# BASIC HEMODYNAMICS and Its Role in Disease Processes

by

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and

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**University Park Press**
Baltimore

**UNIVERSITY PARK PRESS**
International Publishers in Science, Medicine, and Education
233 East Redwood Street
Baltimore, Maryland 21202



Typeset by York Graphic Services, Inc.
Manufactured in the United States of America by
Universal Lithographers, Inc.,
and The Maple Press Company



**Library of Congress Cataloging in Publication Data**

Patel, Dali J.
Basic hemodynamics and its role in disease processes.
Bibliography: p.
Includes index.
1. Hemodynamics. 2. Atherosclerosis.
I. Vaishnav, Ramesh N., joint author. II. Title.
[DNLM: 1. Hemodynamics. WG106 P295b]
QP105.P37 612'.1181 79-23980
ISBN 0-8391-1552-0

# Preface

Hemodynamics may be defined as the study of the physical aspects of the circulatory system, and includes, among other things, the study of the blood vessel wall as well as blood flow. The purpose of this book on hemodynamics is threefold: to serve as a basic hemodynamics text for a variety of students; to cover in considerable detail those areas of hemodynamics that we believe will help in the study of disease processes; and to point out, wherever possible, the applications of basic hemodynamic principles to clinical cardiology. We differentiate, somewhat arbitrarily, between the application of basic hemodynamic principles to clinical cardiology and applied hemodynamics as used in cardiology. For instance, measuring a pressure difference across a heart valve at cardiac catherization to estimate valvular stenosis is an example of the latter, whereas using Navier-Stokes equations to compute blood velocity profiles and wall shear stress from a measured pressure gradient in the aorta of cardiac patients is an example of the former.

Over the past twenty years, following the lead of McDonald and co-workers, researchers have studied in great detail the quantitative aspects of pulsatile phenomena in the arterial system. While these studies have furthered our understanding of the mechanics of the circulatory system, the more recent thrust of hemodynamic research is to deliberately shape the concepts and tools of basic hemodynamics to answer questions relative to the pathogenesis of disease. We now ask more difficult questions of hemodynamics; for example, what is the role of hemodynamics in disease processes like atherosclerosis? Before such questions can be answered, we need detailed information on vascular geometry and rheology, local flow fields, and the blood-wall interface. Such information is not presently available, but study of such questions is underway in various laboratories, including our own. Because arteries are the dominant sites of many serious diseases, such as atherosclerosis, and because the arterial system is particularly suitable to illustrate many concepts of hemodynamics, our emphasis in this work has been on the arterial system.

The book is an outgrowth of many years of research in basic hemodynamics at the National Institutes of Health and The Catholic University of America and several years of teaching a course to a mixed audience of advanced graduate students in physiology and bioengineering, and to technicians and physicians engaged in basic and clinical cardiovascular research. The book has therefore been designed not only as a text for a two-semester course in basic hemodynamics for seniors and first-year graduate students from a variety of backgrounds but also to be of use to researchers in the field. The tutorial aspects are emphasized throughout the book and an effort has been made to deal in concepts rather than to review all the work done in the field. Wherever possible, we have tried to illustrate these concepts from our own work, and refer to others via review articles or books. Unfortunately, this scheme has precluded direct citation of many excellent articles in the field. As far as possible, a consistent set of symbols has been used throughout the book. Occasionally, however, we have departed from this in a few situations where it was considered more desirable to do so and where there was no likelihood of ambiguities. In any case, a selected list of symbols has been provided for each chapter. In order to keep the size of the book within reasonable limits, techniques of measurements as well as historical and descriptive aspects of the subject have been minimized. Moreover, for the same reason, some important topics, such as myocardial mechanics and microcirculation, have not been included.

Although the book uses some sophisticated concepts of mathematics and physics, these are introduced in a gradual manner designed to provide an intuitive feel for the subject, even for readers unfamiliar with advanced physical and mathematical concepts. The first two chapters therefore cover some introductory mathematical, mechanical, and physiologic concepts of general use in hemodynamics.

Wherever possible, the mathematical concepts are illustrated with physiologic examples to serve an interdisciplinary audience. These two introductory chapters may be particularly helpful to physiologists and cardiologists and will also provide a physical basis for the subject matter of the later chapters. The rest of the text is modular in nature and chapters may be selected out of order without loss of continuity.

In Chapter 3, the structure of the normal and atherosclerotic vascular wall is discussed, with particular emphasis on the intimal region. This chapter will help provide a structural basis for the phenomenological studies of the arterial tissue to be discussed in later chapters.

Chapters 4, 5, and 6 deal in considerable detail with the rheologic properties of the vascular tissue. In Chapter 4 certain general aspects of vascular mechanics, such as geometry and motion of the vascular wall, longitudinal tethering of the vessel wall to the body cavity, and general material properties, such as incompressibility and elastic symmetry, are discussed. A knowledge of geometry, motion, and tethering is necessary to formulate the boundary conditions for modelling the circulatory system, and the general material properties are needed for formulating rheologic theories for the vessel wall, as is done in Chapter 5. In Chapter 5 we develop the theoretical and experimental basis foı the linear incremental and nonlinear large deformation theories for the elastic and viscoelastic properties of the vessel wall. These formulations provide compact and quantitative rheologic descriptions of the arterial wall. Although such detailed formulations have not been used to date in circulatory mechanics (such as that described in Chapter 7), future, more detailed models of circulatory mechanics will undoubtedly require them. The discrete properties of the endothelial surface and intimal region, a knowledge of which is pertinent to the study of atherosclerosis, are discussed in Chapter 6. In particular, a microindentation method to study the compliance of the intimal region and a jet impingement method to study the yield strength of the endothelium are discussed. Taken together, the three chapters cover the state of the art in the field of blood vessel rheology.

Arterial blood flow fields and pulse propagation form the subject matter of Chapter 7. After introduction of a few fundamental concepts and the basic equations of fluid mechanics, two pertinent examples—steady and periodic flows in rigid tubes—are given. Then the linear and nonlinear theories of blood flow and pulse propagation are discussed. Although we expect the nonlinear theory to be used more often in the future, a detailed exposition of the linear theory is included in this chapter for tutorial purposes. Finally, the chapter ends with a concise discussion of a few special topics, such as entrance flow, flow through the aortic arch, branches, and stenoses.

Chapter 8 illustrates the clinical application of some basic hemodynamic concepts, such as hydraulic power and hydraulic input impedance. The impedance function characterizes the load the ventricle must face and the hydraulic power indicates the rate at which the ventricle is doing work against this load. The two together provide an opportunity to study the interaction between the heart and the rest of the circulatory system. Moreover, the data presented in this chapter are unique in that they were obtained from patients with cardiac pacemakers in whom the heart rate and the stroke volume could be varied independently over a wide range.

An understanding of the mechanical aspects of many physiologic flow problems, such as those in the heart, lung, kidney, and brain, requires a knowledge of the physics of flow in collapsible tubes. The flow in a collapsible tube becomes independent of the outlet pressure when the pressure on its outer wall exceeds the intraluminal pressure. Although this phenomenon has been widely studied experimentally, an understanding of the associated physical mechanisms has emerged only recently. These mechanisms are discussed in terms of two inherently different models in Chapter 9.

Finally, in Chapter 10 transport of material into the arterial wall is discussed with special reference to the pathogenesis of atherosclerosis. The general problems of describing transport processes in arterial tissue systems are discussed with examples of various tentative approaches to specific mathematical descriptions. A number of simplified cases are then solved in detail with an eye toward providing insight into the mathematical methods of studying problems in this complex field.

It is important to point out that the book was designed as an *integrated textbook* rather than as an edited book. As a result, there was a great deal of interaction between us and the invited authors, particularly in Chapters 7, 8, and 10. By the same token, the guest authors, especially Drs. Fry and Atabek, provided significant input to the chapters written by us. In a work like this, it is inevitable that some errors remain in spite of meticulous care. We would be grateful to the readers if they would kindly draw our attention to any errors they may find.

It is our hope that *Basic Hemodynamics* will provide readers with at least a minimal background in the mechanics of the circulatory system. An effort has been made to do so in a clear, intuitive manner, to enable the readers to understand better the pertinent literature in the field, and to pursue independent study.

D.J.P.
R.N.V.

# Acknowledgments

We extend our sincere thanks to Dr. Donald L. Fry, in whose laboratory most of the original work cited in this book was performed. His encouragement, support, and advice through the years are deeply appreciated. More than a few times we have benefited from Dr. Fry's unique insight into biophysical phenomena. We also thank Drs. Fry, Atabek, Ferrans, Greenfield, and their collaborators (Drs. McHale, Rembert, Thomas, and Deshpande) for taking time out from their busy schedules to contribute their chapters.

We are grateful to many individuals who were instrumental in various ways in shaping this book into its present form. First and foremost we thank the late Dr. Alan C. Burton,* Professor Emeritus at University of Ontario, London, Ontario, Canada, for helpful suggestions in the initial planning stages of the book. We also thank Dr. Frederick J. Cornhill of the Ohio State University and Dr. Byron D. McLees of the National Institutes of Health, who critically read the entire manuscript. Mr. Jafar Vossoughi of The Catholic University of America not only read the whole manuscript, but also helped us with innumerable organizational details. Drs. Robert W. Mahley, John T. Young, John J. McCoy, and David M. Wetzel read specific chapters and gave us their valuable comments. Comments of these scholars were very useful to us and we extend to them our sincere gratitude.

We thank the graduate students, research colleagues, and the staff at the Laboratory of Experimental Atherosclerosis at The National Institutes of Health for their contributions over the years to the research upon which this book is based. In particular, we thank Mr. Fred Plowman for design and fabrication of some important instrumentation, Messrs. Joseph M. Pearce, Leander Brown, George Johnson, and Rufus Seabron for technical assistance in animal experiments, and Ms. Kathleen Holcombe for editorial assistance. We also thank various authors and institutions (Academic Press, American Heart Association, American Physiological Society, Edward Arnold Publ. Ltd., Elsevier/North Holland Biomedical Press, Grune and Stratton, McGraw Hill Book Co., C. V. Mosby Co., The New York Academy of Sciences, Pergamon Press, Raven Press, Rockefeller University Press, and Year Book Medical Publishers) for granting permission to reproduce various figures and tables as identified in the text.

In addition, Dr. Patel wishes to thank Dr. Fry for his support and encouragement during the years he worked under Dr. Fry at the National Institutes of Health. Dr. Vaishnav takes this opportunity to express his deep gratitude to The Catholic University of America for granting him a sabbatical leave during which the bulk of the work was performed, as well as for a generous grant in the form of computer time toward preparation of this book. He also acknowledges the support over the years of various grants from the National Science Foundation and The Public Health Service, on which part of the research work described in Chapters 4, 5, and 6 was based. He is particularly thankful to his able secretary, Ms. Elizabeth Gurubatham, who computerized the manuscript and was in charge of its general organization. She took pride and interest in pushing the manuscript to completion while suffering through the constant changes we made in our struggle to achieve clarity and perfection. He also thanks his student assistant, Ms. Mary Jane Flynn, who checked all the equations in Chapter 10 and critically read the page proofs of all the chapters. Above all, he thanks his wife Marianne, who helped us in many ways

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*Dr. Burton died on June 27, 1979. Physiologists all over the world will remember him as the father of modern circulatory physics, but his students, including the senior author, will remember him as the kind, unselfish man they all loved.

during the preparation of this work. She also undertook the arduous task of preparing the index.

Finally, both of us extend our sincere thanks to Ms. Maria Coughlin, Mrs. Joan Sanow, and Mr. Albert A. Belskie of University Park Press. We owe a great deal to the efficiency and patience of all these fine people.

D.J.P.
R.N.V.

# Contents

# CHAPTER 1
# MATHEMATICAL PRELIMINARIES



## LIST OF SYMBOLS

| | |
|---|---|
| A | area |
| a | acceleration; real part of a complex number z; also used as a constant |
| $a$ | attenuation constant |
| b | imaginary part of a complex number z; also used as a constant |
| $b$ | phase constant |
| $\mathcal{C}$ | capacitance |
| $\mathcal{C}'$ | capacitance per unit length |
| C | damping coefficient; also used as a constant |
| $C_c$ | critical damping coefficient |
| F | $F_{acc}$ = acceleration force; $F_{app}$ = applied force; $F_s$ = spring force; $F_d$ = force in dashpot; $F_{visc}$ = viscous force |
| f | frequency |
| $\mathcal{G}$ | conductance |
| $\mathcal{G}'$ | conductance per unit length |
| h | thickness of blood vessel wall |
| $\mathcal{I}$ | current |

| | |
|---|---|
| $\mathscr{I}m$ | denotes imaginary part of a complex variable |
| j | $= \sqrt{-1}$ |
| K | spring constant |
| $\mathcal{L}$ | inductance |
| $\mathcal{L}'$ | inductance per unit length |
| L | length |
| lim | limit |
| $l_1, l_2, l_3$ | inductances |
| M | mass; amount of substance |
| NE | norepinephrine |
| p | pressure |
| $p_i$ | inside pressure |
| $p_o$ | outside pressure |
| $\lvert p_n \rvert$ | magnitude of $n^{th}$ harmonic of pressure |
| $\mathcal{Q}$ | charge |
| $\lvert Q_n \rvert$ | magnitude of $n^{th}$ harmonic of flow |
| Q | cardiac output; volume flow rate |
| $\mathcal{R}$ | resistance; hydraulic resistance |
| $\mathcal{R}'$ | resistance per unit length |
| R | radius; also reflection coefficient |
| r | radial variable |
| $r_1, r_2, r_3$ | resistances |
| $\vec{r}$ | radius vector |
| $\mathcal{R}e$ | denotes real part of a complex variable |
| Re | Reynold's number |
| $S_\theta$ | circumferential stress |
| T | period |
| TMP | transmural pressure |
| t | time |
| u, v, w | components of $\vec{V}$ |
| V | volume |
| $\mathcal{V}$ | voltage |
| $\vec{V}$ | vector; velocity vector |
| $V_x, V_y, V_z$ | cartesian components of $\vec{V}$ |
| $\lvert \vec{V} \rvert$ | magnitude of $\vec{V}$ |
| v | velocity |
| $v_p$ | phase velocity |
| W | work |
| $X_c$ | complementary solution |
| $X_p$ | particular solution |
| x, y, z | Cartesian coordinates |
| $x_s$ | extension of spring |
| $x_d$ | extension in dashpot |
| z | complex variable; coordinate variable in axial direction |
| Z | impedance |
| $Z_o$ | characteristic impedance |
| $\beta_o$ | damping factor |
| $\Delta c$ | concentration difference |
| $\gamma$ | propagation constant |
| $\zeta$ | damping coefficient |
| $\eta$ | viscosity coefficient |
| $\theta$ | angle |
| $\theta_n$ | phase angle of $n^{th}$ harmonic |
| $\lambda$ | wavelength |
| $\rho$ | density |
| $\tau$ | shear stress |

| | |
|---|---|
| $\phi$ | a scalar; phase angle |
| $\phi_n$ | phase angle of $n^{th}$ harmonic |
| $\phi_f$ | starting angle for flow vector |
| $\phi_p$ | starting angle for pressure vector |
| $\omega$ | angular frequency |
| $\omega_0$ | undamped natural frequency |
| $\omega_d$ | damped natural frequency |
| $\vec{\nabla}$ | vector operator "del" |

The subject of hemodynamics is vast in scope, and the cardiovascular system, which it addresses, is highly complex. Not only are the components of this system complex in nature, but also the interactions of these components in the living system are complicated and varied. Characterization of such a system necessarily requires sophisticated mathematical and mechanical concepts and tools with which the average physiologist may not be familiar. As a matter of fact, some concepts of mechanics used in modern hemodynamics are too specialized even for an average mechanician. The first two chapters of this book have therefore been set out solely to explain some fundamental concepts of mathematics, solid mechanics, and fluid mechanics. Biologic examples are used whenever possible. Once these concepts have been introduced, we can continue the development of the subject with minimal interruption. To facilitate understanding of some of the complicated concepts of hemodynamics to be dicussed later on, the subject is developed from an elementary to a more sophisticated level. The tutorial aspects of the subject are emphasized throughout.

A rudimentary knowledge of calculus is essential to the understanding of the mathematical concepts presented in this book. If a brief review of the subject is desired, we recommend two sources, the books by Ayres (1964) and Richmond (1971), which contain many worked examples and can be adapted for self-study. In the following pages we state, explain, and illustrate a few useful concepts from calculus and other pertinent branches of mathematics.

## FUNCTIONS

If, for each value of a variable x, there exists a corresponding value of y, then y is called a *function* of x. The usual notation for such a correspondence is $y = f(x)$. Simple examples of the general statement $y = f(x)$ are: $y = x^2$, $y = \sin x$, and $y = x^2 \log x$, with x as the *independent* variable and y, whose value depends on x, as the *dependent* variable. These are examples of an *explicit* function, as contrasted with an *implicit* function, such as $x^2y^2 + \sin xy = 2$, which is not expressed explicitly as $y = f(x)$.

If, for a function $y = f(x)$, y has a value $y_0$ when $x = x_0$, this can be expressed as

$$y|_{x=x_0} = f(x_0) = y_0$$

For example, if $y = x^2$, then

$$y|_{x=2} = f(2) = 4$$

If, as in Figure 1.1a, there is only one value of y for each value of x, then f is said to be *single-valued.* In Figure 1.1b, f is *multi-valued* at $x_0$, because there are three values of y corresponding to $x = x_0$. Finally, f is said to be *discontinuous* at $x_0$ if different values of $f(x_0)$ are obtained, depending on whether we approach $x_0$ by gradually increasing x or by gradually decreasing it, as shown in Figure 1.1c.

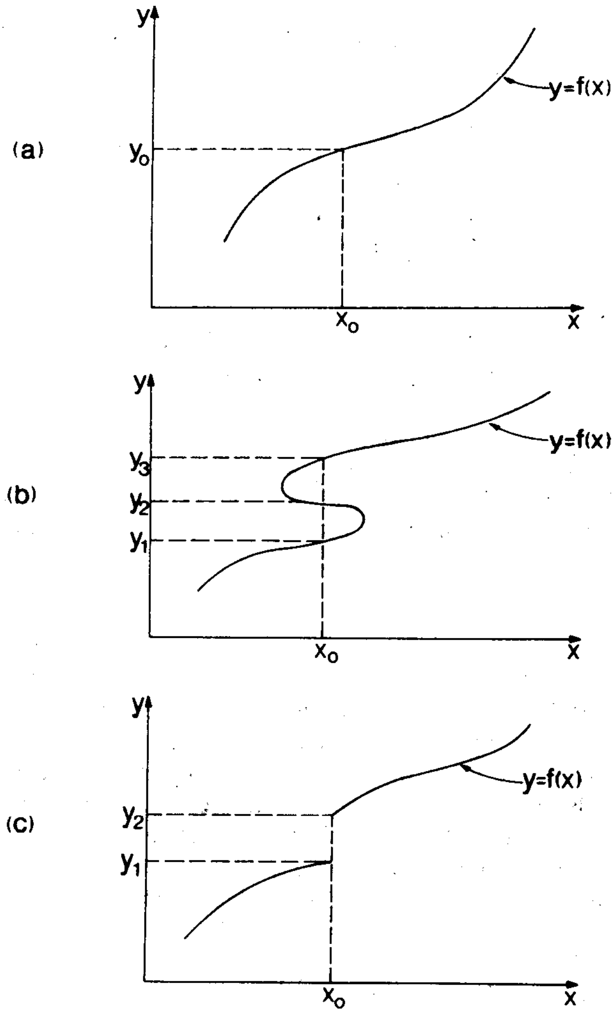


**Figure 1.1.** Graph of a function $y = f(x)$. **(a)** A single-valued continuous function. **(b)** A multi-valued continuous function. **(c)** A function with a discontinuity at $x = x_0$.