Kronecker-based infinite level-dependent QBDs: Matrix analytic solution versus simulation

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Systems are formed of *interacting subsystems*
⇒ systems have *multi-dimensional state spaces*
Each subsystem corresponds to separate dimension

*Kronecker* product models *interaction* among subsystems
There are different kinds of interactions
Subsystem has small matrix for each interaction
Order of small matrix is state space size of subsystem
Small matrices of interacting subsystems in Kronecker product $\neq I$

*Infinitesimal generator* $Q$ of irreducible CTMC with state space $S$
represented using sums of Kronecker products of smaller matrices

(Plateau, ACM Sigmetrics, 1985)
Kronecker (or tensor) product

of two (rectangular) matrices \( A, B \) with \( A = [a(i_A, j_A)] \):

\[
A \otimes B = [a(i_A, j_A)B]
\]

More formally, \( A \in \mathbb{R}^{n_A \times m_A} \), \( B \in \mathbb{R}^{n_B \times m_B} \):

\[
A \otimes B = C \in \mathbb{R}^{n_A n_B \times m_A m_B}
\]

where

\[
c(i_C, j_C) = a(i_A, j_A)b(i_B, j_B)
\]

\( i_C = i_A n_B + i_B, \quad j_C = j_A m_B + j_B \)

\( (i_A, j_A) \in \{0, \ldots, n_A - 1\} \times \{0, \ldots, m_A - 1\} \)

\( (i_B, j_B) \in \{0, \ldots, n_B - 1\} \times \{0, \ldots, m_B - 1\} \)

\( \times : \text{Cartesian product operator} \)
Preliminaries (continued)

Kronecker product is *associative*

Kronecker product of $H$ (rectangular) matrices:

\[
X = X^{(1)} \otimes \cdots \otimes X^{(H)} = \bigotimes_{h=1}^{H} X^{(h)}
\]

where

\[
\mathcal{S}^{(h)} = \{0, \ldots, n_h - 1\} \\
\tilde{\mathcal{S}}^{(h)} = \{0, \ldots, m_h - 1\} \\
X^{(h)} \in \mathbb{R}^{n_h \times m_h} \\
X \in \mathbb{R}^{n \times m} \text{ with } n = \prod_{h=1}^{H} n_h, m = \prod_{h=1}^{H} m_h \\
\text{row index of } X: \vec{i} = (i_1, \ldots, i_H) \in \times_{h=1}^{H} \mathcal{S}^{(h)} \\
\text{col index of } X: \vec{j} = (j_1, \ldots, j_H) \in \times_{h=1}^{H} \tilde{\mathcal{S}}^{(h)}
\]

Example. $Q$ corresponding to CTMC with 12 states

$$Q = \begin{pmatrix}
0 & 1 & 2 & 3 & 4 & 5 & 6 & 7 & 8 & 9 & 10 & 11 \\
0 & * & \lambda_3 & \lambda_2 & & & & & & & & \\
1 & \mu_3 & * & \lambda_2 & & & & & & & & \\
2 & \mu_2 & * & \lambda_3 & \lambda_2 & & & & & & & \\
3 & \mu_2 & \mu_3 & * & \lambda_2 & & & & \lambda_1 & & & \\
4 & \mu_2 & * & \lambda_3 & & & \lambda_1 & & & & & \\
5 & & \mu_2 & \mu_3 & * & & & & \lambda_1 & & & \\
6 & \mu_1 & & * & \lambda_3 & \lambda_2 & & & & & & \\
7 & \mu_1 & & & \lambda_3 & * & \lambda_2 & & & & & \\
8 & \mu_1 & & & \mu_2 & * & \lambda_3 & \lambda_2 & & & & \\
9 & \mu_1 & & & \mu_2 & \mu_3 & * & \lambda_2 & & & & \\
10 & \mu_1 & & & & \mu_2 & \mu_3 & * & \lambda_3 & & & \\
11 & \mu & & & & \mu_1 & & \mu_2 & \mu_3 & * & \\
\end{pmatrix}$$

where $*$: negated off–diagonal row sums

$Q$ has 41 off-diagonal nonzeros among 132 possible ones $\Rightarrow$ sparse matrix
Availability model with 3 subsystems having respectively 1, 2, and 1 redundant component(s) only one of which is working in each subsystem

\( H = 3, n_1 = n_3 = 2, n_2 = 3 \) and

\[
Q = \sum_{k=1}^{4} \bigotimes_{h=1}^{3} Q_k^{(h)} + Q_D
\]

where

\[
Q_2^{(1)} = Q_3^{(1)} = I_2, \quad Q_1^{(1)} = \begin{pmatrix} \mu_1 & \lambda_1 \\ \mu_1 & \lambda_1 \end{pmatrix}, \quad Q_4^{(1)} = \begin{pmatrix} \mu \\ \mu \end{pmatrix}
\]

\[
Q_1^{(2)} = Q_3^{(2)} = I_3, \quad Q_2^{(2)} = \begin{pmatrix} \mu_2 & \lambda_2 \\ \mu_2 & \lambda_2 \end{pmatrix}, \quad Q_4^{(2)} = \begin{pmatrix} 1 \\ 1 \end{pmatrix}
\]

\[
Q_1^{(3)} = Q_2^{(3)} = I_2, \quad Q_3^{(3)} = Q_4^{(3)} = \begin{pmatrix} \mu_3 & \lambda_3 \\ \mu_3 & \lambda_3 \end{pmatrix}, \quad Q_4^{(3)} = \begin{pmatrix} 1 \\ 1 \end{pmatrix}
\]

If absence of matrix in Kronecker representation indicates \( I \), then 11 floating-point values stored for small matrices and 12 for diagonal entries in \( Q_D \), thus 23, whereas 53 for flat representation
Vector–Kronecker product multiplication

Kronecker product is *compatible* with matrix multiplication:

\[ \bigotimes_{h=1}^{H} X^{(h)} = \left( \prod_{h=1}^{H} I_{m_1} \otimes \cdots \otimes I_{m_{h-1}} \otimes X^{(h)} \otimes I_{n_{h+1}} \otimes \cdots \otimes I_{n_H} \right) \]

or more simply

\[ \bigotimes_{h=1}^{H} X^{(h)} = \prod_{h=1}^{H} \left( I_{\prod_{l=1}^{h-1} m_l} \otimes X^{(h)} \otimes I_{\prod_{l=h+1}^{H} n_l} \right) \]

Given \( \vec{x} \in \mathbb{R}^{1 \times n} \), length of \( \vec{y} = \vec{x} \bigotimes_{h=1}^{H} X^{(h)} \) ranges from

\[ m_1 \prod_{h=2}^{H} n_h \text{ to } \prod_{h=1}^{H} m_h = m \]

during vector–Kronecker product multiplication
Handling unreachable states

**Problem:** \( \prod_{h=1}^H S^{(h)} \neq S \)

*Example.* Consider irreducible CTMC with 5 states corresponding to 2 interacting subsystems \( \Rightarrow |S| = 5 \) and \( H = 2 \)

Unless \(|S^{(1)}| = 1 \) and \(|S^{(2)}| = 5 \) or vice versa, \(|S^{(1)} \times S^{(2)}| \neq |S| \)

Let \(1 < |S^{(1)}| \leq |S^{(2)}| \leq 5 \) and do not consider *isomorphic* cases

\(N\): \# of partitions in the representation of \( S \) \((N > 1)\)

1. \(|S^{(1)}| = |S^{(2)}| = 5\)

\(S^{(1)}\) and \(S^{(2)}\) are partitioned into \(N = 5\) subsets

\(S^{(h)}_p = \{p - 1\}, \ p = 1, \ldots, N\) and \(S^{(h)} = \bigcup_{p=1}^N S^{(h)}_p, \ h = 1, 2\)

Then \(|S^{(1)} \times S^{(2)}| = 25\), but

\[ S = \bigcup_{p=1}^N S^{(1)}_p \times S^{(2)}_p = \{(0, 0)\} \cup \{(1, 1)\} \cup \{(2, 2)\} \cup \{(3, 3)\} \cup \{(4, 4)\} \]
Handling unreachable states (continued)

2. \(|S^{(1)}| = 4, |S^{(2)}| = 5\)
   
   \(S^{(1)}\) and \(S^{(2)}\) are partitioned into \(N = 4\) subsets
   
   \(S_{p}^{(h)} = \{p - 1\}, p = 1, 2, 3, \quad S_{4}^{(1)} = \{3\}, \quad S_{4}^{(2)} = \{3, 4\}\) and
   
   \(S^{(h)} = \bigcup_{p=1}^{N} S_{p}^{(h)}, \quad h = 1, 2.\) Then \(|S^{(1)} \times S^{(2)}| = 20\), but
   
   \[S = \bigcup_{p=1}^{N} S_{p}^{(1)} \times S_{p}^{(2)} = \{(0, 0)\} \cup \{(1, 1)\} \cup \{(2, 2)\} \cup \{(3, 3), (3, 4)\}\]

3. \(|S^{(1)}| = 3, |S^{(2)}| = 5\)
   
   \(S^{(1)}\) and \(S^{(2)}\) are partitioned into \(N = 3\) subsets
   
   \(S_{1}^{(1)} = S_{1}^{(2)} = \{0\}, \quad S_{2}^{(1)} = \{1\}, \quad S_{2}^{(2)} = \{1, 2\}, \quad S_{3}^{(1)} = \{2\}, \quad S_{3}^{(2)} = \{3, 4\}\) and
   
   \(S^{(h)} = \bigcup_{p=1}^{N} S_{p}^{(h)}, \quad h = 1, 2.\) Then \(|S^{(1)} \times S^{(2)}| = 15\), but
   
   \[S = \bigcup_{p=1}^{N} S_{p}^{(1)} \times S_{p}^{(2)} = \{(0, 0)\} \cup \{(1, 1), (1, 2)\} \cup \{(2, 3), (2, 4)\}\]
Handling unreachable states (continued)

4. \[ |S^{(1)}| = 3, \quad |S^{(2)}| = 5 \]
   \(S^{(1)}\) and \(S^{(2)}\) are partitioned into \(N = 3\) subsets
   \(S^{(1)}_1 = S^{(2)}_1 = \{0\}, \quad S^{(1)}_2 = \{1\}, \quad S^{(2)}_2 = \{1\}, \quad S^{(1)}_3 = \{2\}, \quad S^{(2)}_3 = \{2, 3, 4\}\)
   and
   \(S^{(h)} = \bigcup_{p=1}^{N} S^{(h)}_p, \quad h = 1, 2.\)
   Then \(|S^{(1)} \times S^{(2)}| = 15\), but
   \[
   S = \bigcup_{p=1}^{N} S^{(1)}_p \times S^{(2)}_p = \{(0, 0)\} \cup \{(1, 1)\} \cup \{(2, 2), (2, 3), (2, 4)\}
   \]

5. \[ |S^{(1)}| = 2, \quad |S^{(2)}| = 5 \]
   \(S^{(1)}\) and \(S^{(2)}\) are partitioned into \(N = 2\) subsets
   \(S^{(1)}_1 = \{0\}, \quad S^{(2)}_1 = \{0\}, \quad S^{(1)}_2 = \{1\}, \quad S^{(2)}_2 = \{1, 2, 3, 4\}\)
   and
   \(S^{(h)} = \bigcup_{p=1}^{N} S^{(h)}_p, \quad h = 1, 2.\)
   Then \(|S^{(1)} \times S^{(2)}| = 10\), but
   \[
   S = \bigcup_{p=1}^{N} S^{(1)}_p \times S^{(2)}_p = \{(0, 0)\} \cup \{(1, 1), (1, 2), (1, 3), (1, 4)\}
   \]
6. \(|S^{(1)}| = 4, |S^{(2)}| = 4\)

\(S^{(1)}\) and \(S^{(2)}\) are partitioned into \(N = 3\) subsets

\(S^{(1)}_1 = S^{(2)}_1 = \{0\}, S^{(1)}_2 = \{1\}, S^{(2)}_2 = \{1, 2\}, S^{(1)}_3 = \{2, 3\}, S^{(2)}_3 = \{3\}\) and

\(S^{(h)} = \bigcup_{p=1}^{N} S^{(h)}_p, h = 1, 2.\) Then \(|S^{(1)} \times S^{(2)}| = 16\), but

\[
S = \bigcup_{p=1}^{N} S^{(1)}_p \times S^{(2)}_p = \{(0, 0)\} \cup \{(1, 1), (1, 2)\} \cup \{(2, 3), (3, 3)\}
\]

7. \(|S^{(1)}| = 3, |S^{(2)}| = 4\)

\(S^{(1)}\) and \(S^{(2)}\) are partitioned into \(N = 2\) subsets

\(S^{(1)}_1 = \{0\}, S^{(2)}_1 = \{0, 1, 2\}, S^{(1)}_2 = \{1, 2\}, S^{(2)}_2 = \{3\}\) and \(S^{(h)} = \bigcup_{p=1}^{N} S^{(h)}_p, h = 1, 2.\) Then \(|S^{(1)} \times S^{(2)}| = 12\), but

\[
S = \bigcup_{p=1}^{N} S^{(1)}_p \times S^{(2)}_p = \{(0, 0), (0, 1), (0, 2)\} \cup \{(1, 3), (2, 3)\}
\]
Handling unreachable states (continued)

8. $|S^{(1)}| = 3$, $|S^{(2)}| = 3$

$S^{(1)}$ and $S^{(2)}$ are partitioned into $N = 2$ subsets

$S^{(1)}_1 = \{0\}$, $S^{(2)}_1 = \{0\}$, $S^{(1)}_2 = \{1, 2\}$, $S^{(2)}_2 = \{1, 2\}$ and $S^{(h)} = \bigcup_{p=1}^{N} S^{(h)}_p$, $h = 1, 2$. Then $|S^{(1)} \times S^{(2)}| = 9$, but

$S = \bigcup_{p=1}^{N} S^{(1)}_p \times S^{(2)}_p = \{(0, 0)\} \cup \{(1, 1), (1, 2), (2, 1), (2, 2)\}$

8 different ways in which $|S| = 5$ can be obtained from 2-dimensional product state space with $2 \leq N \leq 5$

Certain state space sizes never yield $|S| = 5 \Rightarrow$ e.g., $|S^{(1)}| = 2$ and $|S^{(2)}| = 4$

(Buchholz, Queueing Syst. 31, 1994)
Transition classes

Multi-dimensional Markovian systems can also be modeled using transition classes and state vectors

A transition class $k$ for $k = 1, \ldots, K$ is a pair

$$
(\phi^{(k)} \prod_{h=1}^{H} f^{(k,h)}(i_h), \vec{v}^{(k)})
$$

where

$$
\phi^{(k)} \in \mathbb{R}_{>0} \text{ (state independent transition rate)}
$$

$$
f^{(k,h)}(i_h) : S^{(h)} \rightarrow \mathbb{R}_{\geq 0} \text{ for variable } i_h, h = 1, \ldots, H
$$

$$
\text{ (state dependent transition rate)}
$$

$$
\vec{v}^{(k)} \in \mathbb{Z}^{1 \times H} \text{ (state change vector)}
$$

(Dayar, Orhan, 2011)
Transition classes (continued)

First element of pair

\[ \alpha_k(\vec{i}) := \phi^{(k)} \prod_{h=1}^{H} f^{(k,h)}(i_h) \]

is \textit{transition rate} from state \( \vec{i} \in S \) to state \( \vec{i} + \vec{v}^{(k)} \in S \)

Second element of pair

\[ \vec{v}^{(k)} \in \mathbb{Z}^{1 \times H} \]

specifies successor state of transition where

\[ v_h^{(k)}: \text{change in variable } i_h \text{ due to class } k \text{ transition} \]

Now, let

\[ H_I: \# \text{ of countably infinite variables} \]
\[ H_F: \# \text{ of finite variables} \]
An example

Model of a biological process of *metabolite synthesis with repressilator* (Loinger, Biham, Phys. Rev. E 76, 2007)

Three types of *genes* and three different *control variables*
Genes regulate each other's synthesis in a cyclic manner:

\[
\text{type 1} \rightarrow \text{type 2} \rightarrow \text{type 3} \rightarrow \text{type 1}
\]

Each type of gene has a *single binding site* to which only one *repressor* at a time can bind
Gene regulates another type of gene by producing its own type of repressor
Repressor binds to site of gene to be regulated, and thereby represses (or blocks) other type of gene
An example (continued)
e.g., When $i_4 = 1$, type 1 repressor is bound to site of type 2 genes
When control variable is set to 0, corresponding binding site is unbound

\[ S^{(1)} = S^{(2)} = S^{(3)} = \mathbb{Z}_+ \]

\[ S^{(4)} = S^{(5)} = S^{(6)} = \{0, 1\}, \quad \bar{S} = S^{(4)} \times S^{(5)} \times S^{(6)}, \quad |\bar{S}| = 8 \]

\[ S = S^{(1)} \times S^{(2)} \times S^{(3)} \times \bar{S} \]

$\lambda_h$: state independent production rate of type $h$ gene
$\mu_h$: state independent degradation rates of type $h$ gene
$\beta_0$: state independent binding rate
$\beta_1$: state independent unbinding rate

Note that degradation and binding are in fact state dependent
Table 1: Transition classes of the metabolite synthesis model with repressilator

<table>
<thead>
<tr>
<th>$k$</th>
<th>$\phi^{(k)}$</th>
<th>$f^{(k,1)}(i_1)$</th>
<th>$f^{(k,2)}(i_2)$</th>
<th>$f^{(k,3)}(i_3)$</th>
<th>$f^{(k,4)}(i_4)$</th>
<th>$f^{(k,5)}(i_5)$</th>
<th>$f^{(k,6)}(i_6)$</th>
<th>$\vec{v}^{(k)}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$\lambda_1$</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>$(1 - i_6)$</td>
<td>$\vec{e}_1^T$</td>
</tr>
<tr>
<td>2</td>
<td>$\mu_1$</td>
<td>$i_1$</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>$-\vec{e}_1^T$</td>
</tr>
<tr>
<td>3</td>
<td>$\beta_0$</td>
<td>$i_1$</td>
<td>1</td>
<td>1</td>
<td>$(1 - i_4)$</td>
<td>1</td>
<td>1</td>
<td>$(-\vec{e}_1 + \vec{e}_4)^T$</td>
</tr>
<tr>
<td>4</td>
<td>$\beta_1$</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>$i_4$</td>
<td>1</td>
<td>1</td>
<td>$(\vec{e}_1 - \vec{e}_4)^T$</td>
</tr>
<tr>
<td>5</td>
<td>$\lambda_2$</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>$(1 - i_4)$</td>
<td>1</td>
<td>1</td>
<td>$\vec{e}_1^T$</td>
</tr>
<tr>
<td>6</td>
<td>$\mu_2$</td>
<td>1</td>
<td>$i_2$</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>$-\vec{e}_2^T$</td>
</tr>
<tr>
<td>7</td>
<td>$\beta_0$</td>
<td>1</td>
<td>$i_2$</td>
<td>1</td>
<td>1</td>
<td>$(1 - i_5)$</td>
<td>1</td>
<td>$(-\vec{e}_2 + \vec{e}_5)^T$</td>
</tr>
<tr>
<td>8</td>
<td>$\beta_1$</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>$i_5$</td>
<td>1</td>
<td>$(\vec{e}_2 - \vec{e}_5)^T$</td>
</tr>
<tr>
<td>9</td>
<td>$\lambda_3$</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>$(1 - i_5)$</td>
<td>1</td>
<td>$\vec{e}_2^T$</td>
</tr>
<tr>
<td>10</td>
<td>$\mu_3$</td>
<td>1</td>
<td>1</td>
<td>$i_3$</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>$-\vec{e}_3^T$</td>
</tr>
<tr>
<td>11</td>
<td>$\beta_0$</td>
<td>1</td>
<td>1</td>
<td>$i_3$</td>
<td>1</td>
<td>1</td>
<td>$(1 - i_6)$</td>
<td>$(-\vec{e}_3 + \vec{e}_6)^T$</td>
</tr>
<tr>
<td>12</td>
<td>$\beta_1$</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>$(\vec{e}_3 - \vec{e}_6)^T$</td>
</tr>
</tbody>
</table>

$H = 6, \ H_I = 3, \ H_F = 3, \ \vec{i} = (i_1, i_2, i_3, i_4, i_5, i_6), \ K = 12$

$\lambda_1, \lambda_2, \lambda_3, \mu_1, \mu_2, \mu_3, \beta_0, \beta_1 \in \mathbb{R}_{>0}$
Matrix analytic methods

Matrix analytic methods are geared towards MCs having state spaces that can be partitioned into subsets called *levels*

Infinitesimal generator symmetrically permuted according to increasing level number must have particular nonzero structure: *block tridiagonal* or *block Hessenberg*

*Quasi-birth-and-death processes* (QBDs) lend themselves to steady-state analysis with matrix analytic methods

**Advantage:** Direct method yielding fast solution

(Bright, Taylor, Stoch. Model. 11, 1995)
Levent-dependent QBDs

Continuous-time level-dependent QBDs (LDQBDs) have infinitesimal generators that can be symmetrically permuted as

$$Q = \begin{pmatrix}
Q_{0,0} & Q_{0,1} & & \\
Q_{1,0} & Q_{1,1} & Q_{1,2} & \\
& \ddots & \ddots & \ddots \\
& & Q_{l,l-1} & Q_{l,l} & Q_{l,l+1} & \\
& & & \ddots & \ddots & \\
& & & & \ddots & \\
\end{pmatrix}$$

Nonzero values or dimensions of nonzero block (or both) depend on level number, $l \in \mathbb{Z}_+$

$S_l$: subset of states corresponding to level $l$

$$Q_{l,l-1} \in \mathbb{R}^{\geq 0}_{|S_l| \times |S_{l-1}|}, Q_{l,l} \in \mathbb{R}^{\geq 0}_{|S_l| \times |S_l|}, Q_{l,l+1} \in \mathbb{R}^{\geq 0}_{|S_l| \times |S_{l+1}|}$$
Level-dependent QBDs (continued)

Assuming \( S = \bigcup_{l \in \mathbb{Z}^+} S_l \) and steady-state exists, steady-state vector is

\[
\bar{\pi} = (\bar{\pi}(0), \bar{\pi}(1), \ldots)
\]

Its subvector at level \((l + 1)\) can be obtained from

\[
\bar{\pi}(l+1) = \bar{\pi}(l) R_l
\]

once matrix of conditional expected sojourn times at level \( l \)

\[
R_l = Q_{l,l+1}(-Q_{l+1,l+1} - R_{l+1}Q_{l+2,l+1})^{-1}
\]

is available for \( l \in \mathbb{Z}^+ \)

\( R_l(\vec{i}, \vec{j}) \): expected sojourn time in state \( \vec{j} \in S_{l+1} \) per unit sojourn in state \( \vec{i} \in S_l \) before returning to level \( l \), given process started in state \( \vec{i} \).
Level-dependent QBDs (continued)

\[ R_l \in \mathbb{R}_{\geq 0}^{|S_l| \times |S_{l+1}|} \quad \text{for} \quad l \in \mathbb{Z}_+ \quad \text{is nonnegative and rectangular} \]

\[ \vec{\pi}(0) \] is computed from set of boundary equations:

\[ \vec{\pi}(0) Q_{0,0} + \vec{\pi}(1) Q_{1,0} = \vec{0} \]

corresponding to first column of blocks using \[ \vec{\pi}(1) = \vec{\pi}(0) R_0 \]

\[ \vec{\pi}(0) \] is positive left eigenvector of \((Q_{0,0} + R_0 Q_{1,0})\) corresponding to eigenvalue 0

\[ \vec{\pi} \] should be normalized so that \[ \vec{\pi} \vec{e} = 1 \]

**Problem:** \( S \) is countably infinite
Handling infiniteness

Steady-state exists for irreducible CTMC with state space $S$

if and only if

there exists a Lyapunov function $g(\vec{i}) : S \rightarrow \mathbb{R}_{\geq 0}$ and a finite set $C \subset S$ simultaneously satisfying

(i) $d(\vec{i}) \leq -\gamma$ for all $\vec{i} \in S \setminus C$ and some $\gamma > 0$
(ii) $d(\vec{i}) < \infty$ for all $\vec{i} \in C$
(iii) $\{ \vec{i} \in S \mid g(\vec{i}) \leq r \}$ is finite for all $r < \infty$

where

$$d(\vec{i}) = \sum_{k=1}^{K} \alpha_k(\vec{i})(g(\vec{i} + \vec{v}(k)) - g(\vec{i})) \in \mathbb{R}$$

is drift in state $\vec{i} \in S$

Handling infiniteness (continued)

When \( g(\vec{i}) \) satisfies condition (iii) and \( c = \sup_{\vec{i} \in S} d(\vec{i}) < \infty \) (i.e., conditions (i) and (ii) satisfied), we have

\[
\sum_{\vec{i} \in S \setminus C} \pi(\vec{i}) \leq \varepsilon \quad \text{with} \quad \varepsilon = \frac{c}{c + \gamma} \in (0, 1)
\]

Equivalently,

\[
\gamma = \frac{c}{\varepsilon} - c
\]

constructively defines

\[
C = \{ \vec{i} \in S \mid -\gamma < d(\vec{i}) < \infty \}
\]

Now, if it is further shown that \( C \) is finite, conditions (i)–(iii) hold and

\[
\sum_{\vec{i} \in C} \pi(\vec{i}) \geq 1 - \varepsilon
\]
Handling infiniteness (continued)

To determine $c$, domain of search for extrema should be restricted to $\mathbb{R}^{1 \times H}_{\geq 0}$.

All extrema are computed by equating gradient of $d(\vec{i})$ to zero.

To determine all local extrema including those located on boundaries of domain, same system solved for every projection of $d(\vec{i})$ onto each subspace of $\mathbb{R}^{1 \times H}$ by setting all combinations of $i_h$ for $h = 1, \ldots, H$ to 0.

In the end, all extrema outside $\mathbb{R}^{1 \times H}_{\geq 0}$ should be discarded.

Throughout this process, resulting nonlinear equation systems can be solved, for instance, using the HOM4PS-2.0 package (Lee, Li, Tsai, Comput. 83, 2008) implementing polyhedral homotopy continuation method.
Handling infiniteness (continued)

(If possible) proof that $C$ is finite follows from constructively defining a finite superset of $C$

e.g. when $g(\vec{i}) = ||\vec{i}||_2^2$, define $H_I$ quadratic polynomials

\[
d_h(i_h) = a_{2,h}i_h^2 + a_{1,h}i_h + a_{0,h} \quad \text{with} \quad a_{2,h} < 0 \quad \text{for} \quad h = 1, \ldots, H_I
\]

so as to satisfy

\[
d(\vec{i}) \leq \sum_{h=1}^{H_I} d_h(i_h) \quad \text{for} \quad \vec{i} = (i_1, \ldots, i_H) \in S
\]

Since $d_h(i_h)$ is concave down for $h = 1, \ldots, H_I$ and $\vec{i} \in S$ by construction, upper bound on $d(\vec{i})$ over $S$ is finite $\Rightarrow$ $c = \sup_{\vec{i} \in S} d(\vec{i})$ is finite

Now, add $\gamma \in \mathbb{R}_{\geq 0}$ to both of sides of the inequality so that

\[
0 < \gamma + d(\vec{i}) \leq \gamma + \sum_{h=1}^{H_I} d_h(i_h), \quad \text{or equivalently} \quad -\gamma < d(\vec{i}) \leq \sum_{h=1}^{H_I} d_h(i_h)
\]

$-\gamma < d(\vec{i})$ holds for some $\vec{i} \in S$ and characterizes $C$ when $c = \sup_{\vec{i} \in S} d(\vec{i}) < \infty$
Handling infiniteness (continued)

\[ C = \{ \overrightarrow{i} \in S \mid -\gamma < d(\overrightarrow{i}) < \infty \} \]

Define \[ D = \{ \overrightarrow{i} \in S \mid -\gamma < \sum_{h=1}^{H_I} d_h(i_h) \} \Rightarrow C \subseteq D \]

\( f_h(i_h) \) is concave down and \( i_h \in \mathbb{Z}_+ \) for \( h = 1, \ldots, H_I \) \( \Rightarrow \) \( D \) is finite \( \square \)

Once \( C \) proved finite and \( c \) determined (or equivalently, \( \gamma \) for chosen \( \varepsilon \))

\[ Low = \min\{ l \in \mathbb{Z}_+ \mid S_l \cap C \neq \emptyset \} \quad \text{and} \quad High = \max\{ l \in \mathbb{Z}_+ \mid S_l \cap C \neq \emptyset \} \]

\[ C \subseteq \bigcup_{l=L_{ow}}^{L_{high}} S_l \]
contains at least \( (1 - \varepsilon) \) of steady-state probability
Kronecker representation

Associate \textit{transition rate matrices} with countably infinite variables

$H_I$ such transition rate matrices for each transition class

Transition rate matrix of $i_h$ for $h = 1,\ldots, H_I$ and $k = 1,\ldots, K$

$$S^{(h)}_k \in \mathbb{R}^{\mid S^{(h)}\mid \times \mid S^{(h)}\mid}_{\geq 0}$$

and given entrywise as

$$S^{(h)}_k(i_h, j_h) = \begin{cases} f^{(k,h)}(i_h) & \text{if } j_h = i_h + v_h^{(k)} \\ 0 & \text{otherwise} \end{cases}$$

for $i_h, j_h \in S^{(h)}$
Kronecker representation (continued)

For finite variables when \( H > H_I \), define combined transition rate matrix since in practice \( |S^{(h)}| \) for \( h = H_I + 1, \ldots, H \) is very small

\( \bar{S} \): set of states finite variables can take \( \Rightarrow \bar{S} \subseteq \times_{h=H_I+1}^{H} S^{(h)} \)

When \( H = H_I \), assume that \( |\bar{S}| = 1 \) and \( \bar{S}_k = (1) \)

Combined transition rate matrix of finite variables for \( k = 1, \ldots, K \)

\[
\bar{S}_k \in \mathbb{R}_{\geq 0}^{|\bar{S}| \times |\bar{S}|}
\]

and given entrywise as

\[
\bar{S}_k((i_{H_I+1}, \ldots, i_H), (j_{H_I+1}, \ldots, j_H)) = \begin{cases} 
\prod_{h=H_I+1}^{H} f^{(k,h)}(i_h) & \text{if } (j_{H_I+1}, \ldots, j_H) = (i_{H_I+1}, \ldots, i_H) + (v_{H_I+1}^{(k)}, \ldots, v_H^{(k)}) \\
0 & \text{otherwise}
\end{cases}
\]

for \((i_{H_I+1}, \ldots, i_H), (j_{H_I+1}, \ldots, j_H) \in \bar{S}\)
An example (continued)

Transition rate matrices of \(i_h\) for \(h = 1, \ldots, H_I\)

\[
\begin{align*}
S^{(2)}_1 &= S^{(3)}_1 = S^{(2)}_2 = S^{(3)}_2 = S^{(2)}_3 = S^{(3)}_3 = S^{(2)}_4 = S^{(3)}_4 = S^{(1)}_5 = S^{(3)}_5 \\
&= S^{(1)}_6 = S^{(3)}_6 = S^{(1)}_7 = S^{(3)}_7 = S^{(1)}_8 = S^{(3)}_8 = S^{(1)}_9 = S^{(2)}_9 = S^{(1)}_{10} = S^{(2)}_{10} \\
&= S^{(1)}_{11} = S^{(2)}_{11} = S^{(1)}_{12} = S^{(2)}_{12} = I_{\infty} \\
S^{(1)}_1 &= S^{(1)}_4 = S^{(2)}_5 = S^{(3)}_8 = S^{(3)}_9 = S^{(1)}_{12} = \text{superdiag}((1, 1, \ldots)^T) \\
S^{(1)}_2 &= S^{(1)}_3 = S^{(2)}_6 = S^{(2)}_7 = S^{(3)}_{10} = S^{(3)}_{11} = \text{subdiag}((1, 2, \ldots)^T)
\end{align*}
\]

Combined transition rate matrices corresponding to \(i_h\) for \(h = H_I + 1, \ldots, H\)

\[
\begin{align*}
\bar{S}_1 &= I_2 \otimes I_2 \otimes \text{diag}((1, 0)^T) \\
\bar{S}_2 &= \bar{S}_6 = \bar{S}_{10} = I_2 \otimes I_2 \otimes I_2 \\
\bar{S}_3 &= \text{superdiag}((1)^T) \otimes I_2 \otimes I_2 \\
\bar{S}_4 &= \text{subdiag}((1)^T) \otimes I_2 \otimes I_2 \\
\bar{S}_5 &= \text{diag}((1, 0)^T) \otimes I_2 \otimes I_2 \\
\bar{S}_7 &= I_2 \otimes \text{superdiag}((1)^T) \otimes I_2 \\
\bar{S}_8 &= I_2 \otimes \text{subdiag}((1)^T) \otimes I_2 \\
\bar{S}_{11} &= I_2 \otimes I_2 \otimes \text{superdiag}((1)^T) \\
\bar{S}_{12} &= I_2 \otimes I_2 \otimes \text{subdiag}((1)^T)
\end{align*}
\]
Kronecker representation (continued)

**Problem:** Formulate Kronecker representation for nonzero blocks of $Q$

$S_l$: subset of states corresponding to level $l \in \mathbb{Z}_+$

$$S_l = \left\{ \vec{i} \in S \mid \max_{h=1,\ldots,H_I}(i_h) = l \right\}$$

$$S = \bigcup_{l=0}^{\infty} S_l, \quad S_l \cap S_u = \emptyset \text{ for } l \neq u$$

since maximum valued variable among $i_1, \ldots, i_{H_I}$ in any state $\vec{i} \in S$ changes by at most one through any transition in systems of stochastic chemical kinetics

$\# \text{ of states lying in levels } Low \text{ to } High$

$$N(Low, High) = \sum_{l=Low}^{High} |\tilde{S}| ((l + 1)^{H_I} - (l)^{H_I}) = |\tilde{S}| ((High + 1)^{H_I} - (Low)^{H_I})$$
Kronecker representation (continued)

Let

\[ S_{l,p}^{(h)} = \begin{cases} 
\{ i_h \mid 0 \leq i_h \leq l - 1 \} & \text{if } h < p \\
\{ l \} & \text{if } h = p \\
\{ i_h \mid 0 \leq i_h \leq l \} & \text{if } h > p 
\end{cases} \]

for \( h, p = 1, \ldots, H_I \)

Then partition \( p = 1, \ldots, H_I \) of \( S_l \)

\[
S_{l,p} = \left\{ \vec{i} \in S_l \mid (i_1, \ldots, i_{H_I}) \in \times_{h=1}^{H_I} S_{l,p}^{(h)} \text{ and } (i_{H_I+1}, \ldots, i_H) \in \bar{S} \right\}
\]

Finally

\[
S_l = \bigcup_{p=1}^{H_I} S_{l,p}, \quad S_{l,p} \cap S_{l,w} = \emptyset \quad \text{for } p \neq w
\]

Without loss of generality,
order \( S_{l,p} \) within \( S_l \) according to increasing partition index, \( p \)
In our case, we have

\[ S_{l,1}^{(1)} = \{l\} , \quad S_{l,1}^{(2)} = S_{l,1}^{(3)} = \{0, \ldots, l\} \]

\[ S_{l,2}^{(1)} = \{0, \ldots, l - 1\} , \quad S_{l,2}^{(2)} = \{l\} , \quad S_{l,2}^{(3)} = \{0, \ldots, l\} \]

\[ S_{l,3}^{(1)} = S_{l,3}^{(2)} = \{0, \ldots, l - 1\} , \quad S_{l,3}^{(3)} = \{l\} \]

implying

\[ \times_{h=1}^{3} S_{0,1}^{(h)} = \{(0, 0, 0)\} , \quad \times_{h=1}^{3} S_{0,2}^{(h)} = \times_{h=1}^{3} S_{0,3}^{(h)} = \emptyset \]

\[ \times_{h=1}^{3} S_{1,1}^{(h)} = \{(1, 0, 0), (1, 0, 1), (1, 1, 0), (1, 1, 1)\} \]

\[ \times_{h=1}^{3} S_{1,2}^{(h)} = \{(0, 1, 0), (0, 1, 1)\} , \quad \times_{h=1}^{3} S_{1,3}^{(h)} = \{(0, 0, 1)\} \]

\[ \times_{h=1}^{3} S_{2,1}^{(h)} = \{(2, 0, 0), (2, 0, 1), (2, 0, 2), (2, 1, 0), (2, 1, 1), (2, 1, 2), (2, 2, 0), (2, 2, 1), (2, 2, 2)\} \]
An example (continued)

\[
\times_{h=1}^3 S^{(h)}_{2,2} = \{(0, 2, 0), (0, 2, 1), (0, 2, 2), (1, 2, 0), (1, 2, 1), (1, 2, 2)\}
\]

\[
\times_{h=1}^3 S^{(h)}_{2,3} = \{(0, 0, 2), (0, 1, 2), (1, 0, 2), (1, 1, 2)\}
\]

and so on

Since

\[
\bar{S} = \{(0, 0, 0), \ldots, (1, 1, 1)\}
\]

we obtain

\[
S_{l,1} = \left( \times_{h=1}^3 S^{(h)}_{l,1} \right) \times \bar{S} = \{(l, 0, 0, 0, 0, 0), \ldots, (l, l, l, 1, 1, 1)\}
\]

\[
S_{l,2} = \left( \times_{h=1}^3 S^{(h)}_{l,2} \right) \times \bar{S} = \{(0, l, 0, 0, 0, 0), \ldots, (l - 1, l, l, 1, 1, 1)\}
\]

\[
S_{l,3} = \left( \times_{h=1}^3 S^{(h)}_{l,3} \right) \times \bar{S} = \{(0, 0, l, 0, 0, 0), \ldots, (l - 1, l - 1, l, 1, 1, 1)\}
\]
Kronecker representation (continued)

Nonzero blocks $Q_{0,0}$, $Q_{0,1}$, $Q_{1,0}$, and $Q_{l,m}$ for $l \in \mathbb{Z}_+$, $m = l - 1, l, l + 1$ of $Q$ are respectively $(1 \times 1)$, $(1 \times H_I)$, $(H_I \times 1)$, and $(H_I \times H_I)$ block matrices

$$Q_{0,0} = \begin{pmatrix} Q_{0,0}^{(1,1)} \end{pmatrix}, \quad Q_{0,1} = \begin{pmatrix} Q_{0,1}^{(1,1)} & \cdots & Q_{0,1}^{(1,H_I)} \end{pmatrix}, \quad Q_{1,0} = \begin{pmatrix} Q_{1,0}^{(1,1)} \\ \vdots \\ Q_{1,0}^{(H_I,1)} \end{pmatrix}$$

$$Q_{l,m} = \begin{pmatrix} Q_{l,m}^{(1,1)} & \cdots & Q_{l,m}^{(1,H_I)} \\ \vdots & \ddots & \vdots \\ Q_{l,m}^{(H_I,1)} & \cdots & Q_{l,m}^{(H_I,H_I)} \end{pmatrix}$$
Kronecker representation (continued)

Furthermore, blocks of $Q_{l,m}$ can be written in terms of transition rate matrices and state independent transition rates

$$Q^{(p,w)}_{l,m} = \begin{cases} \tilde{Q}^{(p,w)}_{l,m} - \text{diag} \left( \sum_{m'=l-1}^{l+1} \sum_{w'=1}^{H_I} \tilde{Q}^{(p',w')}_{l,m'} \vec{e} \right) & \text{if } p = w \text{ and } l = m \\ \tilde{Q}^{(p,w)}_{l,m} & \text{otherwise} \end{cases}$$

for $l \in \mathbb{Z}_+$, $m = l - 1, l, l + 1$, $p, w = 1, \ldots, H_I$, where

$$\tilde{Q}^{(p,w)}_{l,m} = \sum_{k=1}^{K} \phi^{(k)} \left( \bigotimes_{h=1}^{H_I} S_{k}^{(h)} \left( S_{l,p}^{(h)}, S_{m,w}^{(h)} \right) \right) \otimes \bar{S}_k$$

$S_{k}^{(h)} \left( S_{l,p}^{(h)}, S_{m,w}^{(h)} \right)$: submatrix of $S_{k}^{(h)}$ incident on row indices in $S_{l,p}^{(h)}$, column indices in $S_{m,w}^{(h)}$
An example (continued)

Nonzero blocks $Q_{0,0}$, $Q_{0,1}$, $Q_{1,0}$, and $Q_{l,m}$ for $l \in \mathbb{Z}_+$, $m = l - 1, l, l + 1$ (except $Q_{1,0}$) are respectively $(1 \times 1)$, $(1 \times 3)$, $(3 \times 1)$, and $(3 \times 3)$ block matrices.

In particular, 7 blocks associated with $Q_{0,0}$, $Q_{0,1}$, $Q_{1,0}$

\[
\tilde{Q}^{(1,1)}_{0,0} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S^{(h)}_{k} (S^{(h)}_{0,1}, S^{(h)}_{0,1}) \right) \otimes \tilde{S}_{k} = (0)_{8 \times 8}
\]

\[
\tilde{Q}^{(1,1)}_{0,1} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S^{(h)}_{k} (S^{(h)}_{0,1}, S^{(h)}_{1,1}) \right) \otimes \tilde{S}_{k}
\]

\[
= \lambda_{1} (1) \otimes (1,0) \otimes (1,0) \otimes \tilde{S}_{1} + \beta_{1} (1) \otimes (1,0) \otimes (1,0) \otimes \tilde{S}_{4}
\]

\[
\tilde{Q}^{(1,2)}_{0,1} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S^{(h)}_{k} (S^{(h)}_{0,1}, S^{(h)}_{1,2}) \right) \otimes \tilde{S}_{k}
\]

\[
= \lambda_{2} (1) \otimes (1) \otimes (1,0) \otimes \tilde{S}_{5} + \beta_{1} (1) \otimes (1) \otimes (1,0) \otimes \tilde{S}_{8}
\]

\[
\tilde{Q}^{(1,3)}_{0,1} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S^{(h)}_{k} (S^{(h)}_{0,1}, S^{(h)}_{1,3}) \right) \otimes \tilde{S}_{k}
\]

\[
= \lambda_{3} (1) \otimes (1) \otimes (1) \otimes \tilde{S}_{9} + \beta_{1} (1) \otimes (1) \otimes (1) \otimes \tilde{S}_{12}
\]
An example (continued)

\[\tilde{Q}^{(1,1)}_{1,0} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S^{(h)}_{k} (S^{(h)}_{1,1}, S^{(h)}_{0,1}) \right) \otimes \bar{S}_{k}\]

\[= \mu_{1} (1) \otimes (1, 0)^T \otimes (1, 0)^T \otimes \bar{S}_{2}\]

\[\tilde{Q}^{(2,1)}_{1,0} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S^{(h)}_{k} (S^{(h)}_{1,2}, S^{(h)}_{0,1}) \right) \otimes \bar{S}_{k}\]

\[= \mu_{2} (1) \otimes (1) \otimes (1, 0)^T \otimes \bar{S}_{6} + \beta_{0} (1) \otimes (1) \otimes (1, 0)^T \otimes \bar{S}_{7}\]

\[\tilde{Q}^{(3,1)}_{1,0} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S^{(h)}_{k} (S^{(h)}_{1,3}, S^{(h)}_{0,1}) \right) \otimes \bar{S}_{k}\]

\[= \mu_{3} (1) \otimes (1) \otimes (1) \otimes \bar{S}_{10} + \beta_{0} (1) \otimes (1) \otimes (1) \otimes \bar{S}_{11}\]

9 blocks associated with \(Q_{l,l-1}\)

\[\tilde{Q}^{(1,1)}_{l,l-1} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S^{(h)}_{k} (S^{(h)}_{l,1}, S^{(h)}_{l-1,1}) \right) \otimes \bar{S}_{k}\]

\[= \mu_{1} (l) \otimes \text{diag}(\bar{e})_{(l+1) \times l} \otimes \text{diag}(\bar{e})_{(l+1) \times l} \otimes \bar{S}_{2}\]

\[+ \beta_{0} (l) \otimes \text{diag}(\bar{e})_{(l+1) \times l} \otimes \text{diag}(\bar{e})_{(l+1) \times l} \otimes \bar{S}_{3}\]
An example (continued)

\[
\tilde{Q}_{l,l-1}^{(1,2)} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S_{k}^{(h)} (S_{l,1}^{(h)}, S_{l-1,2}^{(h)}) \right) \otimes \bar{S}_k = 0_{8(l+1)^2 \times 8(l-1)l}
\]

\[
\tilde{Q}_{l,l-1}^{(1,3)} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S_{k}^{(h)} (S_{l,1}^{(h)}, S_{l-1,3}^{(h)}) \right) \otimes \bar{S}_k = 0_{8(l+1)^2 \times 8(l-1)^2}
\]

\[
\tilde{Q}_{l,l-1}^{(2,1)} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S_{k}^{(h)} (S_{l,2}^{(h)}, S_{l-1,1}^{(h)}) \right) \otimes \bar{S}_k
\]

\[
= \mu_2 \left( \vec{e}_l \right)_{l \times 1} \otimes \left( l e_l^T \right)_{1 \times l} \otimes \text{diag}(\vec{e})_{(l+1) \times l} \otimes \bar{S}_6
\]
\[
+ \beta_0 \left( \vec{e}_l \right)_{l \times 1} \otimes \left( l e_l^T \right)_{1 \times l} \otimes \text{diag}(\vec{e})_{(l+1) \times l} \otimes \bar{S}_7
\]

\[
\tilde{Q}_{l,l-1}^{(2,2)} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S_{k}^{(h)} (S_{l,2}^{(h)}, S_{l-1,2}^{(h)}) \right) \otimes \bar{S}_k
\]

\[
= \mu_2 \text{diag}(\vec{e})_{l \times (l-1)} \otimes (l) \otimes \text{diag}(\vec{e})_{(l+1) \times l} \otimes \bar{S}_6
\]
\[
+ \beta_0 \text{diag}(\vec{e})_{l \times (l-1)} \otimes (l) \otimes \text{diag}(\vec{e})_{(l+1) \times l} \otimes \bar{S}_7
\]

\[
\tilde{Q}_{l,l-1}^{(2,3)} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S_{k}^{(h)} (S_{l,2}^{(h)}, S_{l-1,3}^{(h)}) \right) \otimes \bar{S}_k = 0_{8l(l+1) \times 8(l-1)^2}
\]
\[ \tilde{Q}^{(3,1)}_{l,l-1} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S_{k h}^{(l)} (S_{l,3}^{(h)}, S_{l-l,1}^{(h)}) \right) \otimes \bar{S}_{k} \]

\[ = \mu_3 (\vec{e}_{l}^{T})_{l \times 1} \otimes \text{diag}(\vec{e}_{l})_{l \times l} \otimes (l \vec{e}_{l}^{T})_{1 \times 1} \otimes \bar{S}_{10} \]

\[ + \beta_0 (\vec{e}_{l}^{T})_{l \times 1} \otimes \text{diag}(\vec{e}_{l})_{l \times l} \otimes (l \vec{e}_{l}^{T})_{1 \times 1} \otimes \bar{S}_{11} \]

\[ \tilde{Q}^{(3,2)}_{l,l-1} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S_{k h}^{(l)} (S_{l,3}^{(h)}, S_{l-l,1}^{(h)}) \right) \otimes \bar{S}_{k} \]

\[ = \mu_3 \text{diag}(\vec{e}_{l})_{l \times (l-1)} \otimes (\vec{e}_{l}^{T})_{l \times 1} \otimes (l \vec{e}_{l}^{T})_{1 \times l} \otimes \bar{S}_{10} \]

\[ + \beta_0 \text{diag}(\vec{e}_{l})_{l \times (l-1)} \otimes (\vec{e}_{l}^{T})_{l \times 1} \otimes (l \vec{e}_{l}^{T})_{1 \times l} \otimes \bar{S}_{11} \]

\[ \tilde{Q}^{(3,3)}_{l,l-1} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S_{k h}^{(l)} (S_{l,3}^{(h)}, S_{l-l,1}^{(h)}) \right) \otimes \bar{S}_{k} \]

\[ = \mu_3 \text{diag}(\vec{e}_{l})_{l \times (l-1)} \otimes \text{diag}(\vec{e}_{l})_{l \times (l-1)} \otimes (l) \otimes \bar{S}_{10} \]

\[ + \beta_0 \text{diag}(\vec{e}_{l})_{l \times (l-1)} \otimes \text{diag}(\vec{e}_{l})_{l \times (l-1)} \otimes (l) \otimes \bar{S}_{11} \]
An example (continued)

9 blocks associated with $Q_{l,l}$

$$\tilde{Q}_{l,l}^{(1,1)} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S_k^{(h)} (S_{l,1}^{(h)}, S_{l,1}^{(h)}) \right) \otimes \tilde{S}_k$$

$$= \lambda_2 \ (1) \otimes \text{superdiag}(\vec{e})(l+1) \times (l+1) \otimes \text{diag}(\vec{e})(l+1) \times (l+1) \otimes \tilde{S}_5$$

$$+ \mu_2 \ (1) \otimes \text{subdiag}((1, \ldots, l)^T)(l+1) \times (l+1) \otimes \text{diag}(\vec{e})(l+1) \times (l+1) \otimes \tilde{S}_6$$

$$+ \beta_0 \ (1) \otimes \text{subdiag}((1, \ldots, l)^T)(l+1) \times (l+1) \otimes \text{diag}(\vec{e})(l+1) \times (l+1) \otimes \tilde{S}_7$$

$$+ \beta_1 \ (1) \otimes \text{superdiag}(\vec{e})(l+1) \times (l+1) \otimes \text{diag}(\vec{e})(l+1) \times (l+1) \otimes \tilde{S}_8$$

$$+ \lambda_3 \ (1) \otimes \text{diag}(\vec{e})(l+1) \times (l+1) \otimes \text{superdiag}(\vec{e})(l+1) \times (l+1) \otimes \tilde{S}_9$$

$$+ \mu_3 \ (1) \otimes \text{diag}(\vec{e})(l+1) \times (l+1) \otimes \text{subdiag}((1, \ldots, l)^T)(l+1) \times (l+1) \otimes \tilde{S}_{10}$$

$$+ \beta_0 \ (1) \otimes \text{diag}(\vec{e})(l+1) \times (l+1) \otimes \text{subdiag}((1, \ldots, l)^T)(l+1) \times (l+1) \otimes \tilde{S}_{11}$$

$$+ \beta_1 \ (1) \otimes \text{superdiag}(\vec{e})(l+1) \times (l+1) \otimes \text{diag}(\vec{e})(l+1) \times (l+1) \otimes \tilde{S}_{12}$$

$$\tilde{Q}_{l,l}^{(1,2)} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S_k^{(h)} (S_{l,1}^{(h)}, S_{l,2}^{(h)}) \right) \otimes \tilde{S}_k$$

$$= \mu_1 \ (le_l^T)_{1 \times l} \otimes (\vec{e}_{l+1})(l+1) \times 1 \otimes \text{diag}(\vec{e})(l+1) \times (l+1) \otimes \tilde{S}_2$$

$$+ \beta_0 \ (le_l^T)_{1 \times l} \otimes (\vec{e}_{l+1})(l+1) \times 1 \otimes \text{diag}(\vec{e})(l+1) \times (l+1) \otimes \tilde{S}_3$$
An example (continued)

\[
\tilde{Q}_{(1,3)}^{(l,l)} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S_k^{(h)} (S_{l,1}^{(h)}, S_{l,3}^{(h)}) \right) \otimes \bar{S}_k \\
= \mu_1 (l\bar{e}_l^T)_{1 \times l} \otimes \text{diag}(\bar{e})(l+1)_{1 \times l} \otimes (\bar{e}_{l+1})(l+1)_{1 \times 1} \otimes \bar{S}_2 \\
+ \beta_0 (l\bar{e}_l^T)_{1 \times l} \otimes \text{diag}(\bar{e})(l+1)_{1 \times l} \otimes (\bar{e}_{l+1})(l+1)_{1 \times 1} \otimes \bar{S}_3
\]

\[
\tilde{Q}_{(2,1)}^{(l,l)} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S_k^{(h)} (S_{l,2}^{(h)}, S_{l,1}^{(h)}) \right) \otimes \bar{S}_k \\
= \lambda_1 (\bar{e}_l)_{1 \times 1} \otimes (\bar{e}_{l+1})_{1 \times (l+1)} \otimes \text{diag}(\bar{e})(l+1)_{1 \times (l+1)} \otimes \bar{S}_1 \\
+ \beta_1 (\bar{e}_l)_{1 \times 1} \otimes (\bar{e}_{l+1})_{1 \times (l+1)} \otimes \text{diag}(\bar{e})(l+1)_{1 \times (l+1)} \otimes \bar{S}_4
\]

\[
\tilde{Q}_{(2,2)}^{(l,l)} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S_k^{(h)} (S_{l,2}^{(h)}, S_{l,2}^{(h)}) \right) \otimes \bar{S}_k \\
= \lambda_1 \text{superdiag}(\bar{e})_{l \times l} \otimes (1) \otimes \text{diag}(\bar{e})(l+1)_{1 \times (l+1)} \otimes \bar{S}_1 \\
+ \mu_1 \text{subdiag}((1, \ldots, l-1)_T)_{l \times l} \otimes (1) \otimes \text{diag}(\bar{e})(l+1)_{1 \times (l+1)} \otimes \bar{S}_2 \\
+ \beta_0 \text{subdiag}((1, \ldots, l-1)_T)_{l \times l} \otimes (1) \otimes \text{diag}(\bar{e})(l+1)_{1 \times (l+1)} \otimes \bar{S}_3 \\
+ \beta_1 \text{superdiag}(\bar{e})_{l \times l} \otimes (1) \otimes \text{diag}(\bar{e})(l+1)_{1 \times (l+1)} \otimes \bar{S}_4 \\
+ \lambda_3 \text{diag}(\bar{e})_{l \times l} \otimes (1) \otimes \text{superdiag}(\bar{e})(l+1)_{1 \times (l+1)} \otimes \bar{S}_9 \\
+ \mu_3 \text{diag}(\bar{e})_{l \times l} \otimes (1) \otimes \text{subdiag}((1, \ldots, l)_T)_{(l+1) \times (l+1)} \otimes \bar{S}_{10} \\
+ \beta_0 \text{diag}(\bar{e})_{l \times l} \otimes (1) \otimes \text{subdiag}((1, \ldots, l)_T)_{(l+1) \times (l+1)} \otimes \bar{S}_{11} \\
+ \beta_1 \text{diag}(\bar{e})_{l \times l} \otimes (1) \otimes \text{superdiag}(\bar{e})(l+1)_{1 \times (l+1)} \otimes \bar{S}_{12}
\]
An example (continued)

\[ \tilde{Q}_{l,l}^{(2,3)} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S_{k}^{(h)}(S_{l,2}^{(h)}, S_{l,3}^{(h)}) \right) \otimes \tilde{S}_{k} \]

\[ = \mu_{2} \ \text{diag}(\vec{e})_{l \times l} \otimes (l\vec{e}_{l}^{T})_{1 \times l} \otimes (\vec{e}_{l+1})_{(l+1) \times 1} \otimes \tilde{S}_{6} \]

\[ + \beta_{0} \ \text{diag}(\vec{e})_{l \times l} \otimes (l\vec{e}_{l}^{T})_{1 \times l} \otimes (\vec{e}_{l+1})_{(l+1) \times 1} \otimes \tilde{S}_{7} \]

\[ \tilde{Q}_{l,l}^{(3,1)} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S_{k}^{(h)}(S_{l,3}^{(h)}, S_{l,1}^{(h)}) \right) \otimes \tilde{S}_{k} \]

\[ = \lambda_{1} (\vec{e}_{l})_{l \times 1} \otimes \text{diag}(\vec{e})_{l \times (l+1)} \otimes (\vec{e}_{l+1})_{1 \times (l+1)} \otimes \tilde{S}_{1} \]

\[ + \beta_{1} (\vec{e}_{l})_{l \times 1} \otimes \text{diag}(\vec{e})_{l \times (l+1)} \otimes (\vec{e}_{l+1})_{1 \times (l+1)} \otimes \tilde{S}_{4} \]

\[ \tilde{Q}_{l,l}^{(3,2)} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S_{k}^{(h)}(S_{l,1}^{(h)}, S_{l,2}^{(h)}) \right) \otimes \tilde{S}_{k} \]

\[ = \lambda_{2} \ \text{diag}(\vec{e})_{l \times l} \otimes (\vec{e}_{l})_{l \times 1} \otimes (\vec{e}_{l+1})_{1 \times (l+1)} \otimes \tilde{S}_{5} \]

\[ + \beta_{1} \ \text{diag}(\vec{e})_{l \times l} \otimes (\vec{e}_{l})_{l \times 1} \otimes (\vec{e}_{l+1})_{1 \times (l+1)} \otimes \tilde{S}_{8} \]
An example (continued)

\[
\tilde{Q}_{l,l}^{(3,3)} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S_{k}^{(h)} (S_{l,3}^{(h)}, S_{l,3}^{(h)}) \right) \otimes \tilde{S}_{k}
\]

\[
= \lambda_{1} \text{ superdiag} (\vec{e})_{l \times l} \otimes \text{diag} (\vec{e})_{l \times l} \otimes (1) \otimes \tilde{S}_{1} + \mu_{1} \text{ subdiag} ((1, \ldots, l - 1)^{T})_{l \times l} \otimes \text{diag} (\vec{e})_{l \times l} \otimes (1) \otimes \tilde{S}_{2} + \beta_{0} \text{ subdiag} ((1, \ldots, l - 1)^{T})_{l \times l} \otimes \text{diag} (\vec{e})_{l \times l} \otimes (1) \otimes \tilde{S}_{3} + \beta_{1} \text{ superdiag} (\vec{e})_{l \times l} \otimes \text{diag} (\vec{e})_{l \times l} \otimes (1) \otimes \tilde{S}_{4} + \lambda_{2} \text{ diag} (\vec{e})_{l \times l} \otimes \text{superdiag} (\vec{e})_{l \times l} \otimes (1) \otimes \tilde{S}_{5} + \mu_{2} \text{ diag} (\vec{e})_{l \times l} \otimes \text{subdiag} ((1, \ldots, l - 1)^{T})_{l \times l} \otimes (1) \otimes \tilde{S}_{6} + \beta_{0} \text{ diag} (\vec{e})_{l \times l} \otimes \text{subdiag} ((1, \ldots, l - 1)^{T})_{l \times l} \otimes (1) \otimes \tilde{S}_{7} + \beta_{1} \text{ diag} (\vec{e})_{l \times l} \otimes \text{superdiag} (\vec{e})_{l \times l} \otimes (1) \otimes \tilde{S}_{8}
\]
An example (continued)

9 blocks associated with $Q_{l,l+1}$

$$\tilde{Q}_{l,l+1}^{(1,1)} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S_{k}^{(h)}(S_{l,1}^{(h)}, S_{l+1,1}^{(h)}) \right) \otimes \tilde{S}_{k}$$

$$= \lambda_1 (1) \otimes \text{diag}(\vec{e})_{(l+1) \times (l+2)} \otimes \text{diag}(\vec{e})_{(l+1) \times (l+2)} \otimes \tilde{S}_1$$

$$+ \beta_1 (1) \otimes \text{diag}(\vec{e})_{(l+1) \times (l+2)} \otimes \text{diag}(\vec{e})_{(l+1) \times (l+2)} \otimes \tilde{S}_4$$

$$\tilde{Q}_{l,l+1}^{(1,2)} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S_{k}^{(h)}(S_{l,1}^{(h)}, S_{l+1,2}^{(h)}) \right) \otimes \tilde{S}_{k}$$

$$= \lambda_2 (\vec{e}_{l+1}^{T})_{1 \times (l+1)} \otimes (\vec{e}_{l+1})_{(l+1) \times 1} \otimes \text{diag}(\vec{e})_{(l+1) \times (l+2)} \otimes \tilde{S}_5$$

$$+ \beta_1 (\vec{e}_{l+1}^{T})_{1 \times (l+1)} \otimes (\vec{e}_{l+1})_{(l+1) \times 1} \otimes \text{diag}(\vec{e})_{(l+1) \times (l+2)} \otimes \tilde{S}_8$$

$$\tilde{Q}_{l,l+1}^{(1,3)} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S_{k}^{(h)}(S_{l,1}^{(h)}, S_{l+1,3}^{(h)}) \right) \otimes \tilde{S}_{k}$$

$$= \lambda_3 (\vec{e}_{l+1}^{T})_{1 \times (l+1)} \otimes \text{diag}(\vec{e})_{(l+1) \times (l+1)} \otimes (\vec{e}_{l+1})_{(l+1) \times 1} \otimes \tilde{S}_9$$

$$+ \beta_1 (\vec{e}_{l+1}^{T})_{1 \times (l+1)} \otimes \text{diag}(\vec{e})_{(l+1) \times (l+1)} \otimes (\vec{e}_{l+1})_{(l+1) \times 1} \otimes \tilde{S}_{12}$$

$$\tilde{Q}_{l,l+1}^{(2,1)} = \sum_{k=1}^{12} \phi^{(k)} \left( \bigotimes_{h=1}^{3} S_{k}^{(h)}(S_{l,2}^{(h)}, S_{l+1,1}^{(h)}) \right) \otimes \tilde{S}_{k} = 0_{8l(l+1) \times 8(l+2)^2}$$
An example (continued)

\[ \tilde{Q}_{l,l+1}^{(2,2)} = \sum_{k=1}^{12} \phi^{(k)} \left( \sum_{h=1}^{3} S_{k}^{(h)}(S_{l,2}^{(h)}, S_{l+1,2}^{(h)}) \right) \otimes \tilde{S}_{k} \]

\[ = \lambda_2 \text{diag}(\tilde{e})_{l \times (l+1)} \otimes (1) \otimes \text{diag}(\tilde{e})_{(l+1) \times (l+2)} \otimes \tilde{S}_5 \]

\[ + \beta_1 \text{diag}(\tilde{e})_{l \times (l+1)} \otimes (1) \otimes \text{diag}(\tilde{e})_{(l+1) \times (l+2)} \otimes \tilde{S}_8 \]

\[ \tilde{Q}_{l,l+1}^{(2,3)} = \sum_{k=1}^{12} \phi^{(k)} \left( \sum_{h=1}^{3} S_{k}^{(h)}(S_{l,2}^{(h)}, S_{l+1,3}^{(h)}) \right) \otimes \tilde{S}_{k} \]

\[ = \lambda_3 \text{diag}(\tilde{e})_{l \times (l+1)} \otimes (\tilde{e}_{l+1}^{T})_{1 \times (l+1)} \otimes (\tilde{e}_{l+1}^{T})_{(l+1) \times 1} \otimes \tilde{S}_9 \]

\[ + \beta_1 \text{diag}(\tilde{e})_{l \times (l+1)} \otimes (\tilde{e}_{l+1}^{T})_{1 \times (l+1)} \otimes (\tilde{e}_{l+1}^{T})_{(l+1) \times 1} \otimes \tilde{S}_{12} \]

\[ \tilde{Q}_{l,l+1}^{(3,1)} = \sum_{k=1}^{12} \phi^{(k)} \left( \sum_{h=1}^{3} S_{k}^{(h)}(S_{l,3}^{(h)}, S_{l+1,1}^{(h)}) \right) \otimes \tilde{S}_{k} = 0_{8l^2 \times 8(l+2)^2} \]

\[ \tilde{Q}_{l,l+1}^{(3,2)} = \sum_{k=1}^{12} \phi^{(k)} \left( \sum_{h=1}^{3} S_{k}^{(h)}(S_{l,3}^{(h)}, S_{l+1,2}^{(h)}) \right) \otimes \tilde{S}_{k} = 0_{8l^2 \times 8(l+1)(l+2)} \]

\[ \tilde{Q}_{l,l+1}^{(3,3)} = \sum_{k=1}^{12} \phi^{(k)} \left( \sum_{h=1}^{3} S_{k}^{(h)}(S_{l,3}^{(h)}, S_{l+1,3}^{(h)}) \right) \otimes \tilde{S}_{k} \]

\[ = \lambda_3 \text{diag}(\tilde{e})_{l \times (l+1)} \otimes \text{diag}(\tilde{e})_{l \times (l+1)} \otimes (1) \otimes \tilde{S}_9 \]

\[ + \beta_1 \text{diag}(\tilde{e})_{l \times (l+1)} \otimes \text{diag}(\tilde{e})_{l \times (l+1)} \otimes (1) \otimes \tilde{S}_{12} \]
We use subscripts as in $g_p, d_p, c_p, \gamma_p, C_p, d_{p,h}$ for $h = 1, \ldots, H_I$, $(Low_p, High_p)$, $N_p$ for Example $p \in \{1, 2, 3, 4\}$, and report values of $c_p$ and $\gamma_p$ in two decimal digits of precision.

**Example 1.** (Gene Expression)


**Table 2: Transition classes of the gene expression model**

<table>
<thead>
<tr>
<th>$k$</th>
<th>$\phi^{(k)}$</th>
<th>$f^{(k,1)}(i_1)$</th>
<th>$f^{(k,2)}(i_2)$</th>
<th>$\vec{v}^{(k)}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$\lambda$</td>
<td>1</td>
<td>1</td>
<td>$\vec{e}_1^T$</td>
</tr>
<tr>
<td>2</td>
<td>$\mu$</td>
<td>$i_1$</td>
<td>1</td>
<td>$\vec{e}_2^T$</td>
</tr>
<tr>
<td>3</td>
<td>$\delta_1$</td>
<td>$i_1$</td>
<td>1</td>
<td>$-\vec{e}_1^T$</td>
</tr>
<tr>
<td>4</td>
<td>$\delta_2$</td>
<td>1</td>
<td>$i_2$</td>
<td>$-\vec{e}_2^T$</td>
</tr>
</tbody>
</table>

$H = H_I = 2$, $H_F = 0$, $\vec{i} = (i_1, i_2)$, $K = 4$, $\lambda, \mu, \delta_1, \delta_2 \in \mathbb{R}_{>0}$

$S_1 = S_2 = \mathbb{Z}_+$, $|\bar{S}| = 1$, $S = S_1 \times S_2 = \mathbb{Z}_+^{1 \times 2}$

$(2l + 1)$ states at level $l \in \mathbb{Z}_+$
Examples (continued)

Example 1. (cntd.)

\[ \lambda = \mu = \delta_2 = 0.05, \delta_1 = 0.015 \quad \text{and} \quad g_1(\vec{i}) = \|\vec{i}\|_2^2 = i_1^2 + i_2^2 \]

\[ \Rightarrow d_1(i_1, i_2) = -0.03i_1^2 - 0.1i_2^2 + 0.1i_1i_2 + 0.165i_1 + 0.05i_2 + 0.05 \]

Finiteness of \( c_1 \) and \( C_1 \) shown by selecting

\[ d_{1,1}(i_1) = -0.001i_1^2 + 0.165i_1 + 0.05, \quad d_{1,2}(i_2) = -0.005i_2^2 + 0.05i_2 \]

\[ d_1(i_1, i_2) - d_{1,1}(i_1) - d_{1,2}(i_2) \leq 0 \]

obtained by axes rotation and eliminating \( i_1i_2 \) term

Using \( HOM4PS2-2.0 \) package, \( c_1 = 1.86 \Rightarrow \text{for } \varepsilon = 0.05, \)
we have \( \gamma_1 = 35.25, (Low_1, High_1) = (0, 105), N_1(0, 105) = 11, 236 \)
Examples (continued)

Example 2. (Metabolite Synthesis with Two Metabolites and One Enzyme)

Table 3: Transition classes of the molecule synthesis model with one enzyme

<table>
<thead>
<tr>
<th>$k$</th>
<th>$\phi^{(k)}$</th>
<th>$f^{(k,1)}(i_1)$</th>
<th>$f^{(k,2)}(i_2)$</th>
<th>$f^{(k,3)}(i_3)$</th>
<th>$\vec{v}^{(k)}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$k_A K_I$</td>
<td>$\frac{1}{i_1 + K_I}$</td>
<td>1</td>
<td>$i_3$</td>
<td>$\vec{e}_1^T$</td>
</tr>
<tr>
<td>2</td>
<td>$k_B$</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>$\vec{e}_2^T$</td>
</tr>
<tr>
<td>3</td>
<td>$k_2$</td>
<td>$i_1$</td>
<td>$i_2$</td>
<td>1</td>
<td>$(-\vec{e}_1 - \vec{e}_2)^T$</td>
</tr>
<tr>
<td>4</td>
<td>$\mu$</td>
<td>$i_1$</td>
<td>1</td>
<td>1</td>
<td>$-\vec{e}_1^T$</td>
</tr>
<tr>
<td>5</td>
<td>$\mu$</td>
<td>1</td>
<td>$i_2$</td>
<td>1</td>
<td>$-\vec{e}_2^T$</td>
</tr>
<tr>
<td>6</td>
<td>$k_E A K_R$</td>
<td>$\frac{1}{i_1 + K_R}$</td>
<td>1</td>
<td>1</td>
<td>$\vec{e}_3^T$</td>
</tr>
<tr>
<td>7</td>
<td>$\mu$</td>
<td>1</td>
<td>1</td>
<td>$i_3$</td>
<td>$-\vec{e}_3^T$</td>
</tr>
</tbody>
</table>

$H = H_I = 3$, $H_F = 0$, $\vec{i} = (i_1, i_2, i_3)$, $K = 7$, $k_A, k_B, K_I, k_2, \mu, K_R, k_E A \in \mathbb{R}_{>0}$

$S_1 = S_2 = S_3 = \mathbb{Z}_+$, $|\vec{S}| = 1$, $S = S_1 \times S_2 \times S_3 = \mathbb{Z}_+^{1 \times 3}$

$(3l^2 + 3l + 1)$ states at level $l \in \mathbb{Z}_+$
Example 2. (cntd.)

\[ k_A = k_B = 0.3, K_I = 16, k_2 = 0.05, \mu = 0.1, K_R = 8, k_{EA} = 0.02 \quad \text{and} \quad g_2(\vec{i}) = ||\vec{i}||^2 \]

\[ \Rightarrow d_2(i_1, i_2, i_3) = \frac{9.6i_1i_3 + 4.8i_3}{i_1 + 16} + \frac{0.32i_3 + 0.16}{i_1 + 8} - 0.1i_1^2i_2 - 0.1i_1i_2^2 + 0.1i_1i_2 \\
-0.2i_1^2 - 0.2i_2^2 - 0.2i_3^2 + 0.1i_1 + 0.7i_2 + 0.1i_3 + 0.3 \]

Finiteness of \( c_2 \) and \( C_2 \) shown by selecting

\[ d_{2,1}(i_1) = -0.2i_1^2 + 0.1i_1 + 0.3, \quad d_{2,2}(i_2) = -0.2i_2^2 + 0.7i_2, \quad d_{2,3}(i_3) = -0.2i_3^2 + 14.82i_3 + 0.16 \]

\textbf{HOM4PS2-2.0} package requires equation systems to consist of polynomials
Therefore partial derivatives of \( i_1 \) and \( i_3 \) put over common denominator
Numerator used since denominator always positive for given parameters

Using \textbf{HOM4PS2-2.0} package, \( c_2 = 4.63 \quad \Rightarrow \quad \text{for} \ \varepsilon = 0.05, \)
we have \( \gamma_2 = 87.89, (Low_2, High_2) = (0, 31), N_2(0, 31) = 32, 768 \)
Example 3. (Metabolite Synthesis with Two Metabolites and Two Enzymes)

Table 4: Transition classes of the molecule synthesis model with two enzymes

<table>
<thead>
<tr>
<th>$k$</th>
<th>$\phi^{(k)}$</th>
<th>$f^{(k,1)}(i_1)$</th>
<th>$f^{(k,2)}(i_2)$</th>
<th>$f^{(k,3)}(i_3)$</th>
<th>$f^{(k,4)}(i_4)$</th>
<th>$\vec{v}^{(k)}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$k_A K_I$</td>
<td>$\frac{1}{i_1 + K_I}$</td>
<td>1</td>
<td>$i_3$</td>
<td>1</td>
<td>$-\vec{e}_1^T$</td>
</tr>
<tr>
<td>2</td>
<td>$k_B K_I$</td>
<td>1</td>
<td>$\frac{1}{i_2 + K_I}$</td>
<td>1</td>
<td>$i_4$</td>
<td>$-\vec{e}_2^T$</td>
</tr>
<tr>
<td>3</td>
<td>$k_2$</td>
<td>$i_1$</td>
<td>$i_2$</td>
<td>1</td>
<td>1</td>
<td>$(\vec{e}_1 - \vec{e}_2)^T$</td>
</tr>
<tr>
<td>4</td>
<td>$\mu$</td>
<td>$i_1$</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>$-\vec{e}_1^T$</td>
</tr>
<tr>
<td>5</td>
<td>$\mu$</td>
<td>1</td>
<td>$i_2$</td>
<td>1</td>
<td>1</td>
<td>$-\vec{e}_2^T$</td>
</tr>
<tr>
<td>6</td>
<td>$k_{EA} K_R$</td>
<td>$\frac{1}{i_1 + K_R}$</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>$-\vec{e}_3^T$</td>
</tr>
<tr>
<td>7</td>
<td>$k_{EB} K_R$</td>
<td>1</td>
<td>$\frac{1}{i_2 + K_R}$</td>
<td>1</td>
<td>1</td>
<td>$\vec{e}_4^T$</td>
</tr>
<tr>
<td>8</td>
<td>$\mu$</td>
<td>1</td>
<td>1</td>
<td>$i_3$</td>
<td>1</td>
<td>$-\vec{e}_3^T$</td>
</tr>
<tr>
<td>9</td>
<td>$\mu$</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>$i_4$</td>
<td>$-\vec{e}_4^T$</td>
</tr>
</tbody>
</table>

$H = H_I = 4, \ H_F = 0, \ \vec{i} = (i_1, i_2, i_3, i_4), \ K = 9$

$k_A, k_B, K_I, k_2, \mu, K_R, k_{EA}, k_{EB} \in \mathbb{R}_{>0}$

$S_1 = S_2 = S_3 = S_4 = \mathbb{Z}_+, \ |\vec{S}| = 1, \ S = S_1 \times S_2 \times S_3 \times S_4$

$(4l^3 + 6l^2 + 4l + 1)$ states at level $l \in \mathbb{Z}_+$
Example 3. (cntd.)

\[ k_A = k_B = 0.3, K_I = 16, k_2 = 0.05, \mu = 0.2, K_R = 8, k_{E_A} = k_{E_B} = 0.02 \text{ and } g_3(\vec{i}) = \|\vec{i}\|^2 \]

\[ \Rightarrow d_3(i_1, i_2, i_3, i_4) = \frac{9.6i_1i_3 + 4.8i_3}{i_1 + 16} + \frac{0.32i_3 + 0.16}{i_1 + 8} + \frac{9.6i_2i_4 + 4.8i_4}{i_2 + 16} + \frac{0.32i_4 + 0.16}{i_2 + 8} - 0.1i_1^2i_2 - 0.1i_1i_2^2 + 0.1i_1i_2 - 0.4i_1^2 \\
-0.4i_2^2 - 0.4i_3^2 - 0.4i_4^2 + 0.2i_1 + 0.2i_2 + 0.2i_3 + 0.2i_4 \]

Finiteness of \( c_3 \) and \( C_3 \) shown by selecting

\[ d_{3,1}(i_1) = -0.4i_1^2 + 0.2i_1, \quad d_{3,2}(i_2) = -0.4i_2^2 + 0.2i_2 \]

\[ d_{3,3}(i_3) = -0.4i_3^2 + 14.92i_3 + 1.6, \quad d_{3,4}(i_4) = -0.4i_4^2 + 14.92i_4 + 1.6 \]

Using \textit{HOM4PS2-2.0} package, \( c_3 = 0.90 \Rightarrow \) for \( \epsilon = 0.05 \),

we have \( \gamma_3 = 17.11, (Low_3, High_3) = (0, 9), N_3(0, 9) = 10,000 \)
Examples (continued)

Example 4. (Repressilator (cntd.))

\[ 8(3l^2 + 3l + 1) \text{ states at level } l \in \mathbb{Z}_+ \]

\[ \lambda_1 = \lambda_2 = \lambda_3 = 1.3, \mu_1 = \mu_2 = \mu_3 = 0.8, \beta_0 = 1, \beta_1 = 0.5 \text{ and } g_4(\vec{i}) = ||\vec{i}||_2^2 \]

\[ \Rightarrow d_4(i_1, i_2, i_3, i_4, i_5, i_6) = -3.6i_1^2 + 2i_1^2i_4 - i_1i_4 - 2.6i_1i_6 + 5.4i_1 - 3.6i_2^2 
+ 2i_2^2i_5 - i_2i_5 - 2.6i_2i_4 + 5.4i_2 - 3.6i_3^2 + 2i_3^2i_6 
- i_3i_6 - 2.6i_3i_5 + 5.4i_3 - 1.3i_4 - 1.3i_5 - 1.3i_6 + 3.9 \]

Finiteness of \( c_4 \) and \( C_4 \) shown by selecting

\[ d_{4,1}(i_1) = -1.6i_1^2 + 5.4i_1 + 1.3, \quad d_{4,2}(i_2) = -1.6i_2^2 + 5.4i_2 + 1.3 \]

\[ d_{4,3}(i_3) = -1.6i_3^2 + 5.4i_3 + 1.3 \]

since \( i_4, i_5, \) and \( i_6 \) each take values from \( \{0, 1\} \)

Using \( \text{HOM4PS2-2.0} \) package, \( c_4 = 9.30 \ \Rightarrow \text{for } \varepsilon = 0.05, \]

we have \( \gamma_4 = 176.7, (\text{Low}_4, \text{High}_4) = (0, 12), N_4(0, 12) = 17,576 \)
Numerical results

Experiments on 4 GB PC with 1.83 GHz Intel Core2 Duo

Matrix analytic approach used: \( R_{High} = 0 \)


\( R_l \) for \( l = Low, \ldots, High - 1 \) computed from

\[
R_l = Q_{l,l+1}(-Q_{l+1,l+1} - R_{l+1}Q_{l+2,l+1})^{-1}
\]

LDQBD solver available in Matlab

Large main memory necessary to store relatively dense \( R_l \)
(see Figure 1 for their nonzero densities in examples; they become very dense as level number moves towards \( Low \)) and temporary factors allocated by Matlab while solving linear systems involving them
Numerical results (continued)

Figure 1: Nonzero densities of $R_l$ for $l = \text{Low}, \ldots, \text{High}$
Numerical results (continued)

Table 5: LDQBD solver results with $g(\vec{i}) = \|\vec{i}\|_2^2$ for $\varepsilon = 0.05$

<table>
<thead>
<tr>
<th>Example</th>
<th>(Low, High)</th>
<th>Time</th>
<th>$|\tilde{\pi}Q|_\infty$</th>
<th>Memory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gene Expression</td>
<td>(0,105)</td>
<td>4 s</td>
<td>2e-17</td>
<td>20 MB</td>
</tr>
<tr>
<td>Molecule Synthesis (One Enzyme)</td>
<td>(0,31)</td>
<td>188 s</td>
<td>9e-17</td>
<td>667 MB</td>
</tr>
<tr>
<td>Molecule Synthesis (Two Enzymes)</td>
<td>(0,9)</td>
<td>55 s</td>
<td>2e-7</td>
<td>180 MB</td>
</tr>
<tr>
<td>Repressilator</td>
<td>(0,12)</td>
<td>133 s</td>
<td>2e-8</td>
<td>335 MB</td>
</tr>
</tbody>
</table>

Figure 2: $\tilde{\pi}(i_1, i_2, i_3)$ across countably infinite state variables for repressilator model
Numerical results (continued)

(a) $||\tilde{\pi}^{(l)}||_1$, $\max(\tilde{\pi}^{(l)})$, and $\min(\tilde{\pi}^{(l)})$ across levels

(b) $\sigma_1(\tilde{R}_l)$ across levels

Figure 3: Plots for the repressilator model
Numerical results (continued)

Figure 4: \( \tilde{\pi}(i_1, i_2) \) across countably infinite state variables for gene expression model

\[ \max(\pi(i_1, i_2)) = 0.048213 \text{ at } (i_1, i_2) = (2, 2) \]
(a) $\|\tilde{\pi}^{(l)}\|_1$, $\max(\tilde{\pi}^{(l)})$, and $\min(\tilde{\pi}^{(l)})$ across levels

(b) $\sigma_1(\tilde{R}_l)$ across levels

Figure 5: Plots for the gene expression model
Numerical results (continued)

Figure 6: $\tilde{\pi}(i_1, i_2, i_3)$ across countably infinite state variables for molecule synthesis model with one enzyme
Numerical results (continued)

(a) $||\tilde{\pi}^{(l)}||_1$, $\max(\tilde{\pi}^{(l)})$, and $\min(\tilde{\pi}^{(l)})$ across levels

(b) $\sigma_1(\tilde{R}_l)$ across levels

Figure 7: Plots for the molecule synthesis model with one enzyme
Numerical results (continued)

Stochastic simulation (Gillespie, J. Phys. Chem. 81, 1977) with StochKit (Sanft, Wu, Roh, Fu, Lim, Petzold, Bioinforma. 11, 2011) discussed in (Li, Cao, Petzold, Gillespie, Biotechnol. Prog. 24, 2008)

31 sample paths are taken to provide confidence intervals (CIs) for 95% probability

StochKit (SK) mean for particular molecule in sample path after $T$ transitions

$$\text{Mean}_{SK}(J) = \frac{\sum_{j=1}^{J} S_j \Delta t_j}{\sum_{j=1}^{J} \Delta t_j}$$

where $\Delta t_j$: exponentially distributed time of transition $j$

$S_j$: state of molecule during $\Delta t_j$

$$\text{Mean}_{SK}(J + 1) = \text{Mean}_{SK}(J) + \frac{(S_{J+1} - \text{Mean}_{SK}(J)) \Delta t_{J+1}}{\Delta t_{J+1} + \sum_{j=1}^{J} \Delta t_j}$$
Numerical results (continued)

Simulation terminated when \( |\text{Mean}_{\text{SK}}(J+1) - \text{Mean}_{\text{SK}}(J)| < 10^{-16} \)

\[
\text{Rel. Err.} = \frac{|\text{Mean}_{\text{LDQBD}} - \text{Mean}_{\text{SK}}|}{\text{Mean}_{\text{LDQBD}}}
\]

Table 6: StochKit simulation results

<table>
<thead>
<tr>
<th>Example</th>
<th>( J )</th>
<th>Time Mol.</th>
<th>Mean(_{\text{SK}})</th>
<th>CI(_{\text{SK}})</th>
<th>Mean(_{\text{LDQBD}})</th>
<th>Rel. Err.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gene Expression</td>
<td>2e+9</td>
<td>324 s</td>
<td>1 3.33334 0.00095</td>
<td>3.33333</td>
<td>2e-5</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>2 3.33345 0.00112</td>
<td>3.33333</td>
<td>4e-5</td>
<td></td>
</tr>
<tr>
<td>Molecule Synthesis</td>
<td>4e+9</td>
<td>784 s</td>
<td>1 0.27258 0.00014</td>
<td>0.28097</td>
<td>3e-2</td>
<td></td>
</tr>
<tr>
<td>(One Enzyme)</td>
<td></td>
<td></td>
<td>2 2.74106 0.00032</td>
<td>2.73546</td>
<td>2e-3</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3 0.19459 0.00009</td>
<td>0.19442</td>
<td>9e-4</td>
<td></td>
</tr>
<tr>
<td>Molecule Synthesis</td>
<td>7e+9</td>
<td>1,241 s</td>
<td>1 0.13530 0.00003</td>
<td>0.13753</td>
<td>2e-2</td>
<td></td>
</tr>
<tr>
<td>(Two Enzymes)</td>
<td></td>
<td></td>
<td>2 0.13529 0.00003</td>
<td>0.13753</td>
<td>2e-2</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3 0.09860 0.00001</td>
<td>0.09858</td>
<td>2e-4</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4 0.09860 0.00002</td>
<td>0.09858</td>
<td>2e-4</td>
<td></td>
</tr>
<tr>
<td>Repressilator</td>
<td>4e+9</td>
<td>761 s</td>
<td>1 0.75708 0.00023</td>
<td>0.75701</td>
<td>1e-4</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 0.75708 0.00019</td>
<td>0.75701</td>
<td>9e-5</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3 0.75699 0.00024</td>
<td>0.75701</td>
<td>2e-5</td>
<td></td>
</tr>
</tbody>
</table>
Conclusion

- Kronecker representation for nonzero blocks of $Q$ underlying LDQBD provided
- Kronecker representation enables to cope with multi-dimensionality
- Memory requirement of the LDQBD solver imcomparably large with respect to simulation
- Compared to simulation, Kronecker based LDQBD solver yields results with higher accuracy in less time for problems considered here
- Efficient implementation of matrix analytic solvers based on Kronecker products for LDQBDs requires further investigation