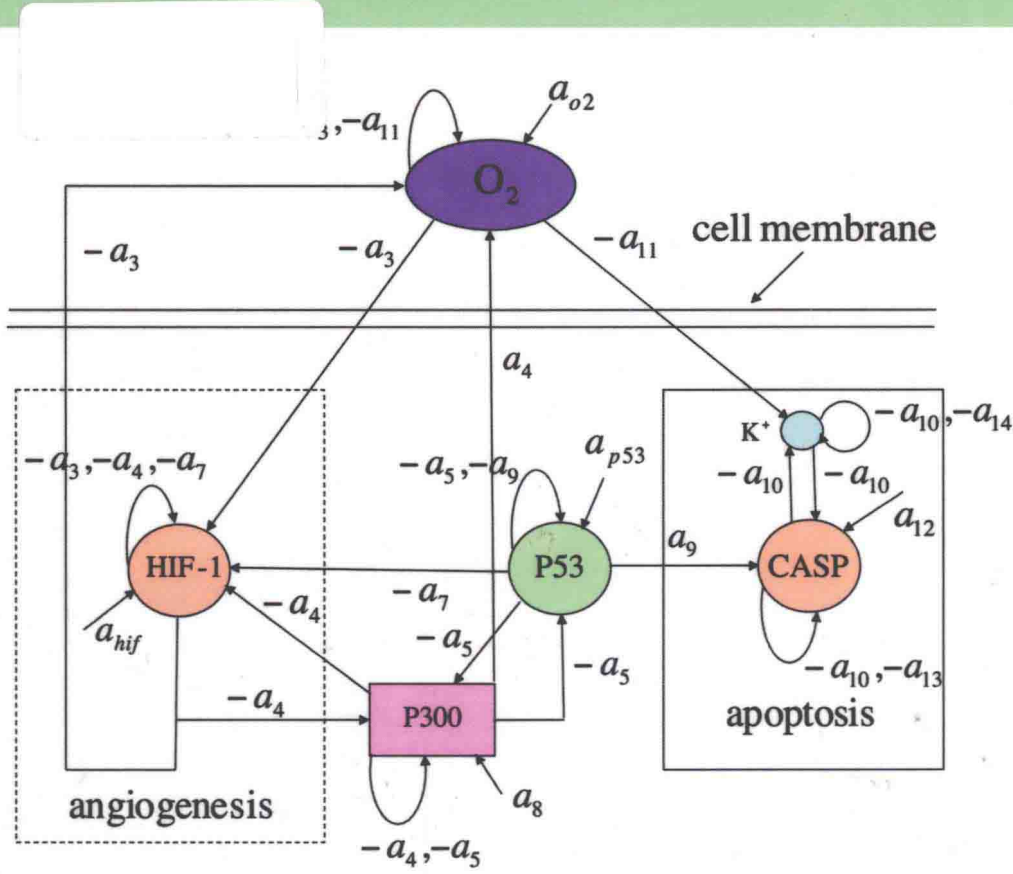


Differential Equation Analysis in Biomedical Science and Engineering

Ordinary Differential Equation Applications with R

William E. Schiesser



Features a solid foundation of mathematical and computational tools to formulate and solve real-world ODE problems across various fields

With a step-by-step approach to solving ordinary differential equations (ODEs), *Differential Equation Analysis in Biomedical Science and Engineering: Ordinary Differential Equation Applications with R* successfully applies computational techniques for solving real-world ODE problems that are found in a variety of fields, including chemistry, physics, biology, and physiology. The book provides readers with the necessary knowledge to reproduce and extend the computed numerical solutions and is a valuable resource for dealing with a broad class of linear and nonlinear ordinary differential equations.

The author's primary focus is on models expressed as systems of ODEs, which generally result by neglecting spatial effects so that the ODE dependent variables are uniform in space. Therefore, time is the independent variable in most applications of ODE systems. As such, the book emphasizes details of the numerical algorithms and how the solutions were computed. Featuring computer-based mathematical models for solving real-world problems in the biological and biomedical sciences and engineering, the book also includes:

- R routines to facilitate the immediate use of computation for solving differential equation problems without having to first learn the basic concepts of numerical analysis and programming for ODEs
- Models as systems of ODEs with explanations of the associated chemistry, physics, biology, and physiology as well as the algebraic equations used to calculate intermediate variables
- Numerical solutions of the presented model equations with a discussion of the important features of the solutions
- Aspects of general ODE computation through various biomolecular science and engineering applications

Differential Equation Analysis in Biomedical Science and Engineering: Ordinary Differential Equation Applications with R is an excellent reference for researchers, scientists, clinicians, medical researchers, engineers, statisticians, epidemiologists, and pharmacokineticists who are interested in both clinical applications and interpretation of experimental data with mathematical models in order to efficiently solve the associated differential equations. The book is also useful as a textbook for graduate-level courses in mathematics, biomedical science and engineering, biology, biophysics, biochemistry, medicine, and engineering.


WILLIAM E. SCHIESSER, PhD, ScD (hon.) is Emeritus McCann Professor of Engineering and Professor of Mathematics at Lehigh University. The author or coauthor of thirteen books, Dr. Schiesser's research interests include numerical software; ordinary, differential algebraic, and partial differential equations; and computational mathematics.

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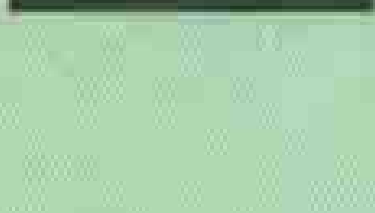


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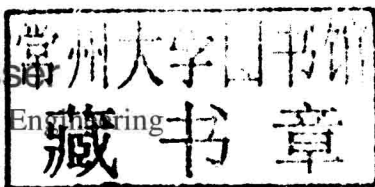


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DIFFERENTIAL EQUATION ANALYSIS IN BIOMEDICAL SCIENCE AND ENGINEERING

ORDINARY DIFFERENTIAL
EQUATION APPLICATIONS WITH R

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**DIFFERENTIAL
EQUATION ANALYSIS IN
BIOMEDICAL SCIENCE
AND ENGINEERING**

*To John Backus and Leon Lapidus,
and their research groups*

PREFACE

This book focuses on the rapidly expanding development and use of computer-based mathematical models in the life sciences, designated here as biomedical science and engineering (BMSE). The mathematical models are stated as systems of ordinary differential equations (ODEs) and generally come from papers in the current research literature that typically include the following steps:

1. The model is presented as a system of ODEs that explain associated chemistry, physics, biology, and physiology.
2. A numerical solution to the model equations is presented, particularly a discussion of the important features of the solution.

What is missing in this two-step approach are the details of how the solution was computed, particularly the details of the numerical algorithms. Also, because of the limited length of a research paper, the computer code used to produce the numerical solution is not provided. Thus, for the reader to reproduce (confirm) the solution and extend it is virtually impossible with reasonable effort.

The intent of this book is to fill in the steps for selected example applications that will give the reader the knowledge to reproduce and possibly extend the numerical solutions with reasonable effort. Specifically, the numerical algorithms are discussed in some detail, with additional background references, so that the reader will have some understanding of how the calculations were performed, and a

set of transportable routines in R¹ is provided so that the reader can execute to produce and extend the solutions.

Thus, the typical format of a chapter includes the following steps:

1. The model is presented as a system of ODEs with explanation of the associated chemistry, physics, biology, and physiology. The requirements of a well-posed set of equations such as the number of dependent variables, the number of ODEs, algebraic equations used to calculate intermediate variables, and the initial conditions for the ODEs are included (which is often not the case in research papers so that all of the details of the model are not included or known to the reader).
2. The features of the model that determine the selection of numerical algorithms are discussed; for example, how derivatives are approximated, whether the ODEs are nonstiff or stiff, and therefore, whether an explicit or implicit integration algorithm is used. The computational requirements of the particular selected algorithms are identified such as the solution of nonlinear equations, banded matrix processing, or sparse matrix processing.
3. The routines that are the programming of the ODEs and numerical algorithms are completely listed and then each section of code is explained, including referral to the mathematical model and the algorithms. Thus, all of the computational details for producing a numerical solution are in one place. Referring to another source for the software, possibly with little or no documentation, is thereby avoided.
4. A numerical solution to the model equations is presented, particularly a discussion of the important features of the solution.

¹R is a quality open source scientific programming system that can be easily downloaded from the Internet (<http://www.R-project.org/>). In particular, R has (i) vector-matrix operations that facilitate the programming of linear algebra, (ii) a library of quality ODE integrators, and (iii) graphical utilities for the presentation of the numerical solutions. All of these features and utilities are demonstrated through the applications in this book.

5. The accuracy of the computed solution is inferred using established methods such as h and p refinement. Alternative algorithms and computational details are considered, particularly to extend the model and the numerical solution.

In this way, a complete picture of the model and its computer implementation is provided without having to try to fill in the details of the numerical analysis, algorithms, and computer programming (often a time-consuming procedure that leads to an incomplete and unsatisfactory result). The presentation is not heavily mathematical, for example, no theorems and proofs, but rather is in terms of detailed examples of BMSE applications.

End of the chapter problems have not been provided. Rather, the instructor can readily construct problems and assignments that will be in accordance with the interests and objectives of the instructor. This can be done in several ways by developing variations and extensions of the applications discussed in the chapters. For example,

1. Parameters in the model equations can be varied, and the effects on the computed solutions are observed and explained. Exploratory questions can be posed such as whether the changes in the solutions are as expected. In addition, the terms in the right-hand sides (RHSs) of the ODEs (without the derivatives in the independent variable) can be computed and displayed numerically and graphically to explain in detail why the parameter changes had the observed effect. The computation and display of ODE RHS terms is illustrated in selected chapters to serve as a guide.
2. Additional terms can be added to the ODE RHSs to model physical, chemical, and biological effects that might be significant in determining the characteristics of the problem system. These additional terms can be computed and displayed along with the original terms to observe which terms have a significant effect on the computed model solution.

3. One or more ODEs can be added to an existing model to include additional phenomena that are considered possibly relevant to the analysis and understanding of the problem system.
4. An entirely new model can be proposed and programmed for comparison with an existing model. The existing routines might serve as a starting point, for example, a template.

These suggested problem formats are in the order of increasing generality to encourage the reader to explore new directions, including the revision of an existing model and the creation of a new model. This process is facilitated through the availability of existing routines for a model that can first be executed and then modified. The trial-and-error development of a model can be explored, particularly if experimental data that can be used as the basis for model development are provided, starting from parameter estimation based on the comparison of experimentally measured data and computed solutions from an existing model up to the development of a new model to interpret the data.

The focus of this book is primarily on models expressed as systems of ODEs that generally result by neglecting spatial effects so that the dependent variables of ODE, for example, concentrations, are uniform in space. The independent variable of the ODE systems is, therefore, time in most applications.

The assumption of spatial uniformity is quite accurate for a spectrum of BMSE systems, for example, a mixed reactor as considered in Chapter 1. However, the assumption of spatial uniformity is not correct for BMSE systems that function according to the spatial distribution of their principal variables, such as corneal curvature discussed in the concluding Chapter 8. This chapter, therefore, serves as an introduction to models based on partial differential equations (PDEs) in which both space and time are the independent variables. The additional spatial variables require boundary conditions for a complete specification of the PDE model. These details are introduced in Chapter 8 and are considered in detail in a companion volume titled *Differential Equation Analysis in Biomedical Science and Engineering: Partial Differential Equation Applications with R*.

In summary, my intention is to provide a set of basic computational procedures for ODE/PDE models in the two volumes that readers can use with modest effort without becoming deeply involved in the details of the numerical methods for ODE/PDEs and computer programming. All of the R routines discussed in the two volumes are available from a software download site, booksupport.wiley.com, which requires the ISBN: 9781118705483 for the ODE volume or 9781118705186 for the PDE volume. I welcome comments and will be pleased to respond to questions to the extent possible by e-mail (wes1@lehigh.edu).

WILLIAM E. SCHIESSER

*Bethlehem, PA
January 2014*

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