

# IDENTIFIABILITY OF LINEAR COMPARTMENT MODELS: THE SINGULAR LOCUS

ELIZABETH 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

**Didier Musso**



## **Identifiability Of Linear Compartment Models The Singular:**

**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

*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

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**Cyber-Physical-Human Systems** Anuradha M. Annaswamy, Pramod P. Khargonekar, Françoise Lamnabhi-Lagarrigue, Sarah K. Spurgeon, 2023-06-08. Cyber Physical Human Systems: A comprehensive edited volume exploring the latest in the interactions between cyber physical systems and humans. In *Cyber Physical Human Systems: Fundamentals and Applications*, a team of distinguished researchers delivers a robust and up-to-date volume of contributions from leading researchers on Cyber Physical Human Systems, an emerging class of systems with increased interactions between cyber physical and human systems communicating with each other at various levels across space and time so as to achieve desired performance related to human welfare, efficiency, and sustainability. The editors have focused on papers that address the power of emerging CPHS disciplines, all of which feature humans as an active component during cyber and physical interactions. Articles that span fundamental concepts and methods to various applications in engineering sectors of transportation, robotics, and healthcare, and general socio-technical systems such as smart cities are featured. Together, these articles address challenges and opportunities that arise due to the emerging interactions between cyber physical systems and humans, allowing readers to appreciate the intersection of cyber physical system research and human behavior in large-scale systems. In the book, readers will also find a thorough introduction to the fundamentals of cyber physical human systems, in-depth discussions of cyber physical human systems with applications in transportation, robotics, and healthcare, a comprehensive treatment of socio-technical systems including social networks and smart cities. Perfect for cyber physical systems researchers, academics, and graduate students, *Cyber Physical Human Systems: Fundamentals and Applications* will also earn a place in the libraries of research and development professionals working in industry and government agencies.

**EPA-600/3**, 1978-12. *Reaction Kinetics: Exercises, Programs and Theorems*. János Tóth, Attila László Nagy, Dávid Papp, 2018-09-18. Fifty years ago, a new approach to reaction kinetics began to emerge, one based on mathematical models of reaction kinetics or formal reaction kinetics. Since then, there has been a rapid and accelerated development in both deterministic and stochastic kinetics, primarily because mathematicians studying differential equations and algebraic geometry have taken an interest in the nonlinear differential equations of kinetics, which are relatively simple yet capable of depicting complex behavior such as oscillation, chaos, and pattern formation. The development of stochastic models was triggered by the fact that novel methods made it possible to measure molecules individually. Now it is high time to make the results of the last half century available to a larger audience: students of chemistry, chemical engineering, and biochemistry, not to mention applied mathematics. Based on recent papers, this book presents the most important concepts and results together with a wealth of solved exercises. The book is accompanied by the authors' Mathematica package *ReactionKinetics*, which helps both students and scholars in their everyday work and which can be

downloaded from <http://extras.springer.com> and also from the authors websites Further the large set of unsolved problems provided may serve as a springboard for individual research

**Mathematical Modeling of Endocrine Systems** Darko Stefanovski, Giovanni Pacini, Ray Boston, 2022-01-04

*Ecological Research Series*, 1978

*New Sampling Theory for Measuring Ecosystem Structure* Robert J. Mulholland, 1978

*Modelling Methodology for Physiology and Medicine* Ewart Carson, Claudio Cobelli, 2000-12-31

Modelling Methodology for Physiology and Medicine offers a unique approach and an unprecedented range of coverage of the state of the art advanced modelling methodology that is widely applicable to physiology and medicine The book opens with a clear and integrated treatment of advanced methodology for developing mathematical models of physiology and medical systems Readers are then shown how to apply this methodology beneficially to real world problems in physiology and medicine such as circulation and respiration Builds upon and enhances the readers existing knowledge of modelling methodology and practice Editors are internationally renowned leaders in their respective fields

*Pharmacokinetic-Pharmacodynamic Modeling and Simulation* Peter L. Bonate, 2006-05-14

A natural hierarchy exists in pharmacokinetic pharmacodynamic modeling culminating in population pharmacokinetic models which are a specific type of nonlinear mixed effects model The purpose of this book is to present through theory and example how to develop pharmacokinetic models both at an individual and population level In order to do so however one must first understand linear models and then build to nonlinear models followed by linear mixed effects models and then ultimately nonlinear mixed effects models This book develops in that manner each chapter builds upon previous chapters by first presenting the theory and then illustrating the theory using published data sets and actual data sets that were used in the development of new chemical entities collected by the author during his years in industry A key feature of the book is the process of modeling Most books and manuscripts often present the final model never showing how the model evolved In this book all examples are presented in an evolutionary manner

*Mixed-Effects Models in S and S-PLUS* José C. Pinheiro, Douglas Bates, 2009-04-15

R linear models random fixed data analysis fit

**Tracer Kinetics in Biomedical Research** Claudio Cobelli, David Foster, Gianna Toffolo, 2007-05-08

1 Introduction 2 Fundamentals of Tracer Kinetics 3 The Noncompartmental Model of Multipool Systems 4 The Compartmental Model 5 Identifiability of the Tracer Model 6 Using the Tracer Model to Estimate Kinetic Parameters 7 Compartmental Versus Noncompartmental Kinetic Parameters 8 Parameter Estimation Some Fundamentals of Regression Analysis 9 Parameter Estimation in Noncompartmental Models 10 Parameter Estimation in Compartmental Models 11 Precursor Product Models Appendices Index

Identification and System Parameter Estimation 1982 G. A. Bekey, G. N. Saridis, 2016-06-06

Identification and System Parameter Estimation 1982 covers the proceedings of the Sixth International Federation of Automatic Control IFAC Symposium The book also serves as a tribute to Dr Naum S Rajbman The text covers issues concerning identification and estimation such as increasing interrelationships between identification estimation and other aspects of system theory including control theory signal

processing experimental design numerical mathematics pattern recognition and information theory The book also provides coverage regarding the application and problems faced by several engineering and scientific fields that use identification and estimation such as biological systems traffic control geophysics aeronautics robotics economics and power systems Researchers from all scientific fields will find this book a great reference material since it presents topics that concern various disciplines      **Atkinson's Principles of Clinical Pharmacology** Shiew-Mei Huang, Juan J.L. Lertora, Paolo Vicini, Arthur J. Atkinson Jr., 2021-10-16 Selected for Doody's Core Titles 2024 in Pharmacology Atkinson's Principles of Clinical Pharmacology Fourth Edition is the essential reference on the pharmacologic principles underlying the individualization of patient therapy and contemporary drug development This well regarded survey continues to focus on the basics of clinical pharmacology for the development evaluation and clinical use of pharmaceutical products while also addressing the most recent advances in the field Written by leading experts in academia industry clinical and regulatory settings the fourth edition has been thoroughly updated to provide readers with an ideal reference on the wide range of important topics impacting clinical pharmacology Presents the essential knowledge for effective practice of clinical pharmacology Includes a new chapter and extended discussion on the role of personalized and precision medicine in clinical pharmacology Offers an extensive regulatory section that addresses US and international issues and guidelines Provides extended coverage of earlier chapters on transporters pharmacogenetics and biomarkers along with further discussion on Phase 0 studies microdosing and PBPK      Transactions of the Society for Computer Simulation ,2001

*Mathematics for Healthcare* Krasimira Tsaneva-Atanasova, Vanessa Diaz-Zuccarini, 2018-09-28 In 1996 and with extraordinary prescience Panfilov and Holden had highlighted in their seminal book Computational Biology of the Heart that biology was potentially the most mathematical of all sciences Fast forward 20 years and we have seen an explosion of applications of mathematics in not only biology but healthcare that has already produced significant breakthroughs not imaginable more than 20 years ago Great strides have been made in explaining through quantitative methods the underlying mechanisms of human disease not without considerable ingenuity and effort Biological mechanisms are bewildering complex ever evolving multi scale variable difficult to fully access and understand This poses immense challenges to the computational physiology community that nevertheless has developed an impressive arsenal of tools and methods in a vertiginous race to combat disease with the tall order of improving human healthcare Mechanistic models are now contending with the advent of machine learning in healthcare and the hope is that both approaches will be used synergistically since the complexity of human pathophysiology and the difficulty of acquiring human datasets will require both deductive and inductive methods This Research Topic presents work that is currently at the frontier in computational physiology with a striking range of applications from diabetes to graft failure and using a multitude of mathematical tools This collection of articles represents a snapshot in a field that is moving at a dizzying speed bringing understanding of

fundamental mechanism and solutions to healthcare problems experienced by healthcare systems all over the world

**Personalized Predictive Modeling in Type 1 Diabetes** Eleni I. Georga, Dimitrios I Fotiadis, Stelios K. Tigas, 2017-12-11  
Personalized Predictive Modeling in Diabetes features state of the art methodologies and algorithmic approaches which have been applied to predictive modeling of glucose concentration ranging from simple autoregressive models of the CGM time series to multivariate nonlinear regression techniques of machine learning. Developments in the field have been analyzed with respect to i feature set univariate or multivariate ii regression technique linear or non linear iii learning mechanism batch or sequential iv development and testing procedure and v scaling properties. In addition simulation models of meal derived glucose absorption and insulin dynamics and kinetics are covered as an integral part of glucose predictive models. This book will help engineers and clinicians to select a regression technique which can capture both linear and non linear dynamics in glucose metabolism in diabetes and which exhibits good generalization performance under stationary and non stationary conditions. Ensure the scalability of the optimization algorithm learning mechanism with respect to the size of the dataset provided that multiple days of patient monitoring are needed to obtain a reliable predictive model. Select a features set which efficiently represents both spatial and temporal dependencies between the input variables and the glucose concentration. Select simulation models of subcutaneous insulin absorption and meal absorption. Identify an appropriate validation procedure and identify realistic performance measures. Describes fundamentals of modeling techniques as applied to glucose control. Covers model selection process and model validation. Offers computer code on a companion website to show implementation of models and algorithms. Features the latest developments in the field of diabetes predictive modeling.

**Principles of Clinical Pharmacology** Mr. Rohit Manglik, 2024-03-20 EduGorilla Publication is a trusted name in the education sector committed to empowering learners with high quality study materials and resources. Specializing in competitive exams and academic support, EduGorilla provides comprehensive and well structured content tailored to meet the needs of students across various streams and levels.

**Characterizing Sources of Indoor Air Pollution and Related Sink Effects** Bruce A. Tichenor, 1996 Based on presentations at a 1994 Symposium these detailed papers review source sink characterization design construction characterization and operation of test chambers and facilities testing protocols for determining emission factors and sink absorption desorption rates models for predicting

**Control and Dynamic Systems V27** C.T. Leonides, 2012-12-02 Control and Dynamic Systems Advances in Theory and Application Volume 27 System Identification and Adaptive Control Part 3 of 3 deals with system parameter identification and adaptive control. It presents useful techniques for adaptive control systems. This volume begins by presenting a powerful approach to multivariable model reference adaptive control based on the ideas and techniques of disturbance accommodating control theory. It then discusses the modeling of biological systems optimal control for air conditioning systems linear programming for constrained multivariable process control finite element approximation development of irreducible state space singular

systems and discrete systems with multiple time scales This book is an important reference for practitioners in the field who want a comprehensive source of techniques with significant applied implications



## **Identifiability Of Linear Compartment Models The Singular** Book Review: Unveiling the Magic of Language

In an electronic digital era where connections and knowledge reign supreme, the enchanting power of language has become more apparent than ever. Its ability to stir emotions, provoke thought, and instigate transformation is really remarkable. This extraordinary book, aptly titled "**Identifiability Of Linear Compartment Models The Singular**," compiled by a very acclaimed author, immerses readers in a captivating exploration of the significance of language and its profound effect on our existence. Throughout this critique, we will delve into the book's central themes, evaluate its unique writing style, and assess its overall influence on its readership.

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