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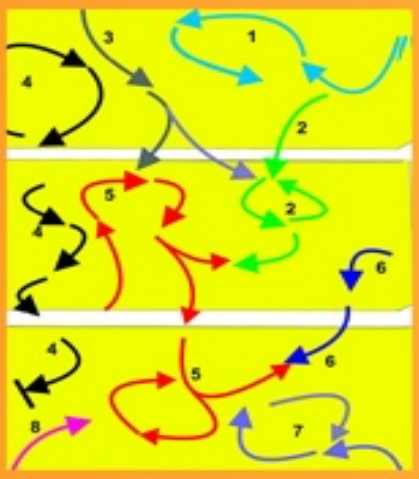
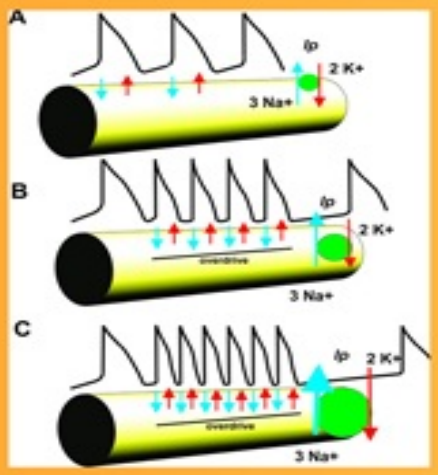
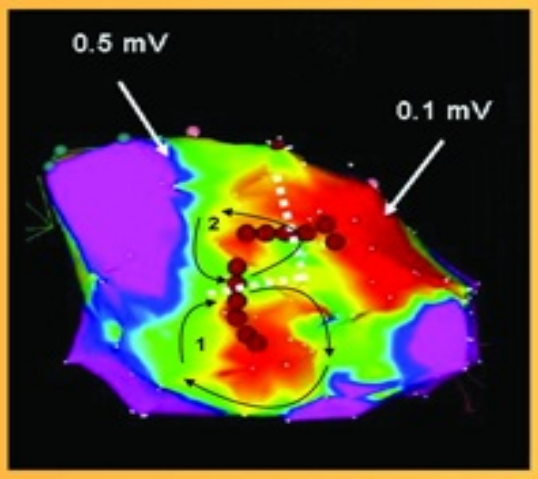
Electrophysiological Foundations of Cardiac Arrhythmias

A Bridge Between Basic Mechanisms and Clinical Electrophysiology







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ELECTROPHYSIOLOGICAL FOUNDATIONS OF CARDIAC ARRHYTHMIAS

A Bridge Between Basic Mechanisms and Clinical Electrophysiology

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Dedication

This book is dedicated to all our teachers who have inspired us to pursue the fascinating study of cardiac arrhythmias and to our families who have traveled with us on this journey.

In Memoriam

Mark E. Josephson passed away on January 11, 2017 as this book went to press. His death is an enormous personal and professional loss to his co-authors and the cardiology community.

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PREFACE

Why Is Basic Cardiac Electrophysiology Important?

Approximately 50 years ago, the introduction of programmed electrical stimulation of the heart together with the recording of intracardiac electrograms, including that of the bundle of His, opened the door for better understanding of the underlying mechanisms of different types of cardiac arrhythmias. This initial diagnostic phase led to new therapeutic possibilities, such as arrhythmia surgery, better selection of antiarrhythmic drugs, antitachycardia pacing, and catheter ablation. In those 50 years, the number of cardiologists involved in cardiac arrhythmia management and the complexity of diagnosis and treatment options increased remarkably. Recent developments using more complex technology include computer-based mapping and ablation therapy for a number of different arrhythmias, atrial fibrillation among them.

Of great importance has been a parallel increase in knowledge of the basic electrophysiology of the heart that has been essential for understanding the mechanisms of arrhythmogenesis and their clinical expression. This has led the authors of this book to the firm belief that practitioners of clinical cardiac electrophysiology must have a solid foundation in the basic electrophysiology responsible for the rhythm abnormalities that they are treating. This reasoning is two-fold.

First, understanding the electrophysiological mechanism of an arrhythmia can help in selecting the appropriate treatment. Initially, the mechanism may not always be evident, but requires some probing to discover it. Appropriate reasoning and interpretations of test results to successfully identify the mechanism is based on knowledge of the electrophysiological properties of the different mechanisms.

Second, the development of modern clinical cardiac electrophysiology has been built on a foundation of the basic science of cardiac electrophysiology, without which the discipline would have stagnated. Discoveries that have moved the field forward and enabled it to accomplish previously unimaginable goals have been based on the interactions of laboratory and clinical research on basic mechanisms. For expert clinical practice and to make new discoveries in the field, current practitioners of clinical cardiac electrophysiology must have a solid basic knowledge foundation of basic electrophysiology.

The Knowledge Gap in Fundamentals of Cardiac Electrophysiology

It has been our observation as teachers and clinicians that the “student” who is entering the field of cardiology and clinical cardiac electrophysiology often does not have the fundamental knowledge necessary for understanding the causes of the abnormalities in electrophysiology of the heart. The reason is that as medical knowledge has expanded, time constraints on medical

education have resulted in a lack of education in fundamental cardiac electrophysiology for students who go on to training programs in cardiology and clinical electrophysiology. Medical education in basic physiology has been reduced to the bare necessities. The basic cellular electrophysiology of transmembrane resting and action potentials are taught mostly as it applies to nerve cells. These concepts are relevant to cardiac cells on the most rudimentary level, but how these basic concepts translate to the cellular electrophysiology of clinical cardiac arrhythmias is barely addressed.

The Purpose of This Book

The purpose of this book is to address this knowledge gap in the cellular electrophysiology of clinical cardiac arrhythmias, while at the same time providing the critical connection of these mechanisms to the arrhythmias.

This book is designed to lead the reader through the pathway from basic cardiac electrophysiology over the bridge to clinical cardiac electrophysiology. Basic cellular electrophysiology of the three main categories of arrhythmogenesis (automaticity, triggered activity, and reentry—see the Introduction and Table i-1) is described in sufficient detail to understand how alterations in cellular electrophysiology cause an arrhythmia. Then, these cellular electrophysiological mechanisms are related to the ECG appearance of that arrhythmia and how the arrhythmia responds to interventions such as programmed electrical stimulation and selected pharmacological agents that are mechanism-specific. Therapy for arrhythmias is not part of this curriculum.

In preparing this book, it has not been our intent to provide a complete review or description of either the basic or the clinical electrophysiology of the heart. These fields are now so extensive that a complete review of both would be impossible undertakings for the authors and would require a number of contributors who are expert in all aspects of both basic and clinical cardiac electrophysiology. Rather, it is our purpose to provide the basic foundations of both cellular electrophysiology and the electrophysiology of selected arrhythmias, so that readers will be able to advance their education with additional texts written by experts. These texts typically assume the fundamental knowledge of basic and clinical electrophysiology found in this book. For more advanced education in clinical electrophysiology built on the fundamentals provided in this book, we recommend another text written by one of us, *Josephson's Clinical Cardiac Electrophysiology: Techniques and Interpretations.*[*]

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[*] Josephson ME. *Josephson's Clinical Cardiac Electrophysiology: Techniques and Interpretations* (5th ed.). Philadelphia, PA: Wolters Kluwer; 2016.

INTRODUCTION

How Is This Book Organized, and How Should It Be Used?

Much of what is known about the electrophysiological mechanisms underlying the occurrence of cardiac arrhythmias comes from the development and utilization of microelectrode techniques for recording transmembrane action potentials and membrane currents from cardiac cells. The properties of cellular electrical events have then been used to assess arrhythmias in experimental laboratory models and arrhythmias in the clinical setting to determine their mechanisms. Although there are many kinds of clinical arrhythmias with many different pathological causes, in the final analysis, they all are the result of critical alterations in cellular electrophysiology.

Since cellular electrophysiology is so important, it is the foundation for the description of mechanisms causing arrhythmias in this book. Therefore, knowledge of basic membrane electrophysiology that can be found in medical physiology textbooks is required as background information to fully utilize this book. We do describe many of the basic concepts as related to the heart throughout the book, but they are not grouped together in a traditional first chapter on basic electrophysiology. Rather, they are presented in the context of an arrhythmia mechanism and the clinical arrhythmias that this mechanism causes.

It is also helpful if the reader has general knowledge of the electrocardiogram, and how to diagnose and classify cardiac arrhythmias. Examples of clinical arrhythmias are described in the book in relation to the cellular electrophysiological mechanisms causing them. The reader is referred to two texts, *The ECG in Emergency Decision Making* (Wellens and Conover) and *Josephson's Clinical Cardiac Electrophysiology* for a more complete description of the clinical arrhythmias.

The purpose of this book is to describe/teach the electrophysiological mechanisms that cause cardiac arrhythmias, a process known as arrhythmogenesis. The different cellular mechanisms that form the organization of the book are presented in **Table i-1**, which has originated from a vast literature on experimental and clinical cardiac electrophysiology. Table i-1 subdivides electrophysiological mechanisms causing arrhythmias into two major headings: I. Arrhythmias Caused by Abnormal Impulse Initiation, and II. Arrhythmias Caused by Altered (Abnormal) Impulse Conduction.

Within this broad framework, this book describes three main classifications of arrhythmia mechanisms: **Part I – Automaticity; Part II – Afterdepolarizations and Triggered Activity; and Part III – Altered (Abnormal) Impulse Conduction and Reentry**.

Table i-1 Electrophysiological Mechanisms of Cardiac Arrhythmias

I. Abnormal Impulse Initiation
   A. **Automaticity**
      - normal automaticity
      - abnormal automaticity
   B. **Afterdepolarizations and Triggered Activity**
      - delayed afterdepolarizations