Master 2 MPRI course 2-19 Biochemical Programming
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Written examination 3 hours
All printed documents allowed
Any electronic devide prohibited
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Abstract

We study the notion of contextual symmetry on the differential semantics of three variants of a model.

We consider a model with only one kind of agent and three sites which can be phosphorylated, or not. Each kind of site is identified by its position, (on the top, on the left, on the right). Unphosphorylated sites carry a white circular while phosphorylated ones carry a black one.

1 First variant of the model

The first variant of the model is described in Fig. 1.

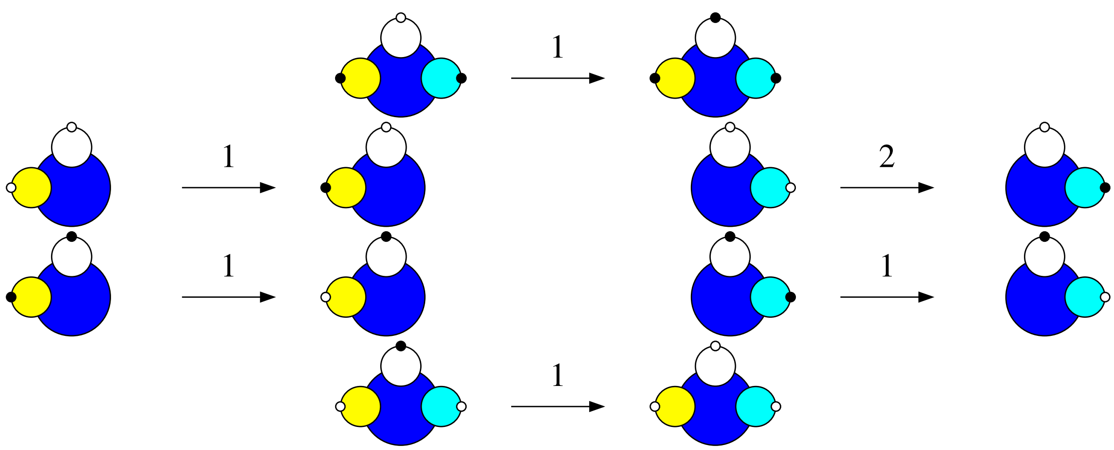


Figure 1: First case study.

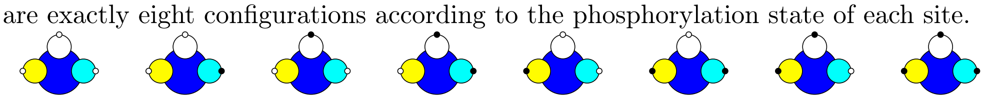
It is worth noticing that when the site on the top is phosphorylated, the site on the left and the site on the right exhibit the same behavior in the sense that they share the same phosphorylation rate. We say that these sites are symmetric when the site on the top is phosphorylated. We call this a contextual symmetry.

Our goal is to investigate the consequence of contextual symmetries on the behavior of models.

Question 1 (Configuration space) *Enumerate all the configurations the protein can take ?*

We denote by $\mathcal{V}$ the set of the configurations of the protein.
Answer:

There are exactly eight configurations according to the phosphorylation state of each site.



Question 2 (Differential semantics) *Write the system of ordinary differential equations that describes the evolution of the concentration of each potential configuration of the protein.*

This system takes the form:

$$\frac{d\vec{X}(t)}{dt} = \mathbb{F}(\vec{X}(t))$$

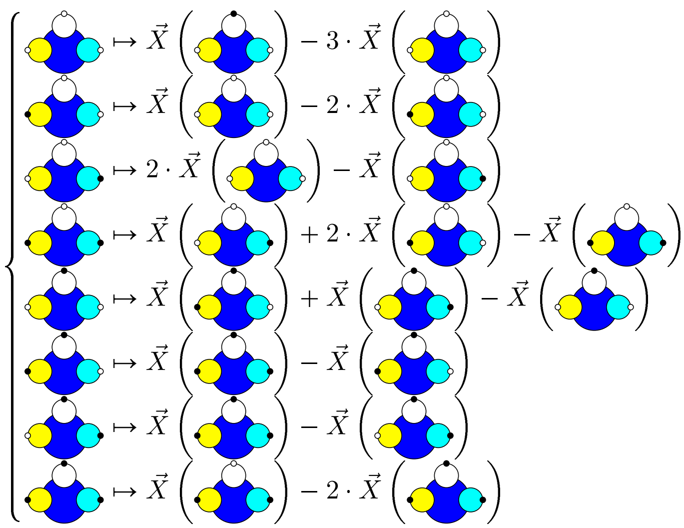
where $\vec{X}(t)$ is the function mapping each configuration $x \in \mathcal{V}$ of the protein to its concentration at time t and $\mathbb{F}$ is a function from $\mathbb{R}^{\mathcal{V}}$ into itself.

Answer:

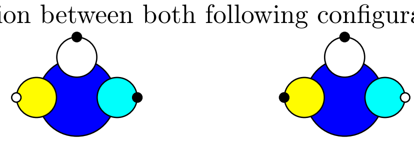
By applying mass action principle, we obtain the following system of differential equations:

$$\frac{\mathrm{d}\vec{X}(t)}{\mathrm{d}t} = \mathbb{F}(\vec{X}(t))$$

where: $\mathbb{F}(\vec{X}) =$



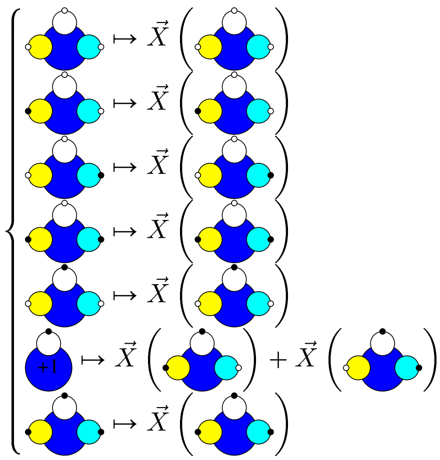
We propose to ignore the distinction between both following configurations of the protein:



which comes down to replace the variables standing for the concentration of these configurations with a single one standing for the sum of their values.

Question 3 (Abstraction) *Introduce a set of abstract observables $\mathcal{V}^{\sharp}$ and a linear function ϕ from the set $\mathbb{R}^{\mathcal{V}}$ into the set $\mathbb{R}^{\mathcal{V}^{\sharp}}$ to model this change of variables.*

Answer:

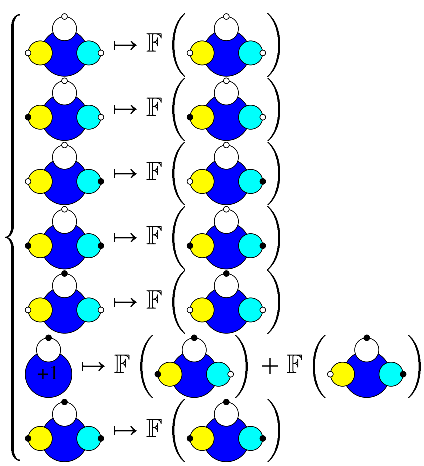
$\phi(\vec{X}) =$ 

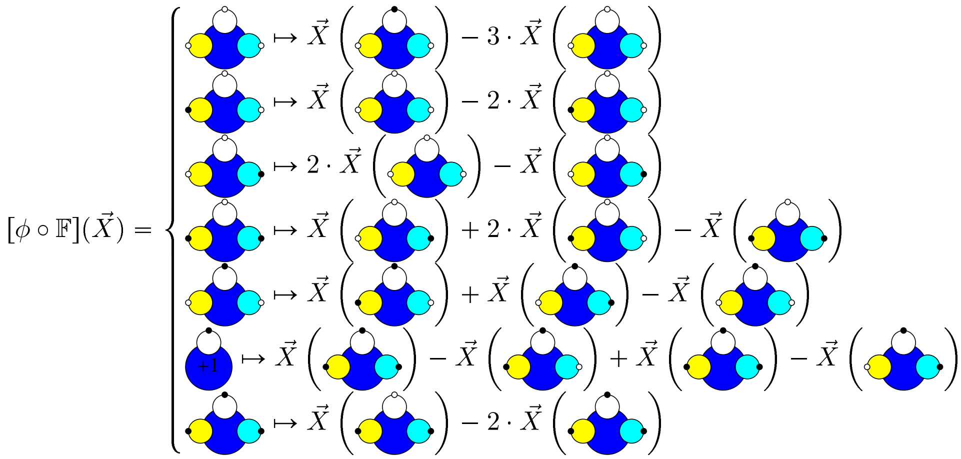
We say that ϕ induces a forward bisimulation is there exists a function $\mathbb{F}^\sharp$ from the set $\mathbb{R}^{\mathcal{V}^\sharp}$ into itself such that the property $\phi \circ \mathbb{F} = \mathbb{F}^\sharp \circ \phi$ is satisfied.

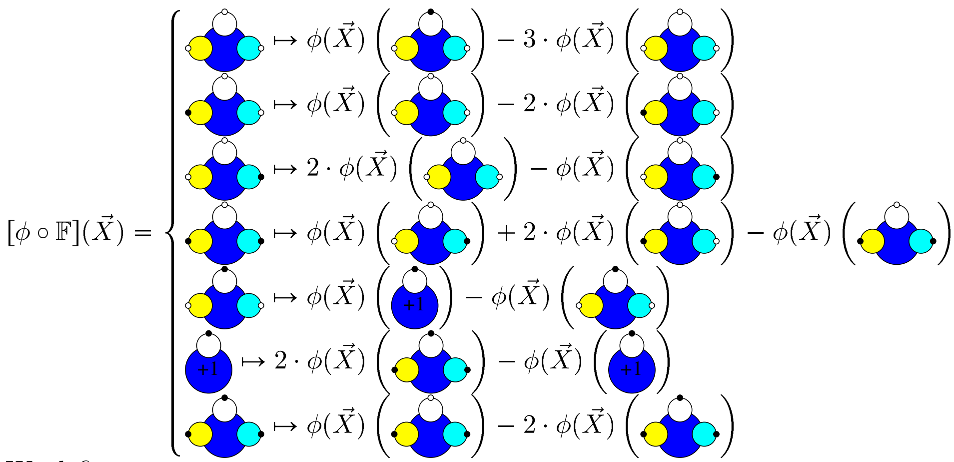
Question 4 (Forward bisimulation) *Does the function ϕ induce a forward bisimulation ?*
If so, express the corresponding function $\mathbb{F}^\sharp$.

Answer:

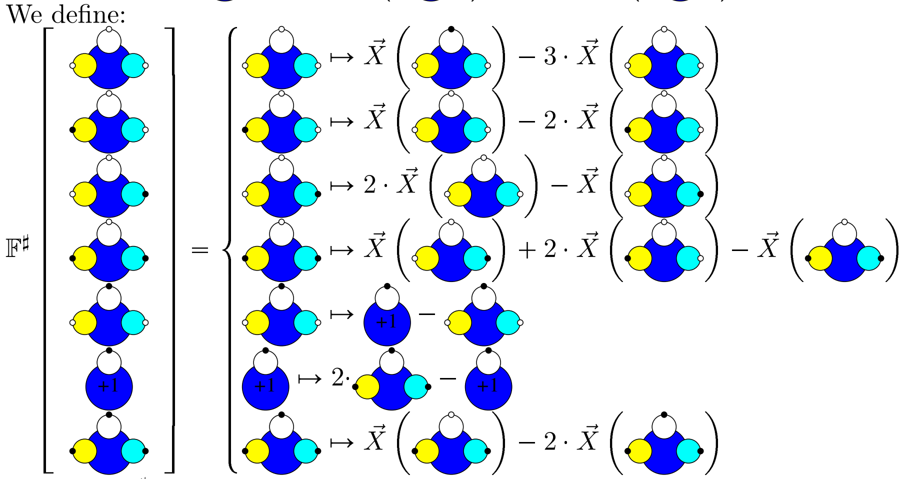
We have:

$[\phi \circ \mathbb{F}](\vec{X}) =$ 





We define:



We have: $\mathbb{F}^\sharp \circ \phi = \phi \circ \mathbb{F}$.

This proves that ϕ induces a forward bisimulation.

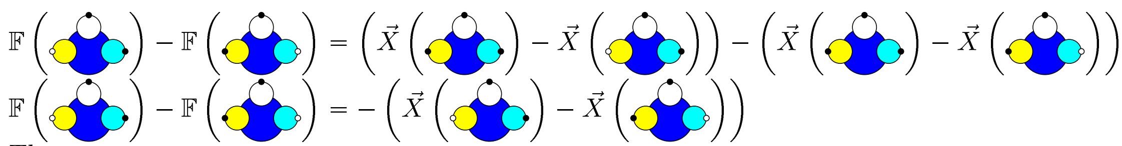
We now investigate about the potential relationships among the concentration of both following configurations:

We say that a pair of configurations induces a backward bisimulation if and only, the concentrations of these configurations remain equal for every solution of the differential semantics that starts in a state when the concentration of these configurations are equal.

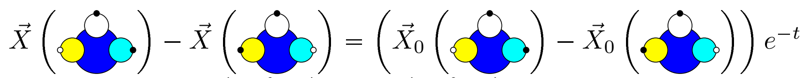
Question 5 (Backward bisimulation) *Does this pair of configurations induce a backward bisimulation?*

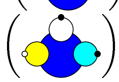
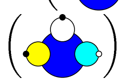
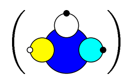
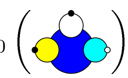
Answer:

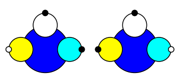
We have:



Thus:



It follows that $\vec{X}$  $= \vec{X}$  forever, provided that $\vec{X}_0$  $= \vec{X}_0$ .

Thus, the pair  induces a backward bisimulation.

2 A second variant of the model

We propose to relax the constraints on the phosphorylation of the site on the top. We obtain the second variant of the model which is described in Fig. 2.

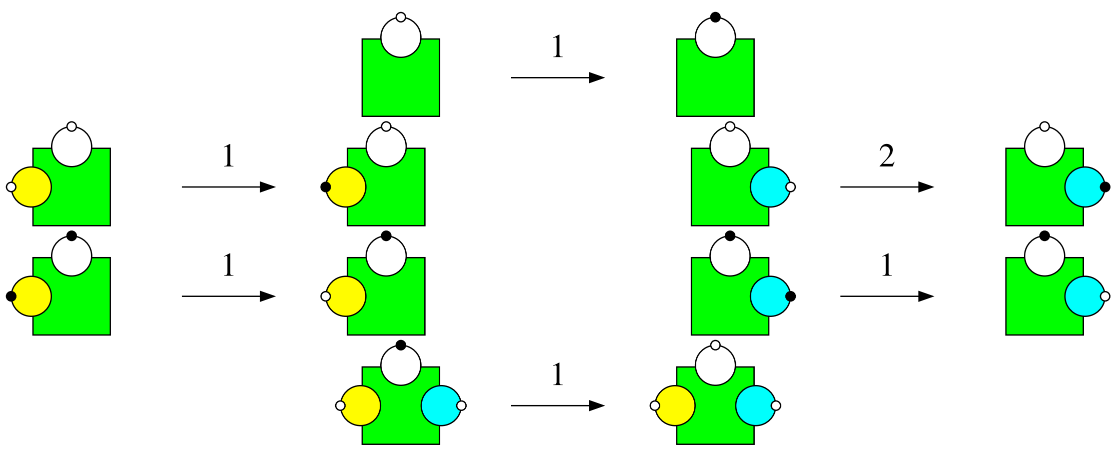
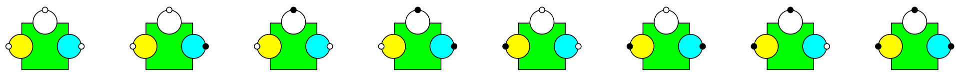


Figure 2: Second variant of the model.

Question 6 *Repeat questions 2, 4, and 5 to the variant of the model that is described in Fig. 2 with the two following configurations of interest:*

Answer:

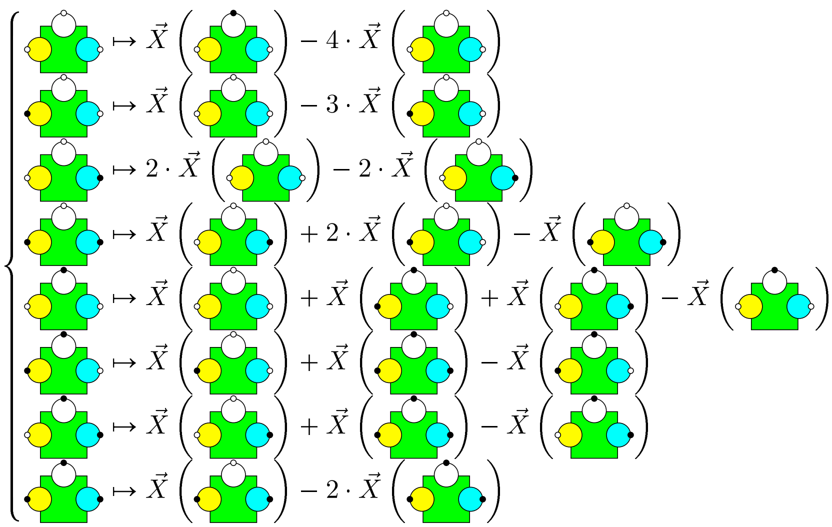
1. There are exactly eight configurations according to the phosphorylation state of each site.



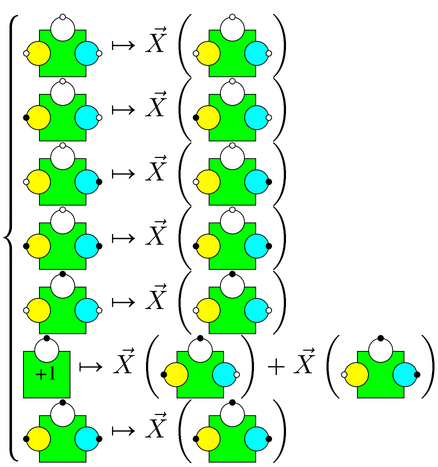
2. By applying mass action principle, we obtain the following system of differential equations:

$$\frac{\mathrm{d}\vec{X}(t)}{\mathrm{d}t} = \mathbb{F}(\vec{X}(t))$$

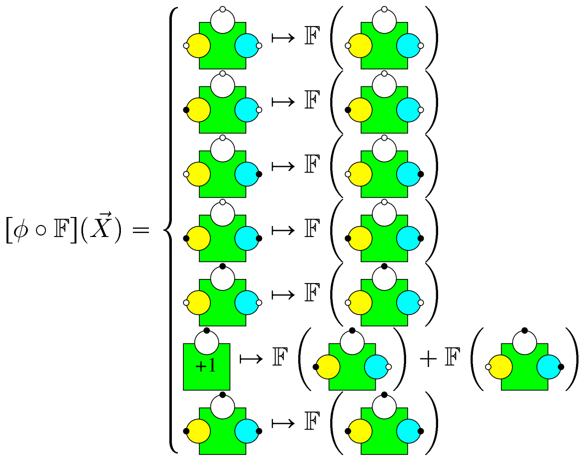
where: $\mathbb{F}(\vec{X}) =$

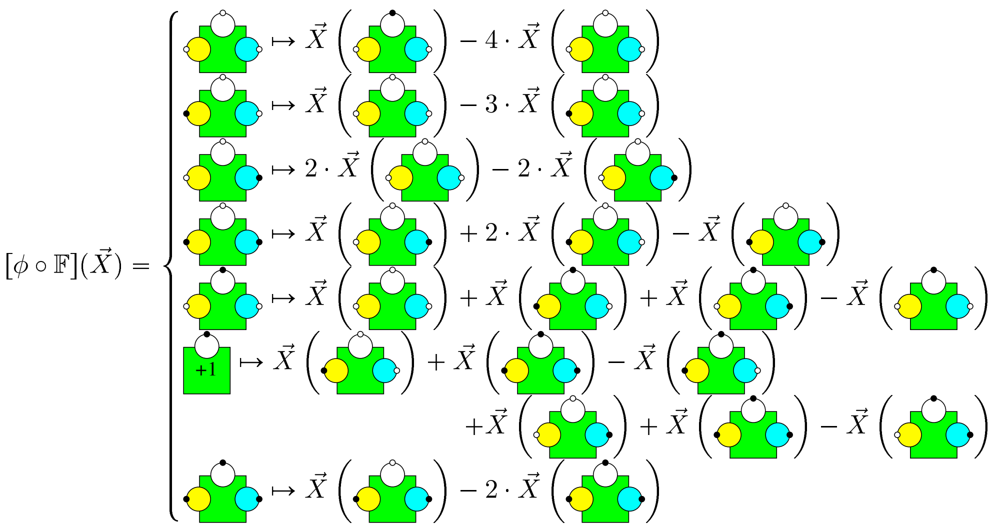


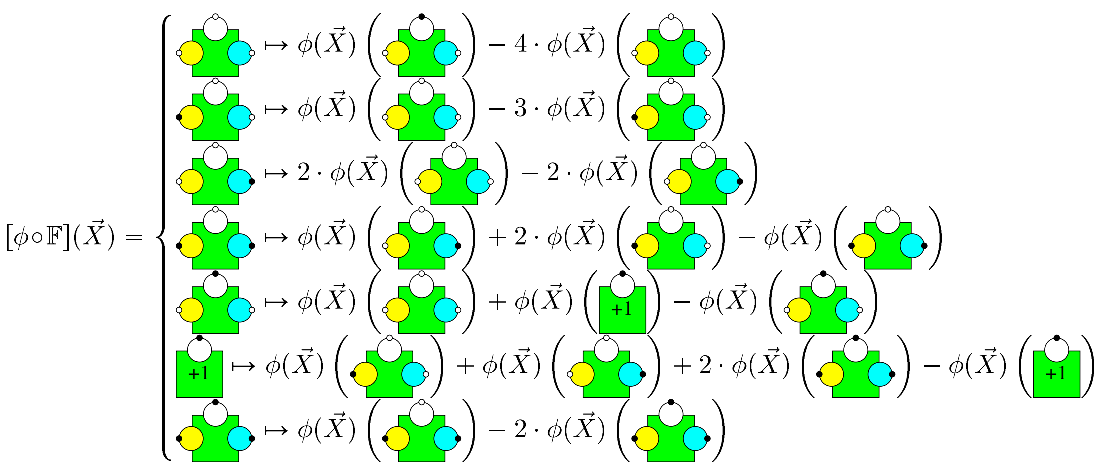
3. $\phi(\vec{X}) =$



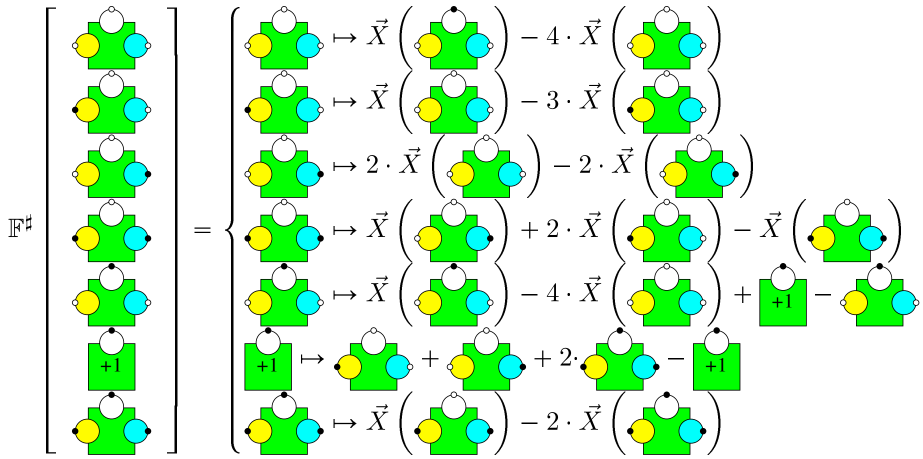
4. We have:


$[\phi \circ \mathbb{F}](\vec{X}) =$


$[\phi \circ \mathbb{F}](\vec{X}) =$

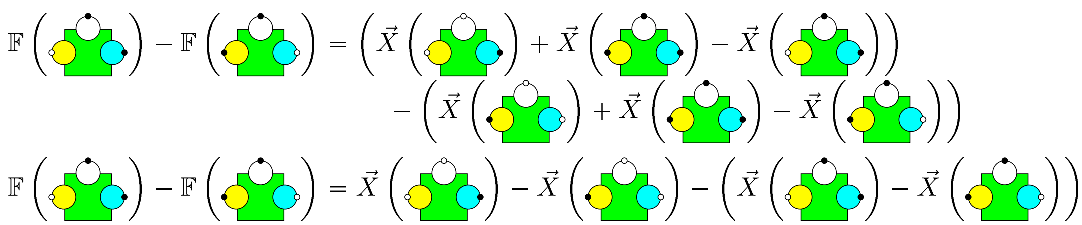

$[\phi \circ \mathbb{F}](\vec{X}) =$

We define:

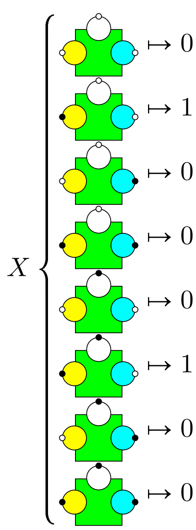


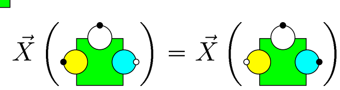
We have: $\mathbb{F}^\sharp \circ \phi = \phi \circ \mathbb{F}$.
This proves that ϕ induces a forward bisimulation.

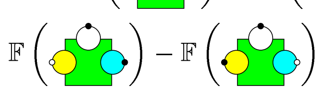
5. We have:

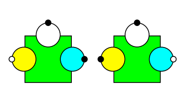


We consider the vector $\vec{X}$ that is defined as follows:



We have: 

But  $\neq 0$.

Thus, the pair of configurations  does not induce a backward bisimulation.

3 A third variant of the model

Now, we propose instead to relax the constraints on the dephosphorylation of the site on the top. This third variant is given in Fig. 3.

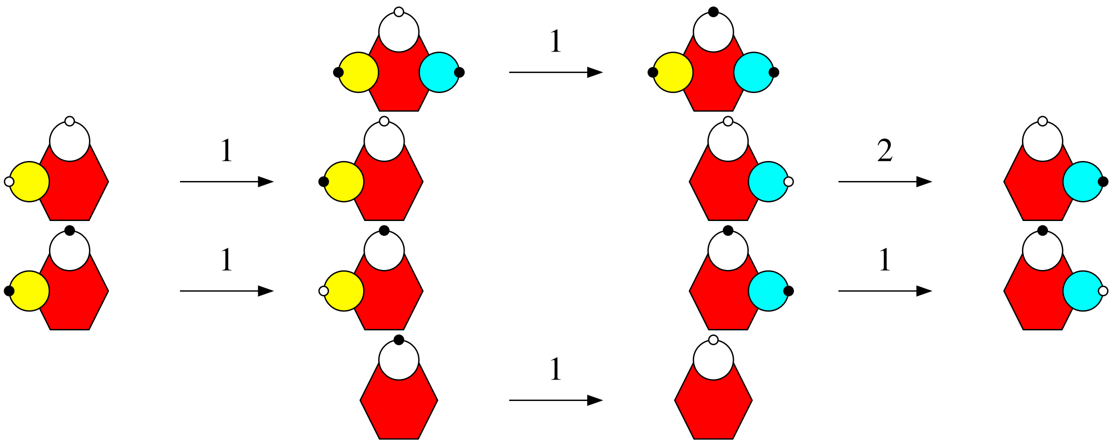
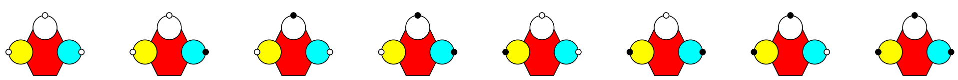


Figure 3: Third case study.

Question 7 *Repeat questions 2, 4, and 5 to the variant of the model that is described in Fig. 3 with the two following configurations of interest:*

Answer:

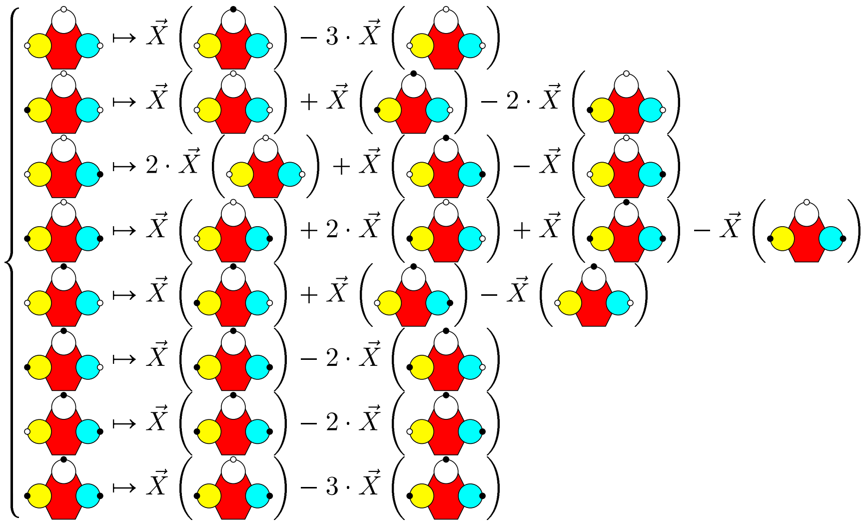
1. There are exactly eight configurations according to the phosphorylation state of each site.



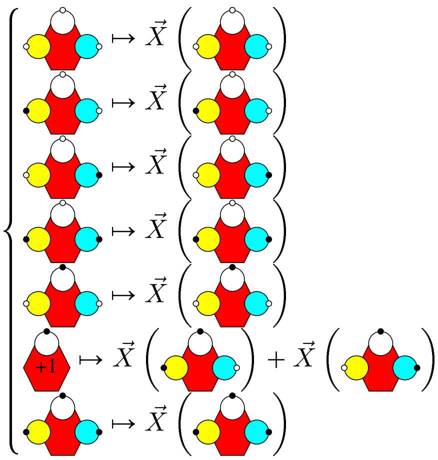
2. By applying mass action principle, we obtain the following system of differential equations:

$$\frac{\mathrm{d}\vec{X}(t)}{\mathrm{d}t} = \mathbb{F}(\vec{X}(t))$$

where: $\mathbb{F}(\vec{X}) =$

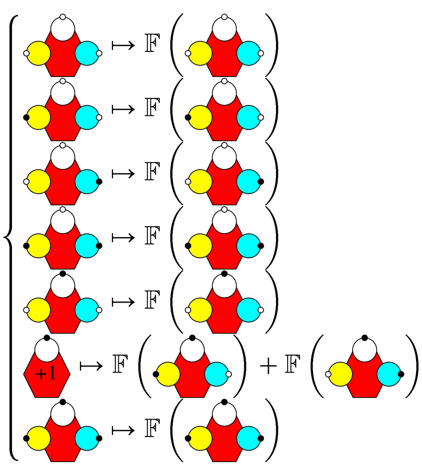


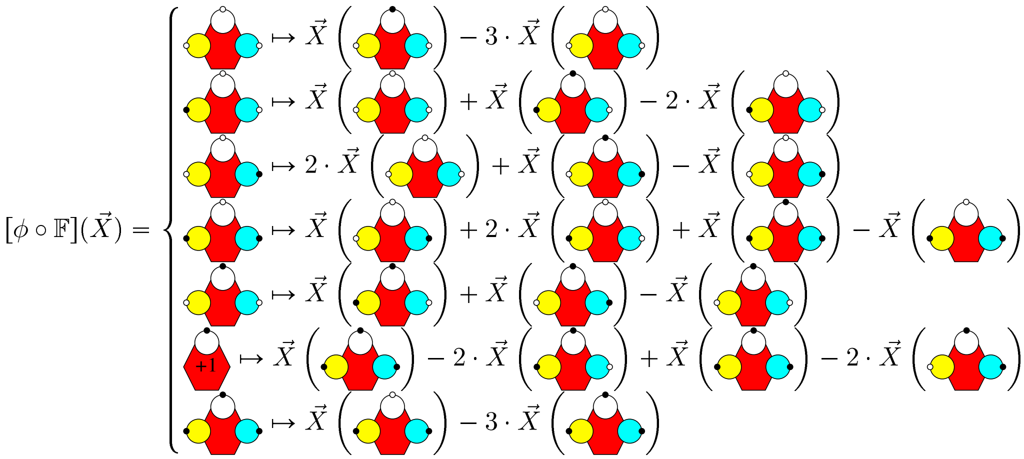
3. $\phi(\vec{X}) =$



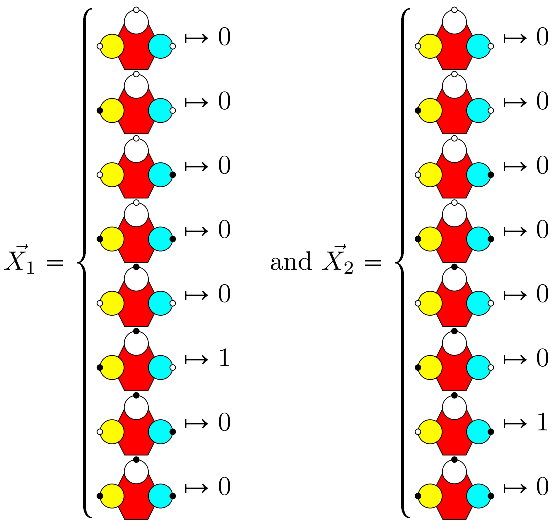
4. We have:

$[\phi \circ \mathbb{F}](\vec{X}) =$

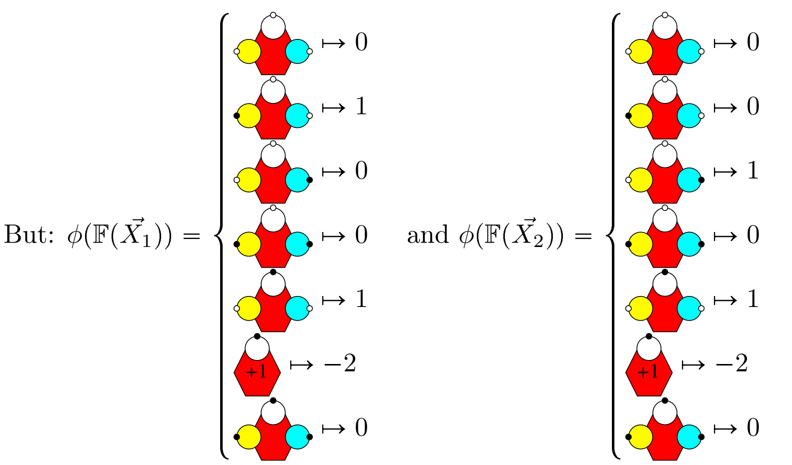




We take the following two vectors $\vec{X}_1$ and $\vec{X}_2$.



We have: $\phi(\vec{X}_1) = \phi(\vec{X}_2)$.

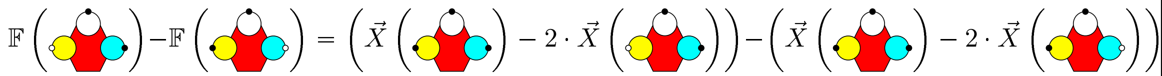


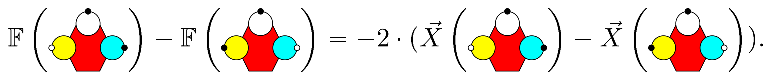
So $\phi(\mathbb{F}(\vec{X}_1)) \neq \phi(\mathbb{F}(\vec{X}_2))$.

So there is no function $\mathbb{F}^\sharp$ such that $[\phi \circ \mathbb{F}] = [\mathbb{F}^\sharp \circ \phi]$.

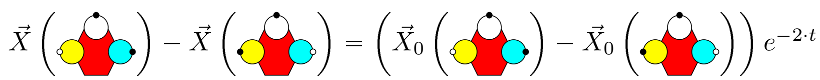
This proves that ϕ does not induce a forward bisimulation.

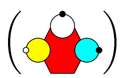
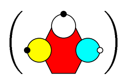
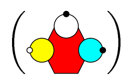
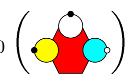
5. We have:

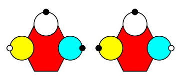




Thus:



It follows that $\vec{X}$  $= \vec{X}$  forever, provided that $\vec{X}_0$  $= \vec{X}_0$ .

Thus, the pair  induces a backward bisimulation.

4 Wrapping-up

Question 8 *Propose some sufficient conditions over the rules of a model to ensure that some contextual symmetries induce a forward bisimulation?*

Answer:

To ensure that some contextual symmetries induce a forward bisimulation, we must check that starting from two symmetric configurations, for any interaction that can be applied to the first one, there is an interaction (not necessarily the same one) that can be applied to the second one, and that leads to a symmetric configuration with the same kinetics.

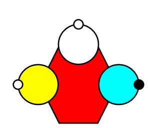
1. In the two first variants of the model.

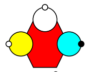
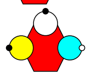
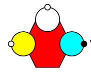
   The only interaction that apply to both symmetric configurations is the phosphorylation of the only remaining unphosphorylated site. This leads to the same configuration (with the three sites phosphorylated) at the same rate (1).

   This ensures that the pair of configurations induces a forward bisimulation.

2. In the third variant of the model.

   Starting for two symmetric configurations:

   we can dephosphorylate the top site at rate 1, to get the configuration: hfill 

But the configuration  has no other symmetric configuration and there is no way to transform the configuration  into .

Thus, our sufficient condition is not satisfied.

Question 9 *Propose some sufficient conditions over the rules of a model to ensure that some contextual symmetries induce a backward bisimulation?*

Answer:

To ensure that some contextual symmetries induce a backward bisimulation, we must check that starting from two symmetric configurations, for any interaction that can be applied to get the first one, there is an interaction (not necessarily the same one) that can be applied to get the second one, and that starts from a symmetric configuration with the same kinetics.

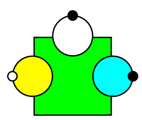
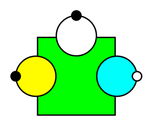
1. In the first and third variant of the model.

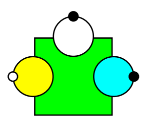
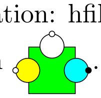
   The only interactions to get symmetric configurations are the phosphorylations of the left or right site from the configuration where only the top site is phosphorylated. They start from the same configuration and have the same rate.

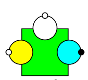
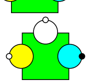
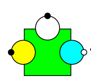
   This ensures that the pair of configurations induces a backward bisimulation.

2. In the second variant of the model.

   Considering the both following symmetric configurations:

   the configuration: hfill  can be obtained by phosphorylating the top site in the configuration .

   But the configuration  has no other symmetric configuration and there is no way to transform the configuration  into .

   Thus, our sufficient condition is not satisfied.