
Preface

Integrative physiological phenomena are difficult to analyze because current experimental techniques do not provide comprehensive information for all hierarchical levels of biological systems. It is difficult to integrate the properties of individual cells to a higher level of organization using a reductionist approach. Interactions of components within a system are often so complicated that their combined activities can be understood only with the application of mathematical and computational tools that serve as universal quantitative approximators. Recent developments in forward dynamic modeling and simulation have attracted considerable attention as non-invasive methods to investigate complex biological phenomena. They have become an essential supplement to experimental techniques that explore inaccessible biological processes and thereby assist researchers to deduce intricate functional mechanisms.

Currently, there are no texts for navigating the extensive field of mathematical and computational modeling in enteric neurobiology. The book is the first research monograph that provides insight into intricate biological mechanisms of intestinal motility that could not have been achieved through *in vivo* and *in vitro* experimental approaches and associated descriptive functional analyses. Although it is written for experts in the field, the book is also intended as a companion text for special courses in integrated system biology, applied mathematics, mathematical modeling, numerical computing, and engineering science for advanced undergraduate and graduate students. It cannot be used though as a traditional textbook to teach either “biology for computer scientists” or “mathematical modeling techniques for biologists.” Classical textbooks on human physiology, molecular biology and numerical

mathematics should be used as a background reading. The emphasis is given to fundamental topics that lie at the interface between biomedical, chemical, physical, computer sciences and recent experimental developments in enteric neurobiology and engages the multidisciplinary approach. Readers learn and understand computer simulations best by following the process of model formulation, and the design and execution of numerical algorithms. We demonstrate applications of the results of computer simulations in several realms, including target identification to treat intestinal motor dysfunction, multiple drug effects on the system, and various medical applications. From a practical point of view, the book will help establish strategies for people with complementary backgrounds who are already involved, or who are planning to work, in multidisciplinary areas.

Therefore, the approach used in the book has been to treat the subject matter with a degree of mathematical rigor while recognizing the complexity of biological structure. Special attention has been given to computer simulations for interpolation and extrapolation of electromechanical and chemo-electrical coupling phenomena, nonlinear self sustained electromechanical wave activity and pharmacological interactions concerned with the effects of co-localization and co-transmission by multiple neurotransmitters, receptor polymodality and heterogeneity, and drug interactions.

A brief introduction to the physiology of the gastrointestinal tract is given in Chapter 1. A one-dimensional mathematical model for electromechanical phenomenon in smooth muscle fibers is developed in Chapter 2, based on actual morphological and electrophysiological data. Numerical algorithms and procedures are outlined.

The results of pharmacological model validation are given in Chapter 3. The effects of drugs that alter the uptake and release of intracellular Ca^{2+} from stores in sarcoplasmic reticulum, specific L-type Ca^{2+} channel antagonists and non-specific weakly selective L-type Ca^{2+} channel agonist, motilides, and benzodiazepines are numerically examined.

Mathematical models and numerical investigations into the processes of chemical neurotransmission are presented in Chapter 4. Special attention is given to electrochemical coupling phenomenon at the synaptic level, including cycles of biochemical conversions for acetylcholine and adrenaline and their derivatives. The effects of tetrodotoxin, β -bungarotoxin, salts of

divalent cations, inhibitors of catechol-O-methyltransferase on neuronal uptake mechanisms, and influence of external Ca^{2+} concentration on the dynamics of signal transduction are analyzed.

Mathematical models of the enteric nervous system as a planar neuronal network are presented in Chapter 5. A traditional network model as a number of interconnected one-dimensional neurons is compared to a novel network model as a syncytium with spacially distributed weakly connected oscillators. The influence of synaptic plasticity on the spread of excitation/inhibition waves within the neuronal network is emphasized. Numerical procedures to solve the governing equations are outlined.

Electrophysiological mechanisms of co-transmission by serotonin (5-HT), acetylcholine, α -amino-3-hydroxy-5-methyl-4-isoxalose propionic acid (AMPA), L-aspartate, N-methyl-D-aspartate (NMDA) and co-expression of different receptors types, including 5-HT type 3 and 4, nicotinic and muscarinic cholinergic, AMPA and NMDA are examined in Chapter 6. Interpretation of numerical results in conjunction with *in vivo* experimental recordings and their possible applications to the development of novel therapeutics to treat diseases associated with altered visceral nociception is provided.

A novel, integrative, computational model that combines information across multiple levels of structural organization for a functional unit by substituting the entire gut with a continuum of overlapping dynamically stable functional elements is presented in Chapter 7. The unit is modeled as a soft biological shell with electromyogenic properties. A combined numerical algorithm is designed to solve the governing system of nonlinear partial and ordinary integro-differential equations. A new phenomenon which is discovered numerically and is related to self-sustained myoelectrical activity is presented and analyzed.

Medical applications for the propulsion of a solid non-deformable bolus, and the neurochemical basis of visceral hypersensitivity are examined in Chapter 8. Results of numerical experiments are discussed in conjunction with the diseases affecting gastrointestinal motility.

All simulations in the book are obtained with ABS Technologies[®] software. The complete version of software is available upon a request at: “abstechservice@gmail.com.”

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Mathematical Modeling and Simulation in Enteric Neurobiology was reviewed by an expert who checked the accuracy of what the reader will learn here, to help ensure that this book will provide the reader with all that he or she would need to know about this modern field of science. We greatly appreciate his or her contribution. Finally, our special thanks are extended to Ms. S. C. Lim, World Scientific Publishing, who supported the project from the very beginning and made its timely publication possible.

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