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ORIGINAL PAPER

Linear compartmental systems. I. kinetic analysis and derivation of their optimized symbolic equations

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Abstract The study of many biological systems requires the application of a compartmental analysis, together with the use of isotopic tracers, parameter identification and methods to evaluate the mean parameters. For all this, the kinetic equations of the compartmental system as a function of its parameters are needed. In this paper, we present some considerations on the diagrams of connectivity of linear compartmental systems and obtain new properties from the matrix corresponding to the ordinary first-order linear differential equation systems which describe their kinetic behaviour. Using these properties, symbolic equations are obtained in a simplified form. These equations provide the instantaneous amount of substance in any compartment of the system when zero input is injected into one or more of the system compartments,

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solely as a function of those parameters of compartmental systems which really have an influence on the sought expression. This is unlike what happens in the other symbolic equations obtained in a previous contribution that included all the fractional transfer coefficients involved in the compartmental system, regardless of whether or not they had an influence on the instantaneous amount of substance.

Keywords Compartmental system · Linear · Open–closed · Kinectics · Symbolic equations

1 Introduction

A compartmental model originating from the pharmacokinetics field where a deterministic, hypothetical and simplified approximation allows the behaviour of drug concentrations in mathematical terms to be described [1,2]. From this classical perspective, and for model construction purposes, all those structures that take a similar blood flow or affinity by the tracer are considered a compartment; therefore, the drug concentration is the same. Thus, the wide use of these dynamic models extends in parallel with the increasing use of stable isotopes in human systems, together with simulation technologies [3,4].

The majority of known drugs that act on the human organism present an absorption, distribution and elimination first-order linear kinetics, and its specific receipts are joined reversiblely and are totally excreted,, therefore behaving like an open system [5,6]. The study of the kinetics behaviour of drugs by means of compartmental models leads, on the one hand, to the evaluation of those parameters related to the absorption, distribution and elimination of drugs and their metabolites, whose measure cannot be taken directly and, on the other hand, to the prediction of behaviour in non accessible places and its time course [7]. Interest in the use of compartment models to define, identify and describe different very important systems in Biology, Medicine, Physiology, Pharmacology, Nutrition, Toxicology, Biochemistry or Kinetic Enzymes has grown in recent years [3,8–24]. Standard and very complete references on compartmental modelling and analyses are those of [25–34]. The kinds of model considered consist in a finite number of compartments related to the transfer rates that control the reaction between them. A compartment may be actually physical or an abstract representation of it [6,7,28,35,36].

The global study of compartmental systems involves the application of determinants and matrix [25], the use of graphic methods [37,38], iterative methods [39] or other methods which require the inversion of matrices. For this reason, systems with a matrix that is not invertible generally have no solution [40,41].

Varon et al. [30] and Garcia-Meseguer et al. [10] developed a kinetic compartmental system analysis of the model parameters (initial amount of substance in each compartment and the fractional transfer coefficients corresponding to the direct connection between compartments).

Such analyses overcome many of the aforementioned difficulties through the introduction of algorithms which facilitate the deduction of kinetic equations (30), while the second analysis mentioned [10] represents a slight improvement over the first one in that it uses symbolic coefficients which are always positive. In these contributions, the symbolic expressions of the coefficients in the kinetic equations were obtained by