Preface

The main objective of this text is to provide a comprehensive, in-depth introduction to the background materials, fundamental concepts, and research challenges in mathematical modeling and computer simulation of electrophysiological heart processes, under both normal and pathological conditions.

Though these topics are closely connected to the field of scientific computing they are interdisciplinary in nature, combining the disciplines of applied mathematics, computer science, physiology, and medicine. From a theoretical point of view these topics are related to the study of a particular type of the more general class of so-called excitable media.

An excitable medium is defined as a nonlinear dynamical system consisting of units distributed in space that interact according to the laws of diffusion. Each unit of the system is itself a nonlinear dynamical system, with its own source of energy. After application of an external over-threshold stimulus, a unit can generate a solitary excitation pulse or a sequence of pulses depending on its nonlinear properties.

The following specific wave phenomena can be observed in excitable media:

- Propagation of traveling waves without decay
- The formation of spiral waves
- Generation of circular waves by autonomous leading centers
- Formation of dissipative structures (e.g. stationary standing wave)

Excitable media are encountered in both biology (cardiac tissue, nerve fiber, smooth and skeletal muscles, eye retina, population of amoeboid cells, some demographical problems, etc.) and technology (specific chemical reactions, some microelectronics devices, burning processes, plasma systems, etc.).

Mathematically, the processes in excitable media are described by a special type of parabolic nonlinear partial differential equations known in literature as reaction-diffusion equations. In contrast to engineering systems, in which mathematical models (descriptions) can be derived from the first principles, biological systems are described in a majority of cases as semi-phenomenological mathematical models partly derived from the first principles and partly represented as the mathematical approximation of experimental data obtained for a specific situation and extrapolated to the more general ones.

The scope of this text is restricted to the mathematical modeling and computer simulations of the dynamical processes in a particular class of these systems – cardiac cells and tissue. It is divided on the following major parts:

I. Electrophysiological background and basic concepts of mathematical modeling and computer simulation.
II. Mathematical modeling and computer simulation of action potential (AP) generation, from simple models such as Van der Pol and FitzHugh-Nagumo to physiological models of the Ist and IInd generations based on the Hodgkin-Huxley formalism.
III. Theory, mathematical modeling, and computer simulations of excitation wave propagation in one-dimensional tissue

IV. Mathematical modeling and computer simulations of excitation wave propagation in uniform and non-uniform two-dimensional tissues including rectilinear and circular wave propagation, theory of stationary and nonstationary spiral waves, and conditions of wave front breakup as analogue of tachyarrhythmia and ventricular fibrillation.

V. The implementation of mathematical models on serial and parallel supercomputers.

Special attention is devoted to new topics such as Markovian representation of cell channel gate processes, and new phenomena appearing in single cells with Ca dynamics under high pacing rates and in cardiac tissues during spiral wave propagation.

The included topics do not cover such important subjects as propagation in three-dimensional tissue with natural heterogeneity of AP characteristics along the thickness of the tissue and directional variability of fiber angles. Computer simulations of these problems have until now been performed using over-simplified non-physiological models such as FitzHugh-Nagumo and simplified ionic models such as the Luo-Rudy I AP model. Application of more realistic models is under intensive investigation. A similar situation is encountered in the investigation of the effect of mechanical cell contractions on conductivity of cell channels and AP propagation. The dynamics of the pacemaker system and the development of cell contraction processes, described in detail in published books, are excluded from the text and replaced by corresponding references.

Despite the many talented scientists working in mathematical modeling and computer simulation of cardiac processes, there are currently no published materials in which these topics are treated systematically, up-to-date with current research and containing the required minimum of materials which allow the specialists in other fields (mathematics, computer science, heart physiology and cardiology) to participate in such interdisciplinary research.

The book, "Simulation of Wave Processes in Excitable Media", by Dr. Zykov (my former PhD student and later colleague) was published in 1984 in the Soviet Union. The English translation of this book (from Russian) was edited by late Dr. Winfree and published in 1987. It includes some of the first approaches and information on the subject matter. The content of the book has become obsolete (except for the kinematics theory of stationary spiral waves), especially as applied to heart processes, because it focuses on simplified, nonionic cell models in which Ca dynamics are not present. J. Keener and J. Sneid's excellent work, "Mathematical Physiology," is devoted to broad topics of mathematical modeling of different physiological systems. Unfortunately the authors, in taking a more general approach, did not consider the heart processes in detail and fully omitted the implementation of mathematical models on modern parallel computer systems, focusing instead on the use of standard programs on desktop computers. Several collections of papers exist (e.g. "Computational Biology of the Heart," edited by A.V. Panfilov and A.V. Holden, 1997) addressing some of the proposed topics, but these collections require extensive prior knowledge of the subject and as such are not functional as an introductory text.

The content of this manuscript is combined from the author's lecture notes for the course "Introduction to Computational Cardiology," delivered to graduate students of the UCLA Computer Science and Biomedical Engineering Departments; the results of his personal research activities and those conducted by his PhD students in the former Soviet Union and United States over the last 30-35 years; and new achievements described in current literature. This book can serve not only as a text book for graduate students specializing in modeling and computer simulation of heart processes, but also as a reference for researchers engaged in mathematical modeling and computer simulation of different bio-medical problems. The latter, among other useful information, may find in the text many challenging problems awaiting solutions.