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.
E. P. M.

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I

Cardiovascular Measurements

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.