#### MPRI 2.19 Biochemical Programming Rule-based Modeling Causal analysis

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#### **Causal traces**



# **Challenges**

Compute minimal traces up to commutation of concurrent events.

This is parametric with respect to:

- the notion of state
- the notion of event

which can be seen at different levels of abstraction.

The choices of the syntax and of the semantics matter.

# The biochemical structure is required

#### Reactions:

$$A \rightarrow {}^{\bullet}A$$
$$A \rightarrow A^{\bullet}$$
$$A \rightarrow {}^{\bullet}A^{\bullet}$$
$$A^{\bullet} \rightarrow {}^{\bullet}A^{\bullet}$$

Causal traces:

$$\begin{array}{ccc} A & \to & \bullet A \\ A & \to & A^{\bullet} & \to & \bullet A^{\bullet} \end{array}$$



## **Counters**

(Rates depend on the number of sites already phosphorylated)

Without counters:



## **Commutative events**

Two events  $\lambda_a$  and  $\lambda_b$  commute if they satisfies the following commutative diagrams:

• No conflicts:



• No precedence:



#### **Case study**



## **Musical notation**

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## **Musical notation**



## **Musical notation**

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#### **Causal flow**



#### First case study: Rules



## First case study: Reachability analysis



## First case study: Local transition system



- Local traces focus on each agent individually (they forget about the context);
- They show the full transition system for each agent.

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### First case study: Causal analysis



## First case study: Causal analysis



# First case study: Causal analysis



- Stories focus on group of individual proteins that interact between each other; (they keep information about the context);
- They focus on the transitions that make progress.

### Second case study: Rules









 $a_2^-$ 



## Second case study: Local transition system



#### Second case study: Simplicial complexes



## **Second case study: Causal analysis**



# **Causal analysis**

- Reachability analysis provides a limited amount of information:
  - It computes potential configurations for patterns of interest.
  - But, it does not explain how to go from one configuration to another one.
- Causal analysis provides only a summary of the model:
  - It focuses on the events that are necessary in potential scenarios.
  - Maybe use to debugging
    Why the hell is this pattern reachable?