Models and Languages for Computational Systems Biology – Lecture 14
Structural Analysis of Petri Nets

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Outline

Quick recap

Structural properties and qualitative behaviour

Small example

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Formal definition of a Petri net

A Petri net is a quadruple $\mathcal{N} = (P, T, f, m_0)$, where

- $P$ and $T$ are finite, non-empty and disjoint sets. $P$ is the set of places and $T$ is the set of transitions.
- $f$, sometimes called the flow relation, is a function $f : ((P \times T) \cup (T \times P)) \rightarrow \mathbb{N}_0$ which defines the set of directed arcs, weighted by nonnegative integer values.
- $m_0 : P \rightarrow \mathbb{N}_0$ is the initial marking.
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The state of the system at any time, is characterised by the distribution of tokens over the places, generally termed a marking: $m : P \rightarrow \mathbb{N}_0$, where $m(p) = n$ means that there are $n$ tokens on place $p$. 
Notation for structural analysis

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$$\bullet x = \{ y \in P \cup T \mid f(y, x) \neq 0 \}$$
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The \textit{preset} of a node $x \in P \cup T$ is defined as

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The \textit{postset} of a node $x \in P \cup T$ is defined as

$$x\cdot = \{ y \in P \cup T \mid f(x, y) \neq 0 \}$$
The firing rule

Let $\mathcal{N} = (P, T, f, m_0)$ be a Petri net.

- A transition $t$ is **enabled** in a marking $m$, written as $m[t]$, if $\forall p \in \bullet t : m(p) \geq f(p, t)$; otherwise $t$ is **disabled**.

- A transition which is enabled in $m$ may **fire**.

- When $t$ in $m$ fires, a new marking $m'$ is reach, written as $m[t]m'$, where $\forall p \in P : m'(p) = m(p) - f(p, t) + f(t, p)$.

- The firing happens **atomically and instantaneously**.
Incidence matrix

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More formally, the incidence matrix $C : P \times T \rightarrow \mathbb{Z}$, indexed by $P$ and $T$, where $C(p, t) = f(t, p) - f(p, t)$. 
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Note that the incidence matrix is independent of the state or marking of the system.
Let $\mathcal{N} = (P, T, f, m_0)$ be a Petri net.

The **reachability graph** of $\mathcal{N}$ is the graph $RG(\mathcal{N}) = (V_N, E_N)$, where

- $V_N = [m_0]$ is the set of nodes,
- $E_N = \{(m, t, m') \mid m, m' \in [m_0], t \in T$ such that $m[t]m'$ is the set of arcs.\}
Structural analysis of Petri nets

There are three key general behavioural properties which can be considered for Petri nets. These are:

**Boundedness:** A Petri net is bounded if each place is bounded; a place is bounded if the number of tokens in the place cannot grow without limit, i.e. it is bounded by some finite constant.

**Liveness:** A Petri net is live if each of its transitions is live; a transition is live if whenever it fires, it is always possible to progress to a state where this transition is enabled.

**Reversibility:** For every marking the net is always able to return to this marking; specifically the net can reinitialise itself.
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You will recall that we considered these are the level of the labelled transition system when we were discussing CSL model checking, but here we consider definition at the level of the Petri net.
Boundedness

A place $p$ is **k-bounded** (bounded for short) if there exists a positive integer $k$, which represents an upper bound for the number of tokens on this place in all reachable markings of the Petri net:

$$k \in \mathbb{N}_0 : \forall m \in [m_0] : m(p) \leq k$$

A Petri net is **k-bounded** if all its places are k-bounded.

A Petri net is **structurally bounded** if it is bounded for any initial marking.
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In biological terms boundedness means that there is no possibility of an unlimited increase of some species within the system.
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A Petri net is **live (strongly live)** if each transition is live.

In biological terms liveness means that all reactions in the system remain possible at some future time.
A Petri net is reversible if the initial marking can be reached again from each reachable marking, i.e. $\forall m \in [m_0] : m_0 \in [m]$. 
Reversibility

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In biological terms reversibility means that the behaviour of the system is recurrent.
Net Structure Classifications

- A Petri net is called a **State Machine (SM)** if
  \[ \forall t \in T : |\bullet t| = |t^\bullet| \leq 1, \text{ i.e. there are neither forward branching or backward branching transitions.} \]
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- A Petri net is called **Extended Free Choice (EFC)** if
  \[ \forall p, q \in P \text{ if } p\cdot \cap q\cdot \neq \emptyset \text{ then } \forall t \in q\cdot \cup p\cdot, f(q, t) = f(p, t), \text{ i.e. transitions in conflict have identical sets of pre-places and the same flow relation. Sometimes termed Equal Conflict (EC).} \]
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- A Petri net is called **Asymmetric Simple (AS)** if \( \forall p, q \in P : p^\cdot \cap q^\cdot = \emptyset \lor p^\cdot \subseteq q^\cdot \lor q^\cdot \subseteq p^\cdot \).
Invariant analysis

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While they are usually defined in terms of the incidence matrix, P-invariants and T-invariants do also have an intuitive meaning at the net level, and an interpretation in terms of the biology.
Place invariants

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A net is **covered by P-invariants** if every place belongs to a P-invariant.
A transition vector is a vector $y : T \to \mathbb{Z}$, indexed by $T$. 
Transition invariants

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A transition vector is called a \textbf{T-invariant} if it is a nontrivial nonnegative integer solution of the linear equation system \( C \cdot y = 0 \).

A net is \textbf{covered by T-invariants} if every transition belongs to a \( T \)-invariant.
Minimal invariants

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An invariant $w$ is called minimal if $\nexists z : \text{supp}(z) \subset \text{supp}(w)$, i.e. its support does not contain the support of any other invariant $z$, and the greatest common divisor of all nonzero entries of $w$ is 1.
Consequences of invariants

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Note the different directions of implication.

Covering with P-invariants is a sufficient condition for structural boundedness, whereas covering with T-invariants is a necessary condition for liveness of a bounded net.
Biological interpretations

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This interpretation makes P-invariants valuable as a model validation tool, as a biologist will generally have a good idea of which species in a model should be conserved through reactions and modifications and calculating P-invariants allows this to be checked.
**Biological interpretations**

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Moreover, if the system has a steady state behaviour (e.g. a metabolic network) then the T-invariant gives relative occurrence rates for the reactions involved.
Consider the following set of biochemical reactions:

\[ r_1 : 2A \xrightarrow{E} 2B \]
\[ r_2 : A \rightarrow B \]
\[ r_3 : B \rightarrow A \]
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Small Example: incidence matrix

\[ E = \begin{array}{c}
\downarrow \\
A \quad \bullet \\
\uparrow \\
B
\end{array} \]

\[ r_1 \]

\[ r_2 \]

\[ r_3 \]

\[ Pre = \begin{pmatrix}
2 & 1 & 0 \\
0 & 0 & 1 \\
1 & 0 & 0
\end{pmatrix} \]

\[ Post = \begin{pmatrix}
0 & 0 & 1 \\
2 & 1 & 0 \\
1 & 0 & 0
\end{pmatrix} \]

\[ C = \begin{pmatrix}
-2 & -1 & 1 \\
2 & 1 & -1 \\
0 & 0 & 0
\end{pmatrix} \]
Small Example: P-invariants

\[ x_1 = (1, 1, 0) = (A, B) \]

\[ x_2 = (0, 0, 1) = (E) \]

\[ \mathcal{C} = \begin{pmatrix} -2 & -1 & 1 \\ 2 & 1 & -1 \\ 0 & 0 & 0 \end{pmatrix} \]
Small Example: T-invariants

\[ y_1 = (1, 0, 2) = (r_1, 2 \cdot r_3) \]

\[ y_2 = (0, 1, 1) = (r_2, r_3) \]

\[ C = \begin{pmatrix} -2 & -1 & 1 \\ 2 & 1 & -1 \\ 0 & 0 & 0 \end{pmatrix} \]
M. Heiner, D. Gilbert and R. Donaldson
Petri Nets for Systems and Synthetic Biology

http://genome.ib.sci.yamaguchi-u.ac.jp/~pnp