

PETRI NETS AS PARTIAL ORDER SEMANTICS FOR BIOCHEMICAL NETWORKS

Monika Heiner

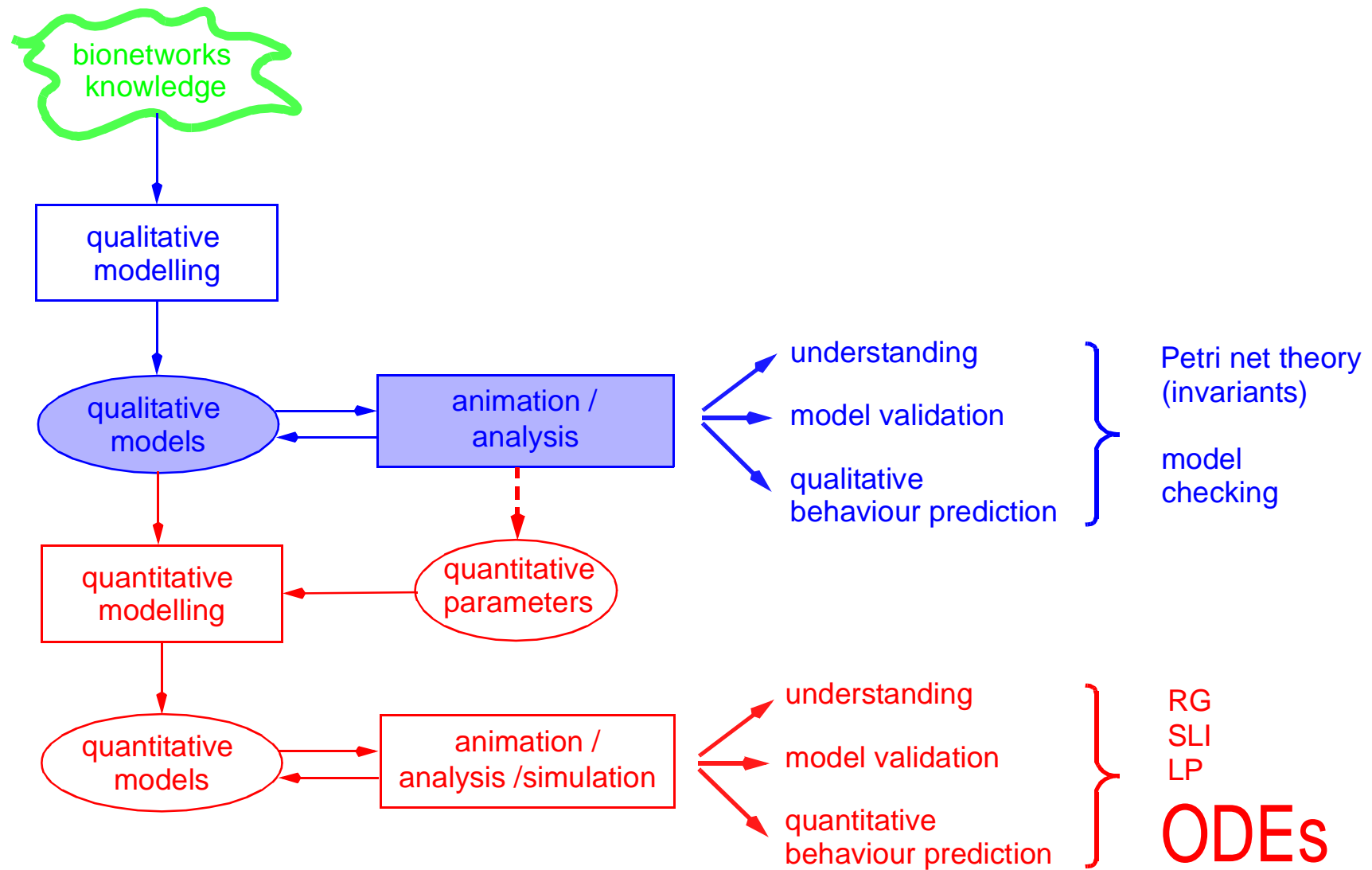
**Brandenburg University of Technology
Cottbus**

Dep. of CS

Ina Koch

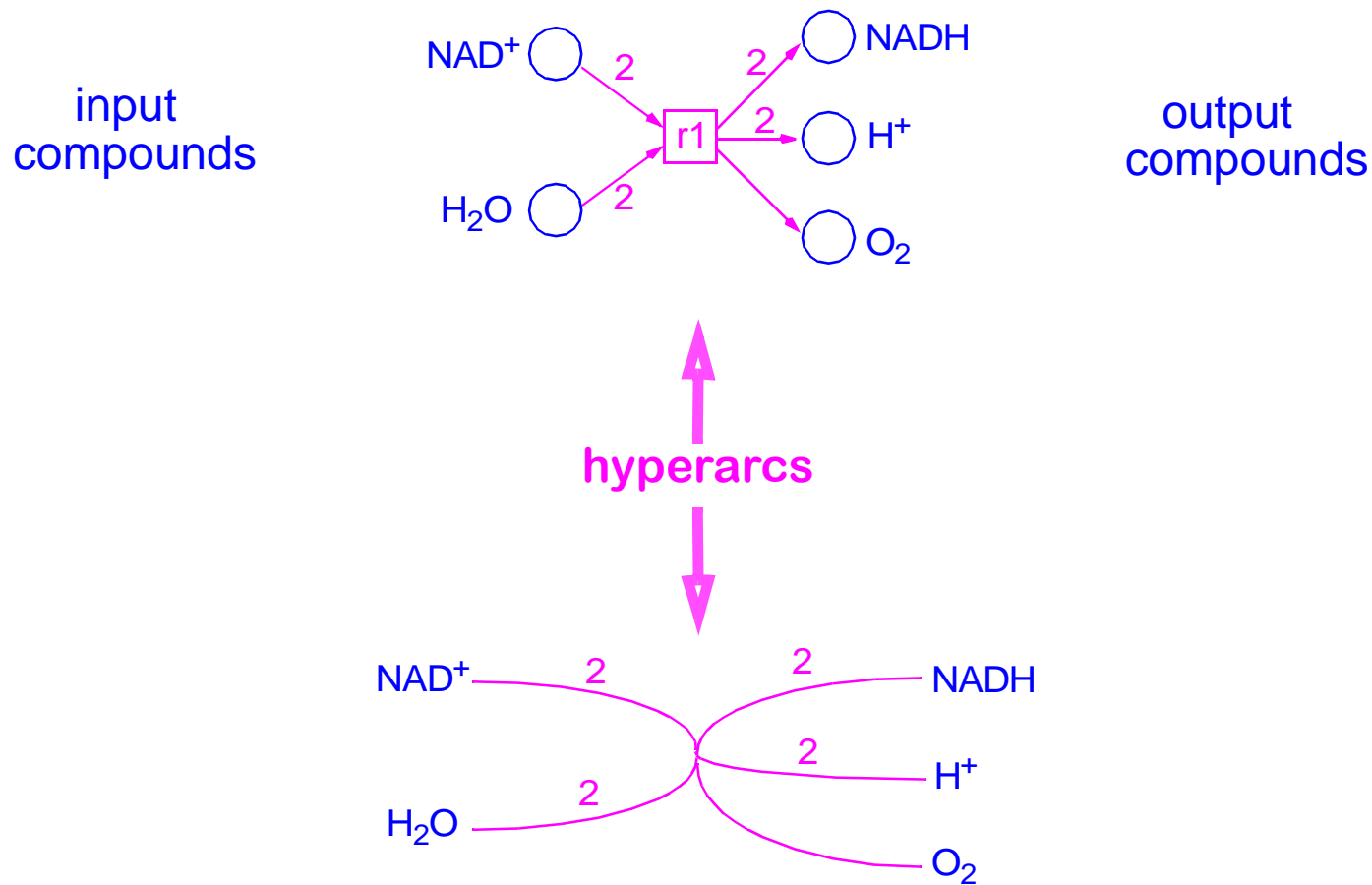
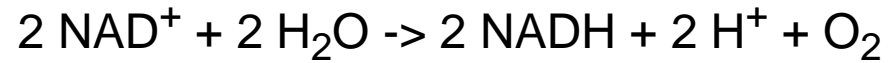
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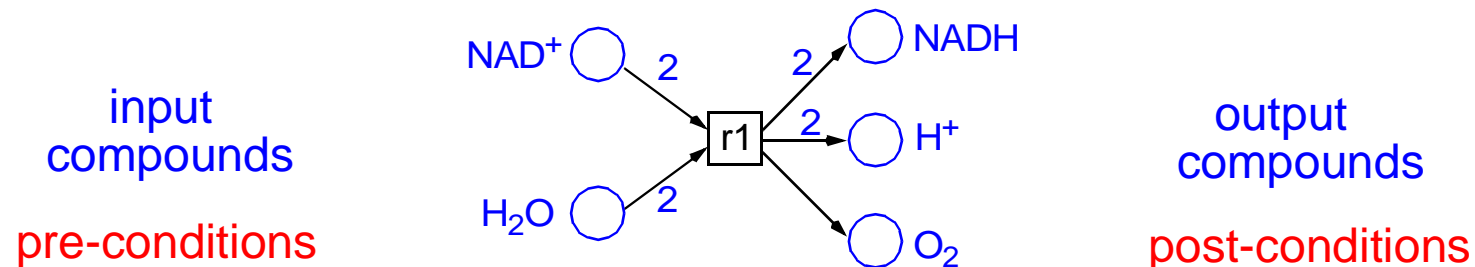
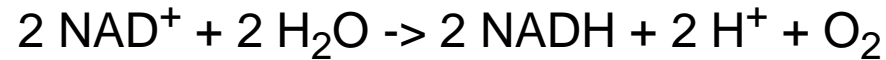


PETRI NETS & PARTIAL ORDER SEMANTICS

□ atomic actions → Petri net transitions → chemical reactions



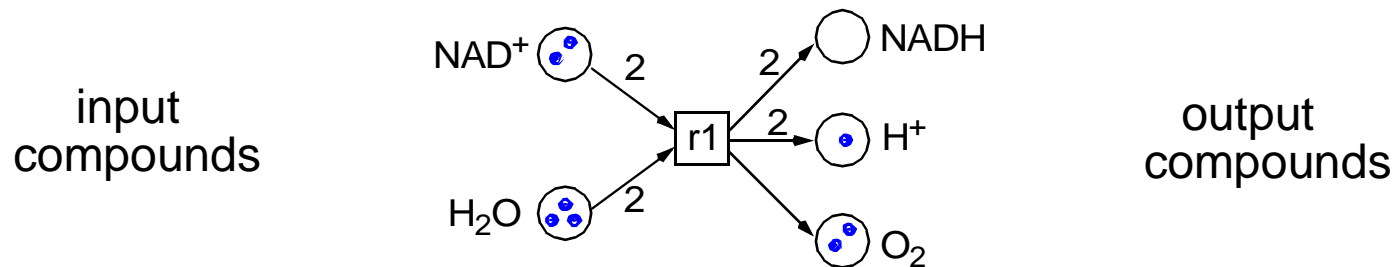
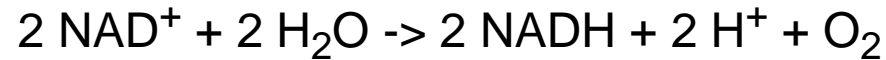
□ atomic actions → Petri net transitions → chemical reactions



□ local conditions → Petri net places → chemical compounds

□ multiplicities → Petri net arc weights → stoichiometric relations

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



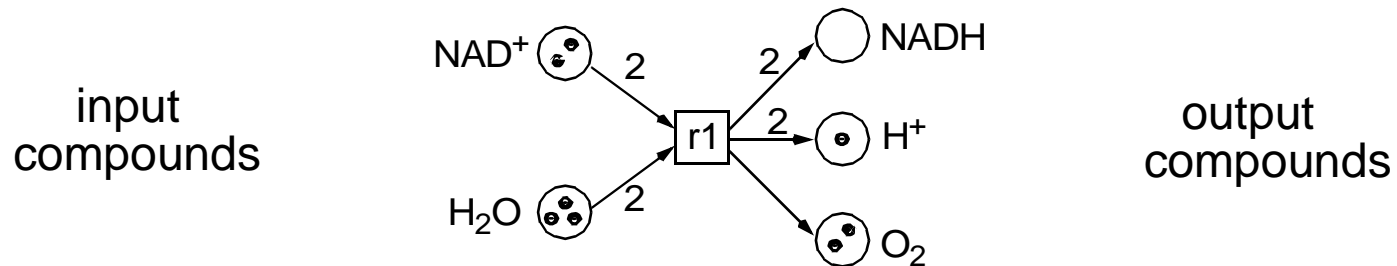
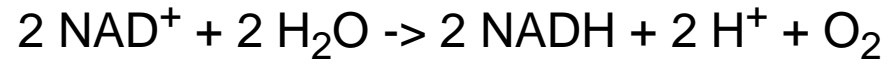
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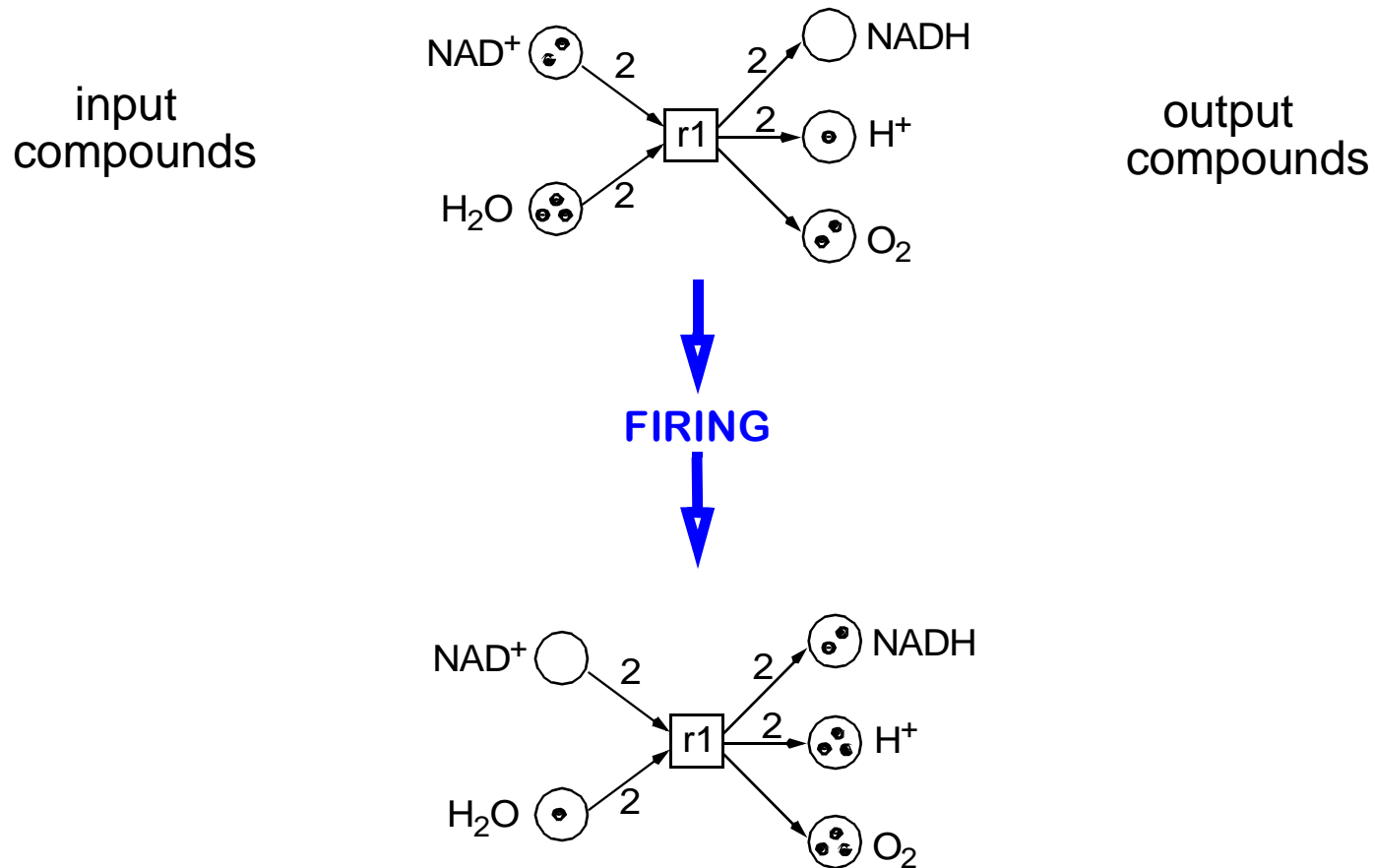
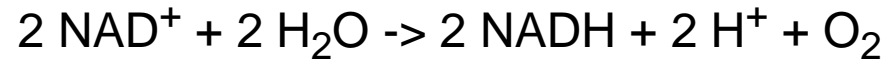
□ condition's state -> token(s) in its place -> available amount (e.g. mol)

□ system state -> marking -> compounds distribution

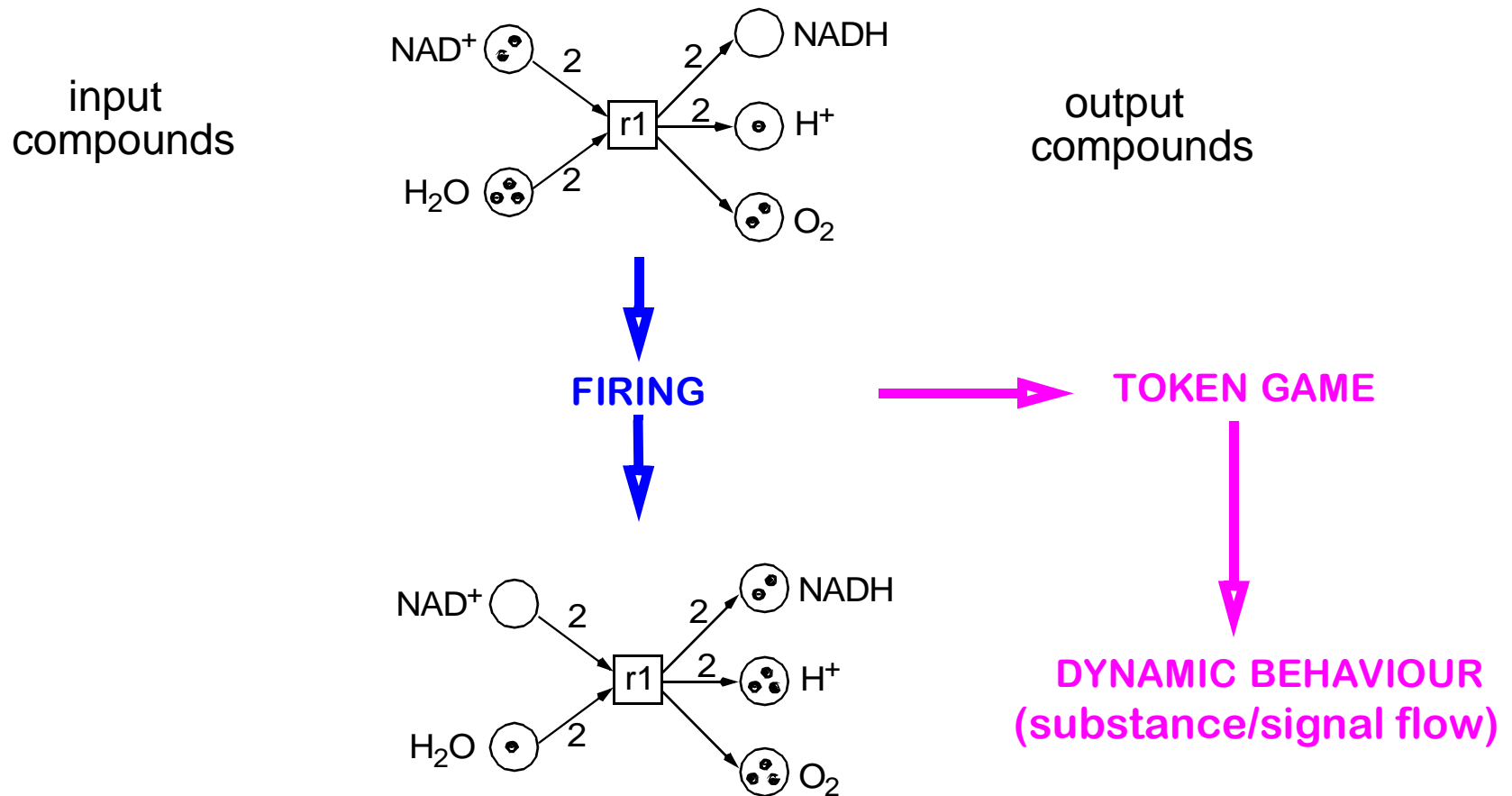
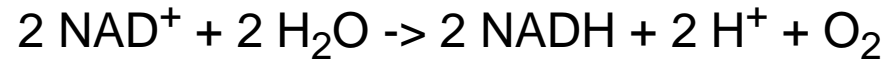
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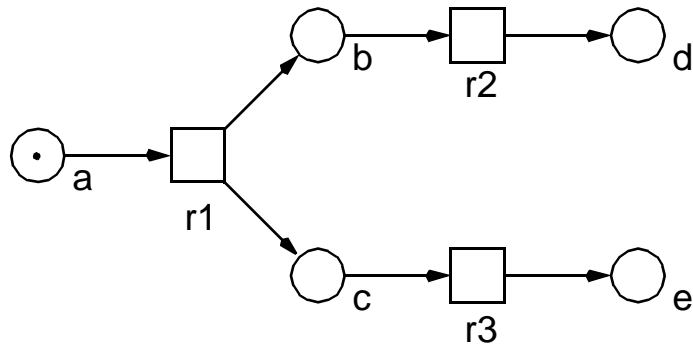


□ atomic actions → Petri net transitions → chemical reactions



□ atomic actions → Petri net transitions → chemical reactions





- order between r1 - r2 and r1 - r3

-> causality $x < y$

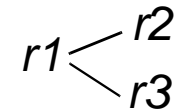
-> dependency

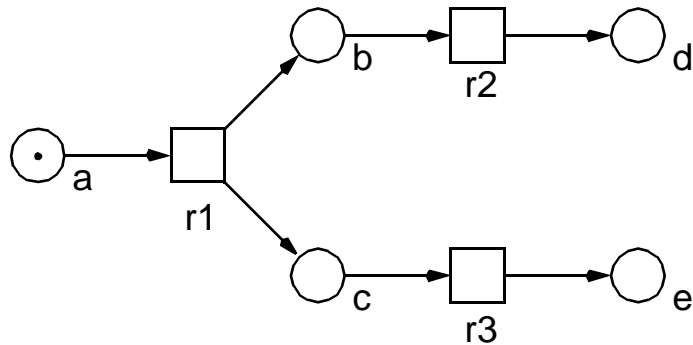
- no order between r2 , r3

-> concurrency $x || y$

-> independency

- partial order run





- order between r1 - r2 and r1 - r3

-> causality $x < y$

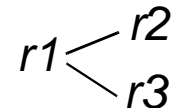
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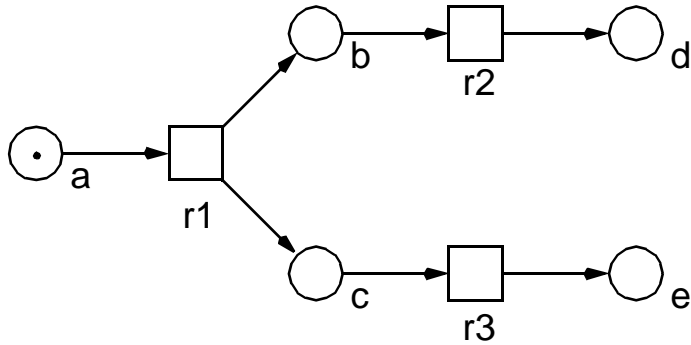
- partial order run



-> PARTIAL ORDER SEMANTICS

“true concurrency semantics”

all partially ordered runs



❑ possible interleaving runs

-> $r1 - r2 - r3$

-> $r1 - r3 - r2$

❑ totally ordered runs

❑ order between $r1 - r2$ and $r1 - r3$

-> causality $x < y$

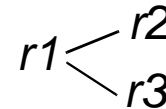
-> dependency

❑ no order between $r2, r3$

-> concurrency $x \parallel y$

-> independency

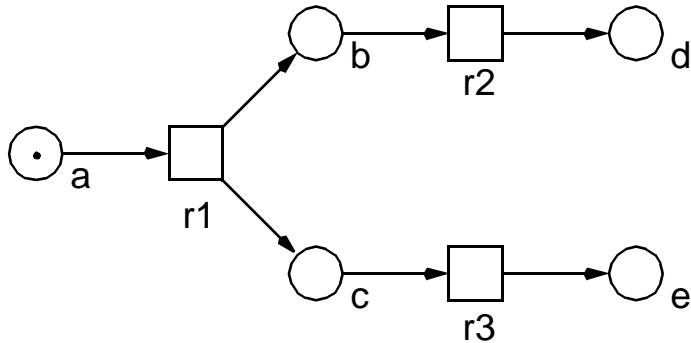
❑ partial order run



-> PARTIAL ORDER SEMANTICS

“true concurrency semantics”

all partially ordered runs



- possible interleaving runs

-> $r1 - r2 - r3$

-> $r1 - r3 - r2$

- totally ordered runs

-> INTERLEAVING SEMANTICS

all totally ordered runs

- order between $r1 - r2$ and $r1 - r3$

-> causality $x < y [x-y]$

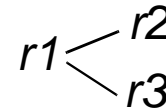
-> dependency

- no order between $r2, r3$

-> concurrency $x || y$

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-> PARTIAL ORDER SEMANTICS

“true concurrency semantics”

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❑ biochemical networks

-> *networks of (abstract) chemical reactions*

❑ biochemically interpreted Petri net

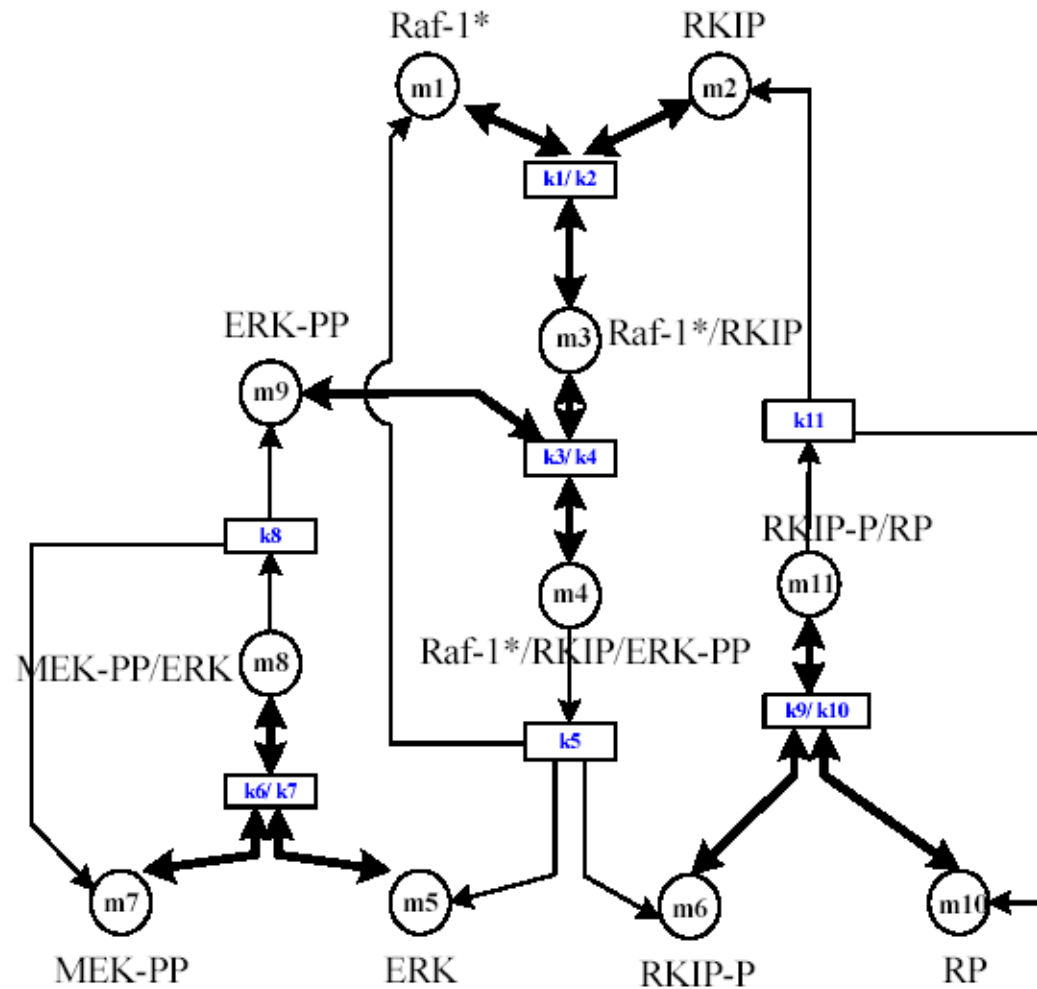
-> *partial order sequences of chemical reactions (= elementary actions)
transforming input into output compounds / signals
[respecting the given stoichiometric relations, if any]*

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

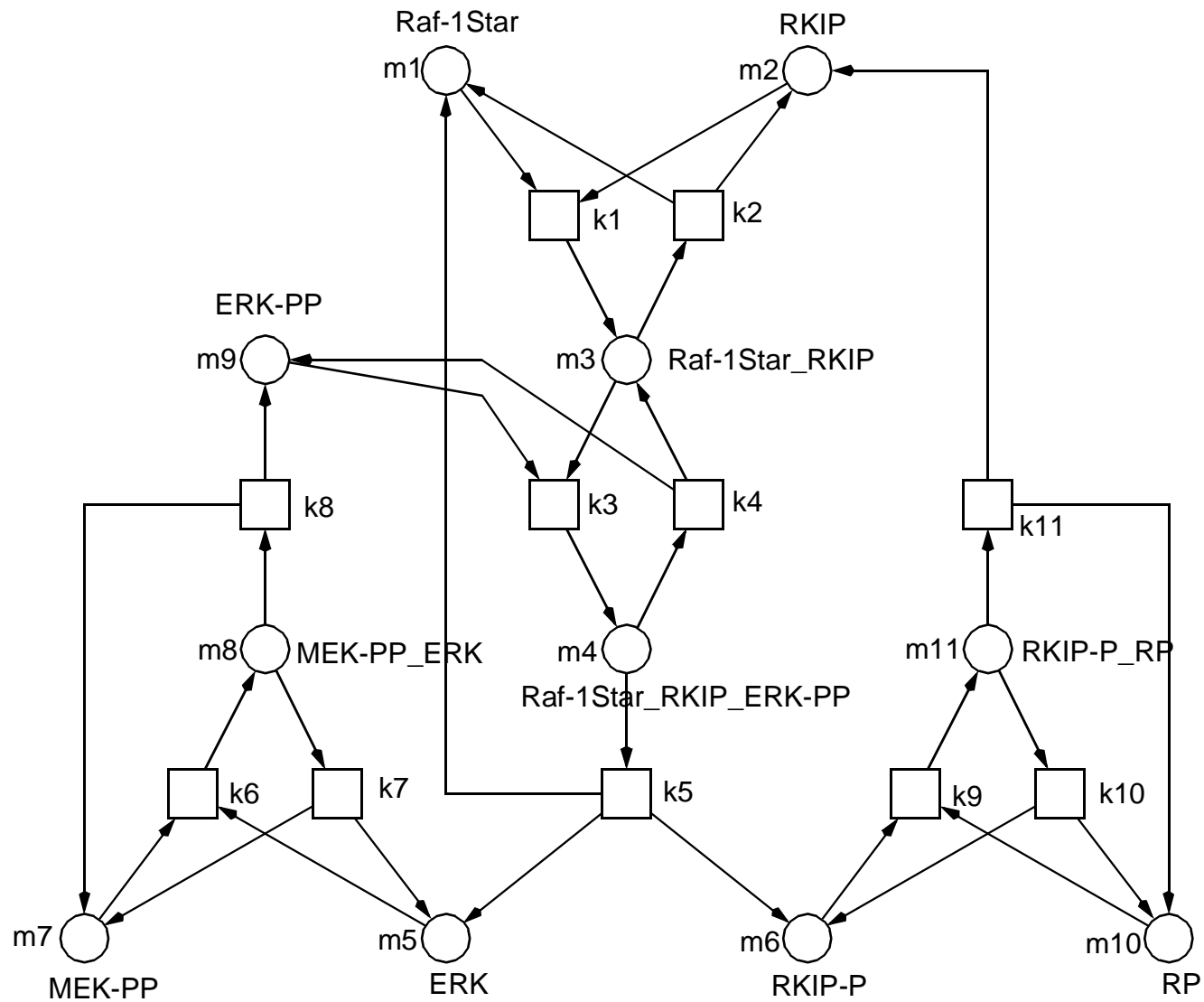
❑ pathway

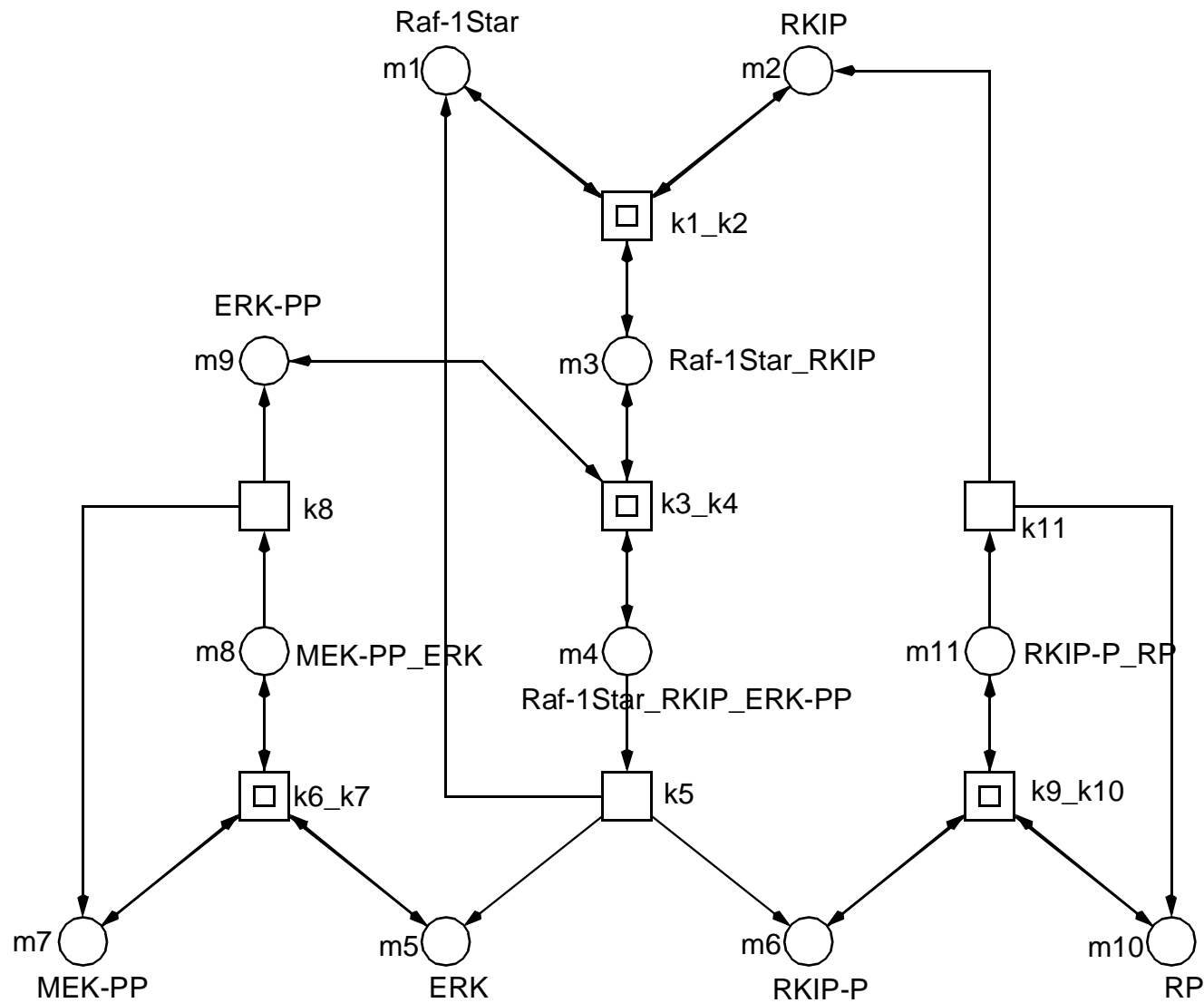
-> *self-contained partial order sequence of elementary (re-) actions*

THE RUNNING EXAMPLE



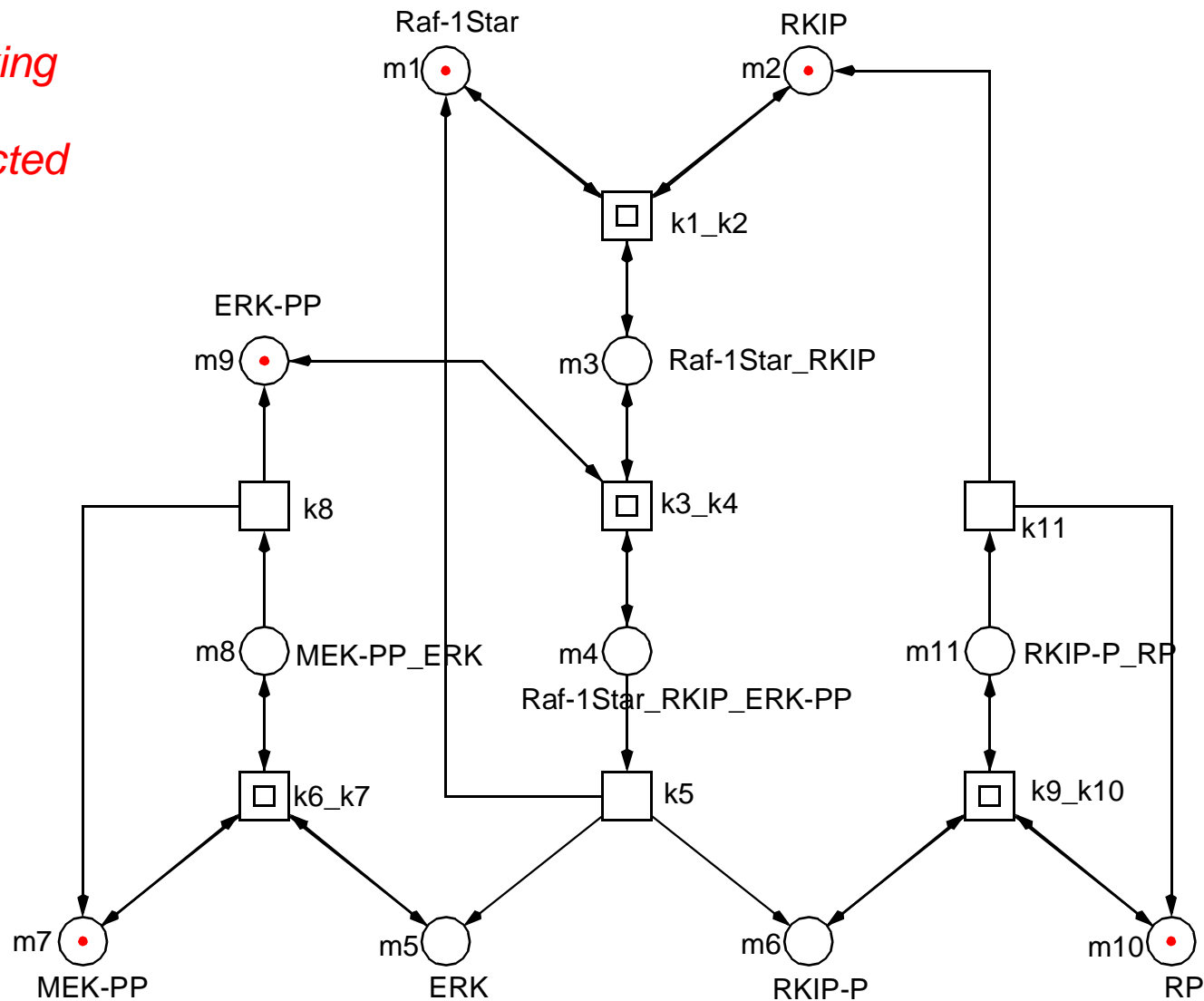
[Cho et al.,
CMSB 2003]





THE RKIP PATHWAY, HIERARCHICAL PETRI NET

initial marking
-> unique
-> constructed



QUALITATIVE ANALYSES

□ Lautenbach, 1973

□ T-invariants

-> integer solutions x of

$$Cx = 0, x \neq 0, x \geq 0$$

-> *multisets of transitions*

-> *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*

$$kx = \sum_i a_i x_i$$

-> **elementary modes [Schuster 1993]**

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

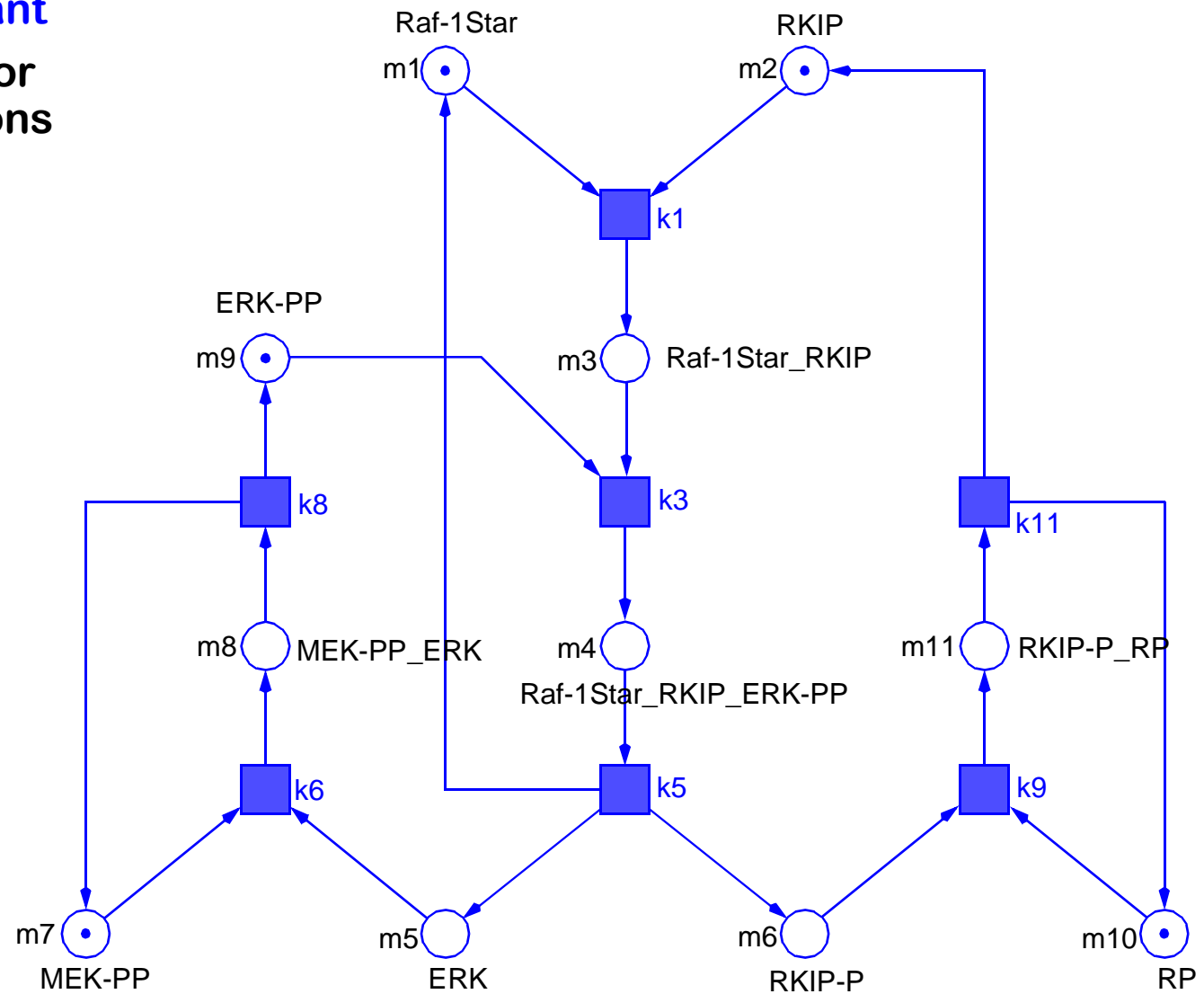
- **two interpretations**
 1. *relative transition firing rates*
of transitions occurring permanently & concurrently
 - > *steady state behaviour*
 2. *partially ordered transition sequence*
of transitions occurring one after the other
 - > *substance / signal flow*

-> behaviour understanding

- **a T-invariant defines a subnet**
 - > *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*

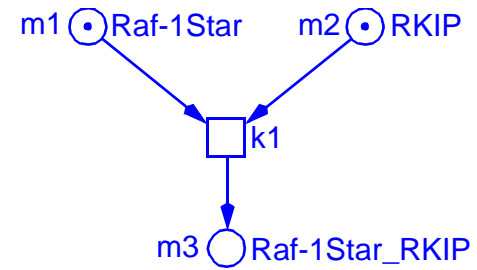
-> partial order structure

-> non-trivial T-invariant
 + four trivial ones for reversible reactions



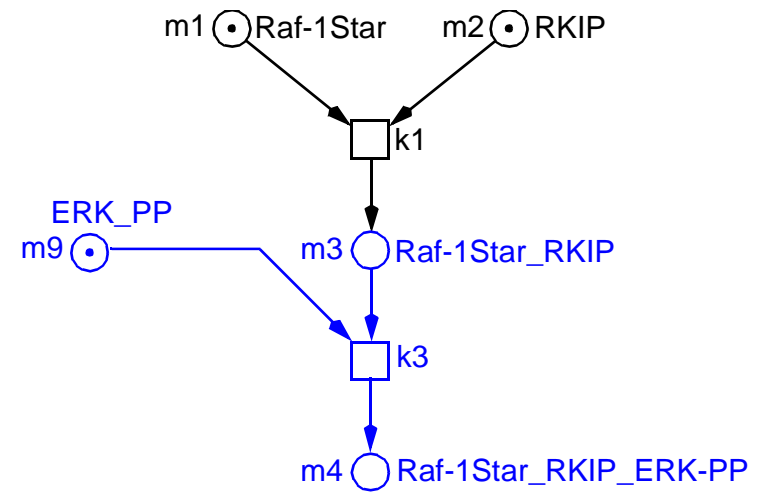
T-INVARIANT'S RUN

- ❑ **partial order structure**
- ❑ T-invariant's unfolding to describe its behaviour



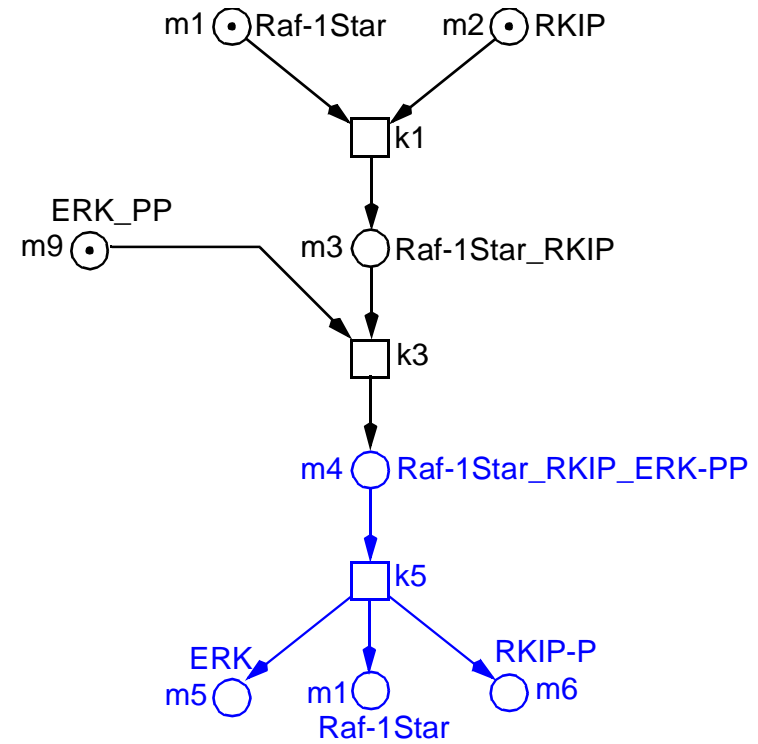
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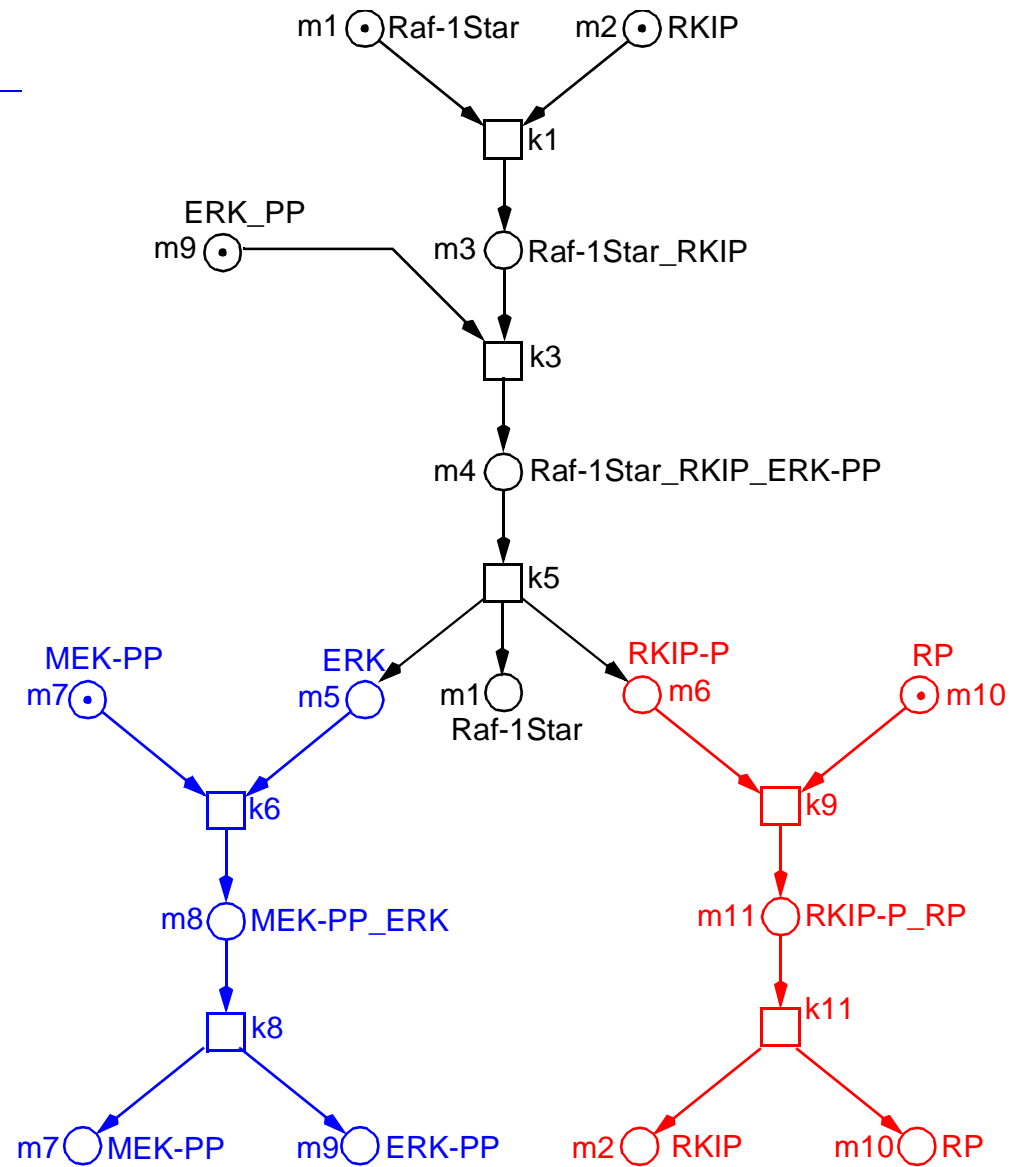
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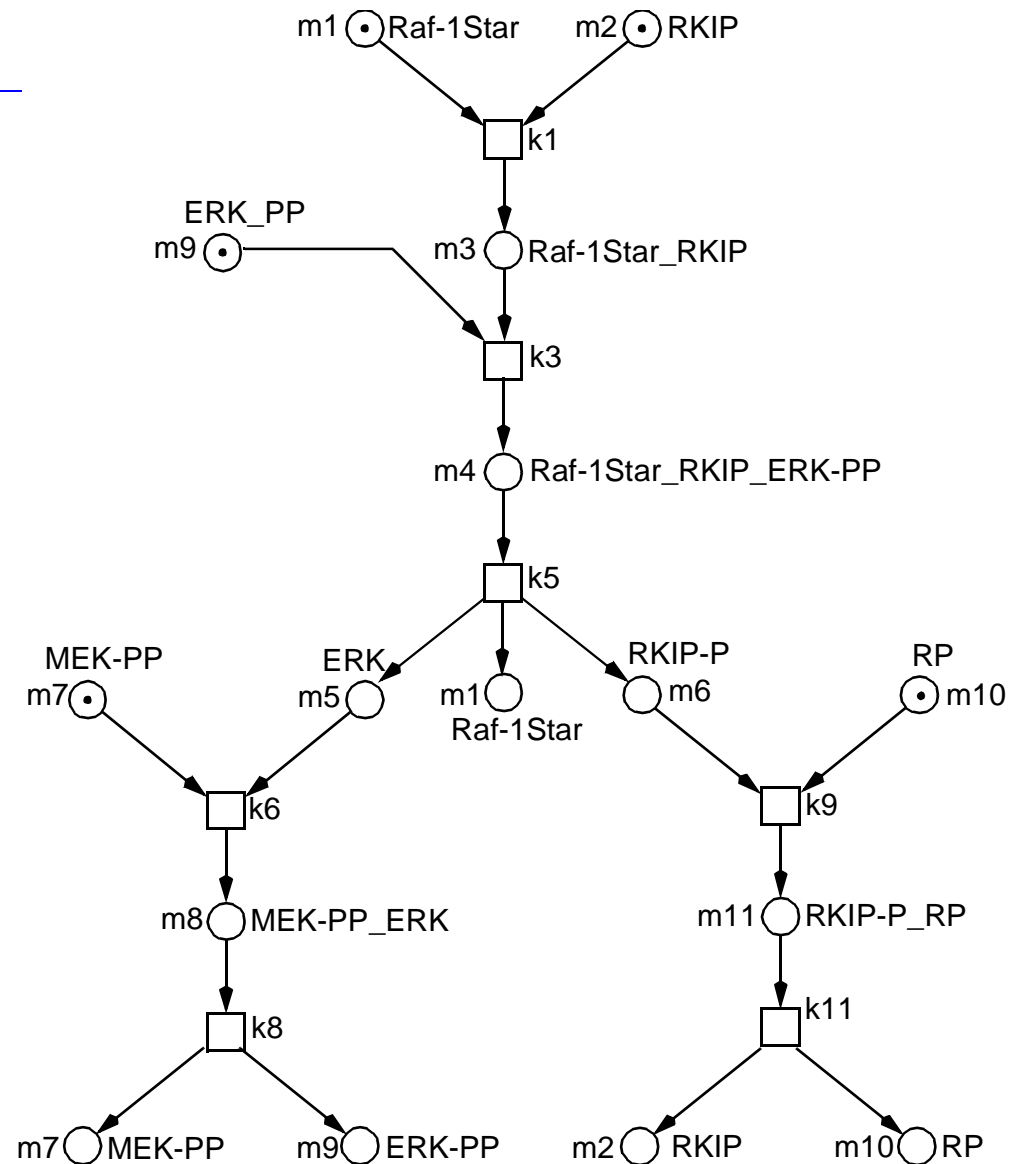
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T-INVARIANT'S RUN

- **partial order structure**
- **T-invariant's unfolding to describe its behaviour**
- **labelled condition / event net**
 - > *events (boxes)*
 - *transition occurrences*
 - > *conditions (circles)*
 - *involved compounds*
- **occurrence net**
 - > *acyclic*
 - > *no backward branching conditions*
 - > *infinite*



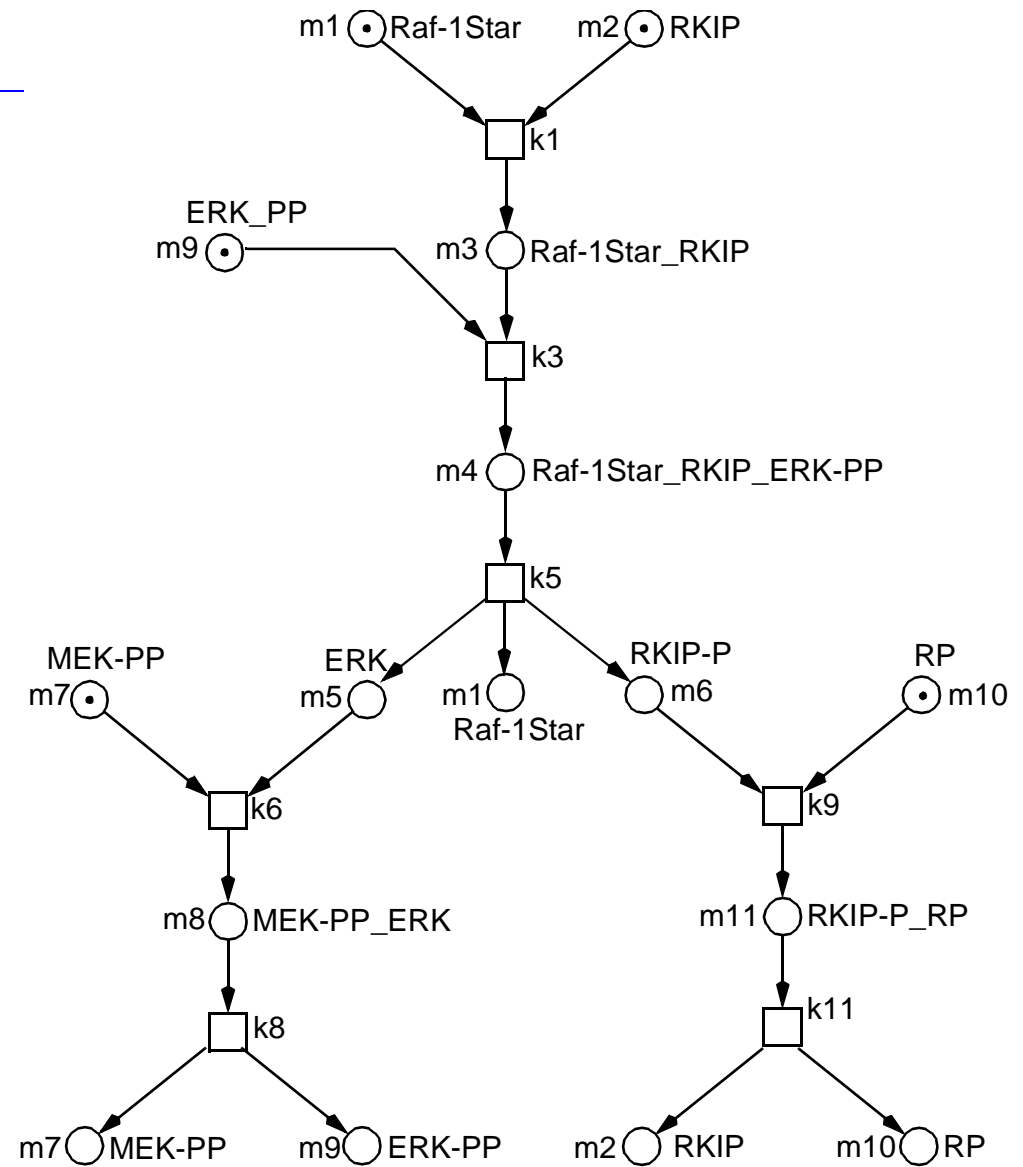
MARKING AND CUTS

marking

- > interleaving semantics
- > system state
- > nodes in reachability graph

cut

- > partial order semantics
- > maximal set of concurrent conditions



MARKING AND CUTS

□ marking

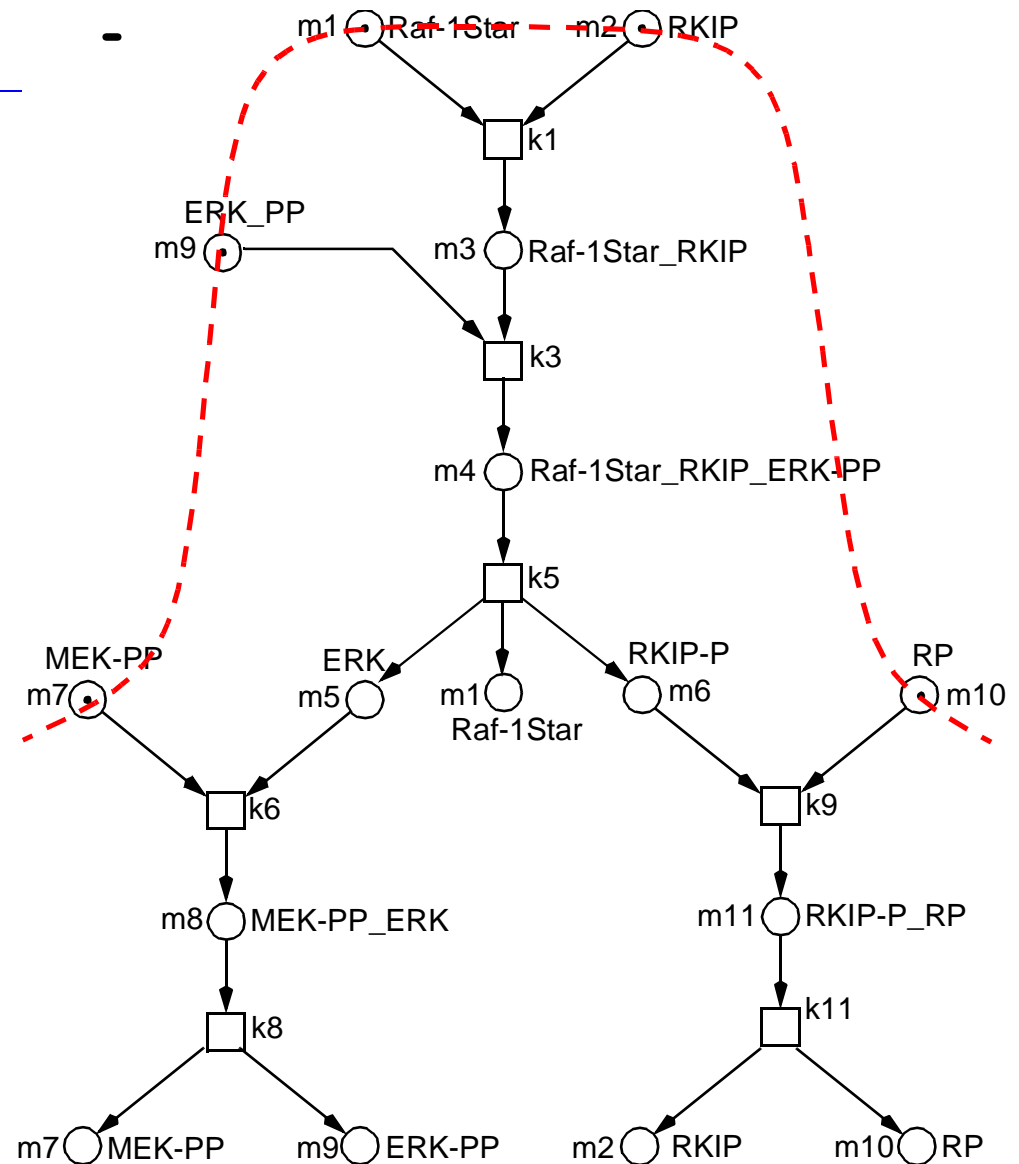
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□ examples

- > initial marking



MARKING AND CUTS

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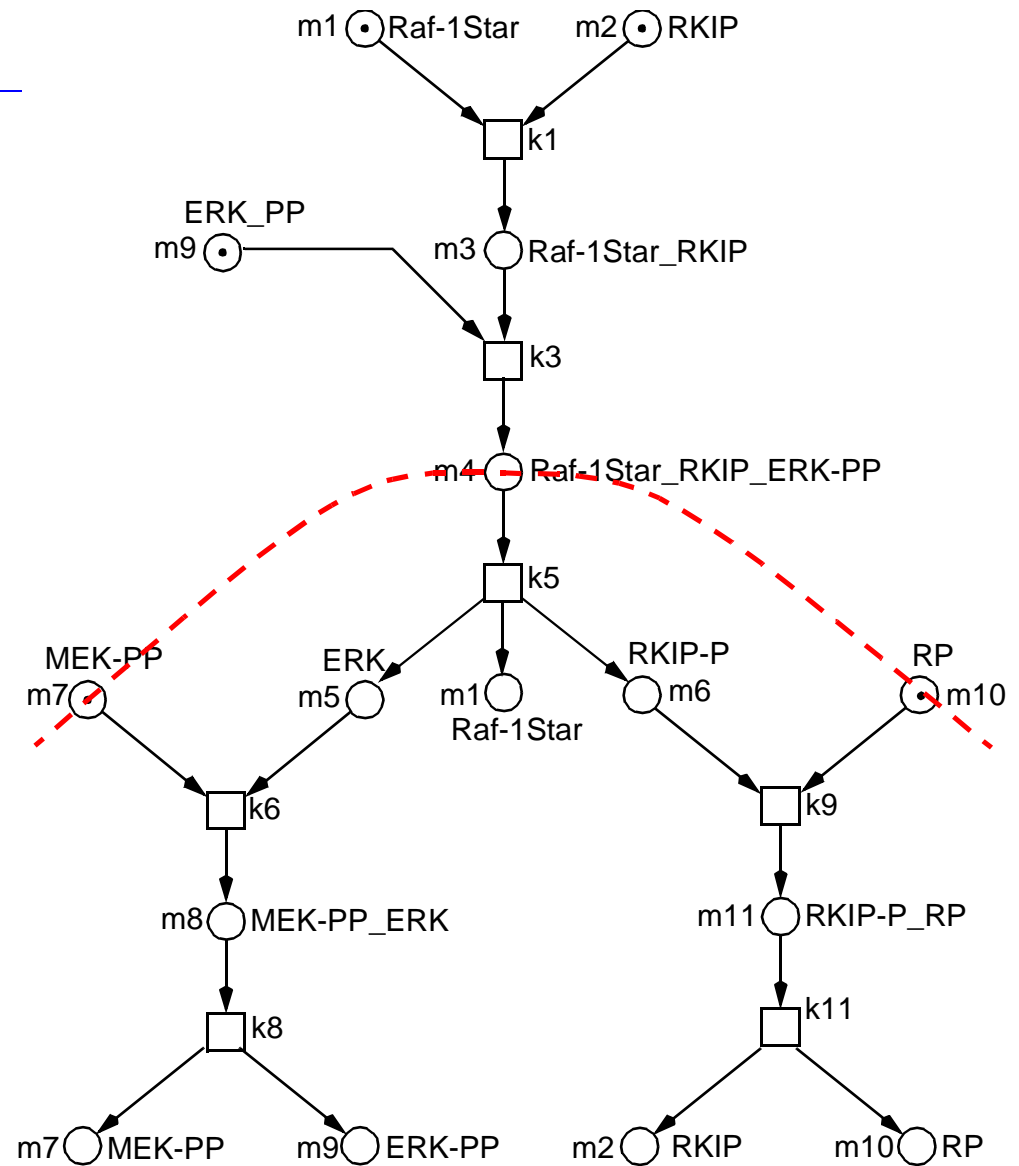
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- > initial marking
- > marking reached by *k1-k3*



MARKING AND CUTS

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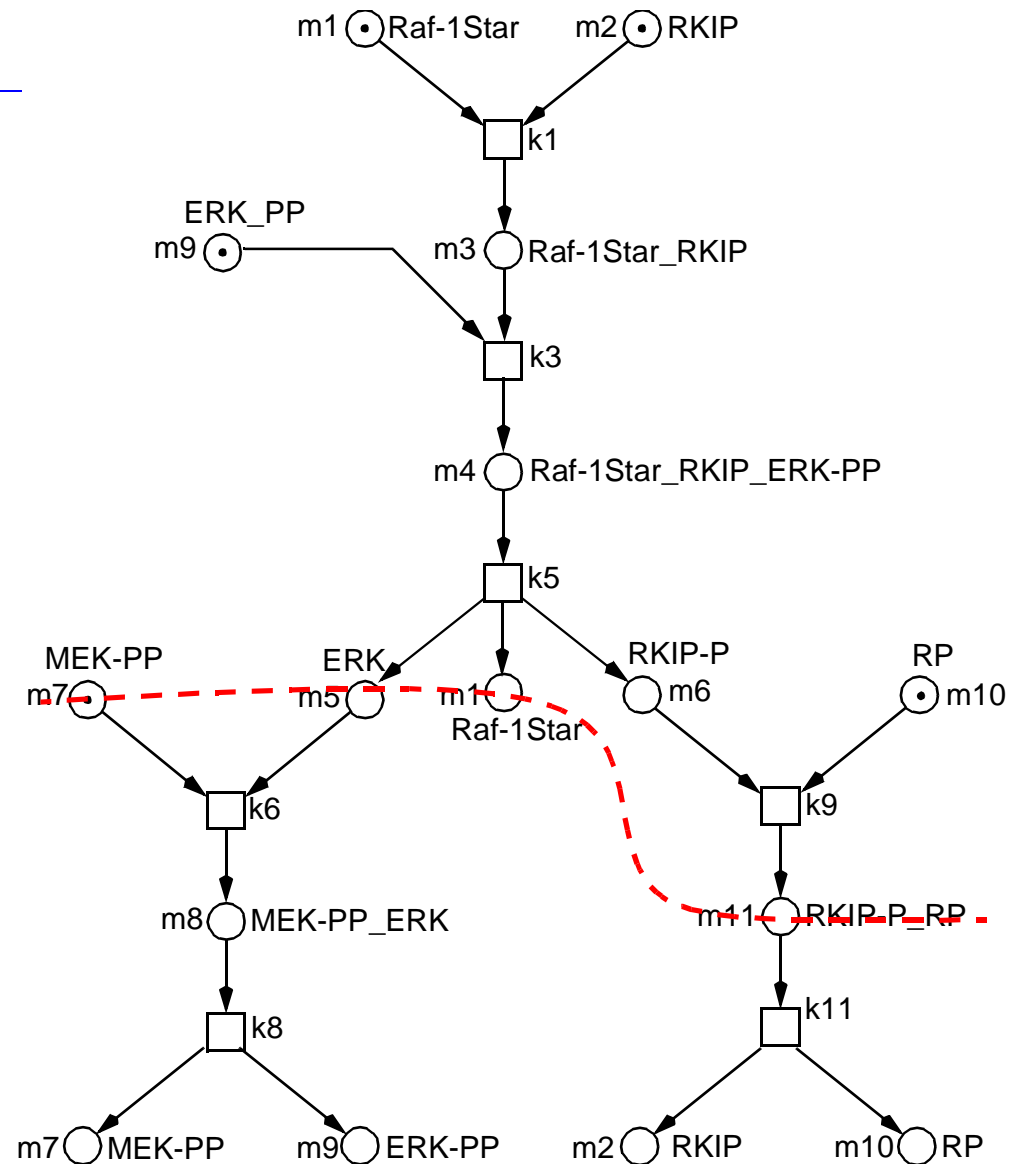
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- > marking reached by *k1-k3-k5-k9*



MARKING AND CUTS

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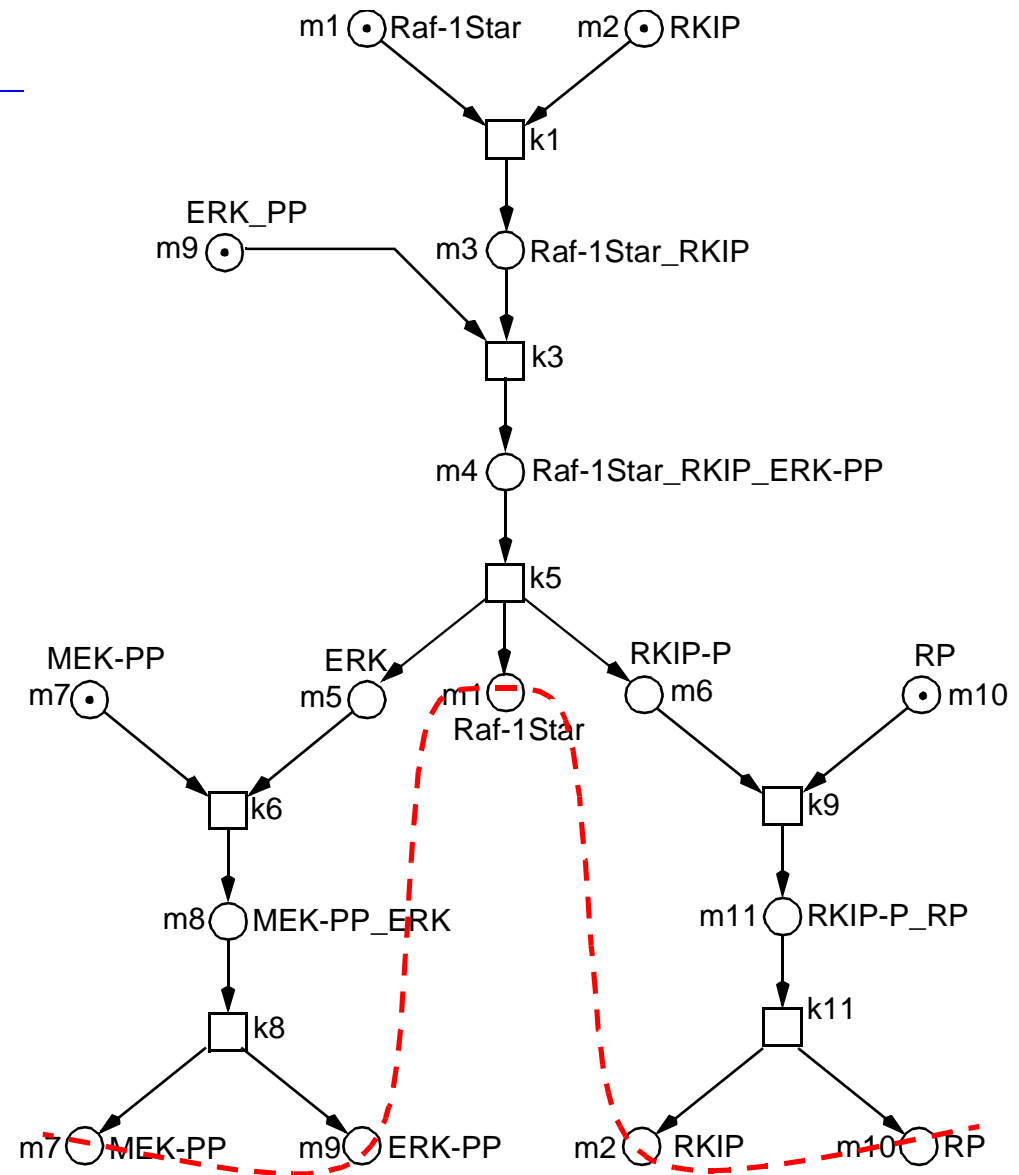
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- > initial marking
- > marking reached by $k1-k3-k5-(k6-k8 \parallel k9-k11)$



MARKING AND CUTS

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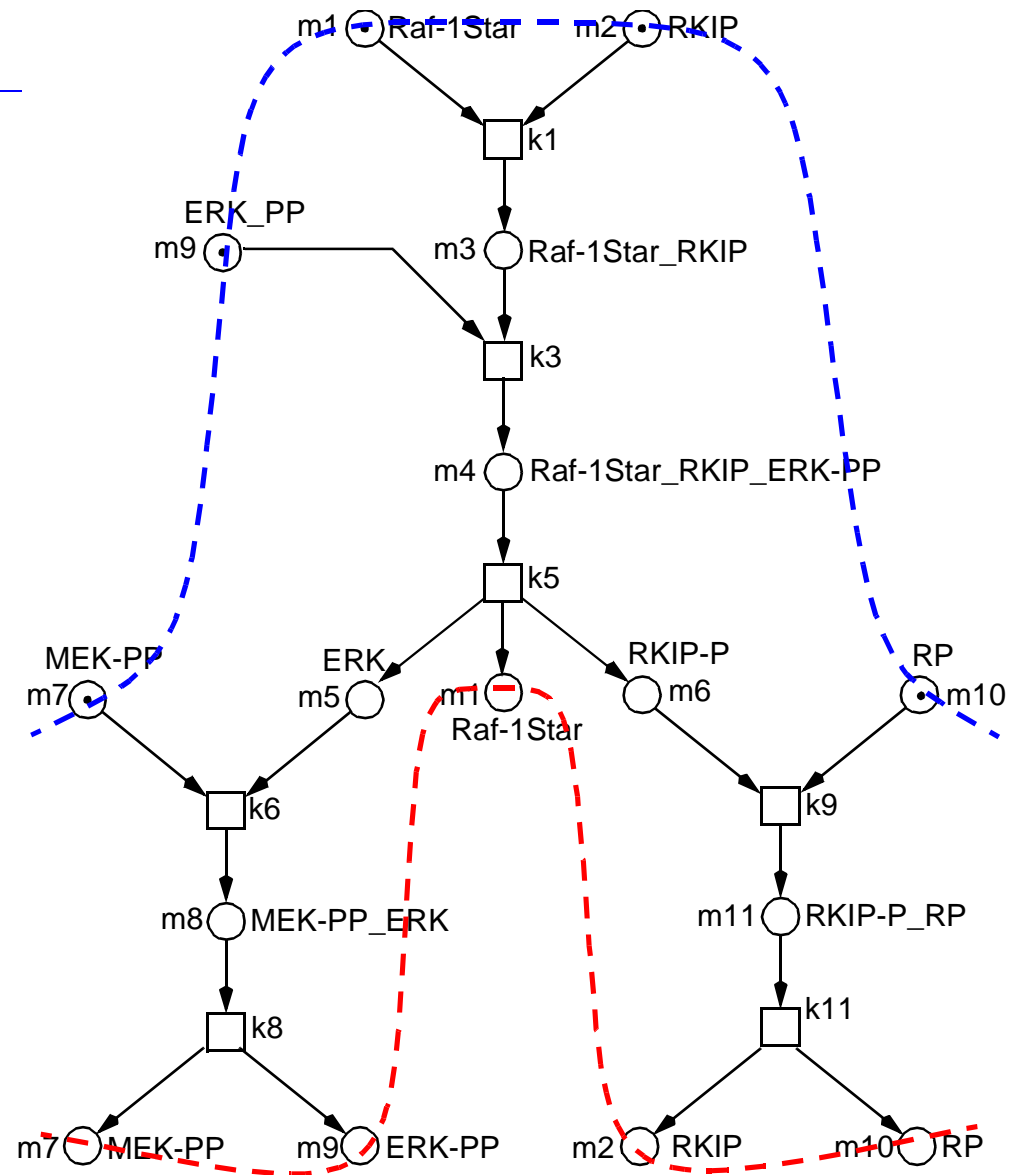
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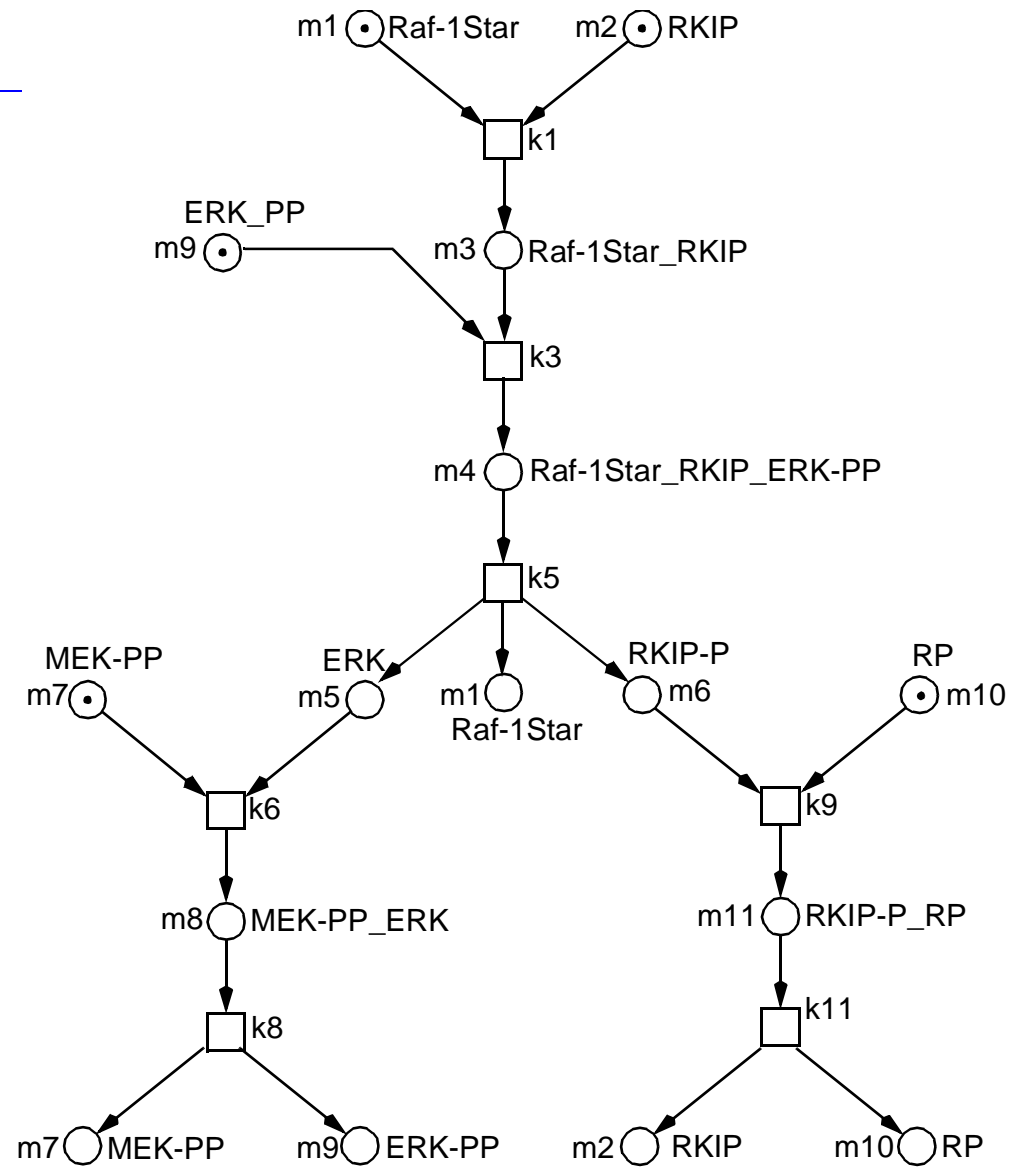
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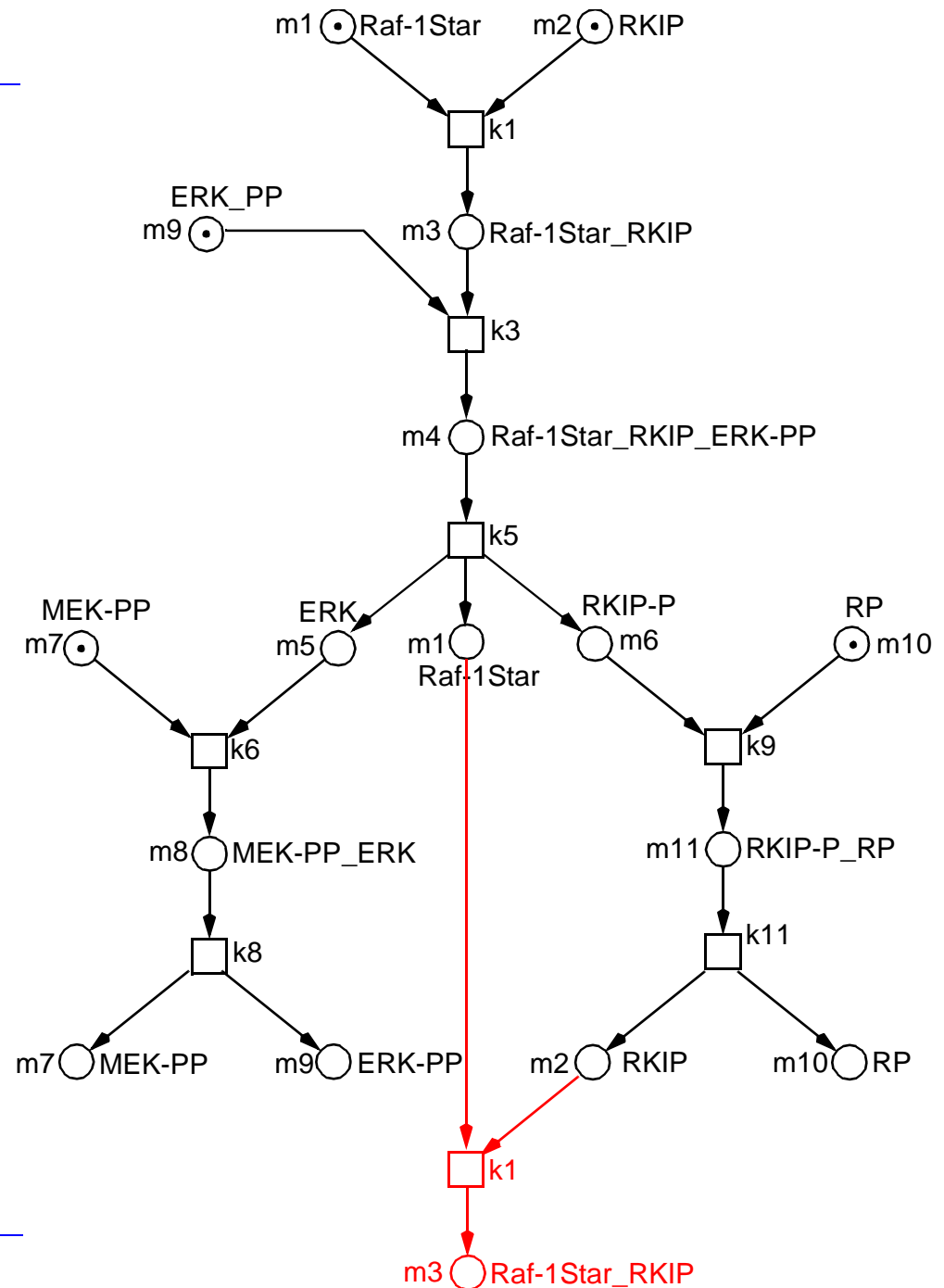
PARTIAL ORDER SEMANTICS

- all (infinite) partial order runs
- any prefix
 - > *finite*
 - > *feasible*
- complete prefix
 - > *markings = cuts*



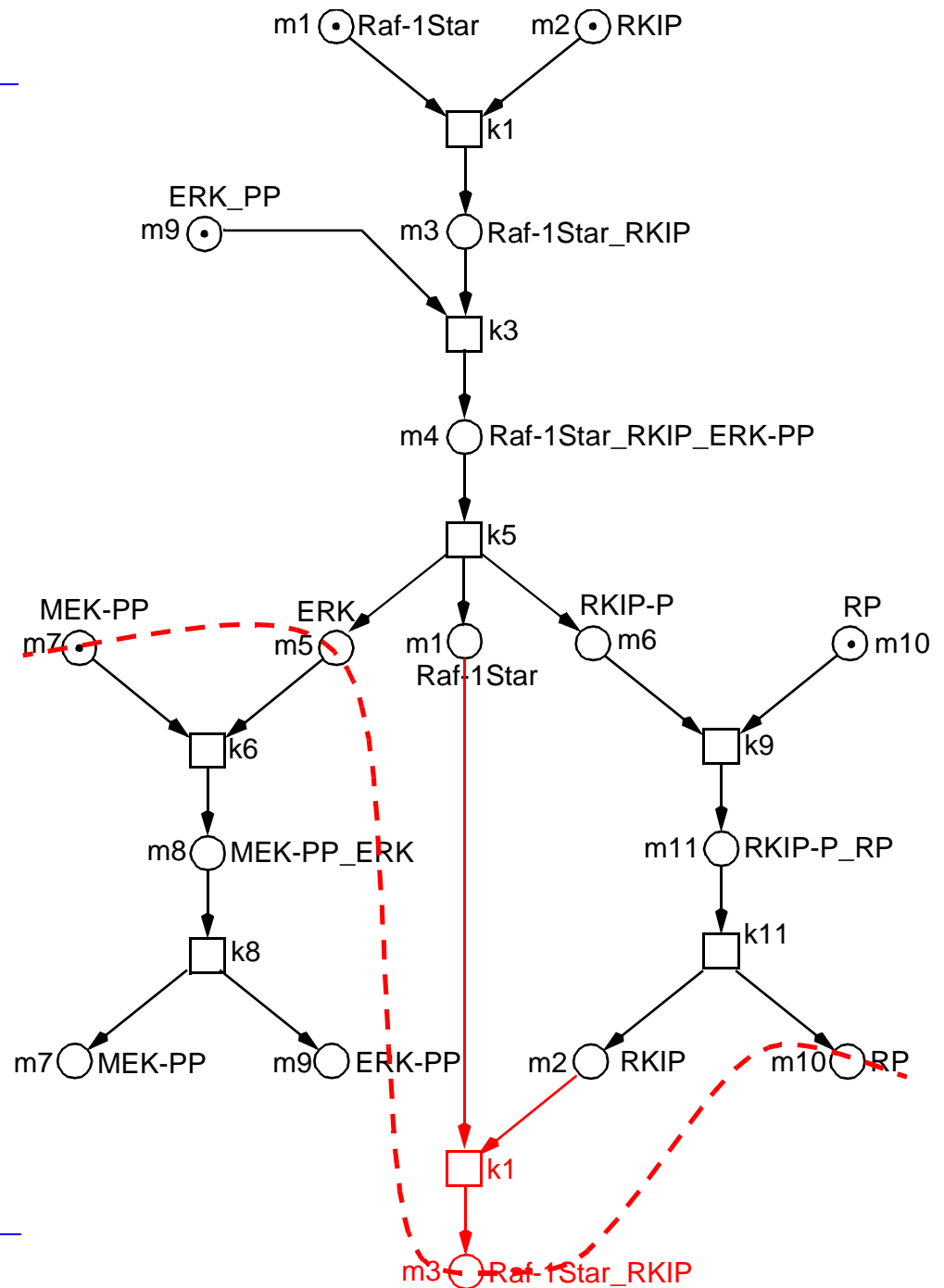
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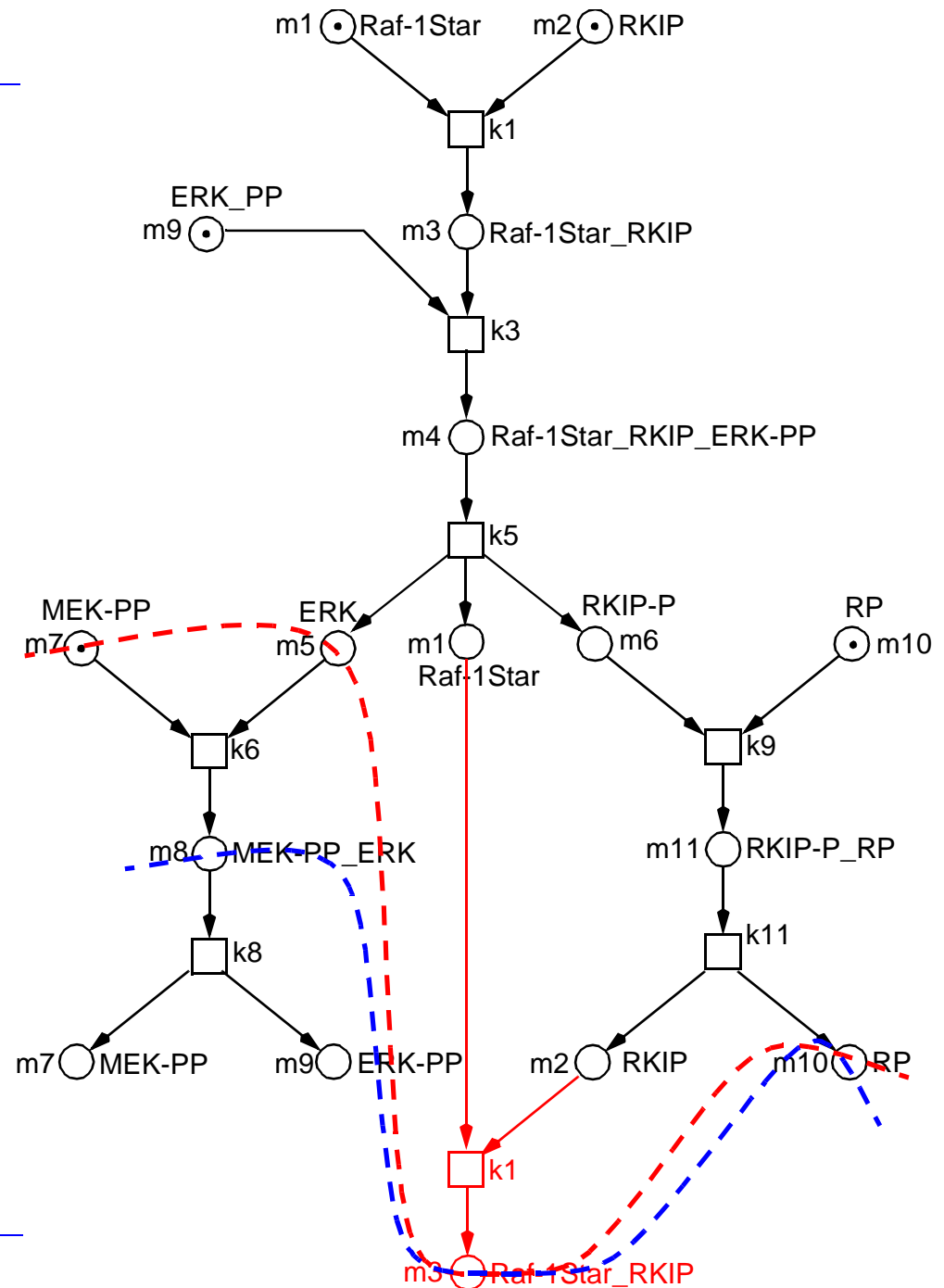
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 - > *markings = cuts*
- **new cuts**
 - > *k1-k3-k5-k9-k11-k1*



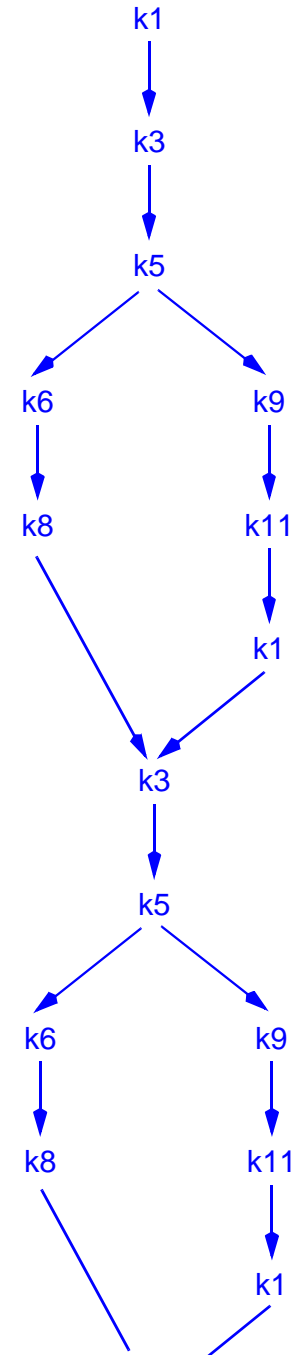
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 - > *markings = cuts*
- **new cuts**
 - > *k1-k3-k5-k9-k11-k1*
 - > *k1-k3-k5-(k6 || k9-k11-k1)*



PARTIAL ORDER SEMANTICS

- infinite partial order run of the essential T-invariant
- short-cut notation



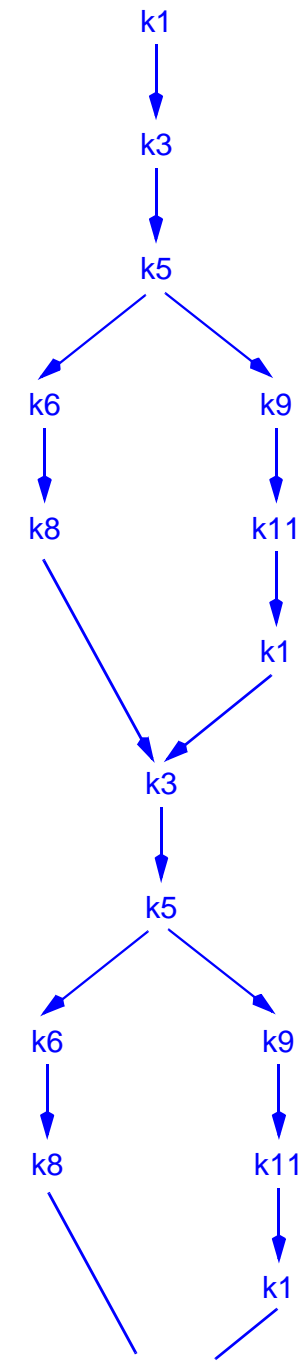
PARTIAL ORDER SEMANTICS

□ infinite partial order run
of the essential T-invariant

□ short-cut notation

□ **DISCLAIMER**

-> *behaviour induced by
trivial t-invariants
not considered here*



□ 1-bounded nets

-> *complete prefix construction*

-> *CTL₀ - model checking*

-> *very efficient if moderate amount of dynamic conflicts*

□ bounded / unbounded nets

-> *algorithms: yes*

-> *tools: ?*

□ representation of bionetworks by Petri nets

-> *partial order representation*

-> *better comprehension*

-> *formal semantics*

-> *various sound analysis techniques*

-> *unifying view*

□ purposes

-> *animation*

-> *to experience the model*

-> *model validation against consistency criteria*

-> *to increase confidence*

-> *qualitative / quantitative behaviour prediction*

-> *new insights*

□ two-step model development

-> *qualitative models* -> *discrete Petri nets*

-> *quantitative models* -> *continuous Petri nets = ODEs*

THANKS !