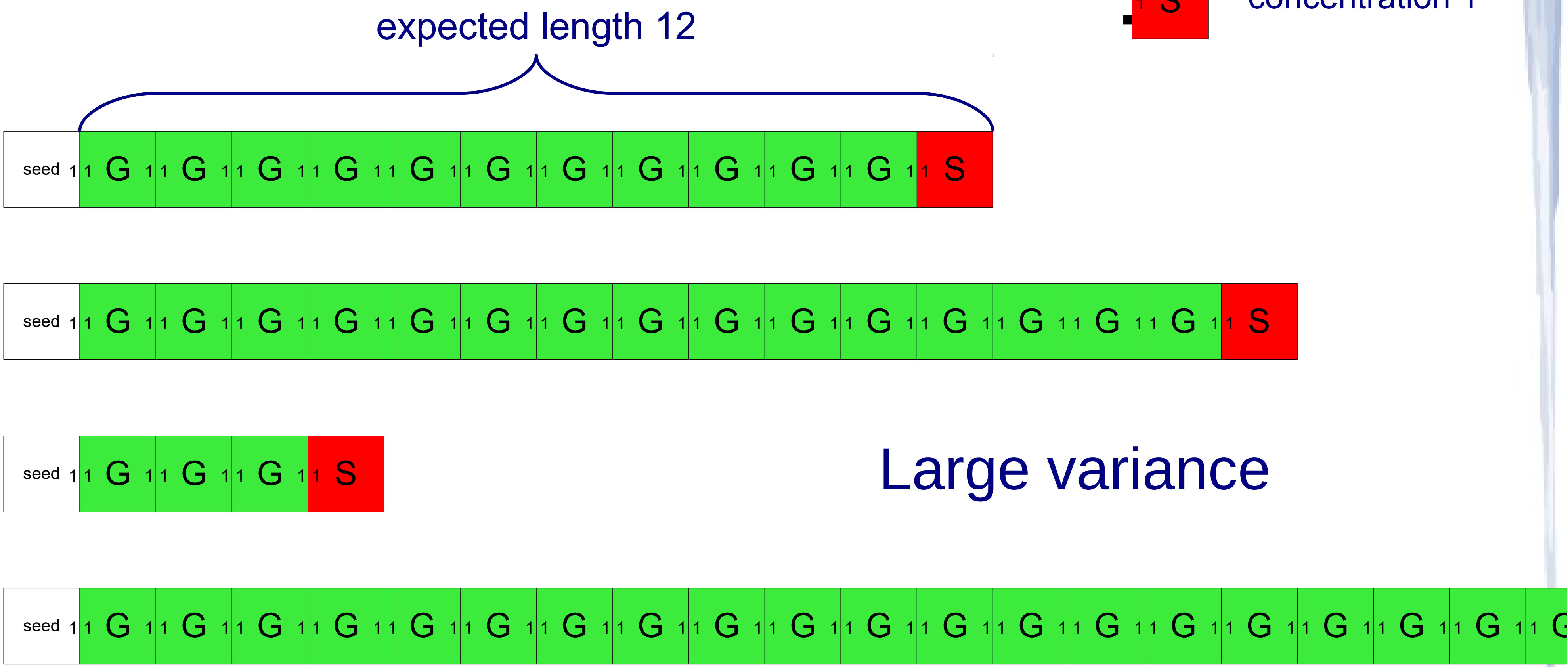
A **singly-seeded** TAS can assemble *any* finite (scaled) shape (with high probability) by mixing them in the right concentrations.



# Programming polymer length with concentrations

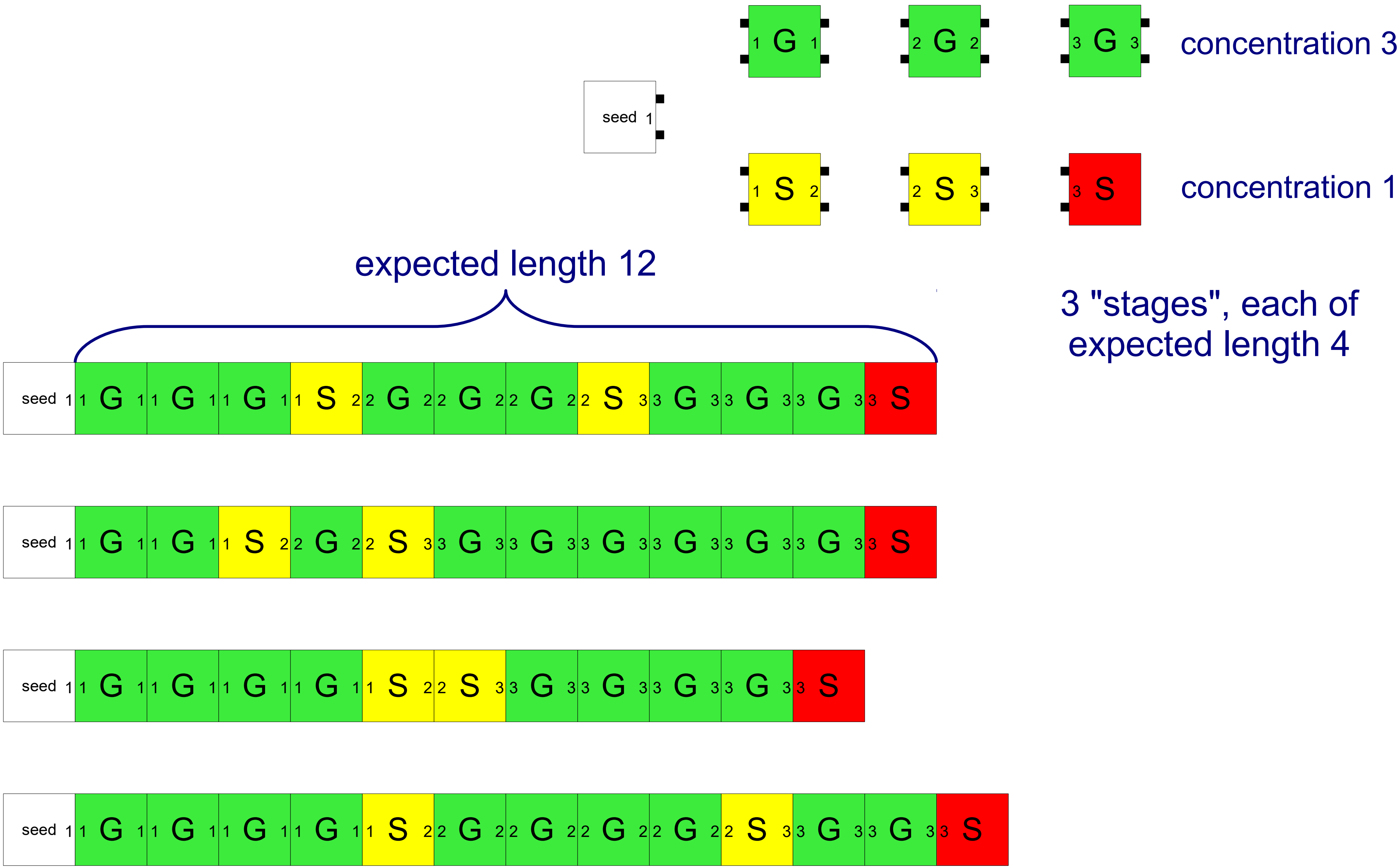
[Becker, Rapaport, Rémila, *FSTTCS* 2006]




Large variance

# Programming polymer length (improved)

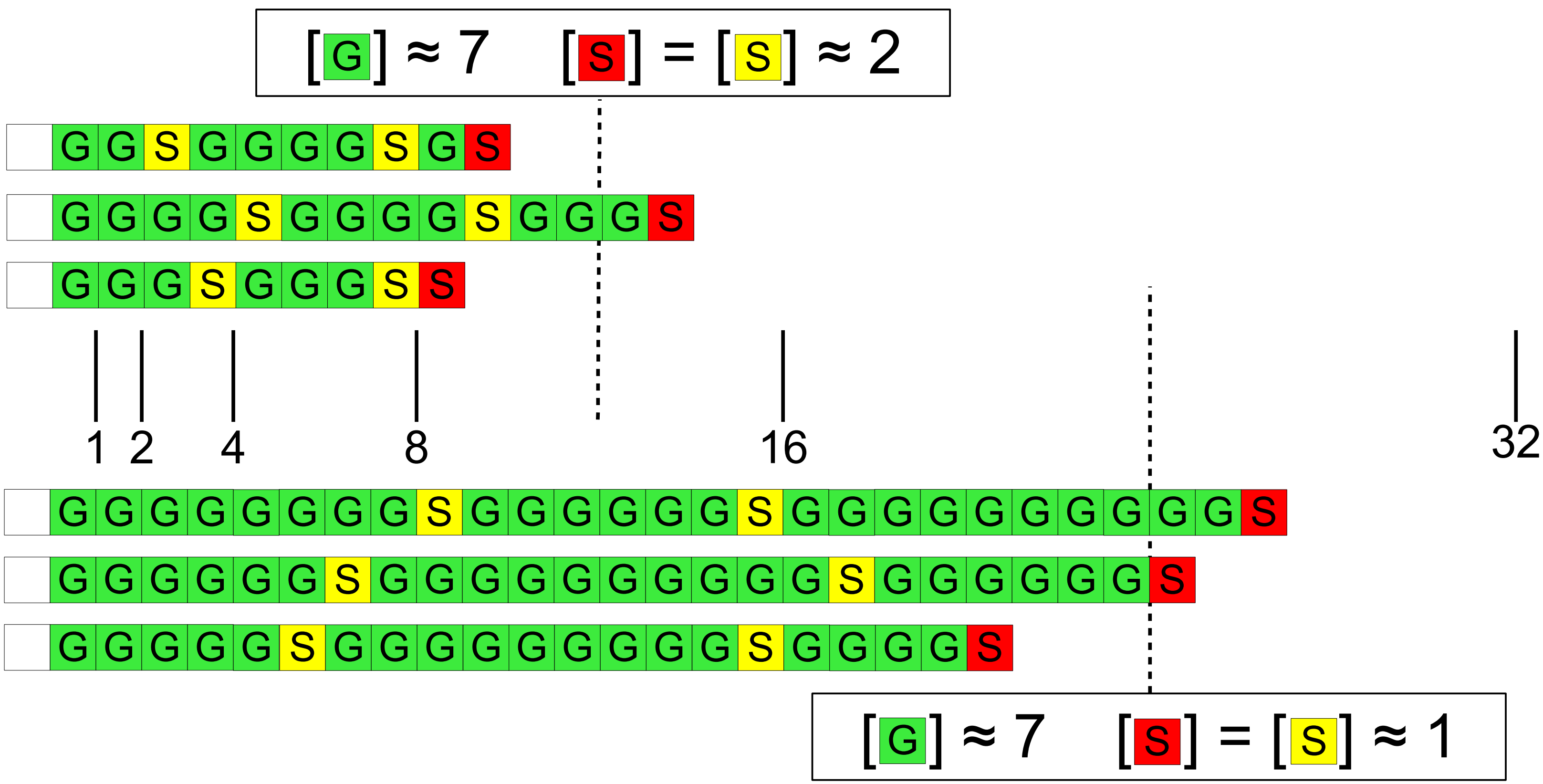



3 "stages", each of expected length 4

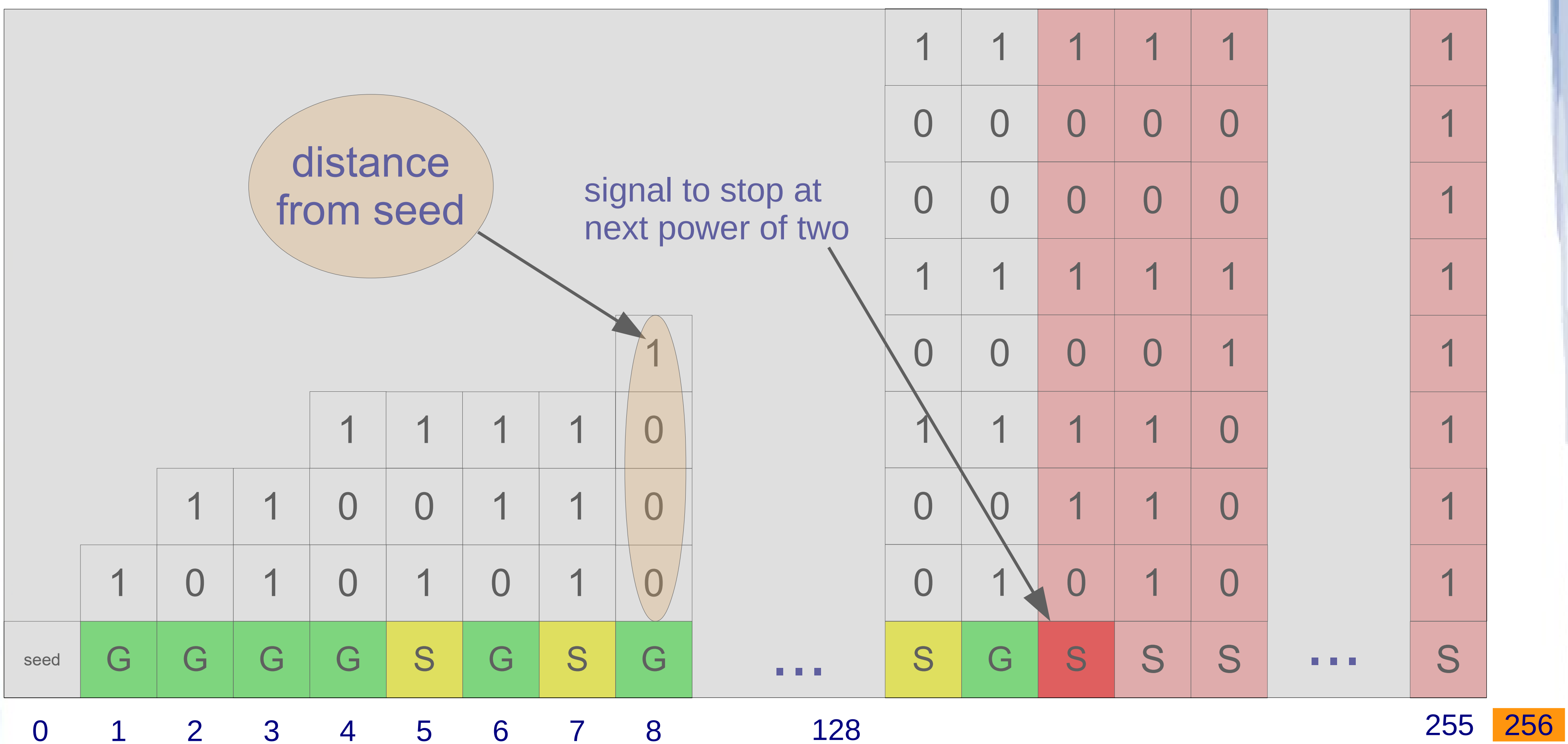
# Programming polymer length (improved)

90 stages, expected length midway in $[2^{a-1}, 2^a)$

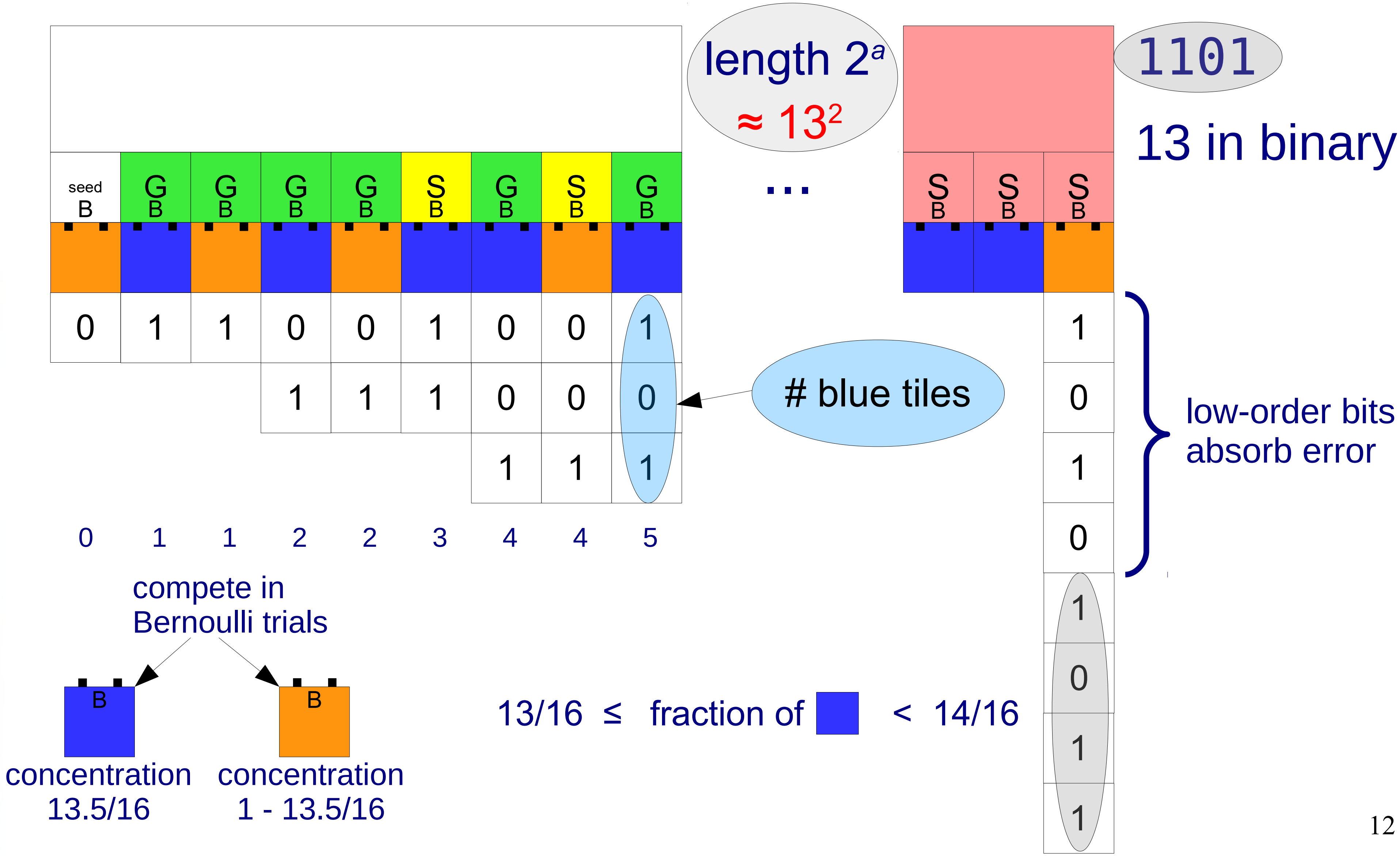
with probability > 99% **actual** length in $[2^{a-1}, 2^a)$



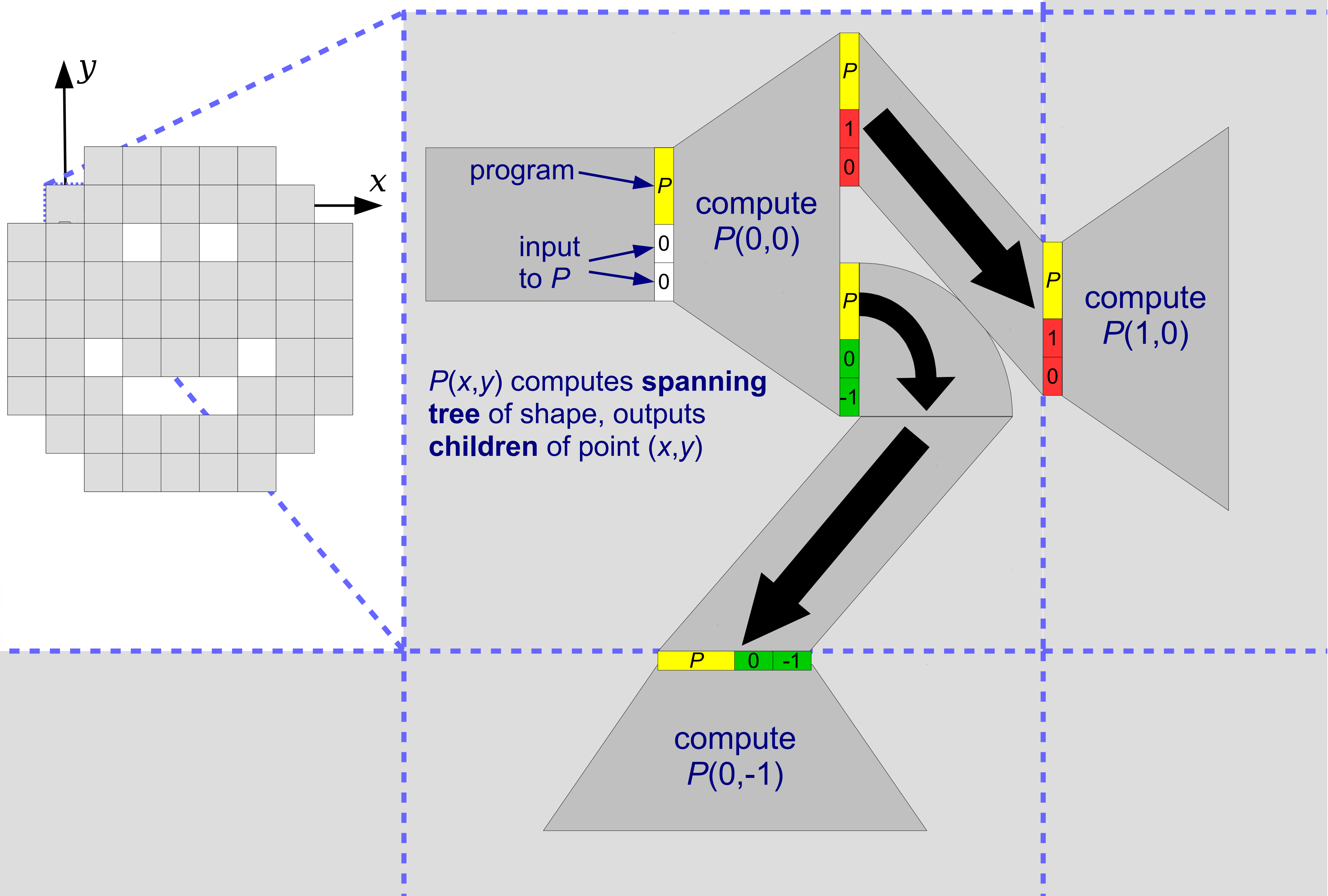
# Programming polymer length $2^a$ precisely



# Programming a binary string



# Programming a shape

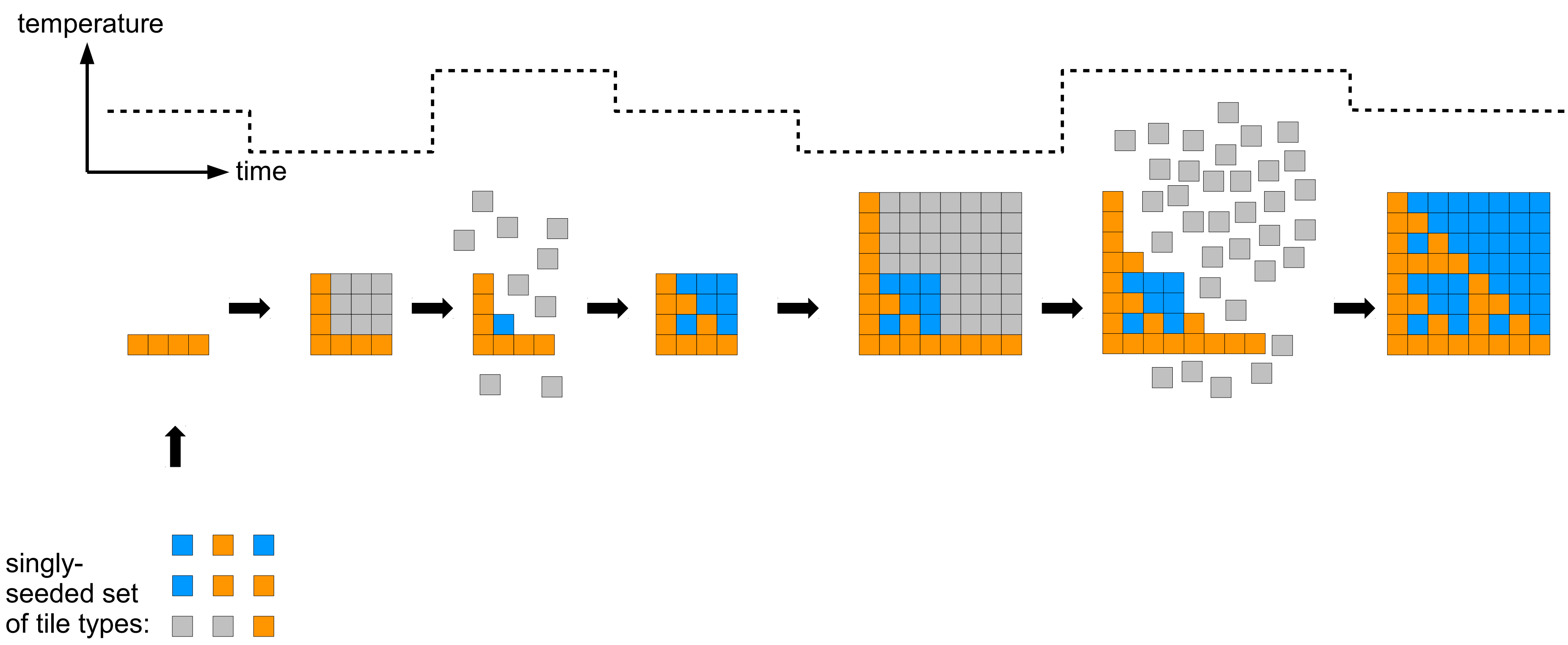



$P(x,y)$ computes **spanning tree** of shape, outputs **children** of point $(x,y)$

# Temperature programming

# Temperature programming

(Kao, Schweller, SODA 2006): Vary temperature (binding strength threshold) throughout assembly to control what assembles.



# Complexity of Temperature Programming

*Scott Summers*: A fixed set of (singly-seeded) tile types can assemble any finite scaled shape through temperature programming.

**Number of tile types** (a self-assembly "resource") is constant (maybe big), no matter the shape.

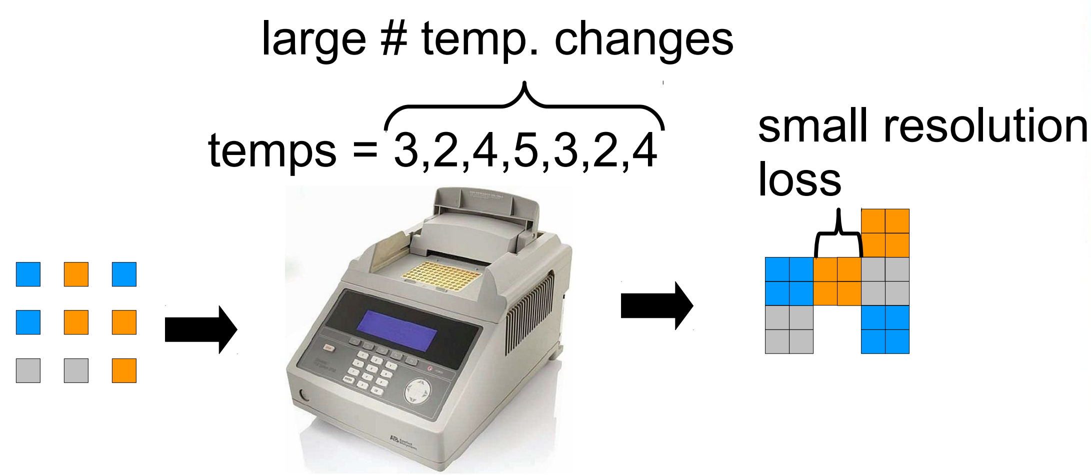
Scott wondered about two other self-assembly resources that might change for each shape:

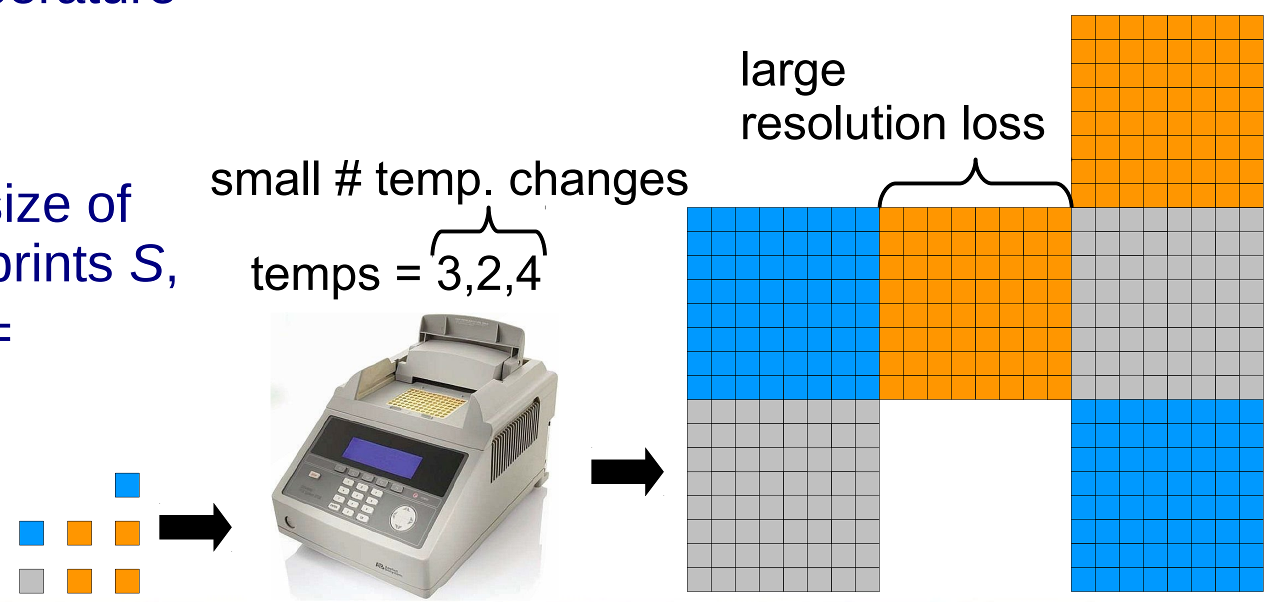
- What **resolution loss** is required?
- What **number of temperature changes** are required?

# Complexity of Temperature Programming

For shape *S* with *n* points, trade-off between **resolution loss** and **number of temperature changes**:

- With *optimal resolution loss* = constant (22 in Scott's paper although shown smaller in the example), need ≈ *n* temperature changes.
- With *optimal number of temperature changes* = size of smallest program *p* that prints *S*, need resolution loss ≈ *t* = running time of *p*.



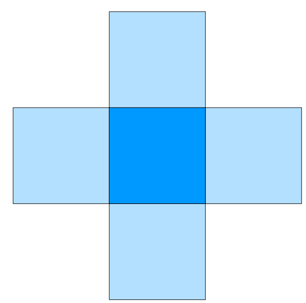
# Hierarchical assembly

# Parallelism in the Model

potential attachment location

attached tile

time step 0

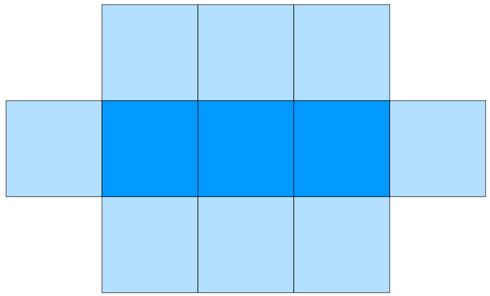


# Parallelism in the Model

potential attachment location

attached tile

time step 1

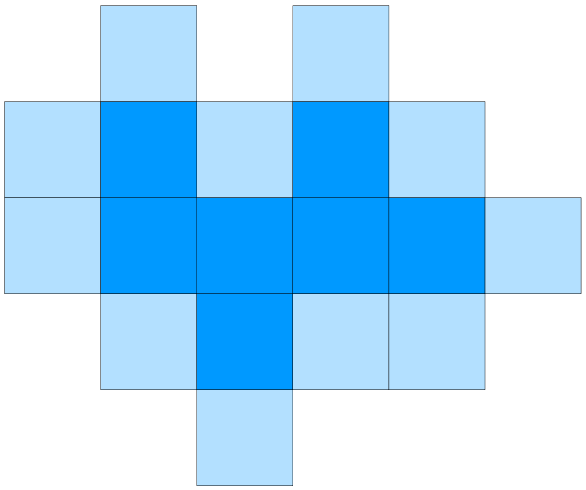


# Parallelism in the Model

potential attachment location

attached tile

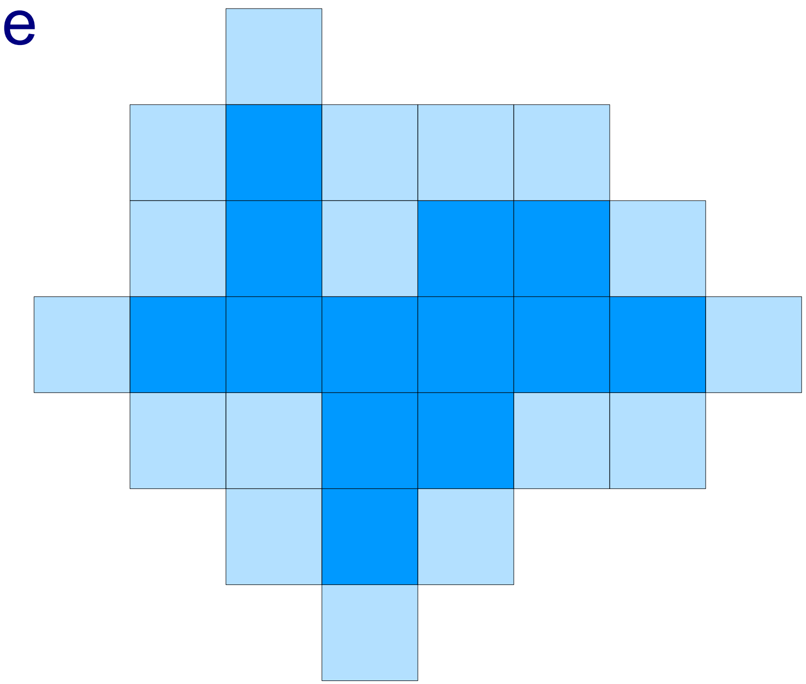
time step 2



# Parallelism in the Model

potential attachment location

attached tile

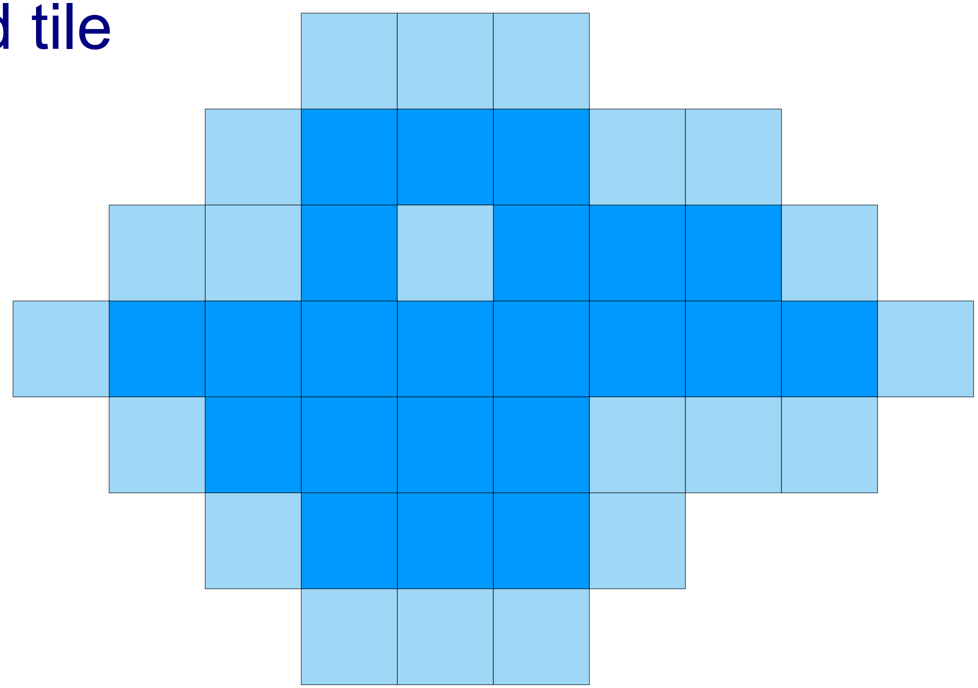


time step 3

# Parallelism in the Model

potential attachment location

attached tile



time step 4

time $t$: perimeter $\leq O(t)$ (with high probability)

$\longrightarrow$ max attachments per time step $\leq O(t)$

$\longrightarrow$ max total attachments after $t$ steps $\leq O(t^2)$

$\longrightarrow$ min time to assemble any shape of size $N \geq \Omega(\sqrt{N})$

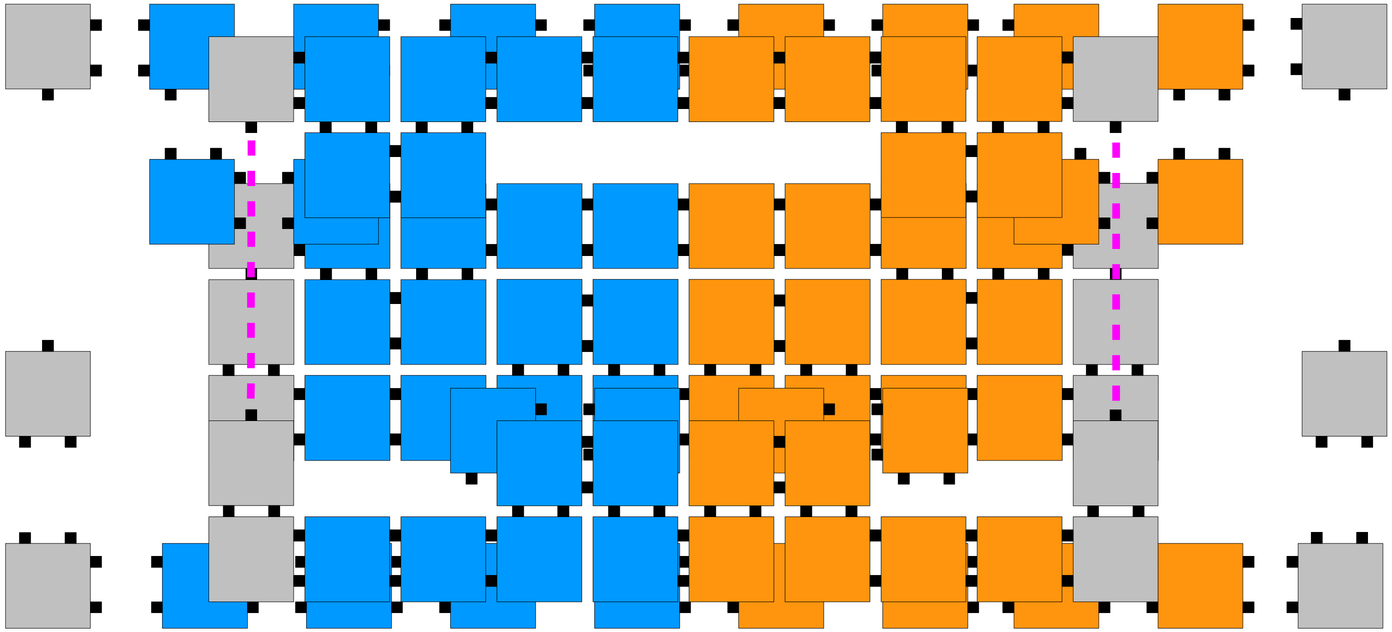
# Parallelism and Time

Can we speed up assembly by allowing large assemblies to form in parallel and then attach to each other in one step?

# Hierarchical Tile Assembly Model

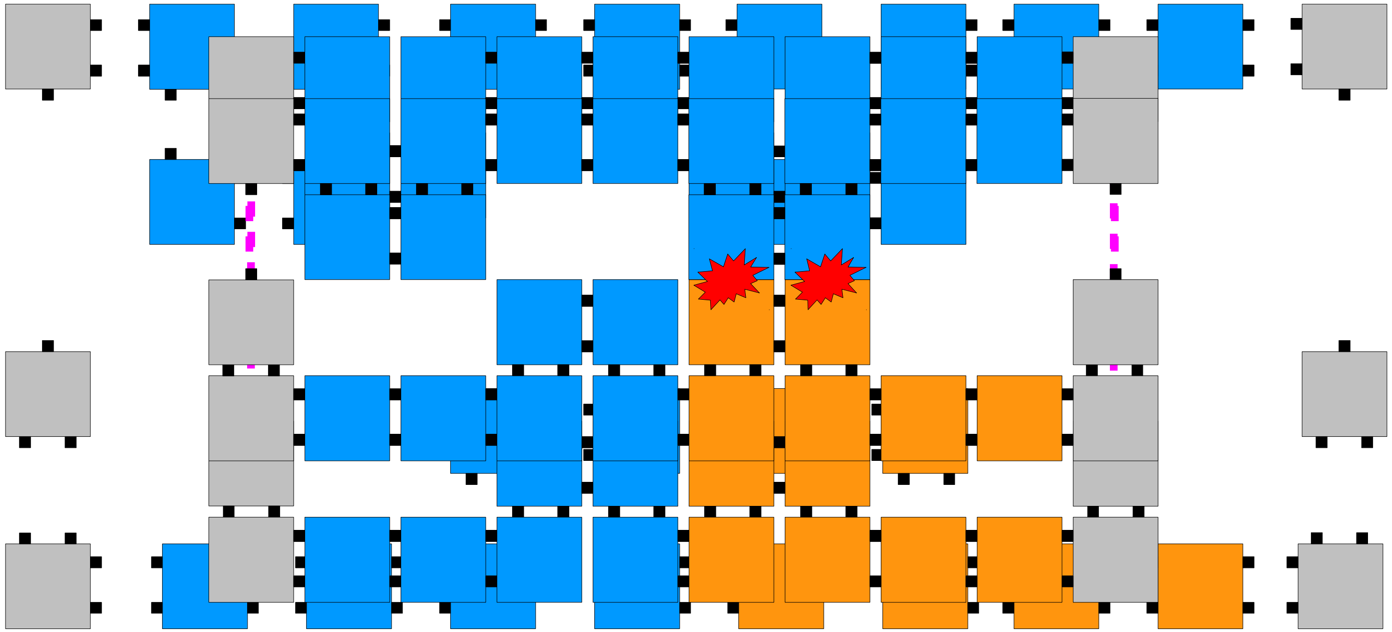
- **seeded** model
  - growth nucleates from a single seed tile
  - tiles attach one at a time
- **hierarchical** model: assembly is producible if
  - <u>base case</u>: it is a single tile, or
  - <u>recursive case</u>: it results from translating two producible assemblies so they *stably attach* without overlap

# Hierarchical Tile Assembly Model



# Hierarchical Tile Assembly Model

Overlap disallowed in attachment events ("steric protection")



# Potentially Unrealistic Aspects of the Hierarchical Assembly Model

- Overlap restriction:
  - DNA is floppy; won't stay in the plane
  - Engineering problem; not fundamental

More fundamental problems:

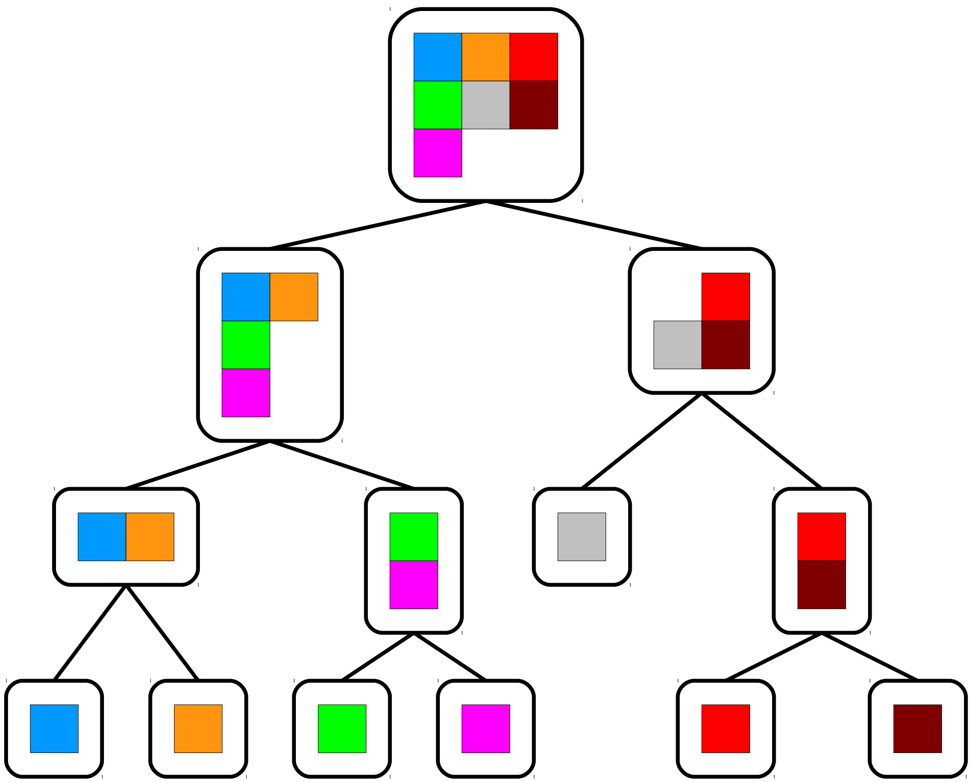
- Large assemblies assumed to diffuse as fast as individual tiles
- Uniform binding strength threshold; should be higher for larger assemblies

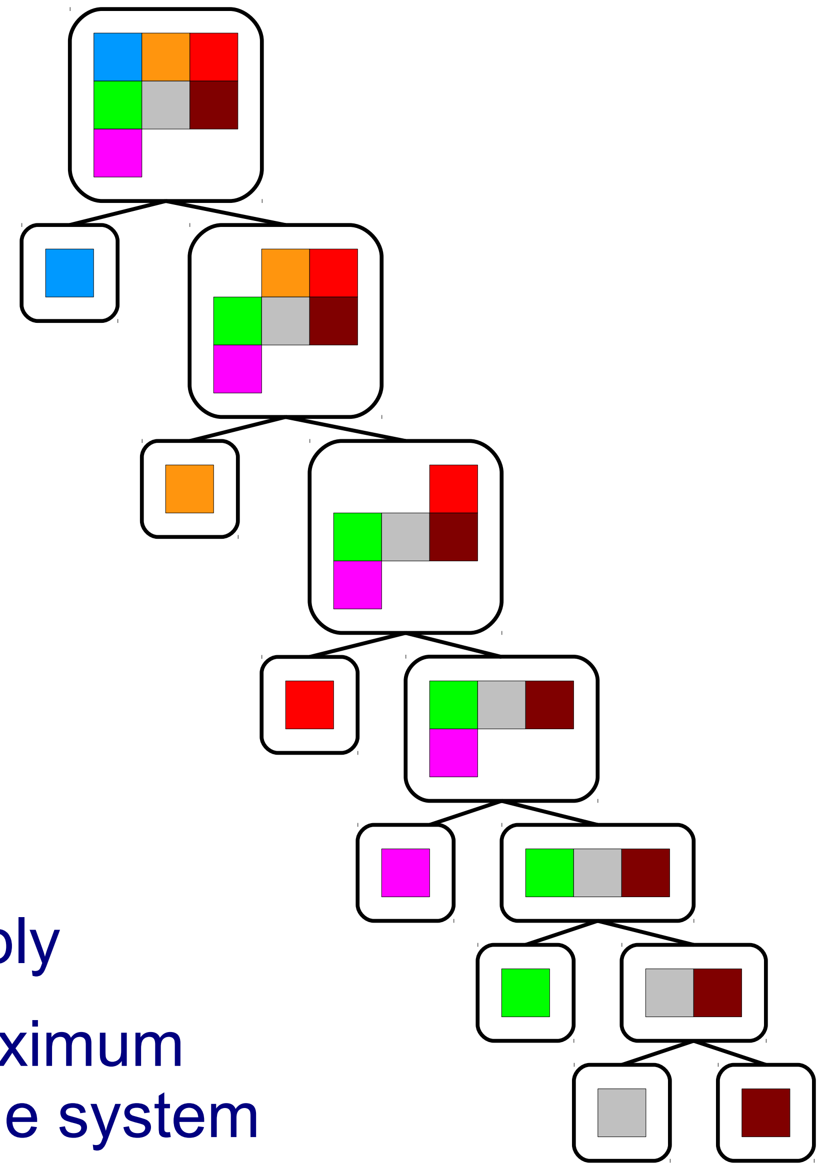
artificially boost assembly speed

# Our Results

- **Previous result:** Assembling an $n$ x $n$ square requires $\Omega(n)$ steps in the **seeded** model; achievable with optimal $O(\log n / \log \log n)$ tile types (Adleman, Cheng, Goel, Huang, *STOC* 2001)
- They asked: Can the extra parallelism in the hierarchical model break the $\Omega(n)$ lower bound?
- <u>We show</u>:
  - $O(\log n / \log \log n)$ tile types can assemble an $n$ x $n$ square using "nearly maximal" parallelism.

# Definition of Hierarchical Parallelism





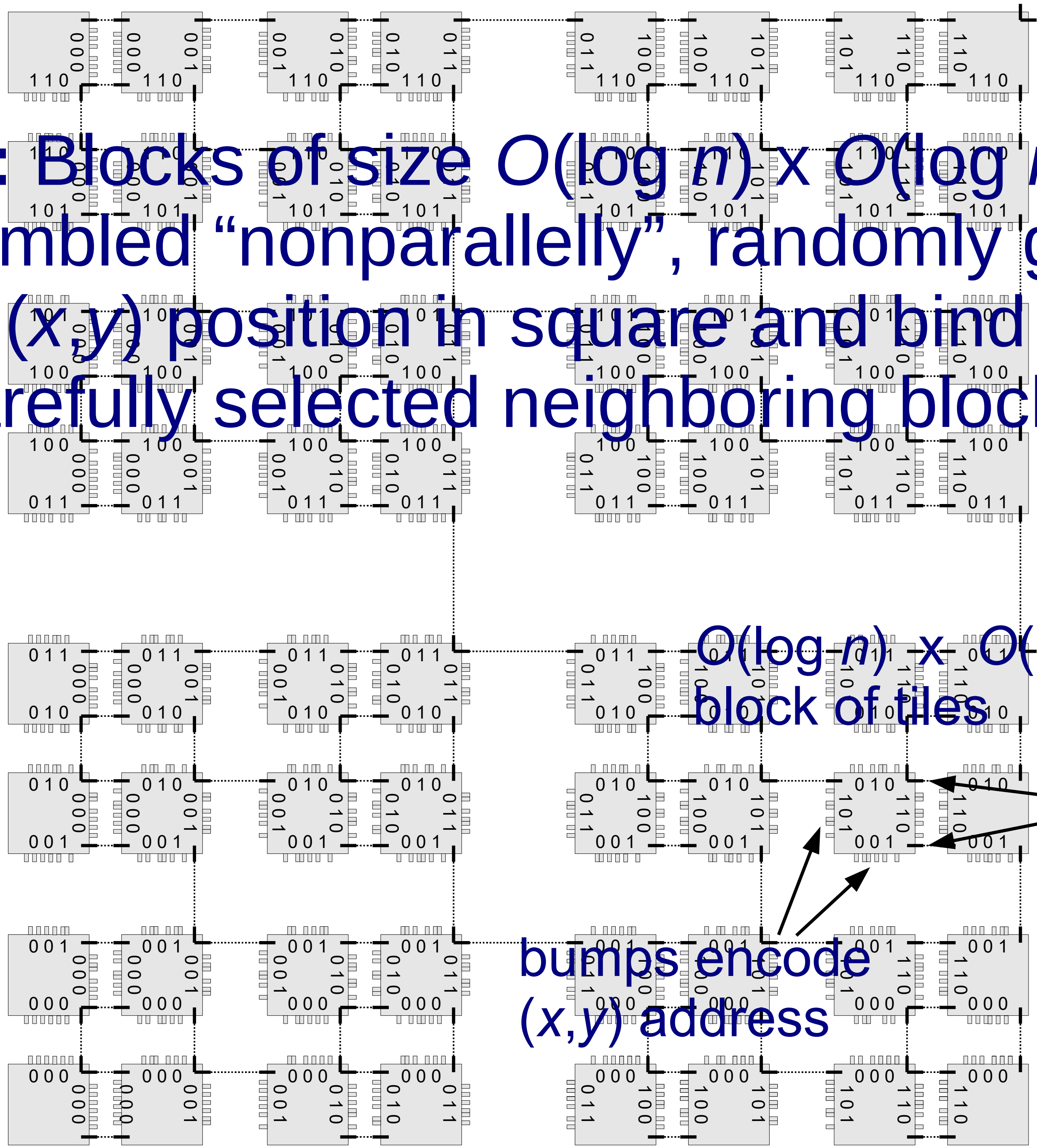
<u>assembly tree</u> = possible order of attachments leading to final assembly

<u>assembly depth</u> of tile system = maximum depth of any assembly tree of the tile system

# Highly Parallel Square Assembly

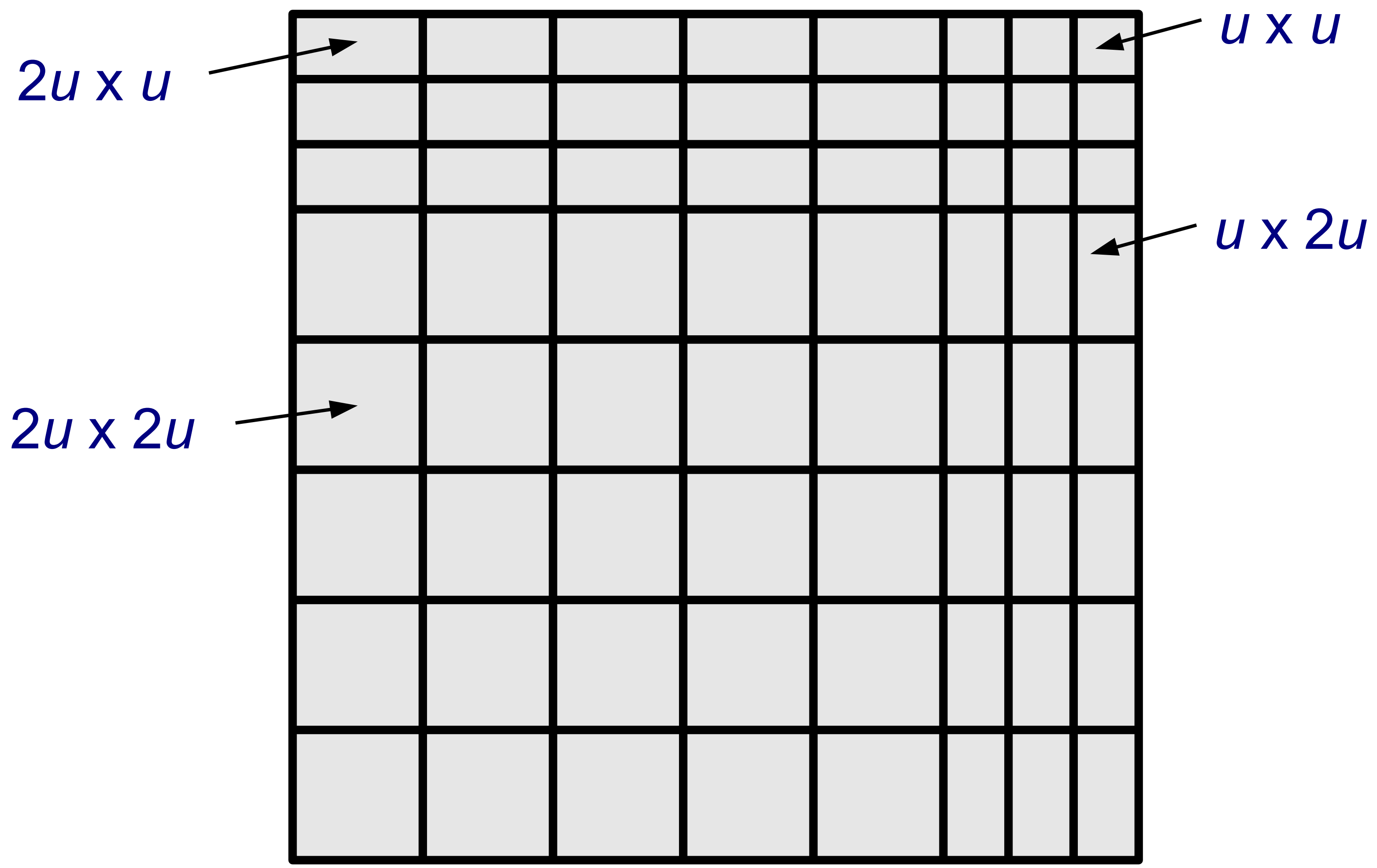
- Best possible assembly depth for any shape with $N$ points is $\log N$.
- **Theorem:** For every positive integer $n$, there is a tile system with $O(\log n / \log \log n)$ tile types and assembly depth $O(\log^2 n)$ that assembles an $n \times n$ square.

**Idea:** Blocks of size $O(\log n)$ x $O(\log n)$, assembled "nonparallelly", randomly guess their $(x,y)$ position in square and bind only to carefully selected neighboring blocks.

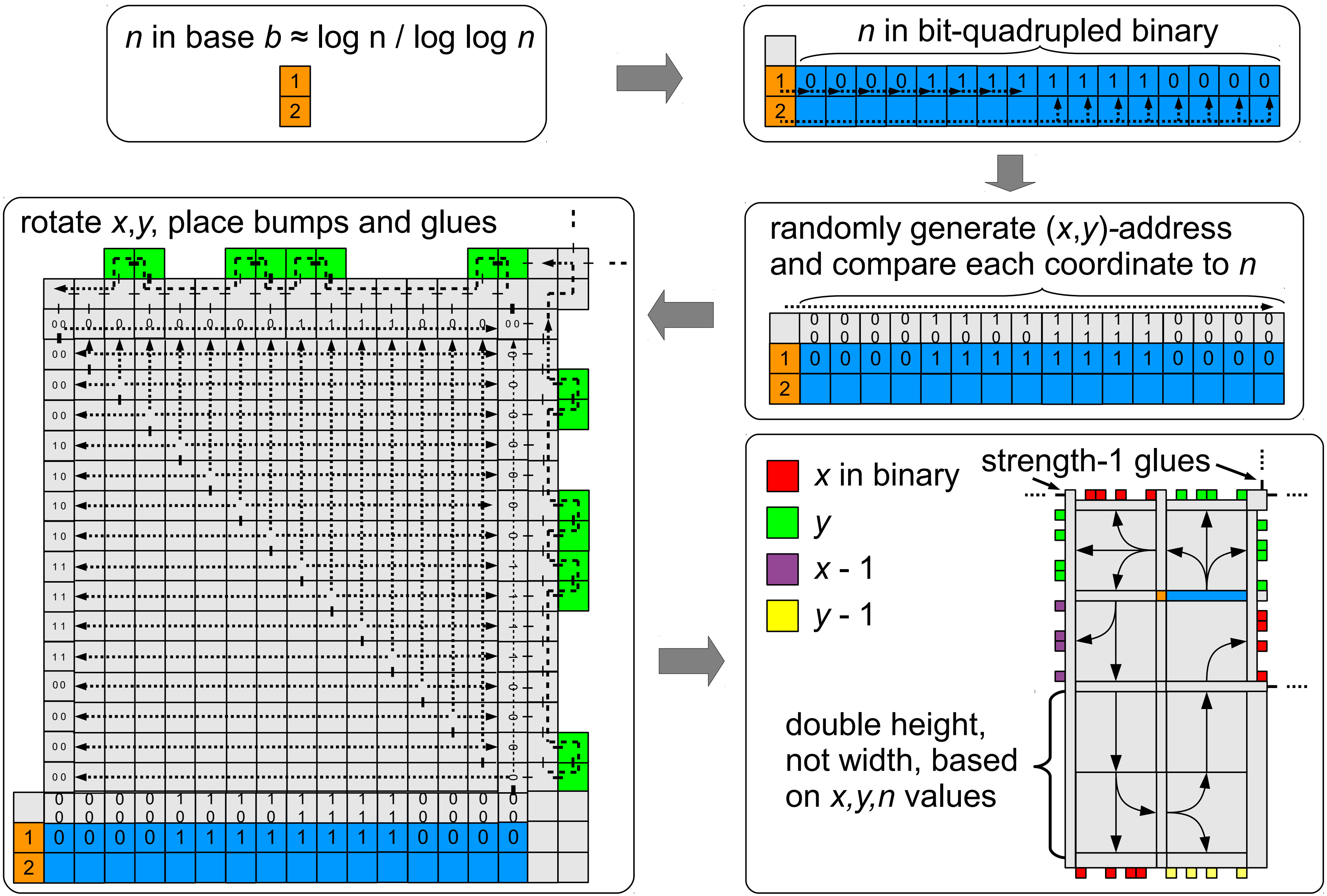


# Handling Non-Powers-of-2

$u = c \log n$



# Assembly of Each Block



# Our Results

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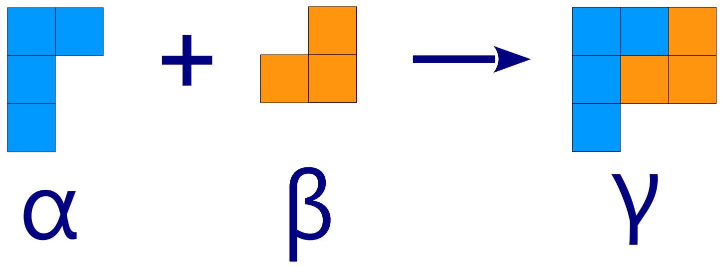
- They asked: Can the extra parallelism in the hierarchical model break the $\Omega(n)$ lower bound?
- We show:
  - $O(\log n / \log \log n)$ tile types can assemble an $n$ x $n$ square using "nearly maximal" parallelism.
  - This construction takes **superlinear** time.
  - **Every** "partial order system" requires time $\Omega(N)$ to assemble any shape of diameter $N$.

The extra parallelism of the hierarchical model is **useless** for speeding up partial order systems.

# Assembly Time Complexity Model

- Assign each tile type $s$ an initial concentration $C(s)$ so that $\sum_s C(s) = 1$ (finite density constraint).
- At time $t = 0$, each assembly $\alpha$ with only a single tile $s$ has initial concentration $[\alpha](t) = C(s)$. All larger assemblies $\alpha$ have $[\alpha](t) = 0$ at time $t = 0$.
- Each attachment $\alpha + \beta \rightarrow \gamma$ is a chemical reaction with rate $[\alpha](t)\cdot[\beta](t)$ at time $t$.

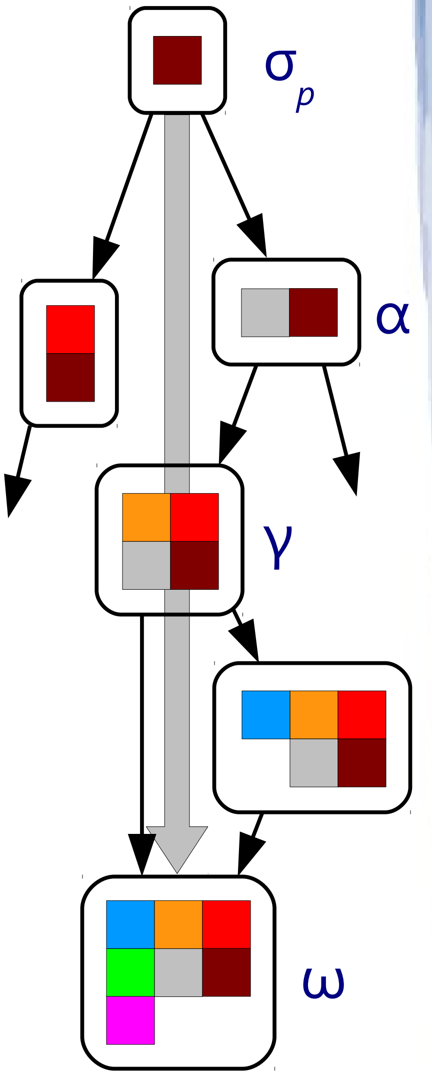



- Concentrations evolve by mass-action kinetics:

$$d[\alpha] / dt \;=\; \sum_{\gamma + \beta \rightarrow \alpha}[\gamma](t)\cdot[\beta](t) \;-\; \sum_{\alpha + \beta \rightarrow \gamma}[\alpha](t)\cdot[\beta](t)$$

# Assembly Time Complexity Model

- Fix a position *p* in the unique final assembly ω, with *initial assembly* $\sigma_p$ with just the tile at position *p*
- $\sigma_p$ changes into ω by a continuous-time Markov chain
- States = assemblies $\sigma_p$, ω, and all possible intermediates
- Transition from α to γ if there is a producible assembly β such that α + β → γ, with time-dependent rate [β](*t*)
- Unique sink state of the Markov chain is ω
- time relative to *p* = expected time to reach ω from $\sigma_p$
- time = $\max_p$ time relative to *p*



# Assembly Time Lower Bound

- partial order system: in the terminal assembly, each pair of adjacent binding tiles have an *assembly order precedence relationship* (one always binds first, or at the same time)
- **Theorem**: Any partial order system whose terminal assembly has diameter $N$ requires time $\Omega(N)$.

# Main Proof Idea

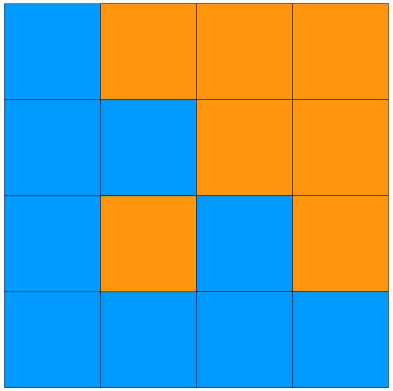
conservation of mass: assemblies of size $n$ and $k$ attach to create assembly of size $n + k$

$\rightarrow (\forall t \geq 0) \quad \sum_{\alpha} [\alpha](t) \cdot |\alpha| \;=\; 1$

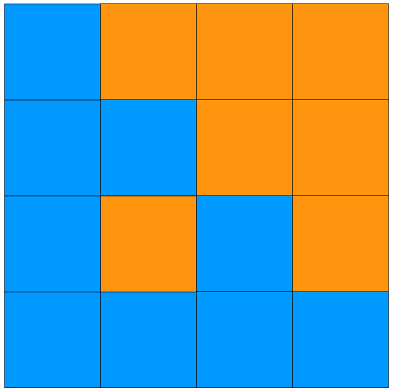
$\rightarrow$ assembly of size $k$ has concentration $\leq 1/k$

$\rightarrow$ growing by size $k$ in a single step takes expected time $\geq k$

seeded



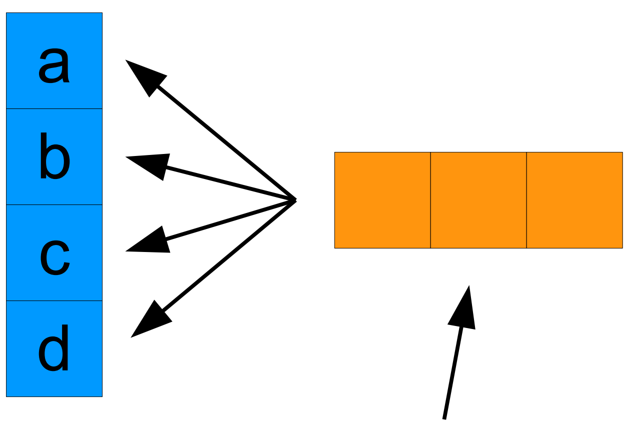
hierarchical

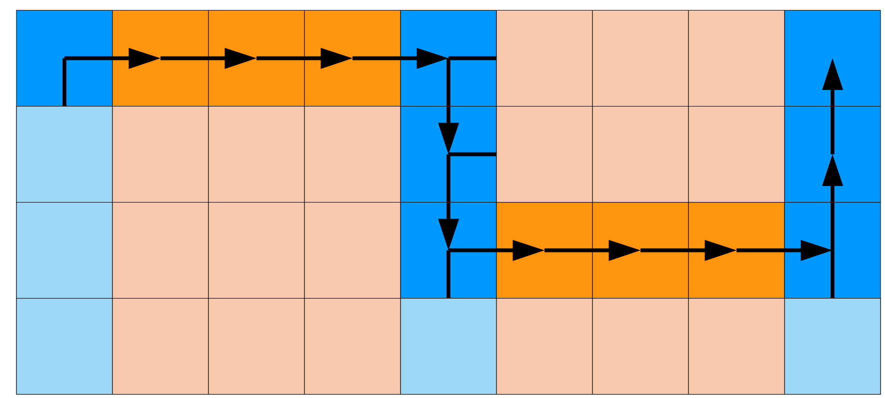


# Why Partial Order Systems?

Argument breaks if a single assembly of size *k* could attach to many positions, any one of which suffices to proceed to terminal assembly.

Any path in partial order DAG must assemble in order



longest path has length ≥ diameter of shape

by concentration argument, path takes time *k* to grow by *k* tiles

concentration ≤ 1/3

E[time to attach to a] ≥ 3

E[time to attach to any of a,b,c,d] ≥ 3 / 4

# Removing tiles (RNase model)

# Removing Tiles

- aTAM is *monotone*: stably attached tiles do not detach
  - "Computation of a shape" with tiles may take a lot of space
  - Need large resolution loss to compute **within** the shape
  - kinetic model allows detachment but not controllable
- RNase model (Abel, Benbernou, Damian, Demaine, Demaine, Flatland, Kominers, Schweller)
  - make some tile types from RNA and some from DNA
  - after some time, add RNase enzyme to dissolve RNA tiles
  - only subassemblies made of DNA tiles remain

# Shape-Building with Small Resolution Loss and Optimal Tile Complexity

*Demaine, Patitz, Schweller, Summers* (STACS 2011)*:*

**given:** finite shape *S*, |*S*|=*n*

there is a TAS T, |T| ≈ K(*S*), that assembles S at scale factor ≈ log *n*, with one step of dissolving RNA tiles

RNA tiles:

DNA tiles: