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

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Overview

1. Context and motivations
2. Case study
3. Kappa semantics
4. Symmetries in site-graphs
5. Symmetric models
6. Conclusion
Bridging the gap between...
Site-graphs rewriting

- a language close to knowledge representation;
- rules are easy to update;
- a compact description of models.
Choices of semantics

interaction map

Markov chain

ordinary differential equations

Markov chain

\[
\begin{align*}
\frac{dx_1}{dt} &= -k_1 \cdot x_1 \cdot x_2 + k_{-1} \cdot x_3 \\
\frac{dx_2}{dt} &= -k_1 \cdot x_1 \cdot x_2 + k_{-1} \cdot x_3 \\
\frac{dx_3}{dt} &= k_1 \cdot x_1 \cdot x_2 - k_{-1} \cdot x_3 + 2 \cdot k_2 \cdot x_3 \cdot x_3 - k_{-2} \cdot x_4 \\
\frac{dx_4}{dt} &= k_2 \cdot x_3^2 - k_2 \cdot x_4 + \frac{x_4 \cdot x_5}{x_4 + x_5} - k_3 \cdot x_4 - k_{-3} \cdot x_5 \\
\frac{dx_5}{dt} &= \ldots \quad i \\
\frac{dx_n}{dt} &= -k_1 \cdot x_1 \cdot c_2 + k_{-1} \cdot x_3
\end{align*}
\]
Complexity walls

![Graph showing different complexity levels with number of instances per molecular species and number of molecular species on axes.](image-url)
Abstractions offer different perspectives on models

concrete semantics

causal traces

information flow

exact projection of the ODE semantics
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!!!.

\[ \text{Diagram showing symmetrical connections and structures.} \]
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
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   (a) Symmetric model with symmetric initial state
   (b) Symmetric model with non-symmetric initial state
   (c) Non-symmetric model
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Case study
State distribution

State distribution VS Time

\[
P(q_0) = 1
\]

with:

\[
\begin{align*}
k_{\bullet, \bullet} &= k_{\bullet, \circ} = 1 \\
 k_{\circ, \bullet} &= k_{\circ, \bullet}^d = k_{\circ, \circ}^d = k_{\circ, \circ}^d = 2 \\
P(q_0 | t = 0) &= 1
\end{align*}
\]
Lumpability

Whenever:

\[
\begin{align*}
2k_{a,b} &= 2k_{c,d} = k_{a,b} \\
k_{a,b} &= k_{c,d} = k_{c,d}
\end{align*}
\]

We can lump the system.
Lumped system
Macrostate distribution

\[
\begin{align*}
Q_0 & : \times 6 \\
Q_1 & : \times 4 \times 1 \\
Q_2 & : \times 2 \times 2 \\
Q_3 & : \times 3
\end{align*}
\]

Lumped system

with:

\[
\begin{align*}
k_\cdot & = 1 \\
k_\cdot^d & = 2 \\
P(q_0 | t = 0) & = 1
\end{align*}
\]
Probability ratios

\[ q_1 : \quad \times 4 \quad \times 1 \]

\[ q_2 : \quad \times 4 \quad \times 1 \]

\[ q_3 : \quad \times 4 \quad \times 1 \]

\[ q_4 : \quad \times 2 \quad \times 2 \]

\[ q_5 : \quad \times 2 \quad \times 2 \]

Probability ratios VS Time

\[ P(q_2)/P(q_1) \]

\[ P(q_3)/P(q_1) \]

\[ P(q_5)/P(q_4) \]

with:

\[
\begin{align*}
&k_{\cdot,\cdot} = k_{\cdot,\cdot} = 1 \\
&k_{\cdot,\cdot} = k^d_{\cdot,\cdot} = k^d_{\cdot,\cdot} = k^d_{\cdot,\cdot} = 2 \\
&P(q_0 | t = 0) = 1
\end{align*}
\]
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State distribution

\[
q_0 : \times 6 \\
q_1 : \times 4 \times 1 \\
q_2 : \times 4 \times 1 \\
q_3 : \times 2 \times 2 \\
q_4 : \times 2 \times 2
\]

State distribution VS Time

\[
P(q_0) \quad P(q_1) \quad P(q_2) \quad P(q_3) \quad P(q_4)
\]

with:

\[
\begin{align*}
k_{\bullet, \bullet} &= k_{\bullet, \circ} = 1 \\
k_{\bullet, \circ} &= k^d_{\bullet, \circ} = k^d_{\circ, \circ} = 2 \\
P(q_3 \mid t = 0) &= 1
\end{align*}
\]
Whenever:

\[
\begin{align*}
2k_{\cdot, \cdot} &= 2k_{\cdot, \cdot} = k_{\cdot, \cdot} \\
k_{\cdot, \cdot}^d &= k_{\cdot, \cdot}^d = k_{\cdot, \cdot}^d
\end{align*}
\]

We can lump the system.
Lumped system
Macrostate distribution

$Q_0 : \times 6$

$Q_1 : \times 4 \times 1$

$Q_2 : \times 2 \times 2$

$Q_3 : \times 3$

Lumped system
Probability ratios (wrong initial condition)

\[ q_1 : \quad \times 4 \quad \times 1 \]

\[ q_2 : \quad \times 4 \quad \times 1 \]

\[ q_3 : \quad \times 4 \quad \times 1 \]

\[ q_4 : \quad \times 2 \quad \times 2 \]

\[ q_5 : \quad \times 2 \quad \times 2 \]

\[ \frac{P(q_2)}{P(q_1)} \]

\[ \frac{P(q_3)}{P(q_1)} \]

\[ \frac{P(q_5)}{P(q_4)} \]

with:

\[ \begin{align*}
    k_{s,s} &= k_{d,s} = 1 \\
    k_{s,d} &= k_{d,s} = k_{d,d} = 2 \\
    P(q_4 \mid t = 0) &= 1
\end{align*} \]
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Model
State distribution

$q_0$: \[ \times 6 \]

$q_1$: \[ \times 4 \times 1 \]

$q_2$: \[ \times 4 \times 1 \]

$q_3$: \[ \times 2 \times 2 \]

$q_4$: \[ \times 2 \times 2 \]

Probabilities

![State distribution VS Time](image)

with:

\[
\begin{align*}
    k_{s_s} &= k_{s_d} = k_{d_s} = 1 \\
    k_{d_s} &= k_{d_d} = 2 \\
    k_{d_d} &= 4 \\
    P(q_0 \mid t = 0) &= 1
\end{align*}
\]
Lumpability

In general, when the following system:

\[
\begin{align*}
2k_{r,s} &= 2k_{r,s} = k_{r,s} \\
k^d_{r,s} &= k^d_{r,s} = k^d_{r,s}
\end{align*}
\]

is not satisfied, we cannot lump the system.
Probability ratios (wrong coefficients)

\[
\begin{align*}
q_1 &: [\times 4] \times 1 \\
q_2 &: [\times 4] \times 1 \\
q_3 &: [\times 4] \times 1 \\
q_4 &: [\times 2] \times 2 \\
q_5 &: [\times 2] \times 2 \\
\end{align*}
\]

Probability ratios VS Time

with:

\[
\begin{align*}
k_{x,x} &= k_{x,d} = k_{d,x} = 1 \\
k_{x,d} &= k_{d,d} = 2 \\
k_{d,x} &= 4 \\
P(q_0 | t = 0) &= 1
\end{align*}
\]
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.
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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:

\[
\begin{array}{c}
\downarrow \quad \downarrow \\
g & \approx & f \\
\uparrow \quad \uparrow \\
\end{array}
\]

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
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. $Q \triangleq \{ [G] \approx \mid G \text{ fully specified site graph} \}$;
3. $L \triangleq \left\{ (r, [f] \approx) \mid r \text{ a rule, } f \text{ an embedding from } lhs(r) \text{ to a fully specified site graph} \right\}$;
4. $[M] \approx (r, [\phi] \approx) \rightarrow [M'] \approx$ if and only if:

$$M \rightarrow M'$$

$$f \uparrow$$

$r \rightarrow$
Semantics

1. A model is a map \( k \) from rules to non negative real numbers;

2. \( Q \triangleq \{ [G] \approx \mid G \text{ fully specified site graph} \}; \)

3. \( L \triangleq \left\{ (r, [f] \approx) \mid r \text{ a rule, } f \text{ an embedding from } \text{lhs}(r) \text{ to a fully specified site graph} \right\}; \)

4. \( [M] \approx (r, [f] \approx) \Rightarrow [M'] \approx \text{ if and only if:} \)

\[
\begin{align*}
&M \xrightarrow{\gamma} M' \\
&\approx \\
&f \\
&r
\end{align*}
\]

The rate of such a transition is defined as:

\[
\gamma(r) \frac{\text{card}\{\phi f \mid \phi \in \text{Aut}(\text{im}(f))\}}{\text{card}(\text{Aut}(\text{lhs}(r)))}.
\]
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.
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   (a) Groups of transformations
   (b) Action of the transformations
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Transformations over site graphs

- For any site graph $G$, we introduce a finite group of transformations $G_G$.

- For any site graph $G$ and any transformation $\sigma \in G_G$, we introduce the site graph $\sigma.G$ and we call it the image of $G$ by $\sigma$.

- We assume that $G_G$ and $G_{(\sigma.G)}$ 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

\[ G \xrightarrow{f} H \]

\[ \sigma \]

\[ \sigma.H \]
Restriction of symmetry to the domain of an embedding
Identity function

\[ E \xleftarrow{i_E} E \xrightarrow{\sigma} E \]
Identity function

\[ E \xleftarrow{i_E} E \]

\[ \sigma \]

\[ \sigma . E \]
Identity function

\[ E \xrightarrow{i_E} E \]

\[ (i_E \cdot \sigma).E \xrightarrow{\sigma \cdot i_E} \sigma.E \]
Identity function

\[
E \xleftarrow{i_E} E
\]

\[
(i_E \cdot \sigma).E \xrightarrow{i(\sigma.E)} \sigma.E
\]

\[
\sigma \cdot i_E
\]
Identity function

We assume that:

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

\[ E \xleftarrow{f} F \]

\[ E = (f \cdot \varepsilon_F) \]
Identity symmetry

\[ E \xrightarrow{f} F \]

\[ \varepsilon_F . F \]

\[ \varepsilon_F \]
Identity symmetry

$$E \xleftarrow{f} F$$

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

\[ E \xrightarrow{f} F \]

\[ E = (f \cdot \varepsilon_F).E \xrightarrow{f} \varepsilon_F.F = F \]
Identity symmetry

\[ E \xrightarrow{f} F \]

\[ E = (f \cdot \varepsilon_F).E \]

We assume that:

- \( \varepsilon_F.F = F \)
- \( f \cdot \varepsilon_F = \varepsilon_E \)
- \( \varepsilon_F.f = f \)
Composition of embeddings

\( E \xrightarrow{f} F \xleftarrow{\sigma} g \rightarrow G \)
Composition of embeddings

\[ E \xrightarrow{gf} G \]

\[ E \xrightarrow{f} F \xrightarrow{g} G \]

\[ \sigma \]
Composition of embeddings

\[
\begin{align*}
E & \xrightarrow{gf} G \\
& \xleftarrow{f} F \\
& \xrightarrow{g} G \\
\end{align*}
\]

\[
\begin{align*}
(gf) \cdot \sigma & \xrightarrow{\sigma} \sigma \cdot (gf) \\
\end{align*}
\]
Composition of embeddings

\[
\begin{align*}
E & \xrightarrow{gf} G \\
E & \xrightarrow{f} F & F & \xrightarrow{g} G \\
((gf) \cdot \sigma) \cdot E & \xrightarrow{\sigma \cdot (gf)} \sigma \cdot G
\end{align*}
\]
Composition of embeddings

\[
\begin{align*}
E & \xrightarrow{gf} G \\
\xrightarrow{f} F & \xrightarrow{g} \phantom{(g.\sigma).E} \\
((gf).\sigma).E & \xrightarrow{\sigma.(gf)} \sigma.G \\
(g.\sigma).F & \xrightarrow{\sigma.g} \phantom{(g.\sigma).E} \\
\xrightarrow{(g.\sigma).f} & \phantom{(g.\sigma).E} \\
(gf).\sigma & \xrightarrow{f.(g.\sigma)} \phantom{(g.\sigma).E} \\
\end{align*}
\]
Composition of embeddings

We assume that:

- \((gf).\sigma = f.(g.\sigma)\)
- \(\sigma.(gf) = (\sigma.g)((g.\sigma).f)\)
Product of transformations

\[ E \xrightarrow{f} F \]

\[ \sigma' \circ \sigma \]

\[ \sigma' \circ \sigma \]
Product of transformations

$E \xlongequal{f} F$

$(f \circ (\sigma' \circ \sigma)) . E \xlongequal{(\sigma' \circ \sigma) . f} (\sigma' \circ \sigma) . F$
Product of transformations

\[ E \xrightarrow{f} F \]

\[ f.\sigma \xrightarrow{\sigma} \sigma.F \]

\[ \sigma'(\sigma' \circ \sigma) \xrightarrow{(\sigma' \circ \sigma).f} (\sigma' \circ \sigma).F \]
Product of transformations

\[
\begin{align*}
\text{Product of transformations:} & \\
E & \xrightarrow{f} F \\
(f \circ \sigma).E & \xrightarrow{\sigma \circ f} \sigma.F \\
(f.\sigma).E & \xrightarrow{(\sigma \circ f).\sigma'} \sigma'.F
\end{align*}
\]
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 $\sigma \in \mathcal{G}_G$ the two following assertions are equivalent:

1. $G$ is fully specified;
2. $\sigma.G$ is fully specified.
For any partial embedding $\phi : L \xleftrightarrow{f} D \xrightarrow{g} R$,
We assume that:

- if

$$\begin{align*}
&f.\sigma_L = g.\sigma_R \\
&f.\sigma'_L = g.\sigma'_R
\end{align*}$$

- then

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

for any $\sigma_L, \sigma'_L \in G_L$, $\sigma_R, \sigma'_R \in G_R$,

We consider:

$$G_{\phi} \triangleq \{(\sigma_L, \sigma_R) \in G_L \times G_R \mid f.\sigma_L = g.\sigma_R\}.$$
Images of rules

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

1. $\phi$ is a rule;

2. $\sigma_L.L \xleftarrow{\sigma_L.f} (f.\sigma_L).D \xrightarrow{\sigma_R.g} \sigma_R.R$ is a rule.
Images of push-outs

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

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

is a push-out, then the following diagram:

\[
\begin{array}{ccc}
\sigma_L \cdot L' & \xrightarrow{(\sigma_L, \sigma_R) \cdot r} & \sigma_R \cdot R' \\
\uparrow \sigma_L \cdot h_L & & \uparrow \sigma_R \cdot h_R \\
(\sigma_L \cdot L') \cdot (h_L \cdot \sigma_L) & \xrightarrow{(h_L \cdot \sigma_L, h_R \cdot \sigma_R) \cdot r'} & (h_R \cdot \sigma_R) \cdot R \\
\end{array}
\]

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 \( \mathcal{G}_G' \) of \( \mathcal{G}_G \);
- for any transformation \( \sigma \in \mathcal{G}_G' \), \( \mathcal{G}_G = \mathcal{G}_{(\sigma,G)}' \);
- for any two \( \sigma, \sigma' \) transformations in \( \mathcal{G}_G' \), \( \sigma \circ \sigma' \in \mathcal{G}_G' \);
- for any transformation \( \sigma \in \mathcal{G}_H' \), \( h.\sigma \in \mathcal{G}_G' \);

then the groups \( (\mathcal{G}_G') \) define a set of transformations.
Example:
Heterogeneous site permutations
Example:
Homogeneous site permutations
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Group actions over site graphs

Let $G, G'$ be two site graphs.

We write $G \approx_G G'$ if and only if there exists $\sigma \in G_G$ such that $G' = \sigma.G$.

The function:

\[
G_G \times [G]_{\approx_G} \to [G]_{\approx_G}
\]

\[
(\sigma, G) \mapsto \sigma.G
\]

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 \( f \approx_G f' \) if and only if there exists \( \sigma \in G_{\mathsf{IM}(f)} \) such that \( f' = \sigma.f \).

The function:

\[
\begin{cases}
G_{\mathsf{IM}(f)} \times [f] \approx_G \rightarrow [f] \approx_G \\
(\sigma, f) \mapsto \sigma.f
\end{cases}
\]

is a group action.
Compatible embeddings

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

$$G_G = \{ f.\sigma | \sigma \in G_H \}$$

(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:

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

(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:

$$G_H \approx \{\sigma \in G_H \mid f.\sigma = \varepsilon_G\} \times \{h.\sigma \mid \sigma \in G_H\}.$$
Decomposition of transformations along an embedding

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

\[
\mathcal{G}_H \approx \{ \sigma \in \mathcal{G}_H \mid f.\sigma = \varepsilon_G \} \times \{ h.\sigma \mid \sigma \in \mathcal{G}_H \}.
\]
Decomposition of transformations along an embedding

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

$$G_H \approx \{\sigma \in G_H \mid f.\sigma = \varepsilon_G\} \times \{h.\sigma \mid \sigma \in G_H\}.$$
Images of isomorphisms

The image of an isomorphism is an isomorphism.

\[ \sigma_{F}.F \xrightarrow{i_{\sigma_{F}.F}} \sigma_{F}.F \]

\[ (f.\sigma_{F}).(f^{-1}) \xrightarrow{(f.\sigma_{F}).E} \sigma_{F}.f \]

The image of an automorphism may be not an automorphism.

Yet, for any site graph \( G \), we have:

\[ \text{Card}(G) = \text{Card}(\{ \phi \mid \phi \in \text{Aut}(G) \}) \times \text{Card}(\{G' \mid G' \approx G \ and \ G' \approx_G G \}). \]
Group actions over rules

Let \( r : L \leftarrow f D \rightarrow g R \) be a rule.

We define the symmetric of \( r \) by a symmetry \( (\sigma_L, \sigma_R) \in G_r \) as follows:

\[
(\sigma_L, \sigma_R).r \overset{\Delta}{=} \sigma_L.L \overset{\sigma_L.f}{\leftarrow} (f.\sigma_L).D \overset{\sigma_R.g}{\rightarrow} \sigma_R.R
\]

We write \( r \approx_{G} r' \) if and only if there exists \( \sigma \in G_r \) such that \( r' = \sigma.r \).

Then:

- \( G_r \) is a group.
- the groups \( G_r \) and \( G_{\sigma.r} \) are the same, for any symmetry \( \sigma \in G_r \).
- The function:

\[
\left\{
\begin{array}{c}
G_r \times [r]_{\approx G} \rightarrow [r]_{\approx G} \\
(\sigma, r) \mapsto \sigma.r
\end{array}
\right.
\]

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:

\[
\mathcal{G}_r \cong \{ \sigma \in \mathcal{G}_L \mid f.\sigma = \varepsilon_D \} \times \{ \sigma \mid \exists (\sigma_L, \sigma_R) \in \mathcal{G}_r, \sigma = f.\sigma_L = f.\sigma_R \} \times \{ \sigma \in \mathcal{G}_R \mid g.\sigma = \varepsilon_D \}.
\]

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

\[
\begin{array}{c}
L' & \xrightarrow{r'} & R' \\
& \downarrow h_L & \downarrow h_R \\
L & \xrightarrow{r''} & R
\end{array}
\]

with $r' \approx_G r$, to the push-out:

\[
\begin{array}{c}
\sigma_L.L' & \xrightarrow{(\sigma_L, \sigma_R).r'} & \sigma_R.R' \\
& \downarrow \sigma_L.h_L & \downarrow \sigma_R.h_R \\
(h_L.\sigma_L).L & \xrightarrow{(h_L.\sigma_L, h_R.\sigma_R).r''} & (h_R.\sigma_R).R
\end{array}
\]

is a group action.
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4. Symmetries in site-graphs
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   (a) Symmetries among set of rules
   (b) Induced bisimulations
6. Conclusion
Isomorphic rules
Isomorphic rules
Symmetric model

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

A model is $G$-symmetric if and only if:

- for any rule $r$ in the model and any pair of symmetries $\sigma \in G_r$, 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:

$$g(r) \triangleq \frac{k(r)}{\text{card}(\{\sigma \in G_r \mid \sigma.r \simeq r\}) \text{card}(\text{Aut}(\text{lhs}(r)))}.$$
Binding rules

\[
\frac{k_{+,-}}{1 \cdot 2} = \frac{k_{-,+}}{1 \cdot 2} = \frac{k_{-,-}}{2 \cdot 2}
\]
Unbinding rules

\[ k^d_{1,2} = k^d_{2,1} \]

\[ \frac{k^d_{1,2}}{1 \cdot 2} = \frac{k^d_{2,1}}{2 \cdot 1} \]
Overview

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Compatible embeddings (reminders)

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

$$G_G = \{f.\sigma \mid \sigma \in G_H\}$$

(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:

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

(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:

```
   x  →  →  x
   ↖  ↗  ↖  ↗
  g  s  f  t
```

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:

```
   x  →  →  x
   ↖  ↗  ↖  ↗
  f  t  s  g
```

the embedding $f$ is compatible.
Lumping states

We say that two states $q, q' \in Q$ are isomorphic if and only if there exist $M \in q$ and $M' \in q'$ such that $M \approx_G M'$.

In such a case, we write $q \approx_G q'$. $\approx_G$ is an equivalence relation.
Lumping the transition labels

We say that two labels $(r, C) \in \mathcal{L}$ and $(r', C') \in \mathcal{L}$ are isomorphic if and only if there exist an embedding $f \in C$, an embedding $f' \in C'$, a pair of symmetries $(\sigma_L', \sigma_R) \in G_{\text{IM}(f)} \times G_{\text{rhs}(r)}$ such that $(f.'\sigma_L', \sigma_R) \in G_r$ and two isomorphisms $\phi$ and $\psi$ such that the following diagram commutes:

In such a case, we write $(r, C) \approx_{G} (r', C')$ (this is also an equivalence relation).
Let $X, X' \subseteq Q$ and $Y \subseteq L$. Let $\omega$ be a function from $Q$ to $\mathbb{R}^+$. We define the flow from $X$ to $X'$ via $Y$, weighted by the reward function $\omega$ by:

$$\text{FLOW}_\omega (X, Y, X') \triangleq \sum_{q \in X, q' \in X', \lambda \in Y, q \xrightarrow{\lambda} q'} \omega(q) \text{RATE}(\lambda)$$
Theorem 4  Let \( q, q', q'' \in Q \) such that \( q \approx_G q' \). 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:

\[
\text{FLOW}_\omega \left( \{q\}, [\lambda]_G \approx_G, [q'']_G \approx_G \right) = \text{FLOW}_\omega \left( \{q'\}, [\lambda]_G \approx_G, [q'']_G \approx_G \right),
\]

with \( \omega(q_1) = 1 \) for any \( q_1 \in Q \).
**Theorem 5** Let $q, q', q'' \in Q$ such that $q' \sim_G q''$. 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:

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

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

**Backward bisimulation (DTMC)**
Backward bisimulation (CTMC)

**Theorem 6** Let $q, q', q'' \in \mathcal{Q}$ such that $q \approx_G q''$. 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. $\omega(q'') \text{FLOW}_\omega \left( \left[ q \right] \approx_G, \left[ \lambda \right] \approx_G, \{ q' \} \right) = \omega(q') \text{FLOW}_\omega \left( \left[ q \right] \approx_G, \left[ \lambda \right] \approx_G, \{ q'' \} \right)$,
   with $\omega(q_1) \overset{\Delta}{=} \frac{1}{\text{card}(\text{Aut}(q))}$, for any $q_1 \in \mathcal{Q}$. 

Jérôme Feret 105 Wednesday, the 23th of October, 2019
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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 that 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).