BASIC HEMODYNAMICS

and Its Role in Disease Processes

by
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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 for 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.

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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

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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.

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

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Complex Numbers
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Fourier Analysis
Use of Fourier Analysis in Hemodynamics
LINEAR MODELS
General Considerations

LIST OF SYMBOLS

Experimental Measurements of Characteristic Impedance, Propagation

Lumped-Parameter Models Distributed Parameter Models

Constant, and Wave Velocities Propagation of a Pressure Wave

Α	area
a	acceleration; real part of a complex number z; also used as a constant
а	attenuation constant
b	imaginary part of a complex number z; also used as a constant
b	phase constant
e	capacitance
e,	capacitance per unit length
C	damping coefficient; also used as a constant
	critical damping coefficient
C _e F	F _{acc} = acceleration force; F _{app} = applied force; F _s = spring force; F _d = force in dashpot; F _{visc} = viscous force
f	frequency
g	conductance
ց ց՝ հ	conductance per unit length
ĥ	thickness of blood vessel wall
ď	current

```
4m
                 denotes imaginary part of a complex variable
  j
  K
                 spring constant
  £
                 inductance
  \mathfrak{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
                inside pressure
 Pi
                outside pressure
 p<sub>o</sub>
  |p_n|
                magnitude of nth harmonic of pressure
 Q
 |Q_n|
                magnitude of nth harmonic of flow
 Q
                cardiac output; volume flow rate
 R
                resistance; hydraulic resistance
 R'
                resistance per unit length
 R
                radius; also reflection coefficient
 r
                radial variable
                resistances
 r_1, r_2, r_3
 Ť
                radius vector
 Re
                denotes real part of a complex variable
 Re
                Reynold's number
 \frac{S_{\theta}}{T}
                circumferential stress
                period
 TMP
                transmural pressure
                time
 t
                components of \vec{V}
    v, w
 V
                volume
                voltage
                vector; velocity vector
\begin{array}{c} V_{\underline{x}^{x}} \ V_{y}, \\ |V| \\ v \\ v_{p} \\ W \\ X_{c} \\ X_{p} \\ x, \ y, \ z \\ x_{d} \\ z \\ Z \end{array}
                cartesian components of \vec{V}
                magnitude of \overrightarrow{V}
                velocity
                phase velocity
                work
                complementary solution
                particular solution
                Cartesian coordinates
               extension of spring
               extension in dashpot
               complex variable; coordinate variable in axial direction
               impedance
Z
               characteristic impedance
               damping factor
Δc
               concentration difference
γ
ζ
               propagation constant
               damping coefficient
\theta
               viscosity coefficient
\theta_{\rm n}
               phase angle of nth harmonic
λ
               wavelength
               density
               shear stress
```

 $\begin{array}{lll} \varphi & & \text{a scalar; phase angle} \\ \phi_n & & \text{phase angle of } n^{\text{th}} \text{ harmonic} \\ \phi_f & & \text{starting angle for flow vector} \\ \phi_p & & \text{starting angle for pressure vector} \\ \omega & & \text{angular frequency} \\ \omega_0 & & \text{undamped natural frequency} \\ \omega_d & & \text{damped natural frequency} \\ \hline \overrightarrow{V} & & \text{vector operator "del"} \end{array}$

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

$$y|_{\mathbf{x}=\mathbf{x}_0} = f(\mathbf{x}_0) = y_0$$

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.

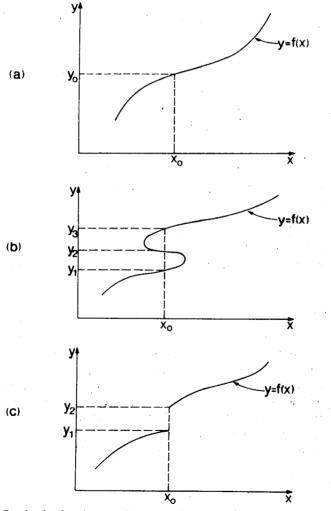


Figure 1.1. Graph of a function y = f(x). (a) A single-valued continuous function. (b) A multi-valued continuous function. (c) A function with a discontinuity at $x = x_0$.