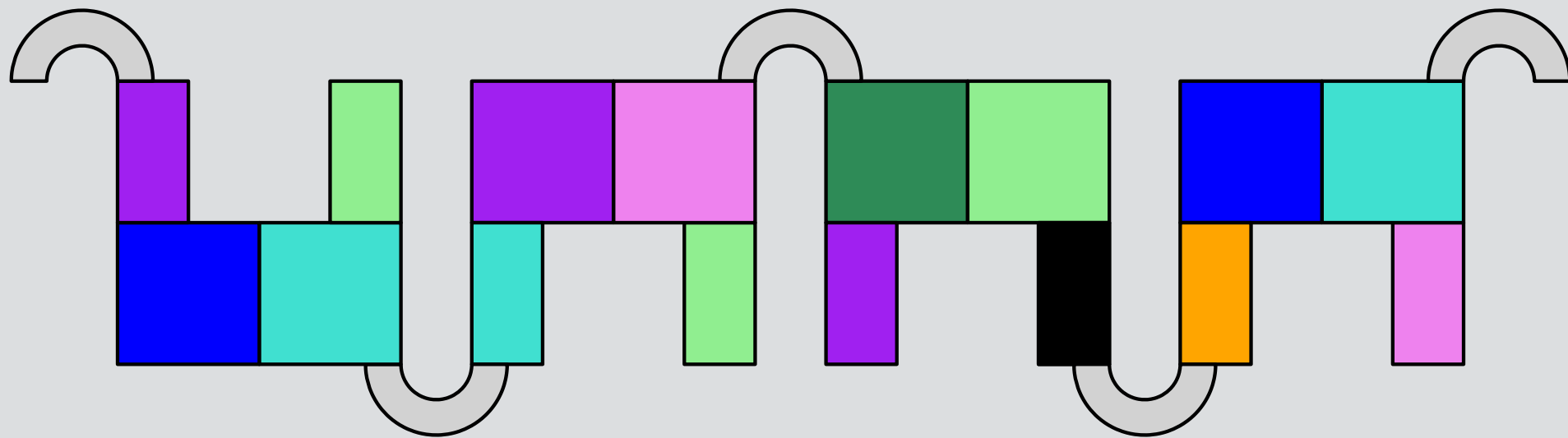


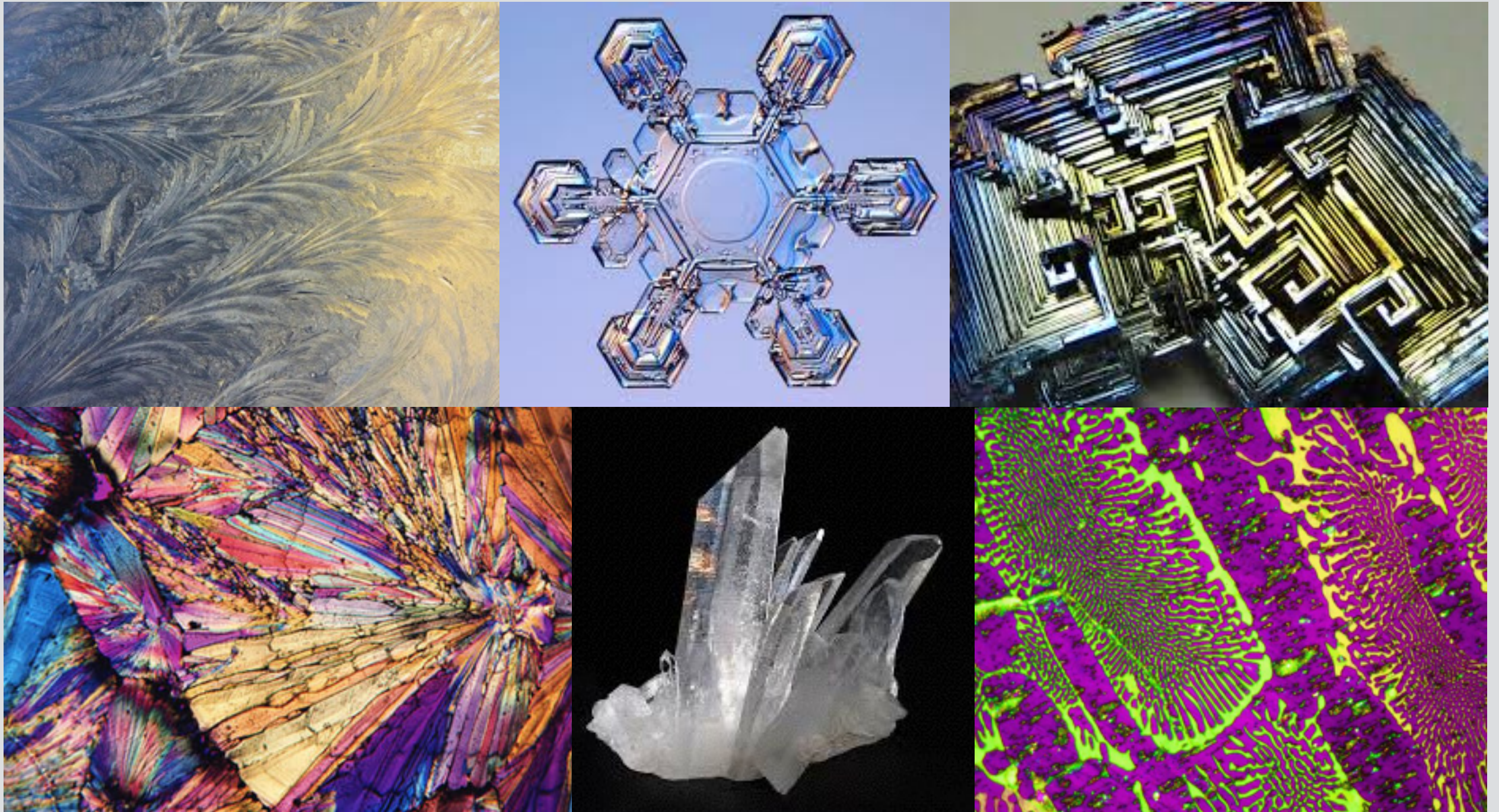
Tight bounds for active self-assembly using an insertion primitive



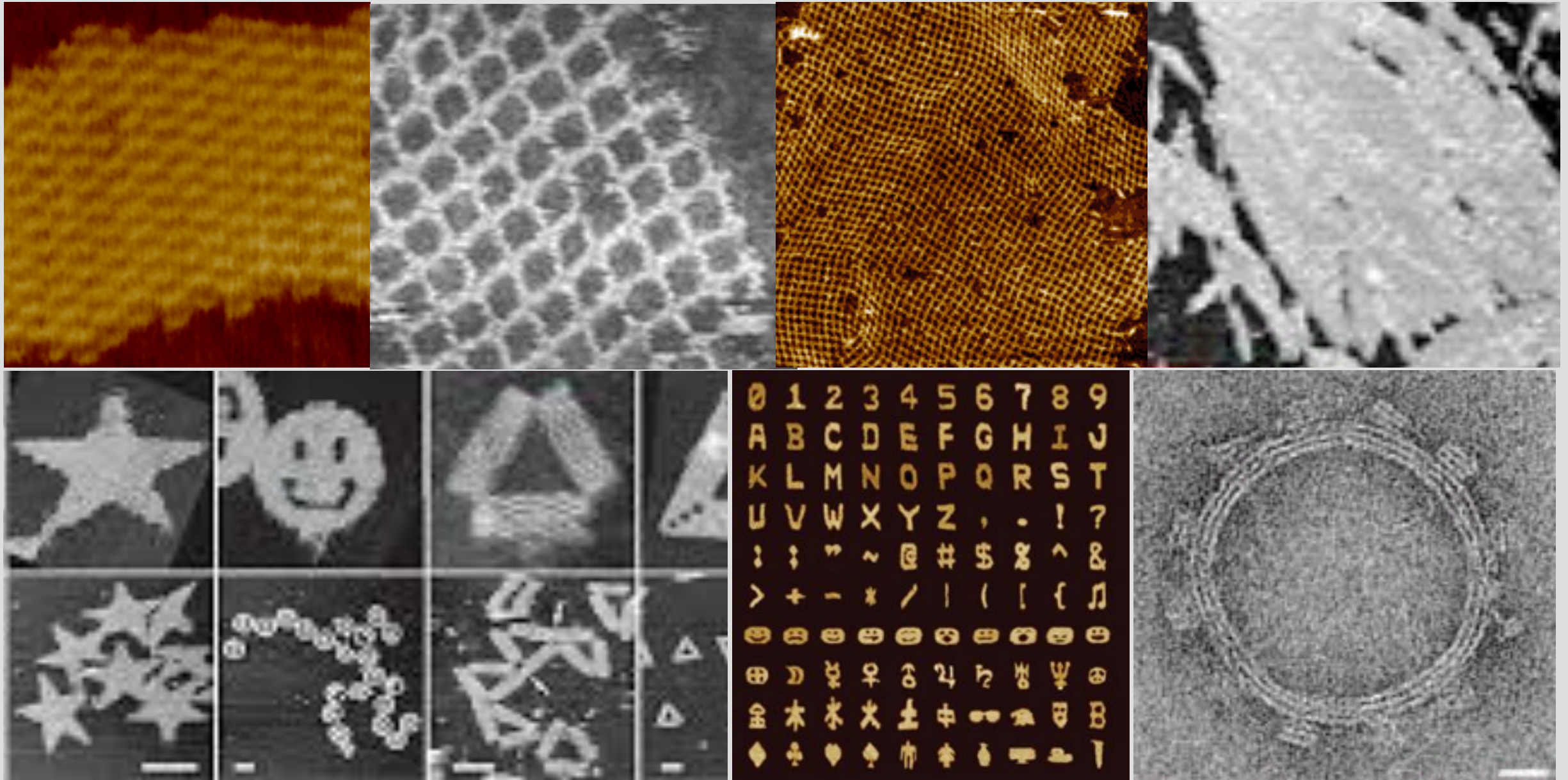
Caleb Malchik and Andrew Winslow



Natural Nanoscale Self-Assembly



Synthetic Nanoscale Self-Assembly



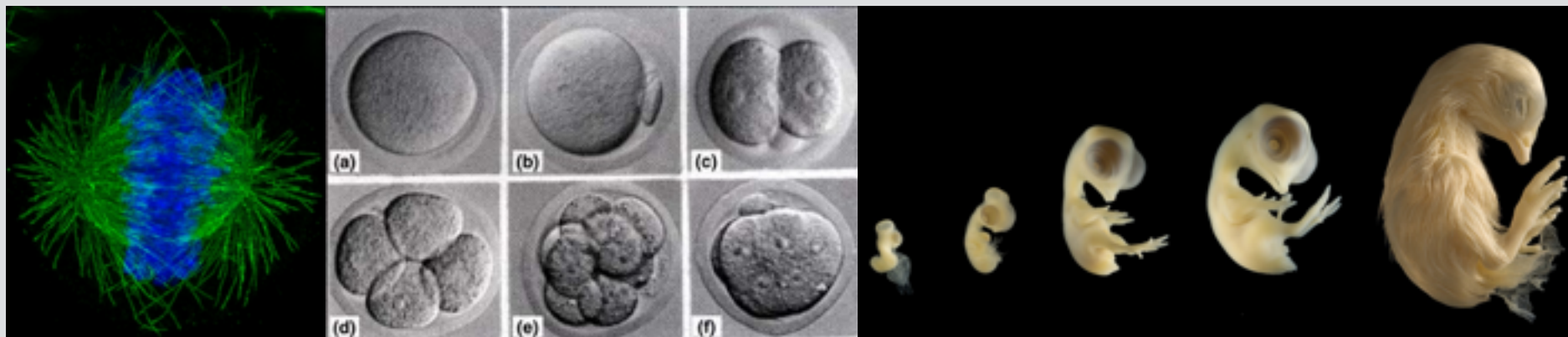
All made of DNA!

DNA Self-Assembly

- Crystal-like growth: single particles attach to a growing lattice structure, starting as a *seed*.
- Particles far from seed can only attach after many other particles.
- Limits growth rates to polynomial.

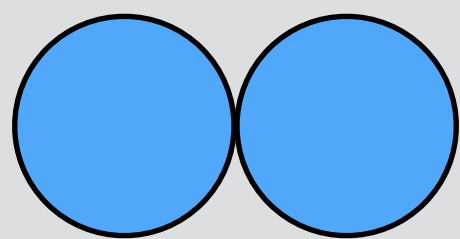
DNA Self-Assembly

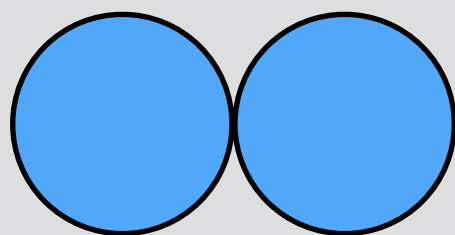
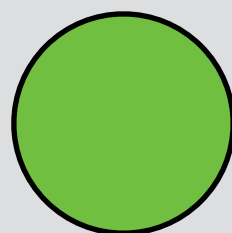
- Crystal-like growth: single particles attach to a growing lattice structure, starting as a *seed*.
- Particles far from seed can only attach after many other particles.
- Limits growth rates to polynomial.
- But some natural systems grow exponentially!

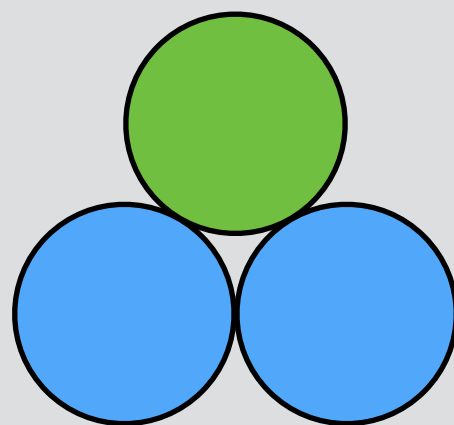


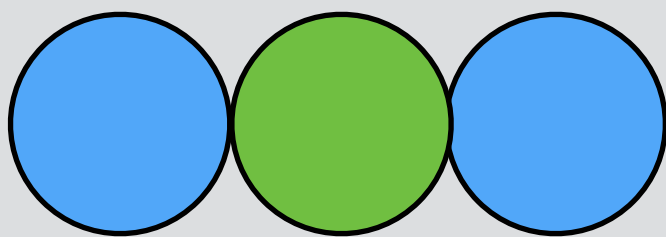
Passive vs. Active Self-Assembly

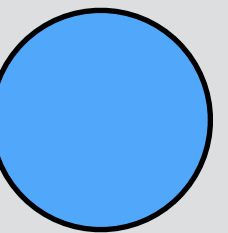
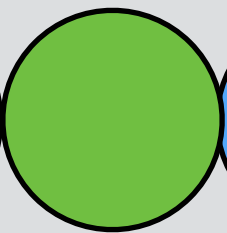
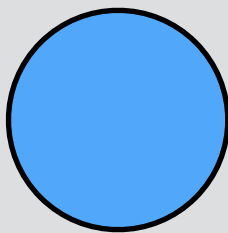
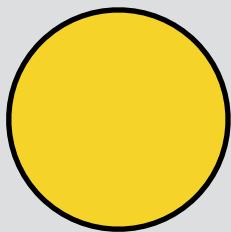
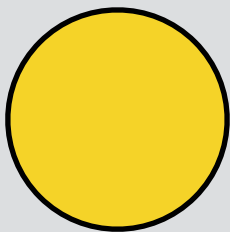
- Most current DNA self-assembly uses crystal-like **passive** growth: bonds and geometry do not change.
- Some natural systems use **active** growth: bonds and geometry change.
- Active growth enables exponential growth rates.

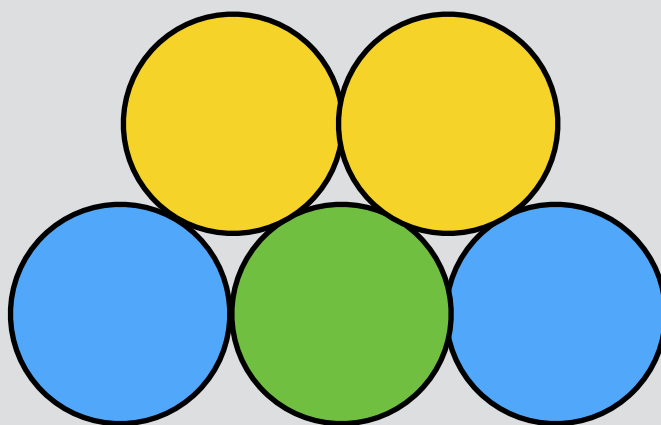


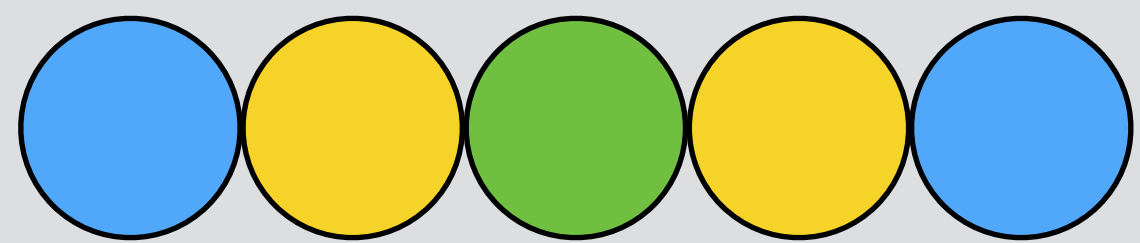


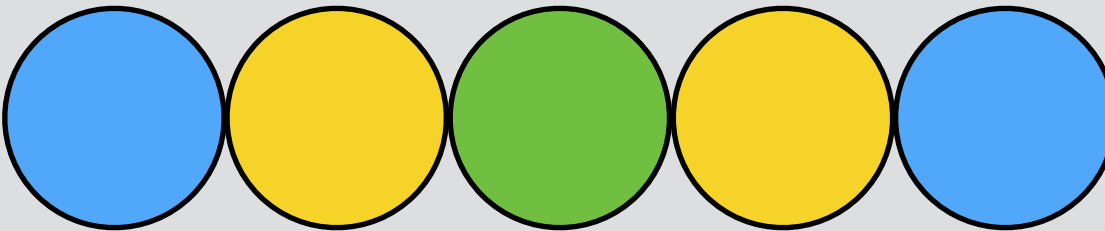
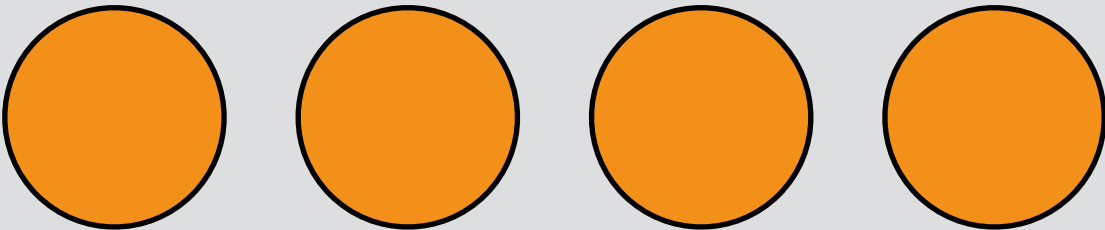


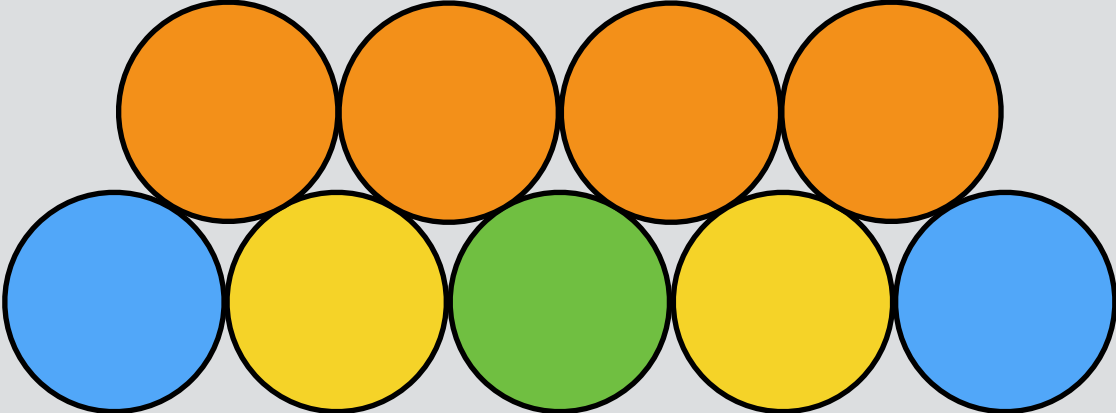


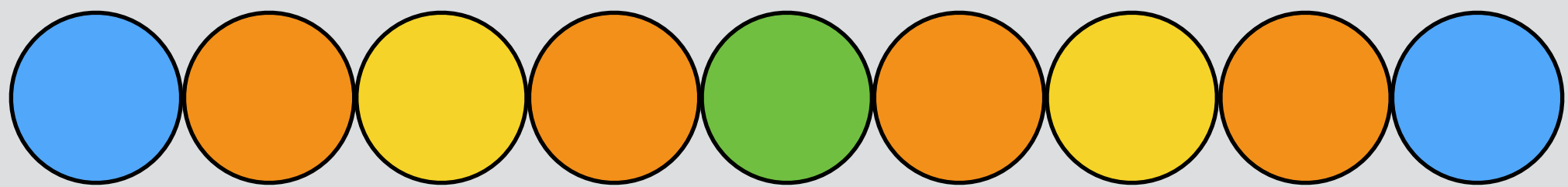


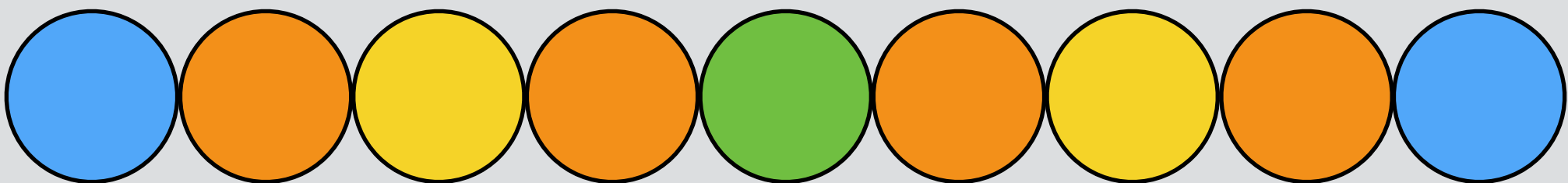
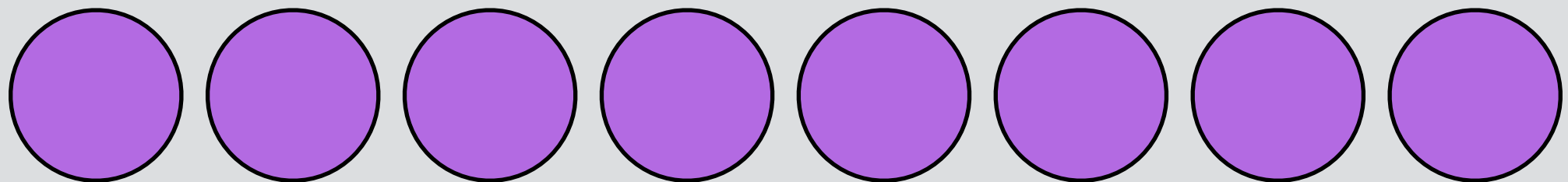


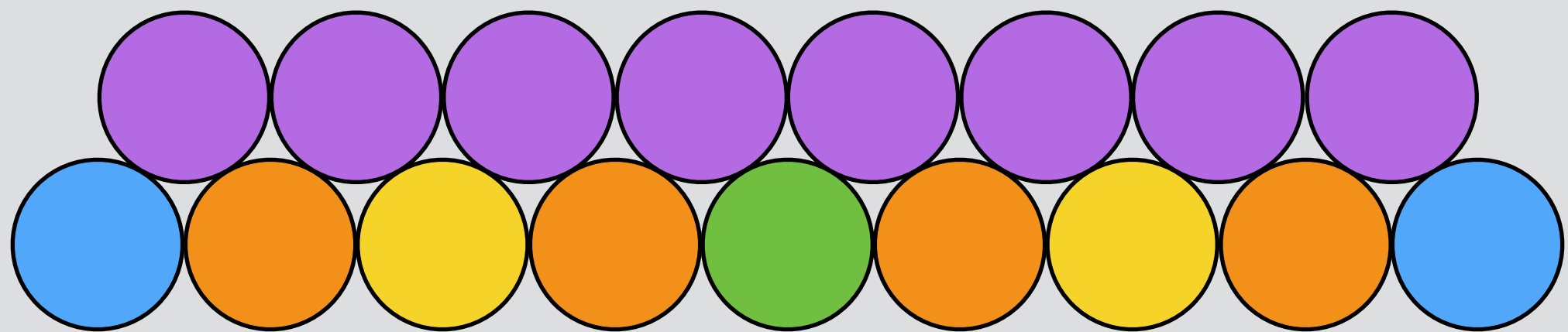


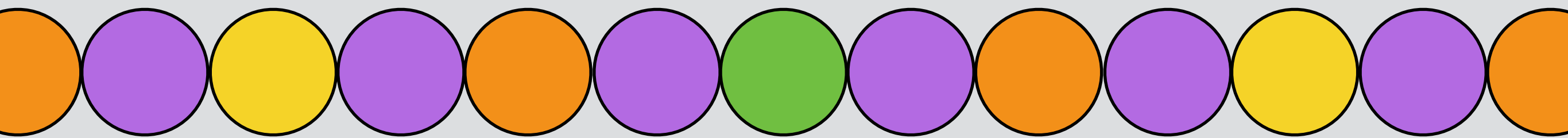




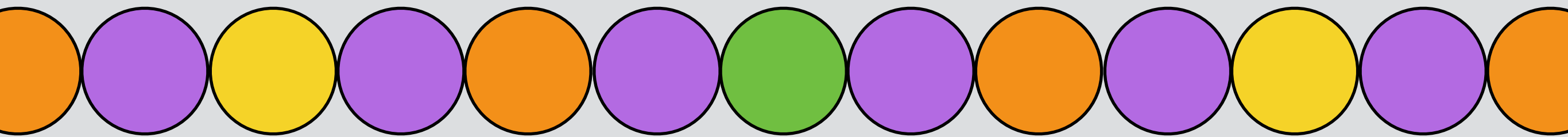






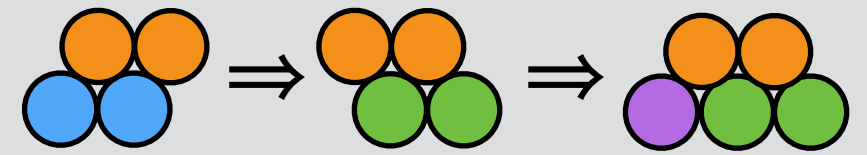


Exponential growth!

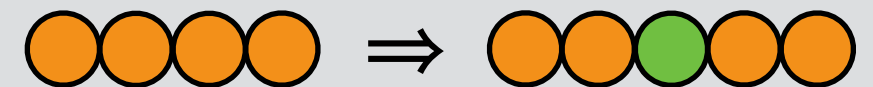


Active self-assembly models

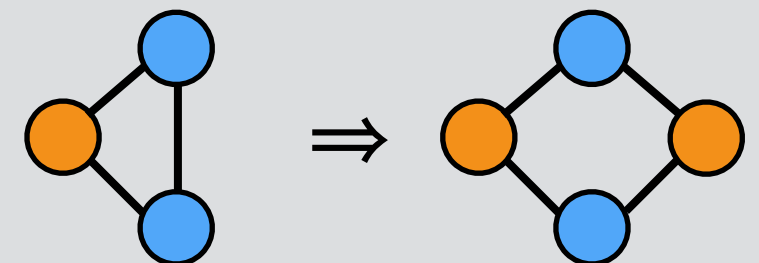
Nubots [Woods et al. ITCS 2012]:
2D, flexible and rigid bonds, stateful particles.



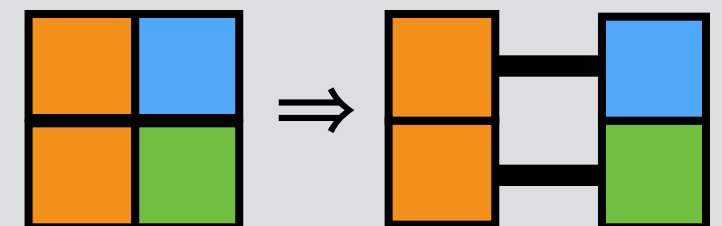
Insertion systems [Dabby, Chen SODA 2013]:
1D, fixed shape, stateless particles.



Graph grammars [Klavins et al. ICRA 2004]:
Geometry-less, stateless particles.



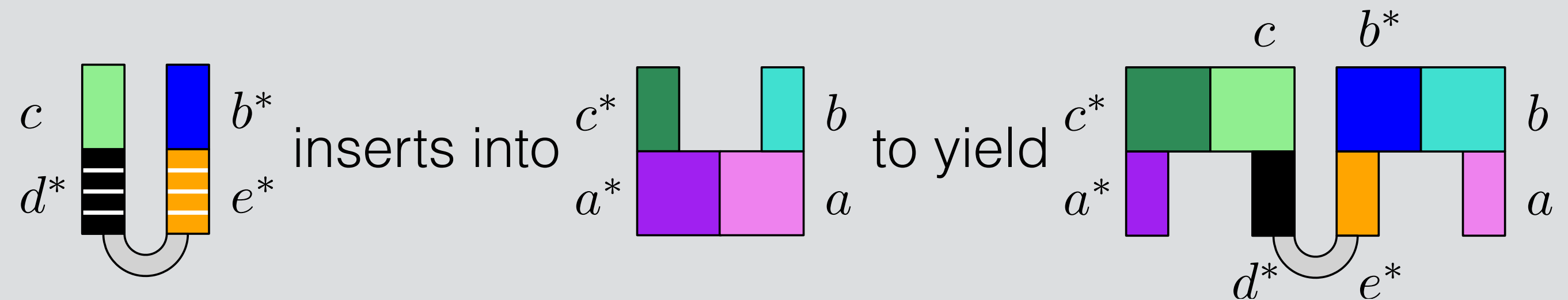
Crystalline robots [Rus, Vona ICRA 1999]:
3D, stateful particles, global communication.



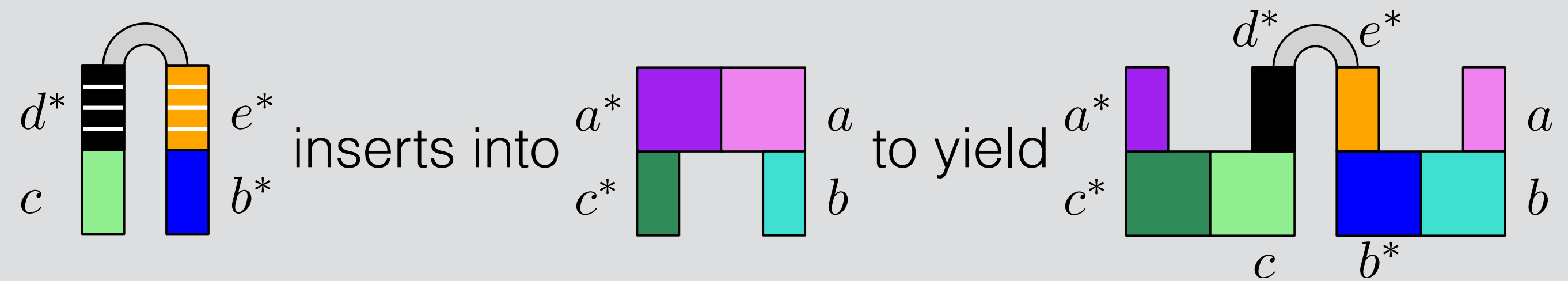
Insertion systems

- Introduced by [Dabby, Chen SODA 2013].
- A model of active self-assembly.
 - Implementable in DNA.
 - Capable of exponential growth.
 - Grows a linear structure by insertion of particles.
- Our work: bound capabilities of insertion systems.

Definitions and examples



$(c, d^*, e^*, b^*)^+$ inserts into $(a^*, c^*)(b, a)$ to yield $(a^*, c^*)(c, d^*, e^*, b^*)(b, a)$



$(d^*, c, b^*, e^*)^-$ inserts into $(c^*, a^*)(a, b)$ to yield $(c^*, a^*)(d^*, c, b^*, e^*)(a, b)$

Insertion system:

Monomer types: $(1, x, 2, b)^+$ $(x, 2^*, a, 3^*)^-$ $(3, x, 4, b)^+$

Initiator: $(a, 1^*)(b^*, a^*)$

Insertion system:

Monomer types: $(1,x,2,b)^+$ $(x,2^*,a,3^*)^-$ $(3,x,4,b)^+$

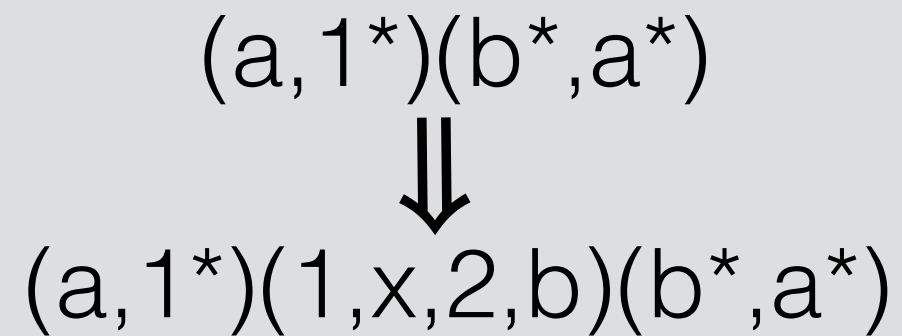
Initiator: $(a,1^*)(b^*,a^*)$

$(a,1^*)(b^*,a^*)$

Insertion system:

Monomer types: $(1,x,2,b)^+$ $(x,2^*,a,3^*)^-$ $(3,x,4,b)^+$

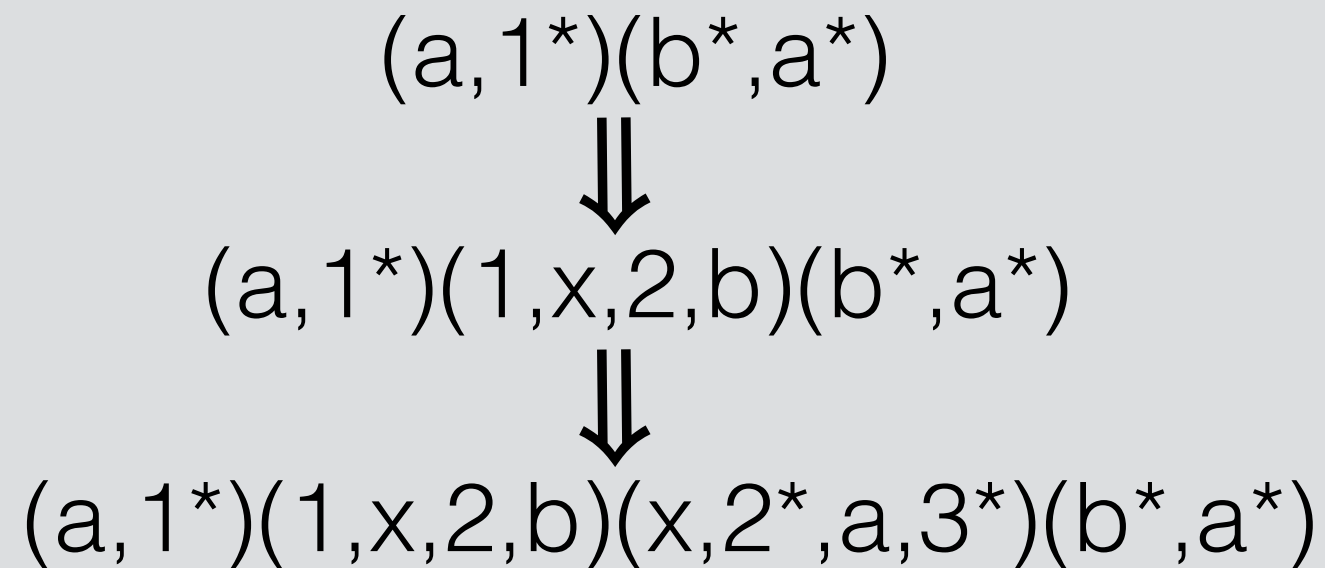
Initiator: $(a,1^*)(b^*,a^*)$



Insertion system:

Monomer types: $(1,x,2,b)^+$ $(x,2^*,a,3^*)^-$ $(3,x,4,b)^+$

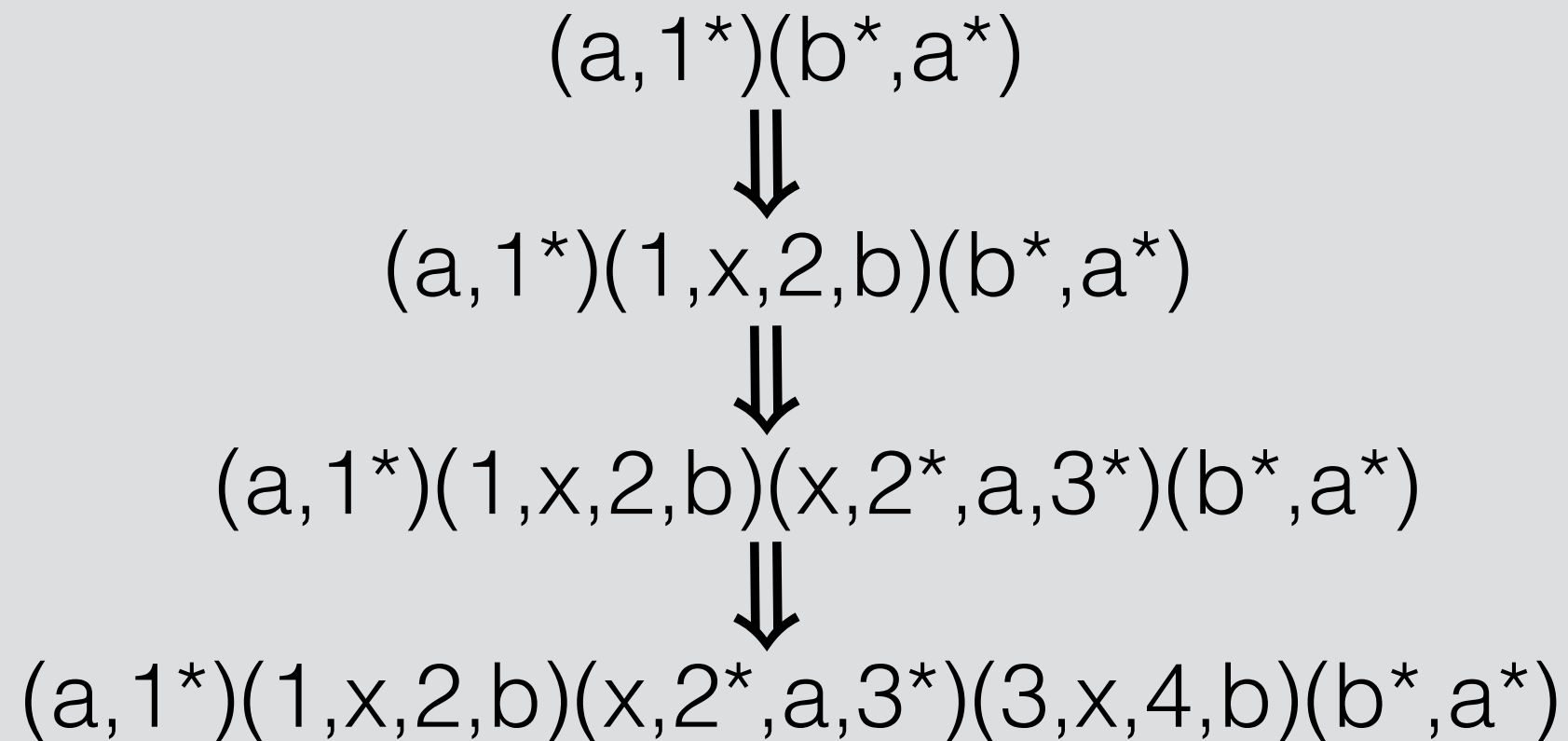
Initiator: $(a,1^*)(b^*,a^*)$



Insertion system:

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Insertion system:

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Initiator: $(a,1^*)(b^*,a^*)$

$(a,1^*)(b^*,a^*)$



$(a,1^*)(1,x,2,b)(b^*,a^*)$



$(a,1^*)(1,x,2,b)(x,2^*,a,3^*)(b^*,a^*)$



$(a,1^*)(1,x,2,b)(x,2^*,a,3^*)(3,x,4,b)(b^*,a^*)$

Terminal polymer of length 5

Insertion time

- Each monomer type has a concentration in $[0,1]$.
- Concentrations of all types in a system must sum to ≤ 1 .
- An insertion occurs after time t with:
 - t an exponential random variable with rate c .
 - c is the total concentration of insertable monomers.

Insertion system:

Monomer types: $(1, x, 2, b)^+$ $(x, 2^*, a, 3^*)^-$ $(3, x, 4, b)^+$

Initiator: $(a, 1^*)(b^*, a^*)$

Insertion system:

Monomer types: $(1,x,2,b)^+$ $(x,2^*,a,3^*)^-$ $(3,x,4,b)^+$

Concentrations: 0.25 0.25 0.5

Initiator: $(a,1^*)(b^*,a^*)$

Insertion system:

Monomer types: $(1,x,2,b)^+$ $(x,2^*,a,3^*)^-$ $(3,x,4,b)^+$

Concentrations: 0.25 0.25 0.5

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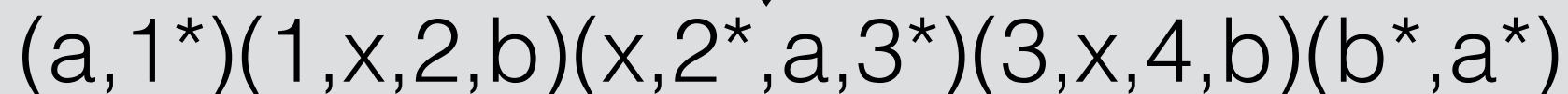
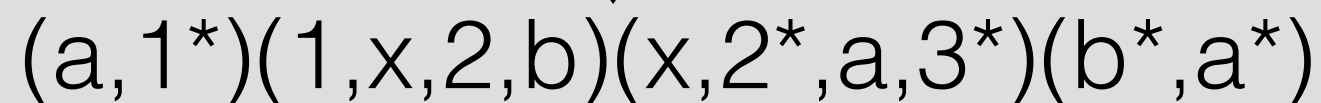
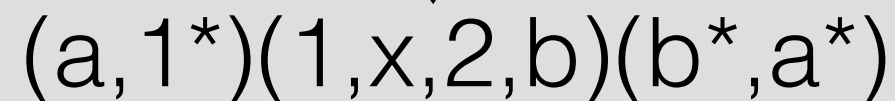
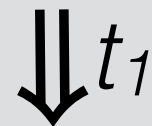
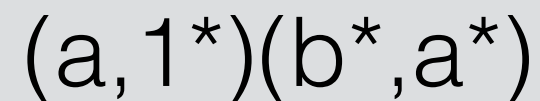
$(a,1^*)(b^*,a^*)$

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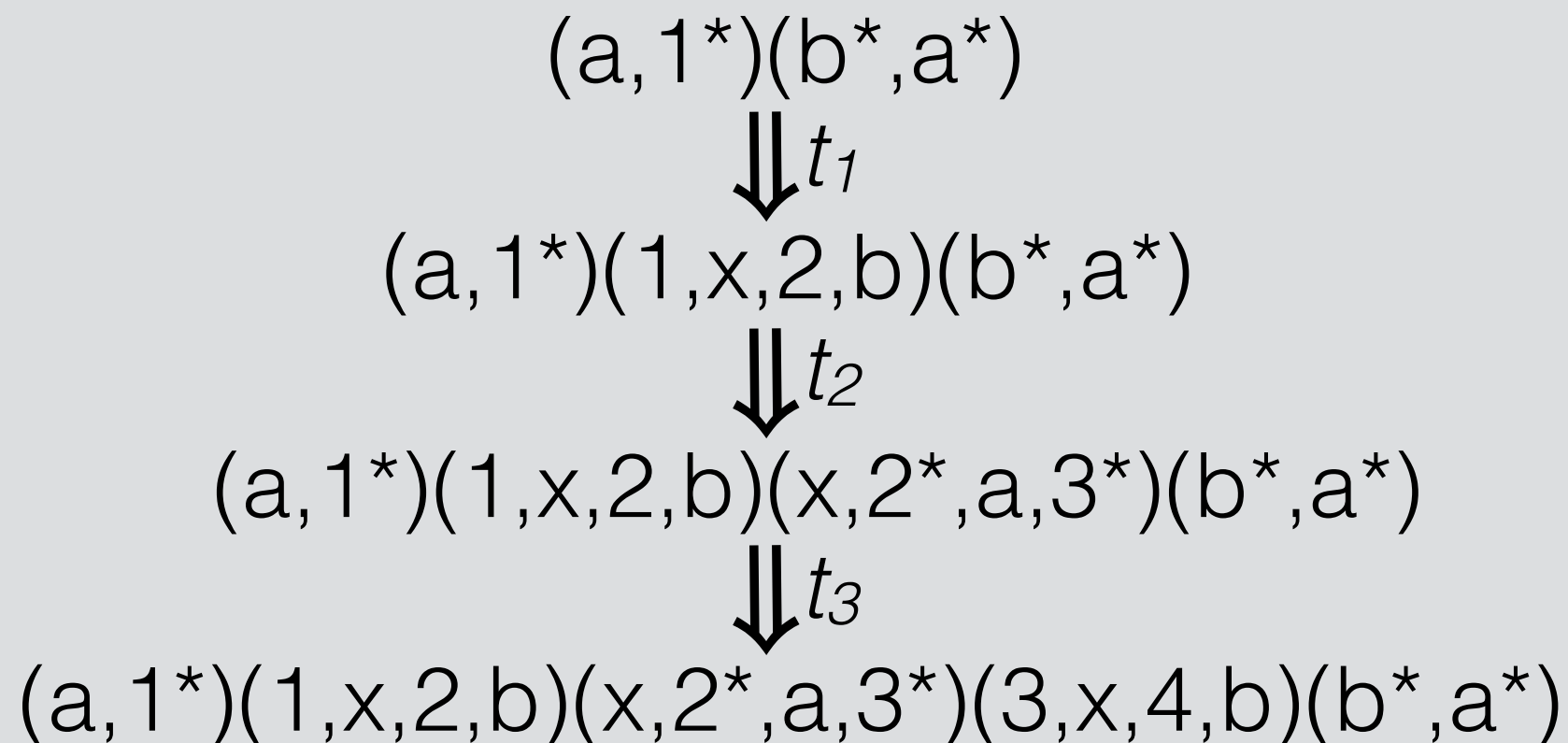
Terminal polymer of length 5

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Concentrations: 0.25 0.25 0.5

Initiator: $(a,1^*)(b^*,a^*)$



Terminal polymer of length 5

Expected time: $t_1 + t_2 + t_3$, with

$$E[t_1] = E[t_2] = 4, E[t_3] = 2.$$

$$4 + 4 + 2 = 12$$

Insertion system:

Monomer types: $(1^*, 2, 2, 1^*)^+$ $(x, 0^*, 2^*, x)^-$ $(x, 2^*, 0, x)^-$

Concentrations: 0.5 0.1 0.4

Initiator: $(0, 1)(1, 0^*)$

$(0, 1)(1, 0^*)$

Insertion system:

Monomer types: $(1^*, 2, 2, 1^*)^+$ $(x, 0^*, 2^*, x)^-$ $(x, 2^*, 0, x)^-$

Concentrations: 0.5 0.1 0.4

Initiator: $(0, 1)(1, 0^*)$

$(0, 1)(1, 0^*)$

$\Downarrow t_1$

$(0, 1)(1^*, 2, 2, 1^*)(1, 0^*)$

Insertion system:

Monomer types: $(1^*, 2, 2, 1^*)^+$ $(x, 0^*, 2^*, x)^-$ $(x, 2^*, 0, x)^-$

Concentrations: 0.5 0.1 0.4

Initiator: $(0, 1)(1, 0^*)$

$(0, 1)(1, 0^*)$

$\Downarrow t_1$

$(0, 1)(1^*, 2, 2, 1^*)(1, 0^*)$

$\Downarrow t_2$

$(0, 1)(x, 0^*, 2^*, x)(1^*, 2, 2, 1^*)(1, 0^*)$

Insertion system:

Monomer types: $(1^*, 2, 2, 1^*)^+$ $(x, 0^*, 2^*, x)^-$ $(x, 2^*, 0, x)^-$

Concentrations: 0.5 0.1 0.4

Initiator: $(0, 1)(1, 0^*)$

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$\Downarrow t_1$

$(0, 1)(1^*, 2, 2, 1^*)(1, 0^*)$

$\Downarrow t_2$

$(0, 1)(x, 0^*, 2^*, x)(1^*, 2, 2, 1^*)(1, 0^*)$

$\Downarrow t_3$

$(0, 1)(x, 0^*, 2^*, x)(1^*, 2, 2, 1^*)(x, 2^*, 0, x)(1, 0^*)$

Insertion system:

Monomer types: $(1^*, 2, 2, 1^*)^+$ $(x, 0^*, 2^*, x)^-$ $(x, 2^*, 0, x)^-$

Concentrations: 0.5 0.1 0.4

Initiator: $(0, 1)(1, 0^*)$

$(0, 1)(1, 0^*)$

$\Downarrow t_1$

$(0, 1)(1^*, 2, 2, 1^*)(1, 0^*)$

$\Downarrow t_2$

$(0, 1)(x, 0^*, 2^*, x)(1^*, 2, 2, 1^*)(1, 0^*)$

$\Downarrow t_3$

$(0, 1)(x, 0^*, 2^*, x)(1^*, 2, 2, 1^*)(x, 2^*, 0, x)(1, 0^*)$

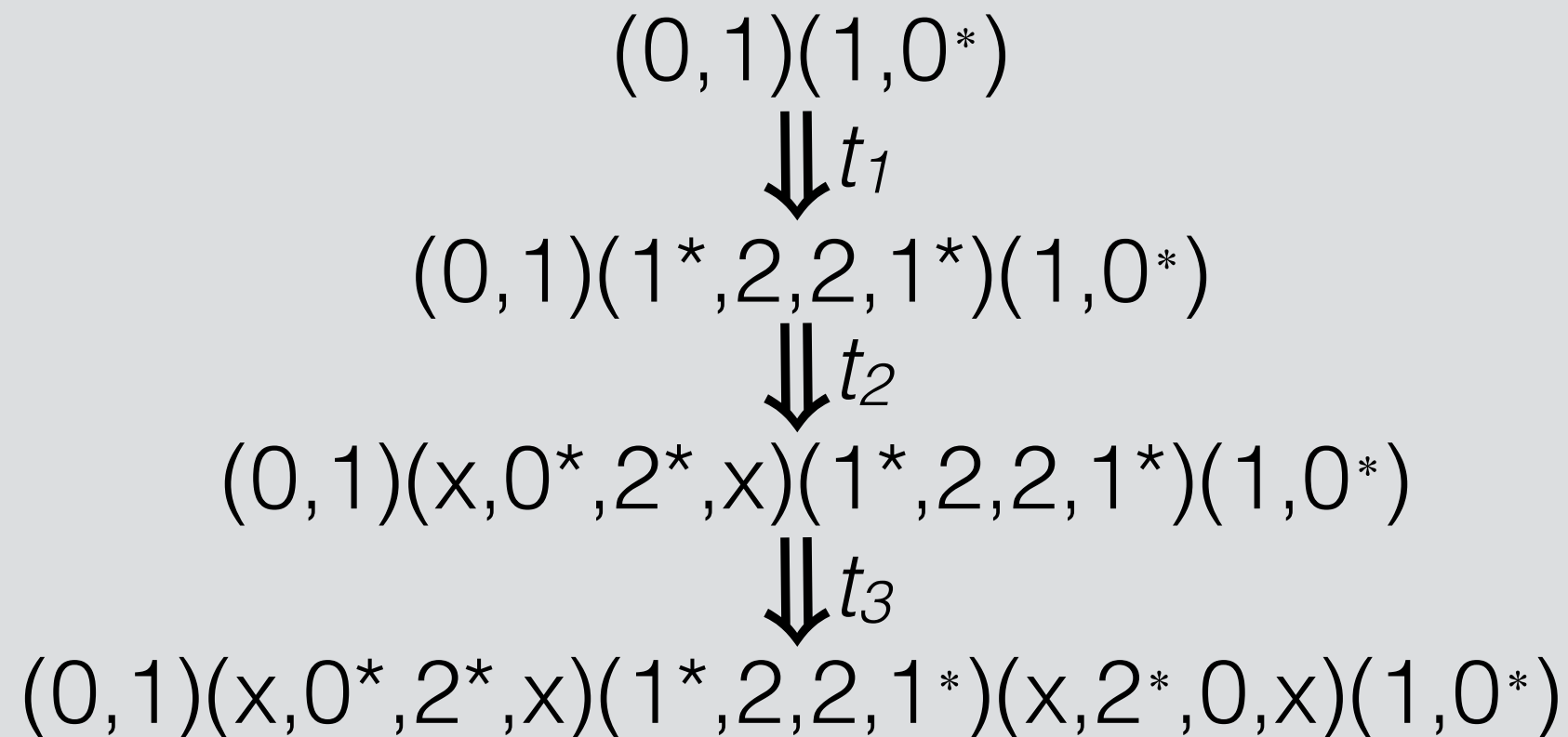
Terminal polymer of length 5

Insertion system:

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Concentrations: 0.5 0.1 0.4

Initiator: $(0, 1)(1, 0^*)$



Terminal polymer of length 5

Expected time: $t_1 + \max(t_2, t_3)$, with

$$E[t_1] = 2, E[t_2] = 10, E[t_3] = 2.5.$$

$$2 + 10.5 = 12.5$$

Insertion system:

Monomer types: $(1,x,2,b)^+$ $(x,2^*,a,1^*)^-$ $(x,2^*,a,x)^-$

Concentrations: 0.5 0.4 0.1

Initiator: $(a,1^*)(b^*,a^*)$

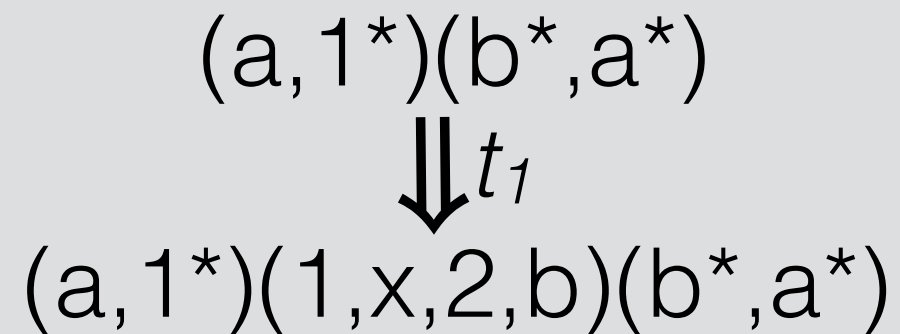
$(a,1^*)(b^*,a^*)$

Insertion system:

Monomer types: $(1,x,2,b)^+$ $(x,2^*,a,1^*)^-$ $(x,2^*,a,x)^-$

Concentrations: 0.5 0.4 0.1

Initiator: $(a,1^*)(b^*,a^*)$



Insertion system:

Monomer types: $(1,x,2,b)^+$ $(x,2^*,a,1^*)^-$ $(x,2^*,a,x)^-$

Concentrations: 0.5 0.4 0.1

Initiator: $(a,1^*)(b^*,a^*)$

$(a,1^*)(b^*,a^*)$

$\Downarrow t_1$

$(a,1^*)(1,x,2,b)(b^*,a^*)$

$\Downarrow t_2$

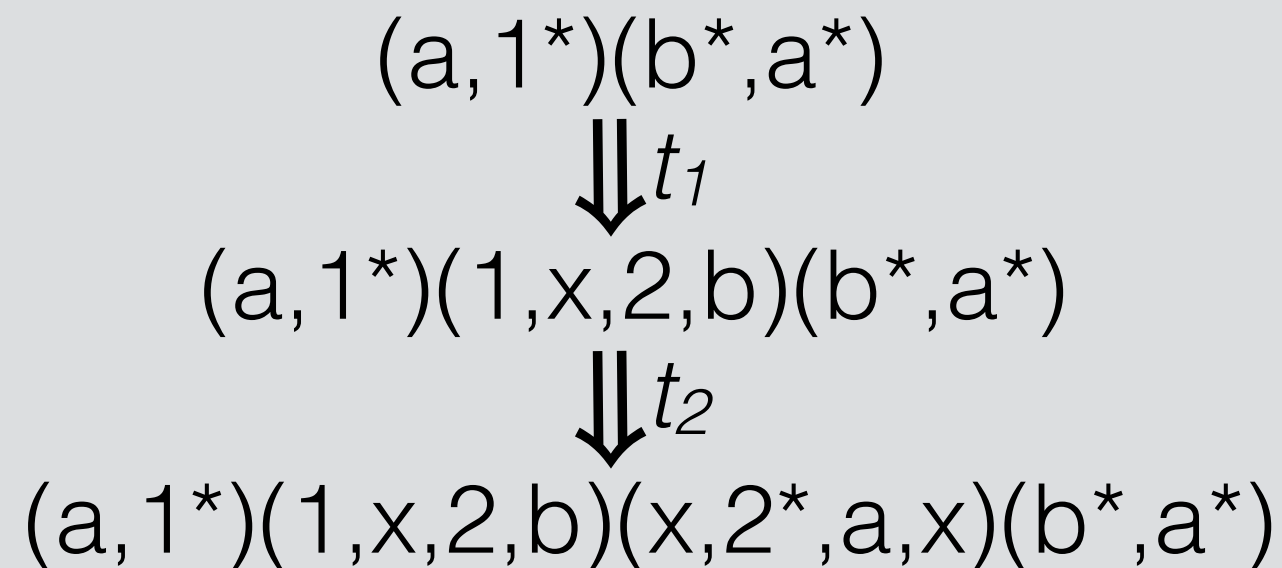
$(a,1^*)(1,x,2,b)(x,2^*,a,x)(b^*,a^*)$

Insertion system:

Monomer types: $(1,x,2,b)^+$ $(x,2^*,a,1^*)^-$ $(x,2^*,a,x)^-$

Concentrations: 0.5 0.4 0.1

Initiator: $(a,1^*)(b^*,a^*)$



Expected time: $t_1 + t_2$, with

$$E[t_1] = E[t_2] = 2.$$

$$2 + 2 = 4$$

Insertion system:

Monomer types: $(1,x,2,b)^+$ $(x,2^*,a,1^*)^-$ $(x,2^*,a,x)^-$

Concentrations: 0.5 0.4 0.1

Initiator: $(a,1^*)(b^*,a^*)$

$(a,1^*)(b^*,a^*)$

$\Downarrow t_1$

$(a,1^*)(1,x,2,b)(b^*,a^*)$

$\Downarrow t_2$

$(a,1^*)(1,x,2,b)(x,2^*,a,x)(b^*,a^*)$

Insertion system:

Monomer types: $(1,x,2,b)^+$ $(x,2^*,a,1^*)^-$ $(x,2^*,a,x)^-$

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Initiator: $(a,1^*)(b^*,a^*)$

$(a,1^*)(b^*,a^*)$

$\Downarrow t_1$

$(a,1^*)(1,x,2,b)(b^*,a^*)$

$\Downarrow t_2$

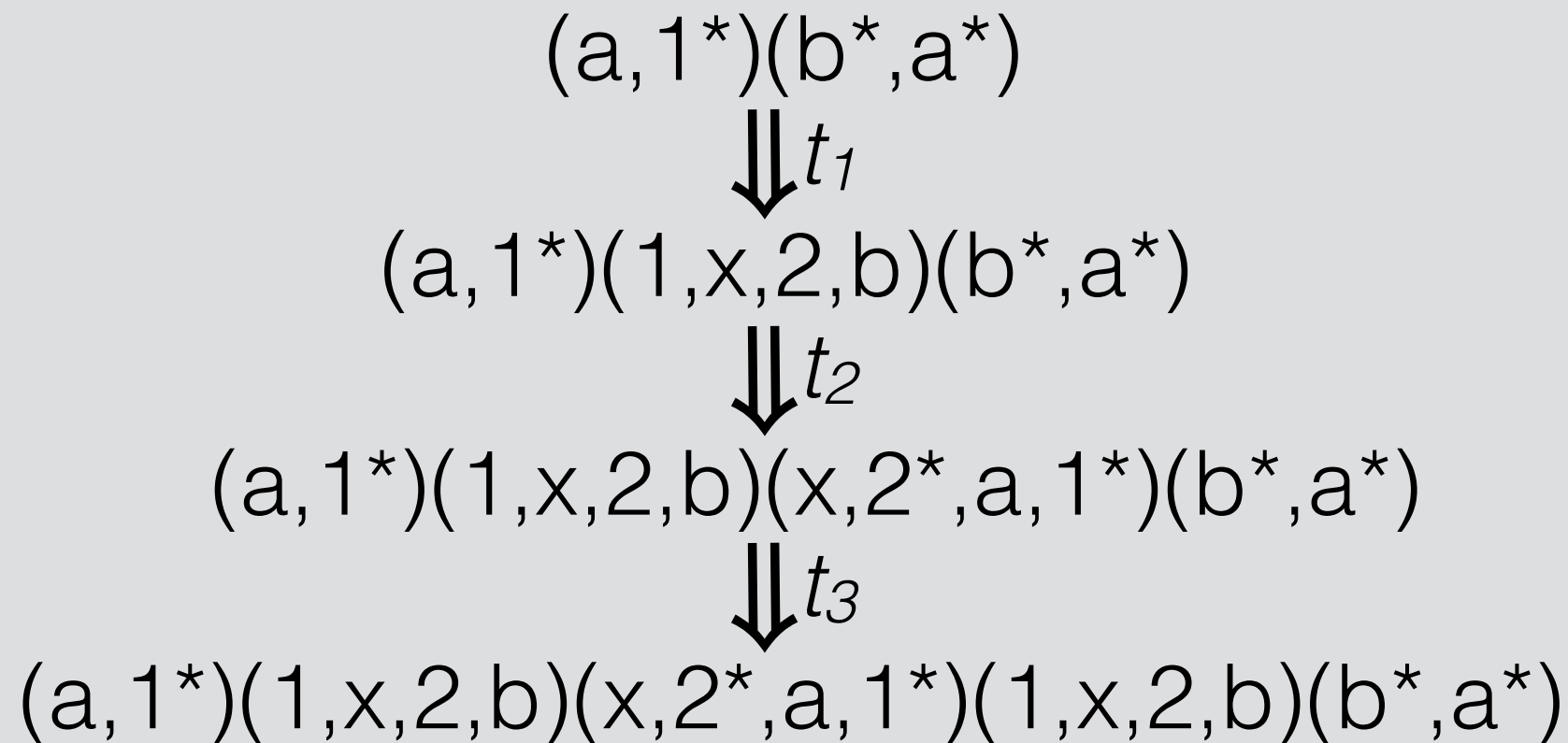
$(a,1^*)(1,x,2,b)(x,2^*,a,1^*)(b^*,a^*)$

Insertion system:

Monomer types: $(1,x,2,b)^+$ $(x,2^*,a,1^*)^-$ $(x,2^*,a,x)^-$

Concentrations: 0.5 0.4 0.1

Initiator: $(a,1^*)(b^*,a^*)$

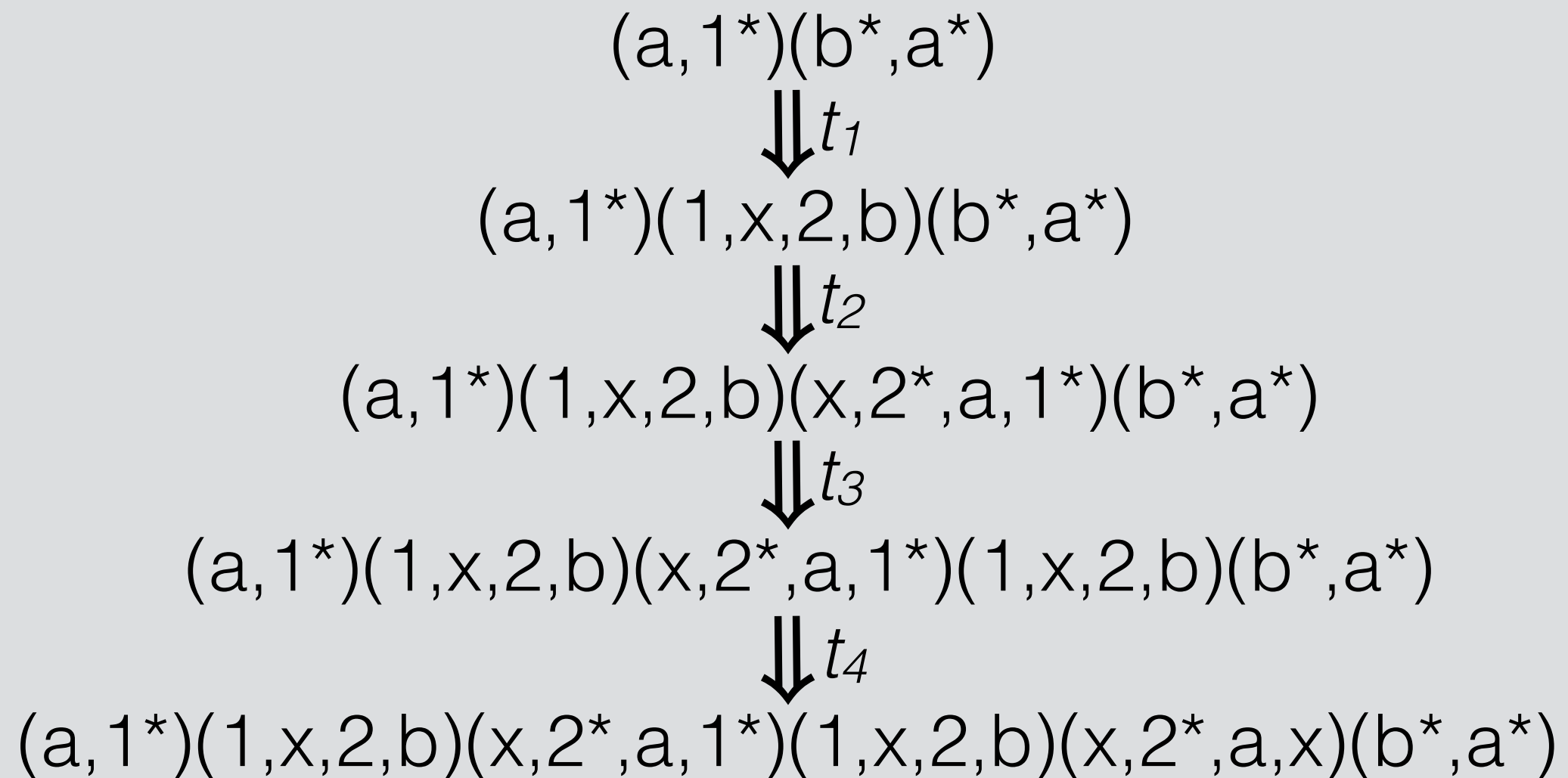


Insertion system:

Monomer types: $(1,x,2,b)^+$ $(x,2^*,a,1^*)^-$ $(x,2^*,a,x)^-$

Concentrations: 0.5 0.4 0.1

Initiator: $(a,1^*)(b^*,a^*)$

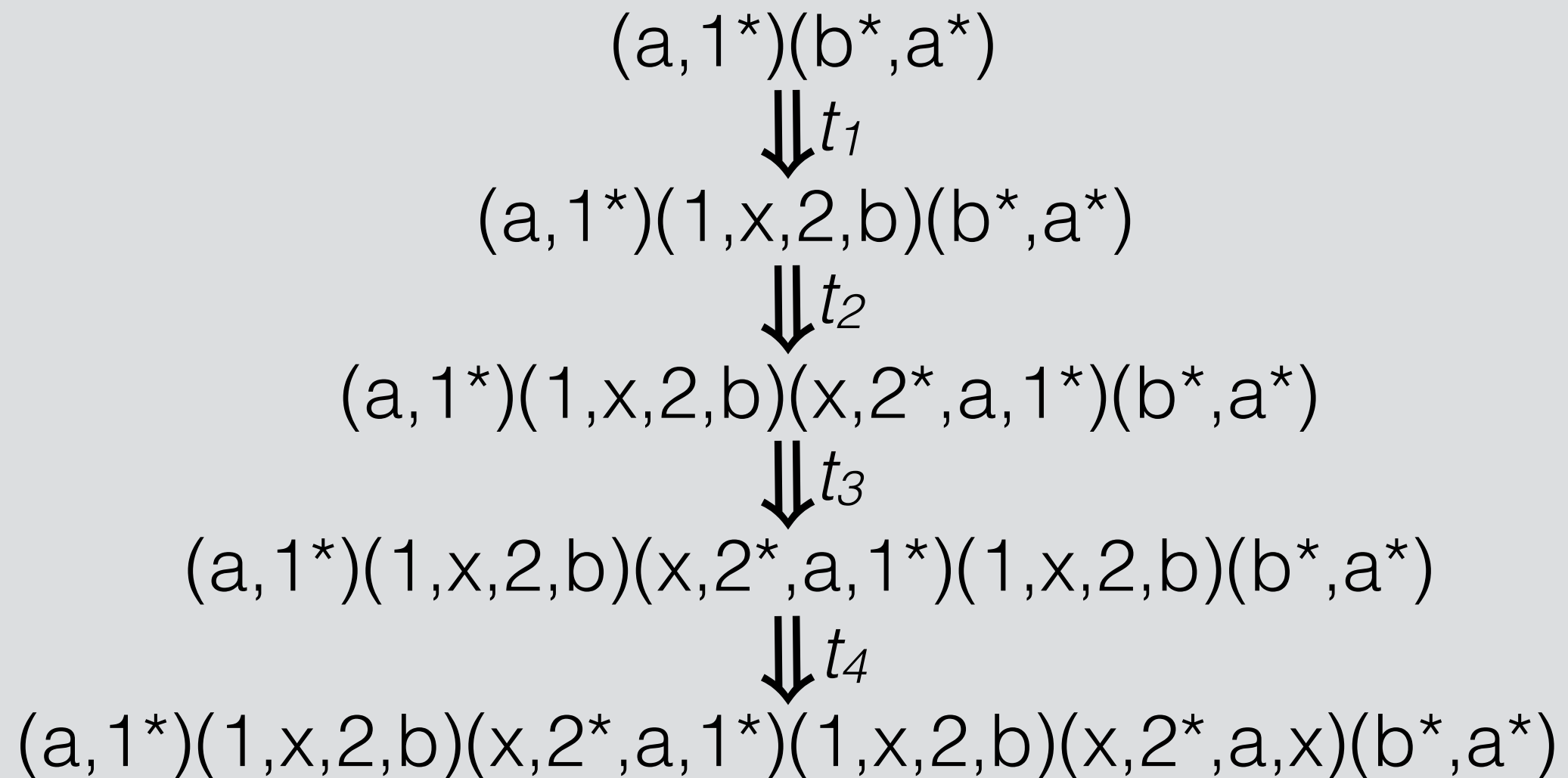


Insertion system:

Monomer types: $(1,x,2,b)^+$ $(x,2^*,a,1^*)^-$ $(x,2^*,a,x)^-$

Concentrations: 0.5 0.4 0.1

Initiator: $(a,1^*)(b^*,a^*)$



Expected time: $t_1 + t_2 + t_3 + t_4$, with

$$E[t_1] = E[t_2] = E[t_3] = E[t_4] = 2.$$

$$2 + 2 + 2 + 2 = 8$$

Expressive power

Expressive Power

- Insertion systems: initiator + set of monomers = set of polymers, with terminal polymer subset.
- Context-free grammars: start symbol + set of rules = set of partial derivations, with string subset.
- Do insertion systems and context-free grammars have equal “expressive-ness”?

Expressive Power

- Insertion systems: initiator + set of monomers = set of polymers, with terminal polymer subset.
- Context-free grammars: start symbol + set of rules = set of partial derivations, with string subset.
- Do insertion systems and context-free grammars have equal “expressive-ness”? *Yes.*

Expressive Power

Theorem: every insertion system can be expressed as a context-free grammar. [Dabby, Chen 2013]

Theorem: every context-free grammar can be expressed as an insertion system. [This work]

Expressive Power

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Insertion system:

Monomer types: $(1,x,2,b)^+$ $(x,2^*,a,3)^-$ $(3,x,4,b)^+$

Concentrations: 0.25 0.25 0.25

Initiator: $(a,1)(b^*,a^*)$

Context-free grammar:

Production rules:

$S_{(a,1)(b^*,a^*)} \rightarrow S_{(a,1)(1,x)} S_{(2,b)(b^*,a^*)}$

$S_{(2,b)(b^*,a^*)} \rightarrow S_{(2,b)(x,2^*)} S_{(a,3)(b^*,a^*)}$

$S_{(a,3)(b^*,a^*)} \rightarrow S_{(a,3)(3,x)} S_{(4,b)(b^*,a^*)}$

$S_{(a,1)(1,x)} \rightarrow (a, 1)(1, x)$

$S_{(2,b)(x,2^*)} \rightarrow (2,b)(x,2^*)$

$S_{(a,3)(3,x)} \rightarrow (a,3)(3,x)$

$S_{(4,b)(x,4^*)} \rightarrow (4,b)(x,4^*)$

Start symbol: $S_{(a,1)(b^*,a^*)}$

Expressive Power

Theorem: every insertion system can be expressed as a context-free grammar. [Dabby, Chen 2013]

Theorem: every context-free grammar can be expressed as an insertion system. [This work]

Expressive Power

Theorem: every insertion system can be expressed as a context-free grammar. [Dabby, Chen 2013]

Theorem: every context-free grammar can be expressed as an insertion system. [This work]

Rule: $A \rightarrow BC$

Derivation step: $eADe \Rightarrow eBCDe$

Monomer type: $(1, x, 2, b)^+$

Insertion: $(a, 1)(b^*, a^*) \Rightarrow (a, 1)(1, x, 2, b)(b^*, a^*)$

Rules completely replace non-terminals.

Insertions do not completely replace insertion sites.

Polymer length

Insertion system:

Monomer types: $(1,x,2,b)^+$ $(x,2^*,a,1^*)^-$ $(x,2^*,a,x)^-$

Concentrations: 0.5 0.4 0.1

Initiator: $(a,1^*)(b^*,a^*)$

$(a,1^*)(1,x,2,b)(x,2^*,a,x)(b^*,a^*)$

$(a,1^*)(1,x,2,b)(x,2^*,a,1^*)(1,x,2,b)(x,2^*,a,x)(b^*,a^*)$

$(a,1^*)(1,x,2,b)(x,2^*,a,1^*)(1,x,2,b)(x,2^*,a,1^*)(1,x,2,b)(x,2^*,a,x)(b^*,a^*)$

• • •

Context-free grammar:

Production rules: $S \rightarrow A$ $A \rightarrow aaA$ $A \rightarrow aa$

Start symbol: S

aa

aaaa

aaaaaa

• • •

Insertion system:

Monomer types: $(1,x,2,b)^+$ $(x,2^*,a,1^*)^-$ $(x,2^*,a,x)^-$

Concentrations: 0.5 0.4 0.1

Initiator: $(a,1^*)(b^*,a^*)$

$(a,1^*)(1,x,2,b)(x,2^*,a,x)(b^*,a^*)$

$(a,1^*)(1,x,2,b)(x,2^*,a,1^*)(1,x,2,b)(x,2^*,a,x)(b^*,a^*)$

Constructing arbitrarily long polymers is easy
if infinite polymers allowed.

Context-free grammar:

Production rules: $S \rightarrow A$ $A \rightarrow aaA$ $A \rightarrow aa$

Start symbol: S

aa

$aaaa$

$aaaaaa$

\dots

Constructing long polymers

Theorem: a system with k monomer types constructing a finite number of polymers can construct:

- polymers of length $2^{\Theta(k^{1/2})}$ [Dabby, Chen 2013]
- polymers of length $2^{\Theta(k^{3/2})}$ [This work]
- only polymers of length $2^{O(k^{3/2})}$ [This work]

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Constructing long polymers

- Consider *insertion sequences*: repeated insertions into the site resulting from previous insertion.

$\dots u, 0)(0, u^* \dots$

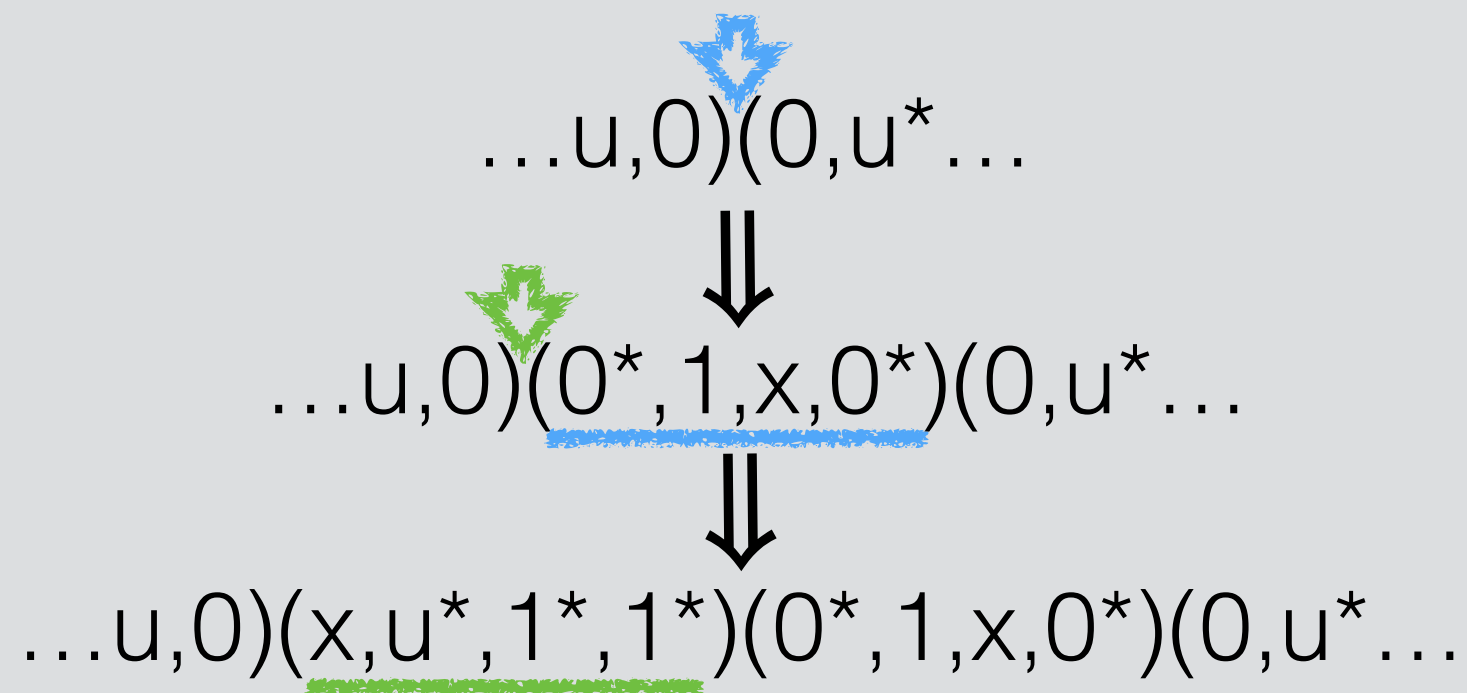
Constructing long polymers

- Consider *insertion sequences*: repeated insertions into the site resulting from previous insertion.

$$\begin{array}{c} \text{...}u,0)(0,u^* \text{...} \\ \Downarrow \\ \text{...}u,0)(\text{0}^*,1,x,\text{0}^*)(0,u^* \text{...} \end{array}$$

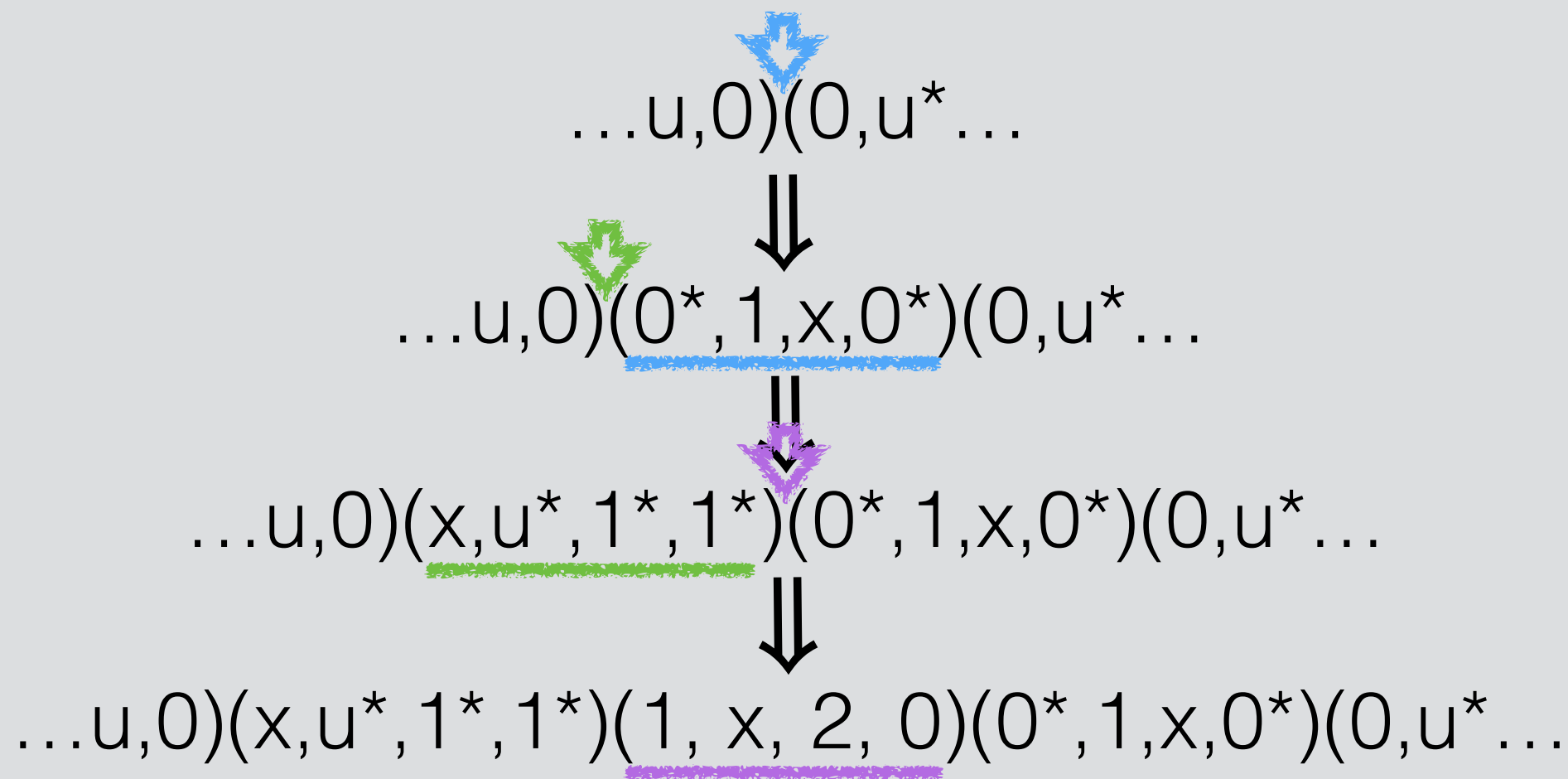
Constructing long polymers

- Consider *insertion sequences*: repeated insertions into the site resulting from previous insertion.



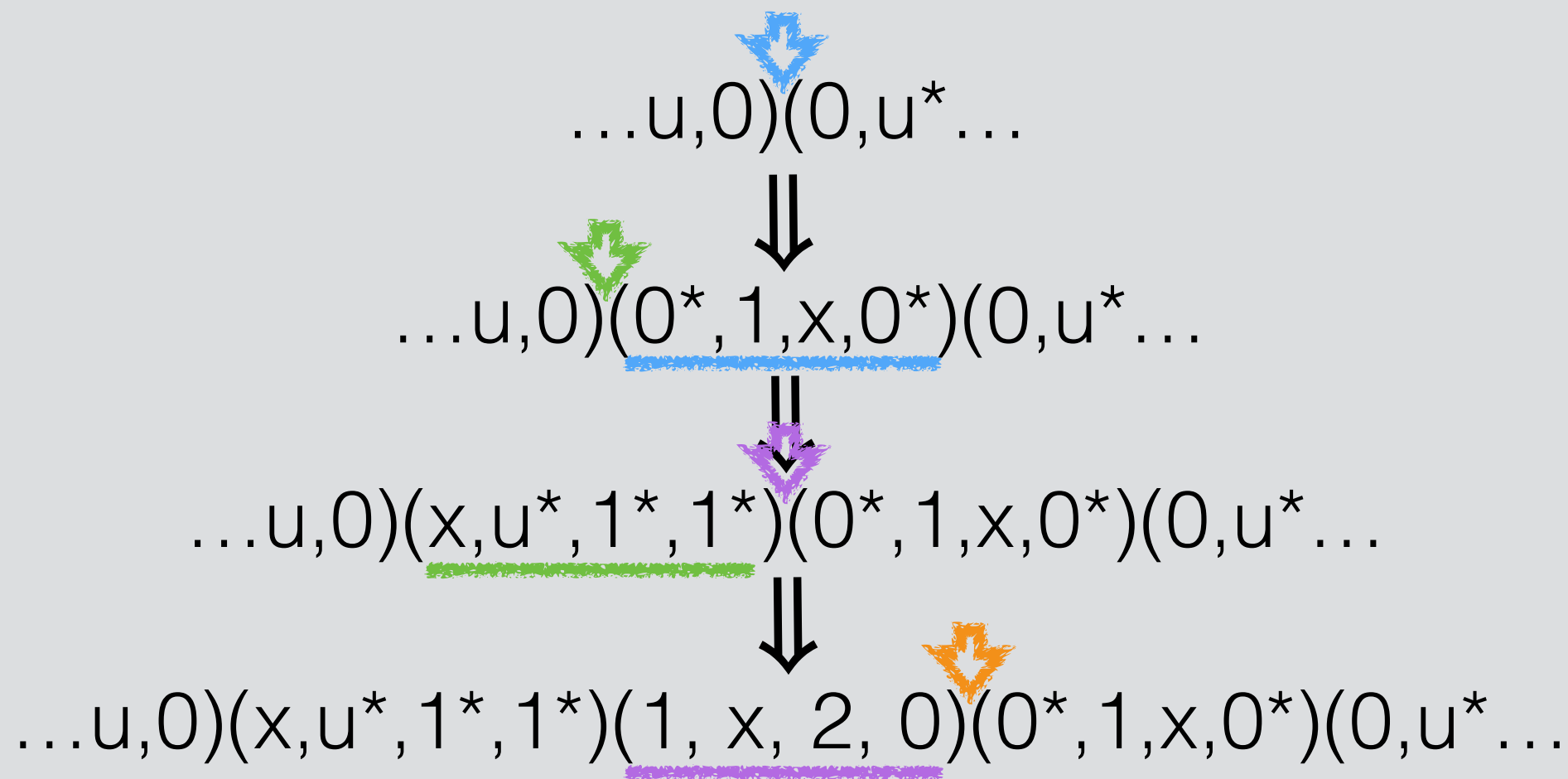
Constructing long polymers

- Consider *insertion sequences*: repeated insertions into the site resulting from previous insertion.



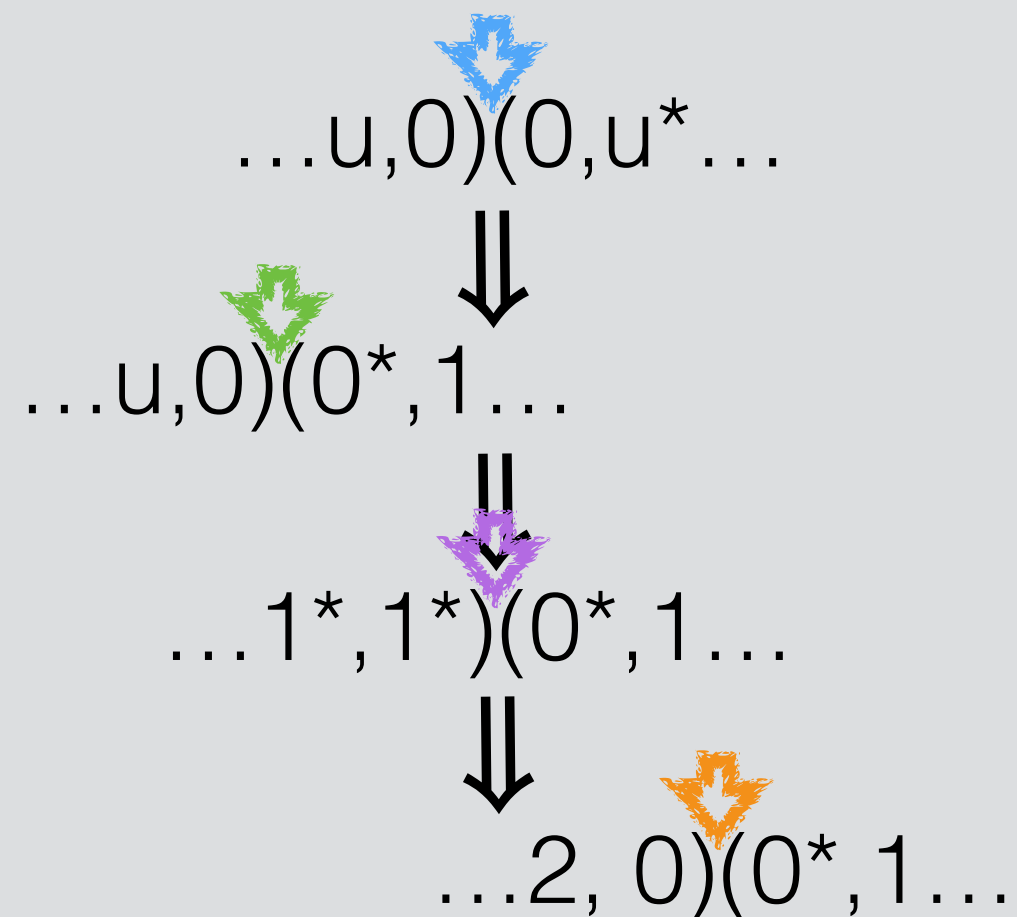
Constructing long polymers

- Consider *insertion sequences*: repeated insertions into the site resulting from previous insertion.



Constructing long polymers

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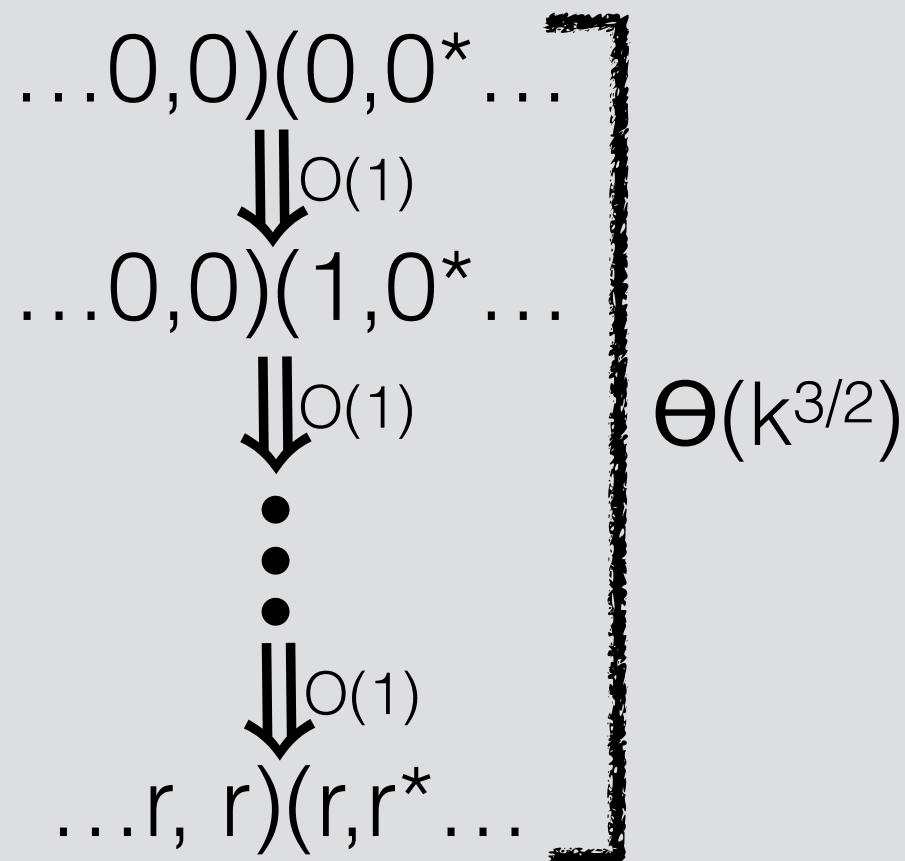
Constructing long polymers

- Consider *insertion sequences*: repeated insertions into the site resulting from previous insertion.

$$\begin{array}{c} \dots u, 0)(0, u^* \dots \\ \Downarrow \\ \dots u, 0)(0^*, 1 \dots \\ \Downarrow \\ \dots 1^*, 1^*)(0^*, 1 \dots \\ \Downarrow \\ \dots 2, 0)(0^*, 1 \dots \end{array}$$

Constructing long polymers

- Consider *insertion sequences*: repeated insertions into the site resulting from previous insertion.
- Ingredient 1: long insertion sequence with no repeated insertion sites.



Constructing long polymers

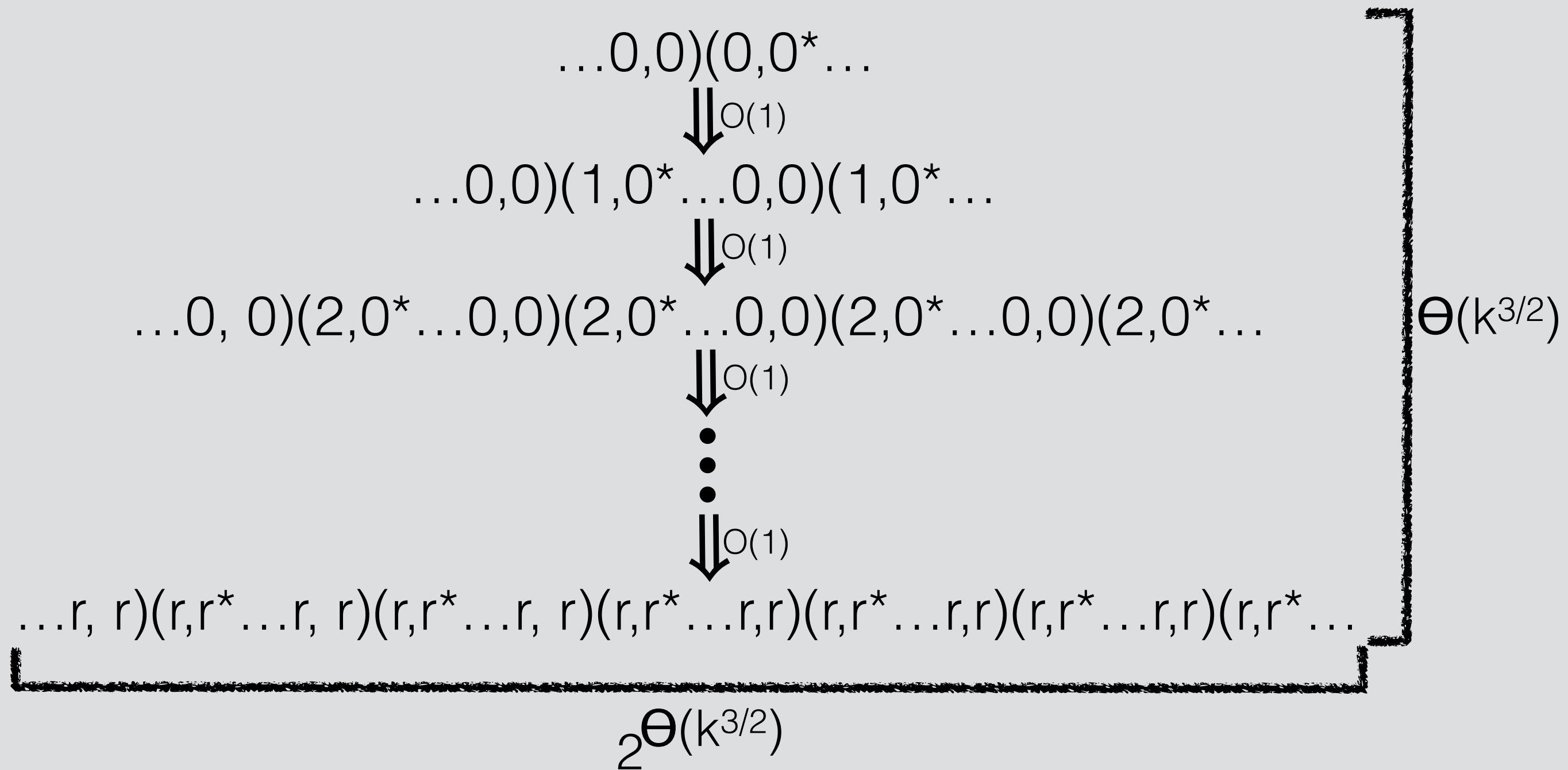
- Consider *insertion sequences*: repeated insertions into the site resulting from previous insertion.
- Ingredient 1: long insertion sequence with no repeated insertion sites.
- Ingredient 2: duplication of each site in sequence.

$$\begin{array}{c}
 \dots 0,0)(0,0^* \dots \\
 \Downarrow^{O(1)} \\
 \dots 0,0)(1,0^* \dots 0,0)(1,0^* \dots \\
 \Downarrow^{O(1)} \\
 \dots 0,0)(2,0^* \dots 0,0)(2,0^* \dots 0,0)(2,0^* \dots
 \end{array}$$

Constructing long polymers

- Consider *insertion sequences*: repeated insertions into the site resulting from previous insertion.
- Ingredient 1: long insertion sequence with no repeated insertion sites.
- Ingredient 2: duplication of each site in sequence.
- Combine these for long polymers.

Constructing long polymers



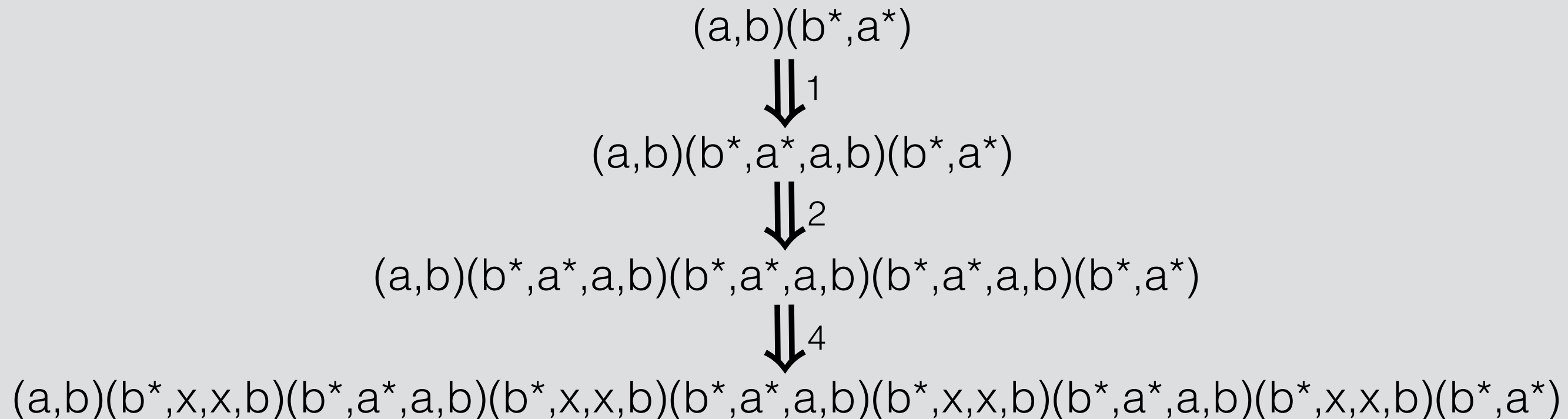
Polymer growth speed

Insertion system:

Monomer types: $(b^*, a^*, a, b)^+$ $(b^*, x, x, b)^+$

Concentrations: 0.5 0.5

Initiator: $(a, b)(b^*, a^*)$



Each round of insertions takes $O(1)$ expected time.

Construction of length $n = 2^i - 1$ takes $O(i)$ expected time.
 $O(\log(n))$

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Monomer types: $(b^*, a^*, a, b)^+$ $(b^*, x, x, b)^+$

Concentrations: 0.5 0.5

Initiator: $(a, b)(b^*, a^*)$

$(a, b)(b^*, a^*)$
 \Downarrow_1
 $(a, b)(b^*, a^*, a, b)(b^*, a^*)$
 \Downarrow_2
 $(a, b)(b^*, a^*, a, b)(b^*, a^*, a, b)(b^*, a^*)$
 \Downarrow_4
 $(a, b)(b^*, x, x, b)(b^*, a^*, a, b)(b^*, x, x, b)(b^*, a^*, a, b)(b^*, x, x, b)(b^*, a^*, a, b)(b^*, x, x, b)(b^*, a^*)$

Constructing polymers in $O(\log(n))$
expected time is easy
if infinite polymers allowed.

Each round of insertions takes $O(1)$ expected time.
Construction of length $n = 2^i - 1$ takes $O(i)$ expected time.
 $O(\log(n))$

Constructing polymers quickly

Theorem: a system constructing a finite number of polymers can **deterministically** construct a polymer of length n in:

- $O(\log^3(n))$ expected time [Dabby, Chen 2013]
- $O(\log^{5/3}(n))$ expected time [This work]
- only $\Omega(\log^{5/3}(n))$ expected time [This work]

Summary

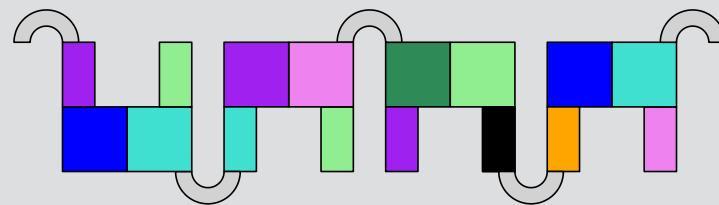
Theorem: insertion systems and context-free grammars are expressively equivalent.

Theorem: a system with k monomer types constructing a finite number of polymers can construct polymers of length $2^{\Theta(k^{3/2})}$ and this is the best possible.

Theorem: a system constructing a finite number of polymers can **deterministically** construct a polymer of length n in $\Theta(\log^{5/3}(n))$ expected time and this is the best possible.

Thank you.

Tight bounds for active self-assembly
using an insertion primitive



Caleb Malchik and Andrew Winslow

