SELF-ORGANIZED BIOLOGICAL DYNAMICS AND NONLINEAR CONTROL

The growing impact of nonlinear science on biology and medicine is fundamentally changing our view of living organisms and disease processes. This book introduces the application to biomedicine of a broad range of interdisciplinary concepts from nonlinear dynamics, such as self-organization, complexity, coherence, stochastic resonance, fractals, and chaos.

The book comprises 18 chapters written by leading figures in the field. It covers experimental and theoretical research, as well as the emerging technological possibilities such as nonlinear control techniques for treating pathological biodynamics, including heart arrhythmias and epilepsy. The chapters review self-organized dynamics at all major levels of biological organization, ranging from studies on enzyme dynamics to psychophysical experiments with humans. Emphasis is on questions such as how living systems function as a whole, how they transduce and process dynamical information, and how they respond to external perturbations. The investigated stimuli cover a variety of different influences, including chemical perturbations, mechanical vibrations, thermal fluctuations, light exposures and electromagnetic signals. The interaction targets include enzymes and membrane ion channels, biochemical and genetic regulatory networks, cellular oscillators and signaling systems, and coherent or chaotic heart and brain dynamics. A major theme of the book is that any integrative model of the emergent complexity observed in dynamical biology is likely to be beyond standard reductionist approaches. It also outlines future research needs and opportunities ranging from theoretical biophysics to cell and molecular biology, and biomedical engineering.

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Toward Understanding Complexity, Chaos and Emergent Function in Living Systems

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Preface

> The real voyage of discovery consists not in seeking new landscapes but in having new eyes.
> *Marcel Proust*

The tools and ideas from nonlinear dynamics such as the concept of self-organization provide scientists with a powerful perspective for viewing living processes in a new light. As in the physical sciences before, the nonlinear dynamical systems approach promises to change scientific thinking in many areas of the biomedical sciences. For example, two rapidly evolving branches of nonlinear dynamics, popularly known as chaos and complexity studies, which have opened up new vistas on the dynamics of the nonliving world, are also beginning to impact deeply on our view of the living world. The key concept at the core of this work states that complex nonlinear systems, under conditions far from equilibrium, have a tendency to self-organize and to generate complex patterns in space and time.

Living organisms are prime examples of nonlinear complex systems operating under far from equilibrium conditions and, hence, self-organization and dynamical pattern formation is the hallmark of any living system. It thus comes as no surprise that knowledge about the nonlinear dynamics of physical systems can be successfully transferred to the study of biological systems. As a result, previously difficult to explain biological phenomena can now be understood on a theoretical basis. Importantly, the nonlinear dynamical approach is quickly leading to the discovery of novel biological behaviors and characteristics also. Many examples of often-unexpected biological insights, as a consequence of the nonlinear systems approach, and the emerging applications for clinical diagnosis and therapy are among the topics discussed in this volume.

Motivated by the growing impact of nonlinear science on biomedicine I proposed the organization of a workshop on 'Self-organized Biodynamics and Control by Chemical and Electromagnetic Stimuli' from which the idea for this volume originated. The workshop, which was jointly sponsored by the US Department of Energy and the Fetzer Institute, was held from 11 to 14 August 1996, at the Fetzer Institute in Kalamazoo, Michigan. Leading investigators, many of whom are the acknowledged authorities in their respective fields, met for three-and-a-half days to review current knowledge and to explore the most promising frontiers in this rapidly developing research field. The unifying theme was the nonlinear sensitivity of biological systems to weak external influences, and the development of novel methods that take advantage of this sensitivity in the study and nonlinear control of biological functions. Because of the demand generated by the first gathering, a second workshop was convened titled 'Towards Information-based Interventions in Biological Systems: From Molecules to Dynamical Diseases' from 23 to 26 August 1998. Between the two workshops a total of 38 stimulating presentations were given. Although this volume is not a workshop proceedings, the contributors, whose work is the subject of this volume, were drawn from the workshop speakers. Because of space constraints, several of the topics then discussed are not represented here, although I have made an effort in their selection to provide the broadest scope possible.

The interdisciplinary topics reflect the importance of the interplay between theoretical work and laboratory experiments in this new research area. While the book's primary goal is to provide an overview, the authors have tried to allow readers of diverse backgrounds to familiarize themselves with some of the details of the experimental and theoretical approaches presented. For example, chapters with a focus on experimental observations often provide important methodological information, so that the reader can better evaluate the challenges as well as opportunities of laboratory work in this area. In a similar fashion, the intent of the chapters that deal with the construction of theoretical models and the development of nonlinear analytical methods is to provide enough detail to enable the nonspecialist but technically oriented reader to follow the basic theoretical reasoning.

The use of concepts from nonlinear biological dynamics, or 'biodynamics' in short, to frame and solve critical research questions is rapidly expanding across many biological disciplines from cell and molecular biology to neuroscience. For example, the formation in 1998 of a program area on 'Quantitative Approaches to the Analysis of Complex Biological Systems' by the US National Institutes of Health is an indication that the nonlinear dynamical systems approach is near the threshold of entering the mainstream of biomedical research. I am convinced that it will be increasingly important for scientists in many biomedical disciplines to become familiar with the concepts outlined here. It is my hope that this book can serve as a useful guide to biodynamics for students and professionals and that it can provide them with a new framework for pursuing their own research interests.

Besides the 30 authors, who have generously given their time to write for this book, there are many other individuals whose support and contributions are directly responsible for making this book become a reality. In particular, this project would not have come to fruition without the enthusiasm and continuing support of the members of the Fetzer Institute's Board of Trustees. The task of planning and organizing the 1996 and 1998 workshops that provided the initial forum for evaluating the results and ideas presented here was carried out by the Fetzer Institute Task Force on 'Biodynamics', which was chaired by Bruce M. Carlson and whose other members included Paul C. Gailey, the late Kenneth A. Klivington, Harold E. Puthoff and myself. I thank my fellow task force members wholeheartedly for their excellent efforts. I also acknowledge the participation of Imre Gyuk, who provided the financial workshop support by the US Department of Energy, and I thank Frank Moss, who made the initial contact with Cambridge University Press. For valuable comments on the contributions written or co-written by me, I am grateful to Adam P. Arkin, Dean R. Astumian, Paul C. Gailey, Friedemann Kaiser, Susan J. Knox and Arnold J. Mandell. At Cambridge University Press, I wish to thank Simon Capelin and Sandi Irvine for patiently working with me to bring this book to completion.

Finally, I am indebted to George Hahn and Jeremy Waletzky for their important roles in the establishment of the Bioelectromagnetics Laboratory at Stanford, where I conducted most of my work in biodynamics. At the laboratory, I thank Jeffrey Carson, Clemens Eichwald, Pamela Killoran, Peter Maxim and Esther Shiu for their commitment to our work. I also want to express my gratitude to my parents and Lark, who were a source of inspiration and steady support throughout this project.

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