Reconstructing $\mathcal{X}'$-deterministic extended Petri nets from experimental time-series data $\mathcal{X}'$

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Outline

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1. Modeling in Biosciences

2. Petri Nets and Extensions

3. Reconstruction Approach
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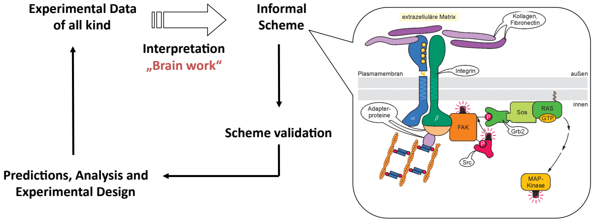
   - Output
   - Representation of the Observed Responses
   - Sequences and their Conflicts
   - Composition of $\mathcal{X}'$-Deterministic Extended Petri Nets

4. Concluding Remarks and Perspectives

Modeling and Model Validation in Biosciences

Molecular Networks:

Modeling and Model Validation in the Biosciences



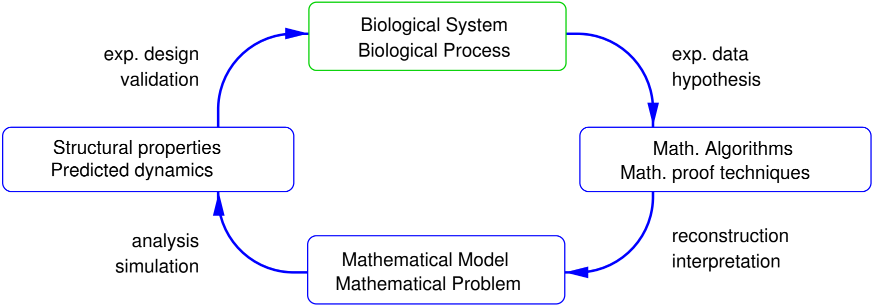
The classical lab approach:

Repeat until the model correctly predicts all experimental results.

Modeling and Model Validation in Biosciences

- **Biological models:** often “cartoon-like” informal schemes
- **Classical lab approaches:** heuristic and hypothesis-driven methods, yield potentially incomplete solution sets

Mathematical Models and Methods for Biological Systems



Mathematics for Biosciences

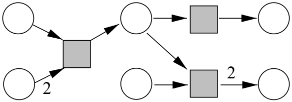
- **Mathematical models:**
  formal schemes representing structure and function of the studied system
- **Mathematical approaches:**
  data-driven methods, can guarantee completeness by mathematical proofs

Outline

Petri nets: The networks

Standard networks $\mathcal{P} = (P, T, A, w)$

- P set of involved **components** ("places" ◯), (molecules, receptors, genes)
- T set of involved **reactions** ("transitions" □), (reactions, activations,...)
- $A \subseteq (P \times T) \cup (T \times P)$ set of directed **links** ("arcs" $\rightarrow$),
- arc weights w as stoichiometric coefficients.



Standard network

Extended networks $\mathcal{P} = (P, T, (A \cup A_R \cup A_I), w)$

- $A_R \subset P \times T$ **read-arcs**
- $A_I \subset P \times T$ **inhibitor-arcs**

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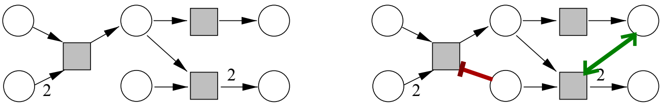

Standard network Extended network

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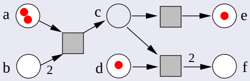
Petri nets: States and state changes

States

- Each place $p \in P$ can be marked with an integral number $\mathbf{x}_p$ of tokens.
- A **state** can be represented as a vector $\mathbf{x} \in \mathbb{N}^{|P|}$ with entries $\mathbf{x}_p$ for all $p \in P$.



$$x = \begin{pmatrix} 2 \\ 0 \\ 0 \\ 1 \\ 1 \\ 0 \end{pmatrix}$$

- If a capacity function $\text{cap} : P \to \mathbb{N}$ is given, $x_p \leq \text{cap}(p) \quad \forall p \in P$.

Switching transitions

- In a **standard** network, $t \in T$ is **enabled** at a state $\mathbf{x}$ if

  $\mathbf{x}_p \geq w(p, t)$ for all p with $(p, t) \in A$, and,
  $\mathbf{x}_p + w(t, p) \leq \text{cap}(p)$ for all p with $(t, p) \in A$.

- In an **extended** network, $t \in T$ is **enabled** at a state $\mathbf{x}$ if in addition

  $\mathbf{x}_p \geq w(p, t)$ for all p with $(p, t) \in A_R$, and,
  $\mathbf{x}_p < w(p, t)$ for all p with $(p, t) \in A_I$.

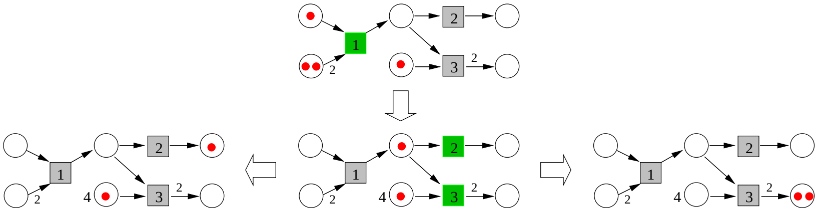
Dynamic processes and reachability

Dynamic processes

Dynamic processes correspond to sequences of system states, obtained by sequences of transition switches.

Starting from an initial state $\mathbf{x}^0$, explore the **dynamic behavior** of the system by

- consecutively switching enabled transitions,
- analyzing the reachability of certain system states.



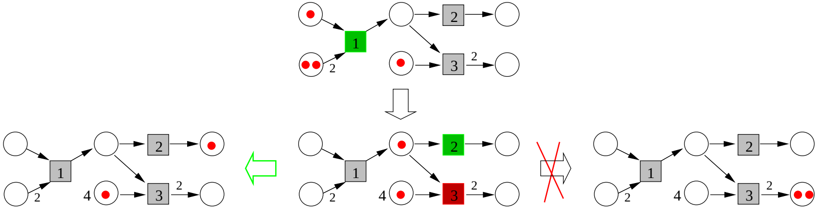
Prediction of the dynamic behavior

Priority relations for transitions

Let G be a network and $\mathcal{O}$ a **priority relation** on its transitions.

- If there are two or more transitions enabled at a state, this transition with **highest priority** will be switched.
- This allows to **predict the dynamic behavior** of the system (instead of listing all potentially possible switching sequences).

Example. Consider the network G with $\mathcal{O} = \{t_2 > t_3\}$.



Outline

AIM:

Reconstruction of **all** extended Petri nets with priorities that reproduce the experimental observations $\mathcal{X}'$ in a simulation, called

$\mathcal{X}'$-deterministic extended Petri nets

Our approach is based on previous works on reconstructing

- **standard networks**
  (Marwan, Wagler, Weismantel 2008; Durzinsky, Wagler, Weismantel 2008, 2011)
- **standard networks with priorities**
  (Marwan, Wagler, Weismantel, 2008; Torres, Wagler 2011)
- **extended Petri nets**
  (Durzinsky, Marwan, Wagler 2011 and 2013)

Outline

The Input

The input $(P, \mathcal{I}_P, \mathcal{X}')$

- a set P of components
- the set $\mathcal{I}_P$ of all known P-invariants (*i.e.* sets $P' \subseteq P$ of components such that the sum of the number of all tokens on all the places in P' is constant).
- time-series data $\mathcal{X}' = \{\mathcal{X}'(\mathbf{x}^1, \mathbf{x}^k) : \mathbf{x}^1 \in \mathcal{X}'_{ini}, \mathbf{x}^k \in \mathcal{X}'_{term}\}$ with
  - initial states $\mathcal{X}'_{ini} \subseteq \mathcal{X}'$, terminal states $\mathcal{X}'_{term} \subseteq \mathcal{X}'$
  - time series $\mathcal{X}'(\mathbf{x}^1, \mathbf{x}^k) = (\mathbf{x}^0; \mathbf{x}^1, \ldots, \mathbf{x}^j, \ldots, \mathbf{x}^k)$

Properties of $\mathcal{X}'$ (Durzinsky, Wagler, Weismantel 2008)

- reproducibility: for each $\mathbf{x}^j \in \mathcal{X}'$ there is a unique observed successor state $\mathrm{succ}_{\mathcal{X}'}(\mathbf{x}^j) = \mathbf{x}^{j+1} \in \mathcal{X}'$.
- monotonicity: for each pair $(\mathbf{x}^j, \mathbf{x}^{j+1}) \in \mathcal{X}'$, the possible intermediate states $\mathbf{x}^j = \mathbf{y}^1, \mathbf{y}^2, ..., \mathbf{y}^{m+1} = \mathbf{x}^{j+1}$ satisfy
  $$y_p^1 \leq y_p^2 \leq \ldots \leq y_p^m \leq y_p^{m+1} \text{ for all } p \in P \text{ with } x_p^j \leq x_p^{j+1} \text{ and}$$
  $$y_p^1 \geq y_p^2 \geq \ldots \geq y_p^m \geq y_p^{m+1} \text{ for all } p \in P \text{ with } x_p^j \geq x_p^{j+1}.$$

Input data

The running example: experimental biologic data

Experimental biologic data from the *light-induced sporulation of Physarum polycephalum* (C. Starostzik and W. Marwan, 1995):

$$
\begin{aligned}
P &= \{FR, R, P_{FR}, P_R, Spo\} & \mathcal{I}_P &= \{P_{FR}, P_R\}\\
\mathcal{X}'(\mathbf{x}^1,\mathbf{x}^3) &= (\mathbf{x}^0;\ \mathbf{x}^1,\mathbf{x}^2,\mathbf{x}^3) & \mathcal{X}'_{ini} &= \{\mathbf{x}^1,\mathbf{x}^4\}\\
\mathcal{X}'(\mathbf{x}^4,\mathbf{x}^0) &= (\mathbf{x}^2;\ \mathbf{x}^4,\mathbf{x}^0) & \mathcal{X}'_{term} &= \{\mathbf{x}^3,\mathbf{x}^0\}
\end{aligned}
$$

$$
\overset{x}{\begin{pmatrix} x_{FR} \\ x_R \\ x_{P_{FR}} \\ x_{P_R} \\ x_{Spo} \end{pmatrix}}
$$

$$
\begin{tikzcd}
 & \overset{x^1}{\begin{pmatrix}1\\0\\1\\0\\0\end{pmatrix}} \arrow[dr, "d^1"] & & \\
\overset{x^0}{\begin{pmatrix}0\\0\\1\\0\\0\end{pmatrix}} \arrow[ur, dashed, "FR"] & & \overset{x^2}{\begin{pmatrix}0\\0\\0\\1\\0\end{pmatrix}} \arrow[r, "d^2"] \arrow[dl, dashed, "R"] & \overset{x^3}{\begin{pmatrix}0\\0\\0\\1\\1\end{pmatrix}} \\
 & \underset{x^4}{\begin{pmatrix}0\\1\\0\\1\\0\end{pmatrix}} \arrow[ul, "d^4"] & &
\end{tikzcd}
$$

Outline

The output

The set of **all** $\mathcal{X}'$-deterministic extended Petri nets $(\mathcal{P}, \text{cap}, \mathcal{O})$ with

- $\mathcal{P} = (P, T, \mathcal{A}, w)$ extended Petri nets on the given set P of places, represented by its incidence matrix $M(\mathcal{P}) \in \mathbb{Z}^{|P|\times|T|}$ having the update vectors $\mathbf{r}^t$ as columns

$$r_p^t = M(\mathcal{P})_{pt} := \begin{cases} -w(p,t) & \text{if } (p,t) \in A, \\ +w(t,p) & \text{if } (t,p) \in A, \\ 0 & \text{otherwise.} \end{cases}$$

  and its control-arcs $A_R \cup A_I$
- the same capacities cap deduced from $\mathcal{X}'$
- a priority relation $\mathcal{O}$ forcing $\mathcal{X}'$-determinism (*i.e.* to show the in $\mathcal{X}'$ experimental observed behavior in a simulation).

Outline

Extraction of difference vectors

Extraction of difference vectors

Observed changes of states from the experimental data:

$$\mathcal{D} := \left\{ \mathbf{d}^j = \mathbf{x}^{j+1} - \mathbf{x}^j \ : \ \mathbf{x}^{j+1} = \mathrm{succ}_{\mathcal{X}'}(\mathbf{x}^j) \in \mathcal{X}' \right\}.$$

$$
\begin{array}{c} x \\ \begin{pmatrix} x_{FR} \\ x_R \\ x_{P_{FR}} \\ x_{P_R} \\ x_{Spo} \end{pmatrix} \end{array}
\qquad
\begin{tikzcd}
 & \begin{array}{c} x^1 \\ \begin{pmatrix} 1 \\ 0 \\ 1 \\ 0 \\ 0 \end{pmatrix} \end{array} \arrow[dr, "d^1"] & & \\
\begin{array}{c} x^0 \\ \begin{pmatrix} 0 \\ 0 \\ 1 \\ 0 \\ 0 \end{pmatrix} \end{array} \arrow[ur, dashed, "\mathrm{FR}"] & & \begin{array}{c} x^2 \\ \begin{pmatrix} 0 \\ 0 \\ 0 \\ 1 \\ 0 \end{pmatrix} \end{array} \arrow[r, "d^2"] \arrow[dl, dashed, "\mathrm{R}"] & \begin{array}{c} x^3 \\ \begin{pmatrix} 0 \\ 0 \\ 0 \\ 1 \\ 1 \end{pmatrix} \end{array} \\
 & \begin{array}{c} \begin{pmatrix} 0 \\ 1 \\ 0 \\ 1 \\ 0 \end{pmatrix} \\ x^4 \end{array} \arrow[ul, "d^4"] & &
\end{tikzcd}
$$

Extraction of difference vectors yields $\mathcal{D} = \{d^1, d^2, d^4\}$ with

$\mathbf{d}^1 = \mathbf{x}^2 - \mathbf{x}^1 = (-1, 0, -1, 1, 0)^T$, $\mathbf{d}^2 = \mathbf{x}^3 - \mathbf{x}^2 = (0, 0, 0, 0, 1)^T$ and
$\mathbf{d}^4 = \mathbf{x}^0 - \mathbf{x}^4 = (0, -1, 1, -1, 0)^T$.

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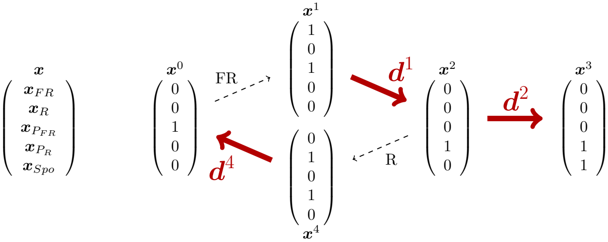

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Which update vectors are suitable ?

Which update vectors are suitable ?

- $\mathbf{x}^j, \mathbf{x}^{j+1} \in \mathcal{X}'$ are not necessarily consecutive system states
- no oscillation in intermediate states between $\mathbf{x}^j$ and $\mathbf{x}^{j+1}$ (monotonicity).

Theorem (Durzinsky, Wagler, Weismantel 2008)

It suffice to consider sign-compatible update vectors from

$$\mathrm{Box}(\mathbf{d}^j) = \left\{ \mathbf{r} \in \mathbb{Z}^{|P|} : \begin{array}{rl} 0 \le r_p \le d_p^j & \text{if } d_p^j > 0 \\ d_p^j \le r_p \le 0 & \text{if } d_p^j < 0 \\ r_p = 0 & \text{if } d_p^j = 0 \\ \sum_{p \in P'} r_p = 0 & \forall P' \in \mathcal{I}_P \end{array} \right\} \setminus \{\mathbf{0}\}.$$

Example:
For $\mathbf{d}^1 = (-1, 0, -1, 1, 0)^T$,
we have

$$\mathrm{Box}(\boldsymbol{d}^1) = \left\{ \underset{\boldsymbol{d}^1}{\begin{pmatrix} -1 \\ 0 \\ -1 \\ 1 \\ 0 \end{pmatrix}}, \underset{\boldsymbol{r}^1}{\begin{pmatrix} -1 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}}, \underset{\boldsymbol{r}^2}{\begin{pmatrix} 0 \\ 0 \\ -1 \\ 1 \\ 0 \end{pmatrix}} \right\}$$

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$$\mathrm{Box}(\boldsymbol{d}^1) = \left\{ \begin{array}{ccccc} \begin{pmatrix} -1 \\ 0 \\ -1 \\ 1 \\ 0 \end{pmatrix} & , & \begin{pmatrix} -1 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} & , & \begin{pmatrix} 0 \\ 0 \\ -1 \\ 1 \\ 0 \end{pmatrix} \\ \\ \boldsymbol{d}^1 & & \boldsymbol{r}^1 & & \boldsymbol{r}^2 \end{array} \right\}$$

Representation of difference vectors

Determine $\Lambda(\mathbf{d}^j)$ and $\mathcal{R}(\mathbf{d}^j, \lambda)$

- $\Lambda(\mathbf{d}^j)$ is the set of all intregral solutions of the equation system:

$$\mathbf{d}^j = \sum_{\mathbf{r}^t \in \text{ Box}(\mathbf{d}^j)} \lambda_t \mathbf{r}^t, \ \lambda_t \in \mathbb{Z}_+.$$

- For each $\boldsymbol{\lambda} \in \Lambda(\mathbf{d}^j)$, the set of update vectors used for this solution $\boldsymbol{\lambda}$ is

$$\mathcal{R}(\mathbf{d}^j, \boldsymbol{\lambda}) = \{r^t \in \text{Box}(\mathbf{d}^j) : \lambda_t \neq 0\}$$

Example: For $\mathbf{d}^1 = (-1, 0, -1, 1, 0)^T$, we have:

solution $\boldsymbol{\lambda}^1$: $\mathbf{d}^1 = \mathbf{d}^1$

solution $\boldsymbol{\lambda}^2$: $\mathbf{d}^1 = \mathbf{r}^1 + \mathbf{r}^2 = (-1, 0, 0, 0, 0)^T + (0, 0, -1, 1, 0)^T$

and accordingly $\mathcal{R}(\mathbf{d}^1, \boldsymbol{\lambda}^1) = \{\mathbf{d}^1\}$, $\mathcal{R}(\mathbf{d}^1, \boldsymbol{\lambda}^2) = \{\mathbf{r}^1, \mathbf{r}^2\}$.

Outline

Sequences

Sequences:

- Every permutation $\pi = (\mathbf{r}^{t_1}, \ldots, \mathbf{r}^{t_m})$ of the elements of a set $\mathcal{R}(\mathbf{d}^j, \boldsymbol{\lambda})$ yields a sequence of intermediate states $\mathbf{x}^j = \mathbf{y}^1, \mathbf{y}^2, ..., \mathbf{y}^m, \mathbf{y}^{m+1} = \mathbf{x}^{j+1}$ with

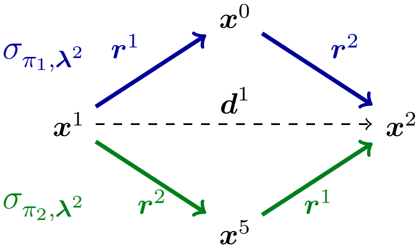
$$\sigma_{\pi,\boldsymbol{\lambda}}(\mathbf{x}^j, \mathbf{d}^j) = \left((\mathbf{y}^1, \mathbf{r}^{t_1}), (\mathbf{y}^2, \mathbf{r}^{t_2}), \ldots, (\mathbf{y}^m, \mathbf{r}^{t_m})\right).$$

- Every sequence σ respects monotonicity and induces a priority relation $\mathcal{O}_\sigma$.

Example: From $\mathcal{R}(\mathbf{d}^1, \boldsymbol{\lambda}^2) = \{\mathbf{r}^1, \mathbf{r}^2\}$, we obtain

$\sigma_{\pi_1,\boldsymbol{\lambda}^2}(\mathbf{x}^1, \mathbf{d}^1) = ((\mathbf{x}^1, \mathbf{r}^1), (\mathbf{x}^0, \mathbf{r}^2))$

with $\mathbf{r}^1 > \mathbf{r}^2$ and $\mathbf{r}^2 > \mathbf{0}$



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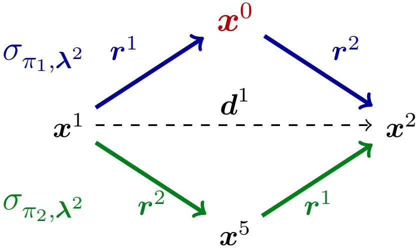

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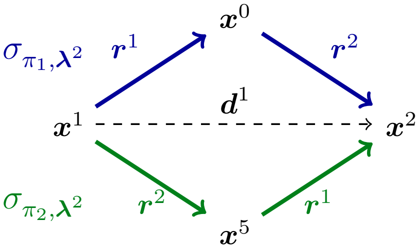
with $\mathbf{r}^1 > \mathbf{r}^2$ and $\mathbf{r}^2 > \mathbf{0}$

$\sigma_{\pi_2,\boldsymbol{\lambda}^2}(\mathbf{x}^1, \mathbf{d}^1) = ((\mathbf{x}^1, \mathbf{r}^2), (\mathbf{x}^5, \mathbf{r}^1))$

with $\mathbf{r}^2 > \mathbf{r}^1$

where $\mathbf{x}^5 = (1, 0, 0, 1, 0)^T$.



Priority conflicts

Sequences and their conflicts:

Sequences σ and σ' are in priority conflict if there are update vectors $\mathbf{r}^t \neq \mathbf{r}^{t'}$ and intermediate states $\mathbf{y}, \mathbf{y}'$ such that t, t' are enabled at $\mathbf{y}, \mathbf{y}'$ but $(\mathbf{y}, \mathbf{r}^t) \in \sigma$ and $(\mathbf{y}', \mathbf{r}^{t'}) \in \sigma'$ (since this implies $t > t'$ in $\mathcal{O}_\sigma$ but $t' > t$ in $\mathcal{O}_{\sigma'}$).

weak priority conflict (WPC):

- if $\mathbf{y} \neq \mathbf{y}'$
- **can** be resolved by adding appropriate control-arcs

strong priority conflict (SPC):

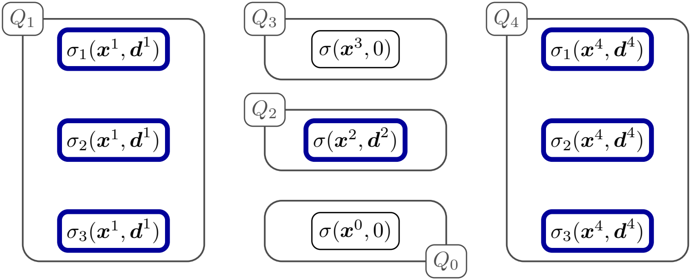
- if $\mathbf{y} = \mathbf{y}'$
- **cannot** be resolved by adding appropriate control-arcs

Note: we have a SPC between the trivial sequence $\sigma(\mathbf{x}^k, \mathbf{0})$ for any terminal state $\mathbf{x}^k \in \mathcal{X}'_{term}$ and any sequence σ containing $\mathbf{x}^k$ as intermediate state.

Example: $\sigma_{\pi_1, \boldsymbol{\lambda}^2}(\mathbf{x}^1, \mathbf{d}^1) = ((\mathbf{x}^1, \mathbf{r}^1), (\mathbf{x}^0, \mathbf{r}^2))$ and $\sigma(\mathbf{x}^0, \mathbf{0})$ are in SPC.

Priority conflict graph $\mathcal{G} = (V_D \cup V_\tau, E_D \cup E_W \cup E_S)$:

- the nodes correspond to sequences
  - V_D: the sequence $\sigma_{\pi,\boldsymbol{\lambda}}(\mathbf{x}^j, \mathbf{d}^j)$ $\forall \boldsymbol{\lambda} \in \Lambda(\mathbf{d}^j)$ and $\forall \pi$ permutations of $\mathcal{R}(\mathbf{d}^j, \boldsymbol{\lambda})$.
  - V_{term}: the trivial sequence $\sigma(\mathbf{x}^k, \mathbf{0})$, $\forall \mathbf{x}^k \in \mathcal{X}'_{term}$.
- the edges to priority conflicts:
  - E_D: all SPC between two sequences σ, σ' from the same difference vector.
  - E_S: all SPC between sequences σ, σ' from distinct difference vectors.
  - E_W: all WPC between sequences σ, σ' from distinct difference vectors.



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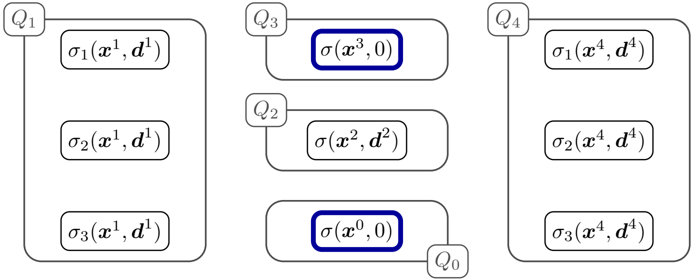
  - E_W: all WPC between sequences σ, σ' from distinct difference vectors.



Priority conflict graph $\mathcal{G} = (V_D \cup V_\tau, E_D \cup E_W \cup E_S)$:

- the nodes correspond to sequences
  - V_D: the sequence $\sigma_{\pi,\boldsymbol{\lambda}}(\mathbf{x}^j, \mathbf{d}^j)$ $\forall \boldsymbol{\lambda} \in \Lambda(\mathbf{d}^j)$ and $\forall \pi$ permutations of $\mathcal{R}(\mathbf{d}^j, \boldsymbol{\lambda})$.
  - V_{term}: the trivial sequence $\sigma(\mathbf{x}^k, \mathbf{0})$, $\forall \mathbf{x}^k \in \mathcal{X}'_{term}$.
- the edges to priority conflicts:
  - E_D: all SPC between two sequences σ, σ' from the same difference vector.
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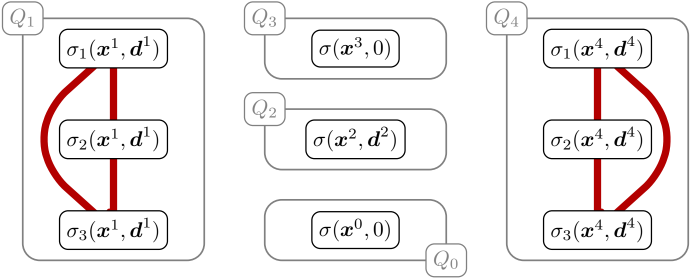

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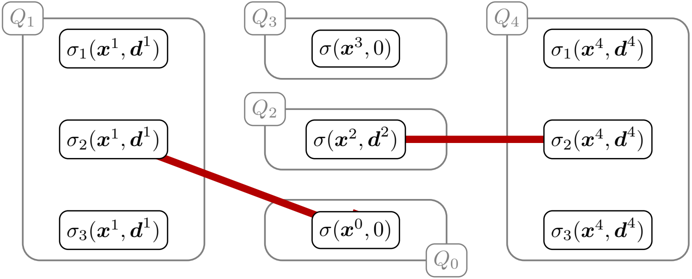

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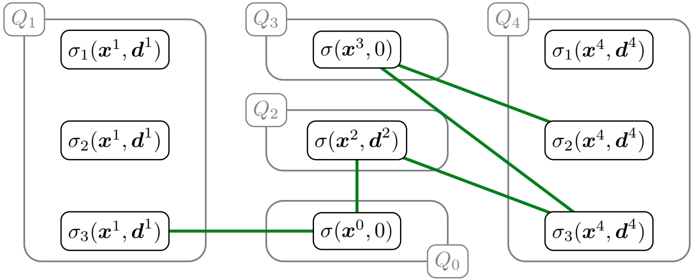

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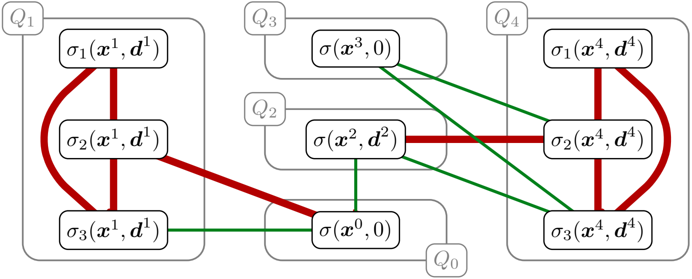


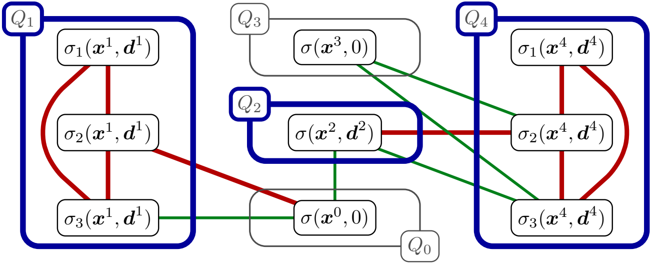
Selection of suitable sequences

We have to select

- a set S containning exactly one sequence $\sigma \in V_D$ for each $\mathbf{d}^j \in \mathcal{D}$
- all nodes from V_{term}

such that no SPCs occur in $S \cup V_{term}$.

Example:



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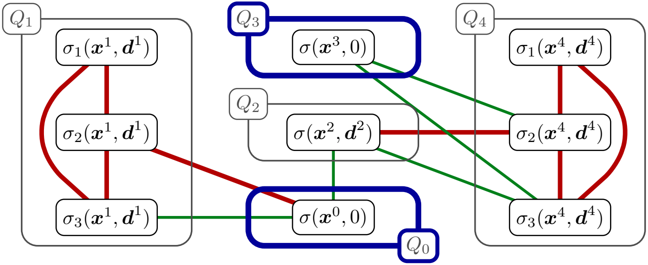

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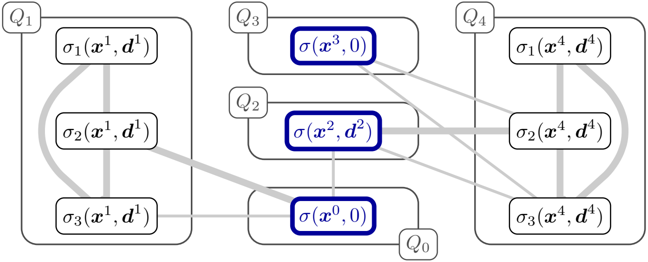

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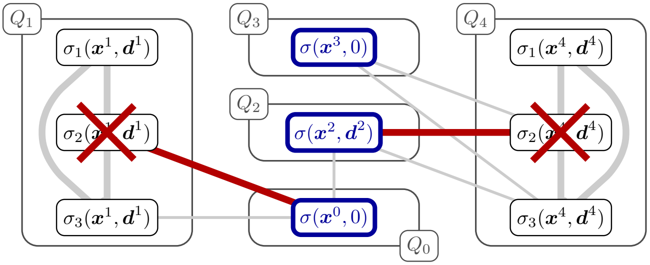

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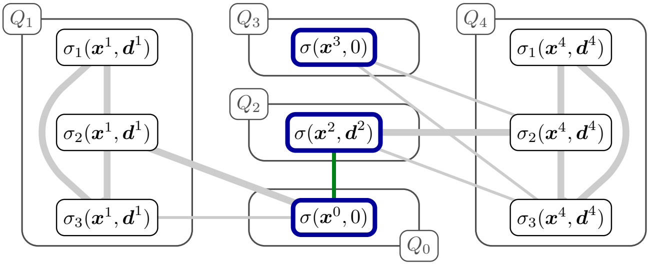

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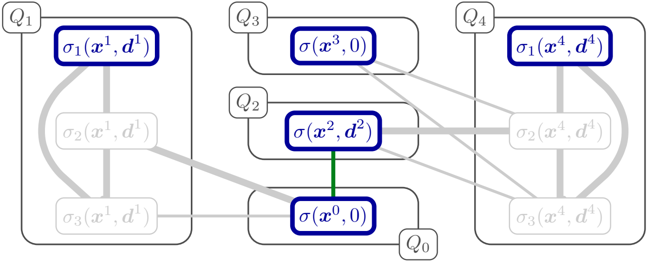
Example: $\mathcal{G}$ contains the following 4 feasible sets $S_i \cup V_{term}$



$S_1 = \{\sigma_1(\mathbf{x}^1, \mathbf{d}^1), \sigma(\mathbf{x}^2, \mathbf{d}^2), \sigma_1(\mathbf{x}^4, \mathbf{d}^4)\}$, $S_3 = \{\sigma_1(\mathbf{x}^1, \mathbf{d}^1), \sigma(\mathbf{x}^2, \mathbf{d}^2), \sigma_3(\mathbf{x}^4, \mathbf{d}^4)\}$,

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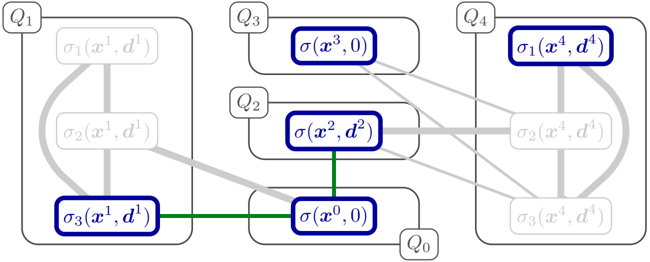

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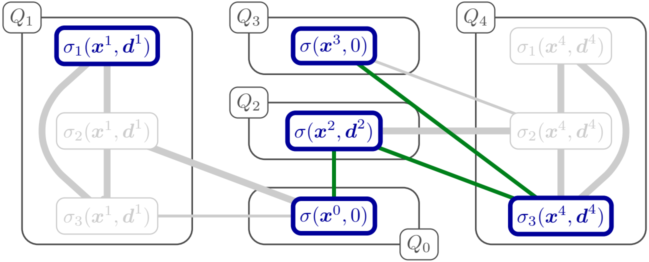

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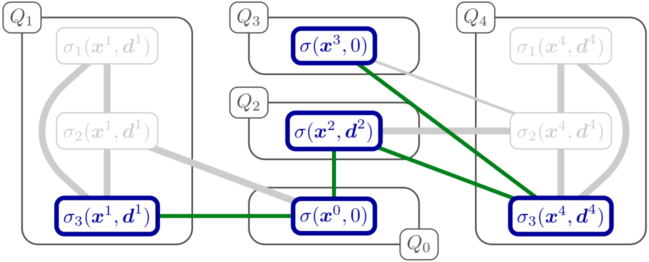

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Outline

1. Modeling in Biosciences
2. Petri Nets and Extensions
3. Reconstruction Approach
    - Input
    - Output
    - Representation of the Observed Responses
    - Sequences and their Conflicts
    - Composition of $\mathcal{X}'$-Deterministic Extended Petri Nets
4. Concluding Remarks and Perspectives

Standard networks with weak priority conflicts

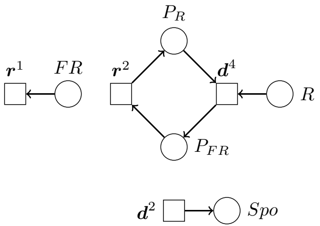
Composition of standard networks

For every selected set $S \cup V_{term}$, we obtain the incidence matrix of a standard network by taking the union of all update vectors in the sets $\mathcal{R}(\mathbf{d}^j, \boldsymbol{\lambda})$ of the sequences $\sigma \in S$.

Example: For solution S_2

Note that there are WPCs:

- between $\sigma(\mathbf{x}^2, \mathbf{d}^2)$ and $\sigma(\mathbf{x}^0, \mathbf{0})$ due to $\mathbf{d}^2, 0 \in T(\mathbf{x}^2) \cap T(\mathbf{x}^0)$ and
- between $\sigma_3(\mathbf{x}^1, \mathbf{d}^1)$ and $\sigma(\mathbf{x}^0, \mathbf{0})$ due to $\mathbf{r}^2, \mathbf{0} \in T(\mathbf{x}^1) \cap T(\mathbf{x}^0)$.



Resolving WPCs by inserting control-arcs

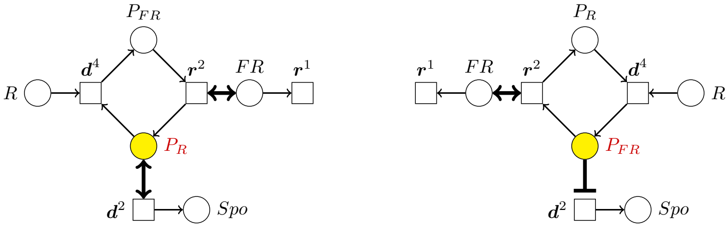
A WPC due to $(\mathbf{y}, \mathbf{r}^t) \in \sigma$ and $(\mathbf{y}', \mathbf{r}^{t'}) \in \sigma'$ can be resolved by

- disabling t at $\mathbf{y}'$ or t' at $\mathbf{y}$ if $\mathbf{y}, \mathbf{y}' \notin \mathcal{X}'_{term}$
- disabling t at $\mathbf{y}'$ if $\mathbf{y}' \in \mathcal{X}'_{term}$

To disable t at $\mathbf{y}'$, insert

- a read-arc (p, t) with weight $w(p, t) > \mathbf{y}'_p$ for some p with $\mathbf{y}_p > \mathbf{y}'_p$ or
- an inhibitor-arc (p, t) with weight $w(p, t) < \mathbf{y}_p$ for some p with $y_p < \mathbf{y}'_p$.

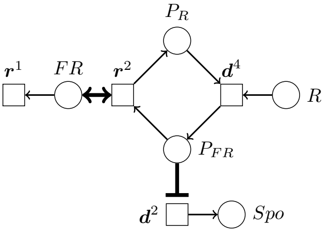
Example: For solution S_2, we resolve the WPC between $\sigma(\mathbf{x}^2, \mathbf{d}^2)$ and $\sigma(\mathbf{x}^0, \mathbf{0})$.

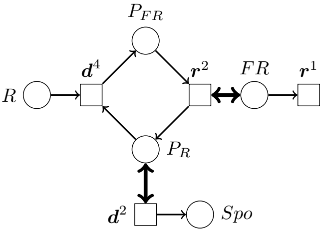


Determining priority relations

Deduce priority relations among so-obtained **transitions** for all selected sequences.

Example:





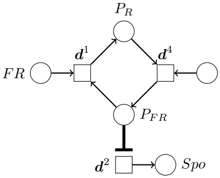
$\mathcal{O}_{S_2,P'} = \{(\mathbf{r}^2 > \mathbf{r}^1)\}$ $\qquad$ $\mathcal{O}_{S_2,P'} = \{(\mathbf{r}^2 > \mathbf{r}^1)\}$

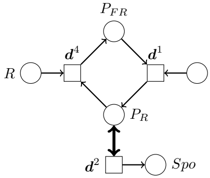
Solution set

Applying this procedure to all feasible sets $S \cup V_{term}$ yields the complete list of **all** $\mathcal{X}'$-deterministic extended Petri nets !

Applying this procedure to all feasible sets $S \cup V_{term}$ yields the complete list of all 12 $\mathcal{X}'$-deterministic extended Petri nets for the running example.

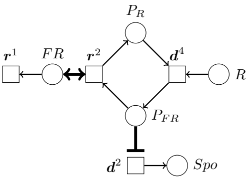
S_1

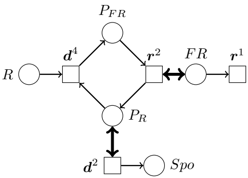




$\mathcal{O}_{S_1,P'} = \emptyset$ $\qquad$ $\mathcal{O}_{S_1,P'} = \emptyset$

S_2

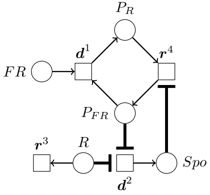




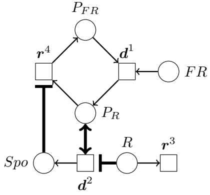
$\mathcal{O}_{S_2,P'} = \{(\mathbf{r}^2 > \mathbf{r}^1)\}$ $\qquad$ $\mathcal{O}_{S_2,P'} = \{(\mathbf{r}^2 > \mathbf{r}^1)\}$

Solution set: Running example

S_3



$$\mathcal{O}_{S_3,P'} = \{(\mathbf{r}^4 > \mathbf{r}^3)\}$$



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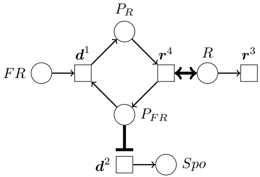

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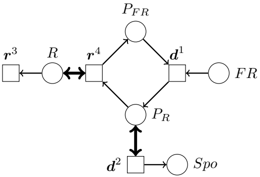

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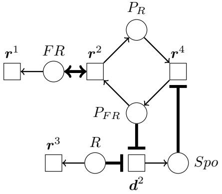
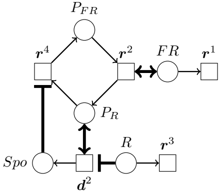
S_4



$$\mathcal{O}_{S_4,P'} = \{(\mathbf{r}^2 > \mathbf{r}^1), (\mathbf{r}^4 > \mathbf{r}^3)\}$$



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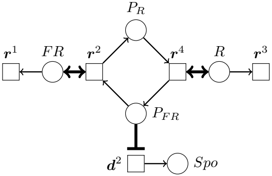

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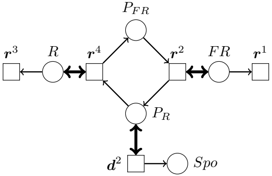

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Outline

Concluding remarks and perspectives

Achieved goals

We proposed an **integrative reconstruction method** to generate **all** possible $\mathcal{X}'$*-deterministic extended Petri nets* from experimental time-series data $\mathcal{X}'$ by:

- representing the observed difference vectors $\mathbf{d}^j$ as in the case of extended networks with priorities (Durzinsky, Marwan, Wagler 2011 and 2013),
- distinguishing weak and strong priority conflicts in the construction of the priority conflict graph,
- resolving weak priority conflicts by inserting control-arcs and determining priorities on the so-obtained transitions.

Perspectives

- Identify groups of WPCs that can be resolved by the same control-arc (definition of a priority conflict **hyper**graph).
- Make the new approach accessible by a suitable implementation.
- Apply the approach to new biological experimental data.

THANK YOU

Marie Favre's work was founded by the French National Research Agency, the European Commission (Feder funds) and the Région Auvergne in the Framework of the LabEx IMobS^3.