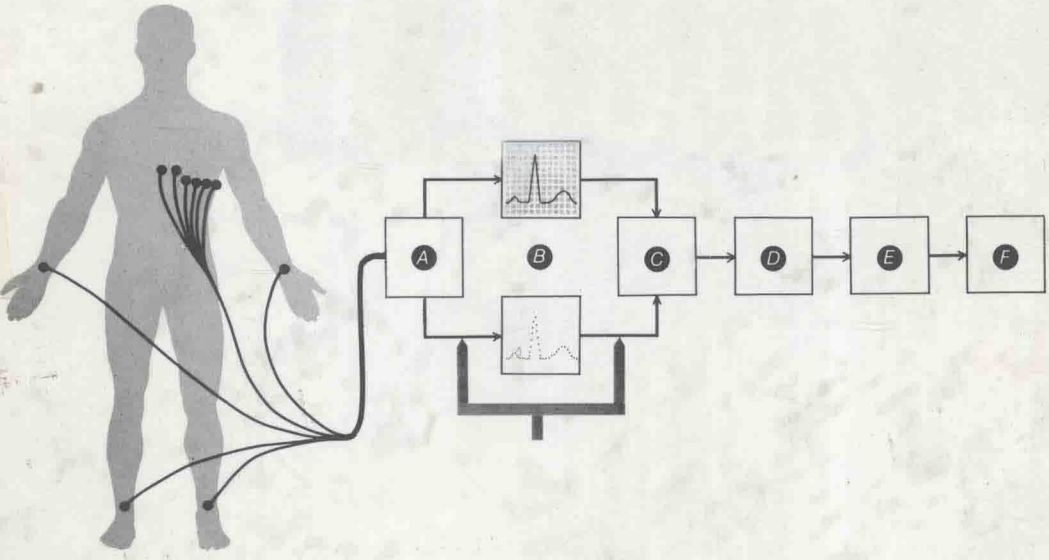
COMPUTER TECHNIQUES IN CARDIOLOGY



edited by Lee D. Cady, Jr.

COMPUTER TECHNIQUES IN CARDIOLOGY

EDITED BY

Lee D. Cady, Jr.

Adjunct Professor of Medicine
University of Southern California
AND
Chief, Cardiopulmonary Laboratory
Department of Personnel
County of Los Angeles
Los Angeles, California

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Edited by

GEORGE A. BEKEY and J. LAWRENCE KATZ

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Los Angeles, California

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PREFACE

Computer techniques are part of the repertoire of many clinicians and most biomedical scientists, and their usefulness is increasing every year. These techniques are useful in medicine because they supply better quantitation and hence provide a sound basis for physicians to work. Each contributor to this book has had one to two decades of experience in applying computers to problems in clinical cardiology, and each author has chosen a particular application to portray the computer techniques used for the solution of problems in cardiology. The presentations have concentrated on both the conceptual and the operational features of computer applications. The discussions offer practical information for readers who are interested in using a computer to provide better medical services. For other readers who are concerned with developing their own solutions to similar problems, the authors provide necessary insights into cost-effective solutions for their specific applications. The techniques, concepts, and computer hardware and software that are described in this book are applicable to medicine generally, although the specific examples given of computer applications are limited to cardiology.

The methods for computations of diagnostic probabilities are sufficiently general to be useful for classification in every field of science. The presentation on medical information systems has broad applications to all fields of medicine. The programs and models for pharmacokinetic systems are useful in determining dosage levels for hundreds of medications, far beyond the three specific examples of digitalis, procainamide, and lidocaine given here. The descriptions of electrical signal processing, pattern recognition, coherent averaging for noise suppression, voltage peak picking, video edge detection, and on-line control of laboratory instrumentation are such useful techniques for industry and science in general that it would be surprising if they were not equally applicable to cardiology.

Each year computer techniques and solutions to medical and biological problems are improving and each lowering in the cost of computer hardware results in more computer applications to medical problems. The cardiological applications for computers can be classified in four ways: (1) recognition and measurement of characteristic patterns in electrical signals (e.g., detection of wave peaks and valleys in electrocardiograms, dynamic video edge detection in ventriculograms); (2) on-line control of physiological variables and instrumentation (e.g., changing ergometer workloads to achieve target heart rates, gating of x-ray photographs during systole or diastole, and dynamic control of drug therapy); (3) mathematical and statistical manipulation of medical data (e.g., filtering electrical signals to reduce electrocardiographic measurement errors and computation of diagnostic probabilities and classifications); (4) orderly bookkeeping of medical information (e.g., clinical trials data management, patient scheduling, and medical records storage and retrieval).

The authors have shared their insights, problem understandings, and solutions with the reader. These presentations describe the current level of advancement of computer applications in cardiology and form a solid base for projecting future applications in cardiology and medicine.

The editor and publisher are indebted to the authors for their openness and willingness to communicate their technological developments in medicine and computing for the benefit of all readers. The authors have taken many hours of scarce time from their professional and personal lives to write and rewrite their manuscripts.

Repeatedly the authors have expressed appreciation and gratitude for the efforts of their technical and secretarial staffs in describing methods, procedures, and results. Finally, the editor is grateful to Jeannine Foreman, Fern Grant, and Darlene Clements for their continuous help with attention to manuscripts, documentation, and details, which are so essential in medical and scientific descriptions of this kind.

Lee D. Cady, Jr.

Albus, John, Cardiopulmonary Laboratory, Occupational Health Service, County Department of Personnel, Los Angeles, California

*Alpert, Joseph S.,** Chief, Division of Cardiovascular Medicine, Professor of Medicine, University of Massachusetts Medical School, Worcester, Massachusetts

Berman, Daniel S., Director of Nuclear Medicine, Cedars-Sinai Medical Center, and UCLA School of Medicine, Los Angeles, California

Bischoff, David P., Cardiopulmonary Laboratory, Occupational Health Service, County Department of Personnel, Los Angeles, California

Cady, Lee D., Jr.,† Chief, Cardiopulmonary Laboratory, Occupational Health Service, County Department of Personnel, Los Angeles, California

Charuzi, Yzhar, Cedars-Sinai Medical Center, and Associate Cardiologist and Assistant Professor of Medicine, UCLA School of Medicine, Los Angeles, California

Clifton, James F., Assistant Professor of Medicine, UCLA School of Medicine, Harbor General Hospital Campus, Torrance, California

Diamond, George A., Senior Research Scientist, Cedars-Sinai Medical Center, and UCLA School of Medicine, Los Angeles, California

Forrester, James S., Assistant Director of Cardiology, Cedars-Sinai Medical Center, and Associate Professor of Medicine, UCLA School of Medicine, Los Angeles, California

Fozzard, Harry A., Professor of Medicine and Physiology, The University of Chicago, Chicago, Illinois

Gray, Richard J., Director of Postoperative Cardiac Care, Cedars-Sinai Medical Center, and Assistant Professor of Medicine, UCLA School of Medicine, Los Angeles, California

Hagan, Arthur D., Director, Clinical Investigation Center, Naval Regional Medical Center, and Associate Clinical Professor of Medicine, University of California at San Diego School of Medicine, San Diego, California

*Affiliations at time of writing: Assistant Professor of Medicine, University of California at San Diego, and Director of the Acute Care Branch, Naval Regional Medical Center, San Diego, California

†Additional affiliation: Adjunct Professor of Medicine (Biomathematics), University of Southern California School of Medicine, Los Angeles, California

Hopkins, W. Barry, C. Horton & Associates, Houston, Texas

Horton, Caroline, C. Horton & Associates, Houston, Texas

Jelliffe, Roger W., Professor of Medicine, Sections of Cardiology and Clinical Pharmacology, University of Southern California School of Medicine, Los Angeles, California

Kinias, Plato, Research Associate (Assistant Professor), The University of Chicago, Chicago, Illinois

Maddahi, Jamshid, Cardiology Fellow, Cedars-Sinai Medical Center, and UCLA School of Medicine, Los Angeles, California

O'Connell, Eugene R., Cardiopulmonary Laboratory, Occupational Health Service, County Department of Personnel, Los Angeles, California

*Okies, J. Edward,** Good Samaritan Hospital and Medical Center, Portland, Oregon

Sapoznikov, Dan, Research Fellow, Department of Medicine, Section of Cardiology, University of Southern California, Rancho Los Amigos Campus, Downey, California

Schwartz, Morton D., Biomedical Engineering Program, California State University, Long Beach, California

Selvester, Ronald H., Professor of Medicine and Chief of Cardiology, Department of Medicine, Section of Cardiology, University of Southern California, Rancho Los Amigos Campus, Downey, California

Shah, Prediman K., Associate Cardiologist, Cedars-Sinai Medical Center, and UCLA School of Medicine, Los Angeles, California

Silverberg, Robert A., Cardiology Research Fellow, Cedars-Sinai Medical Center, Los Angeles, California

Solomon, Joseph, Director of Biomathematics and ECG Fellow, Department of Medicine, Section of Cardiology, University of Southern California, Rancho Los Amigos Campus, Downey, California

Thomas, Phillip C., Cardiopulmonary Laboratory, Occupational Health Service, County Department of Personnel, Los Angeles, California

Vas, Ran, Director of Biophysics, Cedars-Sinai Medical Center, and Associate Professor of Engineering, UCLA, Los Angeles, California

Wartak, Joseph, Director, Medical Education Systems, Kingston, Ontario, Canada

*Affiliation at time of writing: Assistant Professor of Surgery, Division of Cardiopulmonary Surgery, University of Oregon Medical School, Portland, Oregon

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DIFFERENTIATION BETWEEN NORMAL AND ABNORMAL IN CARDIOLOGY

JOSEPH WARTAK

Medical Education Systems
Kingston, Ontario, Canada

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I. INTRODUCTION

In cardiology, as well as in other fields of medicine, the differentiation between normal and abnormal is difficult for two reasons. One reason is that there are no two subjects exactly alike because every biological quantity is a variable influenced by heredity, environment, occupation, nutrition, age, sex, culture, etc. Consequently, even in perfectly normal subjects most biological quantities are scattered over a certain range of values. For example, the amplitude of the ST segment of the electrocardiogram (ECG) in normal subjects may vary from -0.05 mV to +0.3 mV in whites and up to +0.5 mV in blacks. The other reason is that "normality" or "health" has been frequently determined on the basis of a single value such as a mean value or the upper or lower limit of normal values. For example, the limit for a normal Q wave might have been set arbitrarily at 0.2 mV and consequently all Q waves exceeding that limit would have to be regarded as abnormal. Obviously, such an approach greatly simplifies a complex process of differentiation between normal and abnormal.

An optimal separation of pathological conditions from the normal population should be based on normal ranges rather than single values and the demarcation lines should be set according to some statistical rules governing the probability of correct identification of events in various classes. It is also important to employ in the differentiation process those categories of data which have high discriminative power. Such categories of data may not be clinically apparent and can be only discovered by mathematical analysis [1-3]. This, however, involves extensive computation and is feasible only with the assistance of a computer.

II. STATISTICAL NATURE OF NORMALITY

It is by now common knowledge in medicine that most biological quantities being studied in healthy subjects will display values which assume a bell-shaped (Gaussian or normal) frequency distribution which may be described completely by the mean value ($\bar{X}$) and standard deviation (SD). Accordingly, the statistical limits of normality have been arbitrarily chosen at two standard deviations on either side of the mean calculated for a large number of homogeneous, unselected, healthy subjects. Since the area under the frequency distribution curve between the mean - 2SD and the mean + 2SD encloses 95.4% of data, the probability that a value outside the mean ± 2SD range may be normal is only 0.05% (or in other words, it can be found in 1 out of 20 subjects) and can be regarded as negligible (Fig. 1).

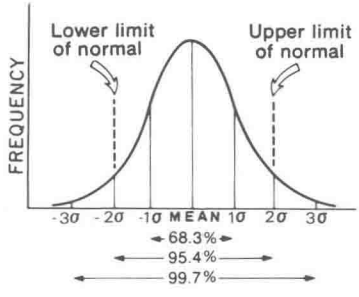

FIG. 1. Gaussian or normal frequency distribution and the limits of normality (σ = standard deviation).

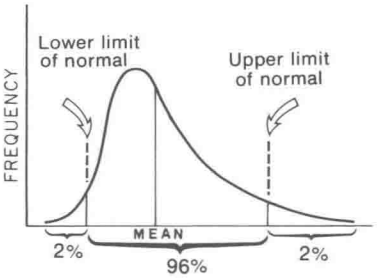

FIG. 2. Non-Gaussian frequency distribution and the limits of normality.

In the case of values which do not follow normal distribution patterns, the normal limits are determined from the 96 percentile ranges as follows: the lower limit is established after eliminating 2% of the cases at the "minimal" end of the distribution, and the upper limit is established after eliminating 2% of the cases at the "maximal" end of the distribution (Fig. 2).

Normal limits have been calculated for all kinds of numerical data in cardiopulmonary medicine. However, their reliability is frequently questionable because not all clinical and statistical requirements can be met in most situations [4]. The primary difficulties include the following:

1. Complete exclusion of pathology in some "normal" cases is impossible because some subjects free from an overt disease process may have had a silent disease.
2. In order for a sample to be representative of a general population it must be very large and demographically diverse to account for physiological variability due to age, sex, race, occupation, physical activity, habitation (including altitude and climate), etc.

The above difficulties are responsible for the fact that in some instances data of a healthy subject may fall beyond the normal limits or data of a sick subject may fall within the normal limits.

III. CONCEPT OF THRESHOLD SETTING

The frequency distributions of most biological data in normal and diseased populations overlap to some extent so that the values found in an overlapping area can belong to either population (Fig. 3). It is obvious that in the overlapping area the separation of the normal population from the diseased one cannot be accomplished without diagnostic errors.

One type of diagnostic error is the conclusion that the patient has a disease when in fact he does not (the so-called false-positive error); a second type of error is the conclusion that the patient does not have a disease when in fact he does (the so-called false-negative error). The relative number of each type of error depends upon where one sets the threshold for the normal population. If the threshold of normality is set too low, many false-positives are obtained, while if the threshold of normality is set too high, many false-negatives result. Thus it follows that criteria for normality, such as the mean ± 2SD, cannot be entirely satisfactory in all situations. In some circumstances one may prefer to avoid one type of error at the expense of the other. This preference is usually dictated by considering the relative harm that might result from each type of error, measured in terms of overall well-being of the patient. For example, the harm of calling a patient with angina pectoris normal

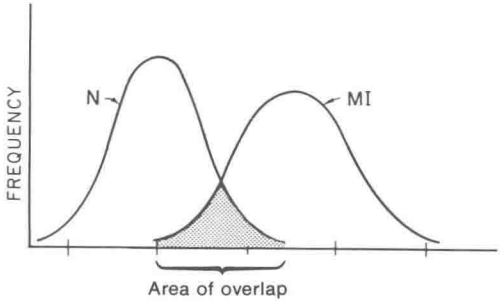

FIG. 3. A hypothetical frequency distribution of the Q wave duration in a normal population (N) and in a population with myocardial infarction (MI).

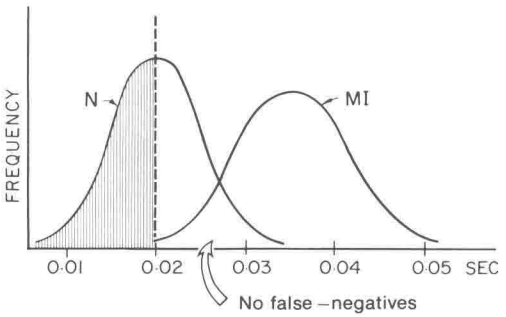

FIG. 4. Setting the threshold of normality resulting in no false-negatives.

would be quite great, in view of the serious consequences of failing to treat this disease properly. Most physicians feel that it is far more culpable to dismiss a sick patient than to call a healthy person sick. Such an attitude is not shared, for example, by the legal profession which thinks that the error that is more important to avoid is to convict the innocent person. Consequently, the rule for decision making in courts is expressed by the aphorism "innocent unless proven guilty," whereas the rule for decision making in hospitals may be expressed by "sick unless proven healthy."

Sensitivity of statistical assessment describes the ability of a diagnostic criterion to give a positive diagnosis when the subject examined is truly diseased, i.e., he or she belongs to the diseased population under the study. Sensitivity can be expressed as a percentage according to the formula

$$\text{Sensitivity (\%)} = \frac{\text{Truly-positive diagnoses}}{\text{All members of the diseased population}} \times 100$$

A hypothetical distribution of the Q wave duration in two populations, one of normal subjects and the other of patients with myocardial infarction is shown in Fig. 4. The upper limit of normal Q wave duration has been set at 0.02 sec (i.e., very low), resulting in a very sensitive diagnostic criterion of pathology because all myocardial infarcts can be diagnosed; however, this is done at the expense of erroneously suggesting that many normal subjects may have myocardial

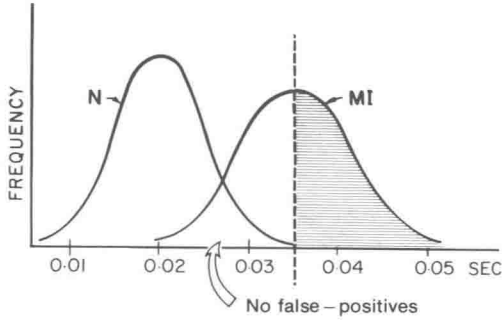

FIG. 5. Setting the threshold of normality resulting in no false-positives.

infarction. If the diagnostic criterion is set at 0.025 sec, a lower sensitivity results, since not all patients with myocardial infarction are diagnosed correctly, but the number of false-positive diagnoses is cut down substantially.

Specificity of statistical assessment describes the ability of a diagnostic criterion to give a negative diagnosis when the subject examined is normal, i.e., he or she belongs to the normal population. Specificity can be expressed in a percentage according to the formula

$$\text{Specificity (\%)} = \frac{\text{Truly-negative diagnoses}}{\text{All members of the normal population}} \times 100$$

A hypothetical distribution of the Q wave duration in two populations, one of normal subjects and the other of patients with myocardial infarction is shown in Fig. 5. The upper limit of normal Q wave duration has been set at 0.035 sec (i.e., very high), resulting in a very specific diagnostic criterion for myocardial infarction, since no normal cases can be diagnosed as infarction; however, this is done at the expense of erroneously suggesting that many patients with myocardial infarction are normal. If the diagnostic criterion is set at 0.03 sec, this results in lower specificity, but at the same time the number of false-negative diagnoses is cut down substantially. The gain in sensitivity of a diagnostic criterion is always negated by a loss in specificity, and vice versa. Consequently, the physician selects a criterion which minimizes either the type of error which

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