

## THE MECHANICS OF THE CIRCULATION

SECOND EDITION

Continuing demand for this book confirms that it remains relevant over 30 years after its first publication. The fundamental explanations are largely unchanged, but in the introduction to this second edition the authors are on hand to guide the reader through major advances of the last three decades.

With an emphasis on physical explanation rather than equations, Part I clearly presents the background mechanics. The second part applies mechanical reasoning to the component parts of the circulation: blood, the heart, the systemic arteries, microcirculation, veins and the pulmonary circulation. Each section demonstrates how an understanding of basic mechanics enhances our understanding of the function of the circulation as a whole.

This classic book is of value to students, researchers and practitioners in bio-engineering, physiology and human and veterinary medicine, particularly those working in the cardiovascular field, and to engineers and physical scientists with multidisciplinary interests.

‘... essential reading for anyone who is interested in the mechanics of the circulation. The normally incomprehensible mechanical laws are explained so clearly that even the non-mathematically minded will have no difficulty, which makes me very sorry that it was not available when I was grappling with these problems.’

DAVID MENDEL, *Journal of the Royal Society of Medicine*

‘Like a good sculpture which leaves no chisel marks on the marble, there are no marks of individual specialization in this book. All is well integrated toward the physiology of circulation . . . After reading the book, one would wonder how can circulation physiology be understood without such a study of mechanics. It cannot! I recommend this book to all physiology teachers and students.’

Y. C. FUNG, *Journal of Biomechanical Engineering*

‘Here is a book on the mechanics of the circulation that is equally accessible to those trained in the life sciences and in the mechanical sciences.’

SIR JAMES LIGHTHILL, *Journal of Fluid Mechanics*

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C.G. Caro, T.J. Pedley, R.C. Schroter and W.A. Seed

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## Foreword

When I arrived at the Physiological Flow Studies Unit, Imperial College, in 1971, the writing of *The Mechanics of the Circulation* was already underway. The book had been commissioned by Oxford University Press to be delivered in 1972 and the Tuesday afternoon book meeting was a regular event. From the outset, the purpose of the book was seen as presenting cardiovascular mechanics in a rigorous but accessible way. It was not meant to be a textbook, but an introduction to the subject that would be useful to a wide range of readers from medical students to experts in either mechanics or cardiovascular physiology.

*The Mechanics of the Circulation* was finally published in 1978 and it was obvious that the authors had succeeded in their purpose. It was a truly interdisciplinary book, its authors having trained in medicine, mathematics and engineering, but there was a continuity of style and content that remains unusual in multidisciplinary, multi-author books. Individual authors wrote the first drafts of the different sections of the book closest to their expertise, but they all had an equal say in the final product which, as evidenced by the time it took to write the book and the heat that was generated in those weekly meetings, was no easy task.

The book had an enormous impact on the emerging field of cardiovascular mechanics and, by extension, on the development of the discipline of bioengineering as an essentially multidisciplinary field of study. It was reprinted and published as a paperback. Then, for reasons known only to the publisher, it was allowed to go out of print. In the years that followed there were occasional discussions about writing a second edition to incorporate the many advances that had taken place in the understanding of the cardiovascular system. But, because of other pressures and activities, the authors never found the time and the book became unavailable (except for the Russian and Chinese translations which continued to be available for several decades).

With the authors all retired, new discussions arose about a second edition and I was very honoured to be asked to be involved. We had many meetings about the changes that were needed and how the book could be made more relevant to the present time. It very quickly became evident, however, that the explosion of knowledge about the

physiology and mechanics of the cardiovascular system during the past 30 years made it impossible to embrace the whole subject in a single book. After much discussion, it was decided that the one thing that has remained constant over the years is the basic mechanics, which was the primary subject of the original book. We therefore decided to republish rather than rewrite the original book. This volume, with the addition of this foreword, a new preface, a few minor corrections and a greatly enhanced index, is the result.

Some flavour of the differences in research on the circulation between 1970 and 2010 can be gained simply by considering the way the old and the new versions of the book were produced. The original book was written in longhand and transcribed by a typist. Editing involved handwritten comments in the margins and the index involved annotated filing cards that were sorted by hand. The book was set by hand and the figures were reproduced using photolithography. The current book was prepared by scanning the original into a text file generated by an optical character recognition program. The text files were edited on a computer into a LaTeX file which generated the final format electronically. The output of the LaTeX program was edited via email and the new index was generated using the 'makeindex' function in LaTeX. Finally, a LaTeX-compatible printing press was used to convert the electronic form of the book into the printed hard copy. Every aspect of cardiovascular science has undergone a similar revolution.

In the compilation of a new, greatly expanded index for this volume, I have been struck by two things about *The Mechanics of the Circulation*: its completeness and its cohesiveness.

In the course of introducing the mechanics of the circulation, the book covers the anatomy and physiology of the circulation in considerable detail and even includes some examples of its pathology. There are, inevitably, some omissions. For instance, the extracellular material at the outer surface of endothelial cells receives only the most fleeting of mentions in Chapter 13 and is never named as the glycocalyx. And in the extensive discussion of waves in the circulation there is no mention of the water hammer equation that so conveniently relates changes in pressure and velocity. It is remarkable, however, how rare these omissions are given the breadth of material covered.

Even more impressive is the cohesiveness of the book. The authors have taken great care in the cross-referencing between the different sections. 'Part I: Background mechanics' provides a thorough grounding in basic mechanics, with extensive links to the application of these principles to the cardiovascular system. 'Part II: Mechanics of the circulation' deals with the different parts of the circulation in turn. Here the links are not only to the basic principles, but also to the other parts of the circulation with similar or opposing properties.

From my personal experience and from the experience of other colleagues working on the circulation, *The Mechanics of the Circulation* is a very valuable book. It

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*Foreword*

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provides an introduction to mechanics for those trained in physiology, medicine and biology and an introduction to the anatomy and physiology of the circulation for those trained in mechanics, engineering and mathematics. Virtually everyone I know in the field has a well-thumbed copy on their bookshelf and many have used it as a basic text for both undergraduate and graduate courses.

Thirty years after its original publication, I am delighted that this classic book is once again being made available to experts and, most importantly, to students – the experts-to-be.

Kim H. Parker

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## Preface to the First Edition

In 1808 Thomas Young introduced his Croonian lecture to the Royal Society on the function of the heart and arteries with the words:

The mechanical motions, which take place in an animal body, are regulated by the same general laws as the motions of inanimate bodies . . . and it is obvious that the inquiry, in what manner and in what degree, the circulation of the blood depends on the muscular and elastic powers of the heart and of the arteries, supposing the nature of those powers to be known, must become simply a question belonging to the most refined departments of the theory of hydraulics.

For Young this was a natural approach to physiology; like many other scientists in the nineteenth century, he paid scant attention to the distinction between biological and physical science. Indeed, during his lifetime he was both a practising physician and a professor of physics; and, although he is remembered today mainly for his work on the wave theory of light and because the elastic modulus of materials is named after him, he also wrote authoritatively about optic mechanisms, colour vision, and the blood circulation, including wave propagation in arteries.

This polymath tradition seems to have been particularly strong among the early students of the circulation, as names like Borelli, Hales, Bernoulli, Euler, Poiseuille, Helmholtz, Fick, and Frank testify; but, as science developed, so did specialization and the study of the cardiovascular system became separated from physical science. This process was not, of course, complete because collaborative work between scientists from different disciplines has always gone on. However, its scale was quite limited, and many medical and physiological workers found it difficult to comprehend because of their inadequate background in mathematics and mechanics, just as physical scientists found the complexity and empiricism of physiological studies, as well as the terminology, forbidding.

The separation caused by specialization has now assumed new importance. Over about the last twenty years physical scientists and engineers have made considerable contributions to the understanding of the mechanics of the circulation. These have strongly stimulated collaborative research, but at the same time have made the field

increasingly difficult for those with a limited training in physics and mathematics. Several recent reviews and monographs bear witness to the importance of this interdisciplinary work, but do little to help the medical reader, since they invariably assume an understanding of mechanics and are often quite mathematical in format.

This book is an attempt to alleviate the problem. It is intended as an introductory text on the mechanics of the circulation which, so far as is practicable, avoids mathematical formulations and presents mechanics in readily comprehensible terms. Our experience in teaching students of physiology and medicine, and cardiological physicians and surgeons, suggests that this approach is helpful, and it is to such a readership that the book is primarily directed. In addition, we think that the book will prove useful to physical scientists, mathematicians, and engineers interested in the field, since it provides the relevant anatomical and physiological background to the mechanics, and gives definitions of terms and numerical data wherever possible.

The book is divided into two parts. The first part, 'Background mechanics', provides a non-mathematical outline of the physical processes and mechanisms which have general importance in the circulation. Thus it forms a physical introduction to the later material, though since it is self-contained and deals in a general rather than a specific way with solid and fluid mechanics and mass transport, it may also prove useful as a background to the study of systems other than the circulation.

The second part, 'The mechanics of the circulation', examines in some detail the physiological events that occur in the circulation and the physical mechanisms that underlie them. It deals first with the relevant properties of blood and then considers the circulation systematically, starting with the heart and moving forward chapter by chapter through the circulation. No attempt is made to deal in detail with active physiological mechanisms such as reflexes, but the resulting changes in the physical properties of the system are studied. In each chapter the relevant anatomical and physiological background is presented first, followed by a discussion of the mechanics. There is extensive cross-referencing to physical processes already examined earlier in the book; more specialized physical processes, relevant to the mechanics of a part of the circulation, are introduced as they arise.

We have attempted to cover all the mechanical features of the circulation which are currently considered important. However, the book is not intended as a research review, and we have therefore largely avoided citing original research references in the text. Instead, we have provided a reading list for each chapter in the second part of the book, chosen to guide readers unfamiliar with the literature to suitable reviews and sources. In addition, we have, wherever possible, taken our illustrations from important sources, in many cases the original research literature, so that the references given in the figure captions supplement the reading list.

A temptation in writing an interdisciplinary book of this kind is to oversimplify, usually at the expense of one of the disciplines; we have tried hard to avoid doing this. We have also tried, wherever possible, to supply numerical data; for convenience

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*Preface to the First Edition*

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the more important measured and derived values, which are referred to repeatedly throughout the book, are collected together in a table reproduced on the end-page. The units used are those of the *Système International*, though with quantities such as pressure, where confusion might arise, we have added the traditional units. Since physical scale is important to so much of mechanics, and the dog is the only species for which anything like a comprehensive range of reliable measurements is available, we have given values from this animal throughout the book. Even so, we have had to turn to other species in describing the microcirculation, though this is a region where inter-species differences in scale appear to be relatively slight. Finally we have referred specifically to the human circulation wherever the mechanics appears to be different, or where we believe that it has relevance to a circulatory disease process.

July 1977

C.G.C.  
T.J.P.  
R.C.S.  
W.A.S.

## Acknowledgements

We owe debts of gratitude to many colleagues for their advice and help. In particular we would like to thank Dr Laurence Smaje, who contributed a major part of the physiological material contained in the chapter on the microcirculation, and without whose guidance we could not have surveyed that topic.

Mr Paul Minton of Imperial College, Dr Giorgio Gabella of University College, and Drs Graham Miller and Derek Gibson of the Brompton Hospital all made available to us original data or material for figures. Dr Michael Sudlow contributed greatly to early discussions on the scope and form of the book, and provided material for the chapter on veins; and Professor Ilsley Ingram and Drs Julien Hoffmann and Michael Hughes made valuable comments and suggestions about the chapters on the blood, heart and pulmonary circulation respectively. In addition, we owe our thanks to all the authors and journals cited in the figure captions for permission to reproduce figures. Every effort has been made to secure necessary permissions to reproduce copyright material in this work, though in some cases it has proved impossible to trace copyright holders. If any omissions are brought to our notice, we will be happy to include appropriate acknowledgements on reprinting.

Finally, we give our special thanks to Miss Evelyn Edwards, whose editorial precision helped (and chastened) us throughout the preparation of the book.

## Introduction to the Second Edition

In the Preface to the first edition, we commented on the benefits and drawbacks of interdisciplinary research; the contributions of specialists to advance our understanding and the difficulty for the non-specialist in understanding these advances. We were thinking particularly about the mechanics of the circulation and the contributions that had been made by engineers, physicists and mathematicians working in collaboration with physiologists and medical doctors. Our goal in writing the book was to alleviate the problem of understanding these advances by providing an introductory text on the mechanics of the circulation that was accessible to physiologists and medical practitioners.

The three decades since the book was published have seen an explosive growth in research on the cardiovascular system. In 1978, bioengineering did not exist as a separate academic discipline and the field of cardiovascular mechanics was relatively small, although it had a long and distinguished history extending over more than three centuries. Today, bioengineering is widely recognized as an academic discipline and interdisciplinary research is generally accepted as essential to progress.

Our understanding of the circulation is immeasurably greater today than it was in 1978, but many problems remain unsolved and cardiovascular disease is still the largest single cause of death world-wide. Again, however, these advances have brought increased difficulty in understanding. We believe that the need for an introductory text on the mechanics of the circulation that is accessible to the non-specialist is even greater now than it was when the book was first published. We consider that the book will be valuable not only to circulatory scientists and practitioners, but also to physical scientists working on imaging, cell biologists working on the responses to mechanical stimuli, molecular biologists interested in cell signalling and researchers using computational fluid dynamics to study haemodynamics; to give only a few examples.

When the idea of a new edition of *The Mechanics of the Circulation* was mooted, we briefly considered expanding the book to include the many advances in cardiovascular science. We soon realized, however, that it would be impossible to be

comprehensive without compromising rigour because of the sheer volume of new work. Since the basic mechanics, the theme of our introductory text, has not changed over the years, we decided to reissue the book with only minor corrections to the original text. As a result, readers will frequently come across phrases such as ‘are incompletely understood’, ‘has not been explored’, ‘is still unknown’ or ‘the data are sparse’. In many cases the more recent developments render these phrases untrue or misleading, although in some cases they are still as true as they were in 1978. Rather than attempt to adjust the text, we have left it unchanged, and hope that this global disclaimer will absolve us from any accusation of egregious ignorance.

In addition to the therapeutic innovations which have transformed clinical practice, most of the advances in cardiovascular science can be categorized into four broad areas: imaging and measurement techniques, computational mechanics, endothelial biology, and molecular biology and genomics. It would be impossible to summarize any one of these fields here, and so we will only mention a few examples and provide some references to books and review articles that will give the interested reader an introduction to modern developments.

#### *Imaging and measurement techniques*

In the 1970s, imaging of the arteries was limited to X-ray methods and direct measurement of arterial blood velocity was difficult and highly invasive. The first quantitative measurements of local blood velocity *in vivo* were made using hot-film anemometers. Doppler ultrasound is mentioned in *The Mechanics of the Circulation*, but only to allude to its ‘tremendous potential’. This tremendous potential of ultrasound has now been realized and the anatomy and function of the cardiovascular system are routinely imaged and measured non-invasively at the bedside. A number of other imaging modalities followed, such as magnetic resonance imaging (MRI), computer tomography (CT) and positron emission tomography (PET). These techniques have been developed in many different ways, enabling not only anatomical images and maps of blood and tissue velocity, but also dynamic functional imaging that could only be dreamt of 30 years ago. Today, the fine degrees of spatial and temporal resolution of imaging techniques allow the observation and consequently dynamic mechanistic modelling of many fast physiological and physico-chemical processes from the scale of whole organs all the way down to the molecular level.

The emergence of fluorescence microscopy and fast-pulsed laser methods have given us a much better understanding of structure and dynamics at the microscopic and sub-microscopic level. It is now possible to image single molecules with two-photon methods and to probe the nano-environment of proteins using state-sensitive fluorescent markers.

All of these imaging techniques progressed rapidly from the research lab to clinical practice, making the flow patterns shown in Chapter 12 of *The Mechanics of the Circulation* look particularly dated. Figures 12.38, 12.40 and 12.41 show velocity

patterns measured in animal experiments and represent the state of the art in the measurement of arterial blood flow in 1978. Now, more detailed and much more accurate measurements are routinely made non-invasively in the clinic or even the GP surgery.

- W. Manning and D. J. Pennell (eds) (2001) *Cardiovascular Magnetic Resonance*, Churchill Livingstone.
- J. B. Pawley (ed.) (2006) *Handbook of Biological Confocal Microscopy*, Springer, ISBN 38725921X 9780387259215.
- G. K. Von Schulthess (2006) *Molecular Anatomic Imaging: PET-CT and SPECT-CT Integrated Modality Imaging*. Lippincott Williams & Wilkins, ISBN 9780781776745.
- G. J. Tearney, S. Waxman, M. Shishkov, B. J. Vakoc, M. J. Suter, M. I. Freilich, A. E. Desjardins, W.-Y. Oh, L. A. Bartlett, M. Rosenberg and B. E. Bouma (2008) Three-dimensional coronary artery microscopy by intracoronary optical frequency domain imaging. *J. Am. Coll. Cardiol. Img.* **1**, 752–761.
- G. T. Herman (2009) *Fundamentals of Computerized Tomography: Image Reconstruction from Projections* (2nd edn). Springer, ISBN 978-1-85233-617-2.
- H. Feigenbaum, W. F. Armstrong and T. Ryan (2010) *Echocardiography* (7th edn). Lippincott Williams & Wilkins, ISBN 0781795575.

#### *Computational mechanics*

The impact of computers on every facet of our lives is self-evident. Since 1978, advances in computer technology have enabled innumerable developments in cardiovascular mechanics. For instance, all the developments in imaging depend upon fast, memory-intensive calculations and many of the advances in molecular biology and genetics would not have been possible without mass data storage and analysis. Advances in computer power have also given rise to computational fluid dynamics (CFD) which has greatly increased our understanding of the complex flows that occur in the cardiovascular system. The basic equations of mechanics are well known and have been rigorously tested for centuries (as described in this book). They are, however, very complex and their solution is well established as a ‘hard’ problem. Powerful computer programs have been developed that enable us to predict the dynamics of the fluid and solid components of the system and, very recently, the interaction between the two. The emerging ability to model these ‘fluid–structure interactions’ in detail will undoubtedly lead to a far greater understanding of how the behaviour of one influences the other, particularly at the cellular and molecular levels.

CFD has a significant advantage, in that it can predict properties of the cardiovascular system, such as wall shear stress, that cannot be measured *in vivo*. CFD has also brought better understanding of the influence of complex three-dimensional geometry on mixing and mass transport in the circulation. It is probably fair to say that many

of the advances in CFD have been stimulated by haemodynamics and that CFD will be necessary to reveal the aetiology of cardiovascular disease.

However, much remains to be done. Because of the nonlinearity of the basic equations, many potential solutions may be possible for the same conditions; for turbulent flows it seems that there can be an infinity of such solutions for some conditions. Thus, finding *an* answer to a patient-specific flow problem is not necessarily the same as finding *the* answer. Consider, for example, the effort that goes into the prediction of the weather, a fluid dynamics problem comparable in complexity to flow in the circulation, with results that have only recently advanced (somewhat) beyond ‘tomorrow’s weather will be like today’s’.

- C. G. Caro, D. J. Doorly, M. Tarnawski, K. T. Scott, Q. Long and C. L. Dumoulin (1996) Non-planar curvature and branching of arteries and non-planar-type flow. *Proc. R. Soc.: Math. Phys. Eng. Sci.*, **452**, 185–197.
- C. A. Taylor and M. T. Draney (2004) Experimental and computational methods in cardiovascular fluid mechanics. *Annu. Rev. Fluid Mech.*, **36**, 197–231.
- Y. S. Chatzizisis, A. U. Coskun, M. Jonas, E. R. Edelman, C. L. Feldman and P. H. Stone (2007) Role of endothelial shear stress in the natural history of coronary atherosclerosis and vascular remodeling. *J. Am. Coll. Cardiol.* **49**, 2379–2393.
- G. Coppola and C. G. Caro (2009) Arterial geometry, flow pattern, wall shear and mass transport: potential physiological significance. *J. R. Soc. Interface*, **6**, 519–528. doi: 10.1098/rsif.2008.0417.
- D. J. Doorly, D. J. Taylor, A. M. Gambaruto, R. C. Schroter and N. Philos (2008) Nasal architecture: form and flow. *Philos. Trans. R. Soc. A* **366**, 3225–3246.
- L. Formaggia, A. Quarteroni and A. Veneziani (eds) (2009) *Cardiovascular Mathematics: Modeling and Simulation of the Circulatory System*. Springer-Verlag Italia, Milan.
- K. H. Parker (2009) An introduction to wave intensity analysis. *Med. Biol. Eng. Comput.*, **47**, 175–188, ISSN:0140-0118.
- C. A. Taylor and C. A. Figueroa (2009) Patient-specific modeling of cardiovascular mechanics. *Annu. Rev. Biomed. Eng.* **11**, 109–134.

#### *Endothelial biology*

Cardiac physiologists were active in the 1970s mapping out the complex control systems that govern the function of the heart, but larger blood vessels were generally considered to be relatively inert. The tone of the smooth muscle in the arteries and arterioles was known to respond to nervous stimulation and to a small number of vasoactive substances circulating in the blood. EDRF (endothelium-derived relaxant factor) was discovered at the end of the decade and NO (nitric oxide) was not identified as the principle EDRF until the early 1980s. In the last three decades, this picture has changed beyond recognition. The endothelium is now recognized as the largest



organ in the body and endothelial cells are known to transduce and respond via normal or disturbed biological changes to subtle alterations in the pattern of blood flow over them.

The NO story provides a prime example of progress in this area of cardiovascular science. The Nobel Prize in Physiology or Medicine was awarded in 1998 to three scientists for their work between 1977 and 1986 on the detection and characterization of the role of NO in cardiovascular signalling. The idea that a short-lived gas which could rapidly diffuse through membranes and tissue could be produced by a cell and used to regulate the function of other cells was a radical departure which had profound effects in virtually every area of physiology and medicine. NO is now recognized as a primary signalling pathway throughout the body and the endothelium is its major producer. NO is also a neurotransmitter, and vascular-derived NO has been shown to regulate neural activity, providing another level of complexity to the cardiovascular control mechanisms. The production, regulation and response to NO is now one of the most studied, and still incompletely understood, topics in physiology and medicine.

- M. H. Friedman, C. B. Barger, O. J. Deters, G. M. Hutchins and F. F. Mark (1987) Correlation between wall shear and intimal thickness at a coronary artery branch. *Atherosclerosis* **68**, 27–33.
- A. M. Malek, S. L. Alper and S. Izumo (1999) Hemodynamic shear stress and its role in atherosclerosis. *JAMA*, **282**, 2035–2042.
- J. Loscalzo and J. A. Vita (eds) (2000) *Nitric Oxide and the Cardiovascular System*. Humana Press, ISBN: 9780896036208.
- J. M. Tarbell (2003) Mass transport in arteries and the localization of atherosclerosis. *Annu. Rev. Biomed. Eng.* **5**, 79–118.
- C. D. Searles (2006) Transcriptional and posttranscriptional regulation of endothelial nitric oxide synthase expression. *Am. J. Physiol. Cell Physiol.* **291**, 803–816.
- P. F. Davies (2007) Hemodynamics in the determination of the endothelial phenotype and flow mechanotransduction. In *Endothelial Biomedicine; A Comprehensive Treatise* (ed. W. C. Aird), Cambridge University Press, pp. 230–245.

#### *Molecular biology and genomics*

The separation of molecular and genetic biology from cell biology is artificial, since one subsumes the other. However, specialists in these areas are making very rapid advances and it is not always clear how they affect particular cells and organs; general texts on molecular cell biology usually omit the cardiovascular system entirely. The complexity of the molecular pathways that govern cell signalling and function is beautiful but bewildering. This is perhaps the field that is currently advancing most rapidly, many of the advances being expressed in a language of acronyms that can seem impenetrable to the newcomer.

The list of molecules involved in the complex transduction and signalling pathways within the endothelial cell now numbers in the thousands and the number of genes

known to be involved increases almost daily. Indeed, the mechanical environment of a cell is now generally recognized to be as important as its chemical environment in determining its function and development. This is particularly true of progenitor cells, and so genetic medicine and tissue engineering are reliant on a good understanding of their micro-mechanical environment. Decoding these influences is one of the most active areas of cardiovascular science and it is difficult to see how this research will progress, other than to say that it is certain to be important.

- S. Chien (1990) *Molecular Biology of the Cardiovascular System*. Lippincott Williams & Wilkins, ISBN-13: 9780812113129.
- K. R. Chien (ed.) (2004) *Molecular Basis of Cardiovascular Disease: A Companion to Braunwald's Heart Disease* W. R. Saunders Company.
- H. Morita, J. Seidman and C. E. Seidman (2005) Genetic causes of human heart failure. *J. Clin. Invest.* **115**, 518–526.
- R. A. Walsh (ed.) (2005) *Molecular Mechanisms of Cardiac Hypertrophy and Failure*, Informa Healthcare/Taylor & Francis, ISBN 1-84214-248-8.
- J. A. Hill and E. N. Olson (2008) Cardiac plasticity. *N. Engl. J. Med.* **358**, 1370–1380.
- R. Passier, L. W. van Laake and C. L. Mummery (2008) Stem-cell-based therapy and lessons from the heart. *Nature* **453**, 322–329.
- E. M. Small, R. J. Frost and E. N. Olson (2010) MicroRNAs add a new dimension to cardiovascular disease. *Circulation* **121**, 1022–1032.

There have been, as we note, major advances in the 30 years between the publication of the first and second editions of this book, both in the understanding of circulatory mechanics and in the technologies applied to its study. But much remains to be done. Recent work has revealed complicated and highly important interactions between cellular pathways and mechanical events that make the need for a better understanding of the mechanics of the circulation ever more apparent. Future developments are certain to be as exciting and unpredictable as those of the past three decades, but, whatever they are, they must adhere to the basic principles of mechanics. This book aims to provide a detailed yet accessible account of these principles and we are delighted that *The Mechanics of the Circulation* is being reissued.

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