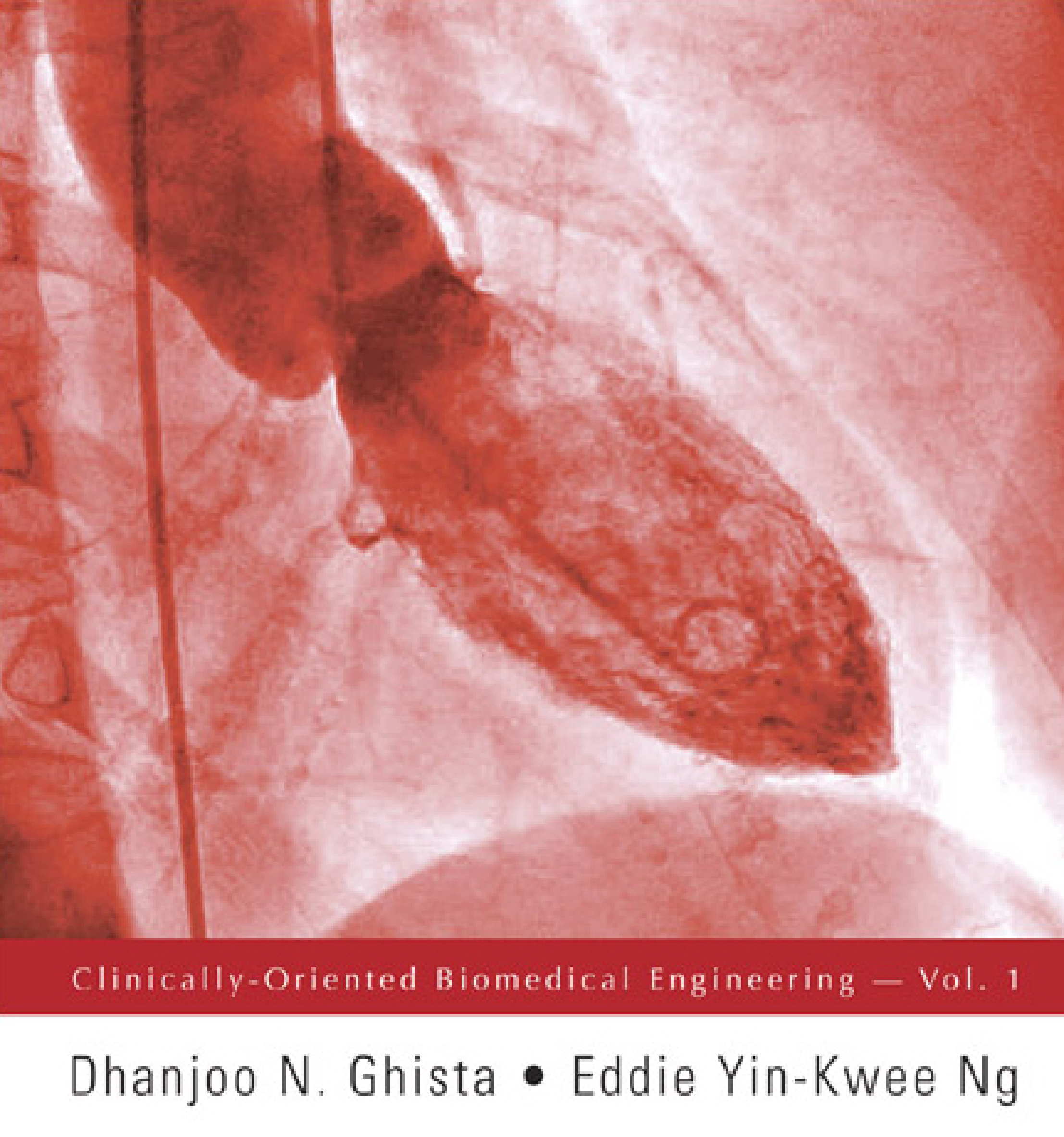

Clinically-Oriented Biomedical Engineering — Vol. 1

Dhanjoo N. Ghista • Eddie Yin-Kwee Ng

Cardiac Perfusion and Pumping Engineering

Cardiac Perfusion and Pumping Engineering

Clinically-Oriented Biomedical Engineering — Vol. 1

Cardiac Perfusion and Pumping Engineering

Dhanjoo N. Ghista
Eddie Yin-Kwee Ng
Nanyang Technological University, Singapore

World Scientific
NEW JERSEY • LONDON • SINGAPORE • BEIJING • SHANGHAI • HONG KONG • TAIPEI • CHENNAI

Published by

World Scientific Publishing Co. Pte. Ltd.
5 Toh Tuck Link, Singapore 596224
USA office: 27 Warren Street, Suite 401-402, Hackensack, NJ 07601
UK office: 57 Shelton Street, Covent Garden, London WC2H 9HE

British Library Cataloguing-in-Publication Data
A catalogue record for this book is available from the British Library.

Clinically-Oriented Biomedical Engineering — Vol. 1
CARDIAC PERFUSION AND PUMPING ENGINEERING

ISBN-13 978-981-270-696-6
ISBN-10 981-270-696-8

Typeset by Stallion Press
Email: enquiries@stallionpress.com

Printed in Singapore.

REVIEWS

"Cardiac Perfusion and Pumping are inter-related, and hence together constitute an intriguing phenomenon that governs cardiac performance. This fascinating book is unique in addressing the clinical features and bioengineering characteristics of cardiac perfusion and pumping. The book also addresses assisted pumping (in the form of left ventricular assist devices) and cardiac tissue engineering (to replace and regenerate myocardial infarcts). The bioengineering formulations of the various chapters are not only sufficiently rigorous to be instructive for bioengineering courses, but are also clinically oriented. The book should be very useful to biomedical engineers as well as cardiologists and cardiac surgeons."

Ghassan S. Kassab
Thomas J. Linnemeier Guidant Endowed Chair
and Professor of Biomedical Engineering
Professor of Surgery, Cellular and Integrative Physiology
Indiana-Purdue University, USA

"This book is unique! It describes the multiple aspects of cardiac ventricular contraction (provided by cardiac perfusion and pumping characteristics), by observing the specific features associated with contraction with an amplified attention. The result is an intermediate step between the well-accepted biomechanical interpretations and fully new and original scientific descriptions. This book is not just a book of a collection of accepted and validated concepts. Nor, is it a special issue of a scientific journal (devoted to perfusion and pumping), with proposals of new concepts and descriptions. Rather, it is an intermediate status of the matter. If you are searching for concrete aspects, you will find therein the relevant models and rules currently accepted by the scientific community. However, if your mind wants to fly out of the actual constraints, you have so many opportunities to compare your most original ideas with those described by the authors, that you will be engaged in a fascinating game.

You will find in the book an acceptable and agreeable scent of science, which impregnates every page of the book and drags a bright mind into a knowledge paradise!"

Romano Zannoli
Professsor of Medical Physics
University of Bologna, Italy

This page intentionally left blank

PREFACE

Cardiac pumping is dependent on cardiac perfusion. Hence, it is only natural that we address both cardiac perfusion and pumping in this book. We have gone one step further in also considering assisted perfusion by coronary bypass surgery and myocardial regeneration by means of stem cells transformed into implantable cardiomyocytes. The book is hence divided into three sections:

(1) Cardiac Perfusion,
(2) Cardiac Pumping Characteristics,
(3) Assisted Perfusion and Pumping, and Myocardial Repair.

Section I on Cardiac perfusion starts out with the chapter on physiomics of coronary microcirculatory perfusion, which supplies nutrients to the heart myocardium for its contraction. The following chapter deals with the phenomenon of myocardial inhomogeneity, and provides an answer to this enigma as the basis of providing cardiac functional reserve. The next chapter is on quantification of cardiac perfusion and function, using nuclear cardiac imaging. The final chapter in this section is a synthesis of cardiac perfusion and pumping. It analyses left-ventricular (LV) pumping in terms of intra-ventricular blood flow velocity and pressure distributions, and also computationally depicts the distribution of pressure and flow velocities in discrete regions of the heart.

Section II is on how cardiac pumping is initiated by myocardial contraction, causing stresses and strains in the myocardium. More importantly, the mechanism of how myocardial contraction causes LV torsion is also discussed. The LV myocardial fibers are spirally wound inside its wall. Thereby, when they contract, the LV twists and then unwinds during relaxation. While this LV torsion is an end-product of LV myocardial fibers geometry and contraction, it can also serve as an index of contractility. Finally, in order for LV to contract or to depict its inability to contract adequately for adequate blood outflow, we have developed indices to assess its contractility, in the form of some intrinsic indices that correlate well with the traditional contractility index of $(\mathrm{d}P/\mathrm{d}t)_{\max}$. In doing so, we have also addressed a hitherto unexplained phenomenon of LV suction during its early filling state. The LV sarcomere is still contracting (albeit decreasing its contractile force and shortening velocity) during early filling. It is this mechanism that causes LV suction (and resulting LV pressure decrease), before the left atrium starts to contract and cause LV filling.

Cardiovascular disease results in *in vivo* bioelectrical abnormalities, blocked coronary vessels and consequently myocardial infarcts. Hence, it is but natural that this book also deals (in Section III) with methods of augmented myocardial perfusion by coronary bypass surgery, mechanical circulatory support in the form of cardiac-assist devices, and myocardial regeneration by means of implantable three-dimensional cardiomyocyte constructs converted from embryonic stem cells. In this regard, this section discusses in detail the reasons for blocked distal coronary graft-occluded vessel anastomosis, the mechanical analysis of circulatory-support ventricular-assist systems, and in particular of an axial blood pump. The last two chapters deal with the basis and prospects of tissue engineering and novel approaches to cell transplantation following the conversion of embryonic stem cells into cardiomyocyte scaffolds for implantation.

We hope that this book can serve as a major reference resource in *cardiology* and *cardiac surgery*, as well be employable as a course text for a course on this topic in a biomedical engineering program. With these aims in mind, the individual chapters deal in adequate rigor with both theory and clinical applications.

Thank you.

Dhanjoo N. Ghista and Eddie Yin-Kwee Ng
Nanyang Technological University
Singapore 639798

October 2006

CONTENTS

This page intentionally left blank

BOOK SUMMARY

Section I. Cardiac Perfusion

Chapter 1. Physiomics of Coronary Perfusion and Cardiac Pumping by Fumihiko Kajiya, Masahito Kajiya, Taro Morimoto, Tatsuo Iwasaki, Yousuke Inai, Masanori Hirota, Takahiko Kiyooka, Yuki Morizane, Takehiro Miyasaka, Satoshi Mohri and Juichiro Shimizu

Physiome is considered to be a powerful successor to the *genome*. Physiome refers to a quantitative description of the physiologic dynamics or functions of the intact organism. It includes integration of knowledge through functional modules and modelling of hierarchic system elements of biologic systems. Biomechanics offers potent tools to promote the *physiome concept*. By using modern microvisualization technology with physiomic model of coronary circulatory network, this chapter introduces our physiomic approach to coronary microcirculation, which supplies oxygen and nutrients to heart muscles.

The heart is unique, among other organs, in that coronary arterial flow is exclusively diastolic while venous flow is systolic. That is, blood pooled in coronary microvessels (during diastole) is squeezed out to the coronary vein by myocardial contraction. In this chapter, we first describe the biomechanical interaction between coronary blood flow and cardiac contraction. Then, the physiome of coronary capillary network and its functions are discussed.

Chapter 2. Left Ventricular Inhomogeneity and the Heart's Functional Reserve by Felix Blyakhman

This chapter concerns with the study of myocardial inhomogeneity in the left ventricular wall. Inhomogeneity is an attribute of both the normal heart and the pathologically compromised heart. In the course of the last couple of decades, this phenomenon has revealed that myocardial inhomogeneity is a modulator of cardiac contractility and/or pump function, although the significance of inhomogeneity for the normal heart has not yet been clarified. Why has nature created such an inhomogeneous device? In this chapter, we seek an answer to this question. We present evidence that the possible role of inhomogeneity in the normal heart is to provide functional reserve for the left ventricle, which is tapped (as needed) to maintain stability of cardiac pumping function throughout the course of life.

Chapter 3. Quantification of Cardiac Perfusion and Function Using Nuclear Cardiac Imaging by Ru-San Tan, Liang Zhong, Terrance Chua and Dhanjoo N. Ghista

Myocardial ischemia occurs when tissue metabolic needs outstrips coronary blood flow or perfusion. The deficiency of the latter is commonly caused by atherosclerotic coronary artery disease, and is diagnosed by various myocardial perfusion imaging techniques that track blood flow heterogeneity between myocardium supplied by normal versus narrowed arteries. Nuclear myocardial perfusion imaging, the most established and ubiquitous of these methods, uses radioactive isotopes (commonly thallium-201- or technetium-99m-based tracer agents) combined with stress and rest imaging protocols, to evaluate regional relative coronary flow reserves, and hence diagnose areas of myocardial ischemia and infarction. Modern image acquisition, using single photon emission computed tomography, allows the reconstruction of a three-dimensional image dataset that facilitates visual analysis as well as quantitation of perfusion. This increases reproducibility of interpretation, and is especially useful in the assessment of myocardial viability. Further, electrocardiographic gating, during the scan acquisition, allows assessment of left ventricular function, which has great prognostic significance. Quantitated perfusion and functional data can be displayed as polar maps that are amenable to comparison with normal databases, thus enhancing the clinical applicability of the technique.

Chapter 4. Regional Mechanics of the Beating Heart by Martyn P. Nash and Peter J. Hunter

Mathematical modeling provides a useful tool to understand the normal and abnormal mechanical function of the heart. The large deformations that take place during the cardiac cycle require that finite deformation elasticity must be used with the governing laws of physics. In addition, the complex geometry and microstructural arrangement of cardiac muscle requires that numerical and computational methods need to be used to solve the resulting nonlinear equations.
This chapter summarizes a continuum mechanics approach to analyzing myocardial soft tissues, and details how the orthotropic nature of the ventricular myocardium may be efficiently represented. Based on this framework, a finite element analysis of canine ventricles is presented, and

the distributions of deformation and regional mechanical stress throughout the heart cycle are quantified.

Chapter 5. Left Ventricular (LV) Pumping–Perfusion Analysis: Myocardial Properties, Intra-LV Velocity and Pressure, Detection of Myocardial Ischemic and Infarcted Segments, Perfusion Depiction by SPECT Imaging, Computation of Blood Flow Pressure and Velocity Patterns Within Myocardial Regions by Eddie Y. K. Ng, Dhanjoo N. Ghista, Jian Jun Shu, Reginald C. Jegathese and Meena Sankaranarayanan

This chapter essentially provides an overview of LV perfusion and pumping (and connects these two LV functions), by employing different methods for characterizing: (i) pumping in terms of LV passive and active myocardial properties, as well as intra-LV flow velocity and pressure distributions; (ii) perfusion based on detection of LV myocardial ischemic and infarcted segments (by means of echocardiographic texture analysis), SPECT imaging, and computational analysis of intra-myocardial regional perfusion.

Section II. Cardiac Pumping Characteristics

Chapter 6. Left Ventricular (LV) Pressure Increase Mechanism During Isovolumic Contraction, and Determination of the Equivalent LV Myocardial Fibers Orientation by Dhanjoo N. Ghista, Li Liu, Liang Zhong, Si Yong Yeo, Leok Poh Chua, Ru-San Tan, and Yong Seng Tan

Herein, a biomechanical thick-walled cylindrical model of the left ventricle (LV) is developed to demonstrate that the mechanisms of LV internal pressure increase during isovolumic contraction is due to the contraction of the LV myocardial fibers helically wrapped inside the LV wall. The contraction of these fibers deforms and twists the LV. Hence, we can indirectly associate LV twisting with LV contractility. Associated with the LV pressure increase, we have determined the LV (radial, longitudinal, and twist) deformation state. We then determine the LV wall stressès associated with the deformations, and thereby the principal stresses in the LV wall, along with the axial shortening force and the torque experienced by the LV.
We now hypothesize that the LV principal stressès orientation corresponds to the orientation of the LV cylindrical model myocardial fibers. This is how we are able to postulate that the contraction of these LV myocardial fibers causes LV deformations, inducing torsion of the LV and associated LV twist angle. Further, the derived orientation of the LV myocardial fibers

may be deemed to be an intrinsic property of the LV, and determine its capacity for adequate blood outflow into the aorta.

Chapter 7. Left Ventricular Filling Performance Characteristics by Dhanjoo N. Ghista, Liang Zhong, Ru-San Tan and Eddie Y. K. Ng

Left ventricular (LV) filling in turn influences LV contraction because inadequate filling will cause inadequate contraction. Hence, it is important to develop an appropriate LV filling index in terms of monitorable LV pressure and volume. Hence, the prime objective of this chapter is to develop an index to assess the filling functional performance of the LV in terms of monitorable LV pressure and volume.

For this purpose, the LV volume response to the driving pressure term is formulated in terms of a differential equation. This equation is solved for LV volume expression (in terms of the model parameters) for two filling phases: (i) the early filling phase due to LV suction, during which the LV myocardial sarcomere contractile element is relaxing and the driving pressure term (in the governing differential equation) is zero, and (ii) the second phase of filling, due to left atrial contraction.

Chapter 8. New Clinically Relevant Left Ventricular Contractility Index (Based on Normalized Wall Stress) by Dhanjoo N. Ghista, Liang Zhong, Ru-San Tan, Eddie Y. K. Ng and Leok Poh Chua

It may be said that any comparative analysis of contractility indices in the intact heart is somewhat arbitrary, due to lack of an ideal descriptor of the contractile state. Hitherto, left ventricular (LV) $(\mathrm{d}P/\mathrm{d}t)_{\max}$ has been employed as a measure of LV contractility, and has been shown to be a relatively load-dependent index. It is however an extrinsic measure of LV contractility, because the LV pressure itself is developed by LV wall stress caused by LV myocardial sarcomeric contraction.

It is hence natural to represent LV contractility by means of this intrinsic property of the LV (namely its circumferential wall stress normalized with respect to LV pressure), which is independent of the preload and afterload. For this purpose, our LV spherical model's wall stress is normalized with respect to LV pressure, and its maximum value is adopted as an index of LV contractility.

Our new index is an intrinsic property of the LV, as well as easily and non-invasively obtainable in terms of measurable LV volume and myocardial volume. For the formulation of this contractility index, the LV is modeled as a pressurized thick-walled sphere; to reduce the mathematical complexity and for clinical application convenience. The high degree of correlation between our new and simple contractility index and $(d\mathrm{P}/d\mathrm{t})_{\max}$ shows that it is well capable of separating normal LVs from LVs with impaired LV contractility.

Chapter 9. Characterization of Cardiac Dysfunction During Systolic Ejection by Dhanjoo N. Ghista, Liang Zhong, Eddie Y. K. Ng and R. S. Tan

It can be said that it is the left ventricular (LV) sarcomere contractility that develops the LV pressure in response to its volume during filling and ejection phases. In this chapter, we develop the governing equations of dynamics of the LV sarcomere contained within the wall of the LV cylindrical model. We then relate the sarcomere stress and displacement to the monitored LV pressure and volume, in terms of the sarcomere elements' parameters (namely the sarcomere contractile element (CE) force and shortening velocity), and evaluate them. We next determine the power generated by the sarcomere (CE) element. All of these indices are deemed to be important LV functional determinants.

Chapter 10. Strain Analysis and Visualization of LV Deformation During a Cardiac Cycle, As an Index of Contractility by Jinah Park and Sang I. L. Park

The three-dimensional (3D) deformation fields of the LV models were initially estimated from tagged MRI data sets, which provide in-plane temporal correspondence of material points. While there is some initial experience in the use of tagged MRI and related techniques to study the 3D motion of a heart, there is still no generally accepted method for analysis and display of the 3D heart motion. Our parameter-function model captures the 3D deformation field in terms of its model parameters, and the volumetric model can then be regenerated based on the estimated parameters, allowing us to select any desired volume element within the myocardium for a conventional strain analysis.
We have verified that the results of a conventional strain analysis performed on the parameter-function model are in agreement with those from a conventional finite element model. Furthermore, we have proposed a new methodology in visualizing multi-dimensional rendition of the LV overall myocardial strain variation. This will help gain a thorough and localized

understanding of the LV motion, and should significantly increase the clinical utility of LV motion analyses.

Section III. Assisted Perfusion and Pumping, and Myocardial Repair

Chapter 11. Augmented Myocardial Perfusion by Coronary Bypass Surgical Procedure: Emphasizing Flow and Shear Stress Analysis at Proximal and Distal Anastomotic Sites Providing the Basis of Better Graft Patency Rates by Dhanjoo N. Ghista, Meena Sankaranarayanan, Leok Poh Chua, Yong Seng Tan and Eddie Y. K. Ng

Coronary artery bypass grafting (CABG) surgery is an effective treatment modality for patients with severe coronary artery disease. CABG is a routine surgical treatment for ischemic heart disease. A large number of CABG cases fail postoperatively due to intimal hyperplasia within months or years, due to deleterious blood-flow velocity and shear–stress distributions at the graft–artery junctions. The conduits used during the surgery include both the arterial and venous conduits. Long-term graft patency rate for the internal mammary arterial graft is superior, but the same is not true for the saphenous vein grafts. At 10 years, more than 50% of the vein grafts would have occluded, and many of them are diseased.

This chapter presents the fluid-dynamics of blood flow in (i) the aorto-right in-plane CABG model (the centerline of the aorta, graft, and the host artery all lie in a plane) and (ii) an out-of-plane CABG model (the centerline of the aorta, graft, and the host artery do not lie in a plane), wherein the left anterior descending artery is bypassed using the sapheneous vein. In our model, the dimensions of the aorta, saphenous vein, and the coronary artery simulate the actual dimensions at surgery, and we employ three-dimensional computational fluid-dynamics, to analyze the blood flow at both proximal and distal anastomoses.

Our results have revealed that (i) maximum perfusion of the occluded artery occurs during mid-diastole, (ii) the maximum wall shear–stress variation is observed around the distal anastomotic region, and (iii) there is a decrease in the magnitude of the peak wall shear–stress at the bed of the anastomosis in the non-planar CABG model as compared to the planar geometry, supporting the view that non-planarity of the blood vessel may lead to better graft patency.

Chapter 12. Numerical Simulation and PIV Measurement of Two Proximal Anastomosis Models by Leok Poh Chua, Jun-Mei Zhang and Dhanjoo N. Ghista

Hemodynamics is widely believed to influence the stenosis of coronary artery bypass graft (CABG). Although distal anastomosis has been extensively investigated, further studies on proximal anastomosis are still necessary, as the extent and initiation of stenosis process may be influenced by the flow at proximal anastomosis *per se*. Therefore, in this study, firstly, two models (namely 90° and 135° anastomotic models) were designed and constructed to mimic the proximal anastomosis of CABG for left and right coronary arteries, respectively. Flow characteristics of these models were studied by both numerical simulation and particle image velocimetry (PIV) measurement, so as to acquire physical insight of hemodynamics in proximal anastomosis and to validate the simulation result simultaneously. The simulation results showed disturbed flow (such as flow separation, stagnation point, etc.) as well as abnormal hemodynamic parameters (HPs) distributions (including the low and high time-averaged wall shear stress (WSS), oscillation shear index, and time-averaged wall shear stress gradient regions in both the models). In contrast to the 90° model studied, the 135° model is proposed to provide better patency rate, as it has reduced disturbed flow and abnormal HPs.
A fair agreement between numerical and experimental data has been observed in terms of flow characteristics, velocity profiles, and WSS distributions. The discrepancy could be due to the difference in detail geometry of the physical and computational models because of manufacturing limitations to have the exact shape of the computational model when making the Pyrex glass model.

Chapter 13. Mechanical Circulatory Support Systems by Mustafa Akdis and Helmut Reul

Mechanical blood pumps for temporary or permanent support of cardiac function are classified into the traditional engineering categories of displacement and rotary pumps. Herein, the clinical use and indications of the various pump categories are outlined, and a detailed description of currently available systems is given. The first part deals with extracorporeal as well as implantable ventricular-assist devices (VADs) of the displacement type, and is followed by a section on current developments in the field of total artificial hearts (TAHs). The second part covers rotary