Dynamical behavior of a Boolean network with different update schedules

Lilian Salinas

Department of Computer Science, U. of Concepción.

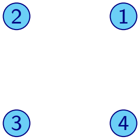
January 7, 2020

Contents

Boolean networks

Boolean Networks

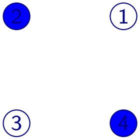
- A finite set V of n element and n states variables $x_v \in \{0,1\}, \; v \in V$



Boolean networks

Boolean Networks

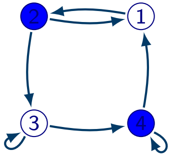
- A finite set V of n element and n states variables $x_v \in \{0, 1\}, \ v \in V$



Boolean networks

Boolean Networks

- A finite set V of n element and n states variables $x_v \in \{0,1\},\ v \in V$
- A global activation function
  $f = (f_v)_{v \in V} : \{0,1\}^n \to \{0,1\}^n$
  - Composed by local activation functions $f_v : \{0,1\}^n \to \{0,1\}$



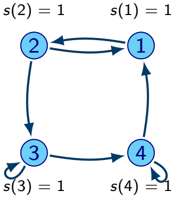
$$f_1(x) = x_2 \wedge x_4$$
$$f_2(x) = x_1$$
$$f_3(x) = x_2 \vee x_3$$
$$f_4(x) = x_3 \wedge x_4$$

Boolean networks

$f_1(x) = x_2 \wedge x_4$
$f_2(x) = x_1$
$f_3(x) = x_2 \vee x_3$
$f_4(x) = x_3 \wedge x_4$

Schedule:

Synchronous: $s = \{1, 2, 3, 4\}$

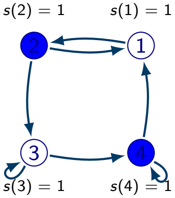


Boolean networks

$f_1(x) = x_2 \wedge x_4$
$f_2(x) = x_1$
$f_3(x) = x_2 \vee x_3$
$f_4(x) = x_3 \wedge x_4$

Schedule:

Synchronous: $s = \{1, 2, 3, 4\}$

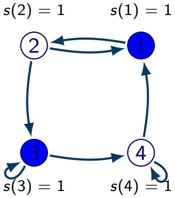


Boolean networks

$f_1(x) = x_2 \wedge x_4$
$f_2(x) = x_1$
$f_3(x) = x_2 \vee x_3$
$f_4(x) = x_3 \wedge x_4$

Schedule:

Synchronous: $s = \{1, 2, 3, 4\}$

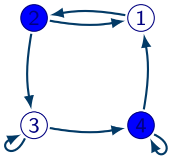


Boolean networks

$f_1(x) = x_2 \wedge x_4$
$f_2(x) = x_1$
$f_3(x) = x_2 \vee x_3$
$f_4(x) = x_3 \wedge x_4$

Schedule:

Asynchronous: $s = \{i\}$

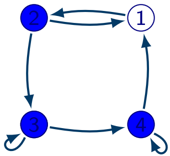


Boolean networks

$f_1(x) = x_2 \wedge x_4$
$f_2(x) = x_1$
$f_3(x) = x_2 \vee x_3$
$f_4(x) = x_3 \wedge x_4$

Schedule:

Asynchronous: $s = \{3\}$

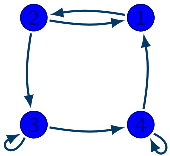


Boolean networks

$f_1(x) = x_2 \wedge x_4$
$f_2(x) = x_1$
$f_3(x) = x_2 \vee x_3$
$f_4(x) = x_3 \wedge x_4$

Schedule:

Asynchronous: $s = \{1\}$

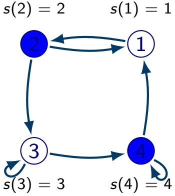


Boolean networks

$f_1(x) = x_2 \wedge x_4$
$f_2(x) = x_1$
$f_3(x) = x_2 \vee x_3$
$f_4(x) = x_3 \wedge x_4$

Schedule:

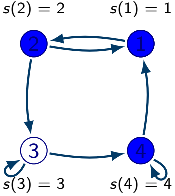
Sequential: $s = \{1\}\,\{2\}\,\{3\}\,\{4\}$



Boolean networks

$f_1(x) = x_2 \wedge x_4$
$f_2(x) = x_1$
$f_3(x) = x_2 \vee x_3$
$f_4(x) = x_3 \wedge x_4$

Schedule:
Sequential: $s = \{1\}\,\{2\}\,\{3\}\,\{4\}$

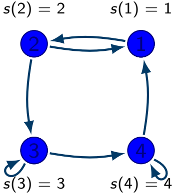


Boolean networks

$$f_1(x) = x_2 \wedge x_4$$
$$f_2(x) = x_1$$
$$f_3(x) = x_2 \vee x_3$$
$$f_4(x) = x_3 \wedge x_4$$

Schedule:

Sequential: $s = \{1\}\,\{2\}\,\{3\}\,\{4\}$

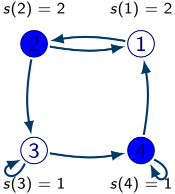


Boolean networks

$$f_1(x) = x_2 \wedge x_4$$
$$f_2(x) = x_1$$
$$f_3(x) = x_2 \vee x_3$$
$$f_4(x) = x_3 \wedge x_4$$

Schedule:

Block-sequential: $s = \{3,4\}\,\{1,2\}$

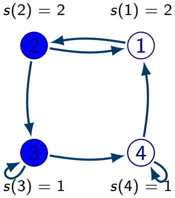


Boolean networks

$f_1(x) = x_2 \wedge x_4$
$f_2(x) = x_1$
$f_3(x) = x_2 \vee x_3$
$f_4(x) = x_3 \wedge x_4$

Schedule:

Block-sequential: $s = \{3, 4\}\{1, 2\}$

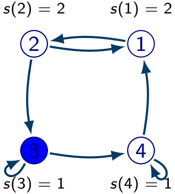


Boolean networks

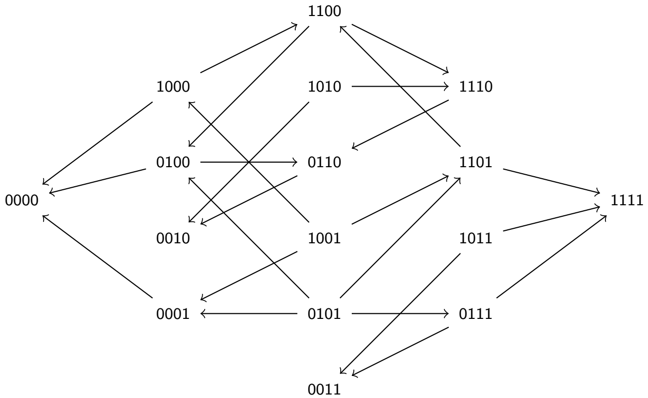
$f_1(x) = x_2 \wedge x_4$
$f_2(x) = x_1$
$f_3(x) = x_2 \vee x_3$
$f_4(x) = x_3 \wedge x_4$

Schedule:

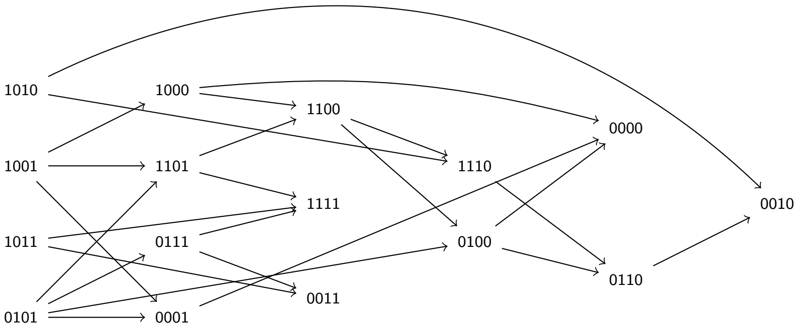
Block-sequential: $s = \{3, 4\}\,\{1, 2\}$



Asynchronous



Asynchronous



Dynamical behavior of deterministic update schedule

The iteration of the Boolean network is given by:

$$x_v^{k+1} = f_v(x_u^{l_u} \colon u \in V), \quad l_u = \begin{cases} k & \text{if } s(v) \leq s(u) \\ k+1 & \text{if } s(v) > s(u) \end{cases}$$

Dynamical behavior of deterministic update schedule

The iteration of the Boolean network is given by:

$$x_v^{k+1} = f_v(x_u^{l_u} \colon u \in V), \quad l_u = \begin{cases} k & \text{if } s(v) \leq s(u) \\ k+1 & \text{if } s(v) > s(u) \end{cases}$$

Dynamical behavior

$f^s : \{0,1\}^n \to \{0,1\}^n$:

$$f_v^s(x) = f_v(g_{v,u}^s(x) \colon u \in V), \quad g_{v,u}^s(x) = \begin{cases} x_u & \text{if } s(v) \leq s(u) \\ f_u^s(x) & \text{if } s(v) > s(u) \end{cases}$$

Example of dynamical behavior

$s_1 = \{1, 2, 3, 4\}$

$$
\begin{aligned}
f_1^{s_1}(x) &= x_2 \wedge x_4 \\
f_2^{s_1}(x) &= x_1 \\
f_3^{s_1}(x) &= x_2 \vee x_3 \\
f_4^{s_1}(x) &= x_3 \wedge x_4
\end{aligned}
$$

Example of dynamical behavior

$s_1 = \{1, 2, 3, 4\}$ $\qquad$ $s_2 = \{1\}\{2\}\{3\}\{4\}$

$$
\begin{aligned}
f_1^{s_1}(x) &= x_2 \wedge x_4 \\
f_2^{s_1}(x) &= x_1 \\
f_3^{s_1}(x) &= x_2 \vee x_3 \\
f_4^{s_1}(x) &= x_3 \wedge x_4
\end{aligned}
$$

Example of dynamical behavior

$s_1 = \{1, 2, 3, 4\}$ $\qquad$ $s_2 = \{1\}\{2\}\{3\}\{4\}$

$$\begin{aligned} f_1^{s_1}(x) &= x_2 \wedge x_4 \\ f_2^{s_1}(x) &= x_1 \\ f_3^{s_1}(x) &= x_2 \vee x_3 \\ f_4^{s_1}(x) &= x_3 \wedge x_4 \end{aligned}$$

$$f_1^{s_2}(x) = x_2 \wedge x_4$$

Example of dynamical behavior

$s_1 = \{1, 2, 3, 4\}$ $\qquad$ $s_2 = \{1\}\{2\}\{3\}\{4\}$

$$f_1^{s_1}(x) = x_2 \wedge x_4 \qquad f_1^{s_2}(x) = x_2 \wedge x_4$$
$$f_2^{s_1}(x) = x_1 \qquad f_2^{s_2}(x) = x_2 \wedge x_4$$
$$f_3^{s_1}(x) = x_2 \vee x_3$$
$$f_4^{s_1}(x) = x_3 \wedge x_4$$

Example of dynamical behavior

$s_1 = \{1, 2, 3, 4\}$ $\qquad$ $s_2 = \{1\}\{2\}\{3\}\{4\}$

$$\begin{array}{ll}
f_1^{s_1}(x) = x_2 \wedge x_4 & \qquad f_1^{s_2}(x) = x_2 \wedge x_4 \\
f_2^{s_1}(x) = x_1 & \qquad f_2^{s_2}(x) = x_2 \wedge x_4 \\
f_3^{s_1}(x) = x_2 \vee x_3 & \qquad f_3^{s_2}(x) = (x_2 \wedge x_4) \vee x_3 \\
f_4^{s_1}(x) = x_3 \wedge x_4 &
\end{array}$$

Example of dynamical behavior

$s_1 = \{1, 2, 3, 4\}$ $\qquad$ $s_2 = \{1\}\,\{2\}\,\{3\}\,\{4\}$

$$\begin{aligned} f_1^{s_1}(x) &= x_2 \wedge x_4 \\ f_2^{s_1}(x) &= x_1 \\ f_3^{s_1}(x) &= x_2 \vee x_3 \\ f_4^{s_1}(x) &= x_3 \wedge x_4 \end{aligned} \qquad \begin{aligned} f_1^{s_2}(x) &= x_2 \wedge x_4 \\ f_2^{s_2}(x) &= x_2 \wedge x_4 \\ f_3^{s_2}(x) &= (x_2 \wedge x_4) \vee x_3 \\ f_4^{s_2}(x) &= ((x_2 \wedge x_4) \vee x_3) \wedge x_4 \end{aligned}$$

Example of dynamical behavior

$s_1 = \{1, 2, 3, 4\}$ $\quad$ $s_2 = \{1\}\,\{2\}\,\{3\}\,\{4\}$ $\quad$ $s_3 = \{3, 4\}\,\{1, 2\}$

$$\begin{aligned} f_1^{s_1}(x) &= x_2 \wedge x_4 \\ f_2^{s_1}(x) &= x_1 \\ f_3^{s_1}(x) &= x_2 \vee x_3 \\ f_4^{s_1}(x) &= x_3 \wedge x_4 \end{aligned}$$

$$\begin{aligned} f_1^{s_2}(x) &= x_2 \wedge x_4 \\ f_2^{s_2}(x) &= x_2 \wedge x_4 \\ f_3^{s_2}(x) &= (x_2 \wedge x_4) \vee x_3 \\ f_4^{s_2}(x) &= ((x_2 \wedge x_4) \vee x_3) \wedge x_4 \end{aligned}$$

Example of dynamical behavior

$s_1 = \{1,2,3,4\}$ $\qquad$ $s_2 = \{1\}\{2\}\{3\}\{4\}$ $\qquad$ $s_3 = \{3,4\}\{1,2\}$

$$
\begin{aligned}
f_1^{s_1}(x) &= x_2 \wedge x_4 \\
f_2^{s_1}(x) &= x_1 \\
f_3^{s_1}(x) &= x_2 \vee x_3 \\
f_4^{s_1}(x) &= x_3 \wedge x_4
\end{aligned}
$$

$$
\begin{aligned}
f_1^{s_2}(x) &= x_2 \wedge x_4 \\
f_2^{s_2}(x) &= x_2 \wedge x_4 \\
f_3^{s_2}(x) &= (x_2 \wedge x_4) \vee x_3 \\
f_4^{s_2}(x) &= ((x_2 \wedge x_4) \vee x_3) \wedge x_4
\end{aligned}
$$

$$
\begin{aligned}
f_3^{s_3}(x) &= x_2 \vee x_3 \\
f_4^{s_3}(x) &= x_3 \wedge x_4
\end{aligned}
$$

Example of dynamical behavior

$s_1 = \{1,2,3,4\}$

$$\begin{aligned} f_1^{s_1}(x) &= x_2 \wedge x_4 \\ f_2^{s_1}(x) &= x_1 \\ f_3^{s_1}(x) &= x_2 \vee x_3 \\ f_4^{s_1}(x) &= x_3 \wedge x_4 \end{aligned}$$

$s_2 = \{1\}\{2\}\{3\}\{4\}$

$$\begin{aligned} f_1^{s_2}(x) &= x_2 \wedge x_4 \\ f_2^{s_2}(x) &= x_2 \wedge x_4 \\ f_3^{s_2}(x) &= (x_2 \wedge x_4) \vee x_3 \\ f_4^{s_2}(x) &= ((x_2 \wedge x_4) \vee x_3) \wedge x_4 \end{aligned}$$

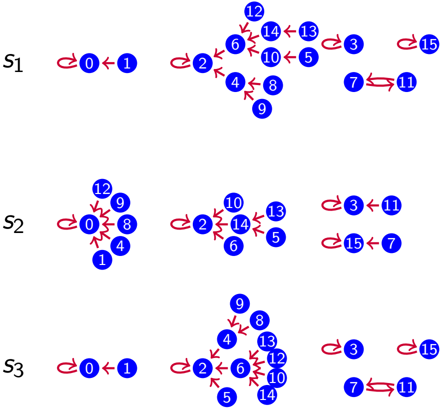
$s_3 = \{3,4\}\{1,2\}$

$$\begin{aligned} f_1^{s_3}(x) &= x_2 \wedge x_3 \wedge x_4 \\ f_2^{s_3}(x) &= x_1 \\ f_3^{s_3}(x) &= x_2 \vee x_3 \\ f_4^{s_3}(x) &= x_3 \wedge x_4 \end{aligned}$$

Dynamics

$s_1 = \{1,2,3,4\}$
$s_2 = \{1\}\{2\}\{3\}\{4\}$
$s_3 = \{3,4\}\{1,2\}$

	State	f^{s_1}	f^{s_2}	f^{s_3}
0	0000	0000	0000	0000
1	0001	0000	0000	0000
2	0010	0010	0010	0010
3	0011	0011	0011	0011
4	0100	0010	0000	0010
5	0101	1010	1110	0010
6	0110	0010	0010	0010
7	0111	1011	1111	1011
8	1000	0100	0000	0100
9	1001	0100	0000	0100
10	1010	0110	0010	0110
11	1011	0111	0011	0111
12	1100	0110	0000	0110
13	1101	1110	1110	0110
14	1110	0110	0010	0110
15	1111	1111	1111	1111



Dynamical problems related to schedule

1. Does there exists some invariant with respect to the update schedule?

Dynamical problems related to schedule

1. Does there exists some invariant with respect to the update schedule?
2. Does there exist two different update schedules s_1, s_2 such that the function f updated with s_1 has the same dynamical behavior, that f updated with s_2?

Dynamical problems related to schedule

1. Does there exists some invariant with respect to the update schedule?
2. Does there exist two different update schedules s_1, s_2 such that the function f updated with s_1 has the same dynamical behavior, that f updated with s_2?
3. Does there exist two update schedules s_1, s_2 such that the function f updated with s_1 has the same attractors that f updated with s_2?

Dynamical problems related to schedule

1. Does there exists some invariant with respect to the update schedule?
2. Does there exist two different update schedules s_1, s_2 such that the function f updated with s_1 has the same dynamical behavior, that f updated with s_2?
3. Does there exist two update schedules s_1, s_2 such that the function f updated with s_1 has the same attractors that f updated with s_2?
4. Does there exist an update schedule s such that the function f updated with s does not have limit cycles?

Dynamical problems related to schedule

1. Does there exists some invariant with respect to the update schedule?
2. Does there exist two different update schedules s_1, s_2 such that the function f updated with s_1 has the same dynamical behavior, that f updated with s_2?
3. Does there exist two update schedules s_1, s_2 such that the function f updated with s_1 has the same attractors that f updated with s_2?
4. Does there exist an update schedule s such that the function f updated with s does not have limit cycles?
5. Does there exist an update schedule s such that the function f updated with s has limit cycles?

Dynamical problems related to schedule

1. Does there exists some invariant with respect to the update schedule?
2. Does there exist two different update schedules s_1, s_2 such that the function f updated with s_1 has the same dynamical behavior, that f updated with s_2?
3. Does there exist two update schedules s_1, s_2 such that the function f updated with s_1 has the same attractors that f updated with s_2?
4. Does there exist an update schedule s such that the function f updated with s does not have limit cycles?
5. Does there exist an update schedule s such that the function f updated with s has limit cycles?
6. Does there exist an update schedule s such that given $x^1, \ldots, x^k, y^1, \ldots, y^k \in \{0,1\}^n$, $f^s(x^i) = y^i$?

Question 1

Fixed points does not change with different update schedules.

Question 1

Fixed points does not change with different update schedules.

The iteration of the Boolean network is given by:

$$x_v^{k+1} = f_v(x_u^{l_u} : u \in V), \quad l_u = \begin{cases} k & \text{if } s(v) \leq s(u) \\ k+1 & \text{if } s(v) > s(u) \end{cases}$$

and the limit cycles?

Theorem (Goles and Salinas (2008))

Let (f, s_p) and (f, s) be two BNs where the loops are monotonic and such that s is a sequential update. Then, there does not exists a common limit cycle of both networks.

and the limit cycles?

Theorem (Goles and Salinas (2008))

Let (f, s_p) and (f, s) be two BNs where the loops are monotonic and such that s is a sequential update. Then, there does not exists a common limit cycle of both networks.

Theorem (Aracena, Goles, Moreira, Salinas (2009))

Let (f, s) be a Boolean network. There exists s' an sequential update schedule such that (f, s') does not preserve the limit cycles of (F, s).

and the limit cycles?

Theorem (Goles and Salinas (2008))

Let (f, s_p) and (f, s) be two BNs where the loops are monotonic and such that s is a sequential update. Then, there does not exists a common limit cycle of both networks.

Theorem (Aracena, Goles, Moreira, Salinas (2009))

Let (f, s) be a Boolean network. There exists s' an sequential update schedule such that (f, s') does not preserve the limit cycles of (F, s).

Proof(Idea)

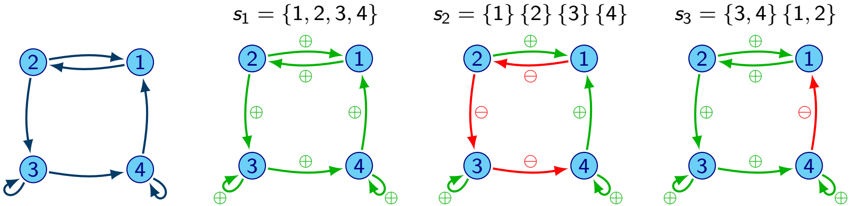
Let $\{i_1, i_2, \ldots, i_n\}$ with $s(i_1) \leq s(i_2) \leq \cdots \leq s(i_n)$. Then,
$s'(i_j) = n + 1 - j$, i.e. $s'(i_1) > s'(i_2) > \cdots > s'(i_n)$, verifies the property.

Update digraph

A labeled digraph is a graph G with a label function lab, (G, lab) such that: $lab : A(G) \to \{\oplus, \ominus\}$

We say that a labeled digraph is an update digraph if there exists $s : V(G) \to \{1, \ldots, n\}$, an update function such that:

$$\forall (u, v) \in A(G), lab(u, v) = \oplus \iff s(u) \geq s(v)$$



Question 2

Theorem (Aracena, Goles, Moreira, Salinas (2009))

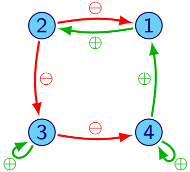
Given two Boolean networks $N_1 = (f, s)$ and $N_2 = (f, s')$ which differ only in the update schedule. If the update digraphs associated to them are equal, then both networks have the same dynamical behavior.

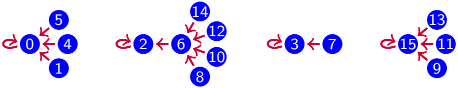
Question 2

Theorem (Aracena, Goles, Moreira, Salinas (2009))

Given two Boolean networks $N_1 = (f, s)$ and $N_2 = (f, s')$ which differ only in the update schedule. If the update digraphs associated to them are equal, then both networks have the same dynamical behavior.

$s = \{2\}\{1\}\{3\}\{4\}$ and $s' = \{2\}\{3\}\{1\}\{4\}$





Of this way, we say that two update schedules are equivalent if and only if they have the same update digraph.

New questions

- Given a labeled digraph. Is it an update digraph?

New questions

- Given a labeled digraph. Is it an update digraph?
- If it is an update digraph. How do we find un update shedule with this update digraph?

New questions

- Given a labeled digraph. Is it an update digraph?
- If it is an update digraph. How do we find un update shedule with this update digraph?
- How many non-equivalent update schedules are there? How many elements does each have?

New questions

- Given a labeled digraph. Is it an update digraph?
- If it is an update digraph. How do we find un update shedule with this update digraph?
- How many non-equivalent update schedules are there? How many elements does each have?
- Given a certain dynamical property. Is there an equivalence class that holds it?

Labels and Update digraphs

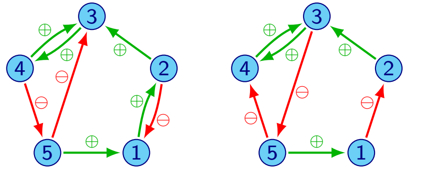
Reverse Digraph

Given (G, lab) a labeled digraph, we define the reverse digraph as (G_r, lab_r), where:

$$\begin{aligned} V(G_r) &= V(G) \\ A(G_r) &= \{(u,v)/((v,u) \in A(G) \wedge lab(v,u) = \ominus) \\ &\quad \vee((u,v) \in A(G) \wedge lab(u,v) = \oplus)\} \end{aligned}$$

$$lab_r(u,v) = \begin{cases} \ominus & (v,u) \in A(G) \wedge lab(v,u) = \ominus \\ \oplus & \text{otherwise} \end{cases}$$

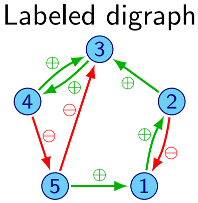
Labeled digraph | Reverse digraph

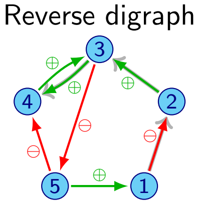


Labels and Update digraphs

Reverse Path

A reverse path is a path in the reverse graph.





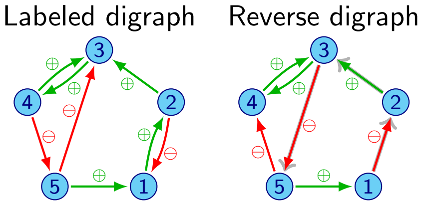
Labels and Update digraphs

Reverse Path

A reverse path is a path in the reverse graph.

Negative Reverse Path

A negative reverse path is a path with an arc labeled $\ominus$ in the reverse graph.



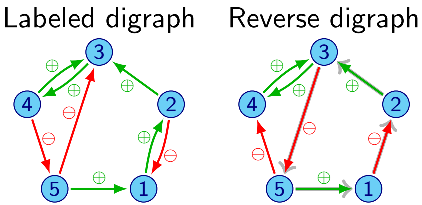
Labels and Update digraphs

Forbidden cycle

A forbidden cycle is a cycle with an arc labeled $\ominus$ in the reverse graph.

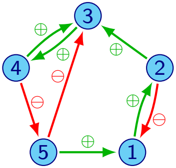
Theorem (Montalva (2012))

A labeled digraph is an update digraph if and only if there does not exist a forbidden cycle in its reverse digraph.



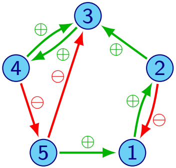
Is it an update digraph?

G :

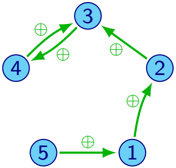


Is it an update digraph?

G :

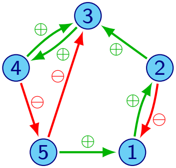


$G_{\oplus}$:

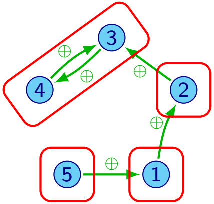


Is it an update digraph?

G :

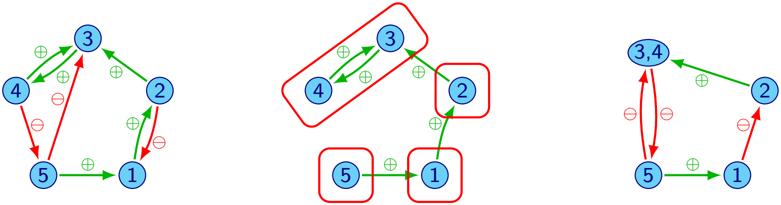


$G_{\oplus}$:



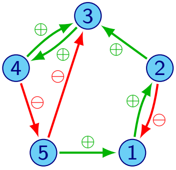
Is it an update digraph?

G : $G_{\oplus}$: G_R :

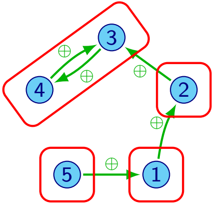


Is it an update digraph?

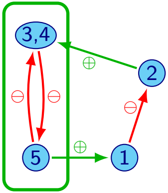
G :



$G_{\oplus}$:



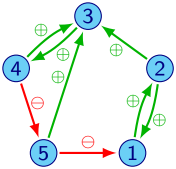
G_R :



Forbidden cycle

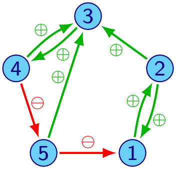
How I find the update schedule of a labeling?

G :

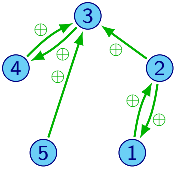


How I find the update schedule of a labeling?

G :

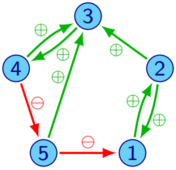


$G_{\oplus}$:

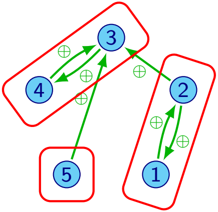


How I find the update schedule of a labeling?

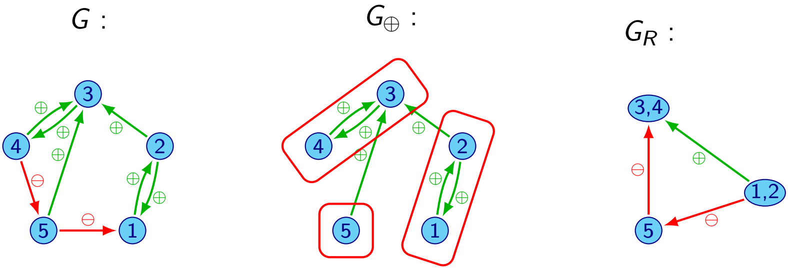
G :



$G_{\oplus}$:

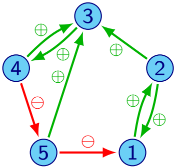


How I find the update schedule of a labeling?

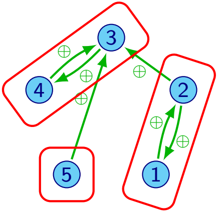


How I find the update schedule of a labeling?

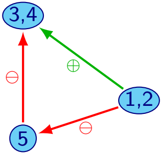
G :



$G_{\oplus}$:



G_R :



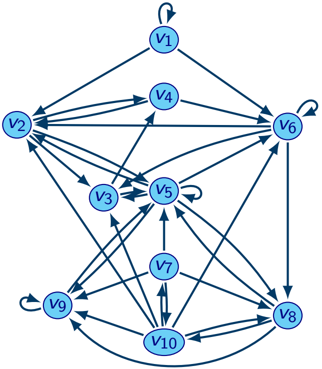
$$s = \{3,4\}\,\{5\}\,\{1,2\}$$

Transition problem (Question 6)

Does there exist an update schedule s such that given $x^1, \ldots, x^k, y^1, \ldots, y^k \in \{0,1\}^n$, $f^s(x^i) = y^i$?

Transition problem (Question 6)

Does there exist an update schedule s such that given $x^1, \ldots, x^k, y^1, \ldots, y^k \in \{0,1\}^n$, $f^s(x^i) = y^i$?



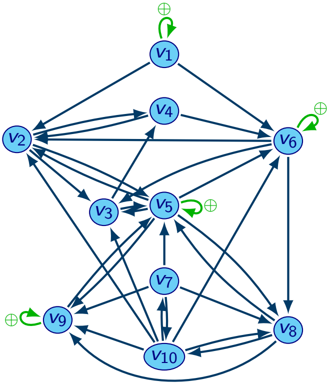
Limit cycle										
$v \in V(G^f)$	v_1	v_2	v_3	v_4	v_5	v_6	v_7	v_8	v_9	v_{10}
x^0	1	0	1	0	0	0	0	1	1	0
x^1	1	0	1	1	0	0	0	1	0	0
x^2	1	0	1	1	1	0	0	1	0	0
x^3	1	0	0	1	1	0	0	0	0	0
x^4	1	0	0	0	1	0	0	0	1	1
x^5	1	0	0	0	1	0	1	0	1	1
x^6	1	0	0	0	0	0	1	1	1	0
x^7	1	0	1	0	0	0	0	1	1	0

$$
\begin{aligned}
f_{v_1}(x) &= x_{v_1}\\
f_{v_2}(x) &= (\neg x_{v_1} \wedge \neg x_{v_{10}}) \wedge ([\neg x_{v_4} \wedge \neg x_{v_5}] \vee x_{v_6})\\
f_{v_3}(x) &= (\neg x_{v_2} \wedge \neg x_{v_5} \wedge \neg x_{v_{10}}) \vee (x_{v_6} \wedge \neg x_{v_2} \wedge \neg x_{v_{10}})\\
f_{v_4}(x) &= x_{v_3} \wedge \neg x_{v_2}\\
f_{v_5}(x) &= (\neg x_{v_2} \wedge \neg x_{v_7} \wedge \neg(x_{v_8} \wedge x_{v_9})) \wedge (x_{v_3} \vee x_{v_5})\\
f_{v_6}(x) &= (\neg x_{v_1} \wedge \neg x_{v_{10}}) \wedge ([\neg x_{v_4} \wedge \neg x_{v_5}] \vee [x_{v_6} \wedge \neg(x_{v_4} \wedge x_{v_5})])\\
f_{v_7}(x) &= x_{v_{10}}\\
f_{v_8}(x) &= (\neg x_{v_5} \wedge \neg x_{v_{10}}) \vee x_{v_7} \vee (x_{v_6} \wedge \neg x_{v_{10}})\\
f_{v_9}(x) &= \neg x_{v_8} \vee (x_{v_8} \wedge x_{v_9} \wedge [x_{v_7} \vee x_{v_5} \vee x_{v_{10}}])\\
f_{v_{10}}(x) &= \neg x_{v_7} \wedge \neg x_{v_8}
\end{aligned}
$$

Fauré, A., Naldi, A., Chaouiya, C., and Thieffry, D. (2006). Dynamical analysis of a generic Boolean model for the control of the mammalian cell cycle. *Bioinformatics*, **22**, 124–131.

Transition problem (Question 6)

Does there exist an update schedule s such that given $x^1, \ldots, x^k, y^1, \ldots, y^k \in \{0,1\}^n$, $f^s(x^i) = y^i$?



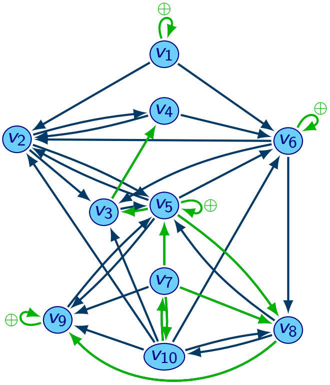
Limit cycle										
$v \in V(G^f)$	v_1	v_2	v_3	v_4	v_5	v_6	v_7	v_8	v_9	v_{10}
x^0	1	0	1	0	0	0	0	1	1	0
x^1	1	0	1	1	0	0	0	1	0	0
x^2	1	0	1	1	1	0	0	1	0	0
x^3	1	0	0	1	1	0	0	0	0	0
x^4	1	0	0	0	1	0	0	0	1	1
x^5	1	0	0	0	1	0	1	0	1	1
x^6	1	0	0	0	0	0	1	1	1	0
x^7	1	0	1	0	0	0	0	1	1	0

$$
\begin{aligned}
f_{v_1}(x) &= x_{v_1} \\
f_{v_2}(x) &= (\neg x_{v_1} \wedge \neg x_{v_{10}}) \wedge ([\neg x_{v_4} \wedge \neg x_{v_5}] \vee x_{v_6}) \\
f_{v_3}(x) &= (\neg x_{v_2} \wedge \neg x_{v_5} \wedge \neg x_{v_{10}}) \vee (x_{v_6} \wedge \neg x_{v_2} \wedge \neg x_{v_{10}}) \\
f_{v_4}(x) &= x_{v_3} \wedge \neg x_{v_2} \\
f_{v_5}(x) &= (\neg x_{v_2} \wedge \neg x_{v_7} \wedge \neg(x_{v_8} \wedge x_{v_9})) \wedge (x_{v_3} \vee x_{v_5}) \\
f_{v_6}(x) &= (\neg x_{v_1} \wedge \neg x_{v_{10}}) \wedge ([\neg x_{v_4} \wedge \neg x_{v_5}] \vee [x_{v_6} \wedge \neg(x_{v_4} \wedge x_{v_5})]) \\
f_{v_7}(x) &= x_{v_{10}} \\
f_{v_8}(x) &= (\neg x_{v_5} \wedge \neg x_{v_{10}}) \vee x_{v_7} \vee (x_{v_6} \wedge \neg x_{v_{10}}) \\
f_{v_9}(x) &= \neg x_{v_8} \vee (x_{v_8} \wedge x_{v_9} \wedge [x_{v_7} \vee x_{v_5} \vee x_{v_{10}}]) \\
f_{v_{10}}(x) &= \neg x_{v_7} \wedge \neg x_{v_8}
\end{aligned}
$$

Fauré, A., Naldi, A., Chaouiya, C., and Thieffry, D. (2006). Dynamical analysis of a generic Boolean model for the control of the mammalian cell cycle. *Bioinformatics*, **22**, 124–131.

Transition problem (Question 6)

Does there exist an update schedule s such that given $x^1, \ldots, x^k, y^1, \ldots, y^k \in \{0,1\}^n$, $f^s(x^i) = y^i$?



Limit cycle										
$v \in V(G^f)$	v_1	v_2	v_3	v_4	v_5	v_6	v_7	v_8	v_9	v_{10}
x^0	1	0	1	0	0	0	0	1	1	0
x^1	1	0	1	1	0	0	0	1	0	0
x^2	1	0	1	1	1	0	0	1	0	0
x^3	1	0	0	1	1	0	0	0	0	0
x^4	1	0	0	0	1	0	0	0	1	1
x^5	1	0	0	0	1	0	1	0	1	1
x^6	1	0	0	0	0	0	1	1	1	0
x^7	1	0	1	0	0	0	0	1	1	0

$$
\begin{aligned}
f_{v_1}(x) &= x_{v_1} \\
f_{v_2}(x) &= (\neg x_{v_1} \wedge \neg x_{v_{10}}) \wedge ([\neg x_{v_4} \wedge \neg x_{v_5}] \vee x_{v_6}) \\
f_{v_3}(x) &= (\neg x_{v_2} \wedge \neg x_{v_5} \wedge \neg x_{v_{10}}) \vee (x_{v_6} \wedge \neg x_{v_2} \wedge \neg x_{v_{10}}) \\
f_{v_4}(x) &= x_{v_3} \wedge \neg x_{v_2} \\
f_{v_5}(x) &= (\neg x_{v_2} \wedge \neg x_{v_7} \wedge \neg(x_{v_8} \wedge x_{v_9})) \wedge (x_{v_3} \vee x_{v_5}) \\
f_{v_6}(x) &= (\neg x_{v_1} \wedge \neg x_{v_{10}}) \wedge ([\neg x_{v_4} \wedge \neg x_{v_5}] \vee [x_{v_6} \wedge \neg(x_{v_4} \wedge x_{v_5})]) \\
f_{v_7}(x) &= x_{v_{10}} \\
f_{v_8}(x) &= (\neg x_{v_5} \wedge \neg x_{v_{10}}) \vee x_{v_7} \vee (x_{v_6} \wedge \neg x_{v_{10}}) \\
f_{v_9}(x) &= \neg x_{v_8} \vee (x_{v_8} \wedge x_{v_9} \wedge [x_{v_7} \vee x_{v_5} \vee x_{v_{10}}]) \\
f_{v_{10}}(x) &= \neg x_{v_7} \wedge \neg x_{v_8}
\end{aligned}
$$

Fauré, A., Naldi, A., Chaouiya, C., and Thieffry, D. (2006). Dynamical analysis of a generic Boolean model for the control of the mammalian cell cycle. *Bioinformatics*, **22**, 124–131.

Update Digraph Extension Problem

UDE

Given a labeled digraph (G, lab), find the set $\mathcal{S}(G, lab)$ of all fully labeled extensions lab' of lab such that (G, lab') is an update digraph.

Complexity

CUDE

Given (G, lab) a labeled digraph, to determine the cardinality of the set $\mathcal{S}(G, lab)$.

Complexity

CUDE

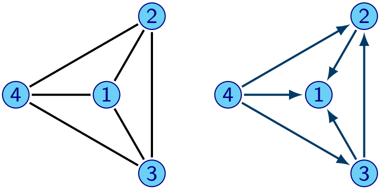
Given (G, lab) a labeled digraph, to determine the cardinality of the set $\mathcal{S}(G, lab)$.

Theorem

CUDE is $\#P$-complete

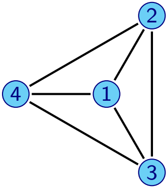
Acyclic orientation problem

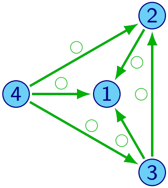
Given a graph to determine the number of acyclic orientations is #P-complete



Acyclic orientation problem

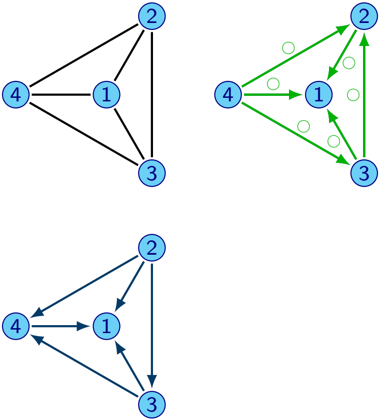
Given a graph to determine the number of acyclic orientations is #P-complete





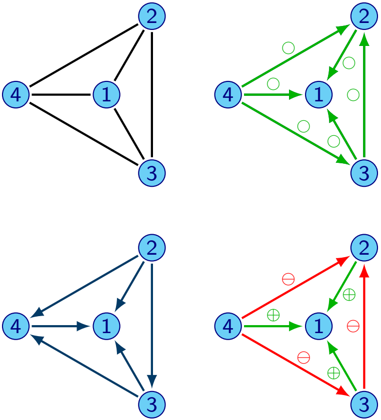
Acyclic orientation problem

Given a graph to determine the number of acyclic orientations is #P-complete



Acyclic orientation problem

Given a graph to determine the number of acyclic orientations is #P-complete



Extension existence

Theorem (Extension)

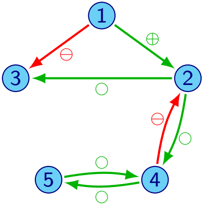
Given G a digraph and G' a subdigraph of G. if (G', lab') is an update digraph, then there exists $lab : A(G) \to \{\oplus, \ominus\}$ such that (G, lab) is an update digraph and $lab|_{A(G')} = lab'$.

Force

Proposition

Given a labeled digraph (G, lab) and an arc (i, j) with $lab(i, j) = \bigcirc$:

- *If there exists a reverse path from i to j, then the arc (i, j) must be labeled $\oplus$*
- *If there exists a negative reverse path from j to i, then the arc (i, j) must be labeled $\ominus$*

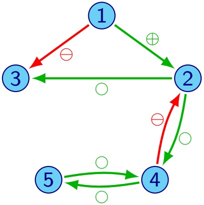


Force

Proposition

Given a labeled digraph (G, lab) and an arc (i,j) with $lab(i,j) = \bigcirc$:

- *If there exists a reverse path from i to j, then the arc (i,j) must be labeled $\oplus$*
- *If there exists a negative reverse path from j to i, then the arc (i,j) must be labeled $\ominus$*



Matrix M

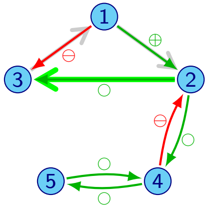
$V(G)$	1	2	3	4	5
1	∞	1	∞	-1	∞
2	∞	∞	∞	-1	∞
3	-1	-1	∞	-1	∞
4	∞	∞	∞	∞	∞
5	∞	∞	∞	∞	∞

Force

Proposition

Given a labeled digraph (G, lab) and an arc (i,j) with $lab(i,j) = \bigcirc$:

- *If there exists a reverse path from i to j, then the arc (i,j) must be labeled $\oplus$*
- *If there exists a negative reverse path from j to i, then the arc (i,j) must be labeled $\ominus$*



Matrix M

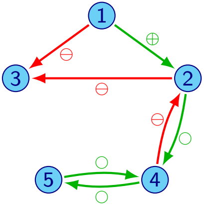
$V(G)$	1	2	3	4	5
1	∞	1	∞	-1	∞
2	∞	∞	∞	-1	∞
3	-1	**-1**	∞	-1	∞
4	∞	∞	∞	∞	∞
5	∞	∞	∞	∞	∞

Force

Proposition

Given a labeled digraph (G, lab) and an arc (i, j) with $lab(i, j) = \bigcirc$:

- *If there exists a reverse path from i to j, then the arc (i, j) must be labeled $\oplus$*
- *If there exists a negative reverse path from j to i, then the arc (i, j) must be labeled $\ominus$*



Matrix M

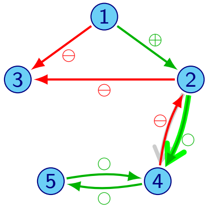
$V(G)$	1	2	3	4	5
1	∞	1	∞	-1	∞
2	∞	∞	∞	-1	∞
3	-1	-1	∞	-1	∞
4	∞	∞	∞	∞	∞
5	∞	∞	∞	∞	∞

Force

Proposition

Given a labeled digraph (G, lab) and an arc (i,j) with $lab(i,j) = \bigcirc$:

- *If there exists a reverse path from i to j, then the arc (i,j) must be labeled $\oplus$*
- *If there exists a negative reverse path from j to i, then the arc (i,j) must be labeled $\ominus$*



Matrix M

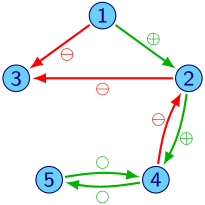
$V(G)$	1	2	3	4	5
1	∞	1	∞	-1	∞
2	∞	∞	∞	-1	∞
3	-1	-1	∞	-1	∞
4	∞	∞	∞	∞	∞
5	∞	∞	∞	∞	∞

Force

Proposition

Given a labeled digraph (G, lab) and an arc (i, j) with $lab(i, j) = \bigcirc$:

- *If there exists a reverse path from i to j, then the arc (i, j) must be labeled $\oplus$*
- *If there exists a negative reverse path from j to i, then the arc (i, j) must be labeled $\ominus$*



Matrix M

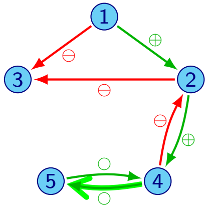
$V(G)$	1	2	3	4	5
1	∞	1	∞	-1	∞
2	∞	∞	∞	-1	∞
3	-1	-1	∞	-1	∞
4	∞	∞	∞	∞	∞
5	∞	∞	∞	∞	∞

Force

Proposition

Given a labeled digraph (G, lab) and an arc (i,j) with $lab(i,j) = \bigcirc$:

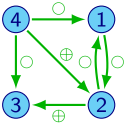
- *If there exists a reverse path from i to j, then the arc (i,j) must be labeled $\oplus$*
- *If there exists a negative reverse path from j to i, then the arc (i,j) must be labeled $\ominus$*



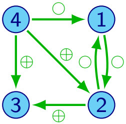
Matrix M

$V(G)$	1	2	3	4	5
1	∞	1	∞	-1	∞
2	∞	∞	∞	-1	∞
3	-1	-1	∞	-1	∞
4	∞	∞	∞	∞	∞
5	∞	∞	∞	∞	∞

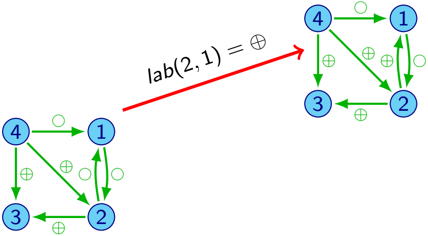
Example of SimpleLabel



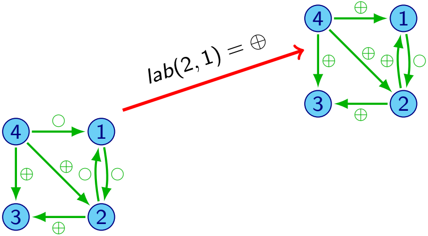
Example of SimpleLabel



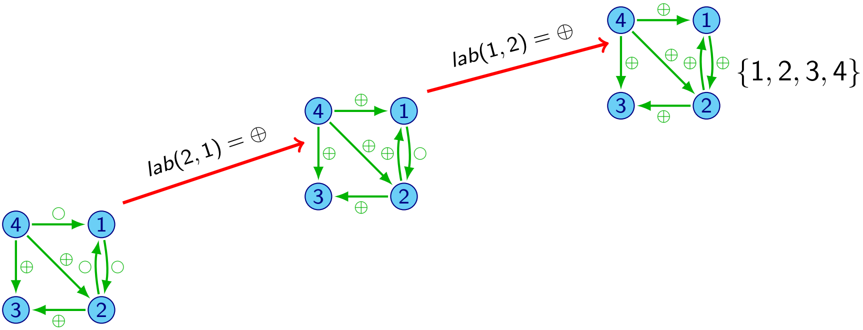
Example of SimpleLabel



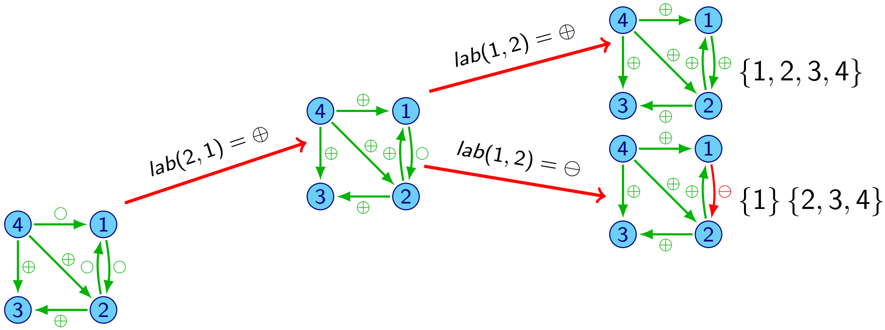
Example of SimpleLabel



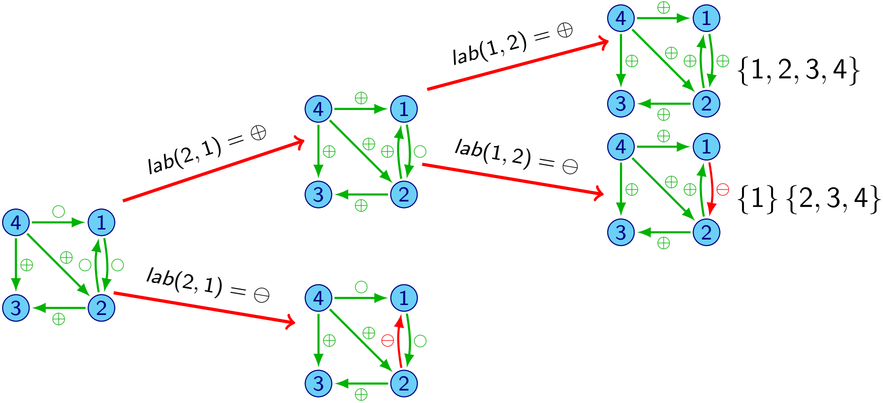
Example of SimpleLabel



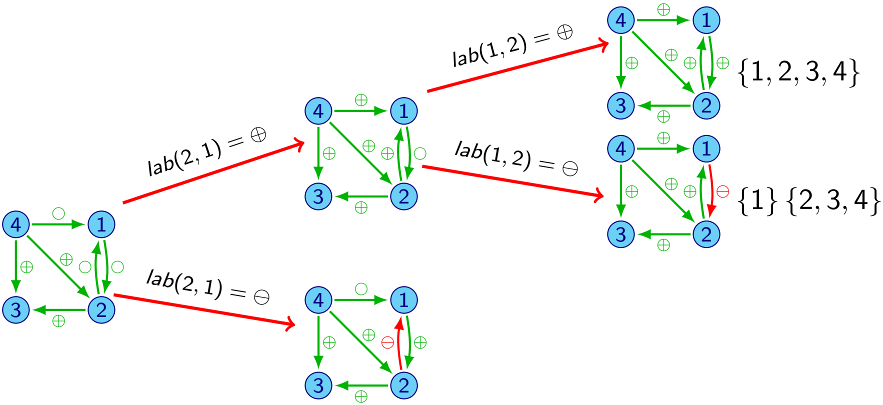
Example of SimpleLabel



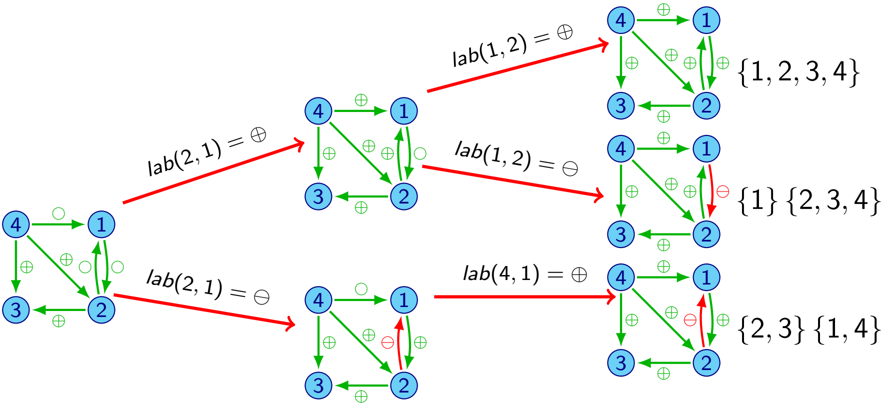
Example of SimpleLabel



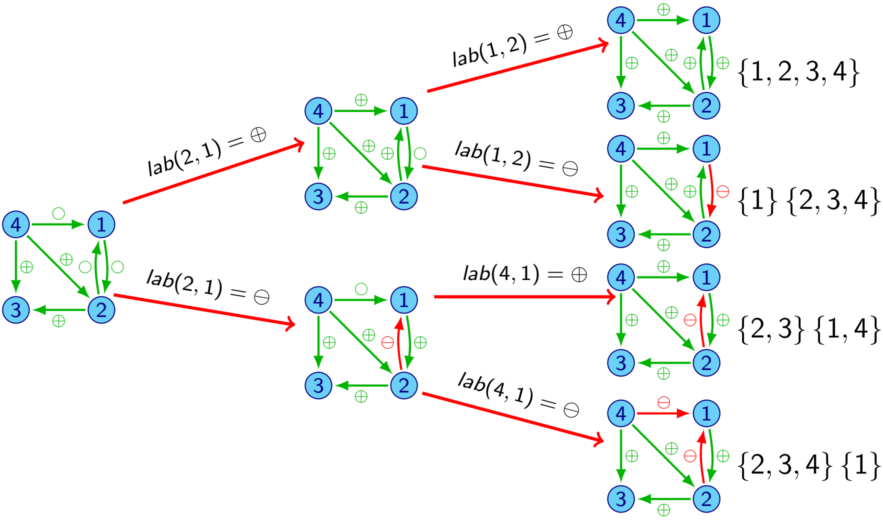
Example of SimpleLabel



Example of SimpleLabel



Example of SimpleLabel



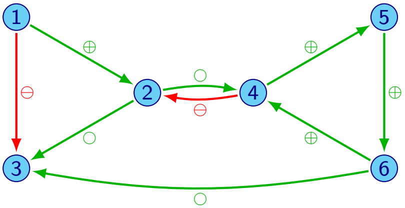
Reduce

Definition

Let (G, lab) be an update digraph and $\{G_1, \ldots, G_k\}$ its positive strongly connected components. We define its reduced labeled digraph by $R(G, lab) = (G_{\text{rd}} = (V_{\text{rd}}, A_{\text{rd}}), lab_{\text{rd}})$, where:

- $V_{\text{rd}} = \{v_1, \ldots, v_k\}$
- $A_{\text{rd}} = \big\{(v_i, v_j) | \exists (u, v) \in A(G) \cap \big(V(G_i) \times V(G_j)\big)\big\}$

$lab_{\text{rd}}(v_i, v_j) = lab(u, v)$, if there exists $(u, v) \in \big(V(G_i) \times V(G_j)\big) \cap \text{Sup}(lab)$ and $lab_{\text{rd}}(v_i, v_j) = \bigcirc$ otherwise



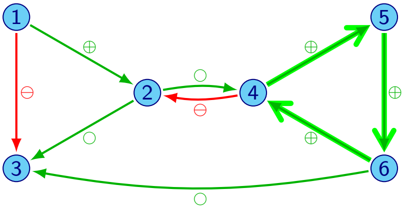
Reduce

Definition

Let (G, lab) be an update digraph and $\{G_1, \ldots, G_k\}$ its positive strongly connected components. We define its reduced labeled digraph by $R(G, lab) = (G_{\text{rd}} = (V_{\text{rd}}, A_{\text{rd}}), lab_{\text{rd}})$, where:

- $V_{\text{rd}} = \{v_1, \ldots, v_k\}$
- $A_{\text{rd}} = \{(v_i, v_j) | \exists (u, v) \in A(G) \cap \left(V(G_i) \times V(G_j)\right)\}$

$lab_{\text{rd}}(v_i, v_j) = lab(u, v)$, if there exists $(u, v) \in \left(V(G_i) \times V(G_j)\right) \cap \text{Sup}(lab)$ and
$lab_{\text{rd}}(v_i, v_j) = \bigcirc$ otherwise



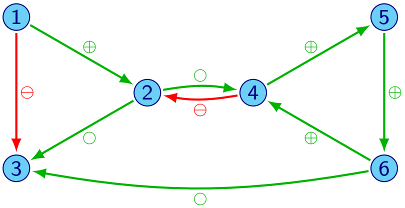
Reduce

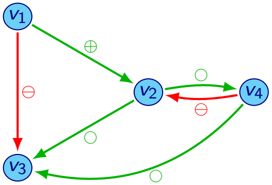
Definition

Let (G, lab) be an update digraph and $\{G_1, \dots, G_k\}$ its positive strongly connected components. We define its reduced labeled digraph by $R(G, lab) = (G_{\text{rd}} = (V_{\text{rd}}, A_{\text{rd}}), lab_{\text{rd}})$, where:

- $V_{\text{rd}} = \{v_1, \dots, v_k\}$
- $A_{\text{rd}} = \left\{(v_i, v_j) | \exists (u, v) \in A(G) \cap \left(V(G_i) \times V(G_j)\right)\right\}$

$lab_{\text{rd}}(v_i, v_j) = lab(u, v)$, if there exists $(u, v) \in \left(V(G_i) \times V(G_j)\right) \cap \text{Sup}(lab)$ and
$lab_{\text{rd}}(v_i, v_j) = \bigcirc$ otherwise



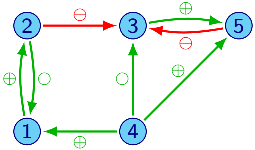


Strongly connected components

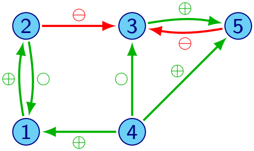
Divide by SCC

Let (G, lab) an update digraph with SCC $G_1, \ldots, G_k$ (ordered) over its reverse extended digraph, then:

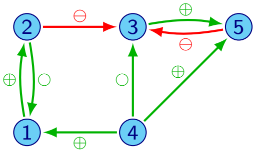
$$\mathcal{S}(G, lab) = \mathcal{S}\left(\widetilde{G}_1, lab|_{A(G_1)}\right) \circ_n \cdots \circ_n \mathcal{S}\left(\widetilde{G}_k, lab|_{A(G_k)}\right)$$

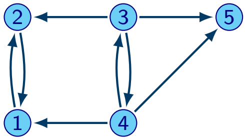


Example: Division by SCC

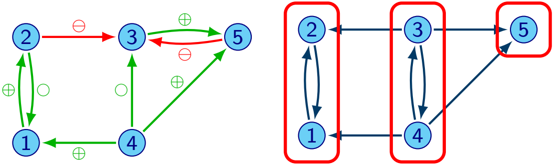


Example: Division by SCC

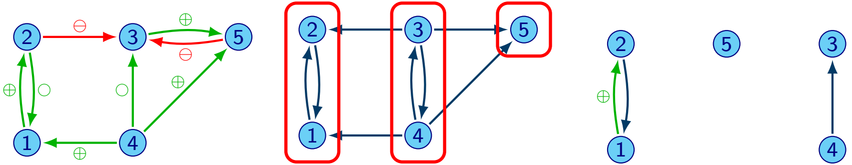




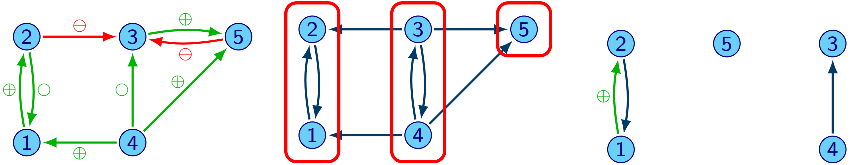
Example: Division by SCC



Example: Division by SCC

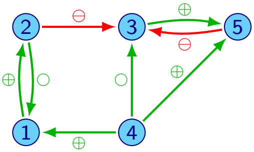


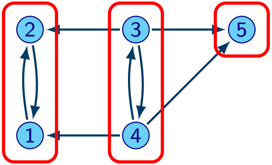
Example: Division by SCC

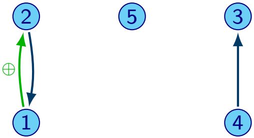


$$\mathcal{S}(G[1,2], lab) = \{\{1,2\}, \{2\}\{1\}\}$$
$$\mathcal{S}(G[5], lab) = \{\{5\}\}$$
$$\mathcal{S}(G[3,4], lab) = \{\{3\}\{4\}, \{4\}\{3\}\}$$

Example: Division by SCC







$$\mathcal{S}(G[1,2], lab) = \{\{1,2\}, \{2\}\{1\}\}$$
$$\mathcal{S}(G[5], lab) = \{\{5\}\}$$
$$\mathcal{S}(G[3,4], lab) = \{\{3\}\{4\}, \{4\}\{3\}\}$$

Then,

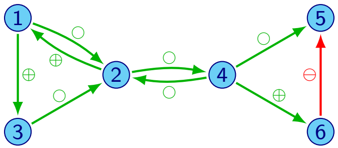
$$\begin{aligned}\mathcal{S}(G, lab) &= \mathcal{S}(G[1,2], lab) \circ_n \mathcal{S}(G[5], lab) \circ_n \mathcal{S}(G[3,4], lab)\\ &= \{\{1,2\}\{5\}, \{2\}\{1\}\{5\}\} \circ_n \{\{3\}\{4\}, \{4\}\{3\}\}\\ &= \Big\{ \{1,2\}\{5\}\{3\}\{4\}, \{1\}\{2\}\{5\}\{3\}\{4\},\\ &\quad \{1,2\}\{5\}\{4\}\{3\}, \{1\}\{2\}\{5\}\{4\}\{3\} \Big\}\end{aligned}$$

Bridges

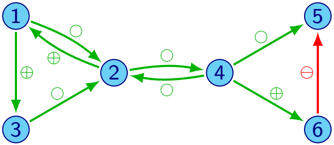
Divide by Bridges

Let (G, lab) a connected digraph, G_U the underlying digraph of G and $uv \in E(G_U)$ a bridge that divide G in G_1 and G_2, then

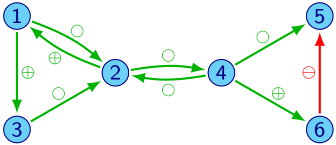
$$\mathcal{S}(G, lab) = \mathcal{S}(G_1, lab|_{A(G_1)}) \circ_{\{u,v\}} \mathcal{S}(G_2, lab|_{A(G_2)})$$

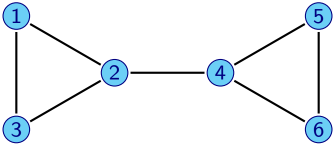


Example: Division by Bridges

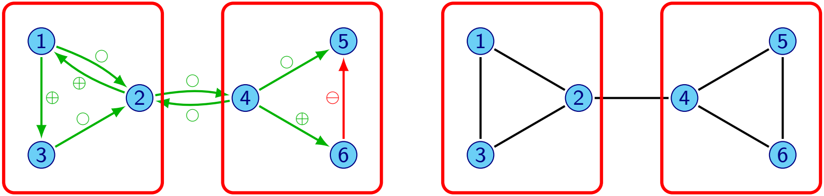


Example: Division by Bridges

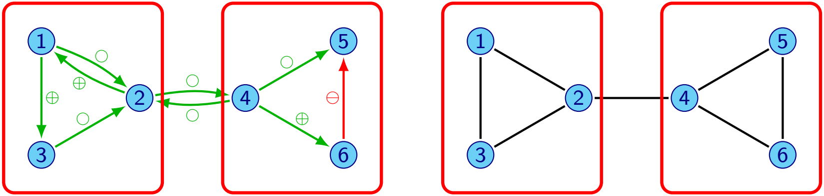




Example: Division by Bridges



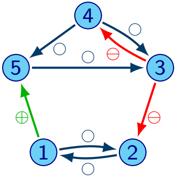
Example: Division by Bridges



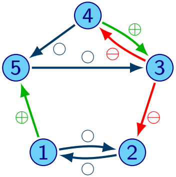
$$S_1 \circ_{nrm_{2,4}} S_2 = \{\{1,2,3\},\{3\}\{1,2\},\{3\}\{1\}\{2\}\} \circ_{nrm_{2,4}} \{\{6\}\{5\}\{4\},\{6\}\{4\}\{5\}\}$$

$\{1,2,3\}\{6\}\{5\}\{4\}$	$\{6\}\{5\}\{4\}\{1,2,3\}$	$\{6\}\{5\}\{4,1,2,3\}$
$\{3\}\{1,2\}\{6\}\{5\}\{4\}$	$\{6\}\{5\}\{4\}\{3\}\{1,2\}$	$\{3\}\{6\}\{5\}\{4,1,2\}$
$\{3\}\{1\}\{2\}\{6\}\{5\}\{4\}$	$\{6\}\{5\}\{4\}\{3\}\{1\}\{2\}$	$\{3\}\{1\}\{6\}\{5\}\{4,2\}$
$\{1,2,3\}\{6\}\{4\}\{5\}$	$\{6\}\{4\}\{5\}\{1,2,3\}$	$\{6\}\{4,1,2,3\}\{5\}$
$\{3\}\{1,2\}\{6\}\{4\}\{5\}$	$\{6\}\{4\}\{5\}\{3\}\{1,2\}$	$\{3\}\{6\}\{4,1,2\}\{5\}$
$\{3\}\{1\}\{2\}\{6\}\{4\}\{5\}$	$\{6\}\{4\}\{5\}\{3\}\{1\}\{2\}$	$\{3\}\{1\}\{6\}\{4,2\}\{5\}$

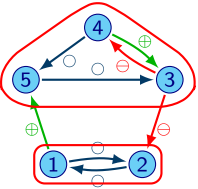
Example: UpdateLabel



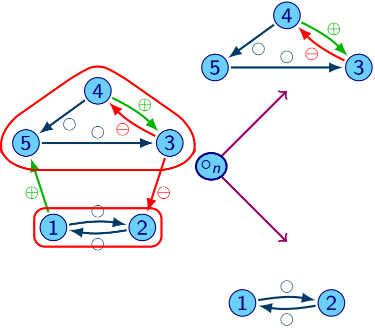
Example: UpdateLabel



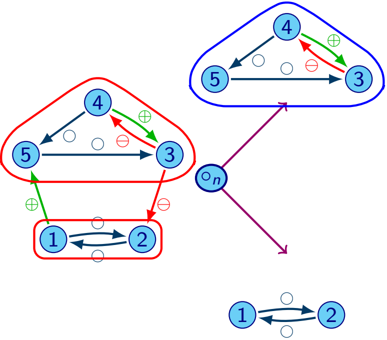
Example: UpdateLabel



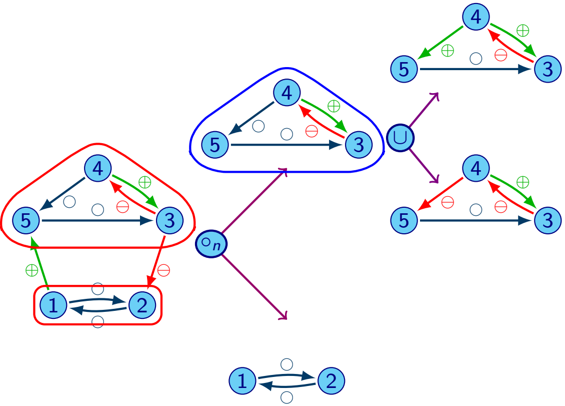
Example: UpdateLabel



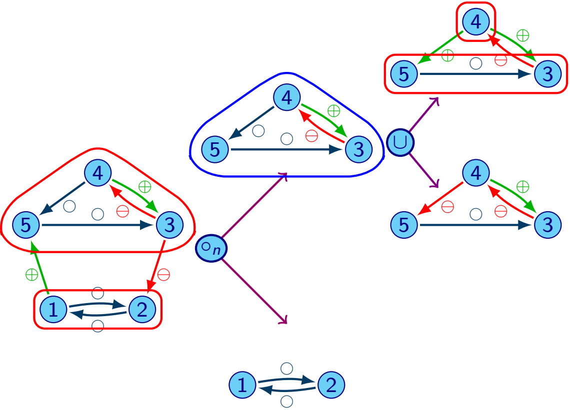
Example: UpdateLabel



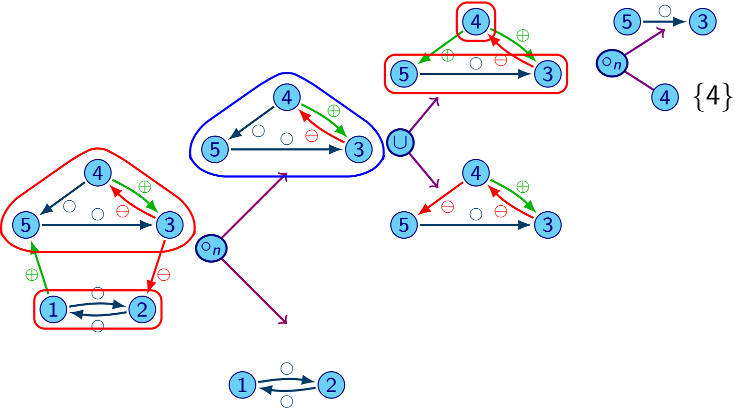
Example: UpdateLabel



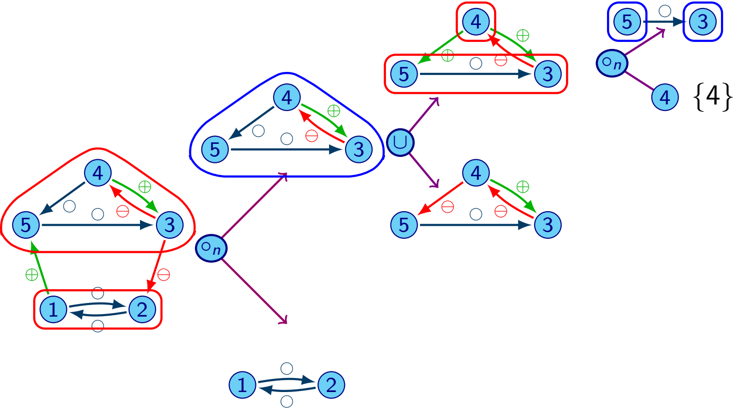
Example: UpdateLabel



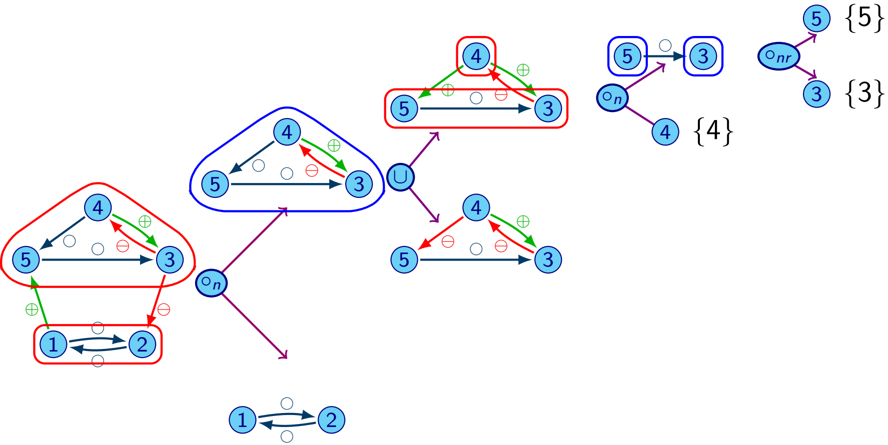
Example: UpdateLabel



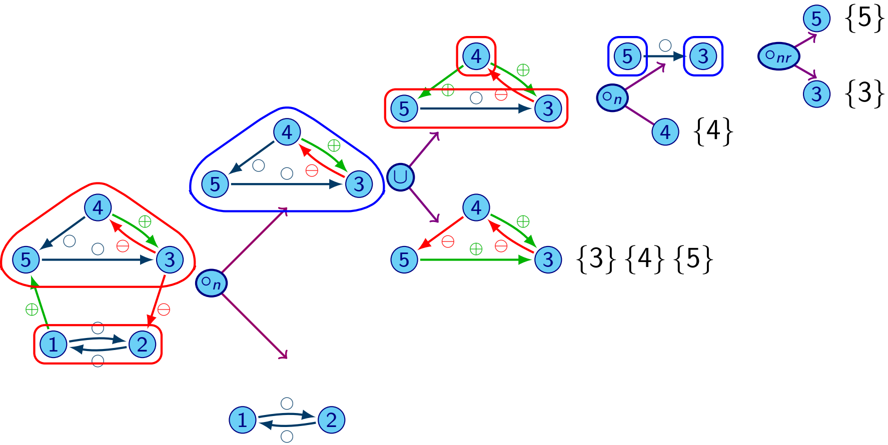
Example: UpdateLabel



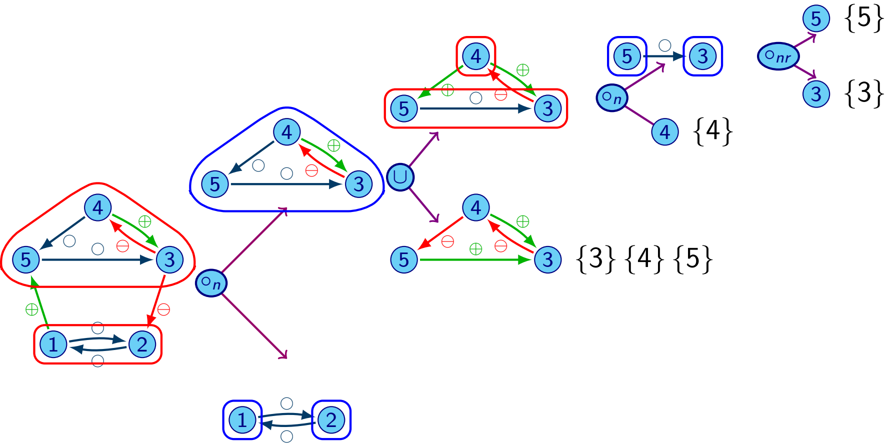
Example: UpdateLabel



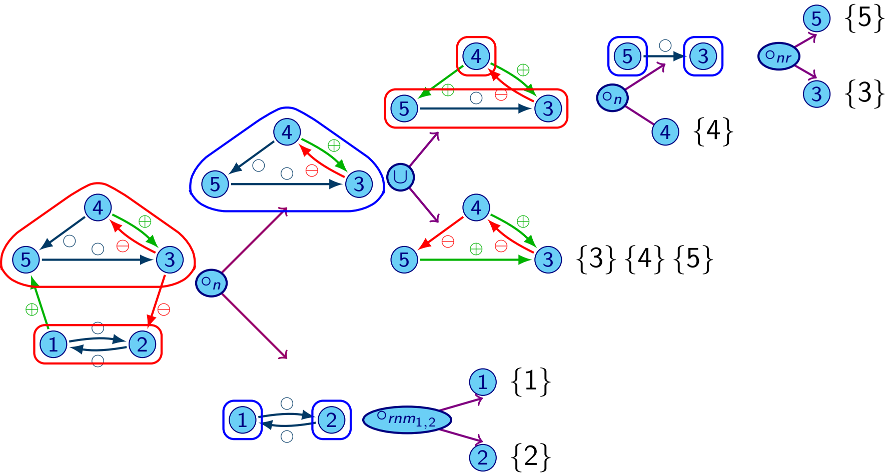
Example: UpdateLabel



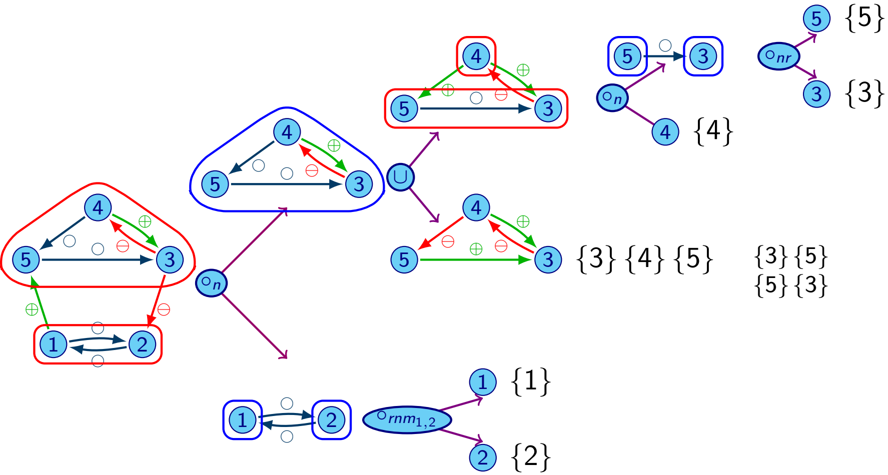
Example: UpdateLabel



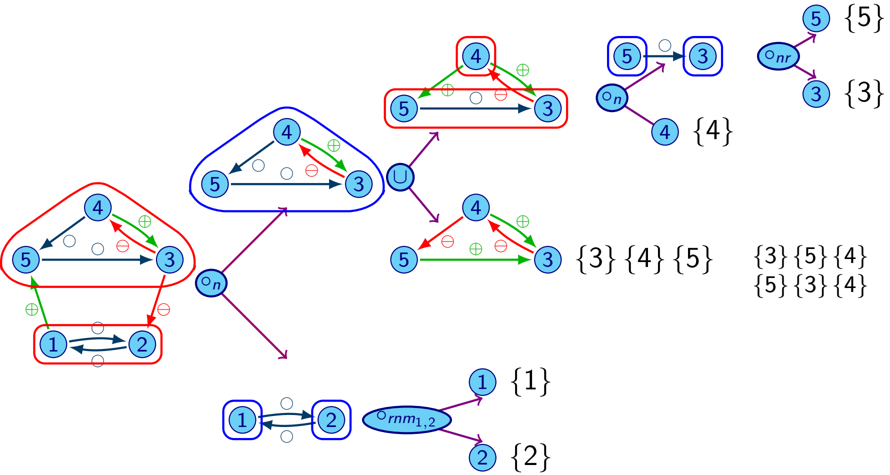
Example: UpdateLabel



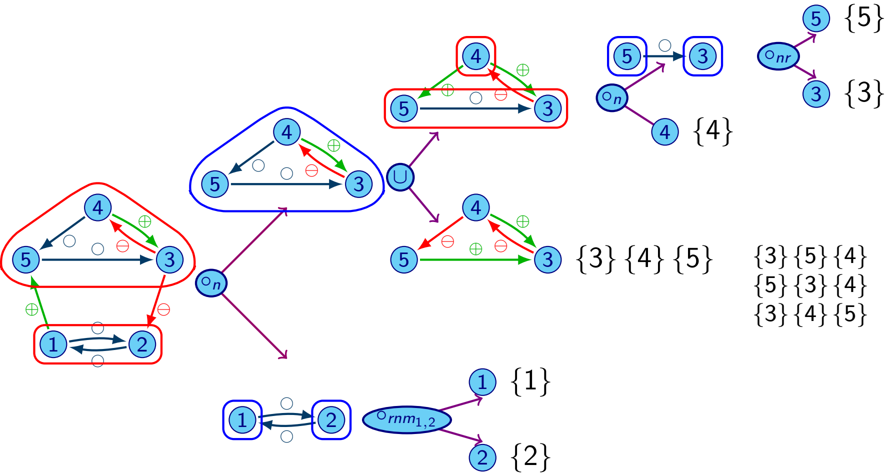
Example: UpdateLabel



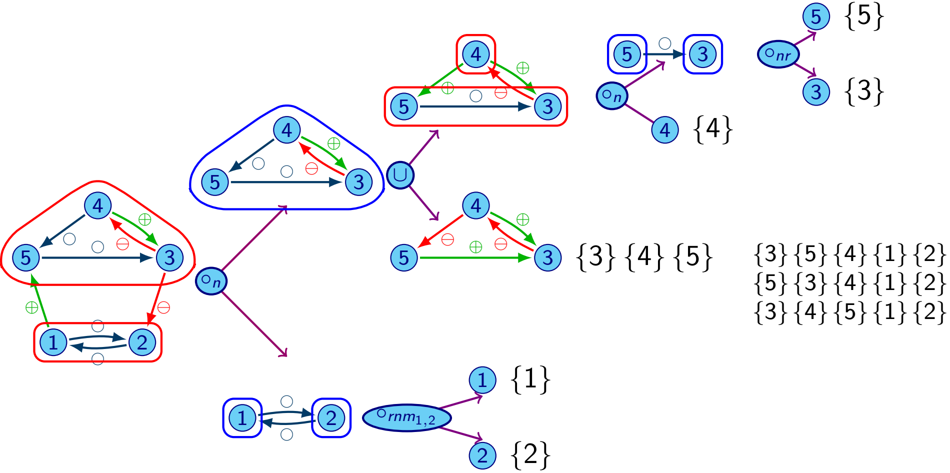
Example: UpdateLabel



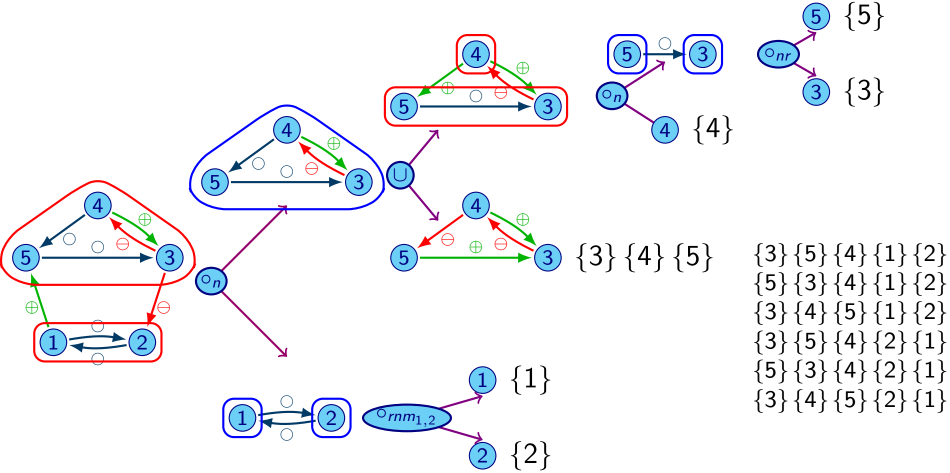
Example: UpdateLabel



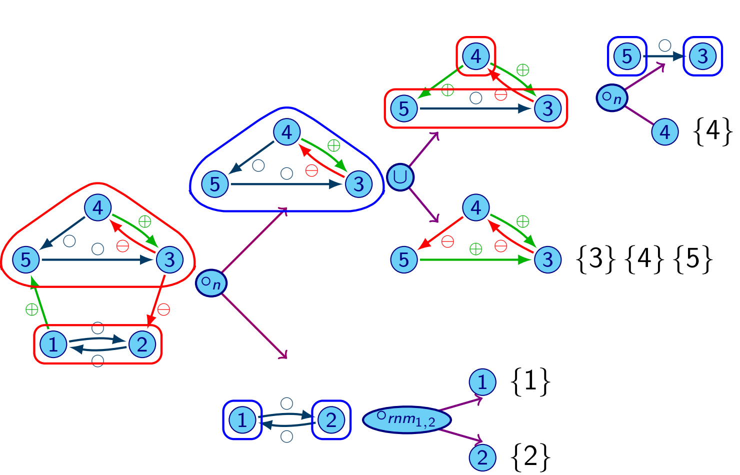
Example: UpdateLabel



Example: UpdateLabel



Example: UpdateLabel



{3} {5} {4} {1} {2}
{5} {3} {4} {1} {2}
{3} {4} {5} {1} {2}
{3} {5} {4} {2} {1}
{5} {3} {4} {2} {1}
{3} {4} {5} {2} {1}
{3} {5} {4} {1, 2}
{5} {3} {4} {1, 2}
{3} {4} {5} {1, 2}

Thank You!