Bisimulations for biology

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Joint work with Jane Hillston and Federica Ciocchetta

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Bio-PEPA

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

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  2. get ideas from biology – fast/slow, lumping of species
  3. use existing equivalences – bisimulation-based
- mostly qualitative – consider action, not rate

Bio-PEPA syntax

- sequential component, species

$$S ::= (\alpha, \kappa) \texttt{ op } S \mid S + S \qquad \texttt{op} \in \{\uparrow, \downarrow, \oplus, \ominus, \odot\}$$

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- well-defined Bio-PEPA model component with levels
  - minimum and maximum concentrations/number of molecules
  - converted to minimum and maximum levels
  - species S: 0 to N_S levels

Example: reaction with enzyme

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S &\stackrel{\mathit{def}}{=} (\alpha, 1) \downarrow S + (\beta, 1) \uparrow S \\
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$$S' \stackrel{\mathit{def}}{=} (\gamma, 1) \downarrow S' \quad E' \stackrel{\mathit{def}}{=} (\gamma, 1) \oplus E' \quad P' \stackrel{\mathit{def}}{=} (\gamma, 1) \uparrow P'$$

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

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Bio-PEPA semantics (continued)

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Example: reaction with enzyme, max level 3

- state vector (S, E, SE, P) and $N_S = N_E = N_{SE} = N_P = 3$

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\begin{tikzcd}
(3,3,0,0) \arrow[r, shift left, "\alpha"] & (2,2,1,0) \arrow[l, shift left, "\beta"] \arrow[r, shift left, "\alpha"] \arrow[d, "\gamma"] & (1,1,2,0) \arrow[l, shift left, "\beta"] \arrow[r, shift left, "\alpha"] \arrow[d, "\gamma"] & (0,0,3,0) \arrow[l, shift left, "\beta"] \arrow[d, "\gamma"] \\
 & (2,3,0,1) \arrow[r, shift left, "\alpha"] & (1,2,1,1) \arrow[l, shift left, "\beta"] \arrow[r, shift left, "\alpha"] \arrow[d, "\gamma"] & (0,1,2,1) \arrow[l, shift left, "\beta"] \arrow[d, "\gamma"] \\
 & & (1,3,0,2) \arrow[r, shift left, "\alpha"] & (0,2,1,2) \arrow[l, shift left, "\beta"] \arrow[d, "\gamma"] \\
 & & & (0,3,0,3)
\end{tikzcd}
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Example: reaction with enzyme, max level 7

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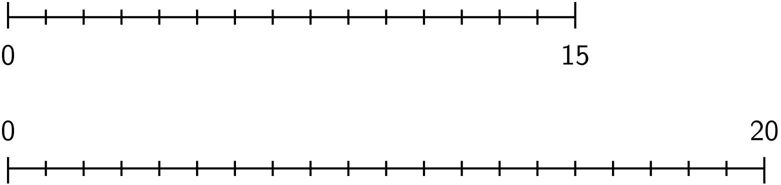
\begin{tikzcd}
7700 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] & 6610 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] \arrow[d, "\gamma"] & 5520 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] \arrow[d, "\gamma"] & 4430 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] \arrow[d, "\gamma"] & 3340 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] \arrow[d, "\gamma"] & 2250 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] \arrow[d, "\gamma"] & 1160 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] \arrow[d, "\gamma"] & 0070 \arrow[d, "\gamma"] \\
 & 6701 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] & 5611 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] \arrow[d, "\gamma"] & 4521 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] \arrow[d, "\gamma"] & 3431 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] \arrow[d, "\gamma"] & 2341 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] \arrow[d, "\gamma"] & 1251 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] \arrow[d, "\gamma"] & 0161 \arrow[d, "\gamma"] \\
 & & 5702 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] & 4612 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] \arrow[d, "\gamma"] & 3522 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] \arrow[d, "\gamma"] & 2432 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] \arrow[d, "\gamma"] & 1342 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] \arrow[d, "\gamma"] & 0252 \arrow[d, "\gamma"] \\
 & & & 4703 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] & 3613 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] \arrow[d, "\gamma"] & 2523 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] \arrow[d, "\gamma"] & 1433 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] \arrow[d, "\gamma"] & 0342 \arrow[d, "\gamma"] \\
 & & & & 3704 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] & 2614 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] \arrow[d, "\gamma"] & 1524 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] \arrow[d, "\gamma"] & 0614 \arrow[d, "\gamma"] \\
 & & & & & 2705 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] & 1615 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] \arrow[d, "\gamma"] & 0525 \arrow[d, "\gamma"] \\
 & & & & & & 1706 \arrow[r, shift left, "\alpha"] \arrow[r, leftarrow, shift right, "\beta"'] & 0616 \arrow[d, "\gamma"] \\
 & & & & & & & 0707
\end{tikzcd}
$$

Motivating example

- $B \stackrel{def}{=} (\alpha, 3) \downarrow B + (\beta, 4) \uparrow B + (\gamma, 1) \uparrow B$



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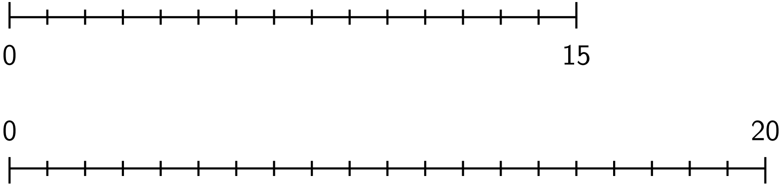

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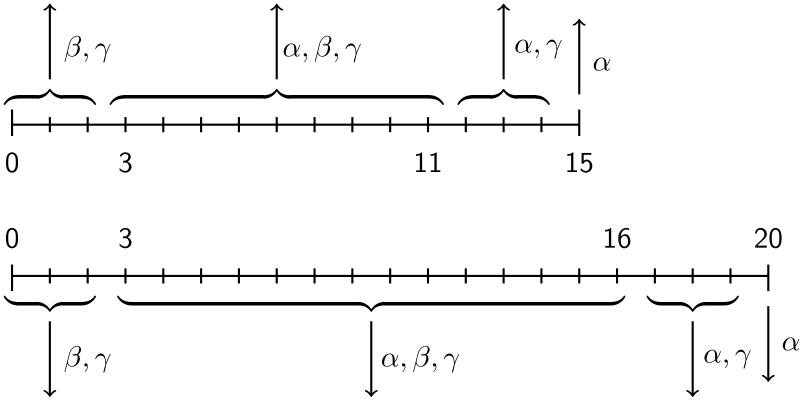

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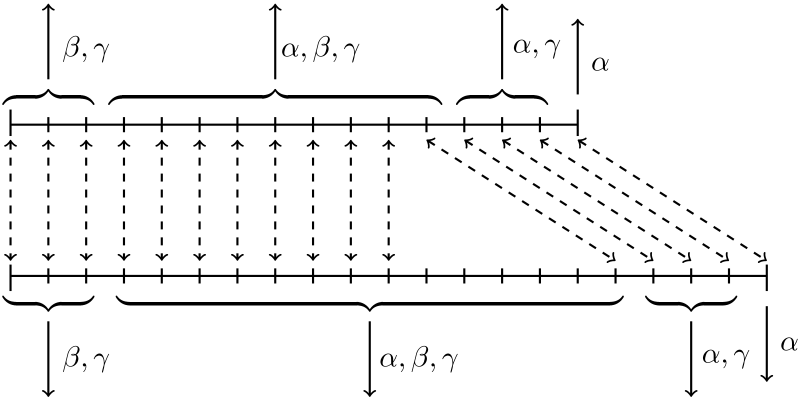

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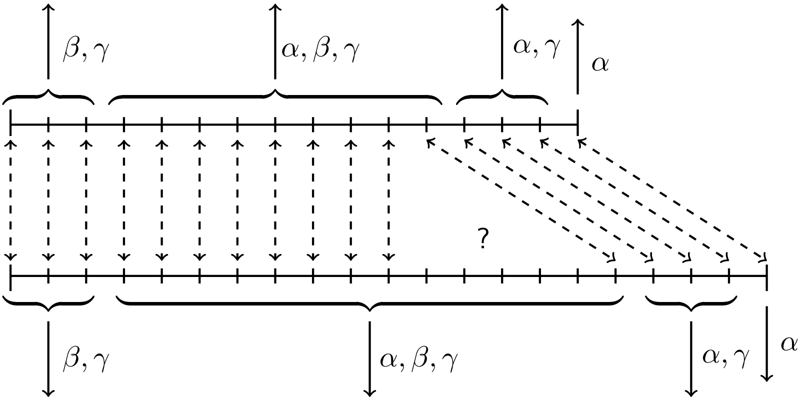

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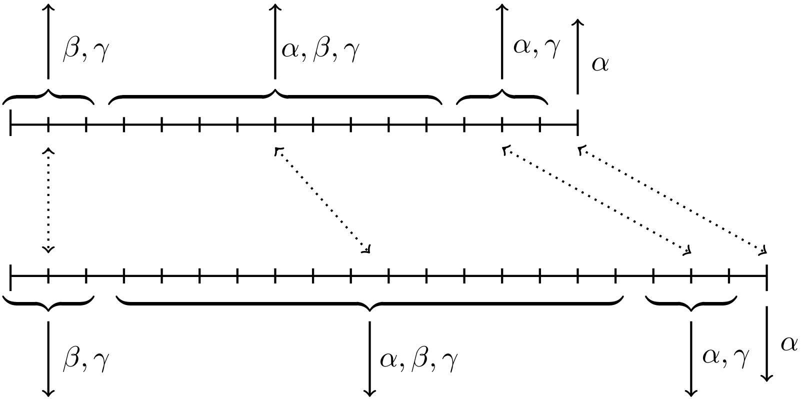

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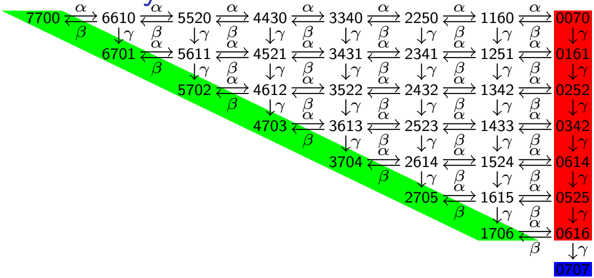
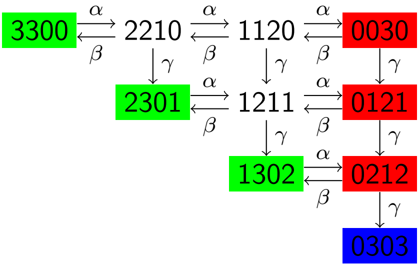
- multiple species: $P^n \doteq P^m$, n and m large enough and a condition necessary for stoichiometry greater than one

Example: reaction with enzyme





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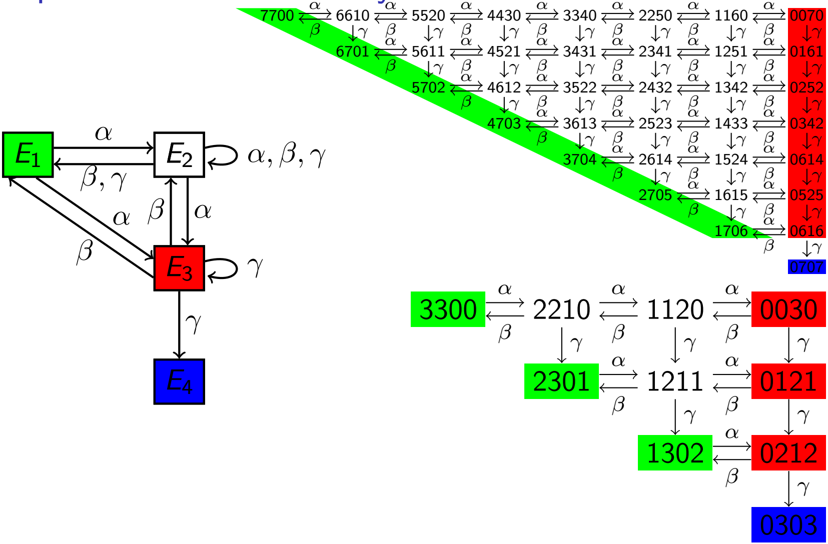

Motivating example

$$S(3) \underset{*}{\bowtie} E(3) \underset{*}{\bowtie} SE(0) \underset{*}{\bowtie} P(0) \qquad S'(3) \underset{*}{\bowtie} E'(3) \underset{*}{\bowtie} P'(0)$$

$$\begin{tikzcd}
3300 \arrow[r, shift left, "\alpha"] & 2210 \arrow[l, shift left, "\beta"] \arrow[r, shift left, "\alpha"] \arrow[d, "\gamma"] & 1120 \arrow[l, shift left, "\beta"] \arrow[r, shift left, "\alpha"] \arrow[d, "\gamma"] & 0030 \arrow[l, shift left, "\beta"] \arrow[d, "\gamma"] \\
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 & & & 0303
\end{tikzcd}
\qquad
\begin{tikzcd}
330 \arrow[d, "\gamma"] \\
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033
\end{tikzcd}$$

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- congruence of cooperation when no shared fast actions

Motivating example revisited

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- consider general notion of bisimulation based on function

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- congruence for all operators under certain conditions

Lumping of species

$$\begin{tikzcd}[column sep=small] & J_1 \arrow[dr] & \\ A \arrow[ur] \arrow[dr] & & B \\ & J_2 \arrow[ur] & \end{tikzcd}$$

$$A \longrightarrow J \longrightarrow B$$

$$\begin{aligned} A' &\stackrel{\mathit{def}}{=} (\alpha_1, 1)\!\downarrow\! A' + (\alpha_2, 1)\!\downarrow\! A' \\ J_1 &\stackrel{\mathit{def}}{=} (\alpha_1, 1)\!\uparrow\! J_1 + (\beta_1, 1)\!\downarrow\! J_1 \\ J_2 &\stackrel{\mathit{def}}{=} (\alpha_2, 1)\!\uparrow\! J_2 + (\beta_2, 1)\!\downarrow\! J_2 \\ B' &\stackrel{\mathit{def}}{=} (\beta_1, 1)\!\uparrow\! B' + (\beta_2, 1)\!\uparrow\! B' \end{aligned}$$

$$\begin{aligned} A &\stackrel{\mathit{def}}{=} (\alpha, 1)\!\downarrow\! A \\ J &\stackrel{\mathit{def}}{=} (\alpha, 1)\!\uparrow\! J + (\beta, 1)\!\downarrow\! J \\ B &\stackrel{\mathit{def}}{=} (\beta, 1)\!\uparrow\! B \end{aligned}$$

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