

# IDENTIFIABILITY OF LINEAR COMPARTMENT MODELS: THE SINGULAR LOCUS

ELEAZBETH GROSS, NICOLETTE MESHKAT, AND ANNE SHIU

**ABSTRACT.** This work addresses the problem of identifiability, that is, the question of whether parameters can be recovered from data, for linear compartment models. Using standard differential algebra techniques, the question of whether a given model is generically locally identifiable is equivalent to asking whether the Jacobian matrix of a certain coefficient map, arising from input-output equations, is generically full rank. We give a formula for these coefficient maps in terms of acyclic subgraphs of the model's underlying directed graph. As an application, we prove that two families of linear compartment models, cycle and mammillary (star) models with input and output in a single compartment, are identifiable, by determining the defining equation for the locus of non-identifiable parameter values. We also state a conjecture for the corresponding equation for a third family: catenary (path) models. These singular-locus equations, we show, give information on which submodels are identifiable. Finally, we introduce the *identifiability degree*, which is the number of parameter values that match generic input-output data. This degree was previously computed for mammillary and catenary models, and here we determine this degree for cycle models. Our work helps shed light on the question of which linear compartment models are identifiable.

## 1. INTRODUCTION

This work focuses on the identifiability problem for linear compartment models. Linear compartment models are used extensively in biological applications, such as pharmacokinetics, toxicology, cell biology, physiology, and ecology [2, 3, 7, 9, 12]. Indeed, these models are now ubiquitous in pharmacokinetics, with most kinetic parameters for drugs (half-lives, residence times, and so on) based at least in part on linear compartment model theory [13, 18].

A mathematical model is *identifiable* if its parameters can be recovered from data. Using standard differential algebra techniques, the question of whether a given linear compartment model is (generically locally) identifiable is equivalent to asking whether the Jacobian matrix of a certain *coefficient map* (arising from certain *input-output equations*) is generically full rank. Recently, Meshkat, Sullivan, and Eisenberg gave a general formula for the input-output equations of a linear compartment model [11]. Using this formula, it is easy to check whether a given model is (generically locally) identifiable. Nevertheless, we would like to bypass this formula. That is, *can we determine whether a model is identifiable by simply inspecting its underlying directed graph?* Or, as a first step, *if a model is identifiable, when can we conclude that a given submodel is too?* Our interest in submodels, obtained by removing edges, has potential applications: the operation of removing an edge in a model may correspond to a biological intervention, such as a genetic knockout or a drug that inhibits some activity. Identifiable submodels have been studied by Vajda and others [14, 16].

# Identifiability Of Linear Compartment Models The Singular

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Identifiability of Parametric Models provides a comprehensive presentation of identifiability This book is divided into 11 chapters Chapter 1 reviews the basic methods for structural identifiability testing The methods that deal with large scale models and propose conjectures on global identifiability are considered in Chapter 2 while the problems of initial model selection and generating the set of models that have the exact same input output behavior are evaluated in Chapter 3 Chapters 4 and 5 cover nonlinear models The relations between identifiability and the well posedness of the estimation problem are analyzed in Chapter 6 followed by a description of the algebraic manipulations required for testing a model for structural controllability observability identifiability or distinguishability in chapter 7 The rest of the chapters are devoted to the relations between identifiability and parameter uncertainty This publication is beneficial to students and researchers aiming to acquire knowledge of the identifiability of parametric models      Modelling and Control in Biomedical Systems 2006 David Dagan Feng,Janan Zaytoon,2006-09-19 Modelling and Control in Biomedical Systems including Biological Systems was held in Reims France 20 22 August 2006 This Symposium was organised by the University of Reims Champagne Ardenne and the Soci t de l Electricit de l Electronique et des TIC SEE The Symposium attracted practitioners in engineering information technology mathematics medicine and biology and other related disciplines with authors from 24 countries Besides the abstracts of the four plenary lectures this volume contains the 92 papers that were presented by their authors at the Symposium The papers included two invited keynote presentations given by internationally prominent and well recognised research leaders Claudio Cobelli whose talk is titled Dynamic modelling in diabetes from whole body to genes and Irving J Bigio whose talk is titled Elastic scattering spectroscopy for non invasive detection of cancer Two prestigious industrial speakers were also invited to give keynote presentations Terry O Brien from LIDCO whose talk is titled LIDCO From the laboratory to protocolized goal directed therapy and Lorenzo Quinzio of Philips whose talk is titled Clinical decision support in monitoring and information systems A valuable source of information on the state of the art in Modelling and Control in Biomedical Systems Including abstracts of four plenary lectures and 92 papers presented by their authors

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