

CONTENTS

PART I Structural and Molecular Bases of Ion Channel Function

1 Voltage-Gated Sodium Channels and Electrical Excitability of the Heart, 1

William A. Catterall

2 Voltage-Gated Calcium Channels, 12

Alexander Kushnir and Steven O. Marx

3 Voltage-Gated Potassium Channels, 25

Gavin Y. Oudit and Peter H. Backx

4 Structural and Molecular Bases of Cardiac Inward Rectifier Potassium Channel Function, 38

Anatoli N. Lopatin and Justus M.B. Anumonwo

5 Mammalian Calcium Pumps in Health and Disease, 49

Marisa Brini and Ernesto Carafoli

6 Structural and Molecular Bases of Sarcoplasmic Reticulum Ion Channel Function, 60

Bin Liu, Sándor Györke, and Przemysław B. Radwański

7 Organellar Ion Channels and Transporters, 66

Jin O-Uchi, Bong Sook Jhun, Jyotsna Mishra, and Shey-Shing Sheu

8 Molecular Organization, Gating, and Function of Connexin-Based Gap Junction Channels and Hemichannels, 80

Feliksas F. Bukauskas

PART II Biophysics of Cardiac Ion Channel Function

9 Structure–Function Relations of Heterotrimeric Complexes of Sodium Channel α - and β -Subunits, 90

Isabelle Deschênes

10 Regulation of Cardiac Calcium Channels, 96

Jonathan Satin

11 Inhibition of Phosphoinositide 3-Kinase and Acquired Long QT Syndrome, 106

Lisa M. Ballou, Richard Z. Lin, and Ira S. Cohen

12 Structural Determinants and Biophysical Properties of hERG1 Channel Gating, 113

Michael C. Sanguinetti and Frank B. Sachse

13 Molecular Regulation of Cardiac Inward Rectifier Potassium Channels by Pharmacological Agents, 122

Manuel Zarzoso, Michelle Reiser, and Sami F. Noujaim

14 Cardiac Stretch-Activated Channels and Mechano-Electric Coupling, 128

Peter Kohl

15 Biophysical Properties of Gap Junctions, 140

Virginijus Valiunas and Peter R. Brink

16 Excitation–Contraction Coupling, 151

Donald M. Bers

PART III Intermolecular Interactions and Cardiomyocyte Electrical Function

17 Ion Channel Trafficking in the Heart, 160

Robin M. Shaw

18 Microdomain Interactions of Macromolecular Complexes and Regulation of the Sodium Channel $\text{Na}_v1.5$, 167

Hugues Abriel

19 Fibroblast Growth Factor Homologous Factors Modulate Cardiac Sodium and Calcium Channels, 177

Geoffrey S. Pitt

20 Macromolecular Complexes and Cardiac Potassium Channels, 180

Stéphane Hatem and Elise Balse

21 Reciprocity of Cardiac Sodium and Potassium Channels in the Control of Excitability and Arrhythmias, 187

Eva Delpón and José Jalife

22 The Intercalated Disc: A Molecular Network That Integrates Electrical Coupling, Intercellular Adhesion, and Cell Excitability, 198

Marina Cerrone, Esperanza Agullo-Pascual, and Mario Delmar

23 Function and Dysfunction of Ion Channel Membrane Trafficking and Posttranslational Modification, 212

Thomas J. Hund and Peter J. Mohler

24 Feedback Mechanisms for Cardiac-Specific MicroRNAs and cAMP Signaling in Electrical Remodeling, 219

Xiao-Dong Zhang and Nipavan Chiamvimonvat

PART IV Cell Biology of Cardiac Impulse Initiation and Propagation

25 Stem Cell–Derived Sinoatrial-Like Cardiomyocytes as a Novel Pharmacological Tool, 226

Andrea Barbuti and Richard B. Robinson

26 Gene Therapy and Biological Pacing, 236

Michael R. Rosen, Ofer Binah, Peter R. Brink, Richard B. Robinson, and Ira S. Cohen

27 Cell-to-Cell Communication and Impulse Propagation, 246

André G. Kléber

28 Mechanisms of Normal and Dysfunctional Sinoatrial Nodal Excitability and Propagation, 259

Brian J. Hansen, Thomas A. Csepe, and Vadim V. Fedorov

29 Cell Biology of the Specialized Cardiac Conduction System, 272

David S. Park and Glenn I. Fishman

30 Cardiac Remodeling and Regeneration, 284

Timon Seeger, Caressa Chen, Ioannis Karakikes, and Joseph C. Wu

PART V Models of Cardiac Excitation

31 Ionic Mechanisms of Atrial Action Potentials, 293

Sandeep V. Pandit

32 Global Optimization Approaches to Generate Dynamically Robust Electrophysiological Models, 304

Trine Krogh-Madsen and David J. Christini

33 Calcium Signaling in Cardiomyocyte Models With Realistic Geometries, 314

Andrew G. Edwards, Johan Hake, Anushka P. Michailova, Masahiko Hoshijima, and Andrew D. McCulloch

34 Theory of Rotors and Arrhythmias, 325

Alexander V. Panfilov and Hans Dierckx

35 Computational Approaches for Accurate Rotor Localization in the Human Atria, 335

Omer Berenfeld

36 Modeling the Aging Heart, 345

Natalia A. Trayanova and Patrick M. Boyle

PART VI Neural Control of Cardiac Electrical Activity

37 Innervation of the Sinoatrial Node, 356

Dainius H. Pauza, Kristina Rysevaite-Kyguoliene, and Neringa Pauziene

38 Mechanisms for Altered Autonomic and Oxidant Regulation of Cardiac Sodium Currents, 362

Gordon F. Tomaselli

39 Pulmonary Vein Ganglia and the Neural Regulation of the Heart Rate, 370

Guillaume Bassil, Manuel Zarzoso, and Sami F. Noujaim

40 Neural Activity and Atrial Tachyarrhythmias, 375

Mark J. Shen, Michael C. Fishbein, Lan S. Chen, Shien-Fong Lin, and Peng-Sheng Chen

41 Sympathetic Innervation and Cardiac Arrhythmias, 387

David Filgueiras-Rama

PART VII Arrhythmia Mechanisms**42** The Molecular Pathophysiology of Atrial Fibrillation, 396

Stanley Nattel, Jordi Heijman, Niels Voigt, Xander H.T. Wehrens, and Dobromir Dobrev

43 Myofibroblasts, Cytokines, and Persistent Atrial Fibrillation, 409

Kuljeet Kaur and José Jalife

44 Role of the Autonomic Nervous System in Atrial Fibrillation, 419

Stavros Stavrakis, Benjamin J. Scherlag, Paul Garabelli, and Sunny S. Po

45 Rotors in Human Atrial Fibrillation, 426

Sanjiv M. Narayan, Junaid A.B. Zaman, David Vidmar, and Wouter-Jan Rappel

46 Body Surface Frequency–Phase Mapping of Atrial Fibrillation, 437

Felipe Ateienza, Andreu M. Climent, and María S. Guillem

47 Panoramic Mapping of Atrial Fibrillation From the Body Surface, 447

Pierre Jaïs, Ashok J. Shah, Remi Dubois, Méléze Hocini, and Michel Haïssaguerre

48 Mechanisms of Human Ventricular Tachycardia and Human Ventricular Fibrillation, 453

Nicholas Jackson, Sigfus Gizurarson, Stéphane Massé, and Kumaraswamy Nanthakumar

49 Genetics of Atrial Fibrillation, 465

Steven A. Lubitz and Patrick T. Ellinor

PART VIII Molecular Genetics and Pharmacogenomics**50** Mechanisms in Heritable Sodium Channel Diseases, 473

Thao P. Nguyen and Alfred L. George, Jr.

51 Genetic, Ionic, and Cellular Mechanisms Underlying the J Wave Syndromes, 483

Charles Antzelevitch and Bence Patocskaï

52 Inheritable Potassium Channel Diseases, 494

Ahmad S. Amin and Arthur A.M. Wilde

53 Inheritable Phenotypes Associated With Altered Intracellular Calcium Regulation, 504

Francisco J. Alvarado and Héctor H. Valdivia

PART IX Pharmacologic, Genetic, and Cell Therapy of Ion Channel Dysfunction**54** Pharmacological Bases of Antiarrhythmic Therapy, 513

Juan Tamargo and Eva Delpón

55 Pharmacogenomics of Cardiac Arrhythmias, 525

Dan M. Roden

56 Gene Therapy to Treat Cardiac Arrhythmias, 531

Silvia G. Priori, Marco Denegri, Rossana Bongianino, and Carlo Napolitano

- 57** Highly Mature Human iPSC-Derived Cardiomyocytes as Models for Cardiac Electrophysiology and Drug Testing, 541

Todd J. Herron

- 58** Cardiac Repair With Human Pluripotent Stem Cell-Derived Cardiovascular Cells and Arrhythmia Risk, 552

Timothy J. Kamp

PART X Diagnostic Evaluation

- 59** Assessment of the Patient With a Cardiac Arrhythmia, 559

Mithilesh K. Das and Douglas P. Zipes

- 60** Differential Diagnosis of Narrow and Wide Complex Tachycardias, 567

John M. Miller and Mithilesh K. Das

- 61** Electroanatomical Mapping for Arrhythmias, 574

Abhishek Deshmukh, Suraj Kapa, and Samuel Asirvatham

- 62** Computed Tomography for Electrophysiology, 587

Alejandro Jimenez Restrepo and Timm M. Dickfeld

- 63** Computed Tomography and Magnetic Resonance Imaging for Electrophysiology, 601

Saman Nazarian and Henry R. Halperin

- 64** Intracardiac Echocardiography for Electrophysiology, 608

Mathew D. Hutchinson and David J. Callans

- 65** Exercise-Induced Arrhythmias, 615

Antonio B. Fernandez, Eric M. Crespo, and Paul D. Thompson

- 66** Cardiac Monitoring: Short- and Long-Term Recording, 623

Andrew D. Krahn, Raymond Yee, Allan C. Skanes, and George J. Klein

- 67** Head-up Tilt Table Testing, 630

Wayne O. Adkisson and David G. Benditt

- 68** Autonomic Regulation and Cardiac Risk, 638

Marek Malik

- 69** T-Wave Alternans, 644

Stefan H. Hohnloser

- 70** Noninvasive Electrocardiographic Imaging of Arrhythmogenic Substrates and Ventricular Arrhythmias in Patients, 655

Yoram Rudy

- 71** Genetic Testing, 668

Christopher Semsarian and Jodie Ingles

PART XI Supraventricular Tachyarrhythmias: Mechanisms, Clinical Features, and Management

- 72** Sinus Node Abnormalities, 674

Dennis H. Lau, Rajiv Mahajan, Jonathan M. Kalman, and Prashanthan Sanders

73 Atrial Tachycardia, 681*Kenneth A. Ellenbogen and Jayanthi N. Koneru***74 Atrial Tachycardia in Adults With Congenital Heart Disease, 700***Dominic James Abrams***75 Typical and Atypical Atrial Flutter: Mapping and Ablation, 713***Chrishan Joseph Nalliah, Saurabh Kumar, Prashanthan Sanders, and Jonathan M. Kalman***76 Atrial Fibrillation: Mechanisms, Clinical Features, and Management, 724***Saurabh Kumar and Gregory F. Michaud***77 Preexcitation, Atrioventricular Reentry, and Variants, 736***Aman Chugh and Fred Morady***78 Electrophysiological Characteristics of Atrioventricular Nodal Reentrant Tachycardia: Implications for the Reentrant Circuits, 746***Deborah J. Lockwood, Hiroshi Nakagawa, and Warren M. Jackman***79 Junctional Tachycardia, 768***Christopher F. Liu, James E. Ip, Steven M. Markowitz, and Bruce B. Lerman***PART XII Ventricular Tachyarrhythmias: Mechanisms, Clinical Features, and Management****80 Premature Ventricular Complexes, 776***Frank Bogun and Rakesh Latchamsetty***81 Outflow Tract Ventricular Tachyarrhythmias: Mechanisms, Clinical Features, and Management, 782***Zian H. Tseng and Edward P. Gerstenfeld***82 Fascicular Ventricular Arrhythmias, 793***Akiko Ueda and Kyoko Soejima***83 Bundle Branch Reentry Tachycardia, 799***Akihiko Nogami and Brian Olshansky***84 Ischemic Heart Disease, 814***David S. Frankel and Francis E. Marchlinski***85 Ventricular Tachycardia in Patients With Dilated Cardiomyopathy, 820***Borislav Dinov, Arash Arya, and Gerhard Hindricks***86 Ventricular Arrhythmias in Hypertrophic Cardiomyopathy: Sudden Death, Risk Stratification, and Prevention With Implantable Defibrillators, 829***Barry J. Maron and Martin S. Maron***87 Ventricular Tachycardias in Arrhythmogenic Right Ventricular Dysplasia/ Cardiomyopathy, 840***Harikrishna Tandri and Hugh Calkins***88 Ventricular Tachycardias in Catecholaminergic Cardiomyopathy (Catecholaminergic Polymorphic Ventricular Tachycardia), 850***Christian van der Werf and Arthur A.M. Wilde*

89 Ventricular Arrhythmias in Heart Failure, 858*Lynne Warner Stevenson, Roy M. John, and Neal K. Lakdawala***90 Arrhythmias and Conduction Disturbances in Noncompaction Cardiomyopathy, 870***Luc Jordaens and Jeffrey A. Towbin***91 Ventricular Arrhythmias in Takotsubo Cardiomyopathy, 878***Abhiram Prasad***92 Brugada Syndrome, 883***Pedro Brugada***93 Long and Short QT Syndromes, 893***Peter J. Schwartz and Lia Crotti***94 Andersen-Tawil Syndrome, 905***Martin Tristani-Firouzi***95 Timothy Syndrome, 910***Silvia G. Priori and Carlo Napolitano***96 J-Wave Syndromes, 917***Sami Viskin and Raphael Rosso***97 Idiopathic Ventricular Fibrillation, 925***Christian Steinberg, Zachary W.M. Laksman, and Andrew D. Krahn***98 Sudden Infant Death Syndrome, 932***Jonathan C. Makielski and Jianding Cheng***99 Sudden Cardiac Death in Adults, 937***Robert J. Myerburg and Jeffrey J. Goldberger***100 Arrhythmia in Neurological Disease, 949***Tarek Zghaib and Saman Nazarian***101 Drug-Induced Ventricular Tachycardia, 962***Lars Eckardt and Günter Breithardt***102 Ventricular Arrhythmias in Congenital Heart Disease, 970***Katja Zeppenfeld, Monique Jongbloed, and Martin Jan Schalij***PART XIII** Syncope and Bradyarrhythmias**103 Syncope, 983***J. William Schleifer, Dan Sorajja, and Win-Kuang Shen***104 Postural Orthostatic Tachycardia Syndrome, 990***Blair P. Grubb and Beverly Karabin***105 Progressive Conduction System Disease, 996***Demosthenes G. Katritsis***106 Atrioventricular Block, 1003***Roy M. John***PART XIV** Arrhythmias in Special Populations**107 Sex Differences in Arrhythmias, 1011***Cevher Ozcan and Anne B. Curtis***108 Sudden Cardiac Deaths in Athletes, Including Commotio Cordis, 1020***Mark S. Link and N.A. Mark Estes III*

109 Arrhythmias in the Pediatric Population, 1032*Edward P. Walsh***110 Sleep-Disordered Breathing and Arrhythmias, 1045***Apoor S. Gami, Sean M. Caples, and Virend K. Somers***111 Ventricular Assist Devices and Cardiac Transplantation Recipients, 1052***Elvis Teijeira Fernández, Karine Nubret Le Coniat, Pierre Jaïs, and Frederic Sacher***PART XV Pharmacologic Therapy****112 Standard Antiarrhythmic Drugs, 1062***Dawood Darbar***113 Innovations in Antiarrhythmic Drug Therapy, 1076***Paulus Kirchhof and Larissa Fabritz***114 Impact of Nontraditional Antiarrhythmic Drugs on Sudden Cardiac Death, 1084***Raul D. Mitrani, Leonard Ilkhanoff, and Jeffrey J. Goldberger***115 Prevention of Stroke in Atrial Fibrillation: Warfarin and New Oral Anticoagulants, 1092***Luciana Armaganijan and Stuart J. Connolly***PART XVI Cardiac Implantable Electronic Devices****116 Implantable Cardioverter Defibrillators: Technical Aspects, 1101***Mohamed H. Kanj and Bruce L. Wilkoff***117 Implantable Cardioverter Defibrillator: Clinical Aspects, 1113***Charles Swerdlow and Paul Friedman***118 Subcutaneous Implantable Cardioverter Defibrillators, 1130***Andrew Grace and Gust H. Bardy***119 Implantable Pacemakers, 1139***Paul J. Wang and David L. Hayes***120 Use of QRS Fusion Complex Analysis in Cardiac Resynchronization Therapy, 1150***Michael O. Sweeney***121 Newer Applications of Cardiac Pacemakers and Extracardiac Stimulation, 1167***Frank Cuoco and Michael R. Gold***122 Remote Monitoring of Cardiac Implantable Electronic Devices, 1173***Emily P. Zeitler, Ruth Ann Greenfield, and Jonathan P. Piccini***PART XVII Catheter Ablation****123 Catheter Ablation: Technical Aspects, 1185***Eric Buch, Noel G. Boyle, and Kalyanam Shivkumar*

124 Catheter Ablation: Clinical Aspects, 1194*Luigi Di Biase, Philip Aagaard, Pasquale Santangeli, and Andrea Natale***125 Ablation for Atrial Fibrillation**, 1211*Nathaniel Thompson, Antonio Frontera, Masateru Takigawa, Arnaud Denis, Nicolas Derval, Méléze Hocini, Pierre Jaïs, and Michel Haïssaguerre***126 Ablation of Supraventricular Tachyarrhythmias**, 1222*Feifan Ouyang, Ardan M. Saguner, Andreas Metzner, and Karl Heinz Kuck***127 Catheter Ablation for Ventricular Tachycardia With or Without Structural Heart Disease**, 1239*William G. Stevenson and Usha B. Tedrow***128 Epicardial Approach in Electrophysiology**, 1253*Arnaud Chaumeil, Frederic Sacher, Michel Haïssaguerre, and Pierre Jaïs***129 Ventricular Fibrillation**, 1263*Méléze Hocini, Ashok J. Shah, Pippa McKelvie-Sebilleau, and Michel Haïssaguerre***130 Ablation in Pediatrics**, 1270*Jennifer N.A. Silva and George F. Van Hare***131 Catheter Ablation in Congenital Heart Disease**, 1280*Edward P. Walsh***132 Anesthesiology Considerations for the Electrophysiology Laboratory**, 1288*Wendy L. Gross, Mark S. Weiss, Lebron Cooper, and William G. Stevenson***PART XVIII** Surgery for Arrhythmias**133 Surgery for Atrial Fibrillation and Other Supraventricular Tachycardias**, 1295*Matthew R. Schill, Spencer J. Melby, Richard B. Schuessler, and Ralph J. Damiano, Jr.***134 Surgery for Ventricular Arrhythmias**, 1307*Sanjay Dixit and Y. Joseph Woo***PART XIX** New Approaches**135 Vagus Nerve Stimulation for the Treatment of Heart Failure**, 1316*Hani N. Sabbah***136 Baroreceptor Stimulation**, 1323*Gino Seravalle and Guido Grassi***137 Spinal Cord Stimulation for Heart Failure and Arrhythmias**, 1328*Mark J. Shen and Douglas P. Zipes***138 Renal Sympathetic Denervation**, 1331*Jacob S. Koruth, Sujata Balulad, and Andre d'Avila***139 Left Atrial Appendage Closure**, 1337*Mohammad Sarraf, Douglas L. Packer, and David R. Holmes, Jr.***Index**, 1345