Termination Problems in Chemical Kinetics

Gianluigi Zavattaro
University of Bologna

Joint work with
Luca Cardelli

Termination Problems in Chemical Kinetics

$A \rightarrow^{r} C_1+\ldots+C_n$ ⟺ $A ::= \tau@r;C_1|\ldots|C_n + b@s;\mathbf{0}$

$A+B \rightarrow^{s} D_1+\ldots+D_m$ ⟺ $B ::= \overline{b}@s;D_1|\ldots|D_m$

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Chemical systems expressed as a set
of mono- and bi-molecular reactions

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Termination Problems in Chemical Kinetics

$$A \xrightarrow{r} C_1+\ldots+C_n \qquad\qquad A ::= \tau@r;C_1|\ldots|C_n + b@s;\mathbf{0}$$

$$A+B \xrightarrow{s} D_1+\ldots+D_m \quad\Longleftrightarrow\quad B ::= \overline{b}@s;D_1|\ldots|D_m$$

Chemical Ground Form (CGF): a process algebraic view of Chemical Kinetics [TCS08]

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Termination Problems in Chemical Kinetics

$A \rightarrow^{r} C_1 + \ldots + C_n$

$A + B \rightarrow^{s} D_1 + \ldots + D_m$

$\Leftrightarrow$

$A ::= \tau@r;C_1|\ldots|C_n + b@s;\mathbf{0}$

$B ::= \overline{b}@s;D_1|\ldots|D_m$

What is the computational power of Chemical Kinetics?

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Termination Problems in Chemical Kinetics

$A \xrightarrow{r} C_1+\ldots+C_n$

$A+B \xrightarrow{s} D_1+\ldots+D_m$

$\Leftrightarrow$

$A ::= \tau@r;C_1|\ldots|C_n + b@s;\mathbf{0}$

$B ::= \overline{b}@s;D_1|\ldots|D_m$

Is TERMINATION decidable in Chemical Kinetics?

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Plan of the talk

- Chemical Kinetics as a Computational Model
  - ... not a new issue
- Chemical Ground Form (CGF) [TCS08]
  - … a new way to analyze chemical kinetics
- Considered TERMINATION problems:
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Is Chemical Kinetics Turing powerful?

- Magnasco. ***Chemical Kinetics is Turing Universal***. *Phys Rev Lett*. 1997
  - Answer: **YES**… but justification not convincing (only Digital Computers with bounded memory are considered)
- Liekens and Fernando. ***Turing Complete Catalytic Particle Computers***. In Proc. *ECAL'07*. 2007
  - Answer: **YES**… but justification not convincing (only Minsky Machines with bounded computation are considered)
- Soloveichik et al. ***Computation with Finite Stochastic Chemical Reaction Networks***. *Nat. Computing*. 2008
  - Answer: **NO**… but all Minsky and Turing Machines can be at least approximated with any given degree of precision

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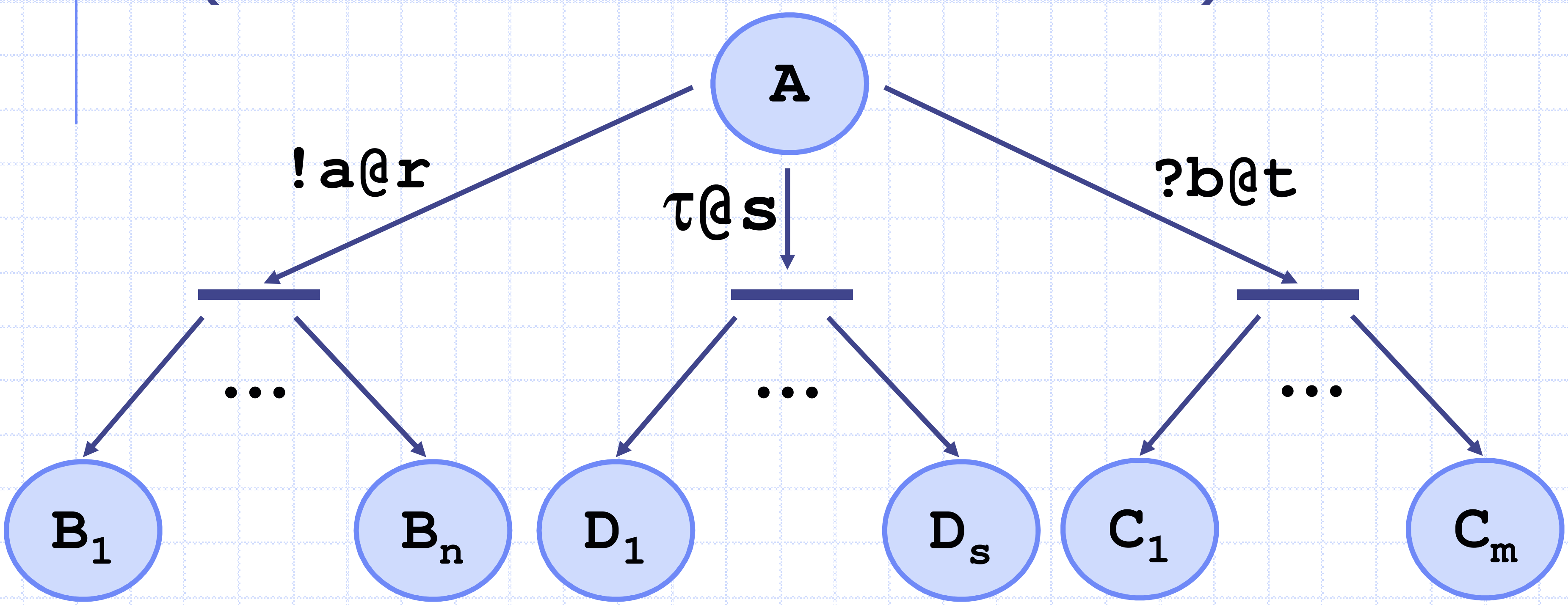
Chemical Ground Forms

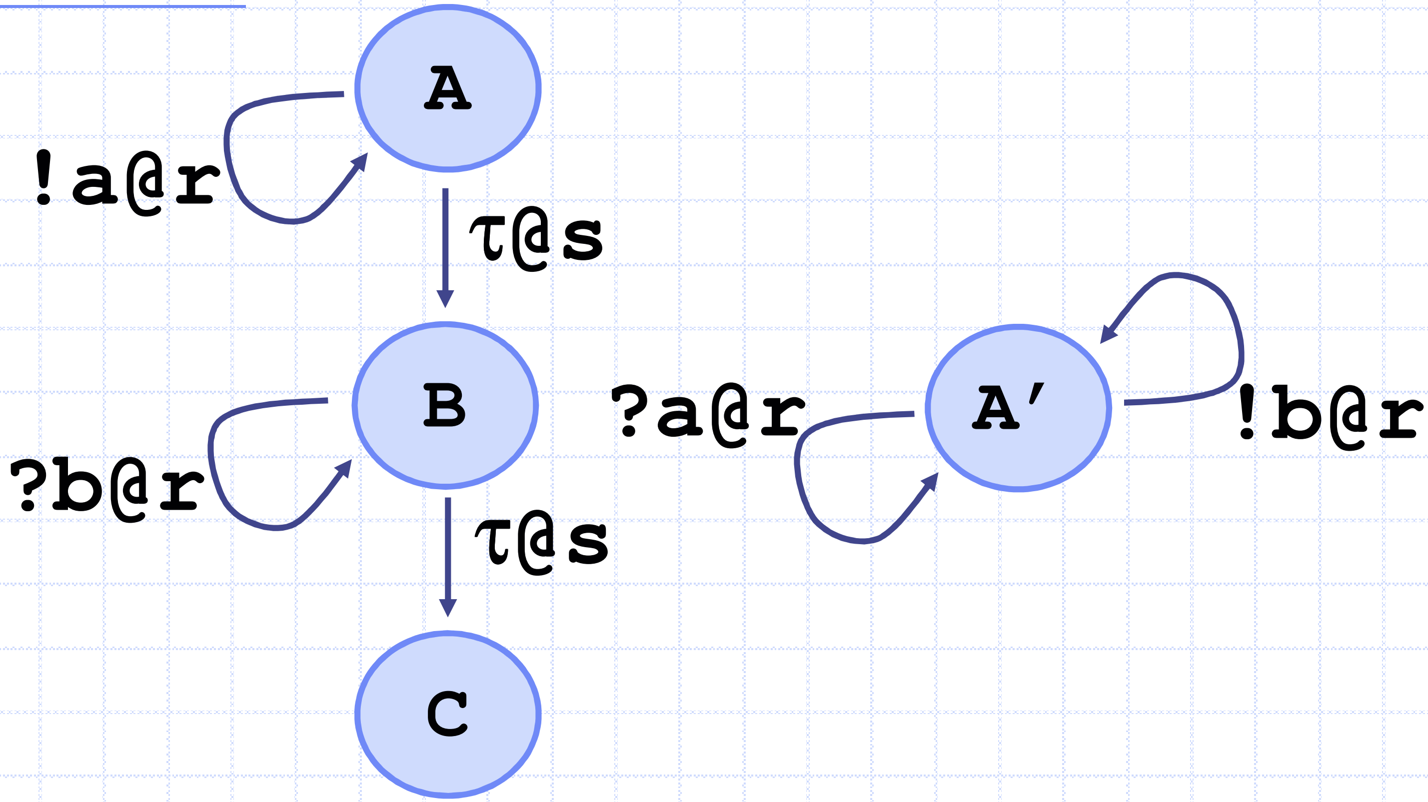
- Stochastic variant of Milner's CCS, with an equivalent graphical notation (Stochastic Collective Automata)



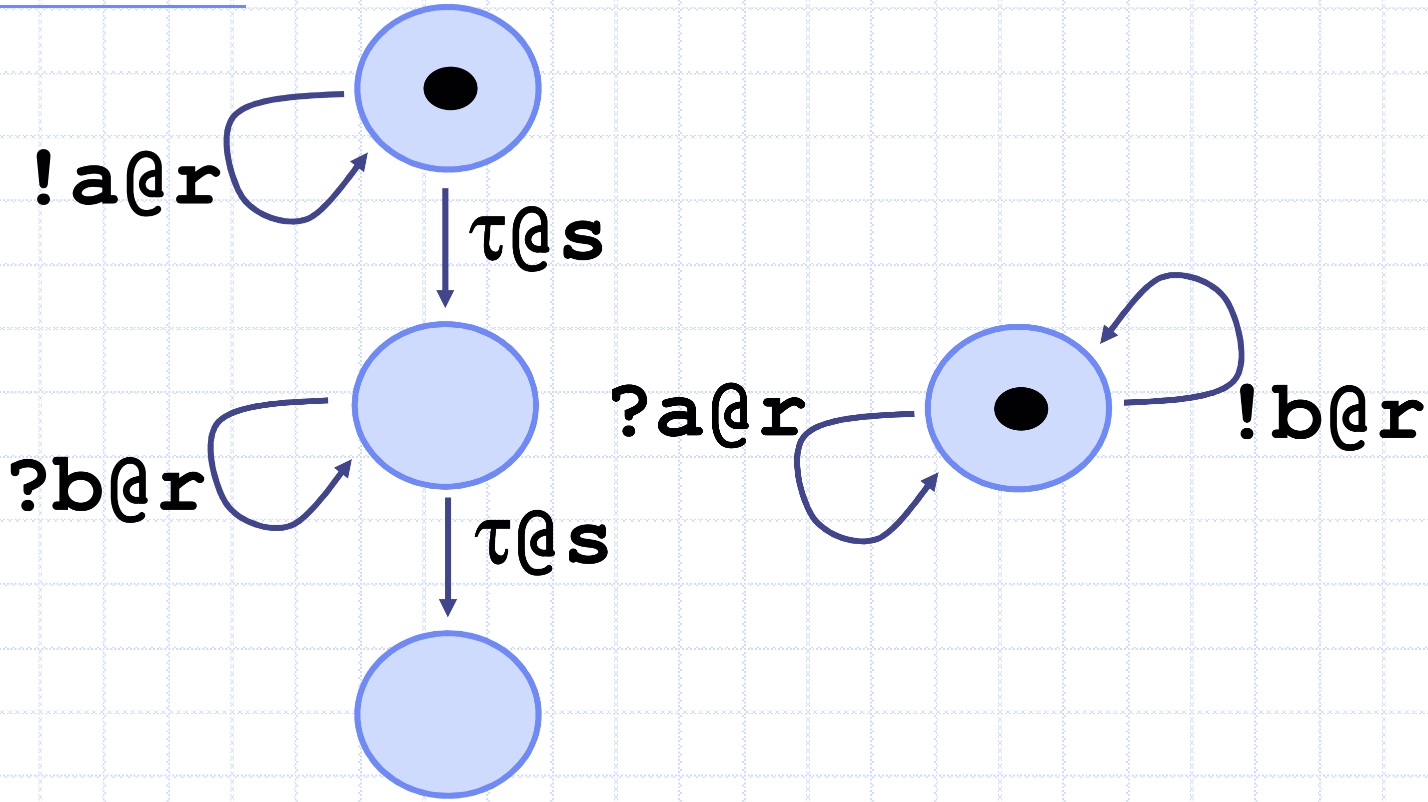
Stochastic semantics

- Actions take (an exponentially distributed amount of) time
  - Internal delay: **τ@r**
    - **Pr(internal delay < t) = 1-e^{-rt}**
  - Synchronization between complementary actions: **?a@r, !a@r**
    - **Pr(synchronization time < t) = 1-e^{-rt}**

Example

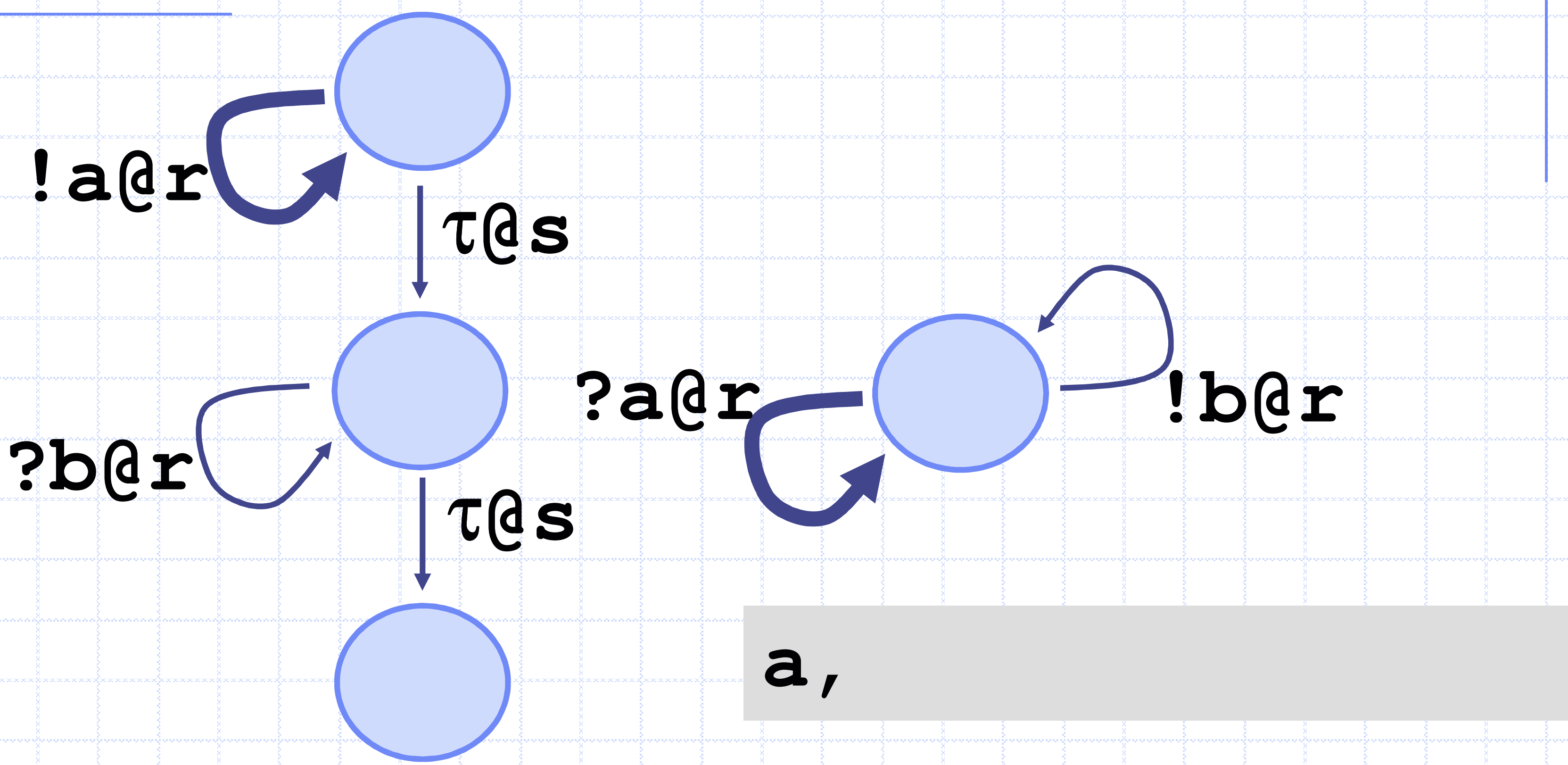


Example



- Starting process: **A|A′**

Example



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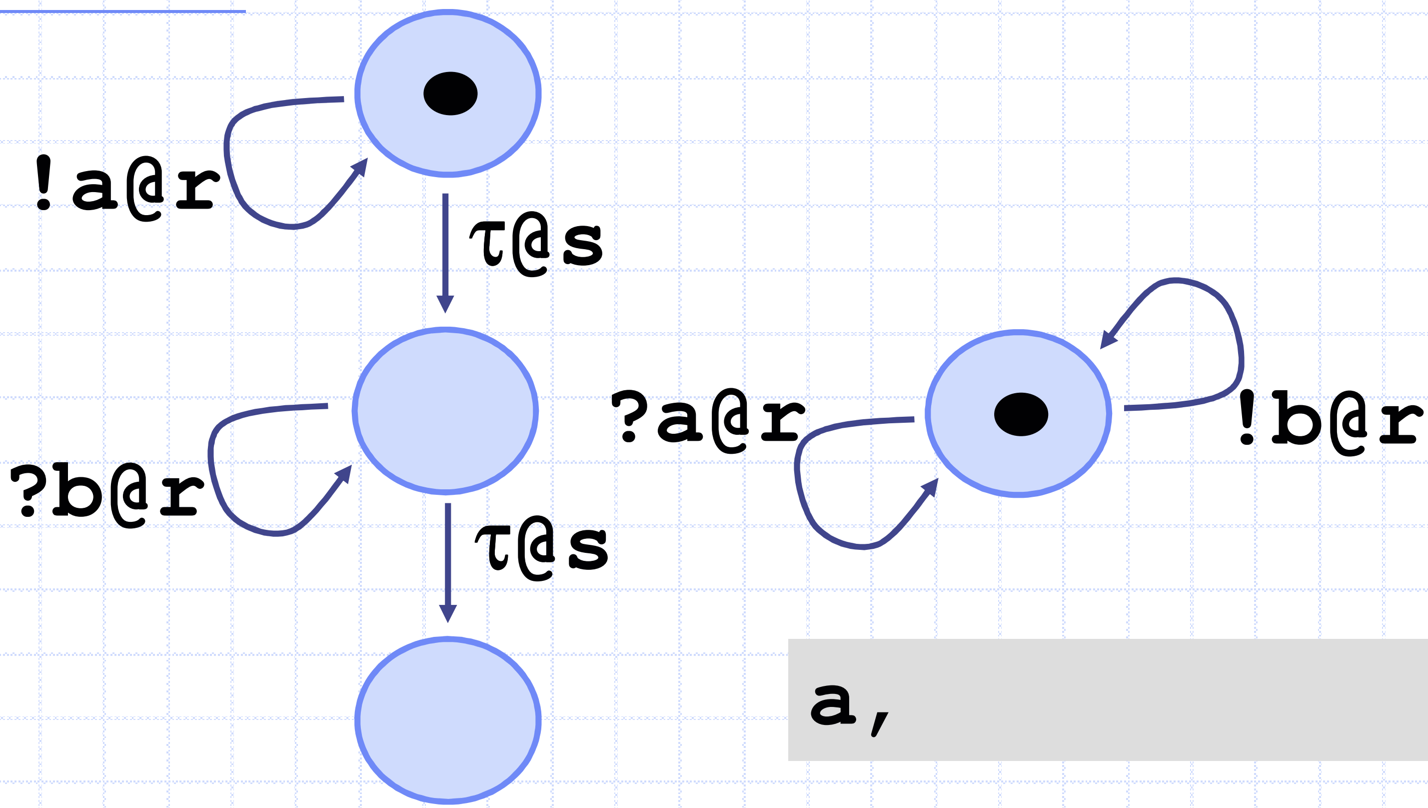

a,

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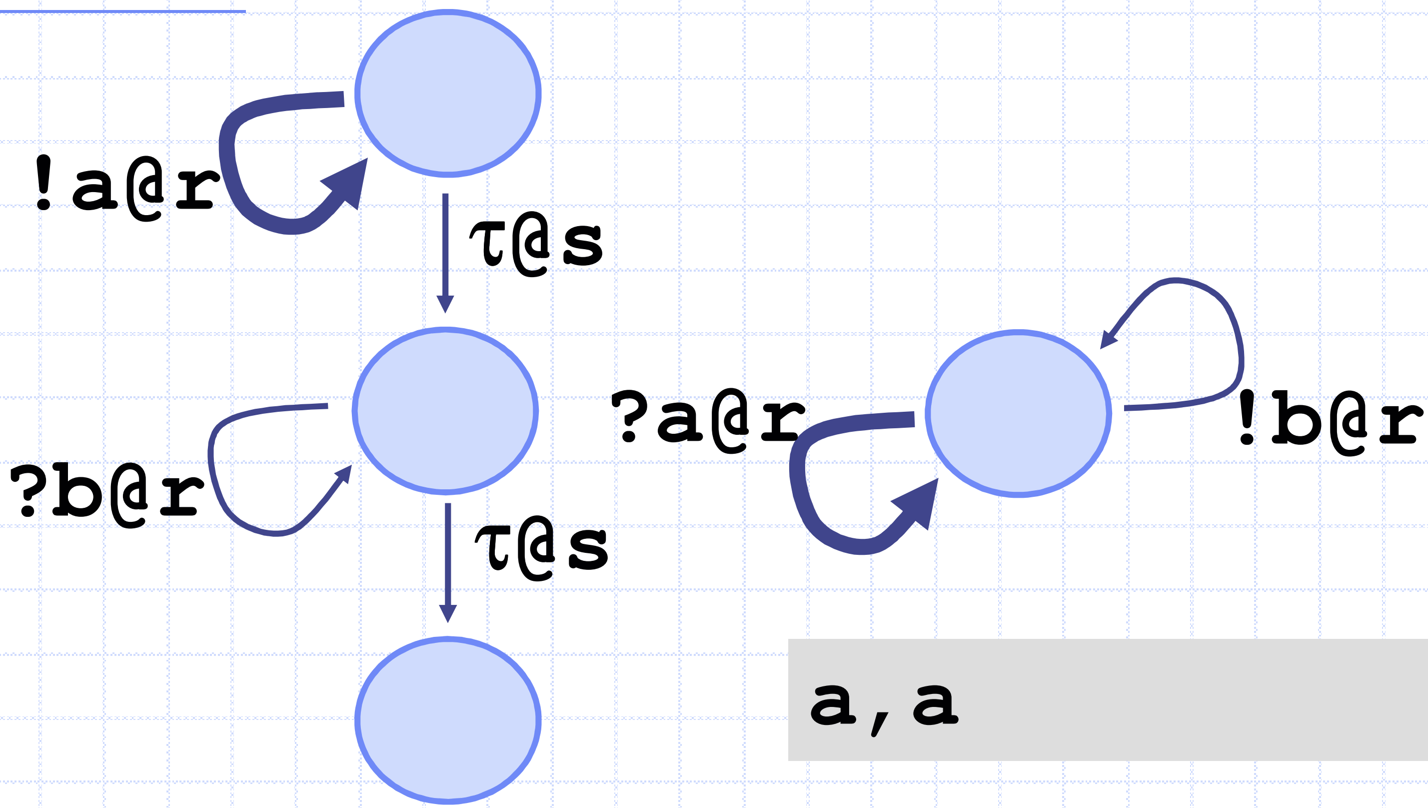
Example



a,a

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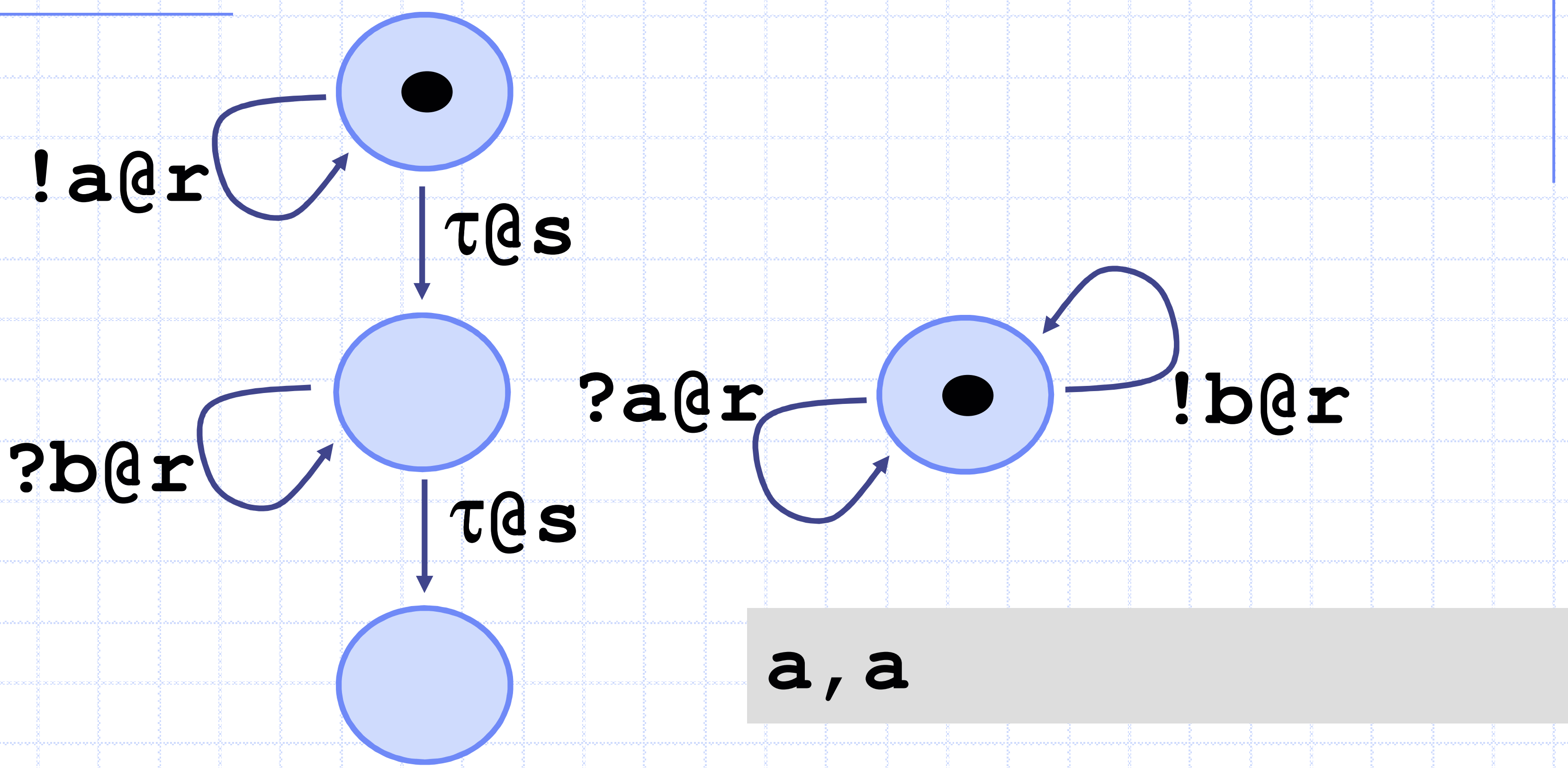
Example



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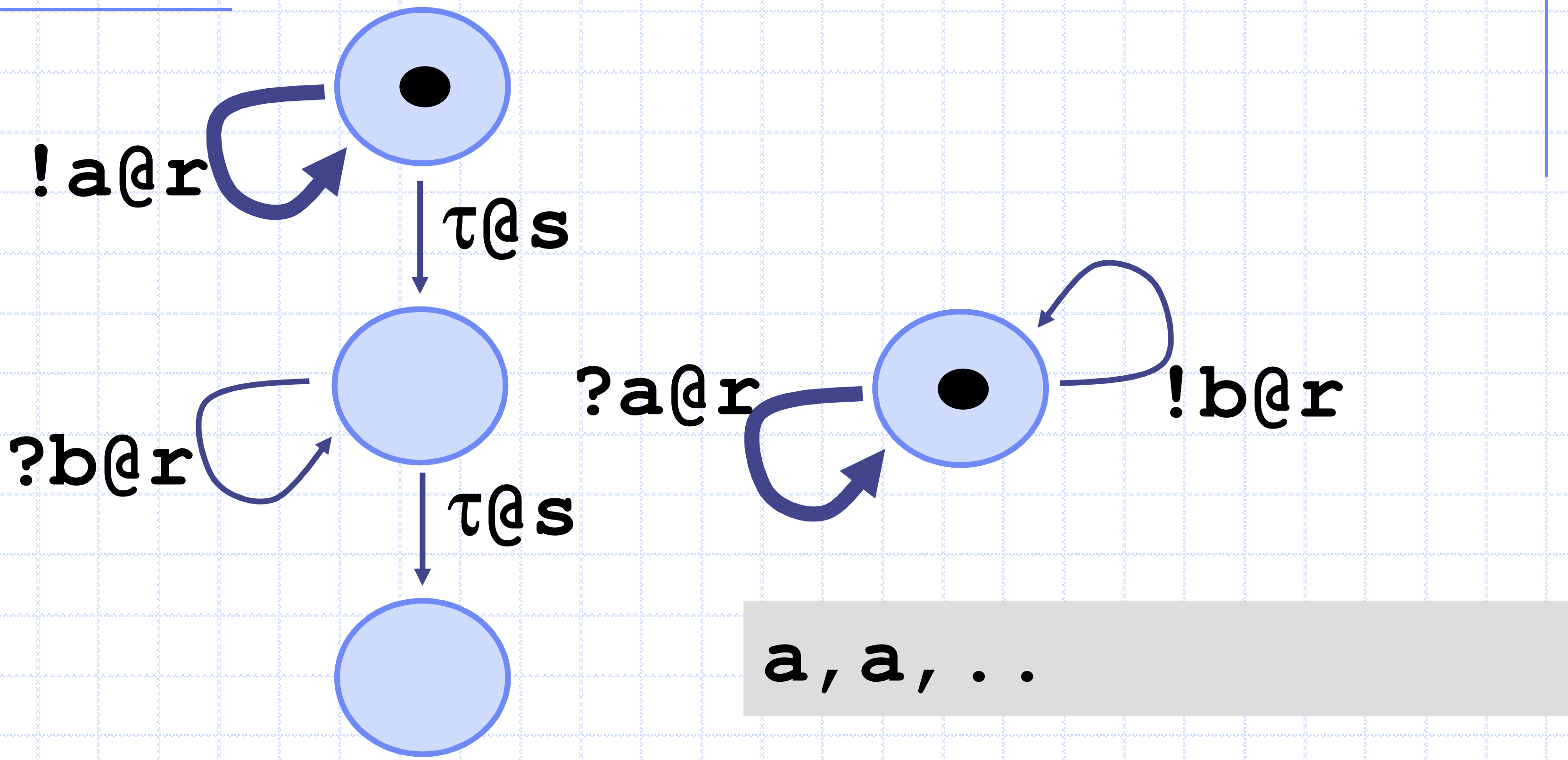

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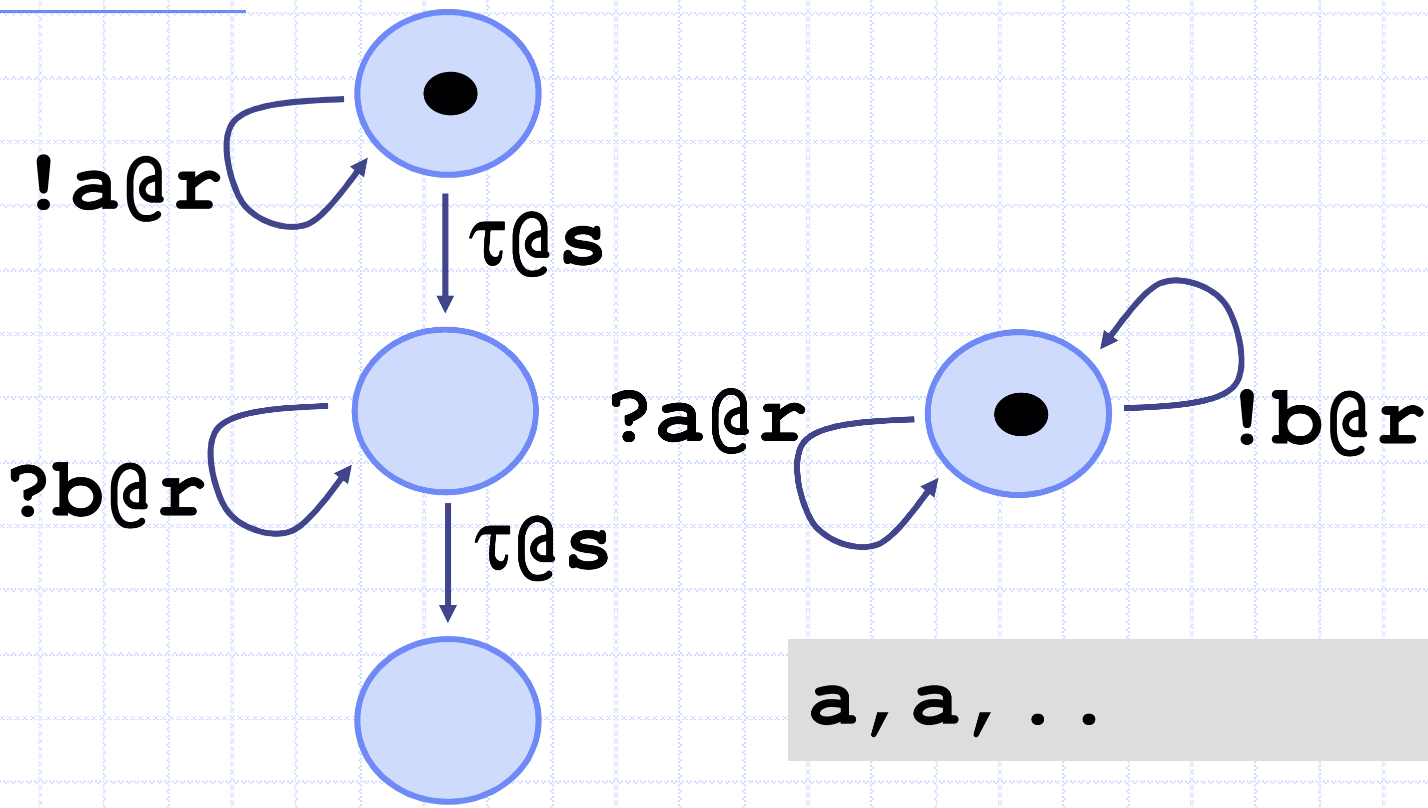

`a,a,..`

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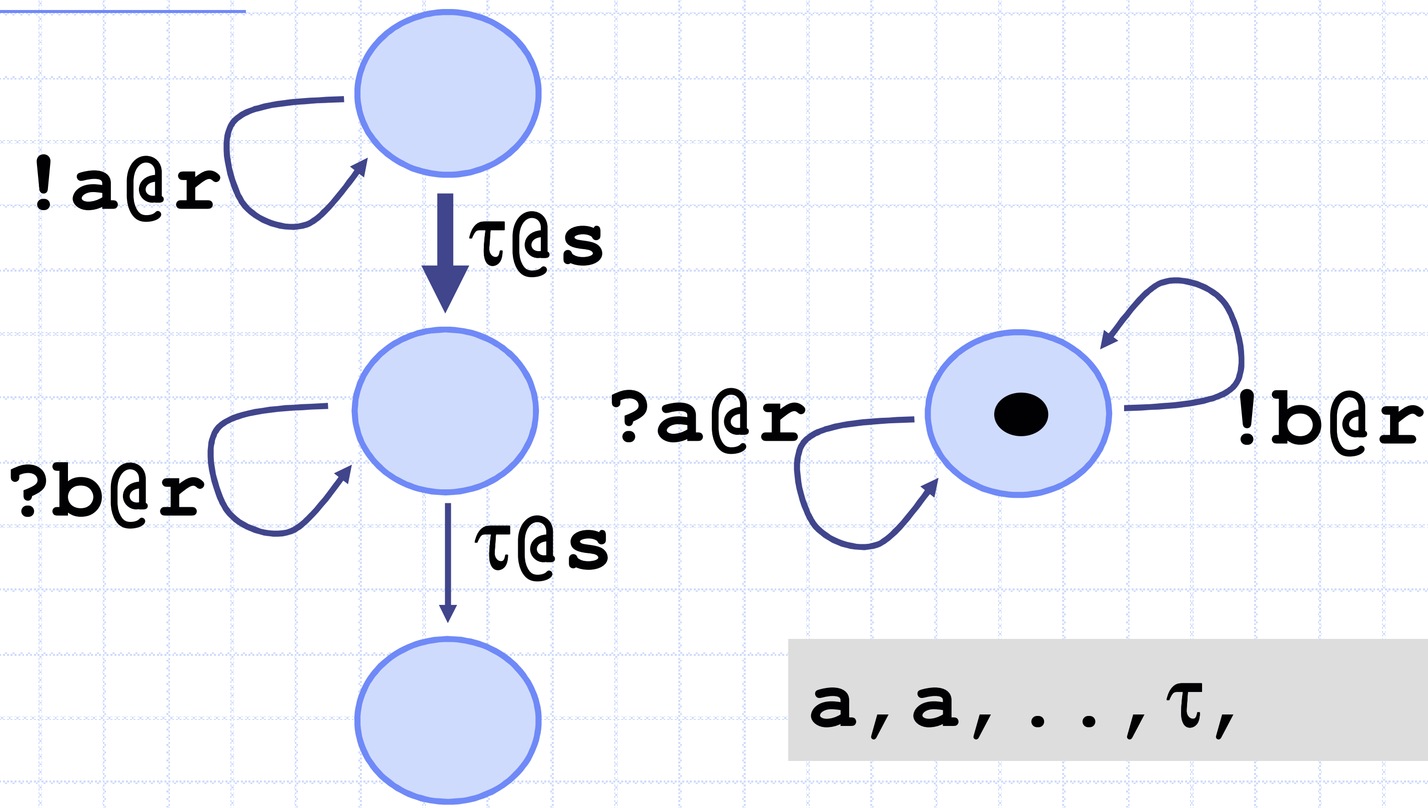

a,a,..,τ,

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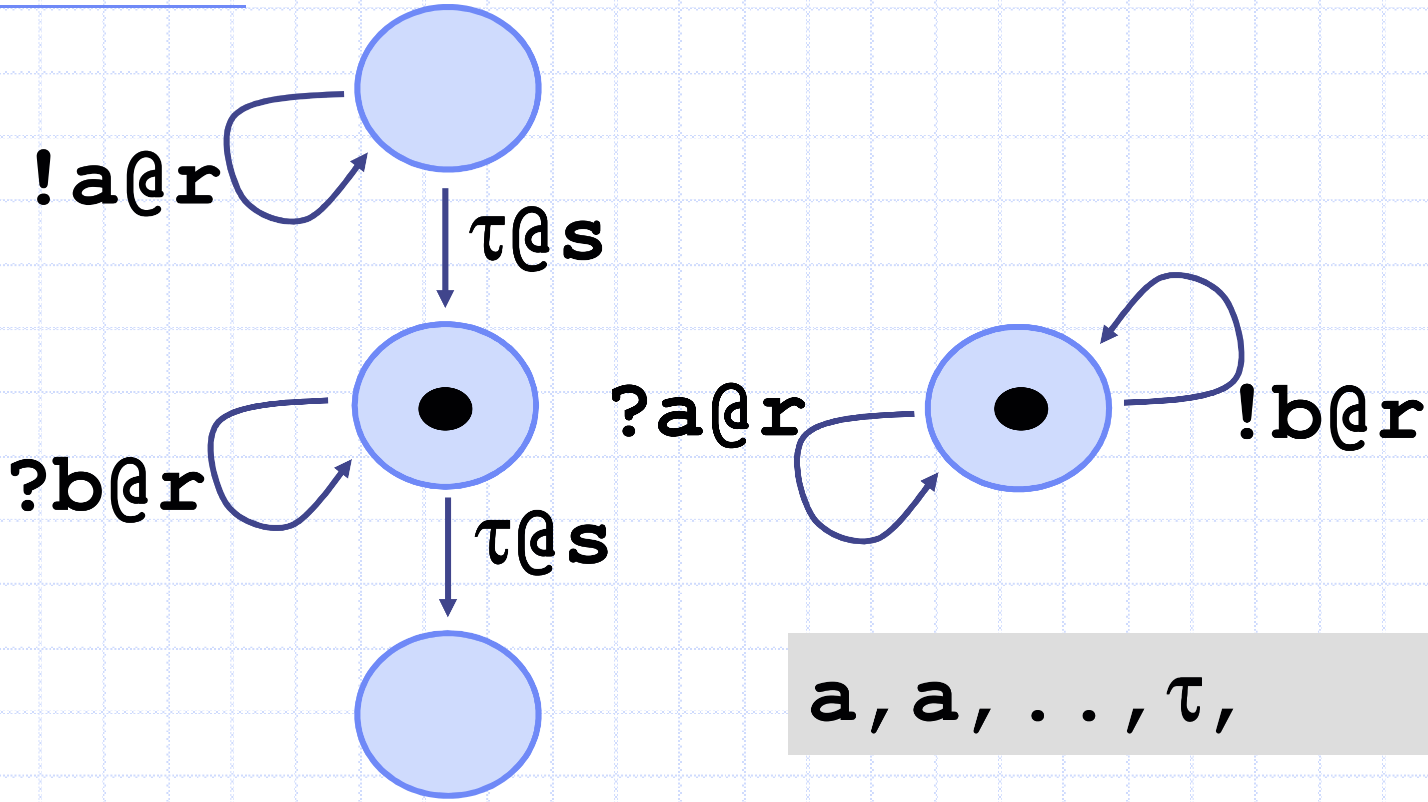
Example



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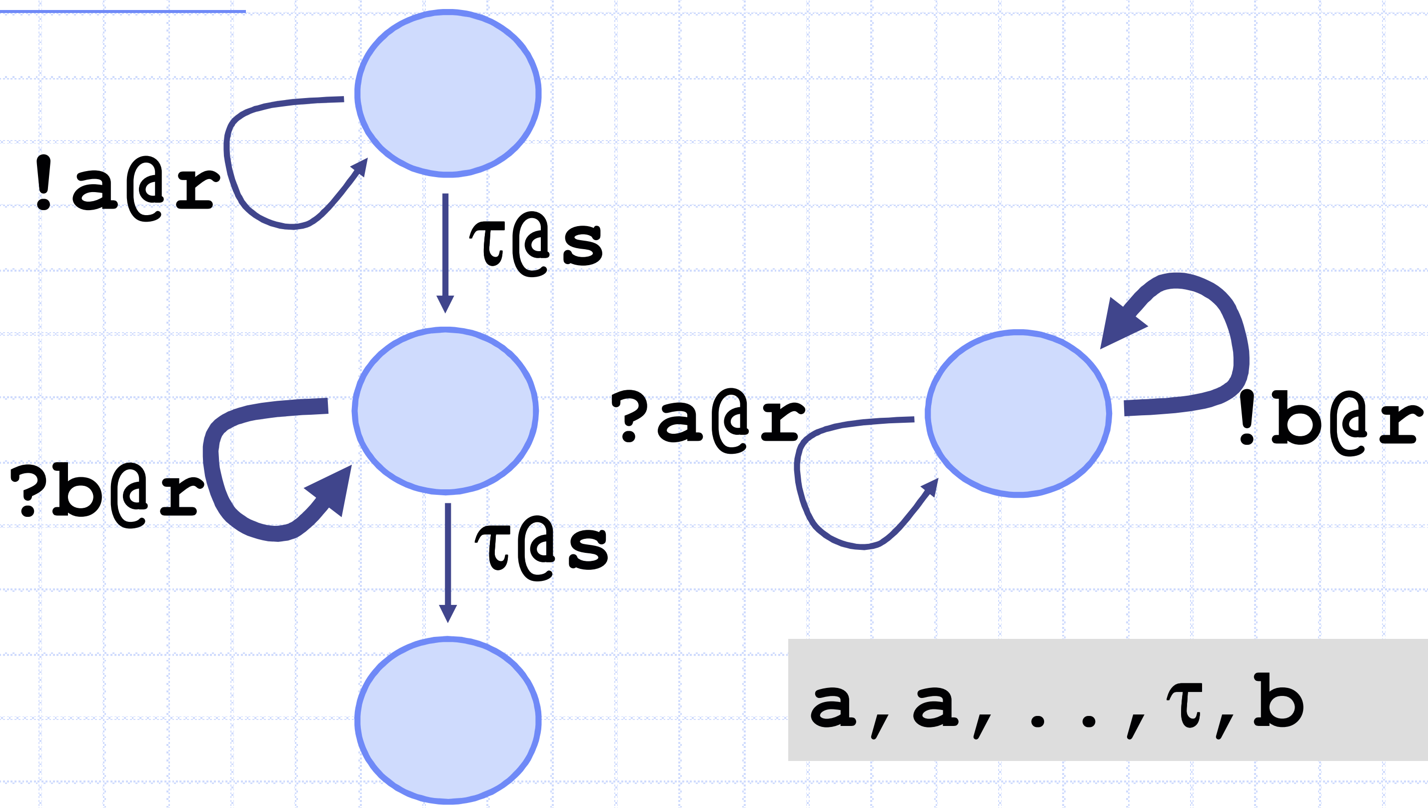

a,a,..,τ,b

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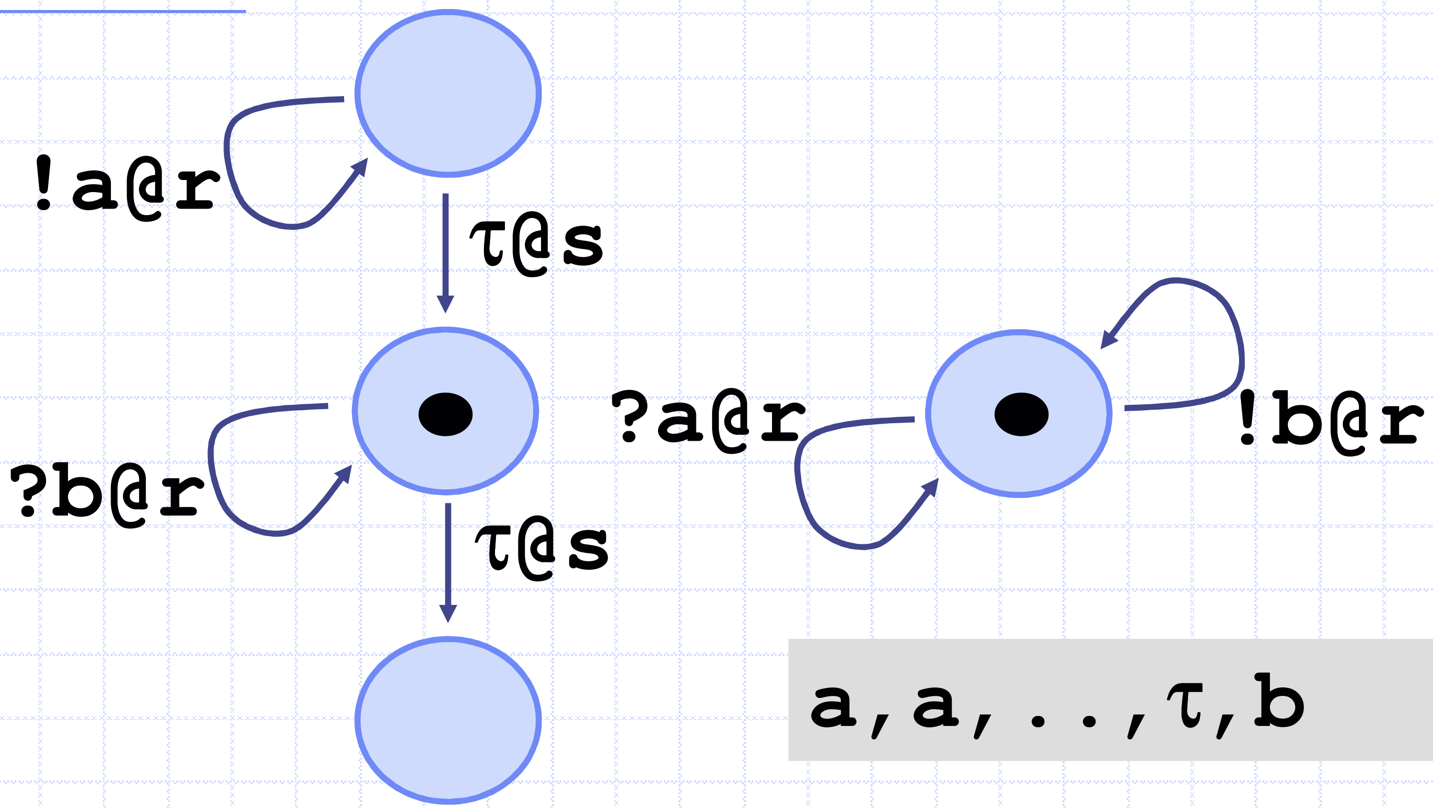
Example



a,a,..,τ,b

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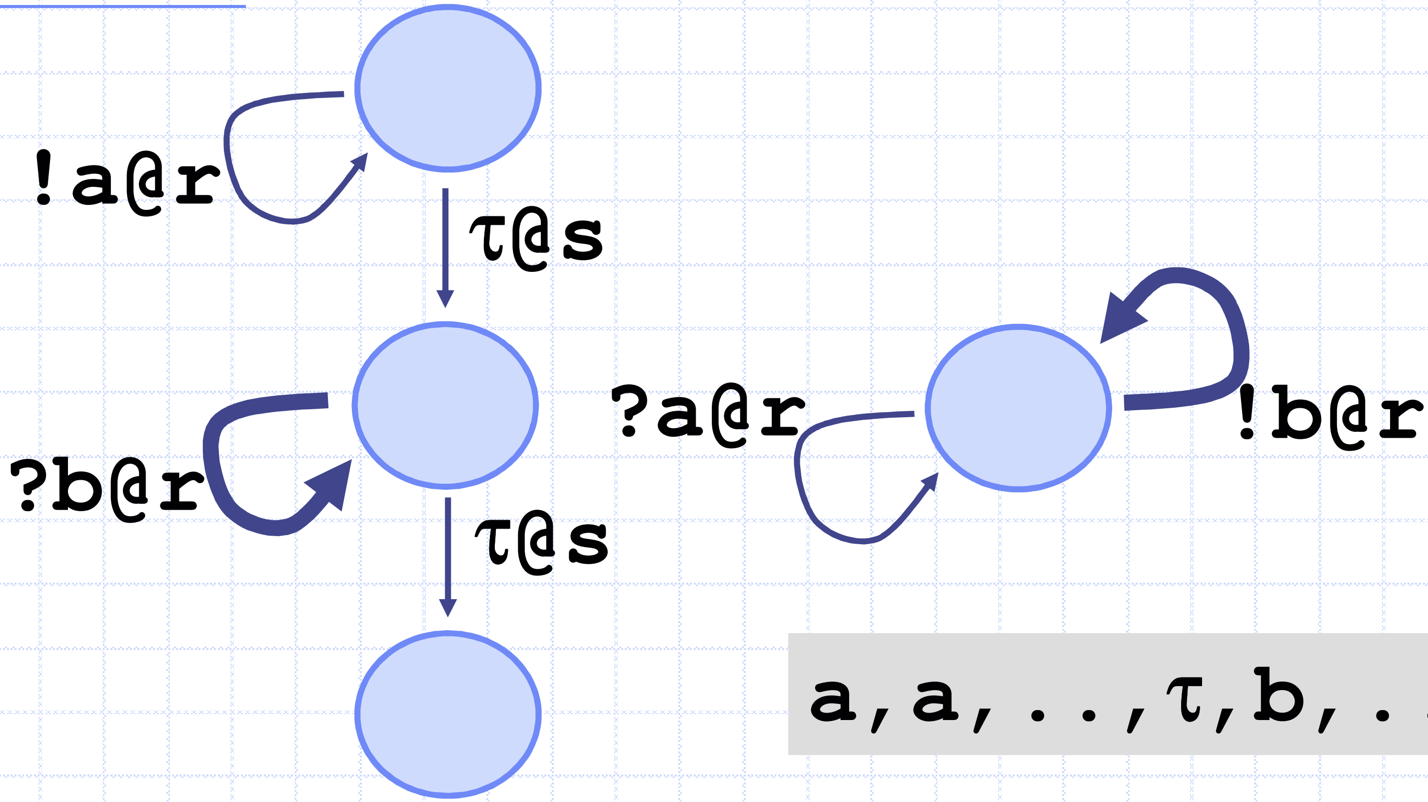
Example



a,a,..,τ,b,..

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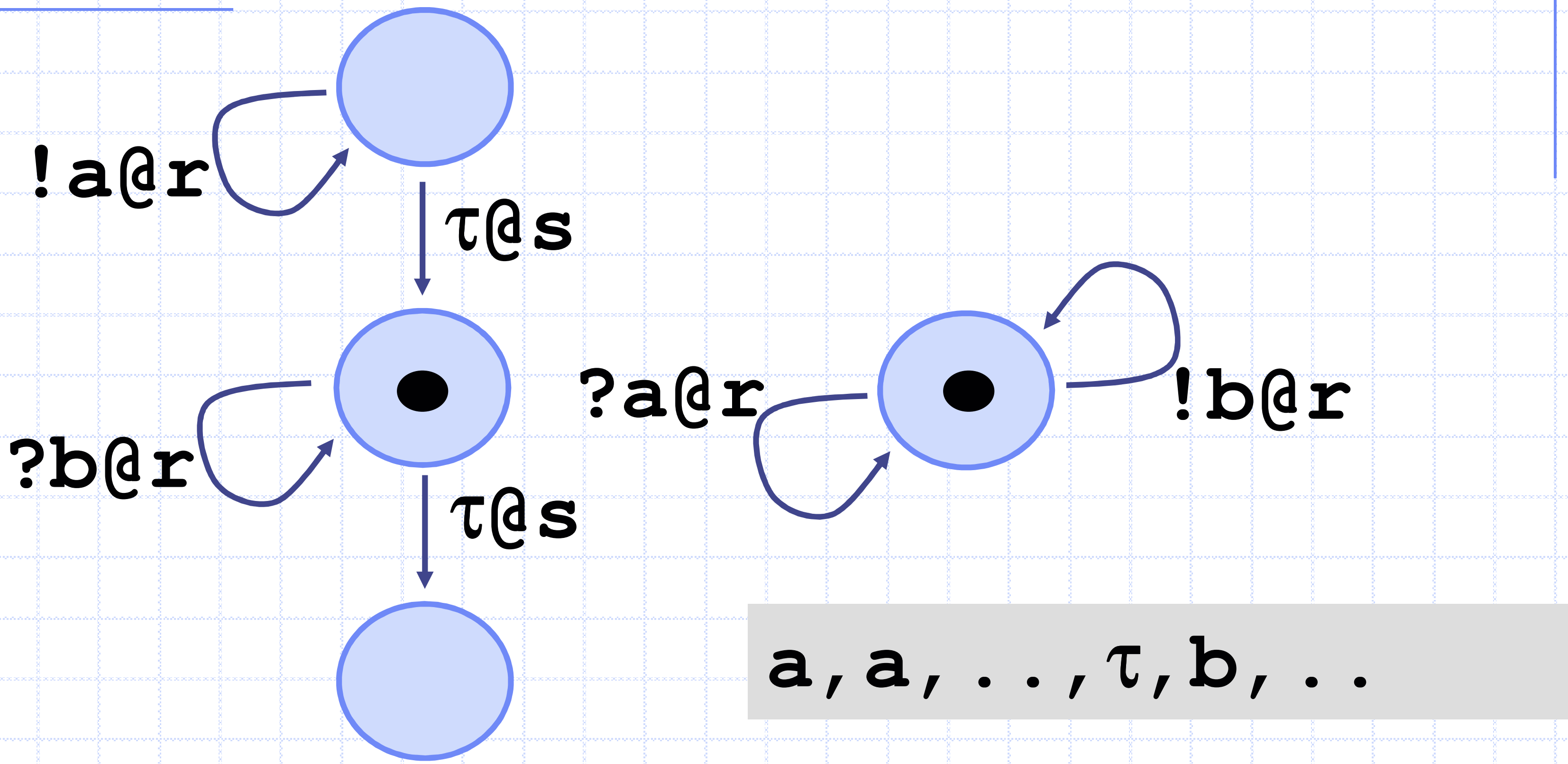
Example



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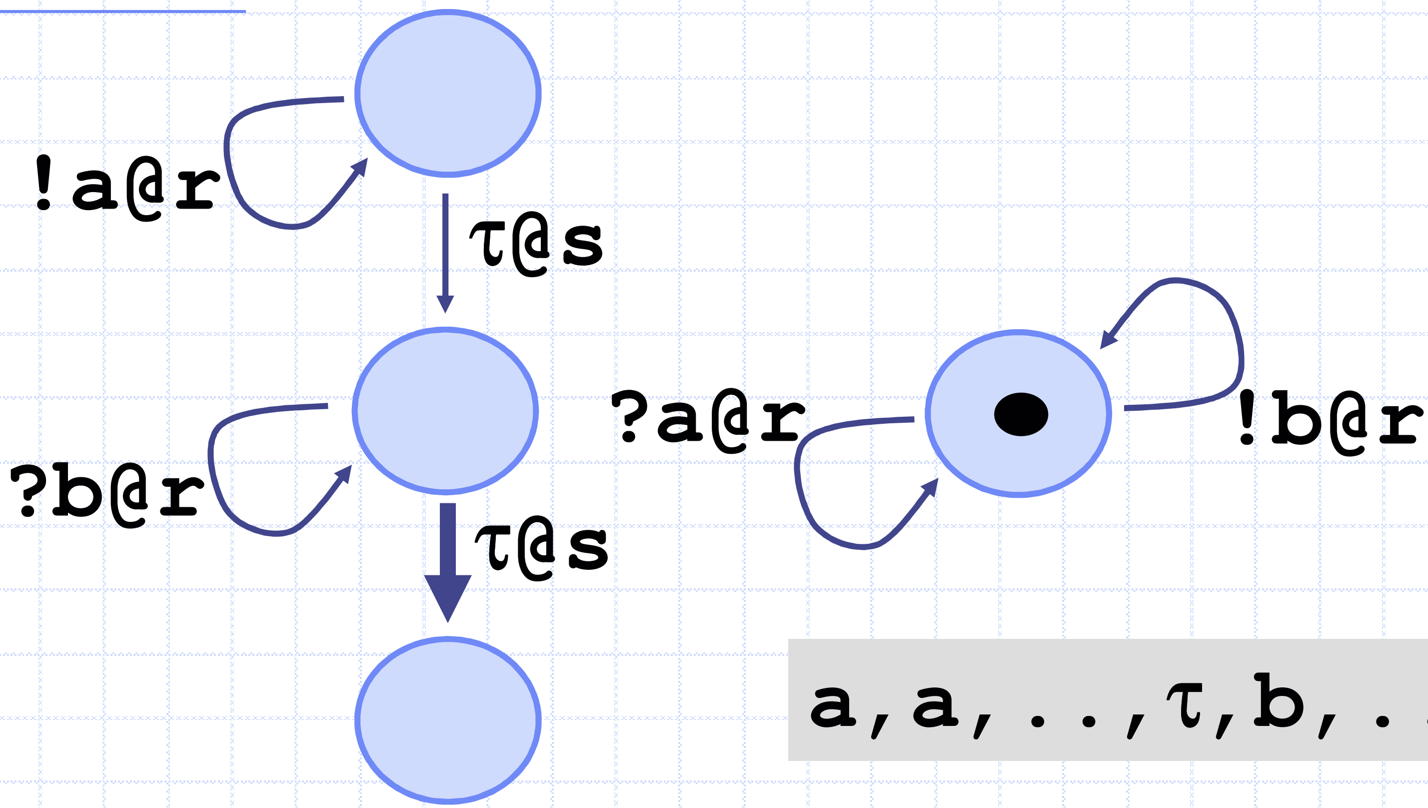

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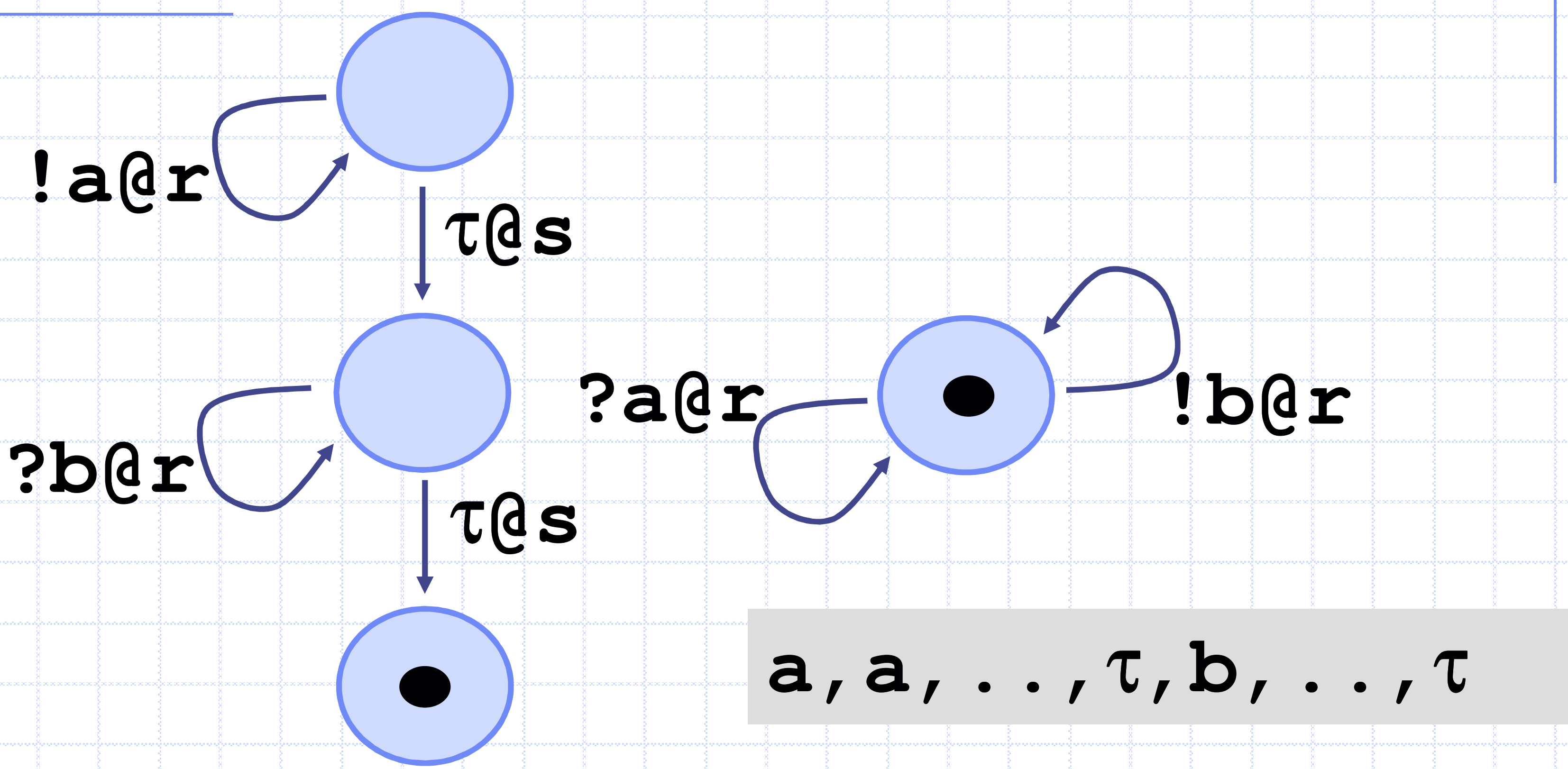

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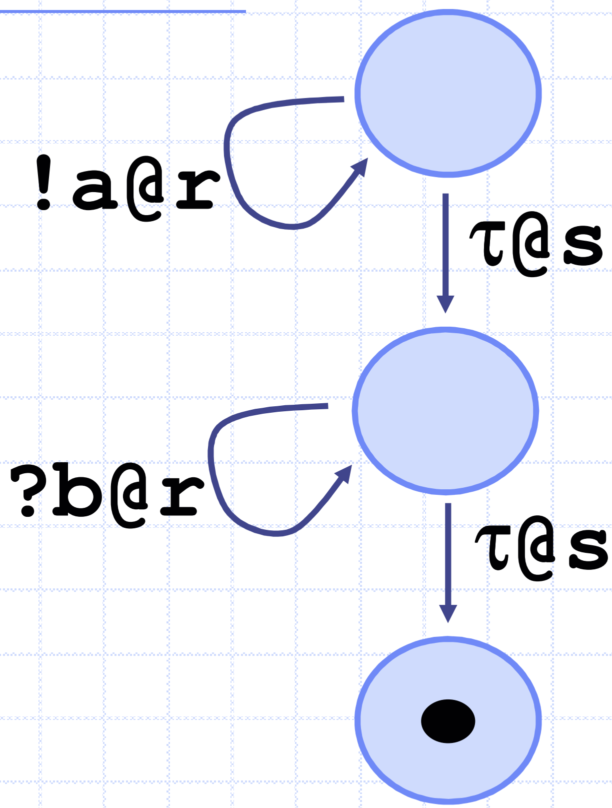

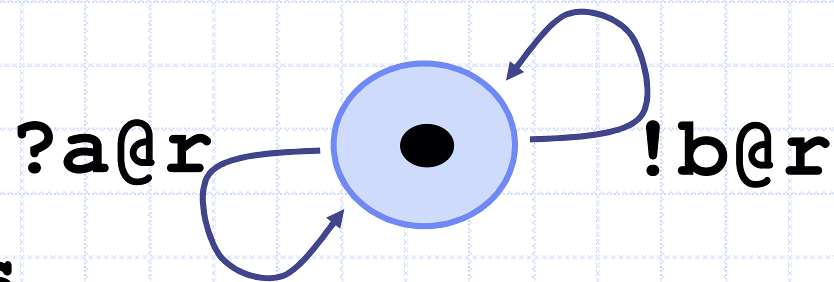

a*τb*τ

- Starting process: **A|A′**

CGF = Chemical Kinetics [TCS08]

Continuous-State Semantics	=	Continuous Chemistry
⬆		⬆
CGF	⟷	**CK**
⬇		⬇
Discrete-State Semantics	=	Discrete Chemistry

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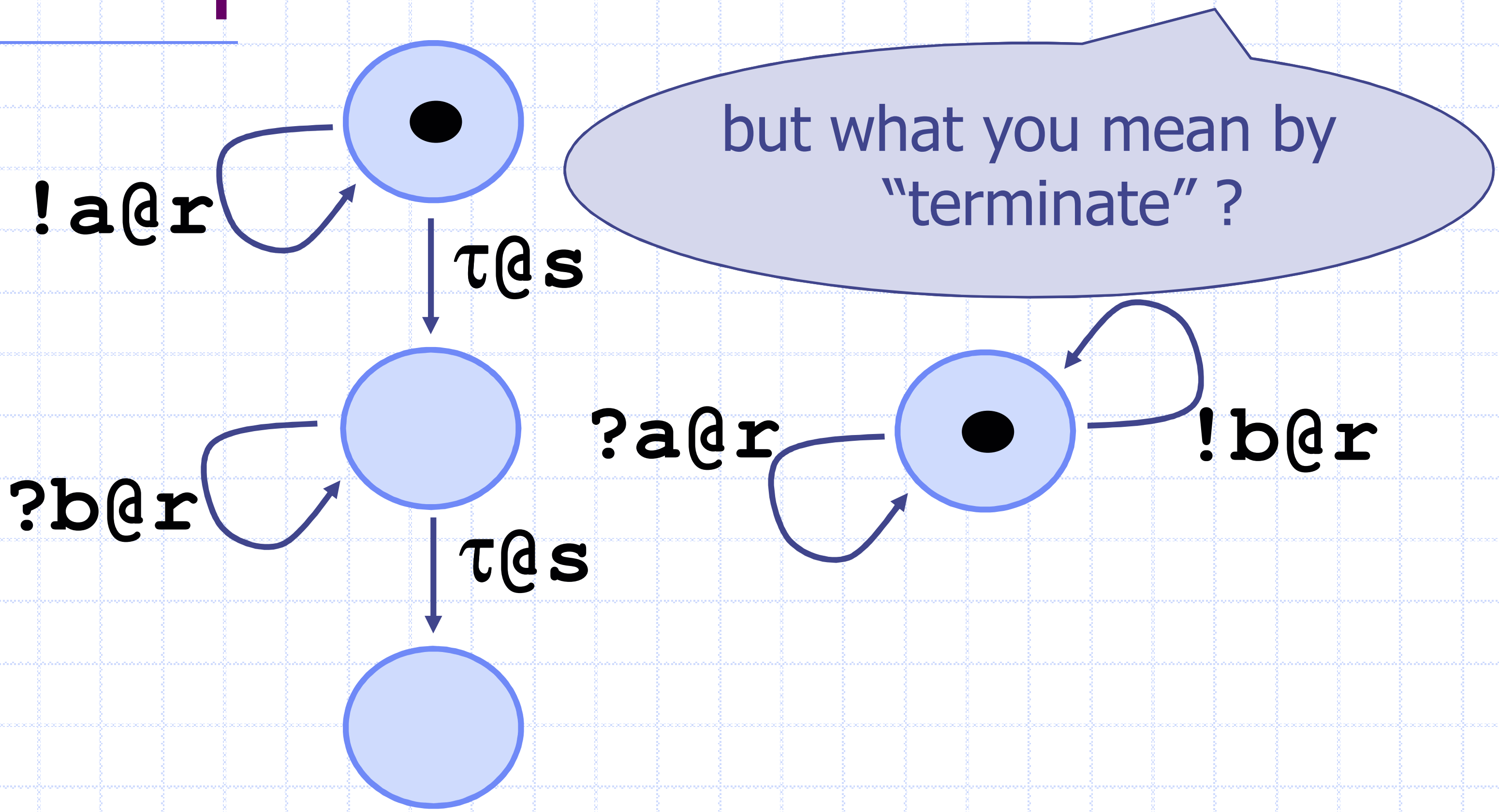
Example: does it terminate?

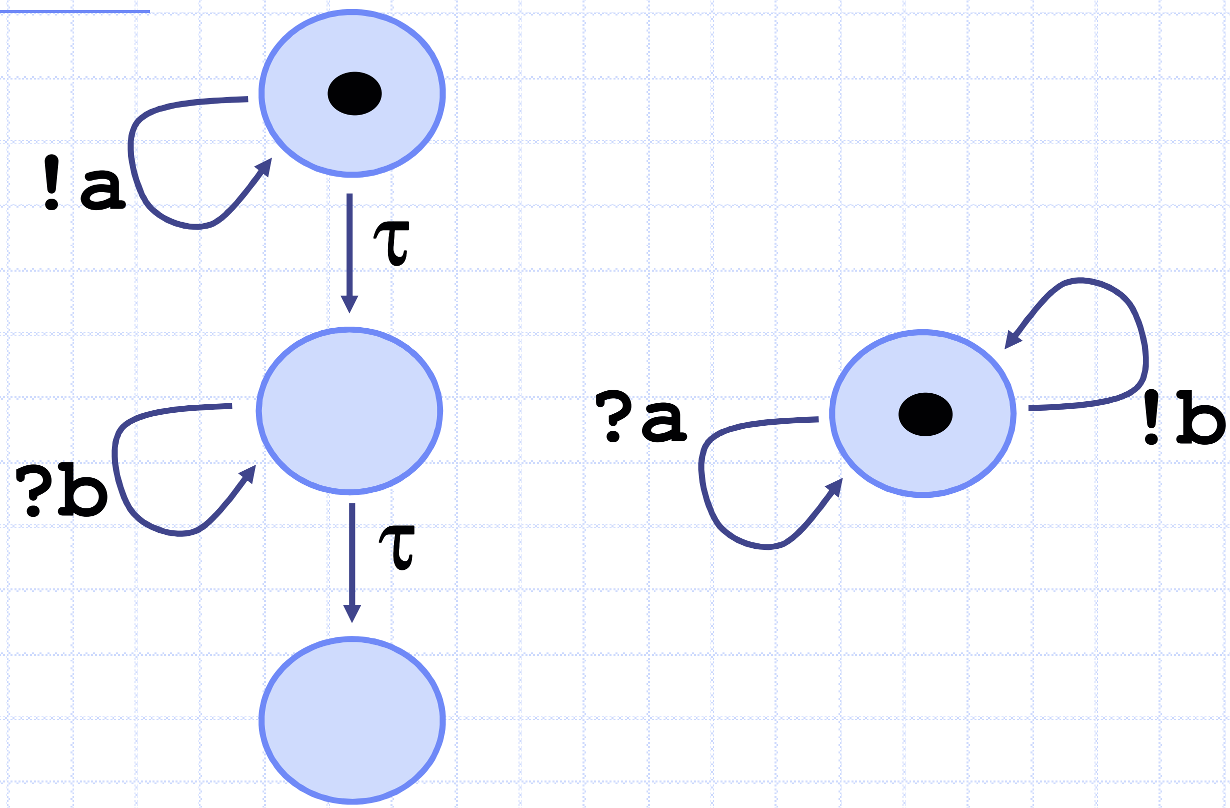


- Starting process: **A|A′**

Several notions of terminations

- Nondeterministic semantics
  - **Existential termination**:
    there exists one terminating computation
  - **Universal termination**: all computations terminate
- Stochastic semantics
  - **Existential termination**:
    the process terminates with prob. > 0
  - **Probabilistic termination**:
    the process terminates with prob. > ε (with $0<\varepsilon<1$)
  - **Universal termination**:
    the process terminates with prob. = 1

Example: does it "existentially" terminate?



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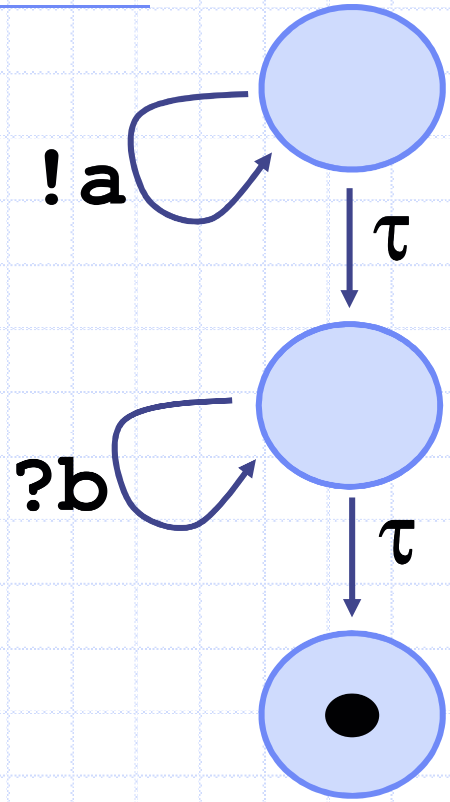
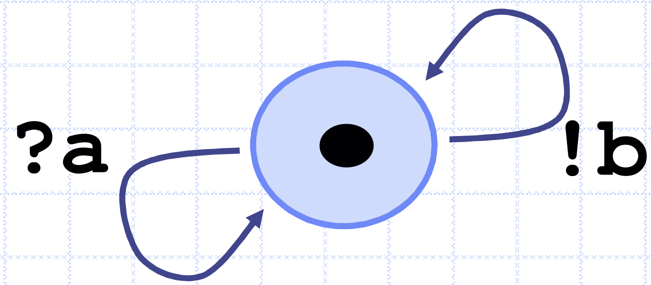


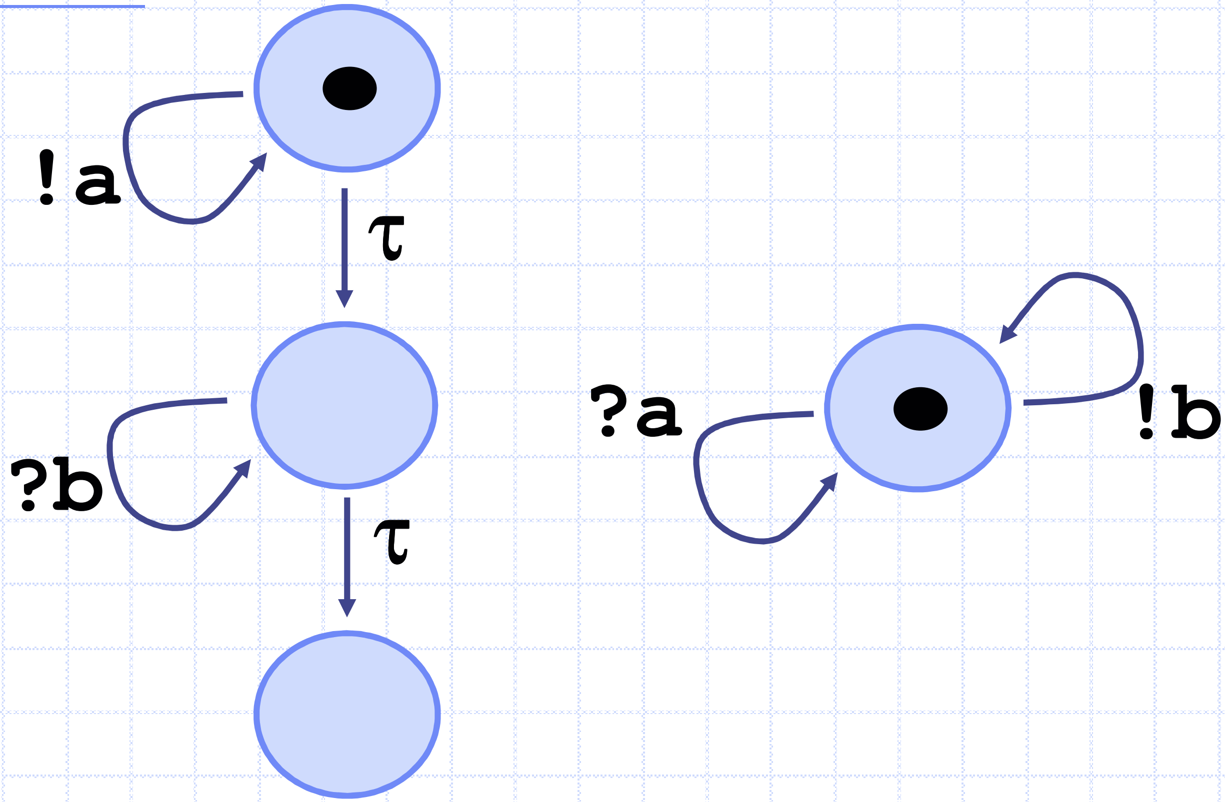
YES



a*τb*τ

- Starting process: **A|A′**

Example: does it "universally" terminate?



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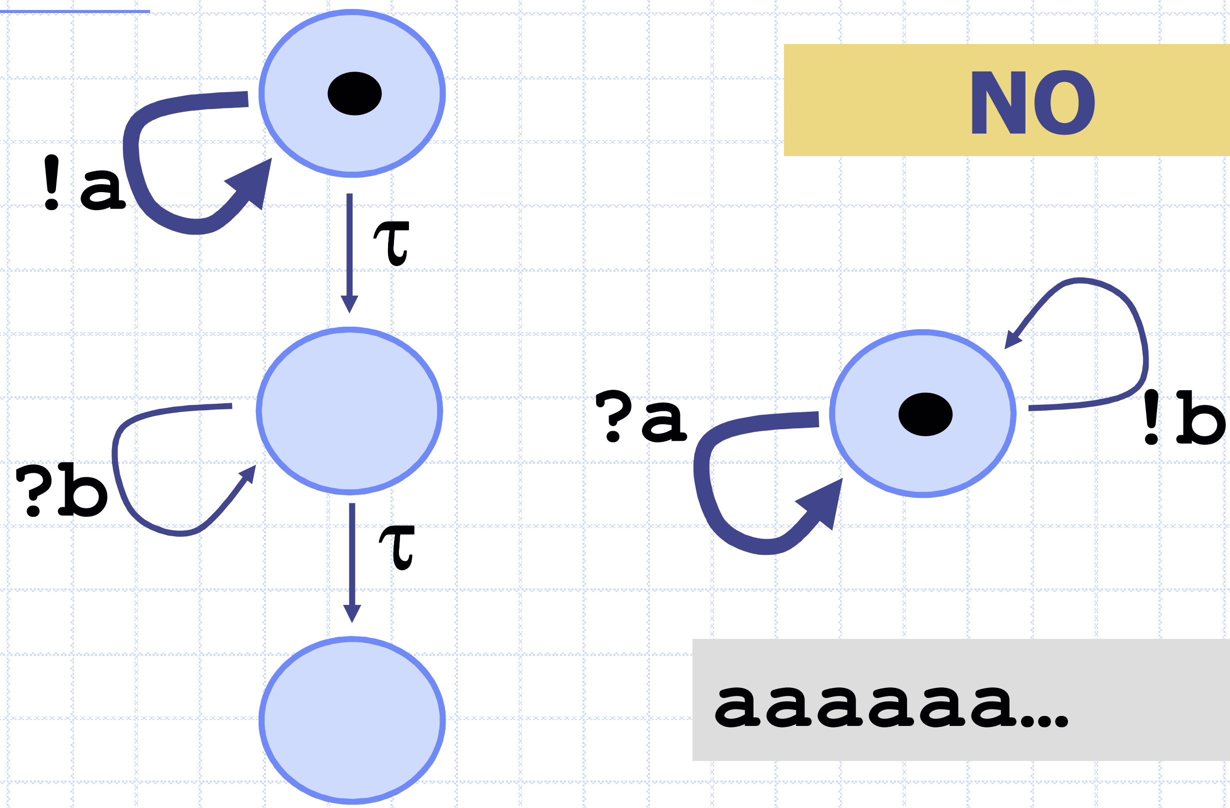

NO

aaaaaa…

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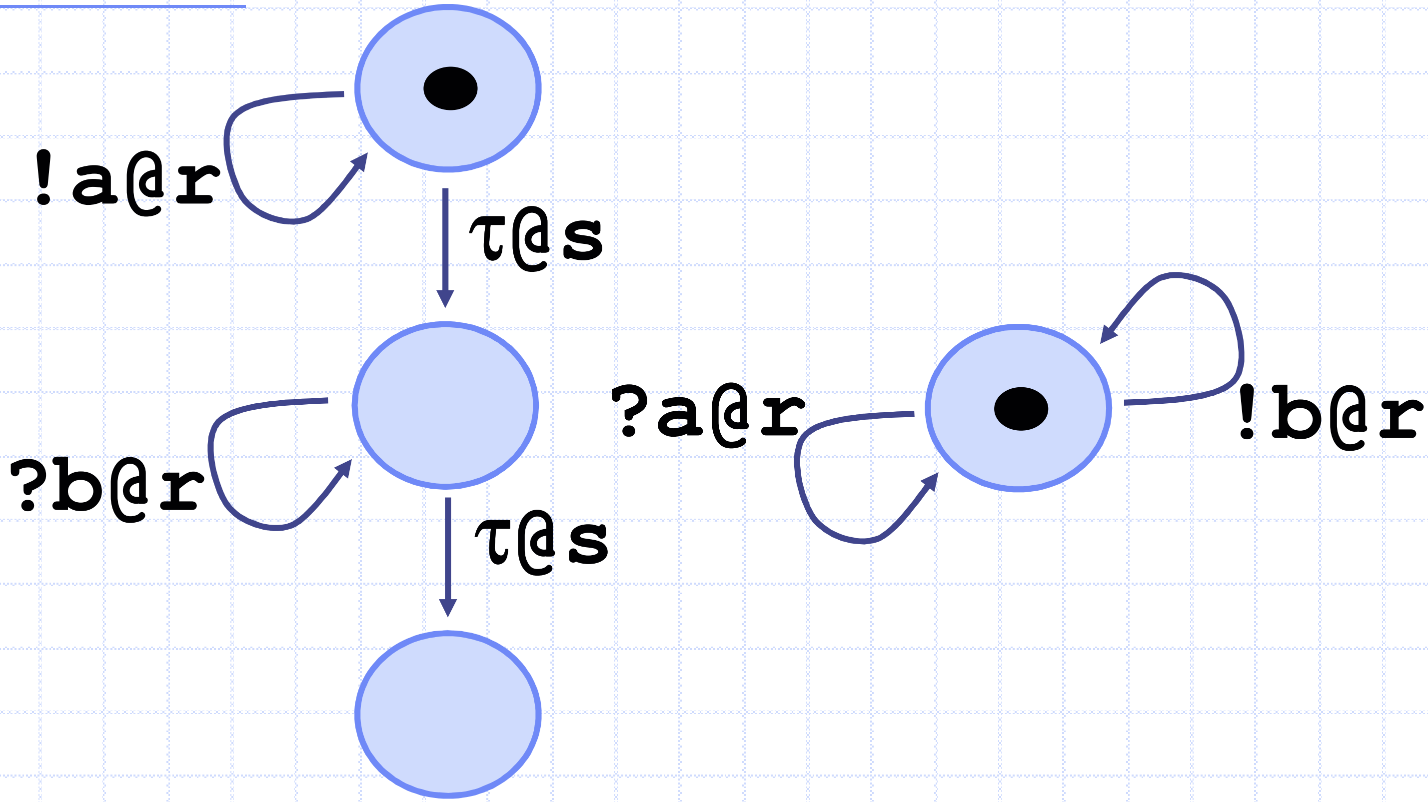

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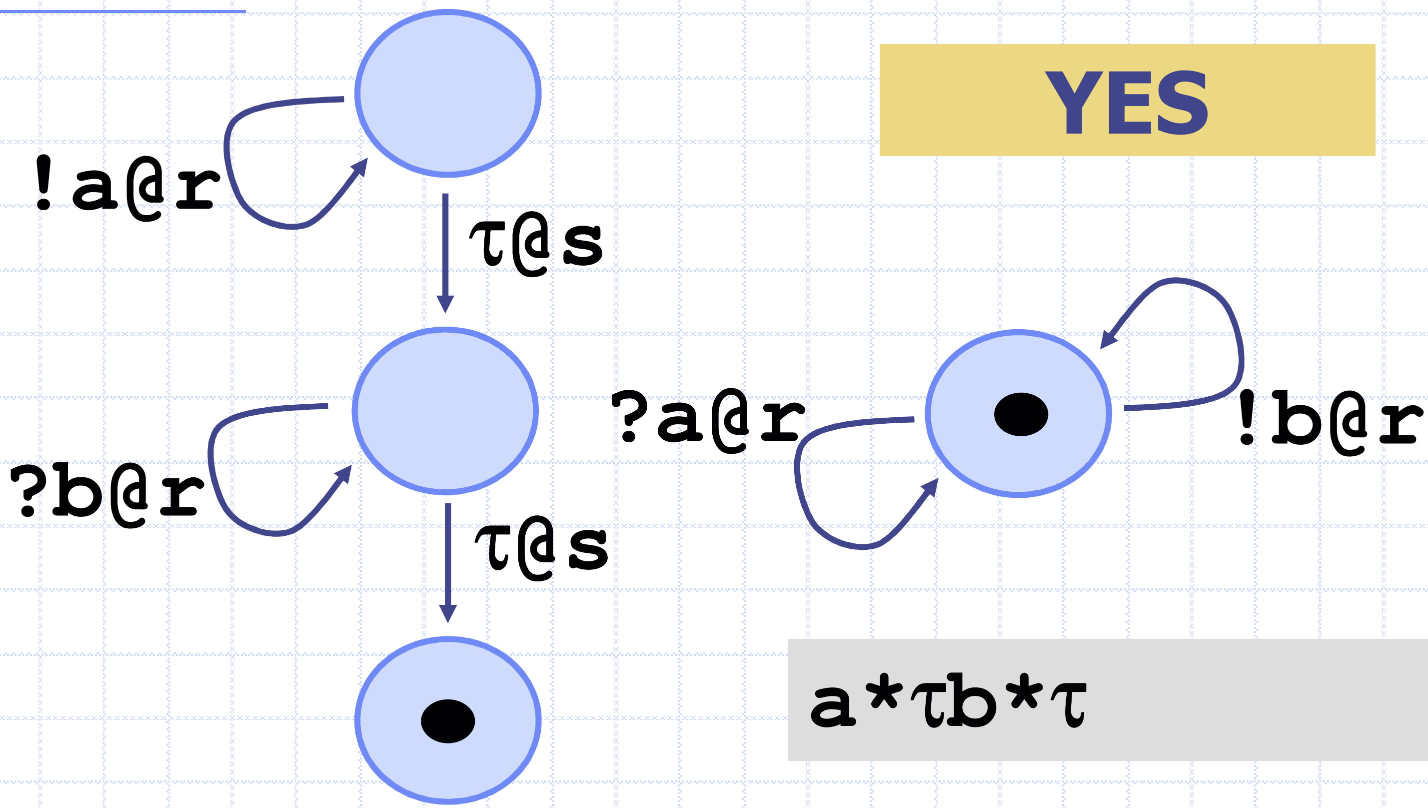

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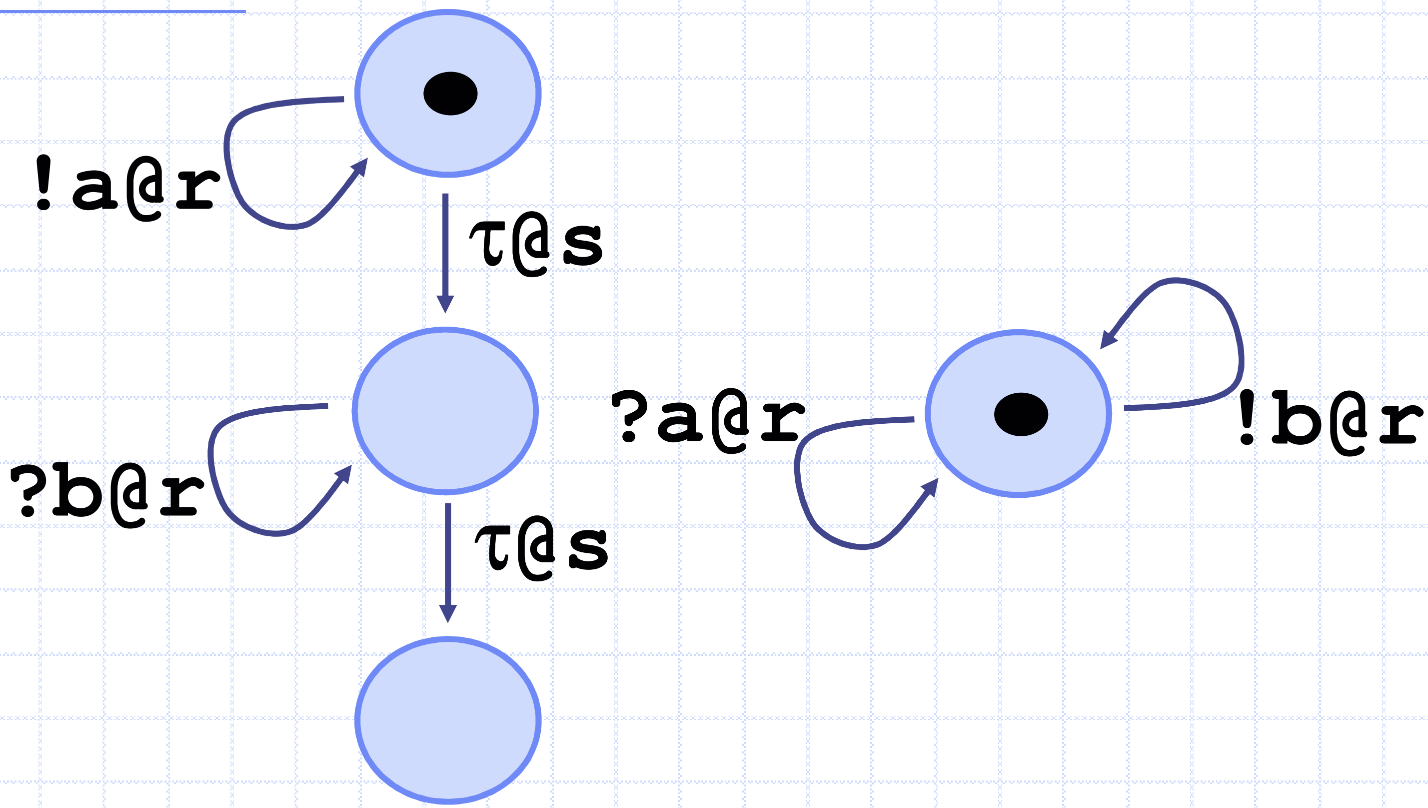

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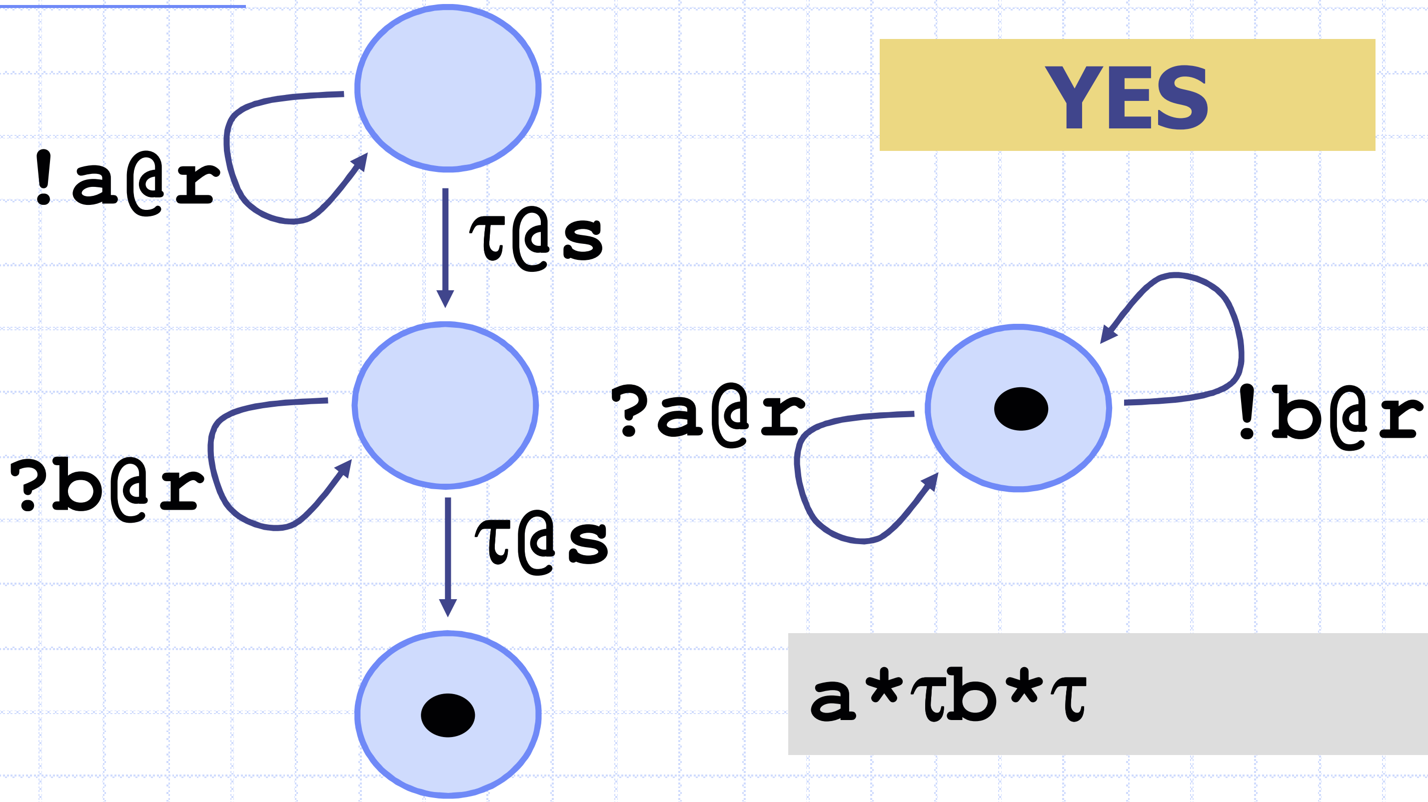

YES

`a*τb*τ`

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Plan of the talk

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Both terminations decidable under nondeterministic semantics

- We reduce **existential** and **universal** termination for CGF to termination for **Petri Nets**
  - In Petri Nets several properties such as reachability, coverability, termination, divergence,… are decidable

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Existential termination (decidable)

- Proof by **reduction** to existential termination under the nondeterministic semantics
  - a CGF process terminates with prob.>0 **iff** it existentially terminates under the nondeterministic semantics

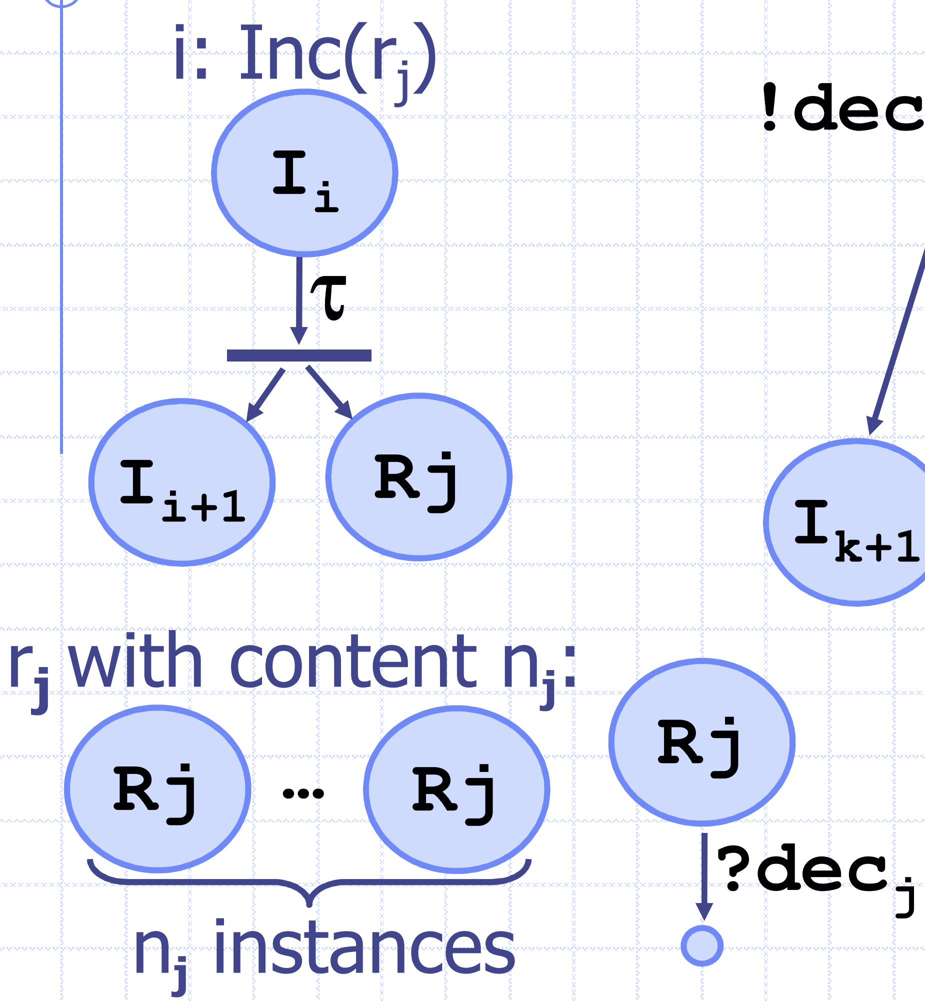
Probabilistic termination (undecidable)

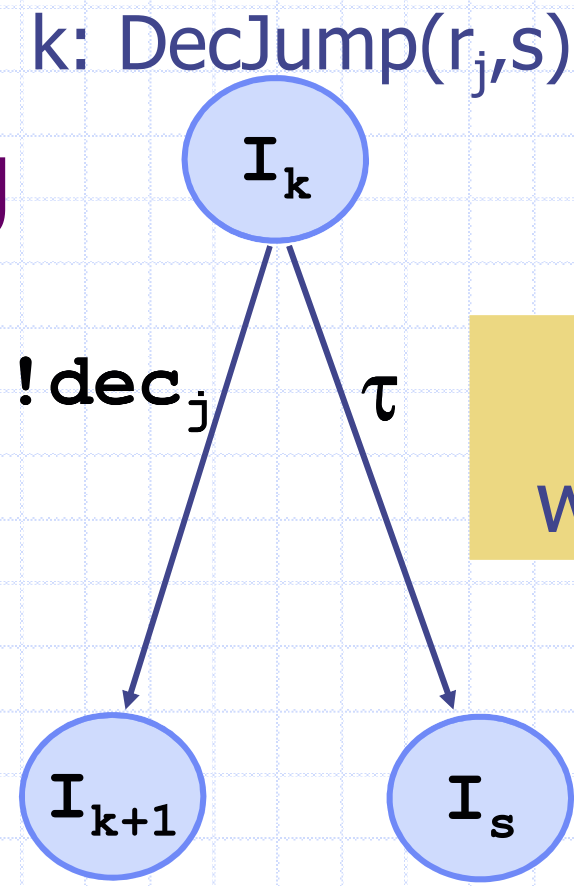
- Proof by reduction to **Random Access Machine** (RAM) termination
- RAMs [Min67]:
  - **Registers**: $r_1 \ldots r_n$ hold natural numbers
  - **Program**: sequence of indexed instructions
    - **i: Inc(r_j)**: add 1 to the content of r_j and go to the next instruction
    - **i: DecJump(r_j,s)**: if the content of r_j is not 0 then decrease by 1 and go to the next instruction; otherwise jump to instruction s

RAM encoding

- RAMs **cannot** be faithfully modeled by a CGF process
  - otherwise (by decidability of existential term. in CGF) RAM termination is decidable
- RAMs **can** be modeled by a CGF process that includes also wrong computations, but the prob. a wrong computation is scheduled is smaller than any given $\varepsilon > 0$

Approximate RAM modeling



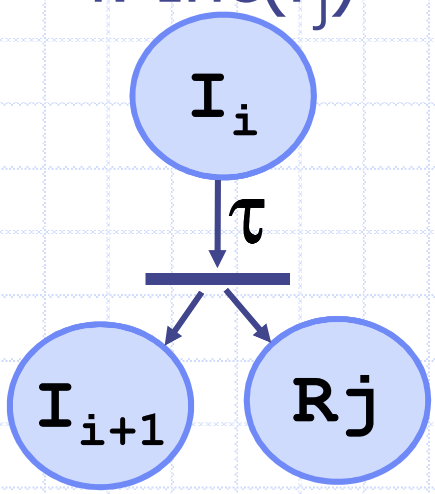


Problem:

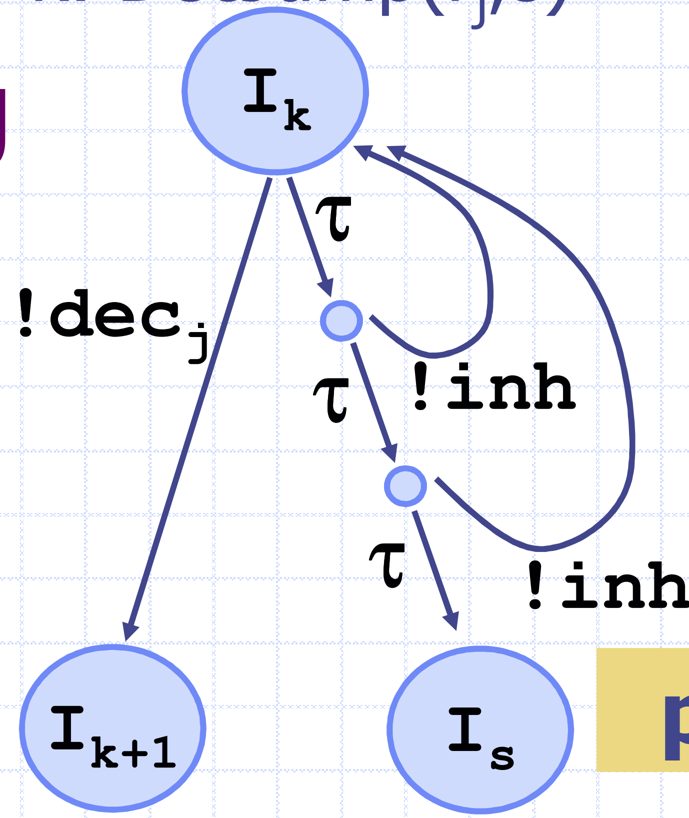
wrong jump!

Approximate RAM modeling

i: Inc(r_j)

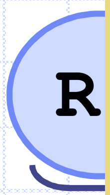


k: DecJump(r_j,s)

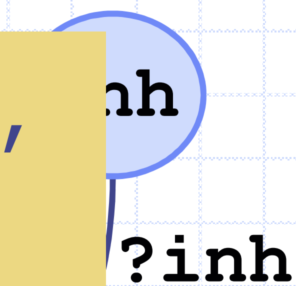


$p < 1/h^2$

r_j wit



r_j



But in an unbounded computation,
with infinitely many DecJump,
the prob. of a wrong jump is 1

Approximate RAM modeling

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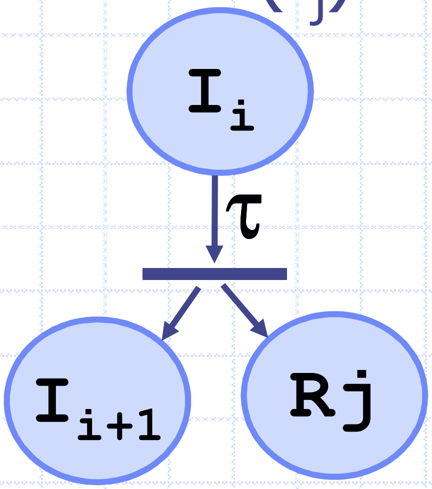

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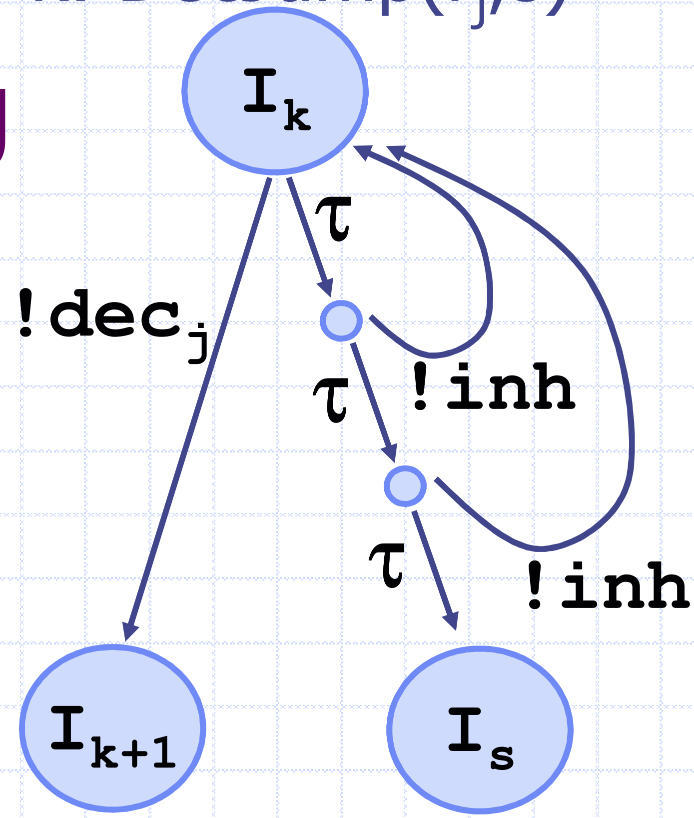
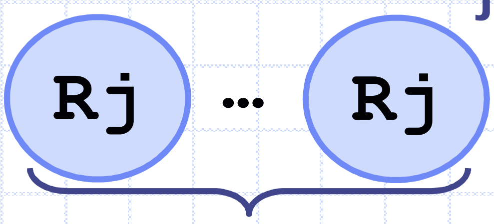
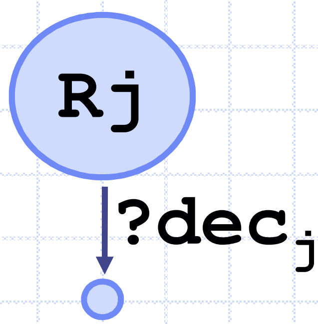
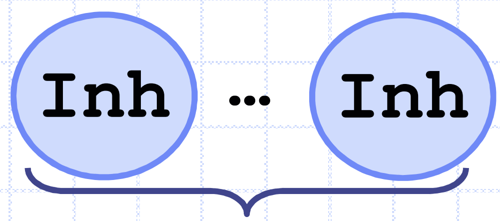


r_j with content n_j:

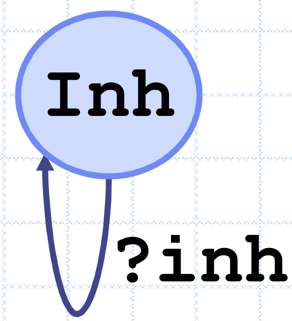


n_j instances

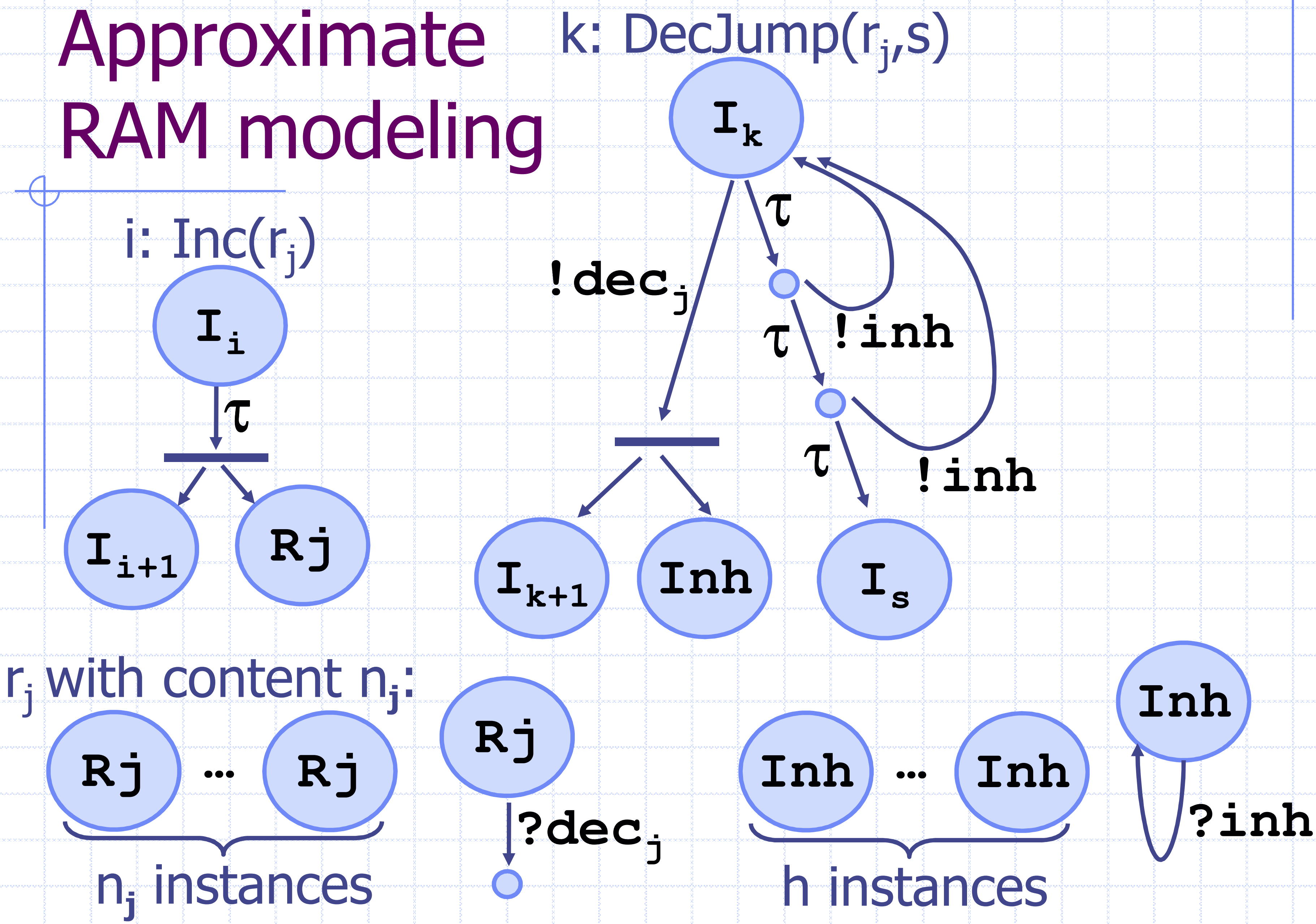




h instances



Approximate RAM modeling



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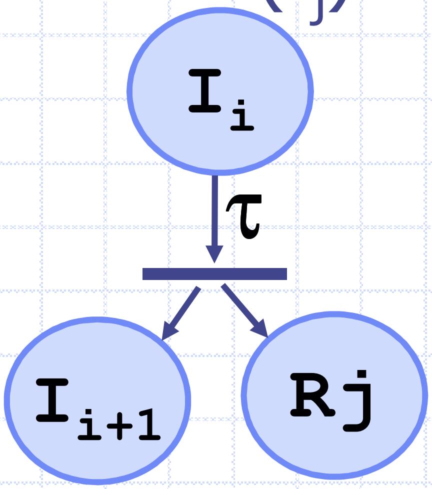

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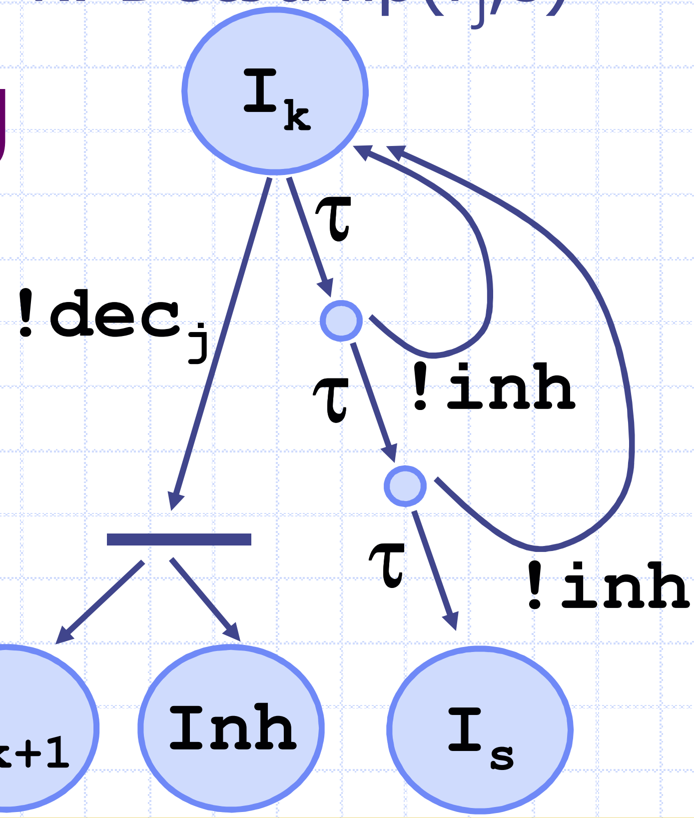


r_j wi

nh

Incrementing the occurrences of **Inh** the prob. of a wrong jump is

$$\mathbf{p} < \Sigma_{i=inith\ldots\infty} \mathbf{1/i^2}$$

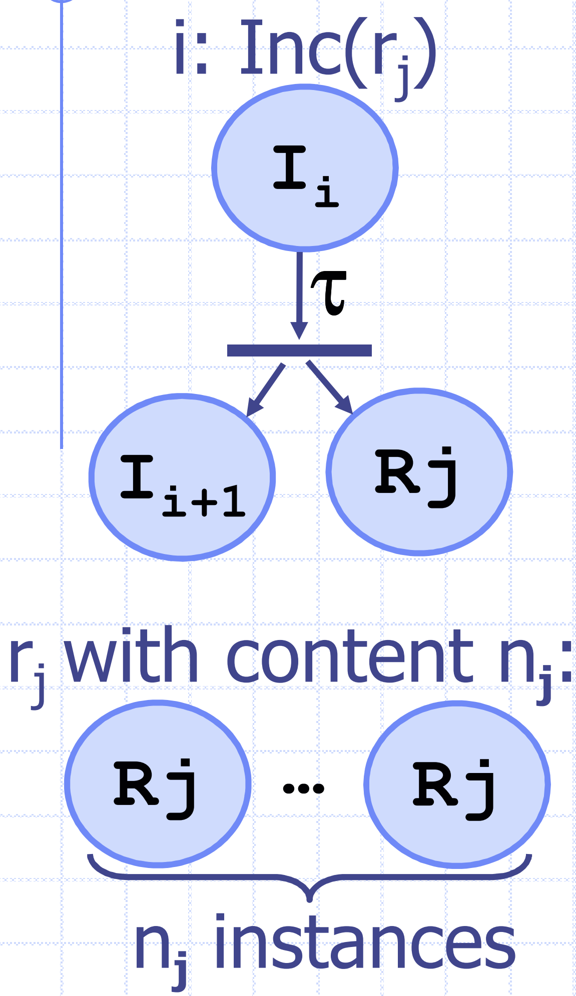
Universal termination (undecidable)

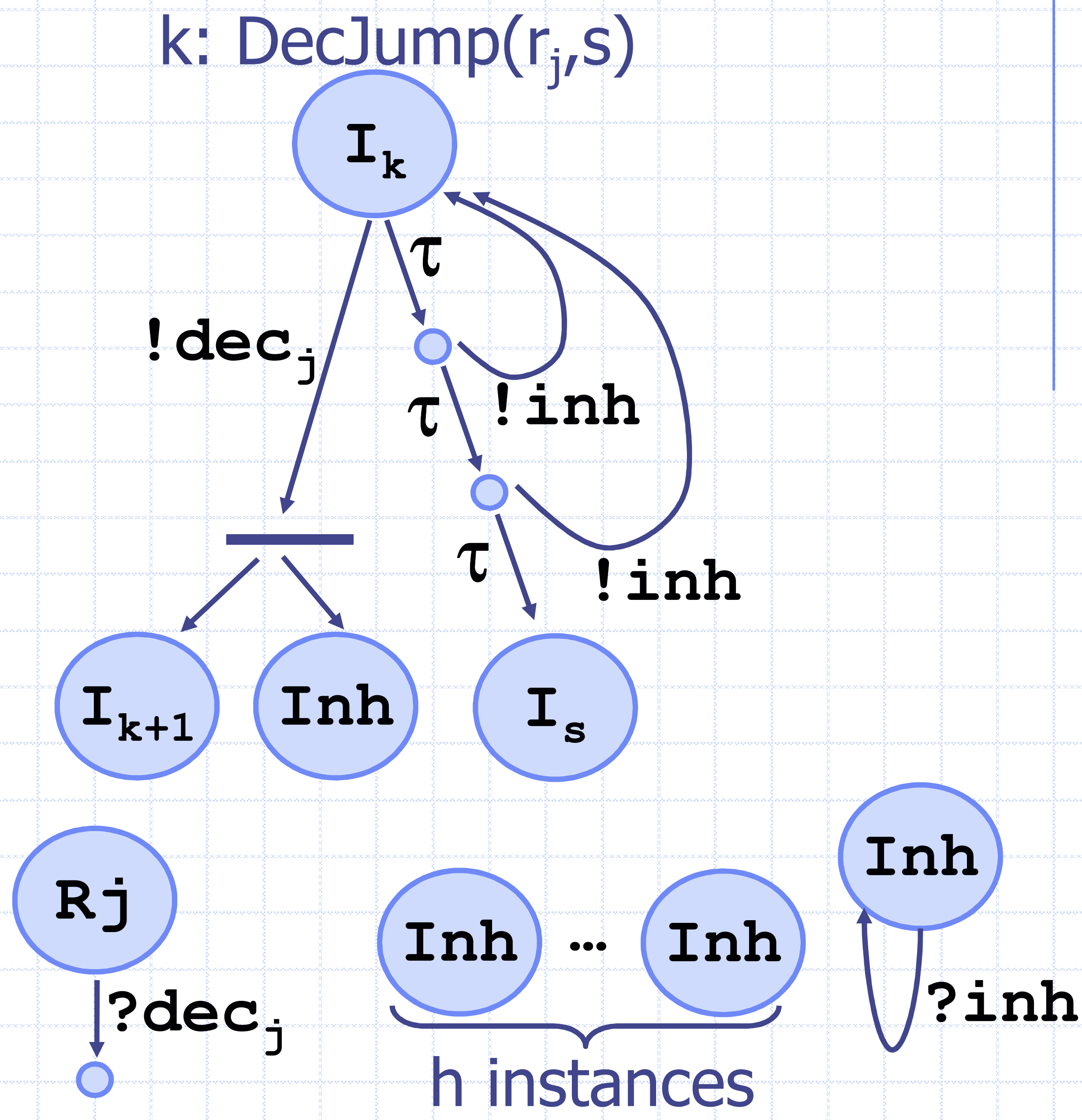
- Proof by **reduction** in two steps:
  - **(step 1)** Reduction of RAM termination to **FinitelyFaultyRAM** (FFRAM) divergence
    - FFRAMs are nondeterministic RAMs that, in case of DecJump with nonempty register, can jump (but only finitely many times!)
  - **(step 2)** Reduction of FFRAM divergence to --the complement of-- universal termination in CGF

First reduction

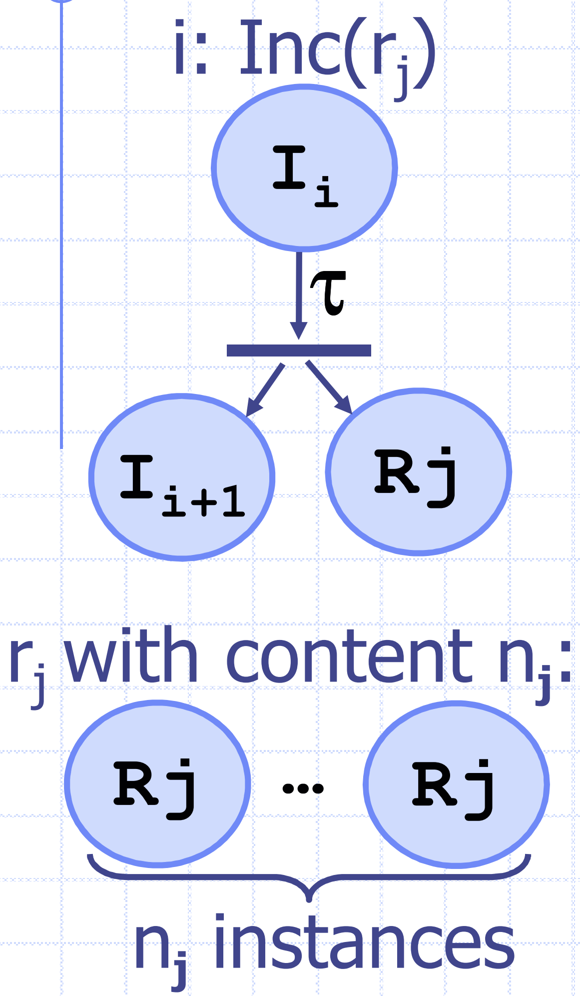
- Given a RAM consider the following FFRAM algorithm:
  1. "Randomly" generate a **value k** (possible thanks to FFRAM nondeterminism)
  2. Simulate **at most k steps** of the RAM
  3. If the simulation reached a **terminated** state return to step 2.
- This algorithm has an infinite computation (i.e. diverges) **iff** the given RAM terminates

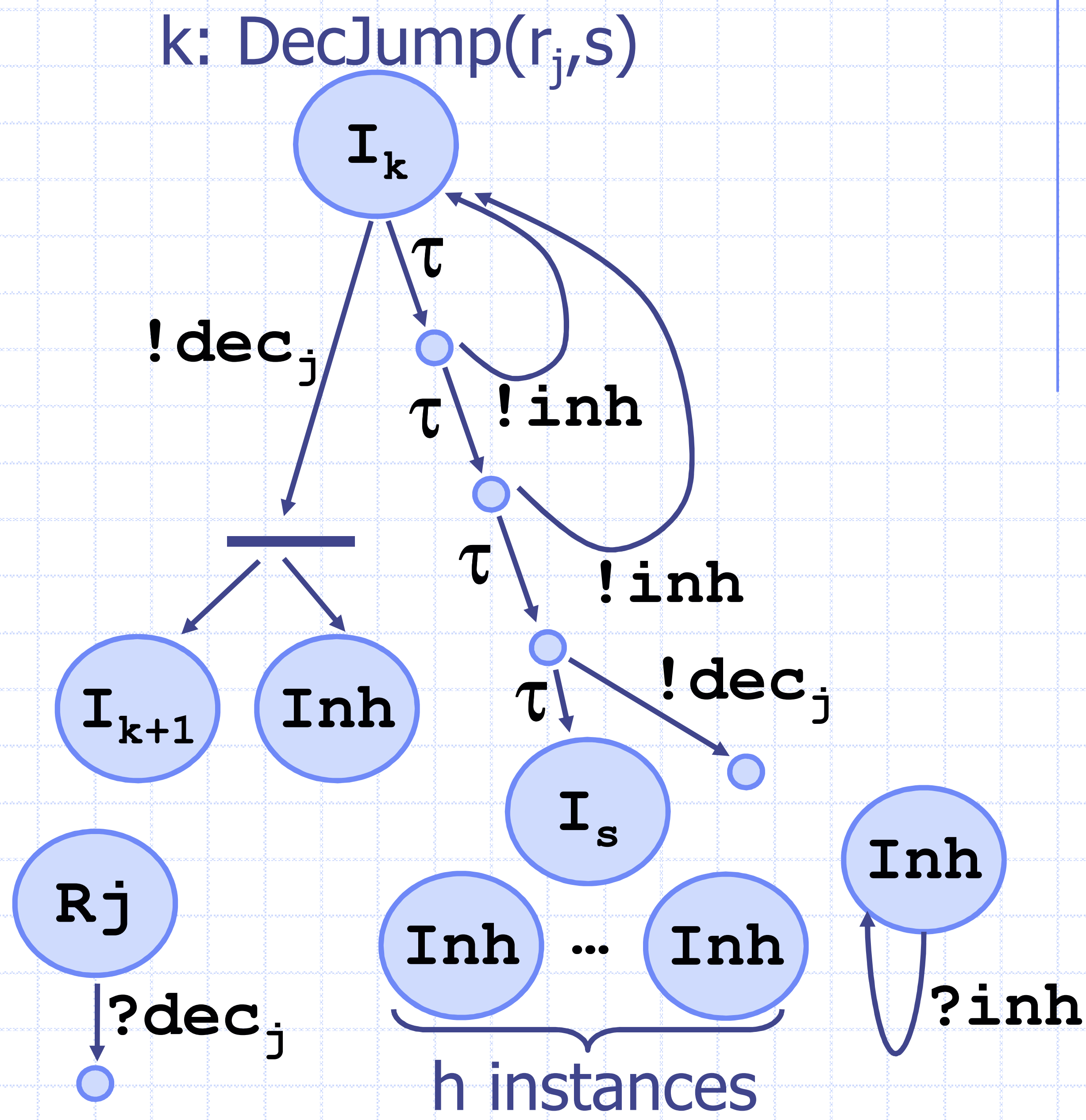
Second Reduction





Second Reduction





Plan of the talk

- Chemical Kinetics as a Computational Model
  - ... not a new issue
- Chemical Ground Form (CGF) [TCS08]
  - … a new way to analyze chemical kinetics
- Considered TERMINATION problems:
  - Purely Nondeterministic semantics:
    - Existential termination (one computation terminates)
    - Universal termination (all computations terminate)
  - Stochastic semantics:
    - Existential termination (terminate with probability $p>0$)
    - Probabilistic termination (terminate with probability $p>\varepsilon$ with $0<\varepsilon<1$)
    - Universal termination (terminate with probability $p=1$)
- **Concluding remarks**

Conclusion

- Is Chemical Kinetics Turing powerful?
  - An additional proof that it is **NOT** but Turing complete formalisms can be **approximated** with any given degree of precision
- "**Perpetual**" and "**ephemeral**" chemical systems
  - Surely "perpetual": DECIDABLE
  - Surely "ephemeral": UNDECIDABLE
  - Possibly "perpetual"/"ephemeral": UNDECIDABLE

Related work

- Petri nets
  - Universal termination is decidable but it is not in **fair** Petri nets [Car87]
- Lossy channels
  - Universal termination is decidable but it is not in **probabilistic** lossy channels [Abd. et al.00]
- "Turifying" chemical kinetics
  - CGF extended with a mechanism for molecule **association/dissociation** (inspired by biochemistry) is Turing powerful [AB08]