On the relation between interaction and state transition graphs

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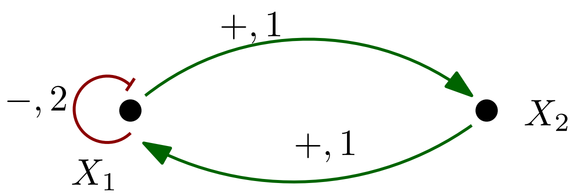
AG MathLife

June 25, 2014

Preliminaries

Interaction graph (IG)

$I = < V, E, \varepsilon, \vartheta, max >$



$V := \{X_1, X_2\}$

$E : V \times V \quad \varepsilon = \{+, -\}$

$\vartheta : E \to \mathbf{N}^+ \quad max : V \to \mathbf{N}$

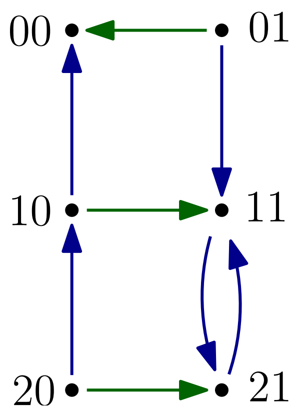
$X_1 \in \{0, 1, 2\}$

$X_2 \in \{0, 1\}$

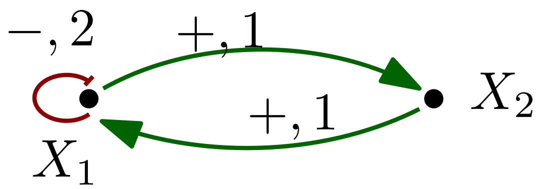
State space $X = \prod_{i \in V} \{0, \dots, max_i\}$

Asynchronous State Transition Graph (ASTG)

$T = (X, S)$



Preliminaries



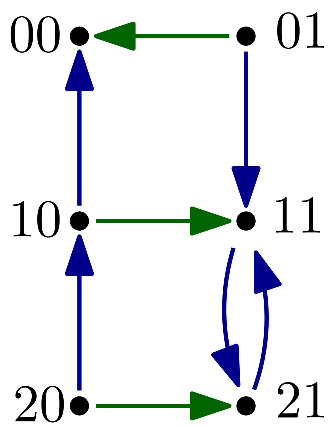
u: component

x: state

$$Res(u,x) = \left\{ v \in Pre(u) \middle| \begin{array}{lll} \varepsilon(v,u) = + & \wedge & x_v \geq \vartheta(v,u) \\ \varepsilon(v,u) = - & \wedge & x_v < \vartheta(v,u) \end{array} \right\}$$

state	$Res(X_1, \cdot)$
00	$\{X_1\}$
01	$\{X_1, X_2\}$
10	$\{X_1\}$
11	$\{X_1, X_2\}$
20	ϕ
21	$\{X_2\}$

state	$Res(X_2, \cdot)$
00	ϕ
01	ϕ
10	$\{X_1\}$
11	$\{X_1\}$
20	$\{X_1\}$
21	$\{X_1\}$



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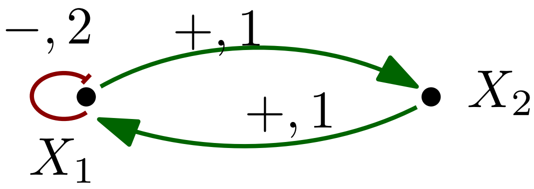

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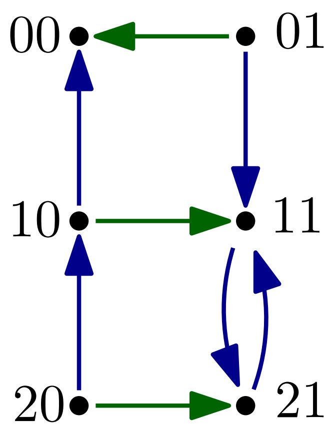
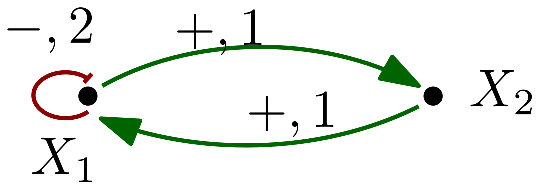
$Res(X_1,\cdot)$	$K(X_1,\cdot)$
ϕ	0
$\{X_2\}$	0
$\{X_1\}$	0
$\{X_1, X_2\}$	2

$Res(X_2,\cdot)$	$K(X_2,\cdot)$
ϕ	0
$\{X_1\}$	1



Model: $M = (I, K)$

Preliminaries

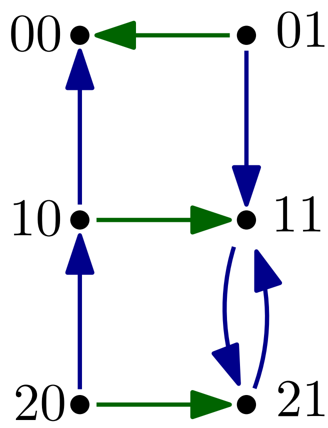


u: component

x: state

$$Res(u,x) = \left\{ v \in Pre(u) \middle| \begin{array}{lll} \varepsilon(v,u) = + & \wedge & x_v \geq \vartheta(v,u) \\ \varepsilon(v,u) = - & \wedge & x_v < \vartheta(v,u) \end{array} \right\}$$

state	$Res(X_1,\cdot)$	$K(X_1, Res(X_1,\cdot))$
00	$\{X_1\}$	0
01	$\{X_1, X_2\}$	2
10	$\{X_1\}$	0
11	$\{X_1, X_2\}$	2
20	ϕ	0
21	$\{X_2\}$	0



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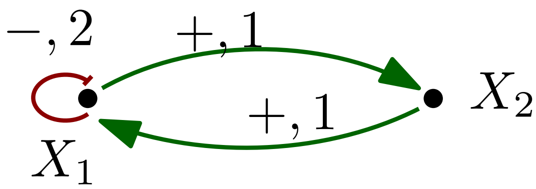

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x: state

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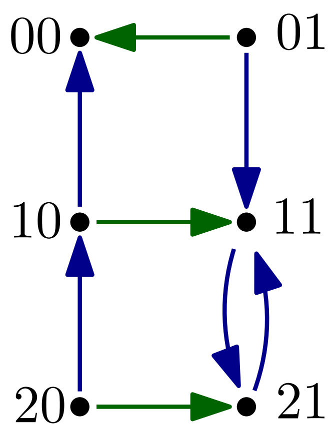
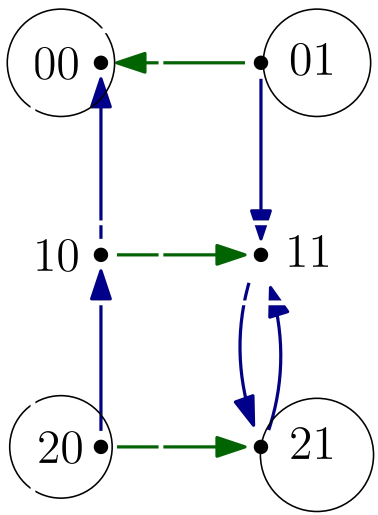
$state$	$Res(X_2,\cdot)$	$K(X_2, Res(X_2,\cdot))$
00	ϕ	0
01	ϕ	0
10	$\{X_1\}$	1
11	$\{X_1\}$	1
20	$\{X_1\}$	1
21	$\{X_1\}$	1



Preliminaries

ASTG $T = (X, S)$

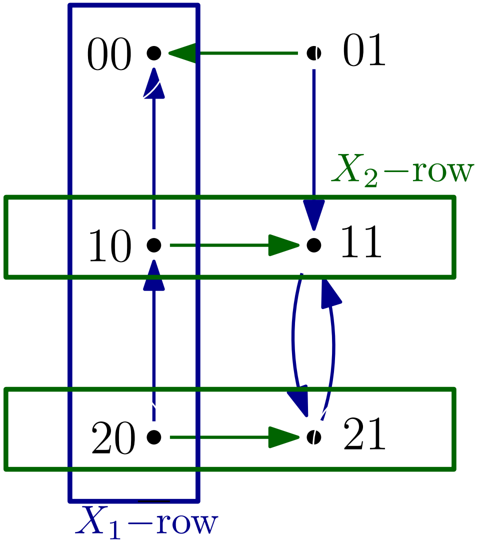


Extreme state

a state $x, \forall u \in V, x_u \in \{0, max_u\}$.

Preliminaries

ASTG $T = (X, S)$



Extreme state

a state $x, \forall u \in V, x_u \in \{0, max_u\}$.

u−**row**

a row of states $\tau(x^0, u) = (x^0, \ldots, x^k)$,

$x^i_u = x^0 + l\mathbf{e}_u, \forall l \in \{0, \ldots, k\}$.

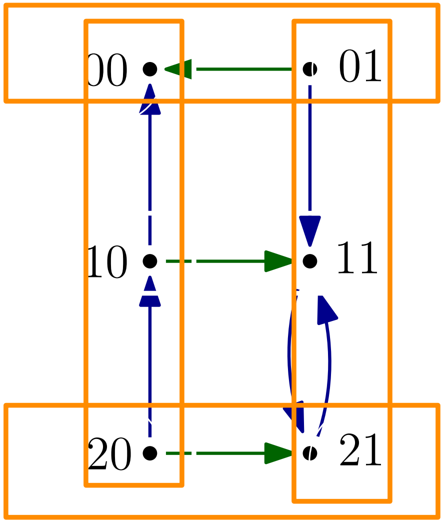
isomorphic u−rows

$(x^0, \ldots, x^k), (y^0, \ldots, y^k)$

if $(x_i, x_j) \in S$ iff $(y_i, y_j) \in S, \forall i, j \in \{0, \ldots, k\}$.

Preliminaries

ASTG $T = (X, S)$



Extreme state

a state $x, \forall u \in V, x_u \in \{0, max_u\}$.

$u-$**row**

a row of states $\tau(x^0, u) = (x^0, \ldots, x^k)$,

$x_u^i = x^0 + l\mathbf{e}_u, \forall l \in \{0, \ldots, k\}$.

Extreme row.

an $u-$row $\tau(x^0, u)$ with

extreme state x^0 and $k = max_u$.

ASTG description using extremal rows

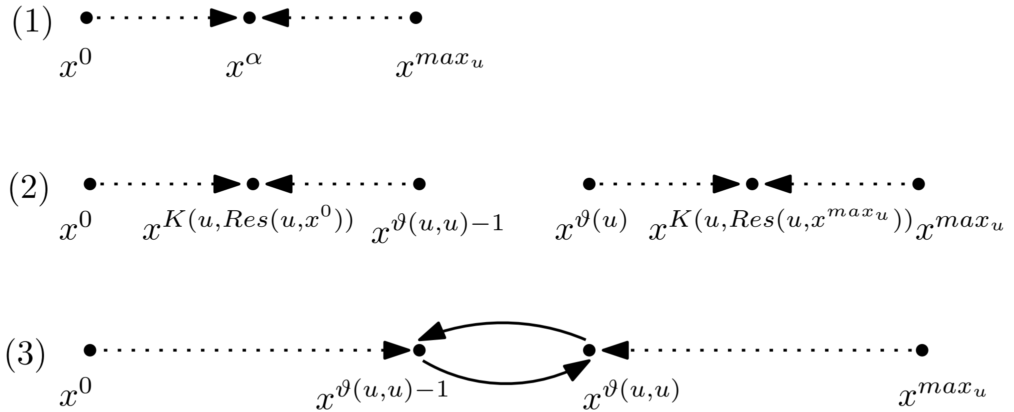
Theorem

For any model $M = (I, K)$, the state transition graph T_M is uniquely determined by IG I and the extremal rows of T_M.[1]

ASTG description using extremal rows

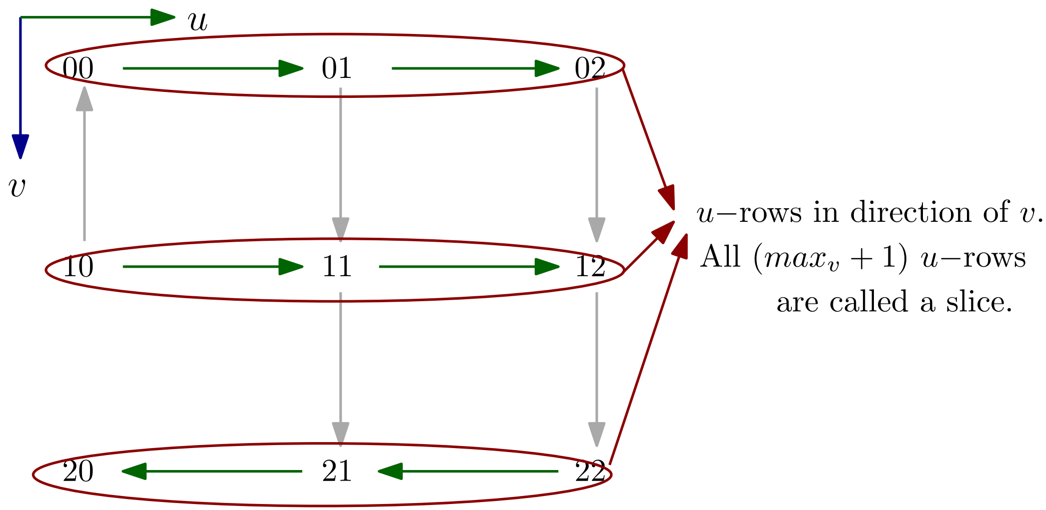
Proposition

All three possible topologies of $u-$rows $(x^0, \ldots, x^{max_u})$ in T_M. [1]



Dotted arrows mean directed path and solid arrows indicate edges.

ASTG description using extremal rows

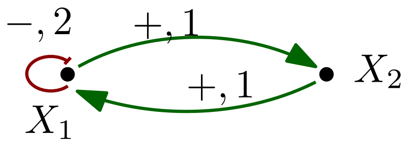


Corollary

Let $u, v \in V, u \neq v$, and $x \in X$ with $x_v = x_u = 0$. For every $i \leq max_v$ $\tau(x + i\mathbf{e}_v, u)$ with start state $(x + i\mathbf{e}_v)$. Then there are:

- *If $(v, u) \notin E$, all rows are isomorphic.*
- *If $(v, u) \in E$, all rows in $\tau^0, \ldots, \tau^{\vartheta(v,u)-1}$ and $\tau^{\vartheta(v,u)}, \ldots, \tau^{max_v}$ are isomorphic respectively. [2]*

Model conditions



$Res(X_1, \cdot)$	$K(\cdot, X_1)$
ϕ	0
$\{X_2\}$	0
$\{X_1\}$	0
$\{X_1, X_2\}$	2

$(u, v) \in E$ is **visible**, if $\exists \omega \subseteq Pre\{v\} \backslash u$,

$K(v, \omega) \neq K(v, \omega \cup \{u\})$.

Eg. (X_2, X_1)

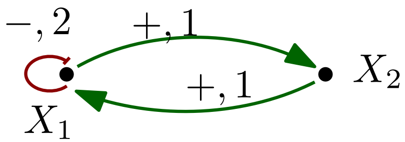
$\exists K(X_1, \{X_1\}) \neq K(X_1, \{X_1, X_2\})$

Visibility Model

A model $M = (I, K)$

where $\forall (u, v) \in E$ is visible.

Model conditions



$Res(X_1, \cdot)$	$K(\cdot, X_1)$
ϕ	0
$\{X_2\}$	0
$\{X_1\}$	0
$\{X_1, X_2\}$	2

$(u, v) \in E$ is **observable**, if $\exists \omega \subseteq Pre\{v\} \backslash u$, $K(v, \omega) < K(v, \omega \cup \{u\})$.

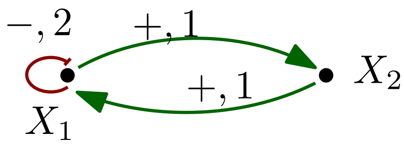
Eg. (X_2, X_1)

$\exists K(X_1, \{X_1\}) < K(X_1, \{X_1, X_2\})$

Observibility Model

A model $M = (I, K)$ where $\forall (u, v) \in E$ is observable.

Model conditions



$Res(X_1, \cdot)$	$K(\cdot, X_1)$
ϕ	0
$\{X_2\}$	0
$\{X_1\}$	0
$\{X_1, X_2\}$	2

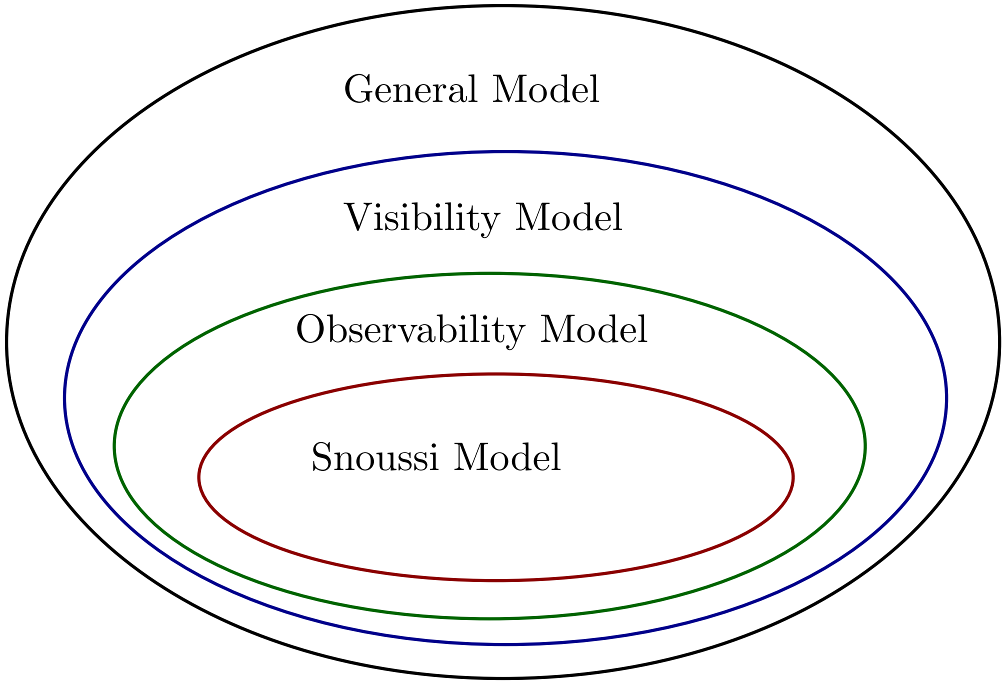
Snoussi condition

A model M satisfies Snoussi-condition
$\forall u \in V, \forall \zeta \subseteq \omega \subseteq Pre(u)$,
$K(u, \zeta) \leq K(u, \omega)$.
This model is

Snoussi model.

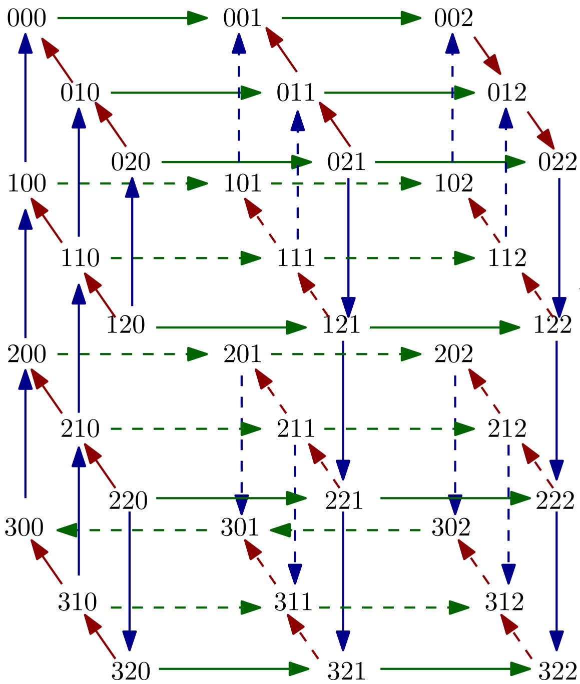
Eg. (X_2, X_1)
$K(X_1, \phi) = K(X_1, \{X_1\})$
$K(X_1, \{X_2\}) < K(X_1, \{X_1, X_2\})$
Satisfies Snoussi condition.

Model conditions



T. Lorenz's Algorithms: Visibility Model

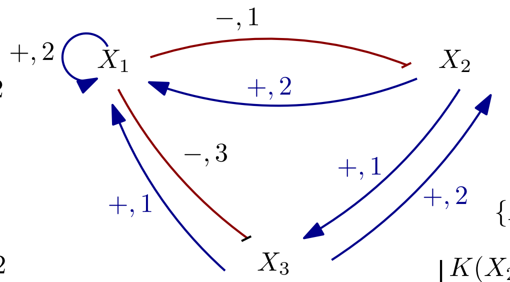
ASTG



Visibility Model $M = (I, K)$

with minimal number of edges.

and $ASTG(M) = T$



	$K(X_1, \cdot)$
ϕ	0
$\{X_3\}$	0
$\{X_2\}$	0
$\{X_2, X_3\}$	3
$\{X_1\}$	0
$\{X_1, X_3\}$	3
$\{X_1, X_2\}$	3
$\{X_1, X_2, X_3\}$	3

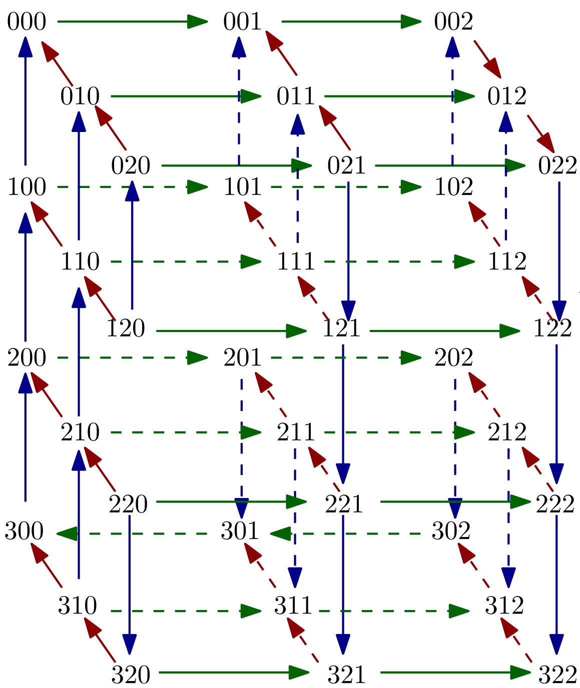
	$K(X_2, \cdot)$
ϕ	0
$\{X_3\}$	0
$\{X_1\}$	0
$\{X_1, X_3\}$	2

	$K(X_3, \cdot)$
ϕ	0
$\{X_2\}$	2
$\{X_1\}$	2
$\{X_1, X_2\}$	2

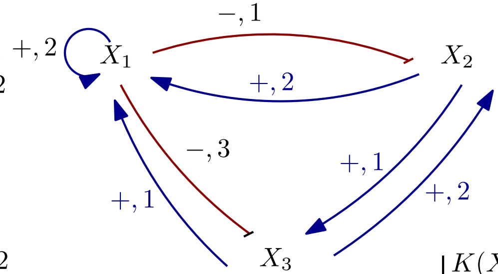
T. Lorenz's Algorithms: Observability-Snoussi Model

Observability-Snoussi Model $M = (I, K)$

ASTG



A model $M = (I, K)$, with minimal number of edges, satisfies: observability condtion, and Snoussi-condition as much as possible, and $ASTG(M) = T$



The difference with Visibility Model

	$K(X_1, \cdot)$
ϕ	0
$\{X_3\}$	0
$\{X_2\}$	0
$\{X_2, X_3\}$	2
$\{X_1\}$	1
$\{X_1, X_3\}$	3
$\{X_1, X_2\}$	3
$\{X_1, X_2, X_3\}$	3

	$K(X_2, \cdot)$
ϕ	0
$\{X_3\}$	0
$\{X_1\}$	0
$\{X_1, X_3\}$	2

	$K(X_3, \cdot)$
ϕ	0
$\{X_2\}$	2
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$\{X_1, X_2\}$	2

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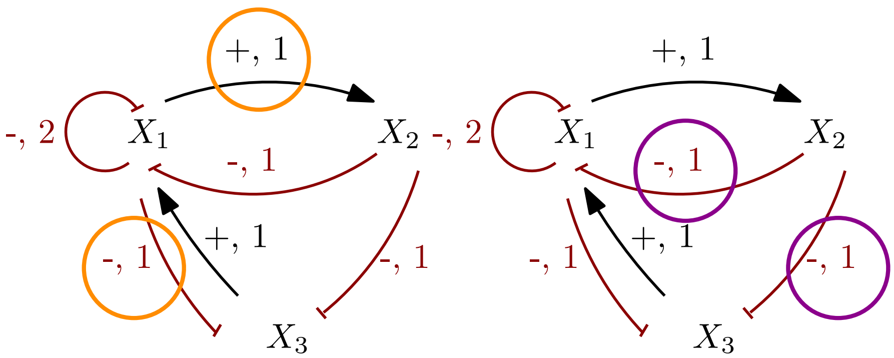
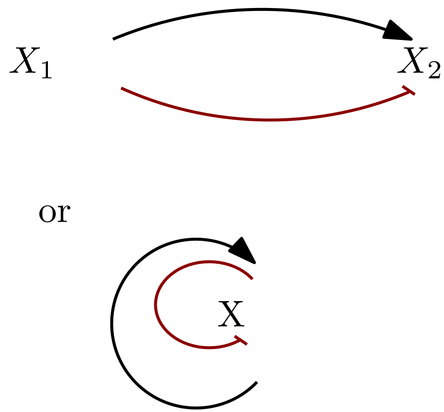
Inverse engineering: From ASTG → Model $M(I, K)$

- Sometimes, the output M can not reproduce the input. Why?
- Multiple edges in the IG corresponding to the input ASTG is not allowed.
- Note: in the corresponding IG, thresholds from one component to others can be the same.(*Different with Thomas' model*)

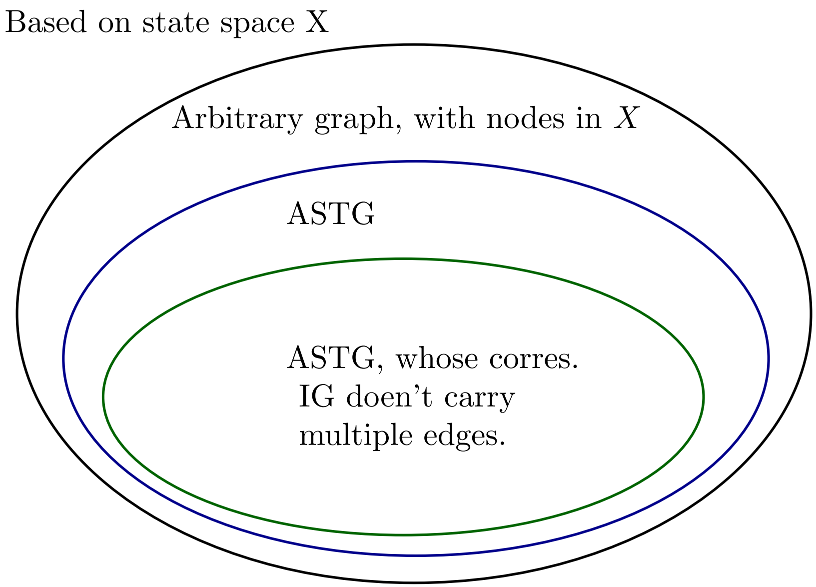


Multiple Edges

X_1, X_2, X are components.



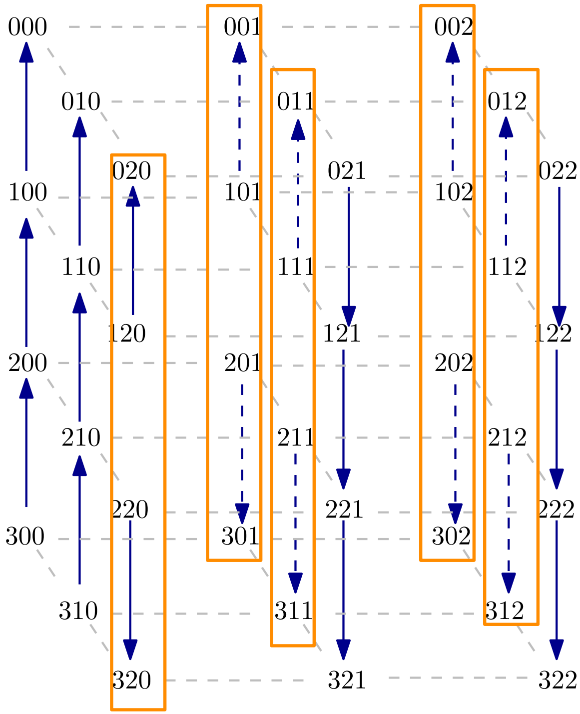
relations


Based on state space X
Arbitrary graph, with nodes in X
ASTG
ASTG, whose corres. IG doen't carry multiple edges.

ASTG Checking

Aim The input ASTG should be checked before using T. Lorenz's algorithms.

- Idea: the ASTG which will be the input of T. Lorenz's algorithms, the IG of this ASTG should have no multiple edges.



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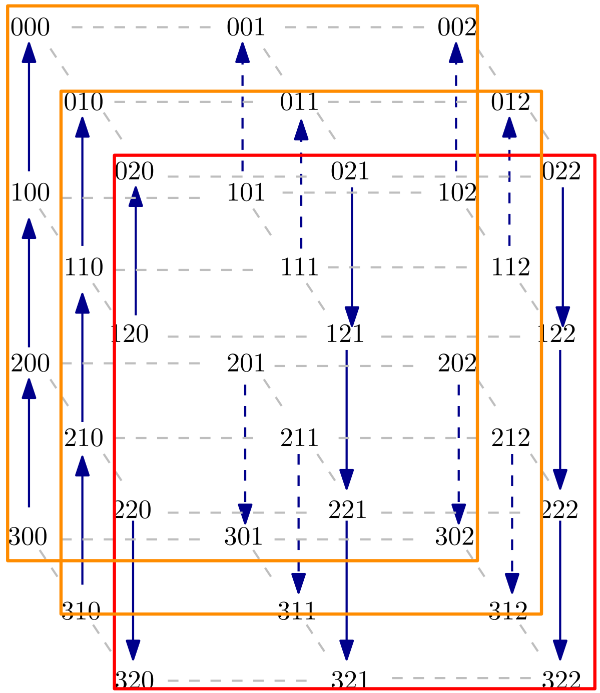

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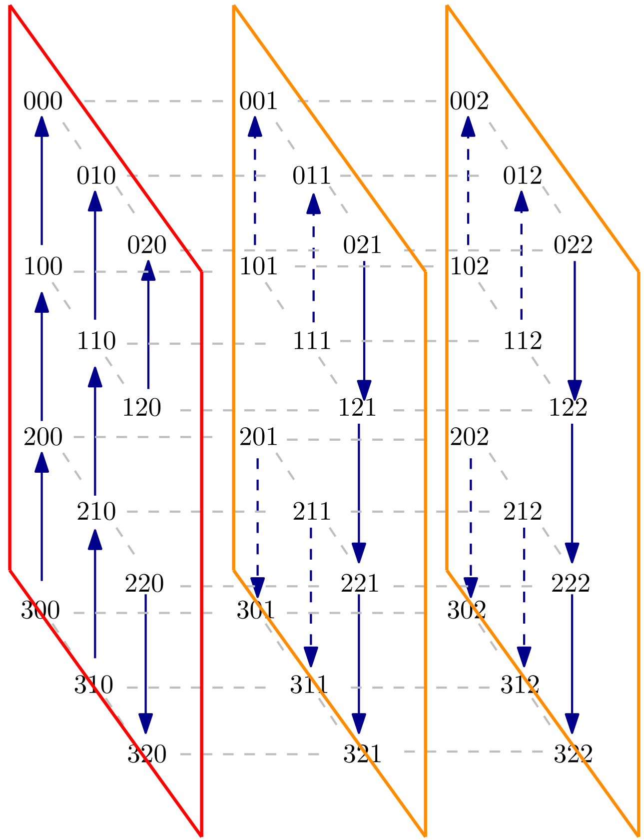

Exploring relations between IG and ASTG

- Method: on small scale, enumerate all possible ASTGs and get corresponding models using T. Lorenz's algorithms.
- Analysis.
  - How many IGs share the same attractors?
  - The changes on ASTGs $\longleftrightarrow$ the changes on IGs.

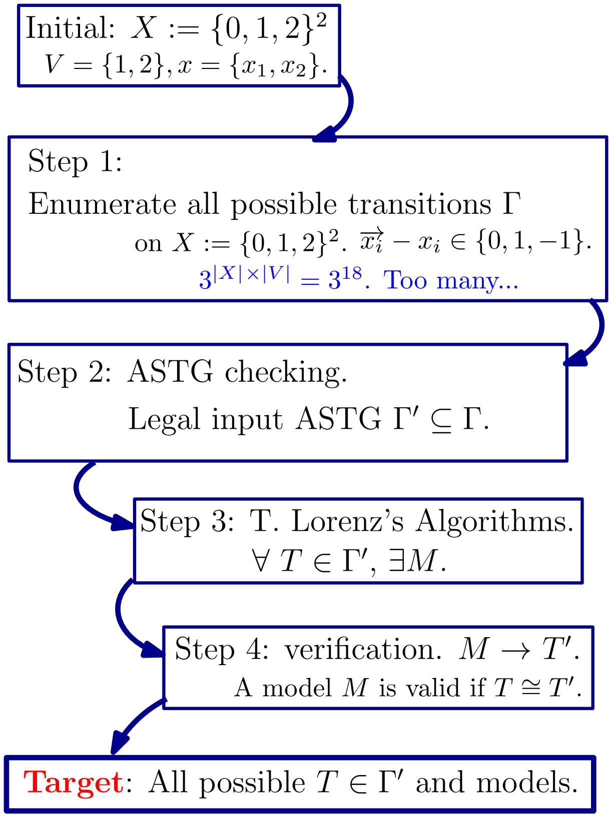

Fig. Experiment process map

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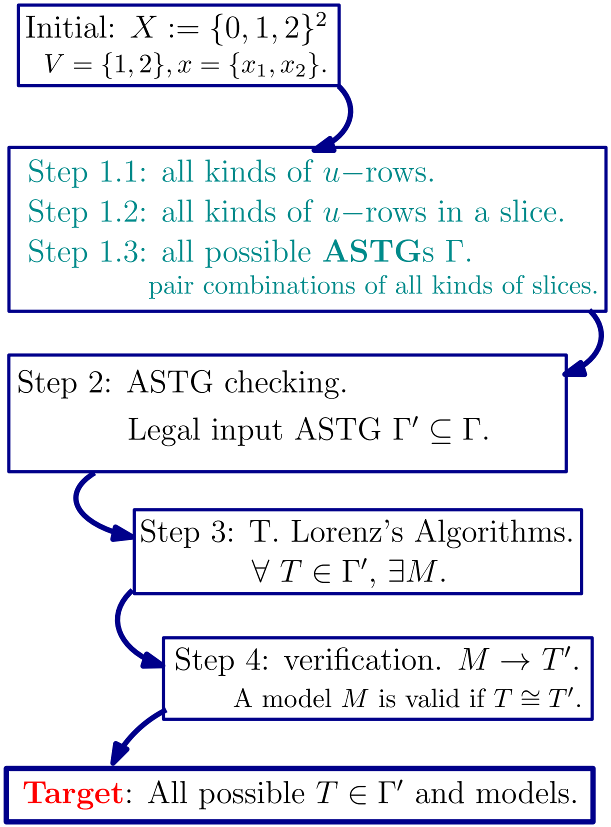
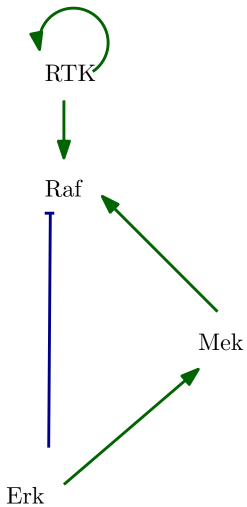
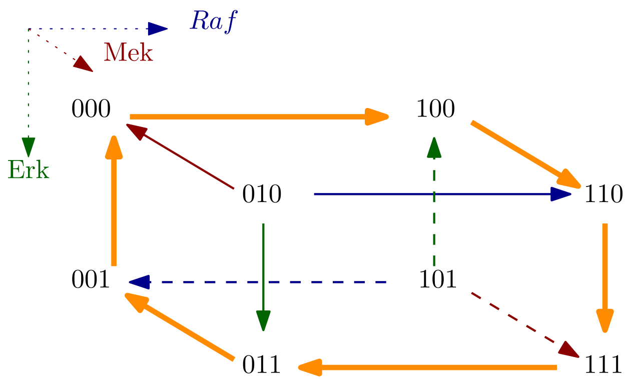


Fig. Experiment process map

Application on 3-node MAPK cascade model

- A reduced MAPK model from Kirsten. ;)
- Set input RTK to 1, the corresponding ASTG is in below on the right.

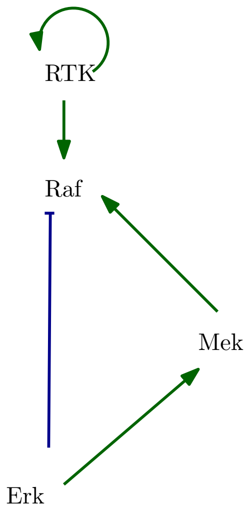


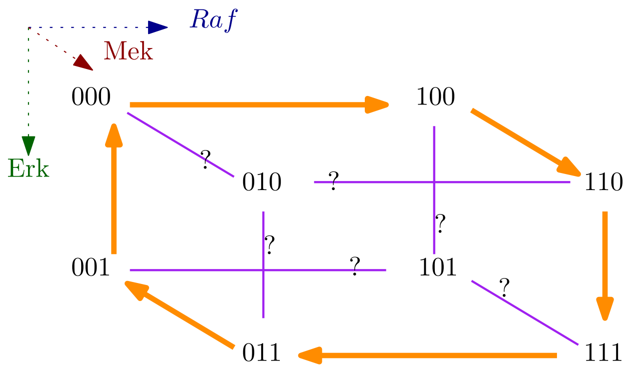


ASTG: Orange path is the cyclic attractor.
Dashed arrows mean in the back of the cube.
All directed arrows are transitions.

Application on 3-node MAPK cascade model

- A reduced MAPK model from Kirsten. ;)
- Set input RTK to 1, the corresponding ASTG is in below on the right.
- Experiment: how many IGs share the same cyclic attractors?
  - Enumerate all possible transitions on $X := \{0, 1\}^3$ which keeps the cyclic cycle. ($2^6 = 64$)
  - Use T. Lorenz's Algorithm: Visibility Model, get all visible models.
  - See the different IGs.





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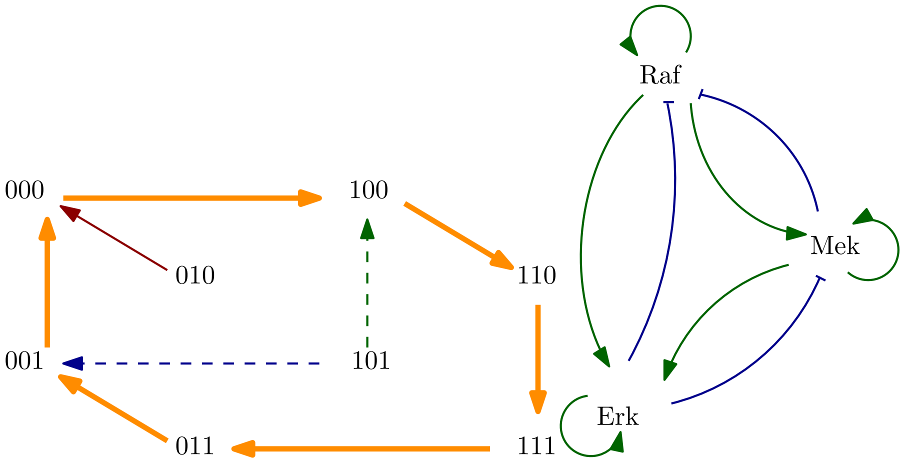
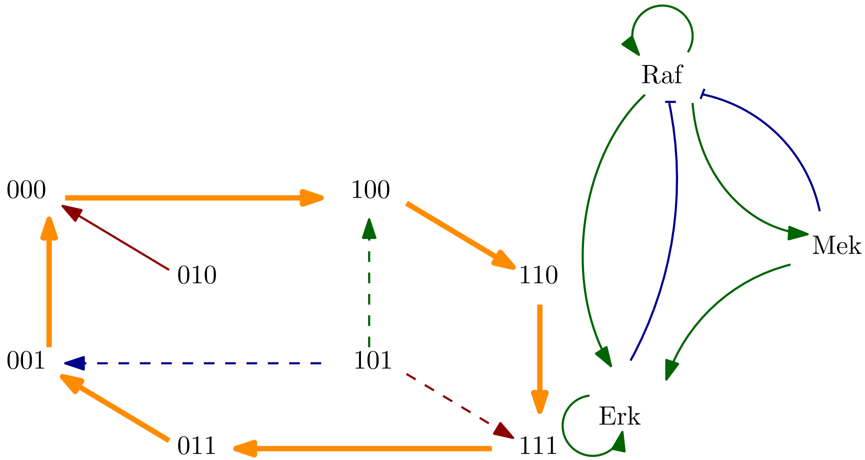
Results

- Different ASTG & corresponding IG.





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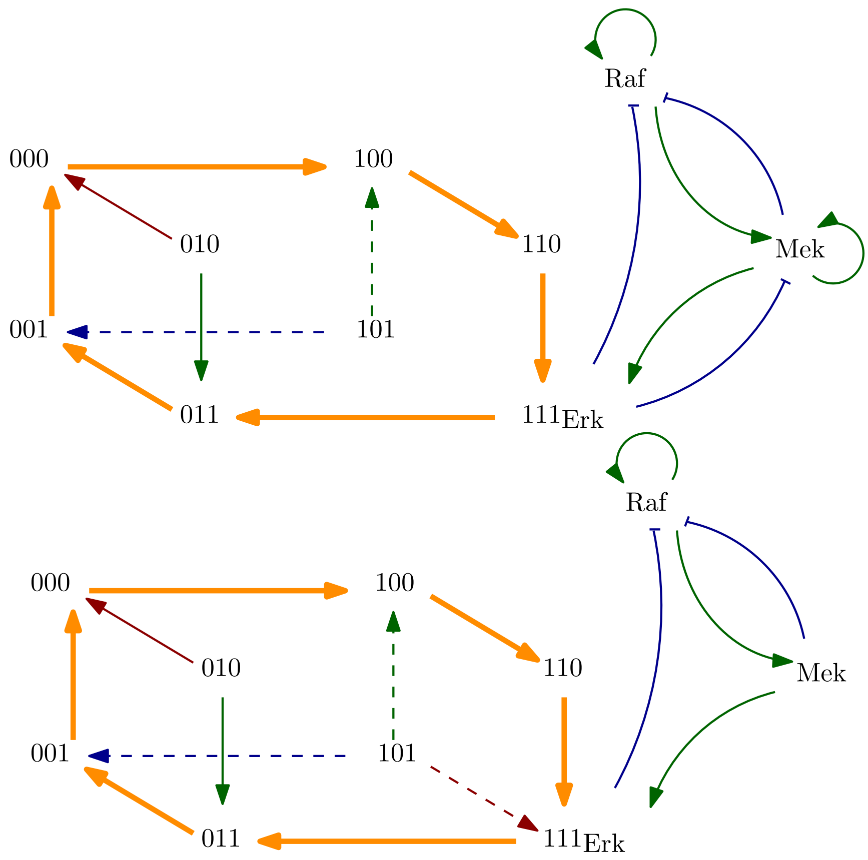

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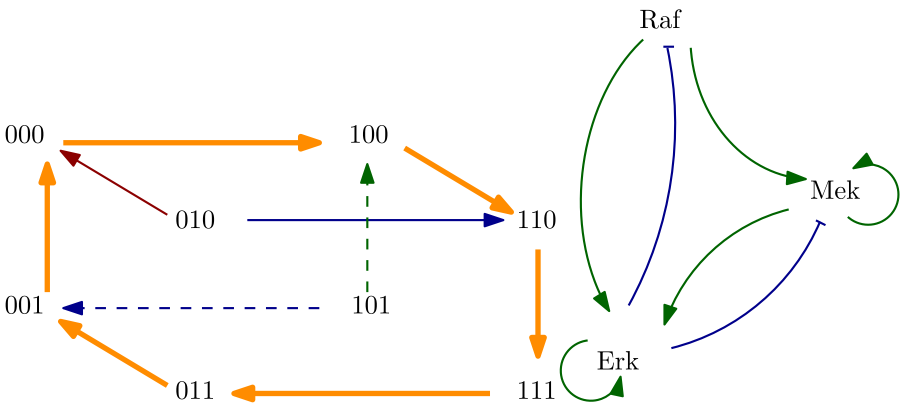

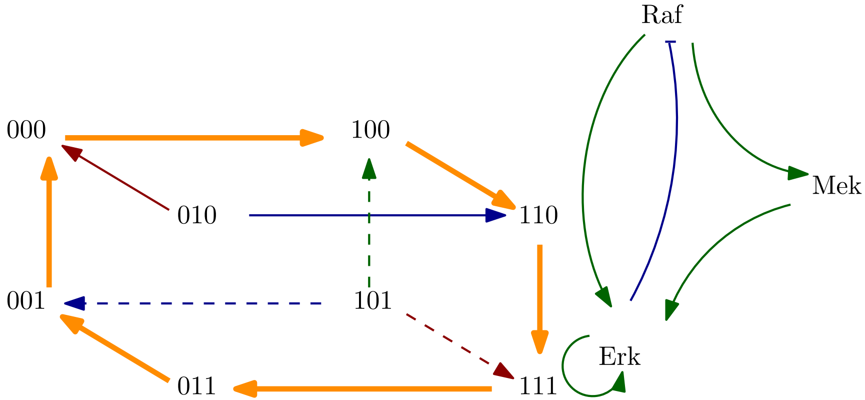

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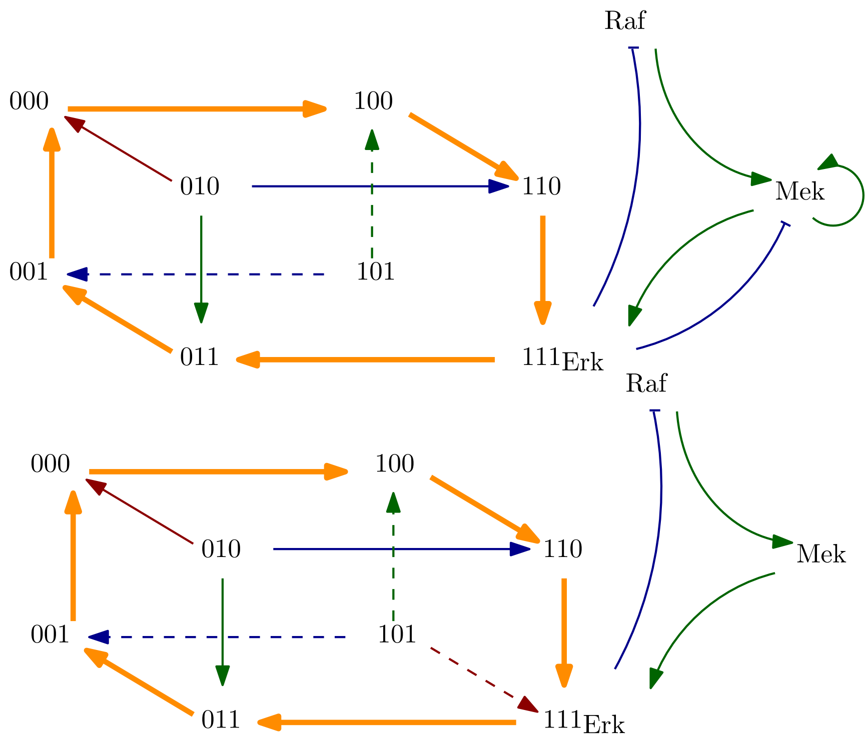
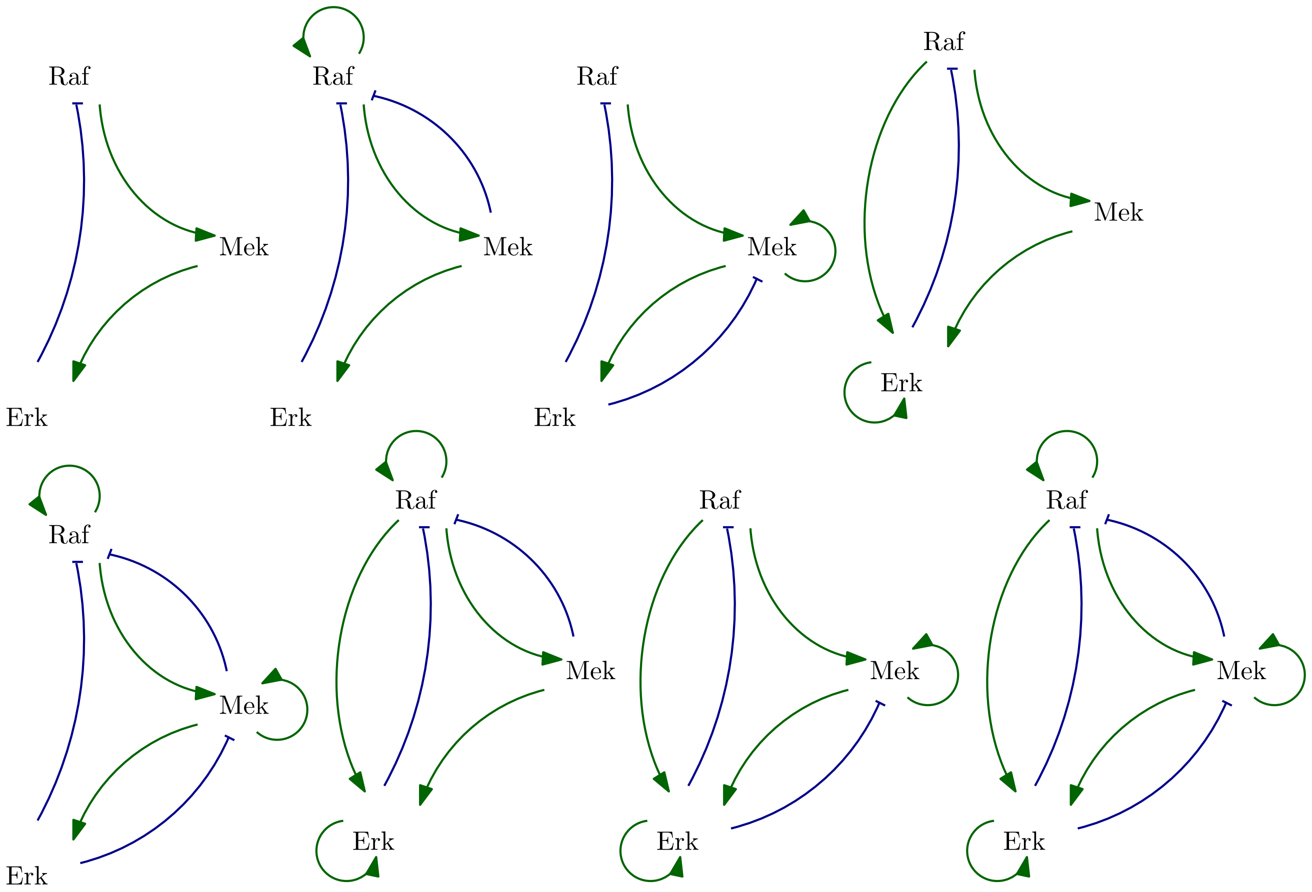
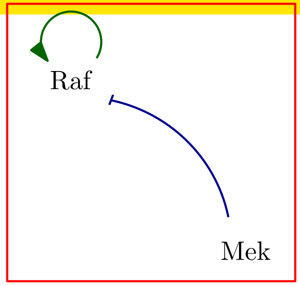


Results

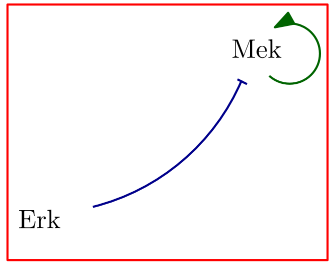
- Eight kinds of interaction graphs.

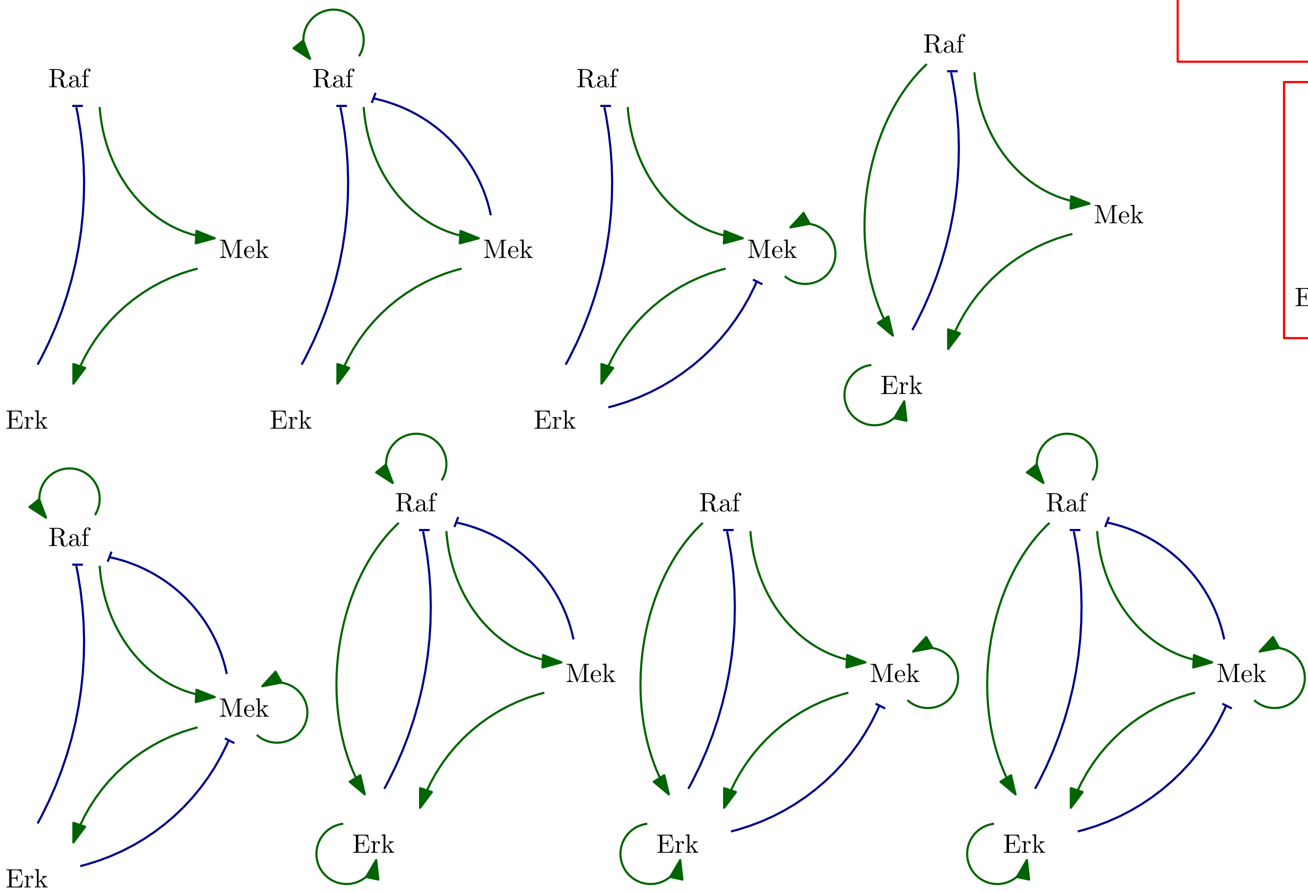


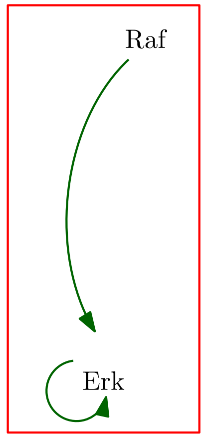
Results



- Eight kinds of interaction graphs.
- Regulations appear in pairs.

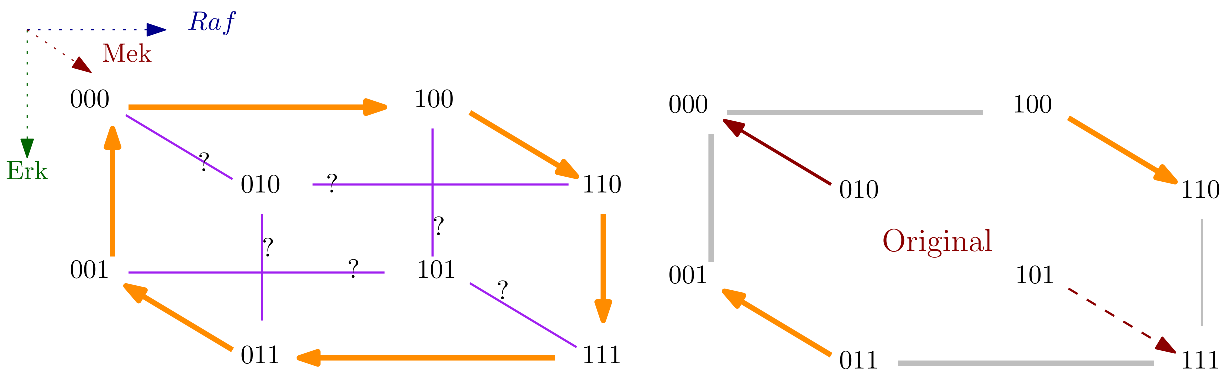






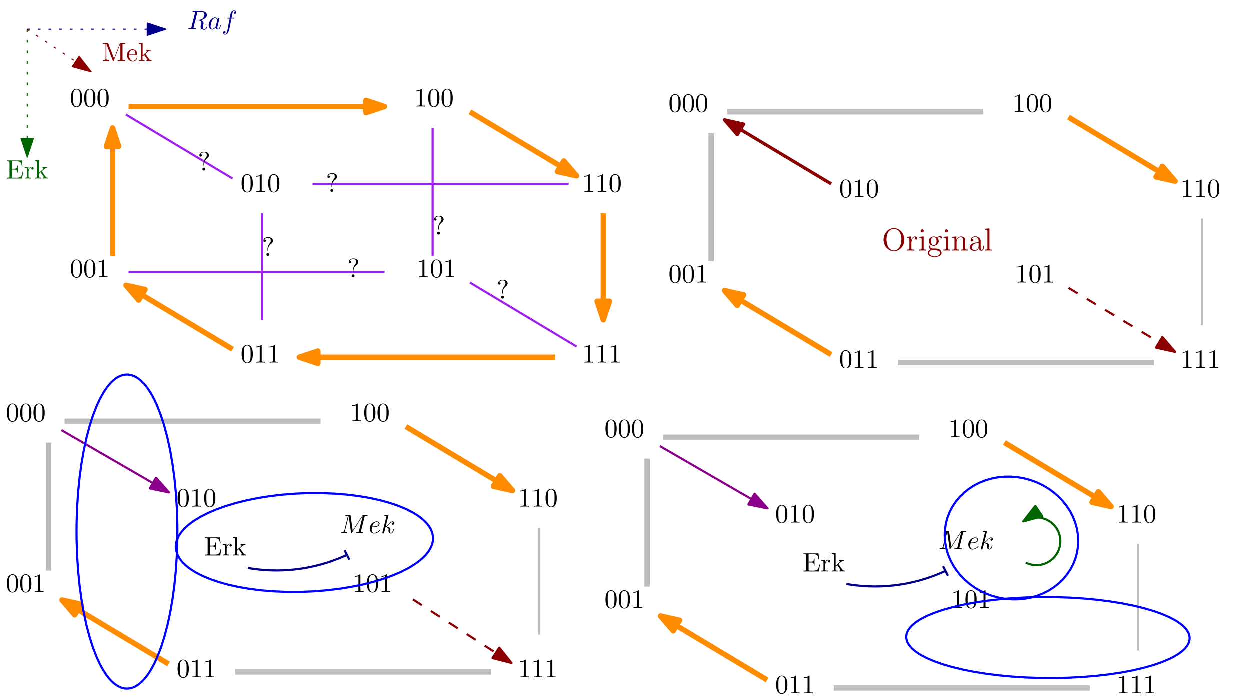
Analysis

- Eg. To understand why *Merk* $\rightarrow$ *Mek* and *Erk* $----|$ *Mek*.



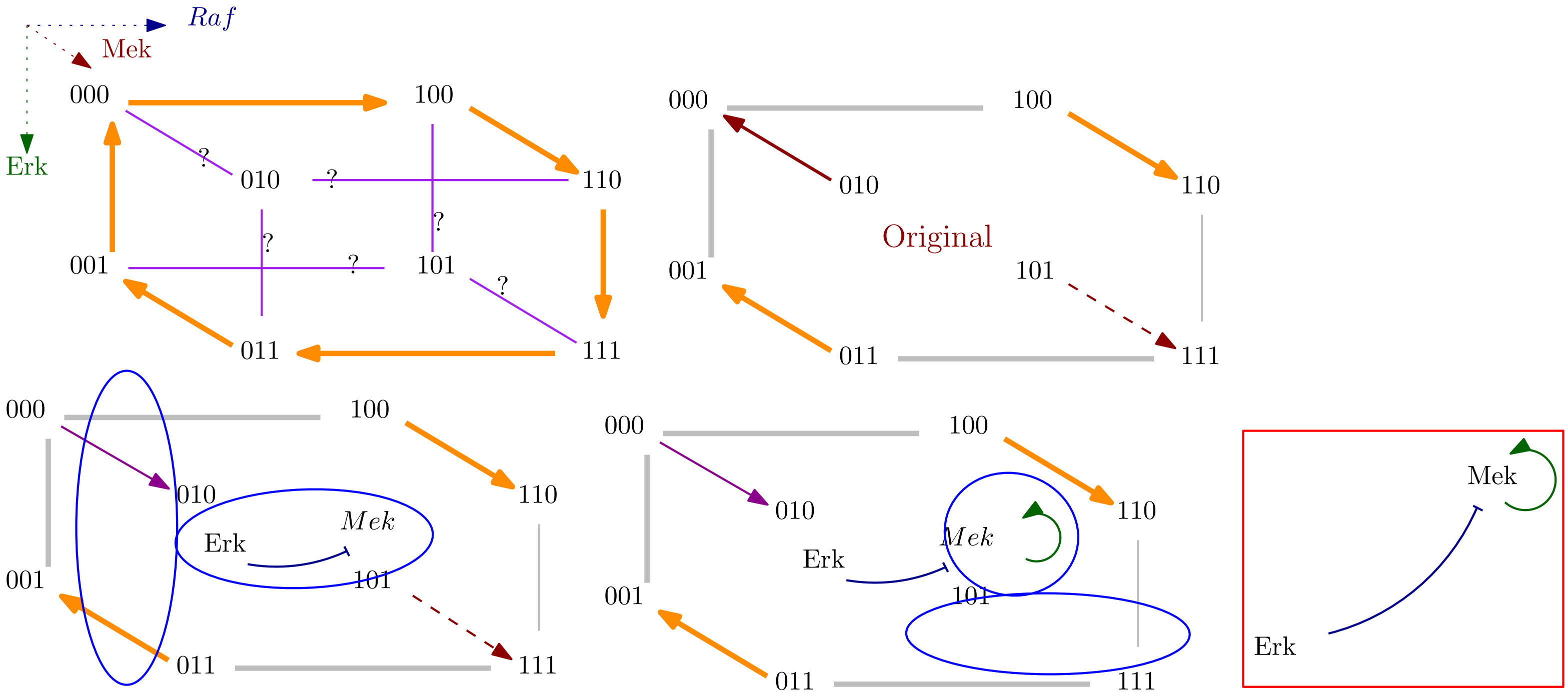
Analysis

- Eg. To understand why *Merk* $\rightarrow$ *Mek* and *Erk* $- - - -|$*Mek*.



Analysis

- Eg. To understand why *Merk* $\to$ *Mek* and *Erk* $----|$*Mek*.



Future work and so on

- Other small network options.
  - Firdevs' Signaling models (4 components).
  - GI/S cell cycle regulation(2 components).
  - Bacteriophage λ infection (4 components).
  - Neural development in Rat (CNS, 4 components).
  - Circadian clock (from 2 to 5 components).

    The last four, from Adam.
- Open question. What kind of graph is a real ASTG? What kind of ASTG doesn't carriy any IG?

Thanks for your attention!

Questions are warmly welcome!

Thanks for all of our group members in
AG MathLife and AG Discrete BioMath.
Also thanks to CSC for the support.