Structural identifiability of strongly connected biological compartmental systems*

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Abstract—*The paper deals with the evaluation of the* a priori *possibility of estimating the unknown parameters of a system having a known structure via an input–output experiment (structural identifiability). The problem is analysed with reference to biological compartmental systems (and precisely to a specific but largely representative class of these systems, i.e. the so-called strongly connected compartmental systems). The analysis is developed by using concepts and methods of system theory and particularly the concepts of 'controllability' and 'observability (i.e. the possibility of influencing the behaviour of the whole system by the input and of estimating it from the output). Two new theorems are proved concerning the necessary and sufficient conditions for the observability and controllability of strongly connected compartmental systems. On the basis of these theorems, a structural identifiability criterion is established and a digital-computer implementation technique for this criterion is given. Some typical tracer-analysis experiments on biological compartmental systems are analysed with the aim of evaluating how many and which parameters of the considered model can be estimated through the chosen input–output experiments.*

Keywords—*Biological compartmental systems, Compartmental mathematical models, Controllability Observability and structural identifiability, Parameter estimation, Input–output tracer experiment,*

1 Introduction

In biomedical engineering, compartmental mathematical models have been more and more used both in research problems (e.g. kinetics of distribution of materials through the organism, pharmacology, chemical kinetics etc.) and in diagnosis and therapy (e.g. clinical pharmacology, pharmacotherapy etc.).

This paper deals with a problem of considerable practical importance in the utilisation of compartmental models; in fact, before performing the experiment on a biological system, for which a compartmental model has been adopted in order to find the values of its parameters, it is necessary to analyse the possibility of estimating the model parameters from the chosen input–output experiment. A solution to this problem is particularly important in the study of *in vivo* phenomena, as the experiment is often non-repeatable because of induced harm, high cost, technical impossibility, trouble etc. (e.g., an experiment involving the injection of radioactive substances).

In the usual terminology of system theory, the methods for estimating the unknown parameters of a system from input–output experiments are called, as is well known, 'identification' methods; therefore the problem considered here is an 'identifiability' problem. As the adopted approach refers only to the system structure, it may be called a 'structural identifiability' problem.

In spite of its inherent interest, the problem of structural identifiability has been considered in the literature only recently (Bellman and Aström, 1970; Hájek, 1972). More precisely, Bellman and Aström (1970) put the problem of structural identifiability in a system-theory context and state precise general definitions. Hájek (1972) provides solution techniques for linear invariant compartmental systems open to the environment, only for the one-input/one-output case (and not directly extendable to multi-input/multi-output case) under restrictive conditions.

The present paper deals with the same matter, but treats it for a more general case than that considered by Hájek (1972) (multi-input/multi-output strongly connected systems, both closed and open to the environment; precise definitions will be given in Section 2). As in the paper by Bellman and Aström (1970), concepts and methods of system theory are adopted, particularly those of controllability (the possibility of influencing independently each state of the system through the inputs) and observability (the possibility of reconstructing each state of the system from the outputs). For the class of strongly connected compartmental systems, a largely representative class of biological systems, two new theorems are proved relating controllability and observability to the

* *First received 29th July and in final form 2nd December 1974*

system structure. The requested conditions stated by the two theorems allow us to establish a structural identifiability criterion. The check of controllability, observability and structural identifiability may be implemented on a digital computer; the corresponding flow chart is given. Examples of tracer-analysis experiments on several biological compartmental systems taken from biomedical literature (bilirubin metabolism, ferrokinetics and thyroxine distribution) are reported.

2 Study of compartmental systems in a system-theory context

2.1 *Controllability, observability and identifiability*

Basic concepts on biological compartmental systems are adequately described in the biomedical literature (see, for instance, SHEPPARD, 1962; RESCIGNO and SEGRE, 1966; ATKINS, 1969; JAQUEZ, 1972; COBELLI *et al.*, 1974). The fundamentals of system theory have also been described (see, for instance, ZADEH and DESOER, 1963; KALMAN, 1963; CHEN, 1970).

In any case, in order to state precisely the terminology and symbols used it seems useful to report some definitions and fundamental relations. Compartmental systems may be studied by linear-system-theory methods. In this context they are described as dynamical, linear, time-invariant systems in their usual input–state–output form:

$$\dot{\mathbf{x}} = A\mathbf{x}+B\mathbf{u} \qquad (1)$$

$$\mathbf{y} = C\mathbf{x} \qquad (2)$$

where $\mathbf{x}$, $\mathbf{u}$ and $\mathbf{y}$ are the state, input and output vectors, respectively.

With reference to the specific form of the compartmental systems, matrices A, B and C show peculiar characteristics. The order n of matrix A is equal to the number of system compartments; its entries are related to the rate constants of the compartmental system by the following equations:

$$a_{ij} = k_{ij} \qquad i \neq j \qquad (3)$$

$$a_{ii} = -k_{oi} - \sum_{j=1}^{n} k_{ji} \qquad (4)$$

where k_{ij} is the rate constant from compartment j to i and k_{oi} is the rate constant from compartment i to the environment. From eqns. 3 and 4, it follows that the eigenvalues of matrix A cannot be purely imaginary and have nonpositive real parts (HEARON, 1963).

Matrix B is of $n \times r_b$ dimension, where $r_b \leqslant n$ is the number of inputs; its entries can assume either value 1 or value 0 under the following conditions:

$$\sum_{i=1}^{n} b_{ij} = 1 \qquad \forall j \qquad (5)$$

$$\sum_{j=1}^{r_b} b_{ij} = \begin{cases} 0 & i \neq i_1, i_2, \ldots, i_{r_b} \\ 1 & i = i_1, i_2, \ldots, i_{r_b} \end{cases} \qquad (6)$$

Matrix C is of dimension $r_c \times n$ where $r_c \leqslant n$ is the number of outputs; its entries can assume either value 1 or value 0 under the following conditions:

$$\sum_{j=1}^{n} c_{ij} = 1 \qquad \forall i \qquad (7)$$

$$\sum_{i=1}^{rc} c_{ij} = \begin{cases} 0 & j \neq j_1, j_2, \ldots, j_{r_c} \\ 1 & j = j_1, j_2, \ldots, j_{r_c} \end{cases} \qquad (8)$$

As was seen in Section 1, heuristically, a system is said to be controllable if all state variables can be independently modified through the inputs, and it is said to be observable when the outputs allow us to reconstruct all the state variables.

As is well known, the above properties may be ascertained by some tests. Rigorous treatments on this subject can be found in the system-theory literature (ZADEH and DESOER, 1963; KALMAN, 1963; CHEN, 1970).

Referring to current criteria, a linear invariant system is completely controllable (c.c.) if and only if the composite $n \times (n-r_b+1).r_b$ matrix (controllability matrix)

$$P = [B|AB|A^2 B|\ldots|A^{n-r_b} B] \qquad (9)$$

is of rank n, and it is completely observable (c.o.) if and only if the composite matrix $(n-r_c+1).r_c \times n$ (observability matrix)

$$Q = [C'|A'C'|A^{2\prime}C'|\ldots|A^{n-r_c\prime}\, C'] \qquad (10)$$

(C' = transpose of C) is of rank n, where n is the order of the system and r_b and r_c are the ranks of matrices B and C.

The input–output behaviour of a c.c. and c.o. system is completely described by its transfer-function matrix $G(s)$. Laplace-transforming eqns. (1) and (2), the relation between input and output vectors can be obtained in the form

$$Y(s) = G(s).U(s) = C.(sI-A)^{-1}.B.U(s) \qquad (11)$$

According to matrix-inversion rules, $G(s)$ may be written in terms of the adjoint matrix of $(sI-A)$

$$G(s) = \frac{1}{\det(sI-A)} C.\mathrm{adj}\,(sI-A).B \qquad (12)$$

The knowledge of $G(s)$ allows the estimation of a certain number of system parameters; the maximum of this number equals the number of independent coefficients of numerator and denominator polynomials of the entries of $G(s)$.

A c.c. and c.o. compartmental system is said to be structurally identifiable when the chosen input–output experiment allows the estimation of all the unknown parameters (rate constants).

If the whole compartmental system is not both c.c. and c.o., the considerations on structural identifiability are to be restricted to the c.c. and c.o. part of the system.

2.2 *Some properties of strongly connected compartmental systems*

Some statements and definitions, useful for the following, are reported in this Section. A compartmental system is strongly connected when every compartment can be reached from every compartment of the system along one path* at least.

Let us consider two matrices K and K_o formed by the rate constants (see eqns. 3 and 4). Matrix K is a square matrix of n rows, where n is the number of compartments, and groups the rate constants between compartments; all its entries are non-negative, and those of the main diagonal are zero. Matrix K_o is a row matrix with n entries, and groups the rate constants from compartments to the environment. If all the entries of K_o are zero the system is said to be closed, otherwise it is open.

The entries of K^r (i.e. the rth power of K) are given by

$$[K^r]_{ij} = \sum_{l_1, l_2, \ldots, l_{r-1}=1, n} k_{il_1} k_{l_1 l_2} \ldots k_{l_{r-1} j} \quad . \quad . \quad (13)$$

Therefore $[K^r]_{ij} > 0$ implies that at least one path of length† r exists that connects compartment j to compartment i.

If matrix

$$R^{(m)} = \sum_{r=1}^{m} K^r$$

is considered, it can be noticed that $[R^{(m)}]_{ij} > 0$ implies that at least one path of length smaller than or equal to m exists connecting compartment j to compartment i. It follows that all entries of matrix $R^{(n)}$ of an n-compartment strongly connected system are positive.

3 Theorems on controllability and observability in a structural sense of strongly connected compartmental systems

A compartmental system can be non-c.c. and/or non-c.o. either because of its own structure or because of a particular combination of the parameter values $\{k_{ij}\}$. In the first case the rank of matrix P and/or Q is always less than n for whatever values of rate constants relative to the system of fixed structure (unchanged topology).

*As is well known in graph theory a path is a succession of branches without bifurcations, that is a subgraph such that each node has at most one entering and at most one outgoing branch and the output node of a branch is also the input node of the next branch of the succession. In compartmental-system theory the notion of a path is usually adopted with reference to a flow-graph representation of the system, where compartments are represented by nodes and rate constants by branches

† The length of a path is the number of its branches

Therefore it seems useful to state the following definition: a compartmental system is said to be non-c.c. (non-c.o.) in a structural sense when it is non-c.c (non-c.o.) for all possible values of the parameters $\{k_{ij}\}$ structurally different from zero.

Two new theorems relating strong connection to controllability and observability are now proved.

Theorem 1: Strong connection is a necessary condition for a compartmental system to be c.c. through any input and c.o. through any output.

Proof by contradiction: Suppose the system is not strongly connected, i.e. there are two compartments, numbered 1 and n for convenience, such that no path exists from 1 to n. Let

$$B = \begin{bmatrix} 1 \\ 0 \\ \vdots \\ 0 \end{bmatrix} \qquad C = [0 \ldots 01] \quad . \quad . \quad . \quad (14)$$

In this case, the entries of the last row of the controllability matrix P:

$$[B]_{n1} | [A]_{n1} | [A^2]_{n1} | \ldots | [A^{n-r_b}]_{n1} \quad . \quad . \quad . \quad (15)$$

are all zero, because compartment n cannot be reached along any path from compartment 1. The rank of P is therefore less than n. The hypothesis is therefore contradicted; q.e.d.

A similar proof holds for the complete-observability condition (the entries of the first column of the observability matrix Q are all zero).

Theorem 2: Strong connection is a sufficient condition for a compartmental system to be both c.c. and c.o. in a structural sense.

Proof: It is necessary to prove that, under such a hypothesis, matrices P and Q cannot have an identically null determinant for any input and any output. It will be proved that P and Q have neither its rows or columns identically null, nor linearly dependent.

With respect to controllability, let:

$$B = \begin{bmatrix} 1 \\ 0 \\ \vdots \\ 0 \end{bmatrix} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (16)$$

Let compartments be numbered as follows: from 2 to r_1 those reached by a path of length 1 from compartment 1, from r_1+1 to r_2 those reached by a path of length 2 from 1, and so on.

Because of the strong connection, all elements on the main diagonal of P are evidently positive; then no null rows or columns can exist. At this point, it can be noticed that:

(*a*) there is no linear dependence either between row 1 and the rows from 2 to r_1, or between these last rows and the rows from r_1+1 to r_2, and so on, since, because of the chosen numbering, entries p_{i1} for $i = 2, 3, \ldots, n$, p_{i2} for $i = r_1+1, r_1+2, \ldots, n$ etc. are zero;

(*b*) there is no linear dependence either among the rows from 1 to r_1, or among those from r_1+1 to r_2 and so on, as each of their entries is a sum of monomials, one of which does not appear in any other entry; q.e.d.

A similar procedure is used for the proof concerning observability. Let

$$C = [1\ 0\ \dots\ 0] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (17)$$

Compartments are numbered by considering the paths from each of them to compartment 1. The remarks made on matrix P also hold for matrix Q.

It is obvious that the proof can be extended to the multi-input and/or multi-output case. Theorem 2 allows us to state that the rank of matrices P and Q can be less than n only in a subspace of the $\{k_{ij} > 0\}$ space. In fact, in the case of one-input/one-output systems, each of the equations $\det P = 0$ and $\det Q = 0$ is the general expression of a hypersurface, therefore the non-c.c. and non-c.o. subspaces are represented by hypersurfaces. For the multi-input/multi-output case, there are as many hypersurface equations as there are submatrices of rank n of matrix P and Q, respectively. Non-c.c. and non-c.o. subspaces are then represented by the intersections of the hypersurfaces described by the equations relative to the considered submatrices of P and Q, respectively.

4 Structural identifiability of strongly connected compartmental systems

As was proved in Section 3, strong connection is a necessary and sufficient condition for a compartmental system to be c.c. and c.o. Therefore a test on $R^{(n)}$, according to Section 2.2, assures controllability and observability. As seen in Section 2.1 the input–output behaviour of a c.c. and c.o. compartmental system is completely described by the transfer-function matrix $G(s)$ (see eqn. 12).

When the whole system is completely controllable through input j and completely observable through output i, there are no cancellations in $[G(s)]_{ij}$ (the transfer function between input j and output i), and the denominator has maximum degree. As previously proved, such a condition is satisfied by each pair ij of a strongly connected compartmental system; in such a case all transfer functions $[G(s)]_{ij}$ have the same denominator.

To determine the number of coefficients that can be estimated, the series expansions of $\det(sI-A)$ and $C.\mathrm{adj}(sI-A).B$ are considered (Chen, 1970; Gantmacher, 1959). The first one is expanded as follows:

$$\det(sI-A) = s^n+\alpha_1 s^{n-1}+\alpha_2 s^{n-2}+\dots+\alpha_n \quad . \quad (18)$$

where: $\alpha_i > 0$ for $i = 2, \dots, n-1$, $\alpha_n > 0$ for open systems and $\alpha_n = 0$ for closed systems.

Properties of α_i follow from the properties of the eigenvalues of A.

adj $(sI-A)$ is expanded as follows:

$$\mathrm{adj}(sI-A) = R_0 s^{n-1}+R_1 s^{n-2}+\dots+R_{n-1} \quad . \quad (19)$$

where

$$\begin{aligned} R_0 &= I \\ R_1 &= A+\alpha_1 I \\ R_2 &= A^2+\alpha_1 A+\alpha_2 I \\ &\vdots \\ R_{n-1} &= A^{n-1}+\alpha_1 A^{n-2}+\dots+\alpha_{n-1} I \quad . \quad . \quad (20) \end{aligned}$$

and α_i for $i = 1, \dots, n-1$, as in the expansion of $\det(sI-A)$, are all positive.

From eqns. 12, 18, 19 and 20,

$$\begin{aligned} G(s) = \frac{1}{\det(sI-A)} &[CB(s^{n-1}+\alpha_1 s^{n-2}+\dots+\alpha_{n-1}) \\ &+CAB(s^{n-2}+\alpha_1 s^{n-3}+\dots+\alpha_{n-2}) \\ &+\dots+CA^{n-2}B(s+\alpha_1)+CA^{n-1}B] \qquad (21) \end{aligned}$$

$[G(s)]_{ij}$ has the same expression as $G(s)$ if we take $[CB]_{ij}$, $[CAB]_{ij}$, ..., $[CA^{n-1}B]_{ij}$, respectively.

About the denominator common to all entries of $G(s)$ and the corresponding numerators, the following remarks can be made:

(i) The denominator is of degree n, and the coefficient of s^n is always 1, therefore n parameters can be estimated in the case $\alpha_n \neq 0$ (open systems), and $n-1$ in the case $\alpha_n = 0$ (closed systems).

(ii) The numerator, if $[CB]_{ij} = 1$, is of degree $n-1$, and the coefficient of s^{n-1} is 1; therefore $n-1$ parameters can be estimated. If $[CA^{l-1}B]_{ij} = [CA^{l-2}B]_{ij} = \dots[CB]_{ij} = 0$ and $[CA^lB]_{ij} \neq 0$, the numerator is of degree $n-l-1$ and the coefficient of the maximum-degree term is a function of $\{k_{ij}\}$, therefore the number of the parameters that can be estimated is $n-l$. Notice that $[CA^lB]_{ij} \neq 0$ implies $[CA^{l+1}B]_{ij} \neq 0$.

Obviously the system is structurally identifiable when the number of parameters that can be estimated from $G(s)$ is not smaller than the number of the unknown system parameters. The existence of redundance does not influence structural identifiability, but is useful for a better numerical parameter estimation, as the measures are generally corrupted by noise.

5 Flow chart for a check of structural identifiability on strongly connected compartmental systems and some operative notes

In this Section, the results obtained in Sections 3 and 4 are utilised for the digital-computer implementation of a program able to perform an analysis of structural identifiability of strongly connected compartmental systems.

In Fig. 1, the flow chart of the program is reported. The main operations are:

(i) input of K, K_0, B and C

(ii) checking strong connection through $R^{(n)}$

(iii) checking structural identifiability through $G(s)$.

Notice that K and K_0 are matrices of binary entries ($k_{ij} = 1$ if a transfer from j to i exists, $k_{ij} = 0$ if it does not). Matrix A is computed as follows: $a_{ij} = k_{ij}$ for $i \neq j$; $a_{ii} = 1$ if $k_{oi} = 1$ or $k_{ij} = 1$ for some j, otherwise $a_{ii} = 0$.

The program, written in PL1 language, was tested on a 370/158 IBM computer through a 2741 terminal.

When the chosen experiment does not allow the model to be identified, some different procedures can be adopted. When possible, either a different experiment is chosen or a different model is developed that can be identified by the chosen experiment; otherwise the problem can be accurately analysed and some relations sought among the parameters which are to be estimated. In examining these possibilities the biological phenomena are always taken into account; sometimes it is impossible to change the input–output experiment, in some other cases there is no further information about the coefficients, not even about the possibility of neglecting some of them.

6 Example

In this Section, some significant biological compartmental systems are considered, and concepts and methods developed in the paper are applied to analyse their structural identifiability. The procedure is examined in detail only for the first example, but results are reported for the other examples.

6.1 *Bilirubin metabolism*

A 3-compartment model (Berk *et al.*, 1967), extravascular spaces-1, plasma-2 and liver-3, is

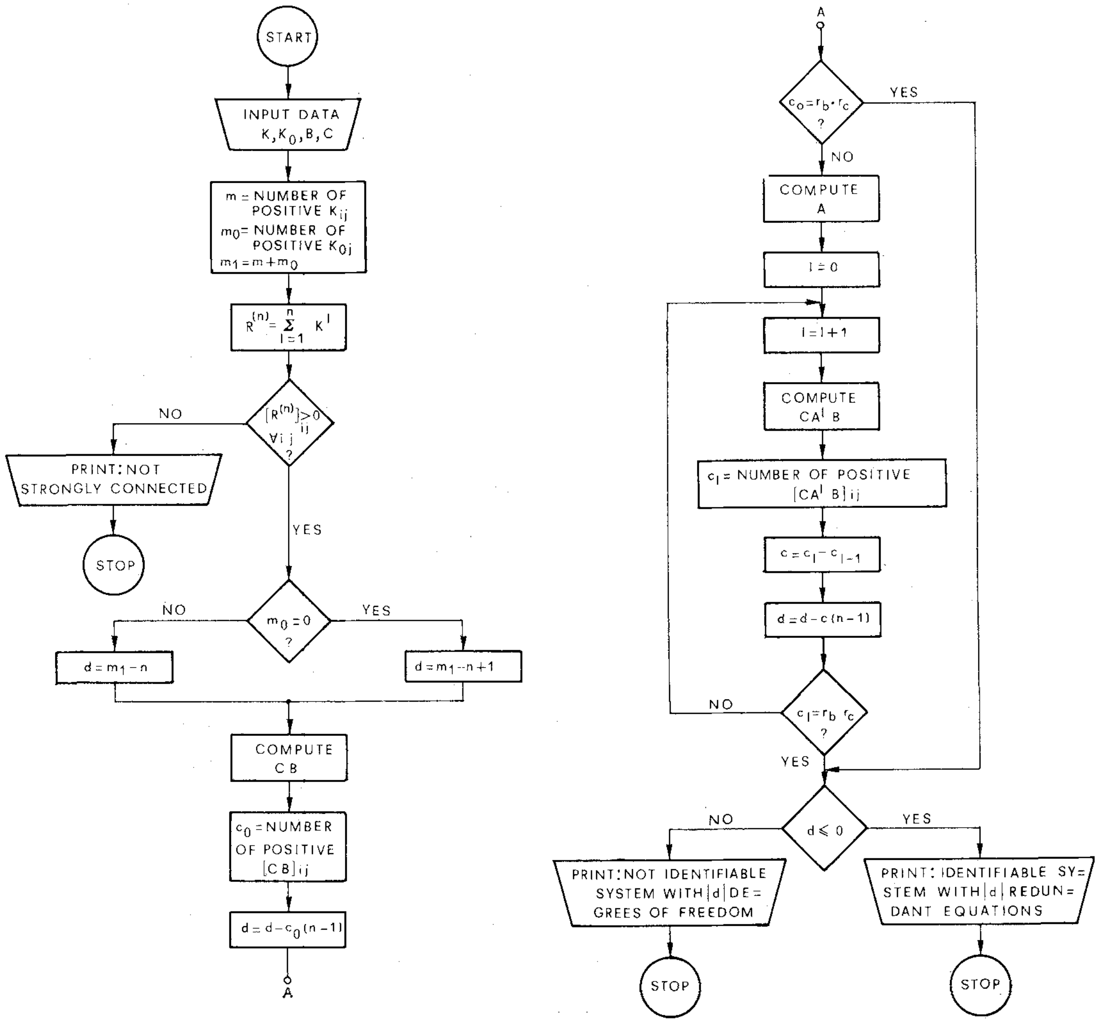

Fig. 1 Flow chart for a check of structurally identifiability of strongly connected compartmental systems

reported in Fig. 2. Exchanges between plasma and extravascular spaces are slower than those between plasma and liver. The experiment is performed with input (injection of radioactive tracer) and output in compartment 2.

Matrices K, K_o are

$$K = \begin{bmatrix} 0 & k_{12} & 0 \\ k_{21} & 0 & k_{23} \\ 0 & k_{32} & 0 \end{bmatrix} \quad K_0 = [0 \quad 0 \quad k_{03}]$$

It can be observed that if $R^{(3)} = \sum_{l=1}^{3} K^l$ has all

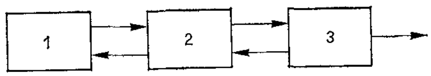

Fig. 2 3-compartment model of bilirubin metabolism

entries positive, the model is strongly connected and is therefore c.c. and c.o.

Matrices A, B and C are

$$A = \begin{bmatrix} -k_{21} & k_{21} & 0 \\ k_{21} & -k_{12}-k_{32} & k_{23} \\ 0 & k_{32} & -k_{23}-k_{03} \end{bmatrix}$$

$$B = \begin{bmatrix} 0 \\ 1 \\ 0 \end{bmatrix}; \quad C = [0 \quad 1 \quad 0]$$

From the expression det $(sI - A)$ (see eqn. 18), it follows that three parameters can be estimated from the denominator of $[G(s)]_{22}$ as the system is open.

Table 1. Computer run of the program for the 3-compartment model of bilirubin metabolism

```
GIVE NUMBER OF COMPARTMENTS
? 3

GIVE K
? 0,1,0
?? 1,0,1
?? 0,1,0

GIVE KO
? 0,0,1

STRONGLY CONNECTED SYSTEM

GIVE NUMBER OF INPUTS
? 1

GIVE: INPUTS IN COMPARTMENTS
? 2

GIVE NUMBER OF OUTPUTS
? 1

GIVE: OUTPUTS IN COMPARTMENTS
? 2

THE SYSTEM IS STRUCTURALLY IDENTIFIABLE
WITH 0 REDUNDANT EQUATIONS
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From $CB = 1$, it follows that two more parameters can be estimated from the numerator, therefore the system is identifiable without redundant equations, as the number of unknown parameters is five.

The computer run of the program for this example is shown in Table 1.

The 3-compartment model represents the biological phenomenon when the output experiment lasts for at least 48 h. Very often the experiment is limited to 4–8 h.; in this case bilirubin metabolism can be studied with the 2-compartment model (BARRET *et al.*, 1968; COBELLI *et al.*, 1974) of Fig. 3, for plasma-1 and liver-2.

Here the experiment is performed with the input (injection of radioactive tracer) and output in compartment 1. In this case too, the system is structurally identifiable without redundant equations

6.2 *Ferrokinetics*

A 4-compartment model (JOHNSON *et al.*, 1973), for

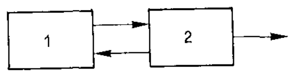

Fig. 3 2-compartment model of bilirubin metabolism

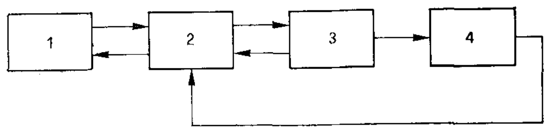

Fig. 4 4-compartment model of ferrokinetics

extravascular spaces-1, plasma-2, bone marrow-3 and red blood cells-4, is reported in Fig. 4.

The experiment is performed with the input (injection of radioactive tracer) and output in compartment 2. It can be proved that the system is structurally identifiable without redundant equations. If a second output in compartment 4 is provided, there are three redundant equations.

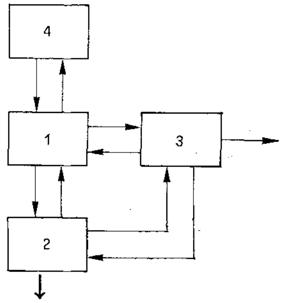

Fig. 5 4-compartment model of thyroxine distribution

6.3 *Thyroxine distribution*

A 4-compartment model (SHARNEY *et al.*, 1965; NICOLOFF and DOWLING, 1968), for interstitial fluids-1, liver-2, plasma-3 and other organs and/or tissues-4 is reported in Fig. 5. Exchanges between compartments 1–2 are slower than those between compartments 1–3 and 2–3; exchanges between 4–1 are slower than those between 1–2. Moreover, outputs from compartments 2 and 3 due to metabolism and excretion, respectively, may be considered as negligible in a first approximation (BENETAZZO *et al.*, 1972).

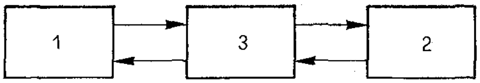

Fig. 6 3-compartment model of thyroxine distribution

The experiment with the input (injection of radioactive tracer) and output in compartment 3 allows us to estimate only seven of the ten unknown parameters; therefore the system is not structurally identifiable via the chosen input–output experiment.

In this case, two procedures can be followed for system identification as seen in Section 6: the first consists in modifying the input–output experiment, when it is physiologically realisable without trouble, the second consists in adopting a model of 'lightly' modified structure from the previous one, but still sufficiently approximate and therefore significant.

For the model of Fig. 5, both procedures can be followed.

In the modified input–output experiment, compartment 2 is also observed: in this case the system is structurally identifiable. A suitably acceptable simplification of the model neglects exchanges between compartments 1–4 and 1–2 and assumes the system to be closed (BENETAZZO *et al.*, 1972) (Fig. 6). In this case, the initially chosen input–output experiment in compartment 3 implies that the system is structurally identifiable.

7 Conclusions

In this paper, the structural identifiability of biological strongly connected compartmental systems has been analysed.

Concepts and methods of linear system theory have been applied to compartmental systems in order to define controllability, observability and structural identifiability.

The relation between strong connection and the properties of controllability and observability has been proved.

The results of the proved theorems make possible an analysis of structural identifiability of strongly connected compartmental systems through the transfer-function matrix $G(s)$. A simple criterion, based on a series expansion of $G(s)$, allows us to check quickly the maximum number of identifiable parameters of the compartmental system.

A flow chart for a digital computer implementation of the whole procedure has been presented.

Finally, the procedure has been applied to several examples concerning biological compartmental systems.

Acknowledgments—The authors wish to thank Prof. A. Lepschy of the Istituto di Elettrotecnica ed Elettronica, Università di Padova, Italy, for their interest and his helpful suggestions.

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Identifiabilite structurelle des systèmes biologiques compartimentés à liaison forte

Sommaire—L'article présente l'évaluation de la possibilité d'estimer à priori les paramètres inconnus d'un système ayant une structure connue, à l'aide d'une expérience entrée-sortie (Identifiabilite structurelle).

Le problème est analysé avec référence aux systèmes biologiques compartimentés (et précisément avec une catégorie spécifique mais bien représentative de ces systèmes, c'est à dire les systèmes compartimentés à liaison forte ainsi nommés). L'analyse est développée à l'aide de concepts et de méthodes pour une théorie de système et en particulier les concepts de 'contrôlabilité' et d''observabilité' (c'est à dire la possibilité d'influencer le comportement de tout le système avec l'entrée et de l'estimer à partir de la sortie).

On démontre deux théorèmes nouveaux se rapportant aux conditions nécessaires et suffisantes pour l'observabilité et la controlabilité des systèmes compartimentés à liaisons fortes. A partir de ces théorèmes, on établit un critère d'identifiabilite structurelle et on donne la mise en effet technique de calcul numérique de ce critère.

Quelques expériences typiques d'analyse de tracés sur des systèmes biologiques compartimentés sont données dans le but d'évaluer le nombre et ceux des paramètres du système considéré pouvant être estimés par l'intermédiaire des expériences entrée-sortie choisies.

Strukturelle Identifizierbarkeit von stark verbundenen biologischen Zellensystemen

Zusammenfassung—Der Aufsatz befaßt sich mit der Beurteilung einer a priori Möglichkeit, die unbekannten Parameter eines Systems mit einer bekannten Struktur über ein Eingabe/Ausgabe-Experiment zu errechnen (strukturelle Identifizierbarkeit).

Das Problem wird in bezug auf biologische Zellensysteme analysiert (und genauer gesagt in bezug auf eine spezifische, jedoch weitgehend repräsentative Klasse dieser Systeme, d.h. die sogenannten stark verbundenen Zellensysteme). Die Analyse wird entwickelt durch Verwnedung von Konzepten und Verfahren der Systemtheorie und insbesondere von Konzepten der Kontrollierbarkeit und Beobachtungsmöglichkeit (d.h. der Möglichkeit, das Verhalten des gesamten Systems durch die Eingabe zu beeinflussen und es durch die Ausgade zu berechnen).

Hinsichtlich der notwendigen und ausreichenden Bedingungen für die Beobachtungsmöglichkeit und Kontrollierbarkeit von stark verbundenen Zellensystemen werden zwei neue Lehrsätze bewiesen. Auf Grund dieser Lehrsätze wird ein Kriterium für die strukturelle Identizierbarkeit aufgestellt, und es wird eine digitale Rechnereinsatztechnik für dieses Kriterium angegeben.

Gewisse typische Spurenmaterialanalysen-Experimente an biologischen Zellensystemen werden analysiert um zu beurteilen, wie viele und welche Parameter des berücksichtigten Modells durch die gewählten Eingabe/Ausgabe-Experimente berechnet werden könenn.