A semantic equivalence motivated by time-scale differences

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Outline

Bio-PEPA

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

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- qualitative – consider action, not rate
- allows parameter fitting on fewer parameters

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- work with a more constrained form

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- well-defined Bio-PEPA species

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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

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

$$((\alpha,\kappa)\uparrow S)(\ell) \xrightarrow{(\alpha,[S:\uparrow(\ell,\kappa)])}_c S(\ell+\kappa) \qquad 0 \le \ell \le N_S - \kappa$$

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Bio-PEPA semantics (continued)

- Cooperation for $\alpha \in L$

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

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- bimolecular model, states have form $(\ell_S, \ell_E, \ell_I, \ell_P, \ell_{EI}, \ell_{SE})$

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- bimolecular model, states have form $(\ell_S, \ell_E, \ell_I, \ell_P, \ell_{EI}, \ell_{SE})$
- abstracted model, states have form $(\ell_{S'}, \ell_{E'}, \ell_{I'}, \ell_{P'})$

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

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- similar definition to Milner's weak bisimilarity
- fast reactions play same role as τ labelled transitions

Competitive inhibition example

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- relation over state vectors

$$\Big\{((n-(k+j), m-j, 0, k, 0, j), (n-k, m, 0, k)) \mid \\ 0 \leq k \leq n, 0 \leq j \leq \min\{m, n-k\}\Big\}$$

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- this is a fast-slow bisimulation
- why?
- consider the labelled transition systems

Transition systems in the case of no inhibitor

$$
\begin{tikzcd}
(5,3,0,0,0,0) \arrow[r, shift left, "\beta_1"] & (4,2,0,0,0,1) \arrow[l, shift left, "\beta_{-1}"] \arrow[r, shift left, "\beta_1"] \arrow[d, "\gamma"] & (3,1,0,0,0,2) \arrow[l, shift left, "\beta_{-1}"] \arrow[r, shift left, "\beta_1"] \arrow[d, "\gamma"] & (2,0,0,0,0,3) \arrow[l, shift left, "\beta_{-1}"] \arrow[d, "\gamma"] & & \\
 & (4,3,0,1,0,0) \arrow[r, shift left, "\beta_1"] & (3,2,0,1,0,1) \arrow[l, shift left, "\beta_{-1}"] \arrow[r, shift left, "\beta_1"] \arrow[d, "\gamma"] & (2,1,0,1,0,2) \arrow[l, shift left, "\beta_{-1}"] \arrow[r, shift left, "\beta_1"] \arrow[d, "\gamma"] & (1,0,0,1,0,3) \arrow[l, shift left, "\beta_{-1}"] \arrow[d, "\gamma"] & \\
 & & (3,3,0,2,0,0) \arrow[r, shift left, "\beta_1"] & (2,2,0,2,0,1) \arrow[l, shift left, "\beta_{-1}"] \arrow[r, shift left, "\beta_1"] \arrow[d, "\gamma"] & (1,1,0,2,0,2) \arrow[l, shift left, "\beta_{-1}"] \arrow[r, shift left, "\beta_1"] \arrow[d, "\gamma"] & (0,0,0,2,0,3) \arrow[l, shift left, "\beta_{-1}"] \arrow[d, "\gamma"] \\
 & & & (2,3,0,3,0,0) \arrow[r, shift left, "\beta_1"] & (1,2,0,3,0,1) \arrow[l, shift left, "\beta_{-1}"] \arrow[r, shift left, "\beta_1"] \arrow[d, "\gamma"] & (0,1,0,3,0,2) \arrow[l, shift left, "\beta_{-1}"] \arrow[d, "\gamma"] \\
 & & & & (1,3,0,4,0,0) \arrow[r, shift left, "\beta_1"] & (0,2,0,4,0,1) \arrow[l, shift left, "\beta"] \arrow[d, "\gamma"] \\
 & & & & & (0,3,0,5,0,0)
\end{tikzcd}
$$

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& & (3,3,0,2,0,0) \arrow[r, shift left, "\beta_1"] & (2,2,0,2,0,1) \arrow[l, shift left, "\beta_{-1}"] \arrow[r, shift left, "\beta_1"] \arrow[d, "\gamma"] & (1,1,0,2,0,2) \arrow[l, shift left, "\beta_{-1}"] \arrow[r, shift left, "\beta_1"] \arrow[d, "\gamma"] & (0,0,0,2,0,3) \arrow[l, shift left, "\beta_{-1}"] \arrow[d, "\gamma"] \\
& & & (2,3,0,3,0,0) \arrow[r, shift left, "\beta_1"] & (1,2,0,3,0,1) \arrow[l, shift left, "\beta_{-1}"] \arrow[r, shift left, "\beta_1"] \arrow[d, "\gamma"] & (0,1,0,3,0,2) \arrow[l, shift left, "\beta_{-1}"] \arrow[d, "\gamma"] \\
& & & & (1,3,0,4,0,0) \arrow[r, shift left, "\beta_1"] & (0,2,0,4,0,1) \arrow[l, shift left, "\beta"] \arrow[d, "\gamma"] \\
& & & & & (0,3,0,5,0,0)
\end{tikzcd}
$$

bimolecular

Transition systems in the case of no inhibitor

$$
\begin{array}{ccccccccccc}
(5,3,0,0,0,0) & \overset{\beta_1}{\underset{\beta_{-1}}{\rightleftarrows}} & (4,2,0,0,0,1) & \overset{\beta_1}{\underset{\beta_{-1}}{\rightleftarrows}} & (3,1,0,0,0,2) & \overset{\beta_1}{\underset{\beta_{-1}}{\rightleftarrows}} & (2,0,0,0,0,3) & & & & \\
 & & \downarrow\gamma & & \downarrow\gamma & & \downarrow\gamma & & & & \\
 & & (4,3,0,1,0,0) & \overset{\beta_1}{\underset{\beta_{-1}}{\rightleftarrows}} & (3,2,0,1,0,1) & \overset{\beta_1}{\underset{\beta_{-1}}{\rightleftarrows}} & (2,1,0,1,0,2) & \overset{\beta_1}{\underset{\beta_{-1}}{\rightleftarrows}} & (1,0,0,1,0,3) & & \\
 & & & & \downarrow\gamma & & \downarrow\gamma & & \downarrow\gamma & & \\
 & & & & (3,3,0,2,0,0) & \overset{\beta_1}{\underset{\beta_{-1}}{\rightleftarrows}} & (2,2,0,2,0,1) & \overset{\beta_1}{\underset{\beta_{-1}}{\rightleftarrows}} & (1,1,0,2,0,2) & \overset{\beta_1}{\underset{\beta_{-1}}{\rightleftarrows}} & (0,0,0,2,0,3) \\
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 & & & & & & & & \downarrow\gamma & & \downarrow\gamma \\
 & & & & & & & & (1,3,0,4,0,0) & \overset{\beta_1}{\underset{\beta}{\rightleftarrows}} & (0,2,0,4,0,1) \\
 & & & & & & & & & & \downarrow\gamma \\
 & & & & & & & & & & (0,3,0,5,0,0)
\end{array}
\qquad
\begin{array}{c}
(5,3,0,0) \\ \downarrow\gamma \\ (4,3,0,1) \\ \downarrow\gamma \\ (3,3,0,2) \\ \downarrow\gamma \\ (2,3,0,3) \\ \downarrow\gamma \\ (1,3,0,4) \\ \downarrow\gamma \\ (0,3,0,5)
\end{array}
$$

bimolecular

abstracted

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& & & & (1,3,0,4,0,0) \arrow[r, shift left, "\beta_1"] & (0,2,0,4,0,1) \arrow[l, shift left, "\beta"] \arrow[d, "\gamma"] \\
& & & & & (0,3,0,5,0,0)
\end{tikzcd}
\qquad
\begin{tikzcd}
(5,3,0,0) \arrow[d, "\gamma"] \\
(4,3,0,1) \arrow[d, "\gamma"] \\
(3,3,0,2) \arrow[d, "\gamma"] \\
(2,3,0,3) \arrow[d, "\gamma"] \\
(1,3,0,4) \arrow[d, "\gamma"] \\
(0,3,0,5)
\end{tikzcd}
$$

bimolecular abstracted

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\begin{array}{ccccccccccc}
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 & & & & & & & & & & (0,3,0,5,0,0)
\end{array}
\qquad
\begin{array}{c}
(5,3,0,0) \\
\downarrow\gamma \\
(4,3,0,1) \\
\downarrow\gamma \\
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(2,3,0,3) \\
\downarrow\gamma \\
(1,3,0,4) \\
\downarrow\gamma \\
(0,3,0,5)
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$$

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& & & & (1,3,0,4,0,0) \arrow[r, shift left, "\beta_1"] & (0,2,0,4,0,1) \arrow[l, shift left, "\beta"] \arrow[d, "\gamma"] \\
& & & & & (0,3,0,5,0,0)
\end{tikzcd}
$$

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(5,3,0,0) \arrow[d, "\gamma"] \\
(4,3,0,1) \arrow[d, "\gamma"] \\
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(1,3,0,4) \arrow[d, "\gamma"] \\
(0,3,0,5)
\end{tikzcd}
$$

bimolecular

abstracted

Transition systems in the case of no inhibitor

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\begin{tikzcd}
(5,3,0,0,0,0) \arrow[r, shift left, "\beta_1"] \arrow[r, <-, shift right, "\beta_{-1}"'] & (4,2,0,0,0,1) \arrow[d, "\gamma"] \arrow[r, shift left, "\beta_1"] \arrow[r, <-, shift right, "\beta_{-1}"'] & (3,1,0,0,0,2) \arrow[d, "\gamma"] \arrow[r, shift left, "\beta_1"] \arrow[r, <-, shift right, "\beta_{-1}"'] & (2,0,0,0,0,3) \arrow[d, "\gamma"] & & \\
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& & & & & (0,3,0,{\color{red}5},0,0) &
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- are $(n, m, p, 0, 0, 0)$ and $(n, m, p, 0)$ fast-slow bisimilar?

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- relation over state vectors

$$\Big\{((n-(k+j), m-(j+l), p-l, k, l, j), (n-k, m, p, k)) \mid$$
$$0 \le k \le n, 0 \le j \le \min\{m, n-k\}, 0 \le l \le p, j+l \le m\Big\}$$

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- further work: use of invariants to capture match list

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

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