

Cardiovascular Function

Principles and Applications

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Preface

This book is designed primarily for second-year graduate students, medical students, residents, and fellows in cardiology and related areas. It is an outgrowth of a course in circulatory physiology taught originally at Indiana University School of Medicine from 1963 to 1975. The absence of a definitive textbook suitable for a second-year graduate student or medical student who had already taken a medical physiology course was a persistent problem. Many textbooks were either too abbreviated for the level of knowledge we expected of our graduate students or, such as the *Handbook of Physiology*, were too detailed. This book is an attempt to provide a comprehensive survey of contemporary cardiovascular physiology, but with a definite emphasis on the methods and instrumentation currently used in investigative work.

At a mid-level of sophistication, this textbook is not designed to be all-encompassing in any particular area, nor is it meant as an up-to-date review of the literature. Rather, it assumes a basic level of knowledge and, it is hoped, will bring students to a second level of knowledge from which they can pursue a particular area in depth by means of standard textbooks in specific subdisciplines and current literature searches. As such, the references are designed to serve as a beginning point and do not by any means include the bulk of the work in the field. In most cases what is stated as fact is, of course, based on a great deal of uncited scientific work. For the most part, such facts are well accepted by the scientific community, but the authors admit to having included their own viewpoints. The authors also admit that they have somewhat arbitrarily selected the areas to be covered and have left out many excellent references in the interest of maintaining a textbook of reasonable size and price.

The book is divided into four parts. The first part deals primarily with methods of instrumentation with which the modern investigator in cardiovascular physiology needs to

be well acquainted. It is our conviction that understanding the principles of cardiovascular measurement is a cornerstone to the understanding of the functional conclusions based on the results of such measurements. Furthermore, our science has reached a point at which conclusions must be based on quantitative findings. Therefore the book begins with a presentation of instrumentation, including data acquisition and processing. The next part deals exclusively with the heart in terms of the mechanical and electrical properties of cardiac muscle and its organization into a pumping system. The third part deals with the properties of the vascular system, arterioles, capillaries, veins, and regional vascular beds. The fourth part deals with the operation of the total system. It begins with a discussion of control systems, the theory and properties of which are all-important for an understanding of integrative mechanisms. The emphasis is on normal function and the broad ranges of adjustment that the system can exhibit without being in a diseased state.

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F. L. A.

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Contents

Contributing Authors
Preface

I. Cardiovascular Measurements

1. Pressure and Stress	5
PRESSURE	5
<i>Definition and Units</i>	5
<i>Direct Measurement</i>	
<i>Techniques (Manometry)</i>	6
<i>Indirect Measurement</i>	
<i>Techniques</i>	
<i>(Sphygmomanometry)</i>	18
STRESS	22
<i>Definitions</i>	22
<i>Low Compliance Devices</i>	24
<i>High Compliance Devices</i>	27
<i>Other Approaches</i>	27
2. Flow, Dimension, and Volume	29
FLOW	29
<i>Definition and Units</i>	29
<i>Mean Flow Methods</i>	29
<i>The Rotameter</i>	
<i>(Shipley-Gregg-Wilson- Rotameter)</i>	32
<i>Pulsatile Flow Methods</i>	34
<i>Indicator Dilution Methods</i>	46
<i>Fick Principle</i>	50
<i>Impedance</i>	
<i>Plethysmography</i>	50
<i>Pulse Contour Method</i>	53
<i>Ballistocardiography</i>	53
DIMENSION AND VOLUME	53
<i>Angiographic Dimension and Volume</i>	
<i>Measurement</i>	54
<i>Ultrasonic Dimension and Volume Measurement</i>	55
<i>Direct Volume</i>	
<i>Determination</i>	58

3. Data Acquisition and Information Processing	61
DATA ACQUISITION SYSTEMS	61
<i>Transducers</i>	61
<i>Amplifiers</i>	61
<i>Output Indicators and Recorders</i>	63
<i>Typical Data Acquisition System</i>	64
<i>Required Frequency Response</i>	65
THE ANALOG COMPUTER	68
<i>General Considerations</i>	68
<i>Elements</i>	68
THE DIGITAL COMPUTER	71
THE HYBRID COMPUTER	73
PATIENT MONITORING SYSTEMS	74
SOME ASPECTS OF DATA MANAGEMENT	75

II. Cardiac Function

4. Electrical Properties of Cardiac Muscle	81
Warren G. Guntheroth	
INTRODUCTION	81
<i>The Generator: Cellular Electrophysiology</i>	81
<i>The Generator: Organ Electrophysiology</i>	90
<i>Conduction from Generator to Body Surface</i>	94
<i>Lead Systems and Recording Method</i>	96
CLINICAL APPLICATION: THE NORMAL	101
<i>Duration and Interval Measurements</i>	101
<i>Voltage Amplitude</i>	103
<i>Orientation of the ECG Complexes in Space</i>	103
<i>Vectorcardiographic Terminology and Criteria</i>	108
<i>Normal Trends with Age</i>	108

ABNORMAL ELECTROCARDIOGRAMS	109
<i>Disorders of Rate, Mechanism, and Rhythm</i>	109
<i>Hypertrophy</i>	118
<i>Disorders of the Sequence of Excitation</i>	121
<i>Disorders of Repolarization</i>	129
<i>Conclusions</i>	133
5. Contractile Properties of Cardiac Muscle	135
STRUCTURE OF CARDIAC SARCOMERE	135
MYOCARDIAL METABOLISM	138
MECHANICAL PROPERTIES OF ISOLATED SKELETAL MUSCLE	140
<i>Force-Length Relationship</i>	140
<i>Force-Time Relationship</i>	141
<i>Force-Velocity-Length Relationship</i>	144
<i>Skeletal Muscle Mechanics and Heat Production</i>	146
<i>Limitations of These Concepts</i>	148
MECHANICAL PROPERTIES OF ISOLATED CARDIAC MUSCLE	150
<i>Force-Length Relationship</i>	150
<i>Force-Time Relationship</i>	151
<i>Force-Velocity-Length Relationship</i>	153
<i>Inotropic Effect</i>	153
<i>Cardiac Muscle Mechanics and Heat Production</i>	155
<i>Expression of Active State</i>	155
<i>Limitations of These Concepts</i>	157
IMPLICATIONS FOR PERFORMANCE EVALUATION IN THE INTACT HEART	158
6. Cardiac Cycle, Heart Sounds, and Cardiodynamics	161
MECHANICAL ASPECTS OF CARDIAC ACTIVITY	161

<i>Functional Anatomy</i>	161
<i>Arrangement of the Valves</i>	163
THE CARDIAC CYCLE	163
<i>Pressure and Flow Events</i>	163
<i>Heart Sounds and Murmurs</i>	169
<i>Time Relationships Within the Cardiac Cycle</i>	175
<i>Central Venous Pressure</i>	175
<i>Electrocardiographic Relationships</i>	176
<i>Cardiodynamics</i>	176
<i>Alterations in Heart Rate</i>	177
<i>Alterations in Stroke Volume</i>	178
 7. Cardiac Work, Heterometric and Homeometric Autoregulation, and Influence of Autonomic Nerves	181
POWER AND WORK	181
HETEROMETRIC AUTOREGULATION	184
HOMEOMETRIC AUTOREGULATION	187
INFLUENCE OF EXTRINSIC NERVES ON CARDIAC PERFORMANCE	189
<i>Effects of Sympathetic Nerve Fibers on the Ventricle</i>	189
<i>Effects of Parasympathetic Nerve Fibers on the Ventricle</i>	191
<i>Effects of the Autonomic Nervous System on the Atrium</i>	194
 8. Evaluation of Ventricular Performance	197
COMPARISON OF ISOLATED MUSCLE AND INTACT HEART	197
<i>Considerations of Cardiac Geometry</i>	197
<i>Other Factors</i>	197
CONTRACTILITY AND PERFORMANCE	198

INVASIVE METHODS	199
<i>End Diastolic Pressure</i>	199
<i>Pressure-Volume Measurements</i>	199
<i>Ventricular Function Curves</i>	200
<i>Rate-Dependent Indexes</i>	203
<i>Isovolumetric Tension-Time Relationships</i>	207
<i>Applications of Force-Velocity Measurements</i>	207
<i>Overall Comparisons</i>	209
<i>Other Parameters</i>	210
NONINVASIVE EVALUATION	211
<i>Systolic Time Intervals (STI)</i>	212
<i>Slopes of Isovolumetric Pressure-Time Curves</i>	213
<i>Ultrasound</i>	214

III. The Vascular System

9. The Arterial System	219
RESISTANCE	219
TURBULENCE	221
FLOW TERMINOLOGY	221
LAPLACE'S LAW	222
OTHER PHYSICAL PROPERTIES OF FLUIDS	223
<i>The Continuity Equation</i>	223
<i>Bernoulli's Equation</i>	223
CRITICAL CLOSING PRESSURE AND CRITICAL CLOSING ACTIVE TENSION	223
IMPEDANCE CONCEPTS IN THE ARTERIAL CIRCULATION	224
AUTOREGULATION	226
<i>Tissue Pressure Theory</i>	226
<i>The Myogenic Hypothesis</i>	226
<i>The Metabolic Theory</i>	226
FACTORS INFLUENCING ARTERIAL PRESSURE DROP	227
<i>Arterial Pressure and Pulse Pressure</i>	228

<i>Arterial Pulse and Its Transmission</i>	232
<i>Relationship Between Pulse Pressure and Heart Rate, Stroke Volume, and Peripheral Resistance</i>	233
<i>Control of Arterial Pressure</i>	235
10. The Microcirculation	239
James E. McNamee	
ARCHITECTURE	239
BLOOD PRESSURE AND FLOW	239
<i>Patterns of Pressure and Flow</i>	240
<i>Pressure and Flow Measurements</i>	241
SOLUTE AND WATER EXCHANGE	242
<i>Diffusion</i>	242
<i>Convection</i>	244
<i>Osmotic Pressure</i>	245
<i>Measurement of Capillary Transport Coefficients</i>	247
<i>Extravascular (Tissue) Pressures</i>	248
<i>Lymphatics</i>	249
11. The Veins and Venous Return	251
ORGANIZATION AND STRUCTURE	251
<i>Passive Properties</i>	253
FACTORS INFLUENCING VENOUS RETURN	255
<i>Vis a Tergo</i>	255
<i>Venous Pressure Measurement</i>	255
<i>The Reference Point</i>	255
<i>Gravity</i>	257
<i>Muscle Pumping Action</i>	257
<i>Abdominal-Thoracic Pump</i>	259
<i>Vis a Fronte</i>	261
<i>Additional Factors</i>	262
NEURAL CONTROL	263
PRESSURE-VOLUME RELATIONSHIPS	264

<i>Mean Circulatory Pressure</i>	270
NORMAL FLOW PATTERNS AND INFLUENCE OF POSTURE	271
12. Regional Vascular Beds	279
THE CORONARY CIRCULATION	279
<i>Anatomy</i>	279
<i>Blood Flow Patterns</i>	281
<i>Regulation of the Coronary Vascular System</i>	283
THE CEREBRAL CIRCULATION	287
<i>Anatomy</i>	287
<i>Cerebral Blood Flow</i>	288
THE PULMONARY CIRCULATION	290
James E. McNamee	
<i>Functional Anatomy</i>	290
<i>Hemodynamics</i>	291
<i>Lung Blood Flow</i>	292
<i>Lung Blood Volume</i>	293
THE RENAL CIRCULATION	294
Philip D. Watson	
<i>General Considerations</i>	294
<i>Anatomy of the Renal Circulation</i>	294
<i>Glomerular Filtration</i>	295
<i>Clearance and the Measurement of Renal Blood Flow</i>	295
<i>Regulation of Renal Blood Flow</i>	296

IV. Circulatory Integration and Regulation

13. Theory and Properties of Control Systems	303
Matthew B. Wolf	
FEEDBACK AND BIOLOGICAL SYSTEMS	303
SYSTEMS	303
TRANSIENT RESPONSE	305
FREQUENCY RESPONSE	305
TRANSFER FUNCTIONS	307
FIRST ORDER SYSTEMS	308

SECOND ORDER SYSTEMS	310
TRANSPORTATION LAG	311
CONTROL SYSTEMS	311
SENSITIVITY AND DISTURBANCE REJECTION	313
STABILITY	314
ANALYSIS OF CARDIOVASCULAR CONTROL SYSTEMS	315
14. Neural Control	319
RECEPTORS AND AFFERENT LIMBS	319
<i>Carotid Sinus and Aortic</i>	
<i>Arch Baroreceptors</i>	319
<i>Cardiac Receptors</i>	321
<i>Other Thoracic</i>	
<i>Mechanoreceptors</i>	325
<i>Other Mechanoreceptors</i>	326
<i>Chemoreceptors</i>	326
CENTRAL CONTROL AREAS	327
EFFERENT MECHANISMS	330
EFFECTORS	331
<i>Adrenergic Effectors</i>	331
<i>Cholinergic Effectors</i>	333
<i>Vascular Pharmacology</i>	333
15. Reserves and Characteristic Responses	337
CARDIOVASCULAR RESERVES	337
CHARACTERISTIC RESPONSES	337
<i>Postural Responses</i>	338
<i>The Defense Reaction</i>	341
<i>Disease States</i>	347
ADJUSTMENTS TO ENVIRONMENTAL CHANGES	349
<i>Responses to Altered</i>	
<i>Ambient Pressure: Diving</i> <i>and Altitude</i>	349
<i>Responses to Altered</i>	
<i>Ambient Temperature:</i> <i>Heat and Cold</i>	358

<i>Responses to Altered Gravitational Field: Centrifugation, Weightlessness, and Recumbency</i>	368
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Appendix

ANALOG COMPUTER CIRCUITS	387
DIGITAL COMPUTER PROGRAMS	390
<i>Integration</i>	390
<i>Differentiation</i>	391
<i>Blood Volume Calculation</i>	392
<i>Dye Dilution Analysis</i>	393
<i>Maximum Routine</i>	395
<i>Cardiac Cycle</i>	396
<i>Coronary Program</i>	398
<i>Power Spectral Analysis</i>	404
<i>Fourier Analysis</i>	408
<i>Cycle Averaging Routine</i>	408
<i>Decimal to Base Conversion</i>	409

<i>Index</i>	411
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Cardiovascular Measurements

I

Scientific observations depend on methodology, and our understanding of circulatory function must inevitably reflect our capability for measuring its fundamental physical properties. Before proceeding with the analysis of system function, we require detailed information on the applicable measurement techniques to determine how much confidence can be placed in the results. The factors of key significance for estimating measurement validity can be summed up by the term *accuracy*. Classically, all measurement is comparison, and accuracy refers to the correctness or exactness of correspondence between a measurement and a reference standard. The issue is more complicated for biological systems than for inanimate objects. In biological applications the type of measurement chosen and the requirements for accuracy are more likely to be influenced by the depth of our understanding of the system. As our understanding increases, our requirements for accuracy are also likely to increase.

Instrument accuracy is expressed by a statistical statement about the probable value of the measured variable as derived from the output of a measurement system. The basis for a statement about accuracy begins with *calibration*. The judgment of accuracy can be no broader than the range covered by the calibration procedure. Calibration may be required in both *static* (steady-state or slowly changing) and *dynamic* (transient or rapidly changing) terms, covering the expected input amplitudes and frequencies and including the entire measurement system under conditions as similar as possible to the experimental situation.

A group of factors can be identified that affect the outcome of the calibration and the determination of accuracy, that is, finding the most representative value. *Directness* refers to the proximity of the measurement transducer to the target variable. A pressure-sensing manometer placed inside an artery is

direct; the cuff technique on the arm is indirect (and inferential), since events in the artery are detected only at the skin, and the relationship to arterial pressure has been established by empirical correlations. *Specificity*, or selectivity, refers to the degree to which a measurement is affected solely by the target variable. For instance, some pressure measurement devices are also extremely sensitive to temperature variations. *Reactance*, the degree to which the biological process is altered by the measurement, is a related effect. Whether the measurement conditions were *acute* or *chronic* is highly significant; for example, it is clear that anesthesia and surgery profoundly alter many aspects of cardiovascular function. With internal placement, examination of tissue changes caused by the presence of a transducer is comparatively direct. In many circumstances, however, the effect that making the measurement has on the measured process is the most difficult determination of all. The interactions may be subtle and complex and range from local biochemical to psychological and environmental influences. Very often, however, these effects can be controlled, even if not quantified.

Range identifies not only the limits of acceptable accuracy with respect to the load imposed by the target variable, but also the limits tolerated by the device without damage. The data are easier to manage if the device output has *linearity* over the input range of interest. An input-output relationship that plots as a straight line is not a requirement. But the form and stability of the input-output function must be known in detail. *Stability*, the degree of baseline and input-output variability with time, can be obtained in conjunction with linearity assessments. Determination of *reproducibility*, *precision*, or test-retest *reliability* is dependent on statistical techniques. Reproducibility may be present even though absolute quantification is limited. *Fidelity* encompasses frequency response and sampling rate: all necessary information must be included, but unneeded data must be excluded. *Sensitivity* includes the slope of the line relating input and output levels, as well as the signal-to-noise ratio, an important component

of the minimal detectable change. Noise is not only the purely random variation generated within the measurement system itself, but frequently also includes unknown sources operating within the biological system. The requirements for accuracy must include the likelihood of functional variation. Therefore a partly subjective judgment may be incorporated in the accuracy specifications. There is little point in measuring changes in cardiac output to levels of 1 ml in 5 liters; or body weight to 1 mg in 100 kg, when the inherent moment-to-moment variations exceed these amounts.

The factors that have been outlined are considerations affecting the subsequent discussion of representative approaches to cardiovascular measurements, even though they may not all be covered explicitly. The reader will find extensive information on measurement principles and applications in the books by Cobbold [4], Geddes and Baker [9], and Webster [26].

For the properties and events of significance in the circulation, the basic descriptors are the quantities of *pressure and stress, flow, dimension and volume, biopotentials*, and *time*. Ancillary factors include variables such as biochemical assessments of blood and other tissues and cells. Measurements of pressure and flow are relatively advanced and merit special treatment; these two topics are presented in Chapters 1 and 2. Dimension-volume considerations are also included in Chapter 2. The biopotentials of greatest cardiovascular significance originate in the heart and are discussed in Chapter 4. The final basic variable of *time* is inherent in each of these areas. Time measurement will not be treated separately, but its continuing significance should be kept in mind. Presentations of the ancillary variables can be found in the references and in standard texts.

The measurement is not complete until the signal has been acquired and processed, and the end result can of course be no better than the entire system. The classes and examples of data management applying to cardiovascular measurements are subjects addressed in Chapter 3.