# Controlling a population

Nathalie Bertrand

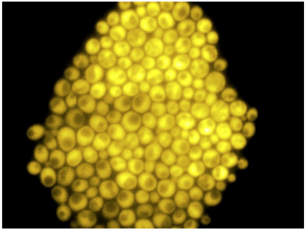
Inria Rennes

**joint work with Miheer Dewaskar (ex CMI student), Blaise Genest (IRISA) and Hugo Gimbert (LaBRI)**

Open Problems in Concurrency Theory, IST

# Motivation

## Control of gene expression for a population of cells



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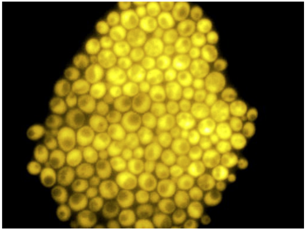

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- drug injections affect all cells
- response varies from cell to cell
- obtain a large proportion of cells with desired gene expression level

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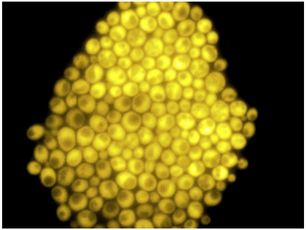

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- arbitrary nb of components
- full observation
- uniform control
- MDP model for single cell
- global quantitative reachability objective

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- population of $N$ identical MDP $\mathcal{M}$
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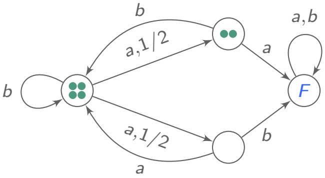


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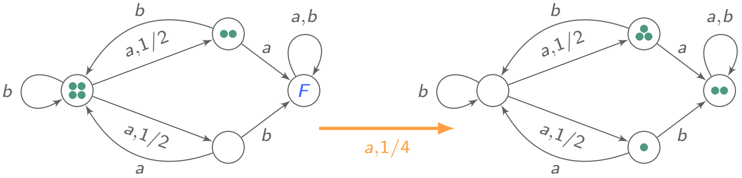


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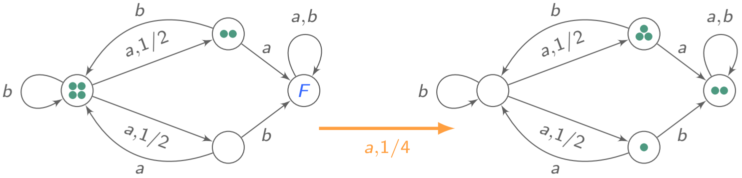


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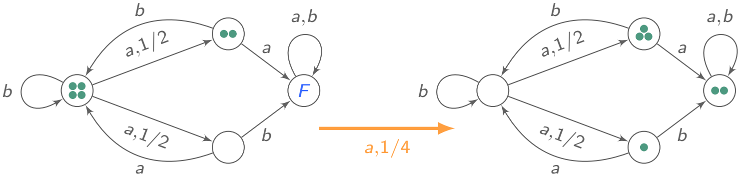


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$$\forall N \max_{\sigma} \mathbb{P}_{\sigma}(\mathcal{M}^N \models \Diamond \text{ at least 80\% of MDPs in F }) \geq .7?$$

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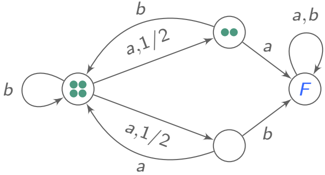


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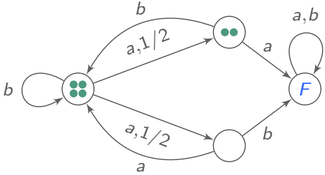


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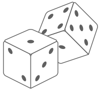

probabilities

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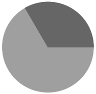

proportions

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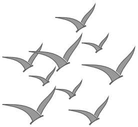

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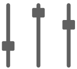

control

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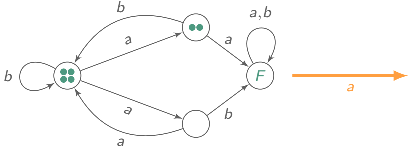


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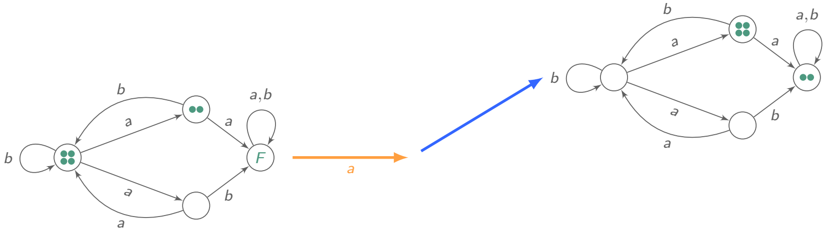


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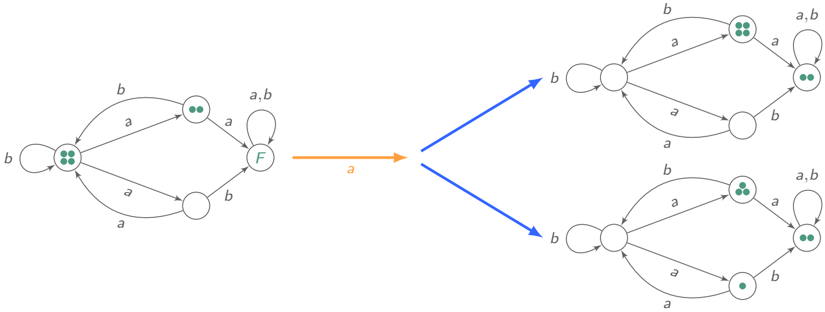


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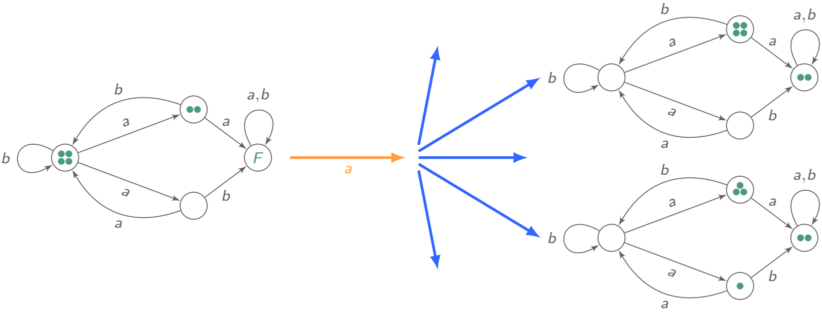


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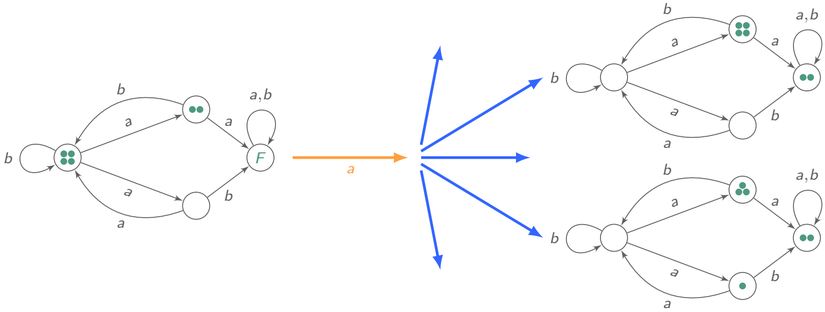


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**Question** can one control the population to ensure that for all non-deterministic choices all NFAs simultaneously reach a target set?

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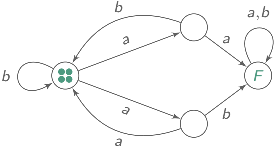


$\forall N \; \exists \sigma \; \forall \tau \; (\mathcal{A}^N, \sigma, \tau) \models \Diamond F^N$?

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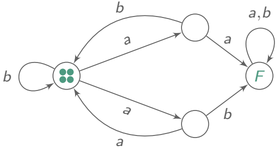


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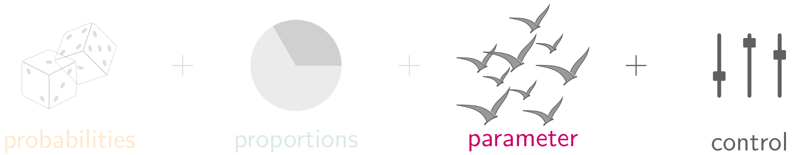

# Monotonicity property and cutoff

Monotonicity property: the larger $N$, the harder for controller

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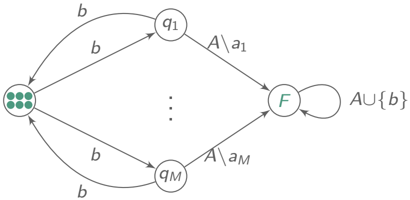


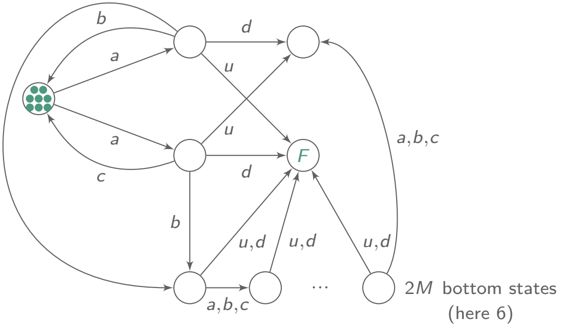

$A = \{a_1, \cdots, a_M\}$
unspecified edges lead to a sink state

winning $\sigma$ if $N < M$
play $b$ then $a_i$ s.t. $q_i$ is empty

winning $\tau$ for $N = M$
always fill all $q_i$'s

cutoff is $M$

# Lower bound on the cutoff




- $\forall N \leq 2^M,\ \exists \sigma,\ \mathcal{A}^N \models \forall_\sigma \Diamond F^N$
  accumulate copies in bottom states, then $u/d$ to converge
- for $N > 2^M$ controller cannot avoid reaching the sink state

Cutoff $\mathcal{O}(2^{|\mathcal{A}|})$

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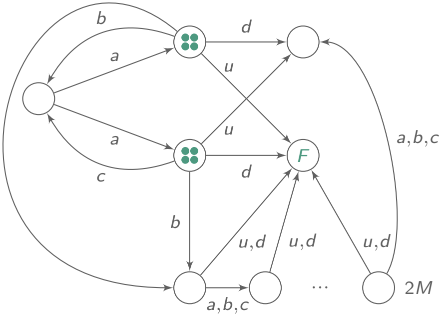


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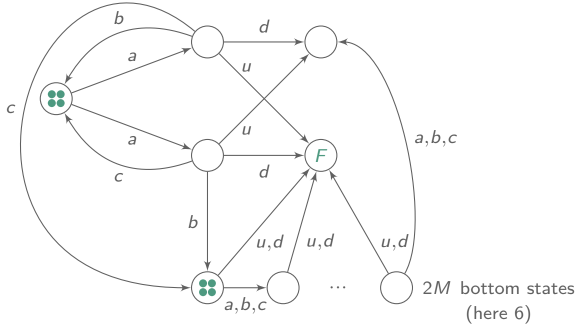


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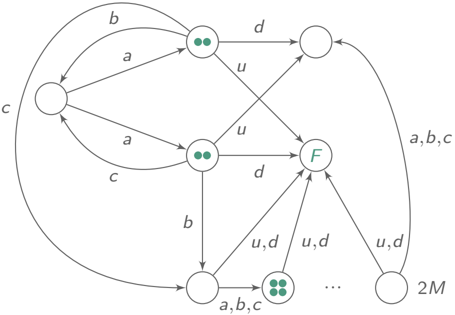


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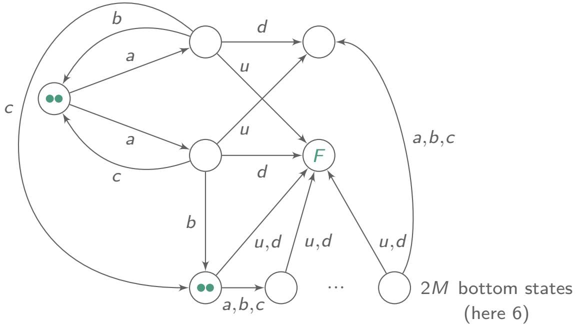


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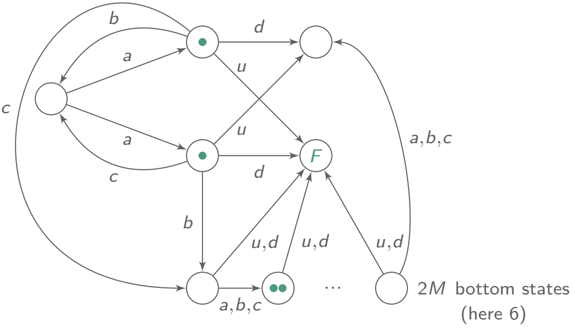


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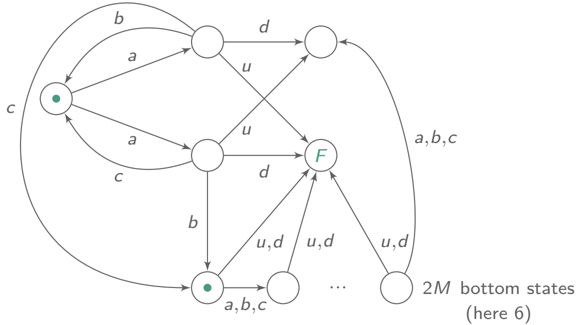


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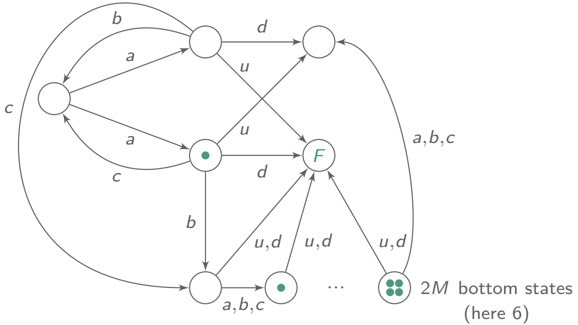


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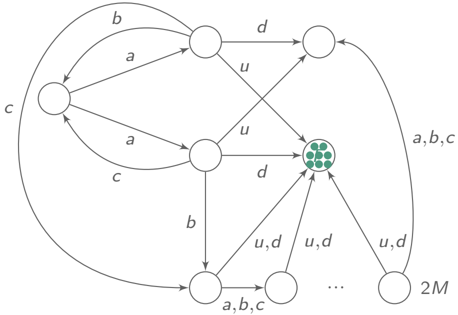


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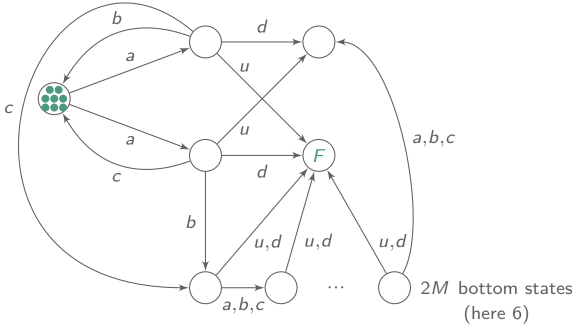


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Combined with a counter, cutoff is even doubly exponential!

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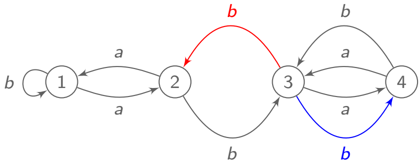


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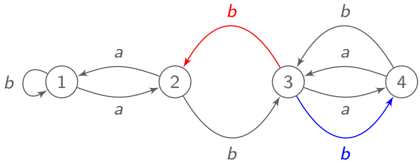


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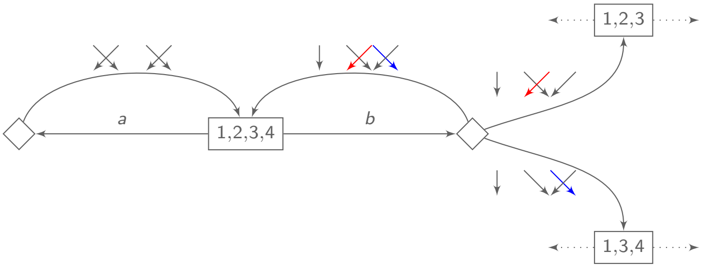

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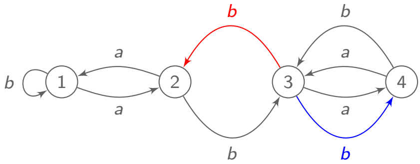


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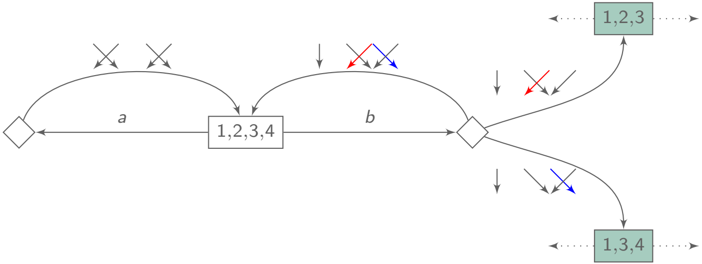
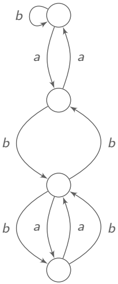
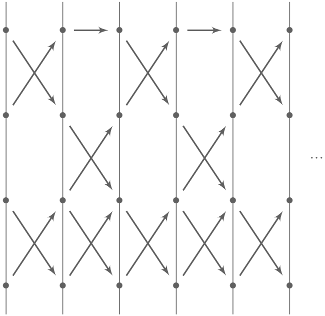



If Eve wins support game then controller has a winning strategy for all $N$

# Support game is not equivalent to population game

- controller alternates $a$ and $b$ ;
- adversary always fills $q_2$ and $q_4$ in the $b$-step



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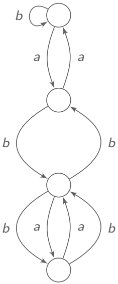


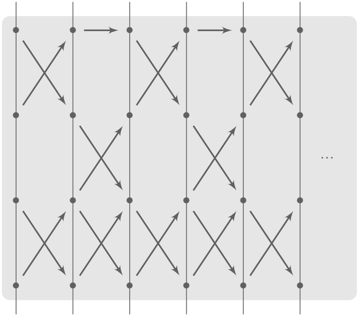

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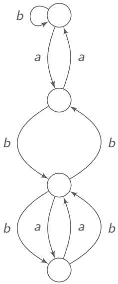


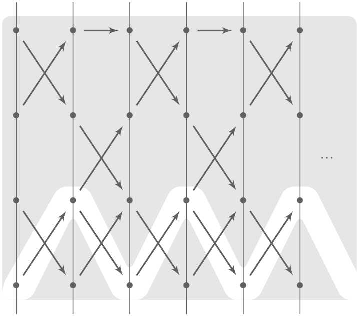

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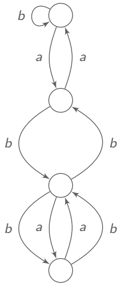


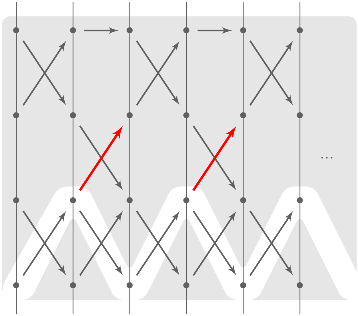

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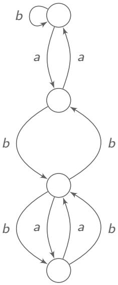


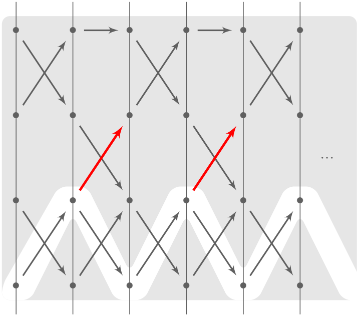


Play in support game is not realisable: Controller wins with $(ab)^\omega$!

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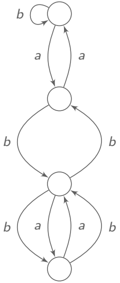
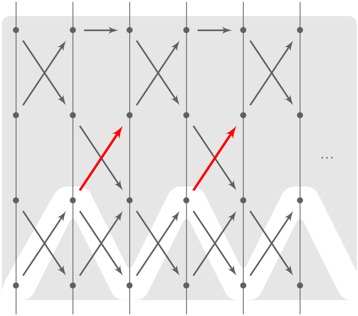
- controller alternates $a$ and $b$ ;
- adversary always fills $q_2$ and $q_4$ in the $b$-step



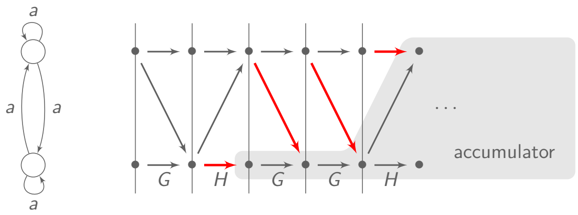




Play in support game is not realisable: Controller wins with $(ab)^\omega$!

Memoryless support-based controllers are not enough!

Exponential memory on top of support may even be needed.

# Capacity game: refining winning condition of support game



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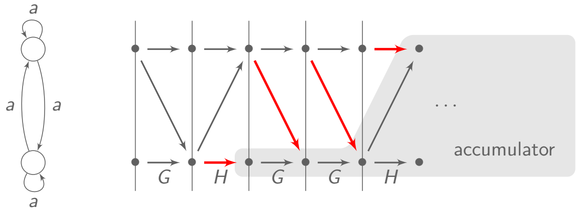


Finite capacity play: all accumulators have finitely many entries
Bounded capacity play: finite bound on # entries for accumulators

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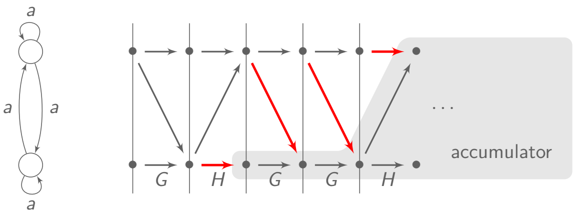


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- corresponds to realizable plays
- does not seem to be regular

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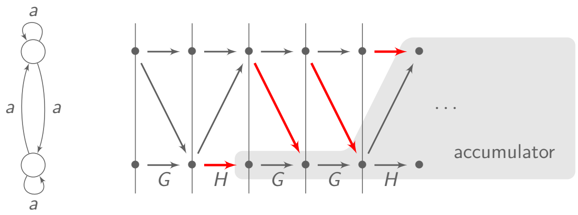


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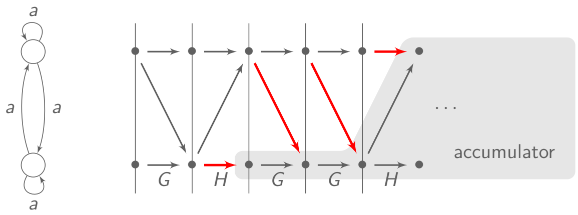


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Capacity game: Eve wins a play if either it reaches a subset of $F$, or it does not have finite capacity.

Eve wins capacity game iff Controller has a winning strategy for all $N$

# Solving the capacity game

## Naive solution

- set of plays with infinite capacity is $\omega$-regular
  non-deterministic Büchi automaton guesses an accumulator, and checks it has infinitely many entries
- winning condition can be determinized into parity condition
  exponential blowup

# Solving the capacity game

Naive solution 2EXPTIME procedure in the size of NFA $\mathcal{A}$

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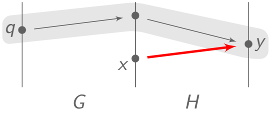
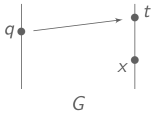
**Naive solution** 2EXPTIME procedure in the size of NFA $\mathcal{A}$

**Better solution** EXPTIME procedure




$x \to y$ enters accumulator from $q$




$G$ separates pair $(t, x)$

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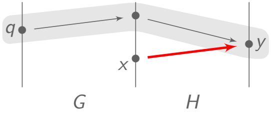


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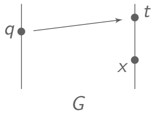


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Parity game:
capacity game enriched with list of separation graphs
priorities reflect how the list evolves

$\#$ states = (simply!) exponential in $|\mathcal{A}|$ $\#$ priorities = polynomial in $|\mathcal{A}|$

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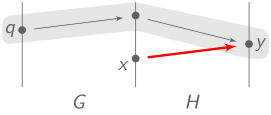


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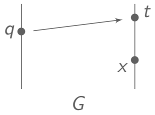


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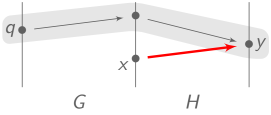


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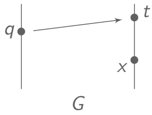


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Parity game is equivalent to capacity game.

**Theorem:**
The population control problem is EXPTIME-complete.

# Summary of results

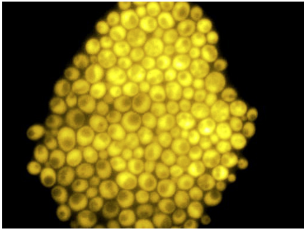
Uniform control of a population of identical NFA

- parameterized control problem: gather all copies in $F$
- (surprisingly) quite involved!
- tight results for complexity, cutoff, and memory
  - complexity: EXPTIME-complete decision problem
  - bound on cutoff: doubly exponential
  - memory requirement: exponential memory (orthogonal to supports) is needed and sufficient for controller

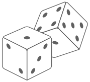
To appear at Concur'17

# Back to motivations

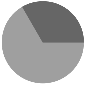
**Control of gene expression for a population of cells**



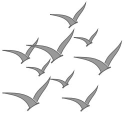
credits: G. Batt



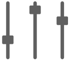
probabilities



proportions



parameter



control

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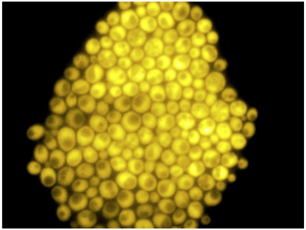

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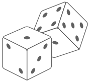

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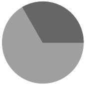

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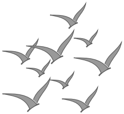

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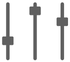

control

- need for truely probabilistic model
  $\rightarrow$ MDP instead of NFA
- need for truely quantitative questions
  $\rightarrow$ proportions and probabilities instead of sure convergence

$$\forall N \max_{\sigma} \mathbb{P}_{\sigma}(\mathcal{M}^N \models \Diamond \text{ at least 80\% of MDPs in } F \,) \geq .7?$$

Thanks!