

A semantic equivalence motivated by time-scale differences

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Outline

Bio-PEPA

Motivating example

Fast-slow bisimilarity

Proof technique

Congruence

Conclusions



Bio-PEPA

- ▶ stochastic process algebra for modelling biological systems [Ciocchetta and Hillston 2008]



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- ▶ quasi-steady-state assumption, Michaelis-Menten
- ▶ qualitative – consider action, not rate
- ▶ allows parameter fitting on fewer parameters

Bio-PEPA syntax

- ▶ two-level syntax



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- ▶ sequential component, species

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- ▶ work with a more constrained form



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- ▶ well-defined Bio-PEPA model component with levels
 - ▶ minimum and maximum concentrations/number of molecules
 - ▶ fix step size, convert to minimum and maximum levels
 - ▶ species S : 0 to N_S levels



Bio-PEPA semantics

- ▶ operational semantics for capability relation \rightarrow_c



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- ▶ Prefix rules

$$((\alpha, \kappa) \downarrow S)(\ell) \xrightarrow{(\alpha, [S: \downarrow(\ell, \kappa)])}_c S(\ell - \kappa) \quad \kappa \leq \ell \leq N_S$$

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Bio-PEPA semantics (continued)

- ▶ Cooperation for $\alpha \in L$

$$\frac{P \xrightarrow{(\alpha, v)}_c P' \quad Q \xrightarrow{(\alpha, u)}_c Q'}{P \boxtimes_L Q \xrightarrow{(\alpha, v::u)}_c P' \boxtimes_L Q'} \quad \alpha \in L$$



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- ▶ operational semantics for stochastic relation \rightarrow_s

$$\frac{P \xrightarrow{(\alpha, v)}_c P'}{\langle \mathcal{V}, \mathcal{N}, \mathcal{K}, \mathcal{F}, \text{Comp}, P \rangle \xrightarrow{(\alpha, f_\alpha(v, \mathcal{N}, \mathcal{K})/h)}_s \langle \mathcal{V}, \mathcal{N}, \mathcal{K}, \mathcal{F}, \text{Comp}, P' \rangle}$$



Bio-PEPA semantics (continued)

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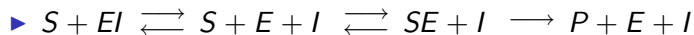
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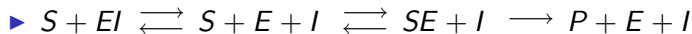
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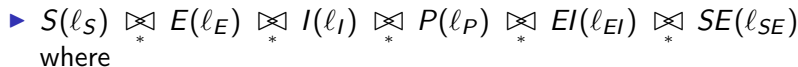
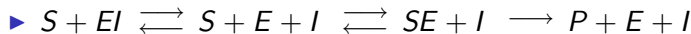
Competitive inhibition, bimolecular



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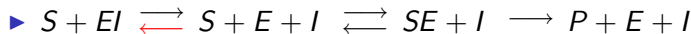
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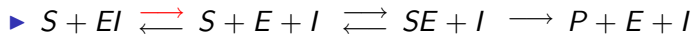
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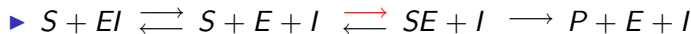
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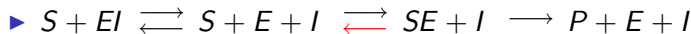
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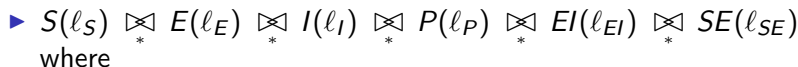
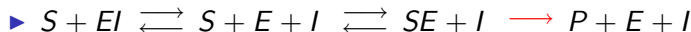
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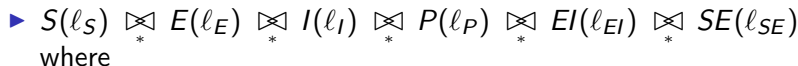
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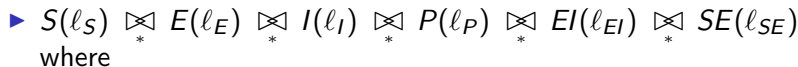
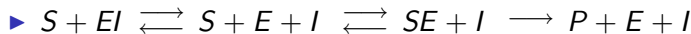
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Competitive inhibition, abstracted



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▶ $S'(l_{S'}) \bowtie_* E'(l_{E'}) \bowtie_* I'(l_{I'}) \bowtie_* P'(l_{P'})$ where



Competitive inhibition, abstracted

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$$\blacktriangleright \text{bimolecular model, states have form } (l_S, l_E, l_I, l_P, l_{EI}, l_{SE})$$



Competitive inhibition, abstracted

$$\blacktriangleright S \xrightarrow{E,I} P$$

$$\blacktriangleright S'(l_{S'}) \boxtimes_* E'(l_{E'}) \boxtimes_* I'(l_{I'}) \boxtimes_* P'(l_{P'}) \text{ where}$$

$$S' \stackrel{\text{def}}{=} (\gamma, 1) \downarrow S'$$

$$E' \stackrel{\text{def}}{=} (\gamma, 1) \oplus E'$$

$$I' \stackrel{\text{def}}{=} (\gamma, 1) \ominus I'$$

$$P' \stackrel{\text{def}}{=} (\gamma, 1) \uparrow P'$$

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 - ▶ partition actions into fast, \mathcal{A}_f and slow, \mathcal{A}_s
 - ▶ define $P \rightarrow P'$ if $P \xrightarrow{(\alpha, w)}_c P'$ and $\alpha \in \mathcal{A}_f$



Fast-slow bisimilarity

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- ▶ fast reactions play same role as τ labelled transitions



Competitive inhibition example

- ▶ first let $\mathcal{A}_f = \{\alpha_1, \alpha_{-1}, \beta_1, \beta_{-1}\}$



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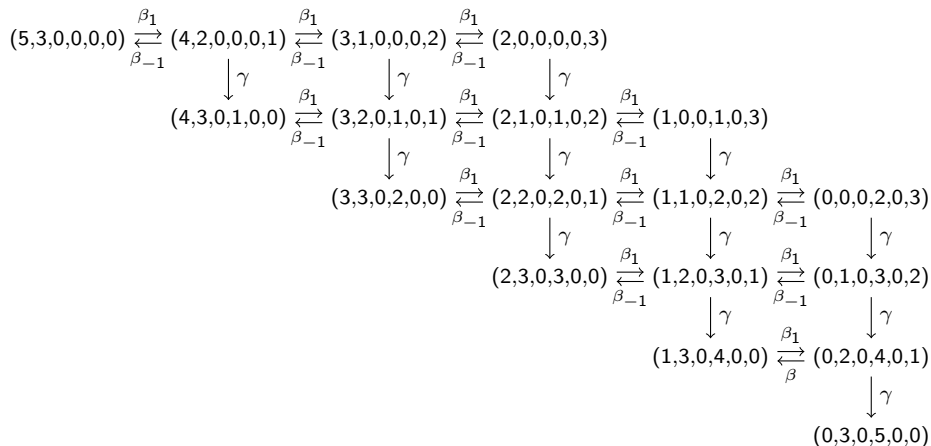
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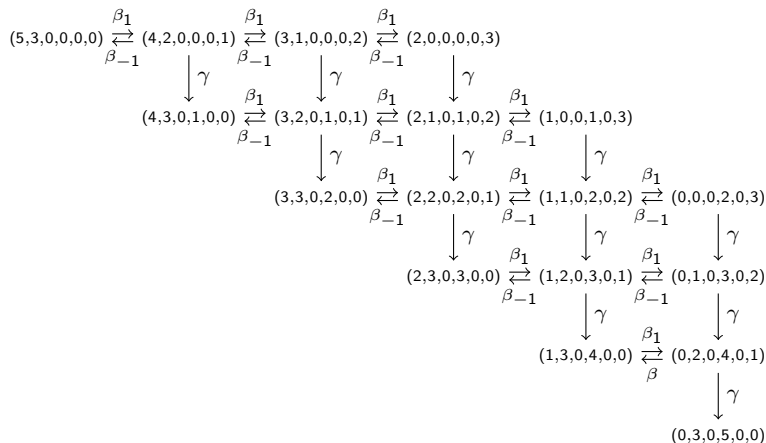
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- ▶ why?
- ▶ consider the labelled transition systems



Transition systems in the case of no inhibitor



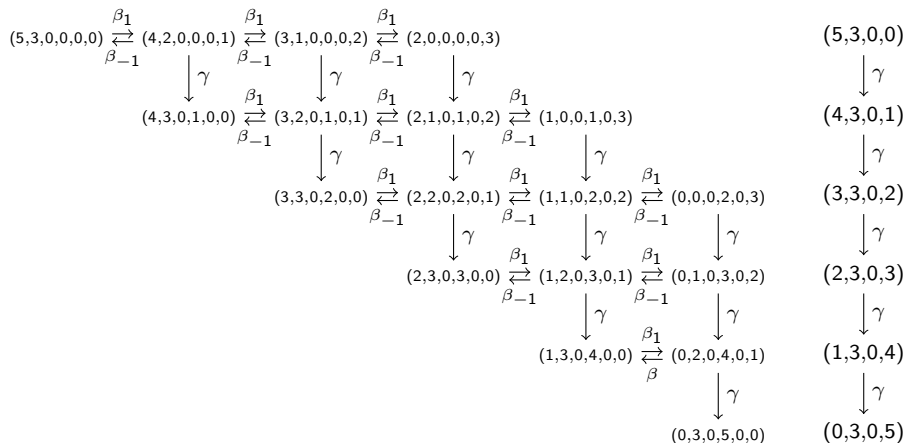
Transition systems in the case of no inhibitor



bimolecular



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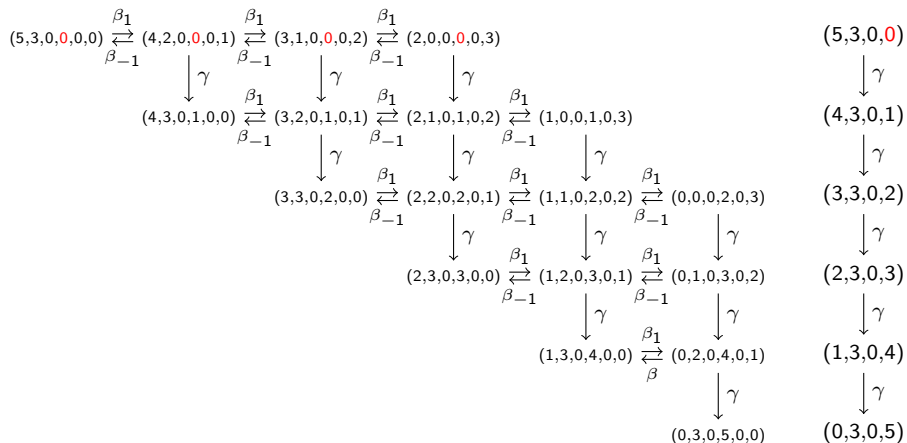


bimolecular

abstracted



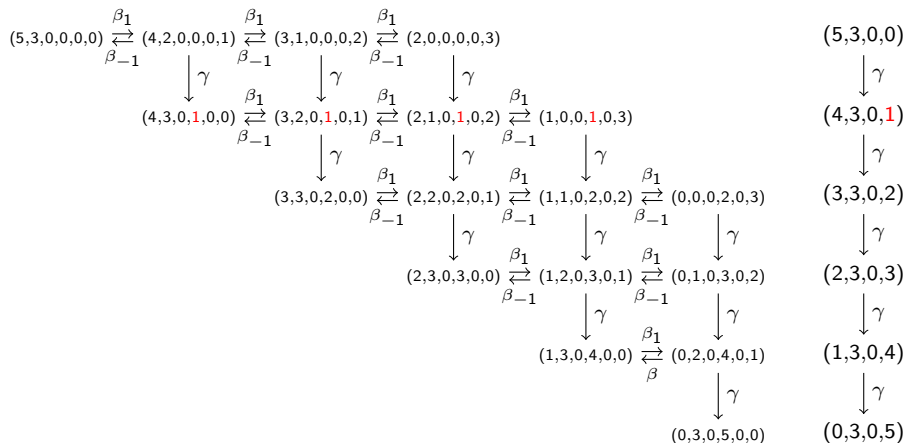
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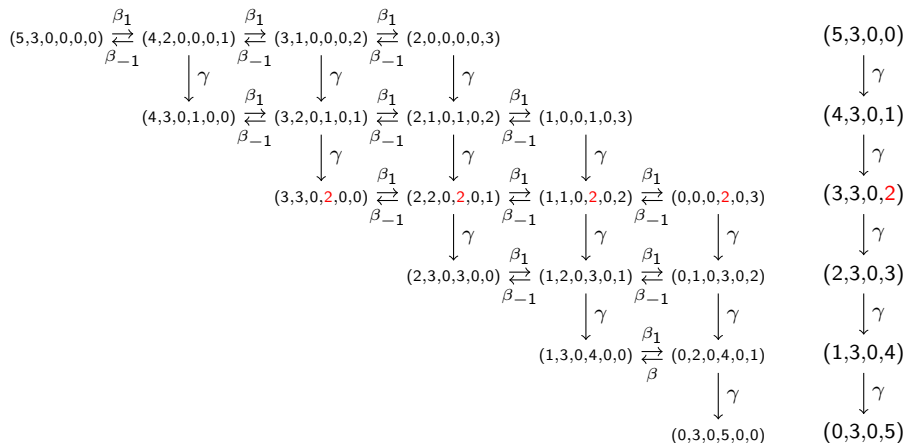
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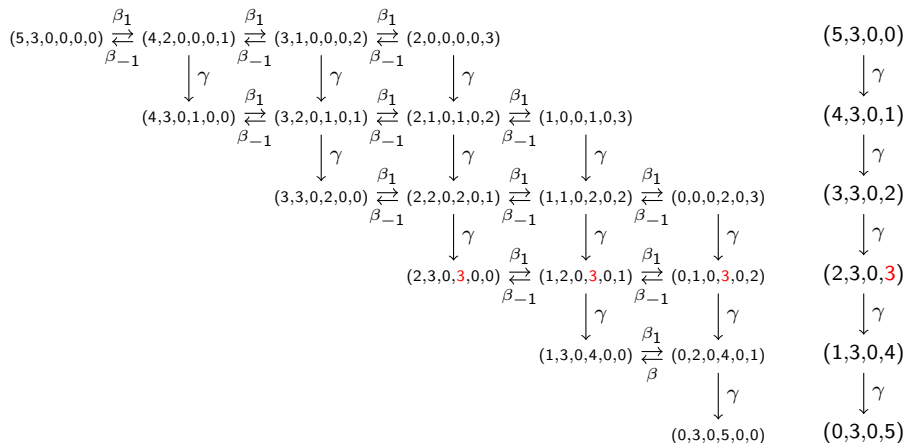


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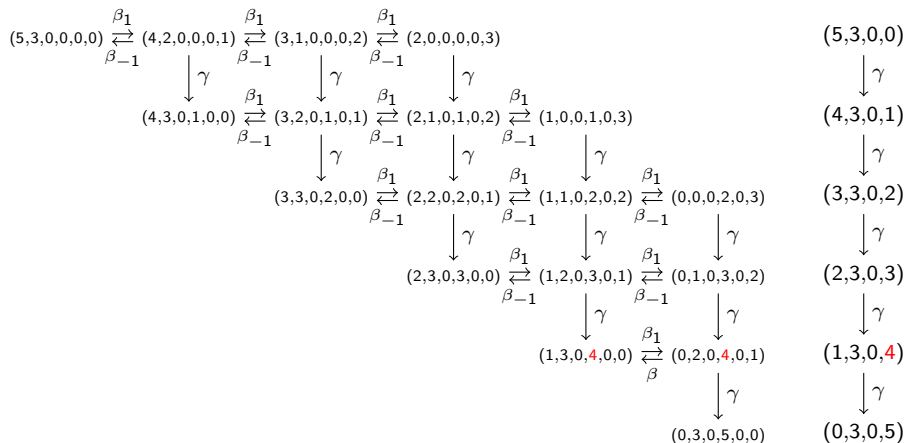
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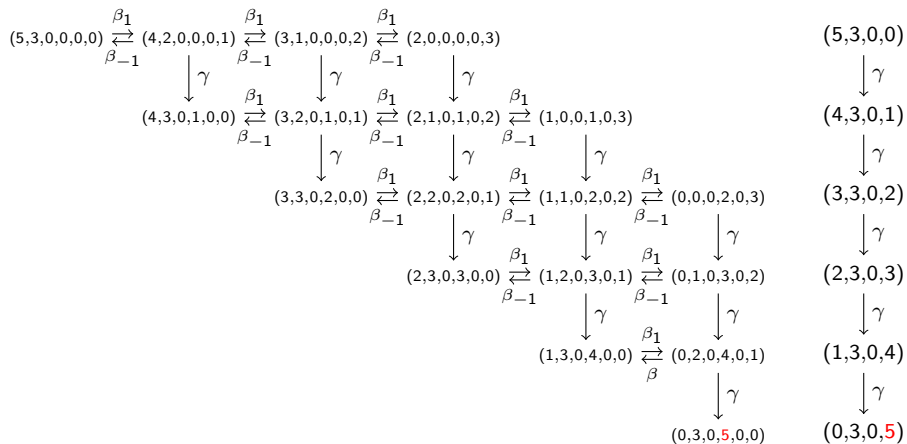


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- ▶ further work: use of invariants to capture match list



Congruence of fast-slow bisimilarity

- ▶ congruence with respect to cooperation if no shared fast reactions, $P_1 \approx_{\mathcal{A}_f} P_2 \Rightarrow P_1 \boxtimes_L Q \approx_{\mathcal{A}_f} P_2 \boxtimes_L Q$



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$$A \stackrel{\text{def}}{=} \sum_{i=1}^n (\alpha_i, \kappa_i) \circ_{\mathbb{P}_i} A \quad \text{and} \quad B \stackrel{\text{def}}{=} \sum_{j=1}^m (\beta_j, \lambda_j) \circ_{\mathbb{P}_j} B$$



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- ▶ congruence with respect to new operator

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Importance of congruence in biological modelling

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- ▶ B , reduced model, smaller state space
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