Preface

> *Je tiens impossible de connaître les parties sans connaître le tout, non plus que de connaître le tout sans connaître particulièrement les parties* –Pascal
>
> *The eternal mystery of the world is its comprehensibility* –Einstein

This book deals with the application of mathematical tools to the study of physiological systems. It is directed toward an audience of physiologists, physicians, physicists, kinesiologists, psychologists, engineers, mathematicians, and others interested in finding out more about the complexities and subtleties of rhythmic physiological processes from a theoretical perspective. We have attempted to give a broad view of the underlying notions behind the dynamics of physiological rhythms, sometimes from a theoretical perspective and sometimes from the perspective of the experimentalist.

This book can be used in a variety of ways, ranging from a more traditional approach such as a textbook in a biomathematics course (at either the advanced undergraduate or graduate level) to a research resource in which someone interested in a particular problem might look at the corresponding discussion here to guide their own thinking. We hope that researchers at all levels will find inspiration from the way we have dealt with particular research problems to tackle completely new areas of investigation, or even approach these in totally new ways.

Mathematically, we expect that readers will have a solid background in differential and integral calculus as well as a first course in ordinary differential equations. From the physiological side, they should have a minimal training in general physiology at the organismal level. We have endeavored in every area to make the book as self-contained as possible given this mathematical and physiological preparation. Furthermore, many of the later chapters stand on their own and can be read independently of the others. When necessary we have added references to other chapters or to appendices.

This book is divided roughly into two sections. Following an introductory Chapter 1, the first section (sort of theory) mainly introduces concepts from nonlinear dynamics using an almost exclusively biological setting for motivation. This is contained in Chapters 2 through 5. Chapter 2 introduces concepts from nonlinear dynamics using the properties of difference and differential equations as a basis. Chapter 3 extends and draws on this material in considering bifurcations from fixed points and limit cycles, illustrating a number of bifurcation patterns with examples drawn from data. This is continued in Chapter 4, which focuses on excitable cell electrophysiology. The first section concludes with a consideration in Chapter 5 of the properties of biological oscillators when perturbed by single stimuli or periodic inputs.

The second part (applications, more or less) consists of five in-depth examples of how the authors have used the concepts of the first part of this book in their research investigations of biological and physiological systems. Thus, Chapter 6 examines the influence of noise in nonlinear dynamical systems using examples drawn from neurobiology. Chapter 7 looks at the properties of spatially extended nonlinear systems as illustrated by the properties of excitable cardiac tissue. In Chapter 8 attention is directed to the dynamics of cellular replication, illustrating how periodic diseases can illuminate underlying dynamics. Chapter 9 returns to the neurobiology arena in considering the properties of a simple neural feedback system, the pupil light reflex. The book continues with this neurobiological emphasis to conclude in Chapter 10 with an examination of the dynamics of tremor.

We have not considered data analysis techniques as a separate subject, but rather have included an Appendix C, explaining those techniques we have found valuable (e.g., Fourier analysis, Lomb periodogram analysis). No doubt, other investigators will have their favorites that are not mentioned.

Since a combination of both analytical and computational techniques are essential to maximize understanding of complex physiological dynamics, we have included both analytic and computer exercises throughout the book using either the freeware `XPP` or the generally available commercial package `Matlab`. Introductions to both `XPP` and `Matlab` are to be found in Appendices A and B, respectively. The source code and data files (and in some cases, help files) for the computer exercises are available on the book's web site, available via `www.springer-ny.com`.

About the Authors and the Audience

The Centre for Nonlinear Dynamics in Physiology and Medicine was officially created in 1988 by the University Senate of McGill University, and from its inception was conceived of as a multiuniversity grouping of researchers and their graduate students and postdoctoral fellows that encompassed people from McGill, the Université de Montréal, the Université du Québec à Montréal, the University of Ottawa, and the University of Chicago. Since then, as young investigators have left to establish their own groups, it has grown to include Concordia University, the University of Victoria, and the University of Waterloo. Thus, in a very real sense, the

Centre for Nonlinear Dynamics in Physiology and Medicine has become a virtual center.

Back in 1995, members of the Centre for Nonlinear Dynamics in Physiology and Medicine hatched the idea of running a novel type of summer school, one that not only tried to convey the art and craft of mathematical modeling of biological systems through lectures, but also employed the use of daily afternoon computer simulation laboratories that would directly engage the students in exploring what they had heard about in morning lectures. The first of these summer schools was held in May 1996 (and dubbed "Montreal96"). Its objective was to teach what our group had learned about modeling physiological systems to interested individuals. Members of the Centre for Nonlinear Dynamics in Physiology and Medicine had as their goal to deliver lectures and laboratories whose material was coordinated between topics, and which were not merely recitals of disparate research topics as is so often the case in summer schools.

This first summer school was an unqualified success. More than 60 students attended "Montreal96" from 16 countries, ranging in subject specialization from biology, medicine, psychology, physiology, and theoretical physics through applied mathematics. At that time a minimal mathematical background of differential and integral calculus resulted in a wide diversity of expertise in the students, though a majority of the students had more advanced levels of preparation. Career levels varied from advanced undergraduates through graduate students, postdoctoral fellows, university faculty members, and physicians. The summer school was repeated in 1997 and 2000, with some variations in the makeup of students and the teaching team.

This book has evolved out of the notes written from these three summer schools. Thus the materials that we used for this book were gathered in a rough form during the 1996 summer school of the Centre for Nonlinear Dynamics in Physiology and Medicine. Therefore, this book is not a collection of disjointed chapters. Rather, a real effort has been made to organize the chapters in an integrated coherent whole even if this was not an easy thing to do, since there is a relatively wide spectrum of contents, some chapters being more mathematical, others more physiological, and still others lying in between. This is one of the few books in the "biomath" field that deals specifically with physiological systems. The description of the makeup of the attendees of these summer schools tells exactly for whom this book is written: a diverse collection of individuals with backgrounds as varied as those who have contributed to the history of this field over the past three hundred years. The one thing that will unite the intended readers of this book will be an absolute driving passion to understand the workings of physiological systems and the willingness to use any available technique (even mathematics!) to achieve that understanding.

We thank the authors and publishers for permission to reproduce many of the figures we have used in the book, and which are acknowledged in the figure captions. In particular, we thank Tom Inoué of Studio i-Design for his tireless efforts in the figure preparation, Dr. Wei Zong of the Research Resource for Complex Physiologic Signals for designing and implementing a collaborative authoring system that greatly facilitated the completion of this project, and Caroline Haurie, who was instrumental in drafts of the book. We thank all the people who attended or taught in the summer schools that were held in 1996, 1997, and 2000 in Montreal, because their feedback and efforts were essential for whatever success this book may achieve. We also thank Springer Verlag, and especially Ms. Achi Dosanjh, for their support during the production of this book. Finally, we thank all the people, colleagues, friends, and students who tested the computer exercises in the summer of 2002 at the Centre for Nonlinear Dynamics in Physiology and Medicine Computer Exercise Pizza Testing Party! All of the remaining errors are, of course, the responsibility of the authors. Our research and the preparation of this book have benefited from funds from many sources, notably the Natural Sciences Engineering and Research Council of Canada, the Canadian Institutes of Health Research, the Mathematics of Information Technology and Complex Systems National Center of Excellence, the Québec Fonds pour la formation de Chercheurs et l'aide à la recherche, and the Research Resource for Complex Physiologic Signals funded by the National Center for Research Resources of the National Institutes of Health (USA).

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