A Framework for Modular Modeling and Analysis of Signaling Networks

Cottbus
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Project Milestones

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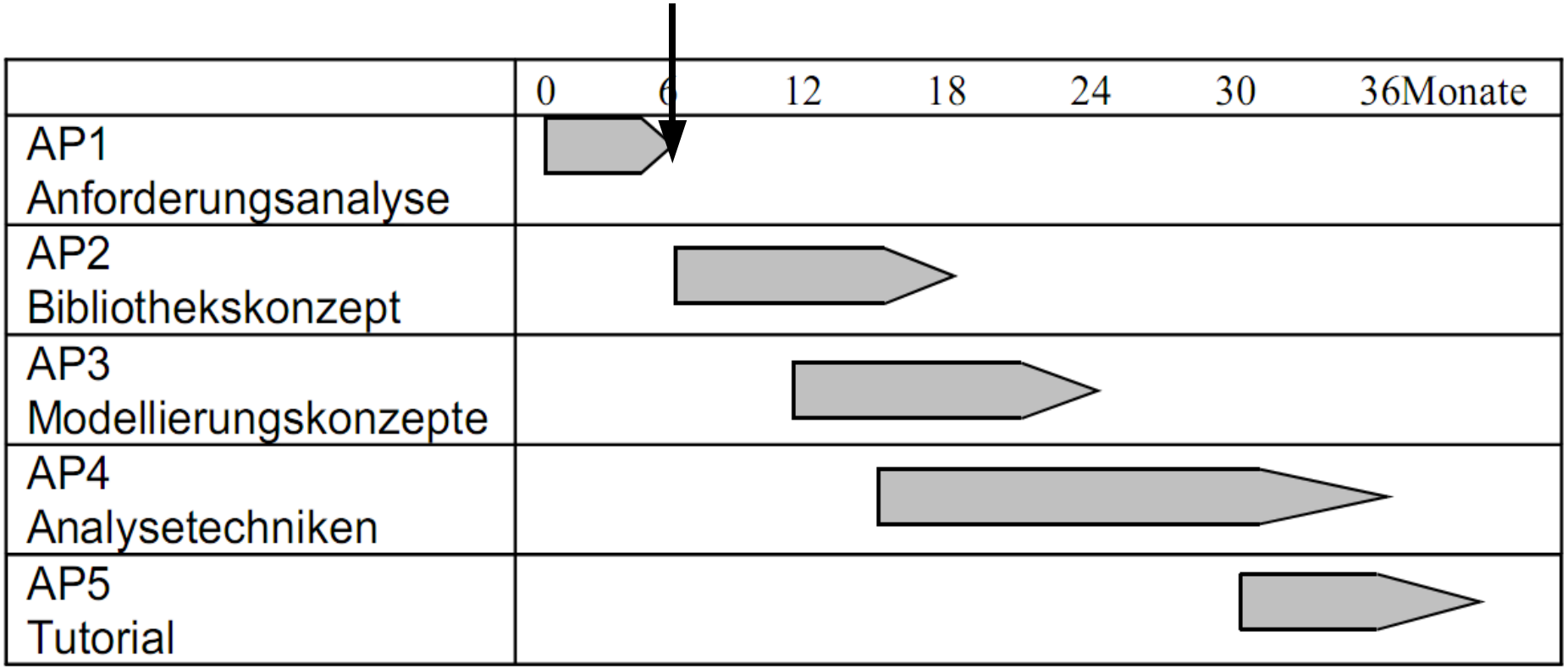
- WP1 - Requirements analysis
- WP2 - Library approach for generic model components
- WP3 - Modeling concepts for dealing with model alternatives
- WP4 - Analysis techniques for identification and Behavior comparison of model components
- WP5 - Tutorial

Schedule


0
6
12
18
24
30
36Monate
AP1
Anforderungsanalyse
AP2
Bibliothekskonzept
AP3
Modellierungskonzepte
AP4
Analysetechniken
AP5
Tutorial

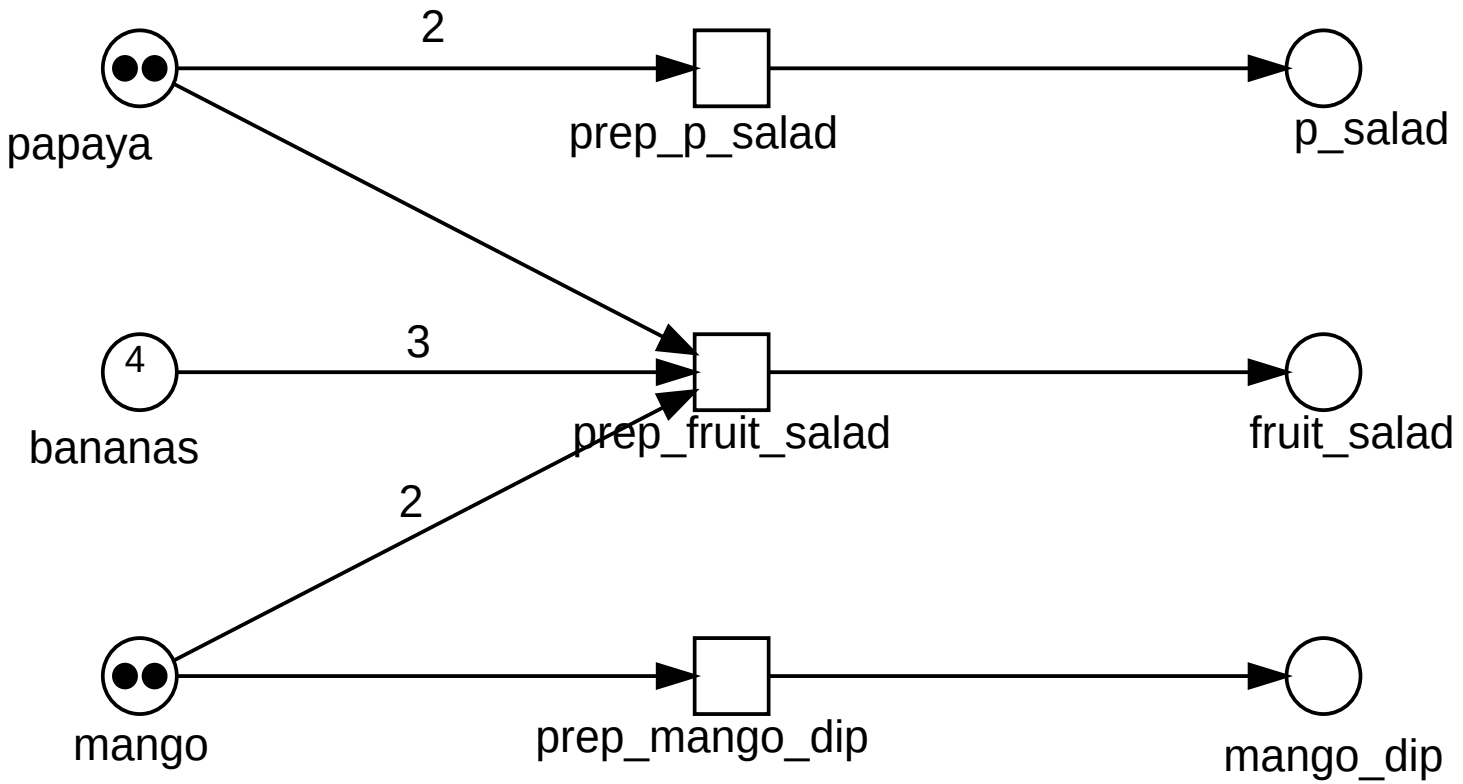
- Building a collection of the relevant network examples which are fully documented in the literature;
- Literature search for techniques to identify structure-based modules; evaluation on automatability, tool availability, and expense of implementation;
- Identification of structural components, manually or using tools, if possible;
- Identification of classes of structural components, which can be grouped together as generic model components;
- Develop a concept for the coupling with the database developed in M2;

Project Results

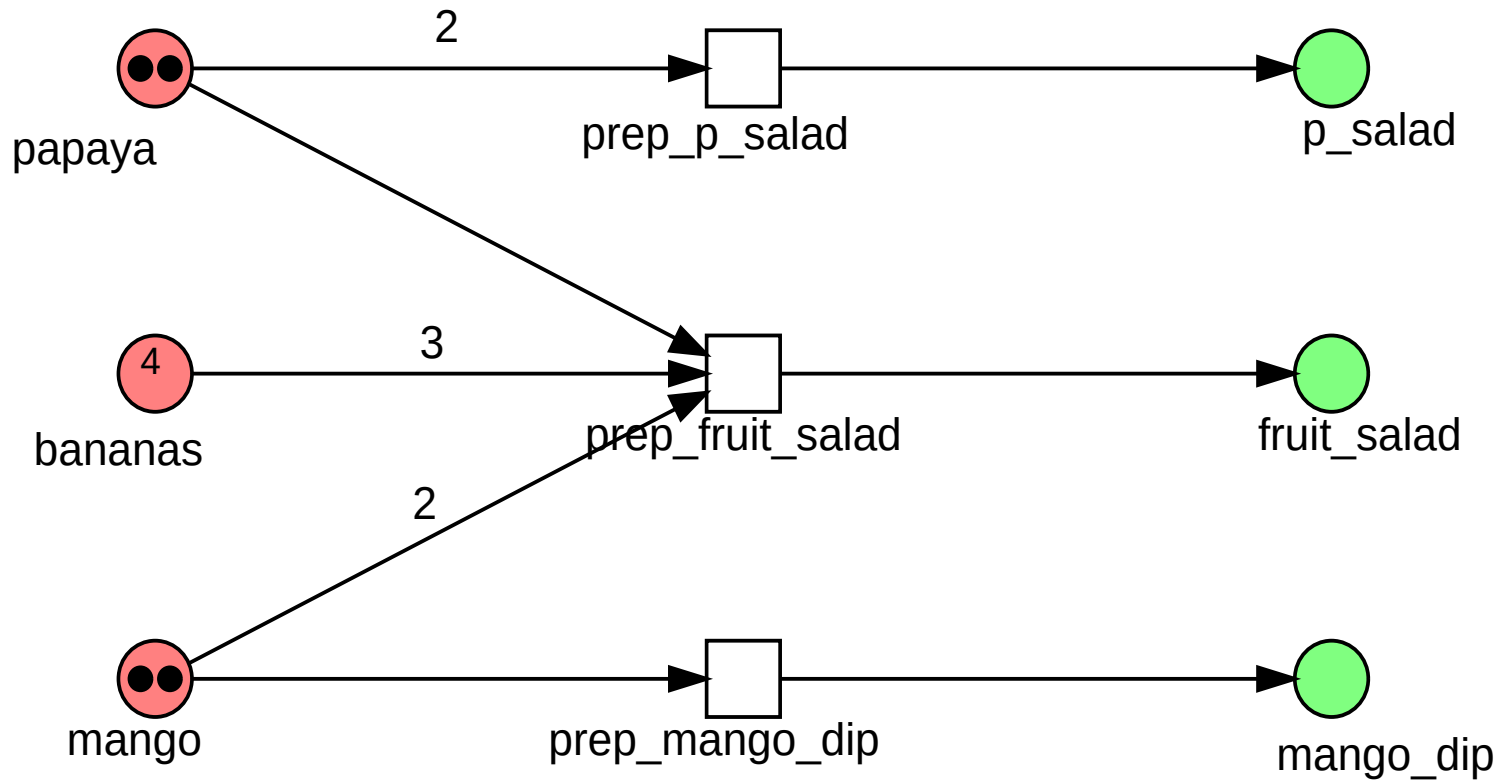
June 2009 --- August 2009

- build a more compact and parametric representation of a system by folding similar subnets
- it is possible to represent very concisely systems that would have required a huge uncoloured net
- these similar subnets when folded are distinguished by coloured tokens

- Prepare salad

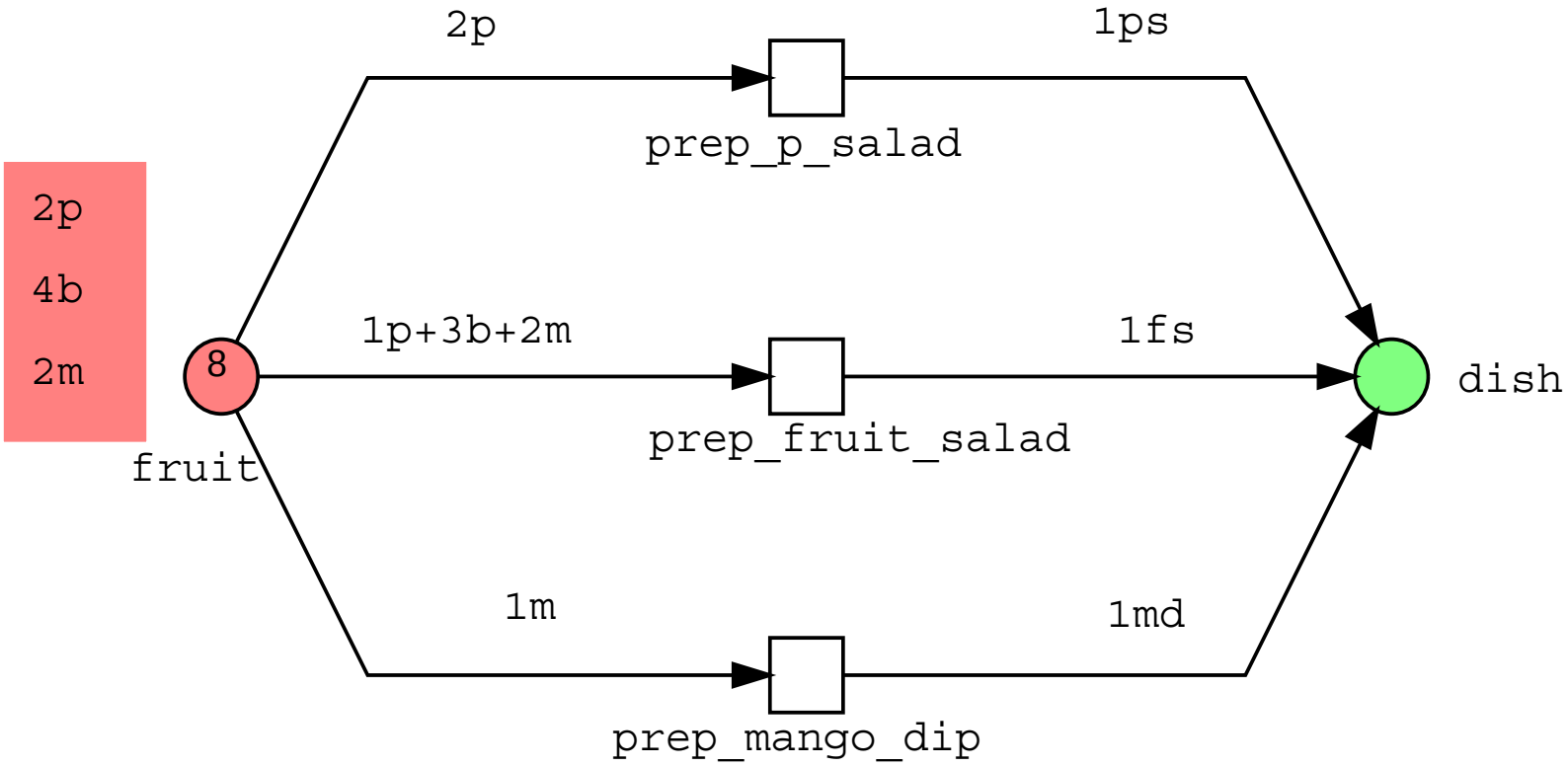


- Prepare salad



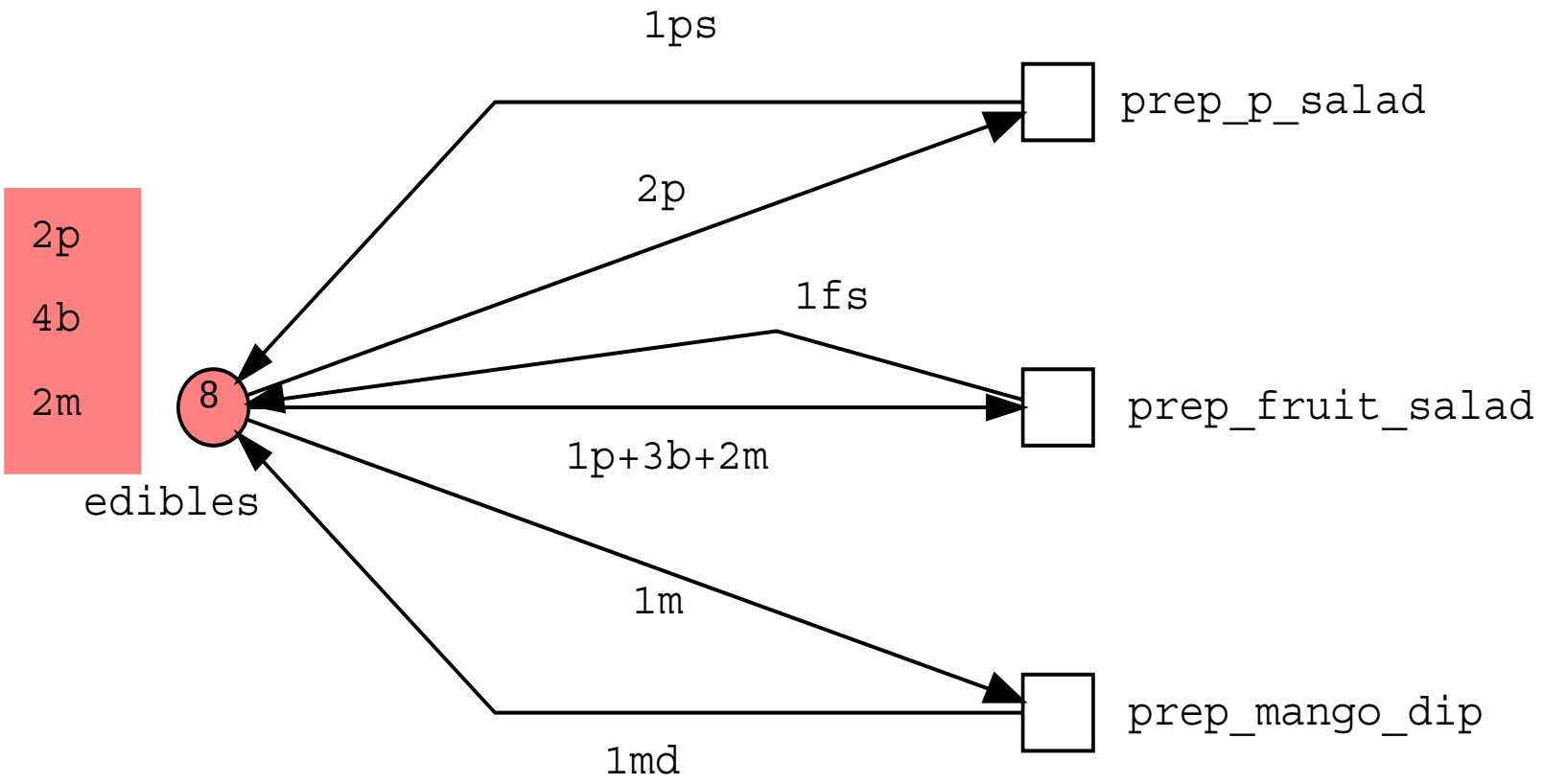
- Prepare salad

Colourset:
Enumeration fruit = {p, b, m}
Enumeration dish = {ps, fs, md}



- Prepare salad

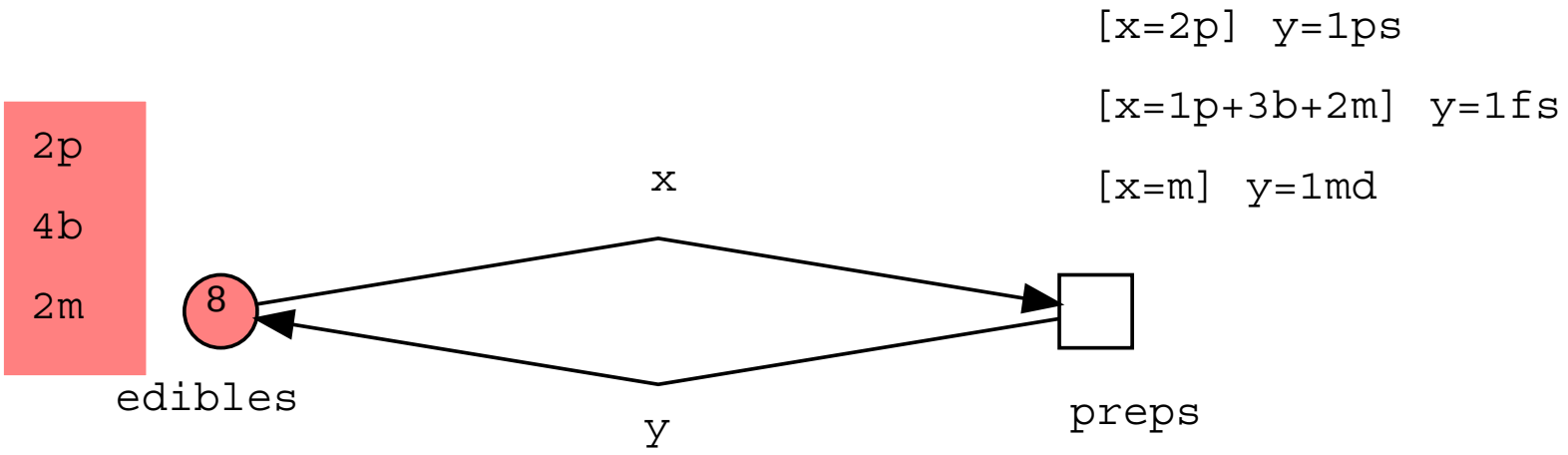
Colourset:
Enumeration fruit = {p, b, m}
Enumeration dish = {ps, fs, md}
union edibles = fruit, dish



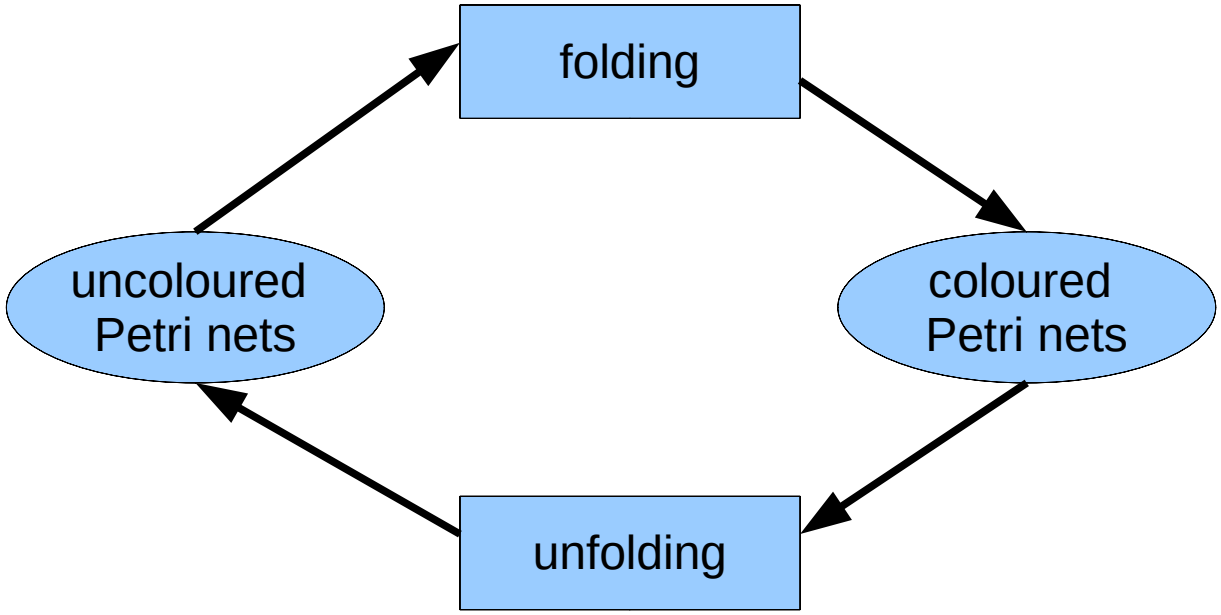
- Prepare salad

Colourset:
enumeration fruit = {p, b, m}
enumeration dish = {ps, fs, md}
union edibles = fruit, dish

Variable:
fruit x
dish y

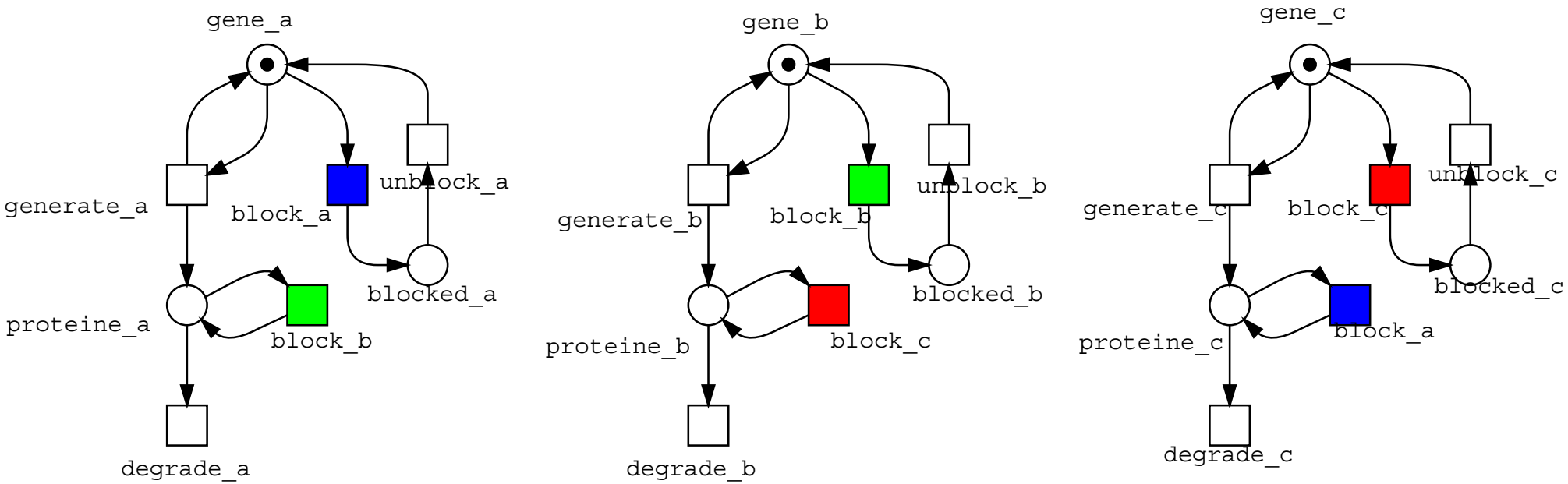


- Coloured Petri nets – uncoloured Petri nets



- Repressilator model

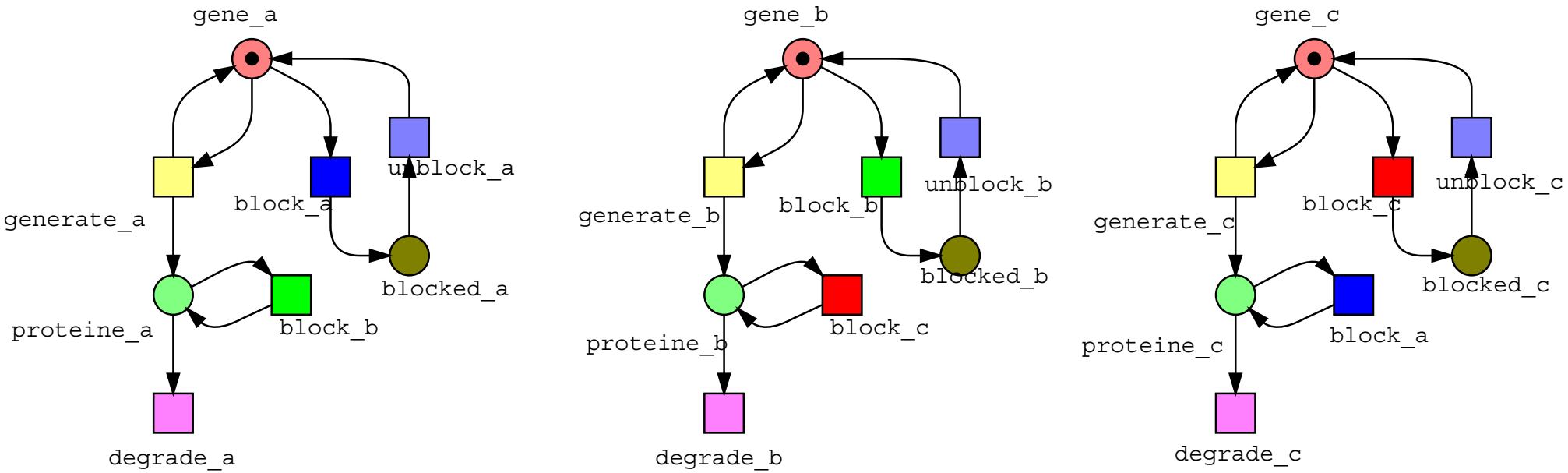
  -> Uncoloured Petri nets model



- Folding repressilator model

  -> subnet partition

  -> node set partition



- Coloured Petri nets for repressilator model

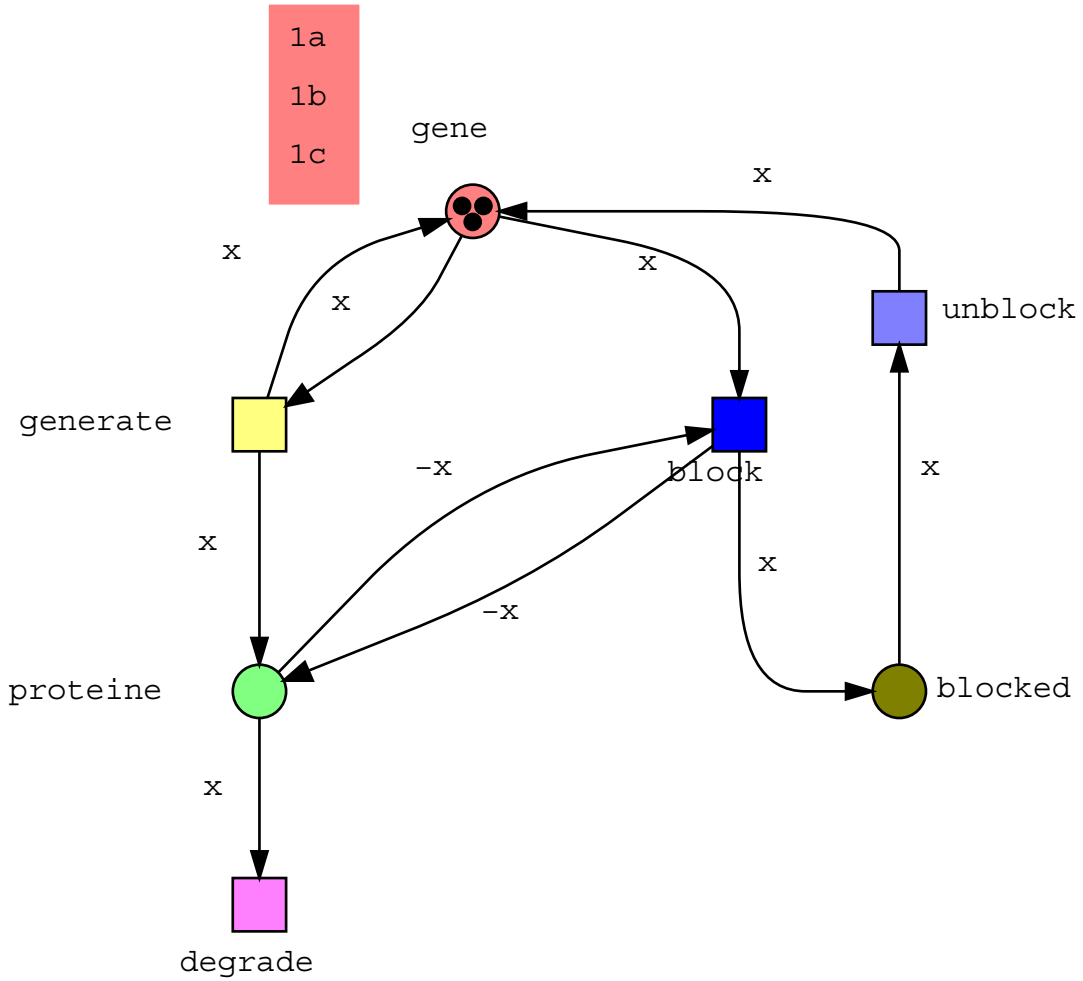
  -> define colour sets

  -> assign colour sets to places and transitions

  -> define arc expressions

Colourset:
enumeration gene = {a, b, c}

Variable:
gene x

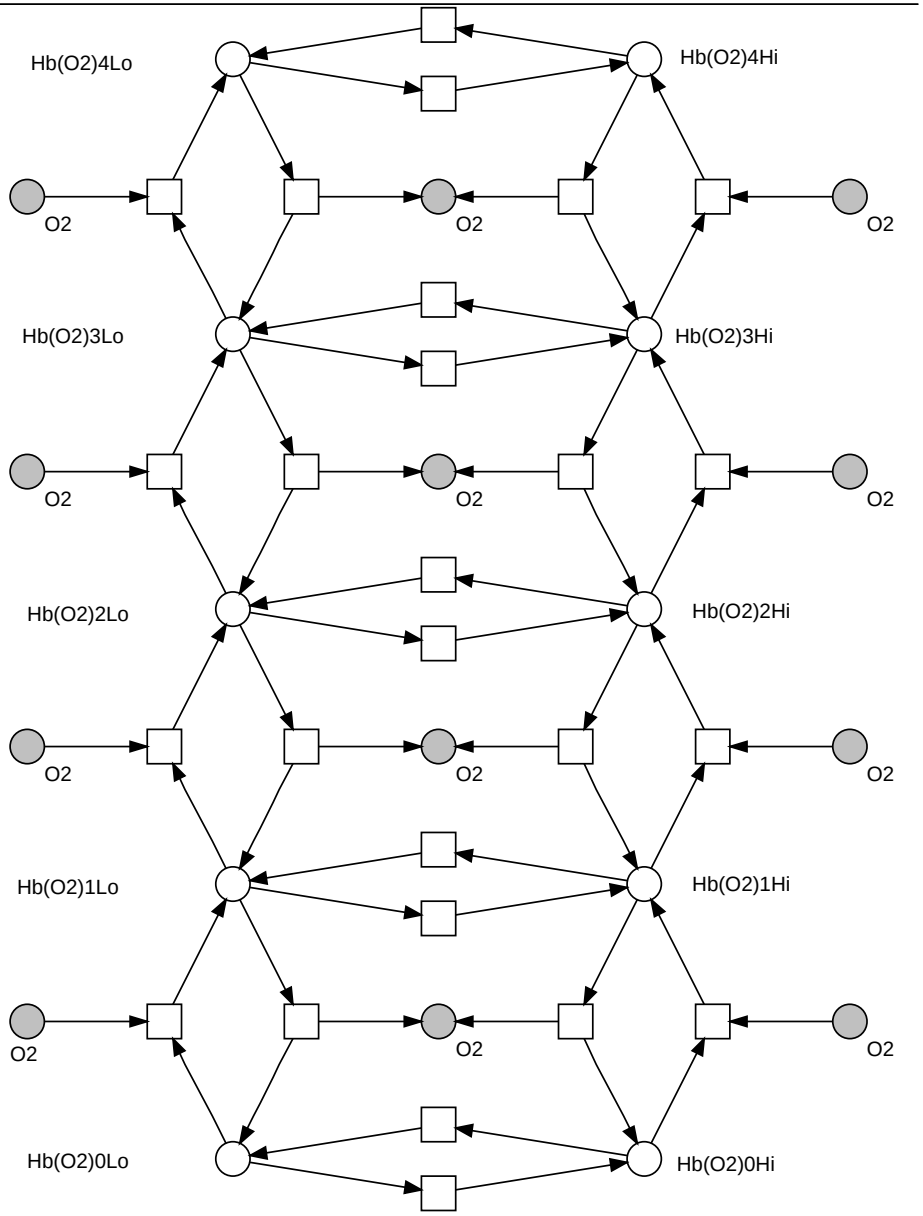


Coloured Petri nets – example 3

- Cooperative ligand binding

  -> Binding of oxygen to the four subunits of a hemoglobin heterotetramer

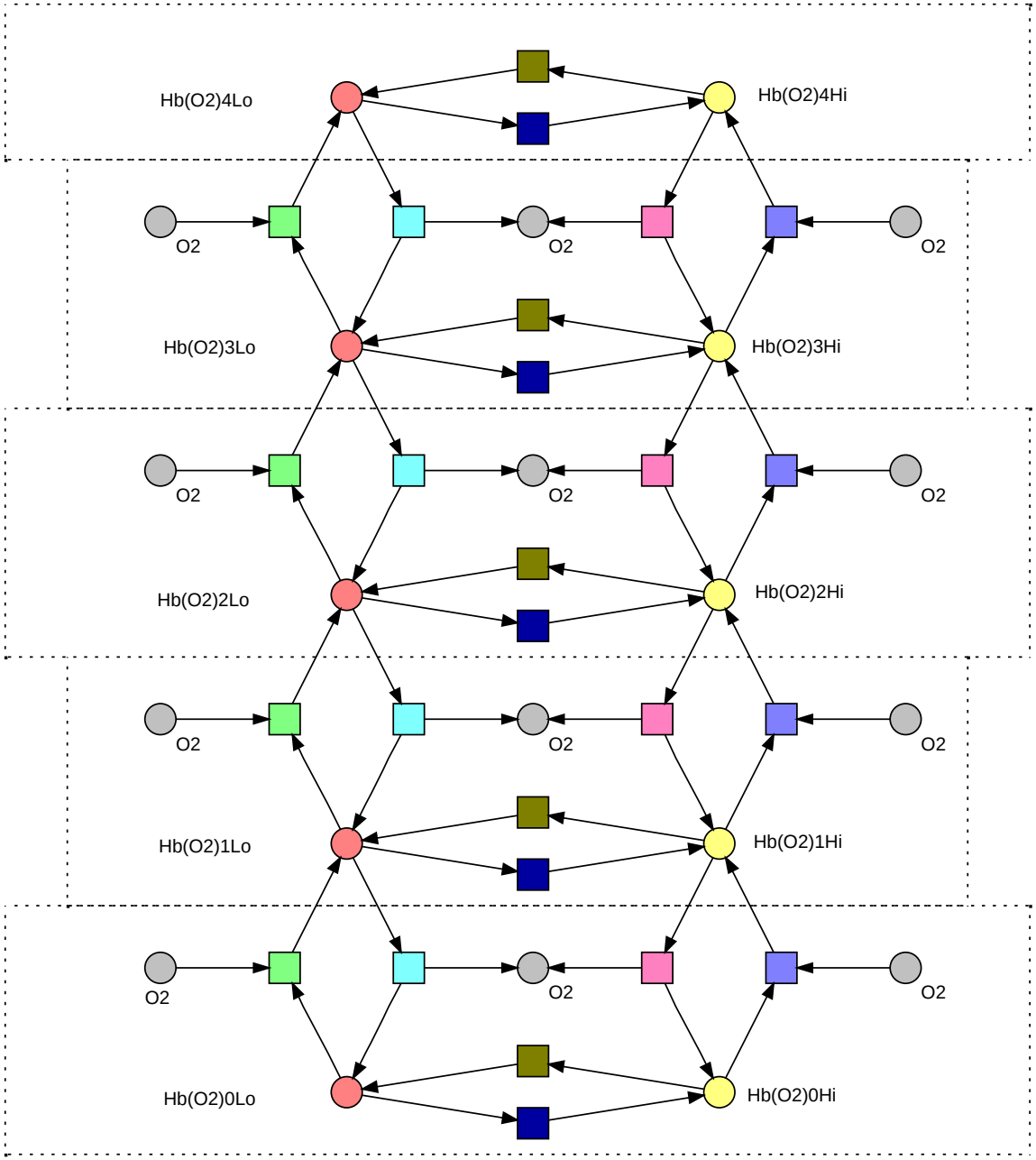
  -> Oxygen (O2) is represented in the form of multiple copies of one logical place



Reference: Annegret Wagler; Robert Weismantel; Wolfgang Marwan. Petri Nets as a Framework for the Reconstruction and Analysis of Signal Transduction Pathways and Regulatory Networks. (so far unpublished)

Coloured Petri nets – example 3

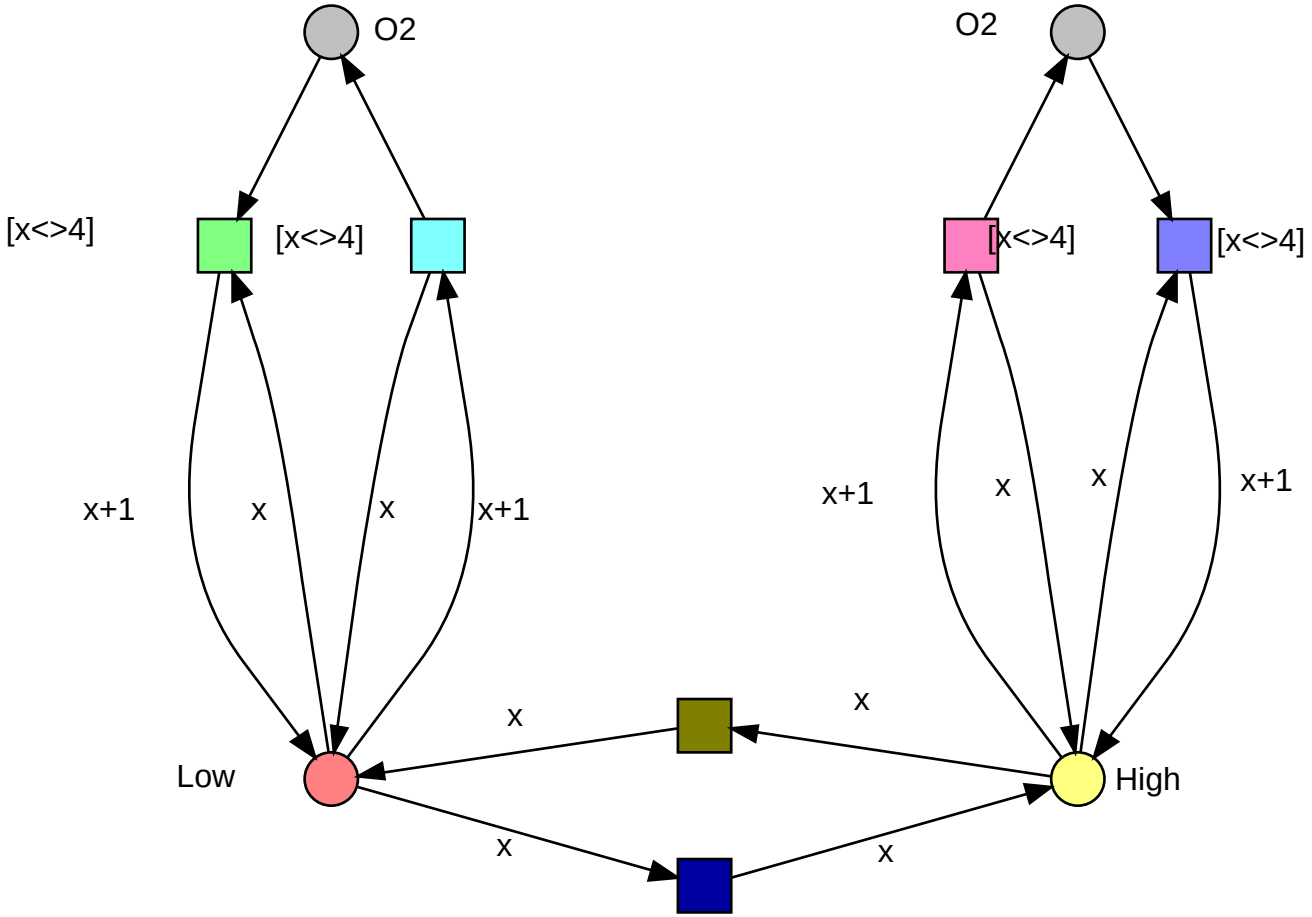
- Folding



- Coloured Petri nets

Colourset:
enumeration Hb(O2)={Hb(O2)0, Hb(O2)1,
Hb(O2)2, Hb(O2)3, Hb(O2)4}

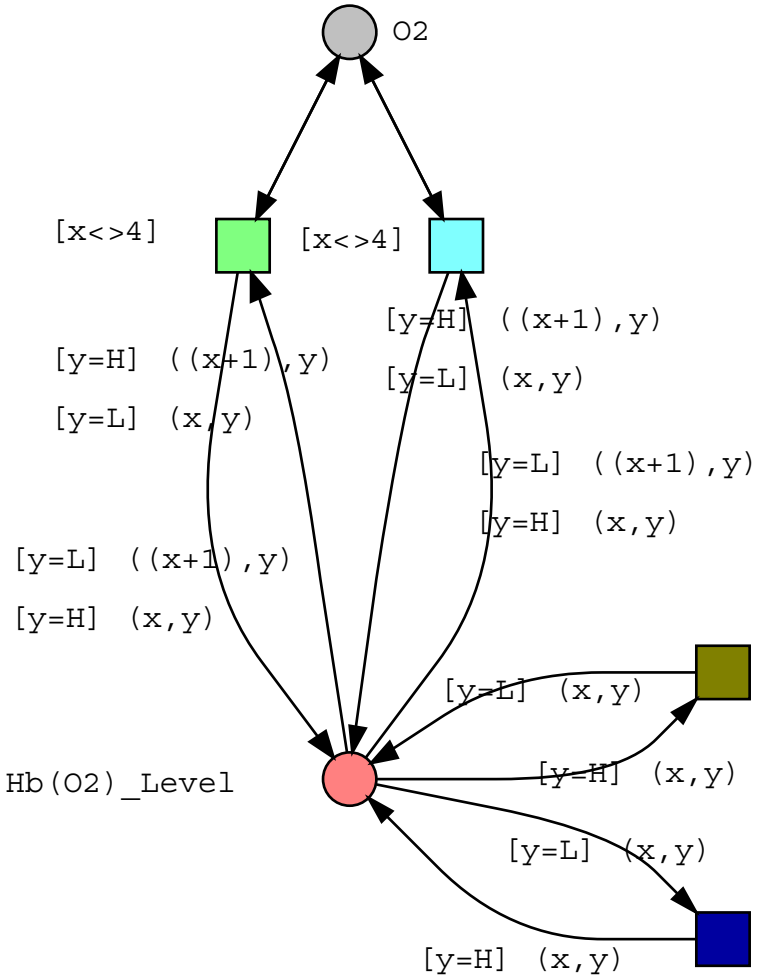
Variable: Hb(O2) x



- Coloured Petri nets

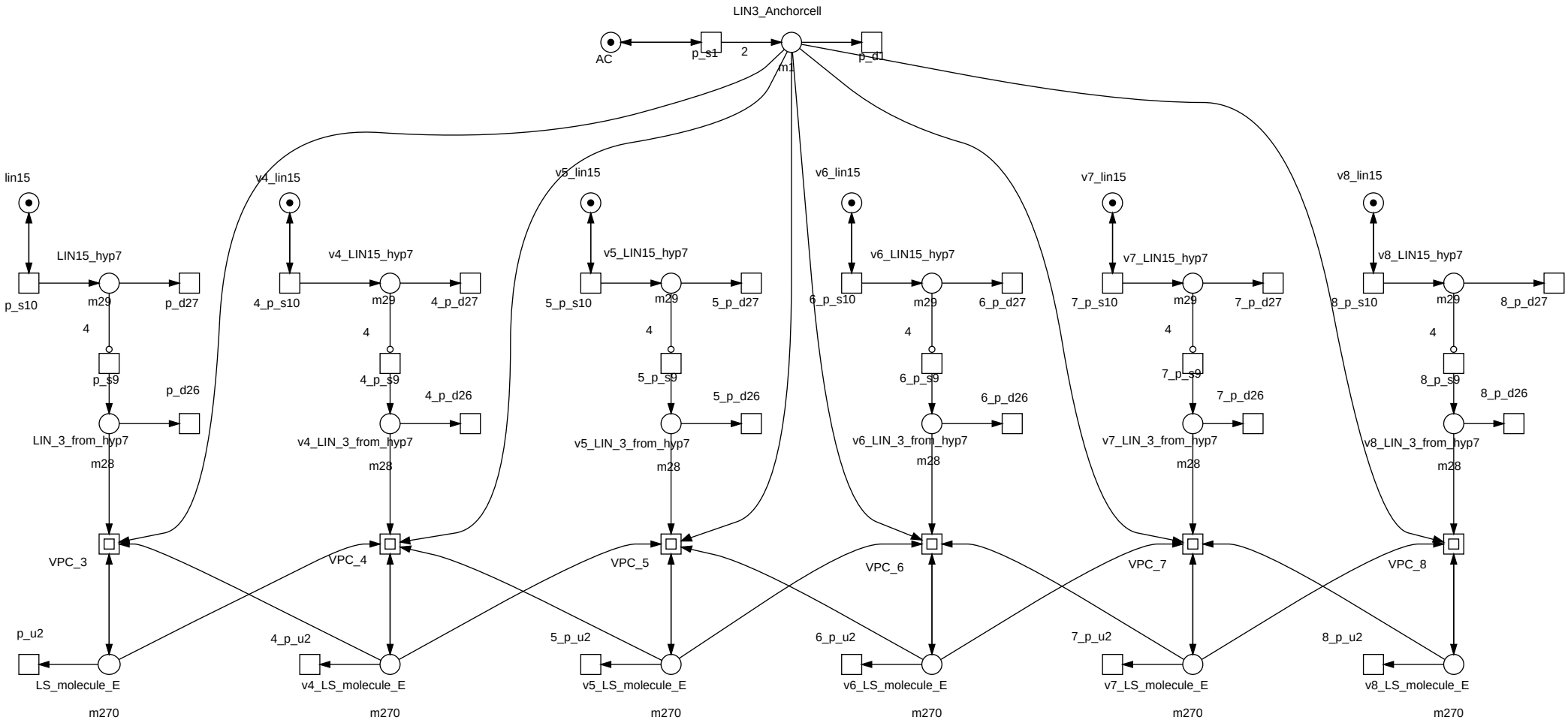
Colourset:
enumeration Hb(O2) = {Hb(O2)0, Hb(O2)1,
Hb(O2)2, Hb(O2)3, Hb(O2)4}
enumeration Level = {H, L}
Product Hb(O2)_Level = Hb(O2) x Level

Variable:
Hb(O2) x
Level y



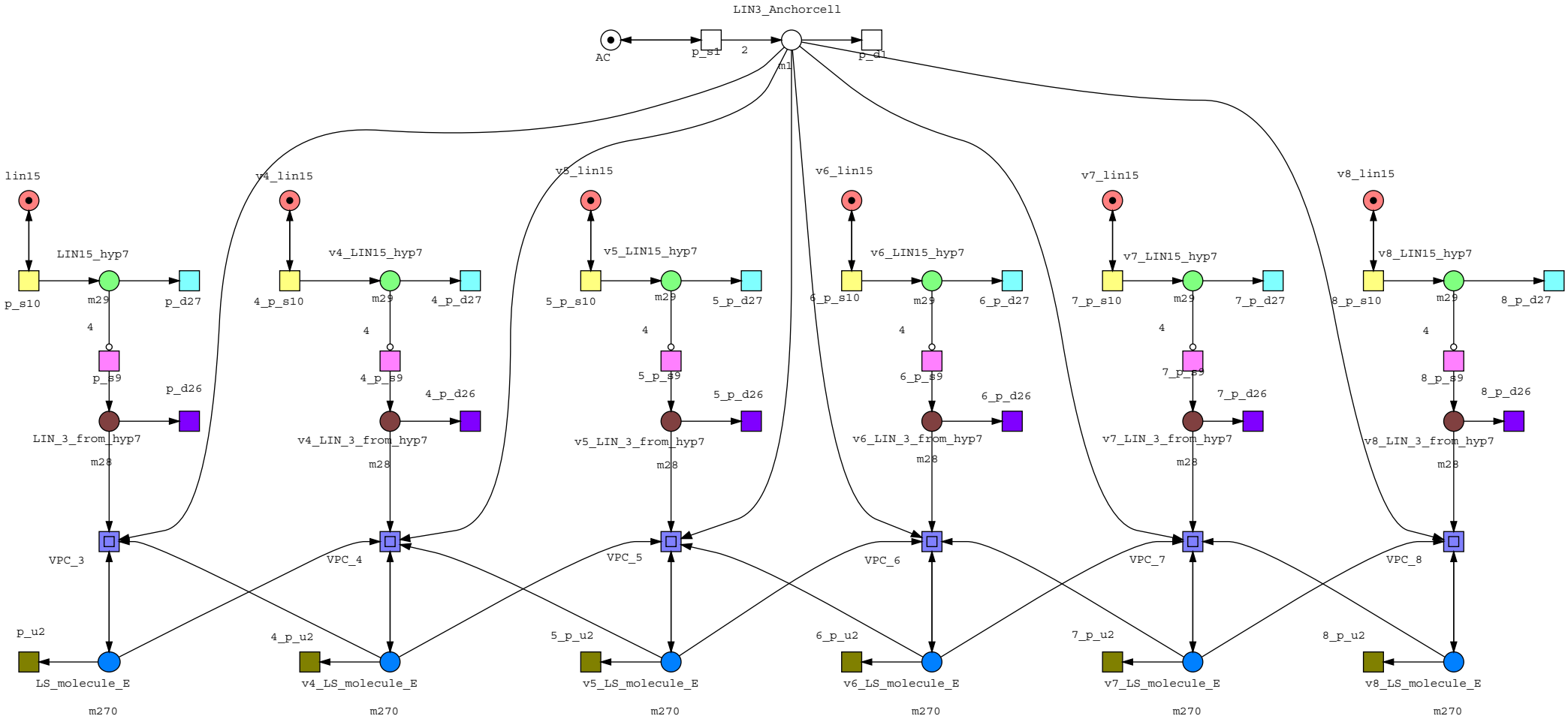
➔ C. elegans vulval development model

Places: 206
Transitions: 360
Kinetics: mass action



Coloured Petri nets – example 4

- Folding

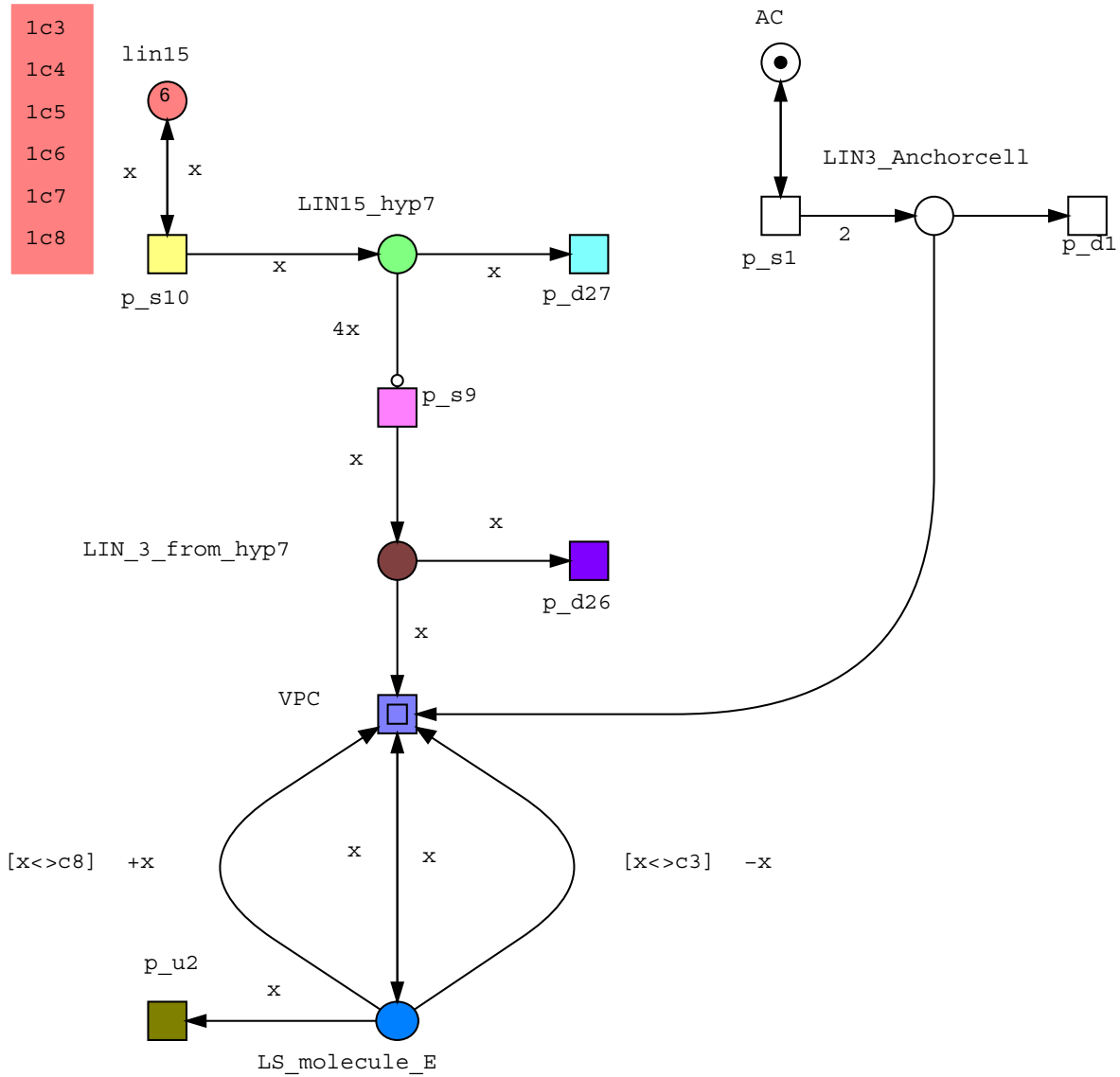


➔ C. elegans vulval development model

-> Coloured Petri net

Colourset:
enumeration
Cell={c3, c4, c5, c6, c7, c8}

Variable:
Cell x



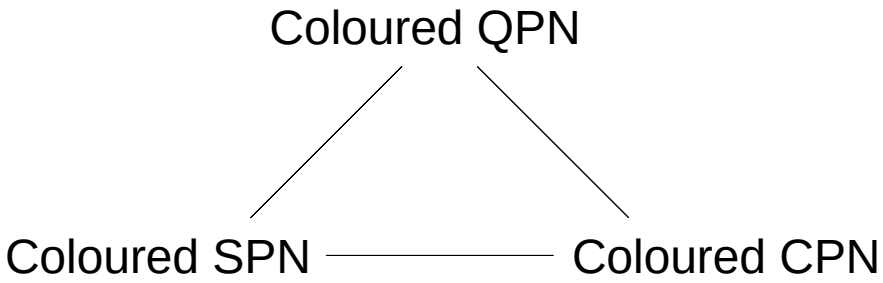
Coloured Petri nets – advantages

- Reduce the size of nets by folding similar subnets
- To increase the colours means to increase the size of the net

  -> E.g. repressilator model, gene= {a,b,c,...}
- Rich analysis techniques

- by unfolding, reuse all P/T net analysis techniques
  - -> invariant analysis
  - -> state equation
  - -> reachability graph
  - -> model checking
- without unfolding, use analysis techniques for coloured Petri nets
  - -> reachability graph
  - -> model checking

- Requirements analysis for coloured Petri nets
- Precisely defining different types of coloured PN
  - -> Coloured qualitative Petri nets (CQPN)
  - -> Coloured stochastic Petri nets (CSPN)
  - -> Coloured continuous Petri nets (CCPN)
- Defining data types or colours that will be supported
- Defining expressions, guards that will be supported



- Definitions of data types

<type> ::= <basic type> | <structured type>
<basic type> ::= <type identifier> | <simple type>
<type identifier> ::= <unsigned integer> | <boolean> | <string>
<unsigned integer> ::= "int"
<boolean> ::= "bool"
<string> ::= "string"
<simple type> ::= <enumeration> | <index>
<enumeration> ::= <identifier list>
<identifier list> ::= <identifier> {,<identifier>}
<index> ::= <identifier> "[" <index specifier> "]"
<index specifier> ::= <type identifier> | <enumeration>
<structured type> ::= <product> | <union>
<product> ::= <type> "x" <type> { "x" <type>}
<union> ::= <type> { "," <type>}

Next Steps

Next steps

- Develop tools for coloured Petri nets
- Consider more network examples especially from the collaborators
- Continue to analyze the capabilities and equivalence of Cell Illustrator and Snoopy
- Coupling with the database developed by M2, needs to be discussed

Thank You !