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Mathematical and Numerical Modeling of the Cardiovascular System and Applications

Springer

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Preface

This book is dedicated to the outstanding career of Piero Colli Franzone, one of the founders of the field of computational electrocardiology. Piero graduated in mathematics from the University of Pavia in 1969. He subsequently became a researcher at the Institute of Numerical Analysis of the National Research Council (CNR) in Pavia (1971–1973), Associated Professor of Mathematical Analysis at the University of Pavia (1973–1981), and Full Professor of Numerical Analysis, first at the University of Udine (1981–1983) and then at the University of Pavia (1983–2016), where he is now Professor Emeritus. During his career, Piero has made pioneering contributions in the field of the inverse problem of electrocardiology, in the development of eikonal models for the propagation of electrical signals in cardiac tissue, in the development of an anisotropic source model for the simulation of electrocardiograms, and more recently in the modeling of cardiac mechanics and electromechanical coupling.

Although Piero's works have mainly focused on computational cardiac electrophysiology and mechanics, this book also contains contributions on the modeling and simulation of the entire cardiovascular system. The increasing use of numerical models and methods in the field of diagnosis/prognosis/therapy of cardiovascular diseases (the main cause of death in Western countries) is considered very important and increasingly appreciated by the scientific and medical community. However, its penetration into clinical practice is slowed by various cultural factors and methodological challenges, in particular by the high computational cost of the complex mathematical, multiscale, and nonlinear models used in computational cardiology.

The quantitative description of cardiovascular activity is based on the construction, analysis, and simulation of models of both the heart and the circulatory system. Cardiac models are composed of nonlinear multiphysical submodels that describe the three main components (electrophysiology, mechanics, and hemodynamics) of cardiac activity, with spatial and temporal scales very different from each other and with specific computational difficulties. The bioelectric models are based on systems of partial and ordinary differential equations that include both the microscopic models of the membrane ionic channels and the macroscopic cardiac models (bidomain, monodomain, and eikonal models). The mechanical models are based on nonlinear orthotropic elastic models for the large deformations of the almost incompressible cardiac tissue and active tension models for the generation of the myocyte contraction. The hemodynamic models are based on the equations of incompressible fluid dynamics in moving domains for blood flow in the cardiac chambers and in the vascular system. Another important process which is described by the interaction between fluid and structures is given by the cardiac valve modeling.

The numerical simulation of these complex multiscale models coupled together by various reaction and feedback terms is very intense, and several aspects are still problematic. The integrated simulation of the three main cardiac phases (bioelectrical, mechanical, and fluid dynamical) is currently a very competitive goal: several leading research groups in the world are working intensively toward this goal, which, if reached in the next few years, could have a major impact on our basic scientific knowledge (regarding cardiac arrhythmogenesis, myocardial infarction, ischemia, heart failure, valve pathologies, etc.), on health technologies, and on the design and development of new biomedical devices.

This volume contains selected invited papers from the conference "Mathematical and Numerical Modeling of the Cardiovascular System and Applications," held at the Aula Volta of the University of Pavia, Italy, on February 21–22, 2017 (http://matematica.unipv.it/pieroconference/), which was also the final workshop of the PRIN Project (funded by the Italian government) 2012HBLYE4 "Metodologie Innovative nella Modellistica Differenziale Numerica" coordinated by Alfio Quarteroni. The conference comprised contributions from recognized international experts in diverse fields of cardiovascular modeling and simulation. The event was sponsored by the Department of Mathematics of the Universities of Pavia and Milan, SISSA, the Polytechnic of Milan, the MIUR Grants PRIN 201289A4LX, PRIN 2012HBLYE4, the INdAM Grant Project GNCS 2017, and the Progetto Cariplo-Regione Lombardia: Problemi variazionali di evoluzione e trasporto ottimo.

The first chapter, entitled "A Distributed Lagrange Formulation of the Finite Element Immersed Boundary Method for Fluids Interacting with Compressible Solids" and coauthored by Daniele Boffi, Lucia Gastaldi, and Luca Heltai, reports on recent advances in the modeling and the numerical approximation of fluids interacting with compressible solids. A version of the Finite Element Immersed Boundary Method is presented which is based on a new variational formulation, thanks to the introduction of a distributed Lagrange multiplier. Stability estimates and numerical validation are included.

The second chapter, entitled "High-Order Operator-Splitting Methods for the Bidomain and Monodomain Models" and coauthored by Jessica Cervi and Raymond J. Spiteri, focuses on high-order operator splitting methods for the reaction-diffusion systems of computational electrocardiology. The methods considered are third and fourth order accurate and are based on use of a combination of explicit and implicit Runge–Kutta schemes. Numerical tests in one and three spatial dimensions and employing both simplified and detailed ionic models are performed to assess the accuracy of the methods.

The third chapter, entitled "Electro-mechanical Modeling and Simulation of Reentry Phenomena in the Presence of Myocardial Infarction" and coauthored by Piero Colli Franzone, Luca F. Pavarino, and Simone Scacchi, presents a review of the cardiac electromechanical coupling models and of the numerical methods for their discretizations. It then reports the results of numerical simulations focusing on the genesis of reentrant arrhythmias in the presence of infarct scars.

The fourth chapter, entitled "Ergotropic Effect in Cardiac Tissue After Electromagnetic and β-Adrenergic Stimulus" and coauthored by Lorenzo Fassina, Marisa Cornacchione, Maria E. Mognaschi, Giovanni Magenes, and Fabio Naro, demonstrates ergotropic effects in murine ventricular cardiomyocytes after electromagnetic field and/or isoproterenol stimulation by means of an innovative image processing technique. The study adds important and significant findings with regard to the structure–function relationship in spontaneously beating primary cultures of murine cardiomyocytes.

The fifth chapter, entitled "Role of Electrotonic Current in Excitable Cells" and coauthored by Emilio Macchi, Ezio Musso, and Stefano Rossi, provides a thorough overview of our understanding of electrotonic current in excitable cells. After a short introduction, the authors go through cable models of conduction, electrotonic currents and potentials, subthreshold current injection, the stimulation threshold, and propagating action potentials. Finally, the authors discuss electrotonic modulation of repolarization by the activation sequence and present some experimental evidence of acute modulation of the activation-recovery interval and the effective refractory period at a test site during ventricular drive and sinus rhythm in the normal rat heart.

The sixth chapter, entitled "Reduced Order Modeling for Cardiac Electrophysiology and Mechanics: New Methodologies, Challenges & Perspectives" and coauthored by Andrea Manzoni, Diana Bonomi, and Alfio Quarteroni, presents an extensive and detailed description of POD-Galerkin methods developed to speed up the solution of parametric coupled electromechanical problems arising in cardiac electrophysiology. In the first part, the authors introduce the models used to describe the electrophysiology and the mechanics of living tissues. Then, after presenting the full-order discretization and reduced-order techniques, they detail the methods used to tackle the challenges of the system considered and the numerical experiments.

The seventh chapter, entitled "Aortic Endovascular Surgery" and coauthored by M. Conti, S. Morganti, A. Finotello, R.M. Romarowski, A. Reali, and F. Auricchio, reports on the use of computer simulations to support two of the most routinely performed endovascular procedures: thoracic endovascular aortic repair (*TEVAR*) and transcatheter aortic valve implantation (*TAVI*). The authors report a short review of simulations (structural for TEVAR and both structural and fluid dynamics for TAVI) and then present two examples of applications.

The eighth chapter, entitled "Combined Parameter and Model Reduction of Cardiovascular Problems by Means of Active Subspaces and POD-Galerkin Methods" and coauthored by Marco Tezzele, Francesco Ballarin, and Gianluigi Rozza, deals with a first example of combination of a priori geometrical parameter space reduction carried out by the active subspace approach combined with a classic computational reduction method for blood flows, based on the POD-Galerkin technique, and applied over a parametrized shape of a patient-specific carotid artery bifurcation. This model problem could be seen as a proof of concept for future, more involved, applications in blood flows.

The ninth chapter, entitled “Extended Finite Elements Method for Fluid-Structure Interaction with an Immersed Thick Non-Linear Structure” and coauthored by Christian Vergara and Stefano Zonca, first introduces an overview of extended finite element methods for general interfaces and heterogeneous coupled problems. Then, it addresses the fluid-structure interaction problem for a thick immersed structure whose thickness is, however, often smaller than the fluid mesh characteristic size. In particular, the authors proposed an inexact Newton method to handle the case of a nonlinear structure described by finite elasticity. Finally, the chapter presents some numerical 3D results.

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Luca F. Pavarino is Professor of Numerical Analysis at the Department of Mathematics of the University of Pavia. He holds a PhD (1992) and master's (1990) in mathematics from the Courant Institute, NYU, USA, and a B.S. degree (1987) in mathematics from the University of Pavia. He was a Postdoctoral Research Associate at Rice University, USA, and Professor at the University of Milan. His current research focuses on domain decomposition methods for PDEs, parallel computing, and biomathematics.

Gianluigi Rozza is Full Professor of Numerical Analysis and Scientific Computing at SISSA, International School for Advanced Studies. He holds a degree in aerospace engineering from Politecnico di Milano (2002) and a PhD in applied mathematics from Ecole Polytechnique Federale de Lausanne (2005). He was a Postdoctoral Research Associate at the Massachusetts Institute of Technology (MIT) Center for Computational Engineering (2006–2008) and then a Researcher and Lecturer at EPFL (2008–2012). He is the author of over 100 scientific publications and recipient of the 2014 ECCOMAS young investigator Jacques Louis Lions Award in Computational Mathematics for researchers under the age of 40. Professor Rozza has been an Associate Editor of the *SIAM/ASA Journal of Uncertainty Quantification* since 2013, of the *SIAM Journal of Numerical Analysis* since 2015, and of *Computing and Visualization in Science* since 2016.

Simone Scacchi is Associate Professor of Numerical Analysis at the Department of Mathematics of the University of Milan. He received a degree in mathematics from the University of Milan (2004) and a PhD in mathematics and statistics from the University of Pavia (2008). He was a Postdoctoral Research Associate at the University of Pavia (2008) and then Assistant Professor at the University of Milan (2008–2015).

Christian Vergara has been Associate Professor of Numerical Analysis at MOX, Dipartimento di Matematica, Politecnico di Milano, since 2015. He received a PhD in mathematical engineering from Politecnico di Milano in 2006. His primary research interests are the numerical approximation of fluid-structure interaction problems, the numerical modeling of the cardiovascular system, both in terms of blood dynamics and electrical activity of the heart, and the application to cases of clinical interests.