KRONECKER-BASED INFINITE LEVEL-DEPENDENT QBDS: MATRIX ANALYTIC SOLUTION VERSUS SIMULATION

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By

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ABSTRACT

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Markovian systems with multiple interacting subsystems under the influence of a control unit are considered. The state spaces of the subsystems are countably infinite, whereas that of the control unit is finite. A recent infinite level-dependent quasi-birth-and-death (LDQBD) model for such systems is extended by facilitating the automatic representation and generation of the nonzero blocks in its underlying infinitesimal generator matrix with sums of Kronecker products. Experiments are performed on systems of stochastic chemical kinetics having two or more countably infinite state space subsystems. Results indicate that, albeit more memory consuming, there are many cases where a matrix analytic solution coupled with Lyapunov theory yields a faster and more accurate steady-state measure compared to that obtained with simulation.

Keywords: Markov processes; numerical analysis; simulation; biology; queues: theory.

ÖZET

KRONECKER-TEMELLİ DÜZEY-BAĞIMLI SONSUZ SÖZDE-DOĞUM-ÖLÜM SÜREÇLERİ: MATRİS ÇÖZÜMLEMELİ YÖNTEM VE BENZETİM KARŞILAŞTIRMASI

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Bu tezde sonlu bir denetim birimi ve sonsuz uzayda tanımlı çoklu etkileşimli altsistemleri olan Markov sistemlerini ele aldık. Bu sistemler için geliştirilmiş olan düzey-bağımlı sonsuz sözde-doğum-ölüm süreci modelini, bu sistemlerin sıfırdan farklı bloklarının Kronecker çarpım toplamlarını kullanarak nasıl tanımlanabileceğini gösterdik. İki ya da daha fazla sonsuz uzayda tanımlı altsistemi olan rassal kimyasal devingen sistemler üzerinde gerçekleştirdiğimiz deneyler, matris çözümlemeli yöntemin pek çok durumda, benzetime oranla, daha hızlı ve doğruya yakın sonuç verdiğini gösterdik.

Anahtar sözcükler: Markov süreçleri; sayısal çözümleme; benzetim; biyoloji; kuyruk kuramı.

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Contents

List of Figures

List of Tables

Chapter 1

Introduction

A Markovian system is a system where history has no effect on the future. In this thesis, we consider Markovian systems with interacting subsystems under the influence of a control unit. The state space is countably infinite and n-dimensional with n_I countably infinite state variables and n_F finite state variables, where $n_I \geq 2$, $n_F \geq 0$, and $n = n_I + n_F$. We will be leaving out the word state and just calling the state variables as variables throughout our presentation. The n_I countably infinite variables are used to represent the interacting n_I subsystems and the n_F finite variables are associated with the control unit. When the control unit does not exist, we have $n = n_I$. The state space of variable i in the n-dimensional state space is denoted by $\mathcal{S}_i$ and $\mathcal{S}_i \subseteq \mathbb{Z}_+$ for $i = 1, \ldots, n$. Without loss of generality, let us assume that the first n_I indices are assigned to the interacting subsystems. Hence, $\mathcal{S}_i$ is countably infinite for $i = 1, \ldots, n_I$ and finite for $i = n_I + 1, \ldots, n$.

We let $\mathcal{S}$ be the state space of the underlying time-homogeneous irreducible continuous-time Markov chain (CTMC) [12, 27] corresponding to the system. Clearly, not all states in the product state space $\times_{i=1}^{n} \mathcal{S}_i$, where $\times$ is the Cartesian product operator, are necessarily reachable. However, each state in $\mathcal{S}$ is reachable from every other state in $\mathcal{S}$ by definition since the associated CTMC is assumed to be irreducible. In many cases, $\mathcal{S}$ is a proper subset of the product state space (i.e., $\mathcal{S} \subset \times_{i=1}^{n} \mathcal{S}_i$). In this thesis, we assume that the CTMC associated with $\mathcal{S}$ is ergodic. An ergodic CTMC is irreducible and positive-recurrent which guarantees that the initial state loses its effect on its state probability distribution as time progresses and the expected revisiting time of each state is finite. We are interested in computing steady-state probability measures [12, 27] of such systems whose existence is guaranteed by the ergodicity assumption of the corresponding CTMCs.

A stochastic chemical system [15, 20, 25, 30] exhibits a set of chemical reactions where molecules are transformed into other molecules with a certain reaction rate. The mathematical model of a chemical reaction can be represented by stoichiometric equations which include reactants on the left-hand side, products on the right-hand side, and the rate of the reaction over the right arrow indicating the reaction. That is, a stoichiometric equation has the form

$$r_1 X_1 + \cdots + r_{n_I} X_{n_I} \xrightarrow{\alpha} p_1 X_1 + \cdots + p_{n_I} X_{n_I},$$

where $\alpha > 0$ is the reaction rate, X_i denotes molecule i, and $r_i \in \mathbb{Z}_+$ and $p_i \in \mathbb{Z}_+$ respectively represent reactant and product coefficients of X_i for $i \in \{1, \ldots, n_I\}$. The reactant and product coefficients denote the number of molecules that enter the reaction and are produced as a result of the reaction, respectively. In a particular reaction rate, the number of a certain molecule is denoted by the lower-case version of the capital letter used to denote that molecule. Some chemical systems include control variables. A control variable is boolean and either has no effect on the reaction or blocks the reaction according to its existence in the system. It is written as a reactant if it has an effect on the reaction and a product if its state is a result of the reaction. Existence and absence of control variable X is denoted by X and $\bar{X}$, respectively.

Stochastic chemical systems can be modelled using the described n-dimensional state representation where n_I countably infinite variables are the molecules and the remaining n_F finite variables in the n-dimensional state space are the control variables of the system. The state change vector of a reaction is the difference of product coefficients and reactant coefficients and the reaction rate is determined by many factors such as type of the reaction, number of molecules in the system, and environmental factors. The described n-dimensional state representation can also be used to model queueing networks [4, 12, 14, 16] where the n_I countably infinite variables represent the occupancies of queues with unbounded waiting space in the network and the remaining n_F finite variables in the n-dimensional state space can be perceived as forming the control unit. It is the former class of problems we consider in this thesis.

Recently, in Dayar et al. [9] it has been shown that systems of stochastic chemical kinetics can be modeled as infinite level-dependent quasi-birth-and-death processes (LDQBDs). In particular, the maximum value among the n_I countably infinite variables determines the level number, and the number of different possibilities for the n_I countably infinite variables times the number of different possibilities for the n_F finite variables determines the number of states within a level. Assuming that the subset of states in $\mathcal{S}$ corresponding to level l is denoted by $\mathcal{S}^{(l)}$, this yields a block tridiagonal infinitesimal generator matrix [3, 24]

$$Q = \begin{pmatrix} Q_{0,0} & Q_{0,1} & & & & \\ Q_{1,0} & Q_{1,1} & Q_{1,2} & & & \\ & \ddots & \ddots & \ddots & & \\ & & Q_{l,l-1} & Q_{l,l} & Q_{l,l+1} & \\ & & & \ddots & \ddots & \ddots \end{pmatrix} \tag{1.1}$$

in which the nonzero blocks at level l are given by $Q_{l,l-1} \in \mathbb{R}_{\geq 0}^{|\mathcal{S}^{(l)}| \times |\mathcal{S}^{(l-1)}|}$, $Q_{l,l} \in \mathbb{R}^{|\mathcal{S}^{(l)}| \times |\mathcal{S}^{(l)}|}$, $Q_{l,l+1} \in \mathbb{R}_{\geq 0}^{|\mathcal{S}^{(l)}| \times |\mathcal{S}^{(l+1)}|}$. These blocks are generally very sparse and their nonzero entries may have values depending on the level number. The off-diagonal entries of Q are nonnegative, whereas its diagonal entries are negative. Level 0 forms the boundary and has two nonzero blocks. Clearly, the ordering of states within a level is only fixed up to a permutation. Observe that transitions are possible only between adjacent levels and the number of states within each level increases with increasing level number. The latter is due to the increase in the number of different possibilities for the n_I countably infinite variables according to the level definition being used.

We let $X(t) = (X_1(t), \ldots, X_n(t))$ denote the state of the LDQBD at time t and $\{X(t), t \geq 0\}$ be the associated CTMC process. Then the probability that the LDQBD is in state $x \in \mathcal{S}$ at time t may be written as $Pr\{X(t) = x\} = Pr\{X_1(t) = x_1, \ldots, X_n(t) = x_n\}$, and its steady-state probability distribution row vector, $\pi := \lim_{t\to\infty} Pr\{X(t)\}$, satisfies $\pi Q = 0$ and $\sum_{x\in\mathcal{S}} \pi(x) = 1$ [12, 27]. By using a judiciously chosen Lyapunov function [11, 29], we can obtain the values of lower and higher level numbers (called *Low* and *High*, respectively) as in Dayar et al. [9] between which a specified percentage of the steady-state probability mass lies. Once these two level numbers are available, the computation of π follows from a matrix analytic method [13, 16, 21] developed by Bright and Taylor [3]. In this method, firstly the conditional expected sojourn time matrix at level *High*, R_{High}, is computed. By using the recursive relationship

$$R_l = Q_{l,l+1}(-Q_{l+1,l+1} - R_{l+1}Q_{l+2,l+1})^{-1} \quad \text{for } l \geq 0,$$

the conditional expected sojourn time matrices between *Low* and *High* are computed. After obtaining these matrices, steady-state probability subvectors for levels *Low* to *High* are computed by the equation

$$\pi^{(l+1)} = \pi^{(l)} R_l \quad \text{for } l \geq 0,$$

where $\pi^{(l)}$ and $\pi^{(l+1)}$ are the steady-state probability subvectors of levels l and $(l+1)$, respectively. The advantage of this approach compared to approximative methods (including simulation) lies in the fact that steady-state measures can be computed exactly up to machine precision by prescribing the difference between *High* and *Low* sufficiently large.

The motivation for this study is based on the observation that, although it may be relatively easy to manually enumerate the states and generate the sparse nonzero blocks $Q_{l,l-1}$, $Q_{l,l}$, $Q_{l,l+1}$ within each level when $n_I = 2$, the task becomes unmanageable once $n_I > 2$. Hence, there is a need to be able to do this from the problem specification in an automated manner. We will see that this problem can be handled smoothly by introducing Kronecker products [4, 6, 22, 23] to cope with multi-dimensionality. Yet, an important requirement in this procedure is to be able to represent only the irreducible set of states associated with the underlying CTMC. Thanks to hierarchical Markovian models (HMMs) introduced by Buchholz [4], this second problem can be solved without much difficulty as well. Armed with a Kronecker-based representation for infinite LDQBDs, we finally undertake possibly for the first time a comparative study between the stochastic simulation of Gillespie [10] and the matrix analytic approach.

In the next chapter, we introduce a specification for the class of problems we consider and build a Kronecker representation of the corresponding sparse nonzero blocks in Q. In the third chapter, we provide a detailed example showing how this all works in practice. In the same chapter, we also introduce three- and four-dimensional examples from the same domain. In the fourth chapter we discuss implementation issues related to the matrix analytic approach and the simulation algorithm. The fifth chapter reports on the results of numerical experiments with the matrix analytic approach on the examples introduced earlier and with simulation. In the sixth chapter, we conclude. In the appendices, we provide proofs, the code used for solving the problem with its readme files and the configuration files of the examples discussed in the thesis.

Throughout the thesis, all vectors are column vectors except state vectors, and state probability vectors. e represents a column vector of ones. e_i represents the ith column of the identity matrix, I. diag(a), subdiag(a), and superdiag(a) denote matrices with the entries of vector a along their diagonal, subdiagonal, and superdiagonal, respectively. All other entries of these martices are zero. A subscript under I is used to indicate its order. Similarly, the subscript $m \times n$ under a matrix indicates that the matrix is $(m \times n)$. The lengths of the vectors are determined by the context in which they are used and ^{T} stands for transposition.

Chapter 2

Kronecker Representation

We first define the Kronecker product operation [5, 31].

Definition 1 *Given two matrices $A \in \mathbb{R}^{r_A \times c_A}$ and $B \in \mathbb{R}^{r_B \times c_B}$ as*

$$A = \begin{pmatrix} a_{1,1} & a_{1,2} & \cdots & a_{1,c_A} \\ a_{2,1} & a_{2,2} & \cdots & a_{2,c_A} \\ \vdots & \vdots & \ddots & \vdots \\ a_{r_A,1} & a_{r_A,2} & \cdots & a_{r_A,c_A} \end{pmatrix}, \quad B = \begin{pmatrix} b_{1,1} & b_{1,2} & \cdots & b_{1,c_B} \\ b_{2,1} & b_{2,2} & \cdots & b_{2,c_B} \\ \vdots & \vdots & \ddots & \vdots \\ b_{r_B,1} & b_{r_B,2} & \cdots & b_{r_B,c_B} \end{pmatrix},$$

their Kronecker product $C = A \otimes B \in \mathbb{R}^{r_A r_B \times c_A c_B}$ is defined as

$$C = \begin{pmatrix} a_{1,1}B & a_{1,2}B & \cdots & a_{1,c_A}B \\ a_{2,1}B & a_{2,2}B & \cdots & a_{2,c_A}B \\ \vdots & \vdots & \ddots & \vdots \\ a_{r_A,1}B & a_{r_A,2}B & \cdots & a_{r_A,c_A}B \end{pmatrix}.$$

In this thesis, we consider stochastic chemical systems with n_I molecules, n_F control variables, and J reactions. Each reaction has a corresponding stoichiometric equation and is represented by atransition class over $\mathcal{S}$ and let $x = (x_1, \ldots, x_n) \in \mathbb{Z}_+^{1 \times n}$ denote a state in $\mathcal{S}$ which represents the number of molecules in the system and the states of the control variables.

Definition 2 *A transition class* $j \in \{1, \ldots, J\}$ *is a pair* $(\psi^{(j)} \prod_{i=1}^{n} h^{(j,i)}(x_i), v^{(j)})$*, where* $\psi^{(j)} \in \mathbb{R}_{>0}$*,* $h^{(j,i)}(x_i) : \mathcal{S}_i \to \mathbb{R}_{\geq 0}$*, and* $v^{(j)} \in \mathbb{Z}^{1 \times n}$ *are respectively its state independent transition rate, its state dependent transition rate for variable* $i \in \{1, \ldots, n\}$*, and its state change vector. The first element of the pair,*

$$\alpha_j(x) := \psi^{(j)} \prod_{i=1}^{n} h^{(j,i)}(x_i),$$

specifies the transition rate from state $x \in \mathcal{S}$ *to state* $(x + v^{(j)}) \in \mathcal{S}$*. The second element of the pair,* $v^{(j)} \in \mathbb{Z}^{1 \times n}$*, specifies the successor state of the transition, where* $v_i^{(j)}$ *denotes the change in variable* i *due to transition class* j*.*

The following definition associates n_I transition rate matrices with each transition class in Definition 2.

Definition 3 *The transition rate matrix of countably infinite variable* $i \in \{1, \ldots, n_I\}$ *for transition class* $j \in \{1, \ldots, J\}$*, denoted by* $Z^{(j,i)} \in \mathbb{R}_{\geq 0}^{|\mathcal{S}_i| \times |\mathcal{S}_i|}$*, is given entrywise as*

$$Z^{(j,i)}(x_i, y_i) = \begin{cases} h^{(j,i)}(x_i) & \text{if } \; y_i = x_i + v_i^{(j)} \\ 0 & \text{otherwise} \end{cases} \quad \text{for } \; x_i, y_i \in \mathcal{S}_i.$$

Note that in Definition 3, only countably infinite variables are considered. We also define transition rate matrices for finite variables. However, for each transition class, we prefer to define a combined transition rate matrix for all finite variables since we have observed that in practice $|\mathcal{S}_i|$ for $i = n_I + 1, \ldots, n$ is very small. Now, let $\bar{\mathcal{S}}$ denote the set of states which finite variables can take. Then, $\bar{\mathcal{S}} \subseteq \times_{i=n_I+1}^{n} \mathcal{S}_i$.

Definition 4 *When* $n > n_I$*, the combined transition rate matrix of finite variables for transition class* $j \in \{1, \ldots, J\}$*, denoted by* $\bar{Z}^{(j)} \in \mathbb{R}_{\geq 0}^{|\bar{\mathcal{S}}| \times |\bar{\mathcal{S}}|}$*, is given entrywise as*

$$\bar{Z}^{(j)}((x_{n_I+1}, \ldots, x_n), (y_{n_I+1}, \ldots, y_n)) =$$
$$\begin{cases} \prod_{i=n_I+1}^{n} h^{(j,i)}(x_i) & \text{if } \; (y_{n_I+1}, \ldots, y_n) = (x_{n_I+1}, \ldots, x_n) + (v_{n_I+1}^{(j)}, \ldots, v_n^{(j)}) \\ 0 & \text{otherwise} \end{cases}$$

for $(x_{n_I+1}, \ldots, x_n), (y_{n_I+1}, \ldots, y_n) \in \bar{\mathcal{S}}$. *When* $n = n_I$, *it is assumed that* $|\bar{\mathcal{S}}| = 1$ *and* $\bar{Z}^{(j)} = 1$.

We are interested in obtaining a Kronecker representation for the nonzero blocks of Q from the state independent transition rates and the transition rate matrices of Definitions 3 and 4. To this end, let us start by formally defining $\mathcal{S}^{(l)}$.

Definition 5 *The subset of states corresponding to level* $l \in \mathbb{Z}_+$ *is given by*

$$\mathcal{S}^{(l)} = \{x \in \mathcal{S} \mid max(x_1, \ldots, x_{n_I}) = l\}, \ \mathcal{S} = \bigcup_{l=0}^{\infty} \mathcal{S}^{(l)}, \ \mathcal{S}^{(l)} \cap \mathcal{S}^{(k)} = \emptyset \ \ for \ \ l \neq k.$$

The maximum function is justified by observing that the maximum valued variable among $x_1, \ldots, x_{n_I}$ in any state $x \in \mathcal{S}$ changes by at most one through any transition due to the particular form of the state change vectors $v^{(j)}$ in the transition classes for systems of stochastic chemical kinetics.

For each level l, the values a variable can take depend on the values of other variables. Therefore, first we define a partition of the values a countably infinite variable can take where there is no such dependency in a way similar to HMMs in [4]. Then we introduce a partition of $\mathcal{S}^{(l)}$ in Definition 5 based on the partitions of countably infinite variables defined before.

Definition 6 *Let*

$$\mathcal{S}_i^{(l,u)} = \begin{cases} \{x_i \mid 0 \leq x_i \leq l-1\} & if \ \ i < u \\ \{l\} & if \ \ i = u \\ \{x_i \mid 0 \leq x_i \leq l\} & if \ \ i > u \end{cases} \quad for \ \ i, u \in \{1, \ldots, n_I\}.$$

Then partition $u \in \{1, \ldots, n_I\}$ *of* $\mathcal{S}^{(l)}$, *denoted by* $\mathcal{S}^{(l,u)}$, *is given by*

$$\mathcal{S}^{(l,u)} = \{x \in \mathcal{S}^{(l)} \mid (x_1, \ldots, x_{n_I}) \in \times_{i=1}^{n_I} \mathcal{S}_i^{(l,u)} \ \ and \ \ (x_{n_I+1}, \ldots, x_n) \in \bar{\mathcal{S}}\}.$$

Finally,

$$\mathcal{S}^{(l)} = \bigcup_{u=1}^{n_I} \mathcal{S}^{(l,u)}, \ \mathcal{S}^{(l,u)} \cap \mathcal{S}^{(l,w)} = \emptyset \ \ for \ \ u \neq w.$$

Without loss of generality, the partitions $\mathcal{S}^{(l,u)}$ are assumed to be ordered within $\mathcal{S}^{(l)}$ according to increasing partition index, u.

For given level $l \in \mathbb{Z}_+$ and noting that $n \geq n_I \geq 2$, by Definition 6 we have

$$\left|\mathcal{S}^{(l,u)}\right| = (l+1)^{n_I-u}(l)^{u-1}\left|\bar{\mathcal{S}}\right| \quad \text{for} \quad u \in \{1,\ldots,n_I\}.$$

Then the number of states in level l can be obtained as

$$\left|\mathcal{S}^{(l)}\right| = \sum_{u=1}^{n_I}\left|\mathcal{S}^{(l,u)}\right| = \left|\bar{\mathcal{S}}\right|((l+1)^{n_I} - (l)^{n_I}). \tag{2.1}$$

Observe that the number of states at level $l \in \mathbb{Z}_+$ is $O(l^{n_I-1})$.

Now, we are in a position to introduce the Kronecker representation of nonzero blocks in Q following the partitions of subset of states at each level given by Definition 6.

Definition 7 *The nonzero blocks $Q_{0,0}$, $Q_{0,1}$, $Q_{1,0}$, and $Q_{l,m}$ for $l > 0$, $m \in \{l-1, l, l+1\}$ are respectively (1×1), $(1 \times n_I)$, $(n_I \times 1)$, and $(n_I \times n_I)$ block matrices as in*

$$Q_{0,0} = \begin{pmatrix} Q_{0,0}^{(1,1)} \end{pmatrix},$$

$$Q_{0,1} = \begin{pmatrix} Q_{0,1}^{(1,1)} & \ldots & Q_{0,1}^{(1,n_I)} \end{pmatrix},$$

$$Q_{1,0} = \begin{pmatrix} Q_{1,0}^{(1,1)} \\ \vdots \\ Q_{1,0}^{(n_I,1)} \end{pmatrix},$$

$$Q_{l,m} = \begin{pmatrix} Q_{l,m}^{(1,1)} & \ldots & Q_{l,m}^{(1,n_I)} \\ \vdots & \ddots & \vdots \\ Q_{l,m}^{(n_I,1)} & \ldots & Q_{l,m}^{(n_I,n_I)} \end{pmatrix}.$$

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

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

for $l, m, u, w \geq 0$ *where*

$$\tilde{Q}_{l,m}^{(u,w)} = \sum_{j=1}^{J} \psi^{(j)} \left(\left(\bigotimes_{i=1}^{n_I} Z^{(j,i)}(\mathcal{S}_i^{(l,u)}, \mathcal{S}_i^{(m,w)}) \right) \otimes \bar{Z}^{(j)} \right)$$

and $Z^{(j,i)}(\mathcal{S}_i^{(l,u)}, \mathcal{S}_i^{(m,w)})$ *denotes the submatrix of* $Z^{(j,i)}$ *incident on row indices in* $\mathcal{S}_i^{(l,u)}$ *and column indices in* $\mathcal{S}_i^{(m,w)}$*. The first summation in diag should have a starting index of 0 rather than* -1 *for the equation of the block* $Q_{0,0}^{(1,1)}$*.*

In the next chapter, we introduce four examples we will be using in the experiments. We employ the two-dimensional one to illustrate the contents of the nonzero blocks of Q as flat sparse matrices so that they may be used to validate the Kronecker representation.

Chapter 3

Examples

Example 1 *(Gene Expression) Consider a system of stochastic chemical kinetics modeling the biological process associated with a gene expression [28]. The reactions and stoichiometric equations, and transition classes of this example are given in Table 3.1 and Table 3.2, respectively. Here, the system includes an mRNA molecule,* X_1*, and a protein molecule,* X_2*, and reactions in which molecules degrade, are translated, and are produced. In this system,* $n = n_I = 2$*,* $n_F = 0$*,* $x = (x_1, x_2)$*,* $J = 4$*, and* $\lambda,\ \mu,\ \delta_1,\ \delta_2 \in \mathbb{R}_{>0}$*. Hence, we have* $\mathcal{S}_1 = \mathcal{S}_2 = \mathbb{Z}_+$*,* $|\bar{\mathcal{S}}| = 1$*, and* $\mathcal{S} = \mathcal{S}_1 \times \mathcal{S}_2 = \mathbb{Z}_+^{1\times 2}$*. Note that (2.1) implies* $(2l+1)$ *states at level* $l \in \mathbb{Z}_+$*.*

Table 3.1: Gene expression model

j	*Reaction*	*Stoichiometric Equation*
1	*Production of mRNA*	$\emptyset \xrightarrow{\lambda} X_1$
2	*Translation of mRNA to protein*	$X_1 \xrightarrow{\mu x_1} X_1 + X_2$
3	*Degradation of mRNA*	$X_1 \xrightarrow{\delta_1 x_1} \emptyset$
4	*Degradation of protein*	$X_2 \xrightarrow{\delta_1 x_2} \emptyset$

Now, from (1.1), Table 3.2, and Definitions 2 and 5, the nonzero blocks of Q *as flat sparse matrices are*

Table 3.2: Transition classes of the gene expression model

j	$\psi^{(j)}$	$h^{(j,1)}(x_1)$	$h^{(j,2)}(x_2)$	$v^{(j)}$
1	λ	1	1	e_1^T
2	μ	x_1	1	e_2^T
3	δ_1	x_1	1	$-e_1^T$
4	δ_2	1	x_2	$-e_2^T$

$$Q_{l,l-1} = \begin{array}{rl} & \begin{array}{cccccc} \scriptstyle (l-1,0) & \scriptstyle \cdots & \scriptstyle (l-1,l-1) & \scriptstyle (0,l-1) & \scriptstyle \cdots & \scriptstyle (l-2,l-1) \end{array} \\ \begin{array}{l} (l,0) \\ \vdots \\ (l,l-1) \\ (l,l) \\ (0,l) \\ \vdots \\ (l-2,l) \\ (l-1,l) \end{array} & \left(\begin{array}{ccc|ccc} l\delta_1 & & & & & \\ & \ddots & & & & \\ & & l\delta_1 & & & \\ & & & & & \\ \hline & & & l\delta_2 & & \\ & & & & \ddots & \\ & & & & & l\delta_2 \\ & & l\delta_2 & & & \end{array} \right) \end{array},$$

$$Q_{l,l+1} = \begin{array}{rl} & \begin{array}{ccccccccc} \scriptstyle (l+1,0) & \scriptstyle \cdots & \scriptstyle (l+1,l) & \scriptstyle (l+1,l+1) & \scriptstyle (0,l+1) & \scriptstyle (1,l+1) & \scriptstyle \cdots & \scriptstyle (1-1,l+1) & \scriptstyle (l,l+1) \end{array} \\ \begin{array}{l} (l,0) \\ \vdots \\ (l,l) \\ (0,l) \\ (1,l) \\ \vdots \\ (l-1,l) \end{array} & \left(\begin{array}{cccc|ccccc} \lambda & & & & & & & & \\ & \ddots & & & & & & & \\ & & \lambda & & & & & & l\mu \\ \hline & & & & & & & & \\ & & & & & \mu & & & \\ & & & & & & \ddots & & \\ & & & & & & & (l-1)\mu & \end{array} \right) \end{array},$$

$$
Q_{l,l} = \begin{array}{l}
(l,0) \\ (l,1) \\ \vdots \\ (l,l-1) \\ (l,l) \\ (0,l) \\ (1,l) \\ \vdots \\ (l-2,l) \\ (l-1,l)
\end{array}
\left(\begin{array}{ccccc|ccccc}
* & l\mu & & & & & & & & \\
\delta_2 & * & l\mu & & & & & & & \\
 & \ddots & \ddots & \ddots & & & & & & \\
 & & (l-1)\delta_2 & * & l\mu & & & & & \\
 & & & l\delta_2 & * & & & & & l\delta_1 \\
\hline
 & & & & & * & \lambda & & & \\
 & & & & & \delta_1 & * & \lambda & & \\
 & & & & & & \ddots & \ddots & \ddots & \\
 & & & & & & & (l-2)\delta_1 & * & \lambda \\
 & & & & \lambda & & & & (l-1)\delta_1 & *
\end{array}\right).
$$

Let us show how the Kronecker representation is obtained. First, the transition rate matrices of the model from Table 3.2 and Definition 3 are obtained as

$$
Z^{(1,2)} = Z^{(3,2)} = Z^{(4,1)} = I_\infty, \quad Z^{(1,1)} = Z^{(2,2)} = \mathit{superdiag}((1,1,\ldots)^T),
$$

$$
Z^{(2,1)} = \mathit{diag}((0,1,\ldots)^T), \quad Z^{(3,1)} = Z^{(4,2)} = \mathit{subdiag}((1,2,\ldots)^T).
$$

Next, the state space partitions from Definition 6 are computed as

$$
\mathcal{S}_1^{(l,1)} = \{l\}, \mathcal{S}_2^{(l,1)} = \{0,\ldots,l\}, \quad \mathcal{S}_1^{(l,2)} = \{0,\ldots,l-1\}, \mathcal{S}_2^{(l,2)} = \{l\},
$$

and therefore,

$$
\mathcal{S}^{(l,1)} = \mathcal{S}_1^{(l,1)} \times \mathcal{S}_2^{(l,1)} = \{(l,0),\ldots,(l,l)\},
$$

$$
\mathcal{S}^{(l,2)} = \mathcal{S}_1^{(l,2)} \times \mathcal{S}_2^{(l,2)} = \{(0,l),\ldots,(l-1,l)\}.
$$

Finally, since $n_I = 2$, from Table 3.2 and Definition 7, the nonzero blocks $Q_{0,0}$, $Q_{0,1}$, $Q_{1,0}$, and $Q_{l,m}$ for $l > 0$, $m \in \{l-1, l, l+1\}$ are respectively (1×1), (1×2), (2×1), and (2×2) block matrices. In particular, the four blocks associated with $Q_{l,l-1}$ are given by

$$
\begin{aligned}
\tilde{Q}_{l,l-1}^{(1,1)} &= \sum_{j=1}^{4} \psi^{(j)} \left(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l-1,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l-1,1)}) \right) \\
&= \delta_1 l \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times l} \\
&= \mathit{diag}((l\delta_1,\ldots,l\delta_1)^T)_{(l+1)\times l},
\end{aligned}
$$

$$
\begin{aligned}
\tilde{Q}^{(1,2)}_{l,l-1} &= \sum_{j=1}^{4} \psi^{(j)} \left(Z^{(j,2)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l-1,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l-1,2)}) \right) \\
&= 0_{(l+1)\times(l-1)},
\end{aligned}
$$

$$
\begin{aligned}
\tilde{Q}^{(2,1)}_{l,l-1} &= \sum_{j=1}^{4} \psi^{(j)} \left(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l-1,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l-1,1)}) \right) \\
&= \delta_2 (0,\ldots,0,1)^T_{l\times 1} \otimes (0,\ldots,0,l)_{1\times l} \\
&= diag((0,\ldots,0,l\delta_2)^T)_{l\times l},
\end{aligned}
$$

$$
\begin{aligned}
\tilde{Q}^{(2,2)}_{l,l-1} &= \sum_{j=1}^{4} \psi^{(j)} \left(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l-1,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l-1,2)}) \right) \\
&= \delta_2\, diag((1,\ldots,1))_{l\times(l-1)} \otimes l \\
&= diag((l\delta_2,\ldots,l\delta_2)^T)_{l\times(l-1)},
\end{aligned}
$$

the four blocks associated with $Q_{l,l}$ are given by

$$
\begin{aligned}
\tilde{Q}^{(1,1)}_{l,l} &= \sum_{j=1}^{4} \psi^{(j)} \left(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l,1)}) \right) \\
&= \mu l \otimes superdiag((1,\ldots,1)^T)_{(l+1)\times(l+1)} \\
&\quad + \delta_2 1 \otimes subdiag((1,\ldots,l)^T)_{(l+1)\times(l+1)} \\
&= superdiag((\mu l,\ldots,\mu l)^T)_{(l+1)\times(l+1)} \\
&\quad + subdiag((\delta_2,\ldots,l\delta_2)^T)_{(l+1)\times(l+1)},
\end{aligned}
$$

$$
\begin{aligned}
\tilde{Q}^{(1,2)}_{l,l} &= \sum_{j=1}^{4} \psi^{(j)} \left(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l,2)}) \right) \\
&= \delta_1 (0,\ldots,0,l)_{1\times l} \otimes (0,\ldots,0,1)^T_{(l+1)\times 1} \\
&= subdiag((0,\ldots,0,l\delta_1)^T)_{(l+1)\times l},
\end{aligned}
$$

$$
\begin{aligned}
\tilde{Q}^{(2,1)}_{l,l} &= \sum_{j=1}^{4} \psi^{(j)} \left(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l,1)}) \right) \\
&= \lambda (0,\ldots,0,1)^T_{l\times 1} \otimes (0,\ldots,0,1)_{1\times(l+1)} \\
&= superdiag((0,\ldots,0,\lambda)^T)_{l\times(l+1)},
\end{aligned}
$$

$$\begin{aligned}
\tilde{Q}_{l,l}^{(2,2)} &= \sum_{j=1}^{4} \psi^{(j)} \left(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l,2)}) \right) \\
&= \lambda \ \mathit{superdiag}((1,\ldots,1)^T)_{l\times l} \otimes 1 \\
&\quad +\delta_1 \mathit{subdiag}((1,\ldots,l-1)^T)_{l\times l} \otimes 1 \\
&= \mathit{superdiag}((\lambda,\ldots,\lambda)^T)_{l\times l} \\
&\quad +\mathit{subdiag}((\delta_1,\ldots,(l-1)\delta_1)^T)_{l\times l},
\end{aligned}$$

and the four blocks associated with $Q_{l,l+1}$ *are given by*

$$\begin{aligned}
\tilde{Q}_{l,l+1}^{(1,1)} &= \sum_{j=1}^{4} \psi^{(j)} \left(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l+1,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l+1,1)}) \right) \\
&= \lambda 1 \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+2)} \\
&= \mathit{diag}((\lambda,\ldots,\lambda)^T)_{(l+1)\times(l+2)},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}_{l,l+1}^{(1,2)} &= \sum_{j=1}^{4} \psi^{(j)} \left(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l+1,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l+1,2)}) \right) \\
&= \mu(0,\ldots,0,l)_{1\times(l+1)} \otimes (0,\ldots,0,1)_{(l+1)\times 1}^T \\
&= \mathit{diag}((0,\ldots,0,l\mu)^T)_{(l+1)\times(l+1)},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}_{l,l+1}^{(2,1)} &= \sum_{j=1}^{4} \psi^{(j)} \left(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l+1,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l+1,1)}) \right) \\
&= 0_{l\times(l+2)},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}_{l,l+1}^{(2,2)} &= \sum_{j=1}^{4} \psi^{(j)} \left(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l+1,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l+1,2)}) \right) \\
&= \mu \ \mathit{diag}((0,\ldots,l-1)^T)_{l\times(l+1)} \otimes 1 \\
&= \mathit{diag}((0,\ldots,(l-1)\mu)^T)_{l\times(l+1)}.
\end{aligned}$$

Example 2 *(Molecule Synthesis with Two Molecules and One Enzyme) Consider a system of stochastic chemical kinetics modeling the biological process of molecule synthesis with two molecules and one enzyme [26]. The reactions and stoichiometric equations, and transition classes of this example are given in Table 3.3 and*

Table 3.4, respectively. The system includes molecules, X_1 and X_2, and enzyme, X_3, and reactions in which enzyme X_3 synthesizes molecule X_1 and molecule X_1 regulates the production of X_3. Besides, molecule X_2 degrades and is produced by a constant reaction rate. Here, $n = n_I = 3$, $n_F = 0$, $x = (x_1, x_2, x_3)$, $J = 7$, and k_A, k_B, K_I, k_2, μ, K_R, $k_{E_A} \in \mathbb{R}_{>0}$. Hence, we have $\mathcal{S}_1 = \mathcal{S}_2 = \mathcal{S}_3 = \mathbb{Z}_+$, $|\bar{\mathcal{S}}| = 1$, and $\mathcal{S} = \mathcal{S}_1 \times \mathcal{S}_2 \times \mathcal{S}_3$. Note that (2.1) implies $(3l^2 + 3l + 1)$ states at level $l \in \mathbb{Z}_+$.

Table 3.3: Molecule synthesis model with one enzyme

j	*Reaction*	*Stoichiometric Equation*
1	*Enzyme X_3 synthesizes molecule X_1*	$\emptyset \xrightarrow{\frac{k_A K_I x_3}{x_1 + K_I}} X_1$
2	*Molecule X_2 is produced*	$\emptyset \xrightarrow{k_B} X_2$
3	*Molecules X_1 and X_2 degrade*	$X_1 + X_2 \xrightarrow{k_2 x_1 x_2} \emptyset$
4	*Molecule X_1 degrades*	$X_1 \xrightarrow{\mu x_1} \emptyset$
5	*Molecule X_2 degrades*	$X_2 \xrightarrow{\mu x_2} \emptyset$
6	*Enzyme X_3 is produced*	$\emptyset \xrightarrow{\frac{k_{E_A} K_R}{x_1 + K_R}} X_3$
7	*Enzyme X_3 degrades*	$X_3 \xrightarrow{\mu x_3} \emptyset$

The transition rate matrices of the model from Table 3.4 and Definition 3 are obtained as

$$\begin{aligned} Z^{(1,2)} &= Z^{(2,1)} = Z^{(2,3)} = Z^{(3,3)} = Z^{(4,2)} = Z^{(4,3)} = Z^{(5,1)} = Z^{(5,3)} = \\ Z^{(6,2)} &= Z^{(7,1)} = Z^{(7,2)} = I_\infty, \end{aligned}$$

$$Z^{(1,1)} = superdiag((K_I^{-1}, (K_I + 1)^{-1}, \ldots)^T), \quad Z^{(1,3)} = diag((0, 1, \ldots)^T),$$

$$Z^{(2,2)} = Z^{(6,3)} = superdiag((1, 1, \ldots)^T), \quad Z^{(6,1)} = diag((K_R^{-1}, (K_R + 1)^{-1}, \ldots)^T),$$

$$Z^{(3,1)} = Z^{(3,2)} = Z^{(4,1)} = Z^{(5,2)} = Z^{(7,3)} = subdiag((1, 2, \ldots)^T.$$

The state space partitions from Definition 6 are computed as

$$\mathcal{S}_1^{(l,1)} = \{l\}, \mathcal{S}_2^{(l,1)} = \mathcal{S}_3^{(l,1)} = \{0, \ldots, l\}, \quad \mathcal{S}_1^{(l,2)} = \{0, \ldots, l-1\}, \quad \mathcal{S}_2^{(l,2)} = \{l\},$$

$$\mathcal{S}_3^{(l,2)} = \{0, \ldots, l\}, \mathcal{S}_1^{(l,3)} = \mathcal{S}_2^{(l,3)} = \{0, \ldots, l-1\}, \mathcal{S}_3^{(l,3)} = \{l\},$$

Table 3.4: Transition classes of the molecule synthesis model with one enzyme

j	$\psi^{(j)}$	$h^{(j,1)}(x_1)$	$h^{(j,2)}(x_2)$	$h^{(j,3)}(x_3)$	$v^{(j)}$
1	$k_A K_I$	$(x_1+K_I)^{-1}$	1	x_3	e_1^T
2	k_B	1	1	1	e_2^T
3	k_2	x_1	x_2	1	$(-e_1-e_2)^T$
4	μ	x_1	1	1	$-e_1^T$
5	μ	1	x_2	1	$-e_2^T$
6	$k_{E_A} K_R$	$(x_1+K_R)^{-1}$	1	1	e_3^T
7	μ	1	1	x_3	$-e_3^T$

and therefore,

$$\mathcal{S}^{(l,1)} = \times_{i=1}^{3}\mathcal{S}_i^{(l,1)} = \{(l,0,0),\ldots,(l,l,l)\},$$
$$\mathcal{S}^{(l,2)} = \times_{i=1}^{3}\mathcal{S}_i^{(l,2)} = \{(0,l,0),\ldots,(l-1,l,l)\},$$
$$\mathcal{S}^{(l,3)} = \times_{i=1}^{3}\mathcal{S}_i^{(l,3)} = \{(0,0,l),\ldots,(l-1,l-1,l)\}.$$

Finally, since $n_I = 3$*, from Table 3.4 and Definition 7, the nonzero blocks* $Q_{0,0}$*,* $Q_{0,1}$*,* $Q_{1,0}$*, and* $Q_{l,m}$ *for* $l > 0$*,* $m \in \{l-1, l, l+1\}$ *are respectively* (1×1)*,* (1×3)*,* (3×1)*, and* (3×3) *block matrices. In particular, the nine blocks associated with* $Q_{l,l-1}$ *are given by*

$$\begin{aligned}
\tilde{Q}_{l,l-1}^{(1,1)} &= \sum_{j=1}^{7}\psi^{(j)}\Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)},\mathcal{S}_1^{(l-1,1)})\otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)},\mathcal{S}_2^{(l-1,1)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)},\mathcal{S}_3^{(l-1,1)})\Big) \\
&= \big(k_2 l \otimes subdiag((1,\ldots,l)^T)_{(l+1)\times l}\otimes diag((1,\ldots,1)^T)_{(l+1)\times l}\big) \\
&\quad + \big(\mu l \otimes diag((1,\ldots,1)^T)_{(l+1)\times l}\otimes diag((1,\ldots,1)^T)_{(l+1)\times l}\big),
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}_{l,l-1}^{(1,2)} &= \sum_{j=1}^{7}\psi^{(j)}\Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)},\mathcal{S}_1^{(l-1,2)})\otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)},\mathcal{S}_2^{(l-1,2)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)},\mathcal{S}_3^{(l-1,2)})\Big) \\
&= 0_{(l+1)^2\times(l-1)l},
\end{aligned}$$

$$\begin{aligned}\tilde{Q}^{(1,3)}_{l,l-1} &= \sum_{j=1}^{7} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l-1,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l-1,3)}) \\ &\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l-1,3)}) \Big) \\ &= 0_{(l+1)^2 \times (l-1)^2},\end{aligned}$$

$$\begin{aligned}\tilde{Q}^{(2,1)}_{l,l-1} &= \sum_{j=1}^{7} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l-1,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l-1,1)}) \\ &\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l-1,1)}) \Big) \\ &= \mu(0,\ldots,0,1)^T_{l\times 1} \otimes (0,\ldots,0,l)_{1\times l} \otimes diag((1,\ldots,1)^T)_{(l+1)\times l},\end{aligned}$$

$$\begin{aligned}\tilde{Q}^{(2,2)}_{l,l-1} &= \sum_{j=1}^{7} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l-1,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l-1,2)}) \\ &\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l-1,2)}) \Big) \\ &= \big(k_2 subdiag((1,\ldots,l-1)^T)_{l\times(l-1)} \otimes l \otimes diag((1,\ldots,1)^T)_{(l+1)\times l} \big) \\ &\quad + \big(\mu diag((1,\ldots,1)^T)_{l\times(l-1)} \otimes l \otimes diag((1,\ldots,1)^T)_{(l+1)\times l} \big),\end{aligned}$$

$$\begin{aligned}\tilde{Q}^{(2,3)}_{l,l-1} &= \sum_{j=1}^{7} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l-1,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l-1,3)}) \\ &\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l-1,3)}) \Big) \\ &= 0_{l(l+1) \times (l-1)^2},\end{aligned}$$

$$\begin{aligned}\tilde{Q}^{(3,1)}_{l,l-1} &= \sum_{j=1}^{7} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l-1,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l-1,1)}) \\ &\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l-1,1)}) \Big) \\ &= \mu(0,\ldots,0,1)^T_{l\times 1} \otimes diag((1,\ldots,1)^T)_{l\times l} \otimes (0,\ldots,0,l)_{1\times l},\end{aligned}$$

$$\begin{aligned}\tilde{Q}^{(3,2)}_{l,l-1} &= \sum_{j=1}^{7} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l-1,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l-1,2)}) \\ &\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l-1,2)}) \Big) \\ &= \mu diag((1,\ldots,1)^T)_{l\times(l-1)} \otimes (0,\ldots,0,1)^T_{l\times 1} \otimes (0,\ldots,0,l)_{1\times l},\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(3,3)}_{l,l-1} &= \sum_{j=1}^{7} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l-1,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l-1,3)}) \\
&\quad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l-1,3)}) \Big) \\
&= \mu\, diag((1,\ldots,1)^T)_{l\times(l-1)} \otimes diag((1,\ldots,1)^T)_{l\times(l-1)} \otimes l,
\end{aligned}$$

the nine blocks associated with $Q_{l,l}$ *are given by*

$$\begin{aligned}
\tilde{Q}^{(1,1)}_{l,l} &= \sum_{j=1}^{7} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l,1)}) \\
&\quad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l,1)}) \Big) \\
&= \big(k_B 1 \otimes superdiag((1,\ldots,1)^T)_{(l+1)\times(l+1)} \otimes diag((1,\ldots,1)^T)_{(l+1)\times(l+1)} \big) \\
&\quad + \big(\mu 1 \otimes subdiag((1,\ldots,l)^T)_{(l+1)\times(l+1)} \otimes diag((1,\ldots,1)^T)_{(l+1)\times(l+1)} \big) \\
&\quad + \big(k_{E_A} K_R (l+K_R)^{-1} \otimes diag((1,\ldots,1)^T)_{(l+1)\times(l+1)} \\
&\quad\quad \otimes superdiag((1,\ldots,1)^T)_{(l+1)\times(l+1)} \big) \\
&\quad + \big(\mu 1 \otimes diag((1,\ldots,1)^T)_{(l+1)\times(l+1)} \otimes subdiag((1,\ldots,l)^T)_{(l+1)\times(l+1)} \big),
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(1,2)}_{l,l} &= \sum_{j=1}^{7} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l,2)}) \\
&\quad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l,2)}) \Big) \\
&= \mu(0,\ldots,0,l)_{1\times l} \otimes (0,\ldots,0,1)^T_{(l+1)\times 1} \otimes diag((1,\ldots,1)^T)_{(l+1)\times(l+1)},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(1,3)}_{l,l} &= \sum_{j=1}^{7} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l,3)}) \\
&\quad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l,3)}) \Big) \\
&= \big(k_2 (0,\ldots,0,l)_{1\times l} \otimes subdiag((1,\ldots,l)^T)_{(l+1)\times l} \otimes (0,\ldots,0,1)^T_{(l+1)\times 1} \big) \\
&\quad + \big(\mu(0,\ldots,0,l)_{1\times l} \otimes diag((1,\ldots,1)^T)_{(l+1)\times l} \otimes (0,\ldots,0,1)^T_{(l+1)\times 1} \big),
\end{aligned}$$

$$\begin{aligned}\tilde{Q}^{(2,1)}_{l,l} &= \sum_{j=1}^{7} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l,1)}) \\ &\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l,1)}) \Big) \\ &= k_A K_I (0,\dots,0,(l-1+K_I)^{-1})^T_{l\times 1} \otimes (0,\dots,0,1)_{1\times(l+1)} \\ &\quad \otimes diag((0,\dots,l)^T)_{(l+1)\times(l+1)},\end{aligned}$$

$$\begin{aligned}\tilde{Q}^{(2,2)}_{l,l} &= \sum_{j=1}^{7} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l,2)}) \\ &\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l,2)}) \Big) \\ &= \big(k_A K_I superdiag((K_I^{-1},\dots,(l-2+K_I)^{-1})^T)_{l\times l} \otimes 1 \\ &\quad \otimes diag((0,\dots,l)^T)_{(l+1)\times(l+1)} \big) \\ &\quad + \big(\mu subdiag((1,\dots,l-1)^T)_{l\times l} \otimes 1 \otimes diag((1,\dots,1)^T)_{(l+1)\times(l+1)} \big) \\ &\quad + \big(k_{E_A} K_R diag((K_R^{-1},\dots,(l-1+K_R)^{-1})^T)_{l\times l} \otimes 1 \\ &\quad \otimes superdiag((1,\dots,1)^T)_{(l+1)\times(l+1)} \big) \\ &\quad + \big(\mu diag((1,\dots,1)^T)_{l\times l} \otimes 1 \otimes subdiag((1,\dots,l)^T)_{(l+1)\times(l+1)} \big),\end{aligned}$$

$$\begin{aligned}\tilde{Q}^{(2,3)}_{l,l} &= \sum_{j=1}^{7} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l,3)}) \\ &\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l,3)}) \Big) \\ &= \big(k_2 subdiag((1,\dots,l-1)^T)_{l\times l} \otimes (0,\dots,0,l)_{1\times l} \otimes (0,\dots,0,1)^T_{(l+1)\times 1} \big) \\ &\quad + \big(\mu diag((1,\dots,1)^T)_{l\times l} \otimes (0,\dots,0,l)_{1\times l} \otimes (0,\dots,0,1)^T_{(l+1)\times 1} \big),\end{aligned}$$

$$\begin{aligned}\tilde{Q}^{(3,1)}_{l,l} &= \sum_{j=1}^{7} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l,1)}) \\ &\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l,1)}) \Big) \\ &= k_A K_I (0,\dots,0,(l-1+K_I)^{-1})^T_{l\times 1} \otimes diag((1,\dots,1)^T)_{l\times(l+1)} \\ &\quad \otimes (0,\dots,0,l)_{1\times(l+1)},\end{aligned}$$

$$\begin{aligned}\tilde{Q}_{l,l}^{(3,2)} &= \sum_{j=1}^{7} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l,2)}) \\ &\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l,2)}) \Big) \\ &= k_B\, diag((1, \ldots, 1)^T)_{l\times l} \otimes (0, \ldots, 0, 1)^T_{l\times 1} \otimes (0, \ldots, 0, 1)_{1\times(l+1)},\end{aligned}$$

$$\begin{aligned}\tilde{Q}_{l,l}^{(3,3)} &= \sum_{j=1}^{7} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l,3)}) \\ &\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l,3)}) \Big) \\ &= \big(k_A K_I\, superdiag((K_I^{-1}, \ldots, (l-2+K_I)^{-1})^T)_{l\times l} \\ &\qquad \otimes diag((1, \ldots, 1)^T)_{l\times l} \otimes l\big) \\ &\quad + \big(k_B\, diag((1, \ldots, 1)^T)_{l\times l} \otimes superdiag((1, \ldots, 1)^T)_{l\times l} \otimes 1\big) \\ &\quad + \big(k_2 subdiag((1, \ldots, l-1)^T)_{l\times l} \otimes subdiag((1, \ldots, l-1)^T)_{l\times l} \otimes 1\big) \\ &\quad + \big(\mu subdiag((1, \ldots, l-1)^T)_{l\times l} \otimes diag((1, \ldots, 1)^T)_{l\times l} \otimes 1\big) \\ &\quad + \big(\mu diag((1, \ldots, 1)^T)_{l\times l} \otimes subdiag((1, \ldots, l-1)^T)_{l\times l} \otimes 1\big),\end{aligned}$$

and the nine blocks associated with $Q_{l,l+1}$ *are given by*

$$\begin{aligned}\tilde{Q}_{l,l+1}^{(1,1)} &= \sum_{j=1}^{7} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l+1,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l+1,1)}) \\ &\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l+1,1)}) \Big) \\ &= k_A K_I (l+K_I)^{-1} \otimes diag((1, \ldots, 1)^T)_{(l+1)\times(l+2)} \\ &\qquad \otimes diag((0, \ldots, l)^T)_{(l+1)\times(l+2)},\end{aligned}$$

$$\begin{aligned}\tilde{Q}_{l,l+1}^{(1,2)} &= \sum_{j=1}^{7} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l+1,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l+1,2)}) \\ &\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l+1,2)}) \Big) \\ &= k_B (0, \ldots, 0, 1)_{1\times(l+1)} \otimes (0, \ldots, 0, 1)^T_{(l+1)\times 1} \\ &\qquad \otimes diag((1, \ldots, 1)^T)_{(l+1)\times(l+2)},\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(1,3)}_{l,l+1} &= \sum_{j=1}^{7} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l+1,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l+1,3)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l+1,3)}) \Big) \\
&= k_{E_A} K_R (0, \dots, 0, (l+K_R)^{-1})_{1\times(l+1)} \otimes diag((1,\dots,1)^T)_{(l+1)\times(l+1)} \\
&\quad \otimes (0,\dots,0,1)^T_{(l+1)\times 1},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(2,1)}_{l,l+1} &= \sum_{j=1}^{7} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l+1,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l+1,1)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l+1,1)}) \Big) \\
&= 0_{l(l+1)\times(l+2)^2},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(2,2)}_{l,l+1} &= \sum_{j=1}^{7} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l+1,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l+1,2)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l+1,2)}) \Big) \\
&= k_B \, diag((1,\dots,1)^T)_{l\times(l+1)} \otimes 1 \otimes diag((1,\dots,1)^T)_{(l+1)\times(l+2)},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(2,3)}_{l,l+1} &= \sum_{j=1}^{7} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l+1,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l+1,3)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l+1,3)}) \Big) \\
&= k_{E_A} K_R \, diag((K_R^{-1}, \dots, (l-1+K_R)^{-1})^T)_{l\times(l+1)} \otimes (0,\dots,0,1)_{1\times(l+1)} \\
&\quad \otimes (0,\dots,0,1)^T_{(l+1)\times 1},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(3,1)}_{l,l+1} &= \sum_{j=1}^{7} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l+1,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l+1,1)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l+1,1)}) \Big) \\
&= 0_{l^2\times(l+2)^2},
\end{aligned}$$

$$
\begin{aligned}
\tilde{Q}^{(3,2)}_{l,l+1} &= \sum_{j=1}^{7} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l+1,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l+1,2)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l+1,2)}) \Big) \\
&= 0_{l^2 \times (l+1)(l+2)},
\end{aligned}
$$

$$
\begin{aligned}
\tilde{Q}^{(3,3)}_{l,l+1} &= \sum_{j=1}^{7} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l+1,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l+1,3)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l+1,3)}) \Big) \\
&= k_{E_A} K_R \, diag((K_R^{-1}, \ldots, (l-1+K_R)^{-1})^T)_{l \times (l+1)} \\
&\quad \otimes diag((1, \ldots, 1)^T)_{l \times (l+1)} \otimes 1.
\end{aligned}
$$

Example 3 *(Molecule Synthesis with Two Molecules and Two Enzymes) Consider a system of stochastic chemical kinetics modeling the biological process of molecule synthesis with two molecules and two enzymes [26]. The reactions and stoichiometric equations, and transition classes of this example are given in Table 3.5 and Table 3.6, respectively. The system includes molecules,* X_1 *and* X_2*, and enzymes,* X_3 *and* X_4*. In this system, enzymes* X_3 *and* X_4 *synthesize molecules* X_1 *and* X_2*, respectively. Also, molecules* X_1 *and* X_2 *respectively regulate the productions of* X_3 *and* X_4*. Here,* $n = n_I = 4$*,* $n_F = 0$*,* $x = (x_1, x_2, x_3, x_4)$*,* $J = 9$*, and* k_A*,* k_B*,* K_I*,* k_2*,* μ*,* K_R*,* k_{E_A}*,* $k_{E_B} \in \mathbb{R}_{>0}$*. Hence, we have* $\mathcal{S}_1 = \mathcal{S}_2 = \mathcal{S}_3 = \mathcal{S}_4 = \mathbb{Z}_+$*,* $|\bar{\mathcal{S}}| = 1$*, and* $\mathcal{S} = \mathcal{S}_1 \times \mathcal{S}_2 \times \mathcal{S}_3 \times \mathcal{S}_4$*. Note that (2.1) implies* $(4l^3 + 6l^2 + 4l + 1)$ *states at level* $l \in \mathbb{Z}_+$*.*

The transition rate matrices of the model from Table 3.6 and Definition 3 are obtained as

$$
\begin{aligned}
Z^{(1,2)} &= Z^{(1,4)} = Z^{(2,1)} = Z^{(2,3)} = Z^{(3,3)} = Z^{(3,4)} = Z^{(4,2)} = Z^{(4,3)} = Z^{(4,4)} = \\
Z^{(5,1)} &= Z^{(5,3)} = Z^{(5,4)} = Z^{(6,2)} = Z^{(6,4)} = Z^{(7,1)} = Z^{(7,3)} = Z^{(8,1)} = Z^{(8,2)} = \\
Z^{(8,4)} &= Z^{(9,1)} = Z^{(9,2)} = Z^{(9,3)} = I_\infty,
\end{aligned}
$$

$$
Z^{(1,1)} = Z^{(2,2)} = superdiag((K_I^{-1}, (K_I+1)^{-1}, \ldots)^T),
$$

Table 3.5: Molecule synthesis model with two enzymes

j	*Reaction*	*Stoichiometric Equation*
1	*Enzyme X_3 synthesizes molecule X_1*	$\emptyset \xrightarrow{\frac{k_A K_I x_3}{x_1+K_I}} X_1$
2	*Enzyme X_4 synthesizes molecule X_2*	$\emptyset \xrightarrow{\frac{k_B K_I x_4}{x_2+K_I}} X_2$
3	*Molecules X_1 and X_2 degrade*	$X_1 + X_2 \xrightarrow{k_2 x_1 x_2} \emptyset$
4	*Molecule X_1 degrades*	$X_1 \xrightarrow{\mu x_1} \emptyset$
5	*Molecule X_2 degrades*	$X_2 \xrightarrow{\mu x_2} \emptyset$
6	*Enzyme X_3 is produced*	$\emptyset \xrightarrow{\frac{k_{E_A} K_R}{x_1+K_R}} X_3$
7	*Enzyme X_4 is produced*	$\emptyset \xrightarrow{\frac{k_{E_B} K_R}{x_2+K_R}} X_4$
8	*Enzyme X_3 degrades*	$X_3 \xrightarrow{\mu x_3} \emptyset$
9	*Enzyme X_4 degrades*	$X_4 \xrightarrow{\mu x_4} \emptyset$

$$Z^{(1,3)} = Z^{(2,4)} = diag((0, 1, \ldots)^T),$$

$$Z^{(6,3)} = Z^{(7,4)} = superdiag((1, 1, \ldots)^T),$$

$$Z^{(6,1)} = Z^{(7,2)} = diag((K_R^{-1}, (K_R + 1)^{-1}, \ldots)^T),$$

$$Z^{(3,1)} = Z^{(3,2)} = Z^{(4,1)} = Z^{(5,2)} = Z^{(8,3)} = Z^{(9,4)} = subdiag((1, 2, \ldots)^T).$$

The state space partitions from Definition 6 are computed as

$$\mathcal{S}_1^{(l,1)} = \{l\}, \mathcal{S}_2^{(l,1)} = \mathcal{S}_3^{(l,1)} = \mathcal{S}_4^{(l,1)} = \{0, \ldots, l\},$$

$$\mathcal{S}_1^{(l,2)} = \{0, \ldots, l-1\}, \mathcal{S}_2^{(l,2)} = \{l\}, \mathcal{S}_3^{(l,2)} = \mathcal{S}_4^{(l,2)} = \{0, \ldots, l\},$$

$$\mathcal{S}_1^{(l,3)} = \mathcal{S}_2^{(l,3)} = \{0, \ldots, l-1\}, \mathcal{S}_3^{(l,3)} = \{l\}, \mathcal{S}_4^{(l,3)} = \{0, \ldots, l\},$$

$$\mathcal{S}_1^{(l,4)} = \mathcal{S}_2^{(l,4)} = \mathcal{S}_3^{(l,4)} = \{0, \ldots, l-1\}, \mathcal{S}_4^{(l,4)} = \{l\},$$

and therefore,

$$\mathcal{S}^{(l,1)} = \times_{i=1}^4 \mathcal{S}_i^{(l,1)} = \{(l, 0, 0, 0), \ldots, (l, l, l, l)\},$$

$$\mathcal{S}^{(l,2)} = \times_{i=1}^4 \mathcal{S}_i^{(l,2)} = \{(0, l, 0, 0), \ldots, (l-1, l, l, l)\},$$

Table 3.6: Transition classes of the molecule synthesis model with two enzymes

j	$\psi^{(j)}$	$h^{(j,1)}(x_1)$	$h^{(j,2)}(x_2)$	$h^{(j,3)}(x_3)$	$h^{(j,4)}(x_4)$	$v^{(j)}$
1	$k_A K_I$	$(x_1+K_I)^{-1}$	1	x_3	1	e_1^T
2	$k_B K_I$	1	$(x_2+K_I)^{-1}$	1	x_4	e_2^T
3	k_2	x_1	x_2	1	1	$(-e_1-e_2)^T$
4	μ	x_1	1	1	1	$-e_1^T$
5	μ	1	x_2	1	1	$-e_2^T$
6	$k_{E_A} K_R$	$(x_1+K_R)^{-1}$	1	1	1	e_3^T
7	$k_{E_B} K_R$	1	$(x_2+K_R)^{-1}$	1	1	e_4^T
8	μ	1	1	x_3	1	$-e_3^T$
9	μ	1	1	1	x_4	$-e_4^T$

$$\mathcal{S}^{(l,3)} = \times_{i=1}^{4} \mathcal{S}_i^{(l,3)} = \{(0,0,l,0),\ldots,(l-1,l-1,l,l)\},$$
$$\mathcal{S}^{(l,4)} = \times_{i=1}^{4} \mathcal{S}_i^{(l,4)} = \{(0,0,0,l),\ldots,(l-1,l-1,l-1,l)\}.$$

Finally, since $n_I = 4$*, from Table 3.6 and Definition 7, the nonzero blocks* $Q_{0,0}$*,* $Q_{0,1}$*,* $Q_{1,0}$*, and* $Q_{l,m}$ *for* $l > 0$*,* $m \in \{l-1, l, l+1\}$ *are respectively* (1×1)*,* (1×4)*,* (4×1)*, and* (4×4) *block matrices. In particular, the sixteen blocks associated with* $Q_{l,l-1}$ *are given by*

$$\begin{aligned}
\tilde{Q}_{l,l-1}^{(1,1)} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l-1,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l-1,1)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l-1,1)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,1)}, \mathcal{S}_4^{(l-1,1)}) \Big) \\
&= \big(k_2 l \otimes \mathit{subdiag}((1,\ldots,l)^T)_{(l+1)\times l} \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times l} \\
&\qquad \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times l} \big) \\
&\quad + \big(\mu l \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times l} \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times l} \\
&\qquad \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times l} \big) ,
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(1,2)}_{l,l-1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l-1,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l-1,2)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l-1,2)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,1)}, \mathcal{S}_4^{(l-1,2)}) \Big) \\
&= 0_{(l+1)^3 \times (l-1)l^2},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(1,3)}_{l,l-1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l-1,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l-1,3)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l-1,3)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,1)}, \mathcal{S}_4^{(l-1,3)}) \Big) \\
&= 0_{(l+1)^3 \times (l-1)^2 l},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(1,4)}_{l,l-1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l-1,4)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l-1,4)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l-1,4)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,1)}, \mathcal{S}_4^{(l-1,4)}) \Big) \\
&= 0_{(l+1)^3 \times (l-1)^3},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(2,1)}_{l,l-1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l-1,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l-1,1)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l-1,1)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,2)}, \mathcal{S}_4^{(l-1,1)}) \Big) \\
&= \mu(0, \ldots, 0, 1)^T_{l \times 1} \otimes (0, \ldots, 0, l)_{1 \times l} \otimes diag((1, \ldots, 1)^T)_{(l+1) \times l} \\
&\quad \otimes diag((1, \ldots, 1)^T)_{(l+1) \times l},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(2,2)}_{l,l-1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l-1,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l-1,2)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l-1,2)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,2)}, \mathcal{S}_4^{(l-1,2)}) \Big) \\
&= \big(k_2 subdiag((1,\dots,l-1)^T)_{l\times(l-1)} \otimes l \otimes diag((1,\dots,1)^T)_{(l+1)\times l} \\
&\quad \otimes diag((1,\dots,1)^T)_{(l+1)\times l} \big) \\
&\quad + \big(\mu diag((1,\dots,1)^T)_{l\times(l-1)} \otimes l \otimes diag((1,\dots,1)^T)_{(l+1)\times l} \\
&\quad \otimes diag((1,\dots,1)^T)_{(l+1)\times l} \big) ,
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(2,3)}_{l,l-1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l-1,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l-1,3)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l-1,3)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,2)}, \mathcal{S}_4^{(l-1,3)}) \Big) \\
&= 0_{l(l+1)^2\times(l-1)^2 l},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(2,4)}_{l,l-1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l-1,4)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l-1,4)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l-1,4)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,2)}, \mathcal{S}_4^{(l-1,4)}) \Big) \\
&= 0_{l(l+1)^2\times(l-1)^3},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(3,1)}_{l,l-1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l-1,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l-1,1)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l-1,1)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,3)}, \mathcal{S}_4^{(l-1,1)}) \Big) \\
&= \mu(0,\dots,0,1)^T_{l\times 1} \otimes diag((1,\dots,1)^T)_{l\times l} \\
&\quad \otimes (0,\dots,0,l)_{1\times l} \otimes diag((1,\dots,1)^T)_{(l+1)\times l},
\end{aligned}$$

$$
\begin{aligned}
\tilde{Q}_{l,l-1}^{(3,2)} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l-1,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l-1,2)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l-1,2)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,3)}, \mathcal{S}_4^{(l-1,2)}) \Big) \\
&= \mu\, diag((1,\ldots,1)^T)_{l\times(l-1)} \otimes (0,\ldots,0,1)_{l\times 1}^T \\
&\quad \otimes (0,\ldots,0,l)_{1\times l} \otimes diag((1,\ldots,1)^T)_{(l+1)\times l},
\end{aligned}
$$

$$
\begin{aligned}
\tilde{Q}_{l,l-1}^{(3,3)} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l-1,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l-1,3)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l-1,3)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,3)}, \mathcal{S}_4^{(l-1,3)}) \Big) \\
&= \mu\, diag((1,\ldots,1)^T)_{l\times(l-1)} \otimes diag((1,\ldots,1)^T)_{l\times(l-1)} \\
&\quad \otimes l \otimes diag((1,\ldots,1)^T)_{(l+1)\times l},
\end{aligned}
$$

$$
\begin{aligned}
\tilde{Q}_{l,l-1}^{(3,4)} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l-1,4)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l-1,4)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l-1,4)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,3)}, \mathcal{S}_4^{(l-1,4)}) \Big) \\
&= 0_{l^2(l+1)\times(l-1)^3},
\end{aligned}
$$

$$
\begin{aligned}
\tilde{Q}_{l,l-1}^{(4,1)} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,4)}, \mathcal{S}_1^{(l-1,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,4)}, \mathcal{S}_2^{(l-1,1)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,4)}, \mathcal{S}_3^{(l-1,1)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,4)}, \mathcal{S}_4^{(l-1,1)}) \Big) \\
&= \mu (0,\ldots,0,1)_{l\times 1}^T \otimes diag((1,\ldots,1)^T)_{l\times l} \\
&\quad \otimes diag((1,\ldots,1)^T)_{l\times l} \otimes (0,\ldots,0,l)_{1\times l},
\end{aligned}
$$

$$
\begin{aligned}
\tilde{Q}^{(4,2)}_{l,l-1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,4)}, \mathcal{S}_1^{(l-1,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,4)}, \mathcal{S}_2^{(l-1,2)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,4)}, \mathcal{S}_3^{(l-1,2)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,4)}, \mathcal{S}_4^{(l-1,2)}) \Big) \\
&= \mu\, diag((1,\ldots,1)^T)_{l\times(l-1)} \otimes (0,\ldots,0,1)^T_{l\times 1} \\
&\qquad \otimes diag((1,\ldots,1)^T)_{l\times l} \otimes (0,\ldots,0,l)_{1\times l},
\end{aligned}
$$

$$
\begin{aligned}
\tilde{Q}^{(4,3)}_{l,l-1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,4)}, \mathcal{S}_1^{(l-1,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,4)}, \mathcal{S}_2^{(l-1,3)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,4)}, \mathcal{S}_3^{(l-1,3)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,4)}, \mathcal{S}_4^{(l-1,3)}) \Big) \\
&= \mu\, diag((1,\ldots,1)^T)_{l\times(l-1)} \otimes diag((1,\ldots,1)^T)_{l\times(l-1)} \\
&\qquad \otimes (0,\ldots,0,1)^T_{l\times 1} \otimes (0,\ldots,0,l)_{1\times l},
\end{aligned}
$$

$$
\begin{aligned}
\tilde{Q}^{(4,4)}_{l,l-1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,4)}, \mathcal{S}_1^{(l-1,4)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,4)}, \mathcal{S}_2^{(l-1,4)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,4)}, \mathcal{S}_3^{(l-1,4)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,4)}, \mathcal{S}_4^{(l-1,4)}) \Big) \\
&= \mu\, diag((1,\ldots,1)^T)_{l\times(l-1)} \otimes diag((1,\ldots,1)^T)_{l\times(l-1)} \\
&\qquad \otimes diag((1,\ldots,1)^T)_{l\times(l-1)} \otimes l,
\end{aligned}
$$

and the sixteen blocks associated with $Q_{l,l}$ *are given by*

$$\begin{aligned}
\tilde{Q}_{l,l}^{(1,1)} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l,1)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l,1)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,1)}, \mathcal{S}_4^{(l,1)}) \Big) \\
&= \big(k_B K_I 1 \otimes \mathit{superdiag}((K_I^{-1}, \ldots, (l-1+K_I)^{-1})^T)_{(l+1)\times(l+1)} \\
&\quad \otimes \mathit{diag}((1, \ldots, 1)^T)_{(l+1)\times(l+1)} \otimes \mathit{diag}((0, \ldots, l)^T)_{(l+1)\times(l+1)} \big) \\
&\quad + \big(\mu 1 \otimes \mathit{subdiag}((1, \ldots, l)^T)_{(l+1)\times(l+1)} \\
&\quad \otimes \mathit{diag}((1, \ldots, 1)^T)_{(l+1)\times(l+1)} \otimes \mathit{diag}((1, \ldots, 1)^T)_{(l+1)\times(l+1)} \big) \\
&\quad + \big(k_{E_A} K_R (l+K_R)^{-1} \otimes \mathit{diag}((1, \ldots, 1)^T)_{(l+1)\times(l+1)} \\
&\quad \otimes \mathit{superdiag}((1, \ldots, 1)^T)_{(l+1)\times(l+1)} \otimes \mathit{diag}((1, \ldots, 1)^T)_{(l+1)\times(l+1)} \big) \\
&\quad + \big(k_{E_B} K_R 1 \otimes \mathit{diag}((K_R^{-1}, \ldots, (l+K_R)^{-1})^T)_{(l+1)\times(l+1)} \\
&\quad \otimes \mathit{diag}((1, \ldots, 1)^T)_{(l+1)\times(l+1)} \otimes \mathit{superdiag}((1, \ldots, 1)^T)_{(l+1)\times(l+1)} \big) \\
&\quad + \big(\mu 1 \otimes \mathit{diag}((1, \ldots, 1)^T)_{(l+1)\times(l+1)} \\
&\quad \otimes \mathit{subdiag}((1, \ldots, l)^T)_{(l+1)\times(l+1)} \otimes \mathit{diag}((1, \ldots, 1)^T)_{(l+1)\times(l+1)} \big) \\
&\quad + \big(\mu 1 \otimes \mathit{diag}((1, \ldots, 1)^T)_{(l+1)\times(l+1)} \\
&\quad \otimes \mathit{diag}((1, \ldots, 1)^T)_{(l+1)\times(l+1)} \otimes \mathit{subdiag}((1, \ldots, l)^T)_{(l+1)\times(l+1)} \big) ,
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}_{l,l}^{(1,2)} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l,2)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l,2)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,1)}, \mathcal{S}_4^{(l,2)}) \Big) \\
&= \mu (0, \ldots, 0, l)_{1\times l} \otimes (0, \ldots, 0, 1)^T_{(l+1)\times 1} \otimes \mathit{diag}((1, \ldots, 1)^T)_{(l+1)\times(l+1)} \\
&\quad \otimes \mathit{diag}((1, \ldots, 1)^T)_{(l+1)\times(l+1)},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}_{l,l}^{(1,3)} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l,3)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l,3)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,1)}, \mathcal{S}_4^{(l,3)}) \Big) \\
&= \big(k_2(0,\ldots,0,l)_{1\times l} \otimes \mathit{subdiag}((1,\ldots,l)^T)_{(l+1)\times l} \otimes (0,\ldots,0,1)^T_{(l+1)\times 1} \\
&\quad \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \big) \\
&\quad + \big(\mu(0,\ldots,0,l)_{1\times l} \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times l} \otimes (0,\ldots,0,1)^T_{(l+1)\times 1} \\
&\quad \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \big),
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}_{l,l}^{(1,4)} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l,4)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l,4)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l,4)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,1)}, \mathcal{S}_4^{(l,4)}) \Big) \\
&= \big(k_2(0,\ldots,0,l)_{1\times l} \otimes \mathit{subdiag}((1,\ldots,l)^T)_{(l+1)\times l} \\
&\quad \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times l} \otimes (0,\ldots,0,1)^T_{(l+1)\times 1} \big) \\
&\quad + \big(\mu(0,\ldots,0,l)_{1\times l} \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times l} \\
&\quad \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times l} \otimes (0,\ldots,0,1)^T_{(l+1)\times 1} \big),
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}_{l,l}^{(2,1)} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l,1)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l,1)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,2)}, \mathcal{S}_4^{(l,1)}) \Big) \\
&= k_A K_I (0,\ldots,0,(l-1+K_I)^{-1})^T_{l\times 1} \otimes (0,\ldots,0,1)_{1\times(l+1)} \\
&\quad \otimes \mathit{diag}((0,\ldots,l)^T)_{(l+1)\times(l+1)} \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+1)},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}_{l,l}^{(2,2)} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l,2)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l,2)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,2)}, \mathcal{S}_4^{(l,2)}) \Big) \\
&= \big(k_A K_I \mathit{superdiag}(((K_I^{-1}, \ldots, (l-2+K_I)^{-1})^T)_{l\times l} \otimes 1 \\
&\quad \otimes \mathit{diag}((0, \ldots, l)^T)_{(l+1)\times(l+1)} \otimes \mathit{diag}((1, \ldots, 1)^T)_{(l+1)\times(l+1)} \big) \\
&\quad + \big(\mu \mathit{subdiag}((1, \ldots, l-1)^T)_{l\times l} \otimes 1 \otimes \mathit{diag}((1, \ldots, 1)^T)_{(l+1)\times(l+1)} \\
&\quad \otimes \mathit{diag}((1, \ldots, 1)^T)_{(l+1)\times(l+1)} \big) \\
&\quad + \big(k_{E_A} K_R \mathit{diag}((K_R^{-1}, \ldots, (l-1+K_R)^{-1})^T)_{l\times l} \otimes 1 \\
&\quad \otimes \mathit{superdiag}((1, \ldots, 1)^T)_{(l+1)\times(l+1)} \otimes \mathit{diag}((1, \ldots, 1)^T)_{(l+1)\times(l+1)} \big) \\
&\quad + \big(k_{E_B} K_R \mathit{diag}((1, \ldots, 1)^T)_{l\times l} \otimes (l+K_R)^{-1} \otimes \\
&\quad \mathit{diag}((1, \ldots, 1)^T)_{(l+1)\times(l+1)} \otimes \mathit{superdiag}((1, \ldots, 1)^T)_{(l+1)\times(l+1)} \big) \\
&\quad + \big(\mu \mathit{diag}((1, \ldots, 1)^T)_{l\times l} \otimes 1 \otimes \mathit{subdiag}((1, \ldots, l)^T)_{(l+1)\times(l+1)} \\
&\quad \otimes \mathit{diag}((1, \ldots, 1)^T)_{(l+1)\times(l+1)} \big) \\
&\quad + \big(\mu \mathit{diag}((1, \ldots, 1)^T)_{l\times l} \otimes 1 \otimes \mathit{diag}((1, \ldots, 1)^T)_{(l+1)\times(l+1)} \\
&\quad \otimes \mathit{subdiag}((1, \ldots, l)^T)_{(l+1)\times(l+1)} \big) ,
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}_{l,l}^{(2,3)} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l,3)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l,3)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,2)}, \mathcal{S}_4^{(l,3)}) \Big) \\
&= \big(k_2 \mathit{subdiag}((1, \ldots, l-1)^T)_{l\times l} \otimes (0, \ldots, 0, l)_{1\times l} \otimes (0, \ldots, 0, 1)^T_{(l+1)\times 1} \\
&\quad \otimes \mathit{diag}((1, \ldots, 1)^T)_{(l+1)\times(l+1)} \big) \\
&\quad + \big(\mu \mathit{diag}((1, \ldots, 1)^T)_{l\times l} \otimes (0, \ldots, 0, l)_{1\times l} \otimes (0, \ldots, 0, 1)^T_{(l+1)\times 1} \\
&\quad \otimes \mathit{diag}((1, \ldots, 1)^T)_{(l+1)\times(l+1)} \big) ,
\end{aligned}$$

$$
\begin{aligned}
\tilde{Q}_{l,l}^{(2,4)} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l,4)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l,4)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l,4)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,2)}, \mathcal{S}_4^{(l,4)}) \Big) \\
&= \big(k_2 subdiag((1,\ldots,l-1)^T)_{l\times l} \otimes (0,\ldots,0,l)_{1\times l} \\
&\quad \otimes diag((1,\ldots,1)^T)_{(l+1)\times l} \otimes (0,\ldots,0,1)^T_{(l+1)\times 1} \big) \\
&\quad + \big(\mu diag((1,\ldots,1)^T)_{l\times l} \otimes (0,\ldots,0,l)_{1\times l} \otimes diag((1,\ldots,1)^T)_{(l+1)\times l} \\
&\quad \otimes (0,\ldots,0,1)^T_{(l+1)\times 1} \big),
\end{aligned}
$$

$$
\begin{aligned}
\tilde{Q}_{l,l}^{(3,1)} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l,1)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l,1)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,3)}, \mathcal{S}_4^{(l,1)}) \Big) \\
&= k_A K_I (0,\ldots,0,(l-1+K_I)^{-1})^T_{l\times 1} \otimes diag((1,\ldots,1)^T)_{l\times(l+1)} \\
&\qquad \otimes (0,\ldots,0,l)_{1\times(l+1)} \otimes diag((1,\ldots,1)^T)_{(l+1)\times(l+1)},
\end{aligned}
$$

$$
\begin{aligned}
\tilde{Q}_{l,l}^{(3,2)} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l,2)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l,2)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,3)}, \mathcal{S}_4^{(l,2)}) \Big) \\
&= k_B K_I diag((1,\ldots,1)^T)_{l\times l} \otimes (0,\ldots,0,(l-1+K_I)^{-1})^T_{l\times 1} \\
&\qquad \otimes (0,\ldots,0,1)_{1\times(l+1)} \otimes diag((0,\ldots,l)^T)_{(l+1)\times(l+1)},
\end{aligned}
$$

$$
\begin{aligned}
\tilde{Q}_{l,l}^{(3,3)} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l,3)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l,3)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,3)}, \mathcal{S}_4^{(l,3)}) \Big) \\
&= \big(k_A K_I \mathit{superdiag}((K_I^{-1}, \ldots, (l-2+K_I)^{-1})^T)_{l\times l} \\
&\quad \otimes \mathit{diag}((1,\ldots,1)^T)_{l\times l} \otimes l \\
&\quad \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \big) \\
&\quad + \big(k_B K_I \mathit{diag}((1,\ldots,1)^T)_{l\times l} \\
&\quad \otimes \mathit{superdiag}((K_I^{-1}, \ldots, (l-2+K_I)^{-1})^T)_{l\times l} \otimes 1 \\
&\quad \otimes \mathit{diag}((0,\ldots,l)^T)_{(l+1)\times(l+1)} \big) \\
&\quad + \big(k_2 \mathit{subdiag}((1,\ldots,l-1)^T)_{l\times l} \otimes \mathit{subdiag}((1,\ldots,l-1)^T)_{l\times l} \otimes 1 \\
&\quad \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \big) \\
&\quad + \big(\mu \mathit{subdiag}((1,\ldots,l-1)^T)_{l\times l} \otimes \mathit{diag}((1,\ldots,1)^T)_{l\times l} \otimes 1 \\
&\quad \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \big) \\
&\quad + \big(\mu \mathit{diag}((1,\ldots,1)^T)_{l\times l} \otimes \mathit{subdiag}((1,\ldots,l-1)^T)_{l\times l} \otimes 1 \\
&\quad \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \big) \\
&\quad + \big(k_{E_B} K_R \mathit{diag}((1,\ldots,1)^T)_{l\times l} \\
&\quad \otimes \mathit{diag}((K_R^{-1}, \ldots, (l-1+K_R)^{-1})^T)_{l\times l} \otimes 1 \\
&\quad \otimes \mathit{superdiag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \big) \\
&\quad + \big(\mu \mathit{diag}((1,\ldots,1)^T)_{l\times l} \otimes \mathit{diag}((1,\ldots,1)^T)_{l\times l} \otimes 1 \\
&\quad \otimes \mathit{subdiag}((1,\ldots,l)^T)_{(l+1)\times(l+1)} \big) ,
\end{aligned}
$$

$$
\begin{aligned}
\tilde{Q}_{l,l}^{(3,4)} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l,4)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l,4)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l,4)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,3)}, \mathcal{S}_4^{(l,4)}) \Big) \\
&= \mu \mathit{diag}((1,\ldots,1)^T)_{l\times l} \otimes \mathit{diag}((1,\ldots,1)^T)_{l\times l} \otimes (0,\ldots,0,l)_{1\times l} \\
&\quad \otimes (0,\ldots,0,1)^T_{(l+1)\times 1},
\end{aligned}
$$

$$\begin{aligned}
\tilde{Q}^{(4,1)}_{l,l} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}^{(l,4)}_1, \mathcal{S}^{(l,1)}_1) \otimes Z^{(j,2)}(\mathcal{S}^{(l,4)}_2, \mathcal{S}^{(l,1)}_2) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}^{(l,4)}_3, \mathcal{S}^{(l,1)}_3) \otimes Z^{(j,4)}(\mathcal{S}^{(l,4)}_4, \mathcal{S}^{(l,1)}_4) \Big) \\
&= k_A K_I (0, \ldots, 0, (l-1+K_I)^{-1})^T_{l\times 1} \otimes diag((1, \ldots, 1)^T)_{l\times(l+1)} \\
&\quad \otimes diag((0, \ldots, l-1)^T)_{l\times(l+1)} \otimes (0, \ldots, 0, 1)_{1\times(l+1)},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(4,2)}_{l,l} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}^{(l,4)}_1, \mathcal{S}^{(l,2)}_1) \otimes Z^{(j,2)}(\mathcal{S}^{(l,4)}_2, \mathcal{S}^{(l,2)}_2) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}^{(l,4)}_3, \mathcal{S}^{(l,2)}_3) \otimes Z^{(j,4)}(\mathcal{S}^{(l,4)}_4, \mathcal{S}^{(l,2)}_4) \Big) \\
&= k_B K_I \, diag((1, \ldots, 1)^T)_{l\times l} \otimes (0, \ldots, 0, (l-1+K_I)^{-1})^T_{l\times 1} \\
&\quad \otimes diag((1, \ldots, 1)^T)_{l\times(l+1)} \otimes (0, \ldots, 0, l)_{1\times(l+1)},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(4,3)}_{l,l} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}^{(l,4)}_1, \mathcal{S}^{(l,3)}_1) \otimes Z^{(j,2)}(\mathcal{S}^{(l,4)}_2, \mathcal{S}^{(l,3)}_2) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}^{(l,4)}_3, \mathcal{S}^{(l,3)}_3) \otimes Z^{(j,4)}(\mathcal{S}^{(l,4)}_4, \mathcal{S}^{(l,3)}_4) \Big) \\
&= k_{E_A} K_R \, diag((K_R^{-1}, \ldots, (l-1+K_R)^{-1})^T)_{l\times l} \otimes diag((1, \ldots, 1)^T)_{l\times l} \\
&\quad \otimes (0, \ldots, 0, 1)^T_{l\times 1} \otimes (0, \ldots, 0, 1)_{1\times(l+1)},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(4,4)}_{l,l} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}^{(l,4)}_1, \mathcal{S}^{(l,4)}_1) \otimes Z^{(j,2)}(\mathcal{S}^{(l,4)}_2, \mathcal{S}^{(l,4)}_2) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}^{(l,4)}_3, \mathcal{S}^{(l,4)}_3) \otimes Z^{(j,4)}(\mathcal{S}^{(l,4)}_4, \mathcal{S}^{(l,4)}_4) \Big) \\
&= \big(k_A K_I \mathit{superdiag}((K_I^{-1}, \ldots, (l-2+K_I)^{-1})^T)_{l\times l} \\
&\quad \otimes \mathit{diag}((1, \ldots, 1)^T)_{l\times l} \otimes \mathit{diag}((0, \ldots, l-1)^T)_{l\times l} \otimes 1 \big) \\
&\quad + \big(k_B K_I \mathit{diag}((1, \ldots, 1)^T)_{l\times l} \\
&\quad \otimes \mathit{superdiag}((K_I^{-1}, \ldots, (l-2+K_I)^{-1})^T)_{l\times l} \\
&\quad \otimes \mathit{diag}((1, \ldots, 1)^T)_{l\times l} \otimes l \big) \\
&\quad + \big(k_2 \mathit{subdiag}((1, \ldots, l-1)^T)_{l\times l} \otimes \mathit{subdiag}((1, \ldots, l-1)^T)_{l\times l} \\
&\quad \otimes \mathit{diag}((1, \ldots, 1)^T)_{l\times l} \otimes 1 \big) \\
&\quad + \big(\mu \mathit{subdiag}((1, \ldots, l-1)^T)_{l\times l} \otimes \mathit{diag}((1, \ldots, 1)^T)_{l\times l} \\
&\quad \otimes \mathit{diag}((1, \ldots, 1)^T)_{l\times l} \otimes 1 \big) \\
&\quad + \big(\mu \mathit{diag}((1, \ldots, 1)^T)_{l\times l} \otimes \mathit{subdiag}((1, \ldots, l-1)^T)_{l\times l} \\
&\quad \otimes \mathit{diag}((1, \ldots, 1)^T)_{l\times l} \otimes 1 \big) \\
&\quad + \big(k_{E_A} K_R \mathit{diag}((K_R^{-1}, \ldots, (l-1+K_R)^{-1})^T)_{l\times l} \\
&\quad \otimes \mathit{diag}((1, \ldots, 1)^T)_{l\times l} \otimes \mathit{superdiag}((1, \ldots, 1)^T)_{l\times l} \otimes 1 \big) \\
&\quad + \big(\mu \mathit{diag}((1, \ldots, 1)^T)_{l\times l} \otimes \mathit{diag}((1, \ldots, 1)^T)_{l\times l} \\
&\quad \otimes \mathit{subdiag}((1, \ldots, l-1)^T)_{l\times l} \otimes 1 \big),
\end{aligned}$$

and the sixteen blocks associated with $Q_{l,l+1}$ are given by

$$\begin{aligned}
\tilde{Q}^{(1,1)}_{l,l+1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}^{(l,1)}_1, \mathcal{S}^{(l+1,1)}_1) \otimes Z^{(j,2)}(\mathcal{S}^{(l,1)}_2, \mathcal{S}^{(l+1,1)}_2) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}^{(l,1)}_3, \mathcal{S}^{(l+1,1)}_3) \otimes Z^{(j,4)}(\mathcal{S}^{(l,1)}_4, \mathcal{S}^{(l+1,1)}_4) \Big) \\
&= k_A K_I (l+K_I)^{-1} \otimes \mathit{diag}((1, \ldots, 1)^T)_{(l+1)\times(l+2)} \\
&\quad \otimes \otimes\ \mathit{diag}((0, \ldots, l)^T)_{(l+1)\times(l+2)} \mathit{diag}((1, \ldots, 1)^T)_{(l+1)\times(l+2)},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(1,2)}_{l,l+1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l+1,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l+1,2)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l+1,2)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,1)}, \mathcal{S}_4^{(l+1,2)}) \Big) \\
&= k_B K_I (0,\ldots,0,1)_{1\times(l+1)} \otimes (0,\ldots,0,(l+K_I)^{-1})^T_{(l+1)\times 1} \\
&\qquad \otimes diag((1,\ldots,1)^T)_{(l+1)\times(l+2)} \otimes diag((0,\ldots,l)^T)_{(l+1)\times(l+2)},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(1,3)}_{l,l+1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l+1,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l+1,3)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l+1,3)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,1)}, \mathcal{S}_4^{(l+1,3)}) \Big) \\
&= k_{E_A} K_R (0,\ldots,0,(l+K_R)^{-1})_{1\times(l+1)} \otimes diag((1,\ldots,1)^T)_{(l+1)\times(l+1)} \\
&\qquad \otimes (0,\ldots,0,1)^T_{(l+1)\times 1} \otimes diag((1,\ldots,1)^T)_{(l+1)\times(l+2)},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(1,4)}_{l,l+1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l+1,4)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l+1,4)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l+1,4)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,1)}, \mathcal{S}_4^{(l+1,4)}) \Big) \\
&= k_{E_B} K_R (0,\ldots,0,1)_{1\times(l+1)} \otimes diag((K_R^{-1},\ldots,(l+K_R)^{-1})^T)_{(l+1)\times(l+1)} \\
&\qquad \otimes diag((1,\ldots,1)^T)_{(l+1)\times(l+1)} \otimes (0,\ldots,0,1)^T_{(l+1)\times 1},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(2,1)}_{l,l+1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l+1,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l+1,1)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l+1,1)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,2)}, \mathcal{S}_4^{(l+1,1)}) \Big) \\
&= 0_{l(l+1)^2\times(l+2)^3},
\end{aligned}$$

$$\begin{aligned}\tilde{Q}^{(2,2)}_{l,l+1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l+1,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l+1,2)}) \\ &\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l+1,2)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,2)}, \mathcal{S}_4^{(l+1,2)}) \Big) \\ &= k_B K_I \, diag((1,\ldots,1)^T)_{l\times(l+1)} \otimes (l+K_I)^{-1} \\ &\qquad \otimes diag((1,\ldots,1)^T)_{(l+1)\times(l+2)} \otimes diag((0,\ldots,l)^T)_{(l+1)\times(l+2)},\end{aligned}$$

$$\begin{aligned}\tilde{Q}^{(2,3)}_{l,l+1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l+1,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l+1,3)}) \\ &\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l+1,3)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,2)}, \mathcal{S}_4^{(l+1,3)}) \Big) \\ &= k_{E_A} K_R \, diag((K_R^{-1},\ldots,(l-1+K_R)^{-1})^T)_{l\times(l+1)} \otimes (0,\ldots,0,1)_{1\times(l+1)} \\ &\qquad \otimes (0,\ldots,0,1)^T_{(l+1)\times 1} \otimes diag((1,\ldots,1)^T)_{(l+1)\times(l+2)},\end{aligned}$$

$$\begin{aligned}\tilde{Q}^{(2,4)}_{l,l+1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l+1,4)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l+1,4)}) \\ &\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l+1,4)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,2)}, \mathcal{S}_4^{(l+1,4)}) \Big) \\ &= k_{E_B} K_R \, diag((1,\ldots,1)^T)_{l\times(l+1)} \otimes (0,\ldots,0,(l+K_R)^{-1})_{1\times(l+1)} \\ &\qquad \otimes diag((1,\ldots,1)^T)_{(l+1)\times(l+1)} \otimes (0,\ldots,0,1)^T_{(l+1)\times 1},\end{aligned}$$

$$\begin{aligned}\tilde{Q}^{(3,1)}_{l,l+1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l+1,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l+1,1)}) \\ &\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l+1,1)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,3)}, \mathcal{S}_4^{(l+1,1)}) \Big) \\ &= 0_{l^2(l+1)\times(l+2)^3},\end{aligned}$$

$$\begin{aligned}\tilde{Q}^{(3,2)}_{l,l+1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l+1,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l+1,2)}) \\ &\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l+1,2)}) \ otimes Z^{(j,4)}(\mathcal{S}_4^{(l,3)}, \mathcal{S}_4^{(l+1,2)}) \Big) \\ &= 0_{l^2(l+1)\times(l+1)(l+2)^2},\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(3,3)}_{l,l+1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l+1,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l+1,3)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l+1,3)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,3)}, \mathcal{S}_4^{(l+1,3)}) \Big) \\
&= k_{E_A} K_R diag((K_R^{-1}, \ldots, (l-1+K_R)^{-1})^T)_{l\times(l+1)} \\
&\quad \otimes diag((1,\ldots,1)^T)_{l\times(l+1)} \otimes 1 \otimes diag((1,\ldots,1)^T)_{(l+1)\times(l+2)},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(3,4)}_{l,l+1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l+1,4)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l+1,4)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l+1,4)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,3)}, \mathcal{S}_4^{(l+1,4)}) \Big) \\
&= k_{E_B} K_R diag((1,\ldots,1)^T)_{l\times(l+1)} \\
&\quad \otimes diag((K_R^{-1}, \ldots, (l-1+K_R)^{-1})^T)_{l\times(l+1)} \\
&\quad \otimes (0,\ldots,0,1)_{1\times(l+1)} \otimes (0,\ldots,0,1)^T_{(l+1)\times 1},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(4,1)}_{l,l+1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,4)}, \mathcal{S}_1^{(l+1,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,4)}, \mathcal{S}_2^{(l+1,1)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,4)}, \mathcal{S}_3^{(l+1,1)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,4)}, \mathcal{S}_4^{(l+1,1)}) \Big) \\
&= 0_{l^3\times(l+2)^3},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(4,2)}_{l,l+1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,4)}, \mathcal{S}_1^{(l+1,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,4)}, \mathcal{S}_2^{(l+1,2)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,4)}, \mathcal{S}_3^{(l+1,2)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,4)}, \mathcal{S}_4^{(l+1,2)}) \Big) \\
&= 0_{l^3\times(l+1)(l+2)^2},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(4,3)}_{l,l+1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,4)}, \mathcal{S}_1^{(l+1,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,4)}, \mathcal{S}_2^{(l+1,3)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,4)}, \mathcal{S}_3^{(l+1,3)}) \otimes Z^{(j,4)}(\mathcal{S}_4^{(l,4)}, \mathcal{S}_4^{(l+1,3)}) \Big) \\
&= 0_{l^3\times(l+1)^2(l+2)},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(4,4)}_{l,l+1} &= \sum_{j=1}^{9} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}^{(l,4)}_1, \mathcal{S}^{(l+1,4)}_1) \otimes Z^{(j,2)}(\mathcal{S}^{(l,4)}_2, \mathcal{S}^{(l+1,4)}_2) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}^{(l,4)}_3, \mathcal{S}^{(l+1,4)}_3) \otimes Z^{(j,4)}(\mathcal{S}^{(l,4)}_4, \mathcal{S}^{(l+1,4)}_4) \Big) \\
&= k_{E_B} K_R diag((1, \ldots, 1)^T)_{l\times(l+1)} \\
&\quad \otimes diag((K_R^{-1}, \ldots, (l-1+K_R)^{-1})^T)_{l\times(l+1)} \\
&\quad \otimes diag((1, \ldots, 1)^T)_{l\times(l+1)} \otimes 1.
\end{aligned}$$

The following example is different than the first three in that it has a control unit of eight states.

Example 4 *(Repressilator) Consider a system of stochastic chemical kinetics modeling the biological process of molecule synthesis with repressilator [19]. The reactions and stoichiometric equations, and transition classes of this example are given in Table 3.7 and Table 3.8, respectively. The system includes three molecules/genes, X_1, X_2 and X_3, and three control variables, X_4, X_5, and X_6. In this system, each gene has a single binding site and binds to the binding site of another gene. Genes block other genes by binding to their binding sites. Here, X_1 represses X_2, X_2 represses X_3, and X_3 represses X_1. The control variables denote whether the gene is bound to the binding site of the corresponding gene. $X_4 = 1$ if X_1 is bound to X_2, and $X_4 = 0$ otherwise. $X_5 = 1$ if X_2 is bound to X_3, and $X_5 = 0$ otherwise, and $X_6 = 1$ if X_3 is bound to X_1, and $X_6 = 0$ otherwise. Here, $n = 6$, $n_I = 3$, $n_F = 3$, $x = (x_1, x_2, x_3, x_4, x_5, x_6)$, $J = 12$, and λ_1, λ_2, λ_3, δ_1, δ_2, δ_3, β_0, $\beta_1 \in \mathbb{R}_{>0}$. Hence, we have $\mathcal{S}_1 = \mathcal{S}_2 = \mathcal{S}_3 = \mathbb{Z}_+$, $\mathcal{S}_4 = \mathcal{S}_5 = \mathcal{S}_6 = \{0, 1\}$, $\bar{\mathcal{S}} = \mathcal{S}_4 \times \mathcal{S}_5 \times \mathcal{S}_6$, $|\bar{\mathcal{S}}| = 8$, and $\mathcal{S} = \mathcal{S}_1 \times \mathcal{S}_2 \times \mathcal{S}_3 \times \bar{\mathcal{S}}$. Note that (2.1) implies $8(3l^2 + 3l + 1)$ states at level $l \in \mathbb{Z}_+$.*

The transition rate matrices of the model from Table 3.8 and Definition 3 are obtained as

$$\begin{aligned}
Z^{(1,2)} &= Z^{(1,3)} = Z^{(2,2)} = Z^{(2,3)} = Z^{(3,2)} = Z^{(3,3)} = Z^{(4,2)} = Z^{(4,3)} = \\
Z^{(5,1)} &= Z^{(5,3)} = Z^{(6,1)} = Z^{(6,3)} = Z^{(7,1)} = Z^{(7,3)} = Z^{(8,1)} = Z^{(8,3)} = \\
Z^{(9,1)} &= Z^{(9,2)} = Z^{(10,1)} = Z^{(10,2)} = Z^{(11,1)} = Z^{(11,2)} = Z^{(12,1)} = Z^{(12,2)} = I_\infty,
\end{aligned}$$

Table 3.7: Repressilator model

j	*Reaction*	*Stoichiometric Equation*
1	X_3 *is not bound to* X_1 *and* X_1 *can be produced*	$\bar{X}_6 \xrightarrow{\lambda_1(1-x_6)} X_1 + \bar{X}_6$
2	X_1 *degrades*	$X_1 \xrightarrow{\delta_1 x_1} \emptyset$
3	X_1 *binds to the binding site of* X_2	$X_1 + \bar{X}_4 \xrightarrow{\beta_0 x_1(1-x_4)} X_4$
4	X_1 *leaves the the binding site of* X_2	$X_4 \xrightarrow{\beta_1 x_4} X_1 + \bar{X}_4$
5	X_1 *is not bound to* X_2 *and* X_2 *can be produced*	$\bar{X}_4 \xrightarrow{\lambda_2(1-x_4)} X_2 + \bar{X}_4$
6	X_2 *degrades*	$X_2 \xrightarrow{\delta_2 x_2} \emptyset$
7	X_2 *binds to the binding site of* X_3	$X_2 + \bar{X}_5 \xrightarrow{\beta_0 x_2(1-x_5)} X_5$
8	X_2 *leaves the the binding site of* X_3	$X_5 \xrightarrow{\beta_1 x_5} X_2 + \bar{X}_5$
9	X_2 *is not bound to* X_3 *and* X_3 *can be produced*	$\bar{X}_5 \xrightarrow{\lambda_3(1-x_5)} X_3 + \bar{X}_5$
10	X_3 *degrades*	$X_3 \xrightarrow{\delta_3 x_3} \emptyset$
11	X_3 *binds to the binding site of* X_1	$X_3 + \bar{X}_6 \xrightarrow{\beta_0 x_3(1-x_6)} X_6$
12	X_3 *leaves the the binding site of* X_1	$X_6 \xrightarrow{\beta_1 x_6} X_3 + \bar{X}_6$

$$Z^{(1,1)} = Z^{(1,4)} = Z^{(5,2)} = Z^{(8,2)} = Z^{(9,3)} = Z^{(12,3)} = superdiag((1,1,\ldots)^T),$$
$$Z^{(2,1)} = Z^{(3,1)} = Z^{(6,2)} = Z^{(7,2)} = Z^{(10,3)} = Z^{(11,3)} = subdiag((1,2,\ldots)^T).$$

The joint transition rate matrices of the model for finite variables from Table 3.8 and Definition 4 are obtained as follows

$$\bar{Z}^{(2)} = \bar{Z}^{(6)} = \bar{Z}^{(10)} = I_2 \otimes I_2 \otimes I_2, \quad \bar{Z}^{(1)} = I_2 \otimes I_2 \otimes diag((1,0)^T),$$
$$\bar{Z}^{(3)} = superdiag((1)^T) \otimes I_2 \otimes I_2, \quad \bar{Z}^{(4)} = subdiag((1)^T) \otimes I_2 \otimes I_2,$$
$$\bar{Z}^{(5)} = diag((1,0)^T) \otimes I_2 \otimes I_2, \quad \bar{Z}^{(7)} = I_2 \otimes superdiag((1)^T) \otimes I_2,$$
$$\bar{Z}^{(8)} = I_2 \otimes subdiag((1)^T) \otimes I_2, \quad \bar{Z}^{(9)} = I_2 \otimes diag((1,0)^T) \otimes I_2,$$
$$\bar{Z}^{(11)} = I_2 \otimes I_2 \otimes superdiag((1)^T), \quad \bar{Z}^{(12)} = I_2 \otimes I_2 \otimes subdiag((1)^T).$$

Table 3.8: Transition classes of the molecule synthesis model with repressilator

j	$\psi^{(j)}$	$h^{(j,1)}(x_1)$	$h^{(j,2)}(x_2)$	$h^{(j,3)}(x_3)$	$h^{(j,4)}(x_4)$	$h^{(j,5)}(x_5)$	$h^{(j,6)}(x_6)$	$v^{(j)}$
1	λ_1	1	1	1	1	1	$(1-x_6)$	e_1^T
2	δ_1	x_1	1	1	1	1	1	$-e_1^T$
3	β_0	x_1	1	1	$(1-x_4)$	1	1	$(-e_1+e_4)^T$
4	β_1	1	1	1	x_4	1	1	$(e_1-e_4)^T$
5	λ_2	1	1	1	$(1-x_4)$	1	1	e_2^T
6	δ_2	1	x_2	1	1	1	1	$-e_2^T$
7	β_0	1	x_2	1	1	$(1-x_5)$	1	$(-e_2+e_5)^T$
8	β_1	1	1	1	1	x_5	1	$(e_2-e_5)^T$
9	λ_3	1	1	1	1	$(1-x_5)$	1	e_3^T
10	δ_3	1	1	x_3	1	1	1	$-e_3^T$
11	β_0	1	1	x_3	1	1	$(1-x_6)$	$(-e_3+e_6)^T$
12	β_1	1	1	1	1	1	x_6	$(e_3-e_6)^T$

The state space partitions from Definition 6 are computed as in Example 2, but now we also have

$$\bar{\mathcal{S}} = \{(0,0,0),\ldots,(1,1,1)\},$$

and therefore,

$$\mathcal{S}^{(l,1)} = \left(\times_{i=1}^{3}\mathcal{S}_i^{(l,1)}\right) \times \bar{\mathcal{S}} = \{(l,0,0,0,0,0),\ldots,(l,l,l,1,1,1)\},$$

$$\mathcal{S}^{(l,2)} = \left(\times_{i=1}^{3}\mathcal{S}_i^{(l,2)}\right) \times \bar{\mathcal{S}} = \{(0,l,0,0,0,0),\ldots,(l-1,l,l,1,1,1)\},$$

$$\mathcal{S}^{(l,3)} = \left(\times_{i=1}^{3}\mathcal{S}_i^{(l,3)}\right) \times \bar{\mathcal{S}} = \{(0,0,l,0,0,0),\ldots,(l-1,l-1,l,1,1,1)\}.$$

Finally, since $n_I = 3$, from Table 3.8 and Definition 7, the nonzero blocks $Q_{0,0}$, $Q_{0,1}$, $Q_{1,0}$, and $Q_{l,m}$ for $l > 0$, $m \in \{l-1,l,l+1\}$ are respectively (1×1), (1×3), (3×1), and (3×3) block matrices. In particular, the nine blocks associated *with $Q_{l,l-1}$ are given by*

$$\begin{aligned}
\tilde{Q}^{(1,1)}_{l,l-1} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l-1,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l-1,1)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l-1,1)}) \otimes \bar{Z}^{(j)} \Big) \\
&= \big(\mu_1 l \otimes diag((1,\ldots,1)^T)_{(l+1)\times l} \\
&\qquad \otimes diag((1,\ldots,1)^T)_{(l+1)\times l} \otimes \bar{Z}^{(2)} \big) \\
&\quad + \big(\beta_0 l \otimes diag((1,\ldots,1)^T)_{(l+1)\times l} \\
&\qquad \otimes diag((1,\ldots,1)^T)_{(l+1)\times l} \otimes \bar{Z}^{(3)} \big) \,,
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(1,2)}_{l,l-1} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l-1,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l-1,2)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l-1,2)}) \otimes \bar{Z}^{(j)} \Big) \\
&= 0_{8(l+1)^2 \times 8(l-1)l},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(1,3)}_{l,l-1} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l-1,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l-1,3)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l-1,3)}) \otimes \bar{Z}^{(j)} \Big) \\
&= 0_{8(l+1)^2 \times 8(l-1)^2},
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(2,1)}_{l,l-1} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l-1,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l-1,1)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l-1,1)}) \otimes \bar{Z}^{(j)} \Big) \\
&= \big(\mu_2 (0,\ldots,0,1)^T_{l\times 1} \otimes (0,\ldots,0,l)_{1\times l} \\
&\qquad \otimes diag((1,\ldots,1)^T)_{(l+1)\times l} \otimes \bar{Z}^{(6)} \big) \\
&\quad + \big(\beta_0 (0,\ldots,0,1)^T_{l\times 1} \otimes (0,\ldots,0,l)_{1\times l} \\
&\qquad \otimes diag((1,\ldots,1)^T)_{(l+1)\times l} \otimes \bar{Z}^{(7)} \big) \,,
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(2,2)}_{l,l-1} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l-1,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l-1,2)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l-1,2)}) \otimes \bar{Z}^{(j)} \Big) \\
&= \big(\mu_2\, diag((1,\ldots,1)^T)_{l\times(l-1)} \otimes l \\
&\qquad \otimes diag((1,\ldots,1)^T)_{(l+1)\times l} \otimes \bar{Z}^{(6)} \big) \\
&\quad + \big(\beta_0\, diag((1,\ldots,1)^T)_{l\times(l-1)} \otimes l \\
&\qquad \otimes diag((1,\ldots,1)^T)_{(l+1)\times l} \otimes \bar{Z}^{(7)} \big)\,,
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(2,3)}_{l,l-1} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l-1,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l-1,3)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l-1,3)}) \otimes \bar{Z}^{(j)} \Big) \\
&= 0_{8l(l+1)\times 8(l-1)^2}\,,
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(3,1)}_{l,l-1} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l-1,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l-1,1)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l-1,1)}) \otimes \bar{Z}^{(j)} \Big) \\
&= \big(\mu_3 (0,\ldots,0,1)^T_{l\times 1} \otimes diag((1,\ldots,1)^T)_{l\times l} \\
&\qquad \otimes (0,\ldots,0,l)_{1\times l} \otimes \bar{Z}^{(10)} \big) \\
&\quad + \big(\beta_0 (0,\ldots,0,1)^T_{l\times 1} \otimes diag((1,\ldots,1)^T)_{l\times l} \\
&\qquad \otimes (0,\ldots,0,l)_{1\times l} \otimes \bar{Z}^{(11)} \big)\,,
\end{aligned}$$

$$
\begin{aligned}
\tilde{Q}^{(3,2)}_{l,l-1} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l-1,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l-1,2)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l-1,2)}) \otimes \bar{Z}^{(j)} \Big) \\
&= \big(\mu_3\, diag((1,\ldots,1)^T)_{l\times(l-1)} \otimes (0,\ldots,0,1)^T_{l\times 1} \\
&\qquad \otimes (0,\ldots,0,l)_{1\times l} \otimes \bar{Z}^{(10)} \big) \\
&\quad + \big(\beta_0\, diag((1,\ldots,1)^T)_{l\times(l-1)} \otimes (0,\ldots,0,1)^T_{l\times 1} \\
&\qquad \otimes (0,\ldots,0,l)_{1\times l} \otimes \bar{Z}^{(11)} \big),
\end{aligned}
$$

$$
\begin{aligned}
\tilde{Q}^{(3,3)}_{l,l-1} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l-1,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l-1,3)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l-1,3)}) \otimes \bar{Z}^{(j)} \Big) \\
&= \big(\mu_3\, diag((1,\ldots,1)^T)_{l\times(l-1)} \otimes diag((1,\ldots,1)^T)_{l\times(l-1)} \\
&\qquad \otimes l \otimes \bar{Z}^{(10)} \big) \\
&\quad + \big(\beta_0\, diag((1,\ldots,1)^T)_{l\times(l-1)} \otimes diag((1,\ldots,1)^T)_{l\times(l-1)} \\
&\qquad \otimes l \otimes \bar{Z}^{(11)} \big),
\end{aligned}
$$

and the nine blocks associated with $Q_{l,l}$ *are given by*

$$\begin{aligned}
\tilde{Q}^{(1,1)}_{l,l} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l,1)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l,1)}) \otimes \bar{Z}^{(j)} \Big) \\
&= \big(\lambda_2 1 \otimes \mathit{superdiag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \\
&\qquad \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \otimes \bar{Z}^{(5)} \big) \\
&\quad + \big(\mu_2 1 \otimes \mathit{subdiag}((1,\ldots,l)^T)_{(l+1)\times(l+1)} \\
&\qquad \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \otimes \bar{Z}^{(6)} \big) \\
&\quad + \big(\beta_0 1 \otimes \mathit{subdiag}((1,\ldots,l)^T)_{(l+1)\times(l+1)} \\
&\qquad \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \otimes \bar{Z}^{(7)} \big) \\
&\quad + \big(\beta_1 1 \otimes \mathit{superdiag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \\
&\qquad \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \otimes \bar{Z}^{(8)} \big) \\
&\quad + \big(\lambda_3 1 \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \\
&\qquad \otimes \mathit{superdiag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \otimes \bar{Z}^{(9)} \big) \\
&\quad + \big(\mu_3 1 \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \\
&\qquad \otimes \mathit{subdiag}((1,\ldots,l)^T)_{(l+1)\times(l+1)} \otimes \bar{Z}^{(10)} \big) \\
&\quad + \big(\beta_0 1 \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \\
&\qquad \otimes \mathit{subdiag}((1,\ldots,l)^T)_{(l+1)\times(l+1)} \otimes \bar{Z}^{(11)} \big) \\
&\quad + \big(\beta_1 1 \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \\
&\qquad \otimes \mathit{superdiag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \otimes \bar{Z}^{(12)} \big) ,
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(1,2)}_{l,l} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l,2)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l,2)}) \otimes \bar{Z}^{(j)} \Big) \\
&= \big(\mu_1 (0,\ldots,0,l)_{1\times l} \otimes (0,\ldots,0,1)^T_{(l+1)\times 1} \big) \\
&\qquad \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \otimes \bar{Z}^{(2)} \\
&\quad + \big(\beta_0 (0,\ldots,0,l)_{1\times l} \otimes (0,\ldots,0,1)^T_{(l+1)\times 1} \big) \\
&\qquad \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \otimes \bar{Z}^{(3)} \big) ,
\end{aligned}$$

$$
\begin{aligned}
\tilde{Q}^{(1,3)}_{l,l} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}^{(l,1)}_1, \mathcal{S}^{(l,3)}_1) \otimes Z^{(j,2)}(\mathcal{S}^{(l,1)}_2, \mathcal{S}^{(l,3)}_2) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}^{(l,1)}_3, \mathcal{S}^{(l,3)}_3) \otimes \bar{Z}^{(j)} \Big) \\
&= \big(\mu_1 (0,\ldots,0,l)_{1\times l} \otimes diag((1,\ldots,1)^T)_{(l+1)\times l} \\
&\qquad \otimes (0,\ldots,0,1)^T_{(l+1)\times 1} \otimes \bar{Z}^{(2)} \big) \\
&\quad + \big(\beta_0 (0,\ldots,0,l)_{1\times l} \otimes diag((1,\ldots,1)^T)_{(l+1)\times l} \\
&\qquad \otimes (0,\ldots,0,1)^T_{(l+1)\times 1} \otimes \bar{Z}^{(3)} \big),
\end{aligned}
$$

$$
\begin{aligned}
\tilde{Q}^{(2,1)}_{l,l} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}^{(l,2)}_1, \mathcal{S}^{(l,1)}_1) \otimes Z^{(j,2)}(\mathcal{S}^{(l,2)}_2, \mathcal{S}^{(l,1)}_2) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}^{(l,2)}_3, \mathcal{S}^{(l,1)}_3) \otimes \bar{Z}^{(j)} \Big) \\
&= \big(\lambda_1 (0,\ldots,0,1)^T_{l\times 1} \otimes (0,\ldots,0,1)_{1\times(l+1)} \\
&\qquad \otimes diag((1,\ldots,1)^T)_{(l+1)\times(l+1)} \otimes \bar{Z}^{(1)} \big) \\
&\quad + \big(\beta_1 (0,\ldots,0,1)^T_{l\times 1} \otimes (0,\ldots,0,1)_{1\times(l+1)} \\
&\qquad \otimes diag((1,\ldots,1)^T)_{(l+1)\times(l+1)} \otimes \bar{Z}^{(4)} \big),
\end{aligned}
$$

$$
\begin{aligned}
\tilde{Q}_{l,l}^{(2,2)} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l,2)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l,2)}) \otimes \bar{Z}^{(j)} \Big) \\
&= \big(\lambda_1 \mathit{superdiag}((1,\ldots,1)^T)_{l\times l} \otimes 1 \\
&\qquad \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \otimes \bar{Z}^{(1)} \big) \\
&\quad + \big(\mu_1 \mathit{subdiag}((1,\ldots,l-1)^T)_{l\times l} \otimes 1 \\
&\qquad \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \otimes \bar{Z}^{(2)} \big) \\
&\quad + \big(\beta_0 \mathit{subdiag}((1,\ldots,l-1)^T)_{l\times l} \otimes 1 \\
&\qquad \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \otimes \bar{Z}^{(3)} \big) \\
&\quad + \big(\beta_1 \mathit{superdiag}((1,\ldots,1)^T)_{l\times l} \otimes 1 \\
&\qquad \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \otimes \bar{Z}^{(4)} \big) \\
&\quad + \big(\lambda_3 \mathit{diag}((1,\ldots,1)^T)_{l\times l} \otimes 1 \\
&\qquad \otimes \mathit{superdiag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \otimes \bar{Z}^{(9)} \big) \\
&\quad + \big(\mu_3 \mathit{diag}((1,\ldots,1)^T)_{l\times l} \otimes 1 \\
&\qquad \otimes \mathit{subdiag}((1,\ldots,l)^T)_{(l+1)\times(l+1)} \otimes \bar{Z}^{(10)} \big) \\
&\quad + \big(\beta_0 \mathit{diag}((1,\ldots,1)^T)_{l\times l} \otimes 1 \\
&\qquad \otimes \mathit{subdiag}((1,\ldots,l)^T)_{(l+1)\times(l+1)} \otimes \bar{Z}^{(11)} \big) \\
&\quad + \big(\beta_1 \mathit{diag}((1,\ldots,1)^T)_{l\times l} \otimes 1 \\
&\qquad \otimes \mathit{superdiag}((1,\ldots,1)^T)_{(l+1)\times(l+1)} \otimes \bar{Z}^{(12)} \big),
\end{aligned}
$$

$$
\begin{aligned}
\tilde{Q}_{l,l}^{(2,3)} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l,3)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l,3)}) \otimes \bar{Z}^{(j)} \Big) \\
&= \big(\mu_2 \mathit{diag}((1,\ldots,1)^T)_{l\times l} \otimes (0,\ldots,0,l)_{1\times l} \\
&\qquad \otimes (0,\ldots,0,1)^T_{(l+1)\times 1} \otimes \bar{Z}^{(6)} \big) \\
&\quad + \big(\beta_0 \mathit{diag}((1,\ldots,1)^T)_{l\times l} \otimes (0,\ldots,0,l)_{1\times l} \\
&\qquad \otimes (0,\ldots,0,1)^T_{(l+1)\times 1} \otimes \bar{Z}^{(7)} \big),
\end{aligned}
$$

$$\begin{aligned}
\tilde{Q}_{l,l}^{(3,1)} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l,1)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l,1)}) \otimes \bar{Z}^{(j)} \Big) \\
&= \big(\lambda_1 (0,\ldots,0,1)_{l\times 1}^T \otimes \mathit{diag}((1,\ldots,1)^T)_{l\times(l+1)} \\
&\qquad \otimes (0,\ldots,0,1)_{1\times(l+1)} \otimes \bar{Z}^{(1)} \big) \\
&\quad + \big(\beta_1 (0,\ldots,0,1)_{l\times 1}^T \otimes \mathit{diag}((1,\ldots,1)^T)_{l\times(l+1)} \\
&\qquad \otimes (0,\ldots,0,1)_{1\times(l+1)} \otimes \bar{Z}^{(4)} \big) ,
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}_{l,l}^{(3,2)} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l,2)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l,2)}) \otimes \bar{Z}^{(j)} \Big) \\
&= \big(\lambda_2 \, \mathit{diag}((1,\ldots,1)^T)_{l\times l} \otimes (0,\ldots,0,1)_{l\times 1}^T \\
&\qquad \otimes (0,\ldots,0,1)_{1\times(l+1)} \otimes \bar{Z}^{(5)} \big) \\
&\quad + \big(\beta_1 \, \mathit{diag}((1,\ldots,1)^T)_{l\times l} \otimes (0,\ldots,0,1)_{l\times 1}^T \\
&\qquad \otimes (0,\ldots,0,1)_{1\times(l+1)} \otimes \bar{Z}^{(8)} \big) ,
\end{aligned}$$

$$
\begin{aligned}
\tilde{Q}_{l,l}^{(3,3)} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l,3)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l,3)}) \otimes \bar{Z}^{(j)} \Big) \\
&= \big(\lambda_1 \mathit{superdiag}((1,\ldots,1)^T)_{l\times l} \\
&\qquad \otimes \mathit{diag}((1,\ldots,1)^T)_{l\times l} \otimes 1 \otimes \bar{Z}^{(1)} \big) \\
&\quad + \big(\mu_1 \mathit{subdiag}((1,\ldots,l-1)^T)_{l\times l} \\
&\qquad \otimes \mathit{diag}((1,\ldots,1)^T)_{l\times l} \otimes 1 \otimes \bar{Z}^{(2)} \big) \\
&\quad + \big(\beta_0 \mathit{subdiag}((1,\ldots,l-1)^T)_{l\times l} \\
&\qquad \otimes \mathit{diag}((1,\ldots,1)^T)_{l\times l} \otimes 1 \otimes \bar{Z}^{(3)} \big) \\
&\quad + \big(\beta_1 \mathit{superdiag}((1,\ldots,1)^T)_{l\times l} \\
&\qquad \otimes \mathit{diag}((1,\ldots,1)^T)_{l\times l} \otimes 1 \otimes \bar{Z}^{(4)} \big) \\
&\quad + \big(\lambda_2 \mathit{diag}((1,\ldots,1)^T)_{l\times l} \\
&\qquad \otimes \mathit{superdiag}((1,\ldots,1)^T)_{l\times l} \otimes 1 \otimes \bar{Z}^{(5)} \big) \\
&\quad + \big(\mu_2 \mathit{diag}((1,\ldots,1)^T)_{l\times l} \\
&\qquad \otimes \mathit{subdiag}((1,\ldots,l-1)^T)_{l\times l} \otimes 1 \otimes \bar{Z}^{(6)} \big) \\
&\quad + \big(\beta_0 \mathit{diag}((1,\ldots,1)^T)_{l\times l} \\
&\qquad \otimes \mathit{subdiag}((1,\ldots,l-1)^T)_{l\times l} \otimes 1 \otimes \bar{Z}^{(7)} \big) \\
&\quad + \big(\beta_1 \mathit{diag}((1,\ldots,1)^T)_{l\times l} \\
&\qquad \otimes \mathit{superdiag}((1,\ldots,1)^T)_{l\times l} \otimes 1 \otimes \bar{Z}^{(8)} \big) ,
\end{aligned}
$$

and the nine blocks associated with $Q_{l,l+1}$ *are given by*

$$
\begin{aligned}
\tilde{Q}_{l,l+1}^{(1,1)} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l+1,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l+1,1)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l+1,1)}) \otimes \bar{Z}^{(j)} \Big) \\
&= \big(\lambda_1 1 \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+2)} \\
&\qquad \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+2)} \otimes \bar{Z}^{(1)} \big) \\
&\quad + \big(\beta_1 1 \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+2)} \\
&\qquad \otimes \mathit{diag}((1,\ldots,1)^T)_{(l+1)\times(l+2)} \otimes \bar{Z}^{(4)} \big) ,
\end{aligned}
$$

$$\begin{aligned}\tilde{Q}^{(1,2)}_{l,l+1} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l+1,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l+1,2)}) \\ &\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l+1,2)}) \otimes \bar{Z}^{(j)} \Big) \\ &= \big(\lambda_2 (0,\dots,0,1)_{1\times(l+1)} \otimes (0,\dots,0,1)^T_{(l+1)\times 1} \\ &\qquad \otimes diag((1,\dots,1)^T)_{(l+1)\times(l+2)} \otimes \bar{Z}^{(5)}\big) \\ &\quad + \big(\beta_1 (0,\dots,0,1)_{1\times(l+1)} \otimes (0,\dots,0,1)^T_{(l+1)\times 1} \\ &\qquad \otimes diag((1,\dots,1)^T)_{(l+1)\times(l+2)} \otimes \bar{Z}^{(8)}\big)\,,\end{aligned}$$

$$\begin{aligned}\tilde{Q}^{(1,3)}_{l,l+1} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,1)}, \mathcal{S}_1^{(l+1,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,1)}, \mathcal{S}_2^{(l+1,3)}) \\ &\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,1)}, \mathcal{S}_3^{(l+1,3)}) \otimes \bar{Z}^{(j)} \Big) \\ &= \big(\lambda_3 (0,\dots,0,1)_{1\times(l+1)} \otimes diag((1,\dots,1)^T)_{(l+1)\times(l+1)} \\ &\qquad \otimes (0,\dots,0,1)^T_{(l+1)\times 1} \otimes \bar{Z}^{(9)}\big) \\ &\quad + \big(\beta_1 (0,\dots,0,1)_{1\times(l+1)} \otimes diag((1,\dots,1)^T)_{(l+1)\times(l+1)} \\ &\qquad \otimes (0,\dots,0,1)^T_{(l+1)\times 1} \otimes \bar{Z}^{(12)}\big)\,,\end{aligned}$$

$$\begin{aligned}\tilde{Q}^{(2,1)}_{l,l+1} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l+1,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l+1,1)}) \\ &\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l+1,1)}) \otimes \bar{Z}^{(j)} \Big) \\ &= 0_{8l(l+1)\times 8(l+2)^2},\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(2,2)}_{l,l+1} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l+1,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l+1,2)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l+1,2)}) \otimes \bar{Z}^{(j)} \Big) \\
&= \big(\lambda_2\, diag((1,\ldots,1)^T)_{l\times(l+1)} \otimes 1 \\
&\qquad \otimes diag((1,\ldots,1)^T)_{(l+1)\times(l+2)} \otimes \bar{Z}^{(5)} \big) \\
&\quad + \big(\beta_1\, diag((1,\ldots,1)^T)_{l\times(l+1)} \otimes 1 \\
&\qquad \otimes diag((1,\ldots,1)^T)_{(l+1)\times(l+2)} \otimes \bar{Z}^{(8)} \big)\,,
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(2,3)}_{l,l+1} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,2)}, \mathcal{S}_1^{(l+1,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,2)}, \mathcal{S}_2^{(l+1,3)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,2)}, \mathcal{S}_3^{(l+1,3)}) \otimes \bar{Z}^{(j)} \Big) \\
&= \big(\lambda_3\, diag((1,\ldots,1)^T)_{l\times(l+1)} \otimes (0,\ldots,0,1)_{1\times(l+1)} \\
&\qquad \otimes (0,\ldots,0,1)^T_{(l+1)\times 1} \otimes \bar{Z}^{(9)} \big) \\
&\quad + \big(\beta_1\, diag((1,\ldots,1)^T)_{l\times(l+1)} \otimes (0,\ldots,0,1)_{1\times(l+1)} \\
&\qquad \otimes (0,\ldots,0,1)^T_{(l+1)\times 1} \otimes \bar{Z}^{(12)} \big)\,,
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(3,1)}_{l,l+1} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l+1,1)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l+1,1)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l+1,1)}) \otimes \bar{Z}^{(j)} \Big) \\
&= 0_{8l^2\times 8(l+2)^2}\,,
\end{aligned}$$

$$\begin{aligned}
\tilde{Q}^{(3,2)}_{l,l+1} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l+1,2)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l+1,2)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l+1,2)}) \otimes \bar{Z}^{(j)} \Big) \\
&= 0_{8l^2\times 8(l+1)(l+2)}\,,
\end{aligned}$$

$$
\begin{aligned}
\tilde{Q}^{(3,3)}_{l,l+1} &= \sum_{j=1}^{12} \psi^{(j)} \Big(Z^{(j,1)}(\mathcal{S}_1^{(l,3)}, \mathcal{S}_1^{(l+1,3)}) \otimes Z^{(j,2)}(\mathcal{S}_2^{(l,3)}, \mathcal{S}_2^{(l+1,3)}) \\
&\qquad \otimes Z^{(j,3)}(\mathcal{S}_3^{(l,3)}, \mathcal{S}_3^{(l+1,3)}) \otimes \bar{Z}^{(j)} \Big) \\
&= \big(\lambda_3\, diag((1,\ldots,1)^T)_{l\times(l+1)} \otimes diag((1,\ldots,1)^T)_{l\times(l+1)} \\
&\qquad \otimes 1 \otimes \bar{Z}^{(9)}\big) \\
&\quad + \big(\beta_1\, diag((1,\ldots,1)^T)_{l\times(l+1)} \otimes diag((1,\ldots,1)^T)_{l\times(l+1)} \\
&\qquad \otimes 1 \otimes \bar{Z}^{(12)}\big)\,.
\end{aligned}
$$

In the next chapter, after briefly recalling how we compute the *Low* and *High* level numbers of the LDQBD between which a specified percentage of the steady-state probability mass lies, we describe how the simulation is carried out.

Chapter 4

Implementation Issues

It has been shown by [29] that the LDQBD is ergodic if and only if there exists a function $g : \mathcal{S} \to \mathbb{R}_{\geq 0}$, called a Lyapunov function, and a finite attractor set $\mathcal{C} \subset \mathcal{S}$ satisfying the three conditions

(i) $d(x) \leq -\gamma$ for all $x \in \mathcal{S} \setminus \mathcal{C}$ and some $\gamma > 0$,

(ii) $d(x) < \infty$ for all $x \in \mathcal{C}$, and

(iii) $\{x \in \mathcal{S} \mid g(x) \leq r\}$ is finite for all $r < \infty$,

where

$$d(x) = \sum_{j=1}^{J} \alpha_j(x)(g(x + v^{(j)}) - g(x)) \in \mathbb{R} \tag{4.1}$$

is called the drift in state $x \in \mathcal{S}$.

Assuming that g satisfies condition (iii) and letting $c = \sup_{x \in \mathcal{S}} d(x) < \infty$, an upper bound on $\sum_{x \in \mathcal{S} \setminus \mathcal{C}} \pi(x)$ can be a priori specified as $\epsilon = c/(c + \gamma) \in (0, 1)$, which translates to $\gamma = c/\epsilon - c$ and $\mathcal{C} = \{x \in \mathcal{S} \mid d(x) > -\gamma\}$. In addition, if $\mathcal{C}$ is finite, then the three conditions above hold and $\sum_{x \in \mathcal{C}} \pi(x) \geq 1 - \epsilon$.

In order to determine c, the domain of the search for extrema is restricted to $\mathbb{R}^{1 \times n}_{\geq 0}$. All extrema is computed by equating the gradient of $d(x)$ to zero. In order to determine all local extrema including those located on the boundaries of the domain, the same system is solved for every projection of $d(x)$ onto each subspace of $\mathbb{R}^{1\times n}$ by setting all combinations of variables x_i for $i \in \{1,\ldots,n\}$ to zero. In the end, all extrema outside of $\mathbb{R}^{1\times n}_{\geq 0}$ is discarded. Throughout this process, the resulting nonlinear equation systems are solved using the HOM4PS-2.0 package [17], an implementation of the polyhedral homotopy continuation method. For details, see Dayar et al. [7].

We compute the pair of level numbers, $(Low, High)$, of the LDQBD such that the states in levels Low to $High$ include all the states in $\mathcal{C}$. In other words, we set

$$Low = \min\{l \in \mathbb{Z}_+ \mid \mathcal{S}^{(l)} \cap \mathcal{C} \neq \emptyset\} \quad \text{and} \quad High = \max\{l \in \mathbb{Z}_+ \mid \mathcal{S}^{(l)} \cap \mathcal{C} \neq \emptyset\},$$

and the finite set $\bigcup_{Low \leq l \leq High} \mathcal{S}^{(l)}$ contains at least $(1-\epsilon)$ of the steady-state probability. The number of states lieing in levels Low to $High$ are given by

$$N(Low, High) = \sum_{l=Low}^{High} \left|\bar{\mathcal{S}}\right| ((l+1)^{n_I} - (l)^{n_I}) = \left|\bar{\mathcal{S}}\right| ((High+1)^{n_I} - (Low)^{n_I}).$$

The proofs that the four examples satisfy the conditions for $\mathcal{C}$ to be finite are given in the Appendix A. In order to carry out a fair comparison with simulation, for all examples we choose the squared Euclidean norm, that is, $g(x) = \sum_{i=1}^{n} x_i^2$, as the Lyapunov function and set $\epsilon = 0.05$. In other words, the results we present with the LDQBD solver [8] developed in Matlab are not fine-tuned. In Dayar et al. [9], it has already been shown that for smaller ϵ, the accuracy of the computed solution by the matrix analytic approach improves and eventually reaches that of machine precision. We do not undertake such a study here due to memory limitations imposed by the multi-dimensional models we consider. Given more memory (and time) it is always possible to obtain more accurate results with the matrix analytic approach.

The matrix analytic approach used in the solution process is the one called A3 in Dayar et al. [9]. That is, we start by setting the matrix of conditional expected sojourn times at level $High$ to zero [2] and compute the matrices of conditional expected sojourn times at levels $l \in \{Low, \ldots, High-1\}$ recursively.

In order to provide confidence intervals for the stochastic simulation of Gillespie [10], we take 31 sample paths for each example. Furthermore, it is always an issue when to terminate simulations. To that end, we terminate the simulation dynamically by comparing the absolute value of the update on the current mean with a user specified tolerance as follows. Let the current value of the StochKit (SK) mean for a particular molecule in a sample path be given by

$$\mathrm{Mean}_{\mathrm{SK}}(K) = \sum_{k=1}^{K} S_k \Delta t_k / \sum_{k=1}^{K} \Delta t_k,$$

where Δt_k is the exponentially distributed time of transition k, S_k is the state of the molecule during Δt_k, and K is the number of transitions taken up to this point. Then the new mean after transition $(K+1)$ takes place can be written as

$$\begin{aligned}\mathrm{Mean}_{\mathrm{SK}}(K+1) &= \mathrm{Mean}_{\mathrm{SK}}(K) \\ &\quad + (S_{K+1} - \mathrm{Mean}_{\mathrm{SK}}(K))\Delta t_{K+1} / (\Delta t_{K+1} + \sum_{k=1}^{K} \Delta t_k).\end{aligned}$$

We remark that it is relatively easy to carry out the update on $\mathrm{Mean}_{\mathrm{SK}}(K)$. And while it is computed, we can compare the absolute value of the update (that is, the second term) on the right-hand side of $\mathrm{Mean}_{\mathrm{SK}}(K+1)$ with the given tolerance. In our simulations, we have used 10^{-16} as the tolerance. We present the simulation results in the next chapter along with the results of the LDQBD solver.

Chapter 5

Numerical Results

Experiments are performed on a PC with an Intel Core2 Duo 1.83GHz processor having 4 Gigabytes (GB) of main memory. The existence of two cores in the CPU is not exploited for parallel computing in the implementation. Hence, only one of the two cores is busy running the solver in the experiments.

We use subscripts as in d_p, c_p, γ_p, $(Low_p, High_p)$, and N_p for Example $p \in \{1, 2, 3, 4\}$, and report the values of c_p and γ_p in two decimal digits of precision.

Example 1 *(Gene Expression (cntd.)) We let* $\lambda = \mu = \delta_2 = 0.05$*, and* $\delta_2 = 0.015$ *be the parameters. Then the drift for* $\epsilon = 0.05$ *is*

$$d_1(x_1, x_2) = -0.03x_1^2 - 0.1x_2^2 + 0.1x_1x_2 + 0.165x_1 + 0.05x_2 + 0.05.$$

By using the HOM4PS2-2.0 package [17], we obtain the global maximum drift $c_1 = 1.86$*. For* $\epsilon = 0.05$*, we compute* $\gamma_1 = -35.36$*,* $(Low_1, High_1) = (0, 105)$*, and* $N_1(0, 105) = 11,236$*.*

Example 2 *(Molecule Synthesis with Two Molecules and One Enzyme (cntd.)) We let* $k_A = k_B = 0.3$*,* $K_I = 16$*,* $k_2 = 0.05$*,* $\mu = 0.1$*,* $K_R = 8$*, and* $k_{E_A} = 0.02$ *be* *the parameters. Then the drift for* $\epsilon = 0.05$ *is*

$$\begin{aligned} d_2(x_1, x_2, x_3) &= \frac{9.6x_1x_3 + 4.8x_3}{x_1 + 16} + \frac{0.32x_3 + 0.16}{x_1 + 8} - 0.1x_1^2x_2 - 0.1x_1x_2^2 \\ &\quad +0.1x_1x_2 - 0.2x_1^2 - 0.2x_2^2 - 0.2x_3^2 \\ &\quad +0.1x_1 + 0.7x_2 + 0.1x_3 + 0.3. \end{aligned}$$

The HOM4PS2-2.0 package requires the equation systems to consist of polynomials. Therefore we put the partial derivatives of x_1 *and* x_3 *over a common denominator. We use the numerator of the derivative as input since the denominator is always positive for the parameters chosen. Then we obtain the global maximum drift* $c_2 = 4.66$*. For* $\epsilon = 0.05$*, we compute* $\gamma_2 = -88.53$*,* $(Low_2, High_2) = (0, 31)$*, and* $N_2(0, 31) = 32,768$*.*

Example 3 *(Molecule Synthesis with Two Molecules and Two Enzymes (cntd.)) We let* $k_A = k_B = 0.3$*,* $K_I = 16$*,* $k_2 = 0.05$*,* $\mu = 0.2$*,* $K_R = 8$*, and* $k_{E_A} = k_{E_B} = 0.02$ *be the parameters. Then the drift for* $\epsilon = 0.05$ *is*

$$\begin{aligned} d_3(x_1, x_2, x_3, x_4) &= \frac{9.6x_1x_3 + 4.8x_3}{x_1 + 16} + \frac{0.32x_3 + 0.16}{x_1 + 8} + \frac{9.6x_2x_4 + 4.8x_4}{x_2 + 16} \\ &\quad + \frac{0.32x_4 + 0.16}{x_2 + 8} - 0.1x_1^2x_2 - 0.1x_1x_2^2 + 0.1x_1x_2 \\ &\quad -0.4x_1^2 - 0.4x_2^2 - 0.4x_3^2 - 0.4x_4^2 \\ &\quad +0.2x_1 + 0.2x_2 + 0.2x_3 + 0.2x_4. \end{aligned}$$

We proceed as in the previous example and compute the global maximum drift $c_3 = 0.87$*. For* $\epsilon = 0.05$*, we obtain* $\gamma_3 = -16.53$*,* $(Low_3, High_3) = (0, 9)$*, and* $N_3(0, 9) = 10,000$*.*

Example 4 *(Repressilator (cntd.)) We let* $\lambda_1 = \lambda_2 = \lambda_3 = 1.3$*,* $\delta_1 = \delta_2 = \delta_3 = 0.8$*,* $\beta_0 = 1$*, and* $\beta_1 = 0.5$ *be the parameters. Then the drift for* $\epsilon = 0.05$ *becomes*

$$\begin{aligned} d_4(x_1, x_2, x_3, x_4, x_5, x_6) &= -3.6x_1^2 + 2x_1^2x_4 + x_1x_4 - 2.6x_1x_6 + 5.6x_1 \\ &\quad -3.6x_2^2 + 2x_2^2x_5 + x_2x_5 - 2.6x_2x_4 + 5.6x_2 \\ &\quad -3.6x_3^2 + 2x_3^2x_6 + x_3x_6 - 2.6x_3x_5 + 5.6x_3 \\ &\quad -3.3x_4 - 3.3x_5 - 3.3x_6 + 3.9. \end{aligned}$$

Again, by using the HOM4PS2-2.0 package we obtain the global maximum drift $c_4 = 9.60$. *For* $\epsilon = 0.05$, *we compute* $\gamma_4 = -182.31$, $(Low_4, High_4) = (0, 12)$, *and* $N_4(0, 12) = 17,576$.

Although it cannot be used to its full extent, the large main memory is necessary to store the relatively dense matrices of conditional expected sojourn times at levels $l \in \{Low, \ldots, High - 1\}$ (see Figure 5.1 for their nonzero densities in the four examples and note how dense they become as the level number moves towards Low) and the temporary factors allocated by Matlab while solving linear systems with coefficient matrices involving them.

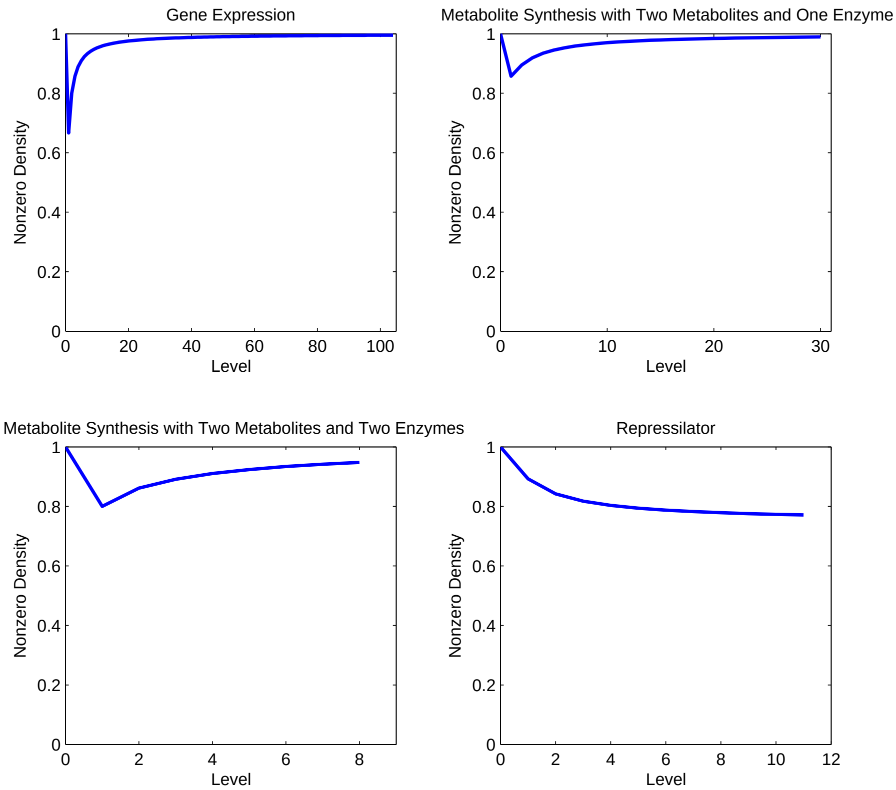

Figure 5.1: Nonzero densities in matrices of conditional expected sojourn times at levels $l \in \{Low, \ldots, High\}$ for the four examples

Now we present the results of LDQBD solvers for the examples discussed in the previous chapters. In Table 5.1, the first two columns give the example name and the corresponding $(Low, High)$ pair for the squared Euclidean norm as the Lyapunov function when we set $\epsilon = 0.05$. Hence, 95 is a lower bound on the percentage of the steady-state probability mass that lies in levels $l \in \{Low, \ldots, High\}$. Column "Time" lists the time in seconds (s) to solve the example with the LDQBD solver [8]. Column "Residual" gives the infinity norm of the residual vector. "Time" includes the time to compute the value in column "Residual". Finally, the last column gives the memory requirement in megabytes (MB) for the solution process associated with the particular example excluding that taken by Matlab itself. In the first two examples, we obtain a residual in the order of machine precision. In the last two examples, the results are still good and we have residuals in the order of at least 10^{-7}.

Table 5.1: LDQBD solver results

Example	$(Low, High)$	Time	Residual	Memory
Gene Expression	(0,105)	4 s	2e-17	20 MB
Molecule Synthesis (One Enzyme)	(0,31)	188 s	9e-17	667 MB
Molecule Synthesis (Two Enzymes)	(0,9)	55 s	2e-7	180 MB
Repressilator	(0,12)	133 s	2e-8	335 MB

Now, we turn to simulation results that is obtained by using the benchmark implementation StochKit [1] of Li et al [18]. In Table 5.2, the first column gives the example name, the second column gives the total number of transitions that are taken for the entire course of simulation (i.e., 31 sample paths) and column "Time" lists the time in seconds (s) for the simulation to terminate for the particular example. Column "Mol." indicates the identity of the molecule whose mean and confidence interval for a confidence probability of 95% are provided in the next two columns named "Mean_{SK}" and "CI_{SK}" The mean computed by the LDQBD solution appears in the next to last column. Finally, in the last column the relative error in Mean_{SK},

$$\text{Rel. Err.} = |\text{Mean}_{\text{LDQBD}} - \text{Mean}_{\text{SK}}|/\text{Mean}_{\text{LDQBD}},$$

is reported.

Table 5.2: StochKit simulation results

Example	Reaction Count	Time	Mol.	Mean_{SK}	CI_{SK}	$\text{Mean}_{\text{LDQBD}}$	Rel. Err.
Gene Expression	2e+9	324 s	X_1	3.74	0.49	3.33	0.12
			X_2	3.68	0.73	3.33	0.11
Molecule Synthesis	4e+9	784 s	X_1	0.32	0.37	0.28	0.14
(One Enzyme)			X_2	3.42	0.83	2.74	0.25
			X_3	0.16	0.18	0.19	0.16
Molecule Synthesis	7e+9	$1,241$ s	X_1	0.41	0.44	0.14	1.92
(Two Enzymes)			X_2	0.29	0.23	0.14	1.07
			X_3	0.52	0.28	0.10	4.20
			X_4	0.45	0.28	0.10	3.50
Repressilator	4e+9	761 s	X_1	0.87	0.45	0.76	0.14
			X_2	1.03	0.37	0.76	0.36
			X_3	1.32	0.41	0.76	0.74

The memory requirement of the simulation is immaterial and therefore not reported. It is clear that the results are obtained with a higher accuracy in less time with the LDQBD solver.

Chapter 6

Conclusion

We have provided a Kronecker representation for the nonzero blocks of the infinitesimal generator matrix underlying an infinite LDQBD. The Kronecker representation seems to be necessary if the problem at hand is multi-dimensional. Thereafter, we have computed the mean number of molecules for examples from systems of stochastic chemical kinetics using the matrix analytic LDQBD solver and Gillespie's stochastic simulation. The memory requirement of the LDQBD solver is incomparably large, but the accuracy of the results is much higher and the time to obtain the solution is much smaller compared to that of simulation. Future work should concentrate on extending the application domain of the LDQBD solver to queueing networks and trying to devise a Kronecker based solver for the systems of linear equations at each level of the matrix analytic approach. The latter should make the LDQBD solver even more scalable.

Bibliography

[1] Stochkit. `http://engineering.ucsb.edu/~cse/StochKit/`, 2011.

[2] H. Baumann and W. Sandmann. Numerical solution of level dependent quasi-birth-and-death processes. *Elsevier Procedia Computer Science*, 1:1555–1563, 2010.

[3] L. Bright and P.G. Taylor. Calculating the equilibrium distribution in level dependent quasi-birth-and-death processes. *Stochastic Models*, 11:497–525, 1995.

[4] P. Buchholz. A class of hierarchical queueing networks and their analysis. *Queueing Systems*, 15:59–80, 1994.

[5] M. Davio. Kronecker products and Shuffle algebra. *IEEE Transactions on Computers*, 30:116–125, 1981.

[6] T. Dayar. Analyzing Markov chains based on Kronecker products. In A.N. Langville and W.J. Stewart, editors, *MAM 2006: Markov Anniversary Meeting*, pages 279–300. Boson Books, Raleigh, NC, 2006.

[7] T. Dayar, H. Hermanns, D. Spieler, and V. Wolf. Bounding the equilibrium distribution of Markov population models. *Numerical Linear Algebra with Applications*, 2011. To appear.

[8] T. Dayar and M.C. Orhan. LDQBD solver version 2. `http://www.cs.bilkent.edu.tr/~tugrul/software.html`, 2011.

[9] T. Dayar, W. Sandmann, D. Spieler, and V. Wolf. Infinite level-dependent QBDs and matrix analytic solutions for stochastic chemical kinetics. *Advances in Applied Probability*, 2011. To appear.

[10] D. T. Gillespie. Exact stochastic simulation of coupled chemical reactions. *The Journal of Physical Chemistry*, 81:2340–2361, 1977.

[11] P. Glynn and A. Zeevi. Bounding stationary expectations of Markov processes. *IMS Collections: Markov Processes and Related Topics*, 4:195–214, 2008.

[12] W.K. Grassman, editor. *Computational Probability*. Kluwer, Norwell, MA, 2000.

[13] W.K. Grassman and D.A. Stanford. Matrix analytic methods. In W.K. Grassman, editor, *Computational Probability*, pages 153–204. Kluwer, Norwell, MA, 2000.

[14] T. Hanschke. A matrix continued fraction algorithm for the multiserver repeated order queue. *Mathematical and Computer Modelling*, 30:159–170, 1999.

[15] T.G. Kurtz. The relationship between stochastic and deterministic models for chemical reactions. *Journal of Chemical Physics*, 57:2976–2978, 1972.

[16] G. Latouche and V. Ramaswami. *Introduction to Matrix Analytic Methods in Stochastic Modeling*. SIAM Press, Philadelphia, PA, 1999.

[17] T.L. Lee, T.Y. Li, and C.H. Tsai. HOM4PS-2.0, A software package for solving polynomial systems by the polyhedral homotopy continuation method. *Computing*, 83:109–133, 2008.

[18] H. Li, Y. Cao, L.R. Petzold, and D. Gillespie. Algorithms and software for stochastic simulation of biochemical reacting systems. *Biotechnology Progress*, 24:56–62, 2008.

[19] A. Loinger and O. Biham. Stochastic simulations of the repressilator circuit. *Physical Review E*, 76:051917, 2007.

[20] D.A. McQuarrie. Stochastic approach to chemical kinetics. *Journal of Applied Probability*, 4:413–478, 1967.

[21] M.F. Neuts. *Matrix-Geometric Solutions in Stochastic Models*. The John Hopkins University Press, Baltimore, MD, 1981.

[22] B. Plateau. On the stochastic structure of parallelism and synchronization models for distributed algorithms. In *Proceedings of the 1985 ACM SIGMETRICS Conference on Measurement and Modeling of Computer Systems, Austin, Texas*, pages 147–154, 1985.

[23] B. Plateau and W.J. Stewart. Stochastic automata networks. In W.K. Grassmann, editor, *Computational Probability*, pages 113–152. Kluwer, Norwell, MA, 2000.

[24] V. Ramaswami and P.G. Taylor. Some properties of the rate operators in level dependent quasi-birth-and-death processes with a countable number of phases. *Stochastic Models*, 12:143–164, 1996.

[25] K. Singer. Application of the theory of stochastic processes to the study of irreproducible chemical reactions and nucleation processes. *Journal of the Royal Statistical Society: Series B*, 15:92–106, 1953.

[26] P.L. Sjöberg, P. Lötstedt, and J. Elf. Fokker-Planck approximation of the master equation in molecular biology. *Computing and Visualization in Science*, 12:37–50, 2009.

[27] W.J. Stewart. *Introduction to the Numerical Solution of Markov Chains*. Princeton University Press, Princeton, NJ, 1994.

[28] M. Thattai and A. van Oudenaarden. Intrinsic noise in gene regulatory networks. *Proceedings of the National Academy of Sciences, USA*, 98:8614–8619, 2001.

[29] R.L. Tweedie. Sufficient conditions for regularity, recurrence and ergodicity of Markov processes. *Mathematical Proceedings of the Cambridge Philosophical Society*, 78:125–136, 1975.

[30] N.G. van Kampen. *Stochastic Processes in Physics and Chemistry*. Elsevier, Amsterdam, The Netherlands, 1992.

[31] C. F. van Loan. The ubiquitous Kronecker product. *Journal of Computational and Applied Mathematics*, 123(1-2):85–100, 2000.

Appendix A

Proofs

In all of the proofs, we define an upper bound on the drift function and show that there exists a finite superset of $\mathcal{C}$ which implies that $\mathcal{C}$ is finite. All four drift functions include parabolas, so we will discuss properties of parabolas before providing the proofs to save space.

Let $f(x) = ax^2 + bx + c$, where $a, b, c, x \in \mathbb{R}$. We assume that $a < 0$ since we only consider such parabolas in the proofs. Since $f(x)$ is a parabola, the maximum of $f(x)$ is attained at $-\frac{b}{2a}$, and equals to $-\frac{b^2}{4a} + c$. There are three cases for the roots of the function:

1. $f(x)$ has no real roots when $b^2 - 4ac < 0$. In this case $f(x) < 0$ for all $x \in \mathbb{R}$,

2. $f(x)$ has a single real root when $b^2 - 4ac = 0$. In this case $f(x) \leq 0$ for all $x \in \mathbb{R}$,

3. $f(x)$ has two real roots, $x_1 = -\frac{b}{2a} + \frac{\sqrt{b^2-4ac}}{2a}$ and $x_2 = -\frac{b}{2a} - \frac{\sqrt{b^2-4ac}}{2a}$, when $b^2 - 4ac > 0$. In this case $f(x) > 0$ for $x_1 < x < x_2$.

Then $\{x \in \mathbb{R} \mid f(x) > 0\}$ is finite. Note that maximum of $f(x)$ is a finite real number for $x \in \mathbb{Z}_+$, and $\{x \in \mathbb{Z}_+ \mid f(x) > 0\}$ is also a finite set.

Example 1 *(Gene Expression (cntd.)) Let* $g(y) = ay_1^2 + by_1y_2 + cy_2^2$*, where* $a, b, c \in \mathbb{R}$*, and* $y \in \mathbb{R}^{1\times 2}$*. The* y_1y_2 *term in the function can be eliminated by rotating the* y_1y_2*-coordinate system in the counterclockwise direction with an angle of* $\theta = \frac{1}{2}\cot^{-1}(\frac{a-c}{b})$ *with respect to the origin (see Figure A.1). This rotation results in the* z_1z_2*-coordinate system in which the relationship between the coordinate systems and the transformation of the function* g*, denoted by* $\tilde{g}$*, can be written as*

$$\begin{aligned} z_1 &= y_1 \cos\theta + y_2 \sin\theta, \\ z_2 &= -y_1 \sin\theta + y_2 \cos\theta, \\ \tilde{g}(z) &= \tilde{a}z_1^2 + \tilde{c}z_2^2, \end{aligned}$$

where

$$\begin{aligned} \tilde{a} &= a\cos^2\theta + b\cos\theta\sin\theta + c\sin^2\theta, \\ \tilde{c} &= a\sin^2\theta - b\cos\theta\sin\theta + c\cos^2\theta. \end{aligned}$$

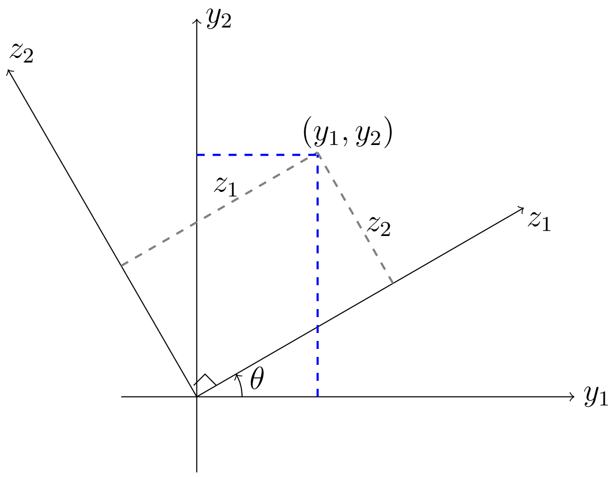

Figure A.1: Rotating the axes

If $a < 0$*,* $c < 0$*, and* $b^2 - 4ac < 0$*, then* $\tilde{a}$ *and* $\tilde{c}$ *are both negative, and* $\tilde{g}(z) \le \max_{z_1\in\mathbb{R}}(\tilde{a}z_1^2) + \max_{z_2\in\mathbb{R}}(\tilde{c}z_2^2) \le 0$*. Therefore, also* $g(y) \le 0$ *for all* $y \in \mathbb{R}^{1\times 2}$ *if* $a < 0$*,* $c < 0$*, and* $b^2 - 4ac < 0$ *hold.*

Now let functions $f_1(x)$, $f_2(x)$, and $g_1(x)$ be defined as follows:

$$
\begin{aligned}
f_1(x) &= -0.001x_1^2 + 0.165x_1 + 0.05,\\
f_2(x) &= -0.005x_2^2 + 0.05x_2,\\
g_1(x) &= -0.029x_1^2 + 0.1x_1x_2 - 0.095x_2^2,
\end{aligned}
$$

and $m_i = \max_{x\in\mathcal{S}}(f_i(x))$ for $i \in \{1,2\}$. Then, for all $x \in \mathcal{S}$, $d(x) = f_1(x) + f_2(x) + g_1(x) \le f_1(x) + f_2(x)$ holds since $g_1(x) \le 0$. Also let us define u_i as

$$u_i(x) = f_i(x) + \sum_{\substack{j=1\\ j\ne i}}^{2} m_j$$

and the set $\mathcal{D}_i$ as

$$\mathcal{D}_i = \{x \in \mathcal{S} \mid u_i(x) > -\gamma\},$$

where $\mathcal{D}_i$ is finite by the properties of the parabola $u_i(x) + \gamma$ for $i \in \{1,2\}$. Now consider $u(x) = max_{x\in\mathcal{S}}(u_1(x), u_2(x)) \ge d(x)$ for $x \in \mathcal{S}$, and $\mathcal{D} = \{x \in \mathcal{S} \mid u(x) > -\gamma\}$, i.e., $\mathcal{D} = \mathcal{D}_1 \cup \mathcal{D}_2$. $\mathcal{D}$ is a finite set since it is a union of two finite sets. Then $\mathcal{C}$ is also a finite set since it is a subset of $\mathcal{D}$.

Example 2 *(Molecule Synthesis with Two Molecules and One Enzyme (cntd.)) Let functions $f_1(x)$, $f_2(x)$ and $f_3(x)$ be defined as follows:*

$$
\begin{aligned}
f_1(x) &= -0.2x_1^2 + 0.1x_1 + 0.3,\\
f_2(x) &= -0.2x_2^2 + 0.7x_2,\\
f_3(x) &= -0.2x_3^2 + (9.6 + 4.8 + 0.32 + 0.1)x_3 + 0.16\\
&= -0.2x_3^2 + 14.82x_3 + 0.16,
\end{aligned}
$$

and $m_i = \max_{x\in\mathcal{S}}(f_i(x))$ for $i \in \{1,2,3\}$. Then $d(x) \le f_1(x) + f_2(x) + f_3(x)$ holds for all $x \in \mathcal{S}$. Also let us define u_i as

$$u_i(x) = f_i(x) + \sum_{\substack{j=1\\ j\ne i}}^{3} m_j$$

and the set $\mathcal{D}_i$ as

$$\mathcal{D}_i = \{x \in \mathcal{S} \mid u_i(x) > -\gamma\},$$

where $\mathcal{D}_i$ is finite by the properties of the parabola $u_i(x)+\gamma$ for $i \in \{1,2,3\}$. Now consider $u(x) = max_{x\in\mathcal{S}}(u_1(x), u_2(x), u_3(x)) \geq d(x)$ for $x \in \mathcal{S}$, and $\mathcal{D} = \{x \in \mathcal{S} \mid u(x) > -\gamma\}$, i.e., $\mathcal{D} = \mathcal{D}_1 \cup \mathcal{D}_2 \cup \mathcal{D}_3$. $\mathcal{D}$ is a finite set since it is a union of three finite sets. Then $\mathcal{C}$ is also a finite set since it is a subset of $\mathcal{D}$.

Example 3 *(Molecule Synthesis with Two Molecules and Two Enzymes (cntd.)) Let functions $f_1(x)$, $f_2(x)$, $f_3(x)$ and $f_4(x)$ be defined as follows:*

$$\begin{aligned}
f_1(x) &= -0.4x_1^2 + 0.2x_1, \\
f_2(x) &= -0.4x_2^2 + 0.2x_2, \\
f_3(x) &= -0.4x_3^2 + (9.6 + 4.8 + 0.32 + 0.2)x_3 + 0.16 \\
&= -0.2x_3^2 + 14.92x_3 + 0.16, \\
f_4(x) &= -0.4x_4^2 + (9.6 + 4.8 + 0.32 + 0.2)x_4 + 0.16 \\
&= -0.2x_4^2 + 14.92x_4 + 0.16,
\end{aligned}$$

and $m_i = max_{x\in\mathcal{S}}(f_i(x))$ for $i \in \{1,2,3,4\}$. Then $d(x) \leq f_1(x) + f_2(x) + f_3(x) + f_4(x)$ holds for all $x \in \mathcal{S}$. Also let us define u_i as

$$u_i(x) = f_i(x) + \sum_{\substack{j=1 \\ j\neq i}}^{4} m_j$$

and the set $\mathcal{D}_i$ as

$$\mathcal{D}_i = \{x \in \mathcal{S} \mid u_i(x) > -\gamma\},$$

where $\mathcal{D}_i$ is finite by the properties of the parabola $u_i(x) + \gamma$ for $i \in \{1,2,3,4\}$. Now consider $u(x) = max_{x\in\mathcal{S}}(u_1(x), u_2(x), u_3(x), u_4(x)) \geq d(x)$ for $x \in \mathcal{S}$, and $\mathcal{D} = \{x \in \mathcal{S} \mid u(x) > -\gamma\}$, i.e., $\mathcal{D} = \mathcal{D}_1 \cup \mathcal{D}_2 \cup \mathcal{D}_3 \cup \mathcal{D}_4$. $\mathcal{D}$ is a finite set since it is a union of four finite sets. Then $\mathcal{C}$ is also a finite set since it is a subset of $\mathcal{D}$.

Example 4 *(Repressilator (cntd.)) Let functions $f_1(x)$, $f_2(x)$ and $f_3(x)$ be defined as follows:*

$$\begin{aligned}
f_1(x) &= (2.4x_4 - 3.6)x_1^2 + (x_4 - 2.6x_6 + 5.6)x_1 + 1.3, \\
f_2(x) &= (2.4x_5 - 3.6)x_2^2 + (x_5 - 2.6x_4 + 5.6)x_1 + 1.3, \\
f_3(x) &= (2.4x_6 - 3.6)x_3^2 + (x_6 - 2.6x_5 + 5.6)x_1 + 1.3.
\end{aligned}$$

where $d(x) \leq f_1(x) + f_2(x) + f_3(x)$ *holds for all* $x \in \mathcal{S}$*. Let* $m_i = max_{x\in\mathcal{S}}(f_i(x))$ *be the maximum of function* f_i *which is a finite real number for* $i \in \{1, 2, 3\}$*. Also let us define* u_i *as*

$$u_i(x) = f_i(x) + \sum_{\substack{j=1 \\ j\neq i}}^{3} m_j$$

and the set $\mathcal{D}_i$ *as*

$$\mathcal{D}_i = \{x \in \mathcal{S} \mid u_i(x) > -\gamma\},$$

where $\mathcal{D}_i$ *is finite by the properties of the parabola* $u_i(x)+\gamma$ *for* $i \in \{1, 2, 3\}$*. Now consider* $u(x) = max_{x\in\mathcal{S}}(u_1(x), u_2(x), u_3(x)) \geq d(x)$ *for* $x \in \mathcal{S}$*, and* $\mathcal{D} = \{x \in \mathcal{S} \mid u(x) > -\gamma\}$*, i.e.,* $\mathcal{D} = \mathcal{D}_1 \cup \mathcal{D}_2 \cup \mathcal{D}_3$*.* $\mathcal{D}$ *is a finite set since it is a union of three finite sets. Then* $\mathcal{C}$ *is also a finite set since it is a subset of* $\mathcal{D}$*.*

Appendix B

Code

The driver of the solver:

```
function [L, comptol, res] = generaldriver(problemfile, ...
                    computesvd, usegth, usemassage, flagU,...
                    Upper, Lower)
% Implements a variant of Algorithm 4 in:
%
% L. Bright and P. G. Taylor,
% Calculating the equilibrium distribution in level dependent
% quasi-birth-and-death processes,
% Stochastic Models 11 (1995), 502-503.
%
% for level numbers in between Lower and Upper.
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%     All Rights Reserved

% The pair UD(i,j) is stored in the cells U{i+1,j+1} and
% D{i+1,j+1}  for which i,j >= 0, since in Matlab indices
% start at 1.
%
```

```
% All matrices are sparse.

% Check for input arguments
if (nargin < 8)
  Lower   = 0;
end
if (nargin < 7)
  disp('Must enter an upper level number!');
  return;
end
if (Upper < Lower)
  disp('Lower must be less than or equal to Upper!');
  return;
end

[params] = readParameters(problemfile);

tic;
[R{Upper-Lower+1},L,comptol] = compute_R(usegth,usemassage,...
                               flagU,Upper,1e-12,params);
tElapsed1 = toc;

tic;
% Recursively compute R{k} for k = Upper-1:-1:Lower+1 using (2.8)
for kp1 = Upper:-1:Lower+1
  [mq1,nq1] = getsizeQ(kp1,kp1,params);
  if (kp1 == Upper)
    [~,nq0] = getsizeQ(kp1,kp1+1,params);
    if (flagU == 4)
      if (usegth == 0)
        if (usemassage > 0)
          R(kp1-Lower) = {massage(-getQ(kp1-1,kp1,params) *...
                         mldivide( getQ(kp1,kp1,params) + ...
```

```
                    sparse(getQ(kp1,kp1+1,params) *...
                    ones(nq0,1) * [zeros(1,nq1-1),1]) + ...
                    R{kp1+1-Lower} * ...
                    getQ(kp1+1,kp1,params), ...
                    speye(mq1)),usemassage)};
   else
     R(kp1-Lower) = {-getQ(kp1-1,kp1,params) * ...
                    mldivide(getQ(kp1,kp1,params) + ...
                    sparse(getQ(kp1,kp1+1,params) * ...
                    ones(nq0,1) * [zeros(1,nq1-1),1]) + ...
                    R{kp1+1-Lower} * ...
                    getQ(kp1+1,kp1,params),speye(mq1))};
   end
 else
   if (usemassage > 0)
     R(kp1-Lower) = {massage(-getQ(kp1-1,kp1,params) * ...
                    gth(getQ(kp1,kp1,params) + ...
                    sparse(getQ(kp1,kp1+1,params) * ...
                    ones(nq0,1) * [zeros(1,nq1-1),1]) + ...
                    R{kp1+1-Lower} * ...
                    getQ(kp1+1,kp1,params), ...
                    speye(mq1)),usemassage)};
   else
     R(kp1-Lower) = {-getQ(kp1-1,kp1,params) * ...
                     gth(getQ(kp1,kp1,params) + ...
                    sparse(getQ(kp1,kp1+1,params) * ...
                    ones(nq0,1) * [zeros(1,nq1-1),1]) + ...
                    R{kp1+1-Lower} * ...
                    getQ(kp1+1,kp1,params),speye(mq1))};
   end
end
elseif (flagU > 4)
   disp('Not implemented yet!');
```

```
        return;
      end
    end
    if (usegth == 0)
      if (usemassage > 0)
        R(kp1-Lower) = {massage(-getQ(kp1-1,kp1,params) * ...
                       mldivide(getQ(kp1,kp1,params) + ...
                       R{kp1+1-Lower} * ...
                       getQ(kp1+1,kp1,params), ...
                       speye(mq1)),usemassage)};
      else
        R(kp1-Lower) = {-getQ(kp1-1,kp1,params) * ...
                       mldivide(getQ(kp1,kp1,params) + ...
                       R{kp1+1-Lower} * ...
                       getQ(kp1+1,kp1,params),speye(mq1))};
      end
    else
      if (usemassage > 0)
        R(kp1-Lower) = {massage(-getQ(kp1-1,kp1,params) * ...
                       gth(getQ(kp1,kp1,params) + ...
                       R{kp1+1-Lower} * ...
                       getQ(kp1+1,kp1,params), ...
                       speye(mq1)), usemassage)};
      else
        R(kp1-Lower) = {-getQ(kp1-1,kp1,params) * ...
                       gth(getQ(kp1,kp1,params) + ...
                       R{kp1+1-Lower} * ...
                       getQ(kp1+1,kp1,params),speye(mq1))};
      end
  end
end

% Preallocate cell array for solution vector
```

```
x = cell(Upper-Lower+1);
for k = Lower:Upper
  [~,nq1] = getsizeQ(k,k,params);
  x(k-Lower+1) = {sparse(1,nq1)};
end

% Solve for boundary subvector x{1}
if (Lower > 0)
  tmp = getQ(Lower,Lower,params) + ...
        R{1} * getQ(Lower+1,Lower,params);
  [~,nq1] = getsizeQ(Lower,Lower,params);
  x(1) = {gth(tmp,(tmp*ones(nq1,1))')};
else
  if (usemassage > 0)
    x(1) = {gth(massage(getQ(Lower,Lower,params) + ...
           R{1} * getQ(Lower+1,Lower,params), usemassage))};
  else
    x(1) = {gth(getQ(Lower,Lower,params) + ...
           R{1} * getQ(Lower+1,Lower,params))};
  end
end

% Compute other subvectors
for k = 2:Upper-Lower+1
  x(k) = {x{k-1}*R{k-1}};

  if (computesvd == 0)
    R(k-1) = {[]};
  end

  % Normalize solution
  s = 0;
  for l = 1:k
```

```
    s = s + sum(x{l});
  end
  s = 1/s;
  for l = 1:k
    x(l) = {s*x{l}};
  end
end

% Compute residual infinity norm
res = max(abs(x{1} * getQ(Lower,Lower,params) + ...
      x{2} * getQ(Lower+1,Lower,params)));

for k = 1:Upper-Lower-1
  newres = max(abs(x{k} * getQ(Lower+k-1,Lower+k,params) + ...
           x{k+1} * getQ(Lower+k,Lower+k,params) + ...
           x{k+2} * getQ(Lower+k+1,Lower+k,params)));
  res = max([res,newres]);
end

newres = max(abs(x{Upper-Lower} * getQ(Upper-1,Upper,params) + ...
         x{Upper-Lower+1} * getQ(Upper,Upper,params)));
res    = max([res,newres]);


tElapsed2 = toc;

% Compute mean values for the distribution
meanVector = findMean(x, Lower, Upper, params);

fp = fopen(['summary_' problemfile '.' int2str(Lower) '_' ...
          int2str(Upper) '_f' int2str(flagU) '_m' ...
          int2str(usemassage)],'w');
```

```
fprintf(fp,'problemfile computesvd usegth usemassage ...
       flagU Upper Lower\n');
fprintf(fp, [problemfile ,'   %3d    %3d        %3d   %3d %5d ...
       %5d\n\n'], computesvd, usegth, usemassage, ...
       flagU, Upper, Lower);

fprintf(fp, 'Time to compute R_Upper = %s\n', tElapsed1);
fprintf(fp, 'L                       = %10d\n', L);
fprintf(fp, 'comptol                 = %10.5e\n', full(comptol));
fprintf(fp, '\n');
fprintf(fp, 'Time to compute pi      = %s\n', tElapsed2);
fprintf(fp, 'res                     = %10.5e\n', full(res));
fprintf(fp, '\n');

for i = 1:params{1,1}
  fprintf(fp, 'Mean of molecule-%d: %20.16f\n', i, meanVector(i));
end
fprintf(fp, '\n');

if (computesvd > 0)
  fprintf(fp, 'k   max(sigma(R{kp1})) ...
          max(sigma(A0{kp1})/sigma(A2{kp1}))\n');
  if (Lower == 0)
    fprintf(fp,'%3d %10.5e\n', 0, max(svds(R{1})));
  else
    fprintf(fp,'%3d %10.5e       %10.5e\n', Lower, ...
           max(svds(R{1})), ...
           max(svds(getQ(Lower,Lower+1,params)))/ ...
           max(svds(getQ(Lower,Lower-1,params))));
  end
  R(1) = {[]};
  for k = Lower+1:Upper
    fprintf(fp,'%3d %10.5e       %10.5e\n', k, ...
```

```
           max(svds(R{k-Lower+1})), ...
           max(svds(getQ(k,k+1,params))) / ...
           max(svds(getQ(k,k-1,params))));
    R(k-Lower+1) = {[]};
  end
  fprintf(fp,'\n');
end

% Print out marginal distribution across levels
fprintf(fp,'k   Pr(k)       max(Pr(k,j)) min(Pr(k,j))\n');
fprintf(fp,'--- ----------- ------------ ------------\n');
for k = Lower+1:Upper+1
  fprintf(fp,'%3d %10.5e %10.5e %10.5e\n', k-1, ...
         sum(full(x{k-Lower})), ...
         max(full(x{k-Lower})), min(full(x{k-Lower})));
end
fclose(fp);

filename = ['pi_' problemfile  '.' int2str(Lower) '_' ...
           int2str(Upper) '_f' ...
           int2str(flagU) '_m' int2str(usemassage)];
fp = fopen(filename,'w');
for k = Lower+1:Upper+1
  fprintf(fp, 'Level = %5d\n', k-1);
  fprintf(fp, '%23.16e\n\n', full(x{k-Lower}));
end
fclose(fp);

fprintf('Time to compute R_Upper = %s\n',tElapsed1);
fprintf('L                       = %10d\n',L);
fprintf('comptol                 = %10.5e\n',full(comptol));

fprintf('Time to compute pi      = %s\n',tElapsed2);
```

```
fprintf('res                          = %10.5e\n',full(res));
for i = 1:params{1,1}
  fprintf('Mean of molecule-%d: %20.16f\n', i, meanVector(i) );
end
fprintf('\n\n');
end
```

The script to read the parameters for the problem to be solved:

```
function [params] = readParameters(problemfile)
% Generate the parameters of the corresponding LDQBD for given
% parameters.
% (C) Copyright 2011 by Muhsin Can Orhan
%     All Rights Reserved

% Open the file that contains the parameters
fid = fopen(problemfile);

% Read the line that contains nI, J and Zfinitesize
C = textscan(fid, '%d %d %f', 1, 'CommentStyle', '%');
nI = double(C{1});
J = C{2};
Zfinitesize = double(C{3});

% Create the format to read the remaining text
format = zeros( 1, 2 + 6 * nI + 3' );
format(1:2) = '%f';
for i = 1:nI
  format((i-1)*6+3:(i-1)*6+8) = ' %s %d';
end
format(nI*6+3:nI*6+5) = ' %s';
```

```
% Read coef, numer/denom, v and Zfinite
C = textscan(fid, char(format), 'CommentStyle', '%');

coef = C{1};
numer = cell(J,nI);
denom = cell(J,nI);
v = zeros(J,nI);
Zfinite = cell(J,1);

for i = 1:nI
  [numerCell,denomCell] = strtok(C{(i-1)*2+2}, '/');
  numerCell = strtok(numerCell, '()');
  denomCell = strtok(denomCell, '/');
  denomCell = strtok(denomCell, '()');
  for j = 1:J
    numer{j,i} = str2num(numerCell{j}); %#ok<ST2NM>
  end
  for j = 1:J
    denom{j,i} = str2num(denomCell{j});  %#ok<ST2NM>
    if isempty( denom{j,i} )
      denom{j,i} = 1;
    end
  end
  v(:,i) = C{(i-1)*2+3};
end

% Obtain Zfinite
C{nI*2+2} = strtok(C{nI*2+2}, '()');
for j = 1:J
  tempZfinite = str2num(cell2mat(C{nI*2+2}(j)));  %#ok<ST2NM>
  Zfinite{j,1} = sparse(tempZfinite(:,1), tempZfinite(:,2), 1, ...
                 Zfinitesize, Zfinitesize);
end
```

```
% params{1,1} : The number of components with infinite state
                space
% params{2,1} : The number of transitions in the model;
% params{3,1} : The coefficient vector for transitions
% params{4,1} : The polynomial matrix for the numerator part for
                transitions
% params{5,1} : The polynomial matrix for the denominator part
                for transitions
% params{7,1} : The transition rate matrix for the components
                with finite state space
% params{8,1} : The size of the transition rate matrix of
                components with finite state space

% Set the params cell array
params = cell(8,1);
params{1,1} = nI;
params{2,1} = J;
params{3,1} = coef;
params{4,1} = numer;
params{5,1} = denom;
params{6,1} = v;
params{7,1} = Zfinite;
params{8,1} = Zfinitesize;

end
```

The script to compute the matrix of the conditional expected sojourn time at level $High$:

```
function [R,L,comptol] = compute_R(usegth, usemassage, flag, ...
                          k, tol, params)
% Implements Algorithms 2 and 3 in:
```

```
%
% L. Bright and P. G. Taylor,
% Calculating the equilibrium distribution in level dependent
% quasi-birth-and-death processes,
% Stochastic Models 11 (1995), 502-503.
%
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%     All Rights Reserved
%

% The pair UD(i,j) is stored in the cells U{i+1,j+1} and
% D{i+1,j+1} for which i,j >= 0, since in Matlab indices
% start at 1.
%
% All matrices are sparse.

l = 1;
k = k+1;

[mq1,~] = getsizeQ(k,k,params);
[mq0,nq0] = getsizeQ(k-1,k,params);
if (flag == 3 || flag == 4)
  L = 0;
  comptol = 1;
  R = sparse(zeros(mq0,nq0));
  return;
end

% Compute UD(1,k)
if (usegth == 0)
  if (usemassage > 0)
    U(l,k) = {massage(-mldivide(getQ(k,k,params),speye(mq1)), ...
              usemassage)};
```

```
  else
    U(1,k) = {-mldivide(getQ(k,k,params),speye(mq1))};
  end
else
  if (usemassage > 0)
    U(1,k) = {massage(-gth(getQ(k,k,params),speye(mq1)), ...
              usemassage)};
  else
    U(1,k) = {-gth(getQ(k,k,params),speye(mq1))};
  end
end

if (usemassage > 0)
  D(1,k+2) = {massage(getQ(k+1,k,params)*U{1,k},usemassage)};
  U(1,k)   = {massage(getQ(k-1,k,params)*U{1,k},usemassage)};
else
  D(1,k+2) = {getQ(k+1,k,params)*U{1,k}};
  U(1,k)   = {getQ(k-1,k,params)*U{1,k}};
end

Utmp   = U{1,k};
Dtmp   = D{1,k+2};
[~,nd] = size(D{1,k+2});
Pi     = speye(nd);
R(k)   = {Utmp};

while (1)
  for i = 1:l
    itmp      = pow2(l-i+1)-1;
    % l is one larger than its actual value, so
    stepsize  = pow2(i-1);
    dstepsize = 2*stepsize;
    for j = k + itmp*stepsize : stepsize : k + itmp*dstepsize
```

```
      if (i > 1)
        % Compute UD(i,j)
        hstepsize = stepsize/2;
        [md,~]   = size(U{i-1,j+stepsize});
        if (usegth == 0)
          if (usemassage > 0)
            U(i,j) = {massage(mldivide(speye(md) - ...
                    U{i-1,j+stepsize} * D{i-1,j+3*hstepsize} - ...
    D{i-1,j+stepsize} * U{i-1,j+hstepsize}, ...
    speye(md)),usemassage)};
          else
            U(i,j) = {mldivide(speye(md) - ...
                    U{i-1,j+stepsize} * D{i-1,j+3*hstepsize} -...
                    D{i-1,j+stepsize} * U{i-1,j+hstepsize}, ...
                    speye(md))};
          end
        else
          if (usemassage > 0)
            U(i,j) = {massage(-gth(-speye(md) + ...
                    U{i-1,j+stepsize} * D{i-1,j+3*hstepsize} + ...
                    D{i-1,j+stepsize} * U{i-1,j+hstepsize}, ...
                    speye(md)),usemassage)};
          else
            U(i,j) = {-gth(-speye(md) + ...
                    U{i-1,j+stepsize} * D{i-1,j+3*hstepsize} + ...
                    D{i-1,j+stepsize} * U{i-1,j+hstepsize}, ...
                    speye(md))};
          end
        end

        if (usemassage > 0)
          D(i,j+dstepsize) = {massage(D{i-1,j+dstepsize} * ...
                            D{i-1,j+3*hstepsize} * ...
```

```
                        U{i,j},usemassage)};
      U(i,j)           = {massage(U{i-1,j} * ...
                        U{i-1,j+hstepsize} * ...
                        U{i,j},usemassage)};
    else
      D(i,j+dstepsize) = {D{i-1,j+dstepsize} * ...
                        D{i-1,j+3*hstepsize} * U{i,j}};
      U(i,j)           = {U{i-1,j} * U{i-1,j+hstepsize} * ...
                        U{i,j}};
    end

    % Clear no longer neeeded cell matrices
    U(i-1,j)             = {[]};
    U{i-1,j+hstepsize}   = {[]};
    D(i-1,j+stepsize)    = {[]};
    D(i-1,j+3*hstepsize) = {[]};
  else

    % Compute UD(1,j)
    [mq1,~] = getsizeQ(j,j,params);
    if (usegth == 0)
      if (usemassage > 0)
        U(i,j) = {massage(-mldivide(getQ(j,j,params), ...
                 speye(mq1)),usemassage)};
      else
        U(i,j) = {-mldivide(getQ(j,j,params),speye(mq1))};
      end
    else
      if (usemassage > 0)
        U(i,j) = {massage(-gth(getQ(j,j,params), ...
                 speye(mq1)),usemassage)};
      else
        U(i,j) = {-gth(getQ(j,j,params),speye(mq1))};
```

```
          end
        end

        if (usemassage > 0)
          D(i,j+2) = {massage(getQ(j+1,j,params) * ...
                     U{i,j}, usemassage)};
          U(i,j)   = {massage(getQ(j-1,j,params) * ...
                     U{i,j},usemassage)};
        else
          D(i,j+2) = {getQ(j+1,j,params) * U{i,j}};
          U(i,j)   = {getQ(j-1,j,params) * U{i,j}};
        end
      end
    end
  end

  l = l+1;

  % Compute UD(l,k)
  % l is one larger than its actual value, so
  stepsize  = pow2(l-1);
  dstepsize = 2*stepsize;
  hstepsize = stepsize/2;
  [md,~]   = size(U{l-1,k+stepsize});
  if (usegth == 0)
    if (usemassage > 0)
      U(l,k) = {massage(mldivide(speye(md) - ...
               U{l-1,k+stepsize} * D{l-1,k+3*hstepsize} - ...
               D{l-1,k+stepsize} * U{l-1,k+hstepsize}, ...
               speye(md)),usemassage)};
    else
      U(l,k) = {mldivide(speye(md) - ...
               U{l-1,k+stepsize} * D{l-1,k+3*hstepsize} - ...
```

```
             D{l-1,k+stepsize} * U{l-1,k+hstepsize}, ...
             speye(md))};
  end
else
  if (usemassage > 0)
    U(l,k) = {massage(-gth(-speye(md) + ...
             U{l-1,k+stepsize} * D{l-1,k+3*hstepsize} + ...
             D{l-1,k+stepsize} * U{l-1,k+hstepsize}, ...
             speye(md)),usemassage)};
  else
    U(l,k) = {-gth(-speye(md) + ...
             U{l-1,k+stepsize} * D{l-1,k+3*hstepsize} + ...
             D{l-1,k+stepsize} * U{l-1,k+hstepsize},speye(md))};
  end
end

if (usemassage > 0)
  D(l,k+dstepsize) = {massage(D{l-1,k+dstepsize} * ...
                     D{l-1,k+3*hstepsize} * ...
                     U{l,k},usemassage)};
  U(l,k)           = {massage(U{l-1,k} * ...
                     U{l-1,k+hstepsize} * U{l,k},usemassage)};
else
  D(l,k+dstepsize) = {D{l-1,k+dstepsize} * ...
                     D{l-1,k+3*hstepsize} * U{l,k}};
  U(l,k)           = {U{l-1,k} * U{l-1,k+hstepsize} * U{l,k}};
end

% Clear no longer needed cell matrices
U(l-1,k)             = {[]};
U(l-1,k+hstepsize)   = {[]};
D(l-1,k+stepsize)    = {[]};
D(l-1,k+3*hstepsize) = {[]};
```

```
  if (usemassage > 0)
    Pi = massage(Dtmp*Pi,usemassage);
  else
    Pi = Dtmp*Pi;
  end
  Utmp  = U{l,k};
  Dtmp  = D{l,k+pow2(l)};

  if (usemassage > 0)
    R_k_new = massage(R{k} + Utmp*Pi,usemassage);
  else
    R_k_new = R{k} + Utmp*Pi;
  end

  comptol = max(max(R_k_new - R{k}));

  if ((comptol < tol) || (flag == 2 && l == 5) )
    break;
  else
    R{k} = R_k_new;
  end % else

end % while

R = R_k_new;
L = l-1;

end
```

The script to compute the requested block of the infinitesimal generator matrix:

```
function [Qkm] = getQ(k,m,params)
```

```
% Generates block Q(k,m) corresponding to the LDQBD for
% given parameters.
%
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if (k == 0 && m == 0)
  Qkm = spdiags( -sum(getQ(0,1,params),2), 0, ...
        params{8,1}, params{8,1});
else
  % Number of partitions in a block is determined
  % by the block index
  if k == 0
    umax = 1;
  else
    umax = params{1,1};
  end
  if m == 0
  wmax = 1;
else
  wmax = params{1,1};
  end

  % Number of rows and columns in block (k,m)
  [rowsize,colsize] = getsizeQ(k,m,params);

  % Row indices, column indices and values of the nonzeros
  % of the partition (u,w) are held in cell (u-1)*wmax+w and
  % these cells are merged in creating the subblock
  rowCell = cell(umax*wmax,1);
  colCell = cell(umax*wmax,1);
  valCell = cell(umax*wmax,1);
```

```
% Create matrix for each partition (u,w)
for u = 1:umax
  % Number of rows of the submatrix for partition (u,w)
  rowPartSize = (k+1)^(params{1,1}-u)* k^(u-1) * params{8,1};

  % Shift the row indices of submatrix (u,w) of
  % Q(k,m) to obtain corresponding row indices of Q(k,m)
  rowshift = params{8,1} * (k+1)^(params{1,1}-u+1) * ...
            ((k+1)^(u-1) - k^(u-1));

  % First create submatrix for partition (u,u) (w = u)
  % Then create submatrix for partition (u,w) where (w ~= u)

  w = u;
  % Shift the column indices of submatrix (u,w)
  % of Q(k,m) to obtain corresponding row indices of Q(k,m)
  colshift = params{8,1} * (m+1)^(params{1,1}-w+1) * ...
            ((m+1)^(w-1) - m^(w-1));

  % Number of columns of the submatrix for partition (u,w)
  colPartSize = (m+1)^(params{1,1}-w)*m^(w-1)*params{8,1};

  Qpart = sparse(rowPartSize, colPartSize);

  % Scan all transition classes j
  for j = 1:params{2,1}
    [Zu,nnzcount] = getZ(j,u,k,m,u,w,params);
    if nnzcount > 0
      Qparttemp = params{3,1}(j) * Zu;
      for i = [1:u-1,u+1:params{1,1}]
        Qparttemp = kron(Qparttemp, getZ(j,i,k,m,u,w,params));
      end
      if params{8,1} == 1
```

```
        Qpart = Qpart + Qparttemp;
      else
        Qpart = Qpart + kron(Qparttemp, params{7,1}{j,1});
      end
    end
  end

  cellInd = (u-1)*wmax + w;
  [rowCell{cellInd,1}, colCell{cellInd,1}, ...
              valCell{cellInd,1}] = find( Qpart );

  % If partition (u,w) is not a zero matrix, create row, column
  % indices and values of the nonzeros
  if ~isempty(rowCell{cellInd,1})
    rowCell{cellInd,1} = rowCell{cellInd,1} + rowshift;
    colCell{cellInd,1} = colCell{cellInd,1} + colshift;
  else
    rowCell{cellInd,1} = zeros(0,1);
    colCell{cellInd,1} = zeros(0,1);
    valCell{cellInd,1} = zeros(0,1);
  end

  for w = [1:u-1,u+1:wmax]
    % Shift the column indices of submatrix (u,w) of
    % Q(k,m) to obtain corresponding row indices of Q(k,m)
    colshift = params{8,1} * (m+1)^(params{1,1}-w+1) * ...
              ((m+1)^(w-1) - m^(w-1));

    % Number of columns of the submatrix for partition (u,w)
    colPartSize = (m+1)^(params{1,1}-w)*m^(w-1)*params{8,1};

    Qpart = sparse(rowPartSize, colPartSize);
```

```
% Submatrices of the transition rate matrices for
% components u and w are row and column matrices,
% respectively
minuw = min(u,w);
maxuw = max(u,w);

for j = 1:params{2,1}
  [Z1,nnzcount1] = getZ(j,minuw,k,m,u,w,params);
  if nnzcount1 == 0
    continue;
  end
  [Z2,nnzcount2] = getZ(j,maxuw,k,m,u,w,params);
  if nnzcount2 == 0
    continue;
  end
  Qparttemp = params{3,1}(j);
  for i = 1:minuw-1
    Qparttemp = kron(Qparttemp,getZ(j,i,k,m,u,w,params));
  end
  Qparttemp = kron(Qparttemp,Z1);
  for i = minuw+1:maxuw-1
    Qparttemp = kron(Qparttemp,getZ(j,i,k,m,u,w,params));
  end
  Qparttemp = kron(Qparttemp,Z2);
  for i = maxuw+1:params{1,1}
    Qparttemp = kron(Qparttemp,getZ(j,i,k,m,u,w,params));
  end

  if params{8,1} == 1
    Qpart = Qpart + Qparttemp;
  else
    Qpart = Qpart + kron(Qparttemp, params{7,1}{j,1});
  end
```

```
      end
      cellInd = (u-1)*wmax + w;
      [rowCell{cellInd,1}, colCell{cellInd,1}, ...
               valCell{cellInd,1}] = find( Qpart );

      % If partition (u,w) is not a zero matrix, create row,
      % column indices and values of the nonzeros
      if ~isempty(rowCell{(u-1)*wmax + w,1})
        rowCell{cellInd,1} = rowCell{cellInd,1} + rowshift;
        colCell{cellInd,1} = colCell{cellInd,1} + colshift;
      else
        rowCell{cellInd,1} = zeros(0,1);
        colCell{cellInd,1} = zeros(0,1);
        valCell{cellInd,1} = zeros(0,1);
      end
    end
  end

  % Create sparse matrix with row indices in rowCell cell
  % array, column indices in colCell cell array and values
  % in valCell cell array.
  Qkm = sparse( cell2mat(rowCell), cell2mat(colCell), ...
        cell2mat(valCell), rowsize, colsize);

  % If requested block is on diagonal, calculate row sum,
  % negate it and write it to the main diaonal
  if k == m
    Qkm = Qkm + ...
          spdiags( -(sum(getQ(k,k-1,params),2) + sum(Qkm,2) + ...
          sum(getQ(k,k+1,params),2)), 0, rowsize, colsize);
  end
end
```

The script to compute the size of the requested block of the infinitesimal generator matrix:

```
function [rowsize,colsize] = getsizeQ(k,m,params)
% Generates dimensions of block (k,m) of matrix Q corresponding
% to the LDQBD.
%
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rowsize = params{8,1}*((k+1)^(params{1,1})-(k)^(params{1,1}));
colsize = params{8,1}*((m+1)^(params{1,1})-(m)^(params{1,1}));

end
```

The script to compute the transition rate of the requsted component and transition:

```
function [Z,nnzcount] = getZ(j, i, k, m, u, w, params)
% Generates the corresponding submatrix of transition rate
% matrix of component i in transition class j, for
% partition (u,w) of block (k,m), and returns the number
% of nonzeros in the matrix
%
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% Obtain the rows and columns of the transition rate matrix
% for the submatrix requested.
if i < u
  rows = (0:k-1)';
  rsize = k;
elseif i == u
```

```
  rows = k;
  rsize = 1;
else
  rows = (0:k)';
  rsize = k + 1;
end

if i < w
  cols = (0:m-1)';
  csize = m;
elseif i == w
  cols = m;
  csize = 1;
else
  cols = (0:m)';
  csize = m + 1;
end

if rsize == 1 && csize == 1
  % Z is a scalar which is located at (rows,cols) of the
  % transition rate matrix
  if cols ~= rows + params{6,1}(j,i)
    nnzcount = 0;
    Z = sparse( rsize, csize );
  else
    nnzcount = 1;
    Z = polyval(params{4,1}{j,i},rows) / ...
        polyval(params{5,1}{j,i},rows);
  end
elseif rsize == 1
  % Z is a row vector of size csize
  ind = find( cols == rows + params{6,1}(j,i) );
  if isempty( ind )
```

```
    nnzcount = 0;
    Z = sparse( rsize, csize );
  else
    nnzcount = 1;
    Z = sparse( 1, ind, polyval(params{4,1}{j,i},rows) / ...
        polyval(params{5,1}{j,i},rows), rsize, csize );
  end
elseif csize == 1
  % Z is a column vector of size csize
  ind = find( rows == cols - params{6,1}(j,i) );
  if isempty( ind )
    nnzcount = 0;
    Z = sparse( rsize, csize );
  else
    nnzcount = 1;
    Z = sparse( ind, 1, polyval(params{4,1}{j,i},rows(ind)) / ...
        polyval(params{5,1}{j,i},rows(ind)), rsize, csize );
  end
else
  % Z is a matrix of size (rsize x csize)
  % Obtain the indices of the submatrix from the transition
  % rate matrix that depends on state change scalar of
  % component i and transition class j
  if params{6,1}(j,i) == 0
    nnzcount = min(rsize,csize);
    rowInds = 1:nnzcount;
    colInds = 1:nnzcount;
  elseif params{6,1}(j,i) == 1
    nnzcount = min(rsize,csize-1);
    rowInds = 1:nnzcount;
    colInds = 2:nnzcount+1;
  else % params{6,1}(j,i) == -1
    nnzcount = min(rsize-1,csize);
```

```
    rowInds = 2:nnzcount+1;
    colInds = 1:nnzcount;
  end

  if isscalar(params{4,1}{j,i})
    vals = params{4,1}{j,i} * ones(nnzcount,1);
  else
    vals = polyval( params{4,1}{j,i}, rows(rowInds) );
  end

  if isscalar(params{5,1}{j,i}) && (params{5,1}{j,i} ~= 1)
    vals = vals / params{5,1}{j,i};
  elseif ~isscalar(params{5,1}{j,i})
    vals = vals ./ polyval( params{5,1}{j,i}, rows(rowInds) );
  end

  Z = sparse( rowInds, colInds, vals, rsize, csize );
end
```

The script that implements the Grassmann-Taksar-Heyman idea of factorizing a (sub-)generator matrix by using positive arithmetic:

```
function [X] = gth(Z,B)
% Implements the Grassmann-Taksar-Heyman idea of factorizing a
% (sub-)generator matrix by using positive arithmetic.
% (C) Copyright 2010 by Tugrul Dayar
%     All Rights Reserved
%
% Input:
%    Z: (nxn) (sub-)generator matrix
%    B: (kxn) right-hand side matrix
%       When B = 0 and k = 1, Z must be singular.
```

```
%       If nargin = 1, then B = 0 and k = 1.
%
% Output:
%    X: (kxn) solution matrix
%       When k = 1 and B = 0, Z must be singular.
%       Then X is a probability vector.
%

[~,n]  = size(Z);

A      = Z';
A(1,1) = sum(A(2:n,1));

if nargin == 2
  rownp1 = -(Z*ones(n,1))';
  A(1,1) = A(1,1) + rownp1(1);
  C      = B';
end

% GTH Reduction
for i = 1:n-1
  s  = 1/A(i,i);
  mu = s*A(i+1:n,i);

  %Added to store multipliers A(i+1:n,i) = mu;
  A(i+1:n,i+1:n) = A(i+1:n,i+1:n) + mu*A(i,i+1:n);
  A(i+1,i+1)     = sum(A(i+2:n,i+1));

  if nargin == 2
    munp1         = s*rownp1(i);

    % Added to store multipliers rownp1(i) = munp1;
    rownp1(i+1:n) = rownp1(i+1:n) + munp1*A(i,i+1:n);
```

```
    A(i+1,i+1)    = A(i+1,i+1) + rownp1(i+1);
    C(i+1:n,:)    = C(i+1:n,:) + mu*C(i,:);
  end
end;

% Initialization
if nargin == 1
  A(n,n)  = 1;
  C(n,1)  = 1;
end;

% Back Substitution
s = 1/A(n,n);
X(n,:) = -s*C(n,:);
for i = n-1:-1:1
  s = 1/A(i,i);
  X(i,:) = s*(-C(i,:) + A(i,i+1:n)*X(i+1:n,:));
end;

% Normalization
if nargin == 1
  [mb,nb] = size(C);
  X = X*diag(ones(1,nb)./(ones(1,mb)*X));
end

X = X';
end
```

The script to set the elements of input matrix smaller than tolerance 10^{-16} to zero.

```
function [X] = massage(X,usemassage)
% Zeroes elements of X less than a tolerance.
```

```
% (C) Copyright 2010 by Tugrul Dayar
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% All matrices are sparse.

if (usemassage == 0)
  tol = -1e308;
else
  tol = 1e-16;
end;

[m,n] = size(X);
[i,j,s] = find(X);
s = s.*(s >= tol);

X = sparse(i,j,s,m,n);

end
```

Appendix C

Readme File

The software tool is coded in Matlab. The tool is capable of solving systems of stochastic chemical kinetics. Specification for the stochastic chemical kinetic system model is written in a configuration file.

The first line includes three integers, number of variables with infinite state space, number of transitions and size of the transition rate matrix of variables with finite state space, respectively. If there are no variables with finite state space, then the last integer should be one.

Each transition is written to a seperate line, after the first line. The transitions include the state independent transition rate, state dependent transition function, state change integer, and the transition rate matrix for the variables with finite state space. At the beginning of the file, the state independent transition rate is written. Then the state dependent transition function and the state change integer are written for each variable with infinite state space. At the end of the line, the transition rate matrix for the variables with finite state space is written. Details of the line are as follows:

- State independent transition rate is a double or integer.
- State dependent transition function can be a polynomial or a polynomial divided by a polynomial. The polynomials are written in Matlab format

which starts with left paranthesis and ends with right paranthesis. For example (a, b, c) denotes the polynomial $ax^2 + bx + c$ in this format. If the denominator of the function is not 1, the denominator polynomial is written after the numerator polynomial. Please note that no space character is allowed between the left and right paranthesis.

- State change integer is either -1, 0 or 1 in the class of problems we consider.
- Transition rate matrix for variables with finite state space is written at the end of the line. The elements of this matrix are either 0 or 1. The nonzero elements of the matrix are given by the row and column indices of the nonzero value. A comma is written between the row and column indices. Also a semicolon is written between the nonzeros. Please note that no space character is allowed between the left and right parantheses.

The solver can be called, after the configuration file for the problem is created. For the experiments we have done for this thesis, we used the third algorithm and did not use `massage`. The command to call driver for configuration file `filename` High value `Upper`, and Low value `Lower` is

```
generaldriver(filename, 0, 0, 0, 3, Upper, Lower)
```

Appendix D

Configuration File Examples

Gene Expression Model:

```
% Configuration file for gene expression problem
% nI J Zfinitesize
2 4 1
%
% coef(j) f(j,1) v(j,1) f(j,2) v(j,2) Zfin{j}
0.05  (1)    1 (1)    0 (1,1)
0.05  (1,0)  0 (1)    1 (1,1)
0.015 (1,0) -1 (1)    0 (1,1)
0.05  (1)    0 (1,0) -1 (1,1)
```

Metabolite Synthesis with One Enzyme Model:

```
% Configuration file for two metabolites and one enzyme
% nI J Zfinitesize
3 7 1
%
% coef(j) f(j,1) v(j,1) f(j,2) v(j,2) f(j,3) v(j,3) Zfin{j}
4.8  (1)/(1,16) 1 (1)    0 (1,0)  0 (1,1)
```

```
0.3  (1)        0 (1)    1 (1)    0 (1,1)
0.05 (1,0)     -1 (1,0) -1 (1)    0 (1,1)
0.1  (1,0)     -1 (1)    0 (1)    0 (1,1)
0.1  (1)        0 (1,0) -1 (1)    0 (1,1)
0.16 (1)/(1,8)  0 (1)    0 (1)    1 (1,1)
0.1  (1)        0 (1)    0 (1,0) -1 (1,1)
```

Metabolite Synthesis with Two Enzymes Model:

```
% Configuration file for two metabolites and two enzymes
% nI J Zfinitesize
4 9 1
%
% coef(j) f(j,1) v(j,1) f(j,2) v(j,2) f(j,3) v(j,3)
%                                              f(j,4) v(j,4) Zfin{j}
4.8  (1)/(1,16) 1 (1)        0 (1,0)  0 (1)    0 (1,1)
4.8  (1)        0 (1)/(1,16) 1 (1)    0 (1,0)  0 (1,1)
0.05 (1,0)     -1 (1,0)     -1 (1)    0 (1)    0 (1,1)
0.2  (1,0)     -1 (1)        0 (1)    0 (1)    0 (1,1)
0.2  (1)        0 (1,0)     -1 (1)    0 (1)    0 (1,1)
0.16 (1)/(1,8)  0 (1)        0 (1)    1 (1)    0 (1,1)
0.16 (1)        0 (1)/(1,8)  0 (1)    0 (1)    1 (1,1)
.2  (1)         0 (1)        0 (1,0) -1 (1)    0 (1,1)
0.2  (1)        0 (1)        0 (1)    0 (1,0) -1 (1,1)
```

Repressilator Model:

```
% Configuration file for repressilator
% nI J Zfinitesize
3 12 8
%
% coef(j) f(j,1) v(j,1) f(j,2) v(j,2) f(j,3) v(j,3) Zfin{j}
1.3 (1)    1 (1)    0 (1)    0 (1,1;3,3;5,5;7,7)
```

```
0.8 (1,0) -1 (1)    0 (1)    0 (1,1;2,2;3,3;4,4;5,5;6,6;7,7;8,8)
1.0 (1,0) -1 (1)    0 (1)    0 (1,5;2,6;3,7;4,8)
0.5 (1)    1 (1)    0 (1)    0 (5,1;6,2;7,3;8,4)
1.3 (1)    0 (1)    1 (1)    0 (1,1;2,2;3,3;4,4)
0.8 (1)    0 (1,0) -1 (1)    0 (1,1;2,2;3,3;4,4;5,5;6,6;7,7;8,8)
1.0 (1)    0 (1,0) -1 (1)    0 (1,3;2,4;5,7;6,8)
0.5 (1)    0 (1)    1 (1)    0 (3,1;4,2;7,5;8,6)
1.3 (1)    0 (1)    0 (1)    1 (1,1;2,2;5,5;6,6)
0.8 (1)    0 (1)    0 (1,0) -1 (1,1;2,2;3,3;4,4;5,5;6,6;7,7;8,8)
1.0 (1)    0 (1)    0 (1,0) -1 (1,2;3,4;5,6;7,8)
0.5 (1)    0 (1)    0 (1)    1 (2,1;4,3;6,5;8,7)
```