

# Preface

The heart is a remarkable electrically activated rhythmic muscular pump responsible for distributing blood to the lungs, brain visceral organs, skeletal muscle other organs and to itself. The intrinsic pumping rate is normally set by pacemaker cells in the sinoatrial node, but the resulting physiological rhythm is variable and highly modulated by the autonomic nervous system and humoral factors. Pathological heart rhythm is a major health issue. Sudden death caused by cardiac arrhythmias is a significant cause of mortality worldwide. In the USA alone, it has been estimated that nearly 300,000 emergency medical services-treated cardiac arrests occur outside a hospital setting each year. In young adults, cardiac arrests are often associated with cardiac abnormalities (either structural or electrical) and can be triggered by intense physical activity or emotion. In adults, the most common underlying cause of lethal arrhythmias (ventricular tachycardia or fibrillation) is coronary artery disease. A minority of cardiac arrests are due to extreme bradycardia or side effects of drug therapy or abuse. Treatment for cardiac arrhythmia includes drugs, implantable pacemakers or cardioverter/defibrillator devices, catheter ablation or surgical resection.

Due to the primary importance of the heart in the life of vertebrates, it is only natural that the molecular and cellular basis of normal and pathophysiological heart rhythms is an intense area of both basic and biomedical research. During the past 50 years, biophysical approaches such as microelectrode recording of intracellular action potentials of isolated cardiac tissue and the voltage clamp technique used to record ionic currents in isolated myocytes led to the remarkable insights into our understanding of the electrical basis of cardiac pacemaking, impulse conduction and myocardial contraction. In the past few decades, molecular biology, genetics, and biochemical approaches have defined the molecular basis, as well as the specific cellular location, of the plethora of ion channels and transporters that underlie the ionic currents identified by voltage clamp techniques and how their synchronized activity controls the basic rate and rhythm of the heart. The resulting information explosion has made it difficult for investigators to keep abreast of new findings in fields outside their areas of expertise and served as motivation for this volume. Here we have endeavored to bring together experts from various fields who share a passion for understanding the mechanisms of cardiac pacemaking and arrhythmogenesis. Individual chapters cover a full range of topics, including the

ionic basis of pacemaking, the role of specific channels and transporters in sinoatrial node pacemaking, altered intracellular  $\text{Ca}^{2+}$  handling in response to disease, computer modeling of the action potentials of pacemaker and working cardiomyocytes, genetic and molecular basis of inherited arrhythmias, development of cardiac conduction system and a review of novel antiarrhythmic agents. Due to the key importance of the specialized pacemaker cells and tissue (sinoatrial and atrioventricular nodes, Purkinje fibers) in maintaining heart rate and rhythm, special emphasis is placed on the peculiar electrophysiology of these cells. The intended audience for this book includes investigators in the fields of cardiac electrophysiology and arrhythmia, advanced graduate students, cardiologists and pharmaceutical industry. It is our hope that the topics and unresolved issues highlighted here will serve to both educate and motivate continued interest in research of the complicated molecular and cellular mechanisms that underlie normal and pathophysiological cardiac rhythms.

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Lucknow, Uttar Pradesh, India  
Dresden, Germany  
Salt Lake City, UT, USA

Onkar N. Tripathi  
Ursula Ravens  
Michael C. Sanguinetti