

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].

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Dissertation Abstracts International, 2005 Identifiability of Parametric Models E. Walter, 2014-05-23 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 Dynamic Systems Biology Modeling and Simulation Joseph DiStefano III, 2015-01-10 Dynamic Systems Biology Modeling and Simulation consolidates and unifies classical and contemporary multiscale methodologies for mathematical modeling and computer simulation of dynamic biological systems from molecular cellular organ system on up to population levels The book pedagogy is developed as a well annotated systematic tutorial with clearly spelled out and unified nomenclature derived from the author s own modeling efforts publications and teaching over half a century Ambiguities in some concepts and tools are clarified and others are rendered more accessible and practical The latter include novel qualitative theory and methodologies for recognizing dynamical signatures in data using structural multicompartmental and network models and graph theory and

analyzing structural and measurement data models for quantification feasibility The level is basic to intermediate with much emphasis on biomodeling from real biodata for use in real applications Introductory coverage of core mathematical concepts such as linear and nonlinear differential and difference equations Laplace transforms linear algebra probability statistics and stochastics topics The pertinent biology biochemistry biophysics or pharmacology for modeling are provided to support understanding the amalgam of math modeling with life sciences Strong emphasis on quantifying as well as building and analyzing biomodels includes methodology and computational tools for parameter identifiability and sensitivity analysis parameter estimation from real data model distinguishability and simplification and practical bioexperiment design and optimization Companion website provides solutions and program code for examples and exercises using Matlab Simulink VisSim SimBiology SAAMII AMIGO Copasi and SBML coded models A full set of PowerPoint slides are available from the author for teaching from his textbook He uses them to teach a 10 week quarter upper division course at UCLA which meets twice a week so there are 20 lectures They can easily be augmented or stretched for a 15 week semester course Importantly the slides are editable so they can be readily adapted to a lecturer's personal style and course content needs The lectures are based on excerpts from 12 of the first 13 chapters of DSBMS They are designed to highlight the key course material as a study guide and structure for students following the full text content The complete PowerPoint slide package 25 MB can be obtained by instructors or prospective instructors by emailing the author directly at joed@cs.ucla.edu [Modeling, Identification, and Control](#), 1980 **Mathematical Reviews**, 2004 **Identifiability and Estimation in Linear and Nonlinear Compartment Models with Application** Jea-Young Lee, 1994 *Proceedings of the Koninklijke Nederlandse Akademie Van Wetenschappen*, 1993 *12th IMACS World Congress, July 18-22, 1988, Paris, France* Robert Vichnevetsky, Pierre Borne, J. Vignes, 1988 **Identification and System Parameter Estimation, 1985** H. A. Barker, Peter C. Young, 1985 **Current Index to Statistics, Applications, Methods and Theory**, 1991 The Current Index to Statistics CIS is a bibliographic index of publications in statistics probability and related fields **Mathematics in Biology and Medicine** Vincenzo Capasso, Enea Grosso, Stefano L. Paveri-Fontana, 2013-03-13 **Modelling and Control in Biomedical Systems** Claudio Cobelli, L. Mariani, 1989 Hardbound This volume provides a complete and up to date review of the recent developments and trends relating to modelling and control in biomedical systems in research diagnosis and therapy Focus is placed on methodological issues relevant to modelling and control as well as to the various physiological systems of the organism visited from a control viewpoint Contains 98 papers **Documentation Abstracts**, 1992 *Large Scale Systems Theory and Applications* André Titli, Madan G. Singh, International Federation of Automatic Control, 1981 The carved and painted figures collected in this exceptional book are excellent examples of a wide spread American folk art tradition that flourished from the middle of the 18th to the end of the 19th century 183 photographic illustrations 4 reproduced in full color on the covers List of illustrations Extensive bibliography *L'Enseignement mathématique*, 1979 [Identification and](#)

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