Master 2 MPRI course 2-19 Biochemical Programming
Jérôme Feret

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Abstract

This problem investigates the impact of structural symmetries on the stochastic behavior of Kappa models. Structural symmetries emerge from equivalence relationships among pairs of sites. That is to say sites having exactly the same capabilities of interaction. We will consider two case studies. In the first one, we introduce a model in which two sites have the same capabilities of interaction in any context. In the second one, we examine a model in which two sites have the same capabilities of interaction only when a third one is activated. We study the impact of these symmetries under the lens of forward bisimulations (which enable to quotient the underlying transition system by discarding the difference between symmetric states) and backward bisimulations (which highlight statistical invariants).

1 Weighted transition systems

Firstly, we introduce the notion of weighted transition systems for describing Markov chains. To make the things simpler, we consider finite Markov chains with discrete time evolution (finite DTMC) only.

Definition 1.1 *A weighted transition system is a pair $(\mathcal{Q}, w)$ where $\mathcal{Q}$ is a finite set of elements, called states, and w is a function mapping every pair of states to a non negative real numbers (in $\mathbb{R}_{\geqslant 0}$) such that for every state $q \in \mathcal{Q}$, the sum $\sum_{q' \in \mathcal{Q}} w(q, q')$ is equal to 1.*

In fact, for every state q, the function mapping every state q' to the real value $w(q, q')$ is the finite probability distribution for the next state of the system. Whenever $w(q, q') = 0$ we say that there is no transition from the state q to the state q', otherwise we say that there is a transition from the state q to the state q' with probability $w(q, q')$. An example of weighted transition system is depicted in Fig. **??**. States are described as ellipses labeled by names whereas transitions are denoted as edges labelled with their probabilities.

We assume until the rest of the section that we are given $(\mathcal{Q}, w)$ a weighted transition system.

Definition 1.2 (Trace) *A (finite) trace is a finite sequence of elements of the set $\mathcal{Q}$.*
The length of a trace is the number of states minus 1.
The probability of the trace $\tau \triangleq (q_i)_{0 \leqslant i \leqslant n}$ is defined as follows:

$$P(\tau \mid q_0) \triangleq \prod_{1 \leqslant i \leqslant n} w(q_{i-1}, q_i).$$

As a direct consequence, a trace has probability 0 whenever it contains two consecutive states not related by any transition. Moreover, we notice that traces of length 0 have probability 1.

Now we define the notion of flow between two sets of states.

Definition 1.3 (Flow) *The flow $\text{FLOW}(X, X')$ from a set of states $X \subseteq \mathcal{Q}$ into a set of states $X' \subseteq \mathcal{Q}$ is defined as follows:*

$$\text{FLOW}(X, X') \triangleq \sum_{q \in X, q' \in X'} w(q, q').$$

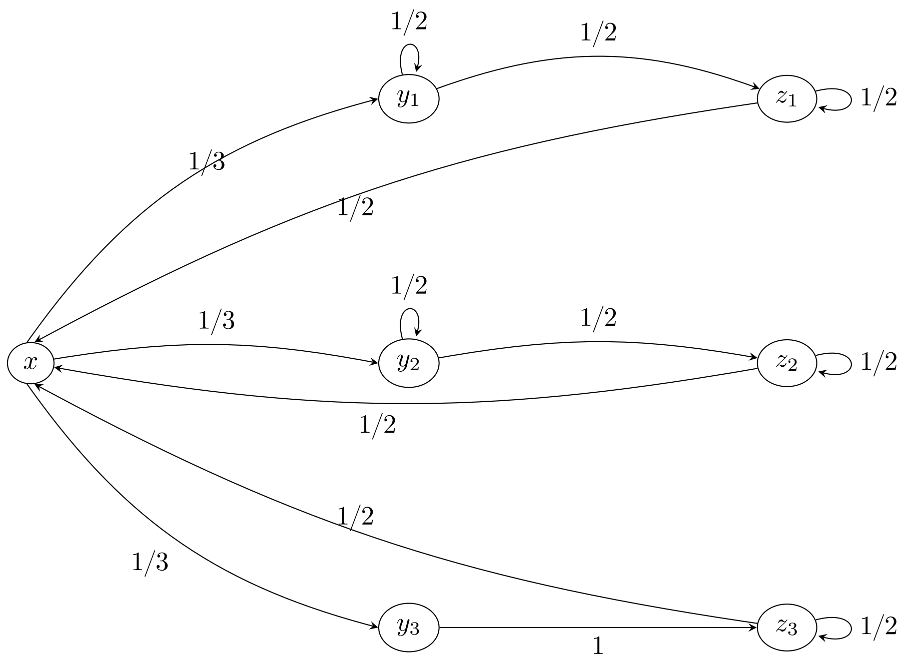


Figure 1: A weighted transition system.

2 Bisimulation over weighted transition system

2.1 Reminder on equivalence relations

The goal of this section is to introduce several notions of equivalence between the states of a weighted transition system. Our goal is to lump the states of the system accordingly.

Definition 2.1 (relation) *A (binary) relation over a set X is a subset of X^2.*

Whenever $\mathcal{R}$ is a relation over a set X, the notation $q\ \mathcal{R}\ q'$ stands for $(q, q') \in \mathcal{R}$.

Definition 2.2 (equivalence relation) *A relation $\mathcal{R}$ over a set X is an equivalence relation whenever it is reflexive, symmetric, and transitive.*

That is to say that, for every $x, y, z \in X$:

- *(reflexivity) $x\ \mathcal{R}\ x$;*
- *(symmetry) $x\ \mathcal{R}\ y \implies y\ \mathcal{R}\ x$;*
- *(transitivity) $[x\ \mathcal{R}\ y \wedge y\ \mathcal{R}\ z \Longrightarrow x\ \mathcal{R}\ z]$.*

Definition 2.3 *An equivalence relation is usually denoted as $\sim$. Given an equivalence relation $\sim$ over a set X and an element $x \in X$, the set of elements x' such that $x \sim x'$ is called the $\sim$-equivalence class of the element x and is denoted as $[x]_\sim$. The set of $\sim$-equivalence classes is denoted as $X_\sim$.*

2.2 Forward bisimulation

Now we study the notion of forward bisimulation which enables to lump the states of a weighted transition system.

Definition 2.4 (Forward bisimulation) *Let $(\mathcal{Q}, w)$ a weighted transition system and $\sim$ be an equivalence relation over the set $\mathcal{Q}$.*

The relation $\sim$ is called a forward bisimulation over the weighted transition system $(\mathcal{Q}, w)$ if and only if for every q, q', q'' such that $q \sim q'$, the following equation:

$$\text{FLOW}(\{q\}, [q'']_\sim) = \text{FLOW}(\{q'\}, [q'']_\sim)$$

is satisfied.

Question 1 *(**) Propose the largest forward bisimulation $\sim$ over the weighted transition systems depicted in Fig.* **??** *such that the state x is $\sim$-equivalent to no other state.*

That is to say that the relation $\sim$ should satisfy the following properties:

1. *$\sim$ is a forward bisimulation over the weighted transition system depicted in Fig.* **??***;*
2. *$[x]_\sim = \{x\}$;*
3. *for every two states $q, q' \in \mathcal{Q}$ and for every forward bisimulation $\sim'$ over the weighted transition system depicted in Fig.* **??** *such that $[x]_{\sim'} = \{x\}$, we have $q \sim' q' \Rightarrow q \sim q'$.*

Answer:

1. Let us show that the relation $\sim$ among the elements of $\mathcal{Q}$ that is defined as follows:

$$\mathcal{Q}_\sim \triangleq \{\{x\}, \{y_1, y_2\}, \{y_3\}, \{z_1, z_2, z_3\}\}$$

is a forward bisimulation.

We compute in the following matrix the flow from every state in $\mathcal{Q}$ to every $\sim$-equivalence class in $\mathcal{Q}_\sim$.

FLOW	$\{x\}$	$\{y_1, y_2\}$	$\{y_3\}$	$\{z_1, z_2, z_3\}$
$\{x\}$	0	$\frac{2}{3}$	$\frac{1}{3}$	0
$\{y_1\}$	0	$\frac{1}{2}$	0	$\frac{1}{2}$
$\{y_2\}$	0	$\frac{1}{2}$	0	$\frac{1}{2}$
$\{y_3\}$	0	0	0	1
$\{z_1\}$	$\frac{1}{2}$	0	0	$\frac{1}{2}$
$\{z_2\}$	$\frac{1}{2}$	0	0	$\frac{1}{2}$
$\{z_3\}$	$\frac{1}{2}$	0	0	$\frac{1}{2}$

We notice that the rows y_1 and y_2 are the same. Moreover, the three rows z_1, z_2, and z_3 are equal as well. Thus $\sim$ is a forward bisimulation.

2. Conversely, let $\sim$ be the largest forward bisimulation such that $[x]_\sim = \{x\}$.

We have, for every $i \in \{1, 2, 3\}$,

$$\text{FLOW}(y_i, [x]_\sim) = 0.$$

and for every $j \in \{1,2,3\}$,

$$\text{FLOW}(z_i, [x]_\sim) = \frac{1}{2}.$$

Thus, for every $i, j \in \{1,2,3\}$, we have $y_i \not\sim z_j$.

So, for every $i \in \{1,2,3\}$, $[y_i]_\sim \subseteq \{y_1, y_2, y_3\}$ and $[z_i]_\sim \subseteq \{z_1, z_2, z_3\}$.

Then, we have:

(a) $\text{FLOW}(y_1, [z_3]_\sim) \in \{0, \frac{1}{2}\}$;

(b) $\text{FLOW}(y_2, [z_3]_\sim) \in \{0, \frac{1}{2}\}$;

(c) $\text{FLOW}(y_3, [z_3]_\sim) = 1$;

Thus $\text{FLOW}(y_3, [z_3]_\sim) \neq \text{FLOW}(y_1, [z_3]_\sim)$ and $\text{FLOW}(y_3, [z_3]_\sim) \neq \text{FLOW}(y_2, [z_3]_\sim)$.

We can conclude that $[y_3]_\sim = \{y_3\}$ and that for every $i \in \{1,2\}$, $[y_i]_\sim \subseteq \{y_1, y_2\}$.

It follows that the equivalence relation that is defined by the following equivalence classes:

$$\{\{x\}, \{y_1, y_2\}, \{y_3\}, \{z_1, z_2, z_3\}\}$$

is the largest forward bisimulation such that $\{x\}$ is an equivalence class.

Question 2 *(*) Let $(\mathcal{Q}, w)$ a weighted transition system and $\sim$ a forward bisimulation over $\mathcal{Q}$. Show that there exists a weighted transition system $(\mathcal{Q}^\sharp, w^\sharp)$ such that both following properties are satisfied:*

1. *the states of the new weighted transition system are the $\sim$-equivalence class of the initial one (i.e. $\mathcal{Q}^\sharp = [\mathcal{Q}]_\sim$);*
2. *for every trace $\tau^\sharp = (C_i)_{0 \leqslant i \leqslant n}$ in the new weighted transition system and any initial state $q^\star \in C_0$, the probability (in the new weighted transition system) of the trace $\tau^\sharp$ is equal to the sum of the probabilities (in the former weighted transition system) of the traces $(q_i)_{0 \leqslant i \leqslant n}$ such that $q_0 = q^\star$ and $q_i \in C_i$ for every i between 1 and n.*

Answer:

We define $w^\sharp([q]_\sim, [q'']_\sim) \stackrel{\Delta}{=} \text{FLOW}(\{q\}, [q'']_\sim)$, for every two states $q, q'' \in \mathcal{Q}$.

The function $w^\sharp$ is well defined, since for every $q, q', q'' \in \mathcal{Q}$, the following condition:

$$\text{FLOW}(\{q\}, [q'']_\sim) = \text{FLOW}(\{q'\}, [q'']_\sim)$$

is satisfied.

Moreover, for every state $q \in \mathcal{Q}$, we have:

$$\begin{array}{rcl} \sum_{C \in \mathcal{Q}_\sim} w^\sharp([q]_\sim, C) & = & \sum_{C \in \mathcal{Q}_\sim} \text{FLOW}(\{q\}, C) \\ & = & \text{FLOW}(\{q\}, \mathcal{Q}) \\ & = & 1. \end{array}$$

We prove the relationship over the probabilities of traces by induction.

1. The probability of the trace (C_0) is equal to 1.

   The probability of the trace $(q^\star)$ is equal to 1 as well.

2. We assume that the relationship holds for traces of size n.

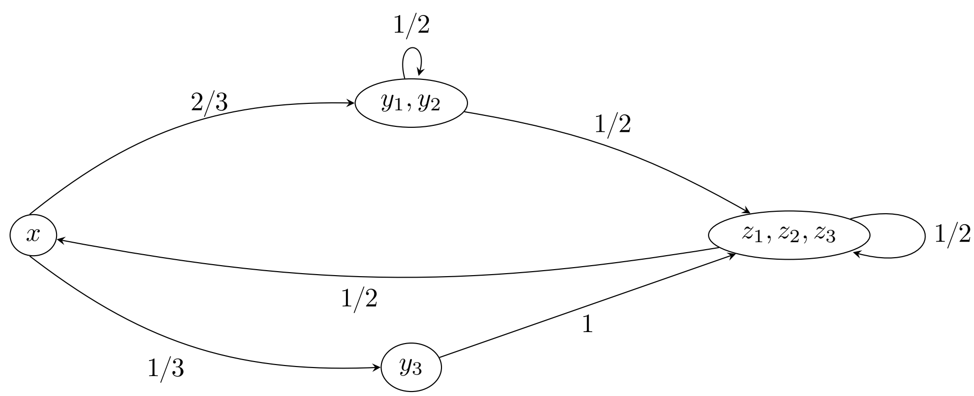
   Let $\tau^\sharp \triangleq (C_i)_{0\leqslant i\leqslant n+1}$ be a trace in the new transition system.

   By induction hypothesis, we assume the probability of the trace $(C_i)_{0\leqslant i\leqslant n}$ is equal to the sum of the probabilities of the traces $(q_i)_{0\leqslant i\leqslant n}$, in the initial transition system, such that $q_0 = q^\star$ and $q_i \in C_i$ for every i between 1 and n.

   We have:

$$\begin{array}{rcl} P(\tau^\sharp \mid C_0) & = & P((C_i)_{0\leqslant i\leqslant n} \mid C_0)\cdot w^\sharp(C_n, C_{n+1}) \\ & = & \left(\sum_{(q_i)_{0\leqslant i\leqslant n}, q_0=q^\star, q_i\in C_i} P((q_i)_{0\leqslant i\leqslant n} \mid q^\star)\right)\cdot w^\sharp(C_n, C_{n+1}) \\ & = & \sum_{(q_i)_{0\leqslant i\leqslant n}, q_0=q^\star, q_i\in C_i} P((q_i)_{0\leqslant i\leqslant n} \mid q^\star)\cdot w^\sharp(C_n, C_{n+1}) \\ & = & \sum_{(q_i)_{0\leqslant i\leqslant n}, q_0=q^\star, q_i\in C_i} P((q_i)_{0\leqslant i\leqslant n} \mid q^\star)\cdot \sum_{q_{n+1}\in C_{n+1}} w(q_n, q_{n+1}) \\ & = & \sum_{(q_i)_{0\leqslant i\leqslant n+1}, q_0=q^\star, q_i\in C_i} P((q_i)_{0\leqslant i\leqslant n+1} \mid q^\star) \end{array}$$

In our case study, we obtain the following coarse-grained transition system:



2.3 Backward bisimulation

Now we study the notion of backward bisimulation which highlights statistical invariants about the time evolution of the state distribution of the underlying weighted transition system.

Definition 2.5 (Backward bisimulation) *Let $(\mathcal{Q}, w)$ a weighted transition system and $\sim$ be an equivalence relation over the set $\mathcal{Q}$.*

The relation $\sim$ is called a backward bisimulation if and only if for every q, q', q'' such that $q \sim q'$, the following equation:

$$\text{FLOW}([q'']_\sim, \{q\}) = \text{FLOW}([q'']_\sim, \{q'\})$$

is satisfied.

Question 3 *(**) Propose the largest backward bisimulation $\sim$ over the weighted transition systems that is depicted in Fig.* **??**.

That is to say that the relation $\sim$ should satisfy both following properties:

1. *$\sim$ is a backward bisimulation over the weighted transition system depicted in Fig.* **??**;
2. *for every states q and q' and for every backward bisimulation $\sim'$ over the weighted transition system depicted in Fig.* **??**, *we have $q \sim' q' \Rightarrow q \sim q'$.*

Answer:

1. Let us show that the relation $\sim$ among the elements of $\mathcal{Q}$ that is defined as follows:

$$\mathcal{Q}_{\sim} \triangleq \{\{x\},\{y_1,y_2\},\{y_3\},\{z_1,z_2\},\{z_3\}\}$$

is a backward bisimulation.

We compute in the following matrix the flow from every $\sim$-equivalence class in $\mathcal{Q}_{\sim}$ to every state in $\mathcal{Q}$.

FLOW	$\{x\}$	$\{y_1\}$	$\{y_2\}$	$\{y_3\}$	$\{z_1\}$	$\{z_2\}$	$\{z_3\}$
$\{x\}$	0	$\frac{1}{3}$	$\frac{1}{3}$	$\frac{1}{3}$	0	0	0
$\{y_1,y_2\}$	0	$\frac{1}{2}$	$\frac{1}{2}$	0	$\frac{1}{2}$	$\frac{1}{2}$	0
$\{y_3\}$	0	0	0	0	0	0	1
$\{z_1,z_2\}$	1	0	0	0	$\frac{1}{2}$	$\frac{1}{2}$	0
$\{z_3\}$	$\frac{1}{2}$	0	0	0	0	0	$\frac{1}{2}$

We notice that the columns y_1 and y_2 are the same.

Moreover, the columns z_1 and z_2 are equal as well.

Thus $\sim$ is a backward bisimulation.

2. Conversely, let $\sim$ be the largest backward bisimulation over the weighted transition system that is depicted in Fig. **??**.

Since $\mathcal{Q}_{\sim}$ is a partition of $\mathcal{Q}$, we get that:

$$\begin{array}{rcl} \text{FLOW}(\mathcal{Q},\{q\}) & = & \sum_{C\in\mathcal{Q}_{\sim}} \text{FLOW}(\mathcal{Q},\{q\}) \\ & = & \sum_{C\in\mathcal{Q}_{\sim}} \text{FLOW}(\mathcal{Q},\{q'\}) \\ & = & \text{FLOW}(\mathcal{Q},\{q'\}). \end{array}$$

We have:

$$\begin{cases} \text{FLOW}(\mathcal{Q},\{x\}) = \frac{3}{2}; \\ \text{FLOW}(\mathcal{Q},\{y_1\}) = \frac{5}{6}; \\ \text{FLOW}(\mathcal{Q},\{y_2\}) = \frac{5}{6}; \\ \text{FLOW}(\mathcal{Q},\{y_3\}) = \frac{1}{3}; \\ \text{FLOW}(\mathcal{Q},\{z_1\}) = 1; \\ \text{FLOW}(\mathcal{Q},\{z_2\}) = 1; \\ \text{FLOW}(\mathcal{Q},\{z_3\}) = \frac{3}{2}; \end{cases}$$

It follows that:

- $[x]_{\sim} \subseteq \{x, z_3\}$;

- $[y_1]_\sim \subseteq \{y_1, y_2\}$;
- $[y_2]_\sim \subseteq \{y_1, y_2\}$;
- $[y_3]_\sim = \{y_3\}$.
- $[z_1]_\sim \subseteq \{z_1, z_2\}$;
- $[z_2]_\sim \subseteq \{z_1, z_2\}$;
- $[z_3]_\sim \subseteq \{x, z_3\}$.

Since $\{y_3\}$ is a $\sim$-equivalence class, we have, for every two states q, q' such that $q \sim q'$:

$$\textsc{flow}(\{y_3\}, \{q\}) = \textsc{flow}(\{y_3\}, \{q'\}).$$

Since $\textsc{flow}(\{y_3\}, \{x\}) = 0$ and $\textsc{flow}(\{y_3\}, \{z_3\}) = 1$, it follows that $x \nsim z_3$.

It follows that the equivalence relation that is defined by the following equivalence classes:

$$\{\{x\}, \{y_1, y_2\}, \{y_3\}, \{z_1, z_2\}, \{z_3\}\}$$

is the largest backward bisimulation for the weigthed transition system that is depicted in Fig. **??**.

Question 4 *(***) Let $(\mathcal{Q}, w)$ a weighted transition system and $\sim$ a backward bisimulation over $\mathcal{Q}$.*

Let $q^\star$ be a state such that $[q^\star]_\sim = \{q^\star\}$ and n be a natural number.

Show that for every two states $q, q' \in \mathcal{Q}$ such that $q \sim q'$, the probability that the system ends in state q after n computation steps knowing that it has started in state $q^\star$ is equal to the probability that the system ends in that q' after n computations knowing that it has started in state $q^\star$.

That is to say that the sum of the probabilities of all the traces of n transitions starting in state $q^\star$ and ending in state q is equal to the sum of the probabilities of all the traces of n transitions starting in state $q^\star$ and ending in state q'.

Answer:

We denote as $\mathcal{T}(q, n, q')$ the set of traces starting from the state q and ending in the state q' in exactly n transitions.

We prove the result by induction over n.

1. For $n = 0$, $\mathcal{T}(q^\star, n, q)$ is equal to $\{q^\star\}$ whenever $q = q^\star$ and to the empty set $\emptyset$ otherwise.

   Let $q, q' \in \mathcal{Q}$ be two states such that $q \sim q'$.

   (a) Whenever $q = q^\star$.
   Since $q^\star$ is the only element of its $\sim$-equivalence class, we have $q' = q^\star$ as well.
   Hence $\sum_{\tau \in \mathcal{T}(q^\star, n, q)} P(\tau \mid q^\star) = 1$ and $\sum_{\tau \in \mathcal{T}(q^\star, n, q')} P(\tau \mid q^\star) = 1$.

   (b) Whenever $q' = q^\star$.
   See previous case.

   (c) Otherwise.
   Both sums $\sum_{\tau \in \mathcal{T}(q^\star, n, q)} P(\tau \mid q^\star)$ and $\sum_{\tau \in \mathcal{T}(q^\star, n, q)} P(\tau \mid q^\star)$ are equal to 0.

   In every case, we have
   $$\sum_{\tau \in \mathcal{T}(q^\star, n, q)} P(\tau \mid q^\star) = \sum_{\tau \in \mathcal{T}(q^\star, n, q)} P(\tau \mid q^\star)$$

2. We assume that the property holds for $n \in \mathbb{N}$, let us show that it holds for the traces of length $n+1$.

   Let q, q' be two states in $\mathcal{Q}$ such that $q \sim q'$.

   For every $\sim$-equivance class C, we choose q_C an element of C.

   We have:

$$
\begin{array}{rcl}
\sum_{\tau \in \mathcal{T}(q^\star, n+1, q)} P(\tau \mid q^\star) & = & \sum_{q'' \in \mathcal{Q}, \tau' \in \mathcal{T}(q^\star, n, q'')} P(\tau' \mid q^\star) \cdot w(q'', q) \\
& = & \sum_{C \in \mathcal{Q}_\sim} \sum_{q'' \in C, \tau' \in \mathcal{T}(q^\star, n, q'')} P(\tau' \mid q^\star) \cdot w(q'', q) \\
& = & \sum_{C \in \mathcal{Q}_\sim} \sum_{q'' \in C} \sum_{\tau' \in \mathcal{T}(q^\star, n, q'')} P(\tau' \mid q^\star) \cdot w(q'', q) \\
& = & \sum_{C \in \mathcal{Q}_\sim} \sum_{q'' \in C} w(q'', q) \cdot \left(\sum_{\tau' \in \mathcal{T}(q^\star, n, q'')} P(\tau' \mid q^\star) \right) \\
& = & \sum_{C \in \mathcal{Q}_\sim} \sum_{q'' \in C} w(q'', q) \cdot \left(\sum_{\tau' \in \mathcal{T}(q^\star, n, q_C)} P(\tau' \mid q^\star) \right) \\
& = & \sum_{C \in \mathcal{Q}_\sim} \left(\sum_{q'' \in C} w(q'', q) \right) \cdot \left(\sum_{\tau' \in \mathcal{T}(q^\star, n, q_C)} P(\tau' \mid q^\star) \right) \\
& = & \sum_{C \in \mathcal{Q}_\sim} (\textsc{flow}(C, q)) \cdot \left(\sum_{\tau' \in \mathcal{T}(q^\star, n, q_C)} P(\tau' \mid q^\star) \right) \\
& = & \sum_{C \in \mathcal{Q}_\sim} (\textsc{flow}(C, q')) \cdot \left(\sum_{\tau' \in \mathcal{T}(q^\star, n, q_C)} P(\tau' \mid q^\star) \right) \\
& = & \sum_{C \in \mathcal{Q}_\sim} \left(\sum_{q'' \in C} w(q'', q') \right) \cdot \left(\sum_{\tau' \in \mathcal{T}(q^\star, n, q_C)} P(\tau' \mid q^\star) \right) \\
& = & \sum_{C \in \mathcal{Q}_\sim} \sum_{q'' \in C} w(q'', q') \cdot \left(\sum_{\tau' \in \mathcal{T}(q^\star, n, q_C)} P(\tau' \mid q^\star) \right) \\
& = & \sum_{C \in \mathcal{Q}_\sim} \sum_{q'' \in C} w(q'', q') \cdot \left(\sum_{\tau' \in \mathcal{T}(q^\star, n, q'')} P(\tau' \mid q^\star) \right) \\
& = & \sum_{C \in \mathcal{Q}_\sim} \sum_{q'' \in C} \sum_{\tau' \in \mathcal{T}(q^\star, n, q'')} P(\tau' \mid q^\star) \cdot w(q'', q) \\
& = & \sum_{C \in \mathcal{Q}_\sim} \sum_{q'' \in C, \tau' \in \mathcal{T}(q^\star, n, q'')} P(\tau' \mid q^\star) \cdot w(q'', q') \\
& = & \sum_{q'' \in \mathcal{Q}, \tau' \in \mathcal{T}(q^\star, n, q'')} P(\tau' \mid q^\star) \cdot w(q'', q') \\
& = & \sum_{\tau \in \mathcal{T}(q^\star, n+1, q')} P(\tau \mid q^\star)
\end{array}
$$

Thus, for every $n \in \mathbb{N}$ and every two $\sim$-equivalent states q, q' in $\mathcal{Q}$, we have:

$$\sum_{\tau \in \mathcal{T}(q^\star, n, q)} P(\tau \mid q^\star) = \sum_{\tau \in \mathcal{T}(q^\star, n, q')} P(\tau \mid q^\star)$$

Question 5 *(**) Let $(\mathcal{Q}, w)$ a weighted transition system and $\sim$ a backward bisimulation over $\mathcal{Q}$. Let $q^\star$ be a state such that $[q^\star]_\sim = \{q^\star\}$. Show that there exists a weighted transition system $(\mathcal{Q}^\sharp, w^\sharp)$ such that*

1. *the states of the new weighted transition system are the $\sim$-equivalence class of the initial one (i.e. $\mathcal{Q}^\sharp = [\mathcal{Q}]_\sim$)*
2. *For every trace $\tau^\sharp = (C_i)_{0 \leqslant i \leqslant n}$ in the new weighted transition system such that $C_0 = \{q^\star\}$, the probability (in the new weighted transition system) of the trace $\tau^\sharp$ is equal to the sum of the probabilities (in the former weighted transition system) of the traces $(q_i)_{0 \leqslant i \leqslant n}$ such that $q_i \in C_i$ for every i between 0 and n.*

Answer:

We define $w^\sharp([q]_\sim, [q'']_\sim) \triangleq \frac{\sum_{q' \in [q]_\sim} \textsc{flow}(\{q'\}, [q'']_\sim)}{\textsc{Cardinal}([q]_\sim)}$, for every two states $q, q'' \in \mathcal{Q}$.

The function $w^\sharp$ is well defined, since for every $q, q', q'' \in \mathcal{Q}$, the following condition:

$$\textsc{flow}(\{q\}, [q'']_\sim) = \textsc{flow}(\{q'\}, [q'']_\sim)$$

is satisfied.

Moreover, for every state $q \in \mathcal{Q}$, we have:

$$\begin{array}{rcl} \sum_{C \in \mathcal{Q}_\sim} w^\sharp([q]_\sim, C) & = & \sum_{C \in \mathcal{Q}_\sim} \frac{\sum_{q' \in [q]_\sim} \textsc{flow}(\{q'\},C)}{\textsc{Cardinal}([q]_\sim)} \\ & = & \frac{\sum_{C \in \mathcal{Q}_\sim} \sum_{q' \in [q]_\sim} \textsc{flow}(\{q'\},C)}{\textsc{Cardinal}([q]_\sim)} \\ & = & \frac{\sum_{q' \in [q]_\sim} \textsc{flow}(\{q'\},\mathcal{Q})}{\textsc{Cardinal}([q]_\sim)} \\ & = & \frac{\sum_{q' \in [q]_\sim} 1}{\textsc{Cardinal}([q]_\sim)} \\ & = & 1 \end{array}$$

We prove the relationship over the probabilities of traces by induction.

1. The probability of the trace (C_0) is equal to 1.

   The probability of the trace $(q^\star)$ is equal to 1 as well.

2. We assume that the relationship holds for traces of size n.

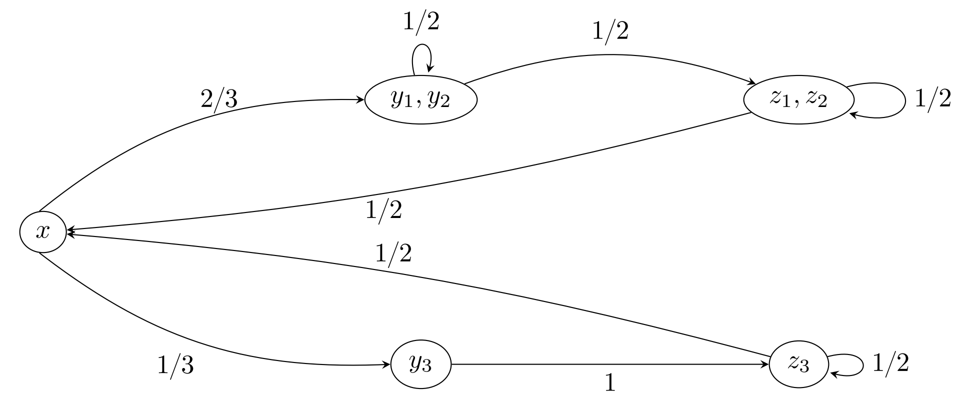
   Let $\tau^\sharp \triangleq (C_i)_{0 \leqslant i \leqslant n+1}$ be a trace in the new transition system.

   By induction hypothesis, we assume the probability of the trace $(C_i)_{0 \leqslant i \leqslant n}$ is equal to the sum of the probabilities of the traces $(q_i)_{0 \leqslant i \leqslant n}$, in the initial transition system, such that $q_0 = q^\star$ and $q_i \in C_i$ for every i between 1 and n.

   We have:

$$\begin{array}{rcl} P(\tau^\sharp \mid C_0) & = & P((C_i)_{0 \leqslant i \leqslant n} \mid C_0) \cdot w^\sharp(C_n, C_{n+1}) \\ & = & \left(\sum_{(q_i)_{0 \leqslant i \leqslant n}, q_0 = q^\star, q_i \in C_i} P((q_i)_{0 \leqslant i \leqslant n} \mid q^\star)\right) \cdot w^\sharp(C_n, C_{n+1}) \\ & = & \sum_{(q_i)_{0 \leqslant i \leqslant n}, q_0 = q^\star, q_i \in C_i} P((q_i)_{0 \leqslant i \leqslant n} \mid q^\star) \cdot w^\sharp(C_n, C_{n+1}) \\ & = & \sum_{(q_i)_{0 \leqslant i \leqslant n}, q_0 = q^\star, q_i \in C_i} P((q_i)_{0 \leqslant i \leqslant n} \mid q^\star) \cdot \frac{\sum_{q'_n \in C_n} w(q'_n, C_{n+1})}{\textsc{Cardinal}(C_n)} \\ & = & \sum_{(q_i)_{0 \leqslant i \leqslant n}, q_0 = q^\star, q_i \in C_i} P((q_i)_{0 \leqslant i \leqslant n} \mid q^\star) \cdot \frac{\sum_{q'_n \in C_n} w(q_n, C_{n+1})}{\textsc{Cardinal}(C_n)} \\ & = & \sum_{(q_i)_{0 \leqslant i \leqslant n}, q_0 = q^\star, q_i \in C_i} P((q_i)_{0 \leqslant i \leqslant n} \mid q^\star) \cdot w(q_n, C_{n+1}) \frac{\sum_{q'_n \in C_n} 1}{\textsc{Cardinal}(C_n)} \\ & = & \sum_{(q_i)_{0 \leqslant i \leqslant n}, q_0 = q^\star, q_i \in C_i} P((q_i)_{0 \leqslant i \leqslant n} \mid q^\star) \cdot w(q_n, C_{n+1}) \\ & = & \sum_{(q_i)_{0 \leqslant i \leqslant n}, q_0 = q^\star, q_i \in C_i} \left(P((q_i)_{0 \leqslant i \leqslant n} \mid q^\star) \cdot \left(\sum_{q_{n+1} \in C_{n+1}} w(q_n, q_{n+1})\right)\right) \\ & = & \sum_{(q_i)_{0 \leqslant i \leqslant n}, q_0 = q^\star, q_i \in C_i} \sum_{q_{n+1} \in C_{n+1}} P((q_i)_{0 \leqslant i \leqslant n} \mid q^\star) \cdot w(q_n, q_{n+1}) \\ & = & \sum_{(q_i)_{0 \leqslant i \leqslant n}, q_0 = q^\star, q_i \in C_i} \sum_{q_{n+1} \in C_{n+1}} P((q_i)_{0 \leqslant i \leqslant n+1} \mid q^\star) \\ & = & \sum_{(q_i)_{0 \leqslant i \leqslant n+1}, q_0 = q^\star, q_i \in C_i} P((q_i)_{0 \leqslant i \leqslant n+1} \mid q^\star) \end{array}$$

In our case study, we obtain the following coarse-grained transition system:



3 Bisimulations induced by perfect symmetries among pairs of sites

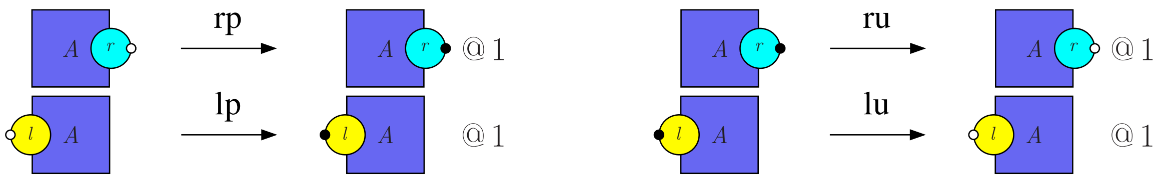


Figure 2: A set of rules with two interaction sites having the same capabilities of interaction.

In this section, we consider the model that is made of the set of rules given in Fig. ??. In this model, the role of sites r and l is intuitively the same. The goal of this section is to investigate what it means with respect to the set of rules and to extrapolate which bisimulations are induced by this property.

Definition 3.1 *The symmetric of an agent is obtained by swapping the states of the sites l and r of this agent.*

In particular:

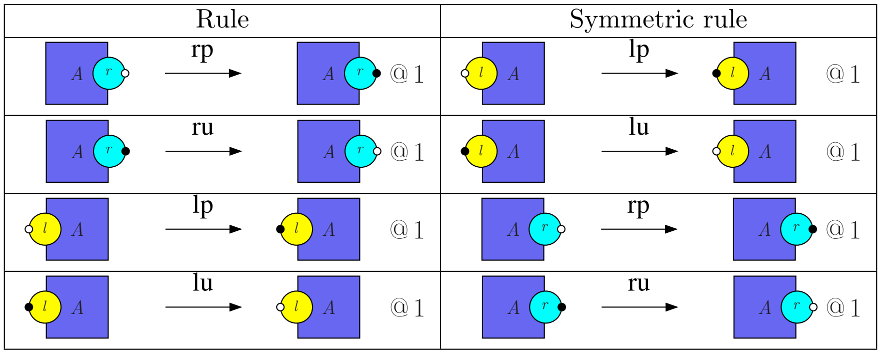
1. *If this agent contains neither the site l, nor the site r, the agent remains unchanged;*
2. *If this agent contains the site l, but not the site r, the site l is replaced with the site r;*
3. *If this agent contains the site r, but not the site l, the site r is replaced with the site l;*
4. *If this agent contains both the site l and the site r, the site l takes the former state of the site r while the site r takes the former state of the site l.*

Definition 3.2 *The symmetric of a rule is obtained by taking the symmetric of the left hand side and the symmetric of the right hand side.*

Question 6 *(*) Show that the symmetric of any rule of the model, is also a rule of the model with the same rate.*

Answer:

In the following array are drawn each rule (left column) and its symmetric (right column):

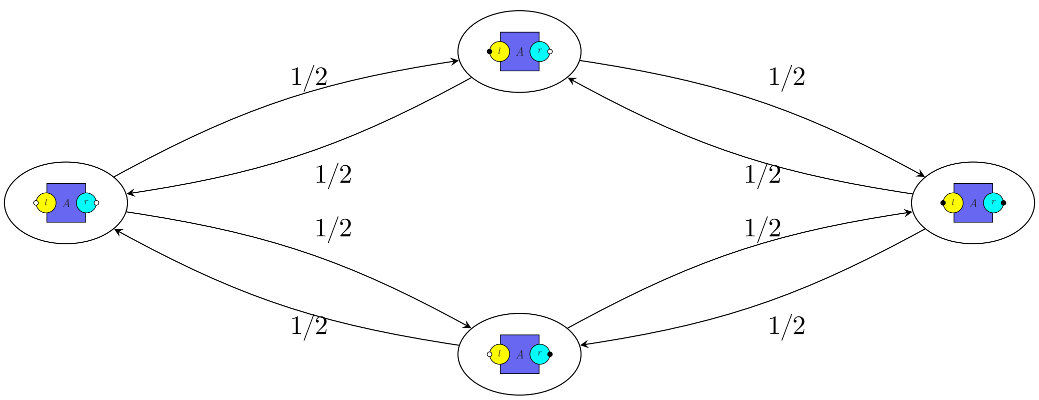


Question 7 *(*) Draw the weighted transition system that is induced by the rules of the model.*

So as to make this transition system easy to write, we consider only the states made of a single agent.

We recall that, an event e stemming from a state q is defined by a rule r and an embedding from the left hand side of the rule r into the state q. The propensity of the event e is equal to the rate of the rule. The state q' that is reached when applying the event is defined by the operational semantics of Kappa. Then the propability $w(q, q')$ is defined as the quotient between the sum of the propensities of the events from the state q to the state q' and the sum of the propensities of all the events stemming from the state q.

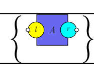
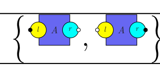
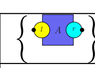
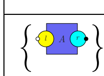
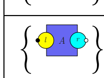
Answer:



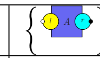
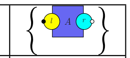
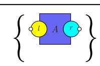
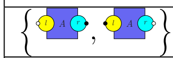
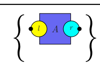
Question 8 *(*) Show that the equivalence relation that gathers states by symmetry-classes induces both a forward bisimulation and a backward bisimulation.*

Answer:

1. Forward bisimulation:

FLOW			
	$\frac{1}{2}$	0	$\frac{1}{2}$
	$\frac{1}{2}$	0	$\frac{1}{2}$

2. Backward bisimulation:

FLOW		
	$\frac{1}{2}$	$\frac{1}{2}$
	0	0
	$\frac{1}{2}$	$\frac{1}{2}$

Thus this equivalence relation induces both a forward bisimulation and a backward bisimulation.

4 Bisimulations induced by contextual symmetries among pairs of sites

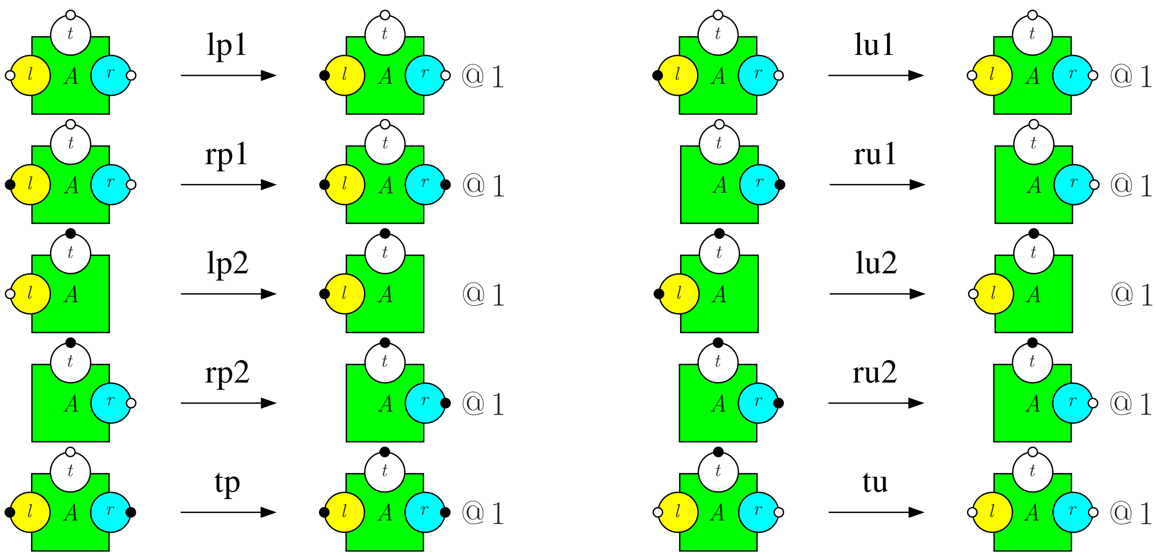


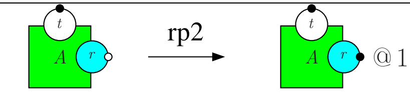
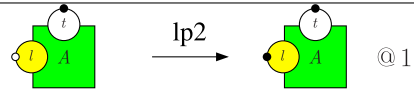
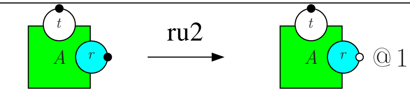
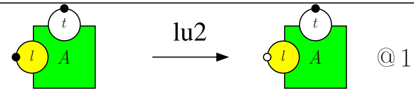
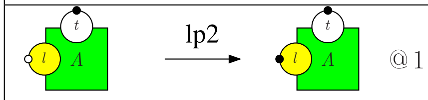
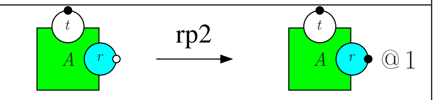
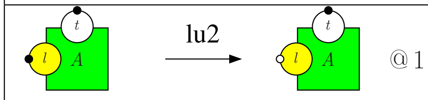
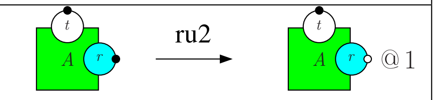
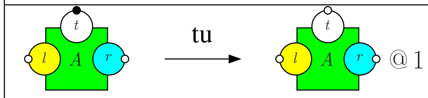
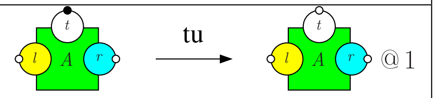
Figure 3: A set of rules in which two sites have the same capabilities of interactions only when a third site is activated.

In this section, we consider the model that is made of the set of rules given in Fig. **??**. In this model, the sites l and r get sequentially activated/deactivated when the site t is not activated, whereas they get activated/deactivated in parallel when this site is activated. Intuitively, the sites l and r have the same capabilities of interaction only when the site t is activated. Hence the symmetry between the site l and r is contextual. The goal of this section is to investigate whether contextual symmetries enjoy the same properties as uncontextual ones and to adapt the framework accordingly.

Question 9 *(*) Show that the symmetric of any rule of the model that requires the site t to be phosphorylated, is also a rule of the model with the same rate.*

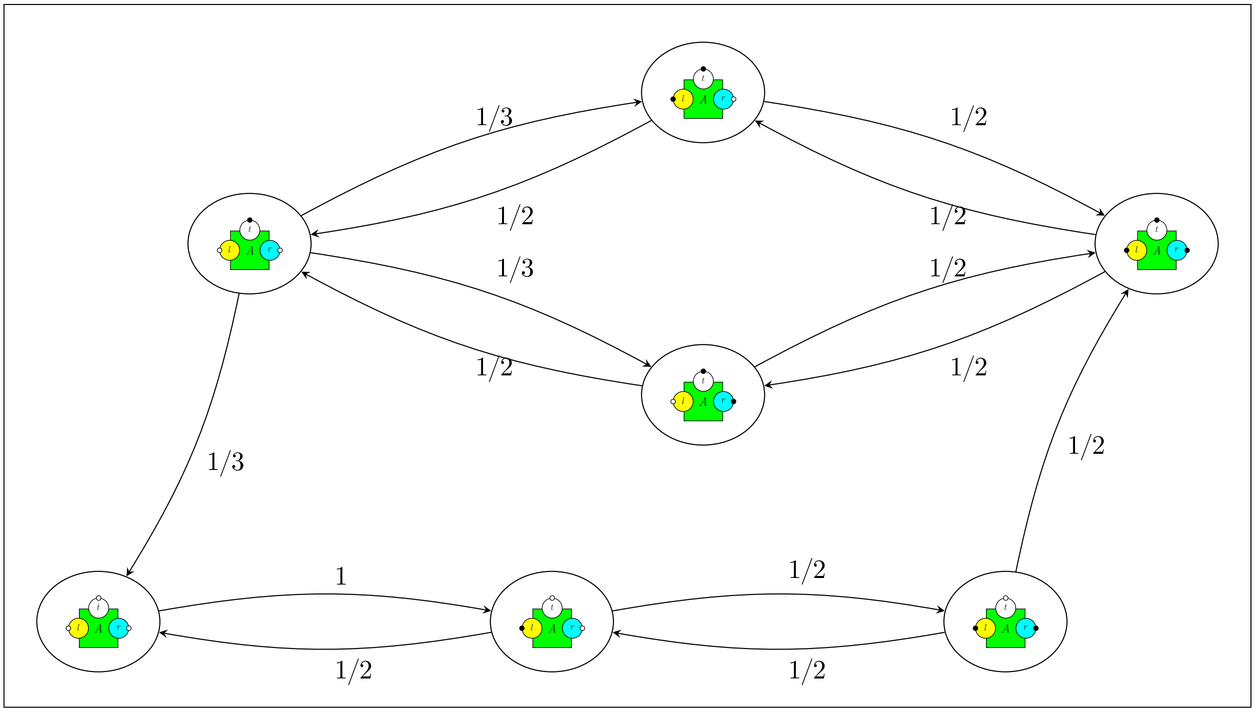
Answer:

In the following array, are drawn each rule (left column) and its symmetric (right column):

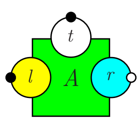
Rule	Symmetric rule
 rp2 @1	 lp2 @1
 ru2 @1	 lu2 @1
 lp2 @1	 rp2 @1
 lu2 @1	 ru2 @1
 tu @1	 tu @1

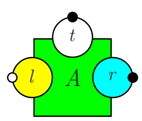
Question 10 *(*) Draw the weighted transition system that is induced by the rule of the model.*
So as to make this transition system easy to write, we consider the states made only of a single agent.

Answer:



We consider the equivalence relation $\sim$ that identifies only the two following configurations:



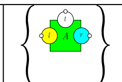
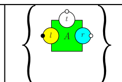
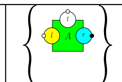
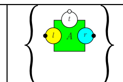
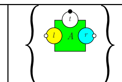
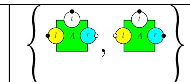
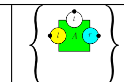
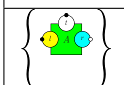
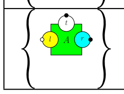


(i.e. any other configuration is the only element of its equivalence class.)

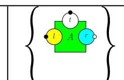
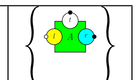
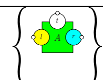
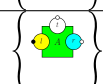
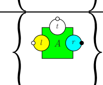
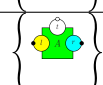
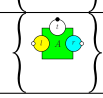
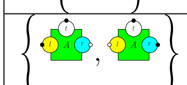
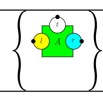
Question 11 *(*) Show that the equivalence relation $\sim$ induces both a forward bisimulation and a backward bisimulation.*

Answer:

1. Forward bisimulation:

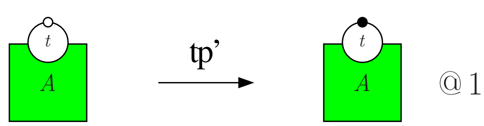
FLOW							
	0	0	0	0	$\frac{1}{2}$	0	$\frac{1}{2}$
	0	0	0	0	$\frac{1}{2}$	0	$\frac{1}{2}$

2. Backward bisimulation:

FLOW		
	0	0
	0	0
	0	0
	0	0
	$\frac{1}{3}$	$\frac{1}{3}$
	0	0
	$\frac{1}{2}$	$\frac{1}{2}$

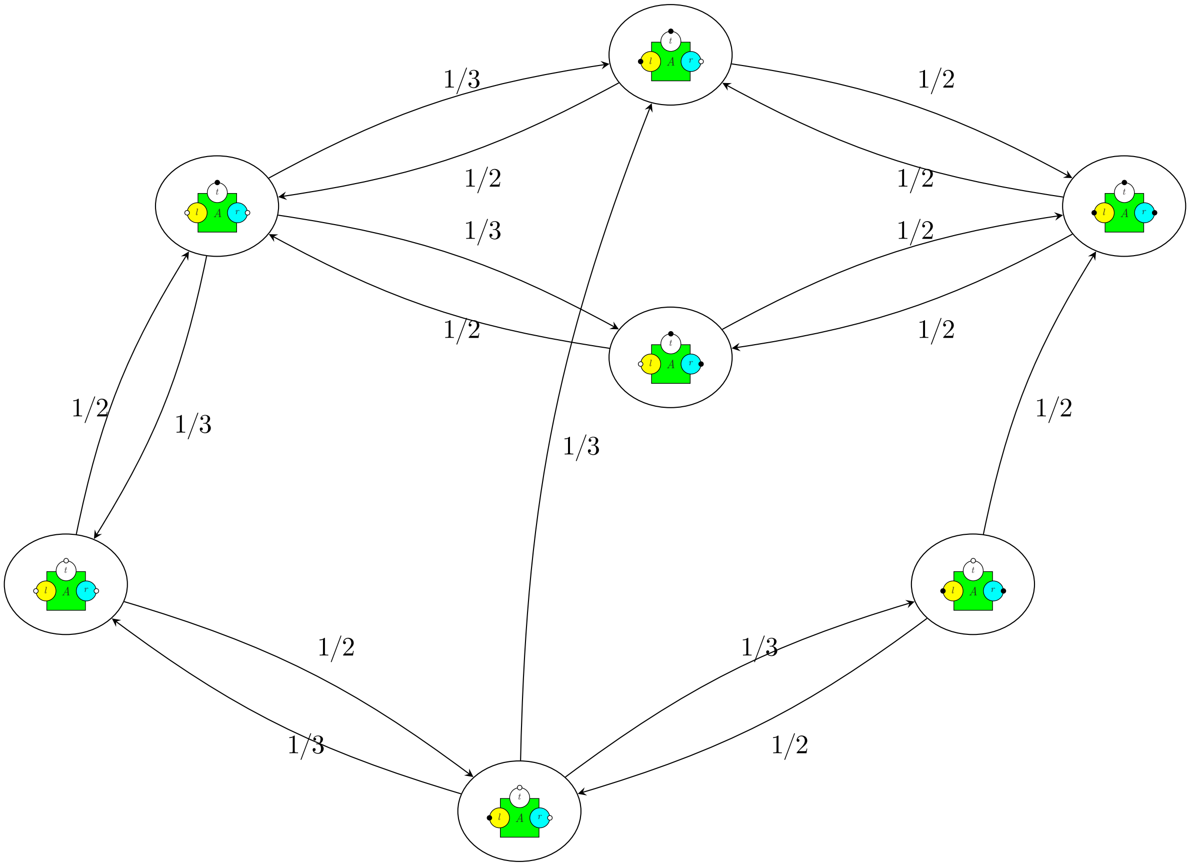
Thus, the relation $\sim$ is both a forward and a backward bisimulation.

Question 12 *(*) In the rules given in Fig.* **??**, *we propose to replace the rule tp by the following one:*

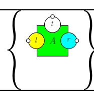
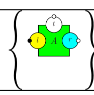
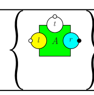
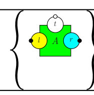
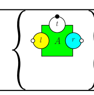
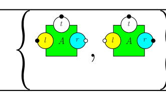
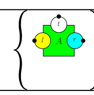
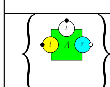
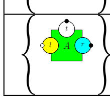


Is the relation $\sim$ still a forward bisimulation over the underlying weighted transition system?
Is the relation $\sim$ still a backward bisimulation over the underlying weighted transition system?

Answer:

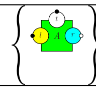
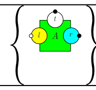
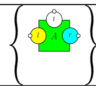
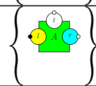
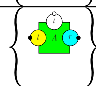
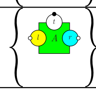
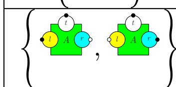
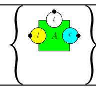


1. Forward bisimulation:

FLOW							
	0	0	0	0	$\frac{1}{2}$	0	$\frac{1}{2}$
	0	0	0	0	$\frac{1}{2}$	0	$\frac{1}{2}$

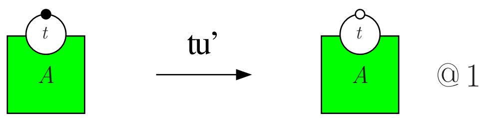
Thus the relation $\sim$ is a forward bisimulation.

2. Backward bisimulation:

FLOW		
	0	0
	$\frac{1}{3}$	0
	0	0
	$\frac{1}{3}$	$\frac{1}{3}$
	0	0
	$\frac{1}{2}$	$\frac{1}{2}$

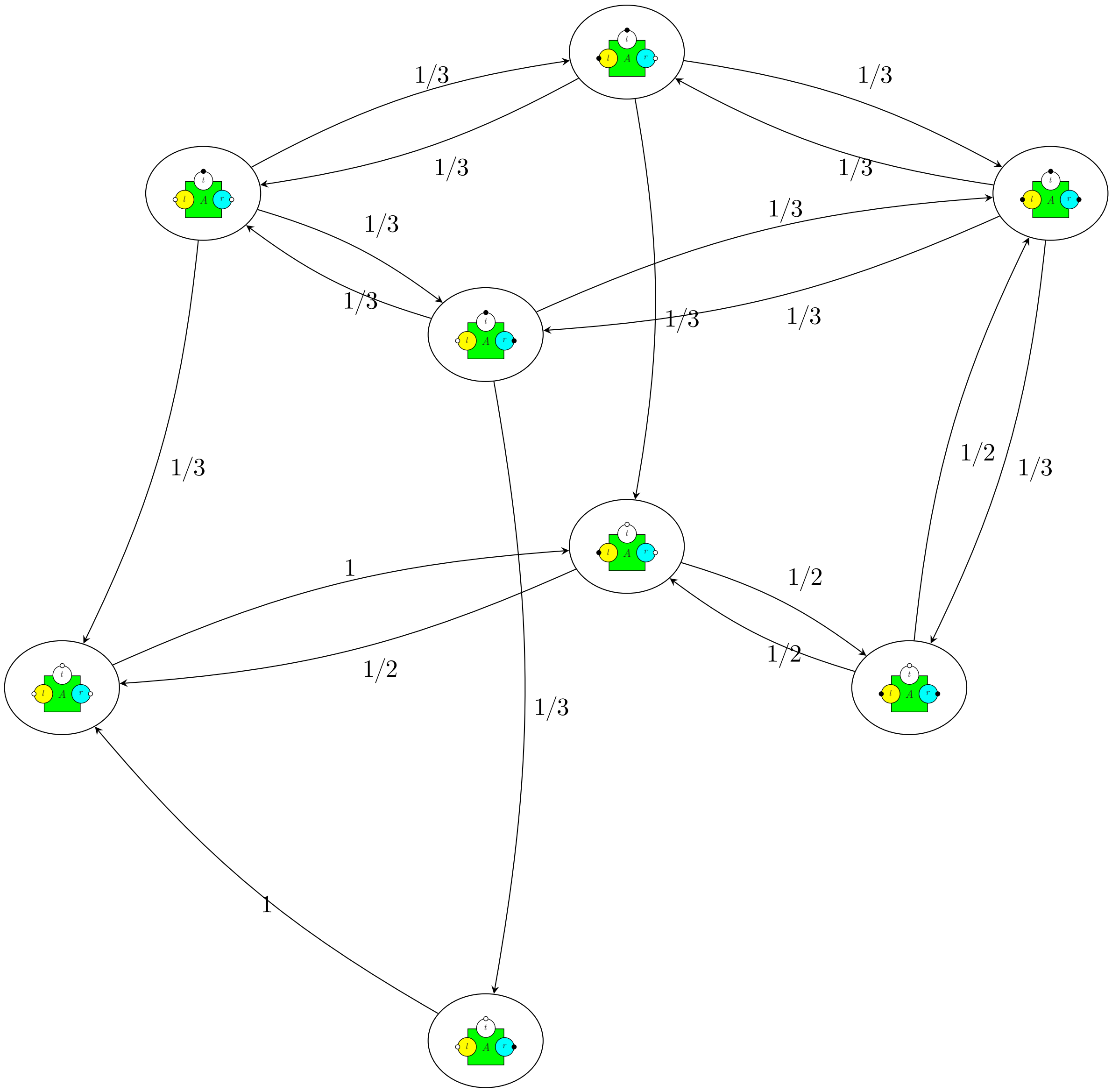
Thus the relation $\sim$ is not a backward bisimulation.

Question 13 *(*) In the rules given in Fig.* **??**, *we propose to replace the rule tu by the following one:*

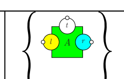
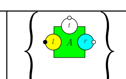
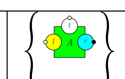
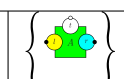
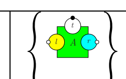
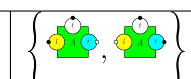
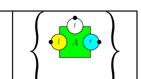
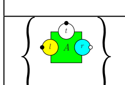
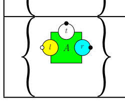


Is the relation $\sim$ still a forward bisimulation over the underlying weighted transition system?
Is the relation $\sim$ still a backward bisimulation over the underlying weighted transition system?

Answer:

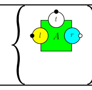
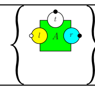
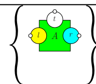
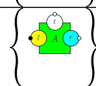
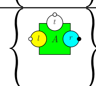
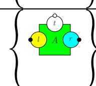
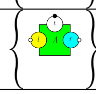
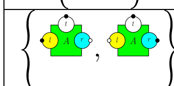
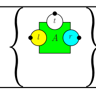


1. Forward bisimulation:

FLOW							
	0	$\frac{1}{3}$	0	0	$\frac{1}{3}$	0	$\frac{1}{3}$
	0	0	$\frac{1}{3}$	0	$\frac{1}{3}$	0	$\frac{1}{3}$

Thus, the relation $\sim$ is not a forward bisimulation.

2. Backward bisimulation:

FLOW		
	0	0
	0	0
	0	0
	0	0
	$\frac{1}{3}$	$\frac{1}{3}$
	0	0
	$\frac{1}{3}$	$\frac{1}{3}$

Thus the relation $\sim$ is a backward bisimulation.

Question 14 *(*****) Propose a criterion over the rules and the state space of a Kappa model so as to ensure that a contextual symmetry among a pair of sites induces a forward bisimulation over the underlying weighted transition system.*

Answer:

To ensure that an equivalence relation induces a forward bisimulation, it is enough to prove that for every pair of symmetric states, any transition from the first state to another one can be mimicked by a transition of same rate from the second one, such that both targeted states are symmetric.

Thus, we require two conditions:

- For every rule r the lhs of which satisfies the contextual condition, the symmetric of the rule is a rule with the same rate.
- Every rule that can potentially break the contextual condition can only be applied on a symmetric configuration.

(The second condition ensures that any symmetry that is valid in the state of system before applying a rule is still valid after having applied this rule. While the first condition ensures that there is a rule to goes from the symmetric of the state before applying the rule to the symmetric of the state before applying the rule.)

Question 15 *(*****) Propose a criterion over the rules and the state space of a Kappa model so as to ensure that a contextual symmetry among a pair of sites induces a backward bisimulation over the underlying weighted transition system.*

Answer:

To ensure that an equivalence relation induces a backward bisimulation, it is enough to prove that for every pair of symmetric states, any transition ending in the first state can be mimicked by a transition of same rate ending in the second one, such that the sources of these both transitions are symmetric.

Thus, we require two conditions:

- For every rule r the lhs of which satisfies the contextual condition, the symmetric of the rule is a rule with the same rate.
- Every rule that can potentially forge the contextual condition can produce only in symmetric configurations.

(The second condition ensures that any symmetry that is valid in the state of system after applying a rule is still valid before having applied this rule. While the first condition ensures that there is a rule to goes from the symmetric of the state before applying the rule to the symmetric of the state before applying the rule.)