Controlling a population of identical NFA

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Inria Rennes

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

LSV 20th anniversary

Back in 2004-2006

Back in 2004-2006

Cheesecake (Tali)
Preparation : 30 min Cuisson: 1h
Ingredients :
une quinzaine de petits beurres (ou de speculoos, ou de vos biscuits secs preferes)
50g de beurre fondu
une pincee de cannelle
500g de creamcheese (si vous n'en trouvez pas, ce qui est probable, utilisez du kiri eventuellement melange a quelques petits suisses)
150g de sucre
1 sachet de sucre vanille (ou 2 pour melanger avec la creme aigre - voir plus bas)
2 cuilleres a soupe de jus de citron
3 oeufs
20cl de creme aigre (si vous n'en trouvez pas, utilisez de la creme fraiche + jus de citron) - facultatif

Prechauffez le four thermostat 5-6. Reduisez les petits beurres en miettes, puis ajoutez le beurre fondu et la cannelle. Chemisez-en un moule (idealement un moule a manque a fond amovible) en pressant bien pour que ca adhere. Reservez au frais.
Mixez a petite vitesse le cream cheese (ou la mixture de substitution de votre choix) ramene a temperature ambiante. Une fois que le melange est homogene, incorporez le sucre, 1 sachet de sucre vanille et le jus de citron et continuez a mixer lentement. Ajoutez ensuite les oeufs un a un et mixez jusqu'a ce que tout soit bien incorpore (mais pas plus). Versez la preparation dans le moule et mettez au four. Normalement, la cuisson se fait au bain-marie, mais ce n'est pas obligatoire. J'ai mis une heure de temps de cuisson mais ca depend beaucoup de l'epaisseur de garniture que vous avez - disons que c'est entre 30 minutes et 1h. Le gateau est cuit quand le centre n'est pas encore tout a fait pris. Si le gateau brunit au cours de la cuisson, couvrez d'aluminium. Une fois que c'est cuit, laissez refroidir completement.
Facultatif : Pendant ce temps, melangez le 2eme sachet de sucre vanille avec la creme aigre et etalez sur le gateau completement froid. Remettez a cuire 5 min a four 7-8 prechauffe.
Reservez au frais minimum 4h (c'est mieux toute la nuit).
Au moment de servir, retirez le cercle du moule si vous pouvez. Vous pouvez servir avec un coulis de fruits rouges, ou deposer sur le dessus des fruits frais (fraises, framboises).

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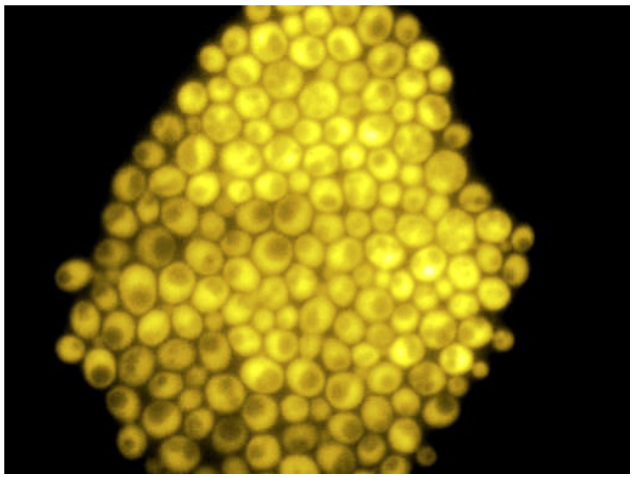
LSV = Loisirs Sport Vacances

Motivation

Control of gene expression for a population of cells



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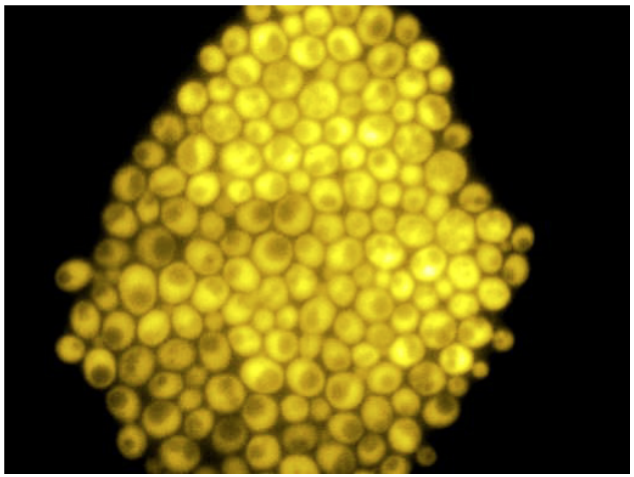

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- gene expression monitored through fluorescence level
- drug injections affect all cells
- response varies from cell to cell
- obtain a large proportion of cells with desired gene expression level

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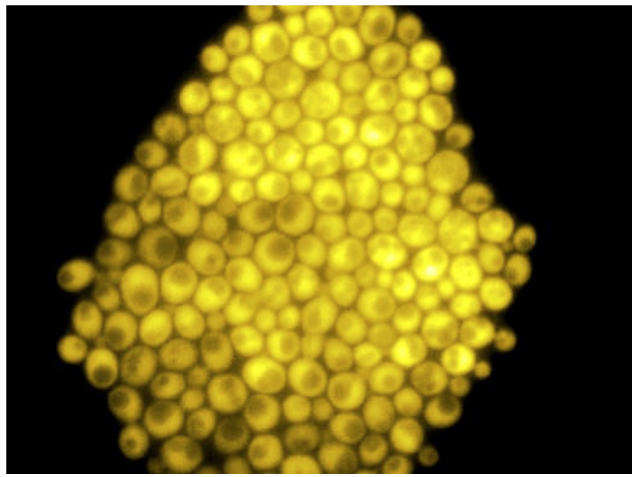

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- cell population
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- arbitrary nb of components
- full observation

- uniform control
- NFA model for single cell
- global reachability objective

Problem formalisation

- population of N identical NFA
- uniform control policy under full observation
- resolution of non-determinism by an adversary

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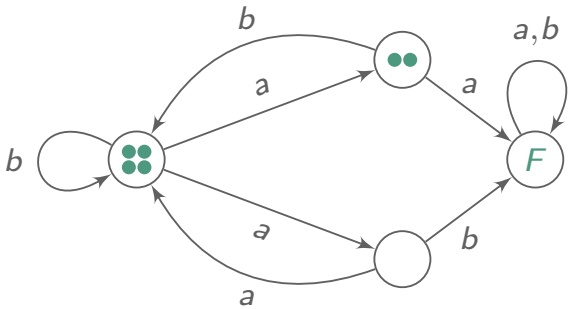

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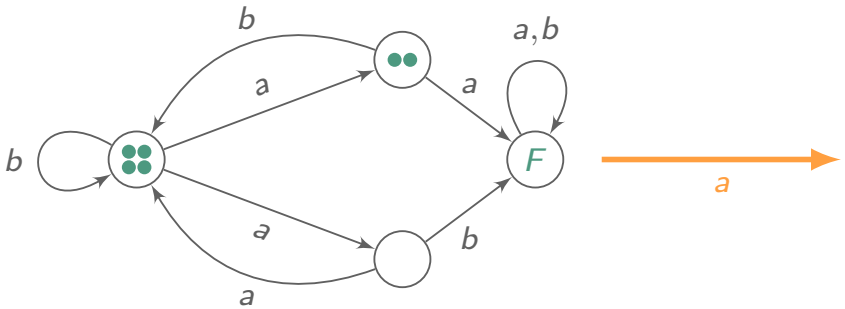

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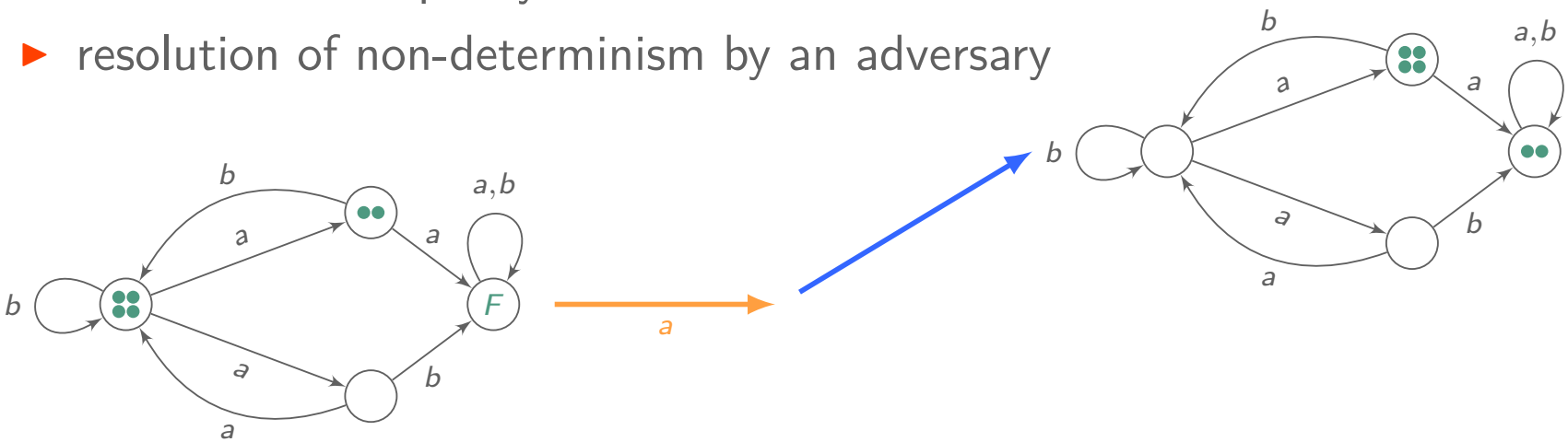

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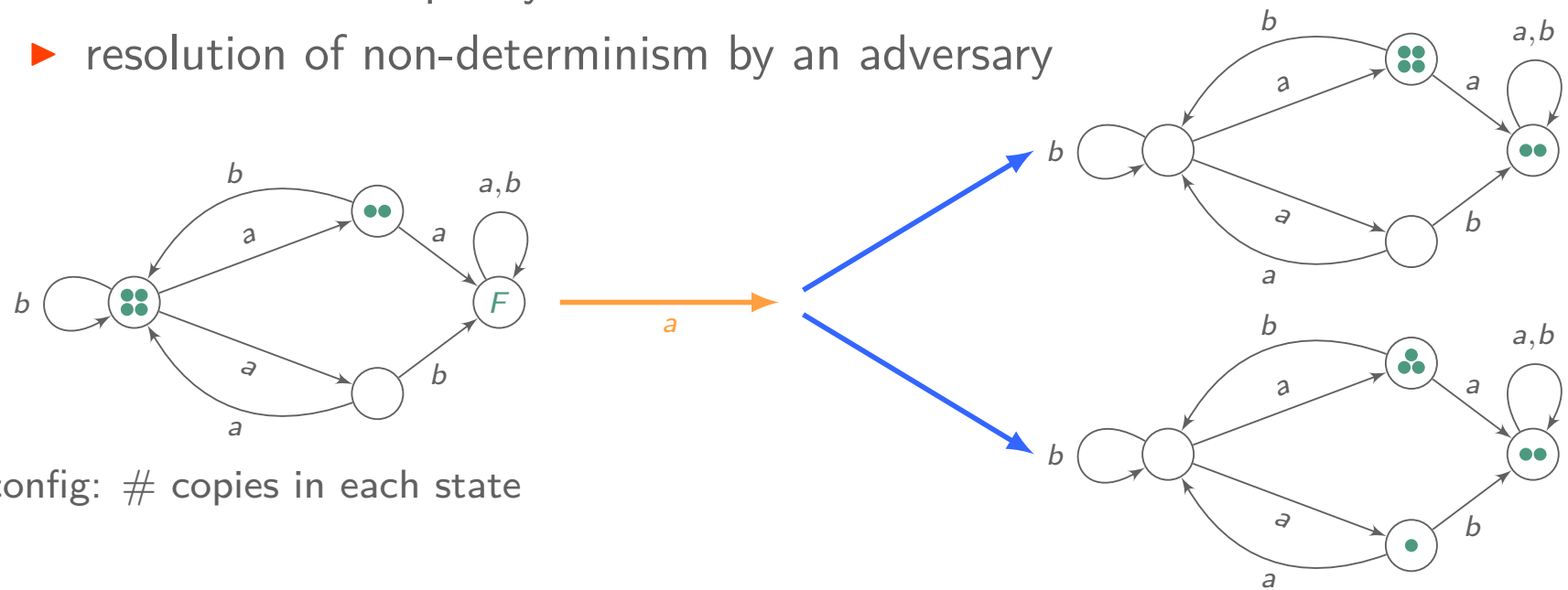

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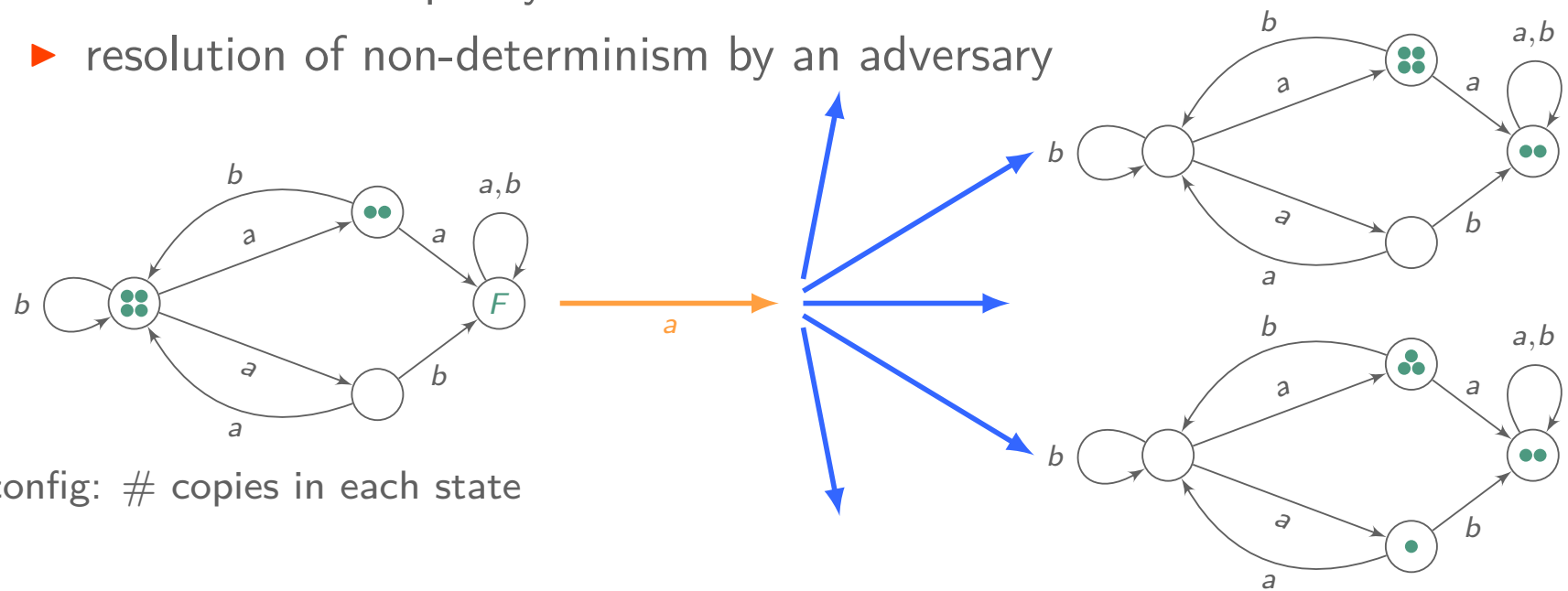

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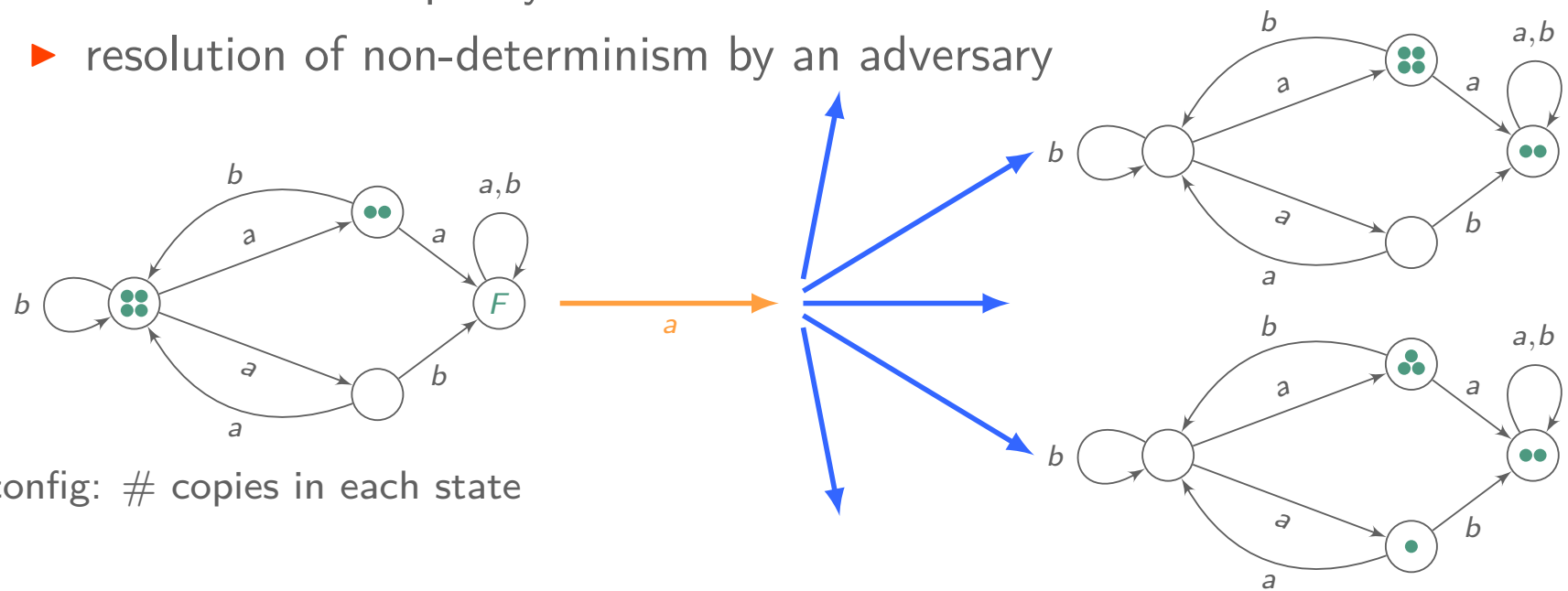

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Question can one control the population to ensure that for all non-deterministic choices all NFAs simultaneously reach a target set?

Population control

Fixed N: build finite 2-player game, identify global target states, decide if controller has a winning strategy for a reachability objective

Challenge: **Parameterized control**

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

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This talk

- decidability and complexity
- memory requirements for controller σ
- admissible values for N

Monotonicity property and cutoff

Monotonicity property: the larger N, the harder for controller

$$\exists \sigma \ \forall \tau (\mathcal{A}^N, \sigma, \tau) \models \Diamond F^N \quad \Longrightarrow \quad \forall M \leq N \ \exists \sigma \ \forall \tau (\mathcal{A}^M, \sigma, \tau) \models \Diamond F^M$$

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Cutoff: smallest N for which controller has no winning strategy

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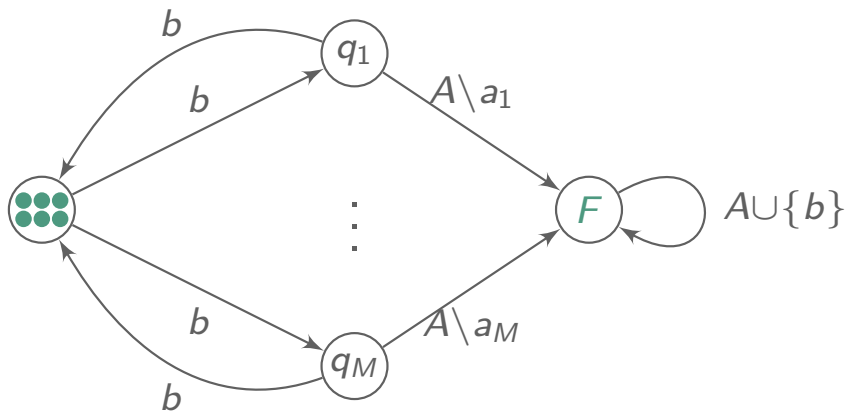


$A = \{a_1, \cdots, a_M\}$

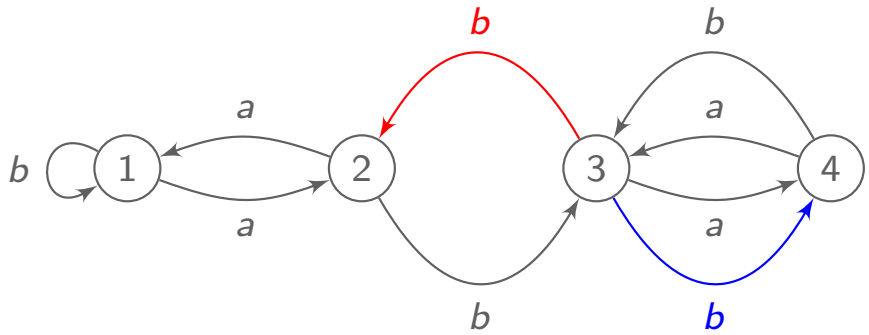
unspecified edges lead to a sink state

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

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

cutoff is M

A natural attempt: the support game



Assumption: if state q_2 or q_4 is empty, controller wins

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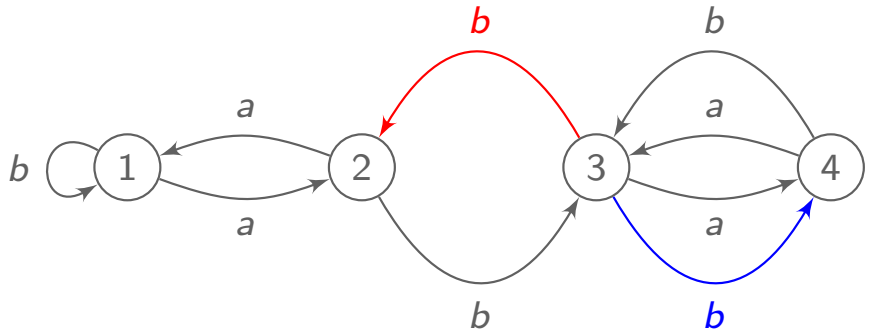

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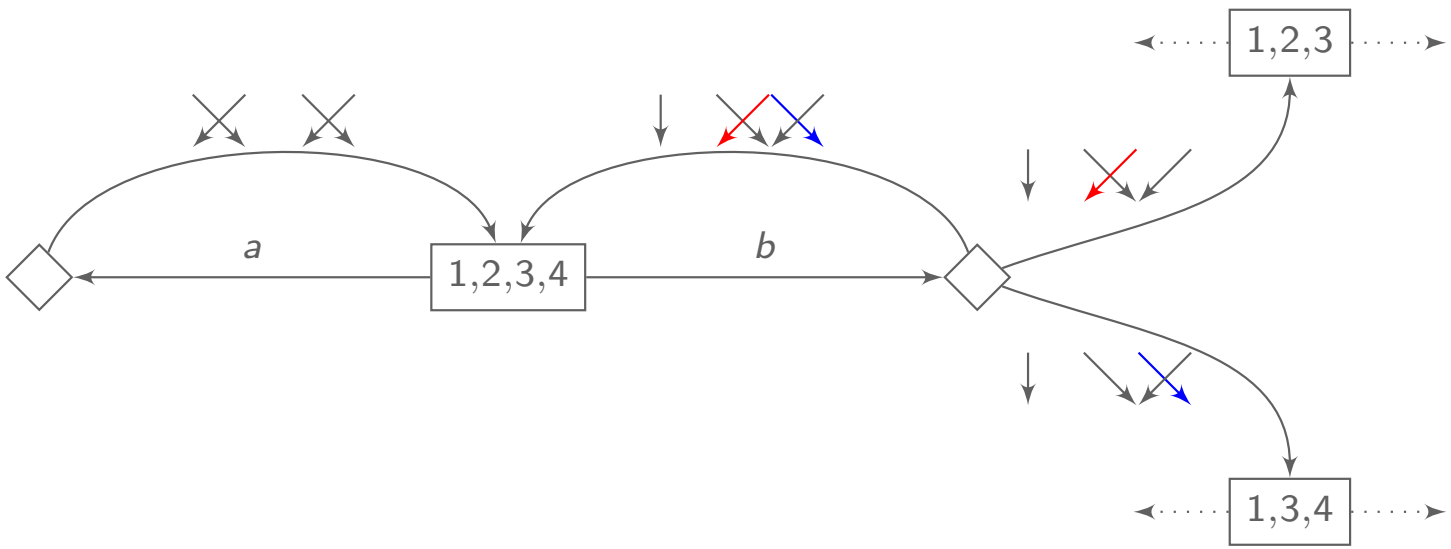
Support game: □ Eve chooses action

◇ Adam chooses transfer graph (footprint of copies' moves)



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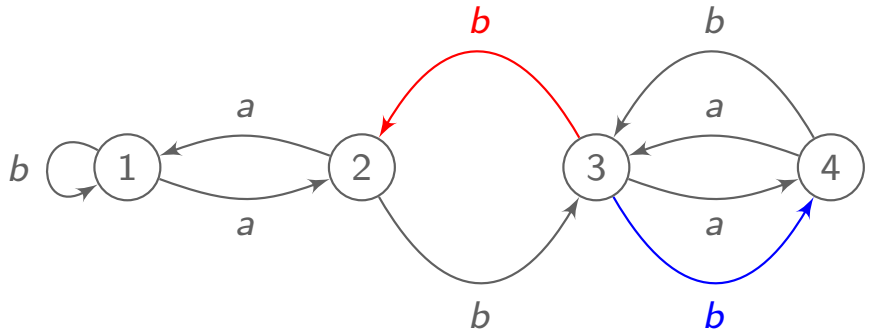

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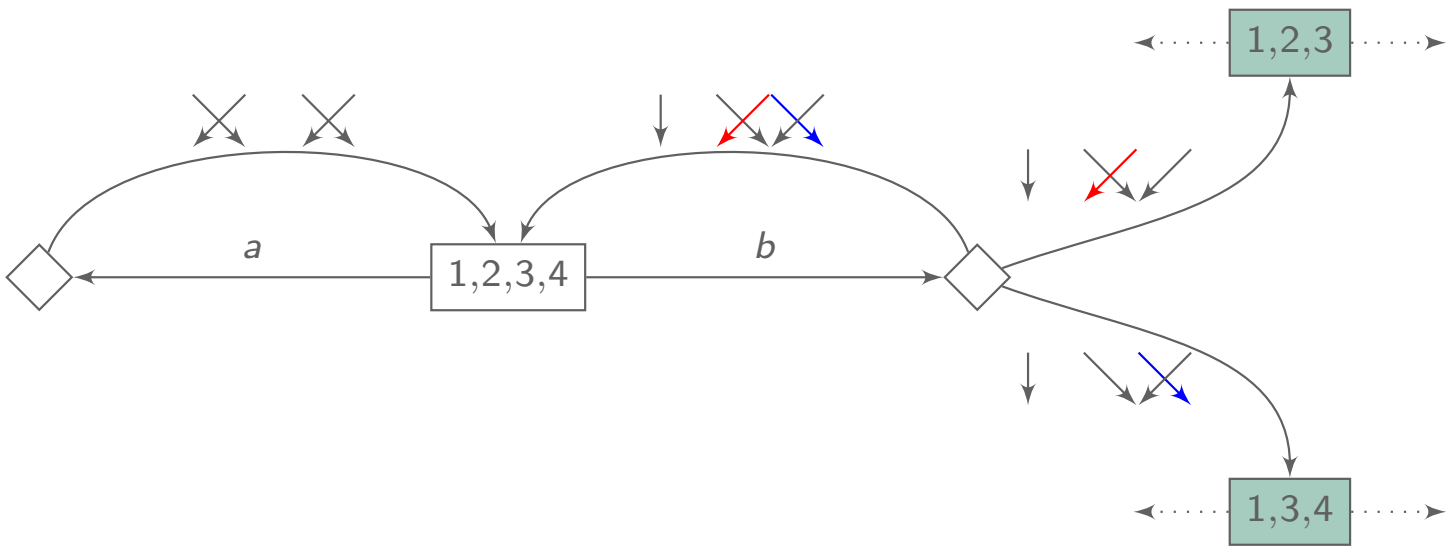
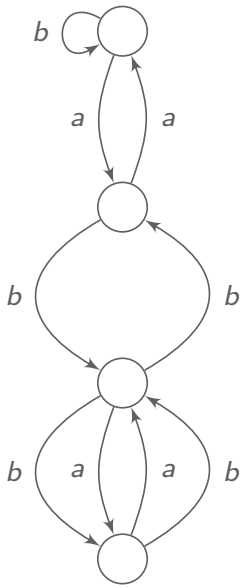
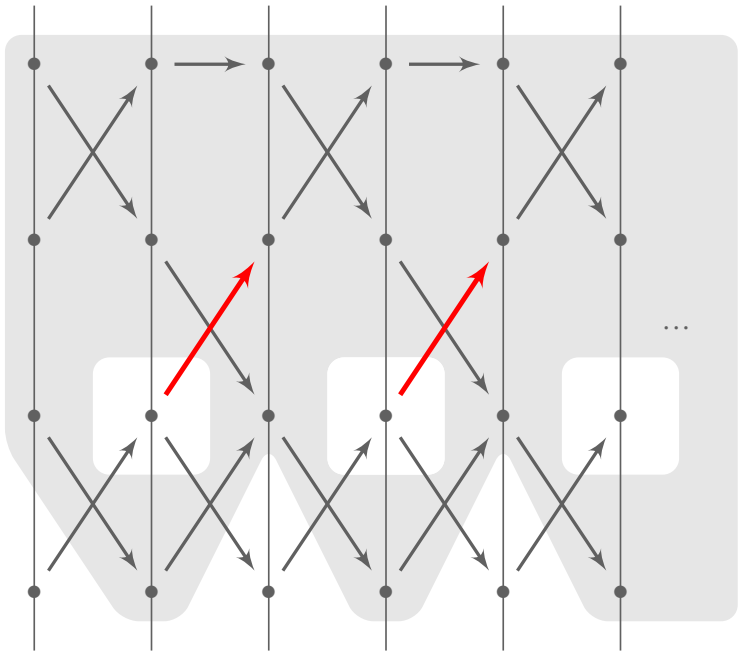


If Eve wins support game then controller has a winning strategy for all N

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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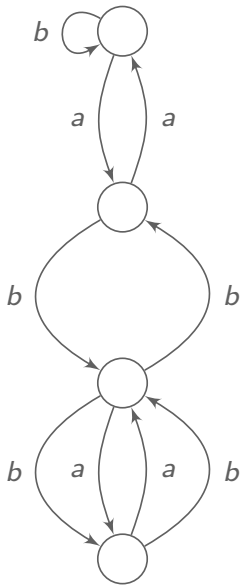

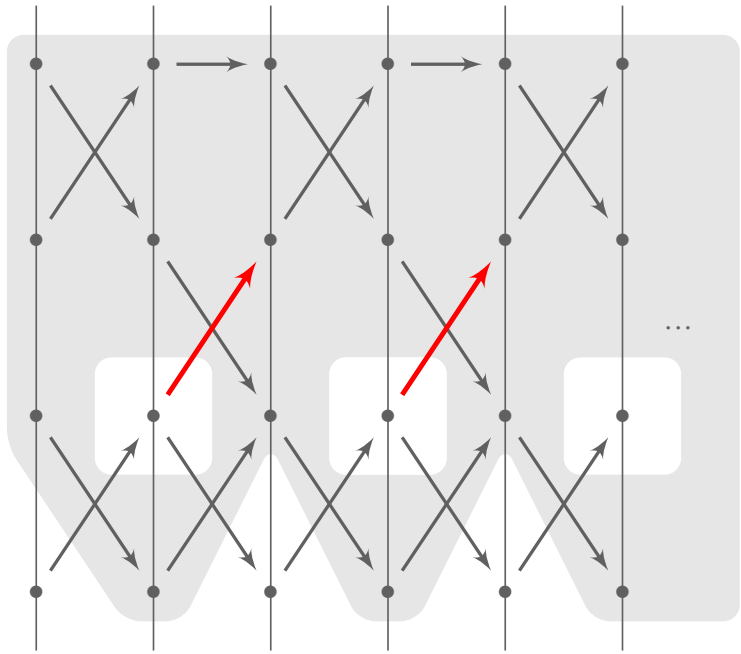

Play in support game is not realisable: Controller wins with $(ab)^\omega$!

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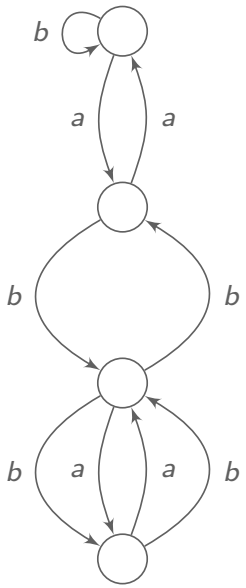

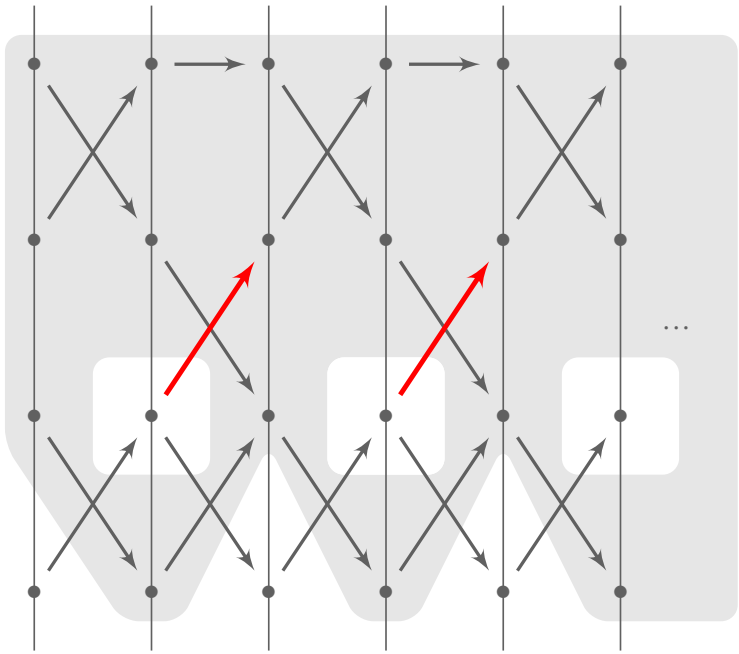

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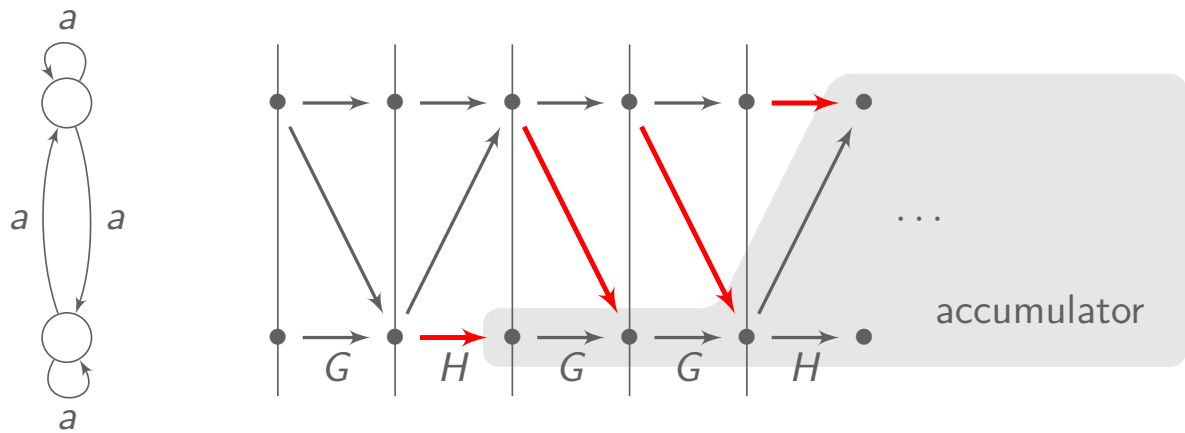
Memoryless support-based controllers are not enough!

Exponential memory on top of support may even be needed.

Capacity game: refining winning condition of support game



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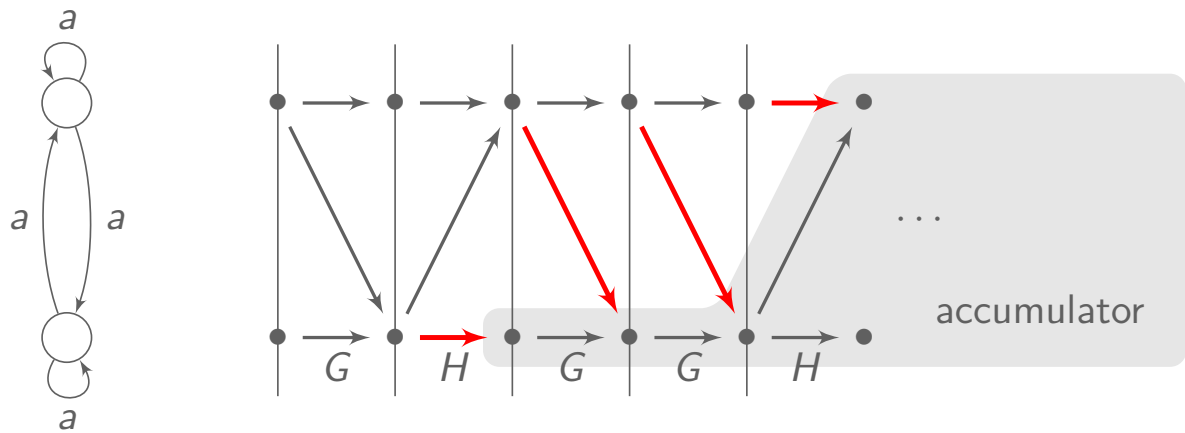

Finite capacity play: all accumulators have finitely many entries
Bounded capacity play: finite bound on # entries for accumulators

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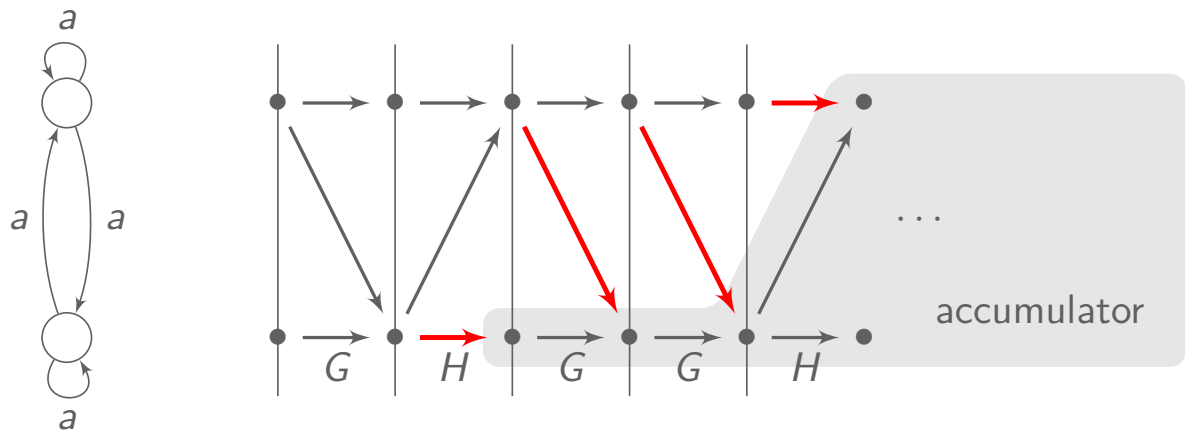

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Bounded capacity

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- does not seem to be regular

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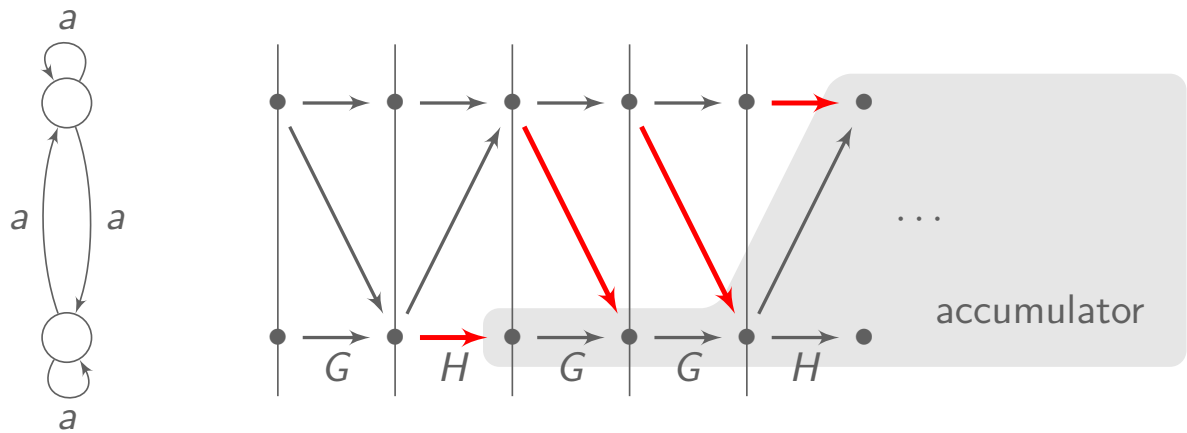

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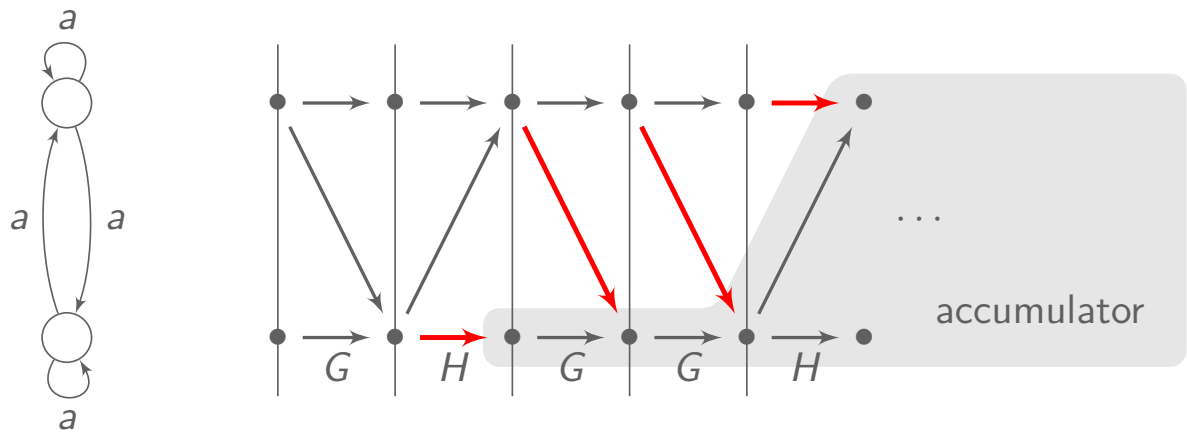

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Capacity game: Eve wins a play if either it reaches a subset of F, or it does not have finite capacity.

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 ω-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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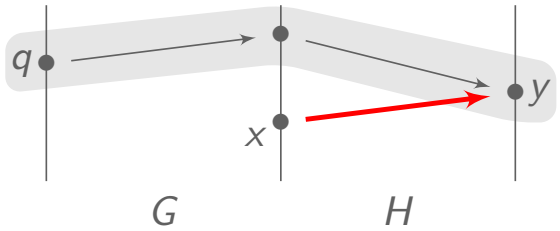
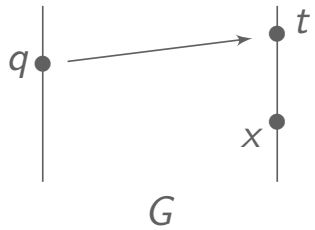
Better solution



$x \to y$ enters accumulator from q



G separates pair (t, x)

- entries arise from separated pairs
- tracking transfer graphs separating new pairs is sufficient

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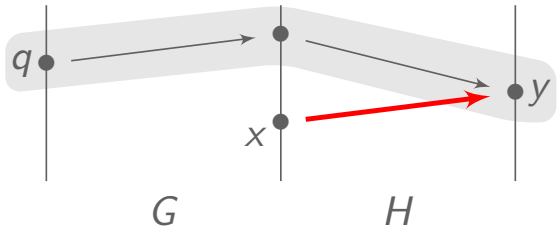

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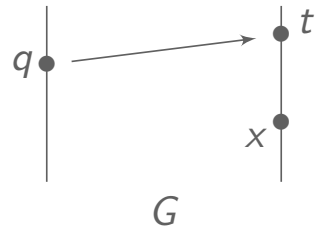


G separates pair (t, x)

- entries arise from separated pairs
- tracking transfer graphs separating new pairs is sufficient

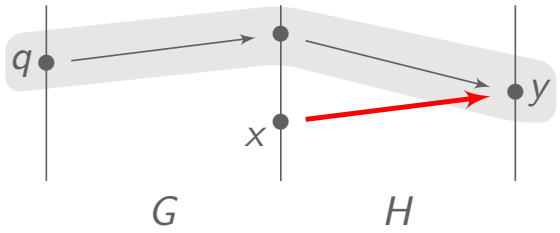
Parity game:
capacity game enriched with tracking lists in states
priorities reflect how the tracking list evolves (removals, shifts, etc.)

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

Solving the capacity game

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

Better solution



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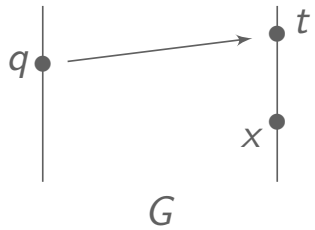

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Parity game is equivalent to capacity game.

Complexity of the population control problem

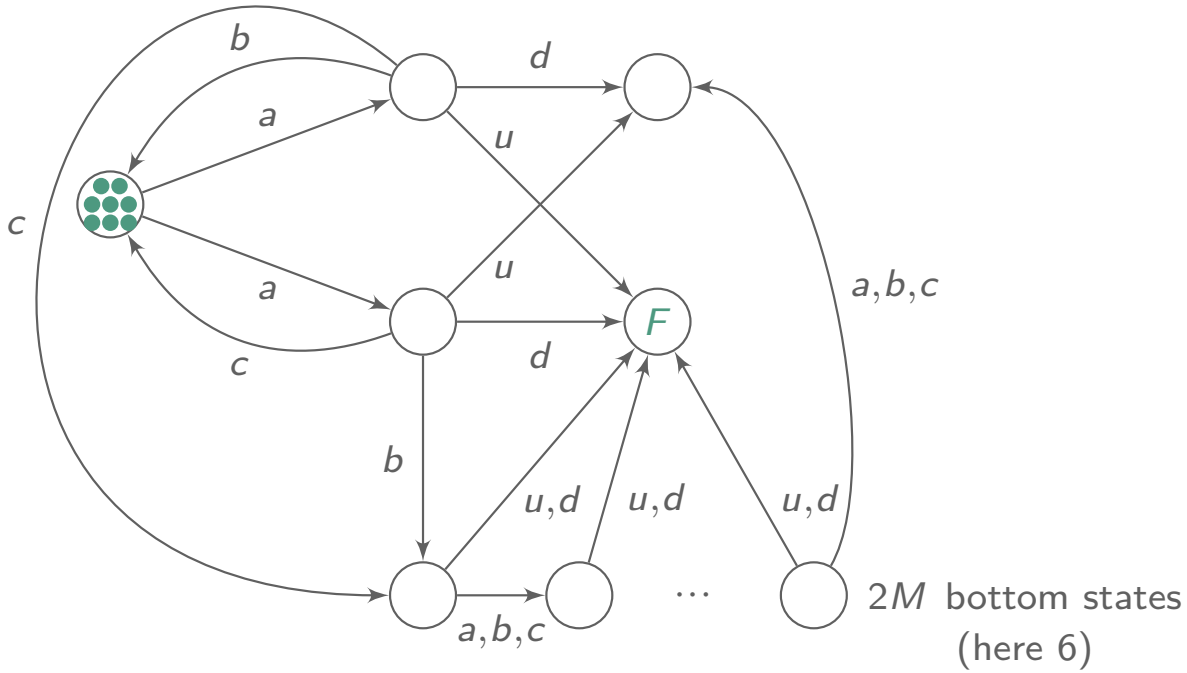
Theorem:
The population control problem is EXPTIME-complete.

Upper bound :

- population control problem $\equiv$ capacity game
- capacity game $\equiv$ to parity game
- solving parity game of size exp. and poly. priorities

Lower bound : encoding of poly space alternating Turing machine

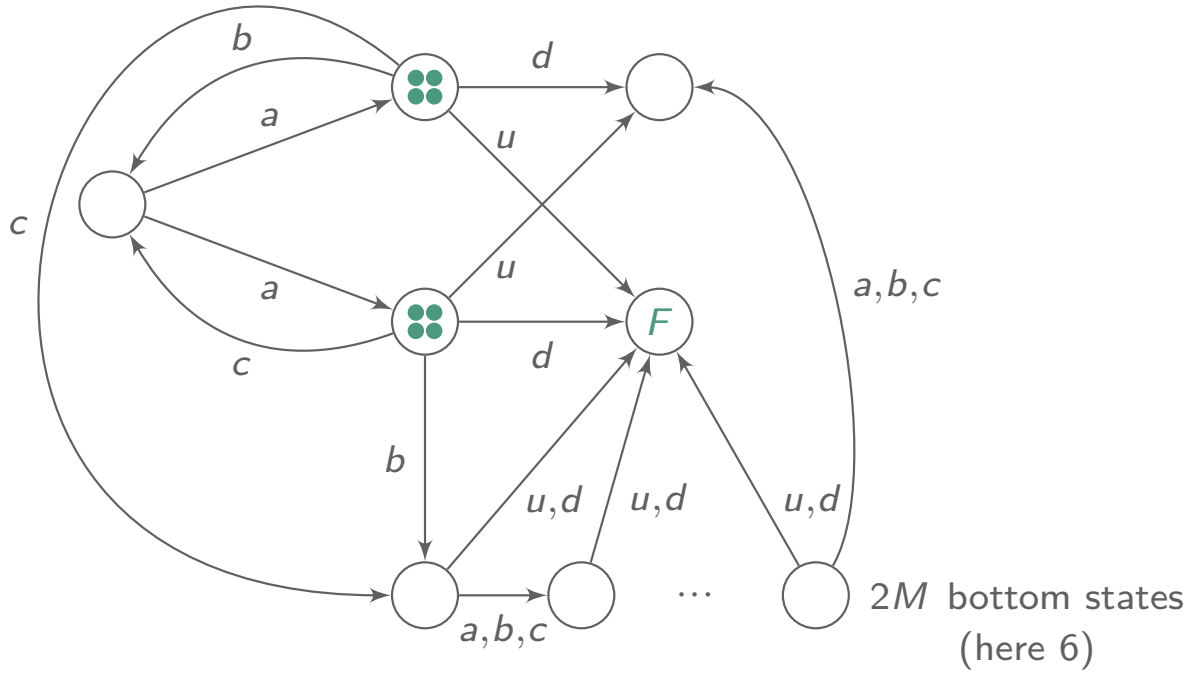
Lower bound on the cutoff



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

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

Lower bound on the cutoff



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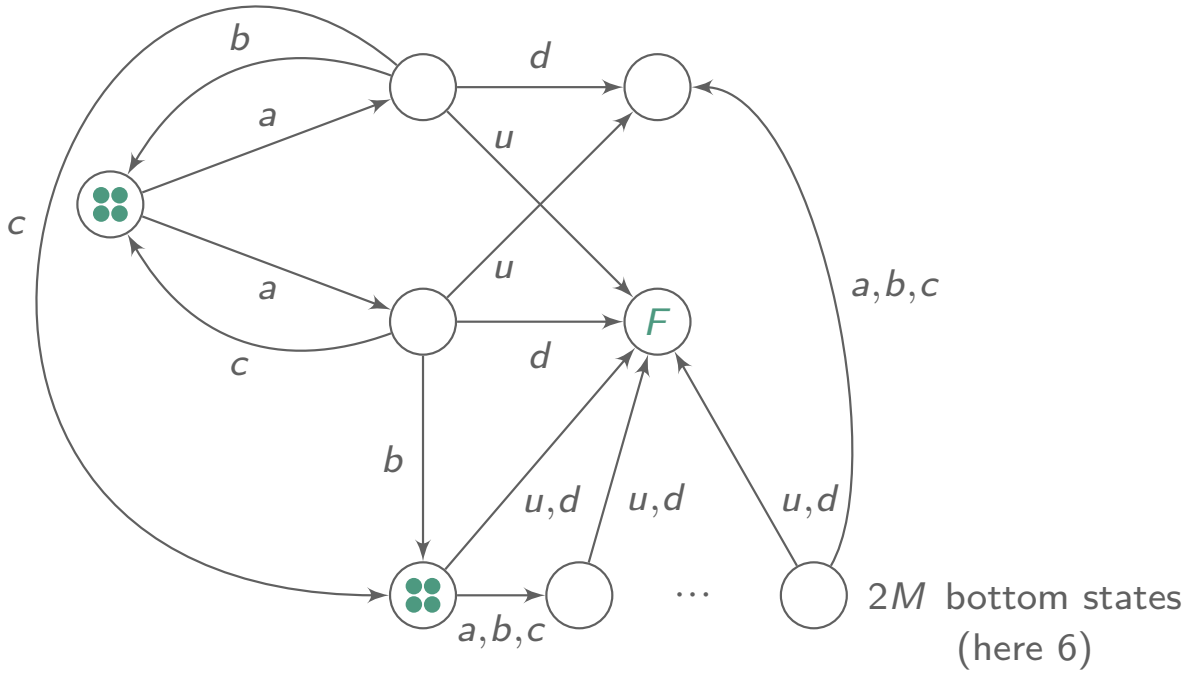

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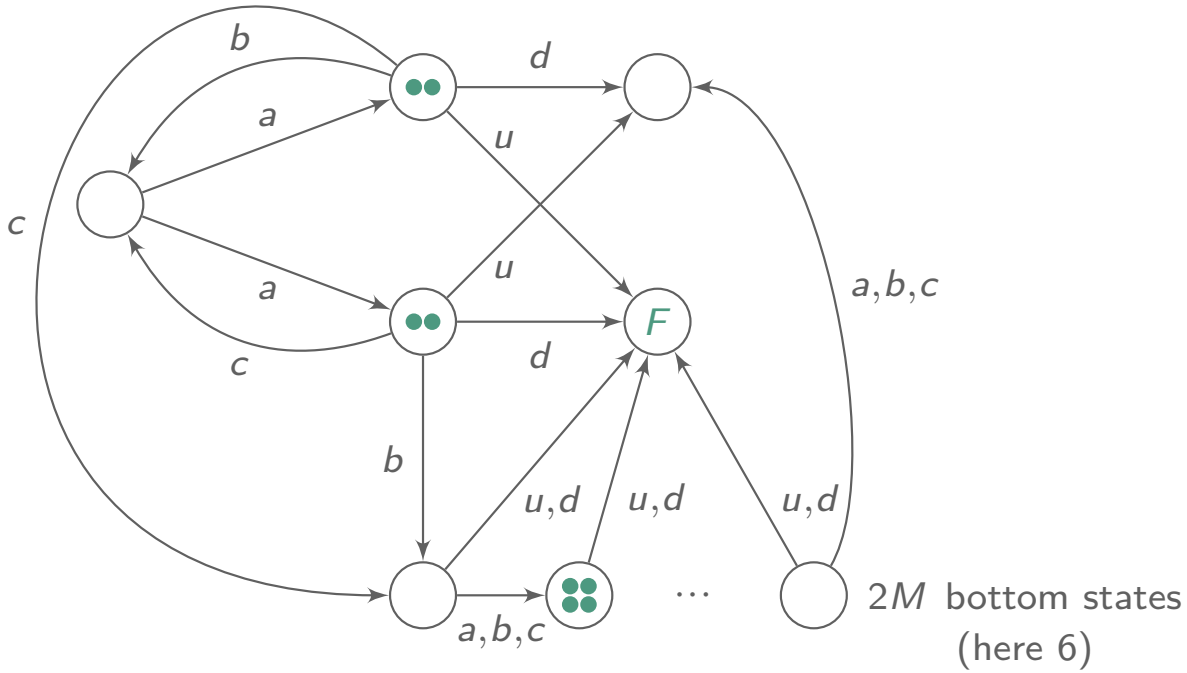

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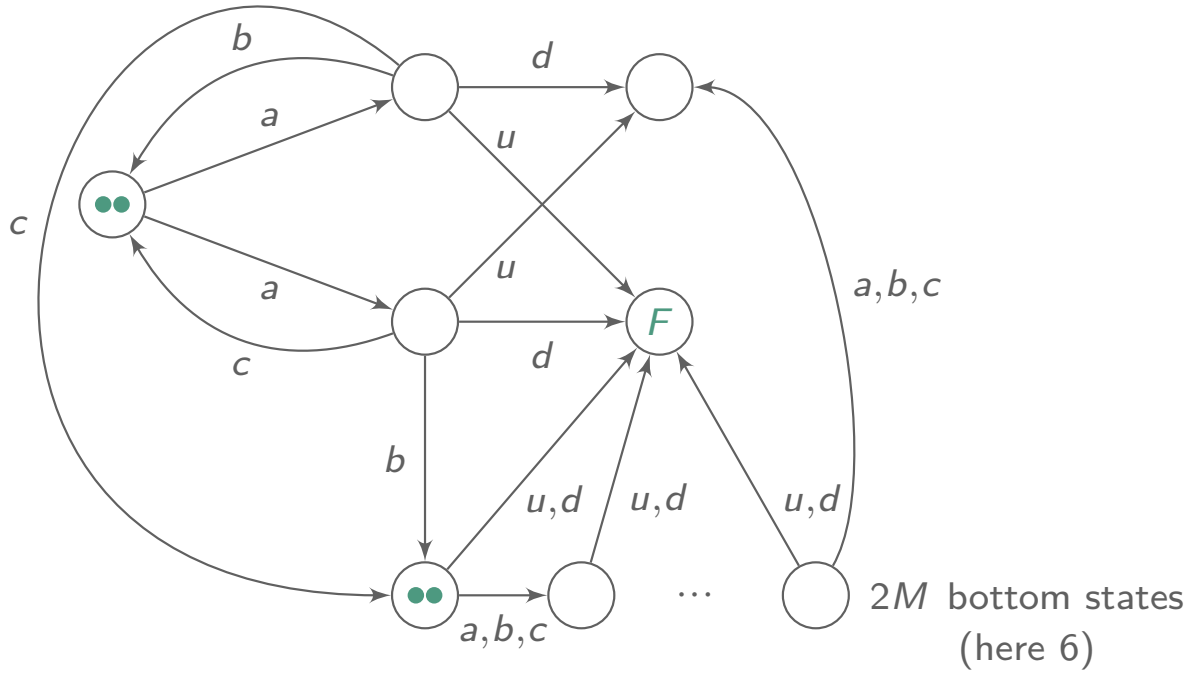

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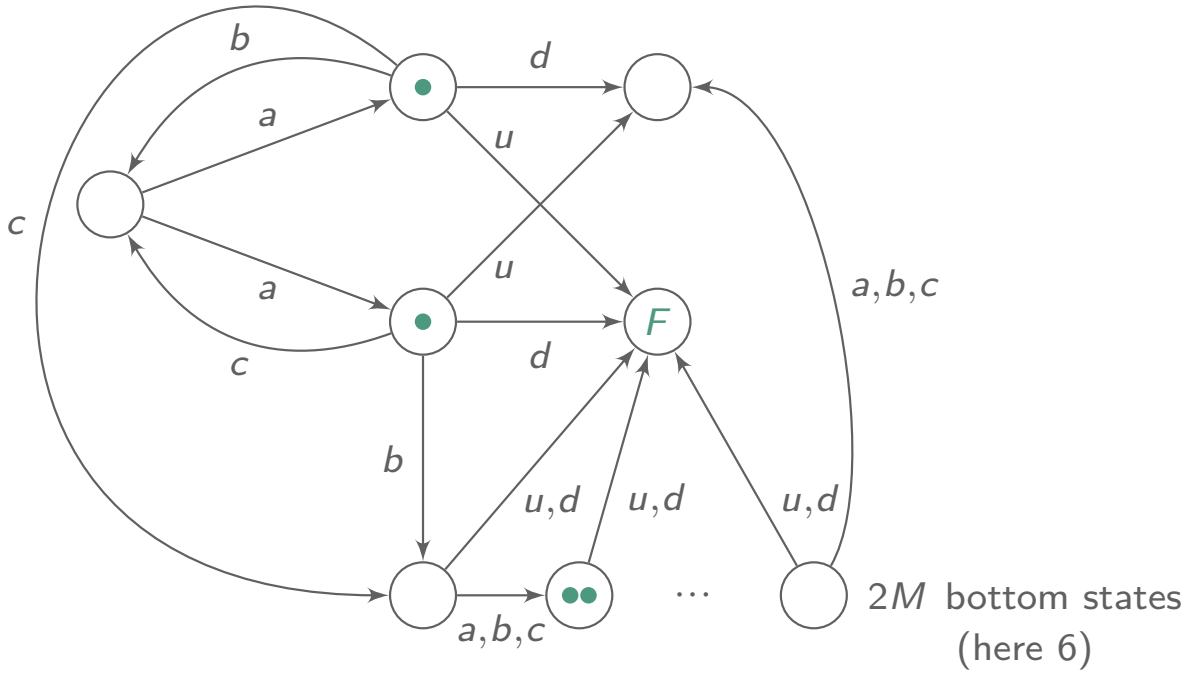

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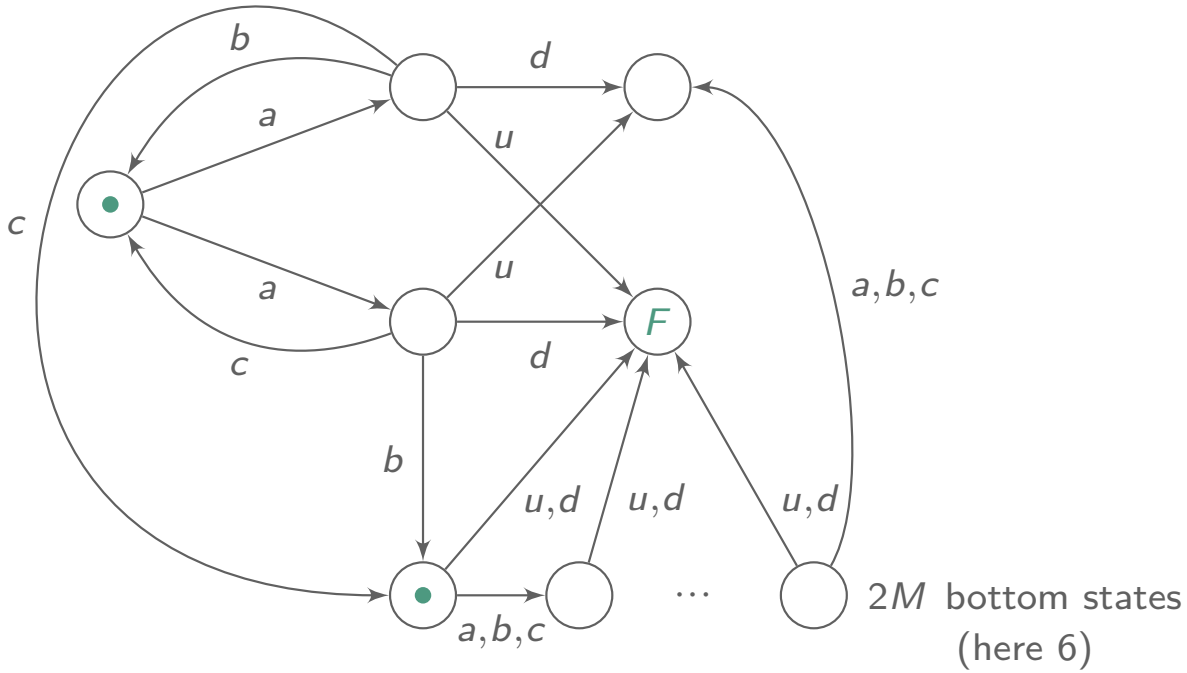

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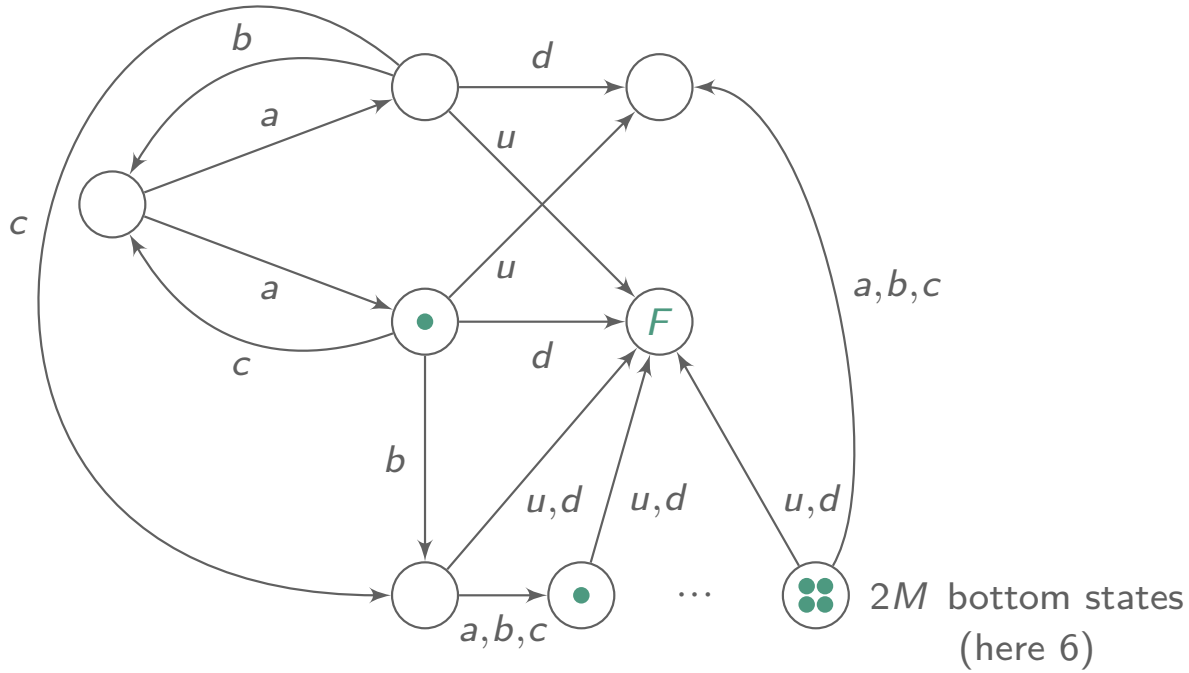

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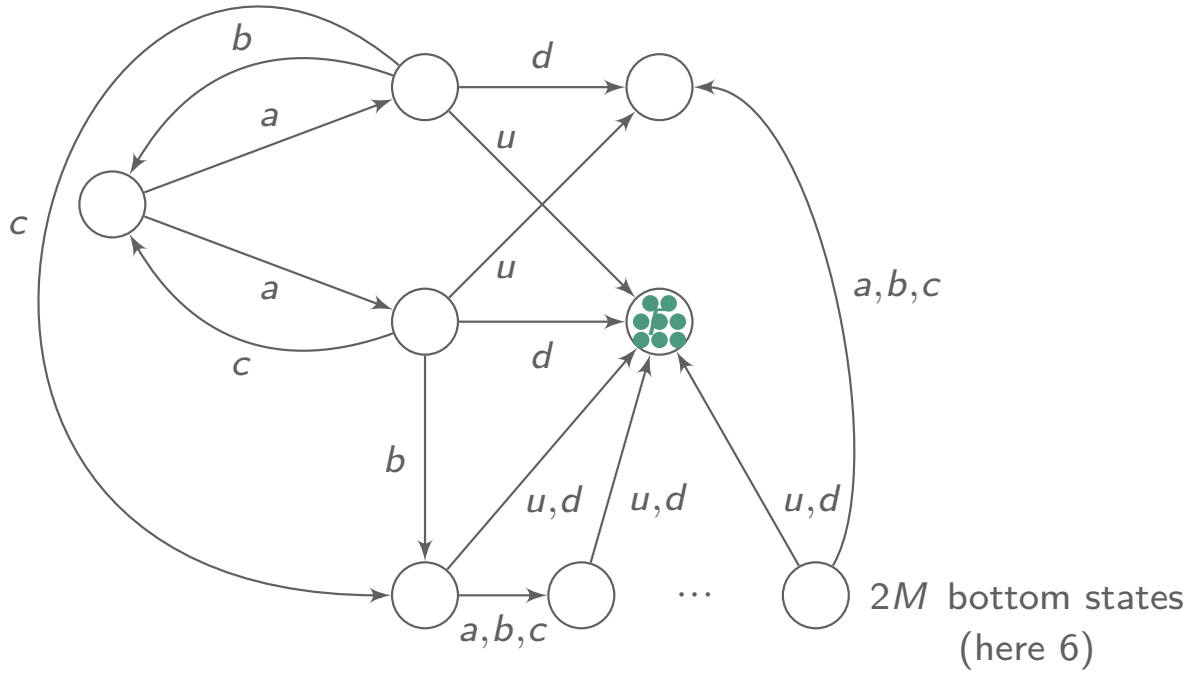

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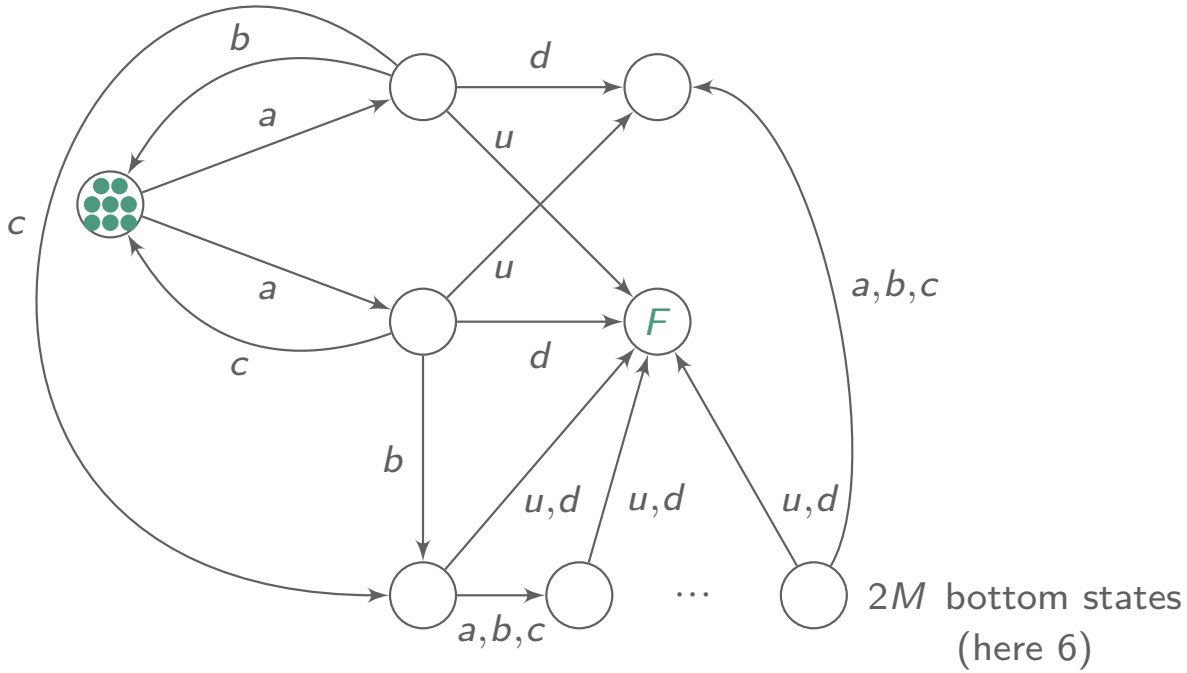

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Cutoff $\mathcal{O}(2^{|\mathcal{A}|})$

Combined with a counter, cutoff is even doubly exponential!

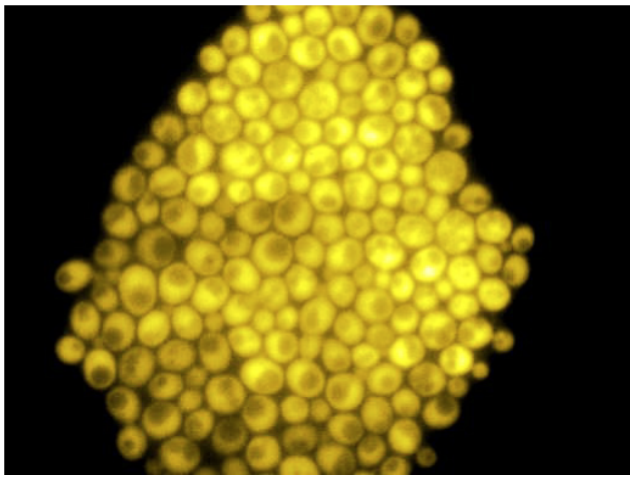
Summary of results

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

Back to motivations

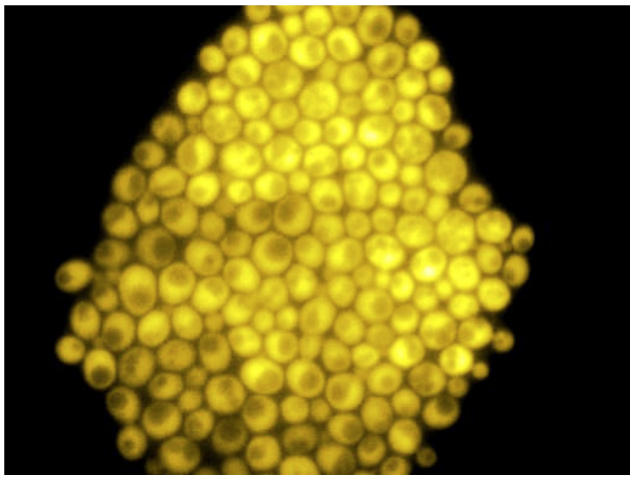
Control of gene expression for a population of cells



credits: G. Batt

Back to motivations

Control of gene expression for a population of cells



credits: G. Batt

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

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

Thanks, and happy anniversary!