

A NUMERICAL METHOD FOR THE IDENTIFICATION OF LINEAR COMPARTMENTAL SYSTEMS*

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Abstract

This paper deals with an inverse problem of a system of ordinary differential equations whose coefficient matrix is the so-called compartmental matrix. This problem arises in a variety of areas such as pharmacokinetics, biology, ecology, economics, and so on. A numerical method applicable to the cases of non-unique solutions is developed, by which the projection of the starting value of iteration onto the manifold of solution can be obtained. The convergence of the method is proved. A few examples are examined, which shows the effectiveness of the given method.

§ 1. Introduction

In recent years, a simple and effective mathematical model, called compartmental model, has been widely used in a variety of areas^[1]. It originated from pharmacokinetics (which is still one of the major fields for use of the compartmental model up to now), and was then applied gradually to other fields such as biology, ecology, medicine, chemistry, and even economics, to explore the quantitative law of transfer and exchange of mass or state. In biological and medical problems, it is used for explaining the processes of distribution, absorption, excretion or metabolism of medicinal, or physiological, or biochemical mass in organisms.

In this model, a system is considered to be made up of a finite number of parts. Each part is assumed to have a specified volume and a uniform distribution of mass (or a same state) at any time. The compartments interact with one another by exchanging the matter (or state). Exchange also occurs with the environment. To this exchange a certain law of conservation applies. A part satisfying the conditions mentioned above is called a compartment, and the whole system called compartmental system.

For instance, in pharmacological problems a part of human body which is homogeneous in drug density is taken as a compartment. (It is possible that different organs belong to one compartment, or one organ belongs to more than one compartment). The drug can diffuse between different compartments through biological membranes. Compartments are infused with drugs from environment by taking medicine or injection, and excrete drugs to environment through urine, excrement and sweat. The law of conservation of mass is valid.

In this paper the simplest case, the linear model, will be taken into consideration. The equations established according to the laws of conservation are usually of the following form:

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$$\begin{cases} \frac{dx(t)}{dt} = Ax(t) + F(t), \\ x(0) = x_0, \end{cases} \quad (1.1)$$

where

$$\begin{aligned} A &= \{a_{ij}\}_{n \times n} \\ a_{ij} &= K_{ij}, \quad i \neq j \\ a_{ii} &= -K_{oi} - \sum_{j=1}^n K_{ji}, \quad i, j=1, \dots, n; \end{aligned} \quad (1.2)$$

K_{ij} is the rate coefficient from compartment j to compartment i , with subscript o denoting the environment; $K_{ij} \geq 0$. Therefore, the matrix A has the following properties:

- 1) Its off-diagonal entries are non-negative.
- 2) Its diagonal entries are negative.
- 3) It is diagonally dominant with respect to the columns,

$$|a_{ii}| \geq \sum_{j=1, j \neq i}^n a_{ji}.$$

We call this kind of matrix compartmental matrix.

In problem (1.2), $F(t)$, $x(0)$ and measurements of part or all of the components of $x(t)$

$$\hat{x}_i(t_j), \quad i=1, \dots, r, \quad r \leq n; \quad j=1, \dots, m$$

are given. Our goal is to find the coefficient matrix A according to known data, that is, to find the solution A of the following least squares problem:

$$\sum_{i=1}^r \sum_{j=1}^m |x_i(t_j, A) - \hat{x}_i(t_j)|^2 = \min_{A \in M_0} \quad (1.3)$$

Here $x(t, A)$ is the solution of problem (1.2) with coefficient matrix A , and M_0 is the set of compartmental matrices

$$M_0 = \{A | a_{ii} < 0, a_{ij} \geq 0 \ (i \neq j), -a_{ii} \geq \sum_{j=1}^n a_{ji}, \ i, j=1, \dots, n\}. \quad (1.4)$$

This is a nonlinear least squares problem. The most common method for solving it is the Gauss-Newton method^[4]. But, some difficulties arise:

The problem is ill-posed. Sometimes its solution is not unique. The examples in § 5 will show the following possibilities in the case that the solution exists:

1. The solution is unique.
2. There is a finite number of solutions
3. There is an infinite number of solutions, which often form a continuous manifold.

For the third case mentioned above, the general Gauss-Newton method can not be used.

Even if the solution is unique, the problem is ill-conditioned, which causes rather large computational error.

To mitigate these difficulties, a numerical method is developed in this paper. Suppose that a rough approximation of the solution is known. Take it as the starting point of iteration. Then an iterative technique based on Tikhonov's regularization^[6] is given to approximate the projection of the starting value onto the manifold of