PATHWAY ANALYSIS OF BIOCHEMICAL NETWORKS WITH PETRI NETS

Monika Heiner

Brandenburg University of Technology Cottbus

Dep. of CS

CONTENTS

BASIC NOTIONS

- ❑
- ❑ minimal T-invariants -> Lautenbach 1973
- ❑ elementary modes -> Schuster 1991
- ❑ extreme pathways -> Schilling, Schuster, Palson 1999
- ❑

MODULAR COMPUTATION

- ❑ approach -> Zaitsev 2005
- ❑ (preliminary) results -> Lehrack 2006 (to appear)

CONTENTS

BASIC NOTIONS

- elementary T-invariants -> Pascoletti 1986
- minimal T-invariants -> Lautenbach 1973
- elementary modes -> Schuster 1991
- extreme pathways -> Schilling, Schuster, Palson 1999
-

MODULAR COMPUTATION

- approach -> Zaitsev 2005
- (preliminary) results -> Lehrack 2006 (to appear)

CONTENTS

BASIC NOTIONS

- proper T-invariants -> Pascoletti 1986
- minimal T-invariants -> Lautenbach 1973
- elementary modes -> Schuster 1991
- extreme pathways -> Schilling, Schuster, Palson 1999
- generic pathways -> Bockmayr 2005

MODULAR COMPUTATION

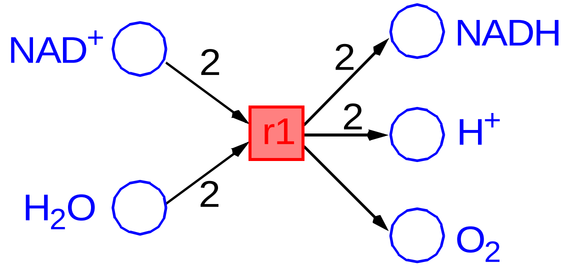
- approach -> Zaitsev 2005
- (preliminary) results -> Lehrack 2006 (to appear)

Petri Nets - Basics

- **atomic actions -> Petri net transitions -> chemical reactions**

$$2\ NAD^+ + 2\ H_2O \rightarrow 2\ NADH + 2\ H^+ + O_2$$

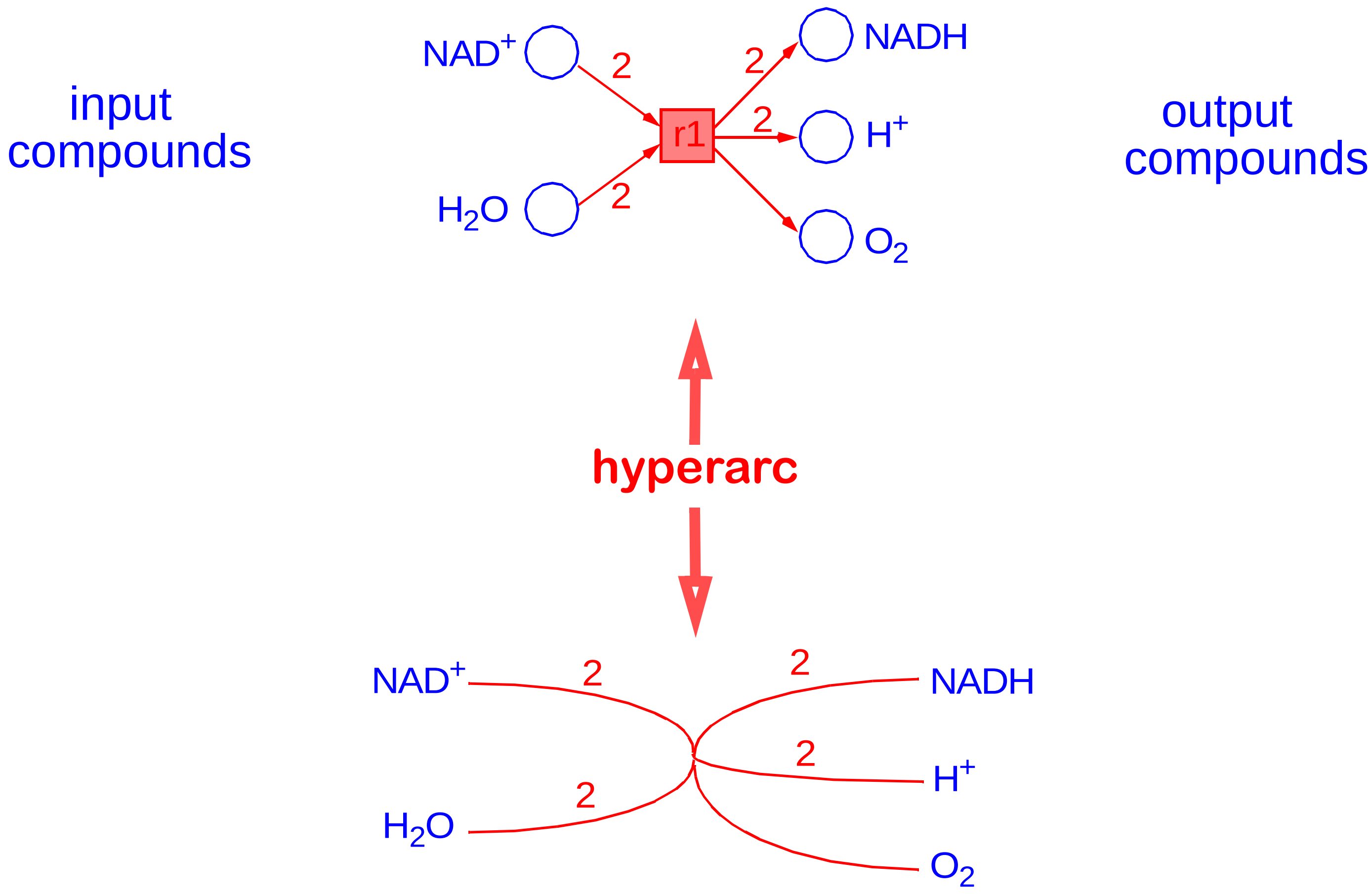
input compounds



output compounds

- **atomic actions -> Petri net transitions -> chemical reactions**

$$2\ NAD^+ + 2\ H_2O \rightarrow 2\ NADH + 2\ H^+ + O_2$$

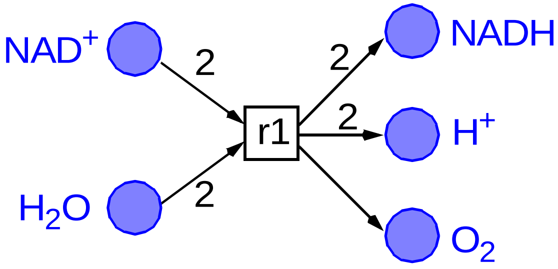


- **atomic actions -> Petri net transitions -> chemical reactions**

$$2\ NAD^+ + 2\ H_2O \rightarrow 2\ NADH + 2\ H^+ + O_2$$

input compounds

pre-conditions



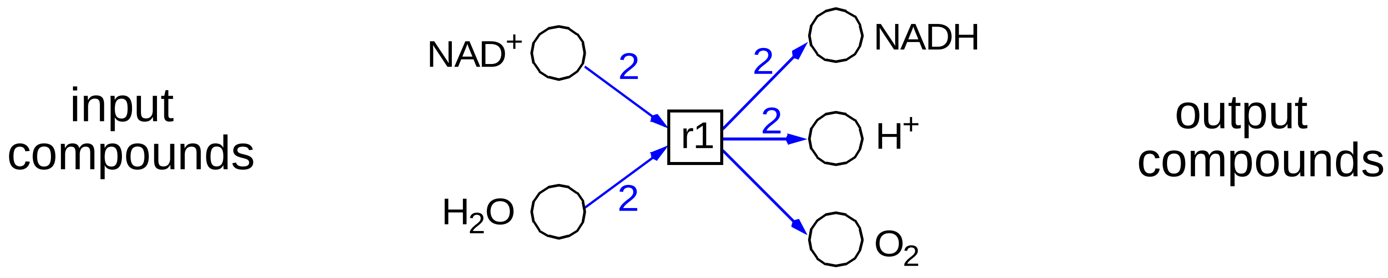
output compounds

post-conditions

- **local conditions -> Petri net places -> chemical compounds**

- **atomic actions -> Petri net transitions -> chemical reactions**

$$2\ NAD^+ + 2\ H_2O \rightarrow 2\ NADH + 2\ H^+ + O_2$$

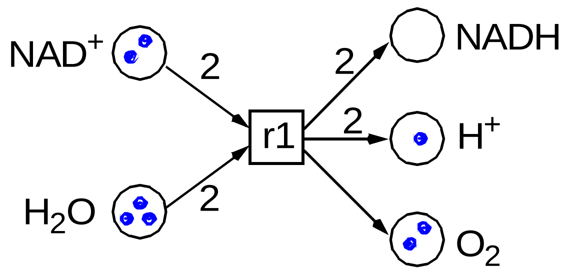


- **local conditions -> Petri net places -> chemical compounds**
- **multiplicities -> Petri net arc weights -> stoichiometric relations**

- **atomic actions -> Petri net transitions -> chemical reactions**

$$2\ NAD^+ + 2\ H_2O \rightarrow 2\ NADH + 2\ H^+ + O_2$$

input compounds



output compounds

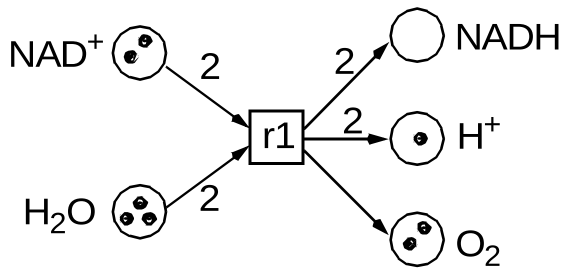
- **local conditions -> Petri net places -> chemical compounds**
- **multiplicities -> Petri net arc weights -> stoichiometric relations**
- **condition's state -> token(s) in its place -> available amount (e.g. mol)**
- **system state -> marking -> compounds distribution**

PETRI NETS, BASICS - THE STRUCTURE

- **atomic actions -> Petri net transitions -> chemical reactions**

$$2\ NAD^+ + 2\ H_2O \rightarrow 2\ NADH + 2\ H^+ + O_2$$

input compounds



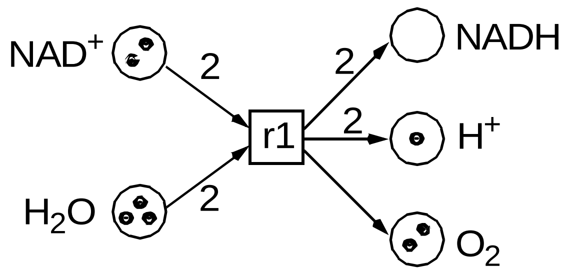
output compounds

- **local conditions -> Petri net places -> chemical compounds**
- **multiplicities -> Petri net arc weights -> stoichiometric relations**
- **condition's state -> token(s) in its place -> available amount (e.g. mol)**
- **system state -> marking -> compounds distribution**
- **PN = (P, T, F, m_0), F: (P x T) U (T x P) -> N_0, m_0: P -> N_0**

- **atomic actions -> Petri net transitions -> chemical reactions**

$$2\ NAD^+ + 2\ H_2O \rightarrow 2\ NADH + 2\ H^+ + O_2$$

input compounds

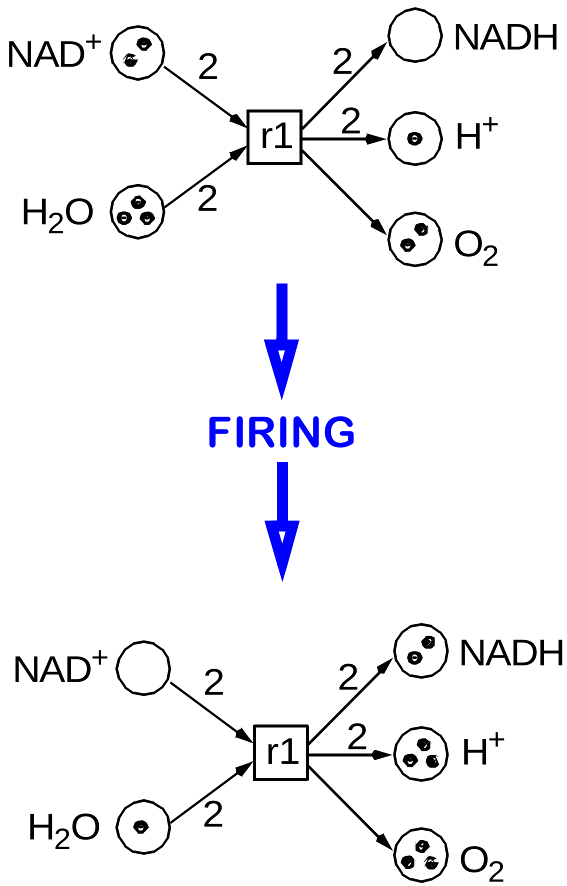


output compounds

- **atomic actions -> Petri net transitions -> chemical reactions**

$$2\ NAD^+ + 2\ H_2O \rightarrow 2\ NADH + 2\ H^+ + O_2$$

input compounds

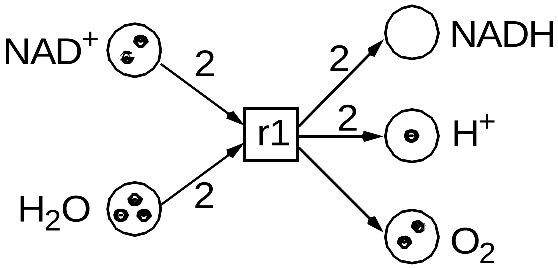


output compounds

- **atomic actions -> Petri net transitions -> chemical reactions**

$$2\ NAD^+ + 2\ H_2O \rightarrow 2\ NADH + 2\ H^+ + O_2$$

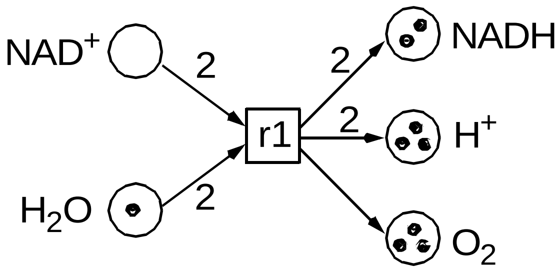
input compounds



output compounds

FIRING

TOKEN GAME



DYNAMIC BEHAVIOUR (substance/signal flow)

BIOCHEMICAL PETRI NETS, SUMMARY

- **biochemical networks**

  -> *networks of (abstract) chemical reactions*

- **biochemically interpreted Petri net**

  -> *partial order sequences of chemical reactions (= elementary actions)*
  transforming input into output compounds / signals
  [respecting the given stoichiometric relations, if any]

  -> *set of all pathways*
  from the input to the output compounds / signals
  [respecting the stoichiometric relations, if any]

- **pathway**

  -> *self-contained partial order sequence of elementary (re-) actions*

INVARIANT ANALYSES

INCIDENCE MATRIX C

- a representation of the net structure **=> stoichiometric matrix**

C =

P \ T	t1 . . .	tj	. . . tm
p1			
pi		cij	
: pn		Δtj	

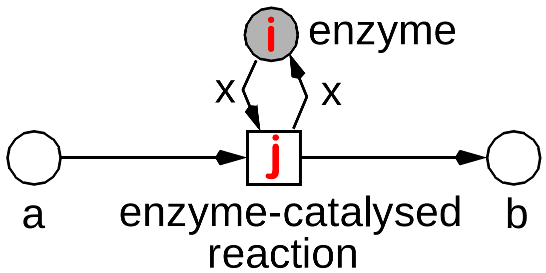
$cij = (pi, tj) = F(tj,pi) - F(pi, tj) = \Delta\ tj(pi)$

$\Delta tj = \Delta\ tj(*)$

- **matrix entry cij:**
  token change in place pi by firing of transition tj

- **matrix column Δtj:**
  vector describing the change of the whole marking by firing of tj

- **side-conditions are neglected**



cij = 0

T-INVARIANTS, BASICS I

- **Lautenbach, 1973**

- **T-invariants** -> *multisets of transitions*
  -> *integer solutions x of* $Cx = 0, x \neq 0, x \geq 0$ -> *Parikh vector*

- **minimal T-invariants**
  -> *there is no T-invariant with a smaller support* -> *sets of transitions*
  -> *gcD of all entries is 1*

- **any T-invariant is a non-negative linear combination of minimal ones**
  -> *multiplication with a positive integer*
  -> *addition*
  -> *Division by gcD*

$$kx = \sum_i a_i x_i$$

- **Covered by T-Invariants (CTI)**
  -> *each transition belongs to a T-invariant*

T-INVARIANTS, BASICS II

- **a T-invariant defines a subnet** **-> partial order structure**
  - -> *the T-invariant's transitions (the support),*
    + all their pre- and post-places
    + the arcs in between
  - -> *pre-sets of supports = post-sets of supports*

monika.heiner@informatik.tu-cottbus.de

- **a T-invariant defines a subnet** **-> partial order structure**
  - -> *the T-invariant's transitions (the support),*
    + all their pre- and post-places
    + the arcs in between
  - -> *pre-sets of supports = post-sets of supports*

-> ANALOGUE DEFINITIONS FOR P-INVARIANTS

$$yC = 0, y \neq 0, y \geq 0$$

T-INVARIANTS, TWO INTERPRETATIONS IN BIO NETWORKS

- **T-invariants = (multi-) sets of transitions = Parikh vector**
  - -> *zero effect on marking*
  - -> *reproducing a marking / system state*

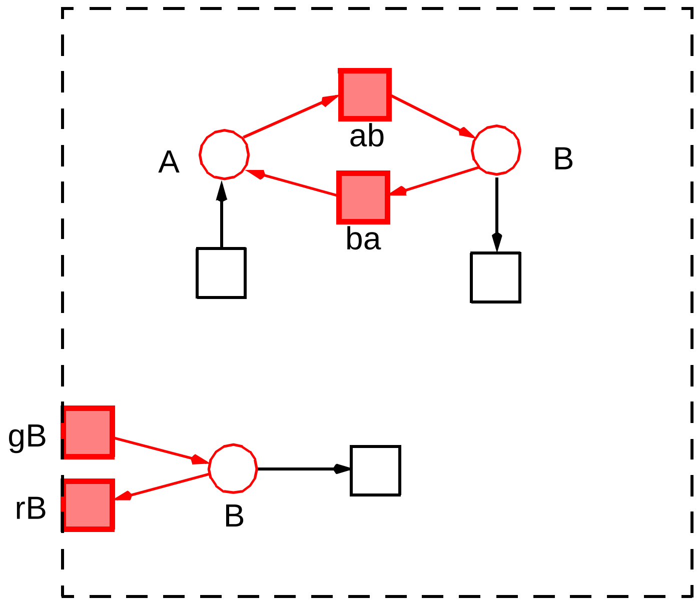
- **partially ordered transition sequence** -> **behaviour understanding**
  of transitions occuring one after the other
  - -> *substance / signal flow*
  - -> *signal transduction networks, gene regulatory networks*

- **relative transition firing rates**
  of transitions occuring permanently & concurrently
  - -> *steady state behaviour*
  - -> *metabolic networks*

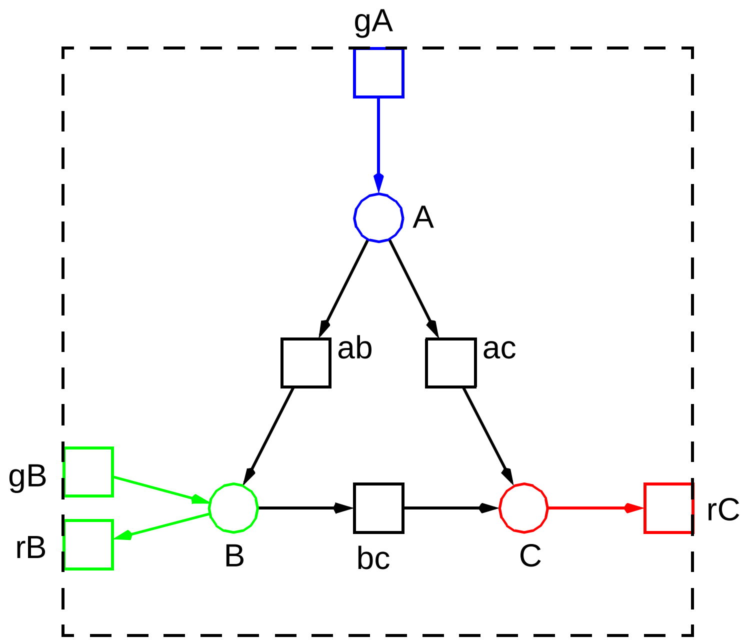
- **trivial minimal T-invariants**
  - -> *reversible reactions*
  - -> *boundary transitions of auxiliary compounds*

- **non-trivial minimal T-invariants**
  - -> *i/o-T-invariants*

    covering boundary transitions of input / output compounds
  - -> *inner cycles*



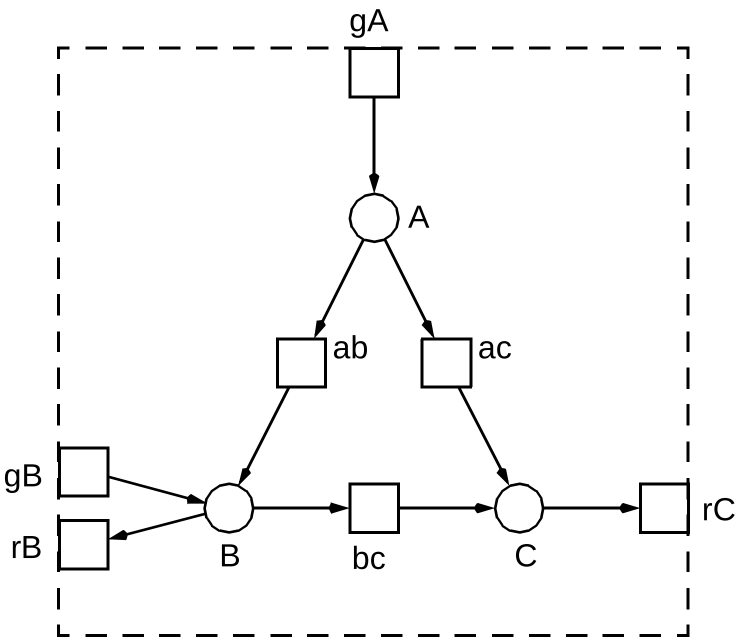
- substances involved
  - -> *input substance A*
  - -> *output substance C*
  - -> *auxiliary substance B*



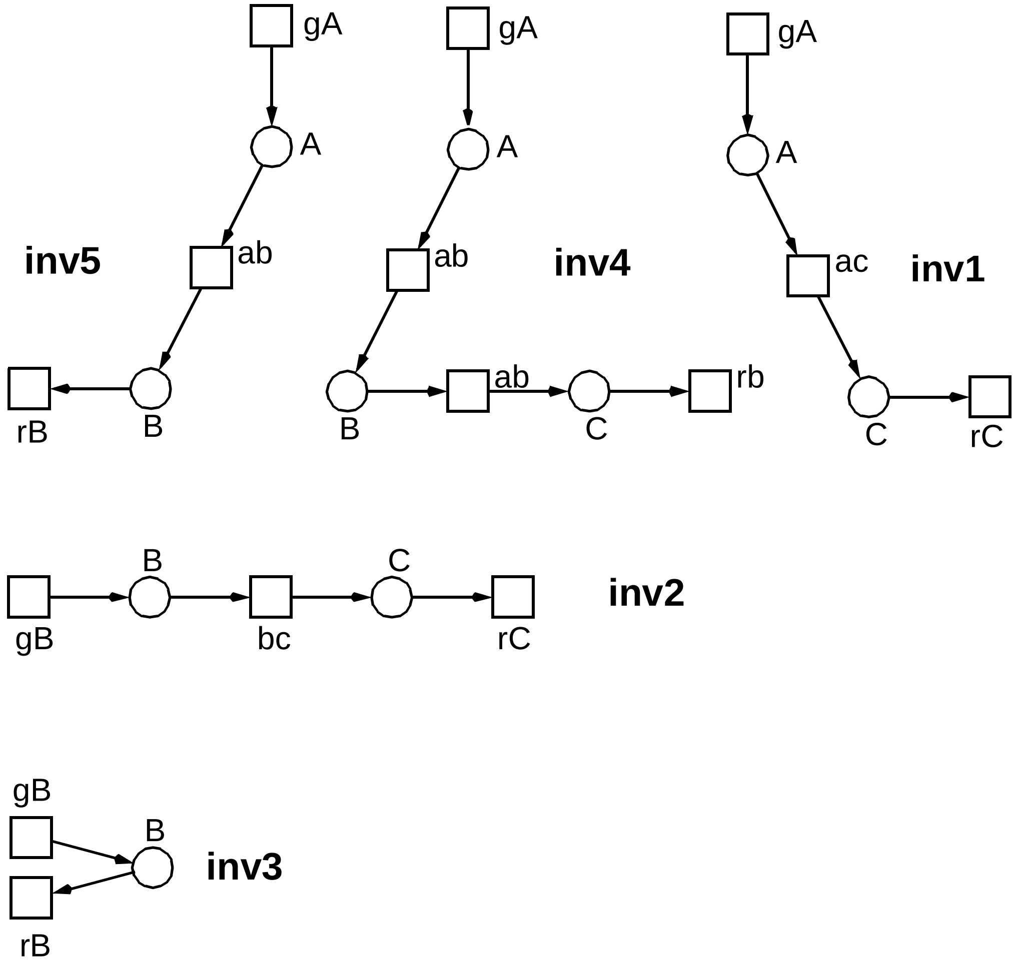
papin2003.spped

EXAMPLE, T-INVARIANTS

- substances involved
  - -> *input substance A*
  - -> *output substance C*
  - -> *auxiliary substance B*

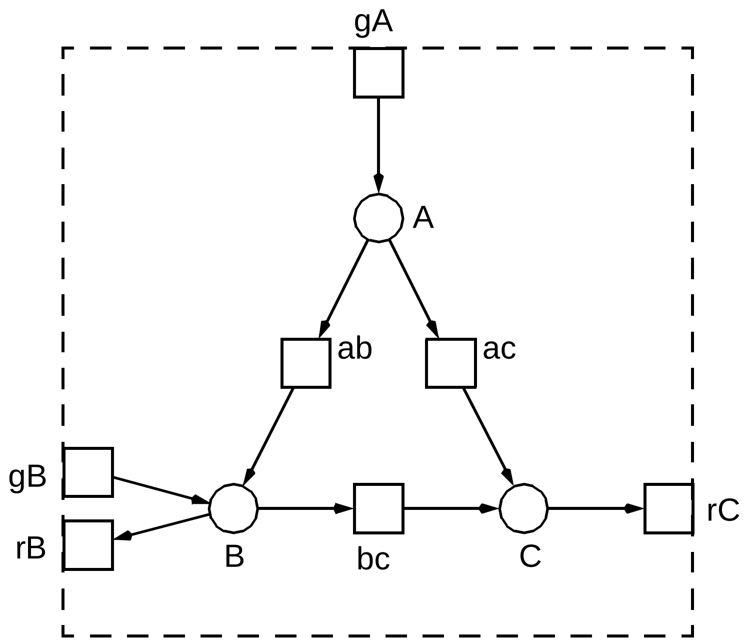


papin2003.spped

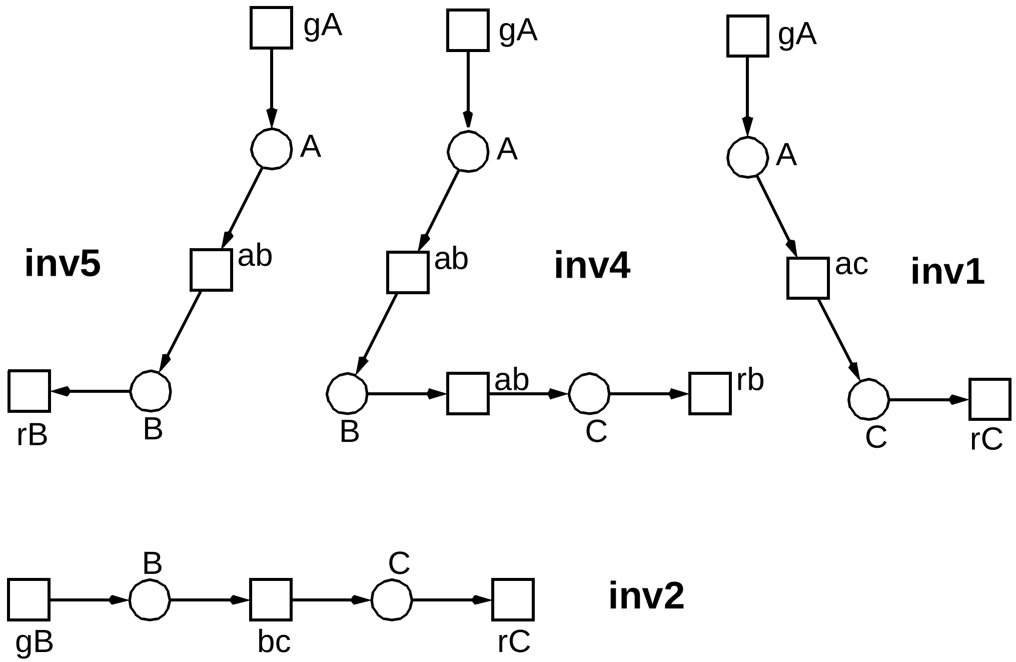


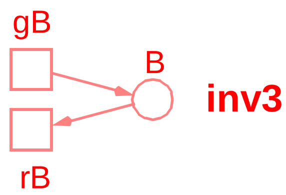
EXAMPLE, ELEMENTARY MODES

- ❑ substances involved
  - -> *input substance A*
  - -> *output substance C*
  - -> *auxiliary substance B*



papin2003.spped

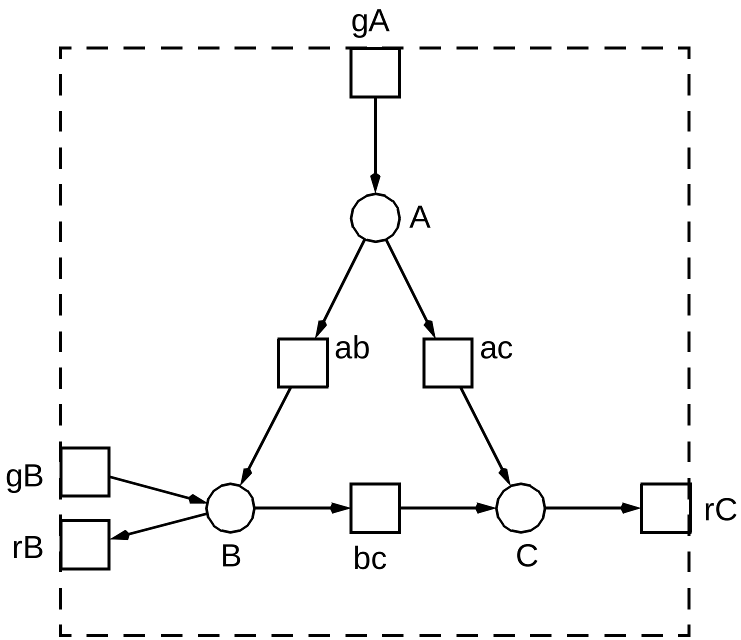




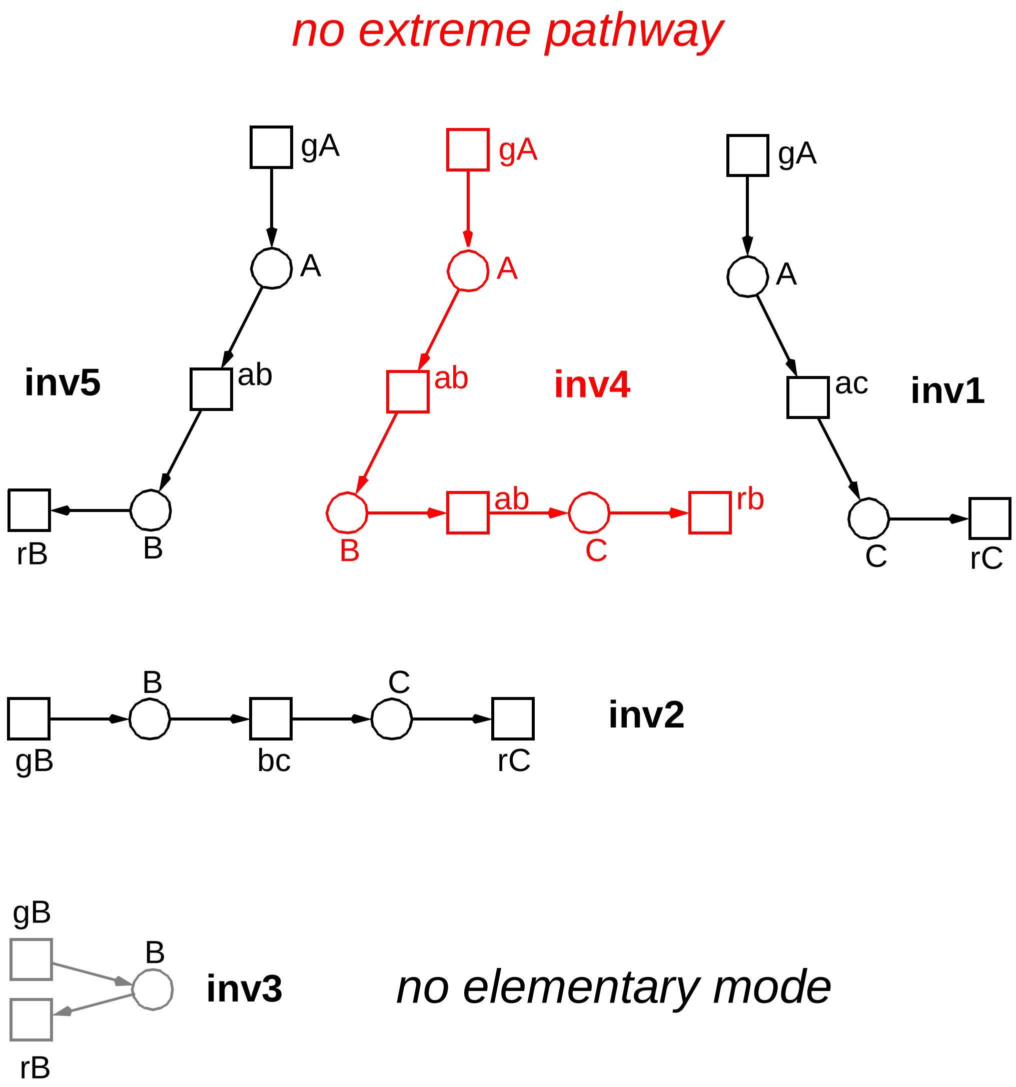
no elementary mode

EXAMPLE, EXTREME PATHWAYS

- substances involved
  - -> *input substance A*
  - -> *output substance C*
  - -> *auxiliary substance B*



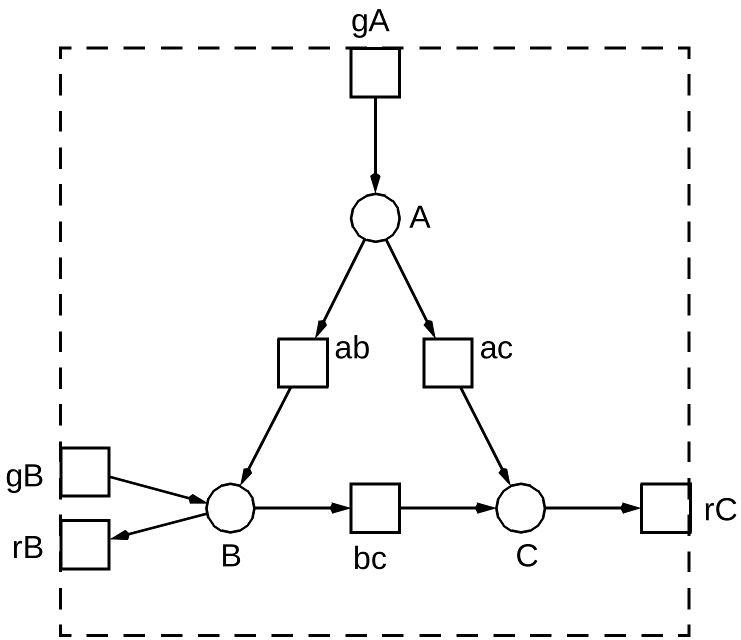
papin2003.spped



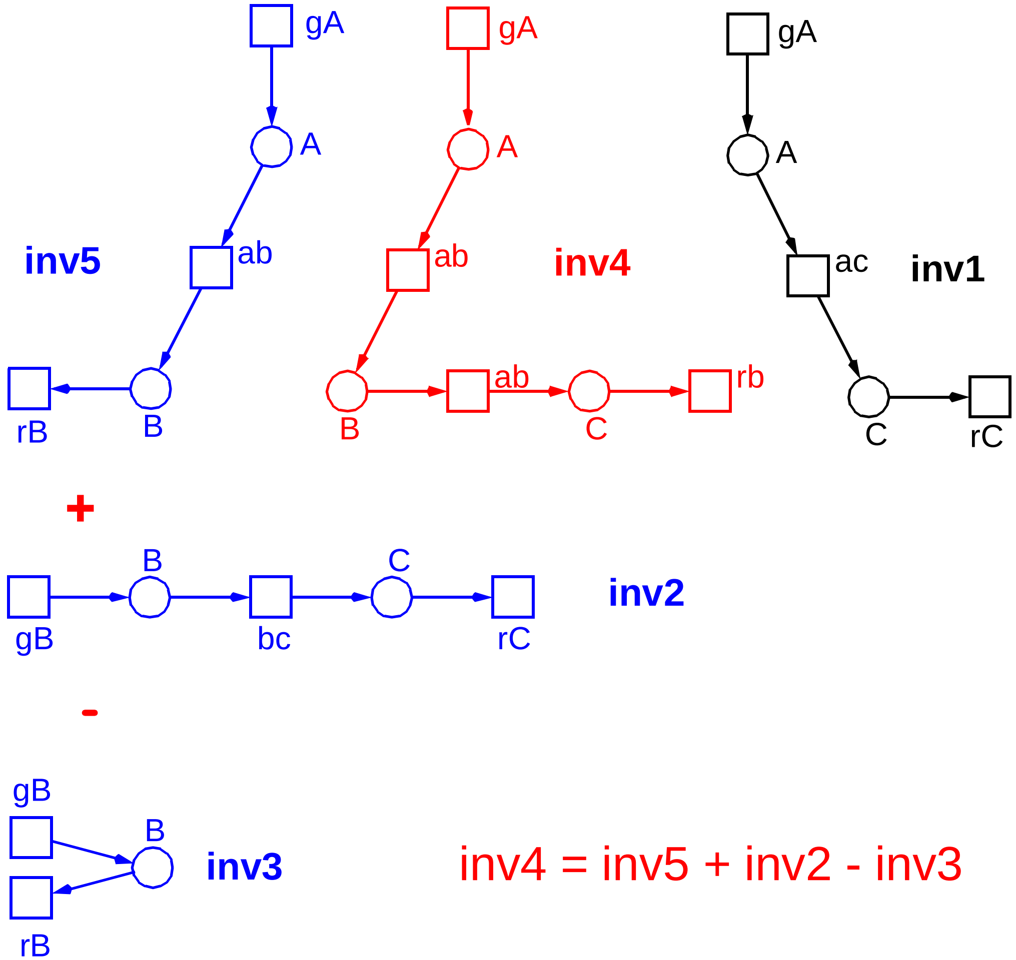
EXAMPLE, EXTREME PATHWAYS

- substances involved
  - -> *input substance A*
  - -> *output substance C*
  - -> *auxiliary substance B*

no extreme pathway



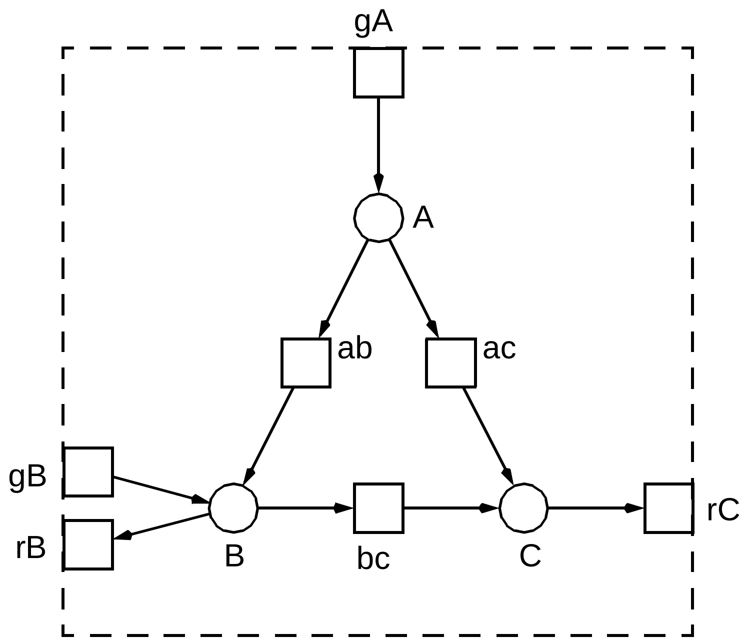
papin2003.spped



inv4 = inv5 + inv2 - inv3

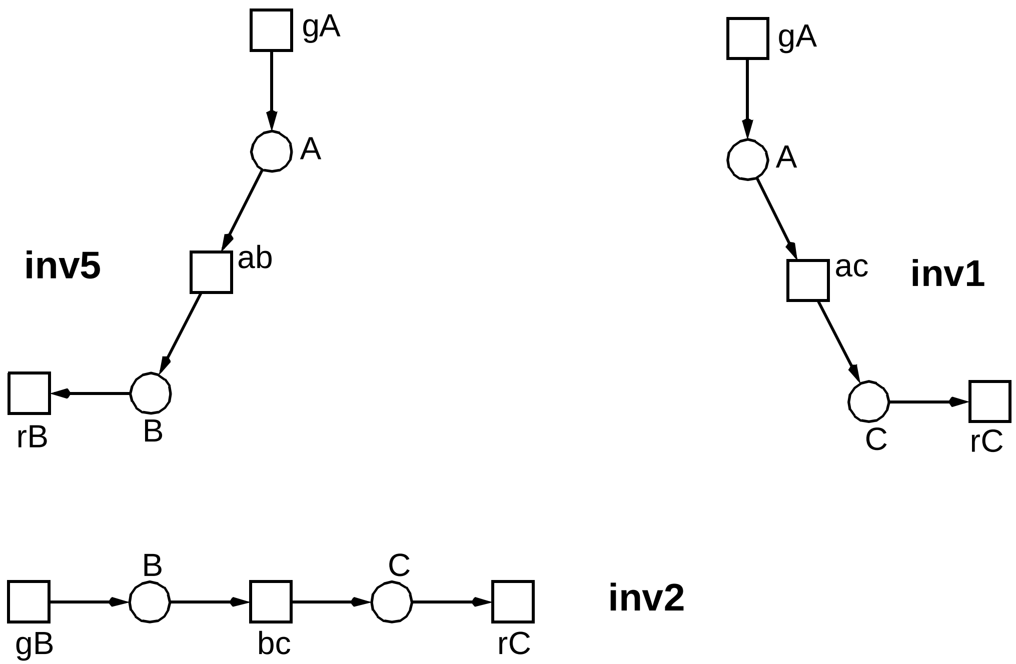
EXAMPLE, SUMMARY

- substances involved
  - -> *input substance A*
  - -> *output substance C*
  - -> *auxiliary substance B*



papin2003.spped

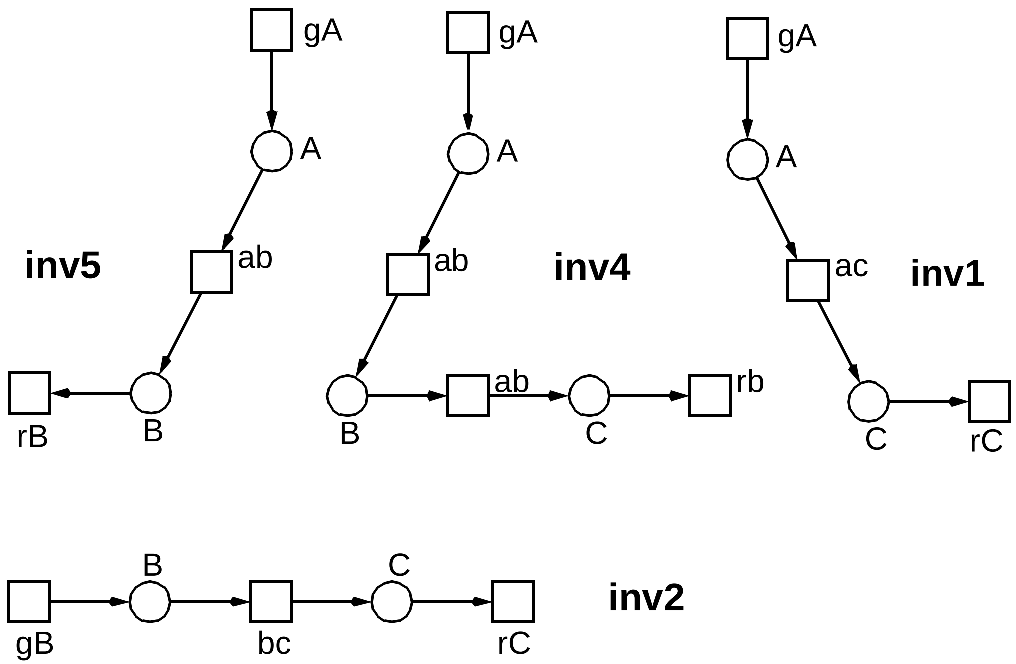
EXTREME PATHWAYS

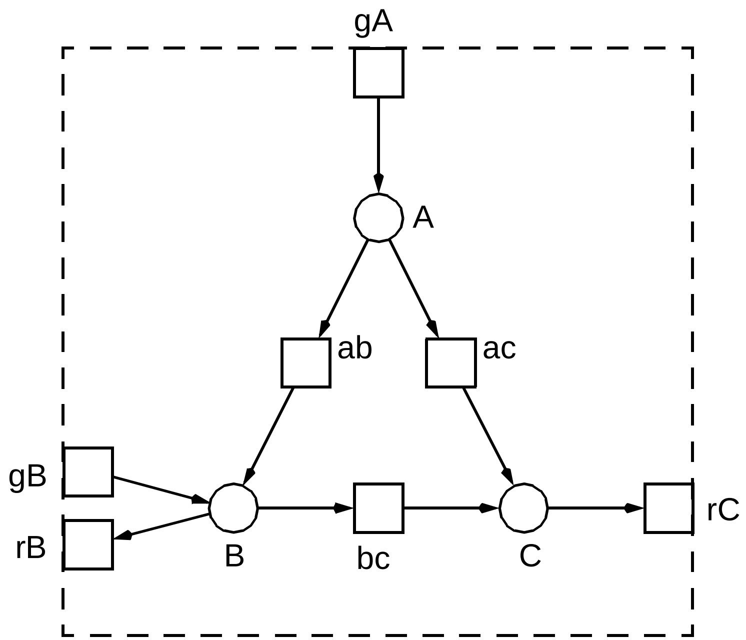


EXAMPLE, SUMMARY

- substances involved
  - -> *input substance A*
  - -> *output substance C*
  - -> *auxiliary substance B*

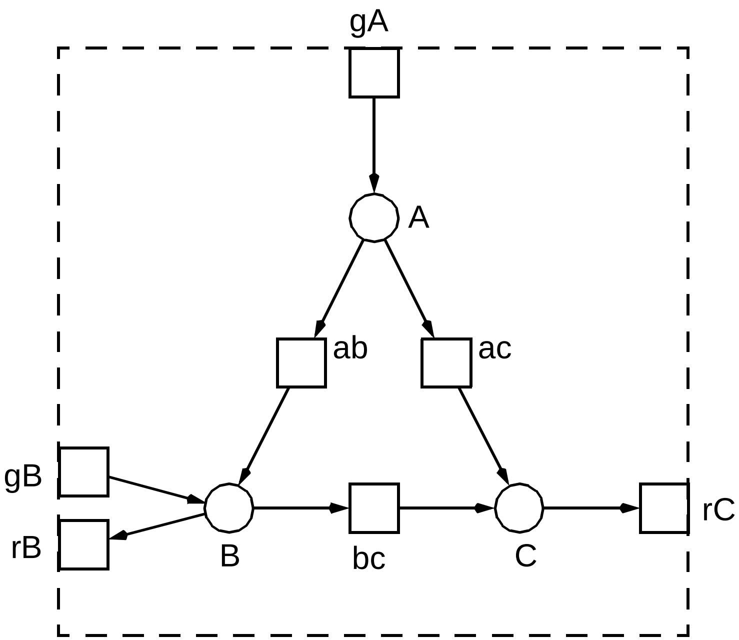
ELEMENTARY MODES





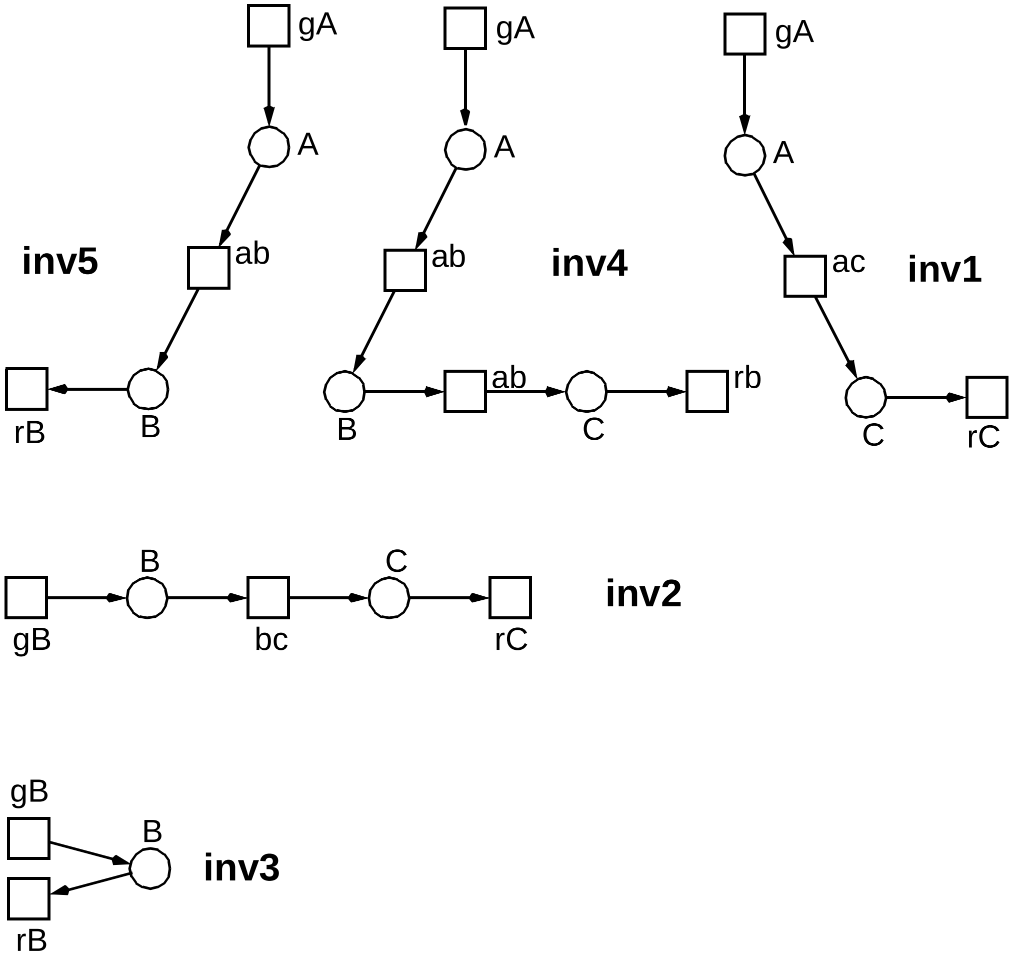
papin2003.spped

- substances involved
  - -> *input substance A*
  - -> *output substance C*
  - -> *auxiliary substance B*

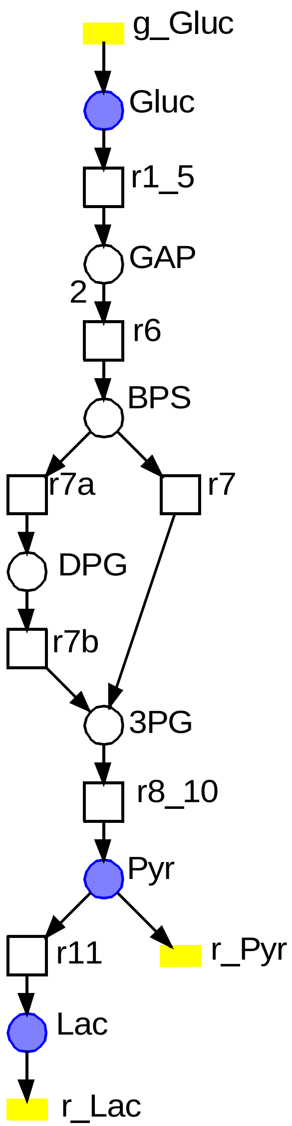


papin2003.spped

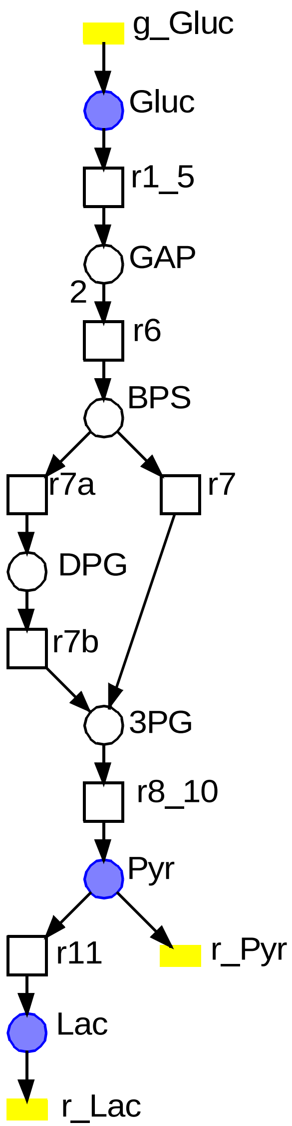
MINIMAL T-INVARIANTS



ELEMENTARY T-INVARIANTS / HILBERT BASIS



Elementary T-invariants / Hilbert basis



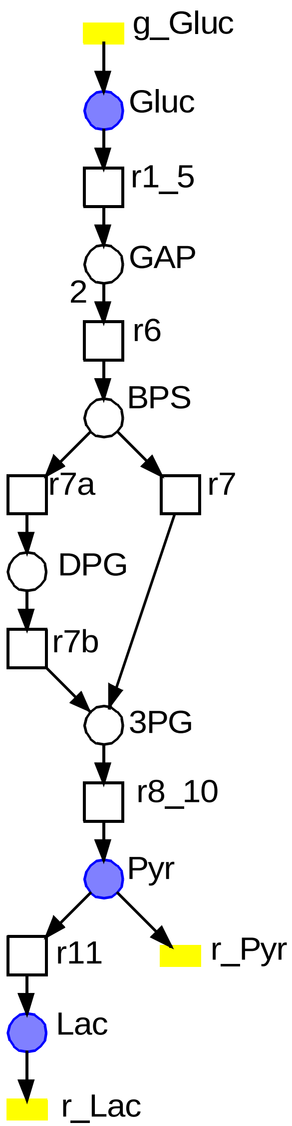
four minimal T-invariants

1. Gluc -> r7 -> 2 Pyr
2. Gluc -> r7 -> 2 Lac
3. Gluc -> r7a, r7b -> 2 Pry
4. Gluc -> r7a, r7b -> 2 Lac

$$\text{Gluc} \rightarrow \begin{bmatrix} \text{r7} \\ \text{r7a, r7b} \end{bmatrix} \rightarrow \begin{bmatrix} \text{2 Lac} \\ \text{2 Pyr} \end{bmatrix}$$

$$kx = \sum_i a_i x_i$$

ELEMENTARY T-INVARIANTS / HILBERT BASIS



four minimal T-invariants

1. Gluc -> r7 -> 2 Pyr
2. Gluc -> r7 -> 2 Lac
3. Gluc -> r7a, r7b -> 2 Pry
4. Gluc -> r7a, r7b -> 2 Lac

Gluc -> [r7 / r7a, r7b] -> [2 Lac / 2 Pyr]

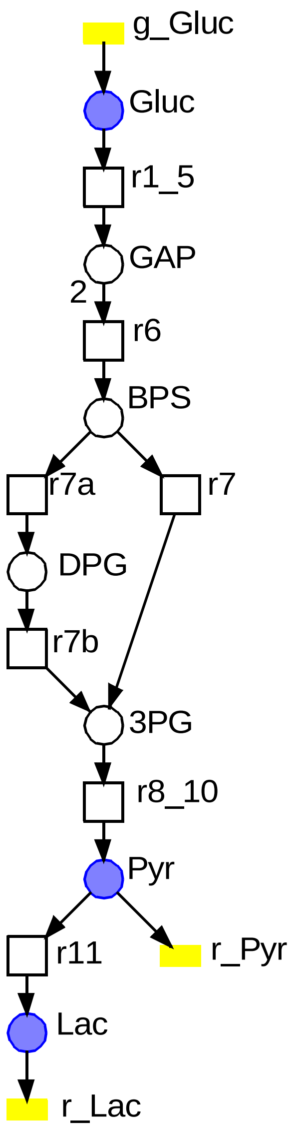
?

Gluc -> [r7 / r7a, r7b] -> [1 Lac / 1 Pyr]

$$kx = \sum_i a_i x_i$$

monika.heiner@informatik.tu-cottbus.de

ELEMENTARY T-INVARIANTS / HILBERT BASIS



four minimal T-invariants

1. Gluc -> r7 -> 2 Pyr
2. Gluc -> r7 -> 2 Lac
3. Gluc -> r7a, r7b -> 2 Pry
4. Gluc -> r7a, r7b -> 2 Lac

five additional T-invariants

inv5 = (inv1 + inv3) / 2
inv6 = (inv2 + inv4) / 2

inv7 = (inv1 + inv2) / 2
inv8 = (inv3 + inv4) / 2

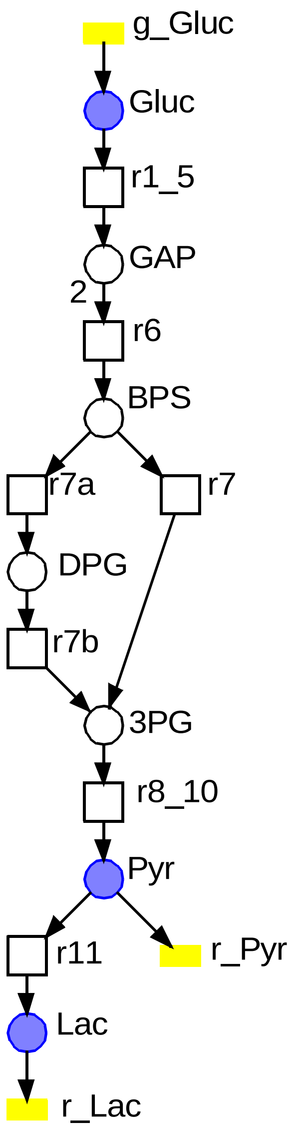
inv9 = (inv1 + inv2 + inv3 + inv4) / 4

Gluc -> [r7 / r7a, r7b] -> [2 Lac / 2 Pyr]

Gluc -> [r7 / r7a, r7b] -> [1 Lac / 1 Pyr]

$$kx = \sum_i a_i x_i$$

Elementary T-invariants / Hilbert basis



four minimal T-invariants

1. Gluc -> r7 -> 2 Pyr
2. Gluc -> r7 -> 2 Lac
3. Gluc -> r7a, r7b -> 2 Pry
4. Gluc -> r7a, r7b -> 2 Lac

$$\text{Gluc} \rightarrow \begin{bmatrix} \text{r7} \\ \text{r7a, r7b} \end{bmatrix} \rightarrow \begin{bmatrix} \text{2 Lac} \\ \text{2 Pyr} \end{bmatrix}$$

$$kx = \sum_i a_i x_i$$

five additional T-invariants

inv5 = (inv1 + inv3) / 2
inv6 = (inv2 + inv4) / 2

inv7 = (inv1 + inv2) / 2
inv8 = (inv3 + inv4) / 2

inv9 = (inv1 + inv2 + inv3 + inv4) / 4

$$\text{Gluc} \rightarrow \begin{bmatrix} \text{r7} \\ \text{r7a, r7b} \end{bmatrix} \rightarrow \begin{bmatrix} \text{1 Lac} \\ \text{1 Pyr} \end{bmatrix}$$

$$x = \sum_i a_i x_i$$

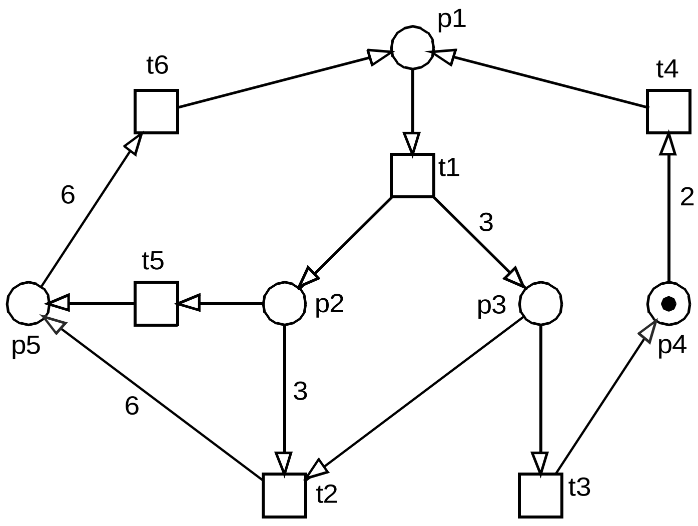
MODULAR COMPUTATION

BASIC IDEA

- **decomposition into subnets**
- **for each subnet: computation of (local) invariants**
- **computation of interface invariants**
- **calculation of system invariants**
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*

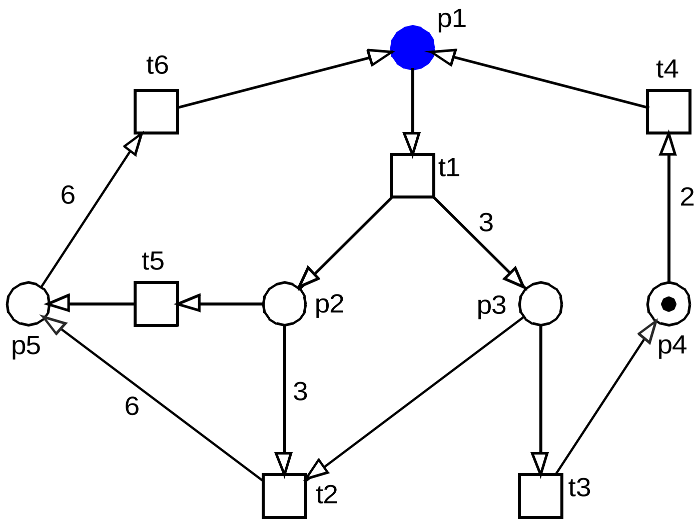
BASIC IDEA

- **decomposition into subnets**
- **for each subnet: computation of (local) invariants**
- **computation of interface invariants**
- **calculation of system invariants**
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*



BASIC IDEA

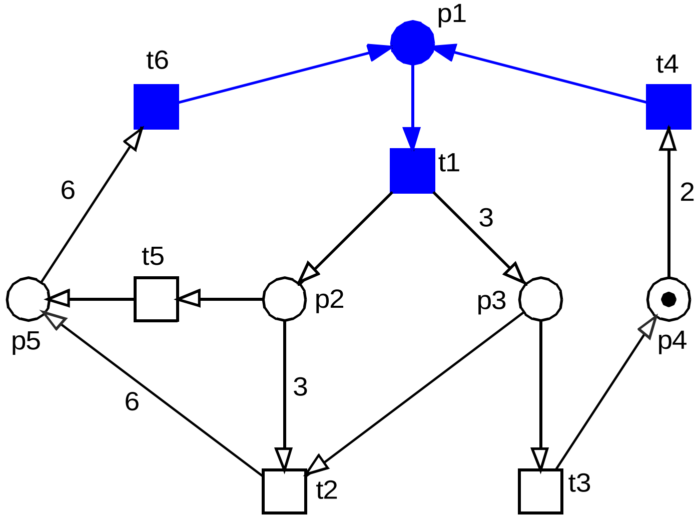
- **decomposition into subnets**
- **for each subnet: computation of (local) invariants**
- **computation of interface invariants**
- **calculation of system invariants**
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*



subnet -
transition-bordered conflict cluster C,
defined by its places

BASIC IDEA

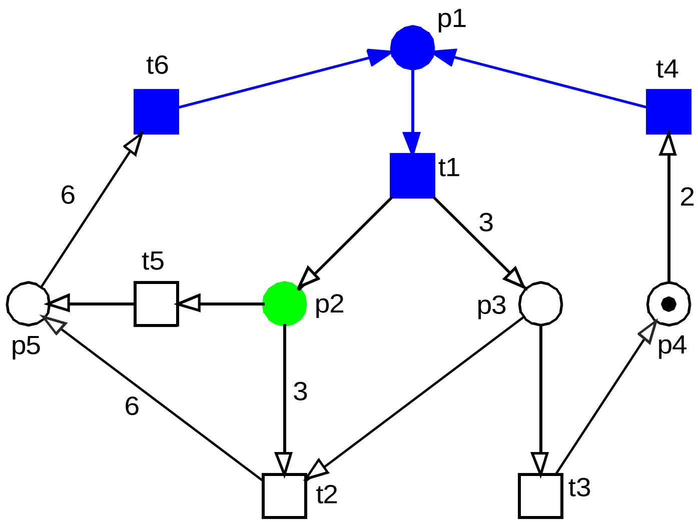
- **decomposition into subnets**
- **for each subnet: computation of (local) invariants**
- **computation of interface invariants**
- **calculation of system invariants**
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*



subnet -
transition-bordered conflict cluster C,
defined by its places

all postplaces of input transitions belong to C
all preplaces of output transitions belong to C

- **decomposition into subnets**
- **for each subnet: computation of (local) invariants**
- **computation of interface invariants**
- **calculation of system invariants**
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*

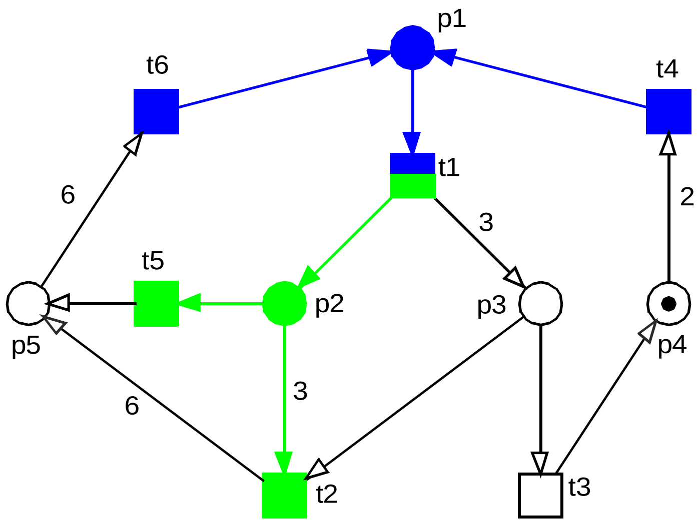


subnet - transition-bordered conflict cluster C, defined by its places

all postplaces of input transitions belong to C
all preplaces of output transitions belong to C

Basic Idea

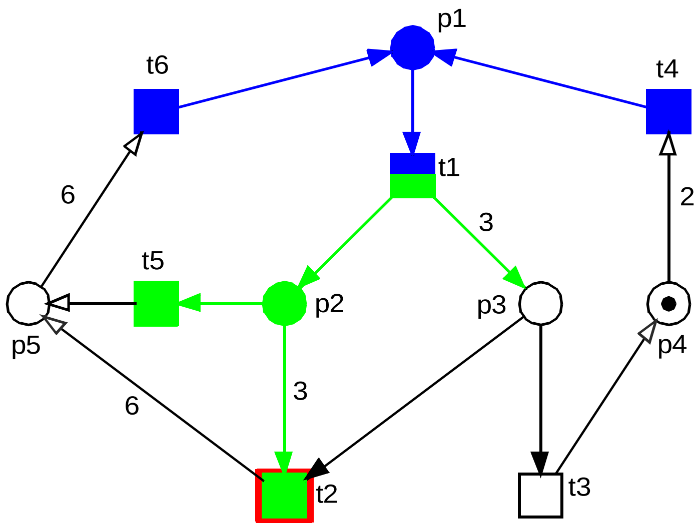
- decomposition into subnets
- for each subnet: computation of (local) invariants
- computation of interface invariants
- calculation of system invariants
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*



subnet -
transition-bordered conflict cluster C,
defined by its places

all postplaces of input transitions belong to C
all preplaces of output transitions belong to C

- decomposition into subnets
- for each subnet: computation of (local) invariants
- computation of interface invariants
- calculation of system invariants
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*

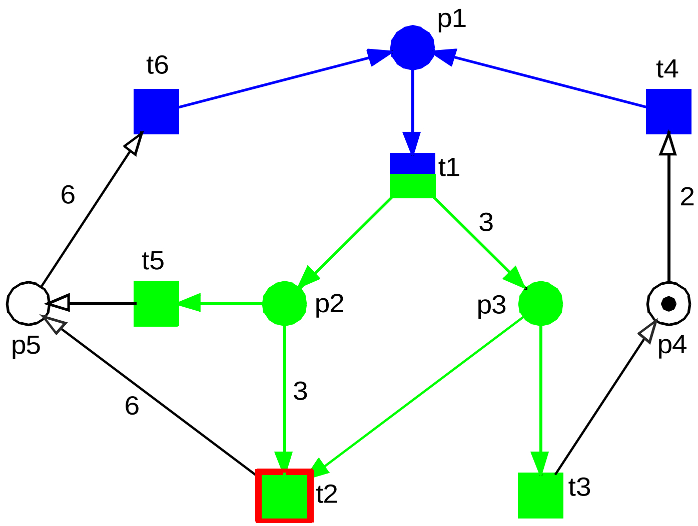


subnets -
transition-bordered conflict clusters C, defined by its places

all postplaces of input transitions belong to C
all preplaces of output transitions belong to C

Basic Idea

- **decomposition into subnets**
- **for each subnet: computation of (local) invariants**
- **computation of interface invariants**
- **calculation of system invariants**
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*

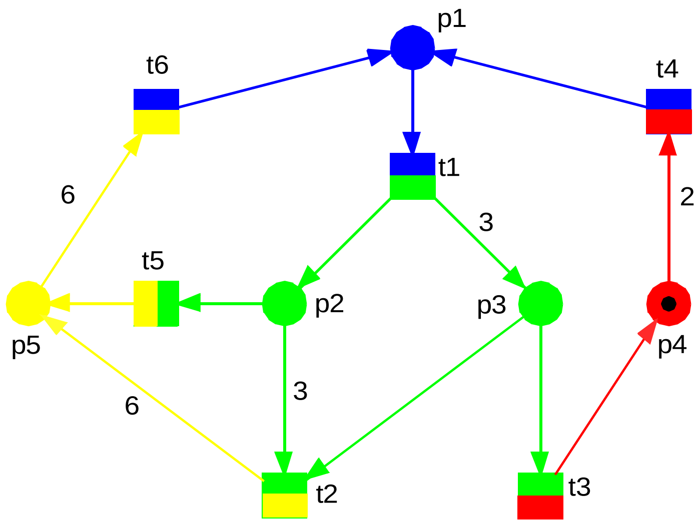


subnet - transition-bordered conflict cluster C, defined by its places

all postplaces of input transitions belong to C
all preplaces of output transitions belong to C

BASIC IDEA

- **decomposition into subnets**
- **for each subnet: computation of (local) invariants**
- **computation of interface invariants**
- **calculation of system invariants**
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*



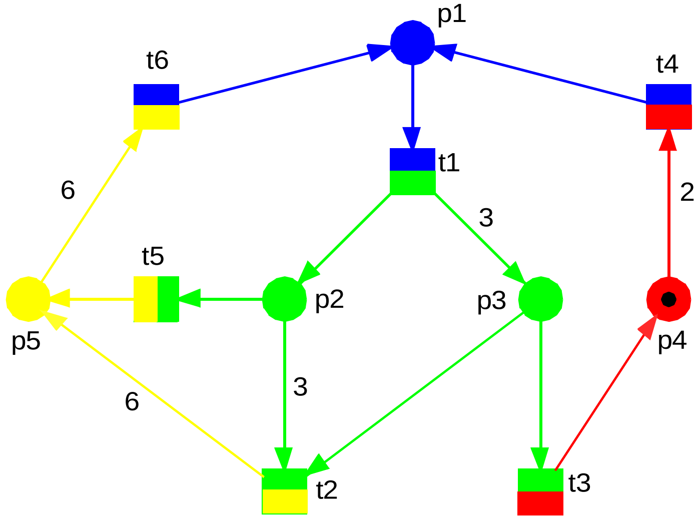
subnet -
transition-bordered conflict cluster C,
defined by its places

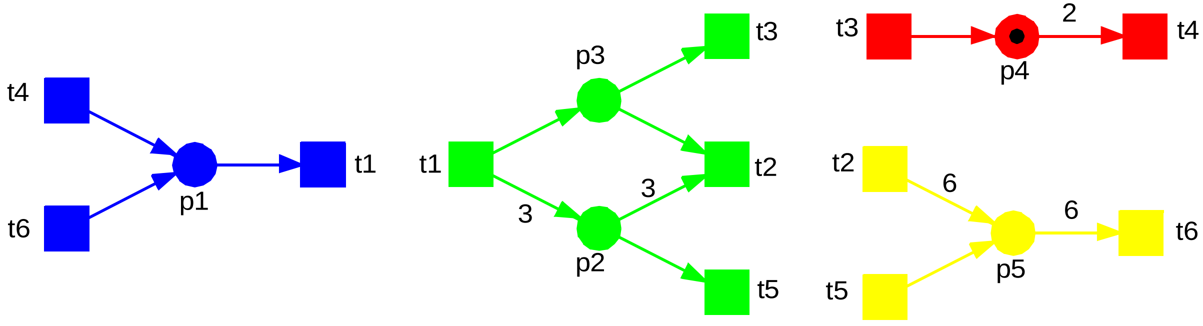
all postplaces of input transitions belong to C
all preplaces of output transitions belong to C

each interface transition has at most
- one input subnet
- one output subnet

Basic Idea

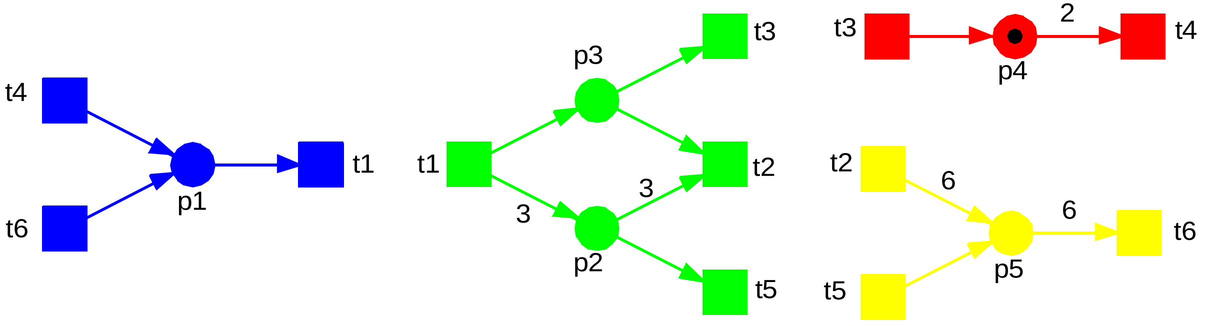
- **decomposition into subnets**
- **for each subnet: computation of (local) invariants**
- **computation of interface invariants**
- **calculation of system invariants**
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*





BASIC IDEA

- decomposition into subnets
- for each subnet: computation of (local) invariants
- computation of interface invariants
- calculation of system invariants
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*



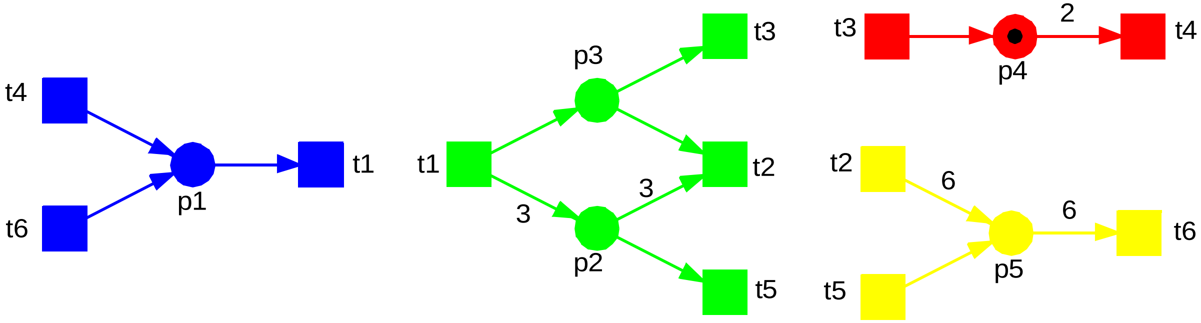
- **decomposition into subnets**
- **for each subnet: computation of (local) invariants**
- **computation of interface invariants**
- **calculation of system invariants**
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*

x1 = (t4, t1)
x2 = (t6, t1)

x3 = (t1, t2)
x4 = (t1, t3, 3 t5)

x5 = (2 t3, t4)

x6 = (t2, t6)
x7 = (6 t5, t6)



- **decomposition into subnets**
- **for each subnet: computation of (local) invariants**
- **computation of interface invariants**
- **calculation of system invariants**
  -> *by composition of subnet invariants*
  -> *guided by interface invariants*

x1 = (t4, t1)
x2 = (t6, t1)

x3 = (t1, t2)
x4 = (t1, t3, 3 t5)

x5 = (2 t3, t4)

x6 = (t2, t6)
x7 = (6 t5, t6)

BASIC IDEA

- decomposition into subnets
- for each subnet: computation of (local) invariants
- **computation of interface invariants**
- calculation of system invariants
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*

FOR EACH CONTACT TRANSITION

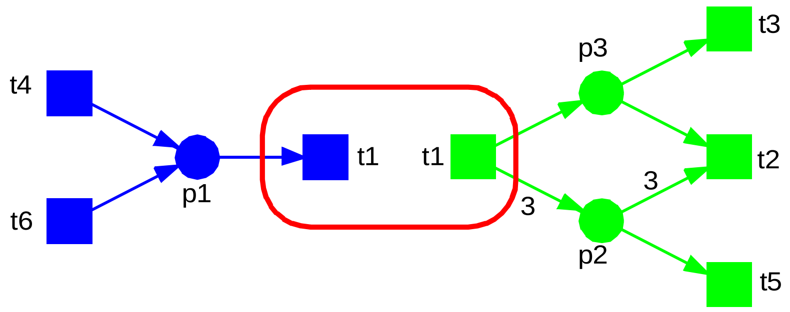
x1 = (t4, t1)
x2 = (t6, t1)

x3 = (t1, t2)
x4 = (t1, t3, 3 t5)

x5 = (2 t3, t4)

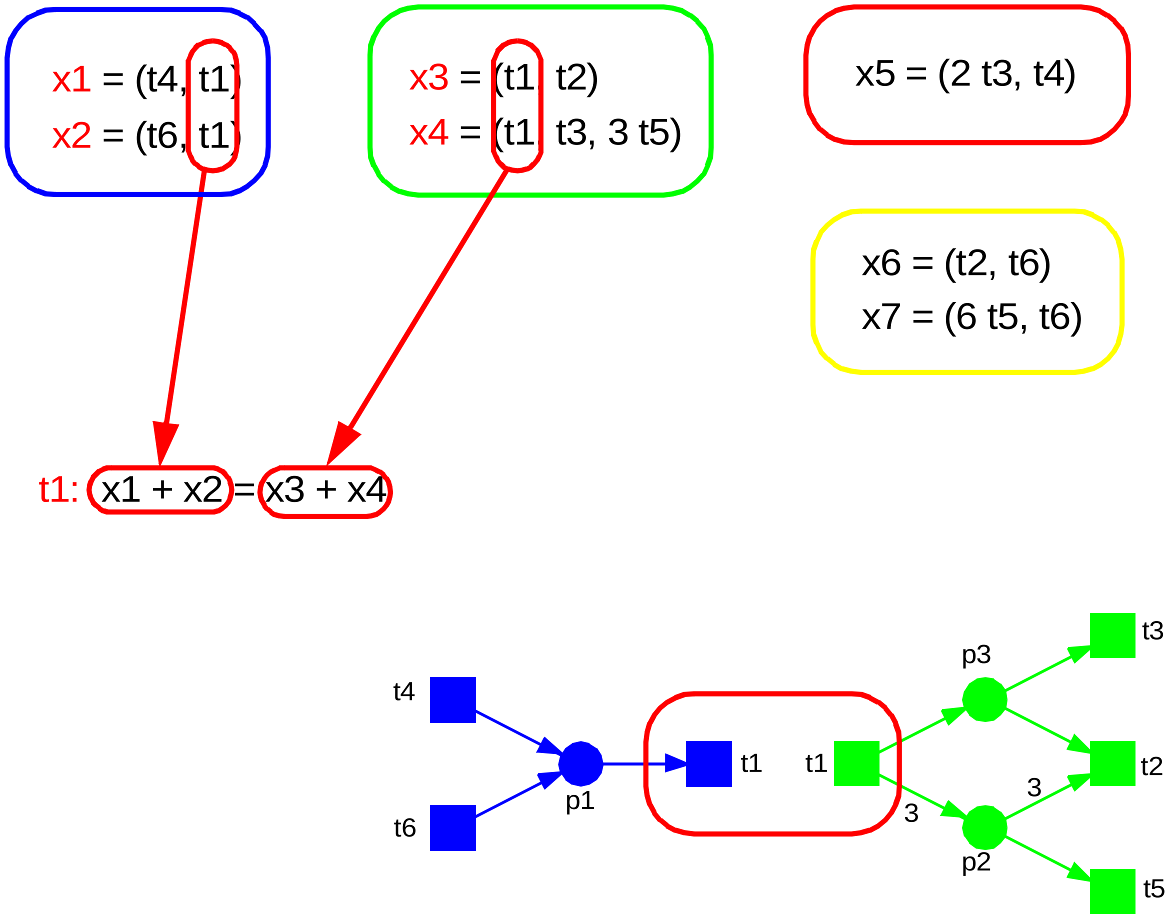
x6 = (t2, t6)
x7 = (6 t5, t6)

t1:



- decomposition into subnets
- for each subnet: computation of (local) invariants
- **computation of interface invariants**
- calculation of system invariants
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*

FOR EACH CONTACT TRANSITION



BASIC IDEA

- decomposition into subnets
- for each subnet: computation of (local) invariants
- computation of interface invariants
- calculation of system invariants
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*

FOR EACH CONTACT TRANSITION

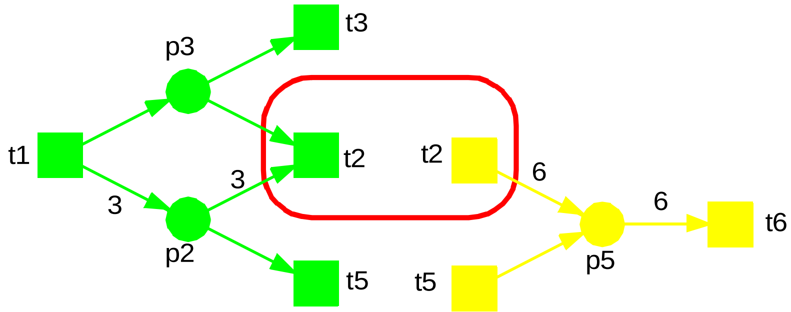
x1 = (t4, t1)
x2 = (t6, t1)

x3 = (t1, t2)
x4 = (t1, t3, 3 t5)

x5 = (2 t3, t4)

x6 = (t2, t6)
x7 = (6 t5, t6)

t1: x1 + x2 = x3 + x4
t2:



- **decomposition into subnets**
- **for each subnet: computation of (local) invariants**
- **computation of interface invariants**
- **calculation of system invariants**
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*

FOR EACH CONTACT TRANSITION

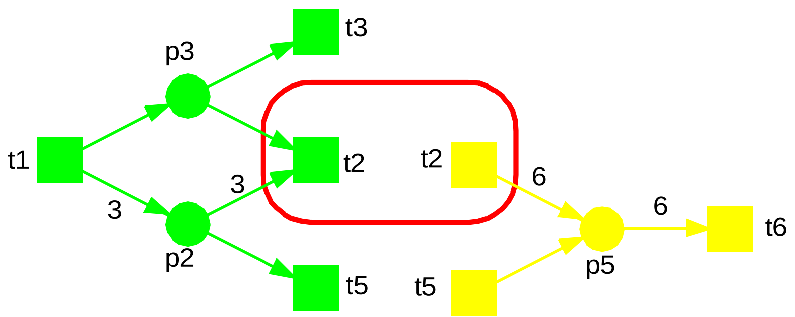
x1 = (t4, t1)
x2 = (t6, t1)

x3 = (t1, t2)
x4 = (t1, t3, 3 t5)

x5 = (2 t3, t4)

x6 = (t2, t6)
x7 = (6 t5, t6)

t1: x1 + x2 = x3 + x4
t2: x3 = x6



- **decomposition into subnets**
- **for each subnet: computation of (local) invariants**
- **computation of interface invariants**
- **calculation of system invariants**
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*

FOR EACH CONTACT TRANSITION

x1 = (t4, t1)
x2 = (t6, t1)

x3 = (t1, t2)
x4 = (t1, t3, 3 t5)

x5 = (2 t3, t4)

x6 = (t2, t6)
x7 = (6 t5, t6)

t1: x1 + x2 = x3 + x4
t2: x3 = x6
t3:
t4:
t5:
t6:

BASIC IDEA

- decomposition into subnets
- for each subnet: computation of (local) invariants
- computation of interface invariants
- calculation of system invariants
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*

FOR EACH CONTACT TRANSITION

x1 = (t4, t1)
x2 = (t6, t1)

x3 = (t1, t2)
x4 = (t1, t3, 3 t5)

x5 = (2 t3, t4)

x6 = (t2, t6)
x7 = (6 t5, t6)

t1: x1 + x2 = x3 + x4
t2: x3 = x6
t3: x4 = 2 x5
t4: x5 = x1
t5: 3 x4 = 6 x7
t6: x6 + x7 = x2

BASIC IDEA

- **decomposition into subnets**
- **for each subnet: computation of (local) invariants**

x1 = (t4, t1)
x2 = (t6, t1)

x3 = (t1, t2)
x4 = (t1, t3, 3 t5)

x5 = (2 t3, t4)

x6 = (t2, t6)
x7 = (6 t5, t6)

- **computation of interface invariants**
- **calculation of system invariants**
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*

t1: x1 + x2 = x3 + x4
t2: x3 = x6
t3: x4 = 2 x5
t4: x5 = x1
t5: 3 x4 = 6 x7
t6: x6 + x7 = x2

→

(x2, x3, x6)
(x1, x2, 2 x4, x5, x7)

BASIC IDEA

- **decomposition into subnets**
- **for each subnet: computation of (local) invariants**
- **computation of interface invariants**
- **calculation of system invariants**
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*

x1 = (t4, t1)
x2 = (t6, t1)

x3 = (t1, t2)
x4 = (t1, t3, 3 t5)

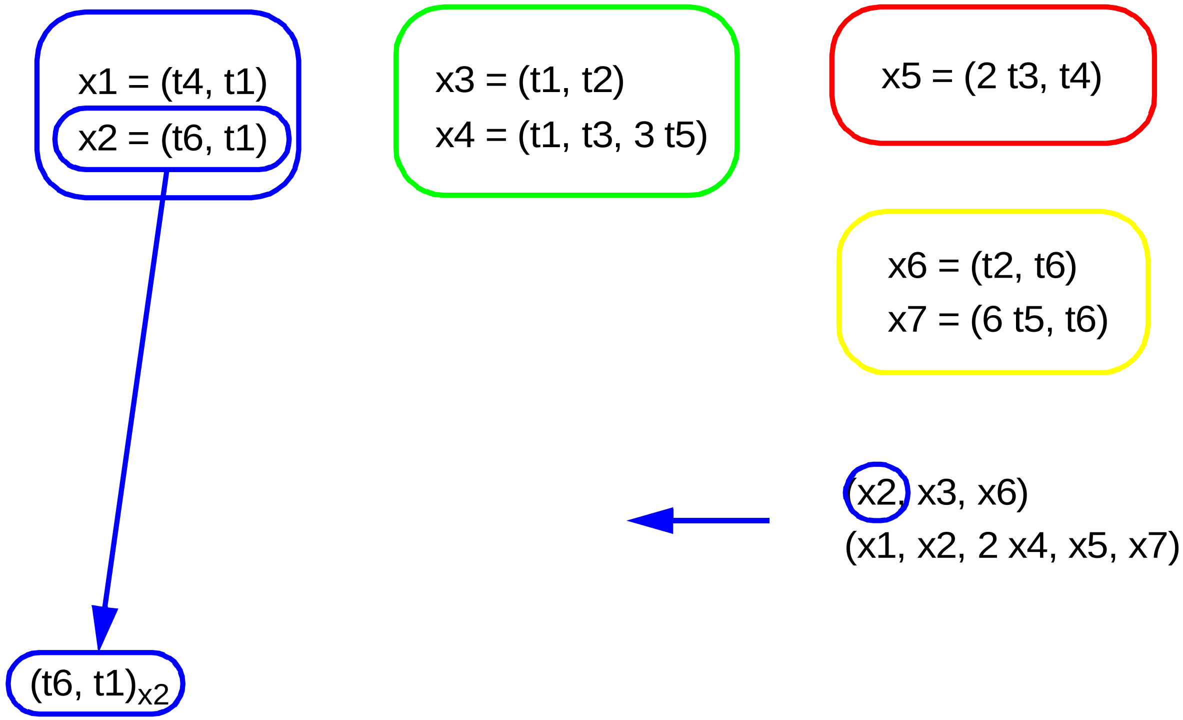
x5 = (2 t3, t4)

x6 = (t2, t6)
x7 = (6 t5, t6)

← (x2, x3, x6)
(x1, x2, 2 x4, x5, x7)

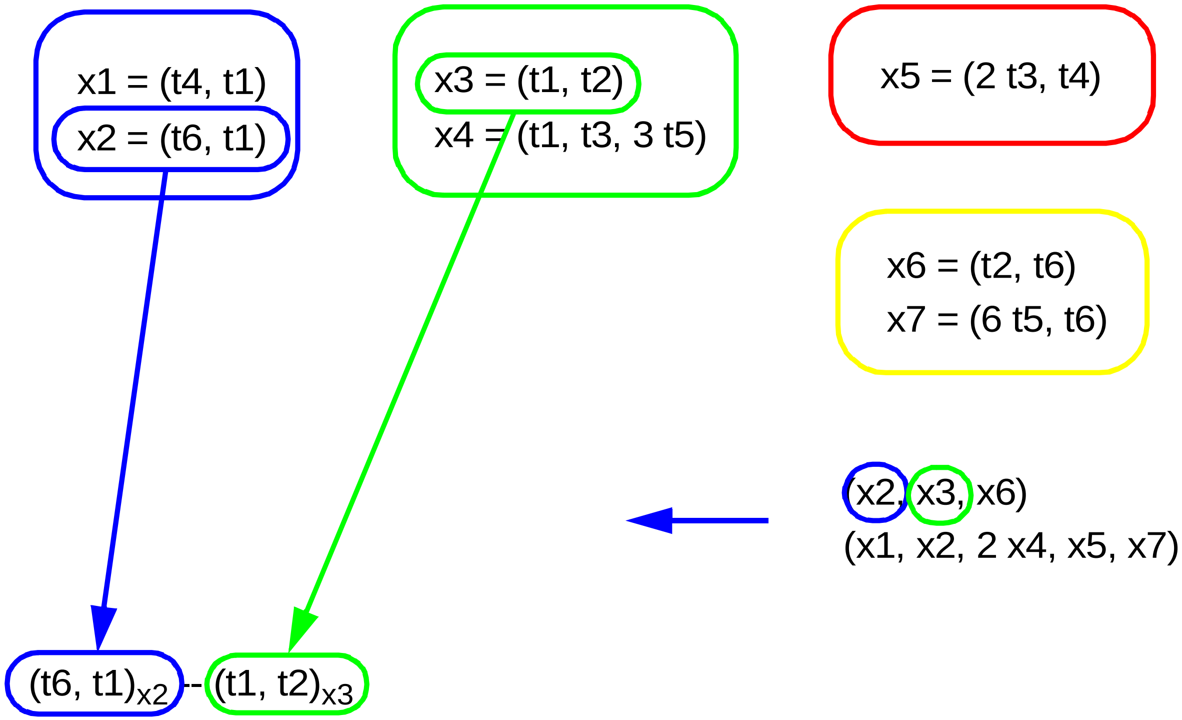
Basic Idea

- **decomposition into subnets**
- **for each subnet: computation of (local) invariants**
- **computation of interface invariants**
- **calculation of system invariants**
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*

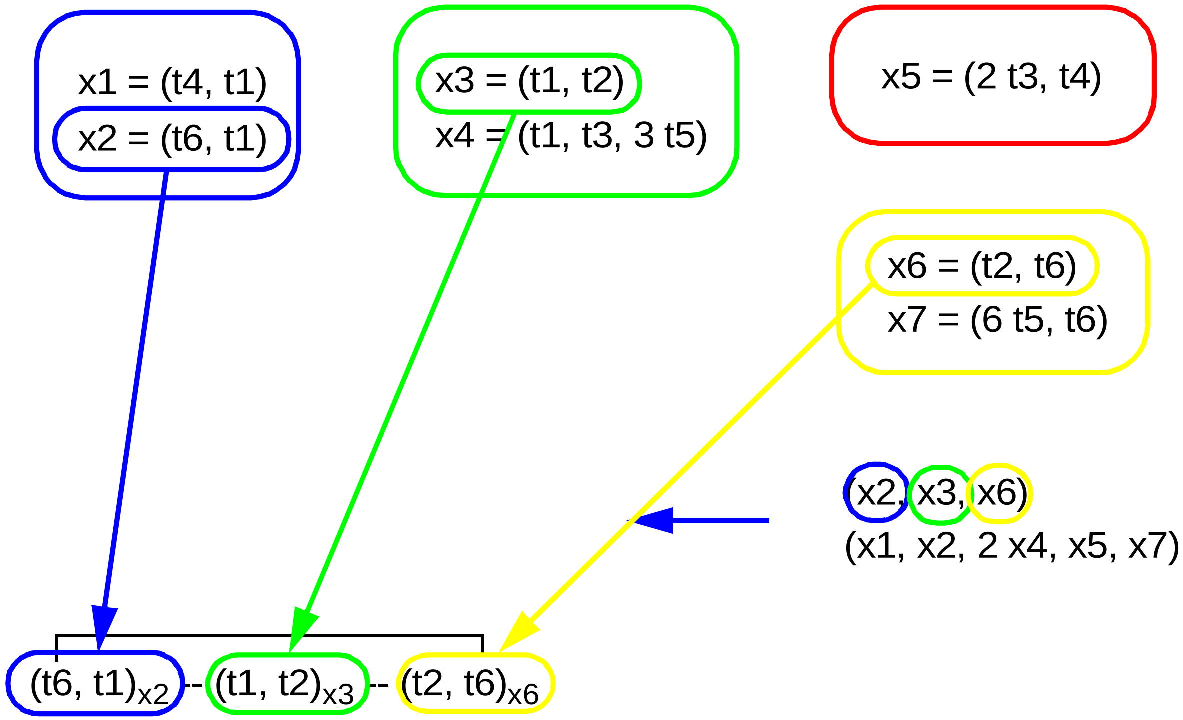


BASIC IDEA

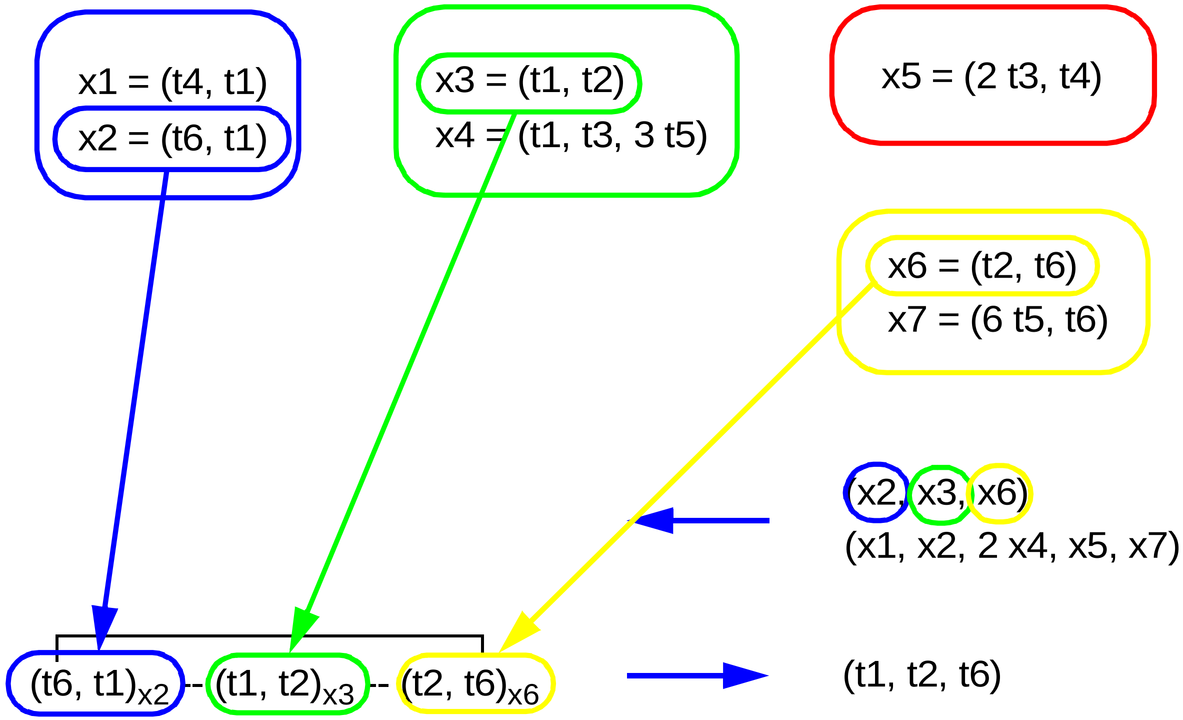
- decomposition into subnets
- for each subnet: computation of (local) invariants
- computation of interface invariants
- calculation of system invariants
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*



- **decomposition into subnets**
- **for each subnet: computation of (local) invariants**
- **computation of interface invariants**
- **calculation of system invariants**
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*



- **decomposition into subnets**
- **for each subnet: computation of (local) invariants**
- **computation of interface invariants**
- **calculation of system invariants**
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*



BASIC IDEA

- **decomposition into subnets**
- **for each subnet: computation of (local) invariants**
- **computation of interface invariants**
- **calculation of system invariants**
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*

x1 = (t4, t1)
x2 = (t6, t1)

x3 = (t1, t2)
x4 = (t1, t3, 3 t5)

x5 = (2 t3, t4)

x6 = (t2, t6)
x7 = (6 t5, t6)

(x2, x3, x6) ← $(t6, t1)_{x2}$ -- $(t1, t2)_{x3}$ -- $(t2, t6)_{x6}$ → (t1, t2, t6)

(x1, x2, 2 x4, x5, x7) ← $2\,(t1,\ t3,\ 3\,t5)_{x4}$ -- $(2\,t3, t4)_{x5}$ -- $(t4, t1)_{x1}$ / -- $(6\,t5, t6)_{x7}$ -- $(t6, t1)_{x2}$

- **decomposition into subnets**
- **for each subnet: computation of (local) invariants**

  $x1 = (t4, t1)$
  $x2 = (t6, t1)$

  $x3 = (t1, t2)$
  $x4 = (t1, t3, 3\ t5)$

  $x5 = (2\ t3, t4)$

  $x6 = (t2, t6)$
  $x7 = (6\ t5, t6)$

- **computation of interface invariants**

  (x2, x3, x6) ←
  (x1, x2, 2 x4, x5, x7)

- **calculation of system invariants**
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*

  $(t6, t1)_{x2} \text{ -- } (t1, t2)_{x3} \text{ -- } (t2, t6)_{x6}$ → (t1, t2, t6)

  $2 \begin{pmatrix} t1, & t3 \\ & 3\ t5 \end{pmatrix}_{x4} \begin{matrix} \text{-- } (2\ t3, t4)_{x5} \text{ -- } (t4, t1)_{x1} \\ \text{-- } (6\ t5, t6)_{x7} \text{ -- } (t6, t1)_{x2} \end{matrix}$ → (2 t1, 2 t3, t4, 6 t5, t6)

BASIC IDEA

- decomposition into subnets
- for each subnet: computation of (local) invariants
- computation of interface invariants
- calculation of system invariants
  - -> *by composition of subnet invariants*
  - -> *guided by interface invariants*

x1 = (t4, t1)
x2 = (t6, t1)

x3 = (t1, t2)
x4 = (t1, t3, 3 t5)

x5 = (2 t3, t4)

x6 = (t2, t6)
x7 = (6 t5, t6)

(x2, x3, x6)
(x1, x2, 2 x4, x5, x7)

$(t6, t1)_{x2}$ -- $(t1, t2)_{x3}$ -- $(t2, t6)_{x6}$ → (t1, t2, t6)

$2\begin{pmatrix} t1, & t3 \\ & 3\ t5 \end{pmatrix}_{x4}$ -- $(2\ t3, t4)_{x5}$ -- $(t4, t1)_{x1}$ -- $(6\ t5, t6)_{x7}$ -- $(t6, t1)_{x2}$ → (2 t1, 2 t3, t4, 6 t5, t6)

(PRELIMINARY) SUMMARY

ASSUMPTION

- the solution of many small systems is less time/space consuming than the solution of a single larger one

MAJOR (KNOWN) DRAWBACK

- the computation of system invariants does not only produce minimal invariants

CASE STUDIES

- -> excel file

Lautenbach, K.:
Exact Liveness Conditions of a Petri Net Class (in German);
Berichte der GMD 82, Bonn 1973.

Pascoletti, K.-H.:
Diophantische Systeme und Lösungsmethoden zur Bestimmung aller Invarianten in Petri-Netzen;
Berichte der GMD 160, 1986.

Starke, P. H.:
Analyse von Petri-Netz-Modellen;
Teubner 1990.

Zaitsev, D.:
Functional Petri Nets;
Univ. Paris-Dauphine, LAMSADE, TR 224, 2005

Schuster, S.; Hilgetag, C.; Schuster, R.:
Determining Elementary Modes of Functioning in Biochemical Reaction Networks at Steady State.
Proc.Second Gauss Symposium (1993) pp. 101-114

Schilling, C. H.; Letscher, D.; Palsson, B. O.:
Theory for the Systemic Definition of Metabolic Pathways and their Use in Interpreting Metabolic Function from a Pathway-Oriented Perspective;
J. Theor. Biol. (2000) 203, pp. 229-248.

THANKS !

HTTP://WWW-DSSZ.INFORMATIK.TU-COTTBUS.DE