Toehold DNA Languages are Regular

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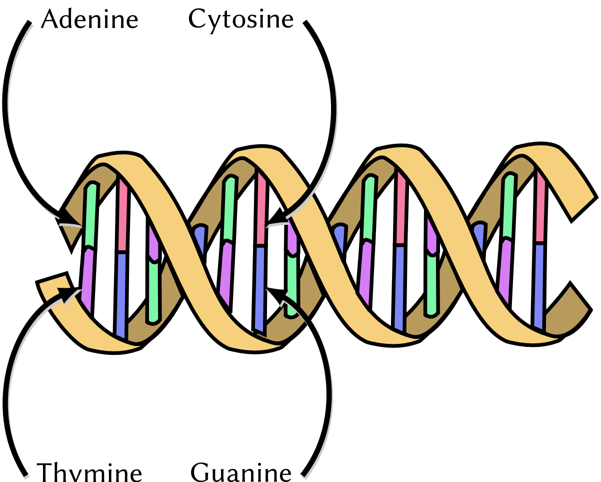
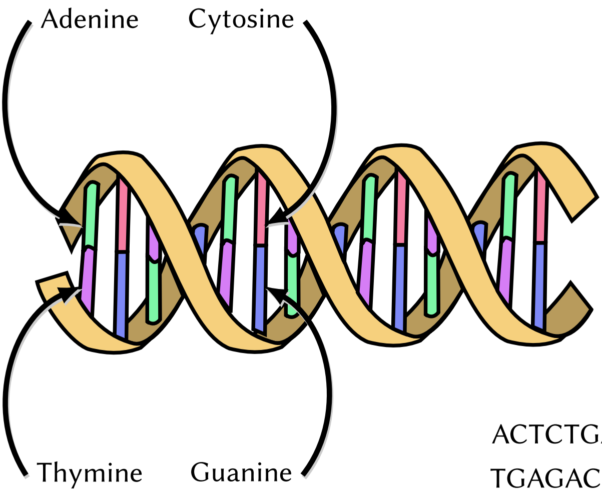
ETH Zurich – Distributed Computing Group – www.disco.ethz.ch

DNA



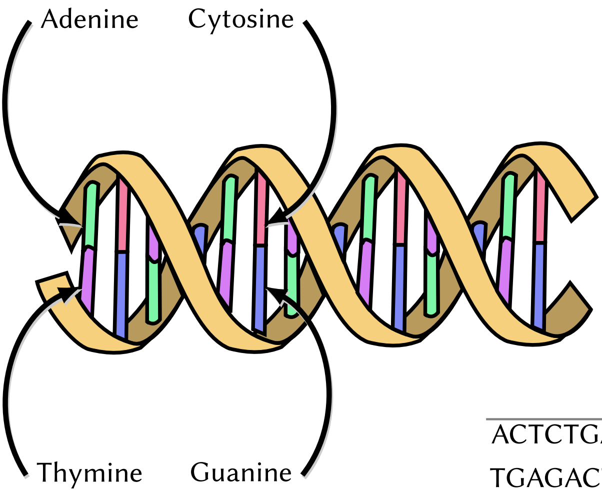
DNA



ACTCTGAGACTCTG

TGAGACTCTGAGAC

DNA



ACTCTGAGACTCTG
TGAGACTCTGAGAC

Domains & Complements

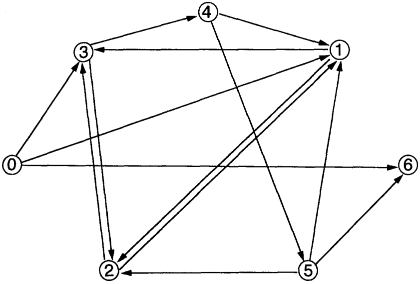
$$\overrightarrow{\mathbf{a}} \equiv \overrightarrow{\mathrm{ATCG}} \qquad \overrightarrow{\bar{\mathbf{a}}} \equiv \overrightarrow{\overline{\mathrm{ATCG}}}$$

$$\overrightarrow{\mathbf{b}} \equiv \overrightarrow{\mathrm{ATT}} \qquad \overrightarrow{\bar{\mathbf{b}}} \equiv \overrightarrow{\overline{\mathrm{ATT}}}$$

$$\overrightarrow{\mathbf{c}} \equiv \overrightarrow{\mathrm{CTC}} \qquad \overrightarrow{\bar{\mathbf{c}}} \equiv \overrightarrow{\overline{\mathrm{CTC}}}$$

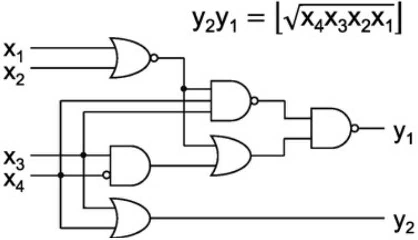
$$\begin{matrix} \overrightarrow{\mathbf{abc}} \\ \underleftarrow{\bar{\mathbf{a}}\bar{\mathbf{b}}\bar{\mathbf{c}}} \end{matrix} \equiv \begin{matrix} \overrightarrow{\mathrm{ATCGATTCTC}} \\ \underleftarrow{\mathrm{TAGCTAAGAG}} \end{matrix}$$

Hamiltonian Path



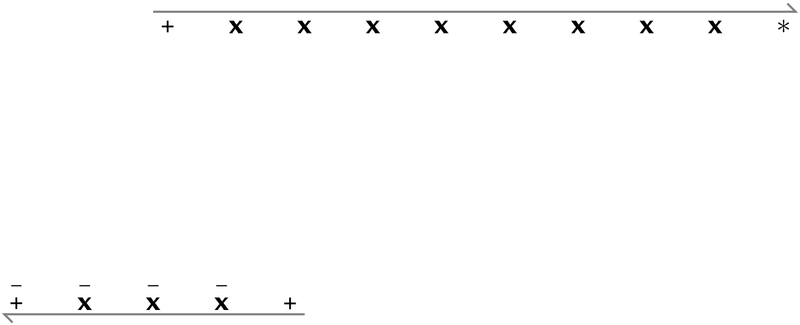
Adleman 1994

Square Root



Qian, Winfree 2011

Strand Binding



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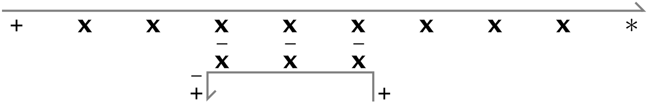
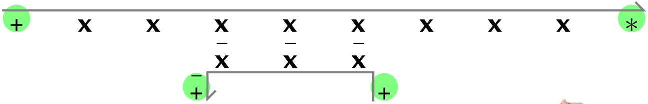
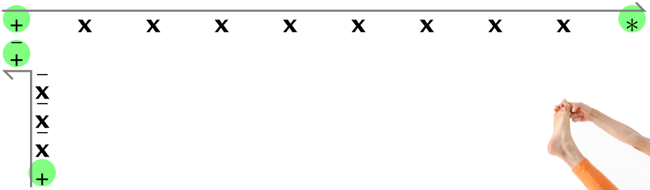


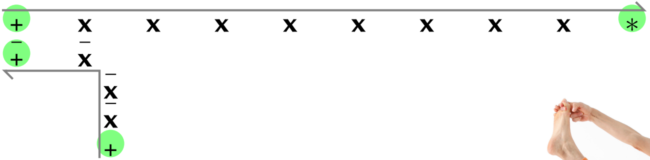
Strand Binding, Toeholds



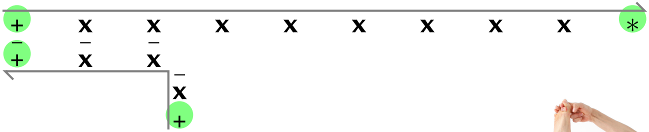
Strand Binding, Toeholds



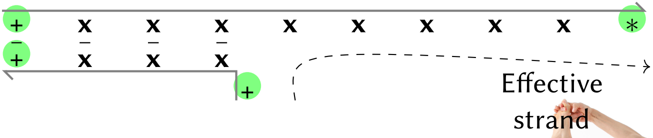
Strand Binding, Toeholds



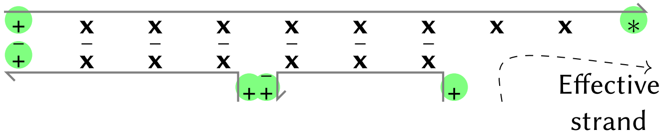
Strand Binding, Toeholds



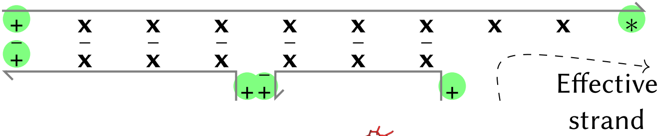
Strand Binding, Toeholds, Effective Strands

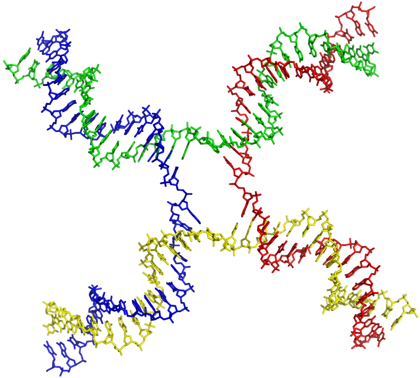


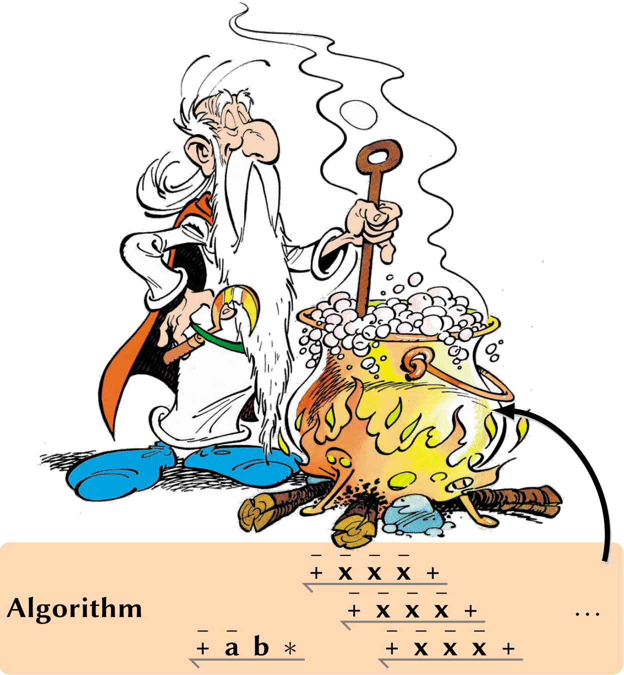
Strand Binding, Toeholds, Effective Strands



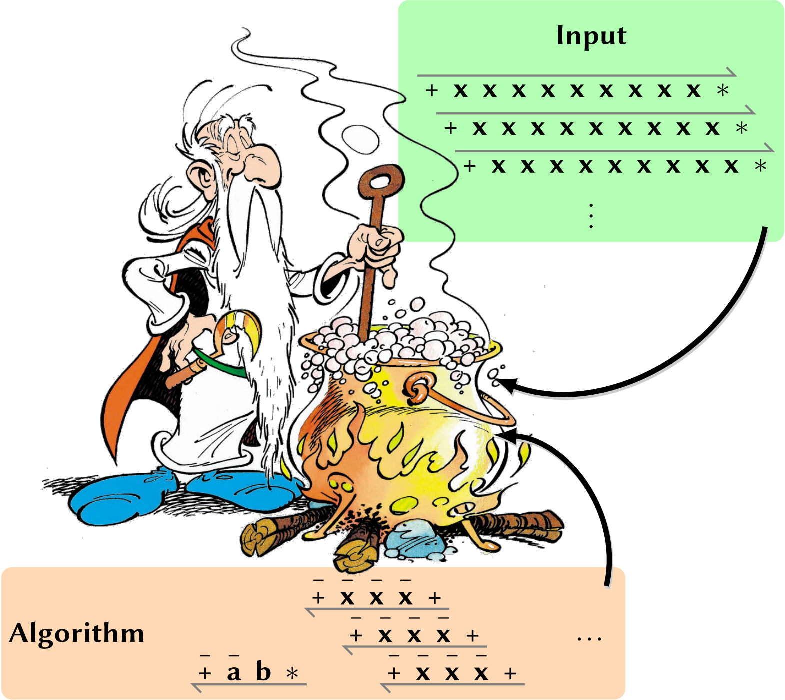
Strand Binding, Toeholds, Effective Strands

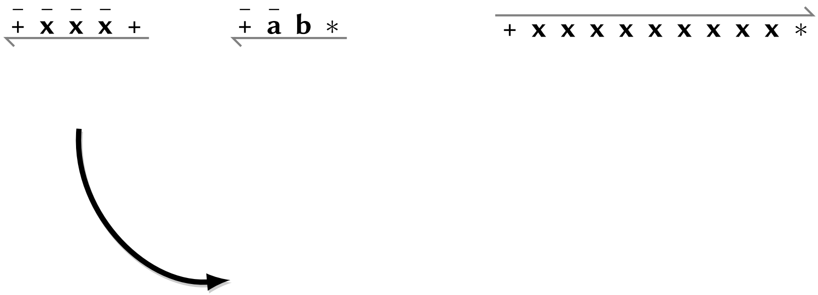




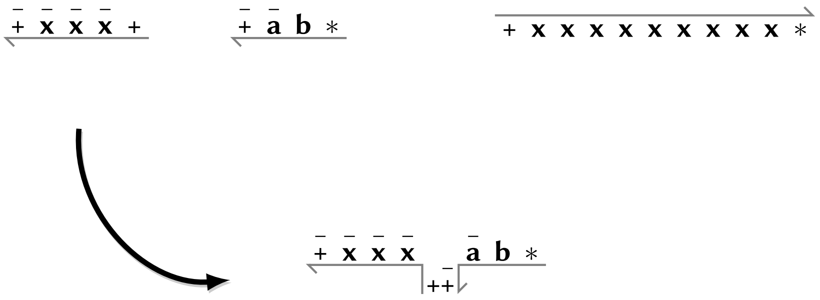


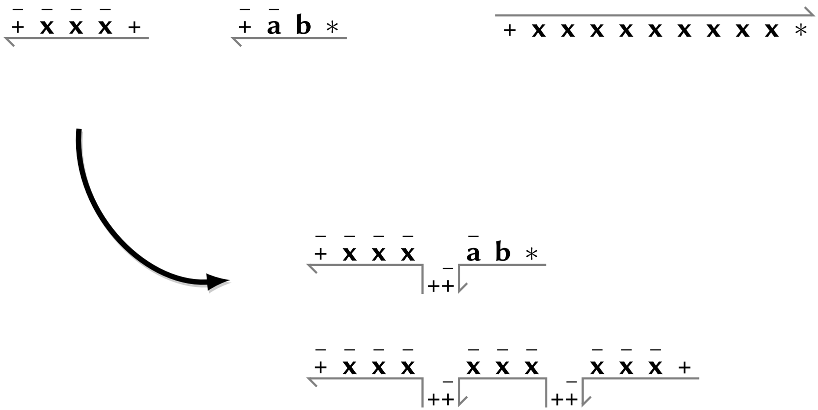
Algorithm
+ x x x +
+ x x x +
+ x x x +
+ a b ∗
...


Input
+ x x x x x x x x x *
+ x x x x x x x x x *
+ x x x x x x x x x *
⋮
Algorithm
+ x x x +
+ x x x +
+ a b *
+ x x x +
...

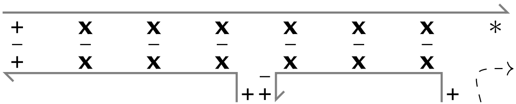


+ x x x +
+ a b *
+ x x x x x x x x x *


+ x x x +
+ a b *
+ x x x x x x x x x *
+ x x x
++
a b *

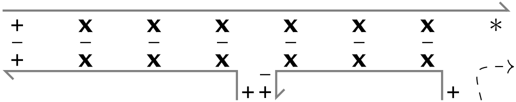


+ x x x +
+ a b *
+ x x x x x x x x x *
+ x x x
++
a b *
+ x x x
++
x x x
++
x x x +

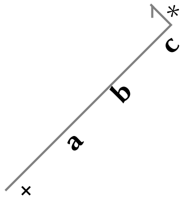


+ x x x x x x *
+ x x x x x x
+ + +


Yes!



Substitution: +abc$*$ $\rightarrow$ +z$*$



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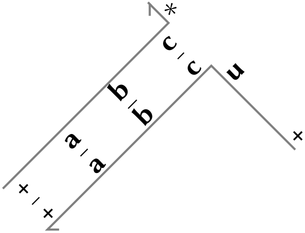

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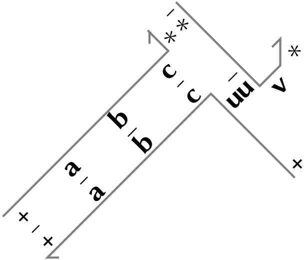

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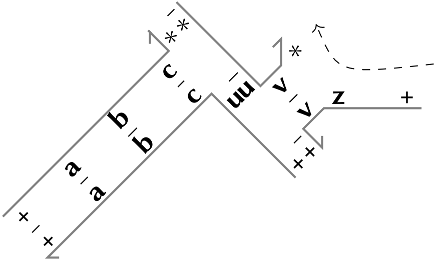
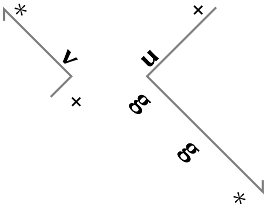


Aggregation: $+\mathbf{abc}* \wedge +\mathbf{def}* \rightarrow +\mathbf{gg}*$

1. $+\mathbf{abc}* \rightarrow +\mathbf{ugg}*$
2. $+\mathbf{def}* \rightarrow +\mathbf{v}*$
3. $\overline{*\mathbf{vu}+}$



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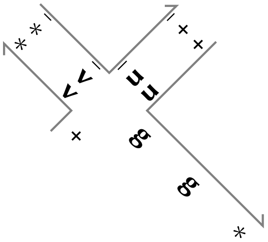

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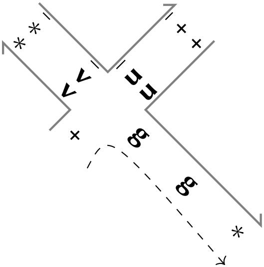

Primality

For $2 \leq j \leq \sqrt{n}$ and $k \leq j - 1$:

1. $\overrightarrow{+\mathbf{b}^j\mathbf{x}\bar{\mathbf{x}}\bar{+}}$
2. $\overrightarrow{+\mathbf{b}^j\bar{\mathbf{x}}^j\bar{\mathbf{b}}^j\bar{+}}$
3. $\overrightarrow{+\mathbf{b}^j\mathbf{x}^k*} \rightarrow \overrightarrow{+\mathbf{b}^j\mathbf{f}*}$
4. $\overrightarrow{+\mathbf{b}^2\mathbf{f}*} \wedge \overrightarrow{+\mathbf{b}^3\mathbf{f}*} \wedge \cdots \wedge \overrightarrow{+\mathbf{b}^{\sqrt{n}}\mathbf{f}*} \rightarrow \overrightarrow{+*}$

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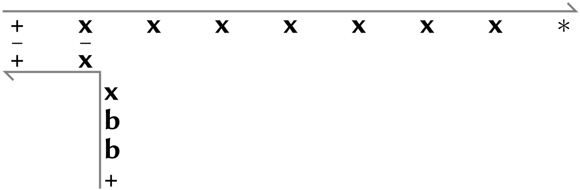

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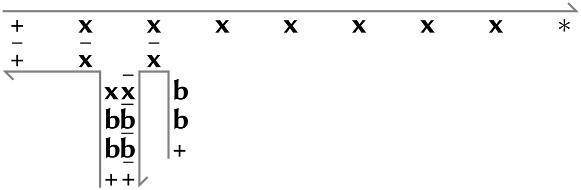

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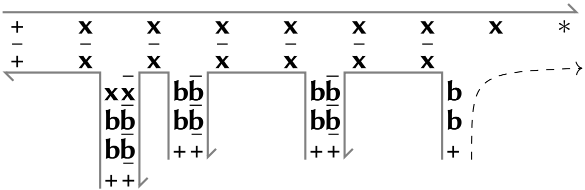

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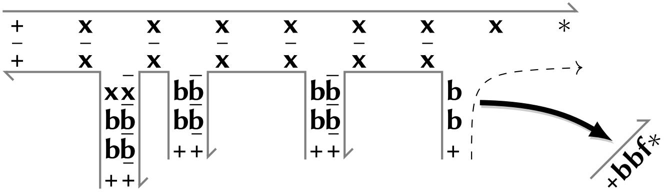

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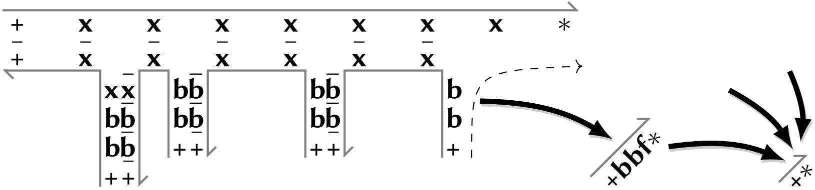

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- $O(n)$ strands
- Binary Encoding: $O(\sqrt{n} \cdot \log n)$ strands
- Good: $O(\sqrt{n} \cdot \log n) \subsetneq O(\frac{n}{\log n})$

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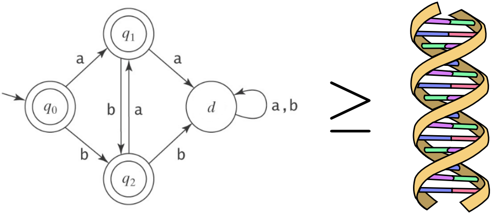
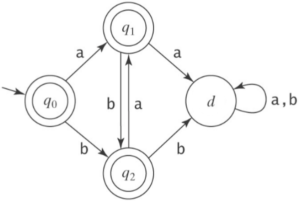
Constant Size Algorithms?

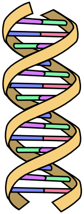


Theorem

Let $\mathcal{A}$ be a DNA algorithm.
If $\mathcal{A}$, interpreted as a set of strands, has finite size,
then $\mathcal{A}$ decides a regular language.



$\geq$



Theorem

Let $\mathcal{A}$ be a DNA algorithm.
If $\mathcal{A}$, interpreted as a set of strands, is a regular language,
then $\mathcal{A}$ decides a regular language.

Basic idea: Define language $\mathcal{I}$ such that

1. $\mathcal{I}$ is regular,
2. every $\iota \in \mathcal{I}$ is accepted by $\mathcal{A}$, and
3. every ι accepted by $\mathcal{A}$ is in $\mathcal{I}$.

The Language $\mathcal{I}$ ...

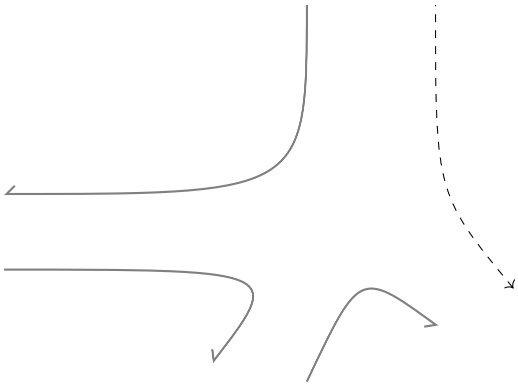
$$\mathcal{I} := \bigcup_{w:\delta(w,*)\in F} \mathcal{X}(\delta(s,+), w, Q \times Q \setminus \{(\delta(s,+), w)\}),$$

$$\mathcal{X}(v,w,J) := \bigcup_{q\in I(v,w,J)} \left(\bigcap_{\substack{(q_i,q_{i+1}):\\ q_i\neq NULL\neq q_{i+1}}} C(q_i, q_{i+1}, J) \ \cap \bigcap_{i:q_i=NULL} D(q_{i-1}, q_{i+1}, J) \right)$$

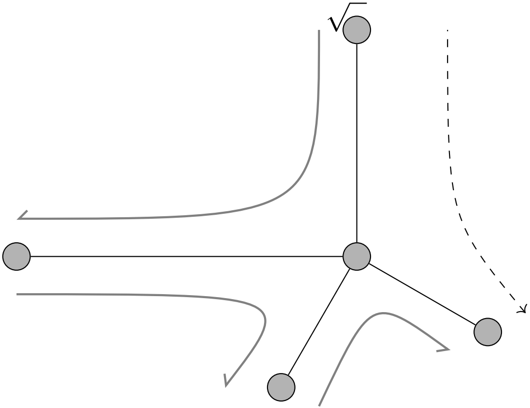
$$C(x,y,J) := \begin{cases} +\Sigma^* *, & \text{if } \exists (z_1,z_2) \in H_{x,y,J} \text{ s.t. } z_2 = s \text{ and } z_1 \in F \\ \bigcup_{(z_1,z_2)\in H_{x,y,J}} \mathcal{X}(z_1, z_2, J \setminus \{(x,y),(z_1,z_2)\}), & \text{otherwise.} \end{cases}$$

$$D(x,y,J) := \bigcup_{K\subseteq J\setminus\{(x,y)\}} \left(\overline{\mathcal{L}(B_{K,x,y})} \cap \bigcap_{(z_1,z_2)\in K} \mathcal{X}(z_1, z_2, J \setminus \{(x,y),(z_1,z_2)\}) \right)$$

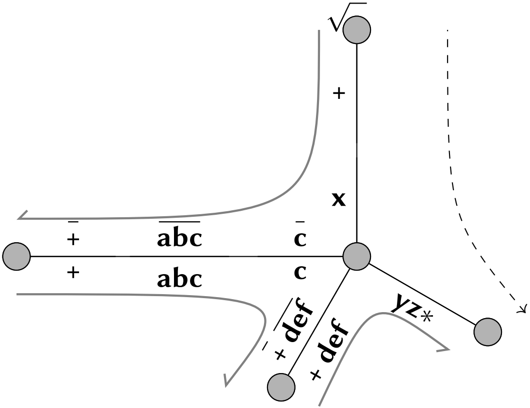
Assemblies



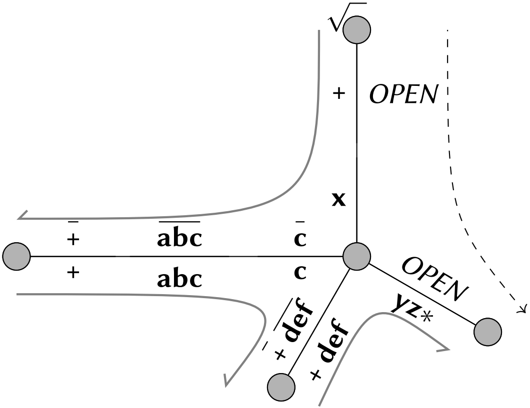
Assemblies



Assemblies

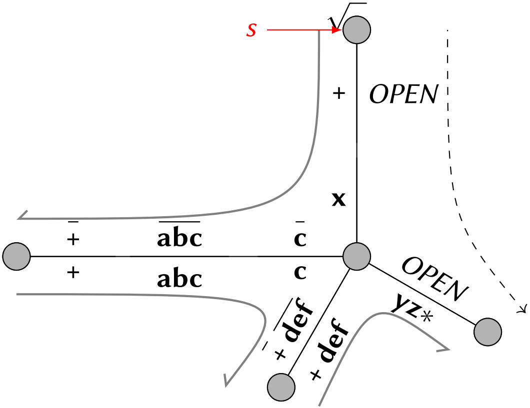


Assemblies



+
OPEN
x
$\overline{+}$
$\overline{\mathbf{abc}}$
$\bar{\mathbf{c}}$
+
abc
c
OPEN
yz*
$\overline{+}\ \overline{\mathbf{def}}$
+ def

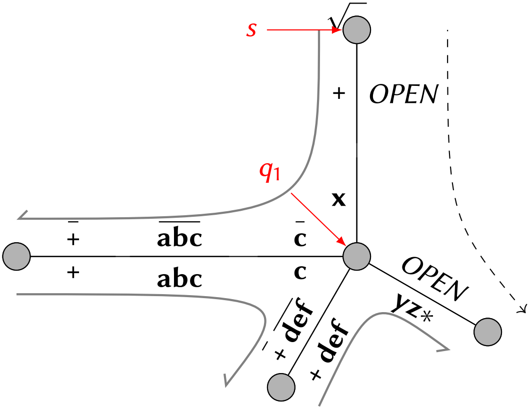
Assemblies & Automata



DNA Algorithm ≈ Finite Automaton

$(Q, \Sigma, \delta, s, F)$

Assemblies & Automata



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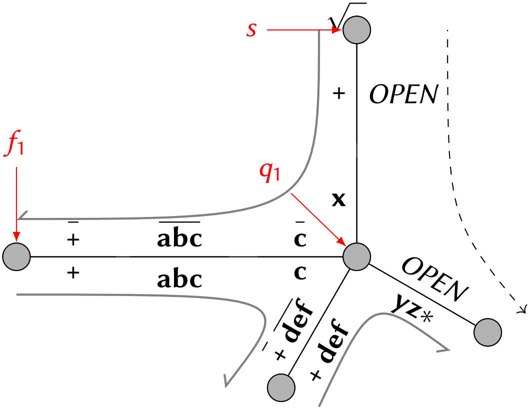
Assemblies & Automata



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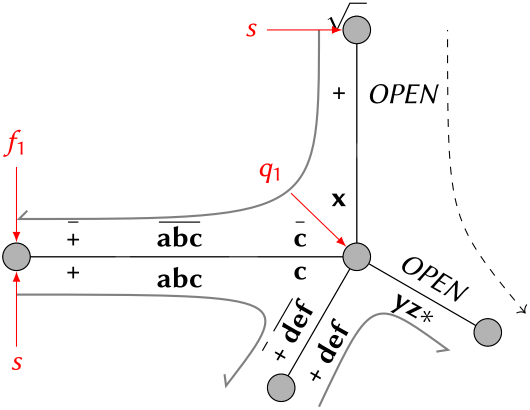
Assemblies & Automata



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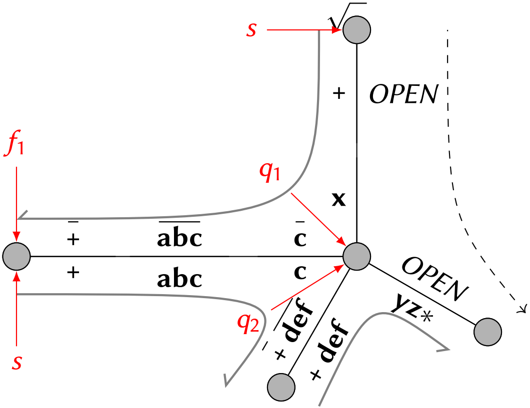
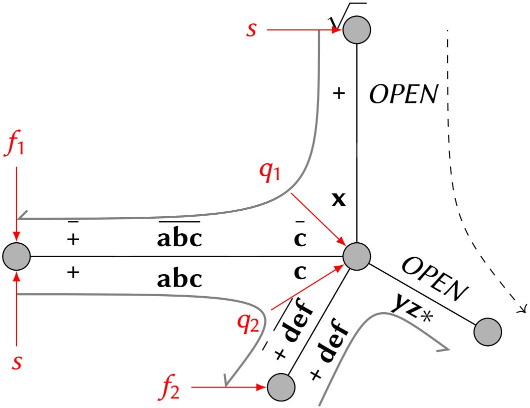
Assemblies & Automata



DNA Algorithm ≈ Finite Automaton

$(Q, \Sigma, \delta, s, F)$

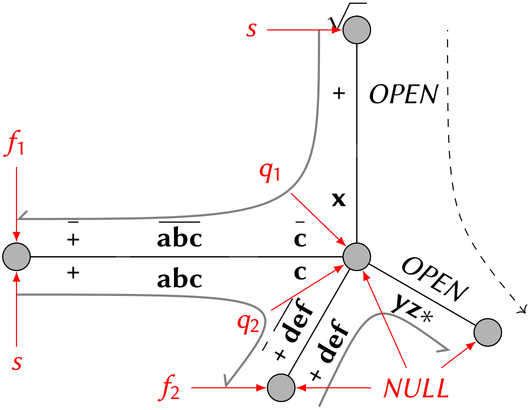
Assemblies & Automata



DNA Algorithm ≈ Finite Automaton

$(Q, \Sigma, \delta, s, F)$

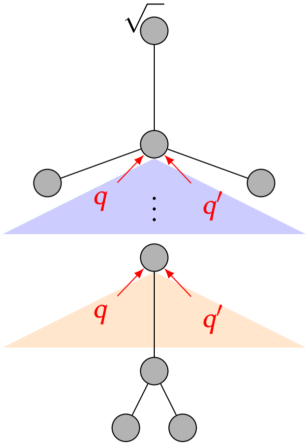
Assemblies & Automata



DNA Algorithm ≈ Finite Automaton

$(Q, \Sigma, \delta, s, F)$

Minimal Assemblies



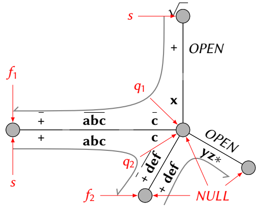
The Laborious Part . . .

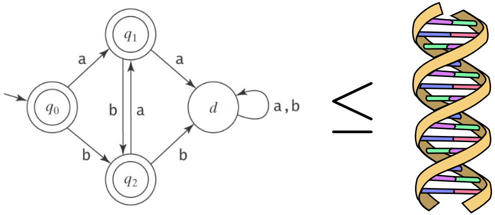
$$\mathcal{I} := \bigcup_{w:\delta(w,*)\in F} \mathcal{X}(\delta(s,+), w, Q\times Q \setminus \{(\delta(s,+), w)\})$$

$$\mathcal{X}(v,w,J) := \bigcup_{q\in I(v,w,J)} \left(\bigcap_{\substack{(q_i,q_{i+1}):\\ q_i\neq NULL\neq q_{i+1}}} C(q_i, q_{i+1}, J) \;\cap \bigcap_{i:q_i=NULL} D(q_{i-1}, q_{i+1}, J) \right)$$

$$C(x,y,J) := \begin{cases} +\Sigma^* * , & \text{if } \exists (z_1,z_2)\in H_{x,y,J} \text{ s.t. } z_2 = s \text{ and } z_1 \in F \\ \bigcup_{(z_1,z_2)\in H_{x,y,J}} \mathcal{X}(z_1, z_2, J\setminus\{(x,y),(z_1,z_2)\}) , & \text{otherwise.} \end{cases}$$

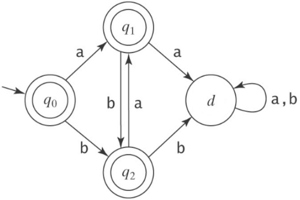
$$D(x,y,J) := \bigcup_{K\subseteq J\setminus\{(x,y)\}} \left(\overline{\mathcal{L}(B_{K,x,y})} \cap \bigcap_{(z_1,z_2)\in K} \mathcal{X}(z_1,z_2,J\setminus\{(x,y),(z_1,z_2)\}) \right)$$



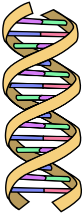


Theorem

Let $\mathcal{L}$ be a regular language.
There is a constant size DNA algorithm that decides $+\mathcal{L}*$.



$\leq$



Theorem

Let $\mathcal{L}$ be a regular language.
There is a constant size DNA algorithm that decides $+\mathcal{L}*$.

- Regular Language $\rightarrow$ FA $(Q, \Gamma, \delta, s, F)$
- $\overrightarrow{+\bar{s}+}$ for the starting state s
- $\overrightarrow{+q'\bar{x}\bar{q}+}$ for all possible transitions $\delta(q, x) = q'$
- $\overrightarrow{\bar{*}\bar{f}*}$ for all $f \in F$.

Summary