BIOSTEACKER 2014

Exhaustive search of dynamical properties in Process Hitting using Answer Set Programming

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Context and Aims

MeForBio team:
Algebric modelling to study
complex dynamical biological systems

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3) What for?

   searching of PH **properties** through ASP (Fixed points, reachability).

The Process Hitting modeling

Sorts: components a, b, z

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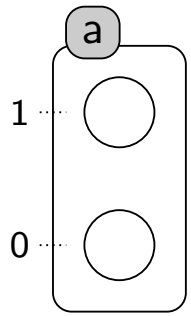

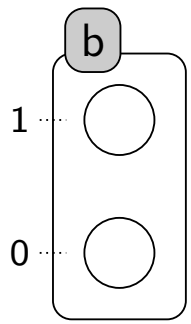

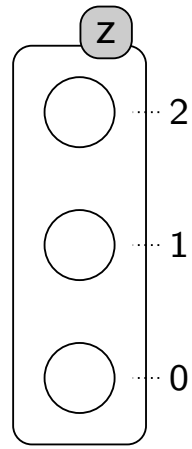

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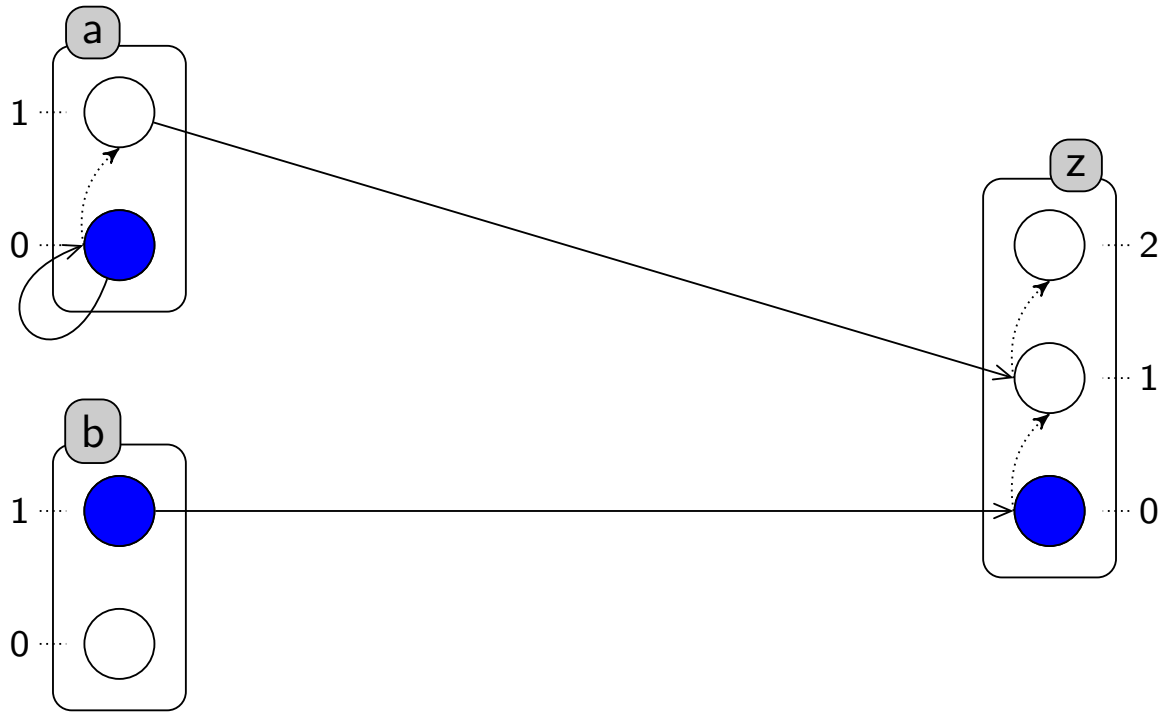

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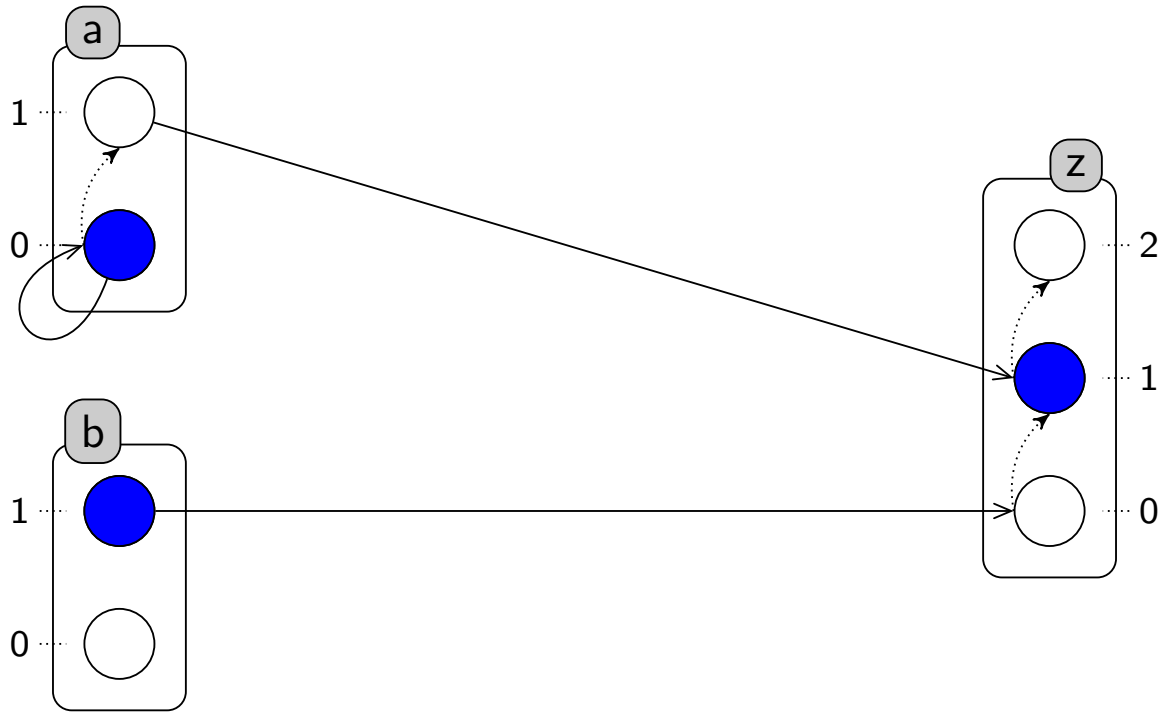

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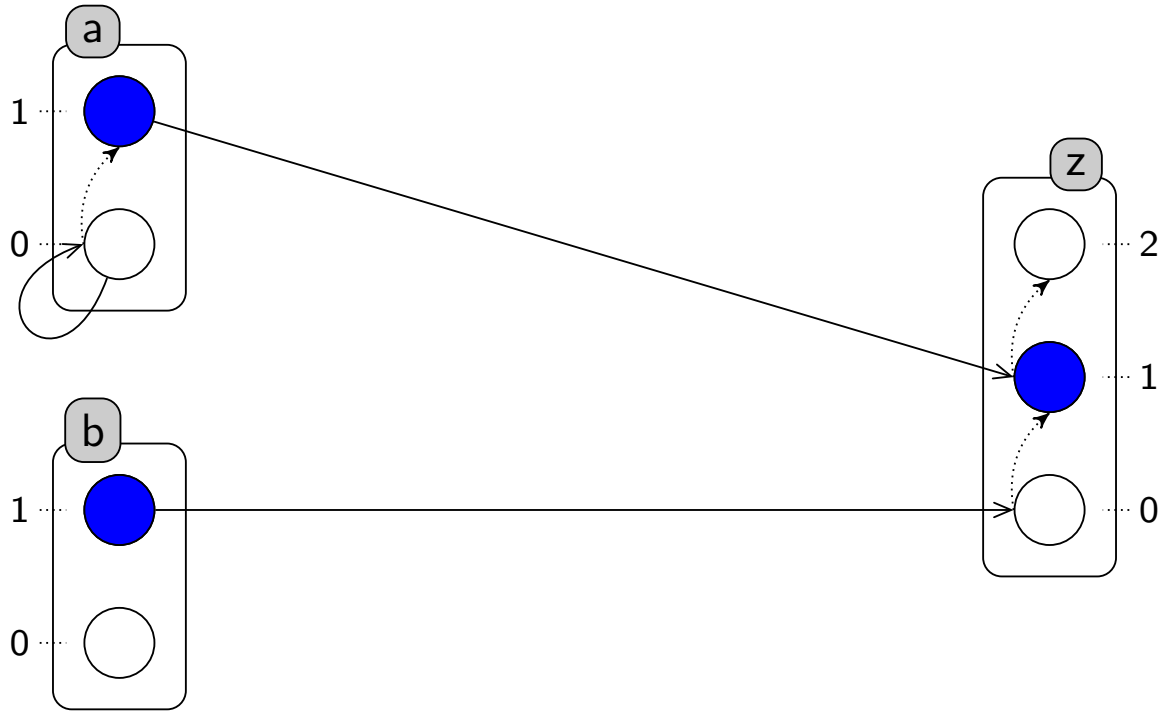

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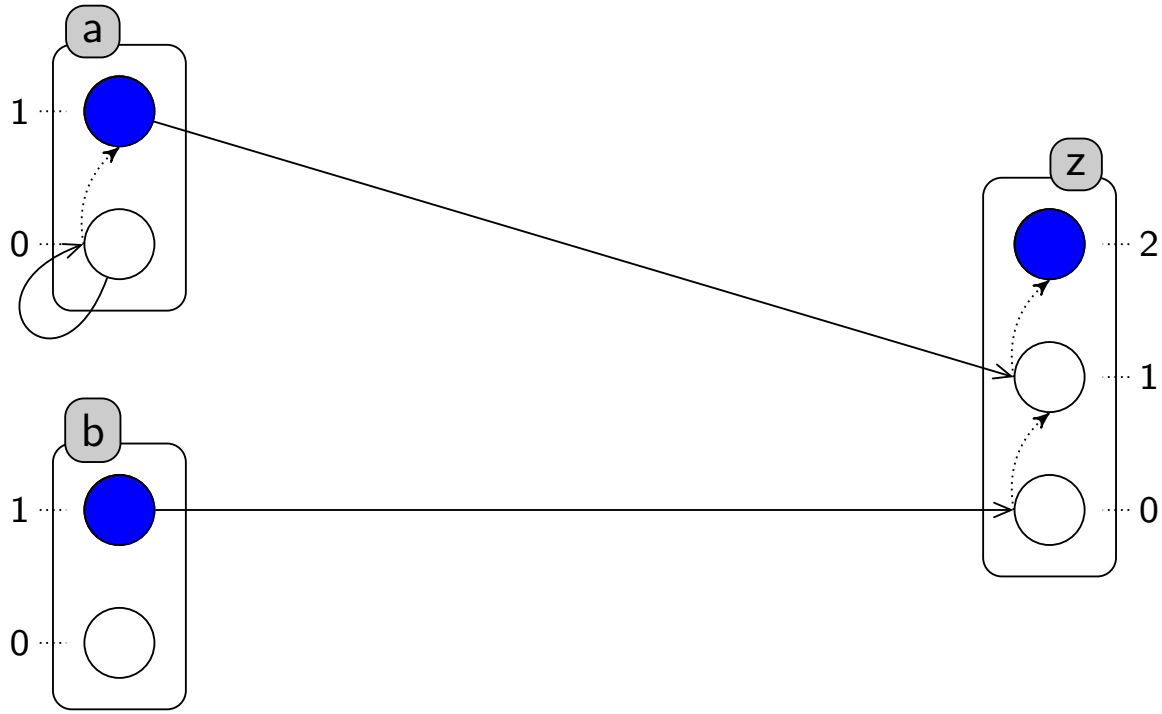

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Answer Set Programming

Answer Set Programming (**ASP**):

- Logic program written in language of AnsProlog*
- Form of rules:

$$L_0 \leftarrow L_k, ..., L_m, \textbf{not } L_{m+1}, ..., \textbf{not } L_n.$$

with each L_i : literal in the sense of classical logic.
Rule's meaning:
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- Constraint:
  $\leftarrow L_k, ..., L_m, \textbf{ not } L_{m+1}, ..., \textbf{ not } L_n.$
- Fact:
  $L_0.$

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Exemple:

$bird(X) \leftarrow lays\_egg(X).$
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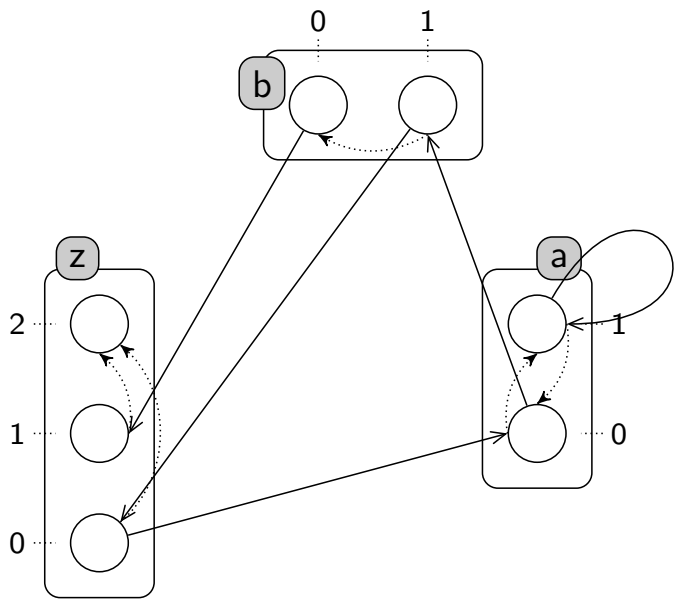
Answer: `fly(tweety), bird(tweety).`

Fixed Points

Fixed point = state where no action can be fired

→ avoid couples of processes bounded by an action



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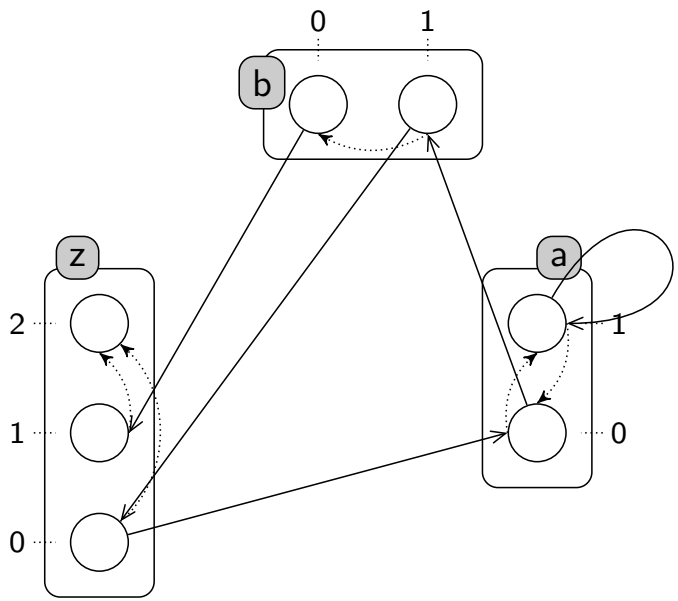

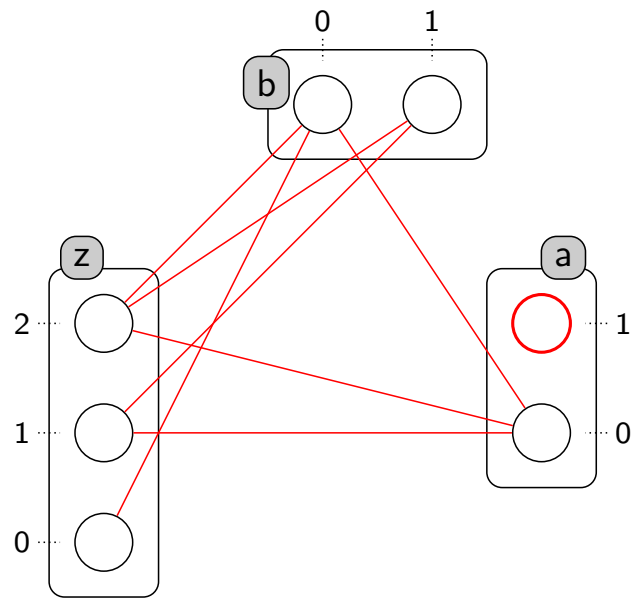

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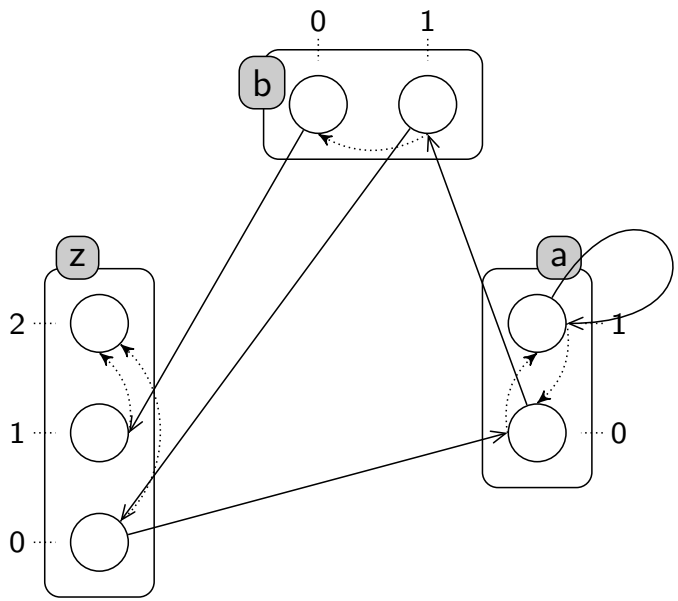

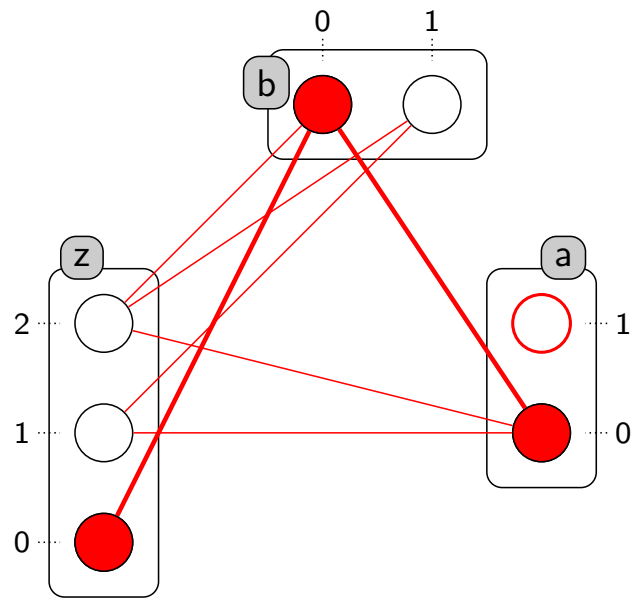

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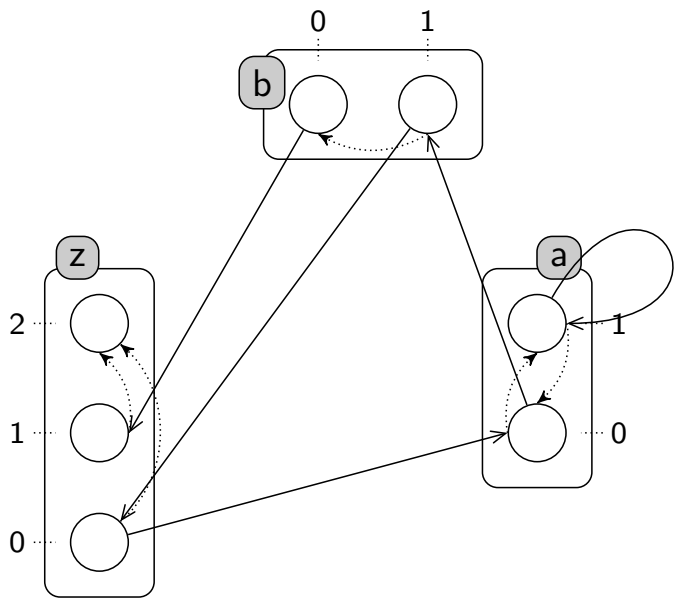
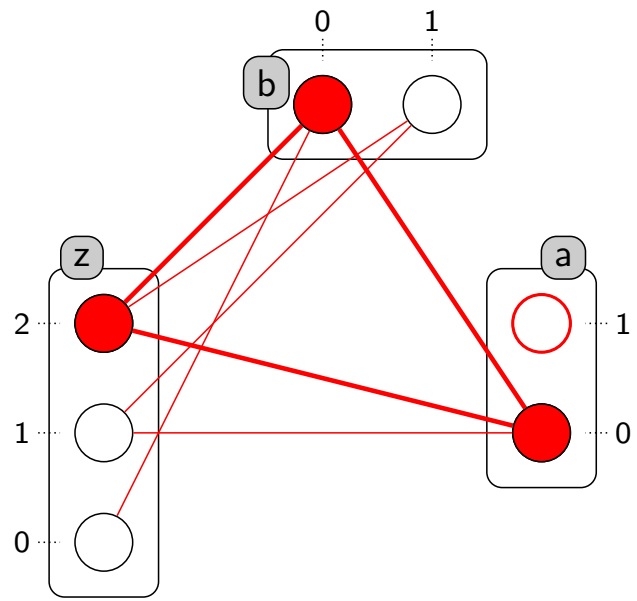
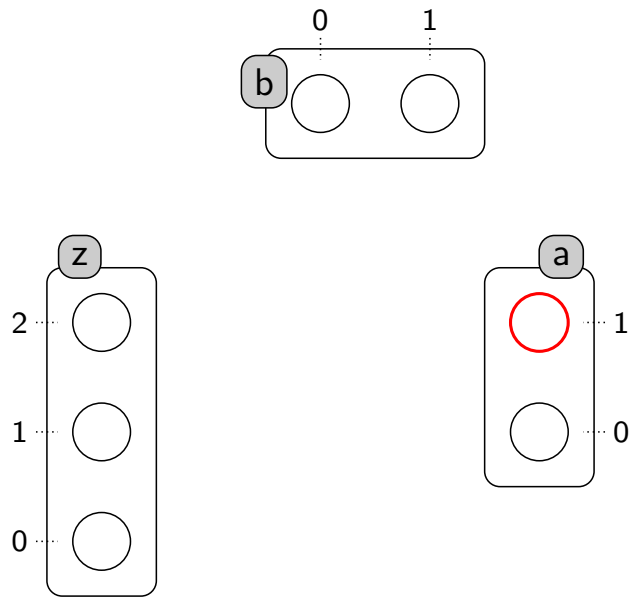




Fixed points through ASP

Implementation of algorithm



Fixed points through ASP

Construct of hitless graph

```
noAction(A,I,B,J) :- not hit(A,I,B,J), not hit(B,J,A,I), A!=B,
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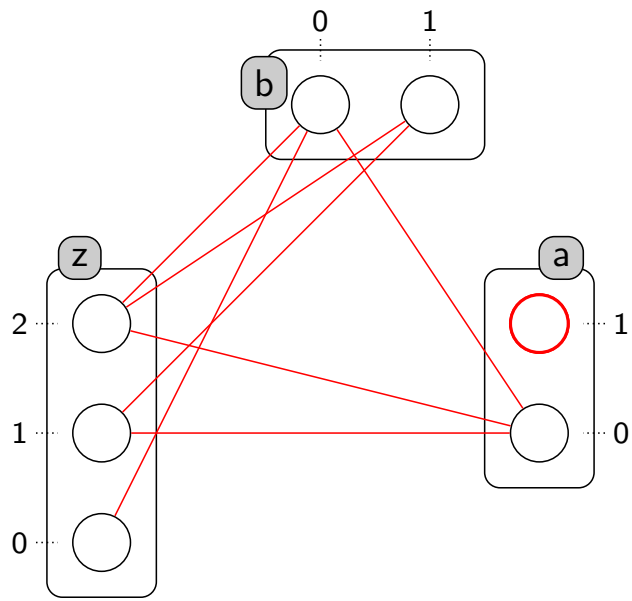

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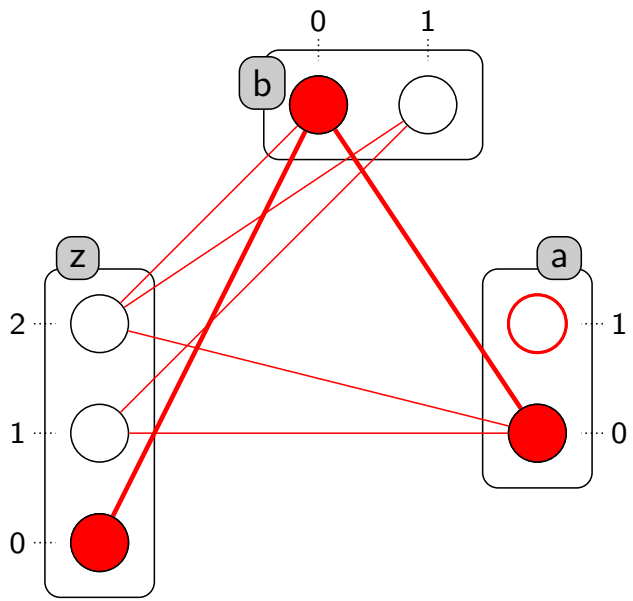

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Find the fixed points

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noExistFixPoint :- X<N, getNumberNoHit(X), N={ sort(_) }.
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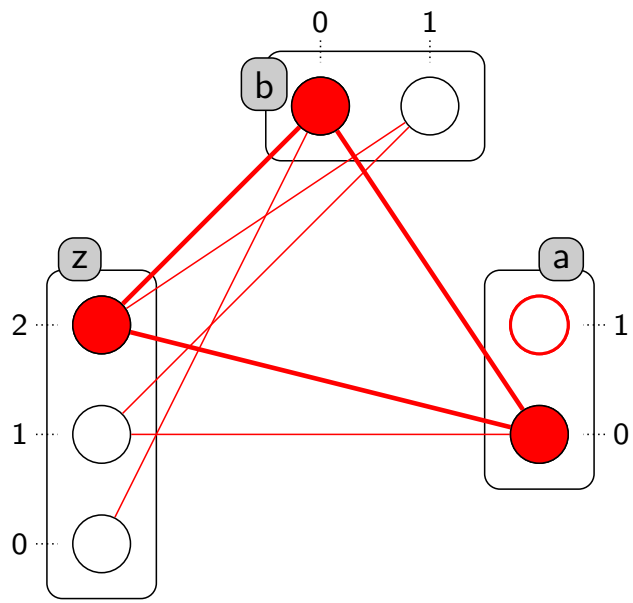

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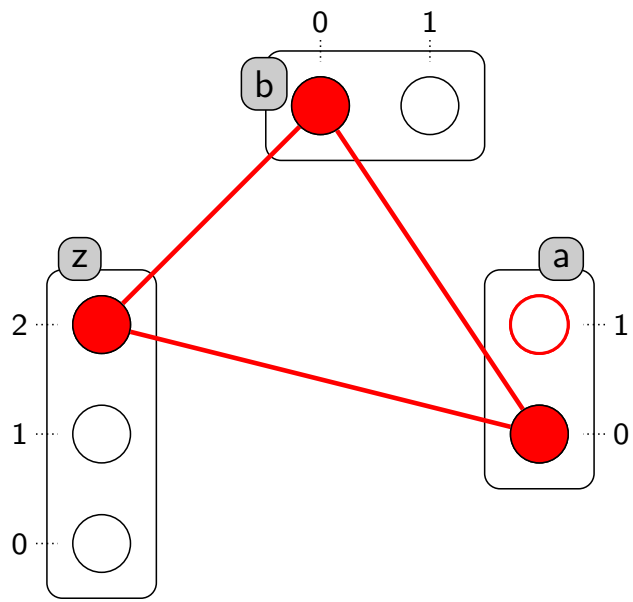
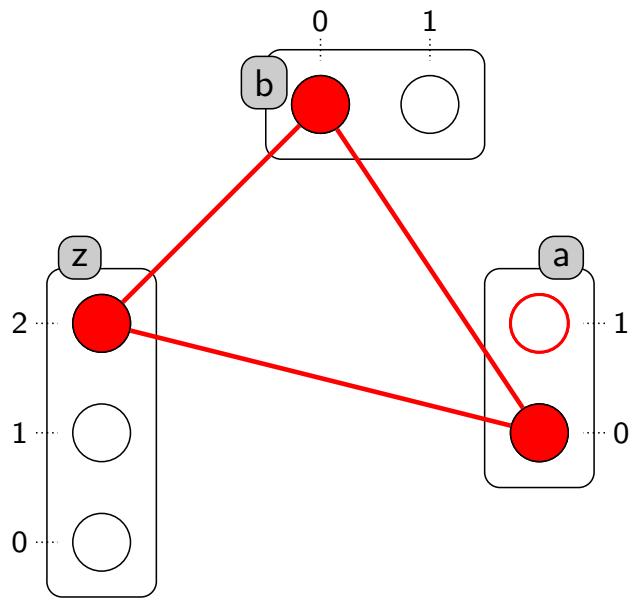


Fixed points through ASP

ASP program answer:

```
Answer 1:  fixProcess(a,0), fixProcess(b,0), fixProcess(z,2).
```



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Optimization:

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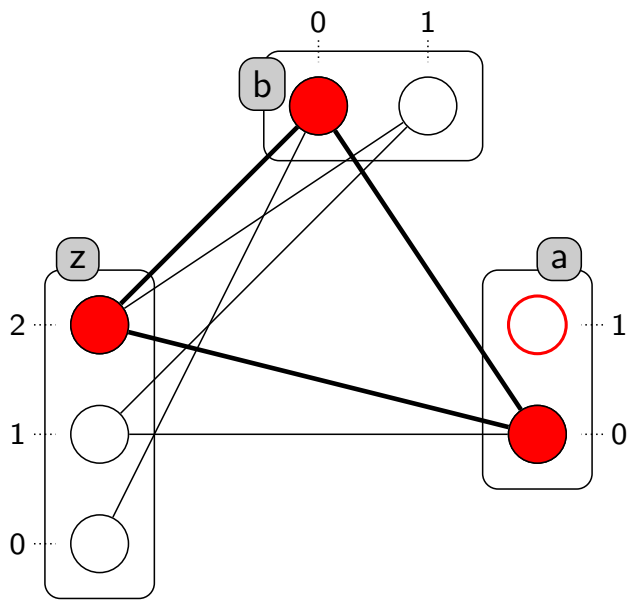

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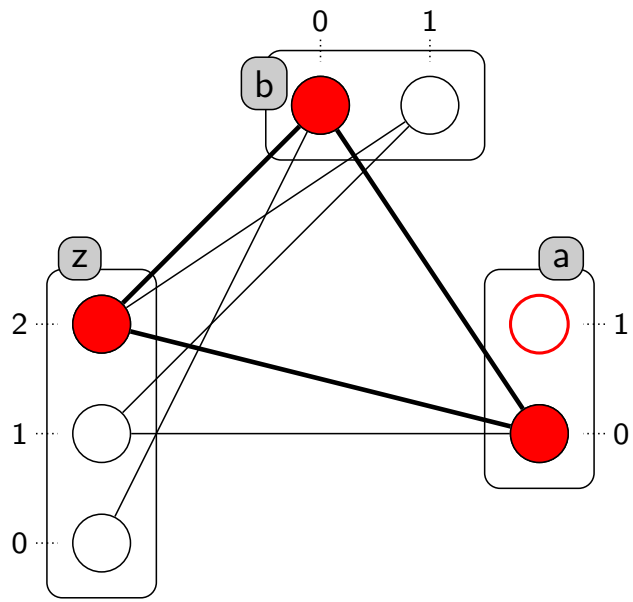


Fixed points through ASP

Comparaison

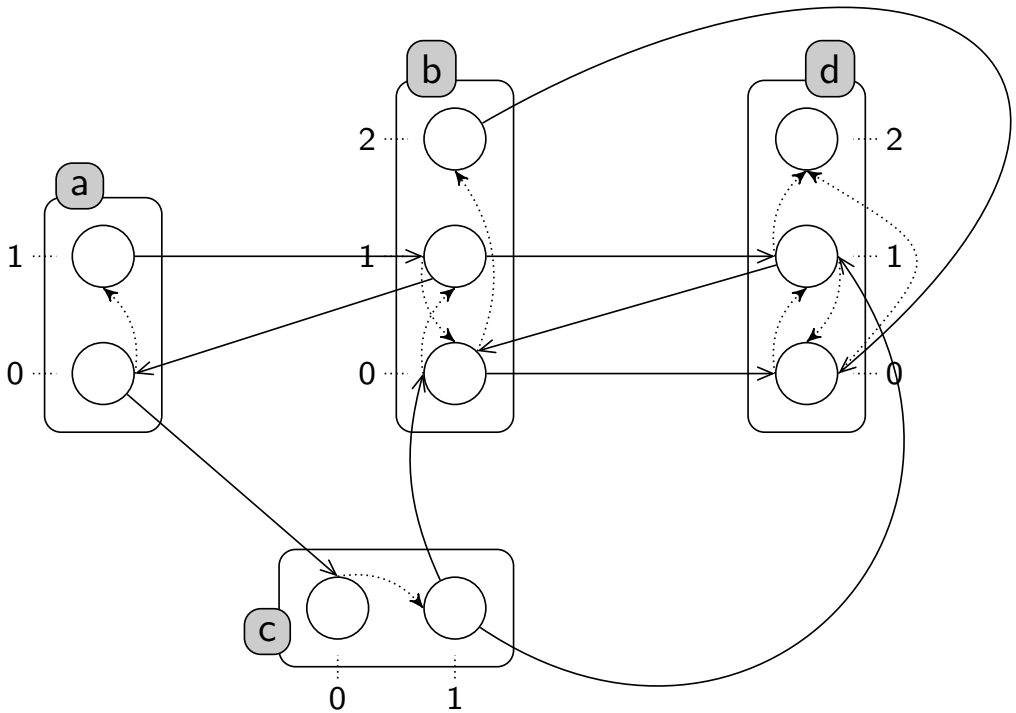
Model	#sorts	#states	#fix-point	PINT	ASP mthd1	mthd2
mvbrn	3	12	1	0.006s	0.000s	0.000s
ERBB_G	42	2^{70}	3	0.017s	0.220s	0.000s
tcrsig40	54	2^{73}	1	0.021s	0.220s	0.020s
tcrsig94	133	2^{194}	0	0.027s	2.540s	0.060s

Figure: Excecution time of ASP metods applied for biological networks with a desktop computer

PINT : a library developed to parse and study PH models

Static analysis: Reachability

Reachability of processes:



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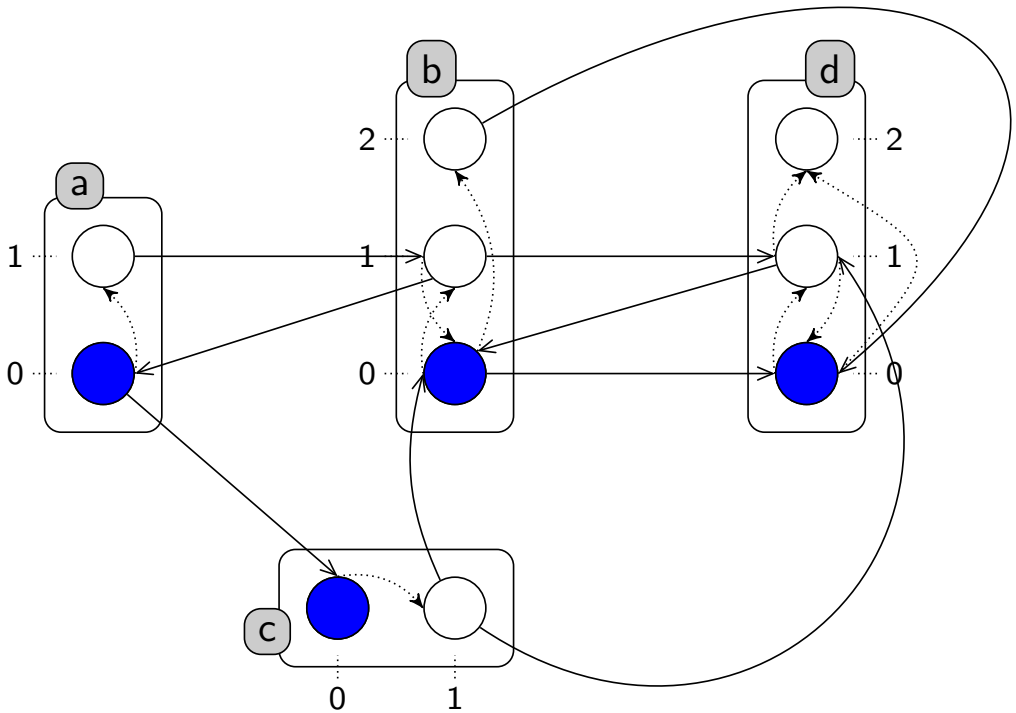

- Initial context

$\langle a_0, b_0, c_0, z_0 \rangle$

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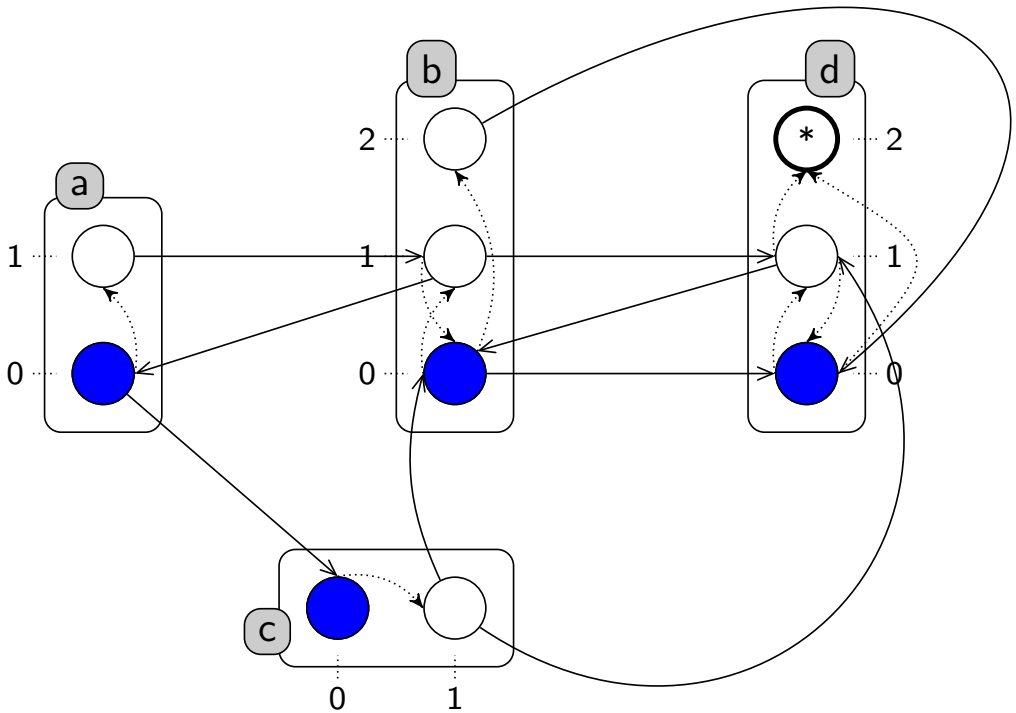

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$$[\ \Rsh\ d_2\ ]$$

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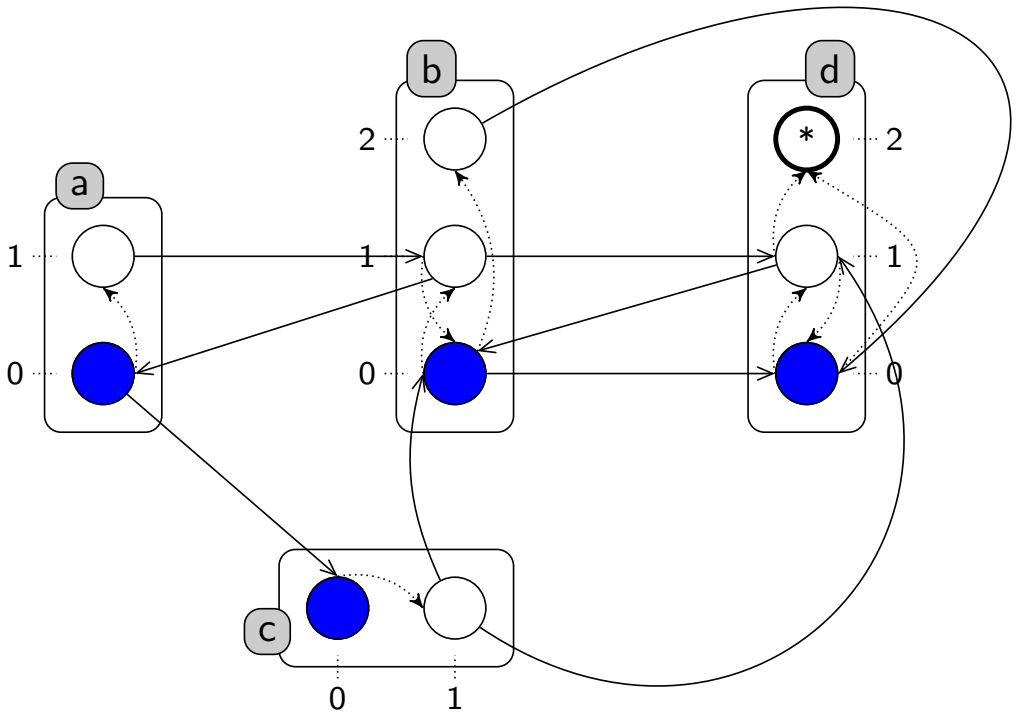

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$\rightarrow$ Concretization of the objective = scenario

$$a_0 \rightarrow c_0 \Rsh c_1 :: \quad b_0 \rightarrow d_0 \Rsh d_1 :: \quad c_1 \rightarrow b_0 \Rsh b_1 :: \quad b_1 \rightarrow d_1 \Rsh d_2$$

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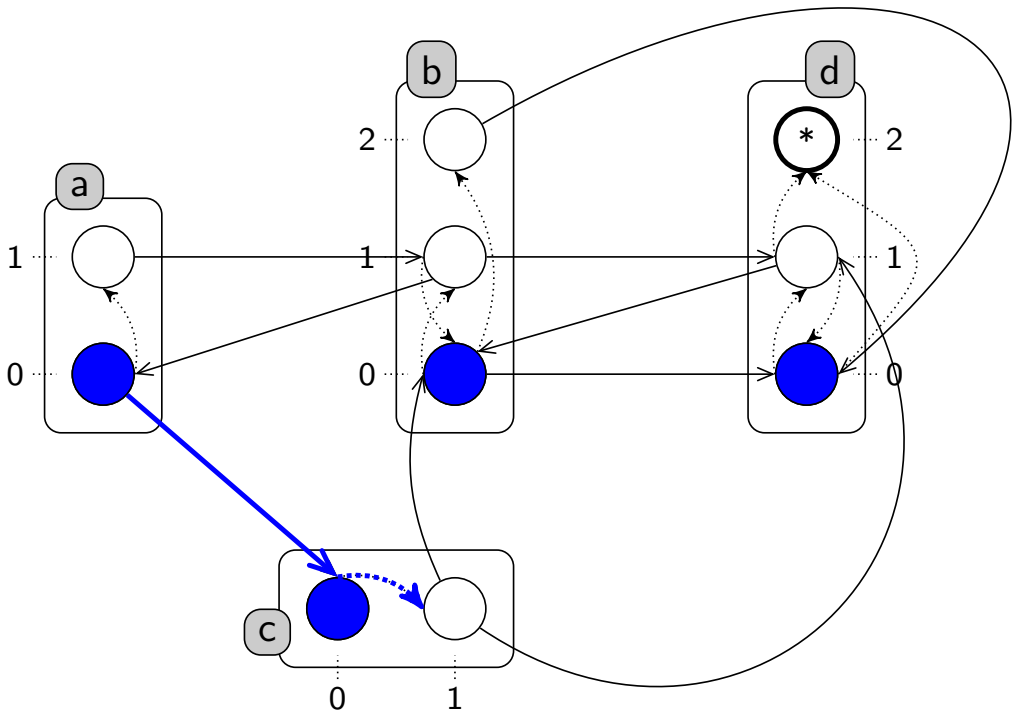

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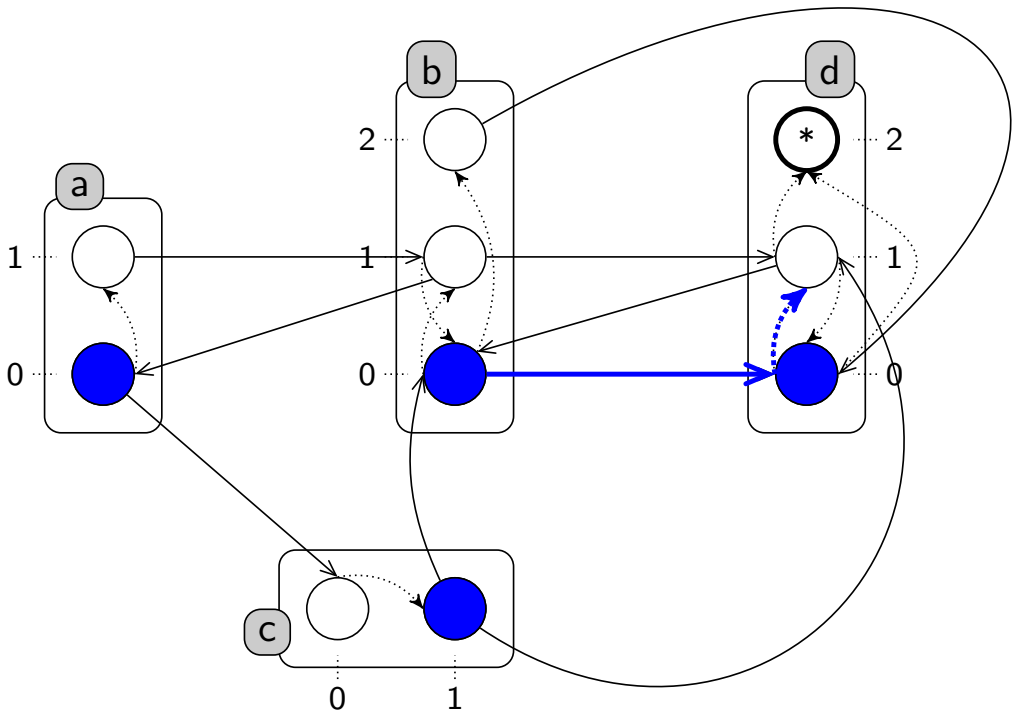

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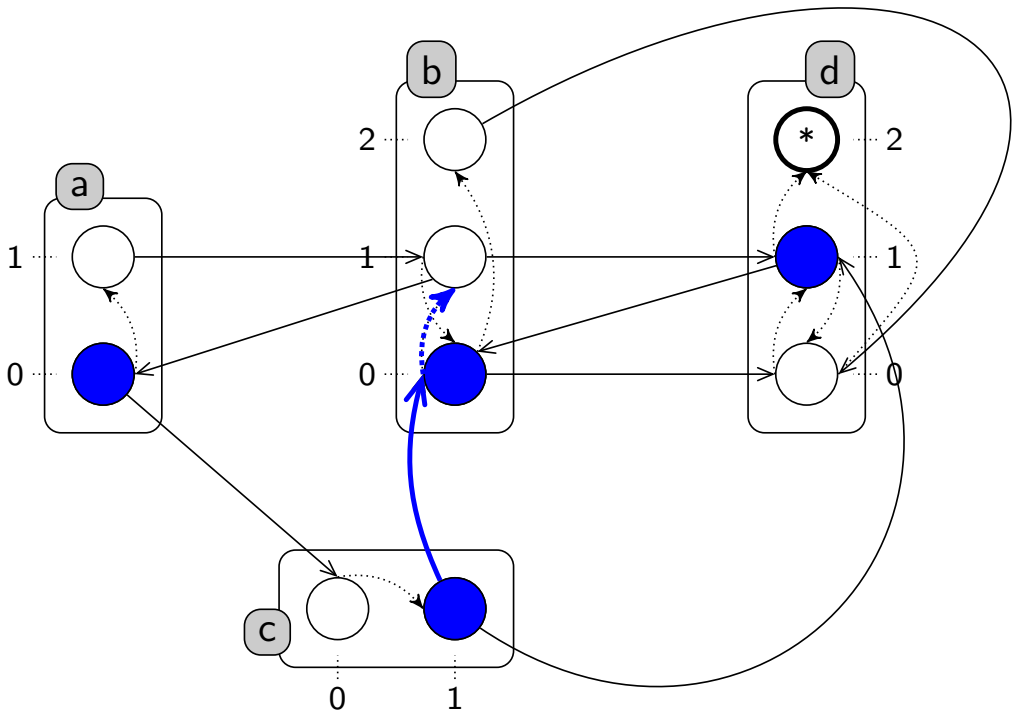

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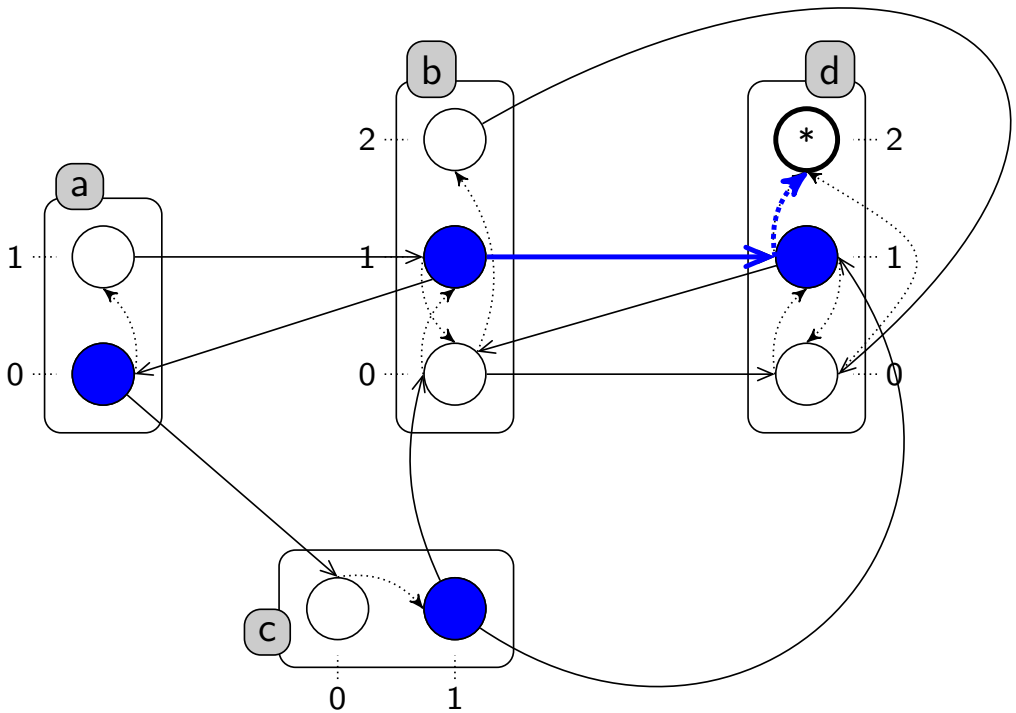

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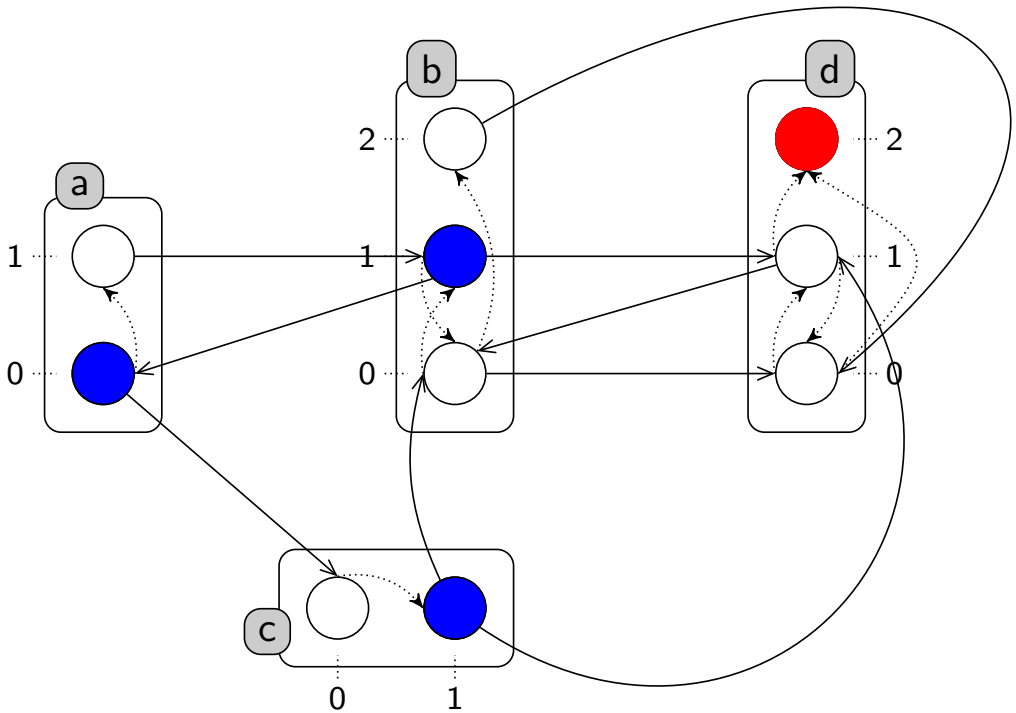
$$[\ \Rsh\ d_2\ ]$$

$\rightarrow$ Concretization of the objective = scenario

$$a_0 \rightarrow c_0 \Rsh c_1 :: \quad b_0 \rightarrow d_0 \Rsh d_1 :: \quad c_1 \rightarrow b_0 \Rsh b_1 :: \quad \underline{b_1 \rightarrow d_1 \Rsh d_2}$$

Static analysis: Reachability

Reachability of processes:



- Initial context

$$\langle a_0, b_0, c_0, z_0 \rangle$$

- Objectives

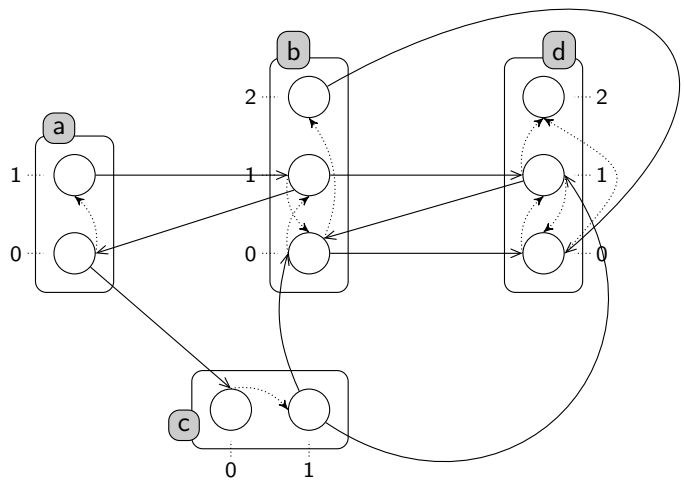
$$[\ \Rsh\ d_2\ ]$$

$\rightarrow$ Concretization of the objective = scenario

$$a_0 \rightarrow c_0 \Rsh c_1 :: \quad b_0 \rightarrow d_0 \Rsh d_1 :: \quad c_1 \rightarrow b_0 \Rsh b_1 :: \quad b_1 \rightarrow d_1 \Rsh d_2$$

Reachability ASP

Network evolution through ASP:

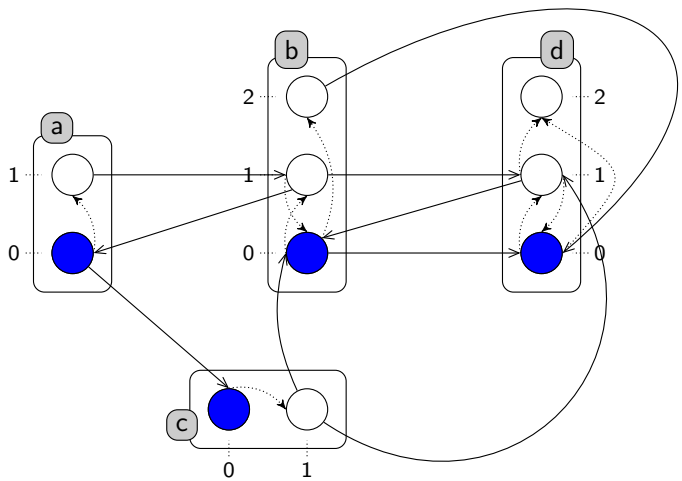


Reachability ASP

Network evolution through ASP:

Initializing :

`init(activeProcess("a",0)).` with `a`: sort, `0`: process index

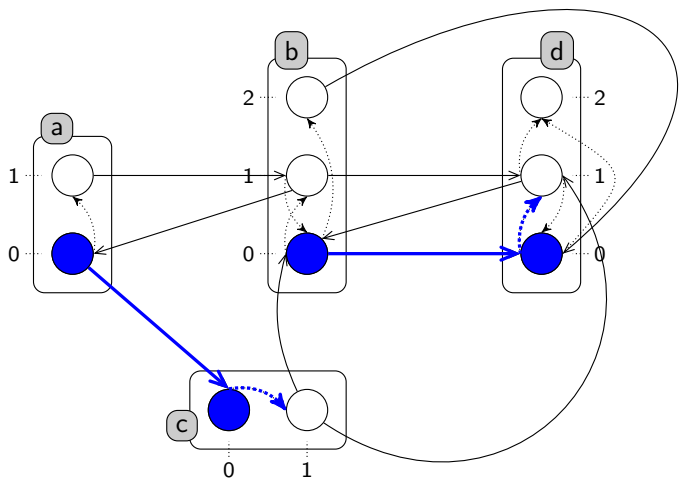


Reachability ASP

Network evolution through ASP:

Playable actions at time T:

```
playableAction(A,I,B,J,K,T) :- action(A,I,B,J,K),
                    instate(actifProcess(B,J),T),
                    instate(actifProcess(A,I),T), time(T).
```

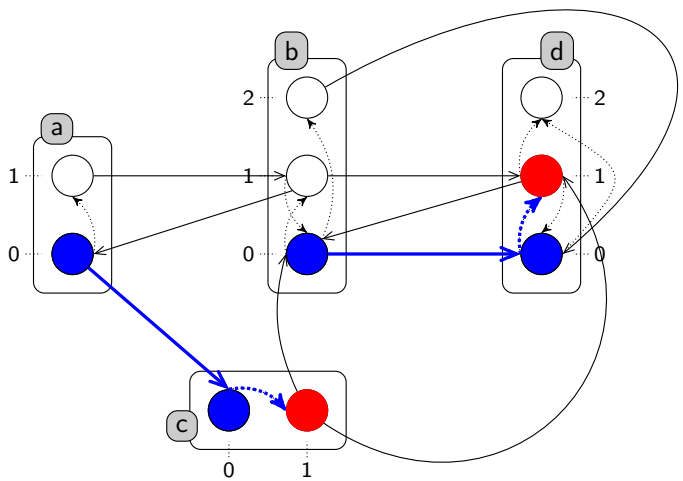


Reachability ASP

Network evolution through ASP:

Change active processes:

```
{activeFromTo(B,J,K,T)} :- playableAction(A,I,B,J,K,T),
                           instate(activeProcess(A,I),T),
                           instate(activeProcess(B,J),T), J!=K, time(T).
                           :- 2{ activeFromTo(B,J,K,T)}, time(T).
```

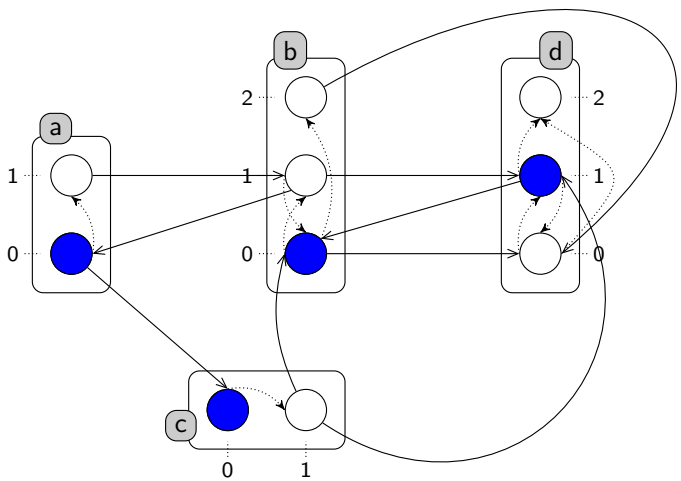


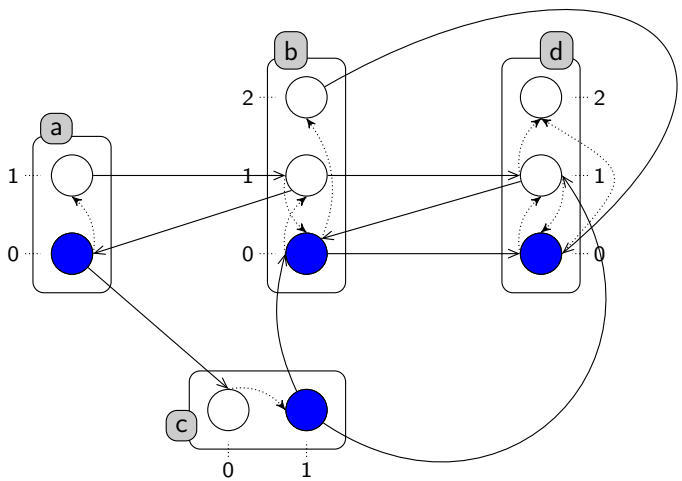
Reachability ASP

Network evolution through ASP:

Active processes at next state (T+1):

```
instate(activeProcess(B,K),T+1) :- activeFromTo(B,J,K,T), time(T).
instate(activeProcess(A,I),T+1) :- instate(activeProcess(A,I),T),
                                   activeFromTo(B,J,K,T), A!=B, time(T).
```

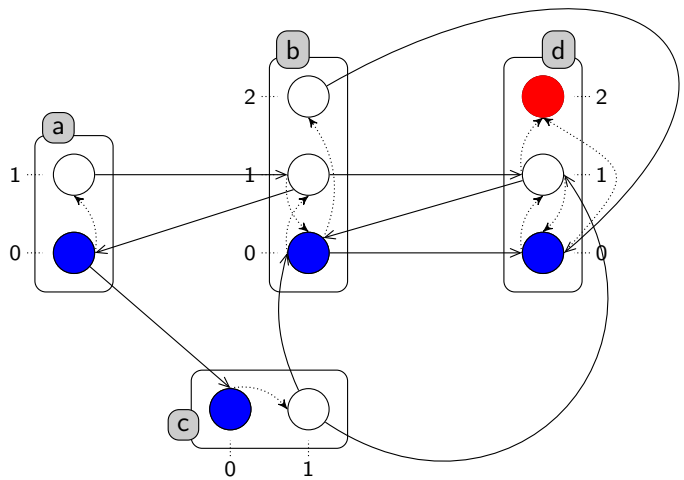




Reachability ASP

Success reachability through ASP:

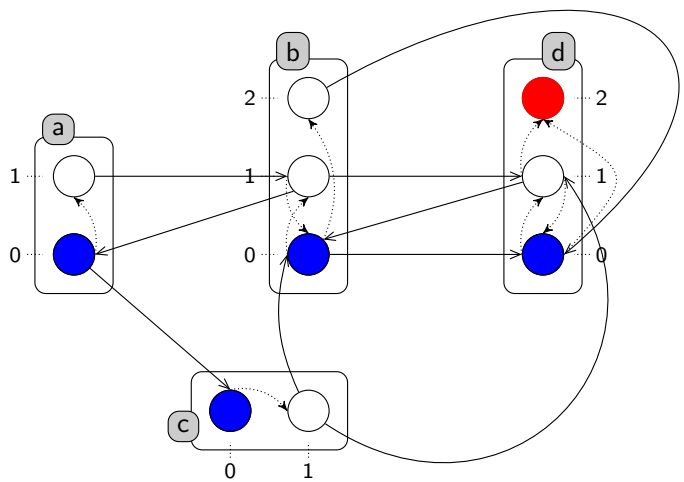
```
goal(activeProcess("d",2)).
```



Reachability ASP

Success reachability through ASP:

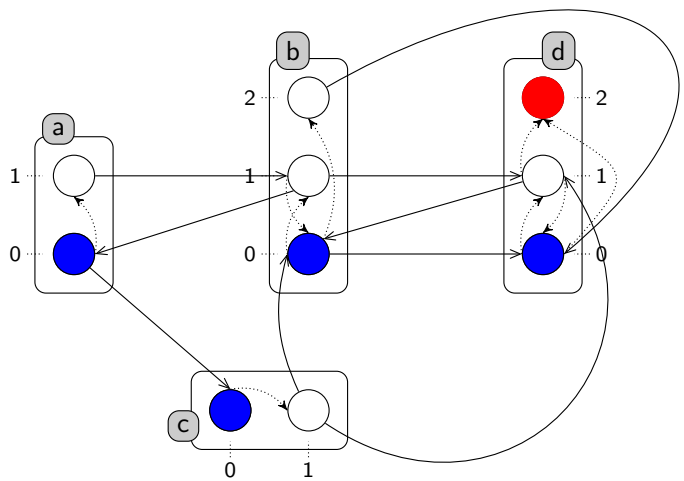
```
goal(activeProcess("d",2)).
satisfaible(F,T) :- goal(F), instate(F,T).
```



Reachability ASP

Success reachability through ASP:

```
goal(activeProcess("d",2)).
satisfaible(F,T) :- goal(F), instate(F,T).
time(0..N).
```

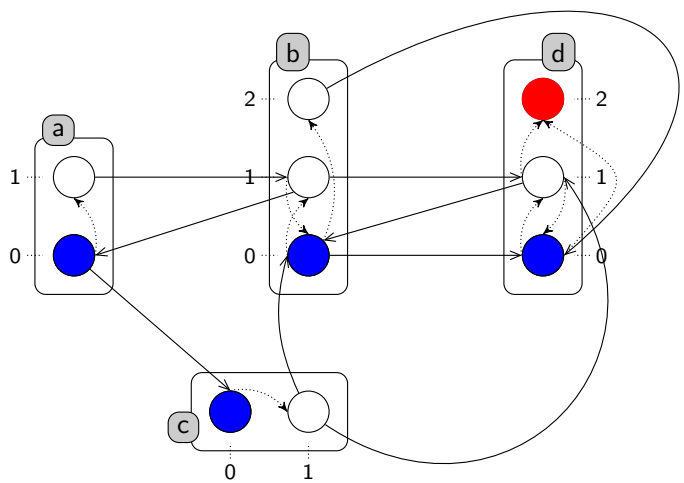


Reachability ASP

Success reachability through ASP:

```
goal(activeProcess("d",2)).
satisfaible(F,T) :- goal(F), instate(F,T).
time(0..N).
```

prédict N –> **Inconvenient**



Reachability ASP

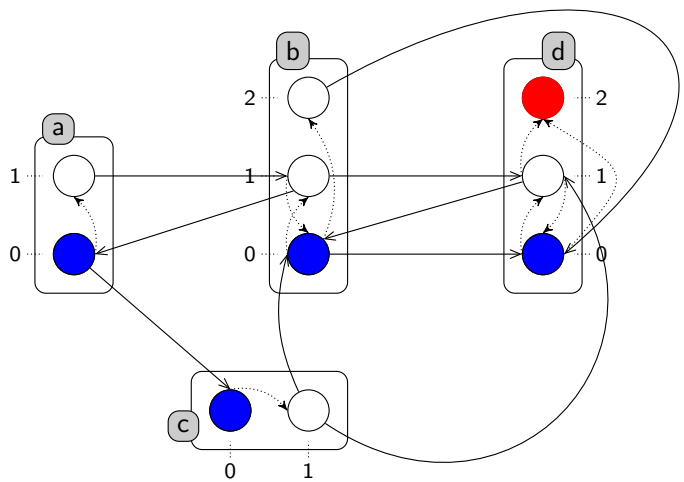
Success reachability through ASP:

Iterative:

```
goal(activeProcess("d",2)).

#cumulative t
playableAction(A, I, B, J, K,t), activeFromTo(B, J, K,t),
instate(activeProcess(A, I),t + 1)...

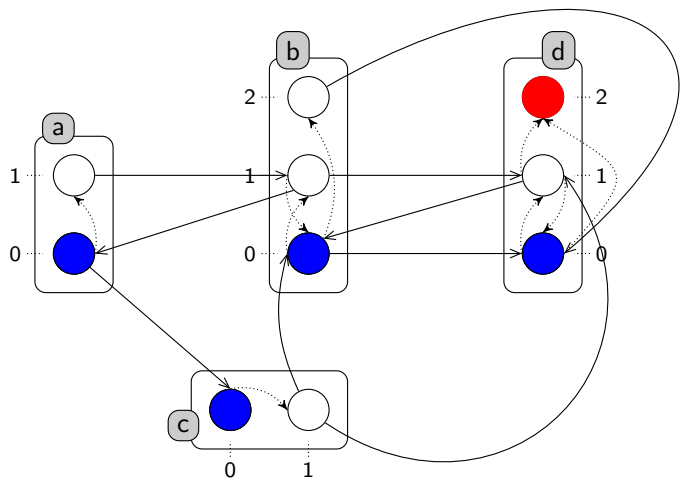
#volatile t
notSatisfaible(t) :- goal(F), not instate(F,t).
:- notSatisfaible(t).
```



Reachability ASP

Success reachability through ASP:

Answer 1: `activeFromTo(c,0,1,0), activeFromTo(d,0,1,1), activeFromTo(b,0,1,2), activeFromTo(d,1,2,3).`



Reachability ASP

Comparaison:

ERBB_G1 : **42** sorts, **152** processes, **399** actions, $2^{\mathbf{70}}$*states*
initialisation: level 0 except 5
obective: $goal(activeProcess("pRB", 1))$.

The Table below describes the results:

Model	#steps	PINT	ASP	ASP iterative
ERBB_G1	18	0.022s	10.620s	5.020s

Conclusion

- New developed dynamic analysis to Process hitting models:
  - Fixed point
  - Network evolution
  - Reachability
- Perspectives:
  - Attractors
  - Network evolution without cycles

Bibliography

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[3] Gebser, Martin and Kaminski, Roland and Kaufmann, Benjamin and Ostrowski, Max and Schaub, Torsten and Thiele, Sven A user's guide to gringo, clasp, clingo, and iclingos, 2008.

Thank you