MPRI

Model reduction of stochastic rules-based models

[CS2Bio'10,MFPS'10,MeCBIC'10,ICNAAM'10]

Jérôme Feret
Laboratoire d'Informatique de l'École Normale Supérieure
INRIA, ÉNS, CNRS

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Joint-work with...

Ferdinanda Camporesi
Bologna / ÉNS

Thomas Henzinger
IST Austria

Heinz Koeppl
ETH Zürich

Tatjana Petrov
EPFL

Overview

1. Introduction
2. Examples of information flow
3. Symmetric sites
4. Stochastic semantics
5. Lumpability
6. Bisimulations
7. Hierarchy of semantics
8. Conclusion

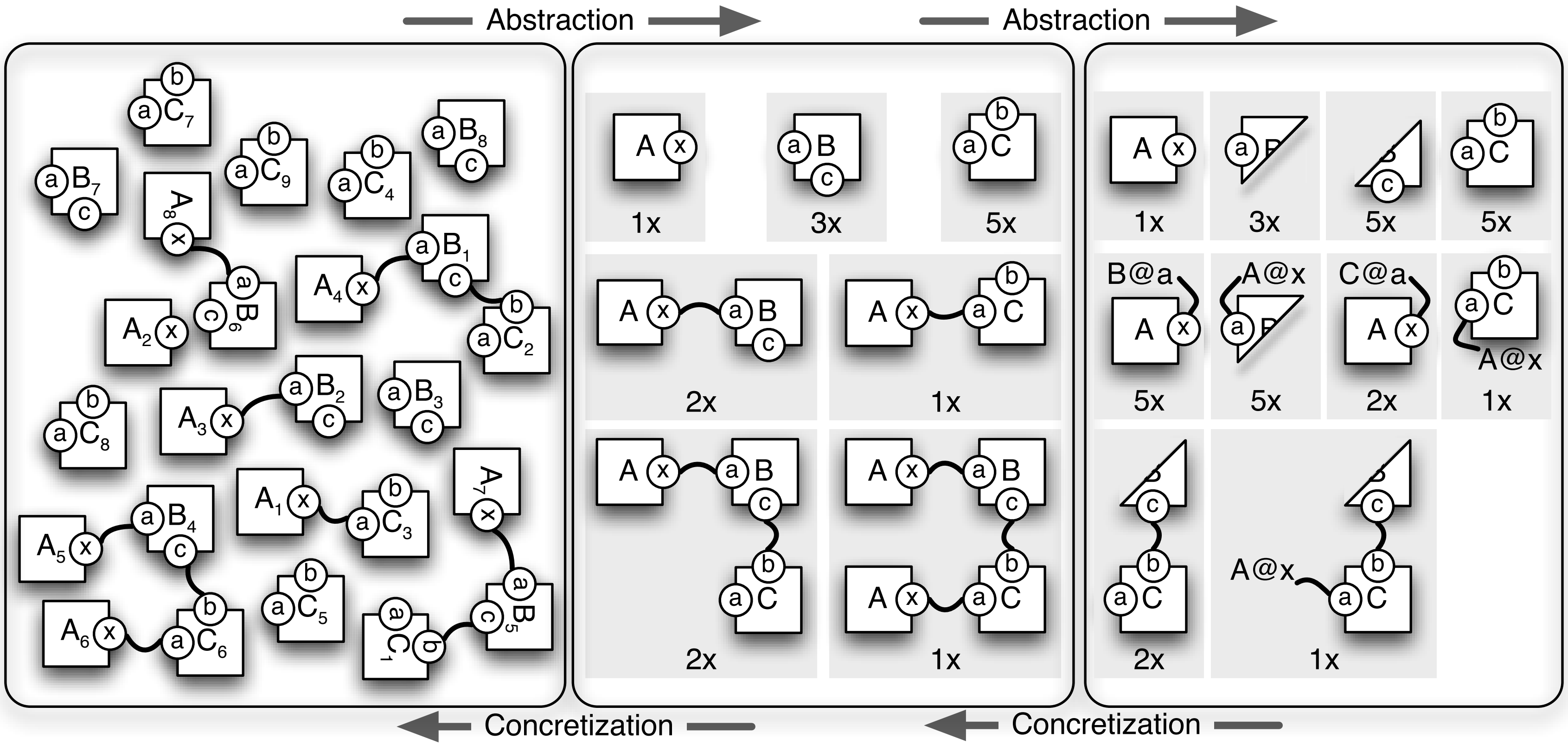
ODE fragments

In the ODE semantics, using the flow of information backward, we can detect which correlations are not relevant for the system, and deduce a small set of portions of chemical species (called fragments) the behavior of the concentration of which can be described in a self-consistent way.

(ie. the trajectory of the reduced model are the exact projection of the trajectory of the initial model).

Can we do the same for the stochastic semantics?

Stochastic fragments ?



Overview

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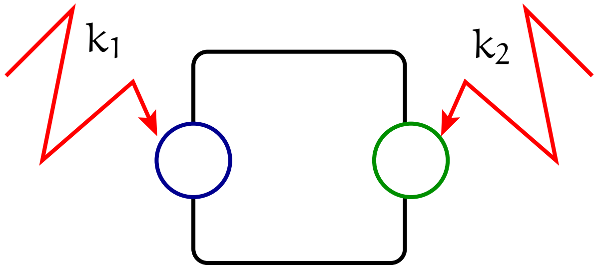
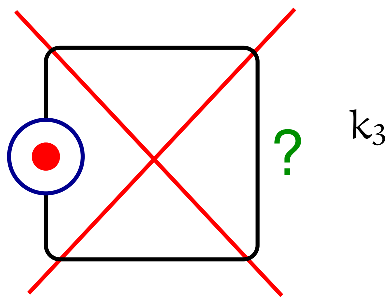
A model with ubiquitination



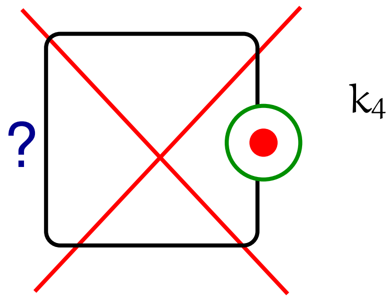
$$P \xrightarrow{k_1} {}^{\star}P \qquad P^{\star} \xrightarrow{k_1} {}^{\star}P^{\star}$$

$$P \xrightarrow{k_2} P^{\star} \qquad {}^{\star}P \xrightarrow{k_2} {}^{\star}P^{\star}$$



$${}^{\star}P \xrightarrow{k_3} \emptyset$$

$${}^{\star}P^{\star} \xrightarrow{k_3} \emptyset$$



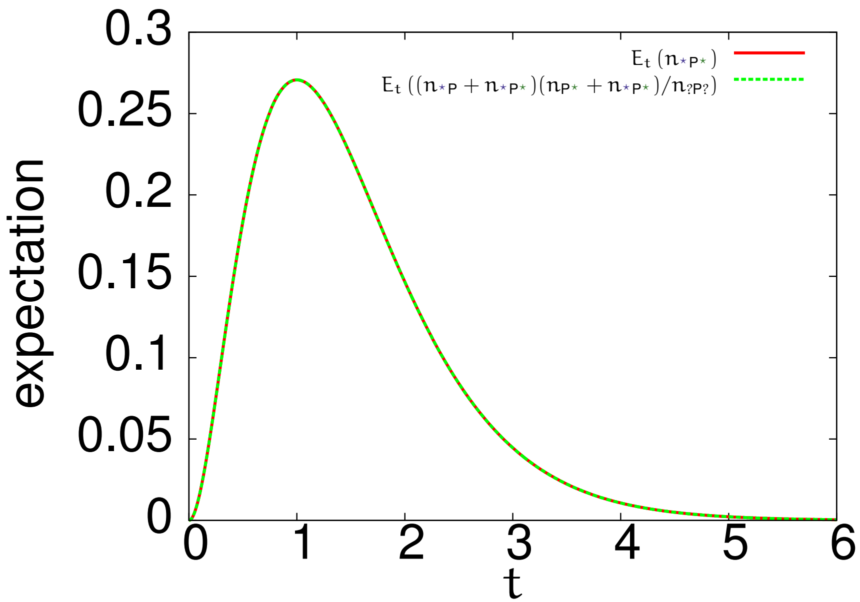
$$P^{\star} \xrightarrow{k_4} \emptyset$$

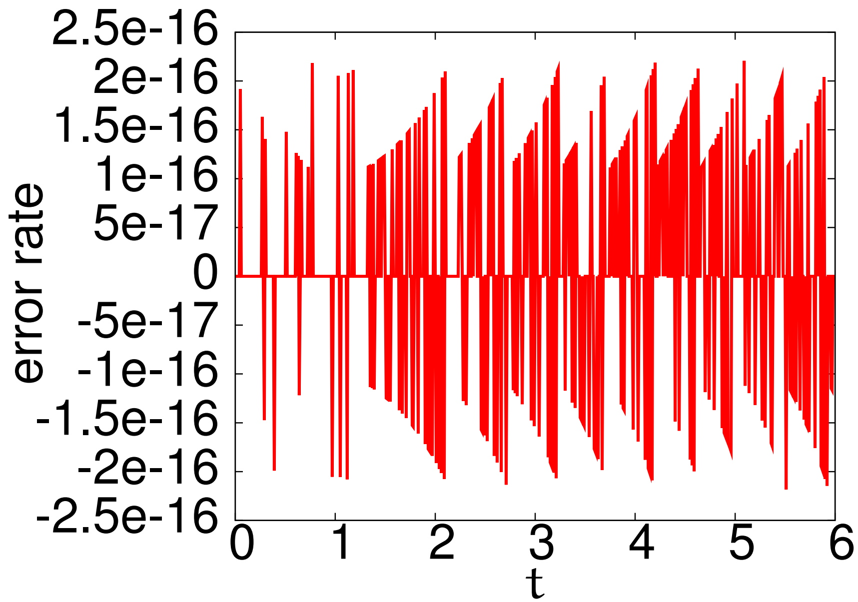
$${}^{\star}P^{\star} \xrightarrow{k_4} \emptyset$$

Statistical independence

We check numerically that:

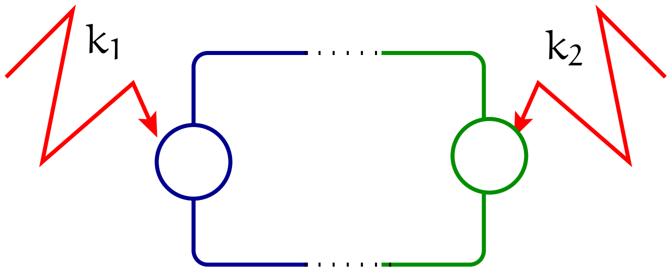
$$E_t\left(n_{\star P\star}\right) = E_t\left(\frac{(n_{\star P}+n_{\star P\star})(n_{P\star}+n_{\star P\star})}{n_{P}+n_{P\star}+n_{\star P}+n_{\star P\star}}\right).$$





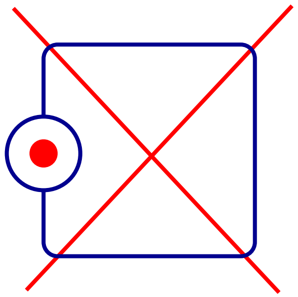
with $k_1 = k_2 = k_3 = k_4 = 1$
and two instances of P at time $t = 0$.

Reduced model



$$P \xrightarrow{k_1} {}^{\star}P$$

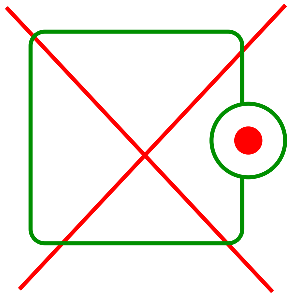
$$P \xrightarrow{k_2} P^{\star}$$



k_3

$${}^{\star}P \xrightarrow{k_3} \emptyset$$

+ side effect: remove one P

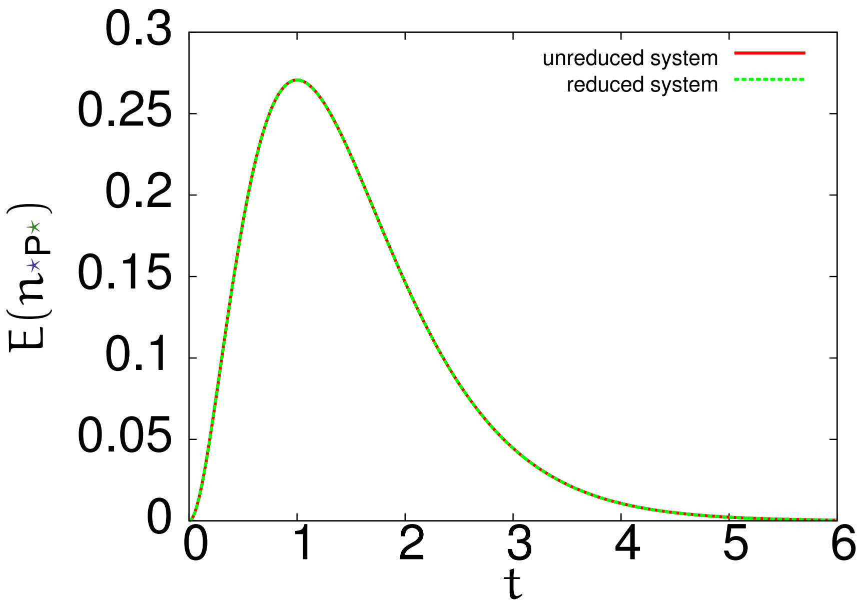


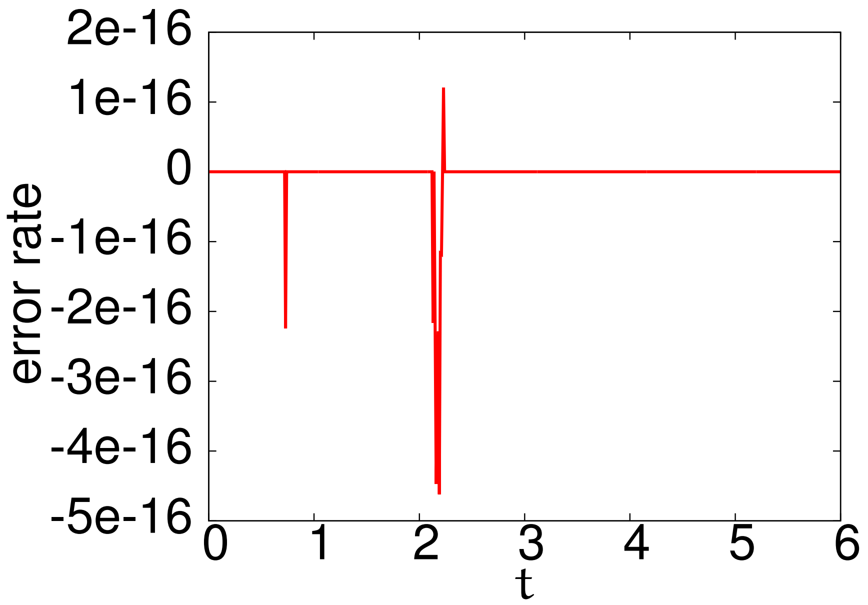
k_4

$$P^{\star} \xrightarrow{k_4} \emptyset$$

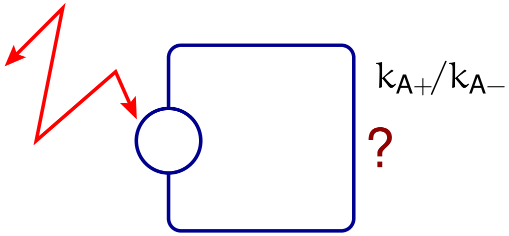
+ side effect: remove one P

Comparison between the two models

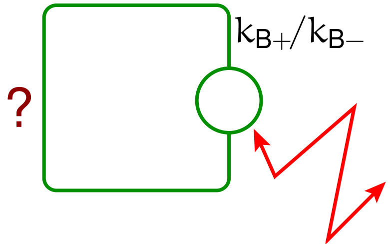




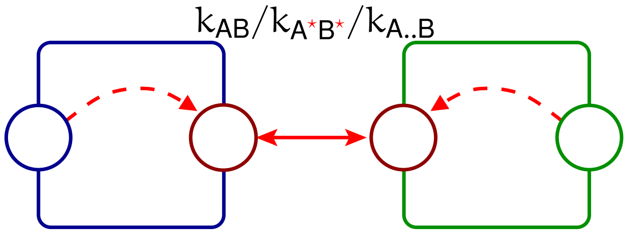
Coupled semi-reactions



$$A \underset{k_{A-}}{\overset{k_{A+}}{\rightleftharpoons}} A^{\star}, \quad AB \underset{k_{A-}}{\overset{k_{A+}}{\rightleftharpoons}} A^{\star}B, \quad AB^{\star} \underset{k_{A-}}{\overset{k_{A+}}{\rightleftharpoons}} A^{\star}B^{\star}$$



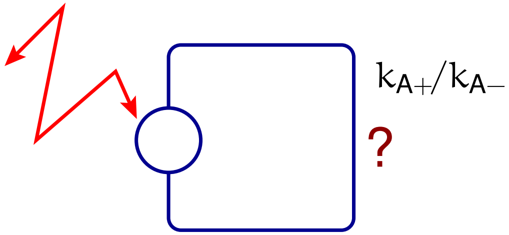
$$B \underset{k_{B-}}{\overset{k_{B+}}{\rightleftharpoons}} B^{\star}, \quad AB \underset{k_{B-}}{\overset{k_{B+}}{\rightleftharpoons}} AB^{\star}, \quad A^{\star}B \underset{k_{B-}}{\overset{k_{B+}}{\rightleftharpoons}} A^{\star}B^{\star}$$



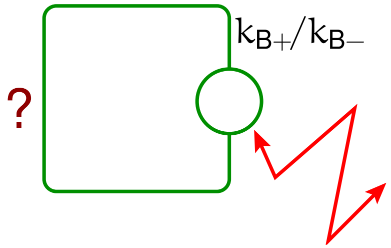
$$A + B \underset{k_{A..B}}{\overset{k_{AB}}{\rightleftharpoons}} AB, \quad A^{\star} + B \underset{k_{A..B}}{\overset{k_{AB}}{\rightleftharpoons}} A^{\star}B,$$

$$A + B^{\star} \underset{k_{A..B}}{\overset{k_{AB}}{\rightleftharpoons}} AB^{\star}, \quad A^{\star} + B^{\star} \underset{k_{A..B}}{\overset{k_{A^{\star}B^{\star}}}{\rightleftharpoons}} A^{\star}B^{\star}$$

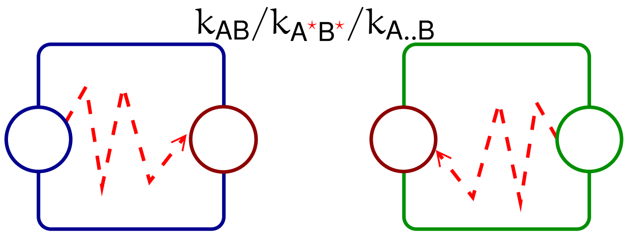
Reduced model



$$A \underset{k_{A-}}{\overset{k_{A+}}{\rightleftharpoons}} A^{\star}, \quad AB^{\diamond} \underset{k_{A-}}{\overset{k_{A+}}{\rightleftharpoons}} A^{\star}B^{\diamond},$$



$$B \underset{k_{B-}}{\overset{k_{B+}}{\rightleftharpoons}} B^{\star}, \quad A^{\diamond}B \underset{k_{B-}}{\overset{k_{B+}}{\rightleftharpoons}} A^{\diamond}B^{\star},$$



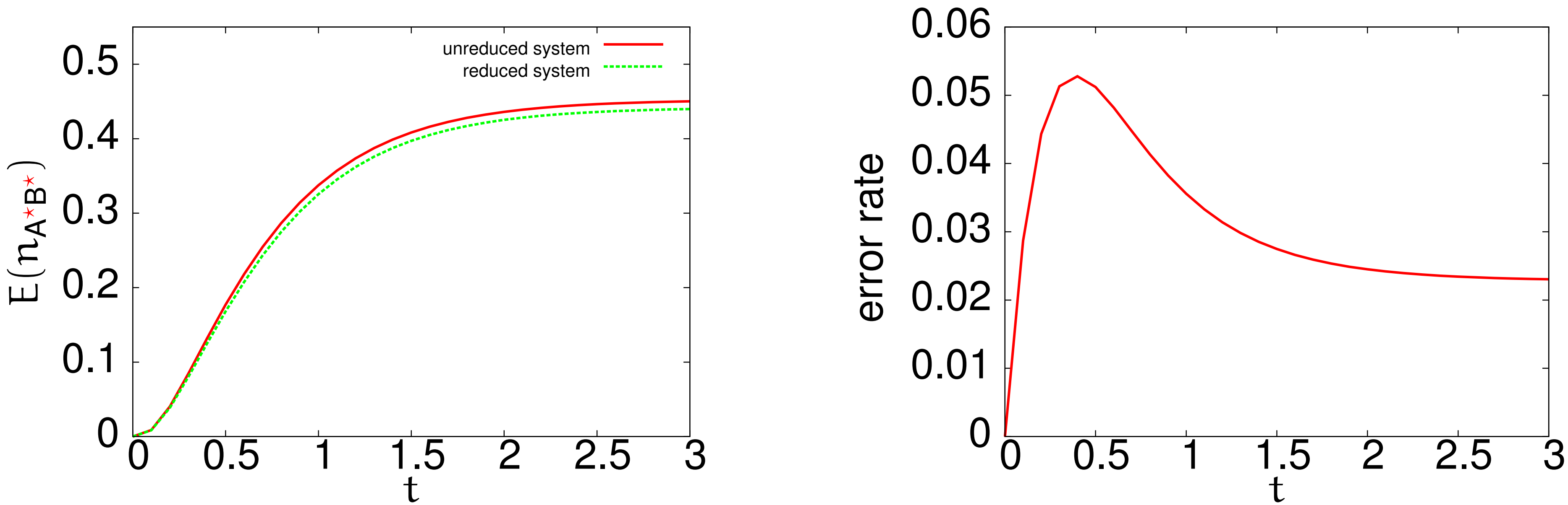
$$A + B \underset{k_{A..B}/(n_{A^{\diamond}B}+n_{A^{\diamond}B^{\star}})}{\overset{k_{AB}}{\rightleftharpoons}} AB^{\diamond} + A^{\diamond}B,$$

$$A^{\star} + B \underset{k_{A..B}/(n_{A^{\diamond}B}+n_{A^{\diamond}B^{\star}})}{\overset{k_{AB}}{\rightleftharpoons}} A^{\star}B^{\diamond} + A^{\diamond}B,$$

$$A + B^{\star} \underset{k_{A..B}/(n_{A^{\diamond}B}+n_{A^{\diamond}B^{\star}})}{\overset{k_{AB}}{\rightleftharpoons}} AB^{\diamond} + A^{\diamond}B^{\star},$$

$$A^{\star} + B^{\star} \underset{k_{A..B}/(n_{A^{\diamond}B}+n_{A^{\diamond}B^{\star}})}{\overset{k_{A^{\star}B^{\star}}}{\rightleftharpoons}} A^{\star}B^{\diamond} + A^{\diamond}B^{\star}$$

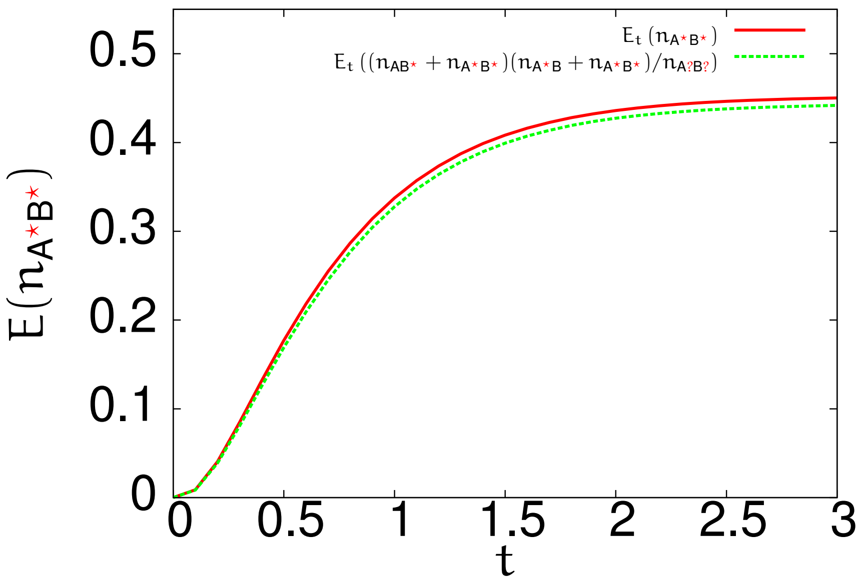
Comparison between the two models

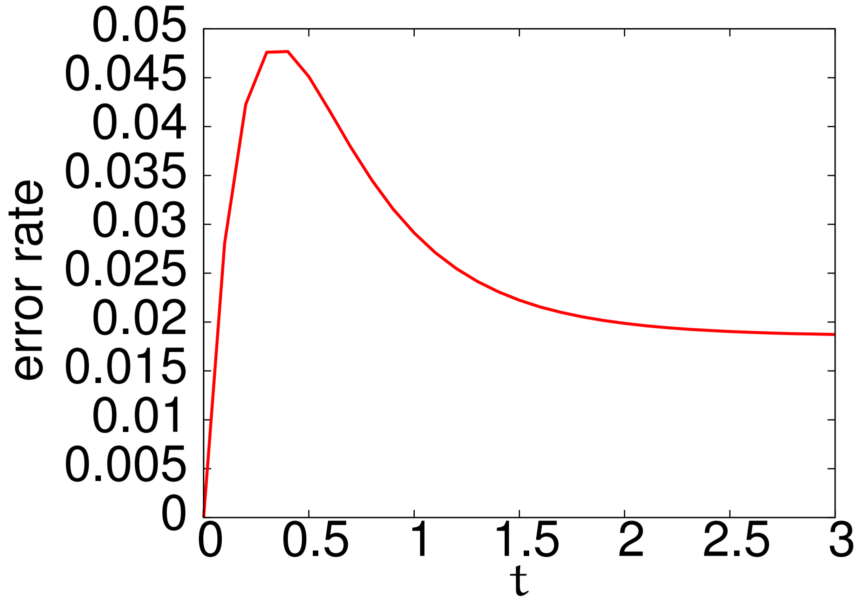


with $k_{A+} = k_{A-} = k_{B+} = k_{B-} = k_{AB} = k_{A..B} = 1$, $k_{A^\star B^\star} = 10$,
and two instances of A and B at time $t = 0$.

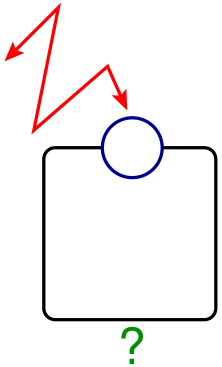
Although the reduction is correct in the ODE semantics.

Degree of correlation
(in the unreduced model)





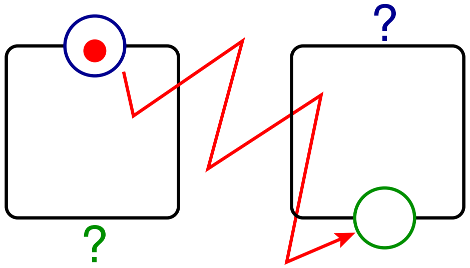
Distant control



k^{+}/k^{-}

$$A \underset{k^{-}}{\overset{k^{+}}{\rightleftharpoons}} A^{\star}$$

$$A_{\star} \underset{k^{-}}{\overset{k^{+}}{\rightleftharpoons}} A^{\star}_{\star}$$



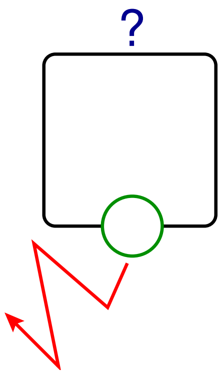
k_{+}

$$A + A^{\star} \xrightarrow{k_{+}} A_{\star} + A^{\star}$$

$$A^{\star} + A^{\star} \xrightarrow{k_{+}} A^{\star}_{\star} + A^{\star}$$

$$A + A^{\star}_{\star} \xrightarrow{k_{+}} A_{\star} + A^{\star}_{\star}$$

$$A^{\star} + A^{\star}_{\star} \xrightarrow{k_{+}} A^{\star}_{\star} + A^{\star}_{\star}$$

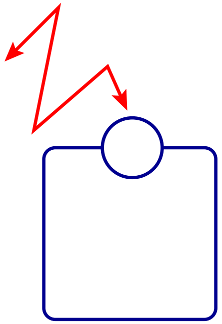


k_{-}

$$A^{\star}_{\star} \xrightarrow{k_{-}} A^{\star}$$

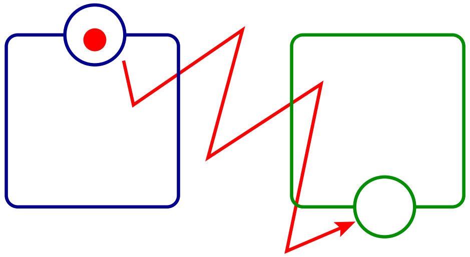
$$A_{\star} \xrightarrow{k_{-}} A$$

Reduced model



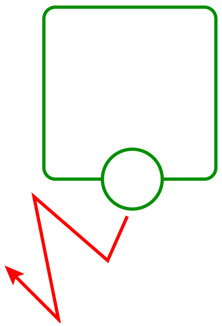
k^+/k^-

$$A \underset{k^-}{\overset{k^+}{\rightleftharpoons}} A^\star$$



k_+

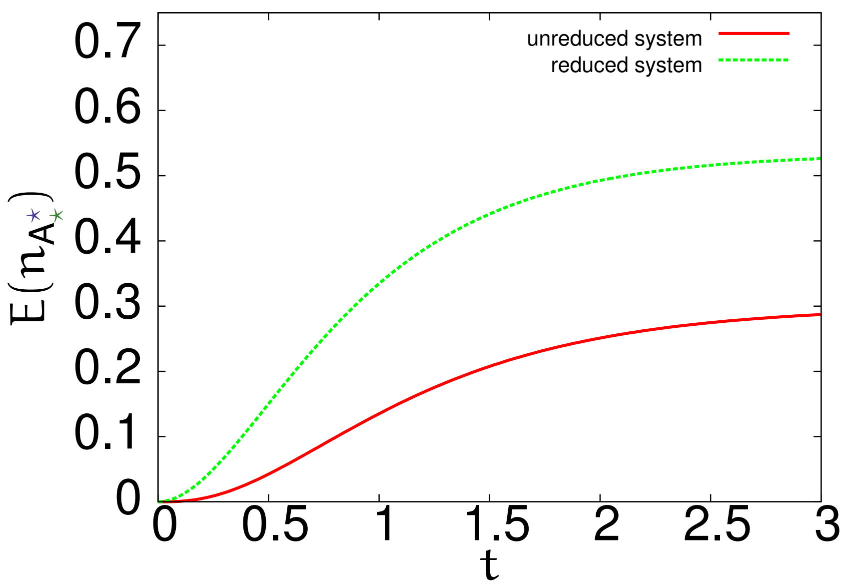
$$A + A^\star \xrightarrow{k_+} A_\star + A^\star$$

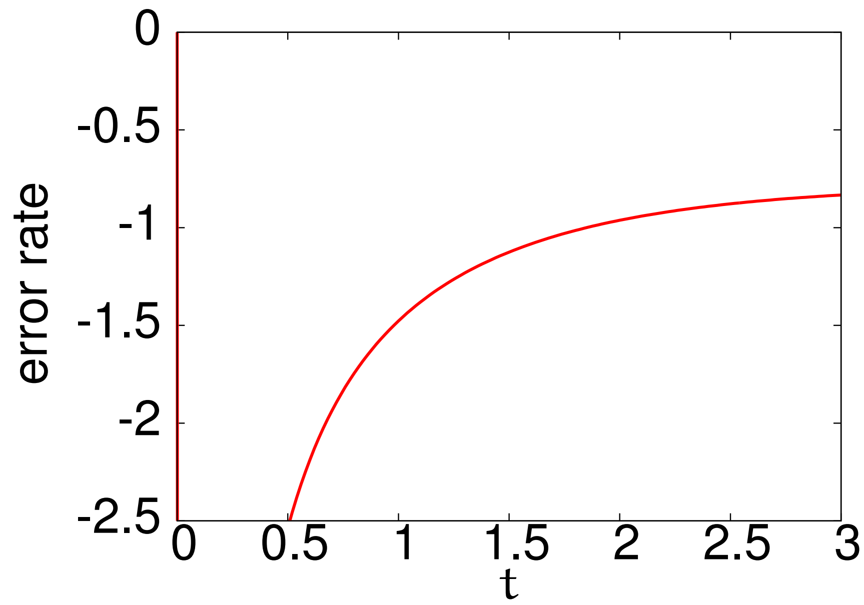


k_-

$$A_\star \xrightarrow{k_-} A$$

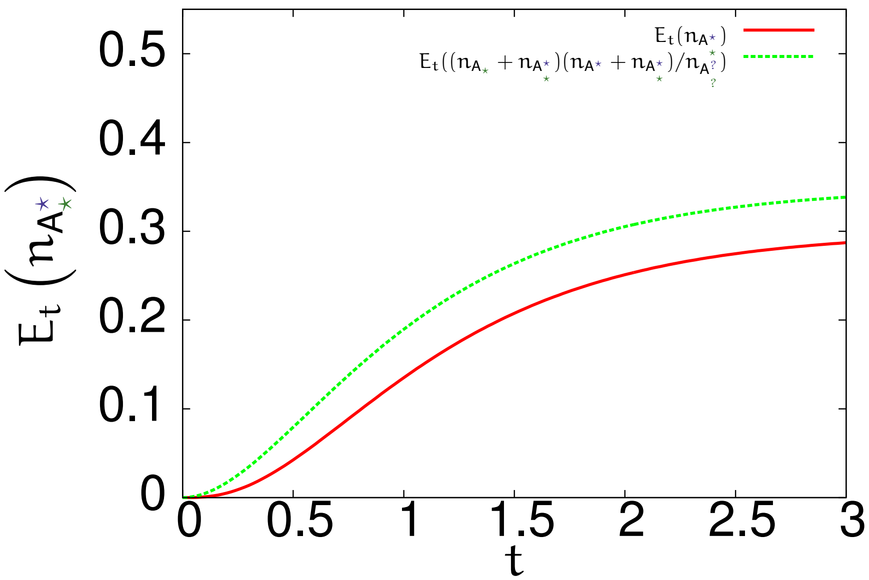
Comparison between the two models

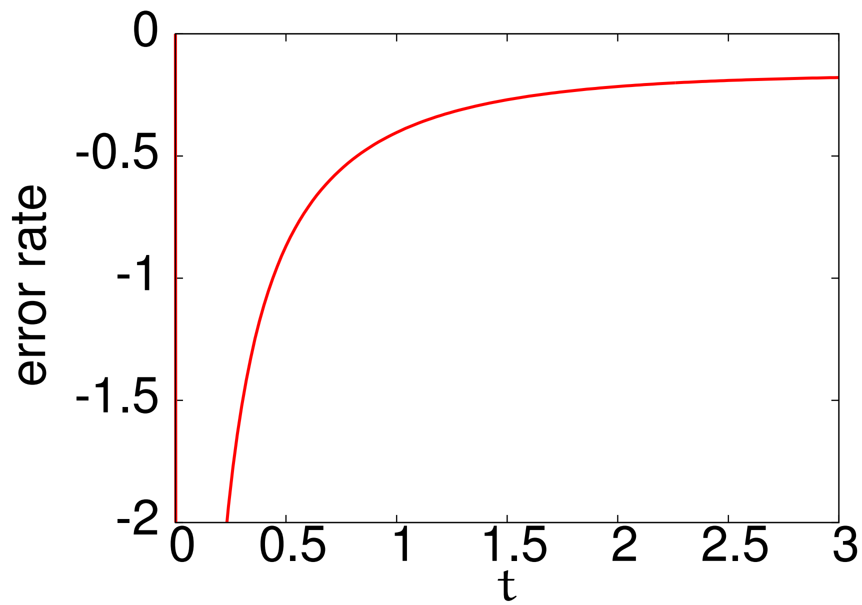




with $k^+ = k^- = k_+ = k_- = 1$,
and two instances of A at time $t = 0$.

Degree of correlation (in the unreduced model)





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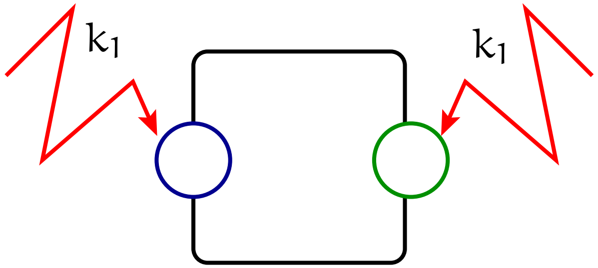
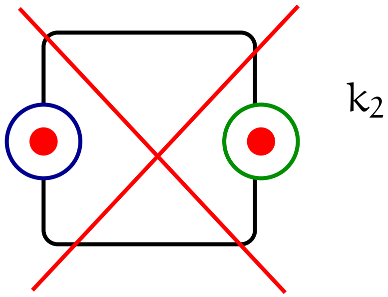
A model with symmetries



$$P \xrightarrow{k_1} {}^{\star}P \qquad P^{\star} \xrightarrow{k_1} {}^{\star}P^{\star}$$

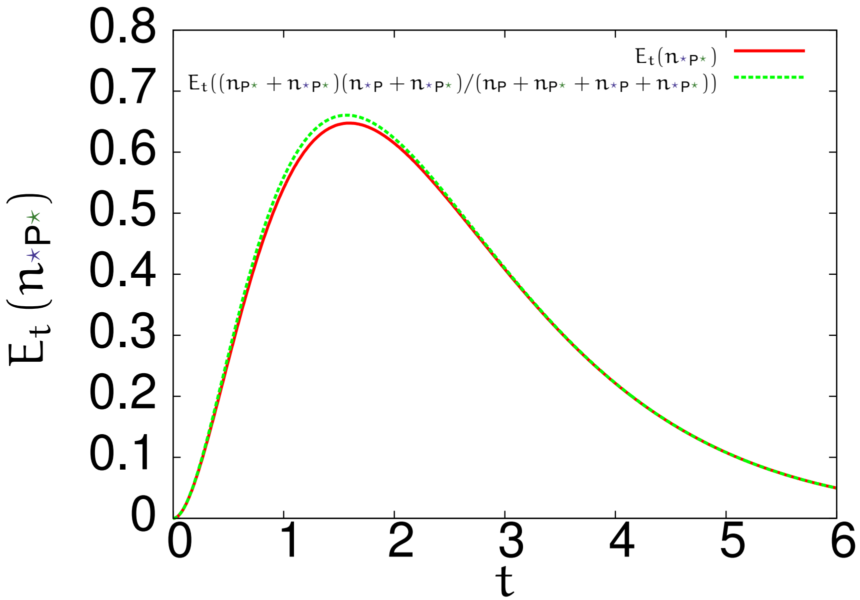
$$P \xrightarrow{k_1} P^{\star} \qquad {}^{\star}P \xrightarrow{k_1} {}^{\star}P^{\star}$$

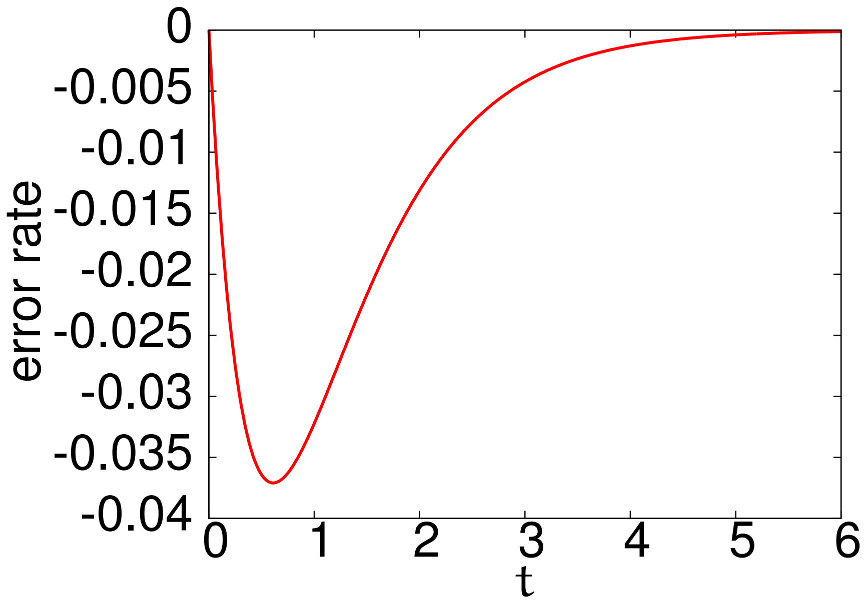


$${}^{\star}P^{\star} \xrightarrow{k_2} \emptyset$$

Degree of correlation (in the unreduced model)

$$\mathsf{E}_t\left(n_{\star P\star}\right) = \mathsf{E}_t\left(\frac{(n_{\star P} + n_{\star P\star})(n_{P\star} + n_{\star P\star})}{n_P + n_{P\star} + n_{\star P} + n_{\star P\star}}\right).$$



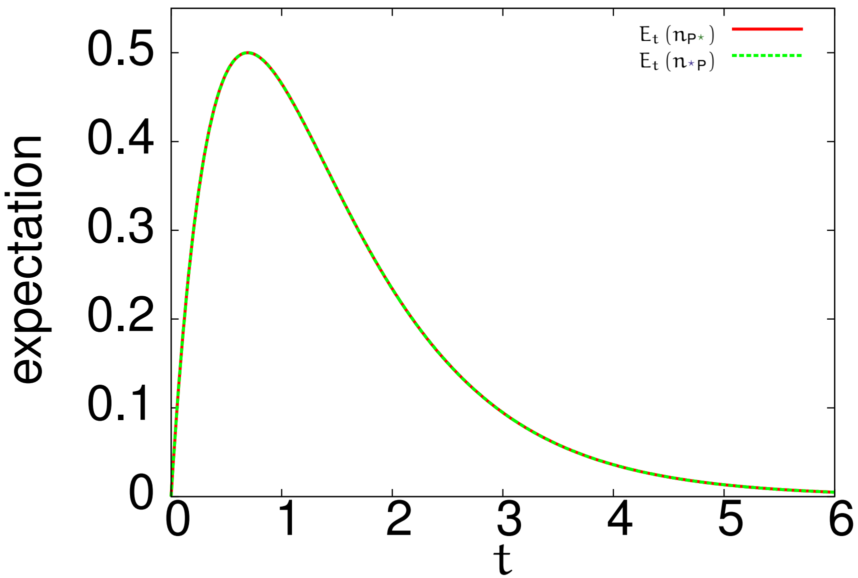


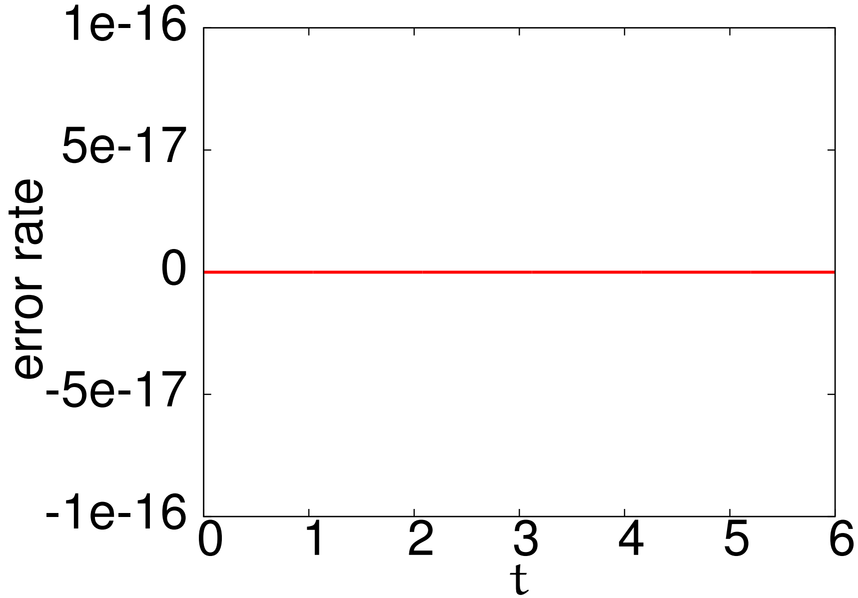
with $k_1 = k_2 = 1$
and two instances of P at time $t = 0$.

Equivalent chemical species

We check numerically that:

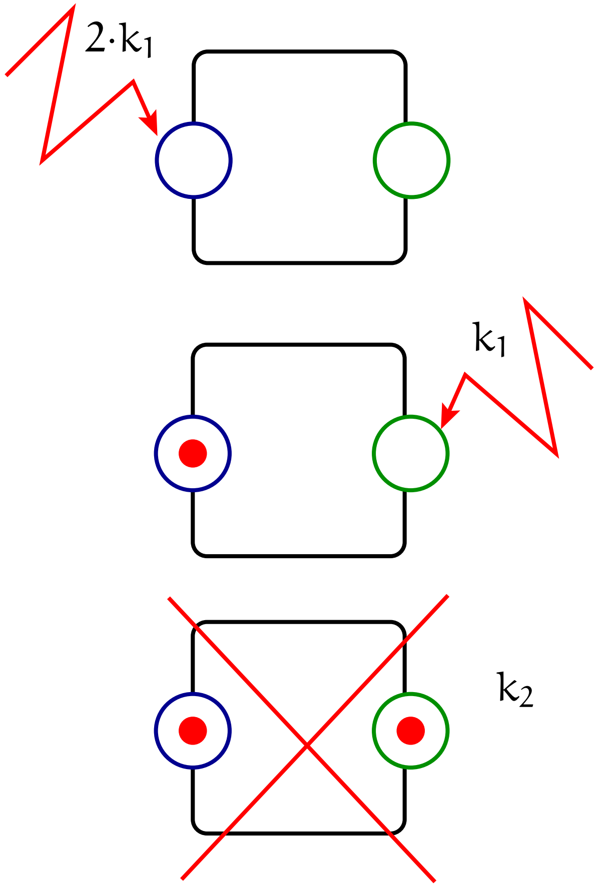
$$E_t(n_{P\star}) = E_t(n_{\star P}).$$





with $k_1 = k_2 = 1$
and two instances of P at time $t = 0$.

Reduced model



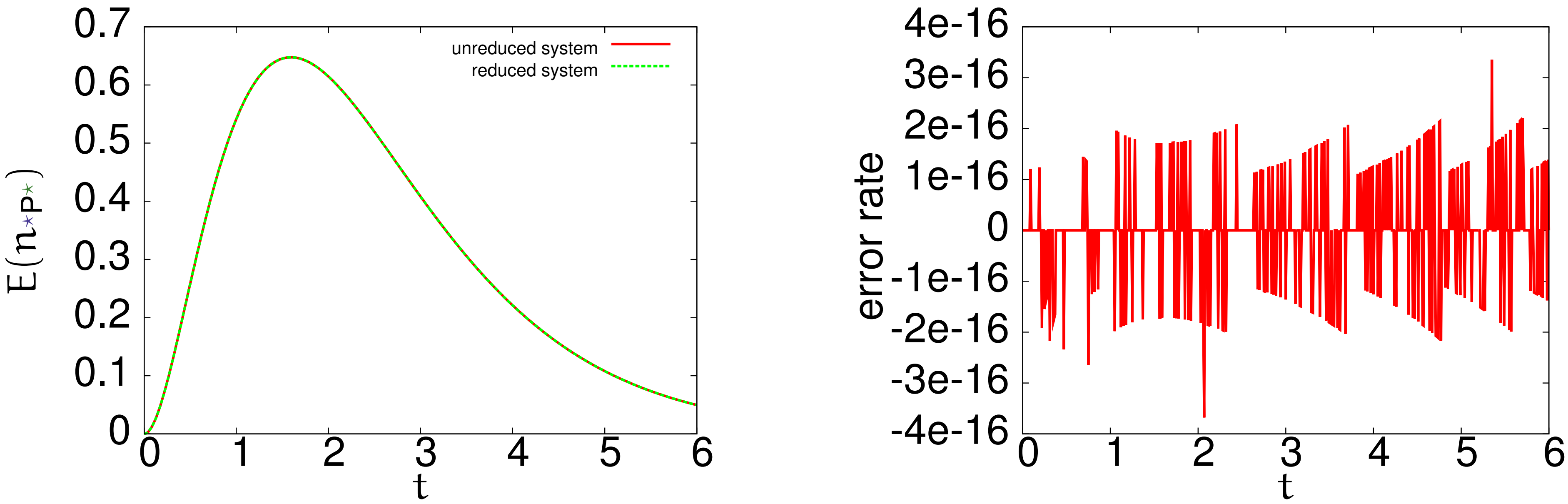
$$P \xrightarrow{2\cdot k_1} {}^{\star}P$$

$$^{\star}P \xrightarrow{k_1} {}^{\star}P^{\star}$$

$$^{\star}P^{\star} \xrightarrow{k_2} \emptyset$$

Exponential reduction!!!

Comparison between the two models



with $k_1 = k_2 = 1$
and two instances of P at time $t = 0$.

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Weighted Labelled Transition Systems

A weighted-labelled transition system $\mathcal{W}$ is given by:

- $\mathcal{Q}$, a countable set of states;
- $\mathcal{L}$, a set of labels;
- $w : \mathcal{Q} \times \mathcal{L} \times \mathcal{Q} \rightarrow \mathbb{R}_0^+$, a weight function;
- $\pi_0 : \mathcal{Q} \rightarrow [0, 1]$, an initial probability distribution.

We also assume that:

- the system is finitely branching, i.e.:
  - the set $\{q \in \mathcal{Q} \mid \pi_0(q) > 0\}$ is finite
  - and, for any $q \in \mathcal{Q}$, the set $\{l, q' \in \mathcal{L} \times \mathcal{Q} \mid w(q, l, q') > 0\}$ is finite.
- the system is deterministic:
  if $w(q, \lambda, q_1) > 0$ and $w(q, \lambda, q_2) > 0$, then: $q_1 = q_2$.

Trace distribution

A cylinder set of traces is defined as:

$$\tau \stackrel{\Delta}{=} q_0 \stackrel{\lambda_1,I_1}{\longrightarrow} q_1 \ldots q_{k-1} \stackrel{\lambda_k,I_k}{\longrightarrow} q_k$$

where:

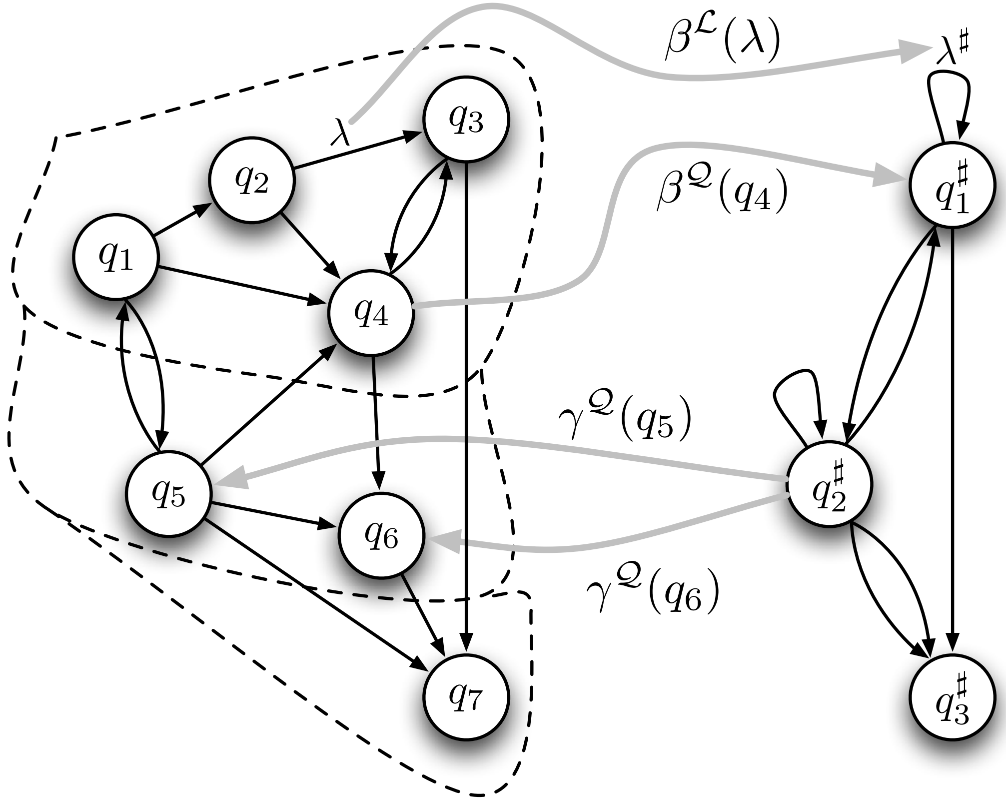
- $(q_i)_{0\leq i\leq k} \in \mathcal{Q}^{k+1}$ and $(\lambda_i)_{1\leq i\leq k} \in \mathcal{L}^k$,
- $(I_i)_{1\leq i\leq k}$ is a family of open intervals in $\mathbb{R}_0^+$.

The probability of a cylinder set of traces is defined as follows:

$$\mathcal{P}r(\tau) \stackrel{\Delta}{=} \pi_0(q_0) \prod_{i=1}^{k} \frac{w(q_{i-1}, l_i, q_i)}{a(q_{i-1})} \left(e^{-a(q_{i-1})\cdot\mathsf{inf}(I_i)} - e^{-a(q_{i-1})\cdot\mathsf{sup}(I_i)}\right),$$

where $a(q) \stackrel{\Delta}{=} \sum_{\lambda,q'} w(q,\lambda,q')$.

Abstraction between WLTS



Soundness

Given:

- two WLTS $\mathcal{S} \stackrel{\Delta}{=} (\mathcal{Q}, \mathcal{L}, \rightarrow, w, \mathcal{I}, \pi_0)$ and $\mathcal{S}^\sharp \stackrel{\Delta}{=} (\mathcal{Q}^\sharp, \mathcal{L}^\sharp, \rightsquigarrow, w^\sharp, \mathcal{I}^\sharp, \pi_0^\sharp)$,
- two abstraction functions $\beta^{\mathcal{Q}} : \mathcal{Q} \rightarrow \mathcal{Q}^\sharp$ and $\beta^{\mathcal{L}} : \mathcal{L} \rightarrow \mathcal{L}^\sharp$,

$\mathcal{S}^\sharp$ is a sound abstraction of $\mathcal{S}$, if and only if, for any cylinder set τ of traces of $\mathcal{S}$, we have:

$$\mathcal{P}r(\beta^{\mathbb{T}}(\tau)) = \sum_{\tau'} (\mathcal{P}r(\tau') \mid \beta^{\mathbb{T}}(\tau) = \beta^{\mathbb{T}}(\tau')),$$

where,

$$\beta^{\mathbb{T}}(q_0 \xrightarrow{\lambda_1, I_1} q_1 \ldots q_{k-1} \xrightarrow{\lambda_k, I_k} q_k)$$
$$\stackrel{\Delta}{=} \beta^{\mathcal{Q}}(q_0) \xrightarrow{\beta^{\mathcal{L}}(\lambda_1), I_1} \beta^{\mathcal{Q}}(q_1) \ldots \beta^{\mathcal{Q}}(q_{k-1}) \xrightarrow{\beta^{\mathcal{L}}(\lambda_k), I_k} \beta^{\mathcal{Q}}(q_k).$$

Completeness

Given:

- two WLTS $\mathcal{S} \stackrel{\Delta}{=} (\mathcal{Q}, \mathcal{L}, \rightarrow, w, \mathcal{I}, \pi_0)$ and $\mathcal{S}^\sharp \stackrel{\Delta}{=} (\mathcal{Q}^\sharp, \mathcal{L}^\sharp, \rightsquigarrow, w^\sharp, \mathcal{I}^\sharp, \pi_0^\sharp)$,
- two abstraction functions $\beta^{\mathcal{Q}} : \mathcal{Q} \rightarrow \mathcal{Q}^\sharp$ and $\beta^{\mathcal{L}} : \mathcal{L} \rightarrow \mathcal{L}^\sharp$,
- a concretization function $\gamma^{\mathcal{Q}} : \mathcal{Q} \rightarrow \mathbb{R}^+$,

$\mathcal{S}^\sharp$ is a sound and complete abstraction of $\mathcal{S}$, if and only if,

1. it is a sound abstraction;
2. for any cylinder set $\tau^\sharp$ of abstract traces of $\mathcal{S}^\sharp$ which ends in the abstract state $q_k^\sharp$, we have:

$$\gamma^{\mathcal{Q}}(s) = \mathcal{P}r(q_k = s \mid \tau \text{ such that } \beta^{\mathbb{T}}(\tau) \in \tau^\sharp) \times \sum \{\gamma^{\mathcal{Q}}(s') \mid \beta^{\mathcal{Q}}(s') = q_k^\sharp\}.$$

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Markovian Property

We consider a stochastic process:

- $\mathbb{T} = \mathbb{R}_0^+$: time range;
- $\mathcal{Q}$: a countable set of states;
- $(\mathcal{X}_t)_{t \in \mathbb{T}}$: a family of random variables over $\mathcal{Q}$;

We say that $(\mathcal{X}_t)$ satisfies the Markovian property,
if, for any family $(s_t)_{t \in \mathbb{T}}$ of states indexed over $\mathbb{T}$, and any time $t_1 < t_2$,
we have:

$$\mathcal{P}r(X_{t_2} = s_{t_2} \mid X_{t_1} = s_{t_1}) = \mathcal{P}r(X_{t_2} = s_{t_2} \mid X_t = s_t, \forall t < t_1).$$

Lumpability property

Given:

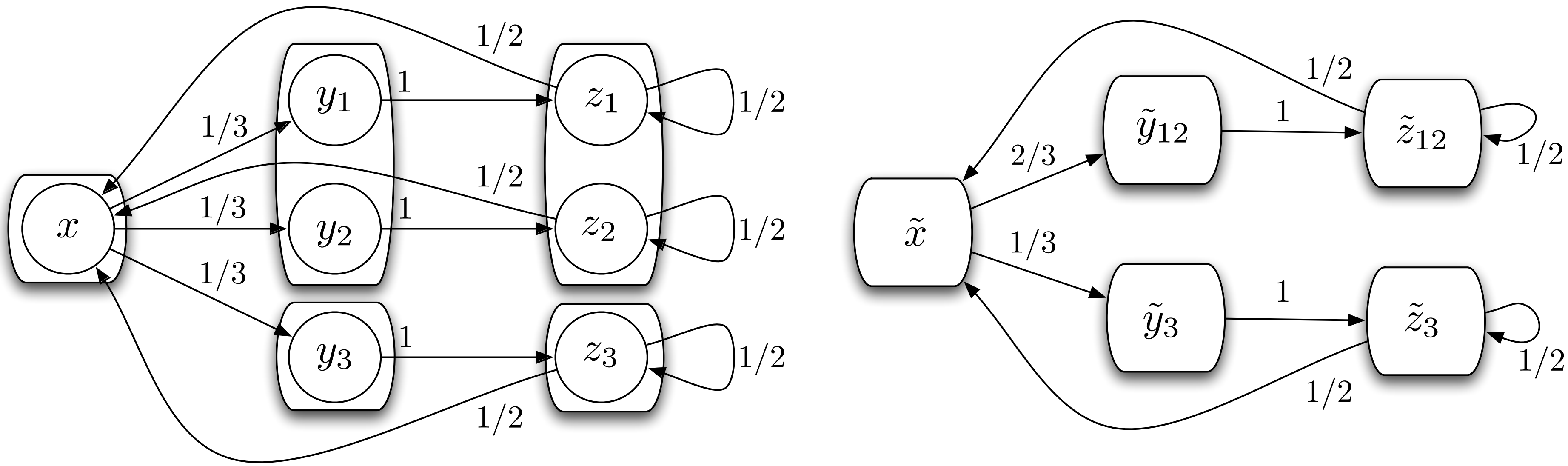
- a stochastic process $(\mathcal{X}_t)$ which satisfies the Markovian property,
- an initial distribution $\pi_0 \; : \; \mathcal{Q} \rightarrow [0, 1]$,
- an equivalence relation $\sim$ over $\mathcal{Q}$,

we define the lumped process $(\mathcal{Y}_t)$ on the state space $\mathcal{Q}_{/\sim}$ as:

$$\mathcal{P}r(\mathcal{Y}_t = [x_t]_{/\sim} \mid \mathcal{Y}_0 = [s_0]_{/\sim}) \stackrel{\Delta}{=} \mathcal{P}r(\mathcal{X}_t \in [s_t]_{/\sim} \mid \mathcal{X}_0 \in [s_0]_{/\sim}).$$

We say that $(\mathcal{X})_t$ is $\sim$-lumpable with respect to π_0 if and only if, the stochastic process $(\mathcal{Y}_t)$ satisfies the Markovian property as well.

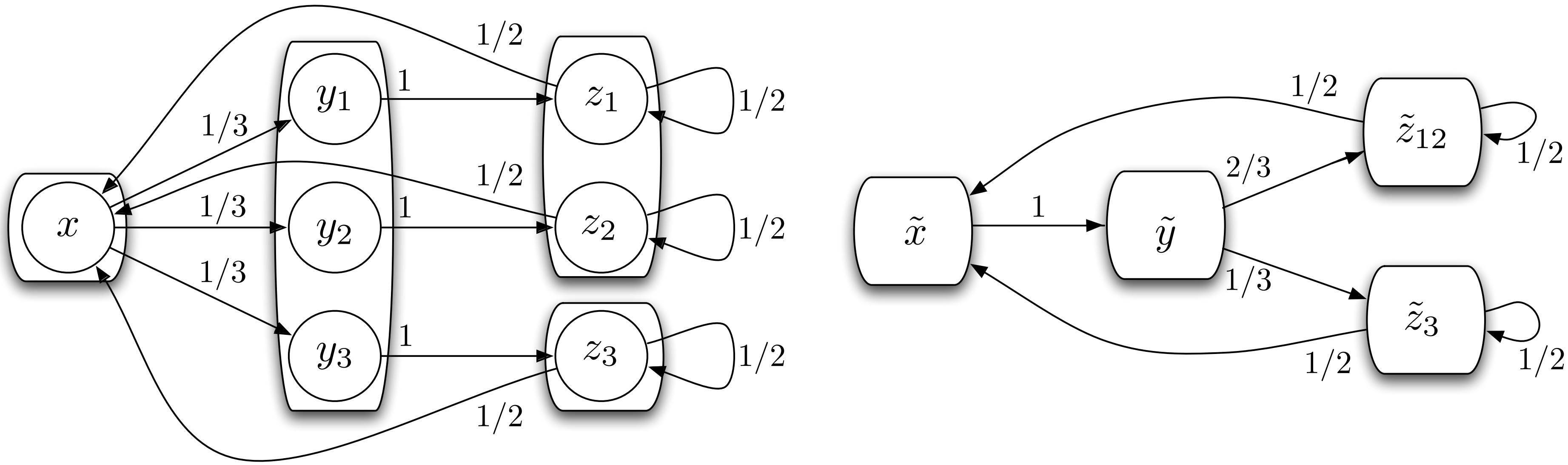
Strong lumpability



A stochastic process is $\sim$-strongly lumpable, if:

it is $\sim$-lumpable with respect to any initial distribution.

Weak lumpability



A stochastic process $(\mathcal{X}_t)$ is $\sim$-weakly lumpable, if:
there exists an initial distribution with respect to which $(\mathcal{X}_t)$ is $\sim$-lumpable.

Overview

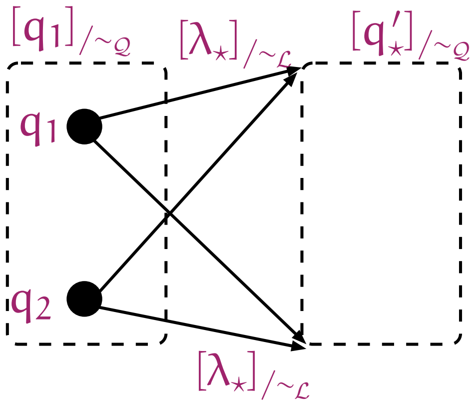
1. Introduction
2. Examples of information flow
3. Symmetric sites
4. Stochastic semantics
5. Lumpability
6. Bisimulations
7. Hierarchy of semantics
8. Conclusion

Forward bisimulation

Let $\sim_{\mathcal{Q}}$ be an equivalence relation over $\mathcal{Q}$ and $\sim_{\mathcal{L}}$ be an equivalence relation over $\mathcal{L}$.

We say that $(\sim_{\mathcal{Q}}, \sim_{\mathcal{L}})$ is a forward bisimulation, if and only if, for any $q_1, q_2 \in \mathcal{Q}$ such that $q_1 \sim_{\mathcal{Q}} q_2$:

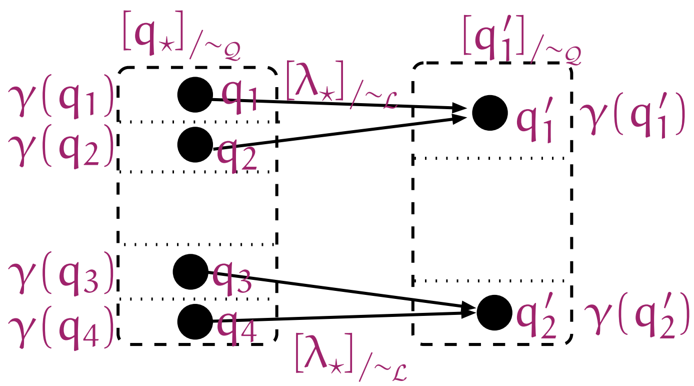
- $a(q_1) = a(q_2)$;
- and for any $\lambda_\star \in \mathcal{L}$, $q'_\star \in \mathcal{Q}$,
  $\mathsf{fwd}(q_1, [\lambda_\star]_{/\sim_{\mathcal{L}}}, [q'_\star]_{/\sim_{\mathcal{Q}}}) = \mathsf{fwd}(q_2, [\lambda_\star]_{/\sim_{\mathcal{L}}}, [q'_\star]_{/\sim_{\mathcal{Q}}})$



where: $\mathsf{fwd}(q, [\lambda_\star]_{/\sim_{\mathcal{L}}}, [q'_\star]_{/\sim_{\mathcal{Q}}}) = \sum_{\lambda', q'} (w(q, \lambda', q') \mid \lambda' \sim_{\mathcal{L}} \lambda_\star,\ q' \sim_{\mathcal{Q}} q'_\star)$.

Backward bisimulation

Let $\sim_{\mathcal{Q}}$ be an equivalence relation over $\mathcal{Q}$ and $\sim_{\mathcal{L}}$ be an equivalence relation over $\mathcal{L}$.



We say that $(\sim_{\mathcal{Q}}, \sim_{\mathcal{L}})$ is a backward bisimulation, if and only if, there exists $\gamma : \mathcal{Q} \to \mathbb{R}^+$, such that: for any $q'_1, q'_2 \in \mathcal{Q}$ which satisfies $q'_1 \sim_{\mathcal{Q}} q'_2$:

- $a(q'_1) = a(q'_2)$;
- and for any $\lambda_\star \in \mathcal{L}$, $q_\star \in \mathcal{Q}$,

  $\mathsf{bwd}([q_\star]_{/\sim_{\mathcal{Q}}}, [\lambda_\star]_{\sim/\mathcal{L}}, q'_1) = \mathsf{bwd}([q_\star]_{/\sim_{\mathcal{Q}}}, [\lambda_\star]_{\sim/\mathcal{L}}, q'_2)$

where: $\mathsf{bwd}([q_\star]_{/\sim_{\mathcal{Q}}}, [\lambda_\star]_{\sim/\mathcal{L}}, q') = \sum_{q,\lambda'} \left(\frac{\gamma(q)}{\gamma(q')} w(q, \lambda', q') \,|\, q \sim_{\mathcal{Q}} q_\star, \lambda' \sim_{\mathcal{L}} \lambda_\star \right)$.

Logical implications

- if $(\sim_{\mathcal{Q}}, \sim_{\mathcal{L}})$ is a forward bisimulation, then the process is $\sim_{\mathcal{Q}}$-strongly lumpable,

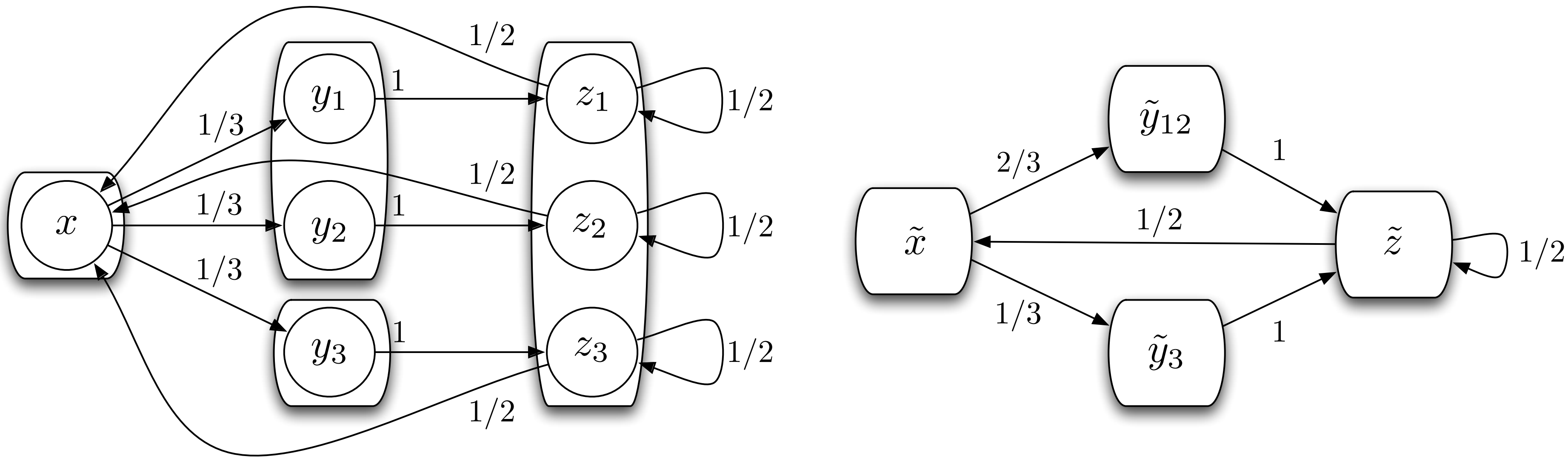
  moreover, it induces a sound abstraction;
- if $(\sim_{\mathcal{Q}}, \sim_{\mathcal{L}})$ is a backward bisimulation, then the process is $\sim_{\mathcal{Q}}$-weakly lumpable, for the initial distributions which satisfy:

  $$q \sim_{\mathcal{Q}} q' \Rightarrow [\pi_0(q) \cdot \gamma(q') = \pi_0(q') \cdot \gamma(q)];$$

  it induces a sound and complete abstraction for these initial distributions;
- there exist forward bisimulations which are not backward bisimulations;
- there exist backward bisimulations which are not forward bisimulations.

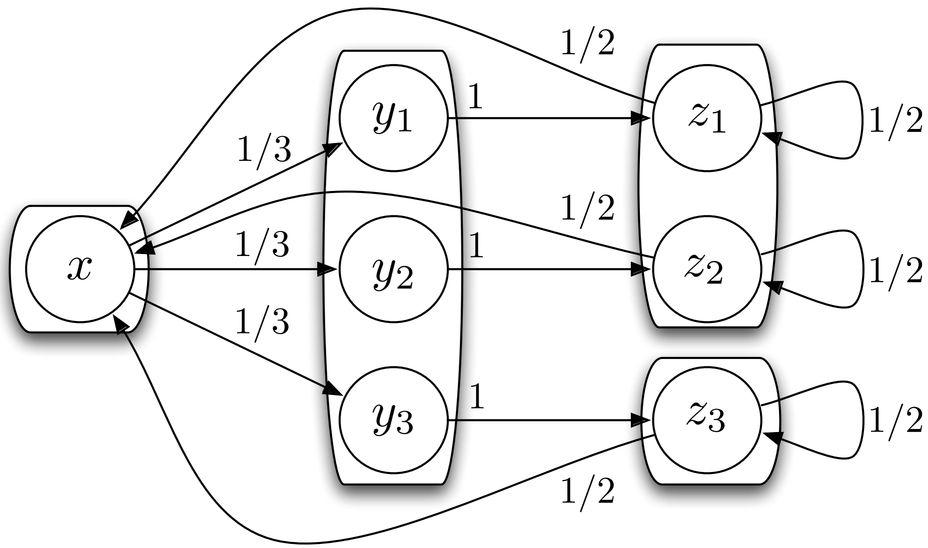
Counter-example I

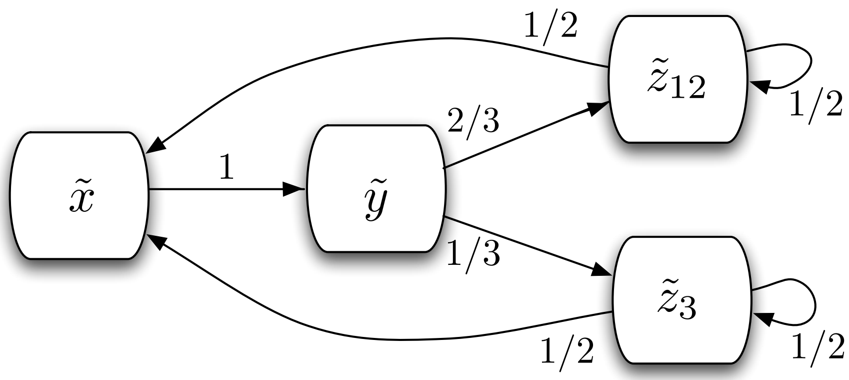
A forward bisimulation which is not a backward bisimulation:



Counter-example II

A backward bisimulation which is not a forward bisimulation:





Uniform backward bisimulation

Given $q_\star, q' \in \mathcal{Q}$ and $\lambda_\star \in \mathcal{L}$, we denote:

$$\mathsf{pred}([q_\star]_{/\sim_\mathcal{Q}}, [\lambda_\star]_{\sim_{/\mathcal{L}}}, q') \stackrel{\Delta}{=} \{(q,\lambda) \mid w(q,\lambda,q') > 0, q \sim_\mathcal{Q} q_\star,\ \lambda \sim_\mathcal{L} \lambda_\star\}.$$

If,

- $q_1 \sim_\mathcal{Q} q_2 \implies a(q_1) = a(q_2)$;
- for any $q_1', q_2' \in \mathcal{Q}$, such that $q_1' \sim_\mathcal{Q} q_2'$, and any $q_\star \in \mathcal{Q}$ and $\lambda_\star \in \mathcal{L}$, there is a 1-to-1 mapping between $\mathsf{pred}([q_\star]_{/\sim_\mathcal{Q}}, [\lambda_\star]_{\sim_{/\mathcal{L}}}, q_1')$ and $\mathsf{pred}([q_\star]_{/\sim_\mathcal{Q}}, [\lambda_\star]_{\sim_{/\mathcal{L}}}, q_2')$ which is compatible with w,

then:

- $(\sim_\mathcal{Q}, \sim_\mathcal{L})$ is a backward bisimulation (with $\gamma(q) = 1,\ \forall q \in \mathcal{Q}$).

Abstraction algebra

(Sound/Complete) abstractions can be:

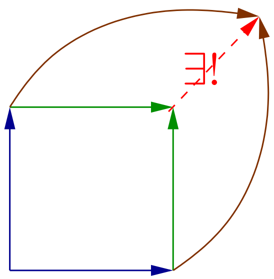
- composed:

$$\begin{tikzcd} \mathcal{S}^\flat \arrow[rr, dashed] \arrow[dr] & & \mathcal{S}^\sharp \\ & \mathcal{S} \arrow[ur] & \end{tikzcd}$$

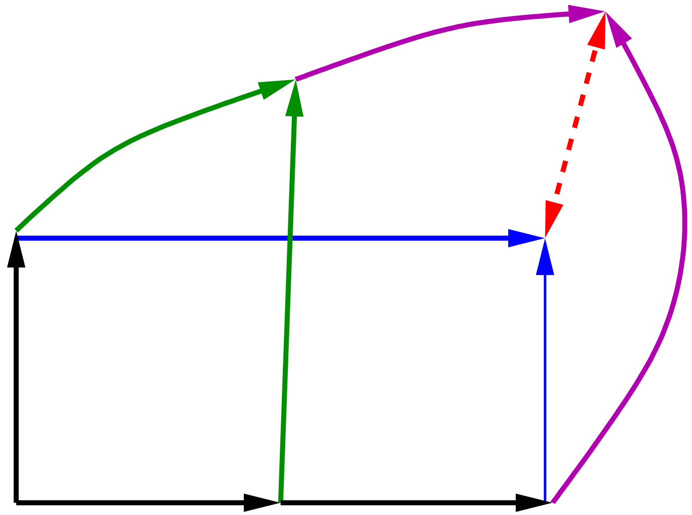
- factored:

$$\begin{tikzcd} \mathcal{S}^\flat \arrow[rr] \arrow[dr] & & \mathcal{S}^\sharp \\ & \mathcal{S} \arrow[ur, dashed] & \end{tikzcd}$$

- combined with a symmetric product (c.f. lub or pushout):



Compatibility between composition and pushout



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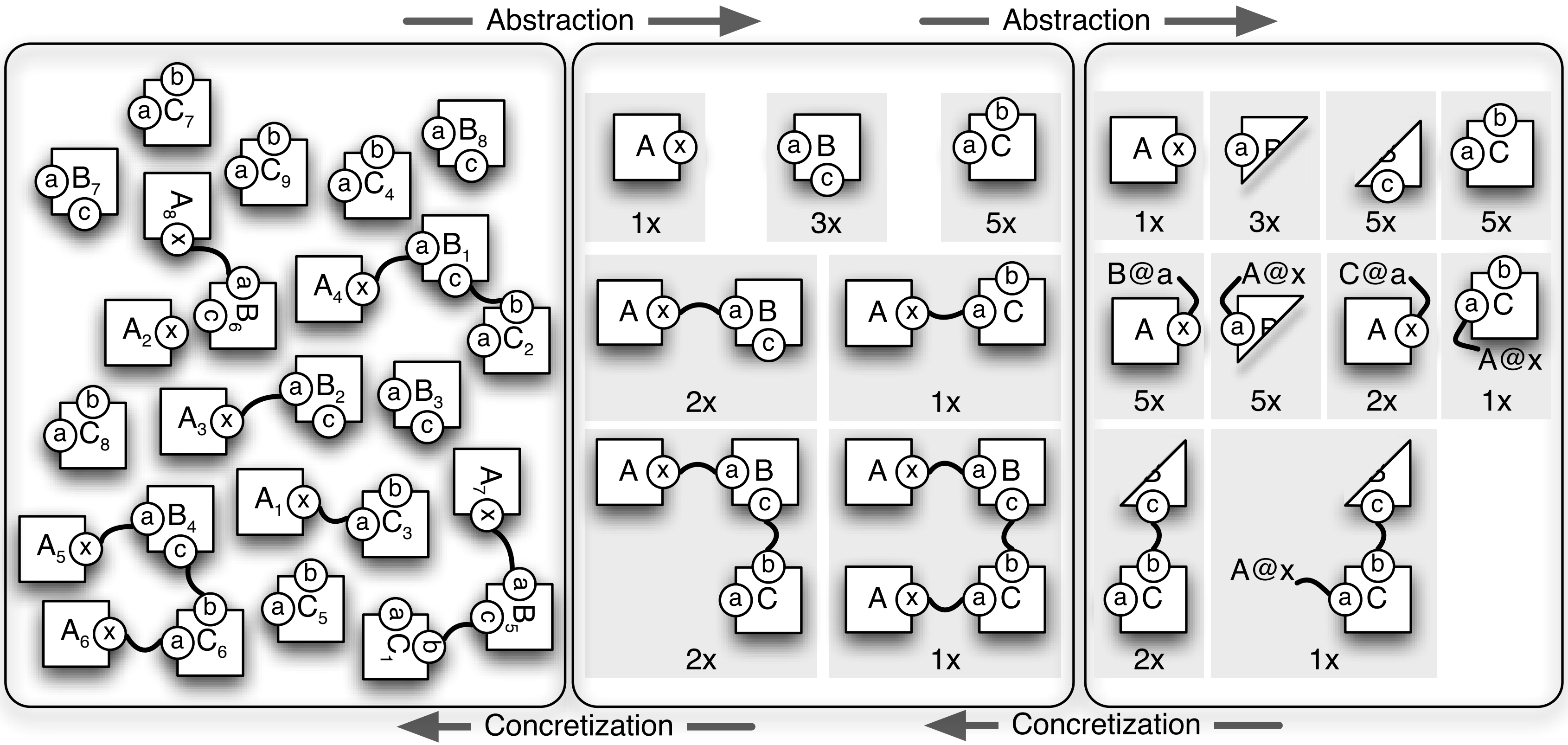

Abstraction
Abstraction
Concretization
Concretization

From individuals to population

- Individual semantics:

  In the individual semantics, each agent is tagged with a unique identifier which can be tracked along the trace;

- Population semantics:

  In the population semantics, the state of the system is seen up to injective substitution of agent identifier;

  equivalently, the state of the system is a multi-set of chemical species.

Fragments

An annotated contact map is valid with respect to the stochastic semantics, if:

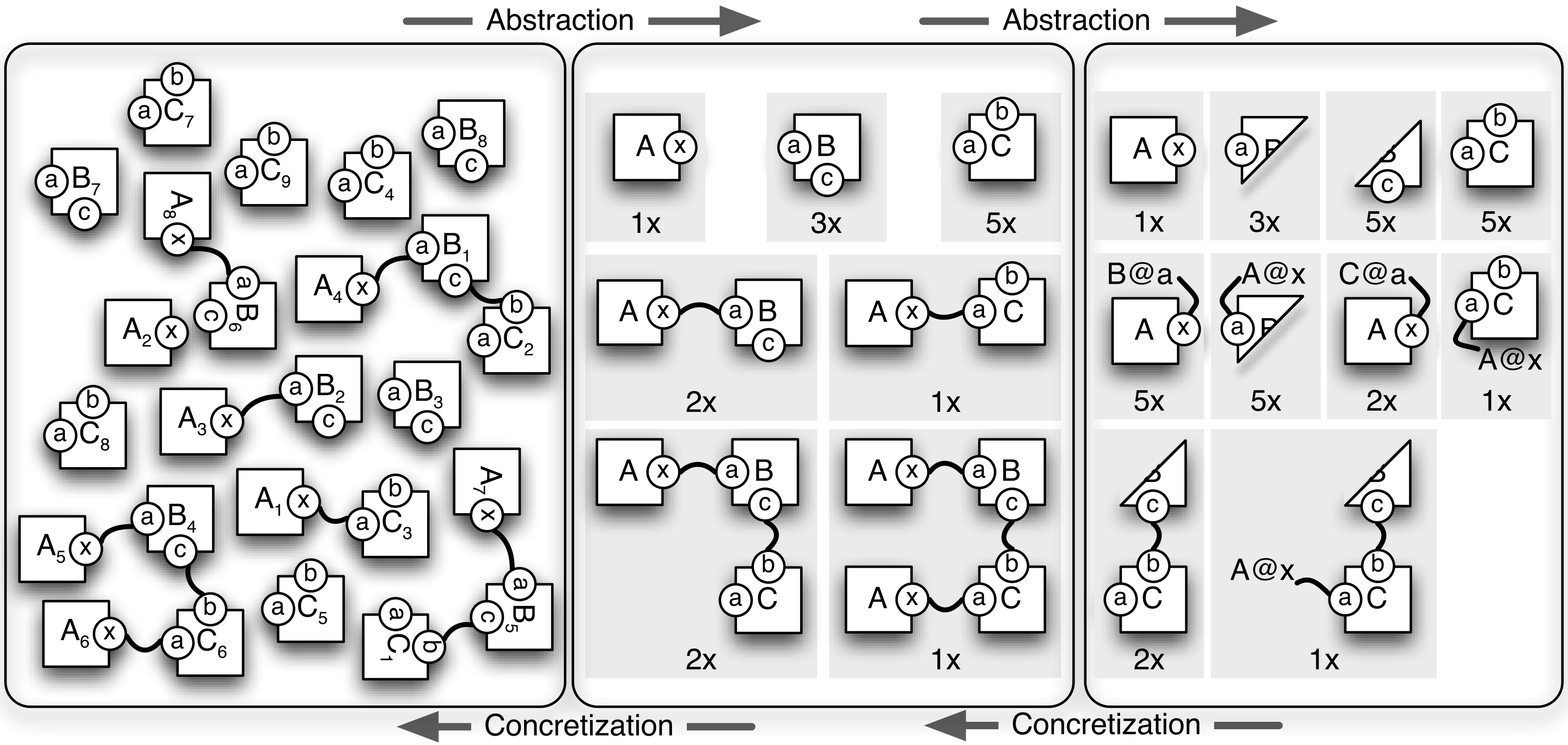
- Whenever the site x and y both occurs in the same or in distinct agent of type A in a rule, then, there should be a bidirectional edge between the site x and the y of A.
- Whenever there is a bond between two sites, each of which either carries an internal state of, is connected to some other sites of its agent, then the bond if oriented in both directions.

From population to fragments

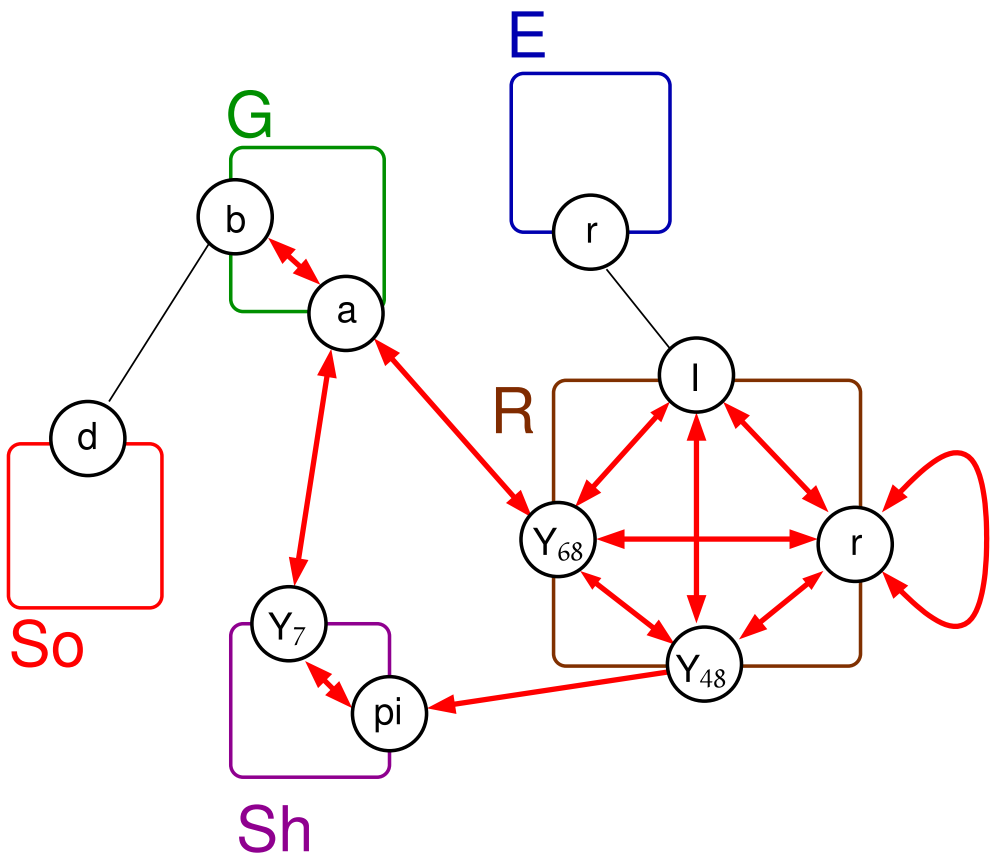
- Population of fragments:

  1. In the annotated contact, each agent is fitted with a binary equivalence over its sites. We split the interface of agents into equivalence classes of sites. Then we abstract away which subagents belong to the same agent.

  2. Whenever an edge is not oriented in the annotated contact map, we cut each instance of this bond into two half bonds, and abstract away which partners are bond together.


Abstraction
Abstraction
1x
3x
5x
2x
1x
2x
1x
1x
3x
5x
5x
B@a
A@x
C@a
A@x
5x
5x
2x
1x
A@x
2x
1x
Concretization
Concretization

Example



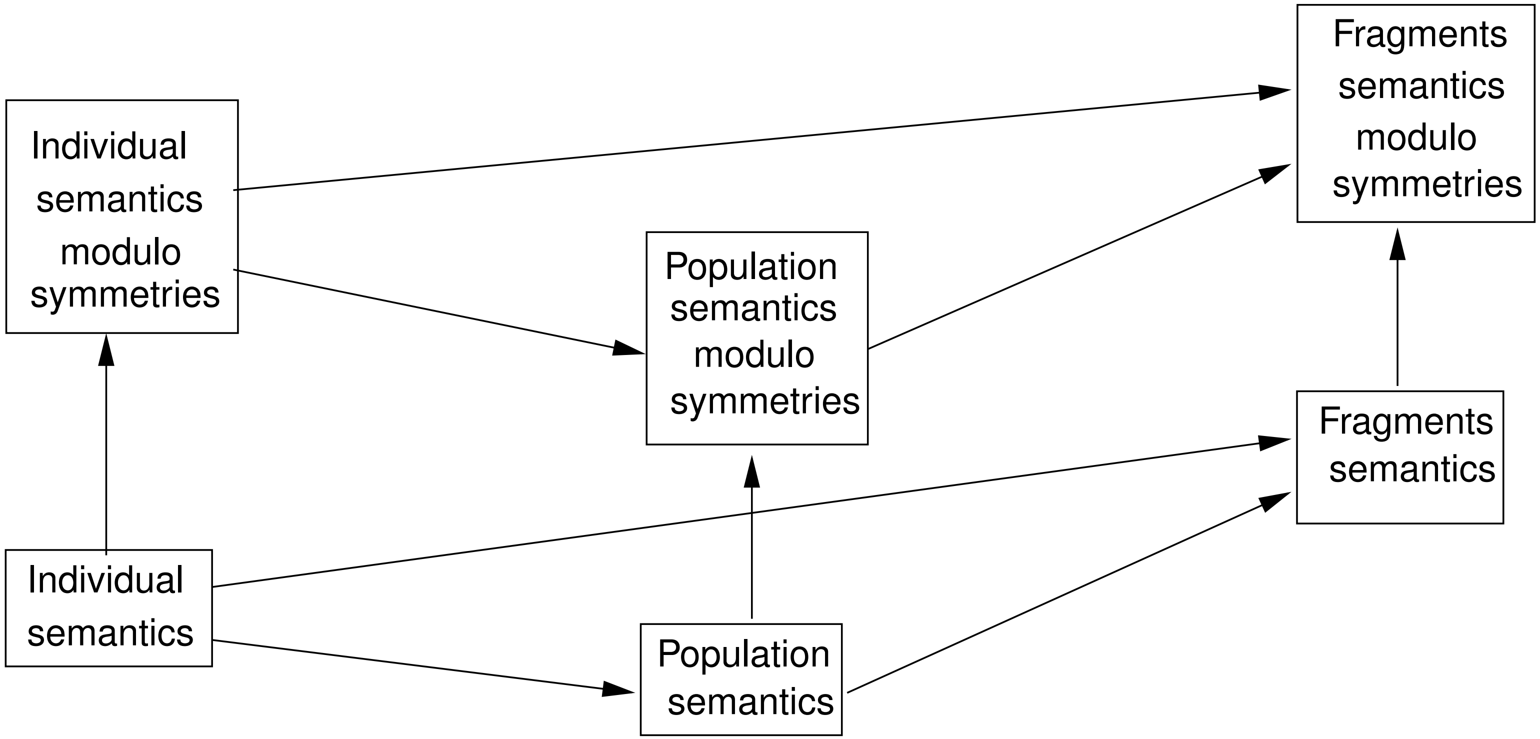
Symmetries among sites

Let $\mathcal{R}$ be a set of rules and $\mathcal{M}_0$ be an initial mixture.

Two sites x_1 and x_2 are symmetric in the agent A in the set of rules $\mathcal{R}$ and the initial mixture $\mathcal{M}_0$ whenever the following three properties are satisfied:

1. for each rule of the model, if we swap the site x_1 and the site x_2 in one instance of A in a rule of $\mathcal{R}$, we get a rule that is isomorphic to a rule in $\mathcal{R}$. (this rule may be the same, or a different one)
2. given two such symmetric rules, the quotient between the sum of the rates of the isomorphic rules and the product between the number of automorphisms in the left hand side, and the number of symmetric isomorphic rules, is the same.
3. each agent A in $\mathcal{M}_0$ has their sites x_1 and x_2 free, with the same internal state.

Hierarchy of semantics



Overview

Conclusion

- A framework for reducing stochastic rule-based models.
  - We use:
    - $*$ the sites the state of which are uncorrelated;
    - $*$ the sites having the same capabilities of interactions.
  - Algebraic operators combine these abstractions.

- We use backward bisimulations in order to prove statistical invariants, we use them to reduce the dimension of the continuous-time Markov chains.

Future works

- Investigate the use of hybrid bisimulation.

- Propose approximated simulation algorithms to approximate different scale rate reactions.
  - hybrid systems,
  - tau-leaping,
  - ...