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Mathematical Modelling of the Human Cardiovascular System

Data, Numerical Approximation, Clinical Applications

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Contents

Introduction

This book is devoted to the mathematical and numerical modelling of the cardiovascular system, a research topic that has attracted remarkable interest from both the mathematical and bioengineering communities over the past 25 years. The driving motivation for this interest is the increasing impact of cardiovascular diseases in our lives. According to Mozaffarian *et al.* (2015), cardiovascular diseases are the major cause of death worldwide, leading to more than 17.3 million deaths per year, a number that is expected to grow to more than 23.6 million by 2030. In Europe this now corresponds to nearly half of all deaths (47%).

We focus on the two principal components of the cardiovascular system: *arterial circulation* and *heart function*, with its electrical and mechanical activities, blood flow in its chambers, and valve dynamics. Geometric complexity, the lack of data to feed the mathematical models, and the multiphysics and multiscale nature of the processes at hand present major challenges when trying to reproduce both function and dysfunction.

Owing to its composite nature, the cardiovascular system is first modelled by means of stand-alone *core components*, each describing a single functionality, for example arterial fluid dynamics, the electrical activity of the heart, and the fluid dynamics in the left ventricle. Each core model needs careful mathematical analysis and efficient numerical approximation, often via specifically devised methods. The next step is integration of the core models into global, coupled integrated models suitable for describing a meaningful and coherent part of the cardiovascular system – or even the entire system. This step requires the introduction of suitable coupling conditions, as well as novel numerical strategies for a stable, robust and computationally effective solution of the global problem.

Clinical data play a decisive role in models of the cardiovascular system, and at the same time dealing with data represents a formidable challenge.

Clinical radiological images (such as *computer tomography* and *magnetic resonance imaging*) are necessary to construct the computational domains wherein the mathematical models (very often based upon a system of differential equations) are defined. The procedure of geometric reconstruction is difficult and, especially for the heart, requires advanced mathematical and numerical tools. Standard radiological images can sometimes be useless: some cardiovascular components may be smaller than the spatial resolution of the imaging device (this is the case for the Purkinje network, for example); in other cases the elevated brightness gap between fluid and vessel wall makes the detection of the latter very hard. Boundary data that feed the mathematical models are also difficult to obtain. When the computational domain results from an artificial truncation, specific physical quantities (*e.g.* fluid velocity or pressure) should be provided at those locations of the arterial tree corresponding to the artificial boundaries. However, this would require invasive measurements that cannot be easily carried out. In some specific circumstances, this calls for suitable parameter identification and data assimilation techniques. Finally, the huge inter- and intra-patient data variability and uncertainty are further sources of concern regarding model calibration and validation.

In spite of all these difficulties, a wealth of models has already been successfully used to address both physiological and pathological instances. The aim is, on one hand, a better understanding of the physical and quantitative processes governing the cardiovascular system, and on the other hand the opening of new frontiers in therapeutic planning and the design of implantable devices (*e.g.* medical stents, cardiac defibrillators, ventricular assisted devices and prosthetic valves).

The literature on the mathematical and numerical modelling of the cardiovascular system is huge, as readers will see by browsing our references, a tiny subset of the total. In the following chapters we will provide a perspective on the main contributions to this field. Here, among the several books, monographs and review papers published so far, we mention Formaggia, Quarteroni and Veneziani (2009*a*), Taylor and Figueroa (2009) and Quarteroni, Veneziani and Vergara (2016*c*) for the circulatory system, and Peskin (2002), Smith, Nickerson, Crampin and Hunter (2004), Colli Franzone, Pavarino and Scacchi (2014), Quarteroni (2015) and Quarteroni, Lassila, Rossi and Ruiz-Baier (2017) for the heart.

The book consists of three main parts: in Part 1 we model the *arterial circulation* (Chapters 1, 2 and 4), in Part 2 we model the *heart function* (Chapters 5, 6 and 7), and in Part 3 we treat *inverse problems* and include *uncertainty* (Chapters 8, 9, 10 and 11). Both Parts 1 and 2 consist of an introductory section on physiology (Chapters 1 and 5), a section describing the available data and their use (Chapters 2 and 6), and a final section on mathematical and numerical modelling (Chapters 4 and 7). In Part 3 we begin by emphasizing the need to move beyond a single (forward) simulation in some applications (Chapter 8). This represents the common denominator of three topics recently applied to cardiovascular mathematics: *control and optimization* (Chapter 9), *parameter estimation* (Chapter 10) and *uncertainty quantification* (Chapter 11).

When appropriate (in particular in Chapters 4, 7, 9, 10 and 11), we report some numerical results to highlight the effectiveness of the numerical strategies presented here. Unless otherwise specified, all the numerical results presented in this book have been obtained using the finite element library LifeV; see www.lifev.org for more details.

Disclaimers. This book is based upon the review paper A. Quarteroni, A. Manzoni and C. Vergara (2017), 'The cardiovascular system: mathematical modelling, numerical algorithms and clinical applications', *Acta Numerica*, 365–390. Several slight (and sometimes more substantial) additions have been made throughout.

Despite the fact that it is 280 pages long,[1] several topics related to the cardiovascular system have not been addressed. Among others, we mention the *venous system* (essential if one wants to consider a closed-loop model of the cardiovascular system, and playing a crucial role in some specific pathologies: see *e.g.* Toro 2016), the *metabolic system* (D'Angelo 2007), the *respiratory system* (Maury 2013, Wall, Wiechert, Comerford and Rausch 2010, Trenhago *et al.* 2016), the *cerebro-spinal fluid circulation* (Fin and Grebe 2003), the *nervous system* (Liang and Liu 2006) the *lymphatic system* (Margaris and Black 2012) and growth and remodelling of the tissue (Humphrey and Rajagopal 2002). For some of them (*e.g.* the venous and respiratory systems) research has made remarkable progress in recent years. Nonetheless, the mathematical investigation of these systems is still in its infancy; in particular, their coupling with the cardiovascular system is almost absent. Many research avenues are open to the contribution of both pure and applied mathematicians, with the dream of enabling mathematical achievements to play a decisive role in everyday clinical practice.

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[1] By slightly rephrasing Blaise Pascal's quotation, we can state that '*we were not good enough* to make it shorter.'

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