Symbolic lumping of some catenary, mamillary and circular compartmental systems

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Abstract

Some of the most important compartmental systems, such as irreversible catenary, mamillary and circular systems are symbolically simplified by the method of exact linear lumping. A few symbolically unmanageable systems are numerically lumped. Transformation of the qualitative properties under lumping are also traced.

Key words: lumping, reduction of the number of variables, circular system, catenary system, mamillary system 

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1 Introduction

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1 Introduction

Compartmental systems are mathematical systems that are frequently used in biology and mathematics. Also a subclass of the class of chemical processes can be modeled as compartmental systems. A compartmental system consists of several compartments with more or less homogeneous amounts of material. The compartments interact by processes of transport and diffusion. The dynamics of a compartmental system is derived from mass balance considerations.

The mathematical theory of compartmental systems is of major importance: it is the bread-and-butter of analysis for medical researchers, pharmacokineticists, physiologists, ecologists, economists as well as other researchers [Cobelli, C., Romanin Jacur, G. (1976)], [Fagarasan, J.T., DiStefano, J. (1987)], [Cobelli, C., Lepschy, A., Romanin Jacur, G., Viaro, U. (1984)], [Jacquez, J. A. (1999)], [Nestorov, I. A., Aarons, L. J., Arundel, P. A., Rowland, M. (1998)].
Sometimes it is useful to reduce a model to get a new one with a lower dimension. The technique’s name is lumping, i.e. reduction of the number of variables by grouping them via a linear or nonlinear function.

The objective of model reduction methods is to obtain a model that can describe the response of the original model accurately and efficiently (cf. [Wilkinson, S. J., Benson, N., Kell, D. B. (2008)]).

Our aim here is to give explicitly possible lumped compartmental systems in a few important classes, mainly of symmetric structure such as: mamillary models, catenary models and circular models. Some classes can be treated in full generality, some only under restrictions on the parameters.

We also show how to lump systems which are only numerically lumpable.

The structure of our paper is as follows. In Section 2 the formal definitions of reactions, compartmental systems, induced kinetic differential equations and that of exact linear lumping are given. Next, our symbolic results are presented. Section 4 shows a few examples which had to be treated numerically. Finally, the results are discussed and further goals are set. We mention that the present work is a continuation of a few simple statements in [Brochot, C., Tóth, J., Bois, F. (2005)] on the symbolic lumping of a general two compartment model.

2 Fundamental definitions

2.1 Reaction mechanism, compartmental system

A chemical reaction mechanism is a set of elementary reactions. Formally, it is a system $\langle \mathcal{M}, \mathcal{R}, \alpha, \beta \rangle$, where

(1) $\mathcal{M}$ and $\mathcal{R}$ are sets with $M$ and $R$ elements ($M, R \in \mathbb{N}$), $\mathcal{R} = \{1, 2, \ldots, R\}$ and $\mathcal{M} = \{X_1, X_2, \ldots, X_M\}$,

(2) $\alpha$ and $\beta$ are matrices with non-negative integers, whose names are stoichiometric coefficients, and for which

(a) for all $r \in \mathcal{R}$, $\alpha(., r) \neq \beta(., r)$,

(b) if $\alpha(., r) = \alpha(., r')$ and $\beta(., r) = \beta(., r')$, then $r = r'$,

(c) for all $m \in \mathcal{M}$ there exists $r \in \mathcal{R}$ such that either $\alpha(m, r) \neq 0$ or $\beta(m, r) \neq 0$ holds.
This mechanism can be represented in the form

$$\sum_{m=1}^{M} \alpha(m, r)X_m \longrightarrow \sum_{m=1}^{M} \beta(m, r)X_m \quad (r \in \mathcal{R}).$$

(1)

The entities on the two sides of the arrow are the reactant and product complexes, respectively.

The number $\max\{\sum_{m=1}^{M} \alpha(m, r), r \in \mathcal{R}\}$ is said to be the order of the reaction; thus, first order reactions are obtained if $\forall r \in \mathcal{R} \sum_{m=1}^{M} \alpha(m, r) \leq 1$. If in a first order reaction it is also true that the length $\sum_{m=1}^{M} \beta(m, r)$ of the product complexes is also less than or equal to 1, then one has a compartmental system. These formal mechanisms are of great practical importance, and are applied in many areas as mentioned in the introduction.

Thus, a compartmental system is a reaction mechanism in which the length of all the complexes is not more than one. In this case we only have reaction steps of the type $X_m \rightarrow X_p$, $X_m \rightarrow O$, $O \rightarrow X_m \ (m, p \in \mathcal{M})$, where $O$ is the empty complex.

A generalized compartmental system is a reaction in which all the complexes contain a single species, and all the species are contained in a single complex, i.e. it is a reaction consisting of elementary reactions of three types

$$y_mX_m \rightarrow y_pX_p, \quad y_mX_m \rightarrow O, \quad O \rightarrow y_mX_m, \quad (m, p \in \mathcal{M}),$$

(2)

and $X_m$ is the constituent of a single complex only.

A generalized compartmental system with no inflow and with some outflow is strictly half-open, while it is strictly open if it contains inflows and possibly outflows.

Reaction (1) is said to be mass-conserving if there exist positive numbers $\rho(1), \rho(2), \ldots, \rho(N)$ such that for all elementary reactions

$$\sum_{m=1}^{M} \alpha(m, r)\rho(m) = \sum_{m=1}^{M} \beta(m, r)\rho(m)$$

(3)

holds. If the atomic structure of the species are not known, it is not trivial to decide whether a reaction is mass-conserving or not [Deák, J., Tóth, J., Vizvári, B. (1992)], [Schuster, S., Höfer, T. (1991)].

A generalized compartmental system is mass-conserving if and only if it is closed: the empty complex is not present.
2.2 Induced kinetic differential equations

The usual continuous time, continuous state deterministic model (or, induced kinetic differential equation) of reaction (1) describing the time evolution of the concentrations \( c_m \) is the polynomial differential equation

\[
\dot{c}_m = \sum_{r=1}^{R} (\beta(m, r) - \alpha(m, r)) k_r \prod_{p=1}^{M} c_p^{\alpha(p,r)},
\]

(4)

where \( k_r \) denotes the rate coefficient, for all \( r \in \mathcal{R} \).

The induced kinetic differential equation of a first order reaction is of the form

\[
\dot{c} = Ac + b
\]

(5)

with

\[
a_{mp} \geq 0 \quad (m \neq p) \quad \text{and} \quad b_m \geq 0 \quad (m, p \in \mathcal{M}).
\]

(6)

The induced kinetic differential equation of a compartmental system has an additional property

\[-a_{mm} \geq \sum_{p \neq m}^{M} a_{pm} \quad (m \in \mathcal{M}).
\]

(7)

Thus, e.g. there is no compartmental system with the induced kinetic differential equation \( \dot{x} = x \) or with \( \dot{x} = -0.5x + y, \quad \dot{y} = -y + x \).

An easy construction proves that the converse of the above statement is also true: a linear differential equation (5) fulfilling the requirements (6) and (7) can be considered as the induced kinetic differential equation of a compartmental system.

This statement can be generalized to get our next theorem showing that if the right hand side of a kinetic differential equation is the sum of univariate monomials and if all the variables have the same exponent in all the rows, then – if an additional condition is also met and only then – there exists an inducing generalized compartmental system to the system of differential equations.

**Theorem 1** There exists an inducing generalized compartmental system of \( M \) compartments to the system of differential equations

\[
\dot{c}_m = \sum_{p=1}^{M} a_{mp}(c_p)^{y_p} + b_m
\]

(8)

(where for all \( m, p \in \mathcal{M}, y^m, y^p \in \mathbb{N}, y^m \neq y^p, \text{if } m \neq p, a_{mp}, b_m \in \mathbb{R} \) which is
(1) closed, if and only if $b_m = 0, -a_{mm}, a_{mp}, d_m \in \mathbb{R}_0^+; a_{mm} = d_my^m,$
(2) strictly half-open, if and only if $b_m = 0, -a_{mm}, a_{mp}, d_m \in \mathbb{R}_0^+; a_{mm} \leq d_my^m, \exists m, a_{mm} < d_my^m,$
(3) strictly open, if and only if $b_m, -a_{mm}, a_{mp}, d_m \in \mathbb{R}_0^+; a_{mm} \leq d_my^m, \exists m b_m \in \mathbb{R}^+,$
where throughout
$$m, p \in \mathcal{M}, m \neq p, d_m := -\sum_{p=1}^{M} a_{pm}/y^m.$$  

Proof.

A) The induced kinetic differential equation of (2) is
$$\dot{c}_m = -y^m(c_m)y^m \sum_p k_{pm} + y^m \sum_p k_{mp}(c_p)y^p,$$
$$\dot{c}_m = -y^m(c_m)y^m \sum_p k_{pm} + y^m \sum_p k_{mp}(c_p)y^p, \quad (\exists k_{0m} \in \mathbb{R}^+)$$
$$\dot{c}_m = -y^m(c_m)y^m \sum_p k_{pm} + y^m \sum_p k_{mp}(c_p)y^p + k_{m0}, \quad (\exists k_{m0} \in \mathbb{R}^+)$$
$$m \in \{1, 2, \ldots, M\}; k_{mp} \in \mathbb{R}_0^+; y^p \in \mathbb{N}; p \in \{0, 1, \ldots, M\}$$
Comparing the coefficients we get the only if part of the Theorem.

B) Given (8) we construct a generalized compartmental system (8) as its induced kinetic differential equation:
$$y^p \chi_{p} \xrightarrow{a_{mp}/y^m} y^m \chi_m, \quad y^p \chi_{p} \xrightarrow{d_p} O, \quad O \xrightarrow{b_m/y^m} y^m \chi_m,$$  
(9)
$$(m, p \in \{1, 2, \ldots, M\}, m \neq p).$$
Reaction (9) induces closed, strictly half-open or strictly open reactions, respectively.

2.3 Exact linear lumping

A special class of lumping is exact linear lumping.

A system $\dot{c} = f \circ c$, with $f, c$ $n$-vectors can be exactly lumped by an $\hat{n} \times n$ real constant matrix $Q$ ($\hat{n} < n$), called lumping matrix, if for $\hat{c} = Qc$ we can find an $\hat{n}$-function vector $\hat{f}$ such that $\dot{\hat{c}} = \hat{f} \circ \hat{c}$.

Not every system is exactly lumpable. A sufficient and necessary condition for the existence of exact lumping is $Qf(c) = Qf(QQc)$, where $Q$ denotes any of
the generalized inverses of $Q$, i.e. $QQ^\perp = I_{\hat{n}}$, and $I_{\hat{n}}$ is the $\hat{n} \times \hat{n}$ identity matrix [Li, G., Rabitz, H. (1989)].

This condition is equivalent to the requirement that the rows of matrix $Q$ span an invariant subspace of $f'^T(c)$ for all $c$, where $f'^T(c)$ denotes the transpose of the Jacobian of $f$ at $c$. Therefore, in order to determine lumping matrices $Q$ we need to determine the fixed $f'^T(c)$-invariant subspaces [Gohberg, I., Lancaster, P., Rodman, L. (1986)].

In the case of linear differential equation (5), the Jacobian matrix is just $A$, and then $f'^T(c) = A^T$. In this situation, fixed invariant subspaces exist, they are spanned by eigenvectors, and they correspond to (constant) eigenvalues. So, a linear system is always exactly lumpable and any $f'^T(c)$-invariant subspaces will give a lumping matrix. In this case therefore, we have to calculate the eigenvectors of $A^T$.

We mention here that, if $Q$ is an $\hat{n} \times n$ lumping matrix and $P$ a nonsingular matrix of dimension $\hat{n}$, then $PQ$ is also a lumping matrix.

It is not true that a given system can be lumped arbitrarily. For example

\begin{align}
S & \xrightarrow{\ !} I_1 \xrightarrow{\ !} \hat{I} \xrightarrow{\ !} P, \\
S & \xrightarrow{\ !} I_2 \xrightarrow{\ !} \hat{I} \xrightarrow{\ !} P,
\end{align}

(10)
cannot lead to a lumped system of the type $S \xrightarrow{\ !} I \xrightarrow{\ !} \hat{I} \xrightarrow{\ !} P$, for $I := I_1 + I_2$, except in the very special case $k_2 = k_4$, contrary to [Conzelmann, H., Saez-Rodriguez, J., Sauter, T., Bullinger, E., Allgöwer, F., Gilles, E. D.].

The next question is whether the lumped system can have an interpretation in terms of reactions (or more specially, in terms of compartments), i.e. is the lumped system kinetic? To formulate this criterion we use the notion of the generalized inverse matrix [Rao, C. R. (1973)].

Farkas [Farkas, Gy. (1999)] gave a sufficient and necessary condition under which certain lumping schemes preserve the kinetic structure of the original system: *A nonnegative lumping matrix leads to a kinetic differential equation if and only if it has a nonnegative generalized inverse.*

For the absence of a nonnegative generalized inverse he proved the following result: *A nonnegative matrix has no nonnegative generalized inverse if and only if it has a row such that in the column of each positive entry there exists another positive entry.*
3 Symbolic results

3.1 Chains

In a chain or catenary system the $M$ compartments are arranged in a linear array such that every compartment exchanges material only with its immediate neighbors and the possible steps are indicated by nonnegative reaction rates. The coefficient matrix for a catenary system has nonzero entries only in the main diagonal and the first sub-diagonal and in the first super-diagonal. The latter case holds only if it is reversible (bidirectional).

3.1.1 Irreversible chains

Let us consider a compartmental system, such as the one in Fig. 2, i.e. a chain with unidirectional steps.

![Diagram of irreversible catenary system]

In this case the coefficient matrix $A$ on the right hand side of (5) takes the form

$$
\begin{bmatrix}
-k_1 & 0 & 0 & \ldots & 0 & 0 & 0 \\
 k_1 & -k_2 & 0 & \ldots & 0 & 0 & 0 \\
 0 & k_2 & -k_3 & \ldots & 0 & 0 & 0 \\
 \vdots & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots \\
 0 & 0 & 0 & \ldots & k_{M-2} & -k_{M-1} & 0 \\
 0 & 0 & 0 & \ldots & 0 & k_{M-1} & 0 \\
\end{bmatrix}
$$

The eigenvalues of the transpose of this triangular matrix are obviously the elements on the diagonal: $-k_1, -k_2, -k_3, \ldots, -k_{M-1}$ and 0 (and are the same as the eigenvalues of the original matrix). So, the corresponding eigenvectors
can be found easily, and they take the form:

\[
\begin{bmatrix}
1 & 0 & 0 & \ldots & 0 & 0 & 0 \\
1 & \frac{k_1 - k_2}{k_1} & 0 & \ldots & 0 & 0 & 0 \\
1 & \frac{k_1 - k_3}{k_1} & \frac{(k_1 - k_3)(k_2 - k_3)}{k_1 k_2} & \ldots & 0 & 0 & 0 \\
\vdots & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots \\
1 & \frac{k_1 - k_{M-1}}{k_1} & \frac{(k_1 - k_{M-1})(k_2 - k_{M-1})}{k_1 k_2} & \ldots & \frac{(k_1 - k_{M-1})(k_2 - k_{M-1})\ldots(k_{M-2} - k_{M-1})}{k_1 k_2 \ldots k_{M-1}} & 0 & 0 \\
1 & 1 & 1 & \ldots & 1 & 1 & 1 \\
\end{bmatrix}
\]

(Here we only consider the robust case when all the reaction rate coefficients are different. Then, the above eigenvectors are independent.)

If we do not neglect inflows and outflows in a catenary system, the principal diagonal of matrix \( A \) will change, i.e. instead of \(-k_i\) we will have \(-k_i - \mu_i\) in the first \( M - 1 \) places (where \( \mu_i \) denotes the outflow coefficient for the species \( X_i \)), and \(-\mu_M\) in the last one, instead of 0. The transpose of the modified matrix has the following eigenvectors:

\[
\begin{bmatrix}
1 & 0 & 0 & \ldots & 0 \\
1 & \frac{k_1 - k_i}{k_1 + \mu_1 - \mu_i} & 1 & 0 & \ldots & 0 \\
1 & \frac{k_1 - k_2 + \mu_1 - \mu_i}{k_1 k_2} & \frac{k_2}{k_2 - k_3 + \mu_2 - \mu_i} & 1 & \ldots & 0 \\
\vdots & \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\
1 & 1 & 1 & \ldots & 1 \\
\end{bmatrix},
\]

corresponding to the eigenvalues \(-k_1 - \mu_1, -k_2 - \mu_2, \ldots, -k_{M-1} - \mu_{M-1}, -\mu_M\).

The graphical representation in this case, when outflows and inflows are incorporated into an irreversible chain, is:

Fig. 2. Irreversible catenary system with inflows and outflows

To get a lumped system for this model, we can take some of the eigenvectors above to generate several lumping matrices.

For example, let us consider an irreversible chain with five compartments.
Then the induced kinetic differential equation has the following coefficient matrix:

\[
\begin{bmatrix}
-k_1 - \mu_1 & 0 & 0 & 0 & 0 \\
   k_1 & -k_2 - \mu_2 & 0 & 0 & 0 \\
   0 & k_2 & -k_3 - \mu_3 & 0 & 0 \\
   0 & 0 & k_3 & -k_4 - \mu_4 & 0 \\
   0 & 0 & 0 & k_4 & -\mu_5
\end{bmatrix}.
\]

Let us compose \(Q\) e.g. putting the eigenvectors \(\frac{k_1}{(k_1-k_2+\mu_1-\mu_2)} 1 0 0 0\) and \(\frac{k_2}{(k_1-k_2+\mu_1-\mu_2)(k_2-k_3+\mu_2-\mu_4)(k_3-k_4+\mu_3-\mu_4)} \frac{k_3}{(k_2-k_4+\mu_2-\mu_4)(k_3-k_4+\mu_3-\mu_4)} 1 0\) into it as rows. Then,

\[
Q^T = \begin{bmatrix}
\frac{k_1}{k_1-k_2+\mu_1-\mu_2} & \frac{k_1k_2k_3}{(k_1-k_2+\mu_1-\mu_2)(k_2-k_3+\mu_2-\mu_4)(k_3-k_4+\mu_3-\mu_4)} \\
1 & \frac{k_2k_3}{(k_2-k_4+\mu_2-\mu_4)(k_3-k_4+\mu_3-\mu_4)} \\
0 & \frac{k_3}{k_3-k_4+\mu_3-\mu_4} \\
0 & 1 \\
0 & 0
\end{bmatrix}.
\]

After some calculations, we get the lumped system \(\dot{A} = QAQ\), which induces the differential equation below:

\[
\begin{bmatrix}
\dot{x}_1 \\
\dot{x}_2
\end{bmatrix} = \begin{bmatrix}
-k_2 - \mu_2 & 0 \\
0 & -k_4 - \mu_4
\end{bmatrix} \begin{bmatrix}
x_1 \\
x_2
\end{bmatrix},
\]

so we got a new compartmental system with two compartments, where

\[
\begin{align*}
\dot{x}_1 &= \frac{k_1}{k_1-k_2+\mu_1-\mu_2}x_1 + x_2 \\
\dot{x}_2 &= \frac{k_1k_2k_3}{(k_1-k_4+\mu_1-\mu_4)(k_2-k_4+\mu_2-\mu_4)(k_3-k_4+\mu_3-\mu_4)}x_1 + \\
&\quad + \frac{k_2k_3}{(k_2-k_4+\mu_2-\mu_4)(k_3-k_4+\mu_3-\mu_4)}x_2 + \frac{k_3}{k_3-k_4+\mu_3-\mu_4}x_3 + x_4.
\end{align*}
\]

The corresponding reaction (actually, a chain with no interaction between the compartments) can be illustrated as follows:
\[ \dot{\hat{X}}_1 \overset{k_2 + \mu_2}{\rightarrow} \hat{X}_2, \]

or it can be the mamillary system \( \hat{X}_1 \rightarrow \hat{X}_3 \leftarrow \hat{X}_2 \), with \( \hat{X}_3 \) neglected in the induced kinetic differential equation.

### 3.1.2 Irreversible chains with nonuniform directions

Let us mention here that the irreversible case with nonuniform direction of the arrows is simpler than the case of a reversible chain.

As an example, consider the compartmental system with the following diagram:

![Fig. 3. An irreversible chain with nonuniform directions](image)

We can associate to it the kinetic differential equation \( \dot{x} = Ax \), where

\[
A = \begin{bmatrix}
-k_1 & 0 & 0 & 0 & 0 \\
0 & k_1 & 0 & k_2 & 0 \\
0 & 0 & -k_2 - k_3 & 0 & 0 \\
0 & 0 & k_3 & 0 & k_4 \\
0 & 0 & 0 & 0 & -k_4 \\
\end{bmatrix}.
\]

The eigenvalues are: \(-k_1, -k_2 - k_3, -k_4, \) and \(0\), with multiplicity 2. From the corresponding eigenvectors, \([1, 0, 0, 0, 0], [0, 0, 1, 0, 0], [0, 0, 0, 0, 1], \left[ \frac{k_2 + k_3}{k_2}, \frac{k_2 + k_3}{k_2}, 1, 0, 0 \right] \)

and \([\frac{k_3}{k_2} - \frac{k_3}{k_2}, 0, 1, 1]\) we can determine a lot of lumping matrices. Depending on our choice, the lumped system can be kinetic or not.

For example, if we take

\[
Q = \begin{bmatrix}
0 & 0 & 0 & 0 & 1 \\
0 & 0 & 1 & 0 & 0 \\
1 & 0 & 0 & 0 & 0 \\
\end{bmatrix},
\]

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then for the lumped system we get the kinetic differential equation system

\[
\begin{bmatrix}
\dot{x}_1 \\
\dot{x}_2 \\
\dot{x}_3 
\end{bmatrix} =
\begin{bmatrix}
-k_4 & 0 & 0 \\
0 & -k_2-k_3 & 0 \\
0 & 0 & -k_1 
\end{bmatrix}
\begin{bmatrix}
x_1 \\
x_2 \\
x_3 
\end{bmatrix},
\]

which can be illustrated via the diagram:

\[\hat{X}_1 \xrightarrow{k_1} O \xleftarrow{k_1} \hat{X}_3\]

\[\uparrow k_2 + k_3\]

\[\hat{X}_2\]

On the other hand, if we take

\[Q = \begin{bmatrix}
1 & 0 & 0 & 0 & 0 \\
0 & 0 & 1 & 0 & 0 \\
k_2 + k_3 & k_2 + k_3 & k_2 & 1 & 0 \\
\end{bmatrix},\]

this leads to the matrix

\[\hat{A} = QAQ = \begin{bmatrix}
-2k_1 & -\frac{k_1k_2}{k_2+k_3} & \frac{k_1k_2}{k_2+k_3} \\
-k_2 & -\frac{k_2^2}{k_2+k_3} - k_2 - k_3 & \frac{k_2^2}{k_2+k_3} - k_2 - k_3 \\
\frac{2k_1(k_2+k_3)}{k_2} - k_2 & -\frac{k_1(k_2+k_3)+k_2^2}{k_2+k_3} - k_2 - k_3 & \frac{k_1(k_2+k_3)+k_2^2}{k_2+k_3} - k_2 - k_3 
\end{bmatrix}.\]

It can be seen that in this case the positivity conditions relative to the convenient elements of the matrix are not fulfilled, as expected in accordance with Lemma 1 in [Farkas, Gy. (1999)]. Consequently, \(\hat{A}\) does not result in a lumped system which has a kinetic differential equation. The new variables are:

\[
\begin{align*}
\hat{x}_1 &= x_1 \\
\hat{x}_2 &= x_3 \\
\hat{x}_3 &= \frac{k_2 + k_3}{k_2} x_1 + \frac{k_2 + k_3}{k_2} x_2 + x_3.
\end{align*}
\]

3.1.3 Reversible chains

To compute the eigenvectors even for a reversible chain consisting of only five compartments is unsolvable symbolically. We shall give a numerical example
3.2 Mamillary systems

In these systems all the compartments communicate only with a central compartment, $X_{M+1}$, and there is no direct communication between the other compartments. The possible steps are indicated by nonnegative reaction rates. We shall call $X_{M+1}$ as the mother compartment and all the other compartments will be called daughter or peripheral compartments.

Only the irreversible case can be treated symbolically; a reversible example will be treated numerically in section 4.2. A class of reversible mamillary systems with a special structure can still be treated symbolically, this will be shown in subsection 3.2.2.

3.2.1 Irreversible mamillary systems

Inward flows

Let us consider an irreversible mamillary system with inward flows such as the one in Fig. 6.
Fig. 6. A mamillary system with inward flows only

The coefficient matrix of the reaction rate constants is

$$
\begin{bmatrix}
-k_1 & 0 & \cdots & 0 & 0 & 0 \\
0 & -k_2 & \cdots & 0 & 0 & 0 \\
\vdots & \vdots & \ddots & \vdots & \vdots & \vdots \\
0 & 0 & \cdots & 0 & -k_M & 0 \\
k_1 & k_2 & \cdots & k_{M-1} & k_M & 0
\end{bmatrix}
$$

The eigenvalues of the transpose of this lower triangular matrix are obviously the elements on the diagonal: \(-k_1, -k_2, -k_3, \ldots, -k_M\) and 0, with the corresponding eigenvectors:

\([1, 0, \ldots, 0, 0], [0, 1, \ldots, 0, 0], \ldots, [0, 0, \ldots, 1, 0], [1, 1, \ldots, 1, 1]\).

Notice that if we denote by \(e_i\) the \(i\)-th element of the standard basis for \(\mathbb{R}^N\), \(i \in \{1, 2, \ldots, N\}\), then \(e_1, e_2, \ldots, e_M\) create the first \(M\) eigenvectors of such a compartmental system.

To lump the system of differential equations induced by this model, we can choose some of these eigenvectors to generate several lumping matrices.

In the first case, if we do not use the vector \([1,1,\ldots,1,1]\) to generate \(Q\), only \(\hat{M}\) of the first \(M\) elements of the standard basis for \(\mathbb{R}^{M+1}\), that appear above, we will receive a new compartmental system, with \(\hat{M}\) compartments, where the new species are taken from the old external ones only. In this case lumping actually discards some peripheral compartments and permutes the remaining ones.

If we take an \(\hat{M} \times \hat{M}\) nonsingular matrix, \(P\), i.e. a basis transformation matrix, then \(PQ\) will be another lumping matrix. It will consist of some of \(P\)'s columns, and values being 0 elsewhere. Accordingly the new compartments
will be the linear combinations of certain old peripheral compartments. An obvious interpretation is that they are measured together.

Assume e.g. we have chosen \( Q \) in the following way: it consists of \( e_i, e_j \) and \( e_k \) of the natural basis \( \mathbb{R}^{M+1}, i, j, k \in \{1, 2, \ldots, M\} \). Let \( P \in \mathbb{R}^{3 \times 3} \) be an invertible matrix. Then

\[
\dot{x} = PQx = x_ip_1 + x_jp_2 + xkp_3,
\]

where \( p_1, p_2, p_3 \) are the linearly independent columns of \( P \), and the coordinates of the new composition vector \( \dot{x} \) are linear combinations of the external species \( x_i, x_j \) and \( x_k \) with (in general) different coefficients.

Now, suppose, the eigenvector \([1, 1, \ldots, 1]\) is contained in the rows of matrix \( Q \). In this case the system of equation \( \dot{x}_j = \sum_{j=1}^{M+1} q_{ij}x_j \) defines new compartments, composed by some of the existing peripheral ones, plus the sum of the original one.

As an example let us consider the following irreversible mamillary system with inward flows:

\[
\begin{align*}
X_3 & \quad \Downarrow k_3 \\
X_1 & \quad k_1 \rightarrow X_4 \quad k_2 \leftarrow X_2
\end{align*}
\]

The induced kinetic differential equation is \( \dot{x} = Ax \), where

\[
A = \begin{bmatrix}
-k_1 & 0 & 0 & 0 \\
0 & -k_2 & 0 & 0 \\
0 & 0 & -k_3 & 0 \\
k_1 & k_2 & k_3 & 0
\end{bmatrix}.
\]

Using the fact that the eigenvectors of \( A^T \) are \([1, 0, 0, 0], [0, 1, 0, 0], [0, 0, 1, 0] \), and \([1, 1, 1, 1]\), we can set e.g.

\[
Q = \begin{bmatrix}
0 & 0 & 1 & 0 \\
1 & 0 & 0 & 0 \\
1 & 1 & 1 & 1
\end{bmatrix}.
\]
The new variables become
\[
\begin{bmatrix}
\dot{x}_1 \\
\dot{x}_2 \\
\dot{x}_3
\end{bmatrix} =
\begin{bmatrix}
0 & 0 & 1 & 0 \\
1 & 0 & 0 & 0 \\
1 & 1 & 1 & 1
\end{bmatrix}
\begin{bmatrix}
x_1 \\
x_2 \\
x_3 \\
x_4
\end{bmatrix}.
\]
and the lumped system has the variables
\[
\begin{align*}
\dot{x}_1 &= x_3 \\
\dot{x}_2 &= x_1 \\
\dot{x}_3 &= x_1 + x_2 + x_3 + x_4.
\end{align*}
\] (11)

The resultant process obeys a differential equation
\[
\begin{bmatrix}
\dot{x}_1 \\
\dot{x}_2 \\
\dot{x}_3
\end{bmatrix} =
\begin{bmatrix}
-k_3 & 0 & 0 \\
0 & -k_1 & 0 \\
0 & 0 & 0
\end{bmatrix}
\begin{bmatrix}
x_1 \\
x_2 \\
x_3
\end{bmatrix}
\]
which is the induced kinetic differential equation e.g. of the reaction
\[
\hat{X}_1 \xrightarrow{k_3} \hat{O} \xleftarrow{k_1} \hat{X}_2,
\]
that is no more a mamillary system. Or, again, we can take $\hat{X}_1 \rightarrow \hat{X}_3 \leftarrow \hat{X}_2$, and say we are not interested in the change of concentration of $\hat{X}_3$; we consider it as an external species.

**Outward flows**

![Fig. 7. Outward flows](image-url)
The induced kinetic differential equation is \( \dot{x} = Ax \), where

\[
A = \begin{bmatrix}
0 & 0 & \ldots & 0 & k_1 \\
0 & 0 & \ldots & 0 & k_2 \\
0 & 0 & \ldots & 0 & \ddots & \ddots & \ddots & \ddots & \ddots & \ddots & \ddots & \ddots & \ddots \\
0 & 0 & \ldots & 0 & k_M \\
0 & 0 & \ldots & 0 & -K
\end{bmatrix},
\]

with \( K = (k_1 + k_2 + \cdots + k_M) \). The transpose of it, \( A^T \), has a single eigenvalue \(-K\) with the eigenvector \([0, 0, \ldots, 0, 1]\), and an eigenvalue 0 with multiplicity \( M \), with the corresponding independent eigenvectors

\[
\begin{bmatrix}
1 & 0 & \ldots & \frac{-k_1}{k_M} & 0 \\
0 & 1 & \ldots & \frac{-k_2}{k_M} & 0 \\
\vdots & \vdots & \ddots & \ddots & \ddots \\
0 & 0 & \ldots & \frac{-k_M}{k_M} & 0 \\
0 & 0 & \ldots & \frac{1}{k_M} & 1
\end{bmatrix}
\]

If we build up a lumping matrix, \( Q \), we get reasonable result only with eigenvectors belonging to the multiple eigenvalue 0, since we get \( \hat{A} = 0 \) in all other cases, and it is not worth taking such a \( Q \).

If the eigenvector \([0, 0, \ldots, 0, 1]\) appears in the lumping matrix, we obtain a lumped system, whose coefficient matrix consists of the 0 elements, except a single element on the principal diagonal, which has the value \(-K\). This can be represented by the extremely simple reaction \( \hat{\mathcal{X}} \xrightarrow{K} \mathcal{O} \).

**Irreversible mamillary systems with inward and outward flows**

Instead of giving a general treatment we shall take an example again, as in subsection 3.1.2. Let us consider the mamillary system below.
Fig. 8. An irreversible mamillary system with inward and outward flows

The coefficient matrix of the induced kinetic differential equation is

\[
\begin{bmatrix}
-k_1 & 0 & 0 & 0 & 0 \\
0 & -k_2 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & k_3 \\
0 & 0 & 0 & 0 & k_4 \\
0 & 0 & 0 & 0 & k_5 \\
0 & 0 & 0 & 0 & -(k_3 + k_4 + k_5)
\end{bmatrix},
\]

with the simple eigenvalues \(-k_1, -k_2, -K := -(k_3 + k_4 + k_5)\), and with the triple eigenvalue 0. The corresponding eigenvectors of its transpose are

\[
\begin{bmatrix}
1, 0, 0, 0, 0 \\
0, 1, 0, 0, 0 \\
0, 0, 0, 0, 1 \\
0, 0, 1, 0, 0 \\
0, 0, 1, -\frac{k_3}{k_4}, 0 \\
0, 0, 1, -\frac{k_3}{k_5}, 0
\end{bmatrix},
\]

Taking the lumping matrix

\[
Q = \begin{bmatrix}
0 & 0 & 1 & 0 & 0 & \frac{k_3}{K} \\
0 & 0 & 1 & -\frac{k_3}{k_4} & 0 & 0 \\
1 & 0 & 0 & 0 & 0 & 0
\end{bmatrix},
\]

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we get the lumped system

\[
\begin{align*}
\dot{x}_1 &= x_3 + \frac{k_3}{K}x_6 \\
\dot{x}_2 &= x_3 - \frac{k_3}{k_4}x_4 \\
\dot{x}_3 &= x_1.
\end{align*}
\]  

(12)

In this case the lumped system’s differential equation will be very simple:

\[
\begin{bmatrix}
\dot{x}_1 \\
\dot{x}_2 \\
\dot{x}_3
\end{bmatrix} =
\begin{bmatrix}
0 & 0 & 0 \\
0 & 0 & 0 \\
0 & 0 & -k_1
\end{bmatrix}
\begin{bmatrix}
\dot{x}_1 \\
\dot{x}_2 \\
\dot{x}_3
\end{bmatrix}.
\]

We can associate it to the reaction \( \dot{X}_3 \xrightarrow{k_1} \mathcal{O} \).

3.2.2 Simplicial compartmental systems

Suppose we have the following formal reaction steps as follows

\[
\mathcal{O} \xrightarrow{d} X_i \xrightarrow{c_{j-i}} X_j \xrightarrow{d} \mathcal{O}, \quad \text{for } i < j; \ i, j \in \{1, 2, \ldots, M\}.
\]

The fact that the reaction rate coefficients are the same for many reaction-antireaction pairs may come from the application when the compartments are physically separated (by a membrane e.g.) parts of the space. In general, such kinds of assumption are made in cases when diffusion is modeled by mass transport between homogeneous boxes; such models often arise [Shapiro, A., Horn, F. (1979a)], [Shapiro, A., Horn, F. (1979b)].

The transpose of the coefficient matrix of the induced kinetic differential equation is

\[
A^T = \begin{bmatrix}
c_0 & c_1 & c_2 & \cdots & c_{M-1} \\
c_{M-1} & c_0 & c_1 & \cdots & c_{M-2} \\
c_{M-2} & c_{M-1} & c_0 & \cdots & c_{M-3} \\
\vdots & \vdots & \vdots & \ddots & \vdots \\
c_1 & c_2 & c_3 & \cdots & c_0
\end{bmatrix},
\]

with \( c_0 := -(c_1 + c_2 + \cdots + c_{M-1} + d) \). Such a matrix \( A^T \) (for which every row is a cyclic permutation of the top row) is called a cyclic, or circulant matrix.
Its eigenvalues can be calculated easily [Gray, R. M. (2006)]. (Certainly, $A$ is a cyclic matrix, as well.)

$$\lambda_1 = \sum_{m=0}^{M-1} c_m$$

$$\lambda_2 = \sum_{m=0}^{M-1} c_m \varepsilon_1^m$$

$$\vdots$$

$$\lambda_M = \sum_{m=0}^{M-1} c_m \varepsilon_{M-1}^m$$

where $\varepsilon_k := e^{\frac{2k\pi i}{M}}$, $(k = 0, 1, \ldots, M - 1)$ are the roots of unity.

The corresponding eigenvectors are

$$\begin{bmatrix} 1 & 1 & 1 & \ldots & 1 \\ 1 & \varepsilon_1 & \varepsilon_1^2 & \ldots & \varepsilon_1^{M-1} \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ 1 & \varepsilon_{M-1} & \varepsilon_{M-1}^2 & \ldots & \varepsilon_{M-1}^{M-1} \end{bmatrix}$$

Here we meet a new problem which we will not discuss here further: obviously, in the applications one needs real lumped systems.

To be more concrete, let us consider the special case (studying the problem of complex numbers in the special case) of Fig. 9. (This system is a special reversible circular system with outflow.)

![Fig. 9. A simplicial compartmental system](image)

Now $\varepsilon_0 = 1, \varepsilon_1 = \frac{-1 + i\sqrt{3}}{2}, \varepsilon_2 =$
\[-\frac{1-i\sqrt{3}}{2},\] thus the eigenvalues of
\[
\begin{bmatrix}
c_0 & c_1 & c_2 \\
c_2 & c_0 & c_1 \\
c_1 & c_2 & c_0
\end{bmatrix}
\] are
\[
\lambda_1 = c_0 + c_1 + c_2, \quad \lambda_2 = c_0 + c_1 \varepsilon_1 + c_2 \varepsilon_1^2 = c_0 + c_1 \frac{-1 + i\sqrt{3}}{2} + c_2 \frac{-1 - i\sqrt{3}}{2},
\]
and
\[
\lambda_3 = c_0 + c_1 \varepsilon_2 + c_2 \varepsilon_2^2 = c_0 + c_1 \frac{-1 - i\sqrt{3}}{2} + c_2 \frac{-1 + i\sqrt{3}}{2}.
\]

For \(c_1 = c_2\) the corresponding eigenvectors are \([1, 1, 1], [-1, 0, 1], [-1, 1, 0]\). In this case we can construct a few lumping matrices which lead to a new, simpler system.

Furthermore, if \(c_1 \neq c_2\) we obtain the following eigenvectors: \([1, 1, 1]\),
\[
\begin{bmatrix}
-|b-c| - i\sqrt{3}(b+c) \\
(2b+c)\text{sign}(b-c) - i\sqrt{3}c \\
(2b+c)\text{sign}(b-c) + i\sqrt{3}c
\end{bmatrix}
\]
\[
\begin{bmatrix}
-|b-c| + i\sqrt{3}(b+c) \\
(2b+c)\text{sign}(b-c) + i\sqrt{3}c \\
(2b+c)\text{sign}(b-c) - i\sqrt{3}c
\end{bmatrix}
\]

The effect of lumping on qualitative properties

One of the major questions connected with lumping is: how are the qualitative properties of the lumped and of the original system connected? We investigated this problem in a more general setting in [Tóth, J. et al., (1997)]; here we add a new statement: suppose we lump a system of \(M\) compartments with a coefficient matrix having real eigenvalues into a compartmental system of \(\hat{M}\) compartments. Then, none of the concentration versus time curves can have more than \(\hat{M} - 2\) local extrema [Póta, Gy. (1981)].

4 A few numerical examples

4.1 A reversible chain

Consider a reversible chain formed by five chemical species, let them be \(X_1, X_2, X_3, X_4\) and \(X_5\). Let the forward and reverse reaction rates be
\[
k_1 = 1, k_2 = 4, k_3 = 2, k_4 = 1 \text{ and } k_{-1} = 2, k_{-2} = 4, k_{-3} = 1, k_{-4} = 2,
\]
respectively, as it can be seen in the following chemical mechanism:
\[ X_1 \equiv X_2 \overset{4}{\equiv} X_3 \overset{2}{\equiv} X_4 \overset{1}{\equiv} X_5 \]

We can associate it with the following induced kinetic differential equation system:

\[
\begin{align*}
\dot{x}_1 &= -x_1 + x_2, \\
\dot{x}_2 &= x_1 - 5x_2 + 4x_3, \\
\dot{x}_3 &= 4x_2 - 6x_3 + 5x_4, \\
\dot{x}_4 &= 2x_3 - 6x_4 + 2x_5, \\
\dot{x}_5 &= x_4 - 2x_5.
\end{align*}
\]

The eigenvectors of the transpose of its coefficient matrix are collected in the rows of the matrix below:

\[
\begin{bmatrix}
0.2 & -0.2 & -0.2 & 0 & 1 \\
-0.689897 & 0.069693 & 0.240408 & 0.449489 & 1 \\
0.289897 & -2.869693 & 4.159591 & -4.449489 & 1 \\
-0.2 & 1 & -0.2 & -2 & 1 \\
1 & 1 & 1 & 1 & 1
\end{bmatrix}
\]

If we take as a lumping matrix

\[
Q = \begin{bmatrix}
0.289897 & -2.869693 & 4.159591 & -4.449489 & 1 \\
0.2 & -0.2 & -0.2 & 0 & 1
\end{bmatrix},
\]

after some calculations we receive

\[
\hat{A} = \begin{bmatrix}
-10.898979 & 0 \\
0 & -2
\end{bmatrix}
\]

and we obtain the lumped model

\[ \hat{X}_1 \overset{10.89}{\rightarrow} \hat{O} \overset{2}{\leftarrow} \hat{X}_1. \]
4.2 A reversible mamillary system

In the following, consider a reversible compartmental system with five compartments. Let $X_5$ be the mother compartment, and $X_1, X_2, X_3, X_4$, the peripheral ones. Suppose that all of the reaction rates corresponding to the reactions from the mother compartment to the peripheral ones have the same value, $K$. Whereas, the reverse reactions also have identical reaction rates, $k$.

To this chemical mechanism we can set up the system

\[
\begin{align*}
\dot{x}_1 &= -kx_1 + Kx_5 \\
\dot{x}_2 &= -kx_2 + Kx_5 \\
\dot{x}_3 &= -kx_3 + Kx_5 \\
\dot{x}_4 &= -kx_4 + Kx_5 \\
\dot{x}_5 &= k(x_1 + x_2 + x_3 + x_4) - 4Kx_5,
\end{align*}
\]

which describes the time evolution of the concentrations of the species taking part in the reaction. Consequently, the coefficient matrix will be

\[
\begin{bmatrix}
-k & 0 & 0 & 0 & K \\
0 & -k & 0 & 0 & K \\
0 & 0 & -k & 0 & K \\
0 & 0 & 0 & -k & K \\
k & k & k & k & -4K
\end{bmatrix}.
\]

Its transpose has a triple eigenvalue, $-k$, and two single eigenvalues, 0 and $-k - 4K$. The corresponding eigenvectors are as follows: $[-1, 0, 1, 0, 0]$, $[-1, 0, 1, 0, 0]$, $[1, 1, 1, 1, 1]$ and $\left[-\frac{k}{4K}, -\frac{k}{4K}, -\frac{k}{4K}, -\frac{k}{4K}, 1\right]$. 

Now, we can take several lumping matrices. For example if

\[
Q = \begin{bmatrix}
-1 & 0 & 0 & 1 & 0 \\
\frac{k}{4K} & \frac{k}{4K} & \frac{k}{4K} & \frac{k}{4K} & 1 \\
-1 & 1 & 0 & 0 & 0
\end{bmatrix},
\]
we obtain the lumped system

\[
\begin{align*}
\dot{x}_1 &= -k \hat{x}_1 \\
\dot{x}_2 &= -(4K + k) \hat{x}_2 \\
\dot{x}_3 &= -k \hat{x}_3,
\end{align*}
\]

and the corresponding model is

\[
\dot{X}_1 \xrightarrow{k} \mathcal{O} \xleftarrow{k} \dot{X}_3 \\
\uparrow 4K + k \\
\dot{X}_2
\]

4.3 Cycles

4.3.1 Irreversible cycles

Consider an irreversible circular system with three compartments, \( X_1, X_2, X_3 \) and the corresponding reaction rates \( k_1, k_2, k_3 \). Then the coefficient matrix of the induced kinetic differential equation is

\[
A = \begin{bmatrix}
-k_1 & 0 & k_3 \\
k_1 & -k_2 & 0 \\
0 & k_2 & -k_3
\end{bmatrix}.
\]

Since the eigenvectors of \( A^\top \) are \([1, 1, 1]\),
\[
\begin{bmatrix}
k_1 + k_2 - k_3 + \sqrt{k_1^2 + (k_2 - k_3)^2 - 2k_1(k_2 + k_3)} \\
k_2(-k_1 + k_2 - k_3 + \sqrt{k_1^2 + (k_2 - k_3)^2 - 2k_1(k_2 + k_3)}) \\
-k_1 - k_2 + k_3 + \sqrt{k_1^2 + (k_2 - k_3)^2 - 2k_1(k_2 + k_3)} \\
k_2(k_1 - k_2 + k_3 + \sqrt{k_1^2 + (k_2 - k_3)^2 - 2k_1(k_2 + k_3)})
\end{bmatrix}, 1
\]
and
\[
\begin{bmatrix}
1 \\
i\sqrt{2} \\
1 \\
-3 - \sqrt{2}i
\end{bmatrix}
\]

respectively, building up \(Q\) from the first two eigenvectors, in the special case \(k_1 = 1, k_2 = 2\) and \(k_3 = 3\) we obtain the lumping matrix
\[
Q = \begin{bmatrix}
1 & 1 & 1 \\
\end{bmatrix}, 1
\]
After some calculations we get \(\hat{A} = \begin{bmatrix} 0 & 0 \\ 0 & -3 - \sqrt{2}i \end{bmatrix}\). To receive a real valued matrix \(\hat{A}\), we should take, for example \(k_1 = 1, k_2 = 1/2\) and \(k_3 = 5/128\).

We can also illustrate the region of those values \(k_2 \in [0, 20]\) and \(k_3 \in [0, 20]\), for which \(k_1 = 1\) results in a lumped system with kinetic structure, that is, a real valued matrix, \(\hat{A}\) (see fig. 11).

![Fig. 11. The preferred values of \(k_2\) and \(k_3\) are those outside the curve](image-url)
4.3.2 Reversible cycles

Consider the reversible cycle with five compartments \( X_1, X_2, X_3, X_4, \) and \( X_5 \). Suppose the reaction rates are all equal to a positive real number \( k \).

Then, we can assign to this mechanism a linear differential equation to describe the time evolution of the species's concentrations, with coefficient matrix

\[
A = \begin{bmatrix}
-2k & k & 0 & 0 & k \\
k & -2k & k & 0 & 0 \\
0 & k & -2k & k & 0 \\
0 & 0 & k & -2k & k \\
k & 0 & 0 & k & -2k
\end{bmatrix}.
\]

This is a special circular matrix. \( A^\top = A \) has two double eigenvalues, \( \frac{-5 + \sqrt{5}}{2} \) and \( \frac{-5 - \sqrt{5}}{2} \), and a single one, 0. With the corresponding eigenvectors,

\[
\begin{bmatrix}
\sqrt{5} - 1 & -\sqrt{5} + 1 \\
2 & 2 \\
\end{bmatrix},
\begin{bmatrix}
1 & -\sqrt{5} + 1 \\
\frac{2}{2} & \frac{2}{2} \\
\end{bmatrix},
\begin{bmatrix}
-\sqrt{5} - 1 & \sqrt{5} + 1 \\
2 & 2 \\
\end{bmatrix},
\begin{bmatrix}
1 & \sqrt{5} + 1 \\
\frac{2}{2} & \frac{2}{2} \\
\end{bmatrix},
\begin{bmatrix}
1, 0, 1 \\
1, 0, 1 \\
1, 0, 1 \\
1, 0, 1 \\
\end{bmatrix},
\]

and \([1, 1, 1, 1, 1]\) we can determine several invariant subspaces in order to find lumping matrices. Choose, for example,

\[
Q = \begin{bmatrix}
1 & 1 & 1 & 1 & 1 \\
-1 & \sqrt{5} + 1 & -\sqrt{5} - 1 & 1 & 0 \\
-\sqrt{\frac{5}{2}} & \sqrt{\frac{5}{2}} & 1 & 0 & 1
\end{bmatrix}.
\]

In this case the lumped system will be

\[
\begin{bmatrix}
\dot{x}_1 \\
\dot{x}_2 \\
\dot{x}_3
\end{bmatrix} = \begin{bmatrix}
0 & 0 & 0 \\
0 & -\frac{5 + \sqrt{5}}{2}k & 0 \\
0 & 0 & -\frac{5 + \sqrt{5}}{2}k
\end{bmatrix} \begin{bmatrix}
\dot{x}_1 \\
\dot{x}_2 \\
\dot{x}_3
\end{bmatrix}.
\]

We can associate it to the model \( \dot{X}_2 \xrightarrow{\frac{5 + \sqrt{5}}{2}k} \mathcal{O} \xrightarrow{\frac{5 + \sqrt{5}}{2}k} \dot{X}_3 \).
5 Discussion, plans

The most important classes of compartmental systems have been reviewed from the point of view of symbolic lumpability. Practically interesting lumped systems mainly arise from numerical calculations, which can be carried out in all cases without difficulties. We used the sentence "which is the induced kinetic differential equation of the reaction" recurrently. However, given a kinetic differential equation the inducing reaction is by far not unique [Érdi, P., Tóth, J. (1978), pages 67–69].

6 Appendix

Suppose we are given two natural numbers, \( n \) and \( \hat{n} \), \( \hat{n} \leq n \), and an \( \hat{n} \times n \) matrix \( Q \) of full rank with real elements. The question arises: what are the necessary and sufficient conditions for the existence of a nonsingular \( \hat{n} \times \hat{n} \) matrix \( P \) such that all elements of \( PQ \) are nonnegative?

This question is hard enough to answer in a general case. Here is a result when \( \hat{n} \leq 2 \). One can see, if \( \hat{n} = 1 \), the elements of \( Q \) must have identical sign, for the existence of such \( P \).

Now, assume \( \hat{n} = 2 \), and take

\[
Q = \begin{bmatrix}
a_{11} & a_{12} & \ldots & a_{1n} \\
a_{21} & a_{22} & \ldots & a_{2n}
\end{bmatrix}. \tag{13}
\]

Furthermore, take

\[
P = \begin{bmatrix}
p_{11} & p_{12} \\
p_{21} & p_{22}
\end{bmatrix}. \tag{14}
\]

Then we obtain

\[
PQ = \begin{bmatrix}
a_{11}p_{11} + a_{21}p_{12} & a_{12}p_{11} + a_{22}p_{12} & \ldots & a_{1n}p_{11} + a_{2n}p_{12} \\
a_{11}p_{21} + a_{21}p_{22} & a_{12}p_{21} + a_{22}p_{22} & \ldots & a_{1n}p_{21} + a_{2n}p_{22}
\end{bmatrix}.
\]

The requirement is that all the elements of the matrix above should be non-negative real numbers. This assumption, i.e. the inequalities \( a_{1j}p_{i1} + a_{2j}p_{i2} \geq 0, \ j = 1, \ldots, n \) determine half-planes in the plane \((p_{i1}, p_{i2})\), passing through the origin, \( i = 1, 2 \). Thus, the problem is to find the cases, when the intersections of the corresponding planes (which is in accordance with the first, resp. the second row in \( PQ \)) are not empty.
Examine the columns of the matrix $Q$. We distinguish 9 cases. In what follows, the symbols $+$, and $-$ indicate the presence of a positive or a negative number in the matrix $Q$.

|   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
| 0 | 0 | + | + | 0 | - | - | - |
| 0 | - | - | 0 | + | + | 0 | - |

For example, suppose the $i$th column of $Q$ is of type 3, i.e. $a_{1i}$ is positive and $a_{2i}$ is negative. Then the inequality $a_{1i}p_{11} + a_{2i}p_{12} \geq 0$ corresponds to the case in the fig. 12.

![Fig. 12. A graphical representation for the case 3.](image)

The slope of the line with equation $a_{1i}p_{11} + a_{2i}p_{12} = 0$ depend on the number $-a_{1i}/a_{2i}$. Here this fraction is a positive number. The shaded region in the figure represents the region that is excluded from the solution.

Thus, after the geometrical consideration, we can conclude: if the matrix $Q$ contains columns of form $[a]$ and $[-a]$ simultaneously, $\forall a, b \in \mathbb{R}$, with $a$ and $b$ different from 0 at the same time, there does not exist nonsingular, $2 \times 2$ matrix $P$, which satisfies the requirement $PQ \geq 0$. This is the case when matrix $Q$ has a pair of columns of type 2 and 6, or 4 and 8, or 3 and 7, or 5 and 9. In the last two cases the elements could only differ in sign. Henceforth, for a shortest notation we will use 26,48,37,59 to point to pair of cases when the matrix $P$ does not exist.
Finding all the cases when the matrix $Q$ contains three columns which precisely exclude together the existence of $P$, we lean on the geometrical representation again. Assume $Q$ does not contain a pair of columns fitting the case described above. If we check the three half-plane cases, we get the following result: 247, 257, 258, 358, 368, 369, 469, 479 and 569 are the cases that exclude each other, i.e. the existence of $P$, by all means. Furthermore, there are other instances for the nonexistence of such a $P$, 259, 347, 357, 359, 367, 378, 379 and 459, but in these cases we still have to verify another condition regarding the slopes. This fact will be illustrated later in an example.

In the case of the intersection of four half-planes, assumed that we did not find in $M$ columns corresponding to either cases given earlier, we get only one case for empty intersection, specifically for 2358, i.e. for a matrix that contains the columns $\begin{bmatrix} 0 \\ -1 \end{bmatrix}$, $\begin{bmatrix} 1 \\ 0 \end{bmatrix}$, $\begin{bmatrix} 1 \\ +1 \end{bmatrix}$, $\begin{bmatrix} -1 \\ 1 \end{bmatrix}$ together, disregarding the order.

The cases presented previously exhaust all the cases, when to a $2 \times n$ matrix given in (13) we cannot find a $2 \times 2$ nonsingular matrix, $P$, so that all the elements of $PQ$ are nonnegative.

Let us take an example to illustrate the problem. Consider the matrix

$$Q = \begin{bmatrix} 5 & 2 & 2 & -3 \\ -2 & 0 & 1 & -1 \end{bmatrix},$$

and $P$ as in (14). Then

$$PQ = \begin{bmatrix} 5p_{11} - 2p_{12} & 2p_{11} & 2p_{11} + p_{12} & -3p_{11} - p_{12} \\ 5p_{21} - 2p_{22} & 2p_{21} & 2p_{21} + p_{22} & -3p_{21} - p_{22} \end{bmatrix},$$

whose elements must satisfy the system of inequalities:

$$\begin{align*}
5p_{11} - 2p_{12} & \geq 0, \\
2p_{11} & \geq 0, \\
2p_{11} + p_{12} & \geq 0, \\
-3p_{11} - p_{12} & \geq 0, \\
5p_{21} - 2p_{22} & \geq 0, \\
2p_{21} & \geq 0, \\
2p_{21} + p_{22} & \geq 0, \\
-3p_{21} - p_{22} & \geq 0.
\end{align*}$$

(15)

Consider the first four of them, and give a geometrical representation as in figure 13.
The picture was created with Maple program, and one can see, that in this case the inequality system (15) does not have any solution. This was only to be expected, because the matrix contains columns of type 3, 4, 5 and 9, and 359 is a critical case, since the slope of the line corresponding to case 9 is smaller than the one corresponding to 5, i.e. \(-(-3)/(-1) < -2/1\).

Notice that if we take \(a_{13} = 18\) in \(Q\), the situation will change, i.e. the existence of \(P\) will be insured, because in this case the direction of the inequality regarding the slopes will change, as it can be seen in Fig. 14.

Choose a point from the region that indicates the solution (the dark region in Fig. 14), such as \((p_{11}, p_{12}) = (1, -5)\). To determine \(p_{21}\) and \(p_{22}\) one must choose their values from the same region, except the case when the point \((p_{21}, p_{22})\) can be found on the line defined by the origin and the point \((p_{11}, p_{12}) = (1, -5)\).

The justification of this statement is as follows. The equation of the line that passes through the points \((0, 0)\) and \((p_{11}, p_{12})\) is \(y = (p_{12}/p_{11})x\). If \((p_{21}, p_{22})\) is a point on this line, then it must satisfy the relation \(p_{11}p_{22} - p_{12}p_{21} = 0\), which is equivalent to the condition \(\det P = 0\), but \(P\) cannot be singular. For example we can choose \((p_{21}, p_{22}) = (1/2, -4)\). In this case \(\det P = -3/2\). Now, check the nonnegativity of the elements of the matrix \(PQ\):

\[
PQ = \begin{bmatrix} 1 & -5 \\ \frac{1}{2} & -4 \end{bmatrix} \begin{bmatrix} 5 & 2 & 18 & -3 \\ -2 & 0 & 1 & -1 \end{bmatrix} = \begin{bmatrix} 15 & 2 & 13 & 2 \\ \frac{21}{2} & 1 & 5 & \frac{5}{2} \end{bmatrix}.
\]

Suppose we are given two natural numbers, \(n\) and \(\hat{n}\), \(\hat{n} \leq n\), and an \(\hat{n} \times n\) matrix \(Q\) of full rank with complex elements. The question arises, what are the necessary and sufficient conditions for the existence of a nonsingular \(\hat{n} \times \hat{n}\) matrix \(P\) such that all elements of \(PQ\) are real?

Observe that for \(\hat{n} = 1\), \(Q\) must have a special form to find a suitable \(P\) to it, i.e. we must have either \(Q = [im_1 \ im_2 \ \ldots \ im_n]\), with \(m_j \in \mathbb{R}, ~ j = 1, \ldots, n\),
or all the elements of $Q$ have to be real, but this is a trivial case.

Consider $\hat{n} > 1$ and $Q$ an $n \times \hat{n}$ matrix, with $Q = Q_1 + iQ_2$ where $Q_1, Q_2 \in \mathcal{M}_{\hat{n}n}(\mathbb{R})$. A sufficient condition for the existence of a $\hat{n} \times \hat{n}$ matrix $P$ such that all elements of $PQ$ are real is:

1. $Q_1$ and $Q_2$ are nonsingular;
2. $Q_1^TQ_2 = Q_2^TQ_1$.

In this case we can choose $P = Q_1^T - iQ_2^T$. Realize that if the conditions above are satisfied, then

$$PQ = (Q_1^T - iQ_2^T)(Q_1 + iQ_2) = Q_1^TQ_1 + iQ_1^TQ_2 - iQ_2^TQ_1 + Q_2^TQ_2$$

$$= Q_1^2 + Q_2^2 + i(Q_1^TQ_2 - Q_2^TQ_1) \in \mathcal{M}_{\hat{n}n}(\mathbb{R}).$$

In what follows suppose that the conditions above are not satisfied and take

$$Q = \begin{bmatrix}
a_{11} + ib_{11} & a_{12} + ib_{12} & \cdots & a_{1n} + ib_{1n} \\
a_{21} + ib_{21} & a_{22} + ib_{22} & \cdots & a_{2n} + ib_{2n} \\
\vdots & \vdots & \cdots & \vdots \\
a_{\hat{n}1} + ib_{\hat{n}1} & a_{\hat{n}2} + ib_{\hat{n}2} & \cdots & a_{\hat{n}n} + ib_{\hat{n}n}
\end{bmatrix},$$

$$P = \begin{bmatrix}
p_{11} + iq_{11} & p_{12} + iq_{12} & \cdots & p_{1\hat{n}} + iq_{1\hat{n}} \\
p_{21} + iq_{21} & p_{22} + iq_{22} & \cdots & p_{2\hat{n}} + iq_{2\hat{n}} \\
\vdots & \vdots & \cdots & \vdots \\
p_{\hat{n}1} + iq_{\hat{n}1} & p_{\hat{n}2} + iq_{\hat{n}2} & \cdots & p_{\hat{n}\hat{n}} + iq_{\hat{n}\hat{n}}
\end{bmatrix}.$$

The requirement that all the elements of $PQ$ are real is equivalent to a linear, homogeneous system

$$\hat{n} \sum_{j=1}^{\hat{n}} (p_{lj}b_{jk} + q_{lj}a_{jk}) = 0, \quad k = 1, n, \quad l = 1, \hat{n},$$

where the number of unknowns are $2\hat{n}^2$ and the number of equations are $\hat{n}n$. Notice that this system has an interesting property: it can be divided into independent subsystems regarding the unknowns. In this case each of these subsystems can be solved separately. Moreover, all of the results can be written in identical form, since they have the same coefficient-matrix. Therefore,
taking $l = 1$, consider and treat only the subsystem with $n$ equations

$$\sum_{j=1}^{\hat{n}} (p_{1j} b_{jk} + q_{1j} a_{jk}) = 0, \quad k = 1, \ldots, n,$$

with unknowns $p_{11}, p_{12}, \ldots, p_{1\hat{n}}$, and $q_{11}, q_{12}, \ldots, q_{1\hat{n}}$. Depending on $n$ and $\hat{n}$ the number of unknowns can be smaller or bigger than the number of equations. The coefficient-matrix is

$$\begin{bmatrix}
  b_{11} & b_{21} & \cdots & b_{\hat{n}1} & a_{11} & a_{21} & \cdots & a_{\hat{n}1} \\
  b_{12} & b_{22} & \cdots & b_{\hat{n}2} & a_{12} & a_{22} & \cdots & a_{\hat{n}2} \\
  \vdots & \vdots & \ddots & \vdots & \vdots & \vdots & \ddots & \vdots \\
  b_{1\hat{n}} & b_{2\hat{n}} & \cdots & b_{\hat{n}\hat{n}} & a_{1\hat{n}} & a_{2\hat{n}} & \cdots & a_{\hat{n}\hat{n}}
\end{bmatrix}.
$$

Denote by $d$ the main determinant for (18). Then, if $d \neq 0$, system (17) has identical zero solution: $(0, \ldots, 0)$, i.e. $\det(P) = 0$, so, $P$ does not satisfy the nonsingularity requirement.

For an adequate $P$ we must have $d = 0$. If it holds, we must specify the rank of (18). Let us denote it by $r$. If $r = 2\hat{n}$, i.e. the system (17) is determined, and has a unique solution. But in this case all the other subsystems mentioned above for (16) has the same (constant) solution. Thus, the matrix $P$ will consist of identical rows, so we have $\det(P) = 0$ again.

For $r = 2\hat{n} - 1$ the system is indefinite, and the solution has the form

$$(\alpha_1 c_1, \alpha_2 c_2, \ldots, \alpha_{2\hat{n}} c_{2\hat{n}}),$$

where $\alpha_i$ are parameters and $c_i$ represent constants, $i = 1, \ldots, 2\hat{n}$. Consequently, $P$ can be given in such a way that its rows will be $k$-times for the others. Thus, we discover a nonsingular $P$ once more.

Finally, if $r < 2\hat{n} - 1$, then there exists an adequate matrix $P$, because in this case the solution of (17) can be expressed with at least two parameters, and this gives possibility for choosing linearly independent lines to $P$.

Now, look at an example. Consider

$$Q = \begin{bmatrix} 1 + i & 2 + i & 4 + 2i & 2 + 2i \\ -1 & 2i & 4i & -2 \end{bmatrix}, \quad \text{and take} \quad P = \begin{bmatrix} p_{11} + iq_{11} & p_{12} + iq_{12} \\ p_{21} + iq_{21} & p_{22} + iq_{22} \end{bmatrix}.$$
In this case the coefficient-matrix (18) is

\[
\begin{bmatrix}
1 & 0 & 1 & -1 \\
1 & 2 & 2 & 0 \\
2 & 4 & 4 & 0 \\
2 & 0 & 2 & -2
\end{bmatrix},
\]

and for it \( r = 2 < 2\hat{n} - 1 \). Thus, we can compute a nonsingular \( P \in \mathcal{M}_{22}(\mathbb{C}) \). Since the homogeneous, linear system with coefficient-matrix above has solution \( (-\alpha + \beta, -\frac{1}{2}(\alpha + \beta), \alpha, \beta) \), we can take \( p_{11} = 0, p_{12} = 1, q_{11} = -1, q_{12} = -1 \) and similarly \( p_{21} = 2, p_{22} = 2, q_{21} = -3, q_{22} = -1 \). After some calculations we obtain

\[
PQ = \begin{bmatrix}
0 & 3 & 6 & 0 \\
3 & 9 & 18 & 8
\end{bmatrix}.
\]
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