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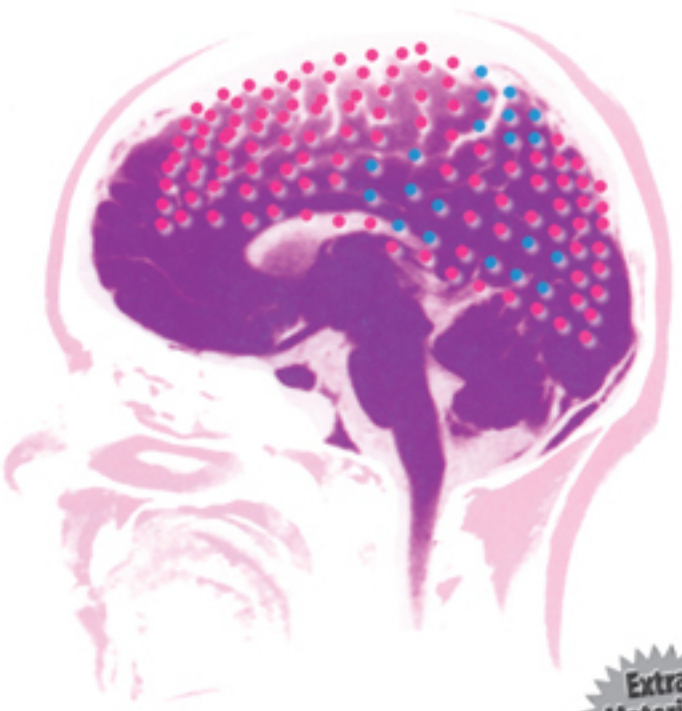
Modeling and Imaging of Bioelectrical Activity

Principles and Applications



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Minneapolis, Minnesota

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PREFACE

Bioelectrical activity is associated with living excitable tissue. It has been known, owing to efforts of numerous investigators, that bioelectrical activity is closely related to the mechanisms and functions of excitable membranes in living organs such as the heart and the brain. A better understanding of bioelectrical activity, therefore, will lead to a better understanding of the functions of the heart and the brain as well as the mechanisms underlying the bioelectric phenomena.

Bioelectrical activity can be better understood through two common approaches. The first approach is to *directly measure* bioelectrical activity within the living tissue. A representative example is the direct measurement using microelectrodes or a microelectrode array. In this direct measurement approach, important characteristics of bioelectrical activity, such as transmembrane potentials and ionic currents, have been recorded to study the bioelectricity of living tissue. Recently, direct measurement of bioelectrical activity has also been made using optical techniques. These electrical and optical techniques have played an important role in our investigations of the mechanisms of cellular dynamics in the heart and the brain.

The second approach is to *noninvasively* study bioelectrical activity by means of *modeling and imaging*. Mathematical and computer models have offered a unique capability of correlating vast experimental observations and exploring the mechanisms underlying experimental data. Modeling also provides a virtual experimental setting, which enables well controlled testing of hypothesis and theory. Based on the modeling of bioelectrical activity, noninvasive imaging approaches have been developed to detect, localize, and image bioelectrical sources that generate clinical measurements such as electrocardiogram (ECG) and electroencephalogram (EEG). Information obtained from imaging allows for elaboration of the mechanisms and functions of organ systems such as the heart and the brain.

During the past few decades, significant progress has been made in modeling and imaging of bioelectrical activity in the heart and the brain. Most literature, however, has treated these research efforts in parallel. The similarity arises from the biophysical point of view that membrane excitation in both cardiac cells and neurons can be treated as volume current sources. The clinical observations of ECG and EEG are the results of volume conduction of currents within a body volume conductor. The difference among bioelectrical activity originating from different organ systems is primarily due to the different physiological mechanisms underlying the phenomena. From the methodological point of view,

therefore, modeling and imaging of bioelectrical activity can be treated within one theoretical framework. Although this book focuses on bioelectric activity of the heart and the brain, the theory, methodology, and state-of-the-art research that are presented in this book should also be applicable to a variety of applications.

The purpose of this book is to provide a state-of-the-art coverage of basic principles, theories, and methods of modeling and imaging of bioelectrical activity with applications to cardiac and neural electrical activity. It is aimed at serving as a reference book for researchers working in the field of modeling and imaging of bioelectrical activity, as an introduction to investigators who are interested in entering the field or acquiring knowledge about the current state of the field, and as a textbook for graduate students and seniors in a biomedical engineering, bioengineering, or medical physics curriculum.

The first three chapters deal with the modeling of cellular activity, cell networks, and whole organ for bioelectrical activity in the heart. Chapter 1 provides a systematic review of one-cell models and cell network models as applied to cardiac electrophysiology. It illustrates how modeling can help elucidate the mechanisms of cardiac cells and cell networks, and increase our understanding of cardiac pathology in three-dimension and whole heart models. Chapter 2 provides a thorough theoretical treatment of the forward problem of bioelectricity, and in particular electrocardiography. Following a review of the theoretical basis of equivalent dipole source models and state-of-the-art numerical methods of computing the electrical potential fields, Chapter 2 discusses the applications of forward theory to whole heart modeling and defibrillation. Chapter 3 reviews important issues in whole heart modeling and its implementation as well as various applications of whole heart modeling and simulations of cardiac pathologies. Chapter 3 also illustrates important clinical applications the modeling approach can offer.

The following two chapters review the theory and methods of inverse imaging with applications to the heart. Chapter 4 provides a systematic treatment of the methods and applications of heart surface inverse solutions. Many investigations have been made in order to inversely estimate and reconstruct potential distribution over the epicardium, or activation sequence, over the heart surface from body surface electrocardiograms. Progress has also been made to estimate endocardial surface potentials and activation sequence from catheter recordings. These approaches and activities are well reviewed in Chapter 4. Chapter 5 reviews the recent development in three dimensional electrocardiography tomographic imaging. Recent research shows that, by incorporating *a priori* information into the inverse solutions, it is possible to estimate three-dimensional distributions of electrophysiological characteristics such as activation time and transmembrane potentials, or equivalent current dipole distribution. In particular, a whole-heart-model based tomographic imaging approach is introduced, which illustrates the close relationship between modeling and imaging and the merits of model-based imaging.

Chapter 6 deals with a noninvasive body surface mapping technology – surface Laplacian mapping. Compared with well-established body surface potential mapping, body surface Laplacian mapping has received relatively recent attention in its enhanced capability of identifying and mapping spatially separated multiple activities. This chapter also illustrates that a noninvasive mapping technique can be applied to imaging of bioelectrical activity originated from different organ systems, such as the heart and the brain.

The subsequent two chapters treat inverse imaging of the brain from neuromagnetic and neuroelectric measurements, as well as functional magnetic resonance imaging (fMRI).

Chapter 7 reviews the forward modeling of magnetoencephalogram (MEG), and neuromagnetic source imaging with a focus on spatial filtering approach. Chapter 8 provides a general review of fMRI, linear inverse solutions for EEG and MEG, and multimodal imaging integrating EEG, MEG and fMRI. Along with Chapters 4 and 5, these four chapters are intended to provide a solid foundation in inverse imaging methods as applied to imaging bioelectrical activity.

Chapter 9 deals with tissue conductivity, an important parameter that is required in bioelectric inverse solutions. The conductivity parameter is needed in establishing accurate forward models of the body volume conductor and obtaining accurate inverse solutions using model-based inverse imaging. As most inverse solutions are derived from noninvasive measurements with the assumption of known tissue conductivity distribution, the accuracy of tissue conductivity is crucial in ensuring accurate and robust imaging of bioelectrical activity. Chapter 9 systematically addresses this issue for various living tissues.

This book is a collective effort by researchers who specialize in the field of modeling and imaging of bioelectrical activity. I am very grateful to them for their contributions during their very busy schedules and their patience during this process. I am indebted to Aaron Johnson Brian Halm, Shoshana Sternlicht, and Kevin Sequeira of Kluwer Academic Publisher for their great support during this project. Financial support from the National Science Foundation, through grants of NSF CAREER Award BES-9875344, NSF BES-0218736 and NSF BES-0201939, is also greatly appreciated.

We hope this book will provide an intellectual resource for your research and/or educational purpose in the fascinating field of modeling and imaging of bioelectrical activity.

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FROM CELLULAR ELECTROPHYSIOLOGY TO ELECTROCARDIOGRAPHY

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INTRODUCTION

Since many cardiac pathologies manifest themselves at the cellular and molecular levels, extrapolation to clinical variables, such as the electrocardiogram (ECG), would prove invaluable to diagnosis and treatment. One ultimate goal of the cardiac modeler is to integrate cellular level detail with quantitative properties of the ECG (a property of the whole heart). This magnificent task is not unlike a forest ranger attempting to document each leaf in a massive forest. Both the modeler and ranger need to place fundamental elements in the context of a broader landscape. But now, with the recent genome explosion, the modeler needs to examine the "leaves" at even much greater molecular detail. Fortunately, the rapid explosion in computational power allows the modeler to span the details of each molecular "leaf" to the "forest" of the whole heart. Thus, cardiac modeling is beginning to span the spectrum from DNA to the ECG, from *nucleotide to bedside*.

Extending cellular detail to whole-heart electrocardiography requires spanning several levels of analysis (Figure 1.1). The **one-cell** model describes an action potential recording from a single cardiac myocyte. By connecting an array of these individual myocytes (via gap junctions), a **linear network** (cable), **two-dimensional (2D) network** or **three-dimensional (3D) network** (slab) model of action potential propagation can be constructed. The bulk electrophysiological signal recorded from these networks is called the local extracellular electrogram. Subsequently, networks representing tissue diversity and realistic heart geometries can be molded into a **whole heart** model, and finally, the whole heart model can be placed in a **torso** model replicating lung, cartilage, bone and dermis. At each level, one can reconstruct the salient electric signal (action potential, electrogram, ECG) from the cardiac sources by solving the forward problem of electrophysiology (Chapter 2).

Simply put, cardiac modeling is equivalent to solving a system of non-linear differential (or partial differential) equations, though vigorous reference must be made to numerous