

MPRI 2.19 Biochemical Programming

Rule-based Modeling

An algebraic approach for inferring and using symmetries in rule-based models

Jérôme Feret

DI - ÉNS

Inria
informatics mathematics



PSL★
RESEARCH
UNIVERSITY

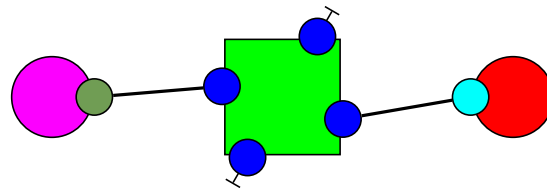
Wednesday, the 14th of January, 2026

Overview

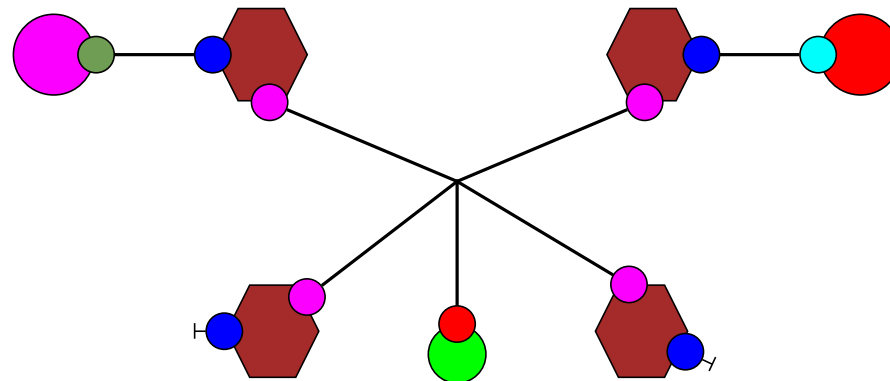
1. Context and motivations
2. Case study
3. Kappa semantics
4. Symmetries in site-graphs
5. Symmetric models
6. Conclusion

Symmetric sites

- in BNGL or MetaKappa (multiple-occurrences of sites):

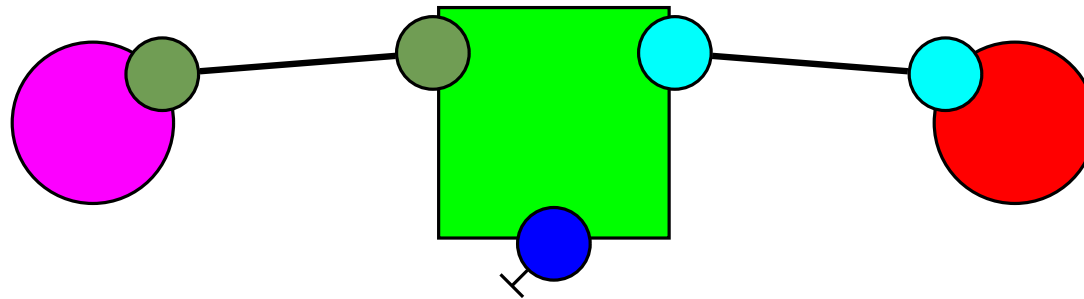


- in Formal Cellular Machinery or React(C) (hyper-edges):

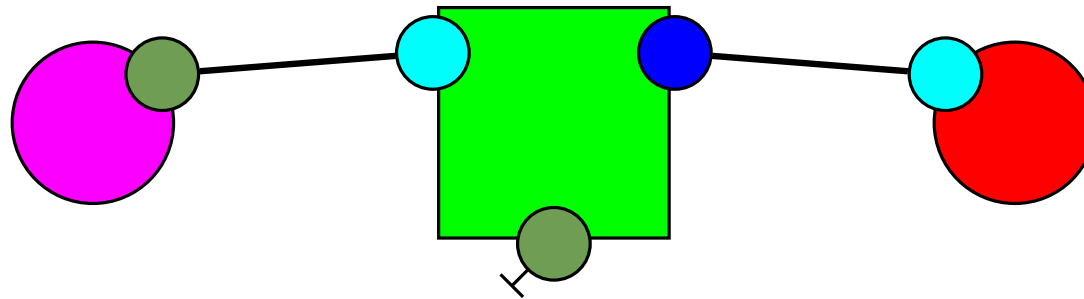


Blinov *et al.*, BioNetGen: software for rule-based modeling of signal transduction based on the interactions of molecular domains, Bioinformatics 2004
Danos *et al.*, Rule-Based Modelling and Model Perturbation, TCSB 2009
Damgaard *et al.*, Formal cellular machinery, Damgaard *et al.*, SASB 2011
John *et al.*, Biochemical Reaction Rules with Constraints, ESOP 2011

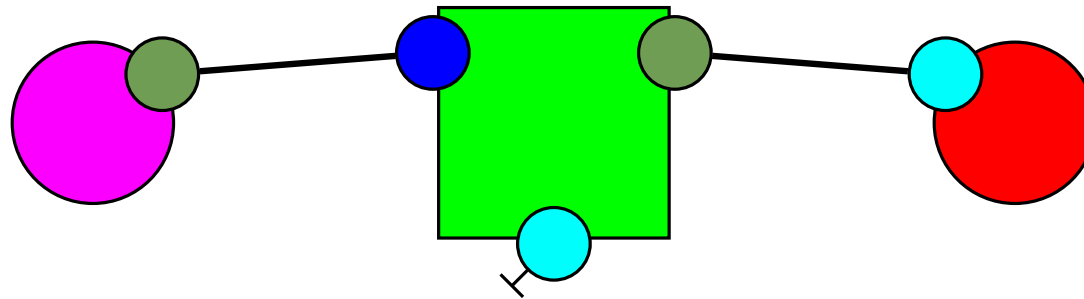
Other kinds of symmetries: Circular permutations



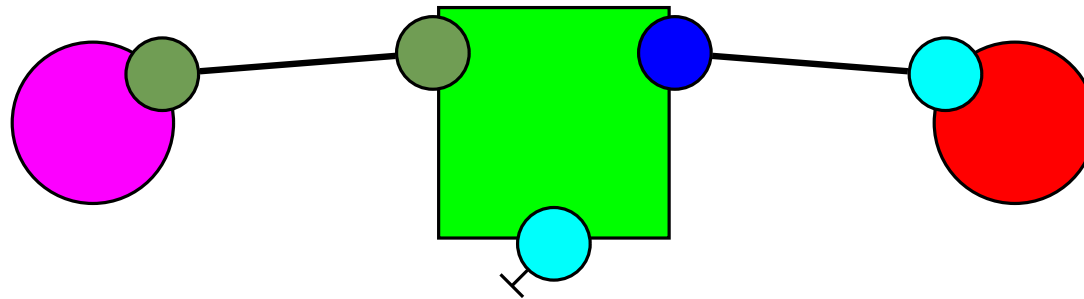
Other kinds of symmetries: Circular permutations



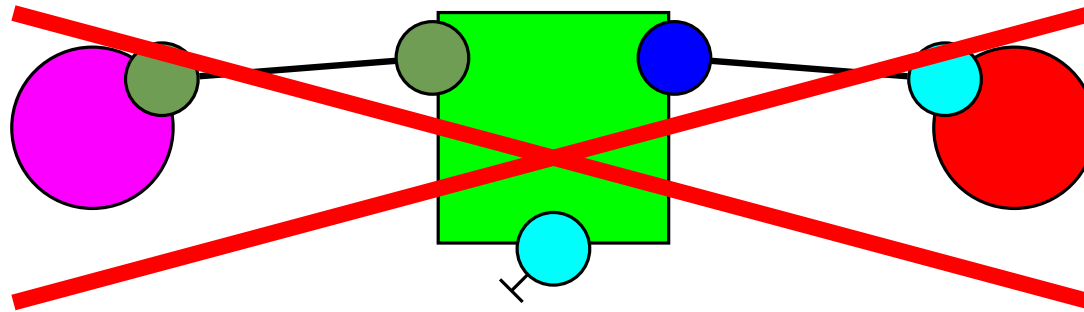
Other kinds of symmetries: Circular permutations



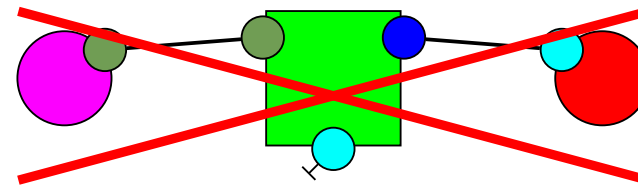
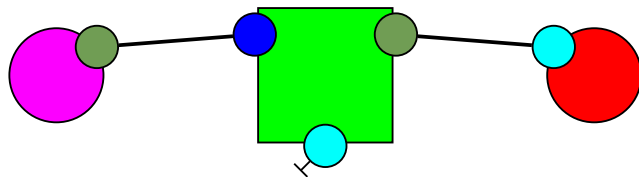
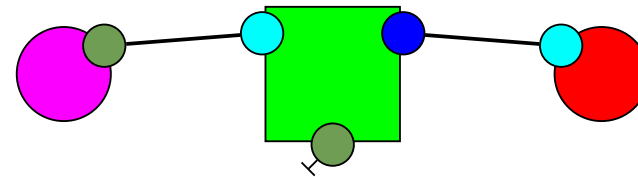
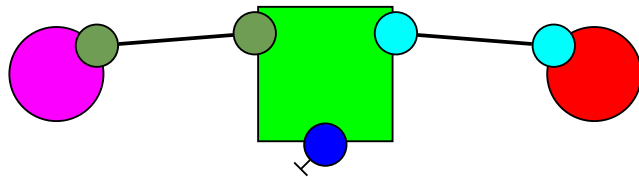
Other kinds of symmetries: Circular permutations



Other kinds of symmetries: Circular permutations

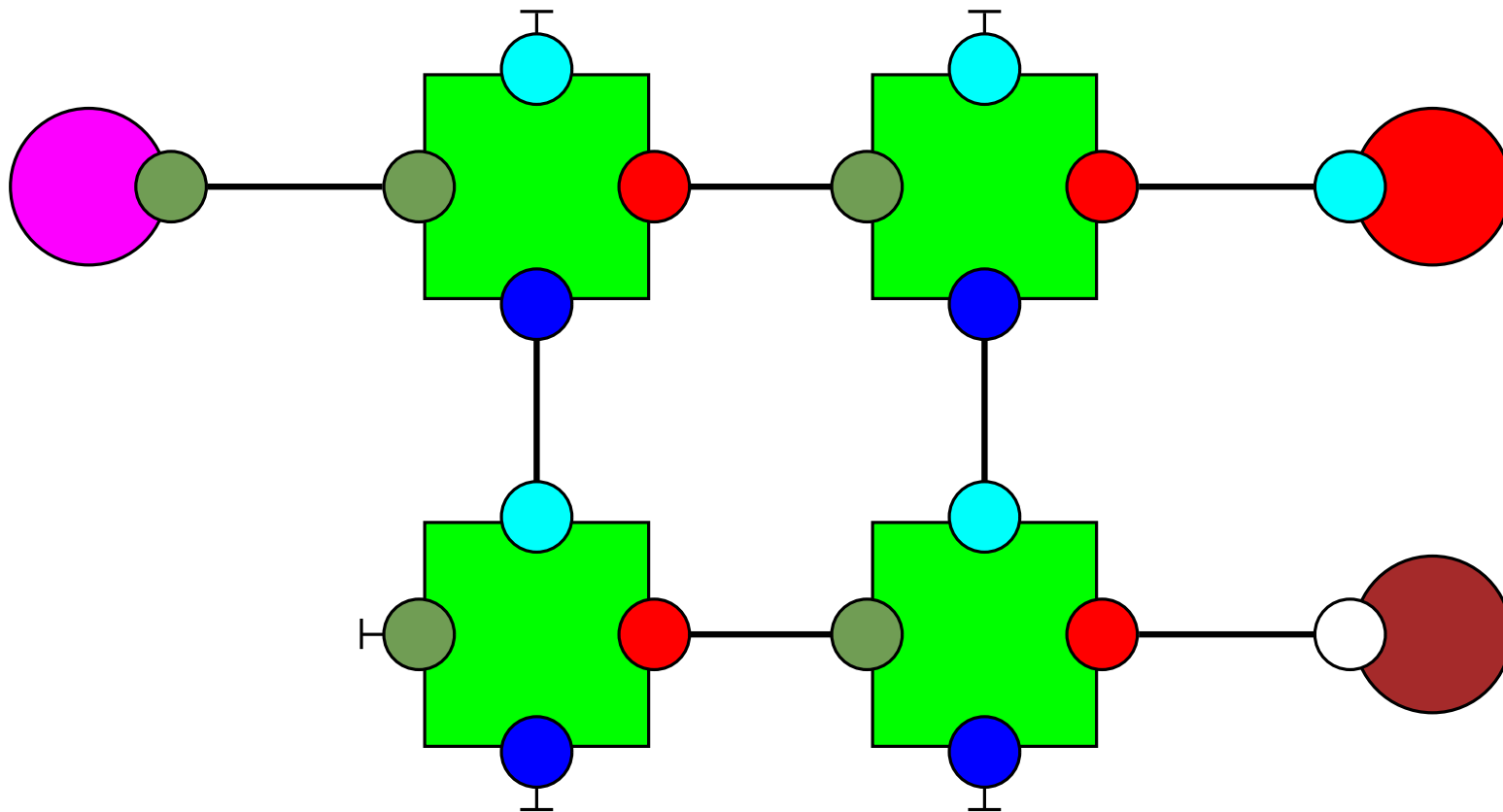


Other kinds of symmetries: Circular permutations



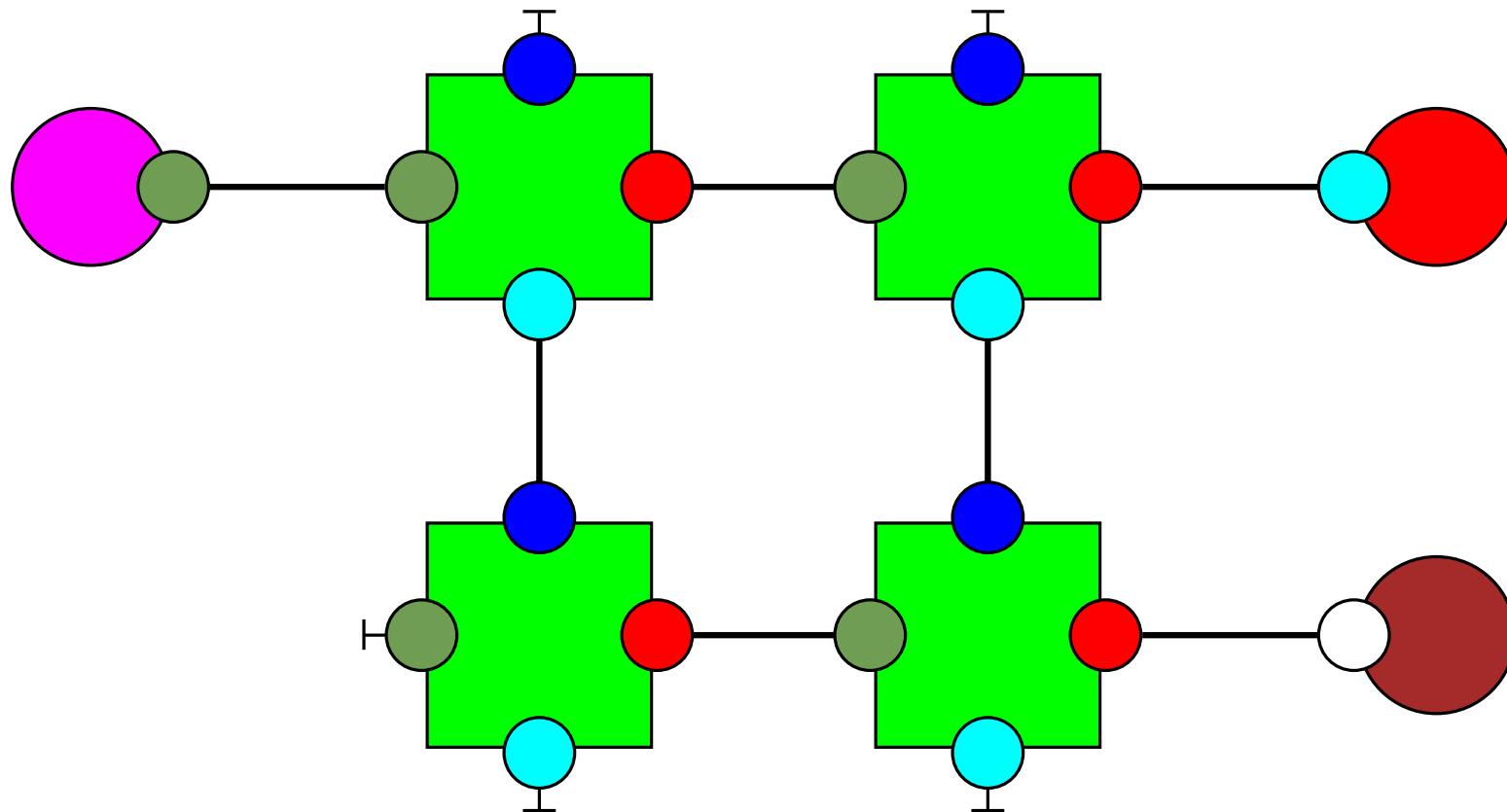
Other kinds of symmetries: Homogeneous symmetries

We can compute a horizontal reflection.



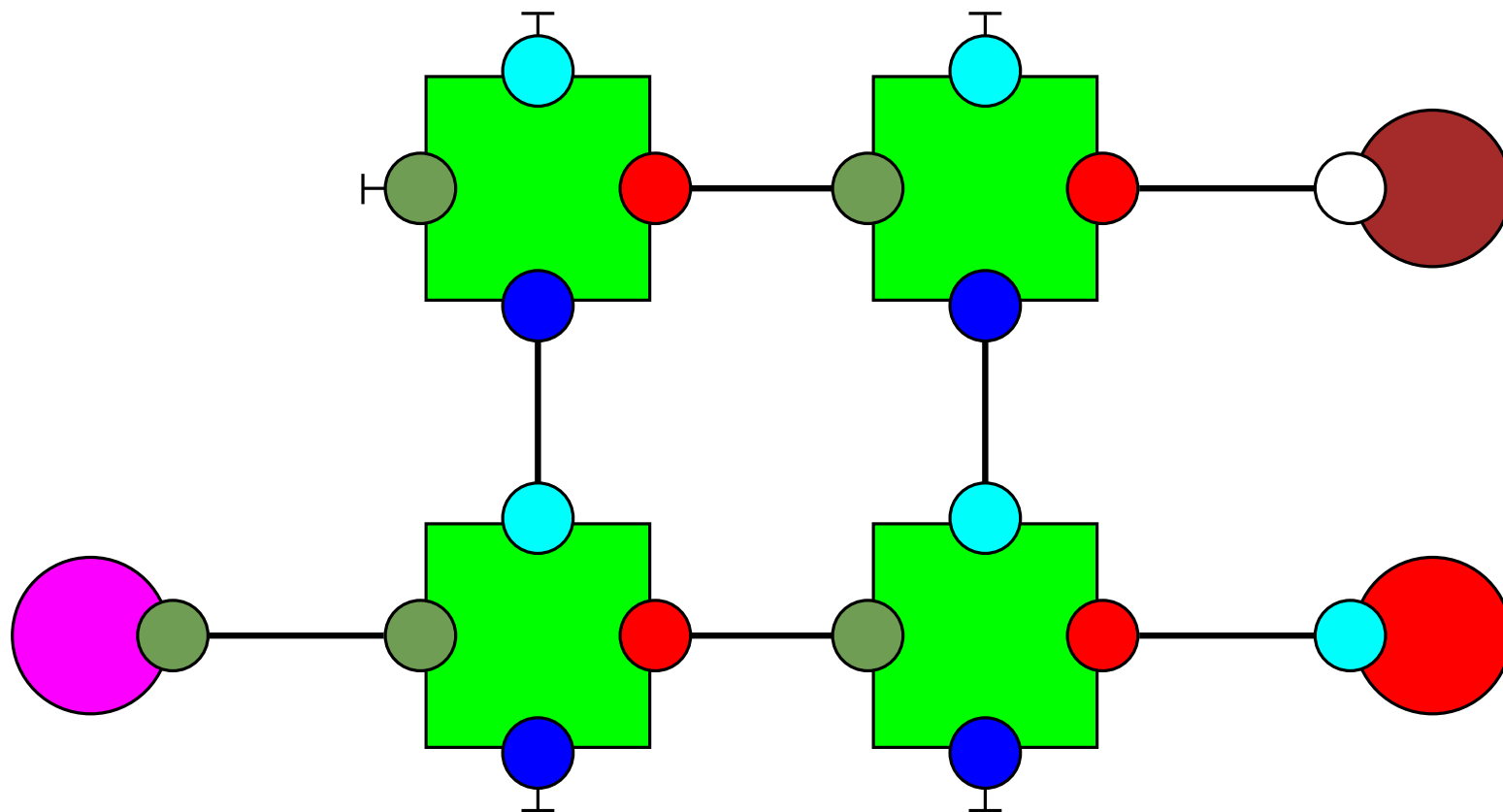
Other kinds of symmetries: Homogeneous symmetries

We can compute a horizontal reflection.



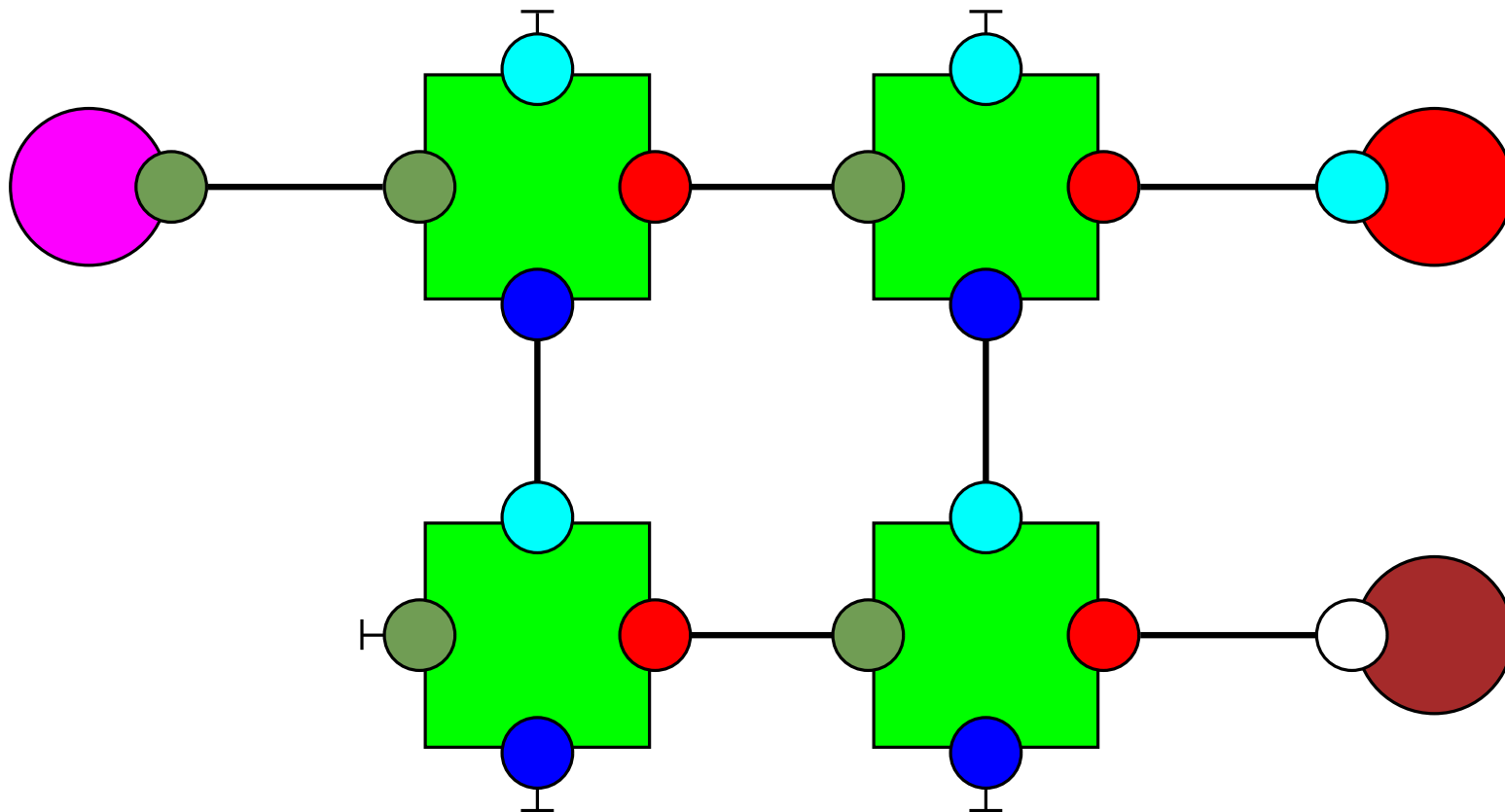
Other kinds of symmetries: Homogeneous symmetries

We can compute a horizontal reflection.



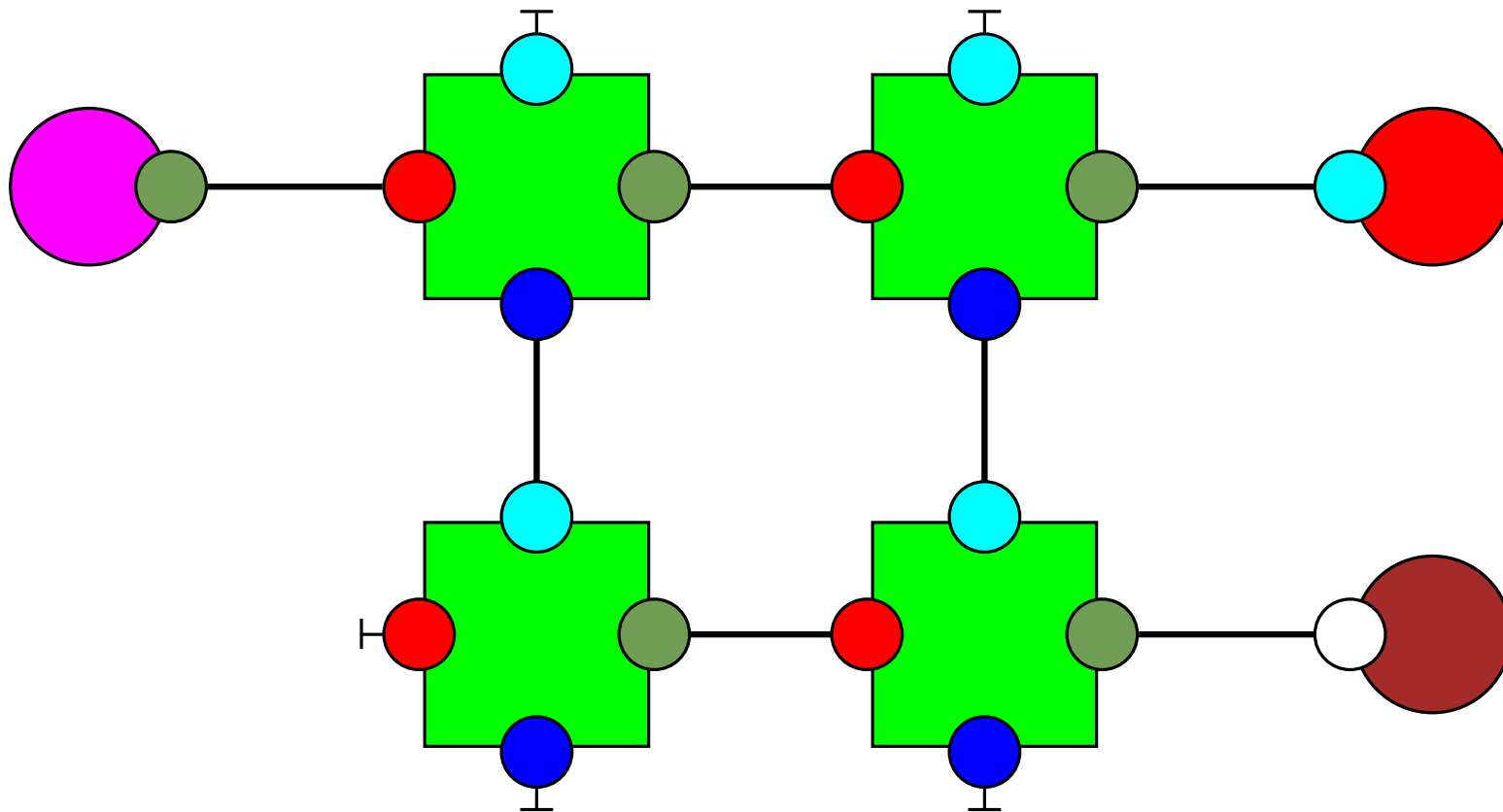
Other kinds of symmetries: Homogeneous symmetries

We can compute a vertical reflection.



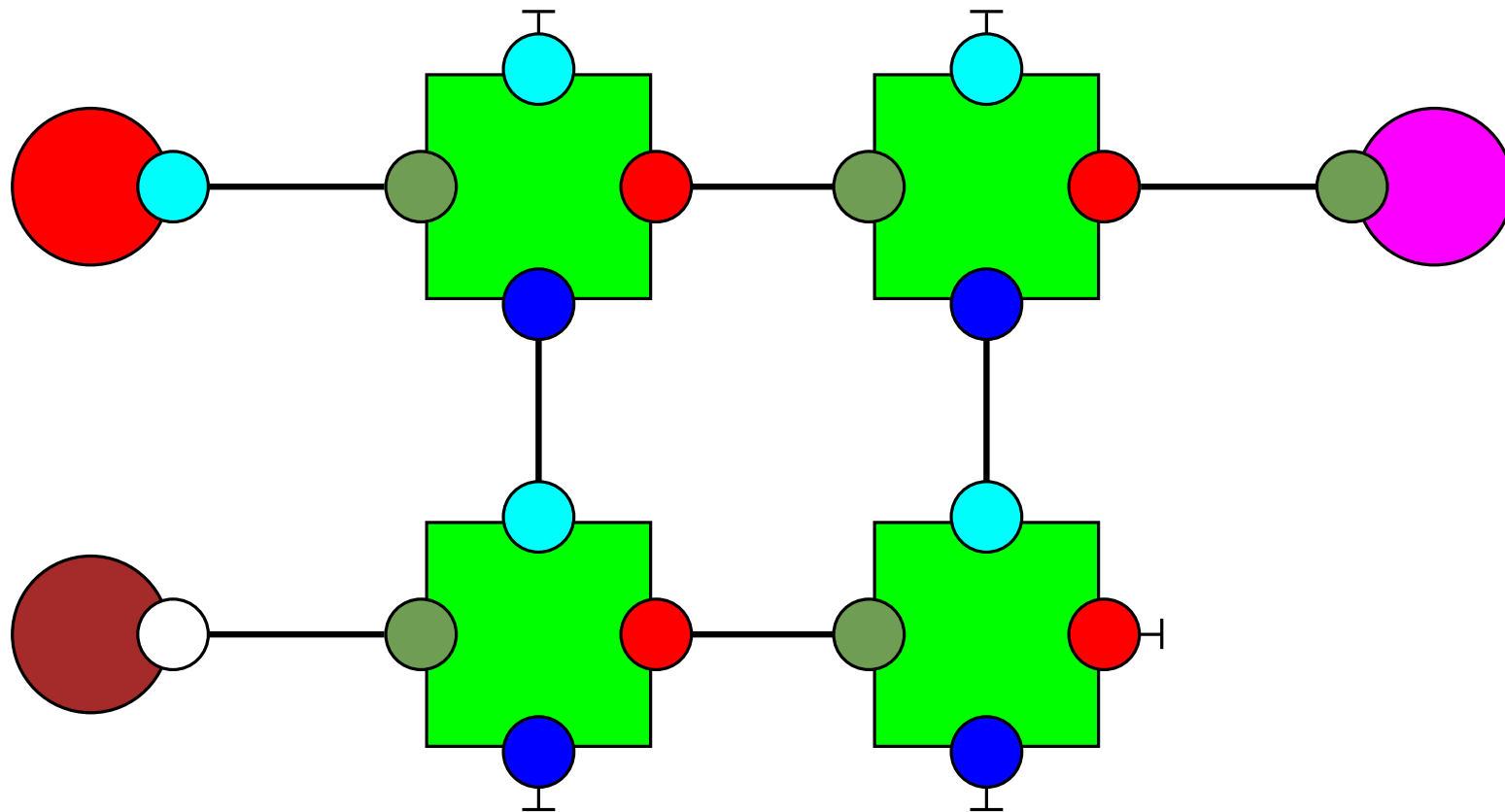
Other kinds of symmetries: Homogeneous symmetries

We can compute a vertical reflection.



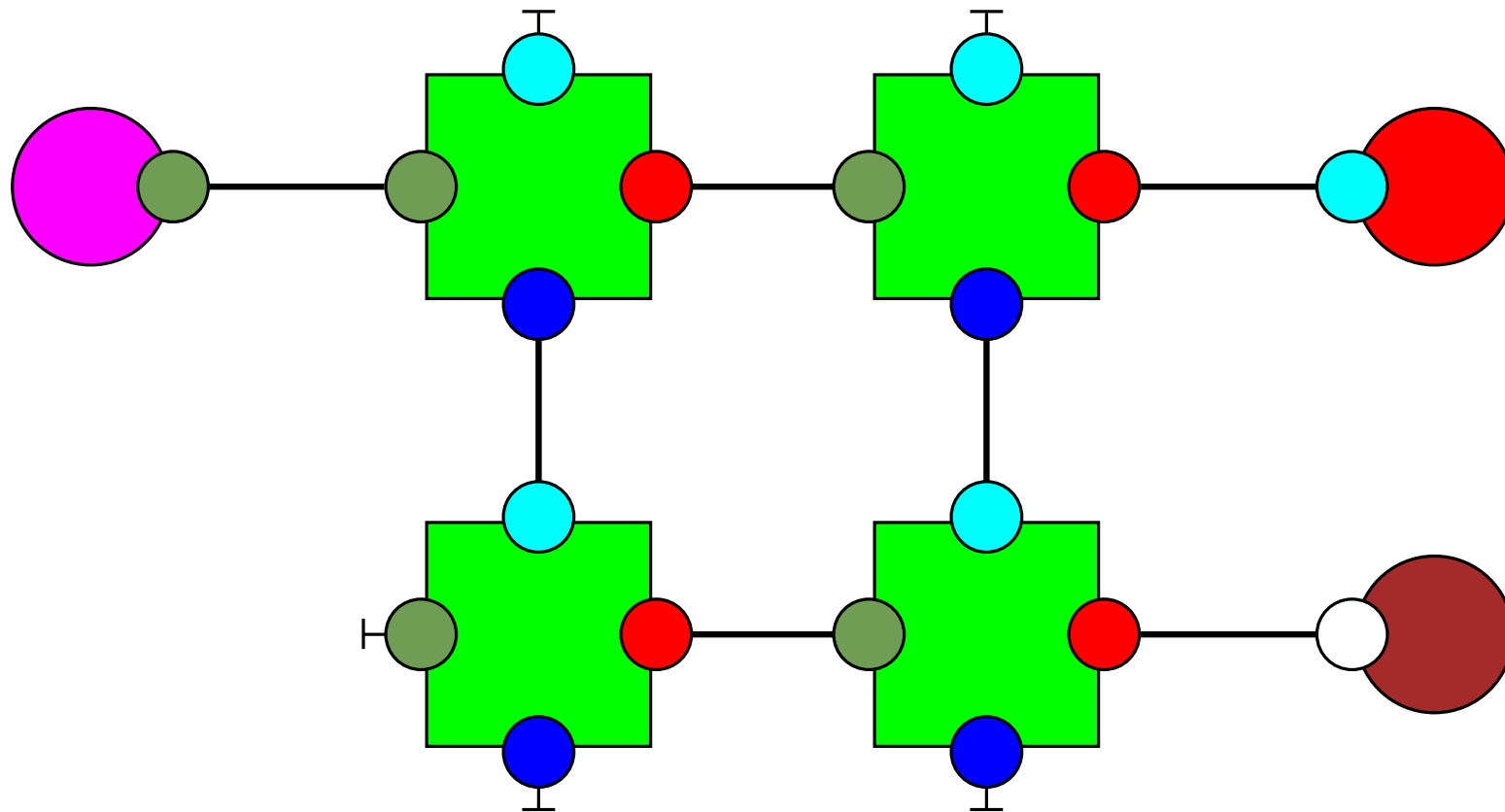
Other kinds of symmetries: Homogeneous symmetries

We can compute a vertical reflection.



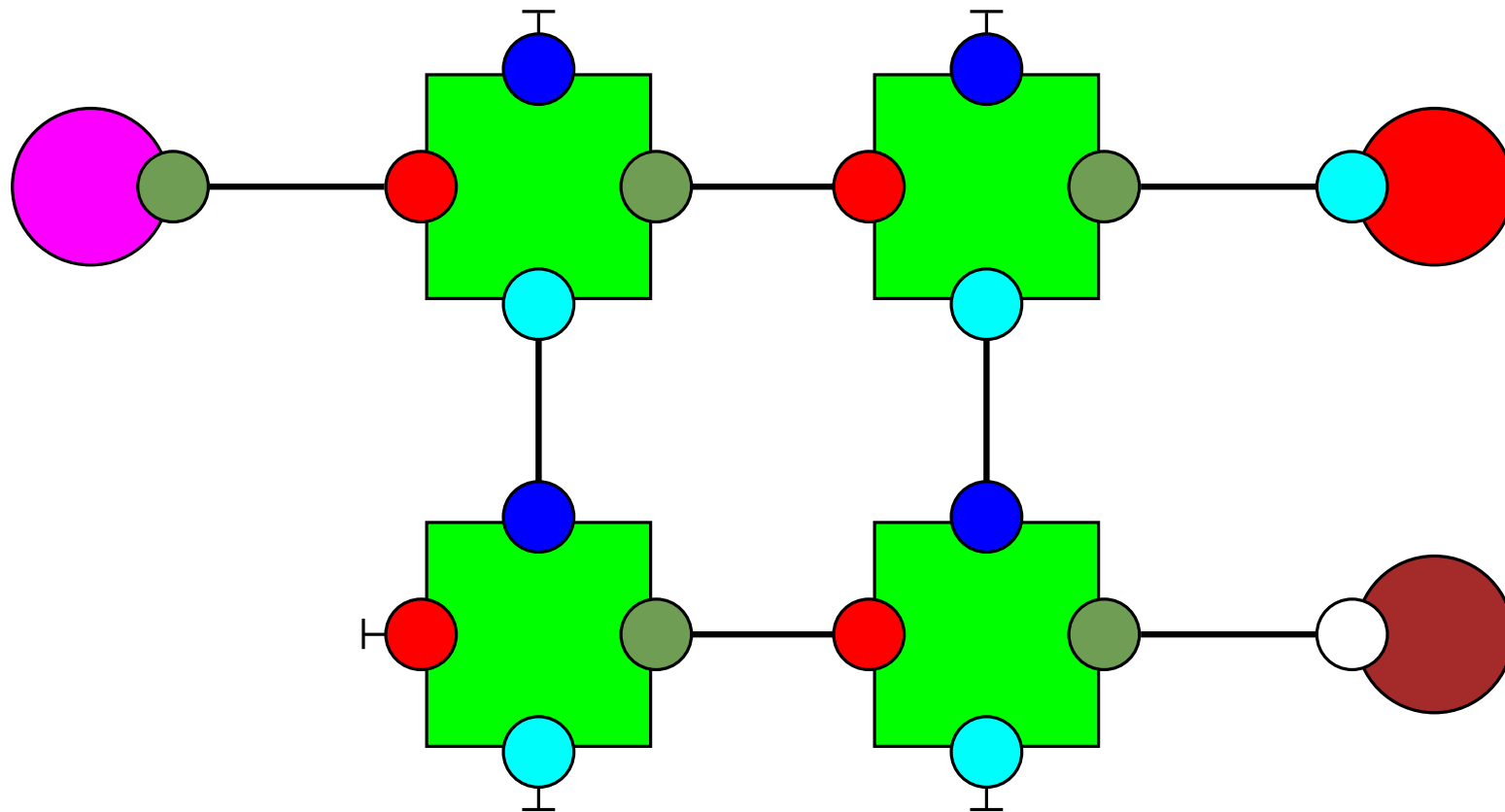
Other kinds of symmetries: Homogeneous symmetries

We can compute both reflections.



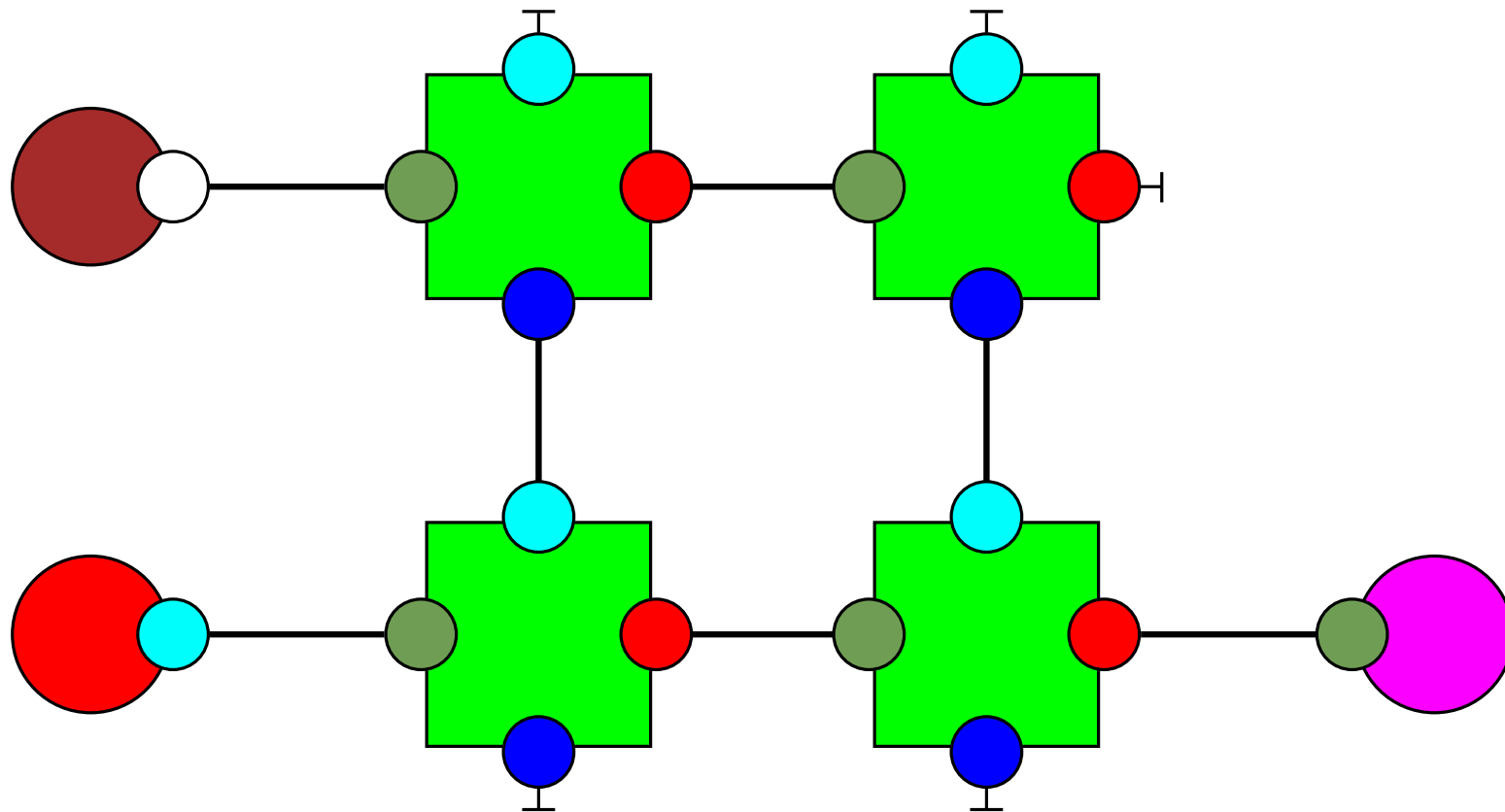
Other kinds of symmetries: Homogeneous symmetries

We can compute both reflections.



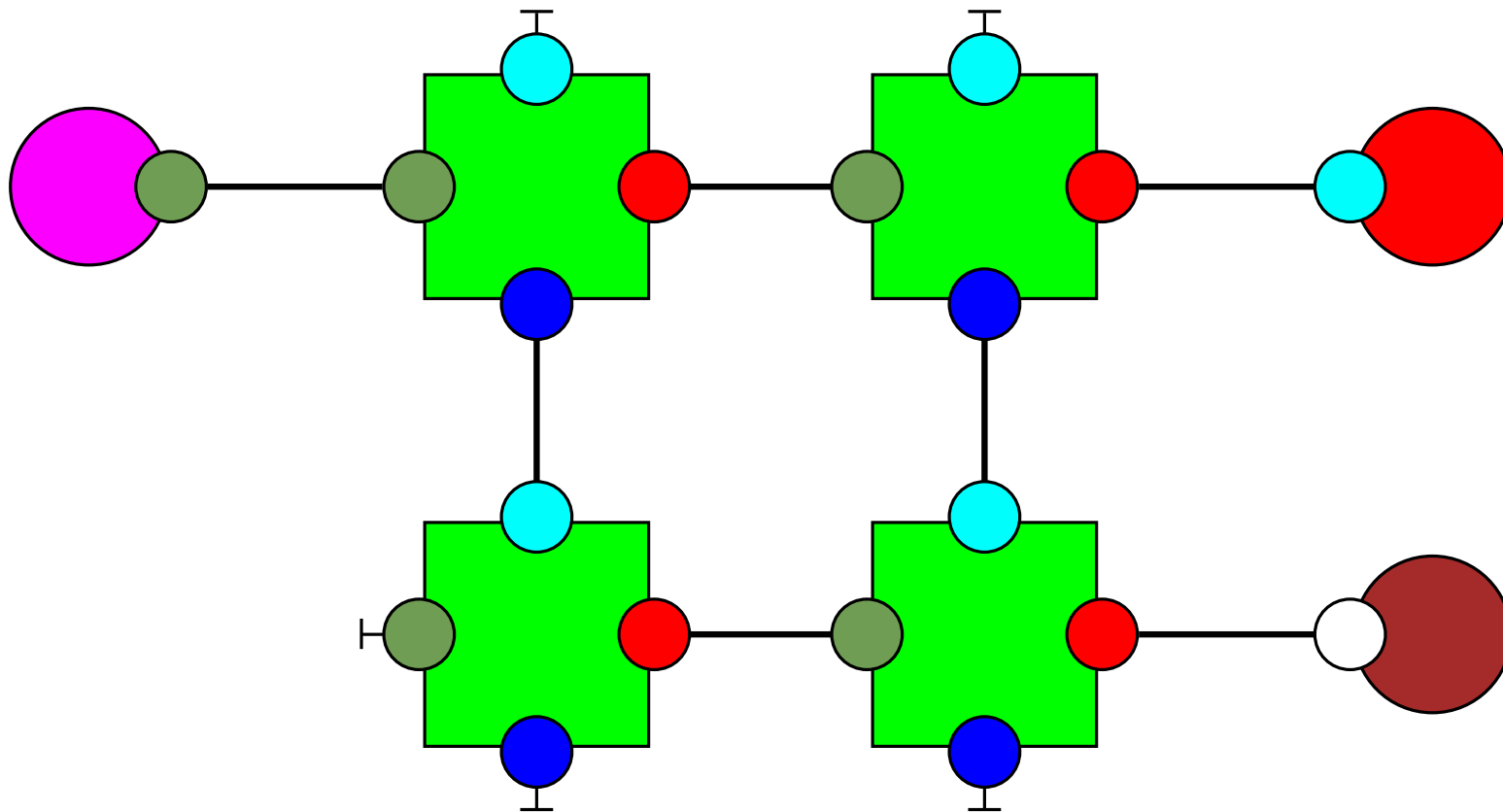
Other kinds of symmetries: Homogeneous symmetries

We can compute both reflections.



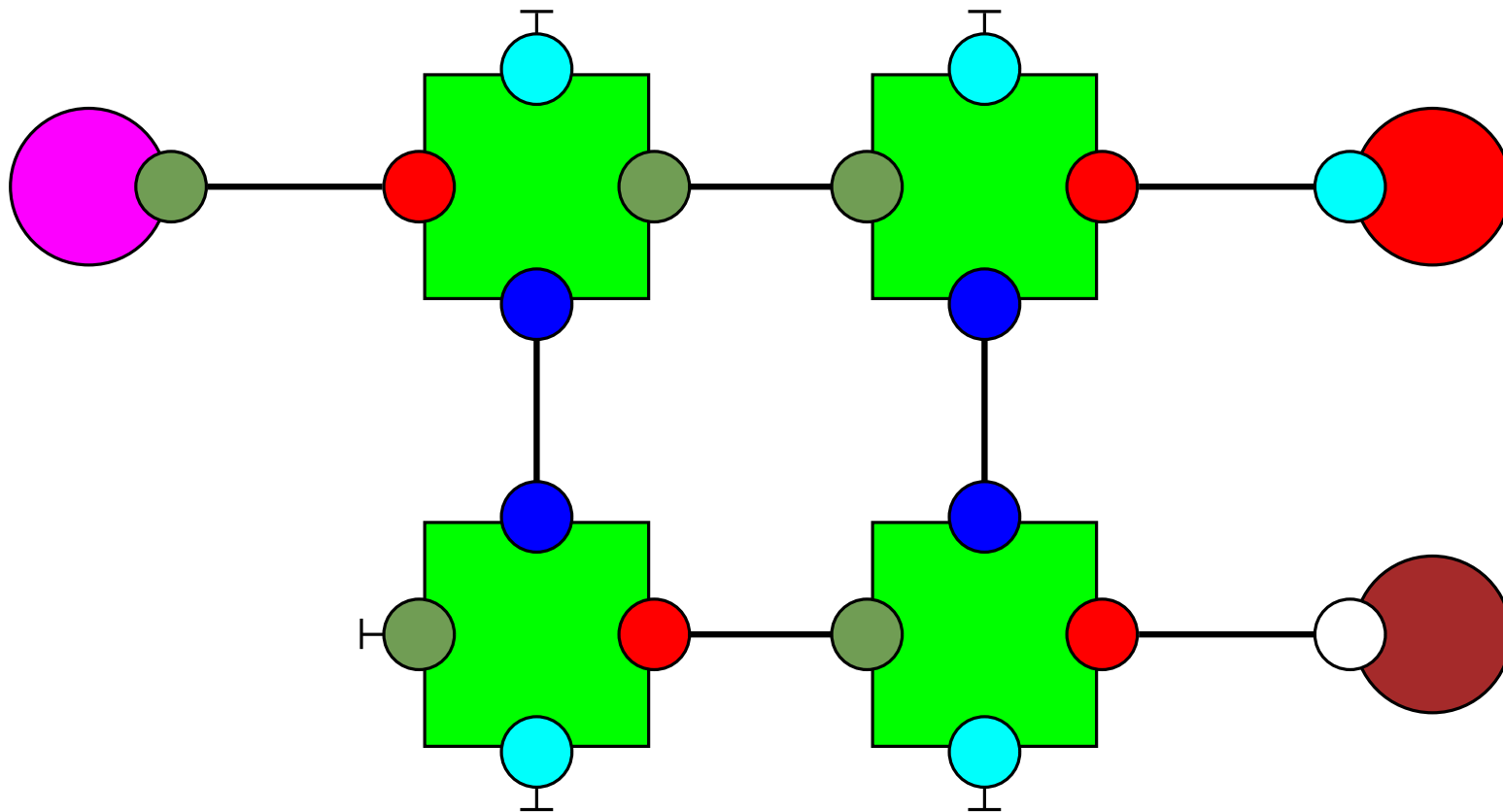
Other kinds of symmetries: Homogeneous symmetries

But we cannot apply different permutations!!!.



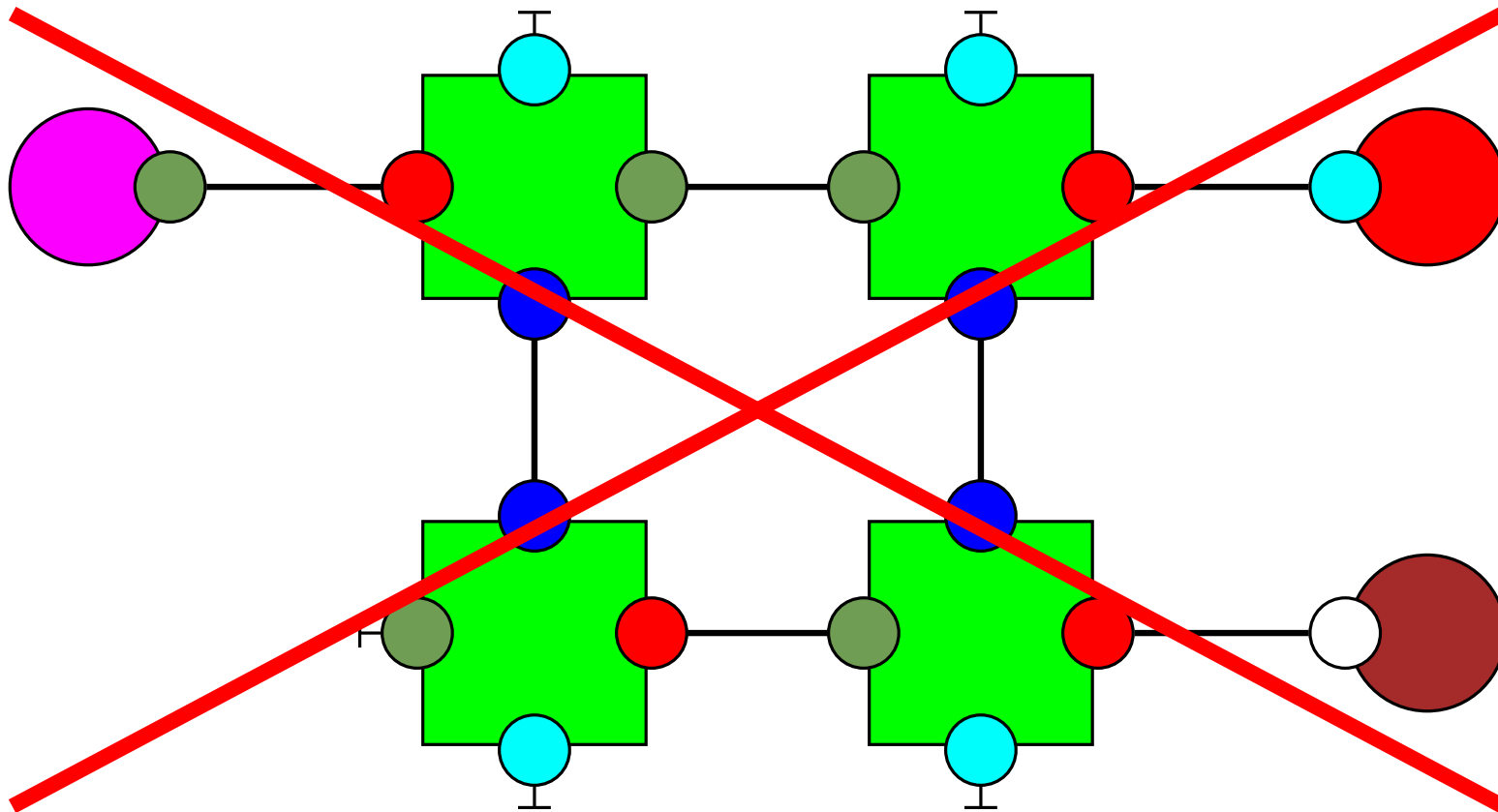
Other kinds of symmetries: Homogeneous symmetries

But we cannot apply different permutations!!!.

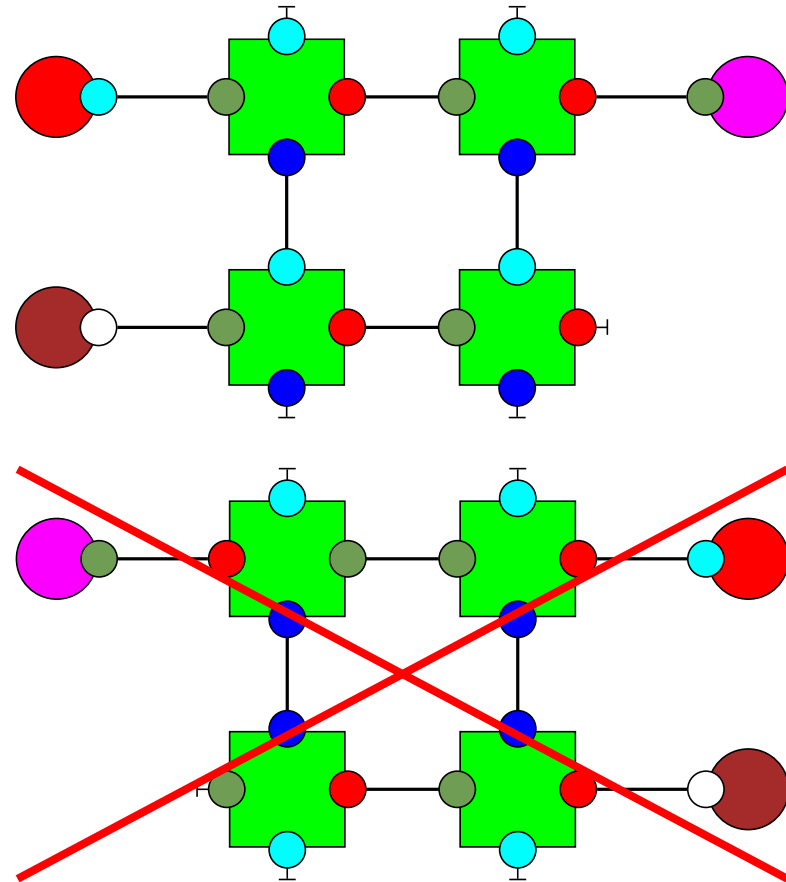
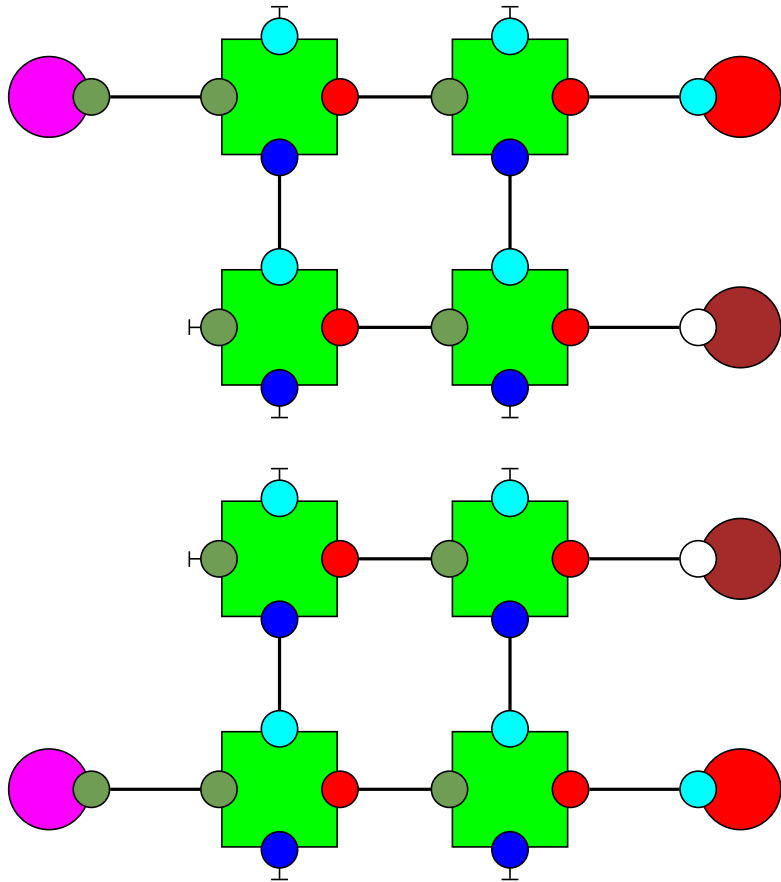


Other kinds of symmetries: Homogeneous symmetries

But we cannot apply different permutations!!!.



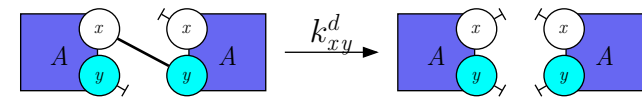
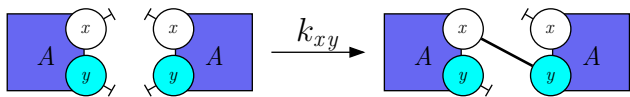
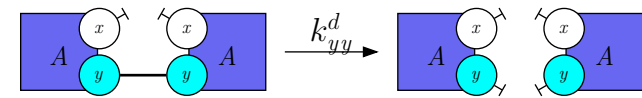
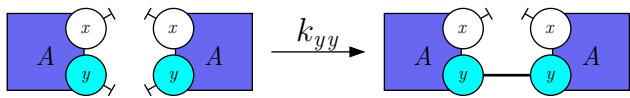
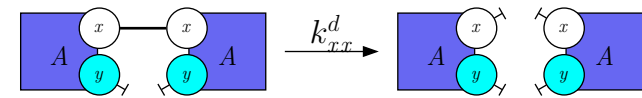
Other kinds of symmetries: Homogeneous symmetries



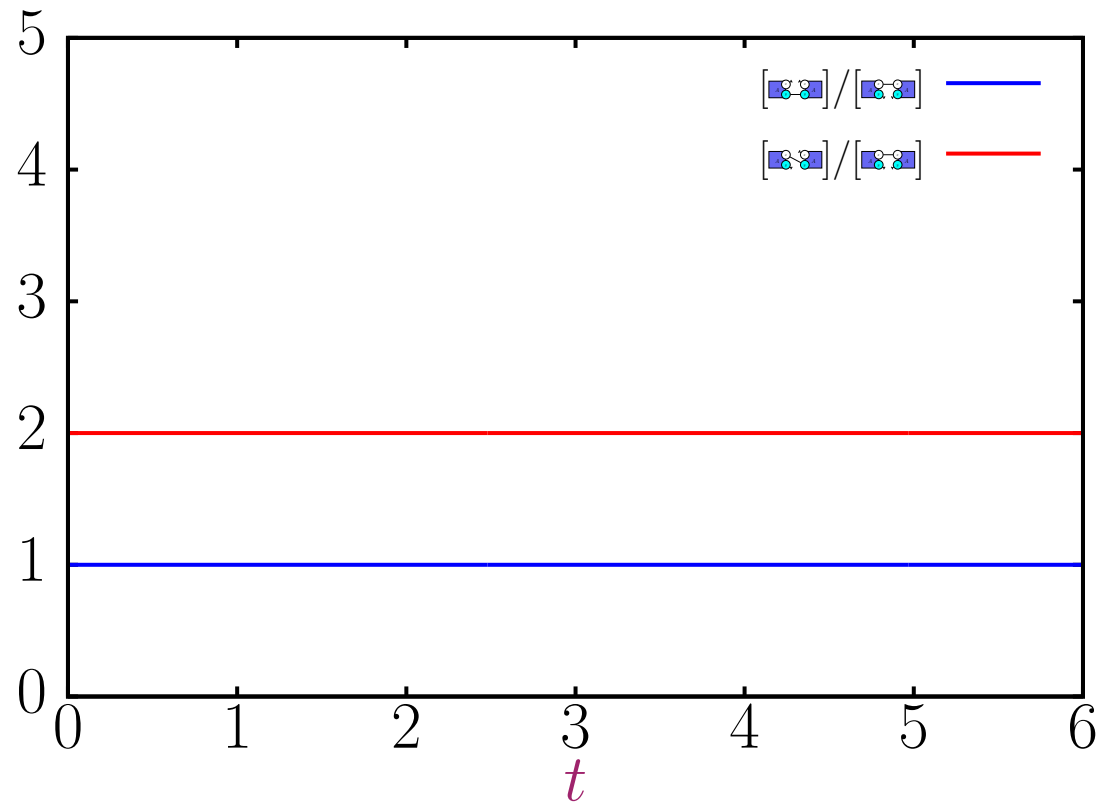
Overview

1. Context and motivations
2. **Case study**
 - (a) Symetric model with symmetric initial state
 - (b) Symmetric model with non-symmetric initial state
 - (c) Non-symmetric model
3. Kappa semantics
4. Symmetries in site-graphs
5. Symmetric models
6. Conclusion

Case study

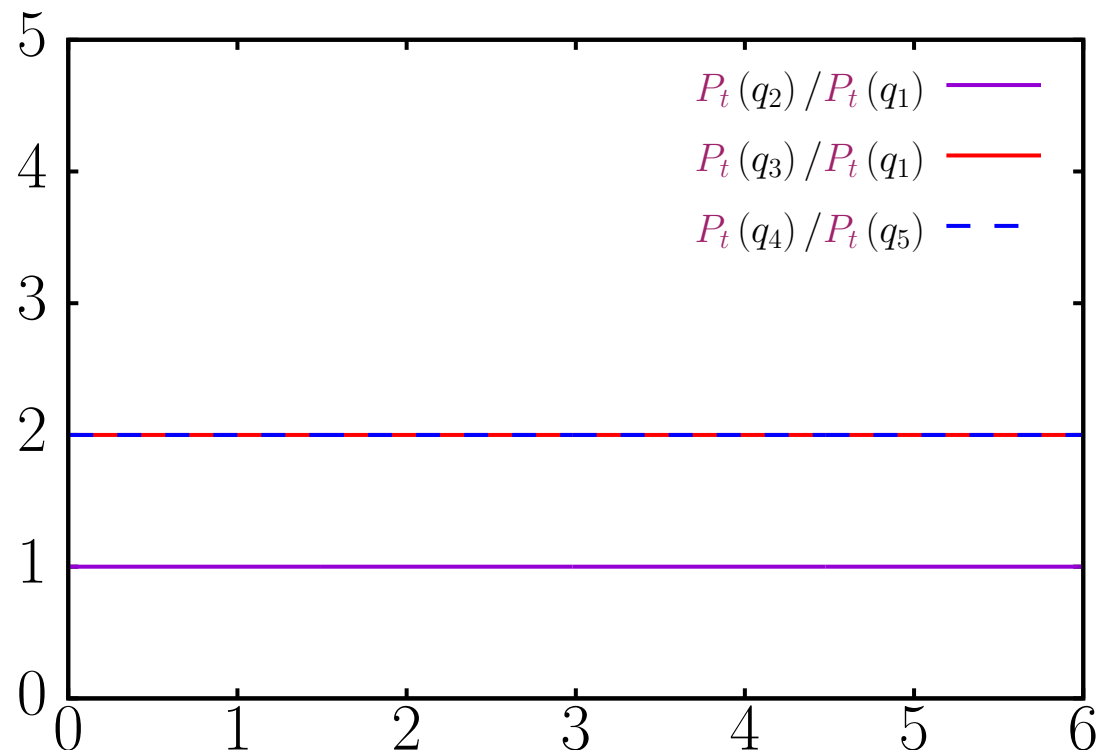
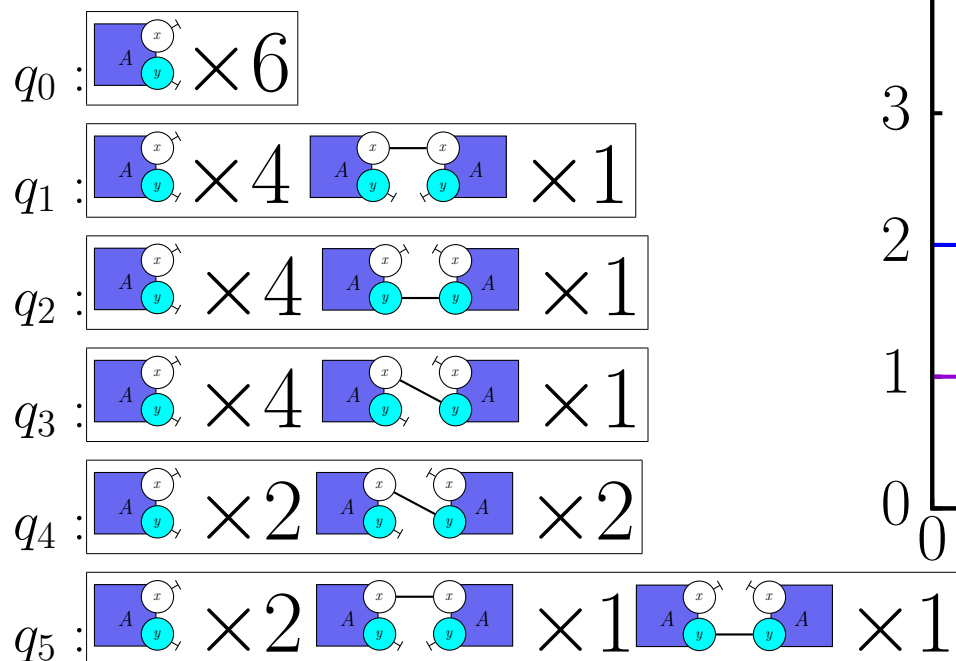


Quotients between concentrations



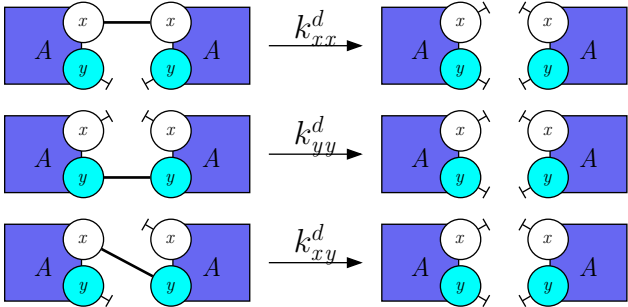
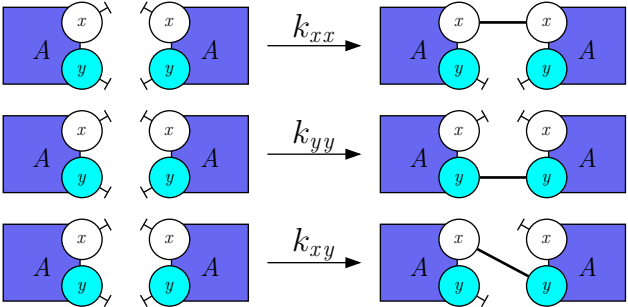
with:
$$\begin{cases} k_{\bullet,\bullet} = k_{\bullet,\bullet} = 0.5, k_{\bullet,\bullet}^d = 2, k_{\bullet,\bullet} = k_{\bullet,\bullet}^d = k_{\bullet,\bullet}^d = 1 \\ [A_2B]_0 = 6, [A_2B]_0 = [A_2B]_0 = [A_2B]_0 = 0 \end{cases}$$

Quotients between state probabilities



with:
$$\begin{cases} k_{\bullet,\bullet} = k_{\bullet,\bullet} = 0.5, & k_{\bullet,\bullet}^d = 2 \\ k_{\bullet,\bullet} = k_{\bullet,\bullet}^d = k_{\bullet,\bullet}^d = 1 \\ P_0(q_0) = 1 \end{cases}$$

Initial model



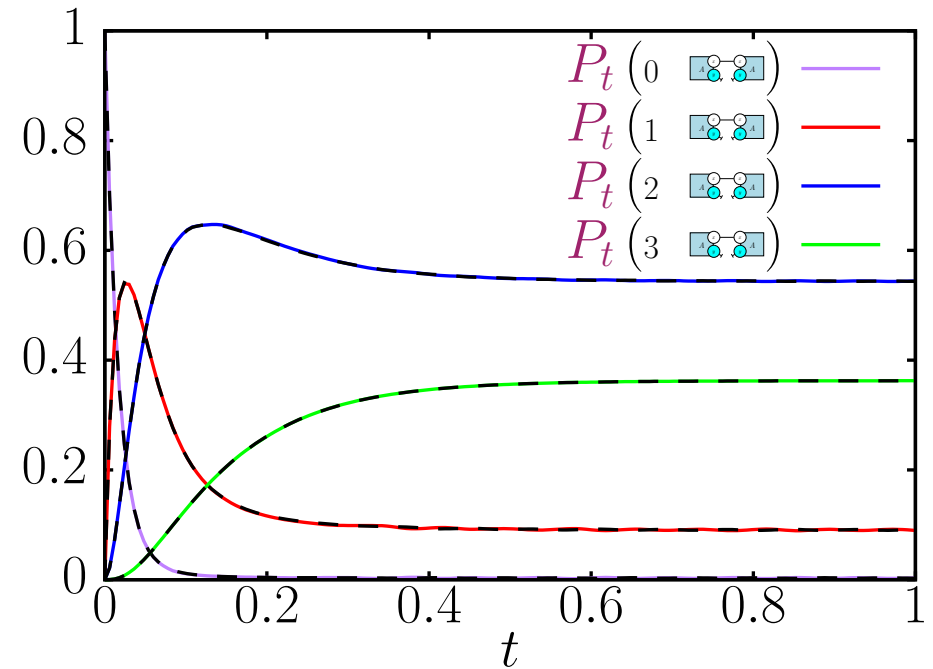
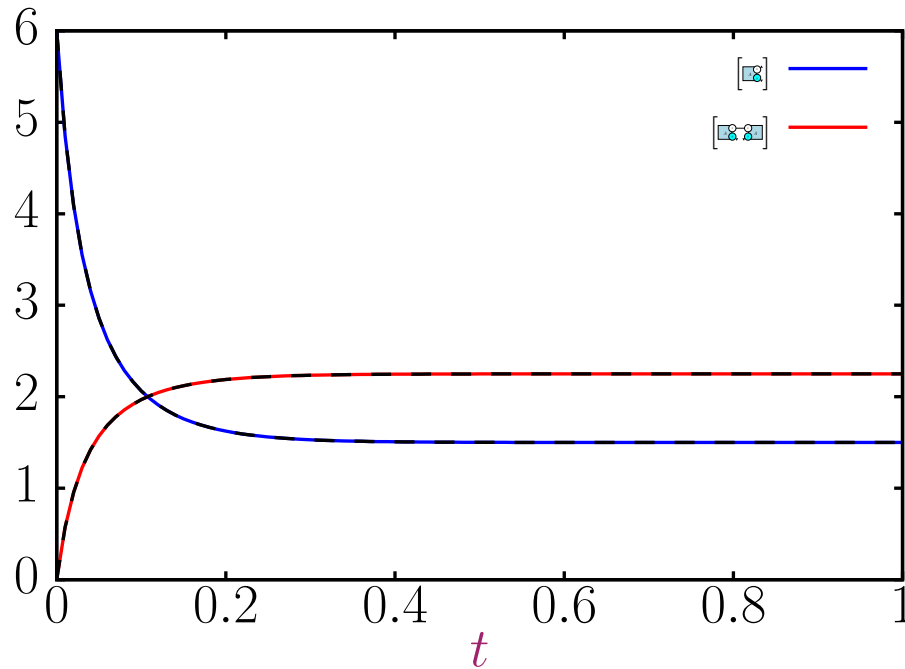
Initial model



Reduced model



Macrostate distribution



with:

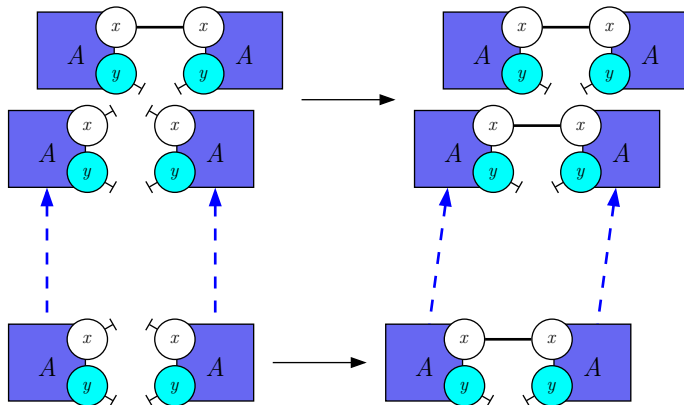
- $k_{\bullet,\bullet} = k_{\bullet,\bullet} = 0.5$, $k_{\bullet,\bullet}^d = 2$, $k_{\bullet,\bullet} = k_{\bullet,\bullet}^d = k_{\bullet,\bullet}^d = 1$;
- $K = 2$, $K^d = 1$,

(continuous lines: initial model; dashed lines: reduced model)

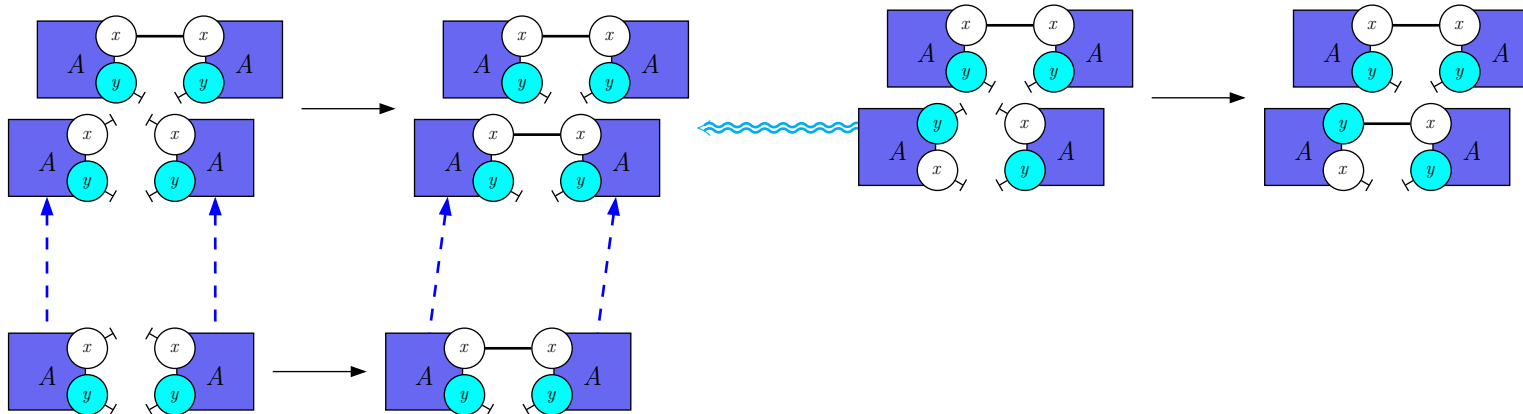
Overview

1. Context and motivations
2. **Case study**
 - (a) Symetric model with symmetric initial state
 - (b) **Symmetric model with non-symmetric initial state**
 - (c) Non-symmetric model
3. Kappa semantics
4. Symmetries in site-graphs
5. Symmetric models
6. Conclusion

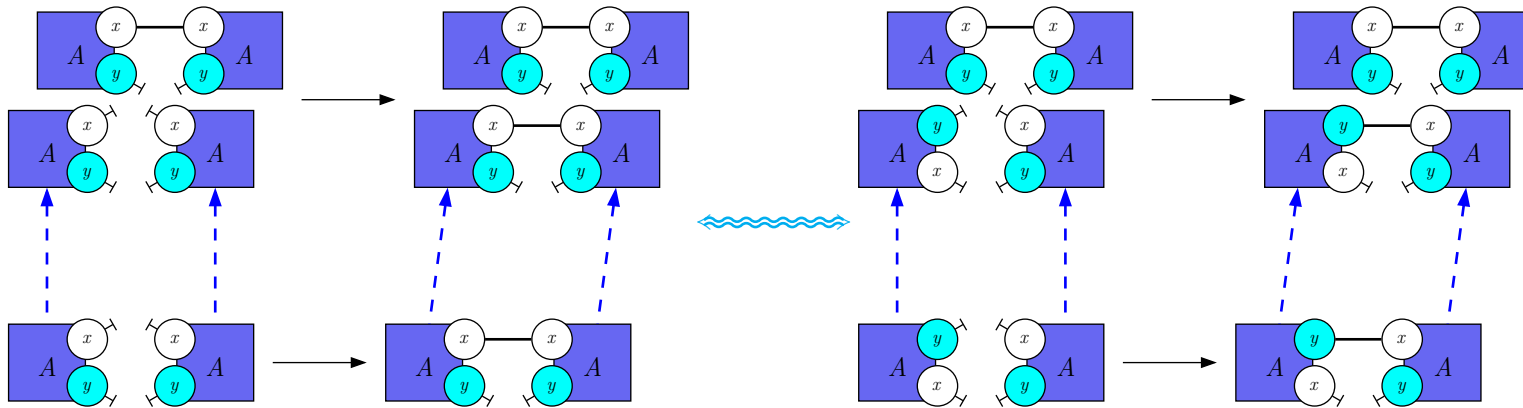
Symmetric of a transition step



Symmetric of a transition step



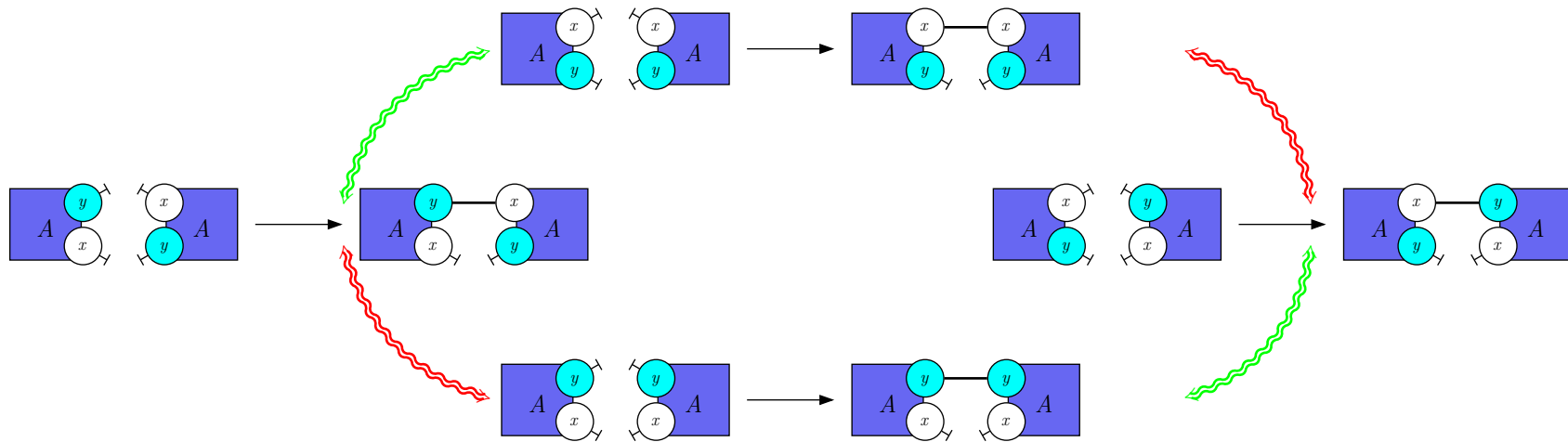
Symmetric of a transition step



Overview

1. Context and motivations
2. **Case study**
 - (a) Symetric model with symmetric initial state
 - (b) Symmetric model with non-symmetric initial state
 - (c) **Non-symmetric model**
3. Kappa semantics
4. Symmetries in site-graphs
5. Symmetric models
6. Conclusion

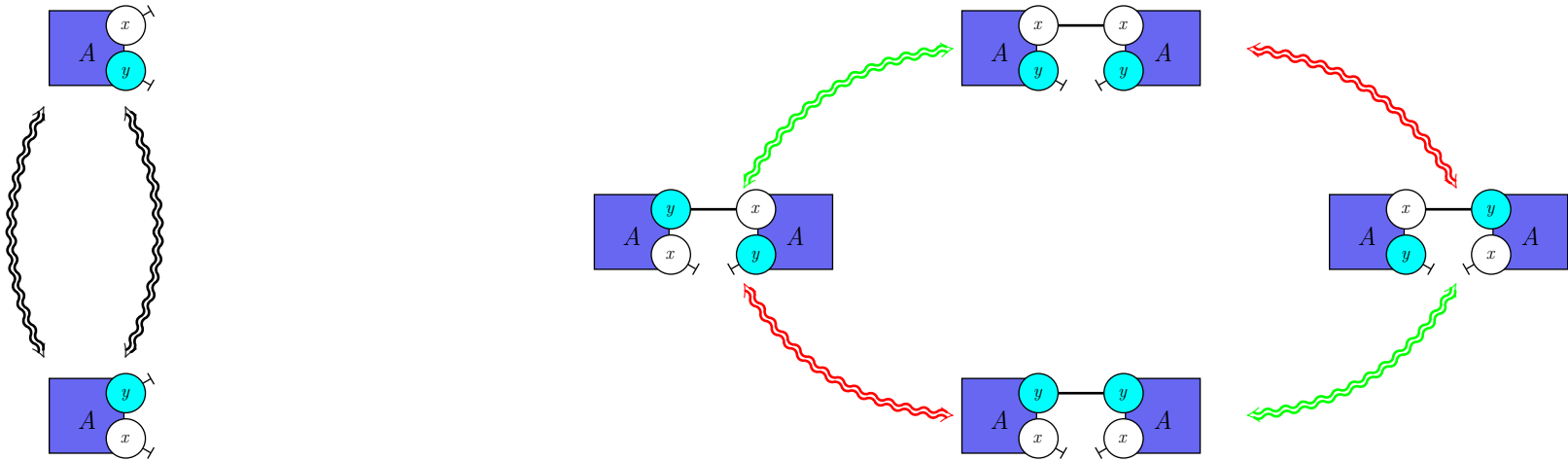
Symmetric sets of rules



A **set of rules is symmetric** if the **rates** of two symmetric rules are **proportional** to their **numbers of occurrences** in the corresponding **orbit**.

Here: $\frac{k_{\bullet, \bullet}}{1} = \frac{k_{\bullet, \bullet}}{1} = \frac{k_{\bullet, \bullet}}{2}$.

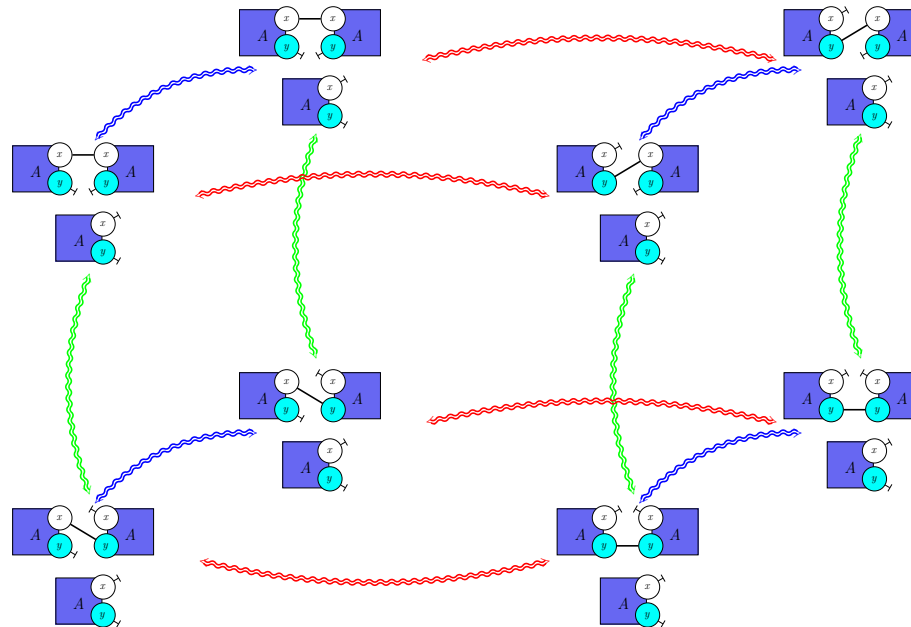
Symmetric continuous states



A **continuous state is symmetric** if the **quantity** of two symmetric biological complexes are **proportional** to their **numbers of occurrences** in the corresponding **orbit**.

Here:
$$\frac{\left[\begin{array}{c} \text{A} \text{---} \text{x} \\ \text{y} \end{array} \right]}{1} = \frac{\left[\begin{array}{c} \text{A} \text{---} \text{x} \\ \text{y} \end{array} \right]}{1} = \frac{\left[\begin{array}{c} \text{A} \text{---} \text{x} \\ \text{y} \end{array} \right]}{2}.$$

Symmetric distributions of states



A **continuous state is symmetric** if the **quantity** of two symmetric biological complexes are **proportional** to their **numbers of occurrences** in the corresponding **orbit**.

Here proportional to their numbers of occurrences of asymmetric dimers.

Overview

1. Context and motivations
2. **Case study**
 - (a) Symetric model with symmetric initial state
 - (b) Symmetric model with non-symmetric initial state
 - (c) Non-symmetric model
3. Kappa semantics
4. Symmetries in site-graphs
5. Symmetric models
6. Conclusion

Properties

Permutations of sites induce **back-and-forth bisimulations**:

- **Forward:**

The semantics can be computed directly on symmetric classes of **states** (resp. **distributions of states**).

- **Backward:**

Starting in a symmetric **state** (resp. **distribution of states**), the **state** (resp. **distribution of states**) is symmetric at any time.

In this talk

An algebraic notion of symmetries over site graphs:

- compatible with the SPO (Single Push-Out) semantics of Kappa;
- with a notion of subgroups of symmetries;
- with a notion of symmetric models.

Some conditions so that symmetries over a model induce

- a forward bisimulation;
- a backward bisimulation.

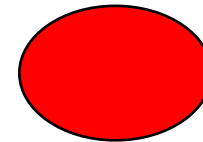
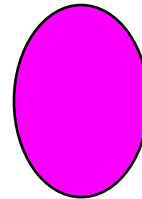
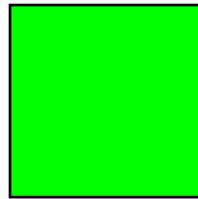
In this talk, we consider only a side-effect free fragment of Kappa.
The full language is handled with in, the paper.

Overview

1. Context and motivations
2. Case study
3. **Kappa semantics**
4. Symmetries in site-graphs
5. Symmetric models
6. Conclusion

Signature

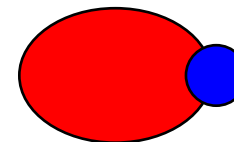
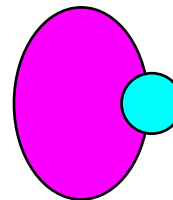
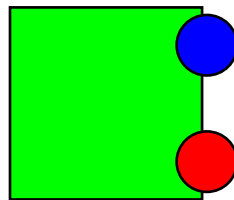
Agents:



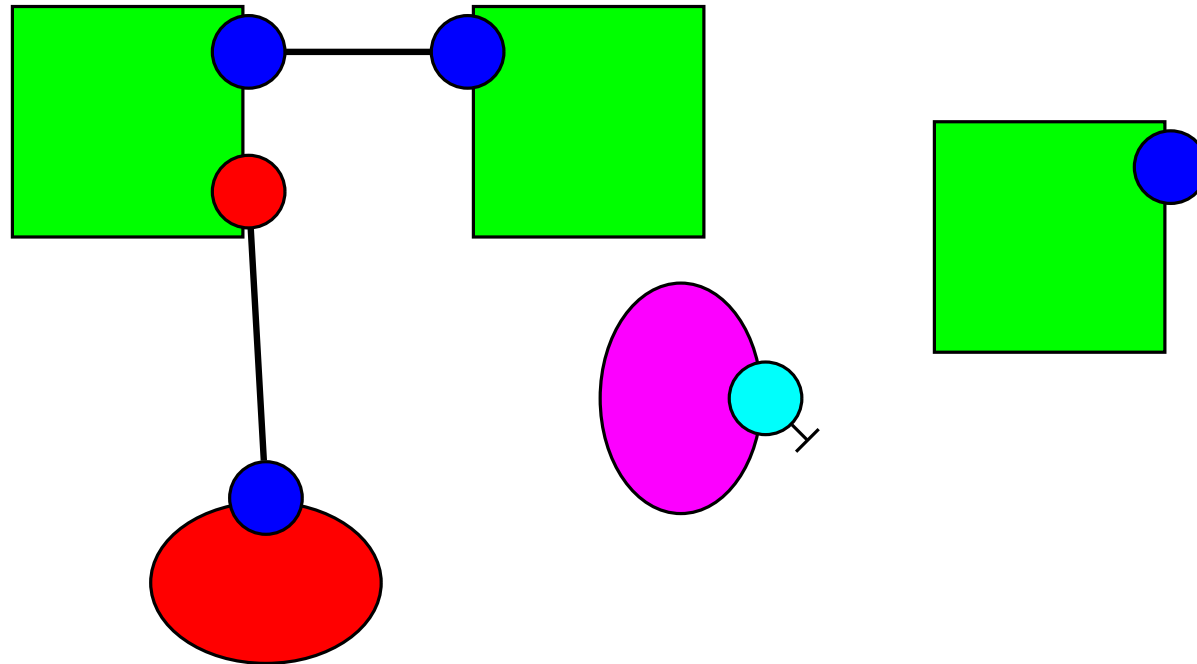
Sites:



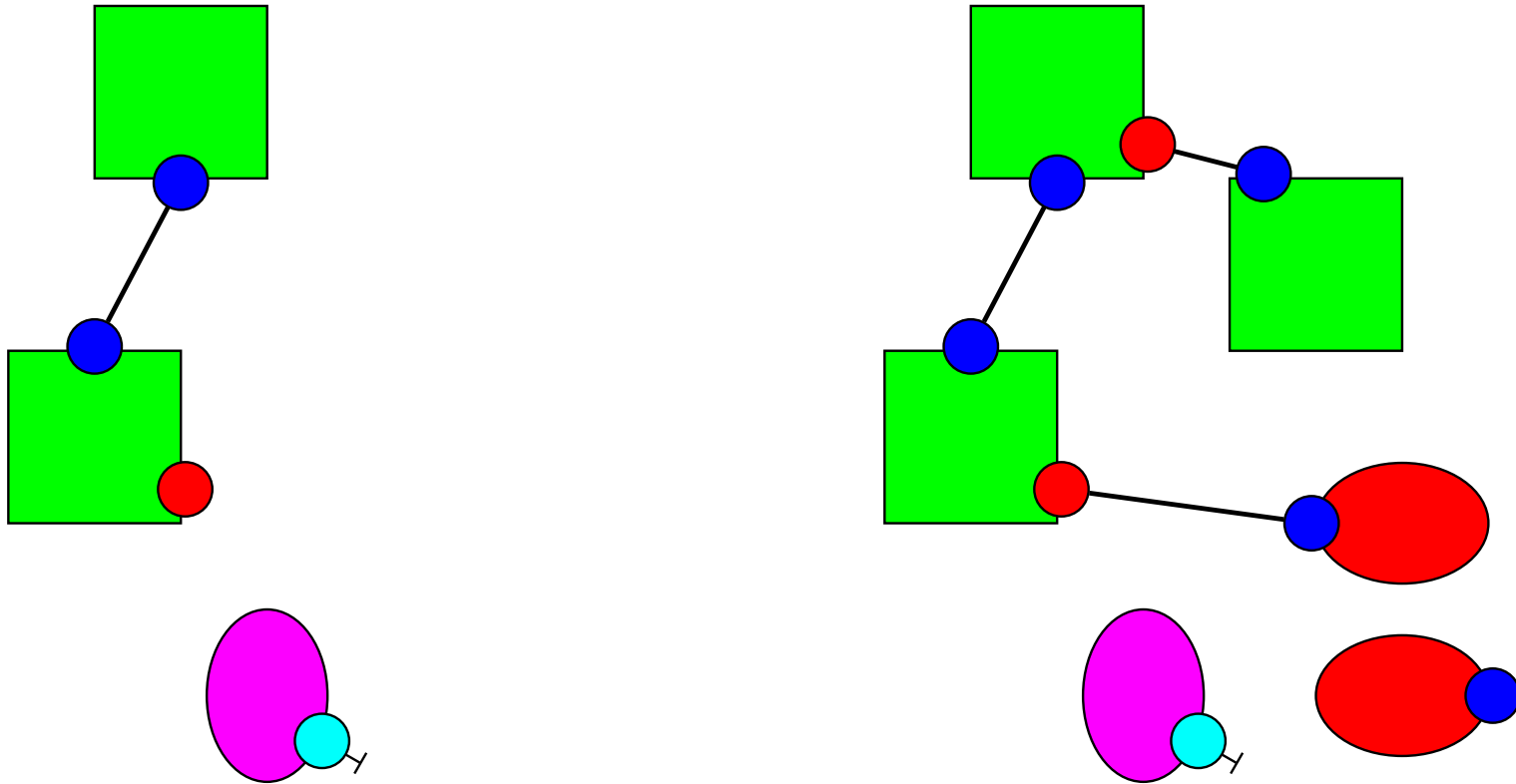
Interface:



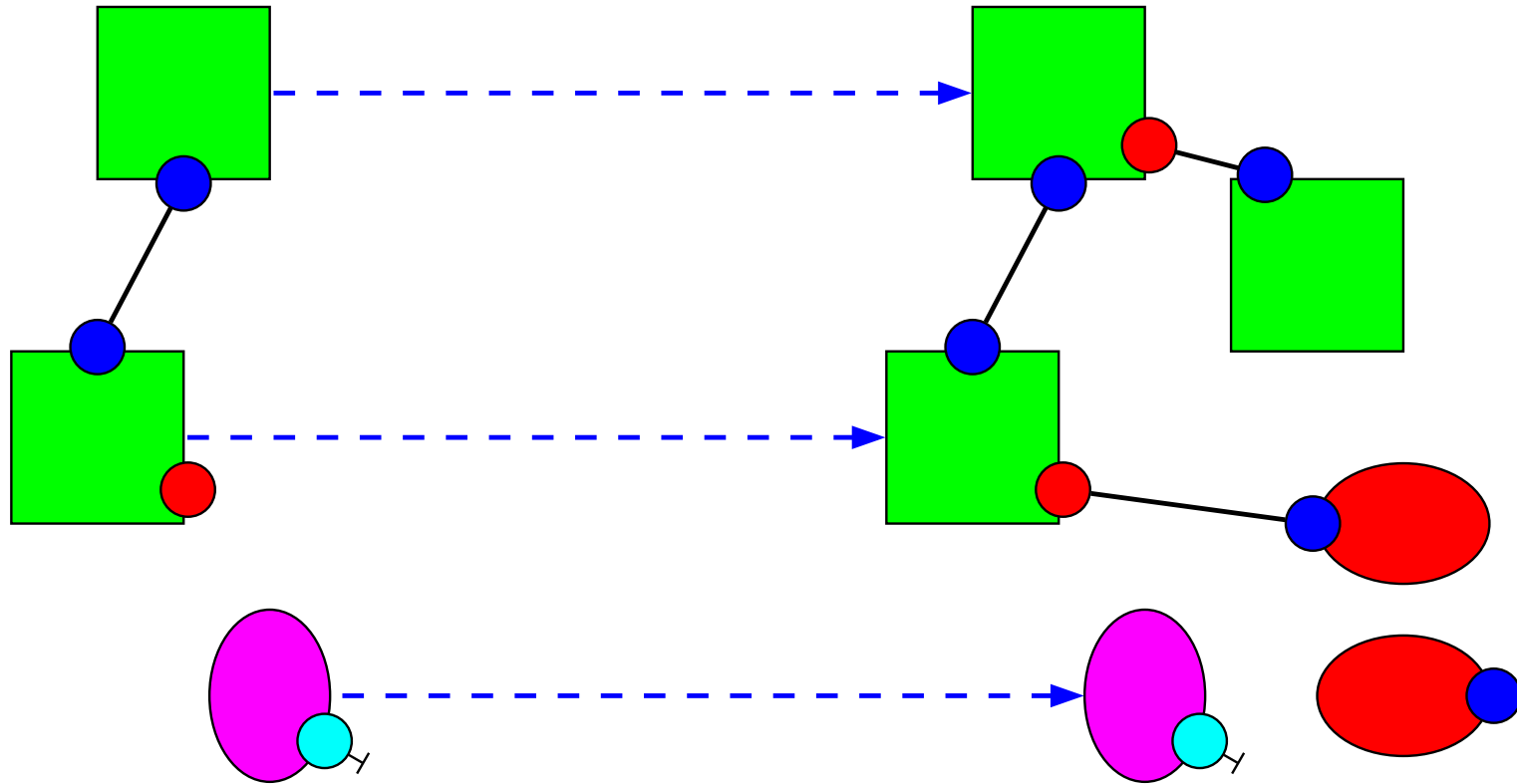
Site graphs



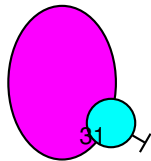
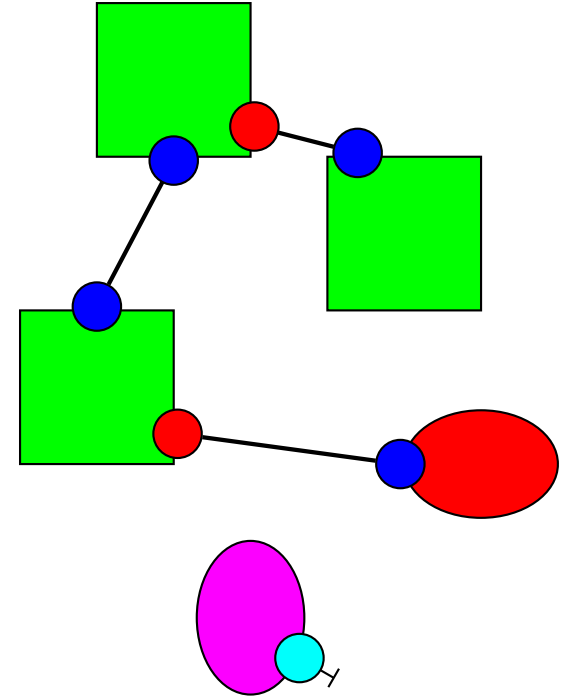
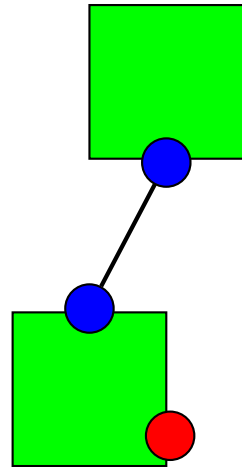
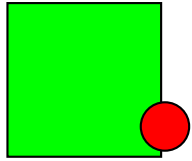
Embeddings



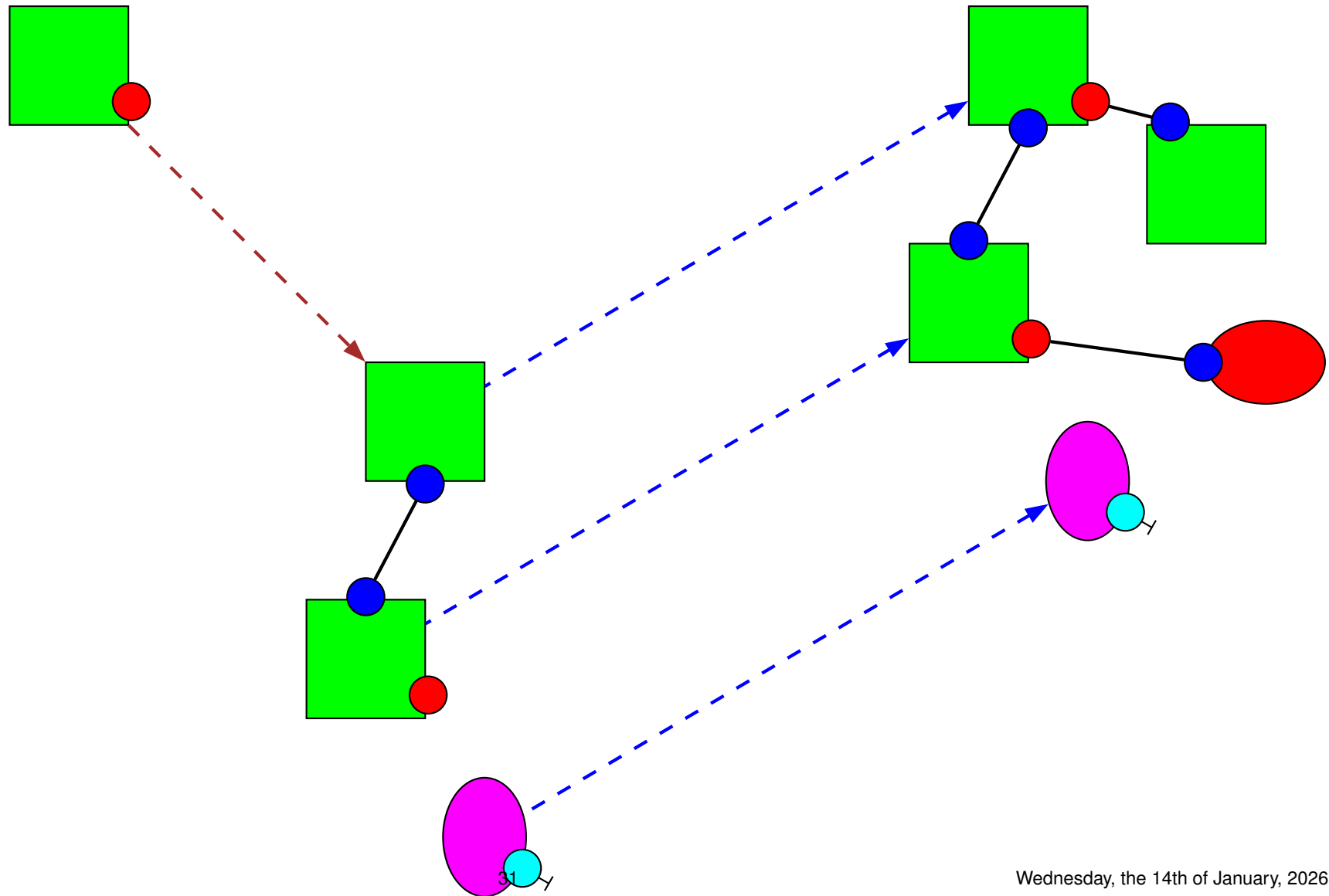
Embeddings



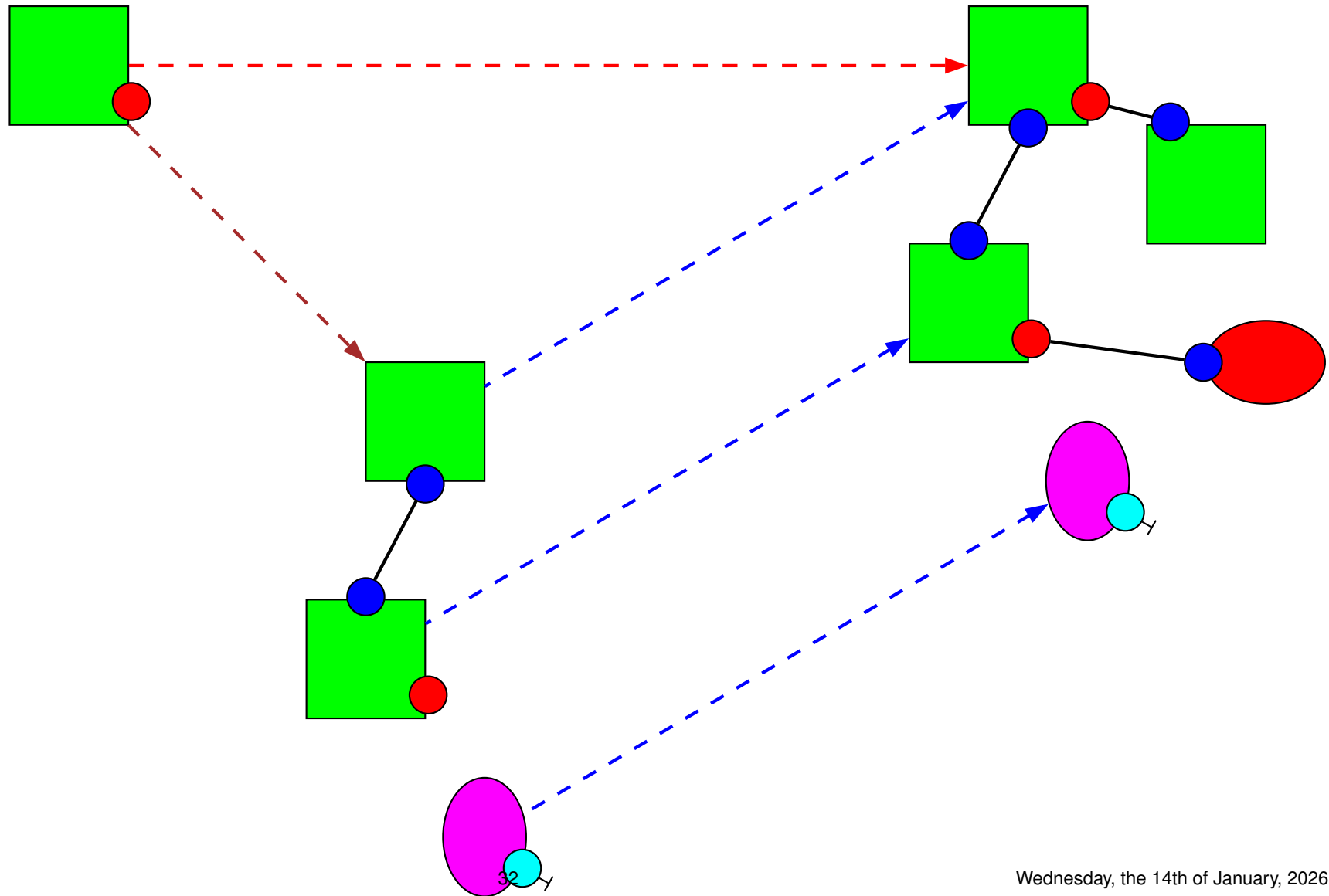
Composition of embeddings



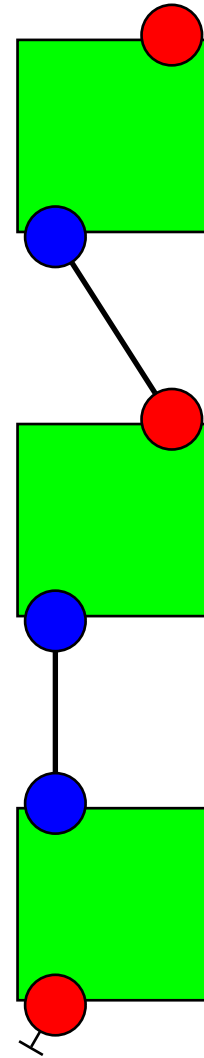
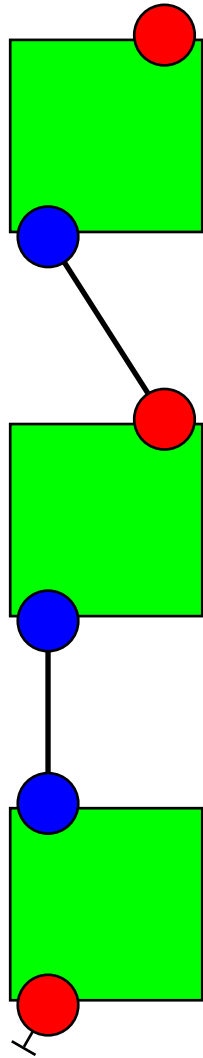
Composition of embeddings



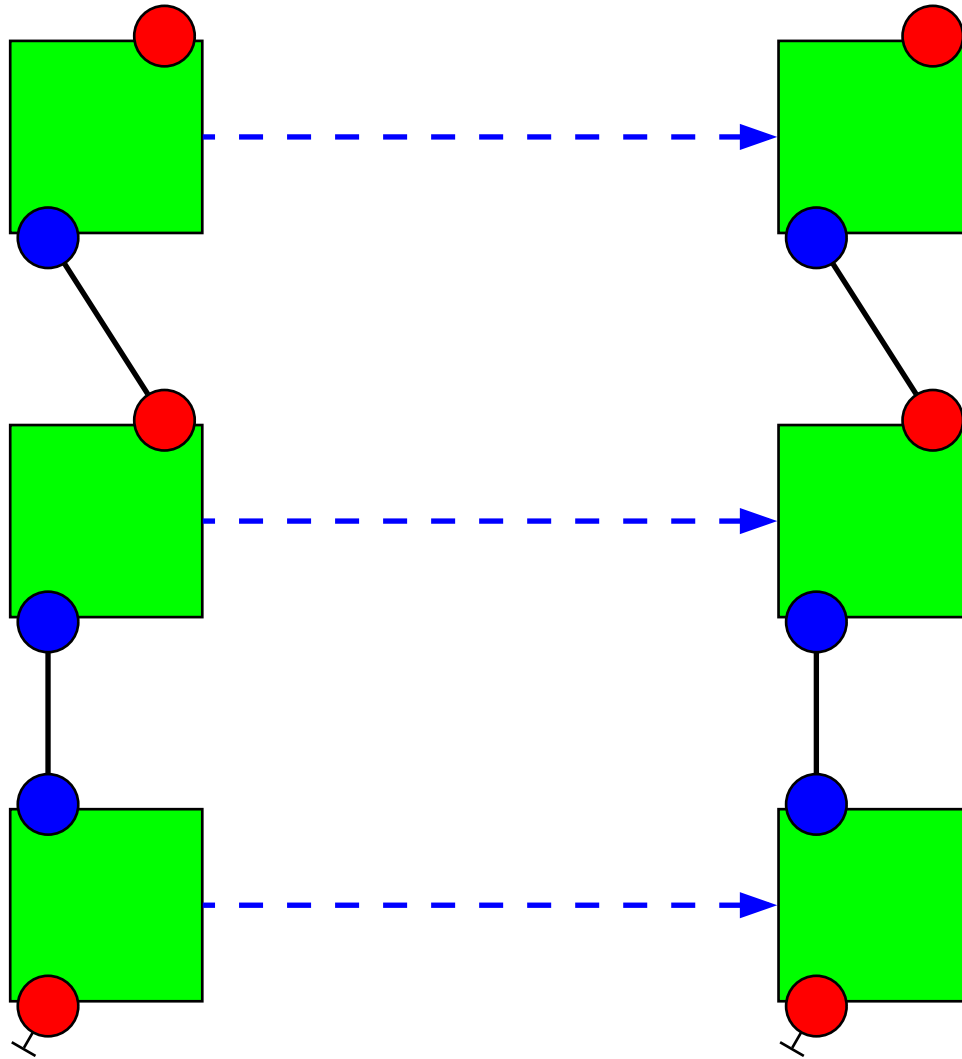
Composition of embeddings



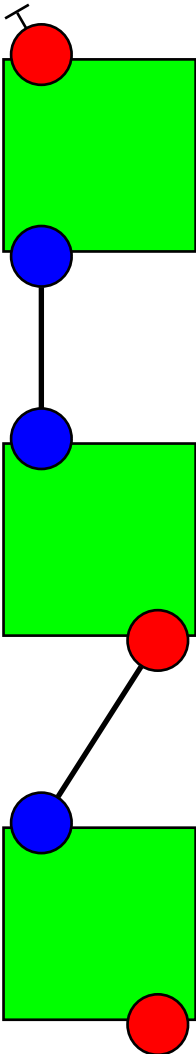
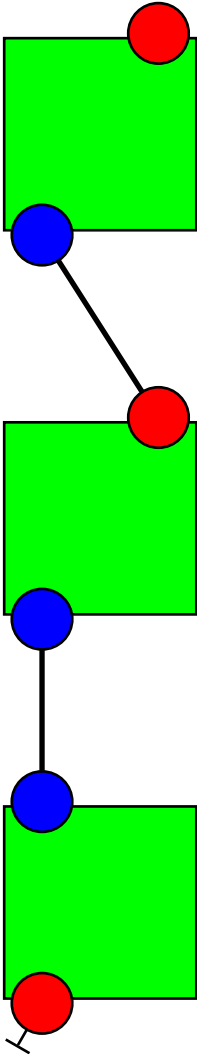
Identity embeddings



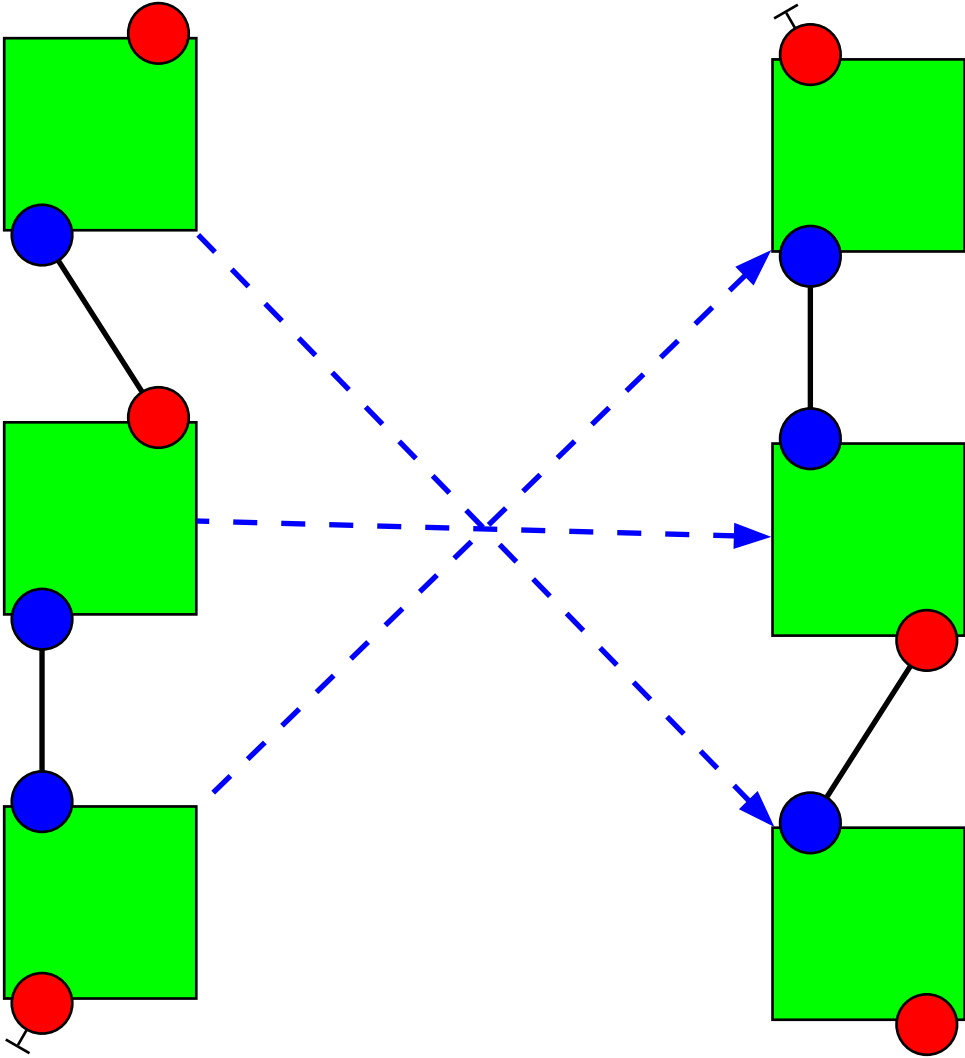
Identity embeddings



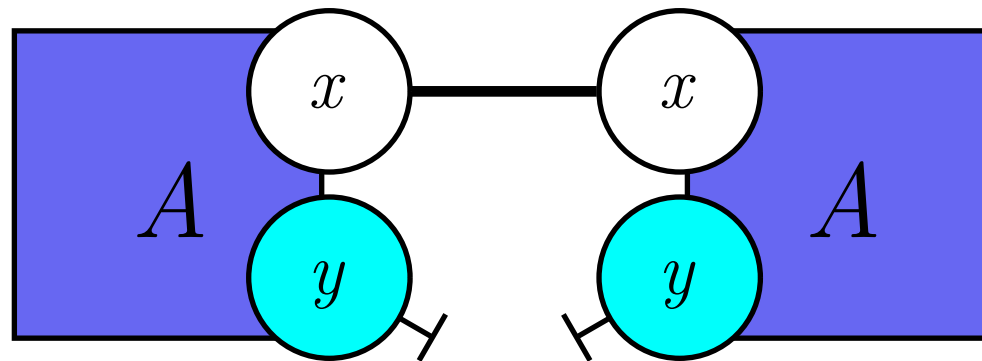
Isomorphisms



Isomorphisms

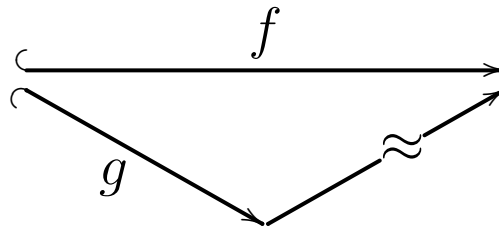


Fully specified site graphs



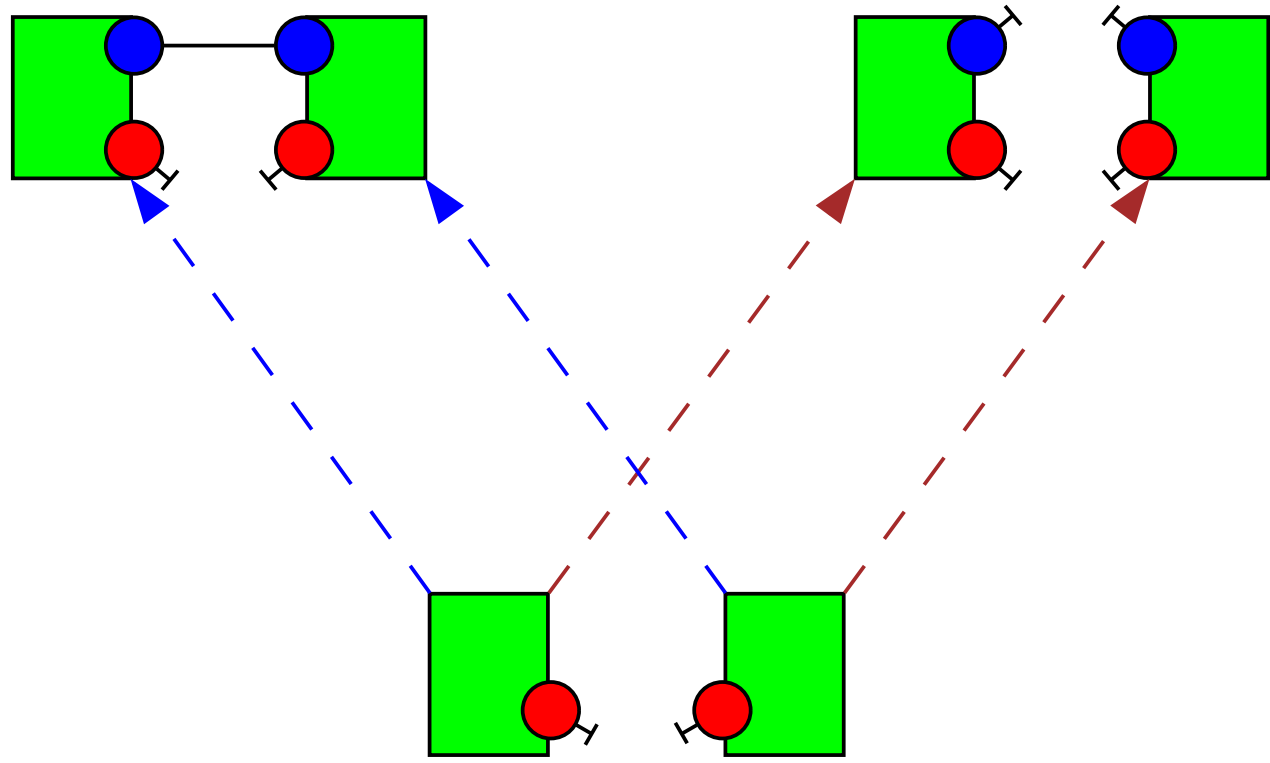
Isomorphic embeddings

When the following diagram:

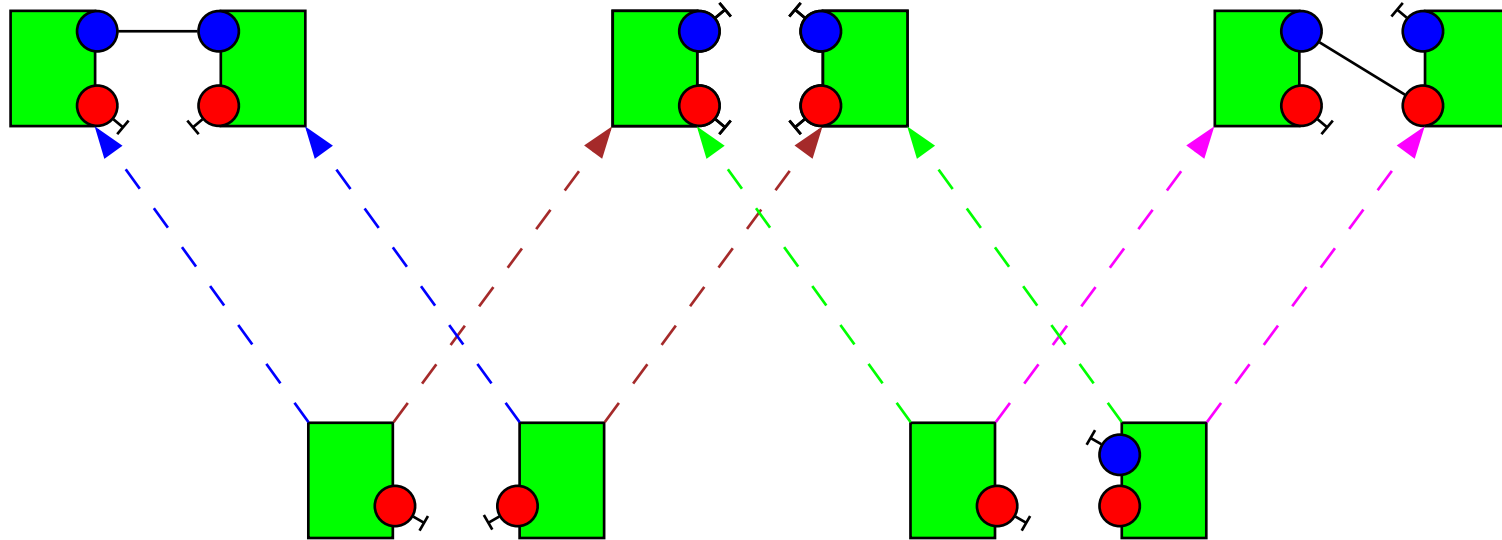


commutes, we say that the embeddings f and g are isomorphic, and we write $f \approx g$.

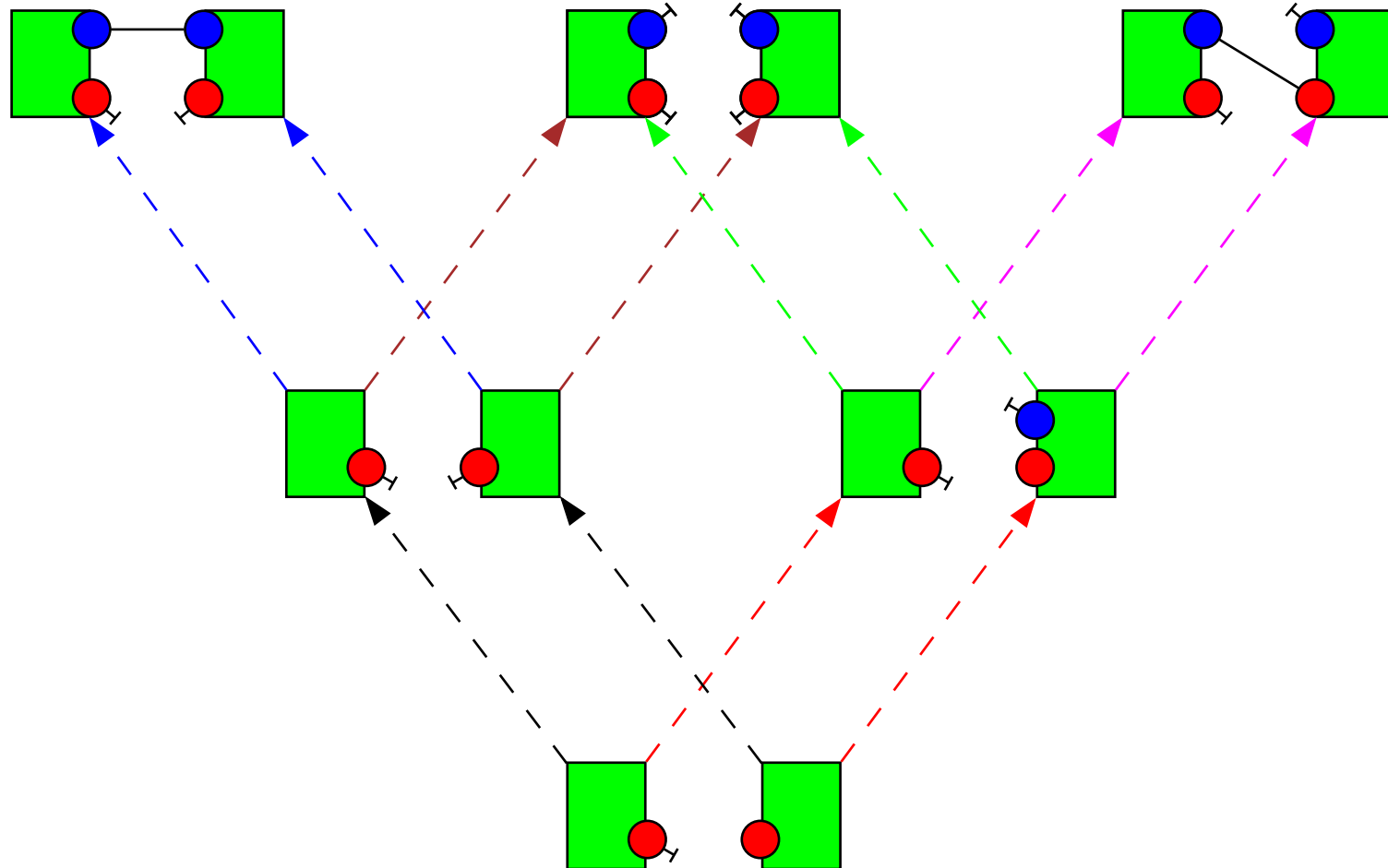
Partial embeddings



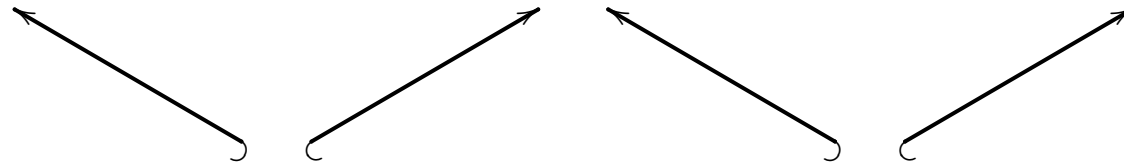
Composition of partial embeddings



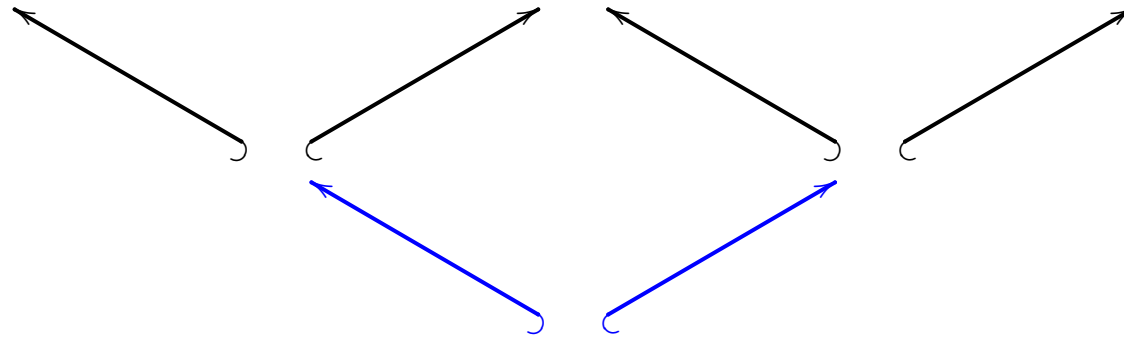
Composition of partial embeddings



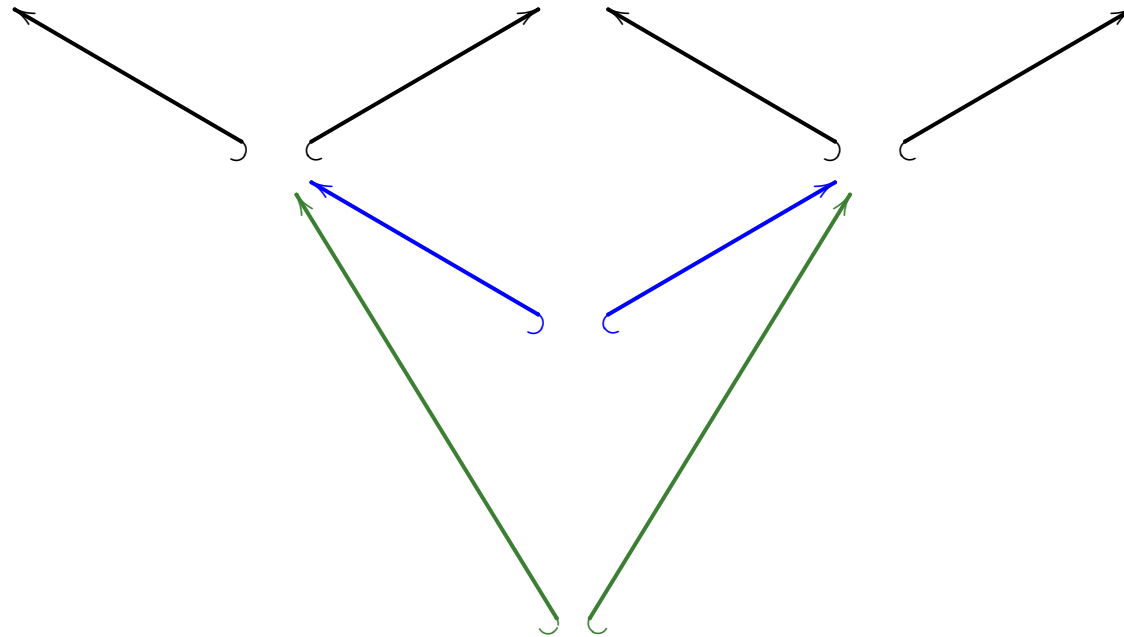
Composition of partial embeddings



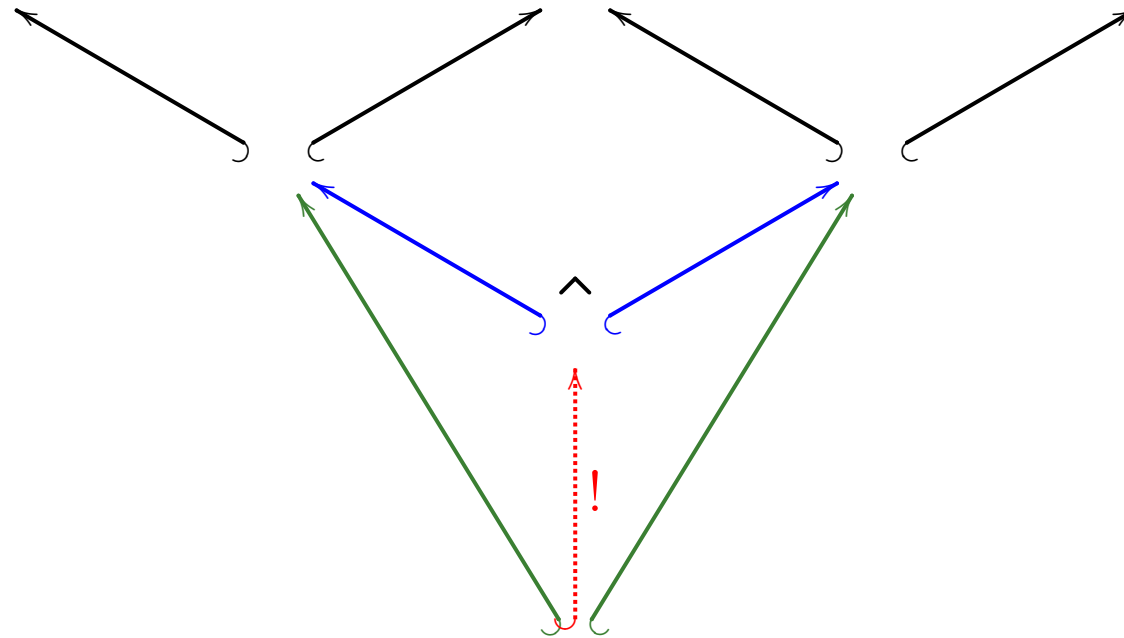
Composition of partial embeddings



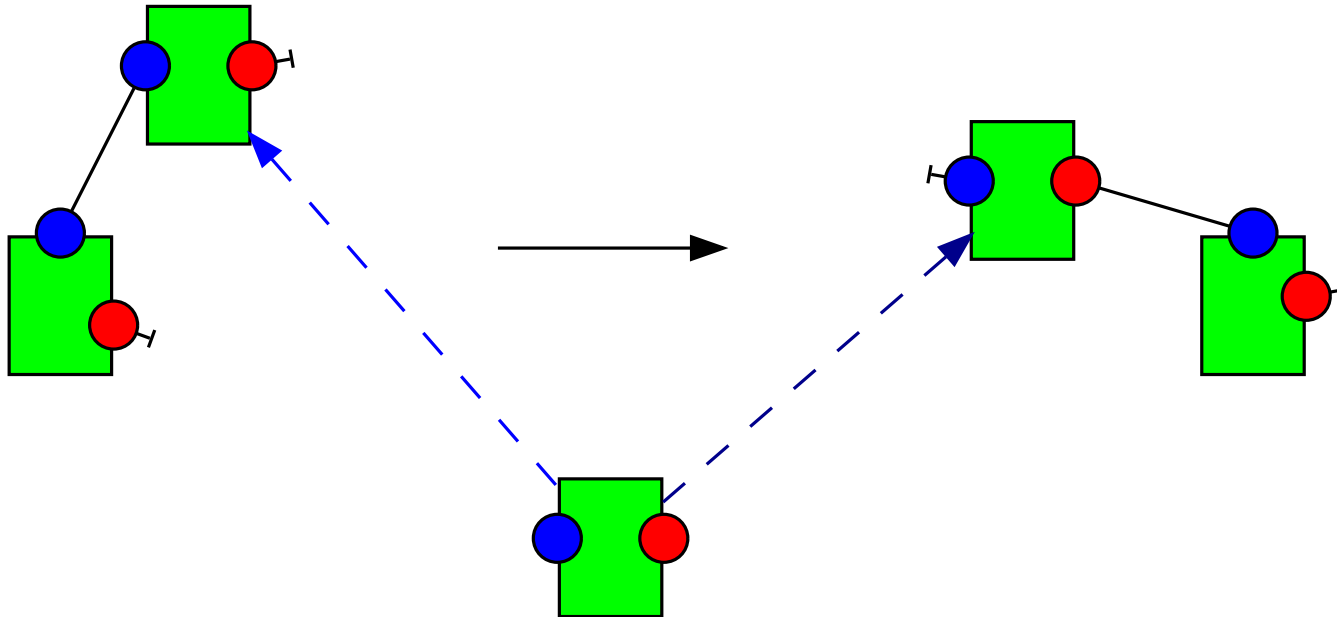
Composition of partial embeddings



Composition of partial embeddings



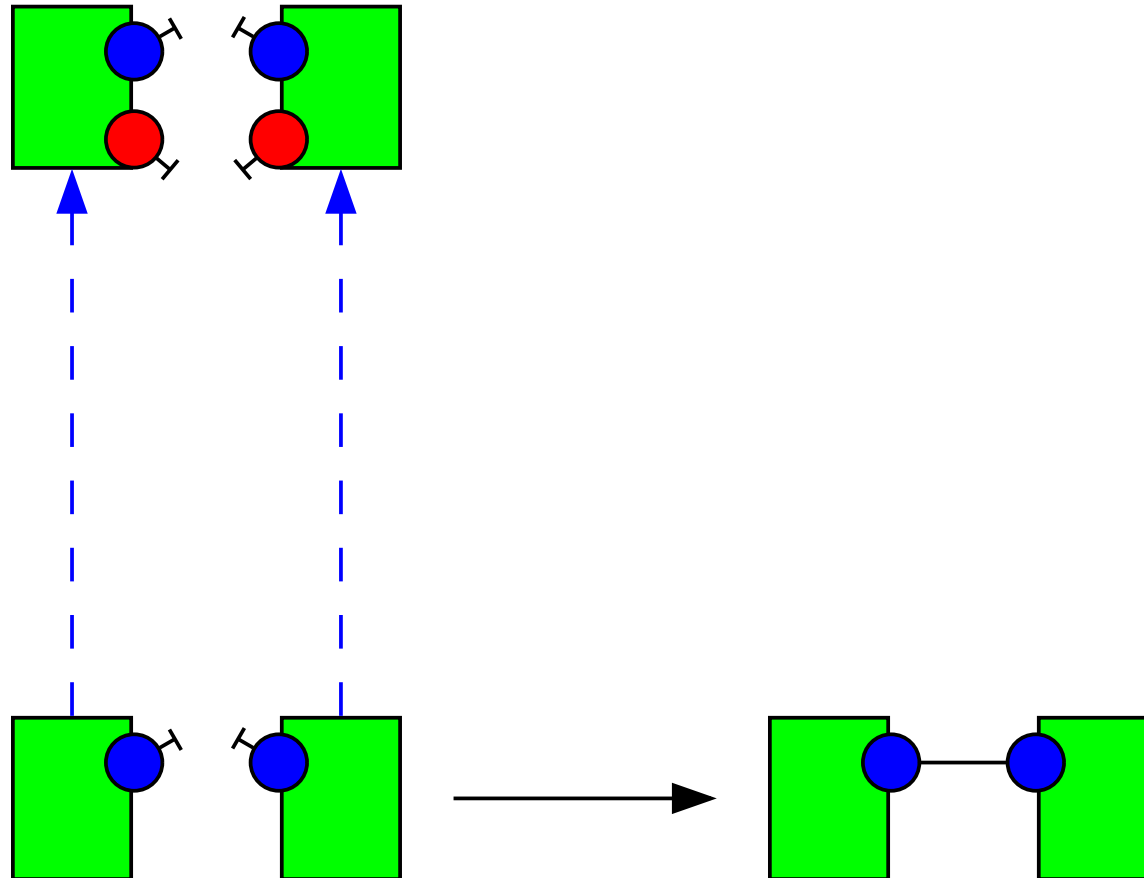
Rules



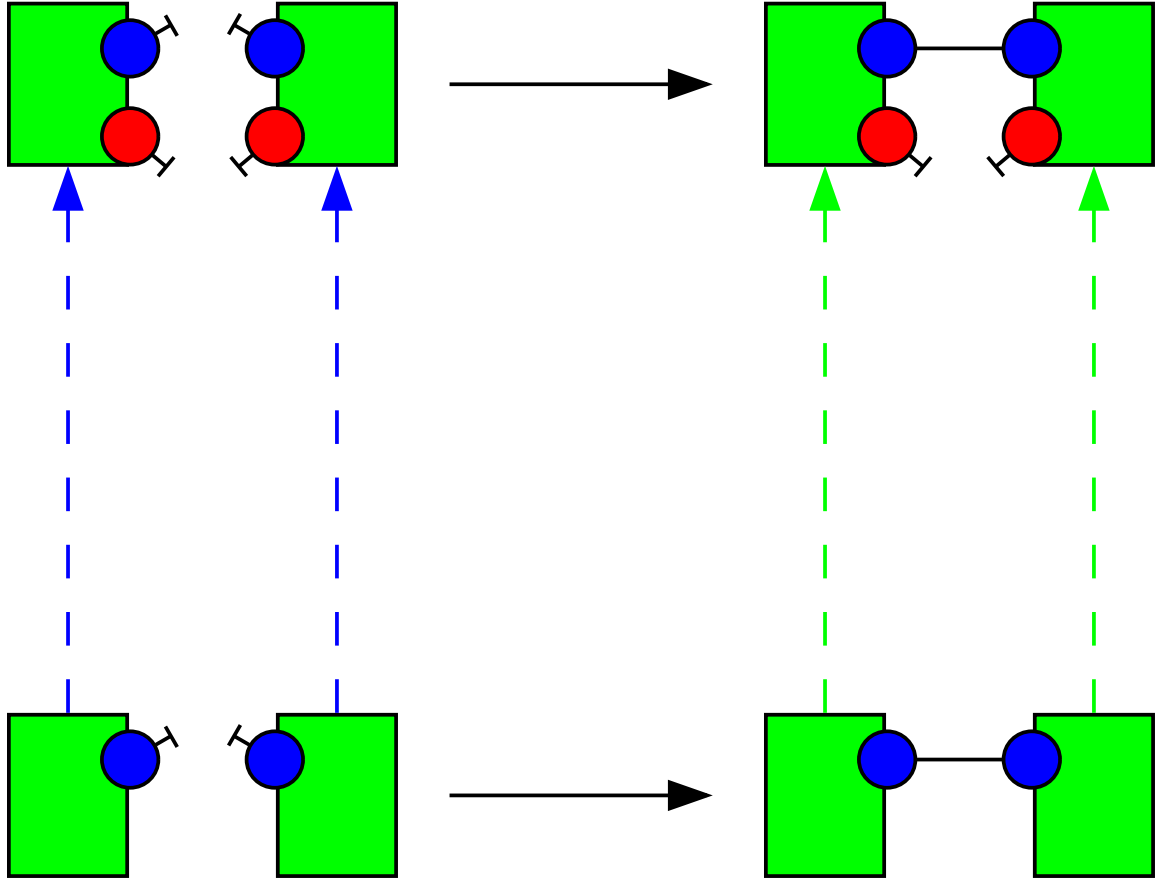
A rule is a partial embedding such that:

- the domain (D) is maximal;
- some constraints that we omit here are satisfied.

Rule application



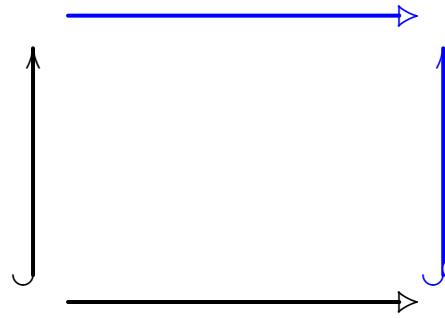
Rule applications



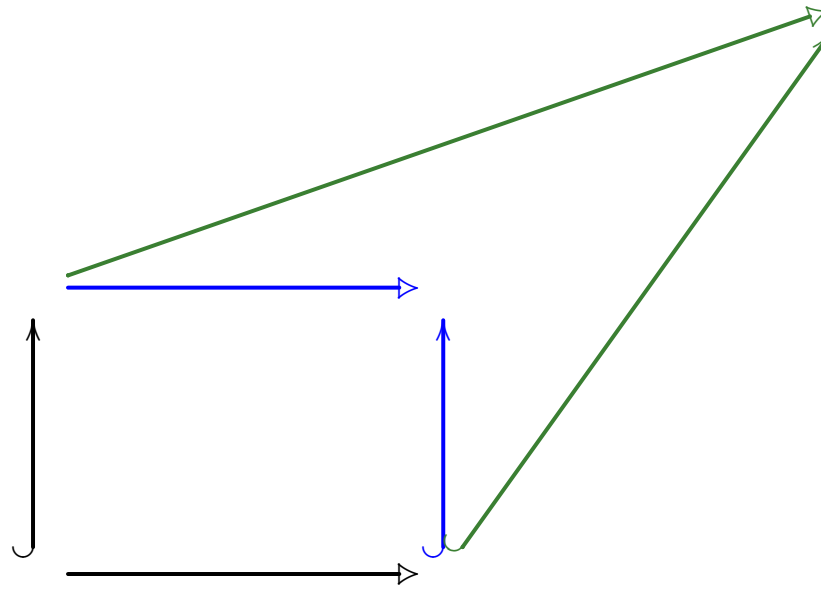
Refinement



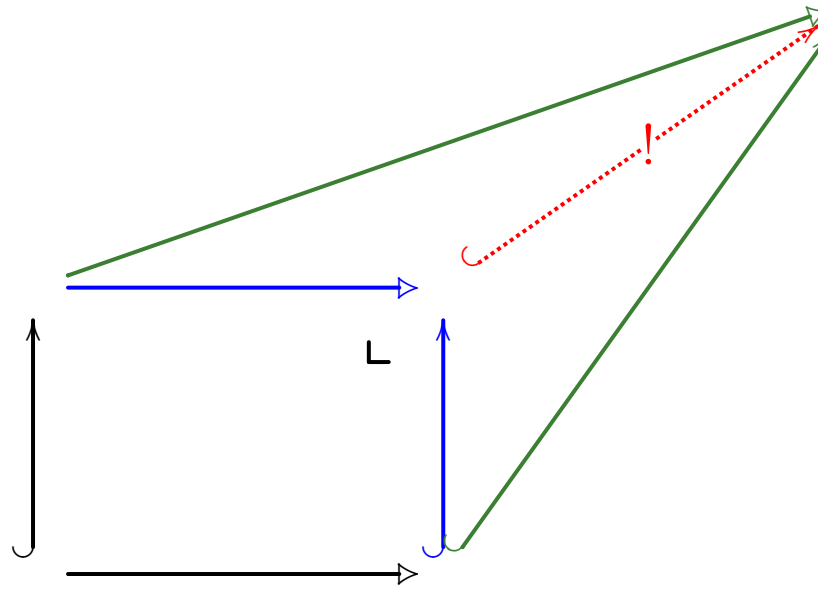
Refinement



Refinement



Refinement



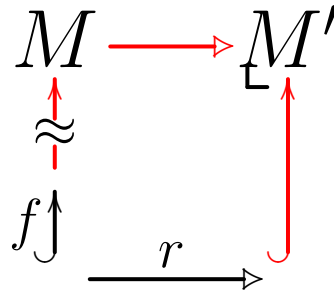
Semantics

1. A model is a map k from rules to non negative real numbers;
2. $\mathcal{Q} \triangleq \{[G]_{\approx} \mid G \text{ fully specified site graph}\}$;
3. $\mathcal{L} \triangleq \left\{ (r, [f]_{\approx}) \mid \begin{array}{l} r \text{ a rule, } f \text{ an embedding from } lhs(r) \\ \text{to a fully specified site graph} \end{array} \right\}$;
4. $[M]_{\approx} \xrightarrow{(r, [f]_{\approx})} [M']_{\approx}$ if and only if:

$$\begin{array}{ccc}
 M & & M' \\
 & \Downarrow f & \\
 & \xrightarrow{r} &
 \end{array}$$

Semantics

1. A model is a map k from rules to non negative real numbers;
2. $\mathcal{Q} \triangleq \{[G]_{\approx} \mid G \text{ fully specified site graph}\};$
3. $\mathcal{L} \triangleq \left\{ (r, [f]_{\approx}) \mid \begin{array}{l} r \text{ a rule, } f \text{ an embedding from } lhs(r) \\ \text{to a fully specified site graph} \end{array} \right\};$
4. $[M]_{\approx} \xrightarrow{(r, [f]_{\approx})} [M']_{\approx}$ if and only if:

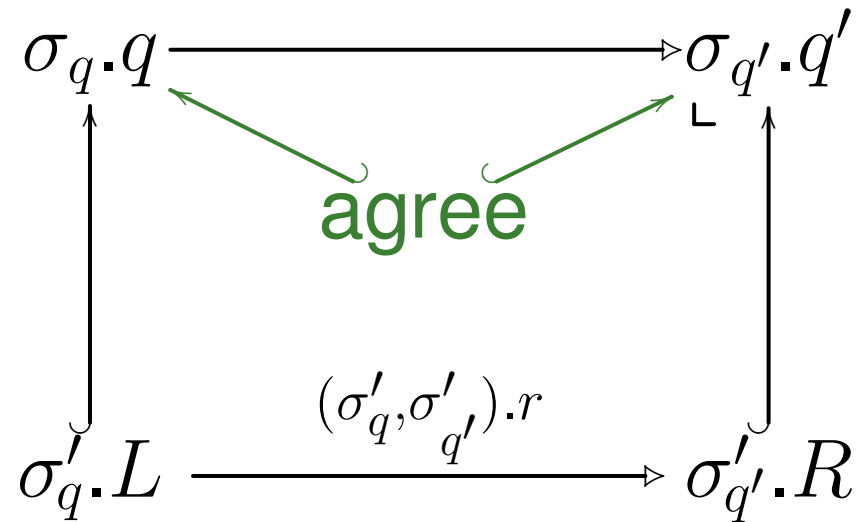
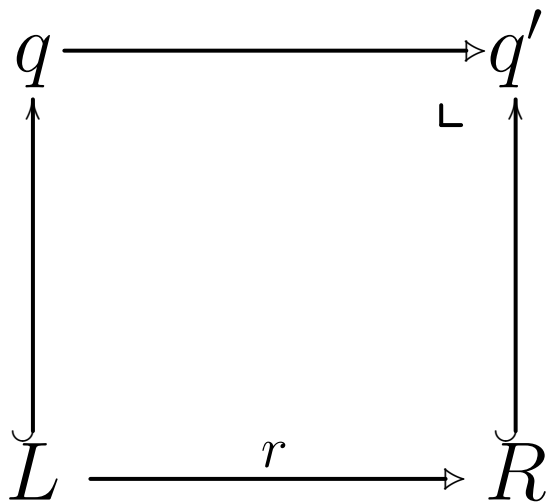


The rate of such a transition is defined as:

$$\frac{\gamma(r) \text{card}(\{\phi f \mid \phi \in \text{Aut}(im(f))\})}{\text{card}(\text{Aut}(lhs(r)))}.$$

Applying transformations over push-outs

We would like to make pairs of transformations act over push-outs,



whenever they act the same way on preserved agents.

Overview

1. Context and motivations
2. Case study
3. Kappa semantics
4. **Symmetries in site-graphs**
 - (a) Groups of transformations
 - (b) Action of the transformations
5. Symmetric models
6. Conclusion

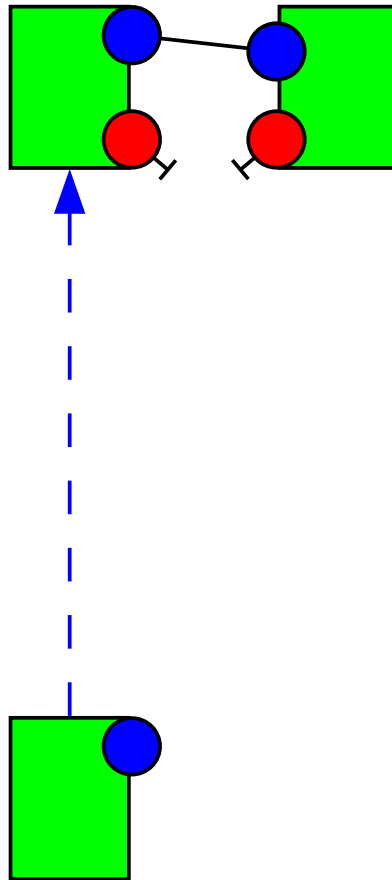
Transformations over site graphs

- For any site graph G , we introduce a finite group of transformations \mathbb{G}_G .

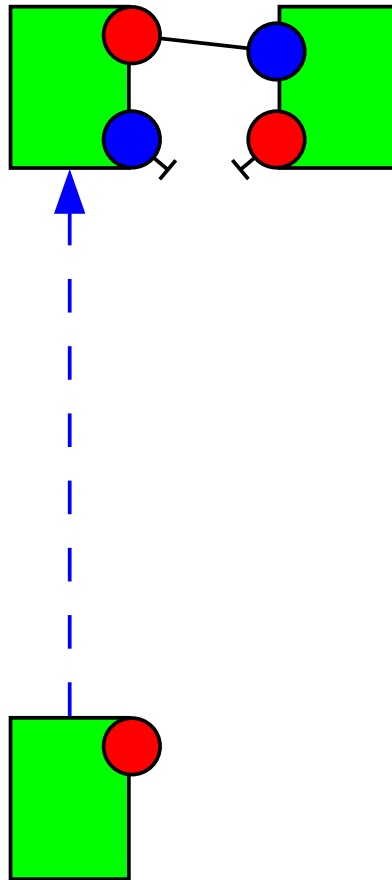


- For any site graph G and any transformation $\sigma \in \mathbb{G}_G$, we introduce the site graph $\sigma.G$ and we call it the image of G by σ .
- We assume that \mathbb{G}_G and $\mathbb{G}_{(\sigma.G)}$ are the same group.

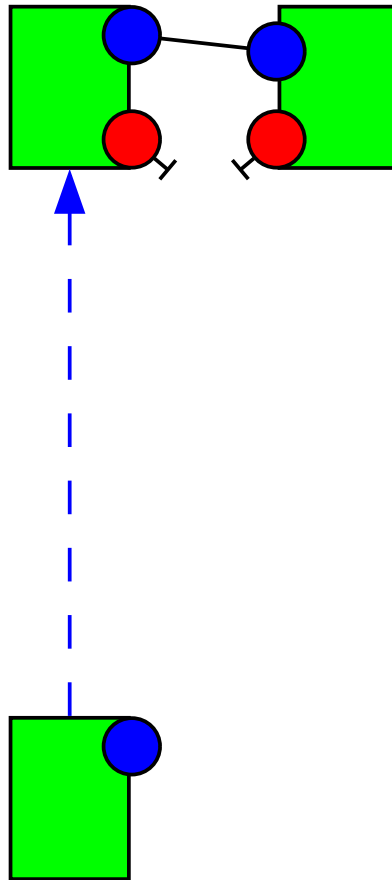
Restricting a transformation to the domain of an embedding



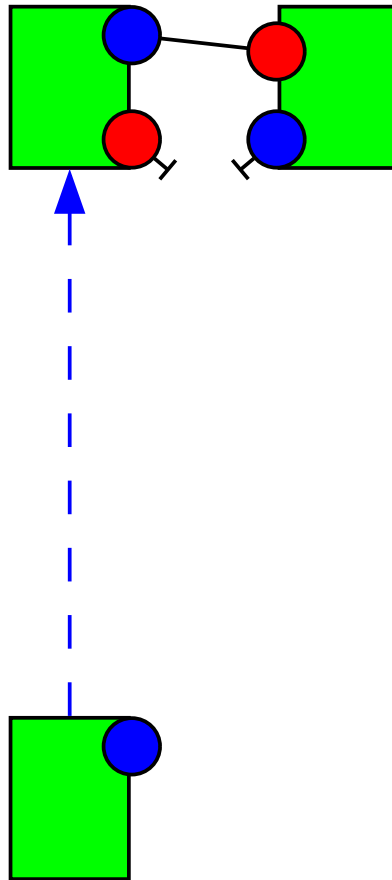
Restricting a transformation to the domain of an embedding



Restricting a transformation to the domain of an embedding



Restricting a transformation to the domain of an embedding



Restriction of symmetry to the domain of an embedding

$$\begin{array}{ccc} G & \xrightarrow{f} & H \\ & & \downarrow \sigma \\ & & \sigma.H \end{array}$$

Restriction of symmetry to the domain of an embedding

$$\begin{array}{ccc} G \hookrightarrow & \xrightarrow{f} & H \\ \downarrow f \cdot \sigma & & \downarrow \sigma \\ (f \cdot \sigma) \cdot G \hookrightarrow & \xrightarrow{\sigma \cdot f} & \sigma \cdot H \end{array}$$

Identity function

$$E \hookrightarrow E \xrightarrow{i_E} E$$

$\Downarrow \sigma$

Identity function

$$E \xrightarrow{i_E} E$$

$$\downarrow \sigma$$

$$\sigma.E$$

Identity function

$$E \xrightarrow{i_E} E$$

$$\begin{array}{ccc} i_E \cdot \sigma \left. \vphantom{\begin{array}{c} \downarrow \\ \downarrow \end{array}} \right\} & & \left. \vphantom{\begin{array}{c} \downarrow \\ \downarrow \end{array}} \right\} \sigma \\ \downarrow & & \downarrow \end{array}$$

$$(i_E \cdot \sigma) \cdot E \xrightarrow{\sigma \cdot i_E} \sigma \cdot E$$

Identity function

$$E \xrightarrow{i_E} E$$

$$\begin{array}{ccc}
 & & \\
 & \begin{array}{c} \left. \begin{array}{l} i_E \cdot \sigma \\ \sigma \end{array} \right\} \\ \downarrow \end{array} & & \begin{array}{c} \left. \right\} \\ \downarrow \end{array} \sigma \\
 & & \\
 (i_E \cdot \sigma) \cdot E & \begin{array}{c} \xrightarrow{i_{(\sigma \cdot E)}} \\ \xleftarrow{\sigma \cdot i_E} \end{array} & \sigma \cdot E
 \end{array}$$

Identity function

$$\begin{array}{ccc}
 E & \xrightarrow{i_E} & E \\
 \left. \begin{array}{c} \text{green} \\ \text{red} \end{array} \right\} i_E \cdot \sigma & & \left. \begin{array}{c} \text{black} \end{array} \right\} \sigma \\
 \left(i_E \cdot \sigma \right) \cdot E & \begin{array}{c} \xrightarrow{i_{(\sigma \cdot E)}} \\ \xrightarrow{\sigma \cdot i_E} \end{array} & \sigma \cdot E
 \end{array}$$

We assume that:

- $i_E \cdot \sigma = \sigma$
- $\sigma \cdot i_E = i_{(\sigma \cdot E)}$

Identity symmetry

$$E \xrightarrow{f} F$$

$$\varepsilon_F$$

Identity symmetry

$$E \xrightarrow{f} F$$

$$\varepsilon_F$$

$$\varepsilon_F \cdot F$$

Identity symmetry

$$E \xrightarrow{f} F$$

$$\begin{array}{ccc} f \cdot \varepsilon_F \left\{ \begin{array}{c} \text{wavy line} \\ \downarrow \end{array} \right. & & \left. \begin{array}{c} \text{wavy line} \\ \downarrow \end{array} \right\} \varepsilon_F \end{array}$$

$$(f \cdot \varepsilon_F) \cdot E \xrightarrow{\varepsilon_F \cdot f} \varepsilon_F \cdot F$$

Identity symmetry

$$E \xrightarrow{f} F$$

$$\begin{array}{ccc}
 f \cdot \varepsilon_F & \left. \vphantom{\begin{array}{c} f \cdot \varepsilon_F \\ \varepsilon_E \end{array}} \right\} & \varepsilon_E \\
 \downarrow & & \downarrow \\
 & & \varepsilon_F
 \end{array}$$

$$E = (f \cdot \varepsilon_F) \cdot E \xrightarrow{\varepsilon_F \cdot f} \varepsilon_F \cdot F = F$$

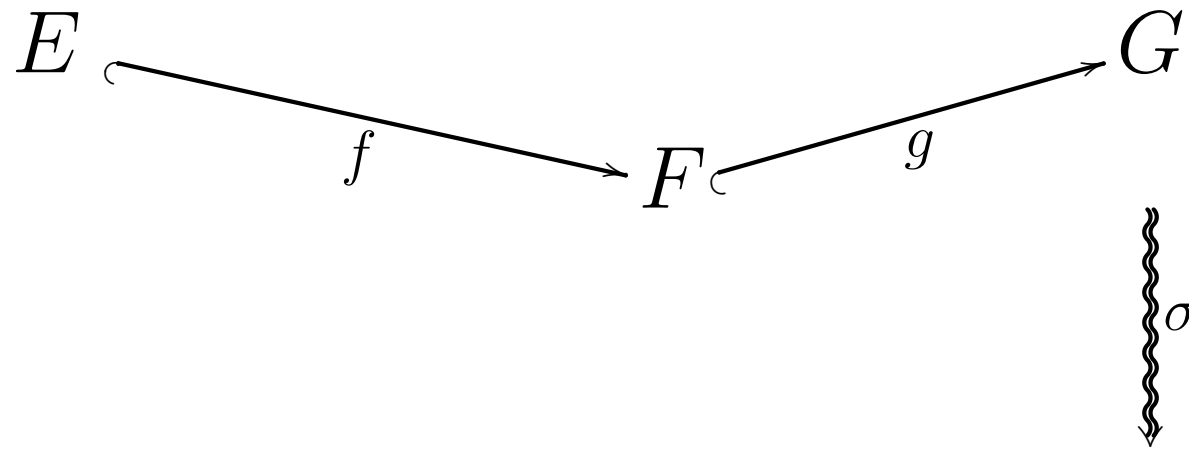
Identity symmetry

$$\begin{array}{ccc}
 E & \xrightarrow{f} & F \\
 \left. \begin{array}{c} f \cdot \varepsilon_F \\ \varepsilon_E \end{array} \right\} & & \left. \varepsilon_F \right\} \\
 \downarrow & & \downarrow \\
 E = (f \cdot \varepsilon_F) \cdot E & \xrightarrow[\varepsilon_F \cdot f]{f} & \varepsilon_F \cdot F = F
 \end{array}$$

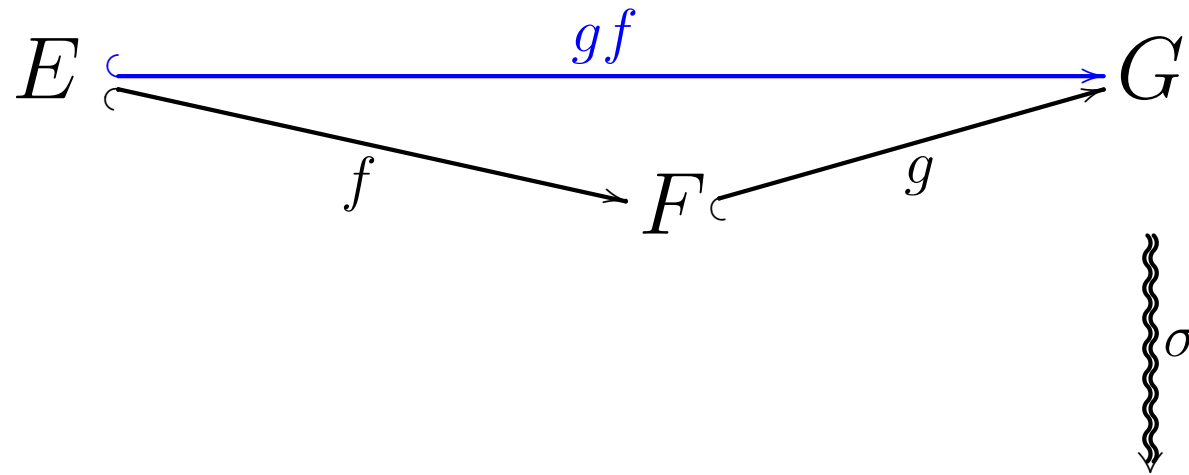
We assume that:

- $\varepsilon_F \cdot F = F$
- $f \cdot \varepsilon_F = \varepsilon_E$
- $\varepsilon_F \cdot f = f$

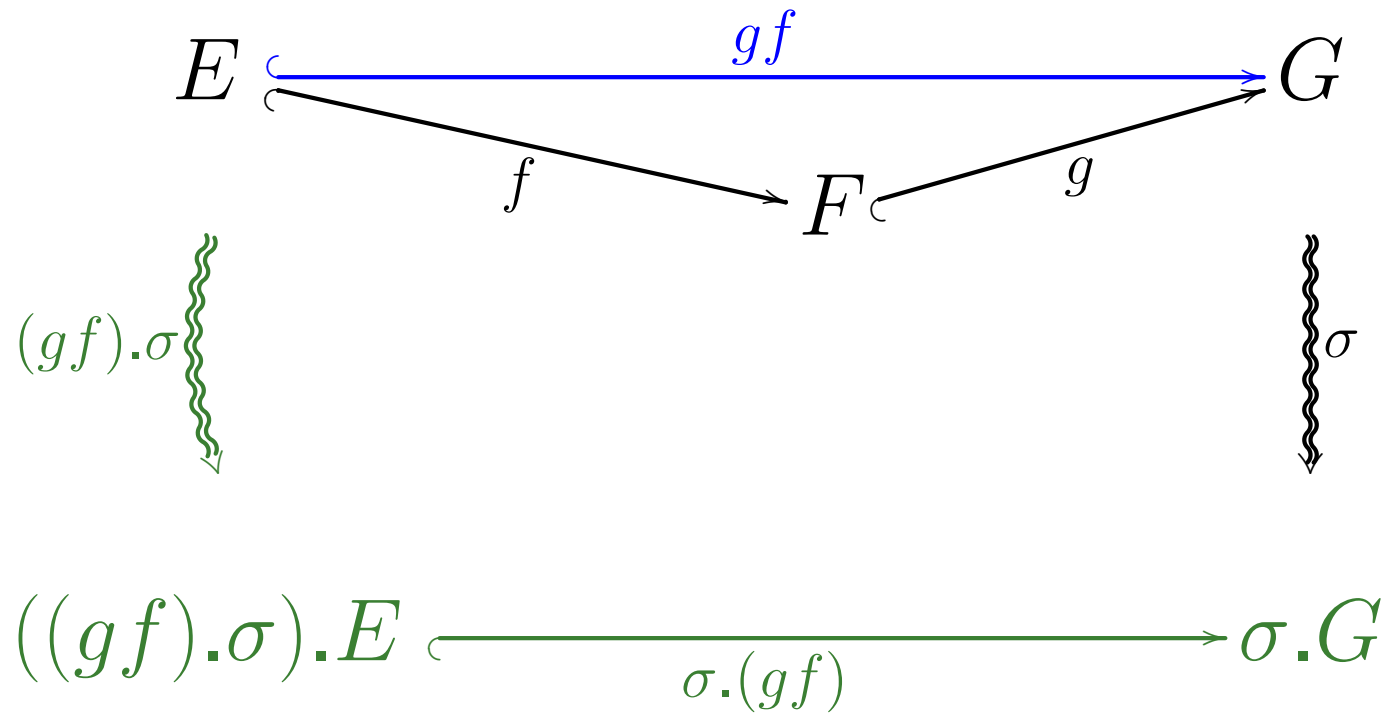
Composition of embeddings



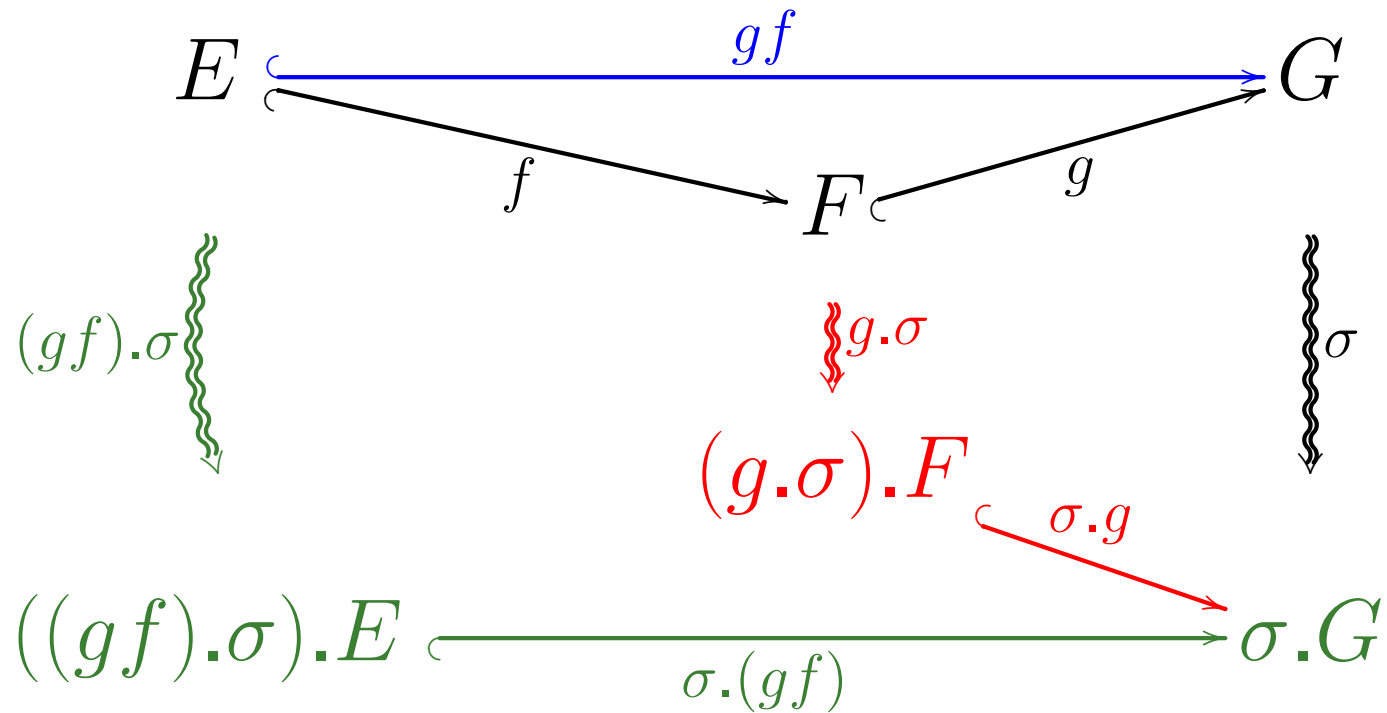
Composition of embeddings



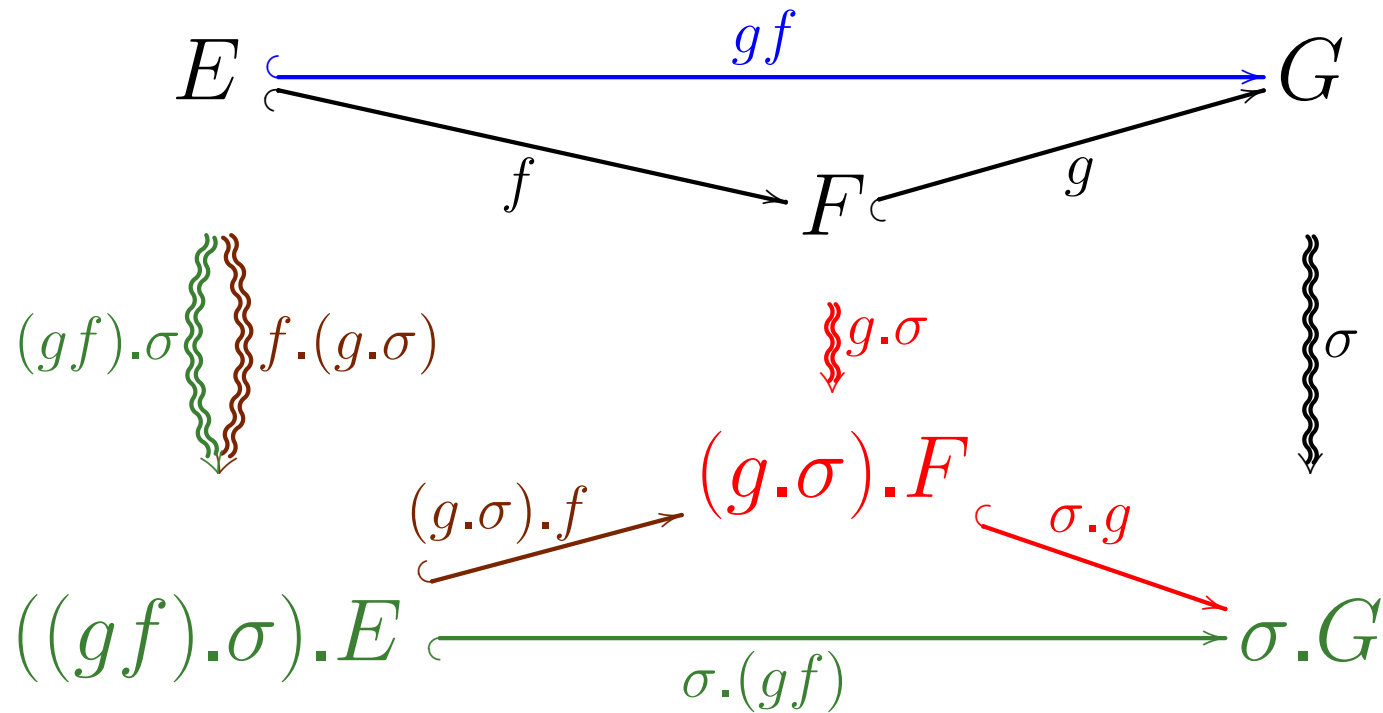
Composition of embeddings



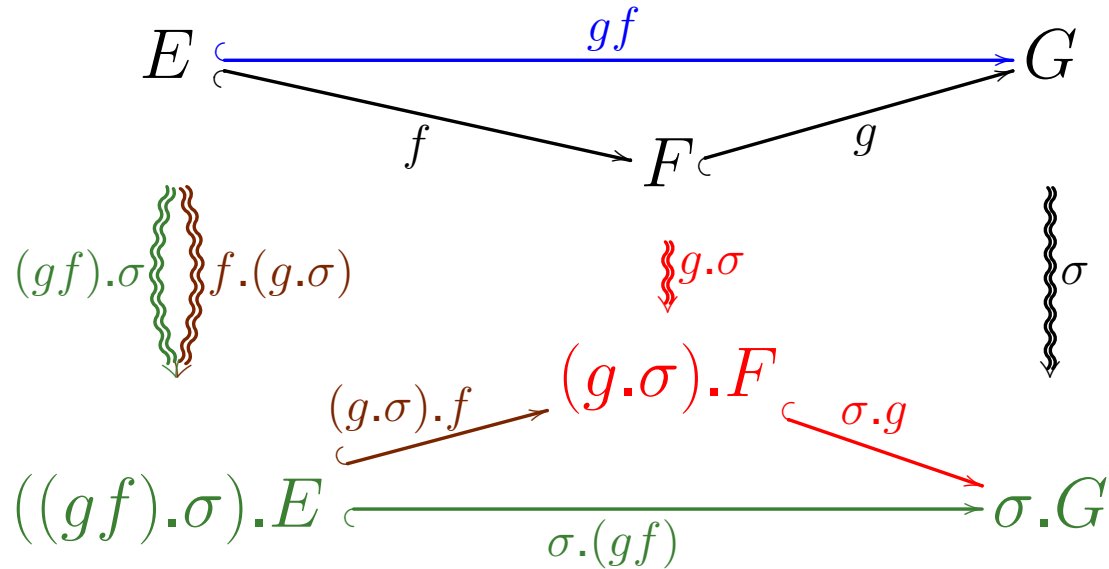
Composition of embeddings



Composition of embeddings



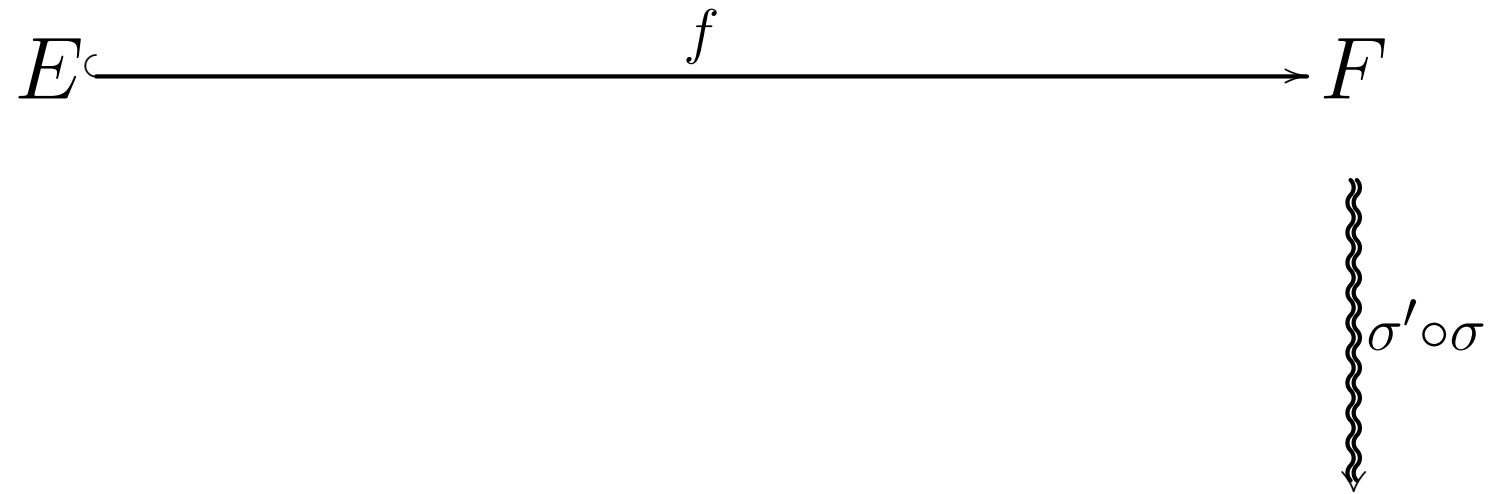
Composition of embeddings



We assume that:

- $(gf).\sigma = f.(g.\sigma)$
- $\sigma.(gf) = (\sigma.g)((g.\sigma).f)$

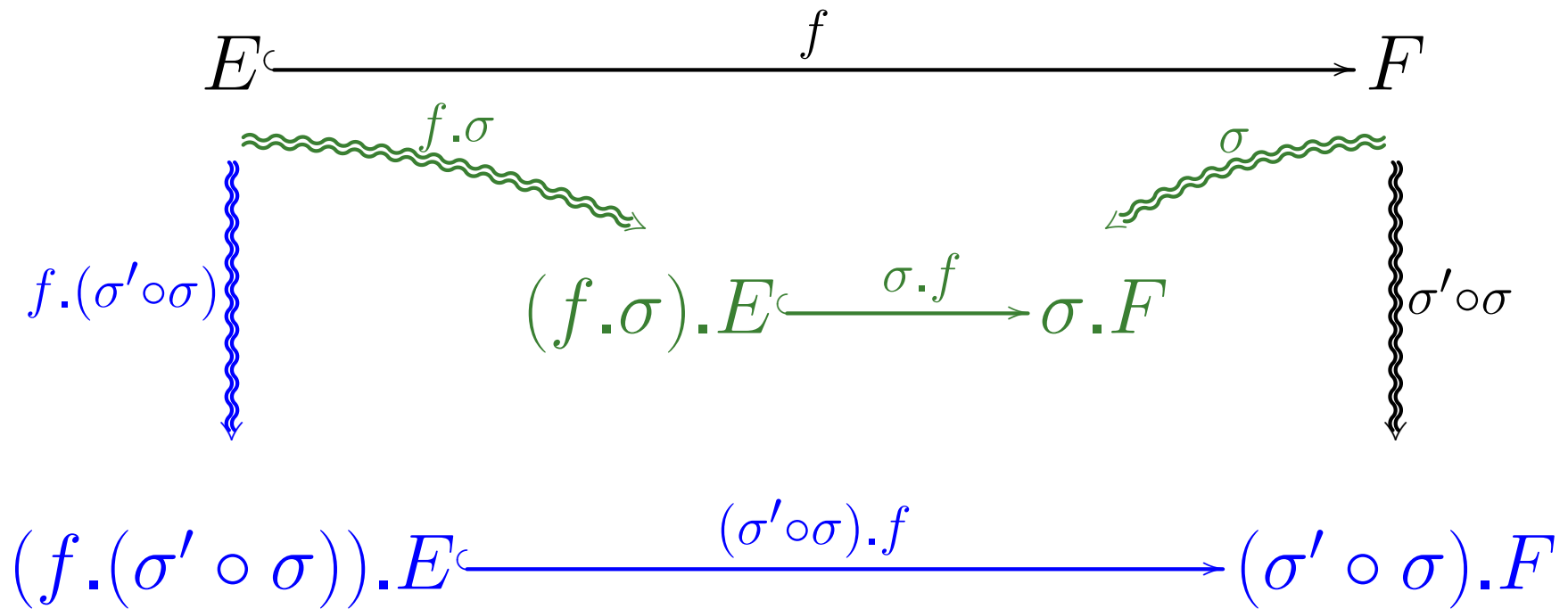
Product of transformations



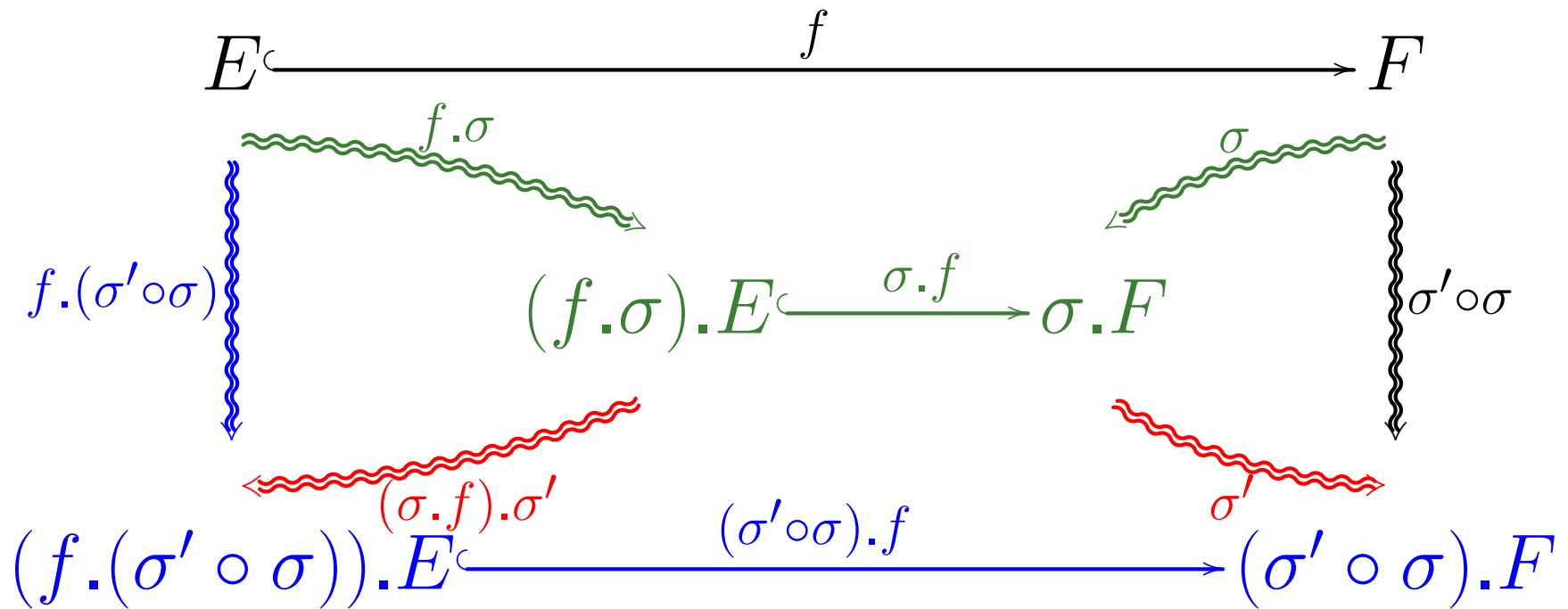
Product of transformations

$$\begin{array}{ccc} E & \xrightarrow{f} & F \\ \left. \begin{array}{c} \text{f.}(\sigma' \circ \sigma) \\ \downarrow \end{array} \right\} & & \left. \begin{array}{c} \downarrow \\ \sigma' \circ \sigma \end{array} \right\} \\ (f.(\sigma' \circ \sigma)).E & \xrightarrow{(\sigma' \circ \sigma).f} & (\sigma' \circ \sigma).F \end{array}$$

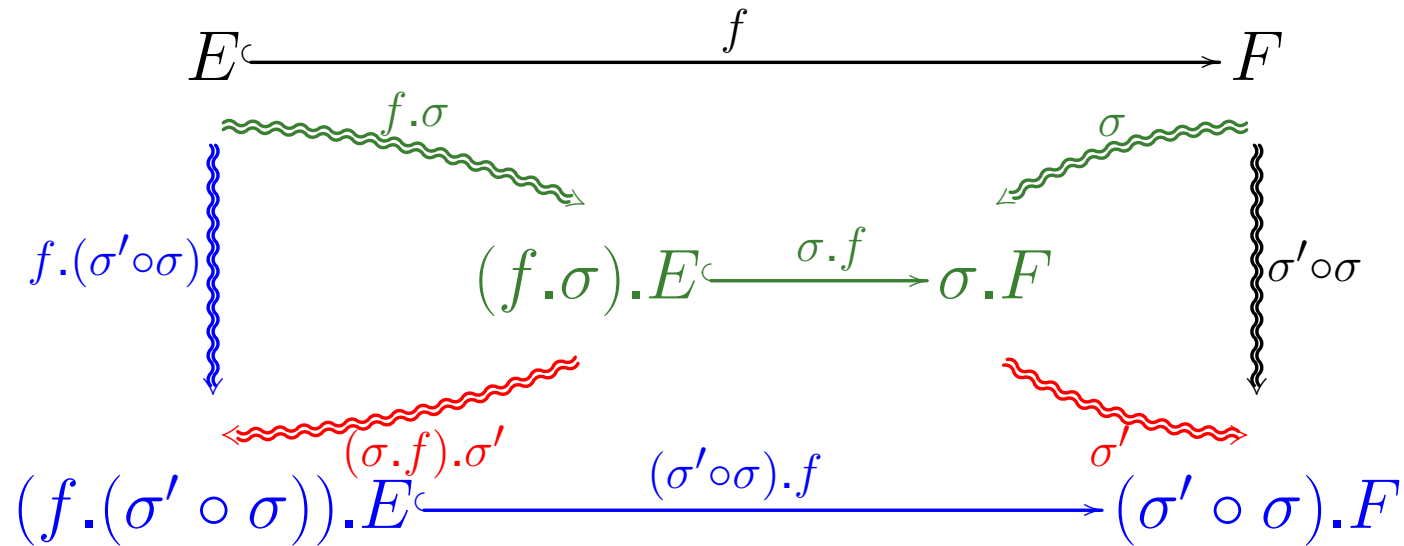
Product of transformations



Product of transformations



Product of transformations



We assume that:

- $(\sigma' \circ \sigma).F = \sigma'.(\sigma.F)$
- $f.(\sigma' \circ \sigma) = ((f.\sigma).\sigma') \circ (f.\sigma)$
- $(\sigma' \circ \sigma).f = \sigma'.(\sigma.f)$

Images of fully specified site graphs

We assume that for any site graph G and any transformation $\sigma \in \mathbb{G}_G$ the two following assertions are equivalent:

1. G is fully specified;
2. $\sigma.G$ is fully specified.

Images of partial embeddings

For any partial embedding $\phi : L \overset{f}{\hookrightarrow} D \overset{g}{\hookrightarrow} R$,

We assume that:

- if

$$\begin{cases} f \cdot \sigma_L = g \cdot \sigma_R \\ f \cdot \sigma'_L = g \cdot \sigma'_R \end{cases}$$

- then

$$f \cdot (\sigma_L \circ \sigma'_L) = g \cdot (\sigma_R \circ \sigma'_R),$$

for any $\sigma_L, \sigma'_L \in \mathbb{G}_L$, $\sigma_R, \sigma'_R \in \mathbb{G}_R$,

We consider:

$$\mathbb{G}_\phi \stackrel{\Delta}{=} \{(\sigma_L, \sigma_R) \in \mathbb{G}_L \times \mathbb{G}_R \mid f \cdot \sigma_L = g \cdot \sigma_R\}.$$

Images of rules

We assume that for any partial embedding $\phi : L \xleftrightarrow{f} D \xrightarrow{g} R$ and any (pair of) transformation(s) $(\sigma_L, \sigma_R) \in \mathbb{G}_\phi$ the two following assertions are equivalent:

1. ϕ is a rule;
2. $\sigma_L.L \xleftrightarrow{\sigma_L.f} (f.\sigma_L).D \xrightarrow{\sigma_R.g} \sigma_R.R$ is a rule.

Images of push-outs

Theorem 1 Let r be a rule, and $(\sigma_L, \sigma_R) \in \mathbb{G}_r$ be a pair of transformations. If the following diagram:

$$\begin{array}{ccc}
 L' & \xrightarrow{r} & R' \\
 h_L \uparrow & & \downarrow h_R \\
 L & \xrightarrow{r'} & R
 \end{array}$$

is a push-out, then the following diagram:

$$\begin{array}{ccc}
 \sigma_L.L' & \xrightarrow{(\sigma_L, \sigma_R).r} & \sigma_R.R' \\
 \sigma_L.h_L \uparrow & & \downarrow \sigma_R.h_R \\
 (h_L.\sigma_L).L & \xrightarrow{(h_L.\sigma_L, h_R.\sigma_R).r'} & (h_R.\sigma_R).R
 \end{array}$$

is a push-out as well.

Subgroups of transformations

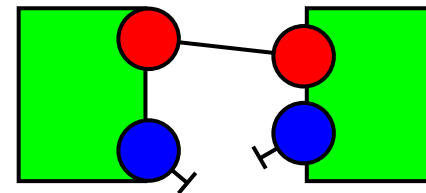
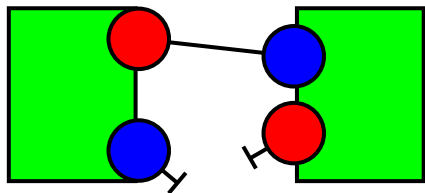
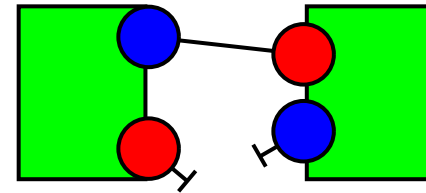
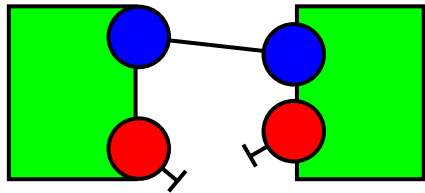
Theorem 2

If, for any embedding h between two site graphs G and H :

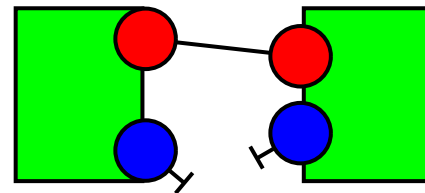
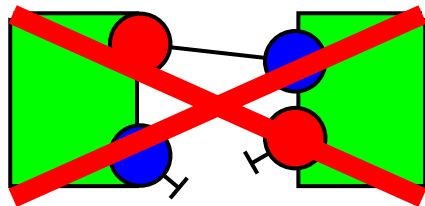
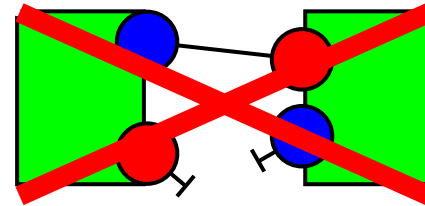
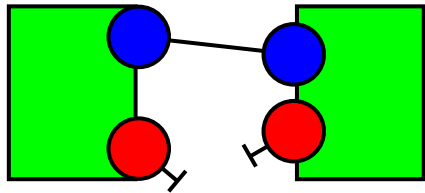
- we have a subset \mathbb{G}'_G of \mathbb{G}_G ;
- for any transformation $\sigma \in \mathbb{G}'_G$, $\mathbb{G}'_G = \mathbb{G}'_{(\sigma.G)}$;
- for any two σ, σ' transformations in \mathbb{G}'_G , $\sigma \circ \sigma' \in \mathbb{G}'_G$;
- for any transformation $\sigma \in \mathbb{G}'_H$, $h.\sigma \in \mathbb{G}'_G$;

then the groups (\mathbb{G}'_G) define a set of transformations.

Example: Heterogeneous site permutations



Example: Homogeneous site permutations



Overview

1. Context and motivations
2. Case study
3. Kappa semantics
4. **Symmetries in site-graphs**
 - (a) Groups of transformations
 - (b) **Action of the transformations**
5. Symmetric models
6. Conclusion

Group actions over site graphs

Let G, G' be two site graphs.

We write $G \approx_{\mathbb{G}} G'$ if and only if there exists $\sigma \in \mathbb{G}_G$ such that $G' = \sigma.G$.

The function:

$$\begin{cases} \mathbb{G}_G \times [G]_{\approx_{\mathbb{G}}} & \rightarrow [G]_{\approx_{\mathbb{G}}} \\ (\sigma, G) & \mapsto \sigma.G \end{cases}$$

is a group action.

That is to say:

- $\varepsilon.G = G$;
- $\sigma'.(\sigma.G) = (\sigma' \circ \sigma).G$.

Group actions over embeddings

Let f, f' be two embeddings.

We write $f \approx_{\mathbb{G}} f'$ if and only if there exists $\sigma \in \mathbb{G}_{\text{IM}(f)}$ such that $f' = \sigma.f$.

The function:

$$\begin{cases} \mathbb{G}_{\text{IM}(f)} \times [f]_{\approx_{\mathbb{G}}} & \rightarrow [f]_{\approx_{\mathbb{G}}} \\ (\sigma, f) & \mapsto \sigma.f \end{cases}$$

is a group action.

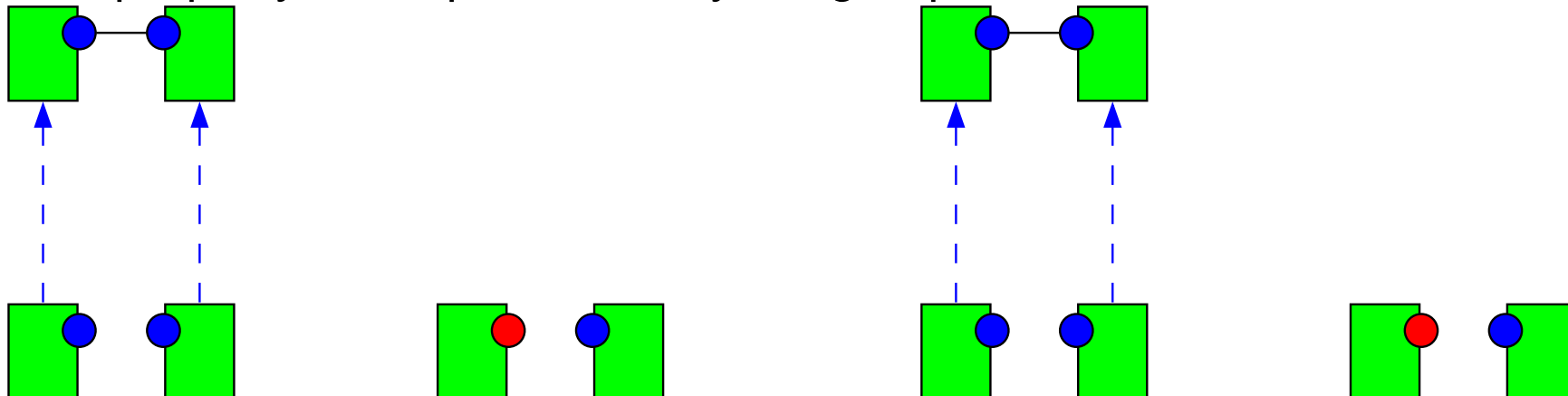
Compatible embeddings

An embedding f between two site graphs G and H is said compatible if and only if:

$$\mathbb{G}_G = \{f \cdot \sigma \mid \sigma \in \mathbb{G}_H\}$$

(that is to say that any transformation that can be applied to the domain of f can be extended to the image of f).

This property is not preserved by subgroups of transformations:



Heterogeneous permutations

Homogeneous permutations

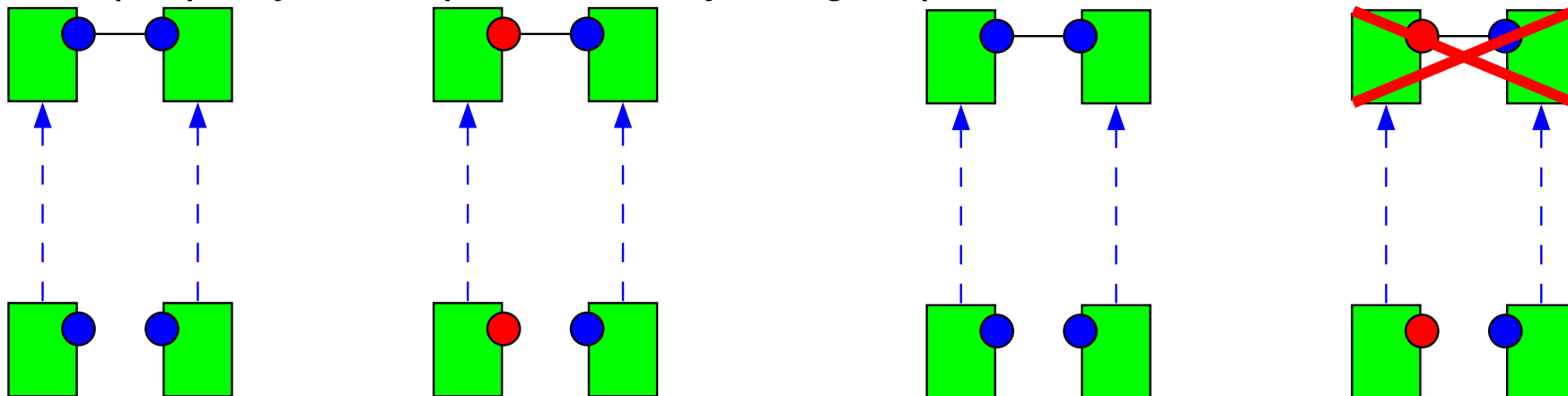
Compatible embeddings

An embedding f between two site graphs G and H is said compatible if and only if:

$$\mathbb{G}_G = \{f \cdot \sigma \mid \sigma \in \mathbb{G}_H\}$$

(that is to say that any transformation that can be applied to the domain of f can be extended to the image of f).

This property is not preserved by subgroups of transformations:



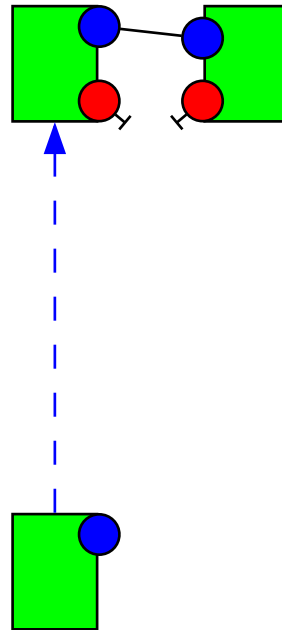
Heterogeneous permutations

Homogeneous permutations

Decomposition of transformations along an embedding

When f is an embedding between two site graphs G and H , we have:

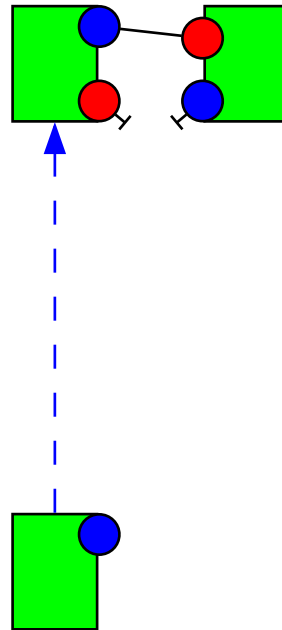
$$\mathbb{G}_H \approx \{\sigma \in \mathbb{G}_H \mid f.\sigma = \varepsilon_G\} \times \{h.\sigma \mid \sigma \in \mathbb{G}_H\}.$$



Decomposition of transformations along an embedding

When f is an embedding between two site graphs G and H , we have:

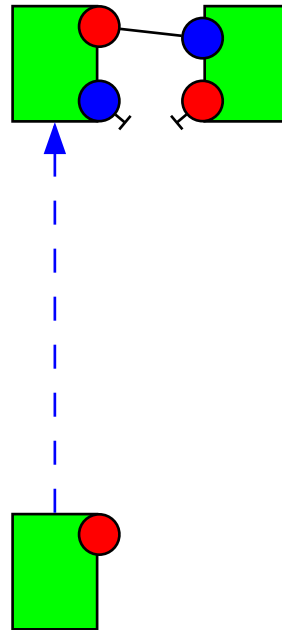
$$\mathbb{G}_H \approx \{\sigma \in \mathbb{G}_H \mid f.\sigma = \varepsilon_G\} \times \{h.\sigma \mid \sigma \in \mathbb{G}_H\}.$$



Decomposition of transformations along an embedding

When f is an embedding between two site graphs G and H , we have:

$$\mathbb{G}_H \approx \{\sigma \in \mathbb{G}_H \mid f.\sigma = \varepsilon_G\} \times \{h.\sigma \mid \sigma \in \mathbb{G}_H\}.$$



Images of isomorphisms

The image of an isomorphism is an isomorphism.

$$\begin{array}{ccc}
 \sigma_F.F & \xrightarrow{i_{\sigma_F.F}} & \sigma_F.F \\
 \searrow^{(f.\sigma_F).(f^{-1})} & & \nearrow^{\sigma_F.f} \\
 & (f.\sigma_F).E &
 \end{array}$$

The image of an automorphism may be not an automorphism.

Yet, for any site graph G , we have:

$$\text{Card}(G) = \text{Card}(\{\phi \mid \phi \in \text{Aut}(G)\}) \times \text{Card}(\{G' \mid G' \approx G \text{ and } G' \approx_{\mathbb{G}} G\}).$$

Group actions over rules

Let $r : L \xleftarrow{f} D \xrightarrow{g} R$ be a rule.

We define the symmetric of r by a symmetry $(\sigma_L, \sigma_R) \in \mathbb{G}_r$ as follows:

$$(\sigma_L, \sigma_R).r \triangleq \sigma_L.L \xleftarrow{\sigma_L.f} (f.\sigma_L).D \xrightarrow{\sigma_R.g} \sigma_R.R$$

We write $r \approx_{\mathbb{G}} r'$ if and only if there exists $\sigma \in \mathbb{G}_r$ such that $r' = \sigma.r$.

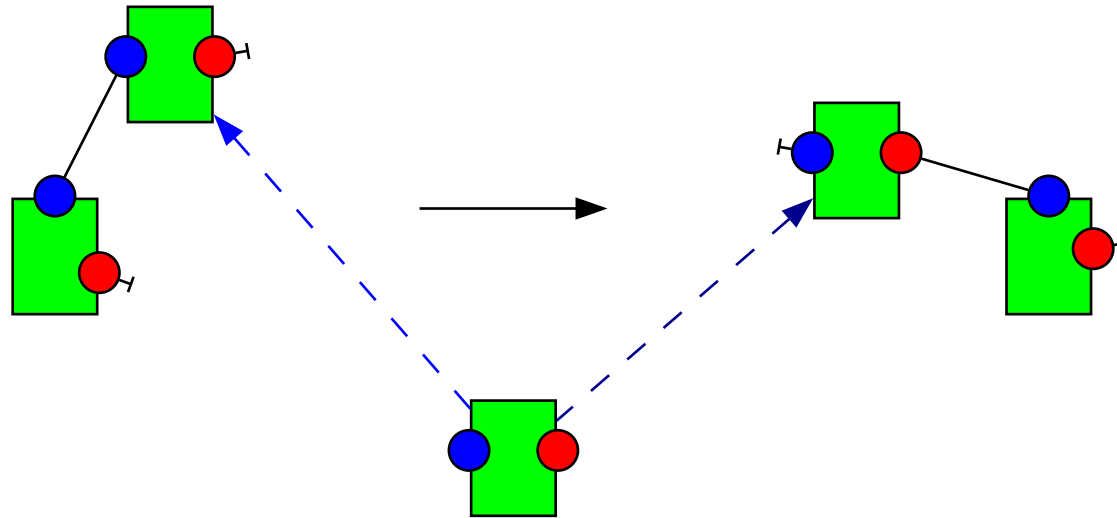
Then:

- \mathbb{G}_r is a group.
- the groups \mathbb{G}_r and $\mathbb{G}_{\sigma.r}$ are the same, for any symmetry $\sigma \in \mathbb{G}_r$.
- The function:

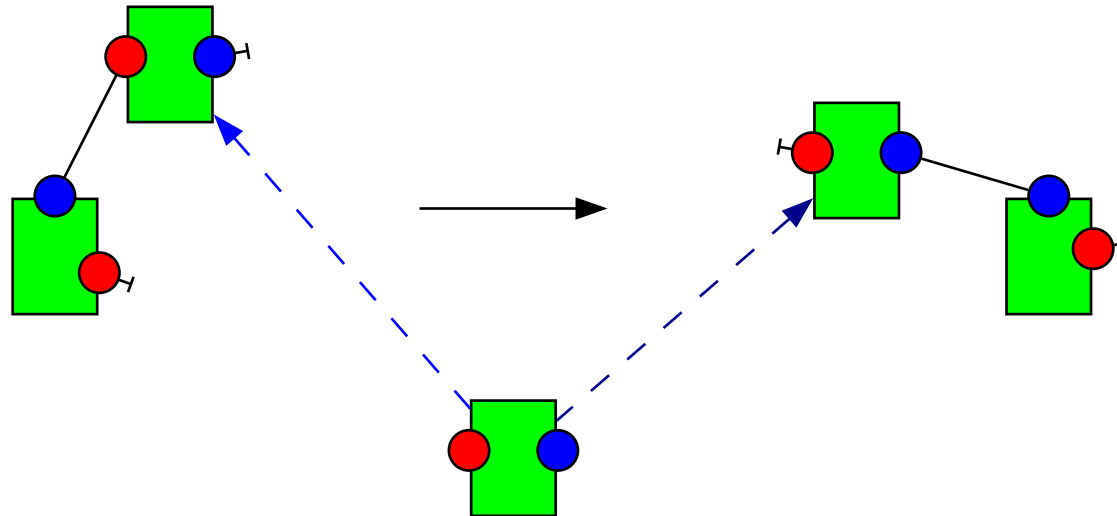
$$\begin{cases} \mathbb{G}_r \times [r]_{\approx_{\mathbb{G}}} & \rightarrow [r]_{\approx_{\mathbb{G}}} \\ (\sigma, r) & \mapsto \sigma.r. \end{cases}$$

is a group action.

Decomposition of the group of transformations over a rule

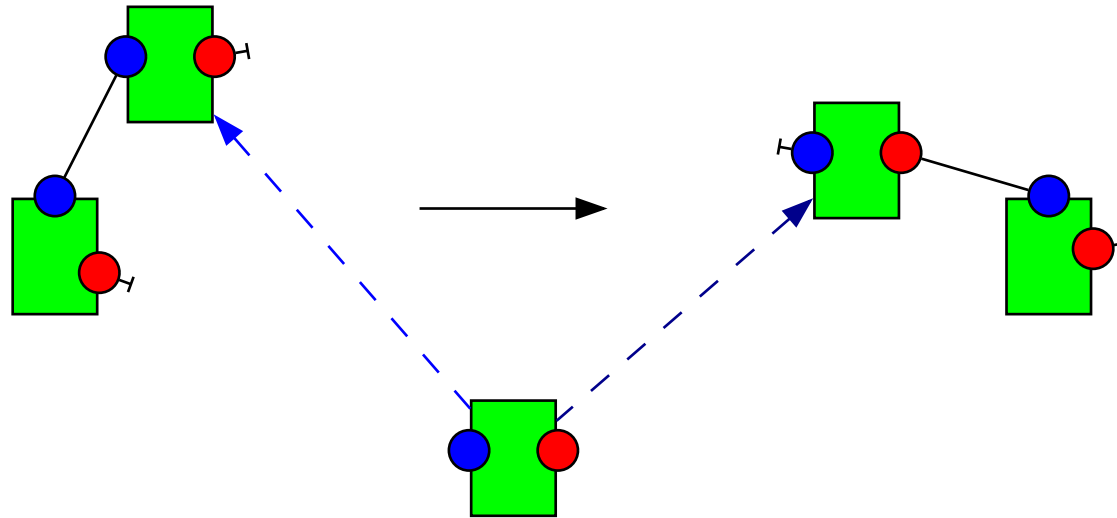


Decomposition of the group of transformations over a rule

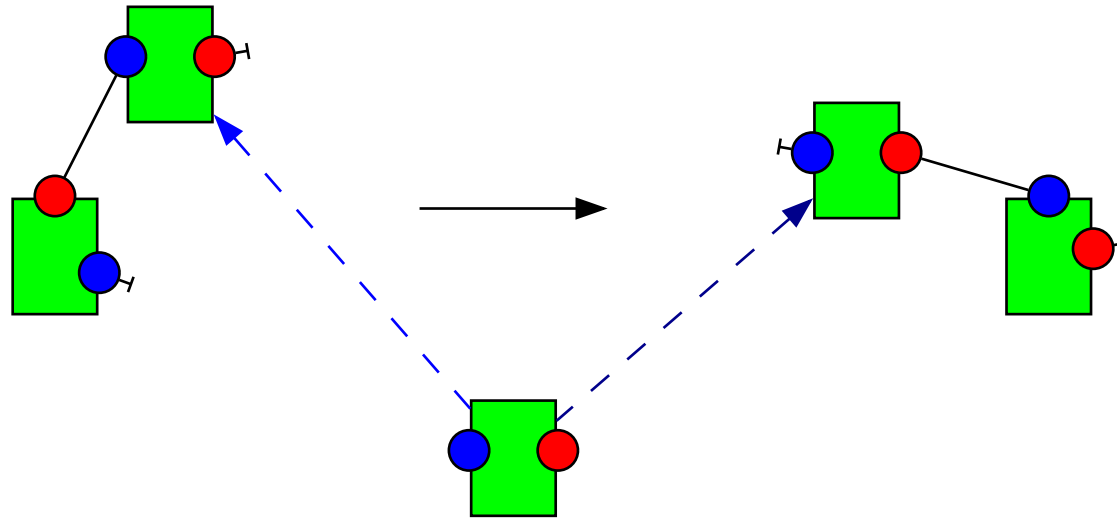


Some transformations operate on the domain of the rule.

Decomposition of the group of transformations over a rule

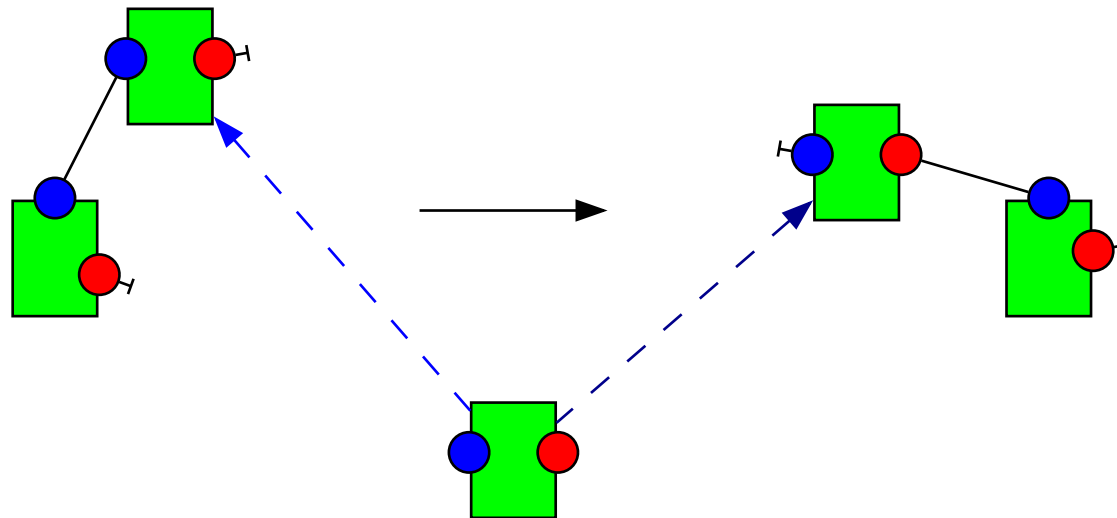


Decomposition of the group of transformations over a rule

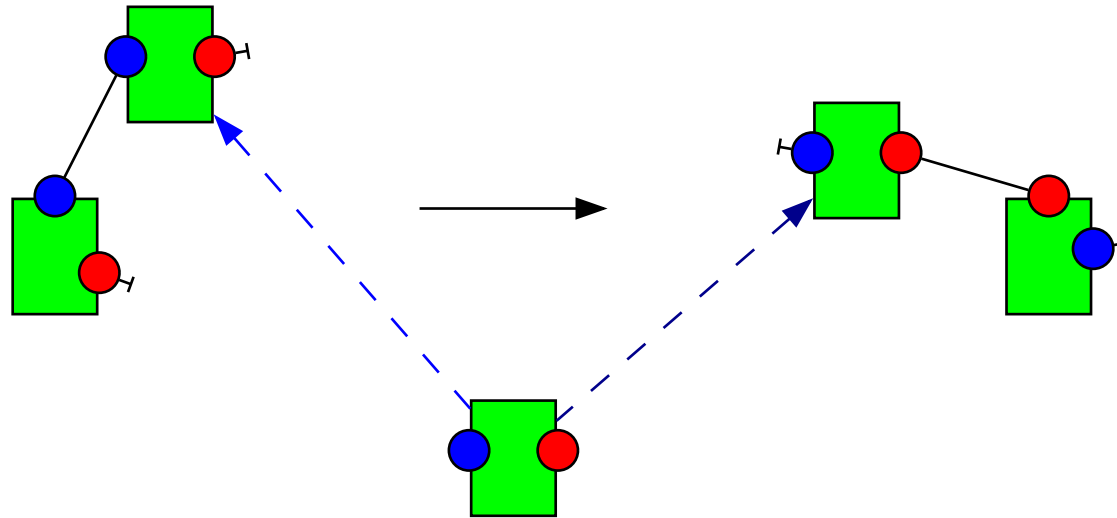


Some transformations operate on degraded agents.

Decomposition of the group of transformations over a rule



Decomposition of the group of transformations over a rule



Some transformations operate on created agents.

Decomposition of the group of transformations over a rule

When $r : L \xleftarrow{f} D \xrightarrow{g} R$ is a rule,
we have:

$$\mathbb{G}_r \approx \{\sigma \in \mathbb{G}_L \mid f.\sigma = \varepsilon_D\} \times \{\sigma \mid \exists(\sigma_L, \sigma_R) \in \mathbb{G}_r, \sigma = f.\sigma_L = f.\sigma_R\} \times \{\sigma \in \mathbb{G}_R \mid g.\sigma = \varepsilon_D\}$$

Symmetries distribute over:

1. the ones on removed agents;
2. the ones on new agents;
3. the ones on the domain which are compatible with rule.

Group actions over push-out

Theorem 3 Let r be a rule. The function which maps each pair of transformations $(\sigma_L, \sigma_R) \in \mathbb{G}_r$ and each push-out of the form:

$$\begin{array}{ccc} L' & \xrightarrow{r'} & R' \\ h_L \uparrow & & \downarrow h_R \\ L & \xrightarrow{r''} & R \end{array}$$

with $r' \approx_{\mathbb{G}} r$, to the push-out:

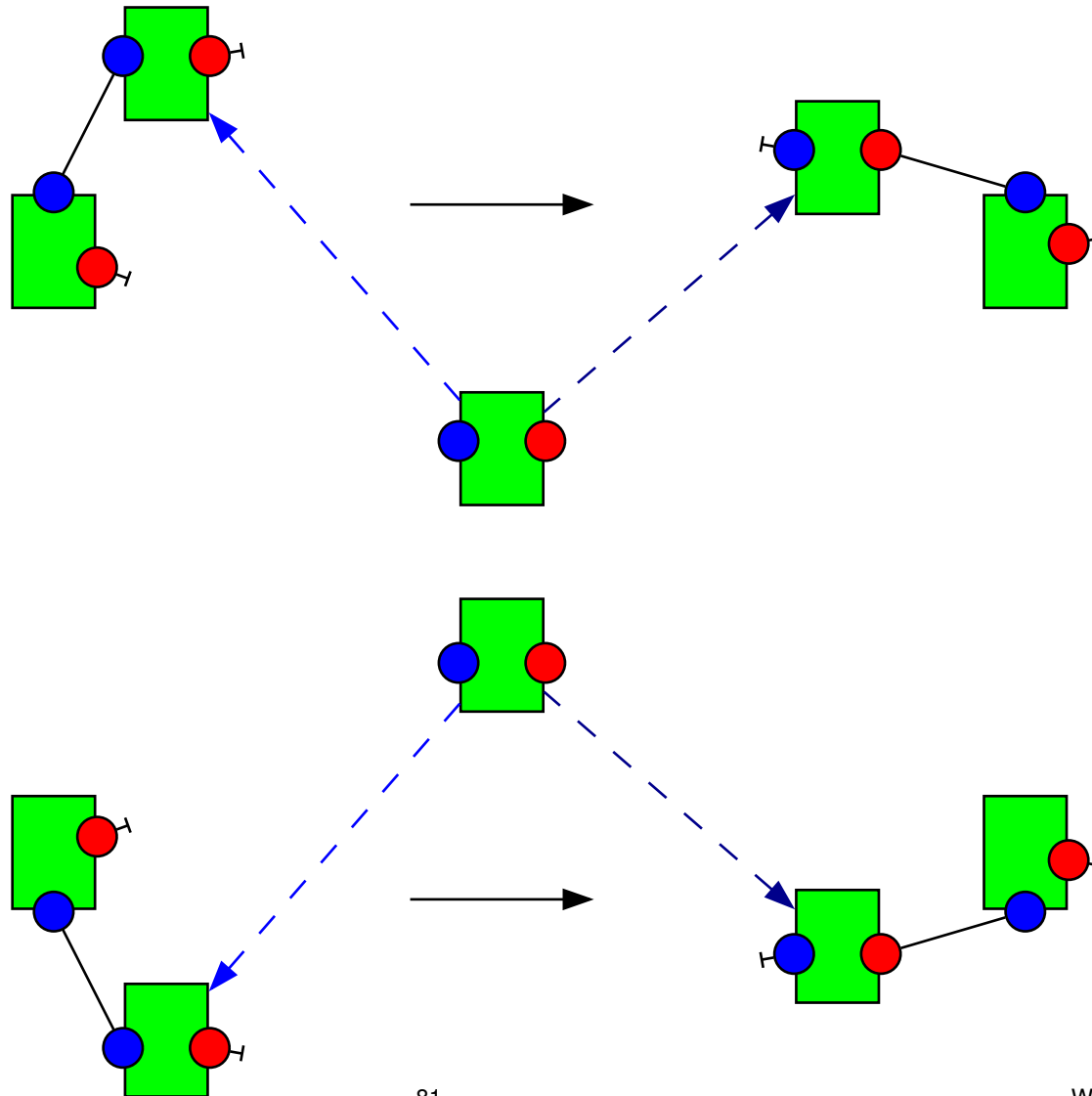
$$\begin{array}{ccc} \sigma_L.L' & \xrightarrow{(\sigma_L, \sigma_R).r'} & \sigma_R.R' \\ \sigma_L.h_L \uparrow & & \downarrow \sigma_R.h_R \\ (h_L.\sigma_L).L & \xrightarrow{(h_L.\sigma_L, h_R.\sigma_R).r''} & (h_R.\sigma_R).R \end{array}$$

is a group action.

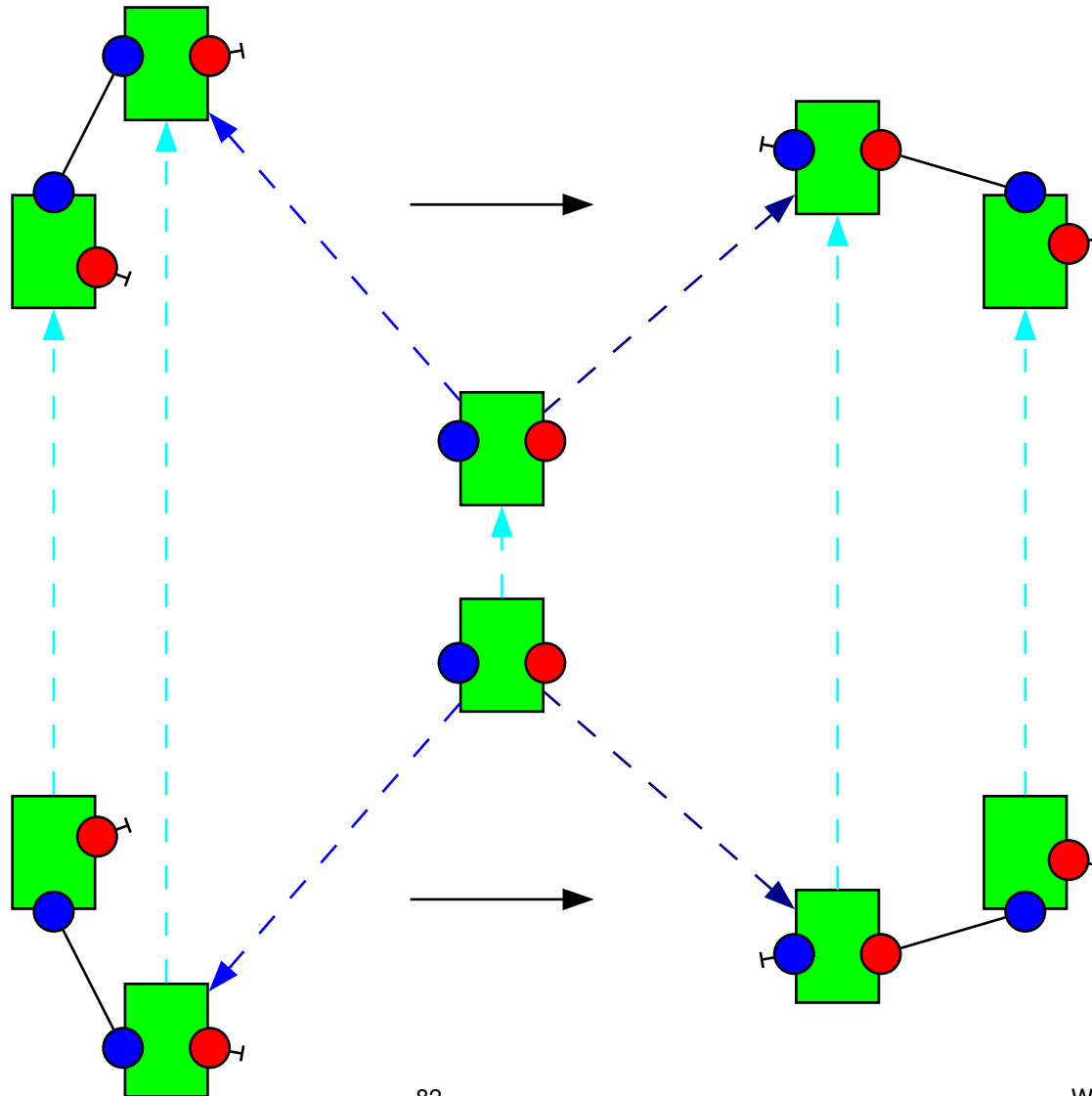
Overview

1. Context and motivations
2. Case study
3. Kappa semantics
4. Symmetries in site-graphs
5. **Symmetric models**
 - (a) Symmetries among set of rules
 - (b) Induced bisimulations
6. Conclusion

Isomorphic rules



Isomorphic rules



Symmetric model

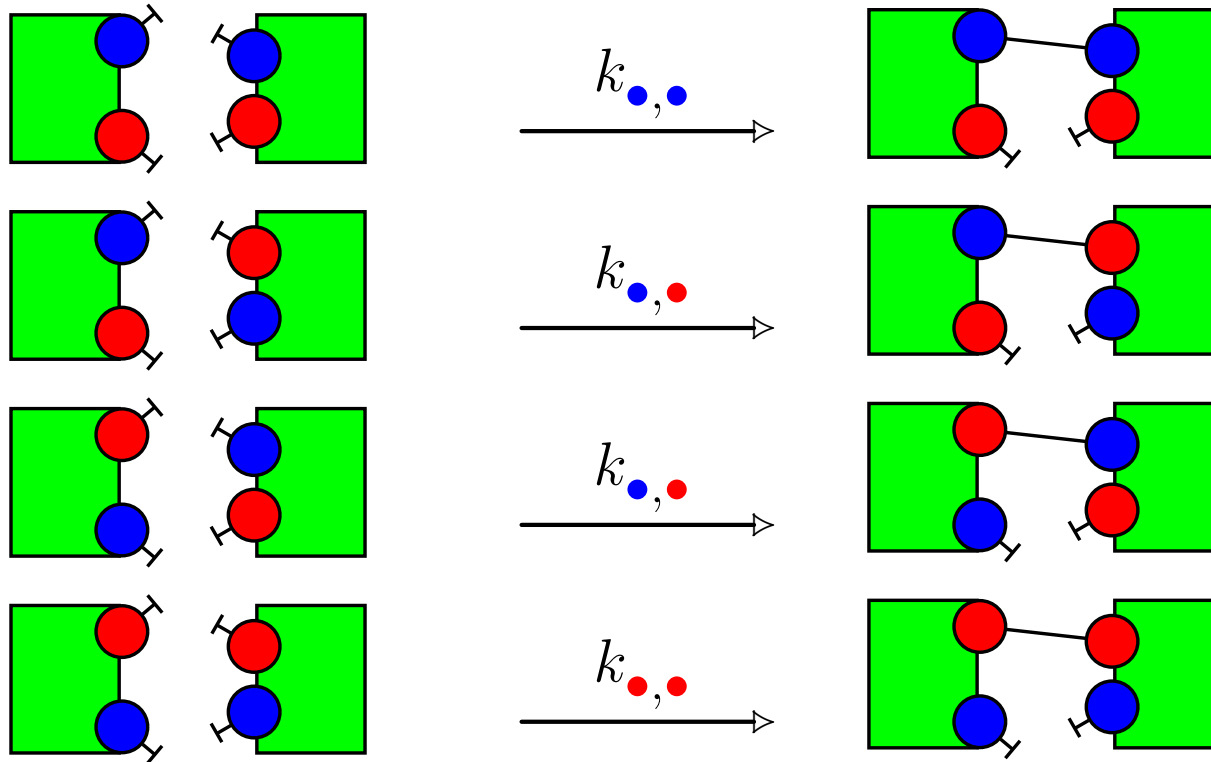
We assume that the model contains at most one rule per isomorphism class.

A model is \mathbb{G} -symmetric if and only if:

- for any rule r in the model and any pair of symmetries $\sigma \in \mathbb{G}_r$, there is (unique) a rule r' in the model that is isomorphic to the rule $\sigma.r$.
- and, with the same notations, we have $g(r) = g(r')$ where:

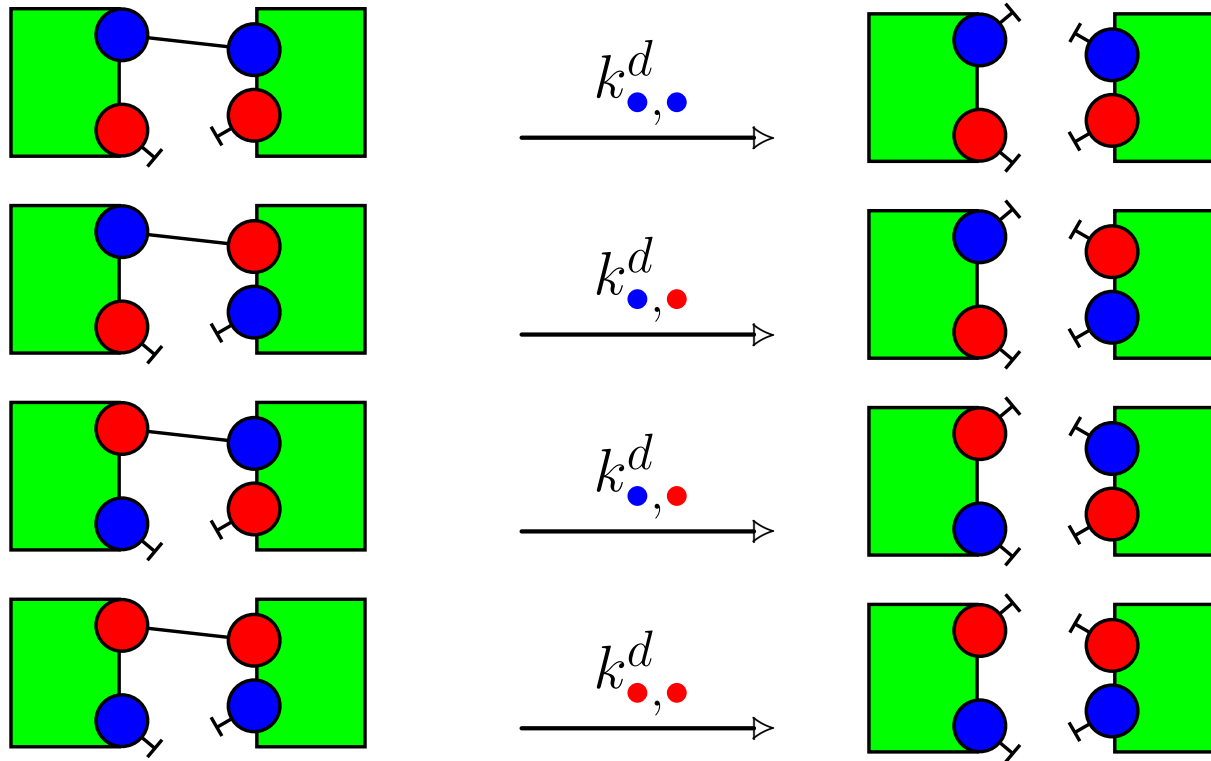
$$g(r) \triangleq \frac{k(r)}{\text{card}(\{\sigma \in \mathbb{G}_r \mid \sigma.r \approx r\}) \text{card}(\text{Aut}(\text{lhs}(r)))}$$

Binding rules



$$\frac{k_{\bullet, \bullet}}{1 \cdot 2} = \frac{k_{\bullet, \bullet}}{1 \cdot 2} = \frac{k_{\bullet, \bullet}}{2 \cdot 2}$$

Unbinding rules



$$\frac{k_{\bullet, \bullet}^d}{1 \cdot 2} = \frac{k_{\bullet, \bullet}^d}{1 \cdot 2} = \frac{k_{\bullet, \bullet}^d}{2 \cdot 1}$$

Overview

1. Context and motivations
2. Case study
3. Kappa semantics
4. Symmetries in site-graphs
5. **Symmetric models**
 - (a) Symmetries among set of rules
 - (b) **Induced bisimulations**
6. Conclusion

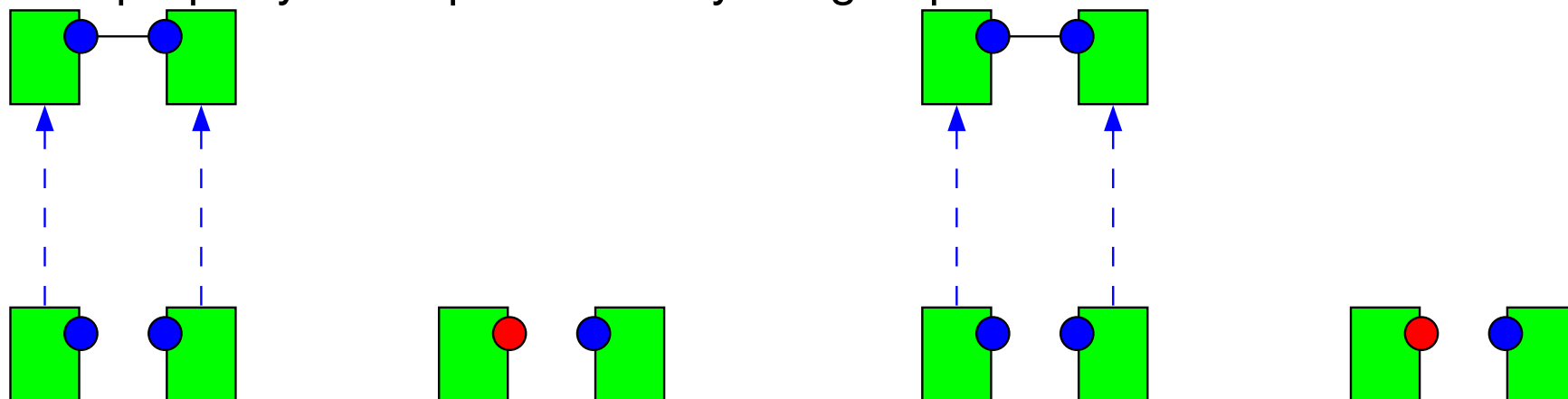
Compatible embeddings (reminders)

An embedding f between two site graphs G and H is said compatible if and only if:

$$\mathbb{G}_G = \{f \cdot \sigma \mid \sigma \in \mathbb{G}_H\}$$

(that is to say that any transformation that can be applied to the domain of f can be extended to the image of f).

This property is not preserved by subgroups of transformations:



Heterogeneous permutations

Homogeneous permutations

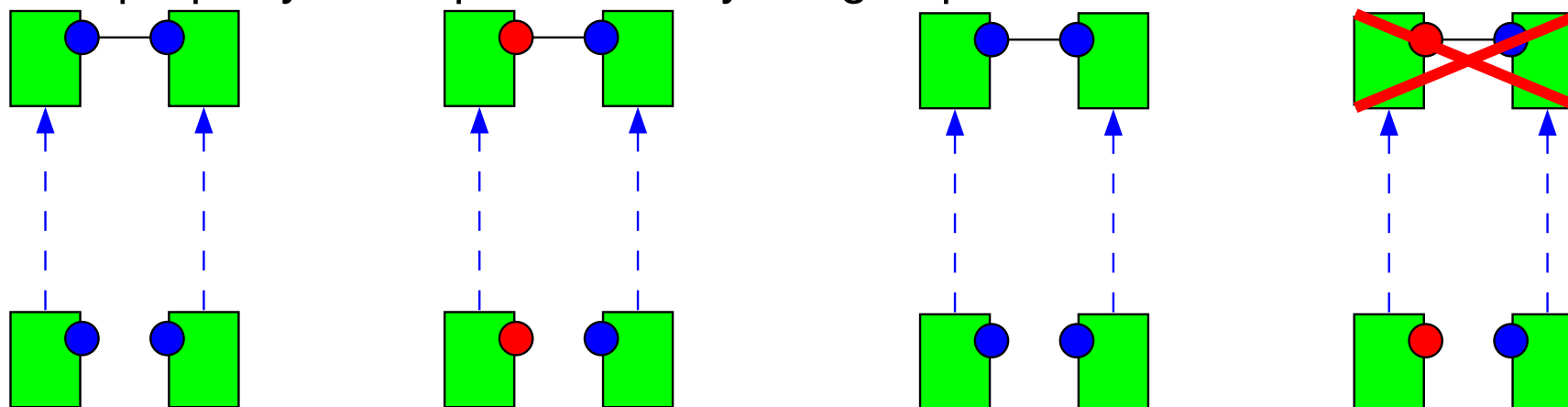
Compatible embeddings (reminders)

An embedding f between two site graphs G and H is said compatible if and only if:

$$\mathbb{G}_G = \{f \cdot \sigma \mid \sigma \in \mathbb{G}_H\}$$

(that is to say that any transformation that can be applied to the domain of f can be extended to the image of f).

This property is not preserved by subgroups of transformations:

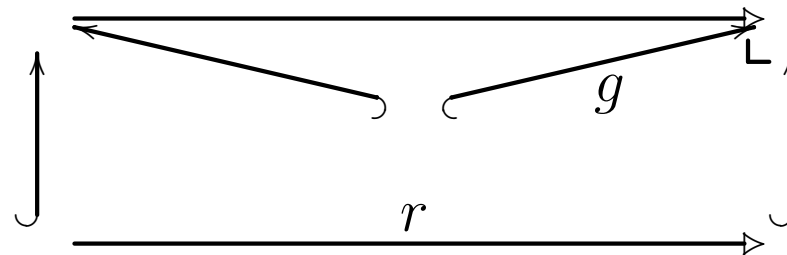


Heterogeneous permutations

Homogeneous permutations

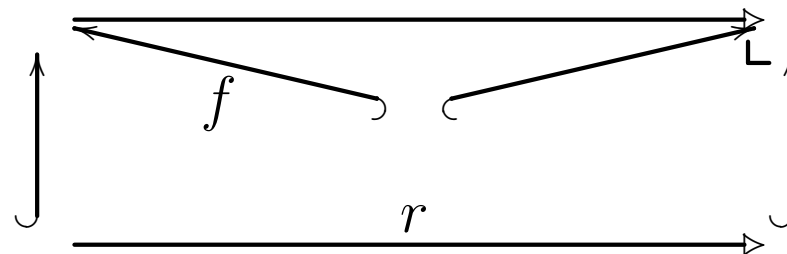
Compatible rules

We say that a rule r is forward-compatible if and only if, for any push-out of the following form:



the embedding g is compatible.

We say that a rule r is backward-compatible if and only if, for any push-out of the following form:



the embedding f is compatible.

Lumping states

We say that two states $q, q' \in \mathcal{Q}$ are isomorphic if and only if there exist $M \in q$ and $M' \in q'$ such that $M \approx_{\mathbb{G}} M'$.

In such a case, we write $q \approx_{\mathbb{G}} q'$.
 $\approx_{\mathbb{G}}$ is an equivalence relation.

Weighted flow

Let $X, X' \subseteq \mathcal{Q}$ and $Y \subseteq \mathcal{L}$.

Let ω be a function from \mathcal{Q} to \mathbb{R}^+ .

We define the flow from X to X' via Y , weighted by the reward function ω by:

$$\text{FLOW}_{\omega}(X, Y, X') \triangleq \sum_{q \in X, q' \in X', \lambda \in Y, q \xrightarrow{\lambda} q'} \omega(q) \text{RATE}(\lambda)$$

Forward bisimulation

Theorem 4 Let $q, q', q'' \in \mathcal{Q}$ such that $q \approx_{\mathbb{G}} q'$. Let $\lambda \in \mathcal{L}$.

If the model is symmetric and if the rules of the models are forward-compatible, then the following equality holds:

$$\text{FLOW}_{\omega} \left(\{q\}, [\lambda]_{\approx_{\mathbb{G}}}, [q'']_{\approx_{\mathbb{G}}} \right) = \text{FLOW}_{\omega} \left(\{q'\}, [\lambda]_{\approx_{\mathbb{G}}}, [q'']_{\approx_{\mathbb{G}}} \right),$$

with $\omega(q_1) = 1$ for any $q_1 \in \mathcal{Q}$.

Backward bisimulation (DTMC)

Theorem 5 Let $q, q', q'' \in \mathcal{Q}$ such that $q' \approx_{\mathbb{G}} q''$. Let $\lambda \in \mathcal{L}$.

If the model is symmetric and if the rules of the models are backward-compatible, then the following equality holds:

$$\omega(q'') \text{FLOW}_{\omega} \left([q]_{\approx_{\mathbb{G}}}, [\lambda]_{\approx_{\mathbb{G}}}, \{q'\} \right) = \omega(q') \text{FLOW}_{\omega} \left([q]_{\approx_{\mathbb{G}}}, [\lambda]_{\approx_{\mathbb{G}}}, \{q''\} \right),$$

with $\omega(q_1) \triangleq \frac{1}{\text{card}(\text{Aut}(q))}$, for any $q_1 \in \mathcal{Q}$.

Backward bisimulation (CTMC)

Theorem 6 Let $q, q', q'' \in \mathcal{Q}$ such that $q' \approx_{\mathbb{G}} q''$. Let $\lambda \in \mathcal{L}$.

If the model is symmetric and if the rules of the models are both forward- and backward-compatible,

then the following equalities holds:

1. $\text{FLOW}_{\omega}(\{q'\}, \mathcal{Q}, \mathcal{L}) = \text{FLOW}_{\omega}(\{q''\}, \mathcal{Q}, \mathcal{L})$,
with $\omega(q_1) = 1$ for any $q_1 \in \mathcal{Q}$;

2. $\omega(q'') \text{FLOW}_{\omega}([q]_{\approx_{\mathbb{G}}}, [\lambda]_{\approx_{\mathbb{G}}}, \{q'\}) = \omega(q') \text{FLOW}_{\omega}([q]_{\approx_{\mathbb{G}}}, [\lambda]_{\approx_{\mathbb{G}}}, \{q''\})$,

with $\omega(q_1) \stackrel{\Delta}{=} \frac{1}{\text{card}(\text{Aut}(q))}$, for any $q_1 \in \mathcal{Q}$.

Overview

1. Context and motivations
2. Case study
3. Kappa semantics
4. Symmetries in site-graphs
5. Symmetric models
6. **Conclusion**

Conclusion

A fully algebraic framework to infer and use symmetries in Kappa;

- Compatible with the SPO semantics (see [\[FSTTCS'2012\]](#));
- Can handle side-effects (see the paper);
- Induces forward and/or back and forth bisimulations;
- Can be applied to discover model reductions for the qualitative semantics, the ODEs semantics, and the stochastic semantics [\[MFPSXXVII\]](#);
- Can be combined with other exact model reductions [\[MFPSXXVI\]](#).

This framework is cleaner and more general than the process algebra based one [\[MFPSXXVII\]](#).

[Camporesi et al.](#), Combining model reductions. MFPS XXVI (2010)

[Camporesi et al.](#), Formal reduction of rule-based models, MFPS XXVII (2011)

[Danos et al.](#), Rewriting and Pathway Reconstruction for Rule-Based Models, FSTTCS 2012

Future work

- Investigate which specific classes of symmetries and which specific classes of rules ensure that rules are forward and/or backward compatible with the symmetries;
- Check the compatibility with the DPO (Double Push-Out) semantics;
- Design approximate symmetries using bisimulation metrics (ask Norman Ferns).



“AbstractCell”
(2009-2013)



“Big Mechanism” (2014-2017)
“CwC” (2015-2018)



“TGF β SysBio”
(2015-2018)