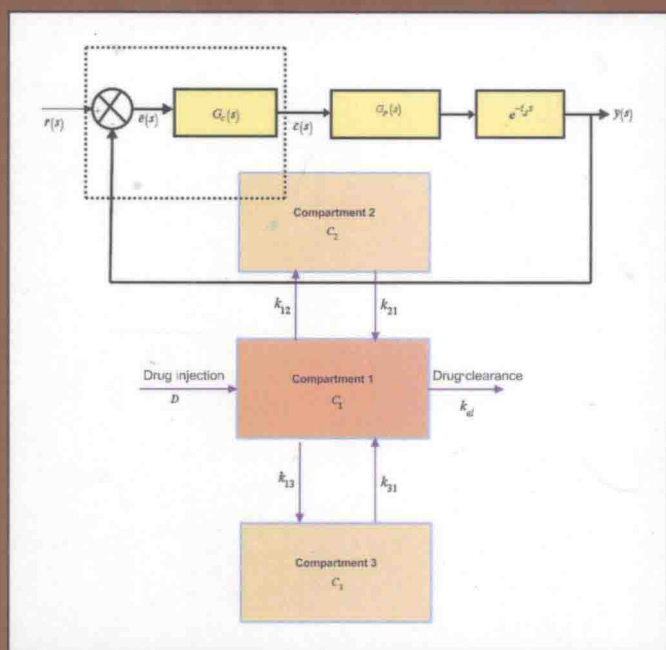


# Control of Biological and Drug-Delivery Systems

## for Chemical, Biomedical, and Pharmaceutical Engineering



LAURENT SIMON

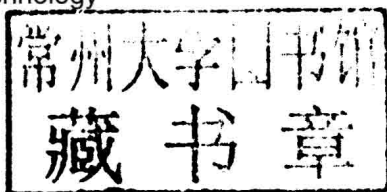
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# CONTROL OF BIOLOGICAL AND DRUG-DELIVERY SYSTEMS FOR CHEMICAL, BIOMEDICAL, AND PHARMACEUTICAL ENGINEERING

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**CONTROL OF BIOLOGICAL  
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ENGINEERING**



# PREFACE

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The control of biological and drug-delivery systems is critical to providing a long and healthy life to millions of people worldwide. In living systems, maintenance of homeostasis is credited to several control mechanisms (e.g., positive and negative feedback loops). Researchers in systems biology and controlled-release devices continue to use dynamics and control theory to increase their understanding of cell behavior, to treat diseases, and to develop drug administration protocols.

As the need to develop and commercialize bio-based products becomes more prevalent, chemical engineering departments throughout the nation have begun to shift their focus from a curriculum centered on the knowledge of chemical plant operations to a program that includes biological and pharmaceutical applications. Consequently, a multidisciplinary approach is mandatory to help ensure that chemical engineering graduates secure employment in industries where expertise in bioprocess and drug delivery is needed.

This textbook combines knowledge of process dynamics and basic control theory to analyze processes in the chemical, biomedical, and pharmaceutical engineering fields. Chemical process control topics, such as external disturbances, transfer functions, and input/output models, will be covered and enhanced by examples selected in the focus areas. Armed with this information, students will be in a strong position to address issues and to solve problems that dominate both fields (i.e., biological sciences and release devices).

Because most textbooks published in these areas are written for graduate-level study, undergraduate chemical engineering students are not exposed to diversified problems in biological sciences. This book is the first of its kind to provide biological and drug-delivery applications for dynamics and control concepts taught at the undergraduate level.

An expected result of the proposed perspective is an enrichment of fundamental concepts and the development of an application-oriented environment that gives students broader career choices and a competitive edge in the job market. The new outlook is also indispensable in developing technologies and in providing effective medicine to millions of people in need of gene therapies, heart–lung bypasses and dialysis machines. Although written primarily for undergraduate chemical and biomedical engineering students, this book's focus on drug-delivery systems and its coverage of a wide range of topics in the biological sciences is expected to appeal to a large audience in pharmaceutical engineering and systems biology.

The textbook is organized so that theory is accompanied by illustrations in several areas. Chapter 1 outlines the role of process dynamics and control in a number of disciplines and a brief overview of instrumentations. Chapter 2 introduces mathematical modeling based on the physical knowledge of a system. In Chapter 3, techniques are developed to linearize process models around nominal points. The concept of deviation variables is also introduced. Stability considerations and phase diagrams are addressed in Chapter 4. The properties of the Laplace operator are described in Chapter 5. Laplace transforms of several functions and ordinary and partial differential equations are computed. Techniques for inverting Laplace transforms are provided in Chapter 6. Partial fraction expansion and the residue theorem are applied to obtain closed-form solutions for differential equations. Chapter 7 discusses derivations of transfer functions from input–output models. This approach is fundamental for controller analysis and design. Physical systems, represented by ordinary and partial differential equations, are discussed. Dynamic behaviors of open-loop systems that are introduced in Chapter 8 deal with rational and transcendental transfer functions. Strategies to derive reduced-order models are also presented. In Chapter 9, control methodologies are developed. The emphasis is placed on three widely used feedback controllers: the proportional, proportional–integral, and proportional–integral–derivative controllers. In Chapter 10, frequency response analyses are studied and methods to draw Bode and Nyquist plots are described. Techniques to analyze the stability of feedback systems are developed in Chapter 11. Examples from biological processes are provided to illustrate the implementation of these tools. In Chapter 12, tuning guidelines for feedback controllers are provided. The Smith predictor, a model-based method to help reduce the effects of dead time on closed-loop performance, is discussed in Chapter 13. Using this structure, the controller acts on a delay-free response. The fundamentals of cascade and feedforward control designs are covered in Chapter 14. Both architectures provide methods for lessening the impact of disturbances on the controlled

variable. A technique for determining a relaxation time for lumped- and distributed-parameter systems is explained in Chapter 15. Based on Laplace transforms, the time to reach a steady-state value can be estimated. Examples of optimum control and design problems encountered in biomedicine are presented in Chapter 16.

This textbook is the result, in part, of my experience as an instructor of process control. I have expertise in process dynamics and control, bioprocesses, and drug-delivery systems and have written over 35 refereed articles and book chapters on biotechnology, controlled release, and mathematical modeling. My unique experiences in teaching biotransport to biomedical and chemical engineering students have exposed me to an assortment of problems that are relevant to both disciplines. My perspective on process dynamics and control has been enriched by courses such as Introduction to Biotechnology and Pharmaceutical Engineering Fundamentals. For additional information, visit my website <http://www.laurentsimeon.com> or <http://web.njit.edu/~lsimeon/>.

LAURENT SIMON





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L. S.



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