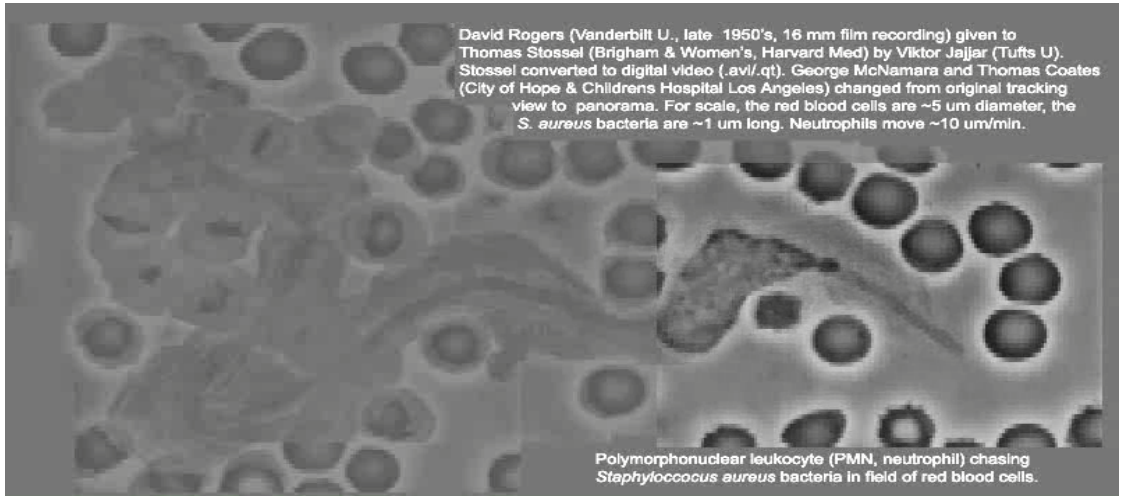
Agents and reagents: Distributed computing in a test tube

David Doty, David Soloveichik

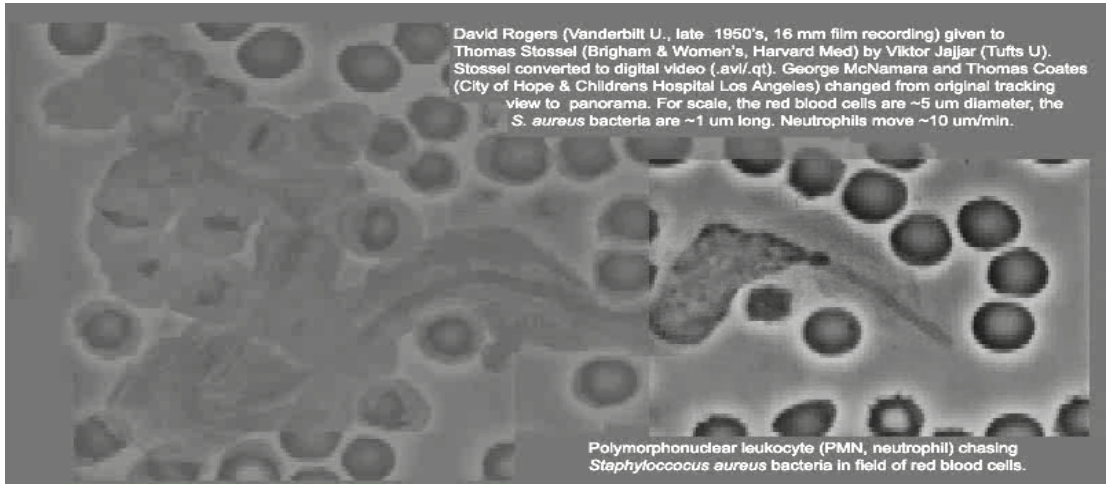
DISC 2014 Tutorial

The software of life



How does the cell compute?

The software of life



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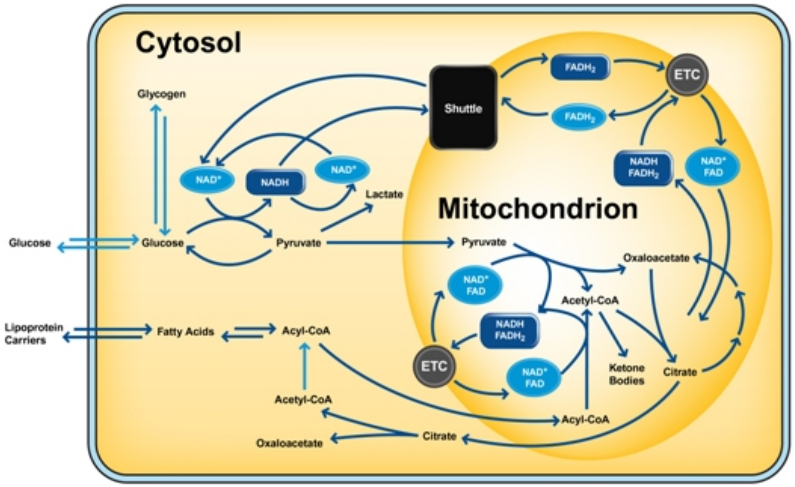
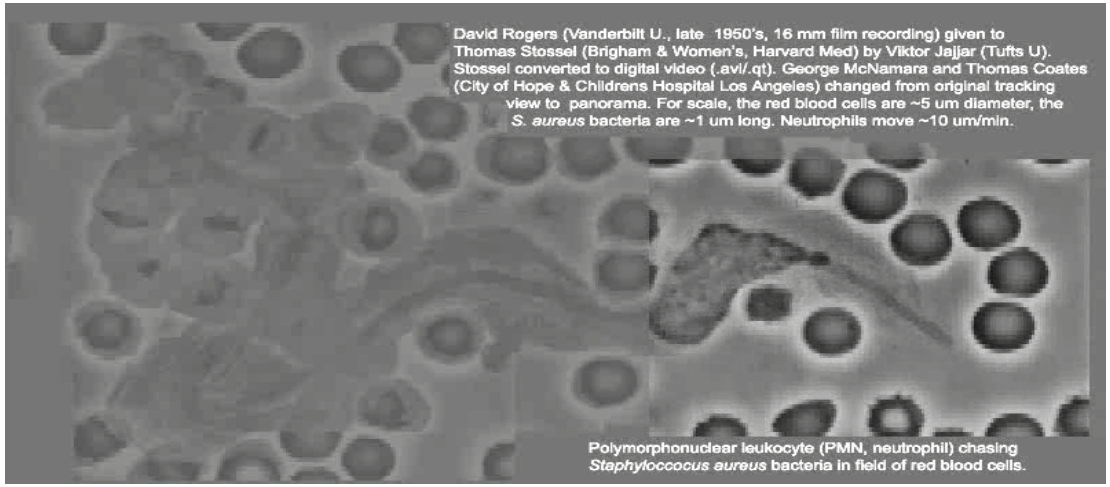


chemistry / geometry

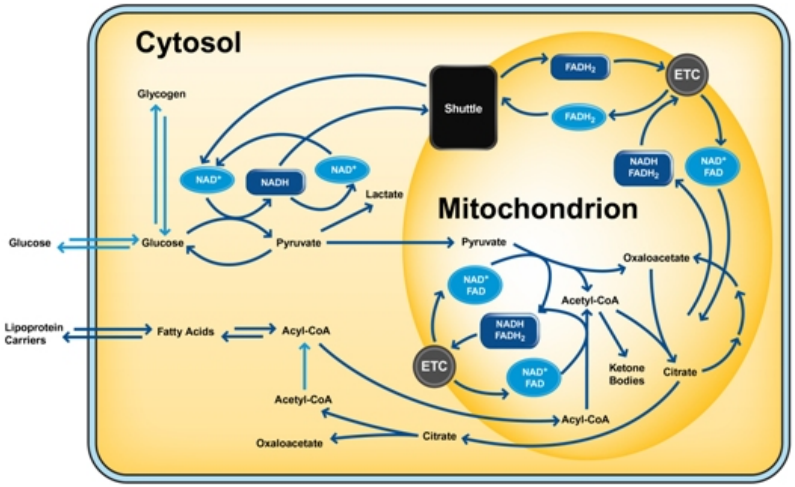
The software of life



~~How does the cell compute?~~

What is possible to compute with chemistry?

~~geometry~~



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$$X \rightarrow 2X$$

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Chemical reaction networks (CRN)

$$R \xrightarrow{2.5} P_1 + P_2$$

$$A + B \xrightarrow{1} C$$

$$X + Y \xrightarrow{5} X + Z$$

$$A + Z \xrightarrow{0.1}$$

(anonymous waste product)

$$X \xrightarrow{0.1} 2X$$

(anonymous fuel source)

What behavior is possible for chemistry in principle?

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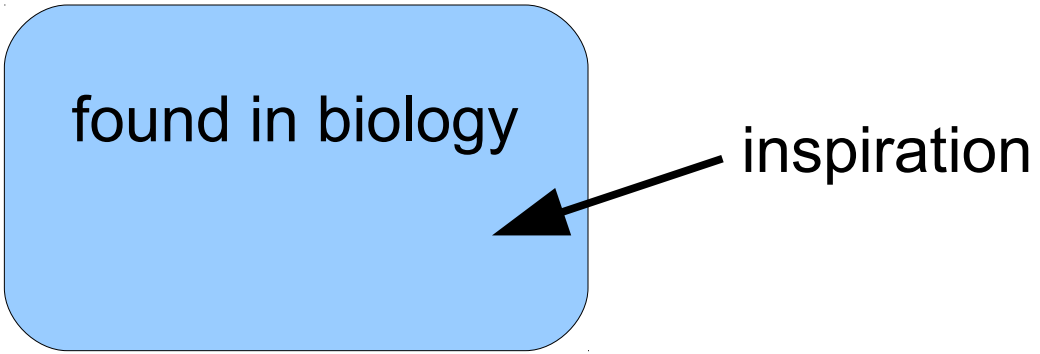

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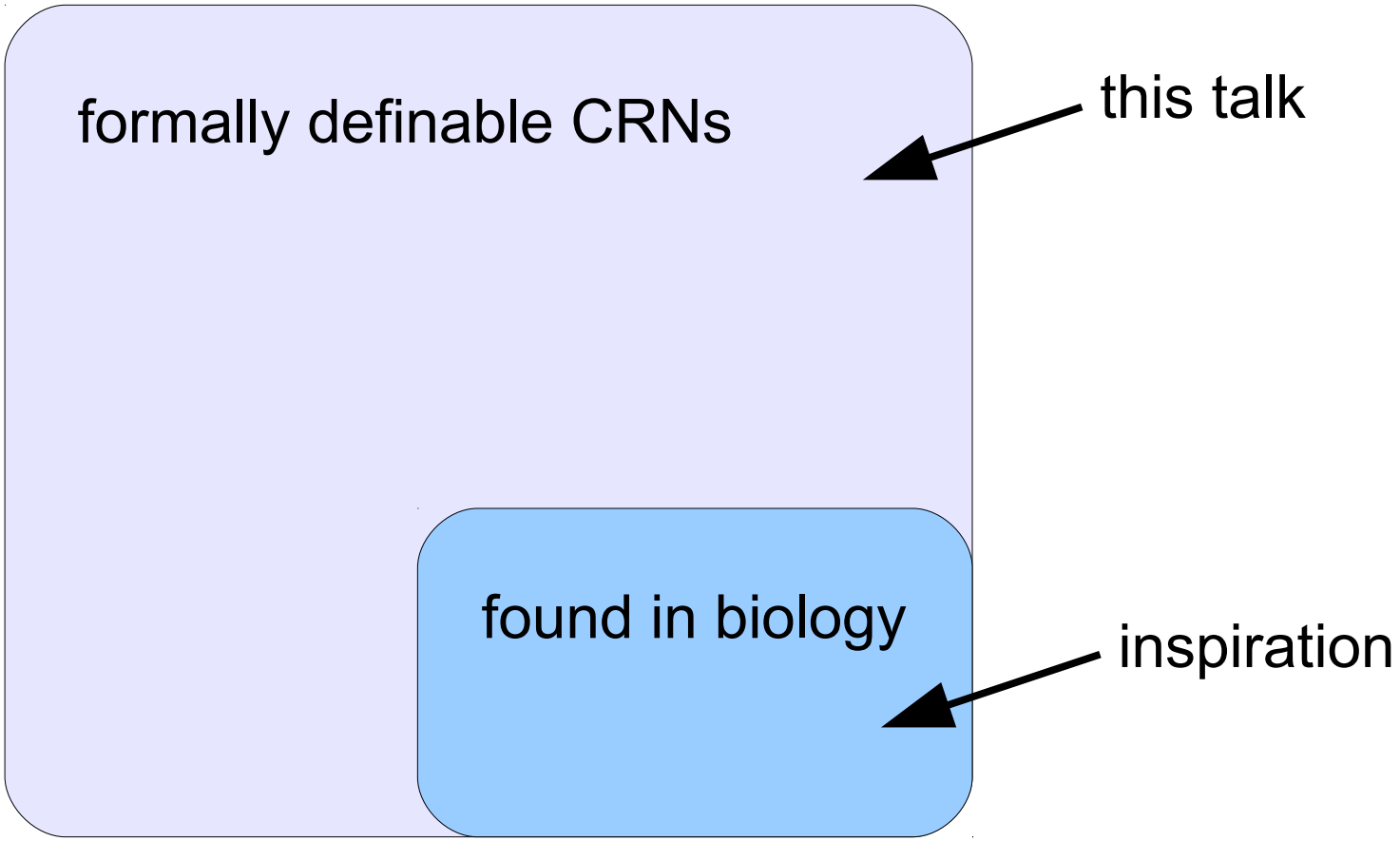

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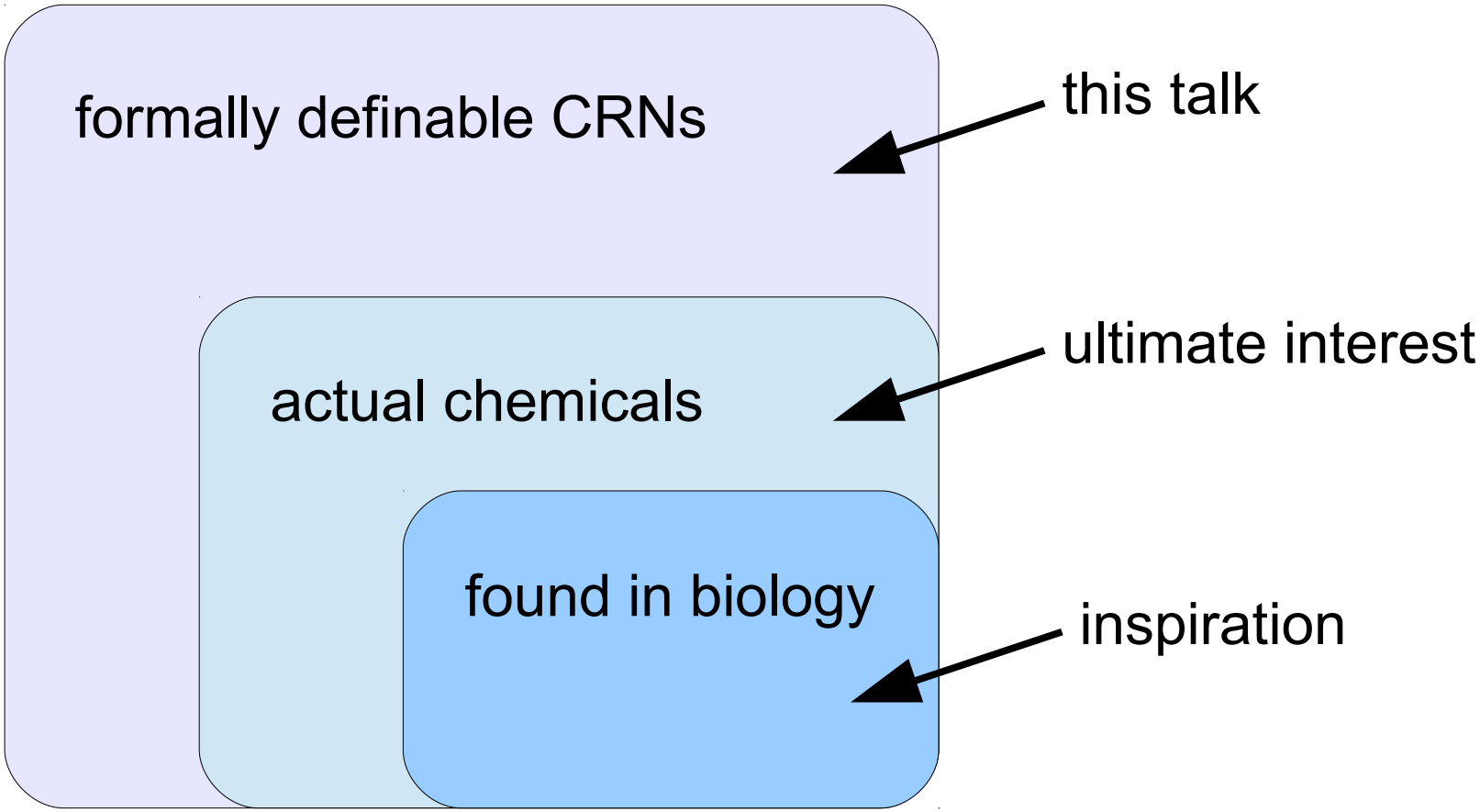

Can we compute with chemistry?

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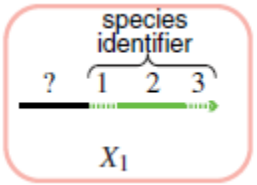

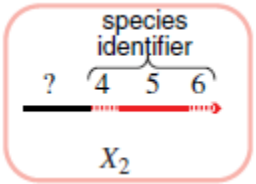

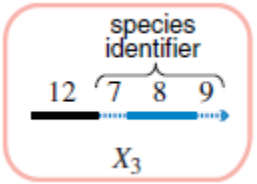

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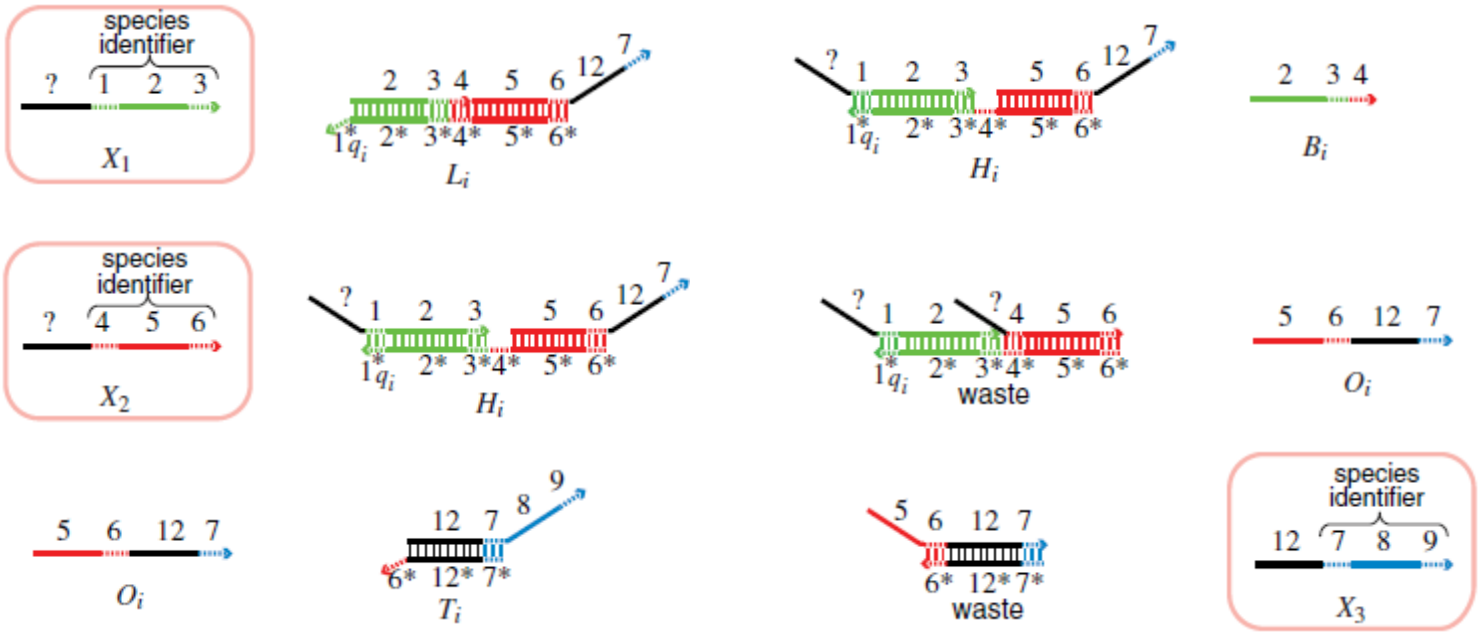

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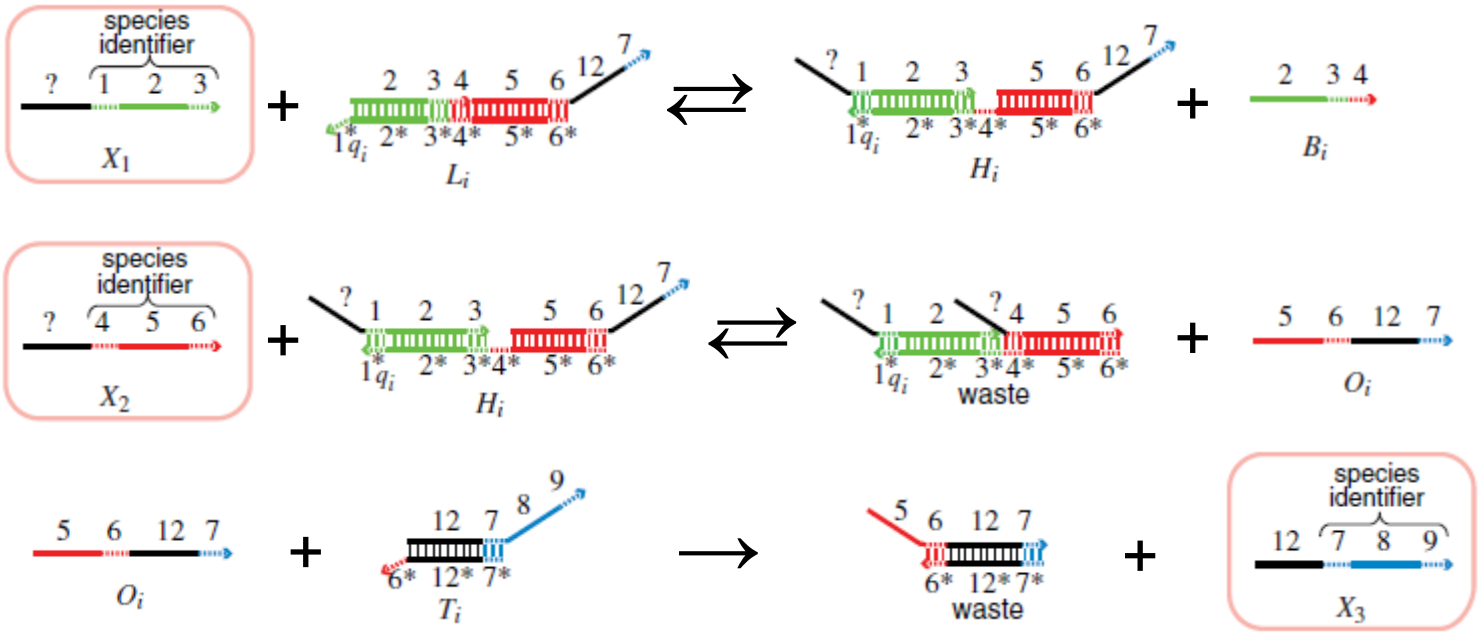

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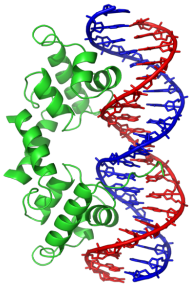
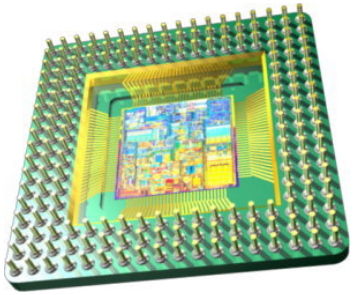


versus



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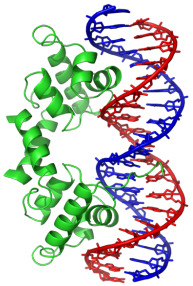

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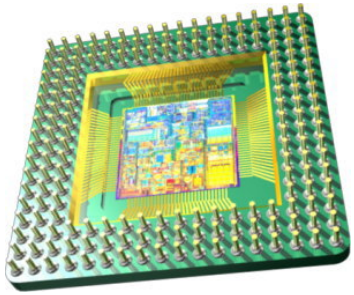

speed?

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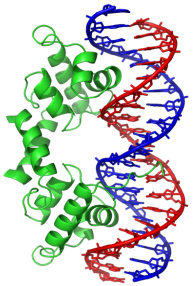

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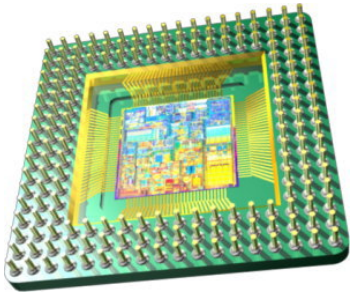

slower speed? faster

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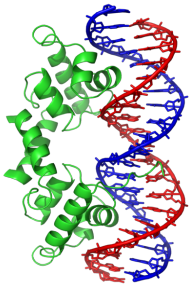

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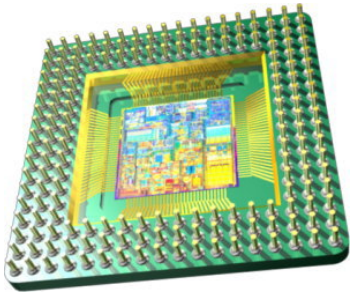

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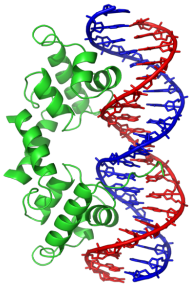

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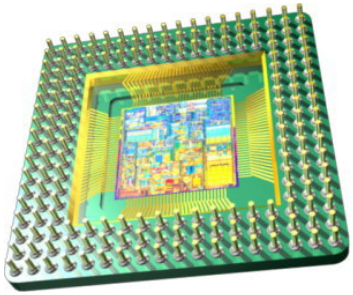

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component size?

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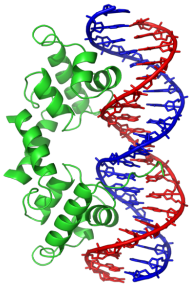

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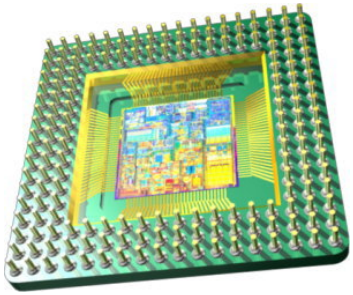

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speed?

faster

≈ 10-100 nm

component size?

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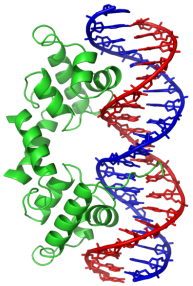

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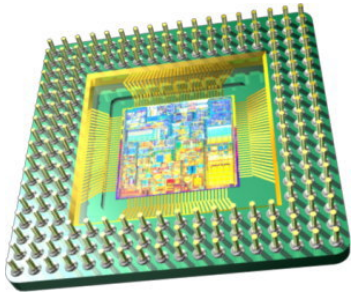

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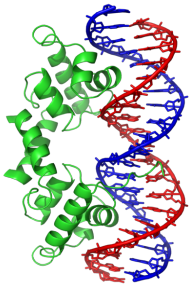

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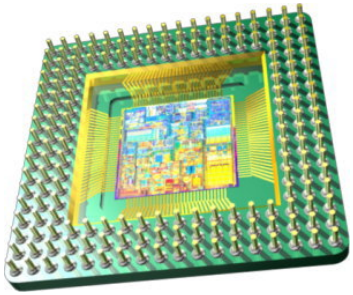

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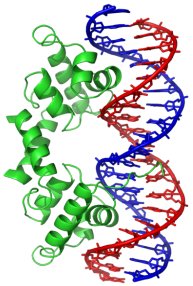

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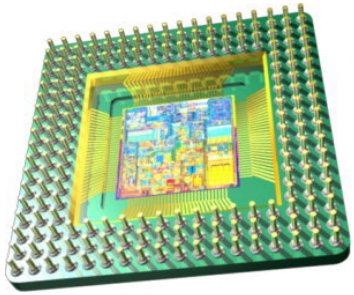
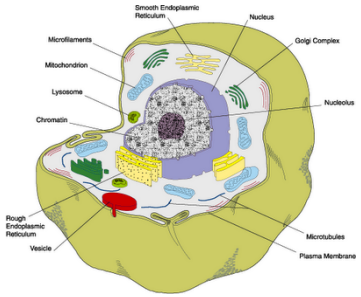


slower	sped?	faster
≈ 10-100 nm	component size?	≈ 10-100 nm
yes	✓ Compatible with biological or other "wet environments"?	not easily

cells



"smart drug" to detect microRNAs levels of cell and release appropriate drug in response

bioreactors

"chemical controller" to increase yield of metabolically produced biofuels/drugs/etc.

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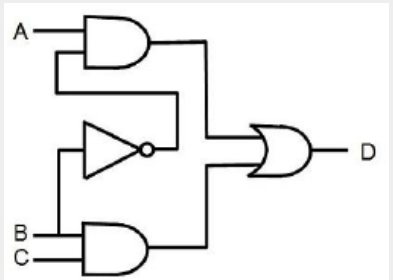

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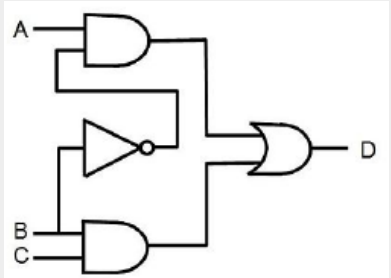
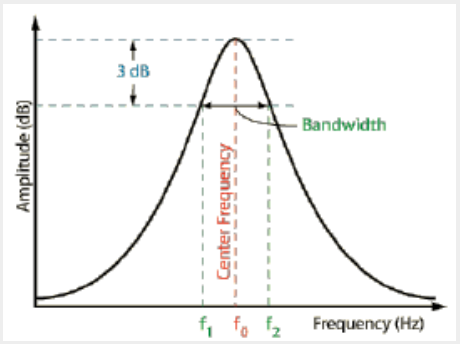


signal processing



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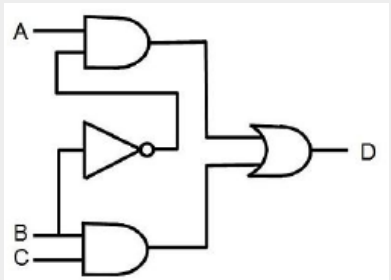
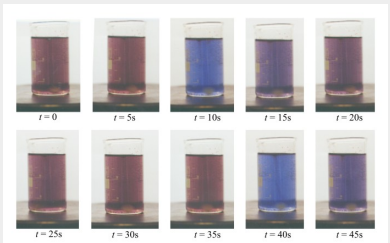


oscillation



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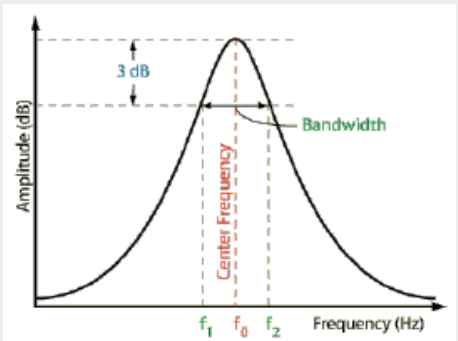

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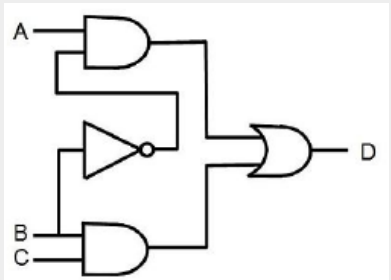

analog computing

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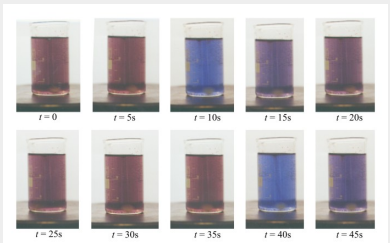

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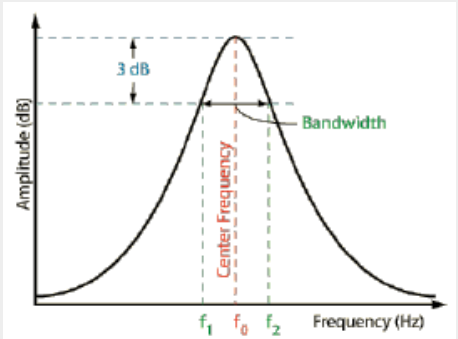

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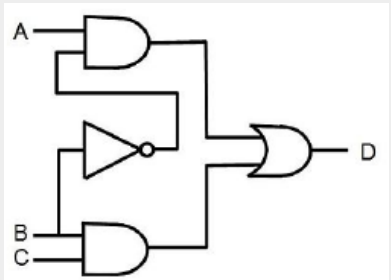
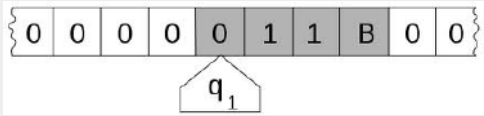


discrete algorithms



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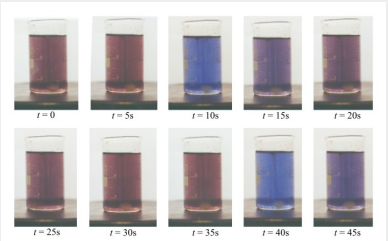

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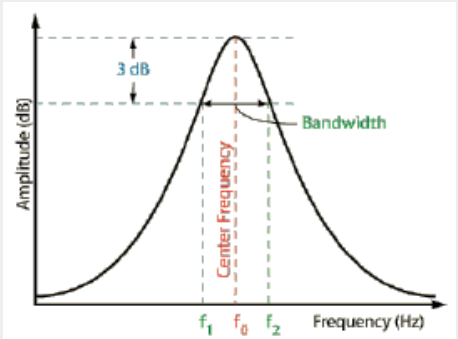

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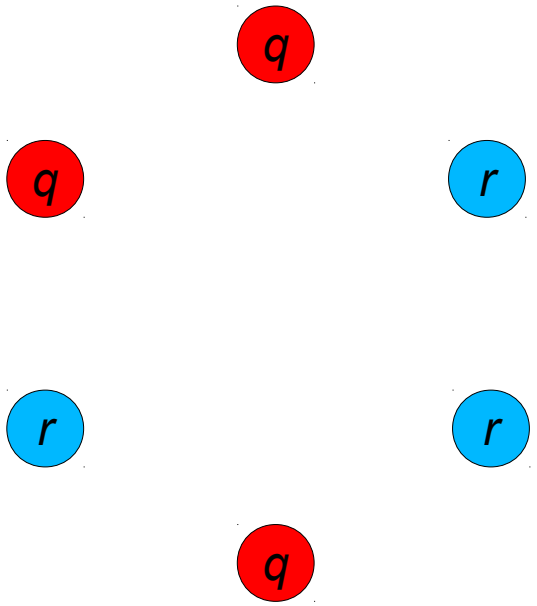
time until next reaction = exponential random variable

Population protocols

n finite-state agents



(Angluin, Aspnes, Diamadi, Fisher, Peralta, PODC 2004)

Population protocols

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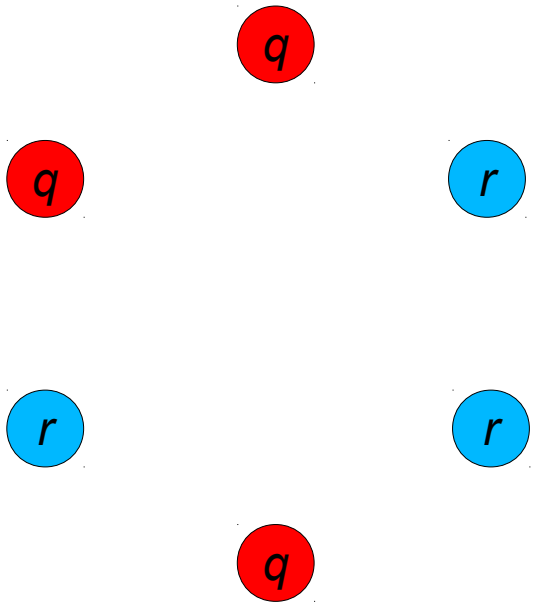
repeatedly pick pair to interact



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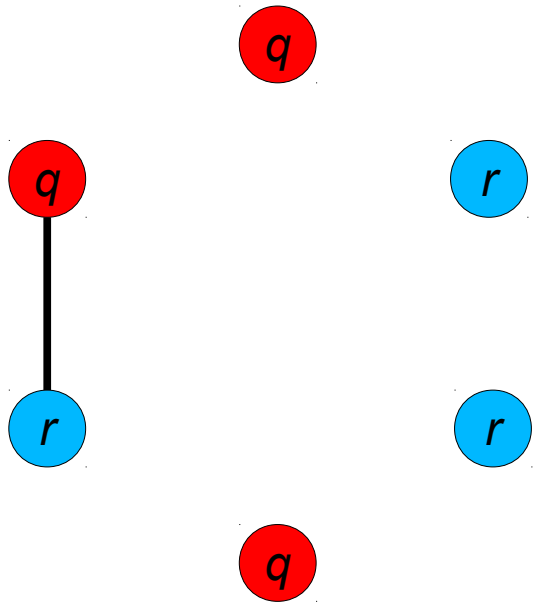

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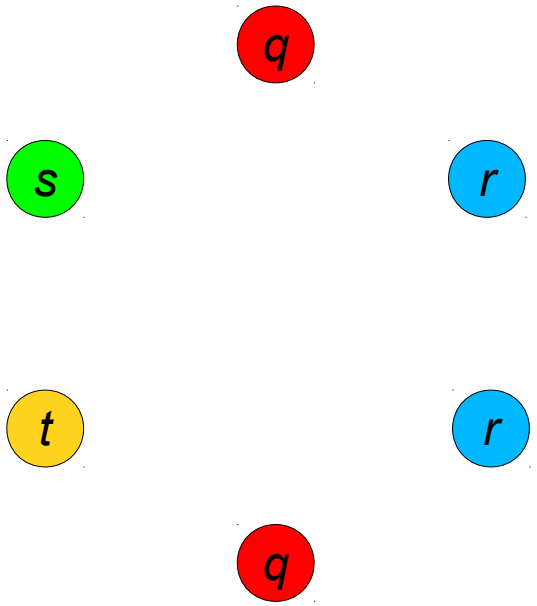

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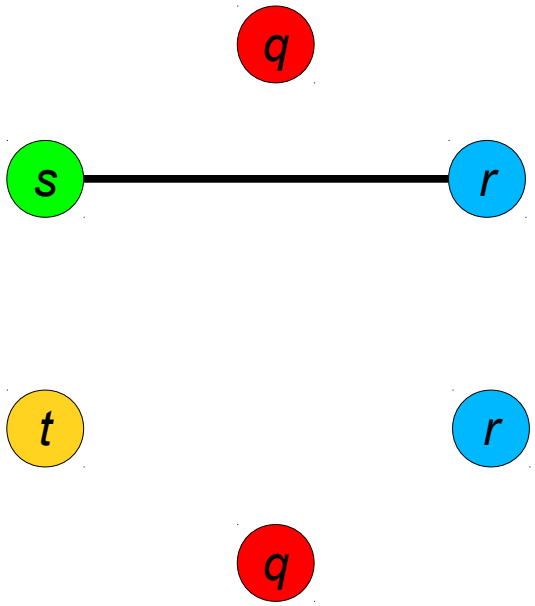

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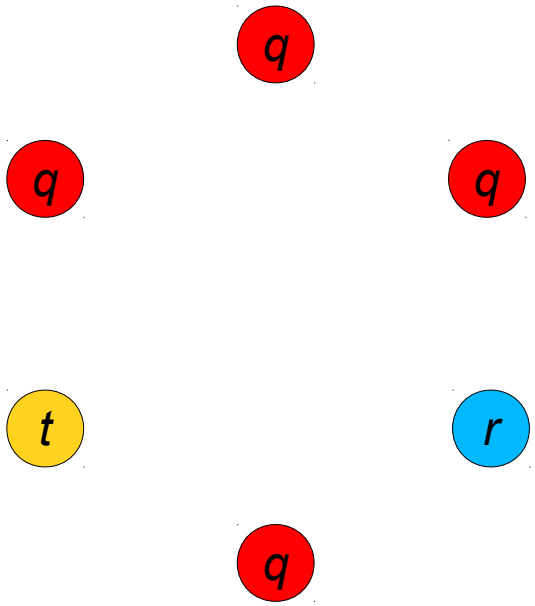

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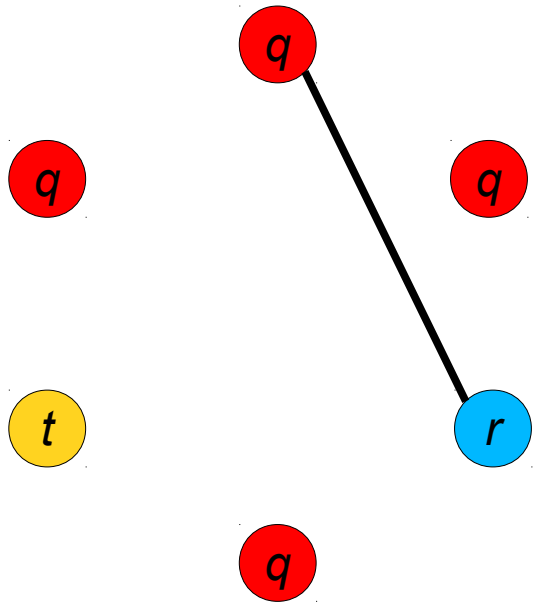

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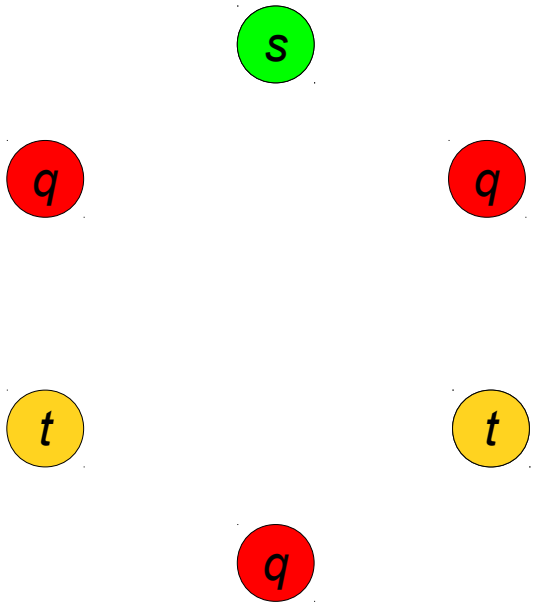

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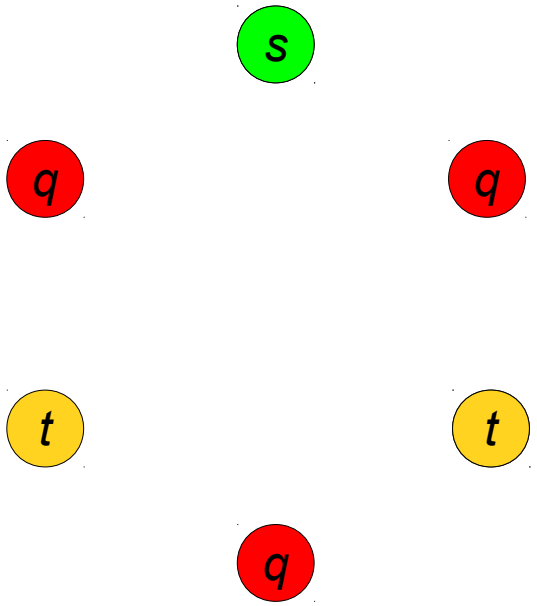

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"parallel time" = # of interactions / *n*

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- sender/receiver states uniquely determine products
  (e.g., cannot have A+B → C+D and A+B → X+Y)

Computation with CRNs: Outline

- Stable computation (“deterministic”)
- Randomized computation:
  - probability of error = small
  - probability of error = 0

Stable (deterministic) CRN computation

Stable CRN predicate computation (definition)

task: compute predicate $p(x_1,...,x_k)$, $x_1,...,x_k \in \mathbb{N}$

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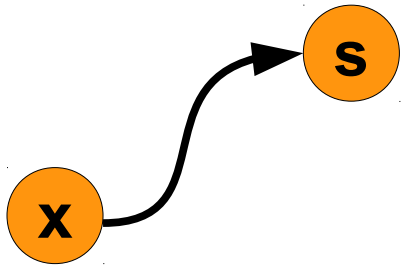

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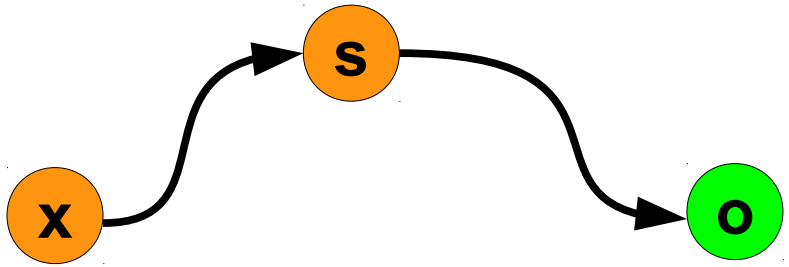

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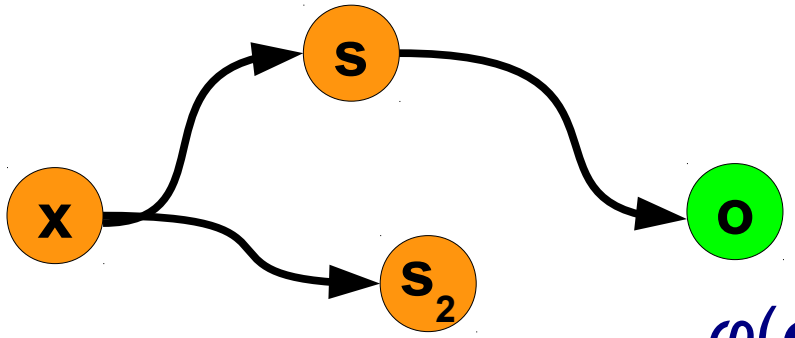

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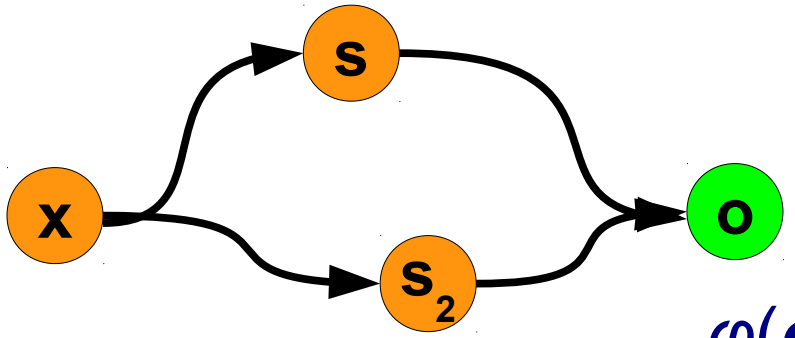

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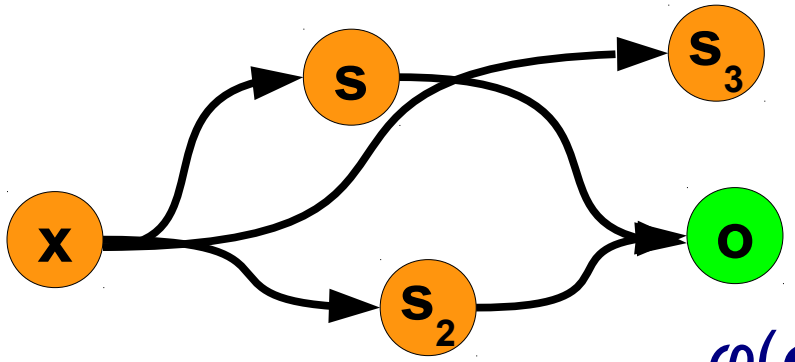

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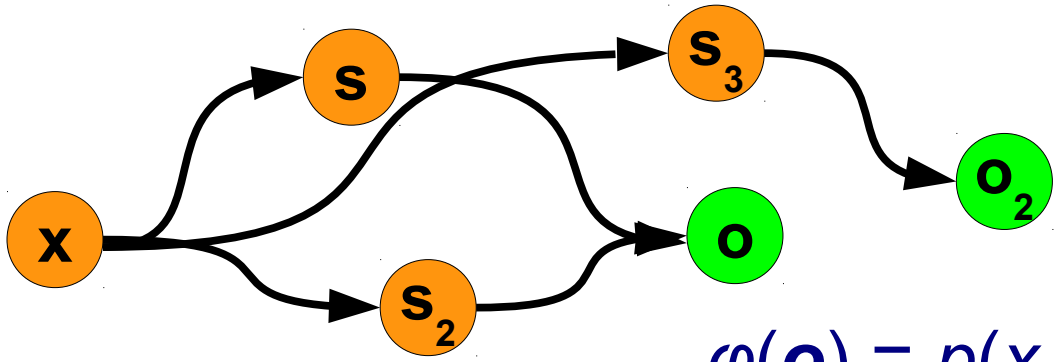

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stable computation: predicate $p(x_1,...,x_k)$ is stably computed if every fair execution contains an output stable state **o** with $\varphi(\mathbf{o}) = p(x_1,...,x_k)$

Stable CRN predicate computation (example)

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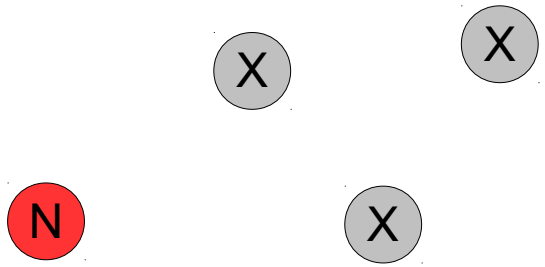

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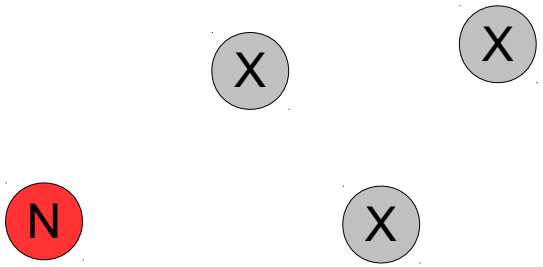

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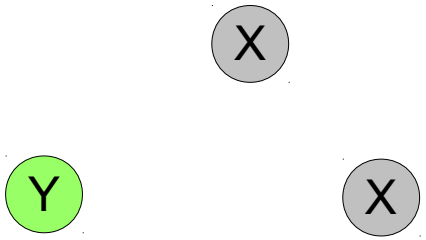

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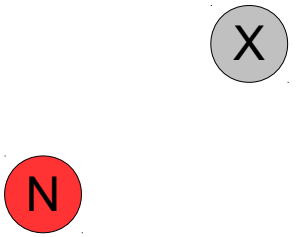

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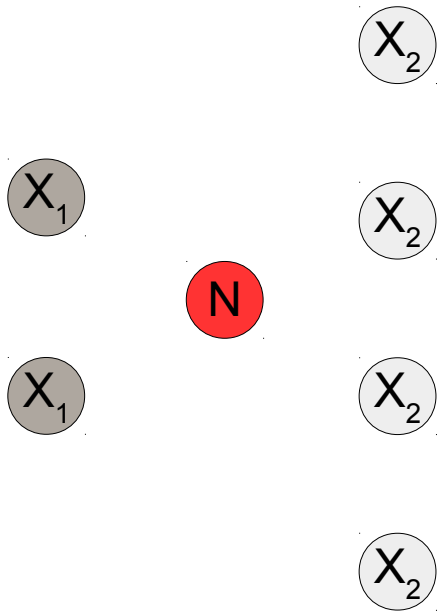

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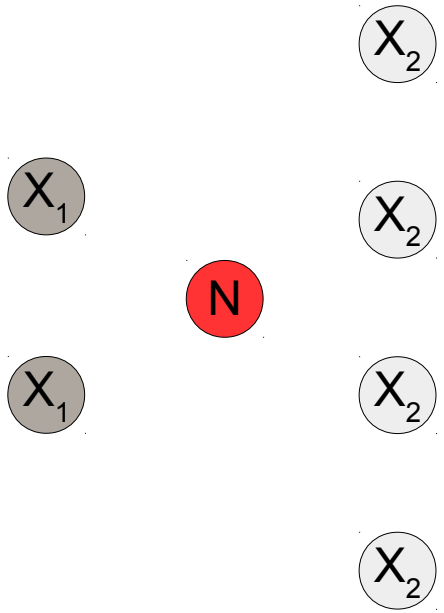

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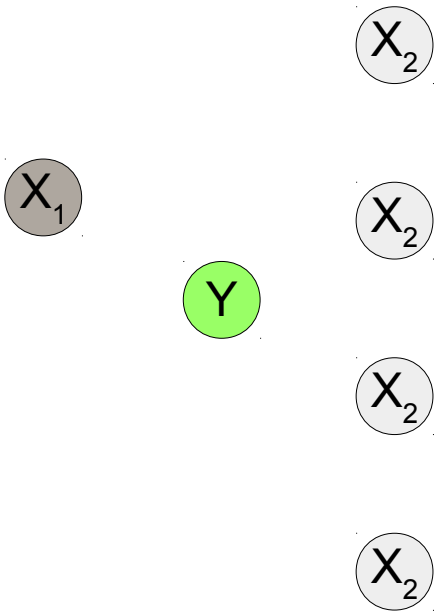

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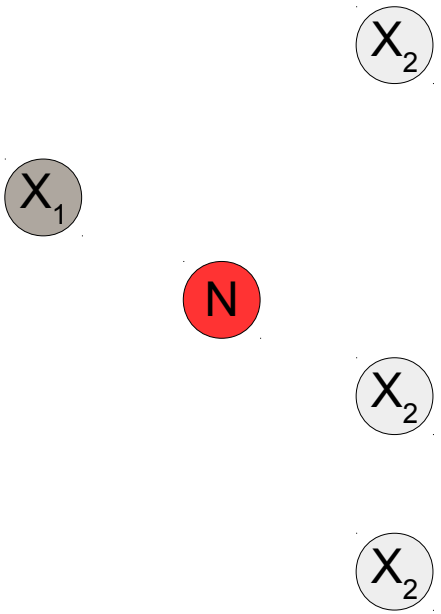

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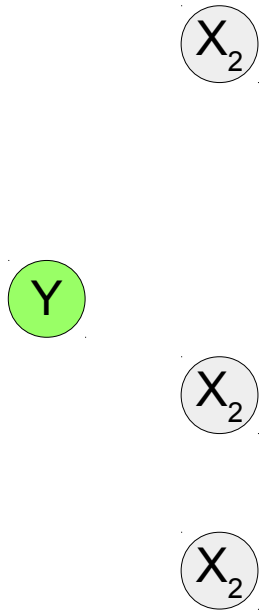

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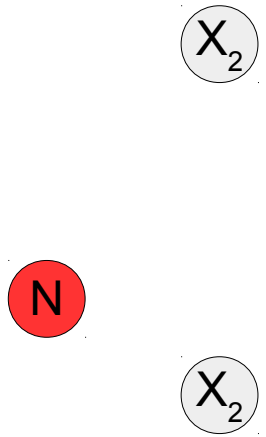

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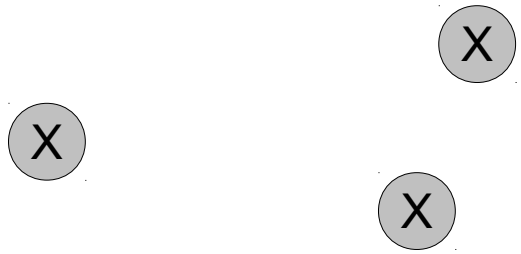

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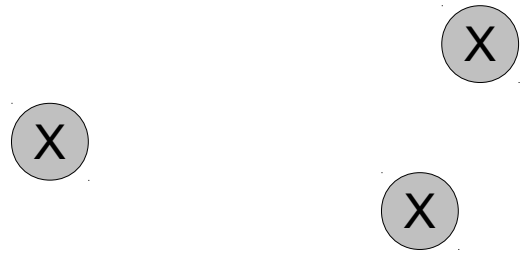

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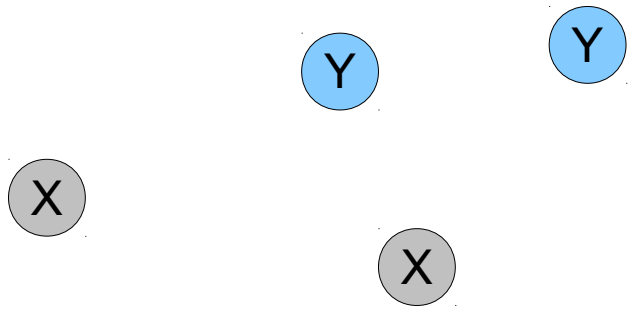

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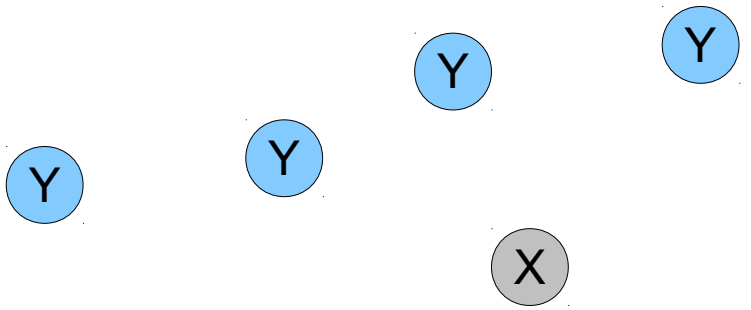

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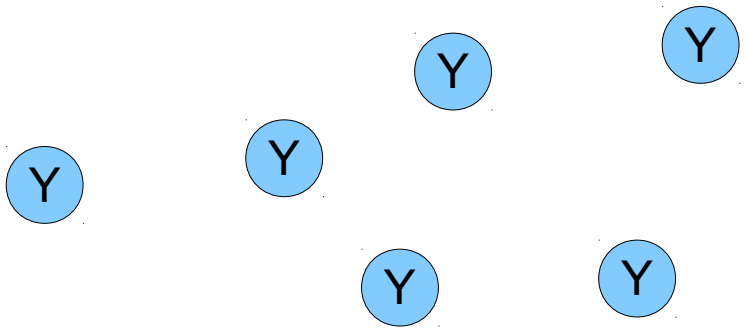

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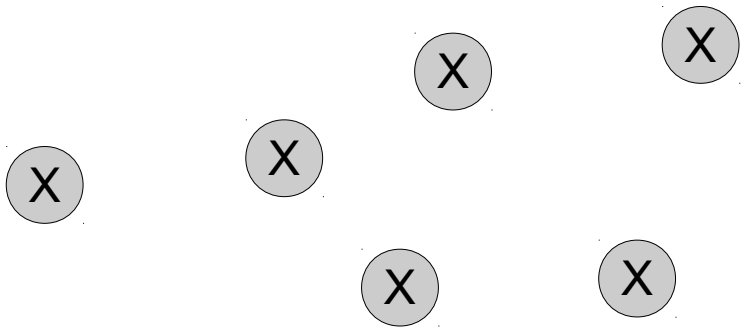

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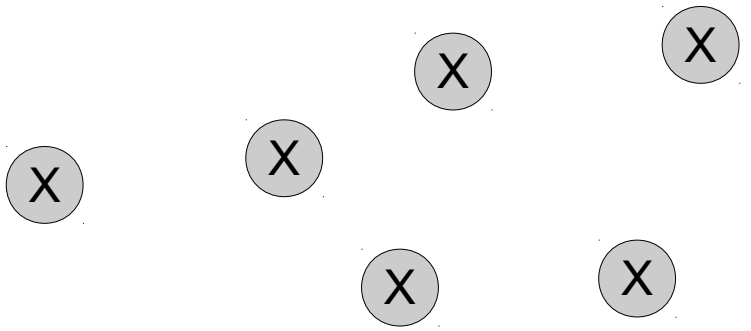

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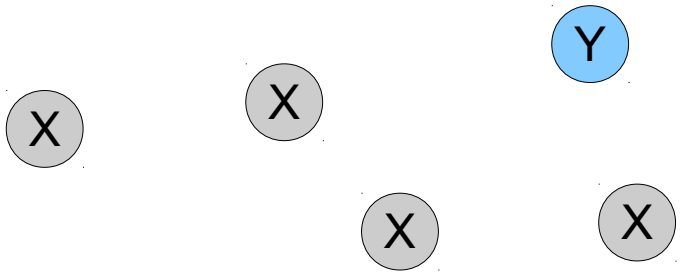

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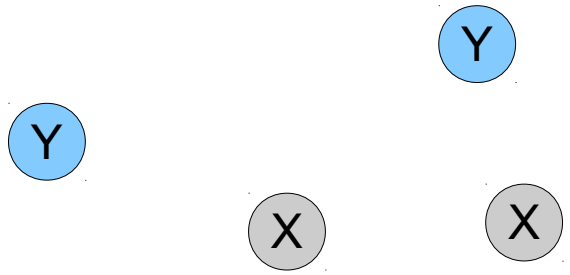

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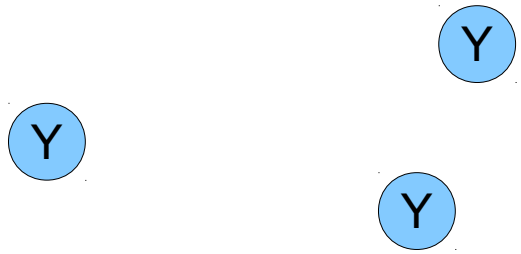

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$$\boxed{\begin{aligned} X_1 &\longrightarrow Y + X_1' \\ X_2 &\longrightarrow Y + X_2' \end{aligned}}$$

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$$K + Y \longrightarrow$$

Stable CRN predicate computation (example)

predicate: $p(x_1,x_2)$: "$3x_1 > x_2/2$"?

initial state: $\{ x_1\ X_1\ ,\ x_2\ X_2\ ,\ 1\ N \}$

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$$N + Z_1 \rightarrow Y$$
$$Y + Z_2 \rightarrow N$$

Stable computation characterization

Theorem: A predicate is stably computed by a CRN if and only if it is *semilinear*.

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- Open question: extension to general CRNs?

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polylogarithmic time = "fast" = polynomial in binary expansion of n

linear time = "slow" = exponential in binary expansion of n

Time complexity in CRNs

time until next reaction = exponential r.v.

reaction	expected time
$X \rightarrow W + 2Y + Z$	$1 / \#X$
$A + B \rightarrow X$	volume / ($\#A \bullet \#B$)

Time complexity (example)

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+ ...
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+ E[time to consume second X]
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= 1/n + 1/(n-1) + 1/(n-2) + … + 1/1

≈ log n

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{*n L*}, volume *n*

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$\{n\ L\}$, volume n

$L + L \rightarrow L$

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What if we allow a small probability of error?
(Randomized CRN computation)

Randomized CRNs are Turing universal

"in a sense"

(Angluin, Aspnes, Eisenstat, DISC 2006)

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Informal: A CRN can simulate a Turing machine with polynomial slowdown and small chance of error.

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Formal: For each TM M, there is a CRN C so that, for each $\varepsilon > 0$ and natural number n, there is an initial state $\mathbf{x}$ of C so that C simulates $M(n)$ with probability ε of error, and expected time poly(s•t), where t and s are the time and space usage of $M(n)$.

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Counter (register) machine

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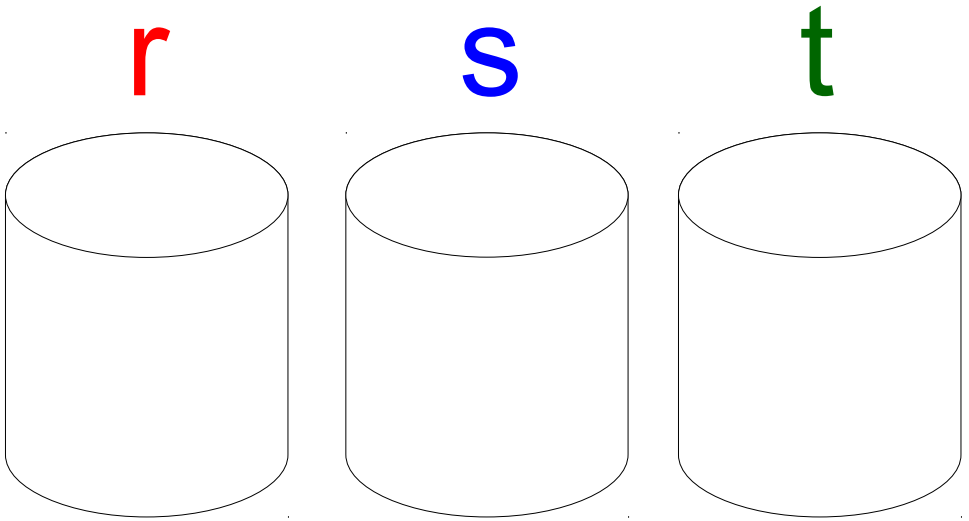

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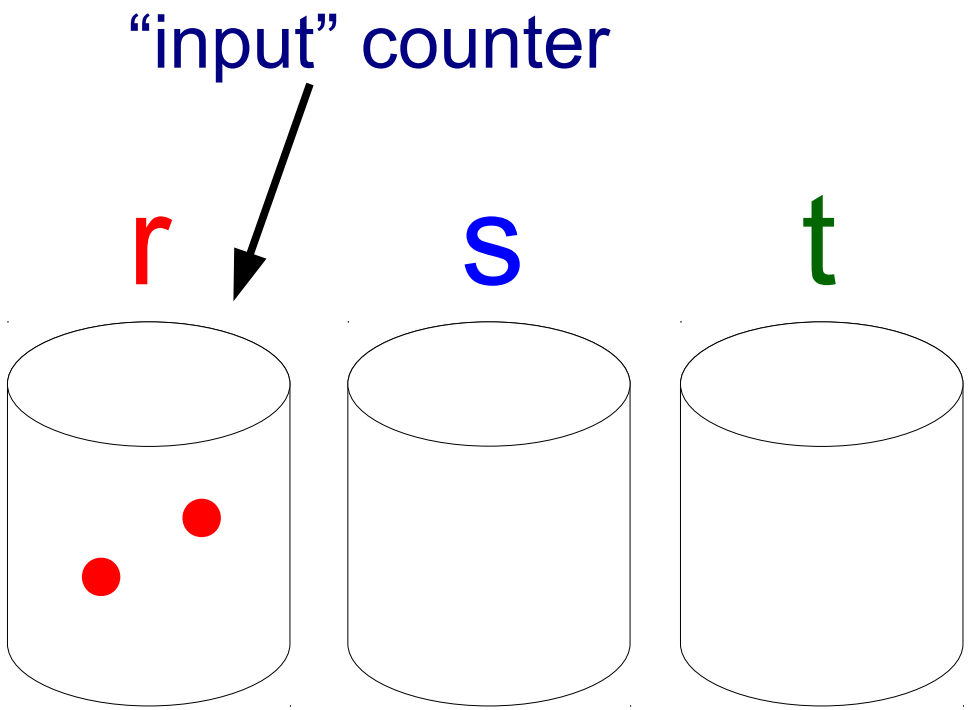

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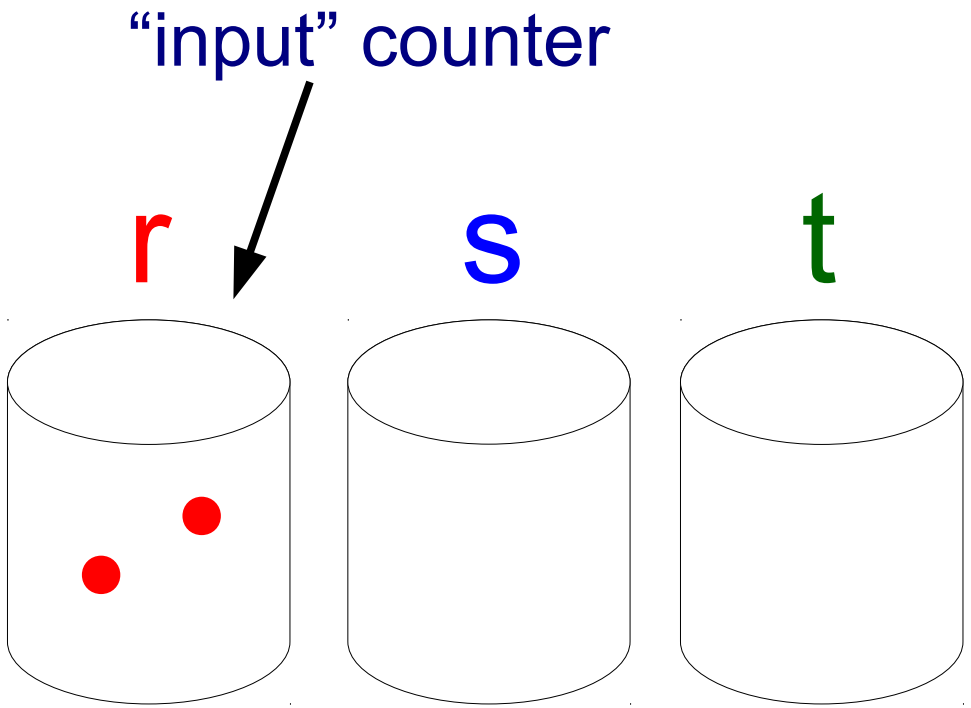

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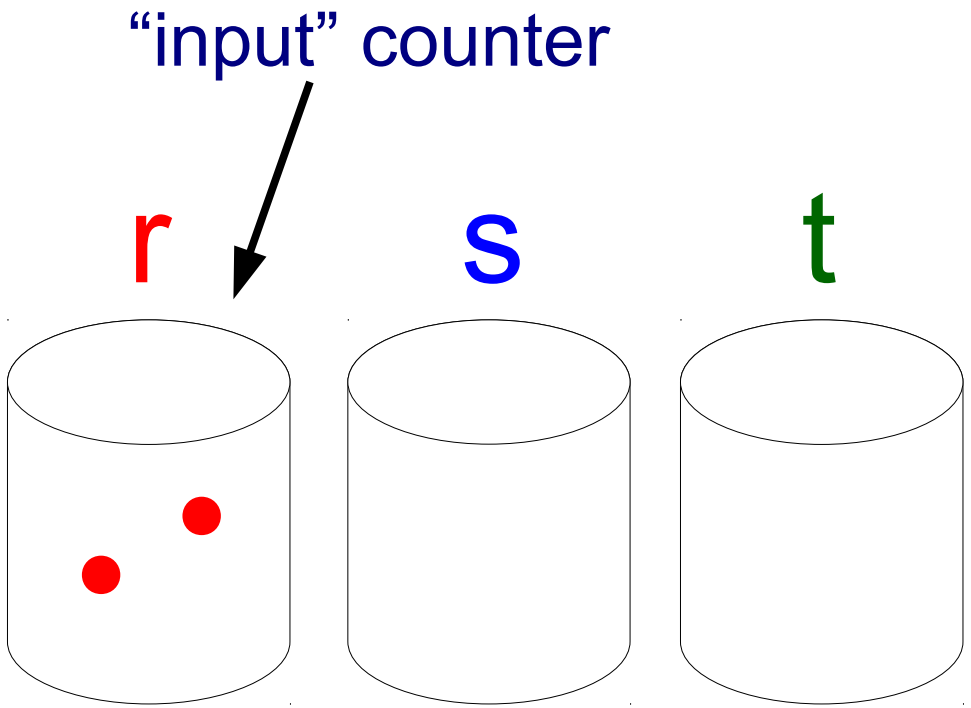

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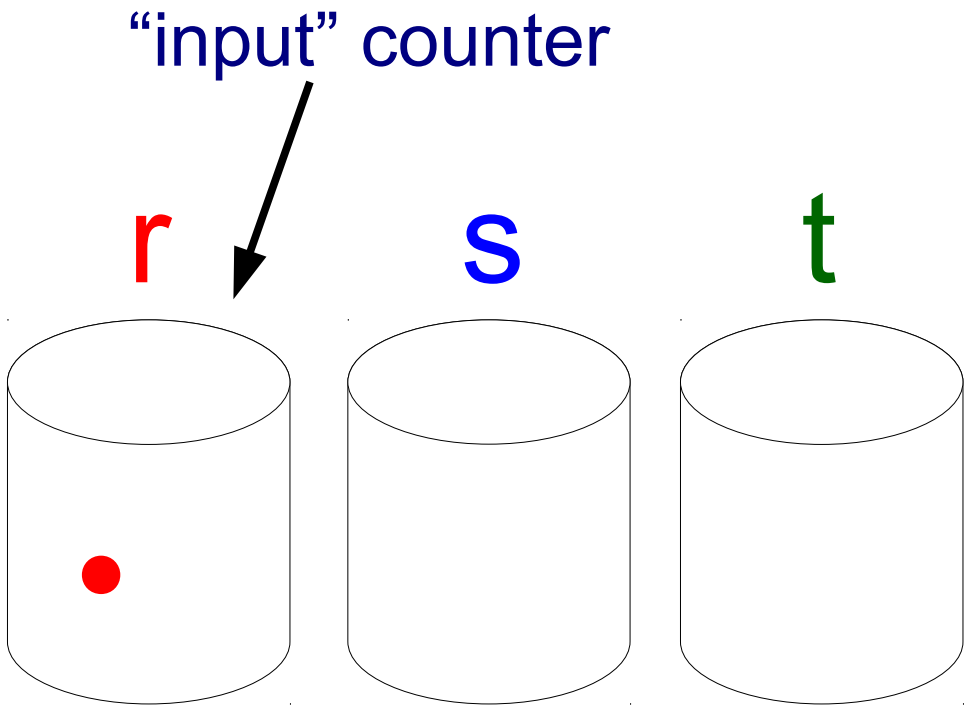

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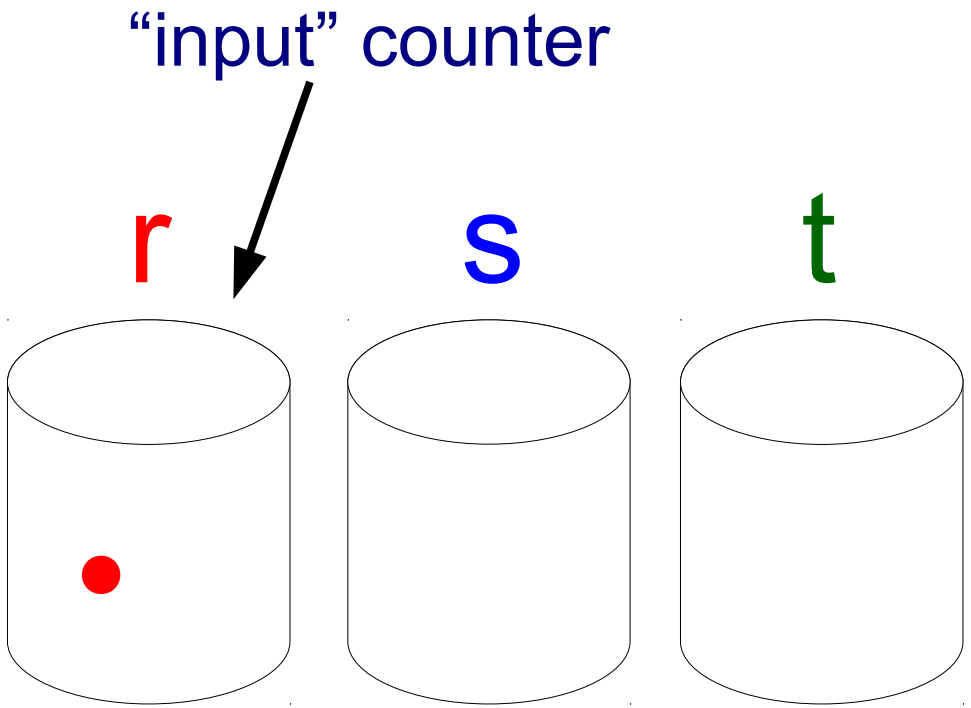

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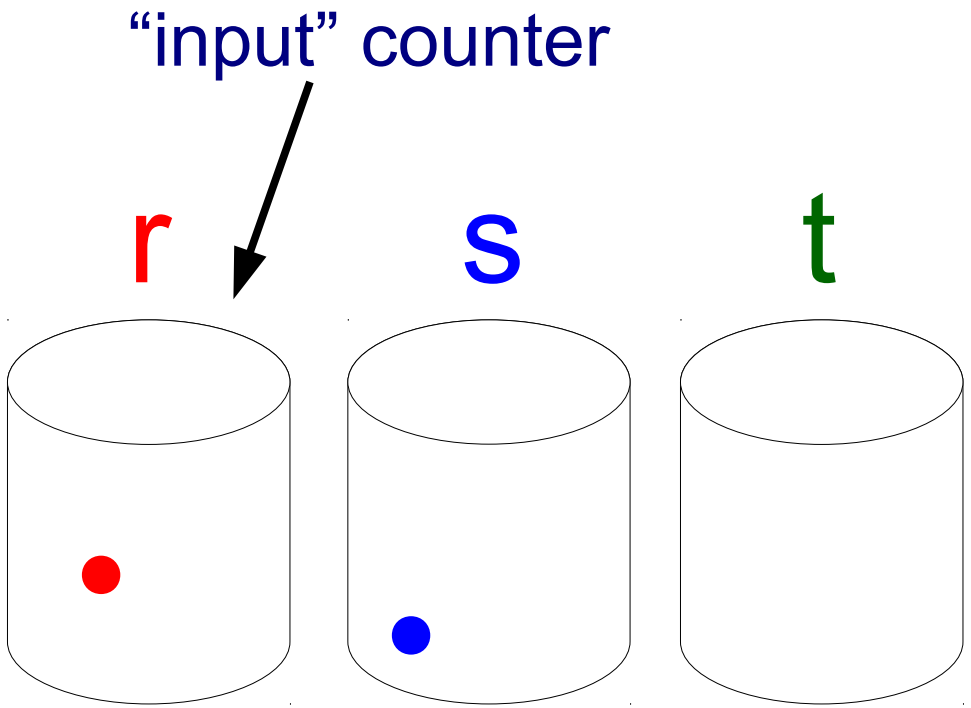

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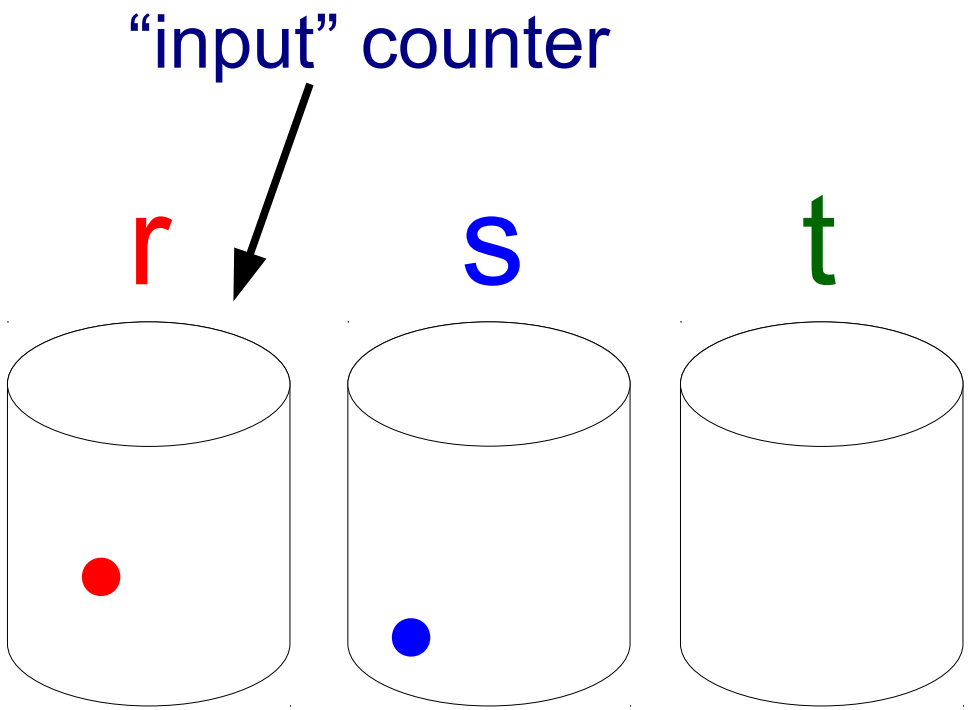

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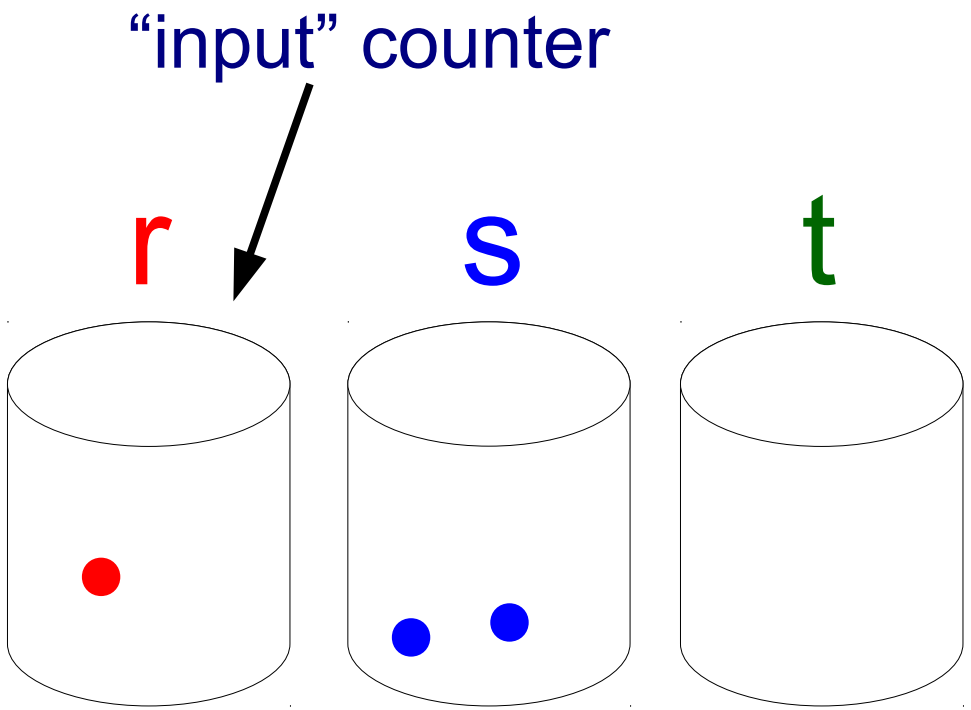

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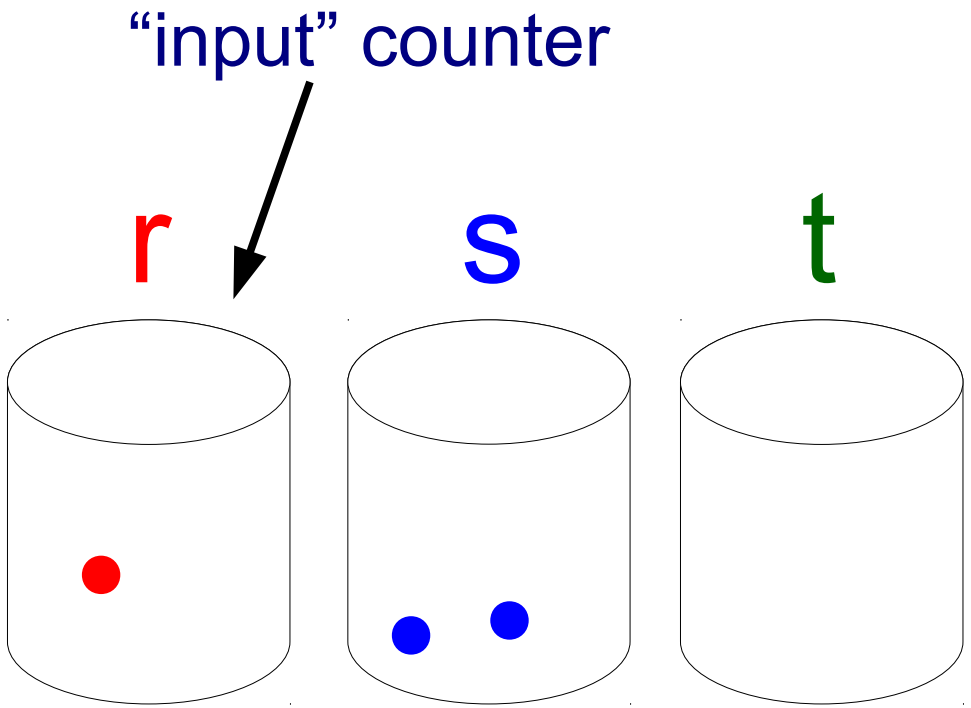

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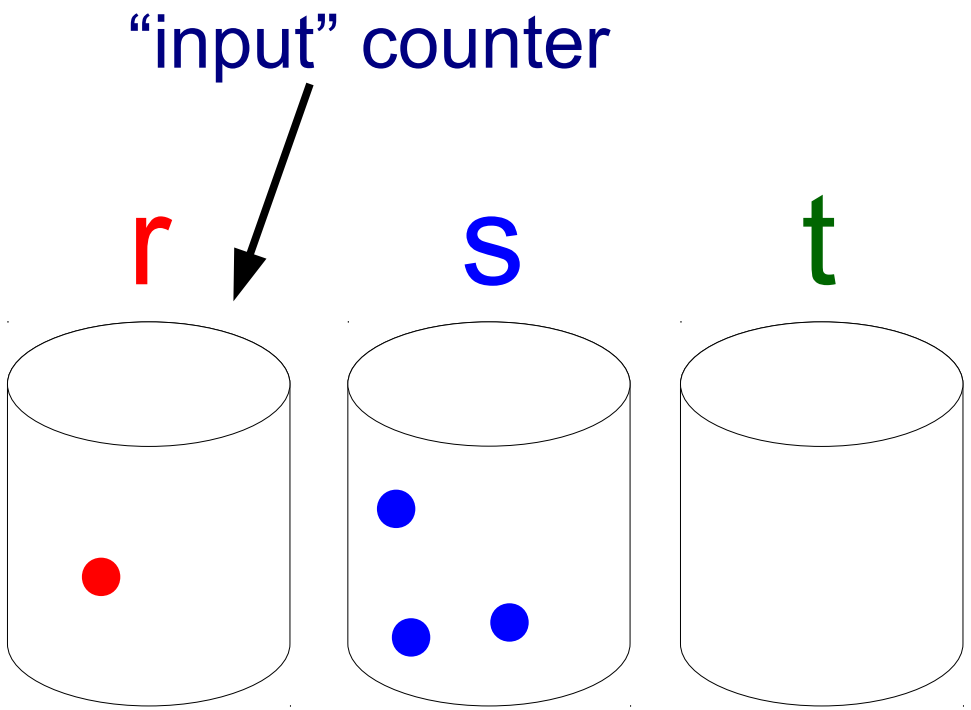

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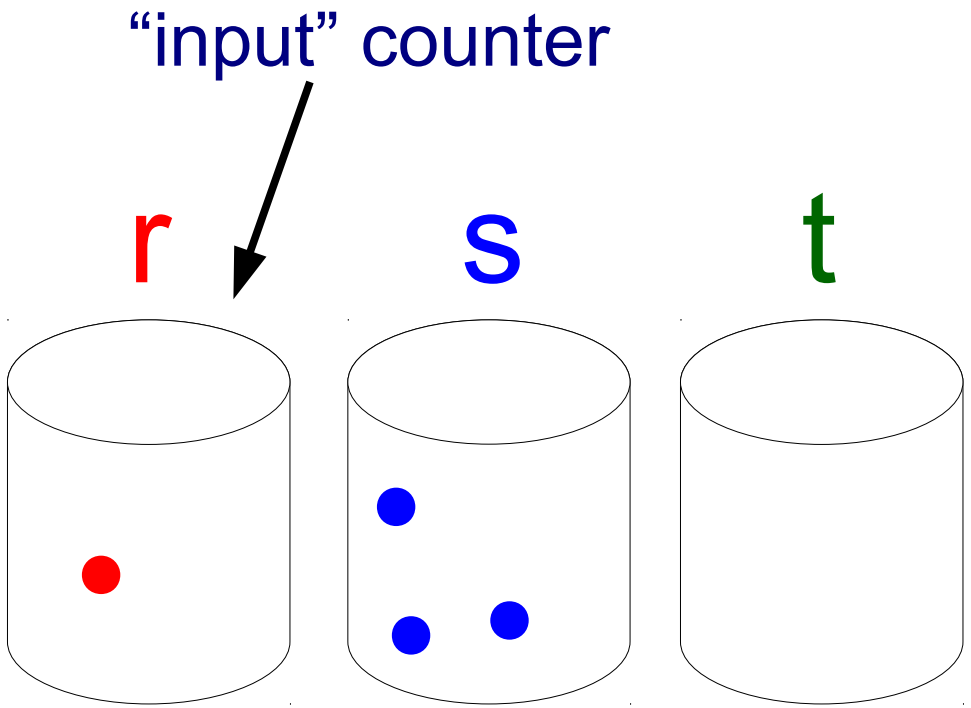

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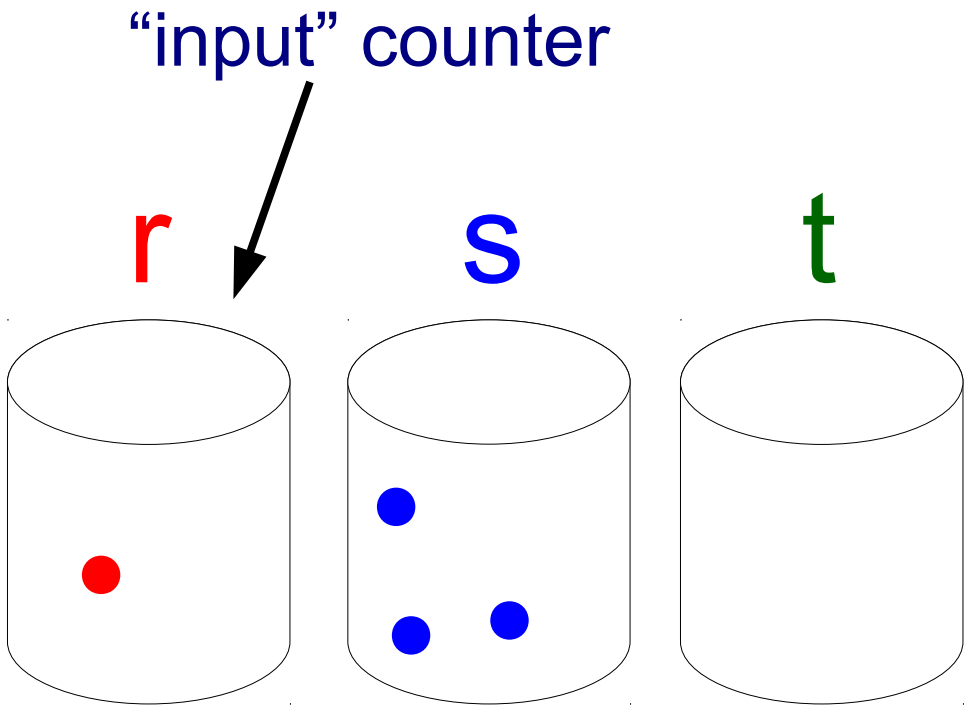

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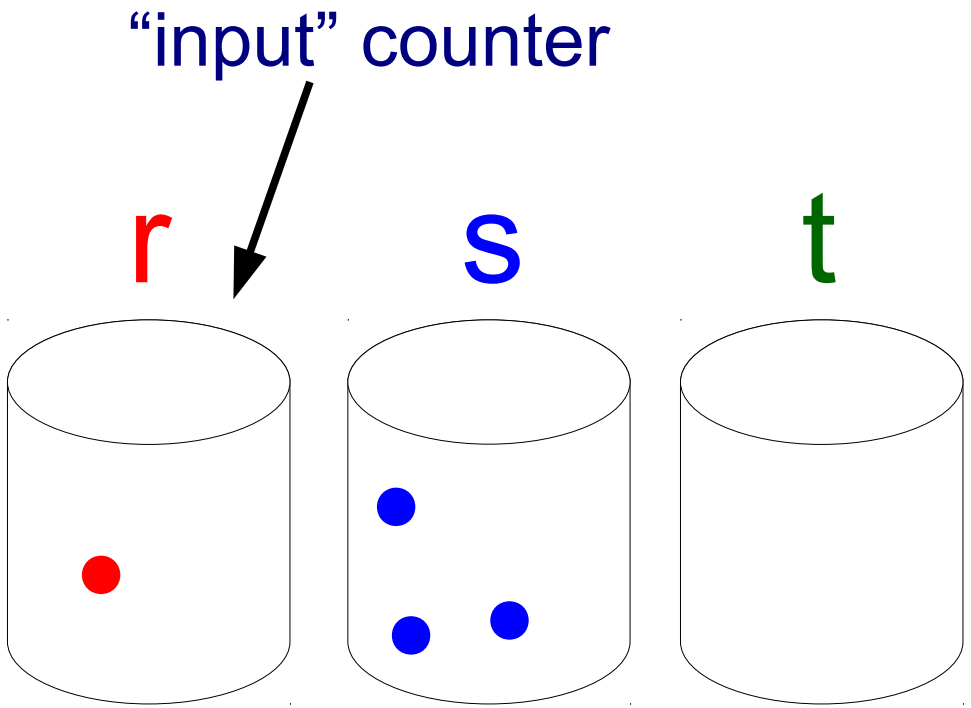

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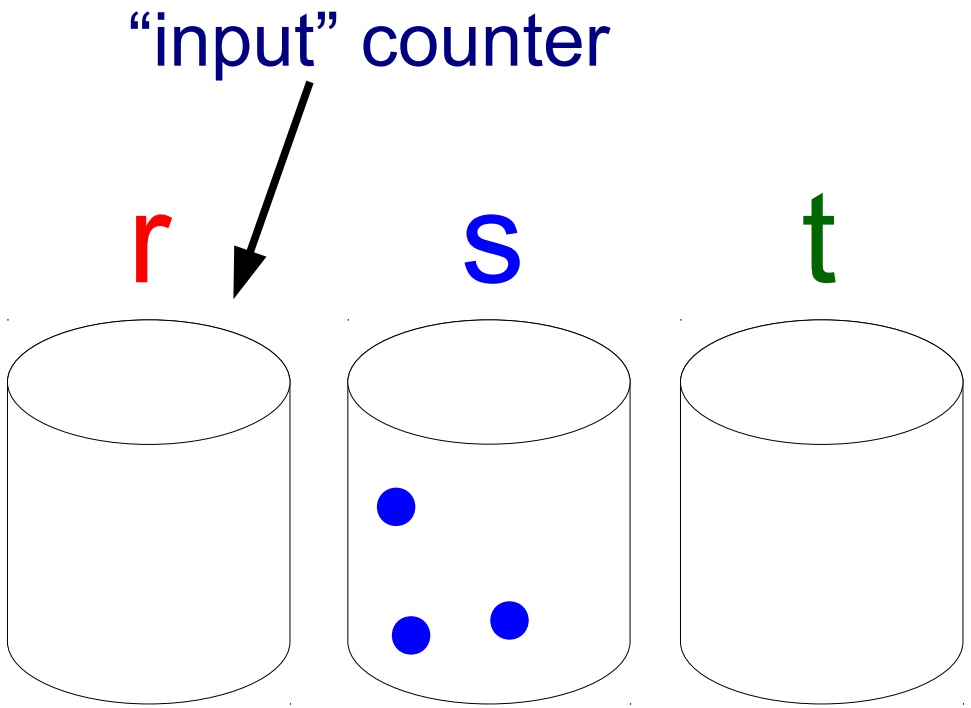

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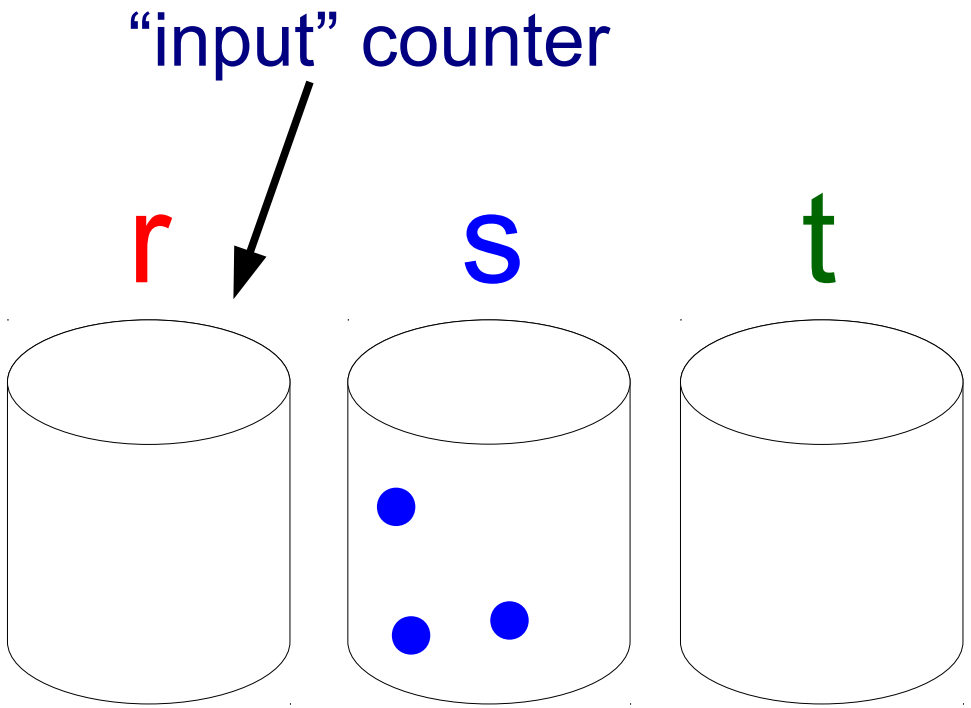

Counter (register) machine

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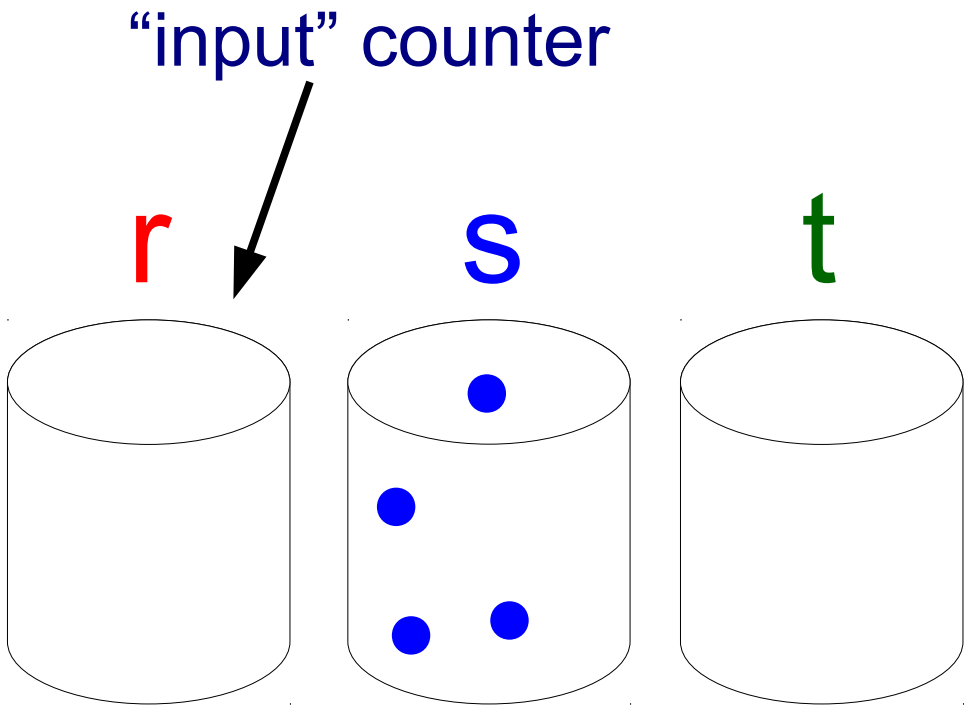

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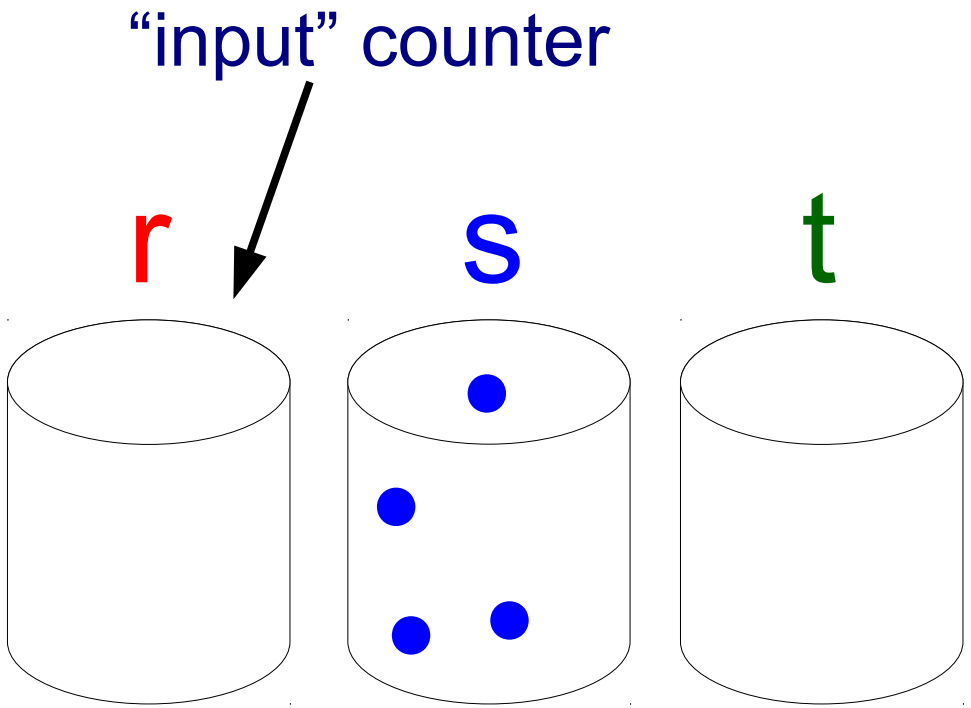

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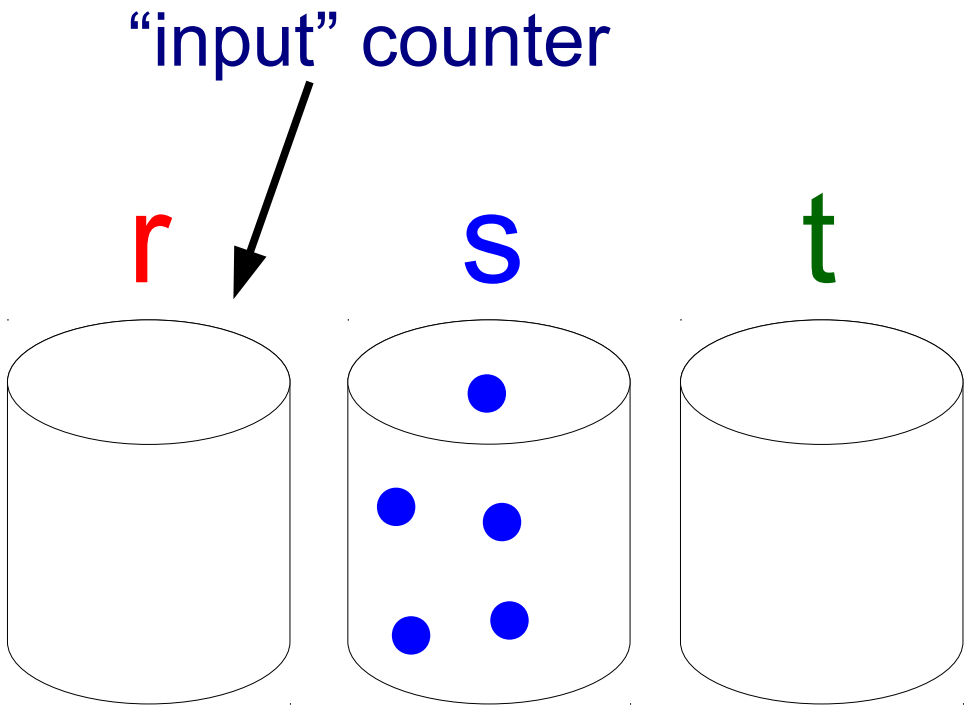

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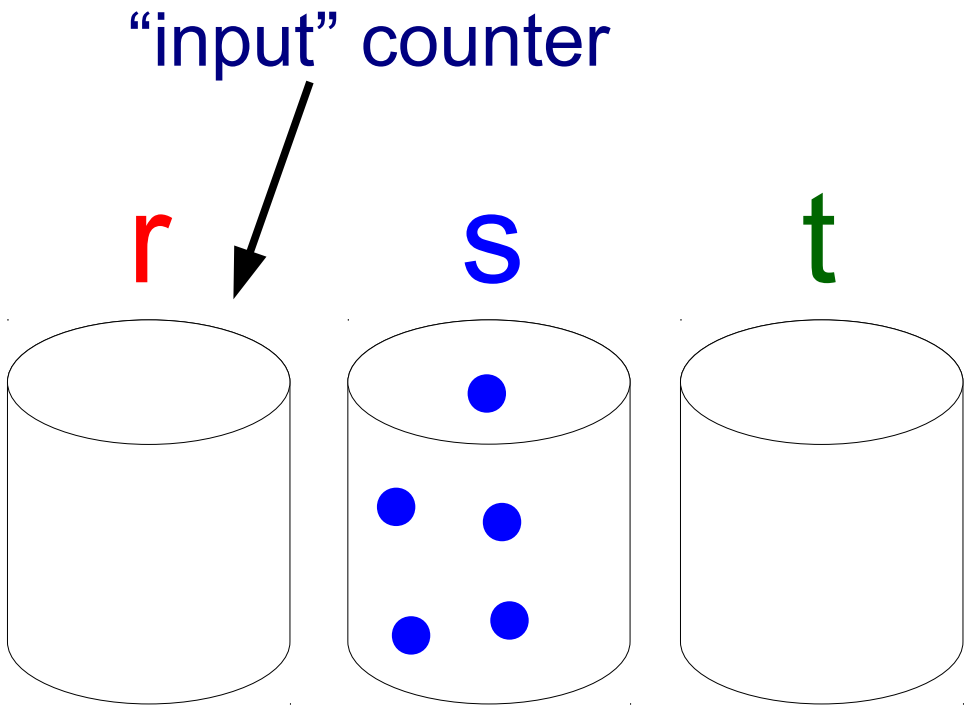

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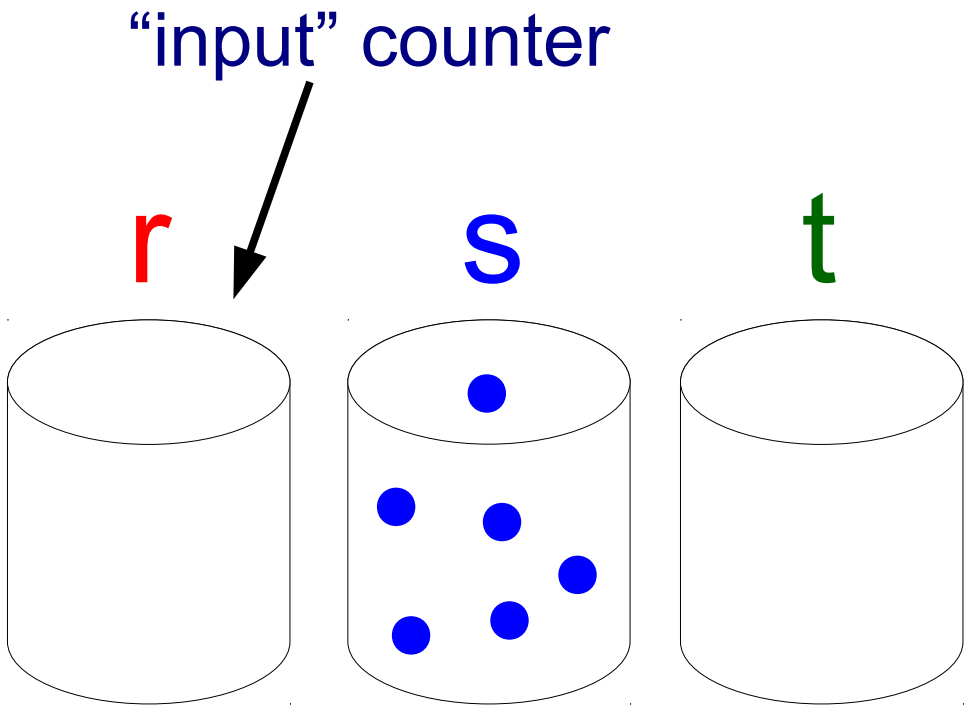

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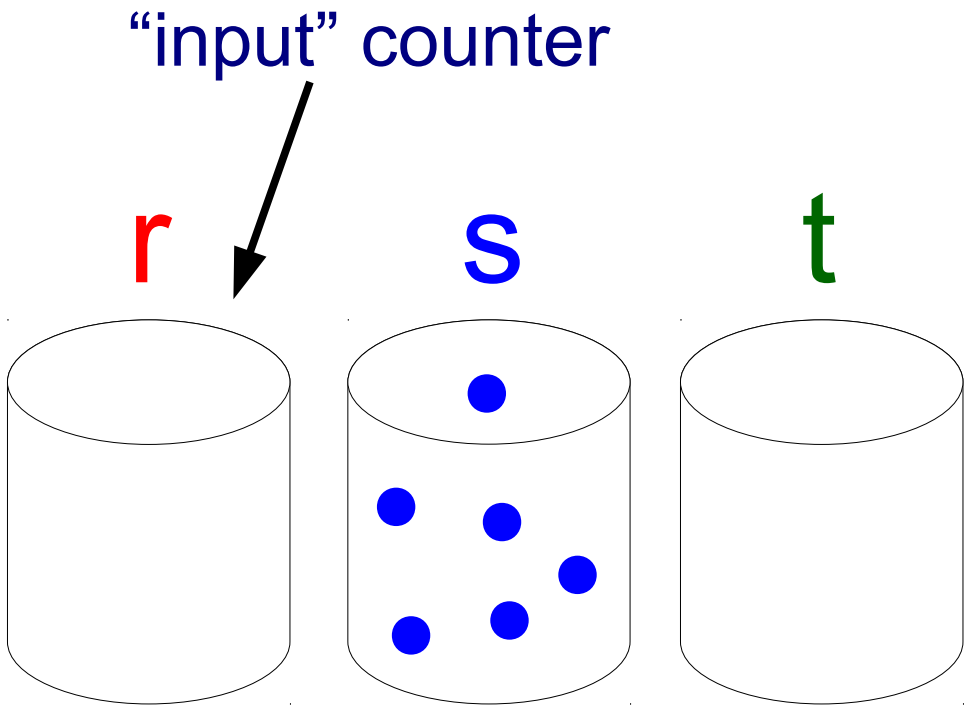

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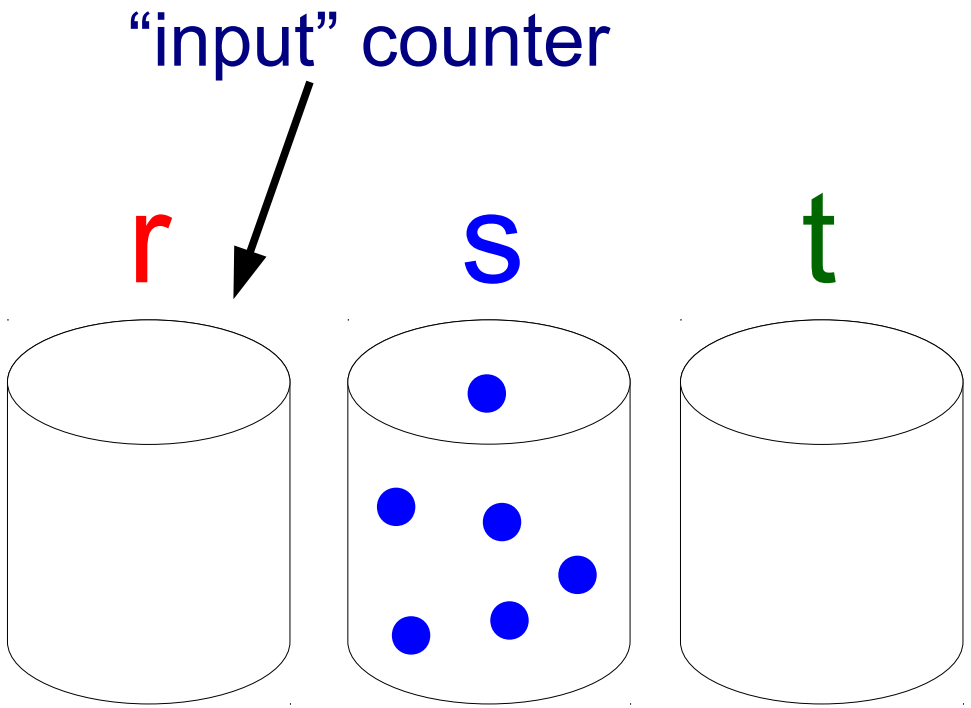

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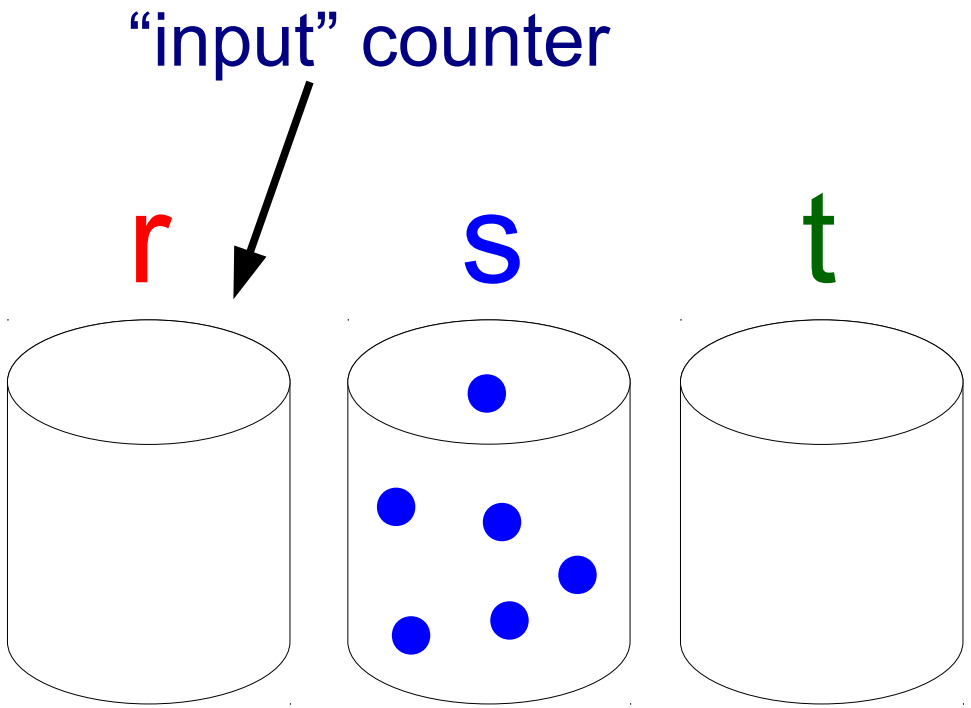

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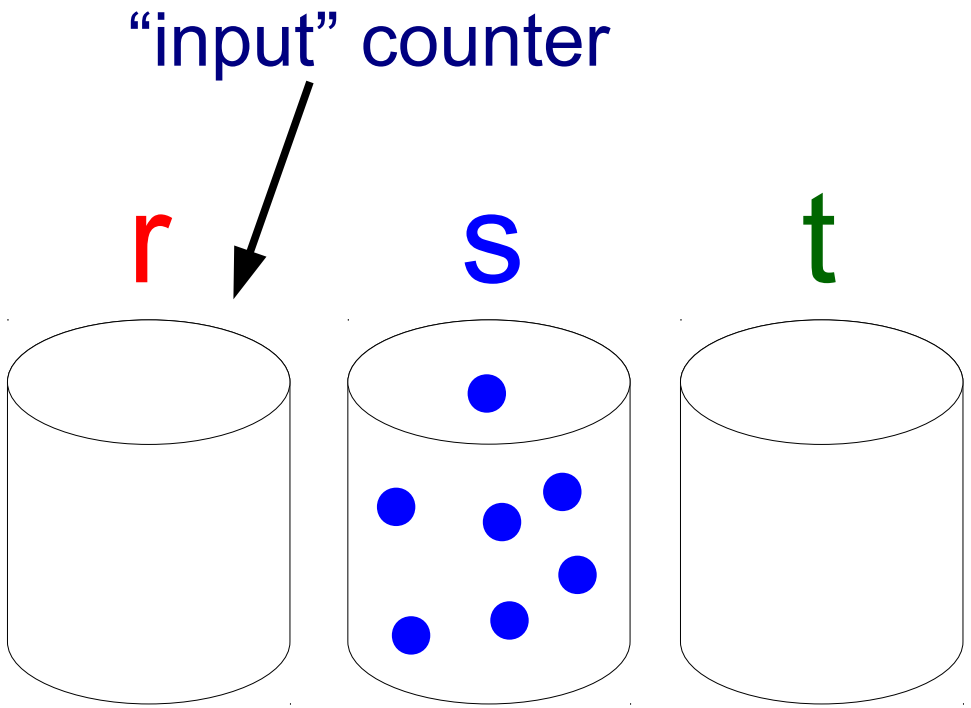

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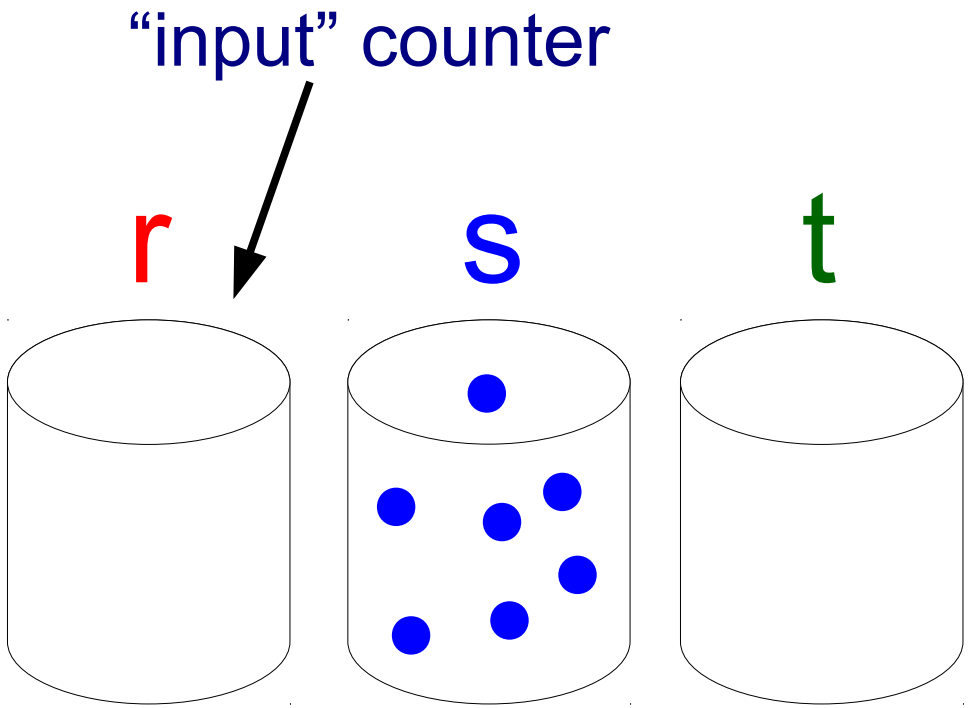

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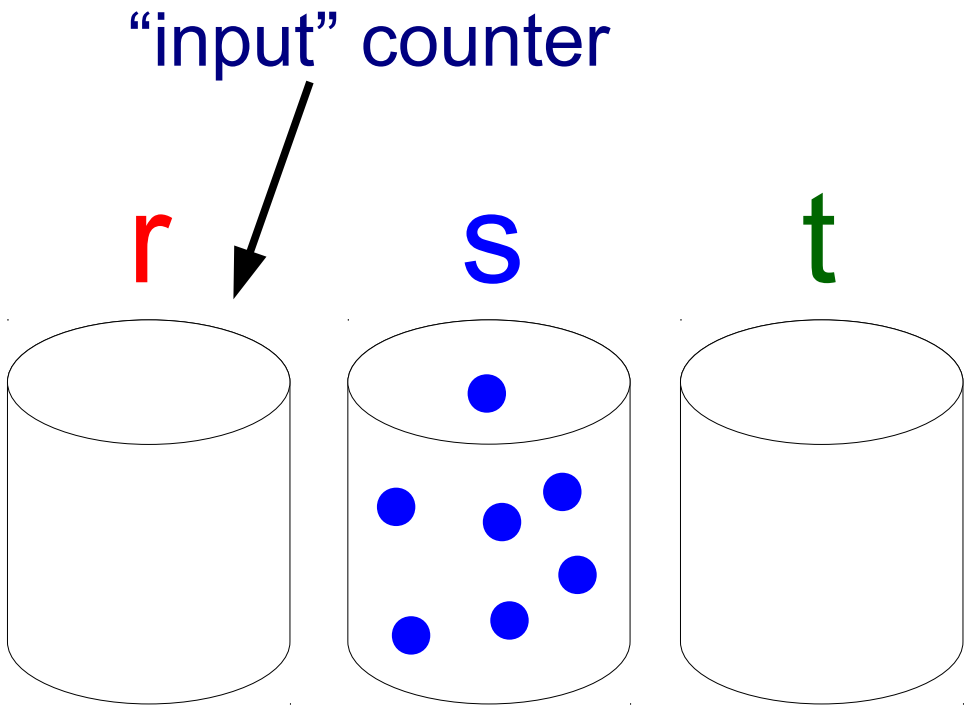

computes $f(n) = 3n+1$

CRNs can simulate counter machines with probability < 1

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Counter machine:

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initial state $\{n\ R, 1\ L_1\}$

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$$L_3 \rightarrow L_4 + S$$

$$L_4 + S \rightarrow L_5 \ ; \ L_4 \rightarrow L_2$$

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Need to be **very** slow!

How to slow down reaction $L_2 \rightarrow L_1$?

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1 C_1, 1 F, n B

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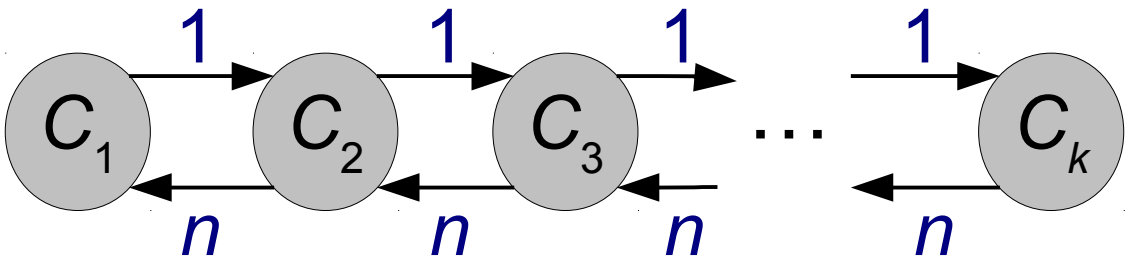

reverse-biased random walk

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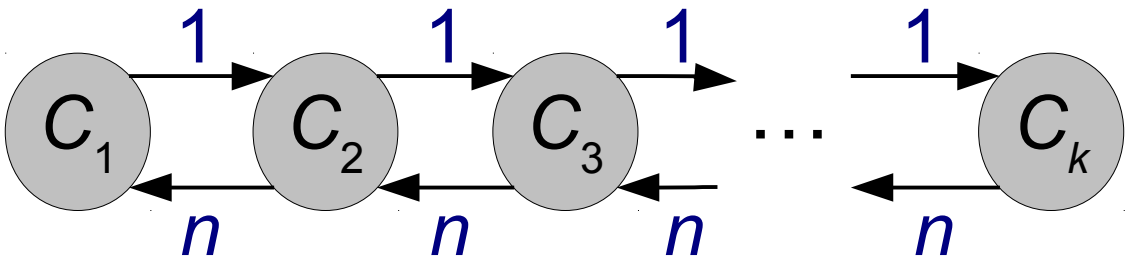

reverse-biased random walk

C_k appears after expected time $\approx n^{k-1}$

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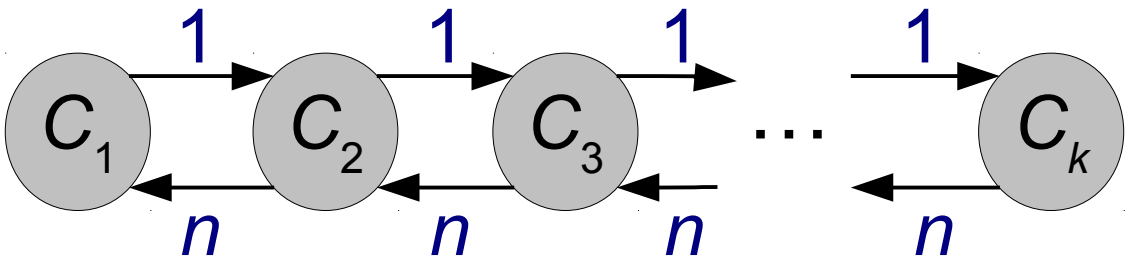

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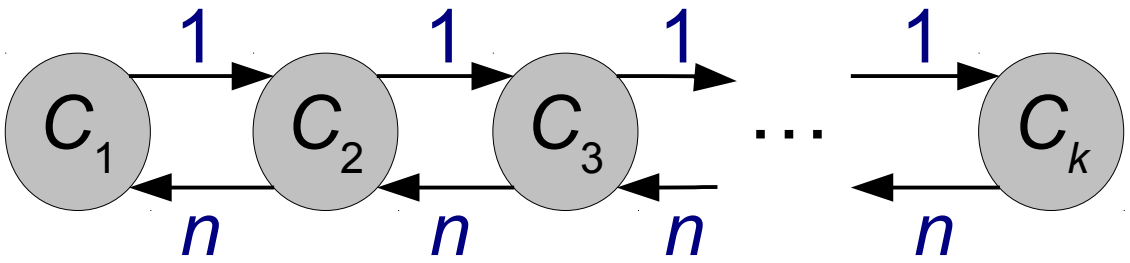

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reverse-biased random walk

E[time for $L_2 + R \to L_3$] $\leq n$

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initial state $\{1Y, 1N\}$

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- Errr... isn't that stable computation?
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Consider... $Y \xrightarrow{2} 2Y$, $Y \xrightarrow{1}$ initial state $\{1Y, 1N\}$

Theorem: All (Turing) computable predicates can be computed by a CRN with probability 1.

(Cummings, Doty, Soloveichik, DNA 2014)