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# Two Qualitative Dynamics Semantics for SBGN Process Description Maps

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## Context

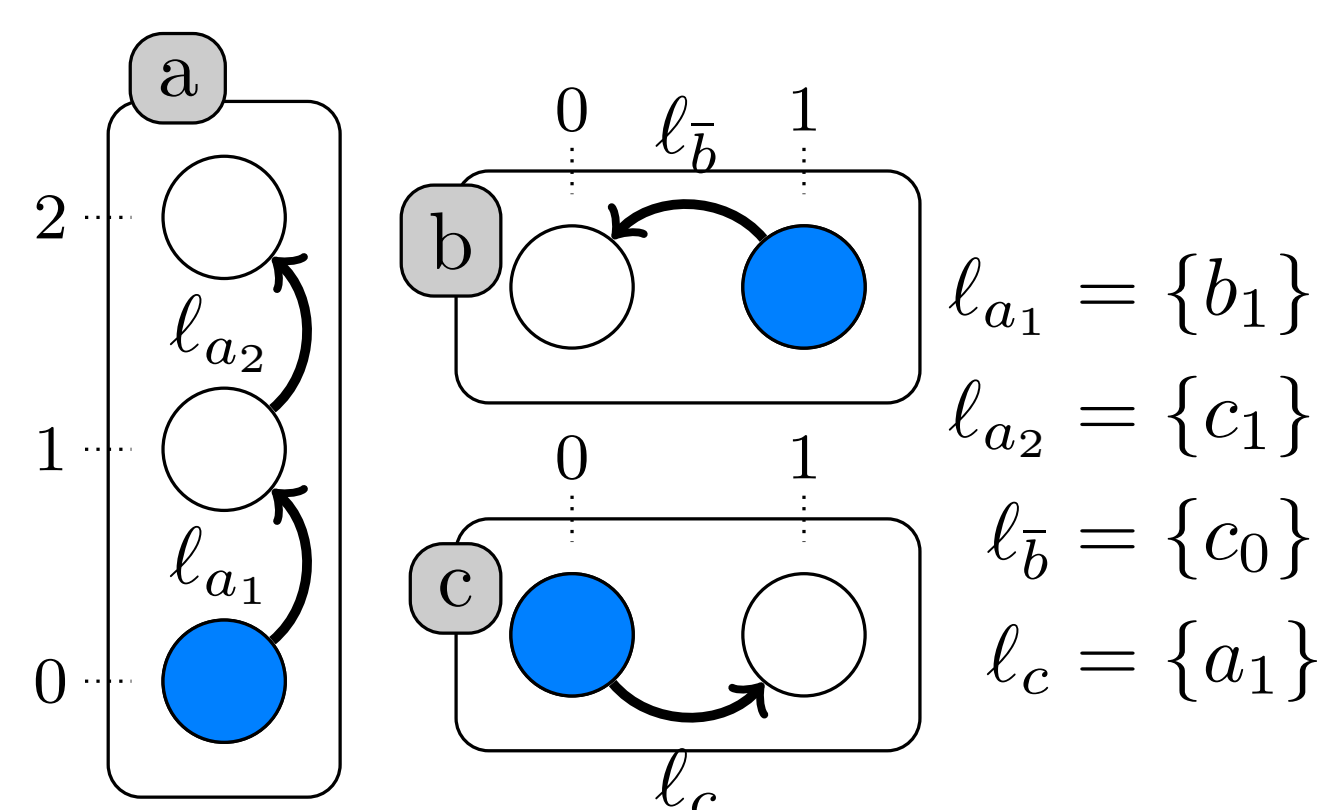
- Larger and larger reaction networks modelling various biological processes (from databases, automatic inference)
- Standards to represent reaction networks: e.g. **Systems Biology Graphical Notation Process Description language (SBGN-PD)**
- Analysis of the dynamics to understand and control these processes

## Motivations

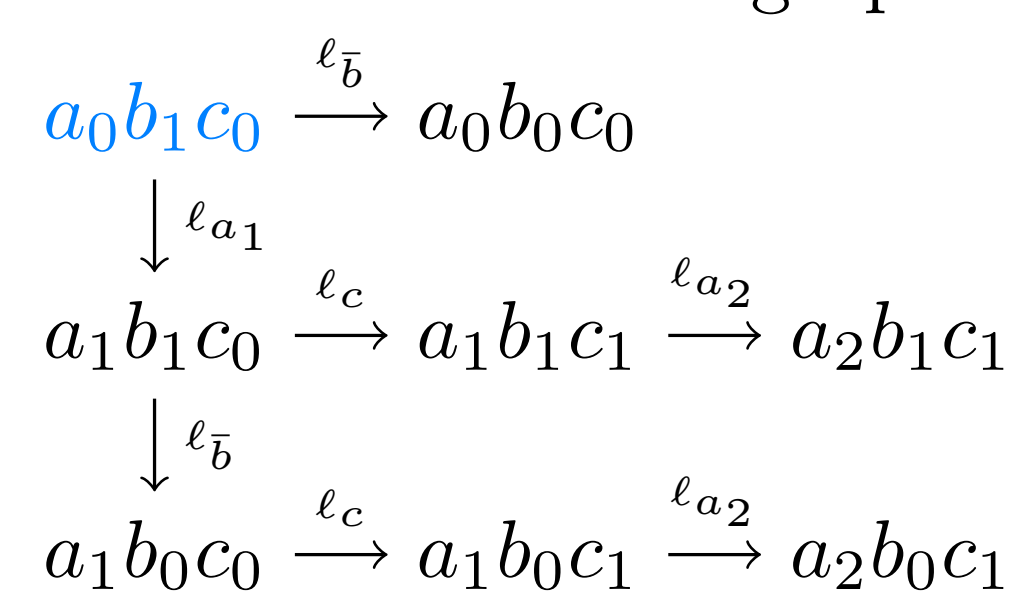
- Qualitative semantics allows to capture **important dynamical features** (e.g. attractors, reachability) without numerical parameters
- Model SBGN-PD maps under **qualitative semantics**

We propose two semantics formalized by **asynchronous automata networks**: the *general semantics*, together with a refinement called *process conflicts*, and the *stories semantics*

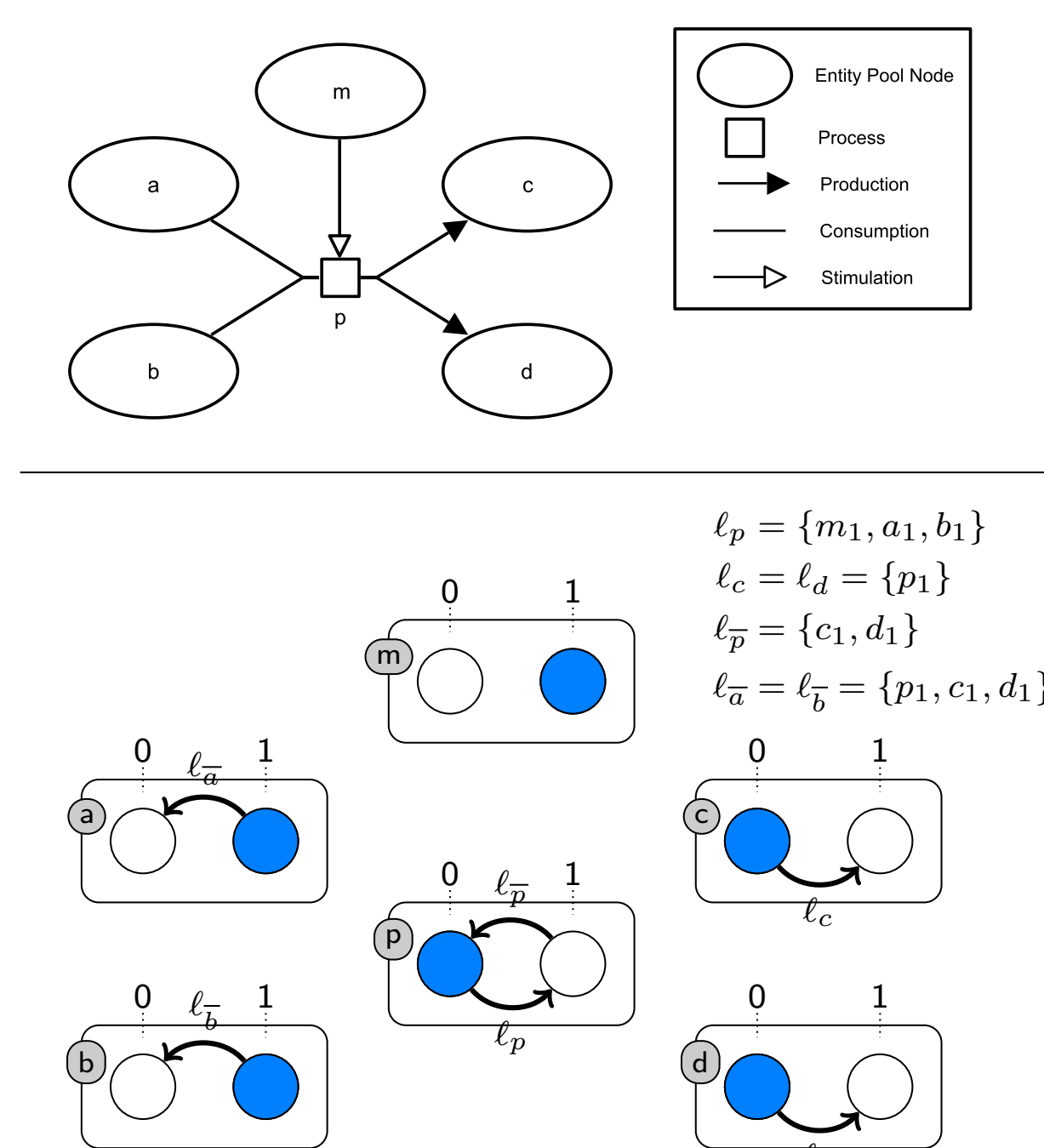
## Asynchronous Automata Networks



State transition graph:

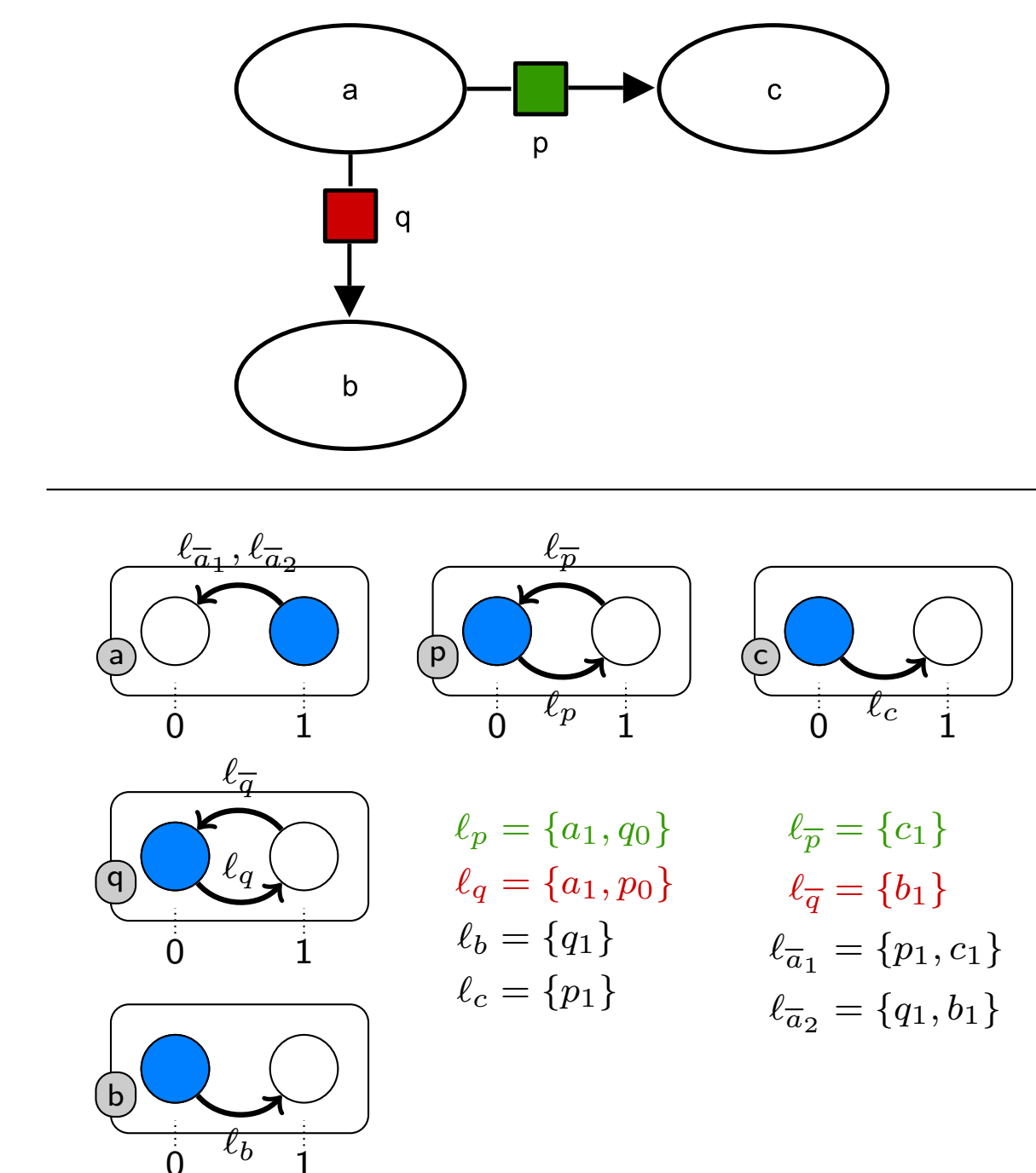


## General Semantics



Each chemical entity is modelled by one automaton

## Refinement 1: Process Conflicts



Processes  $p$  and  $q$  cannot occur at the same time

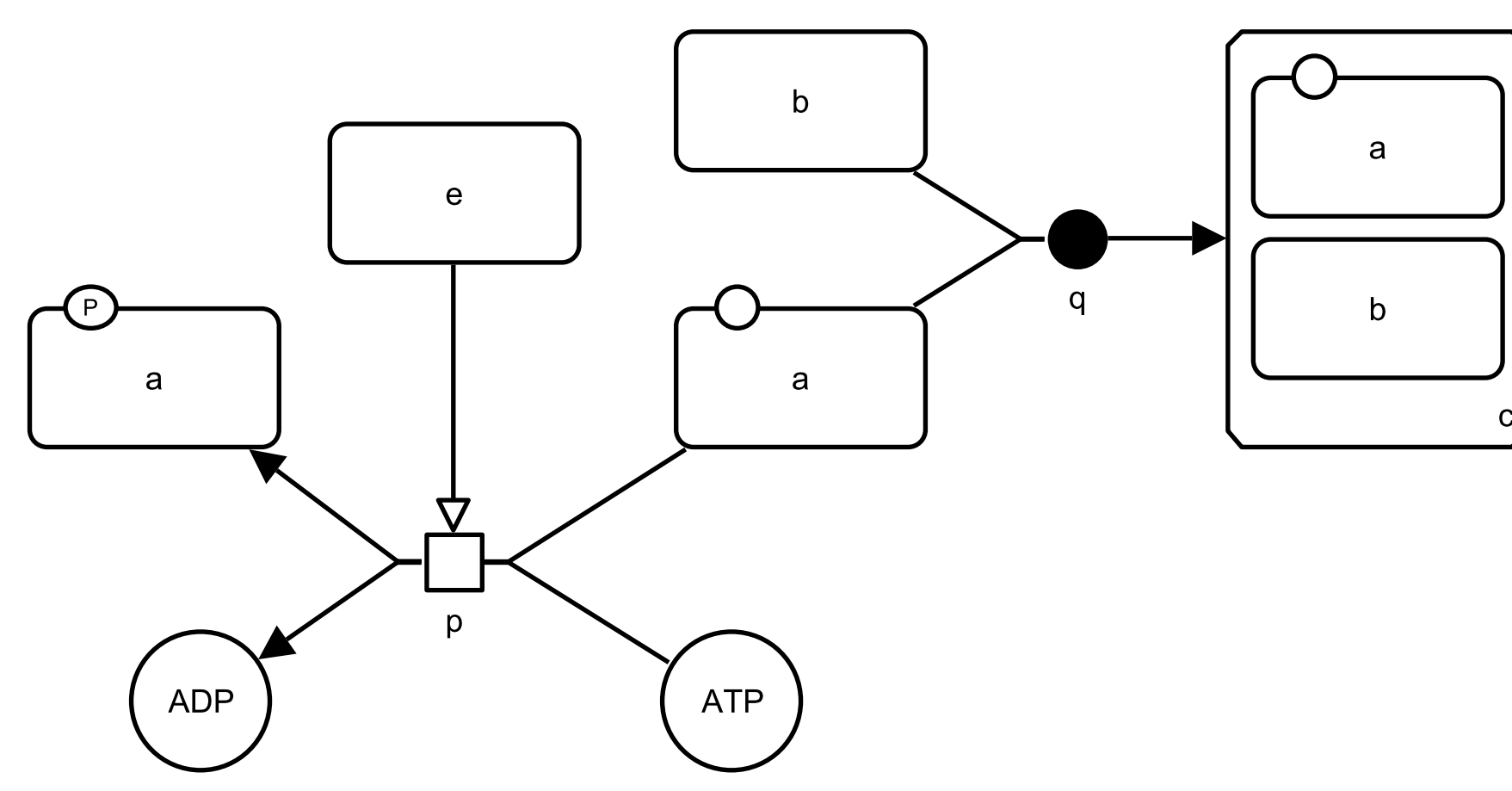
## Refinement 2: Stories Semantics

### Story:

- accounts for **successive transformations** of a chemical entity
- a set of entities that cannot be present at the same time, *i.e.* that are **mutually exclusive**

### Identification of stories:

- **automatic computation**
  - relevance determined by **expert knowledge**
- The stories semantics is a **refinement** of the general semantics driven by **expert knowledge**

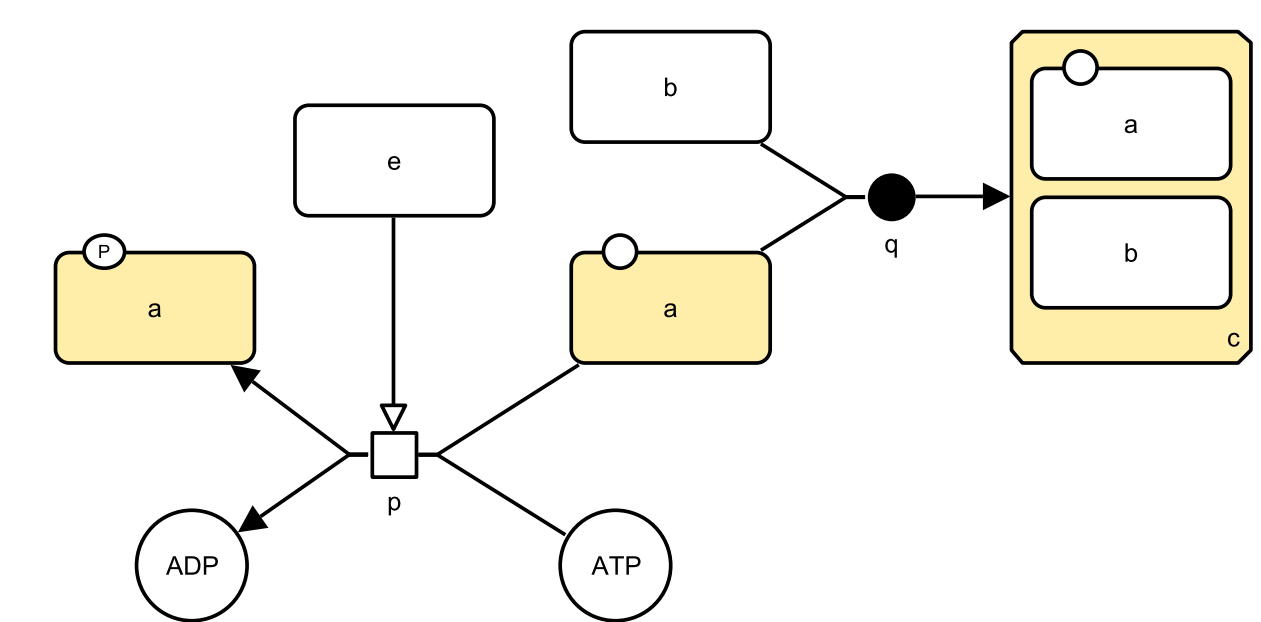


Set of non-singleton stories

$\{a, aP\}, \{a, c\}, \{b, c\}, \{a, aP, c\}$

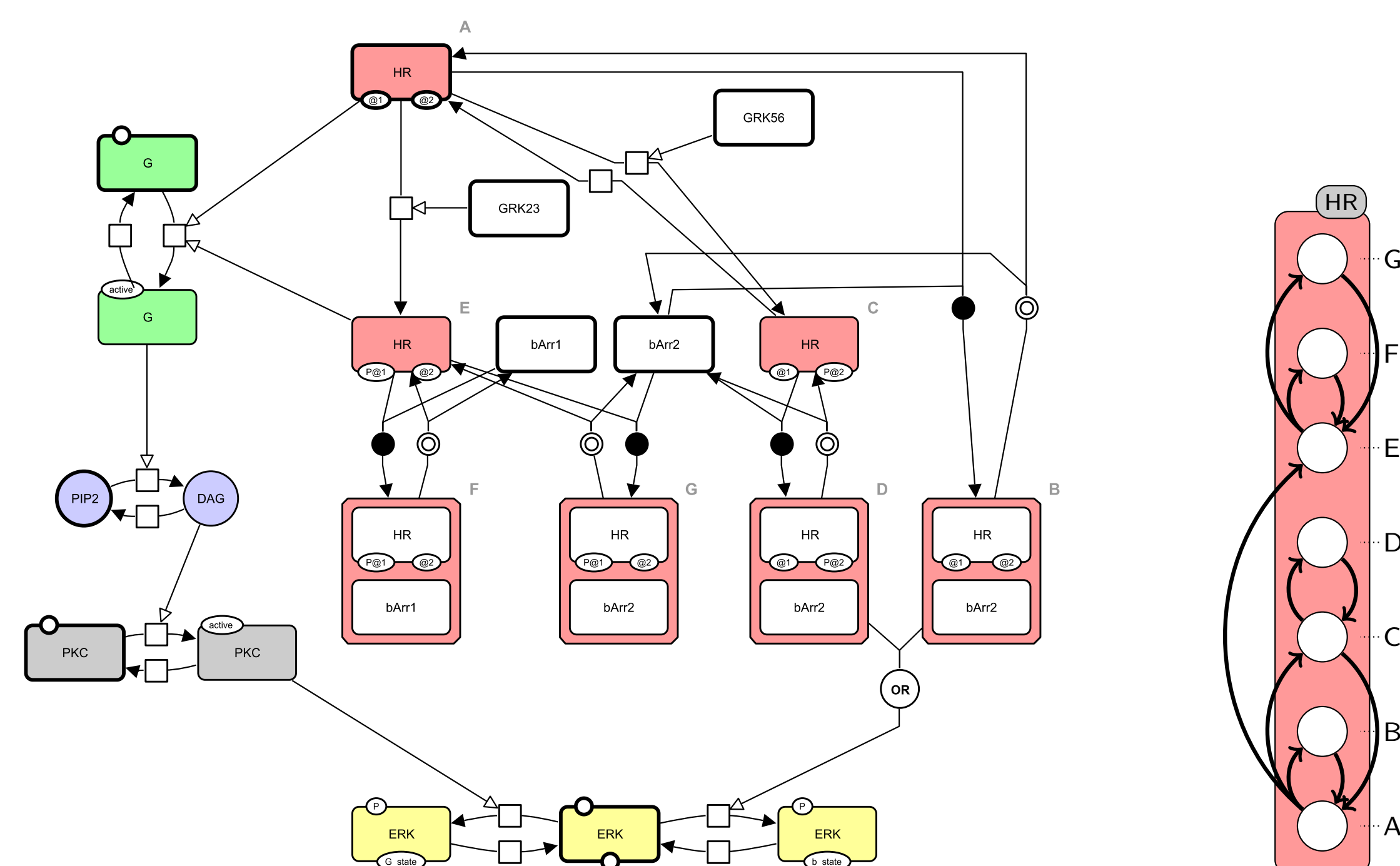
Maximal sets of compatible stories

$\{a, c\}, \{a, aP, c\}, \{a, aP\}, \{b, c\}$



Stories reduce the dimension of the dynamics

## Example: the AT<sub>1</sub>A<sub>R</sub>-induced network



SBGN-PD map adapted from: D. Heitzler et al., *Competing G protein-coupled receptor kinases balance G protein and b-arrestin signaling*, MSB, 2012.

| semantics               | general           | general with conflicts | stories        |
|-------------------------|-------------------|------------------------|----------------|
| No. of automata         | 41                | 41                     | 30             |
| No. of reachable states | $\approx 10^{11}$ | $\approx 10^{10}$      | $\approx 10^5$ |

## Conclusion and Prospects

- **Main features** of SBGN-PD are supported
- The stories semantics is a refinement of the general semantics that:
  - models **several chemical species** with a **unique variable**
  - reduces the state space, **increasing the scalability** of the exhaustive computation of the dynamics
- The dynamics of SBGN-PD maps modelled under both semantics can be analyzed with **state-of-the-art tools** (PRISM, NuSMV ...)

### Ongoing work and prospects:

- Application to a **large network**, the E2F/RB pathway:
  - 153 out of 208 molecules in 28 stories
  - No. of automata reduced from 367 to 242
- Explore the relationship between the stories semantics and **Boolean semantics** applied to SBGN-AF maps