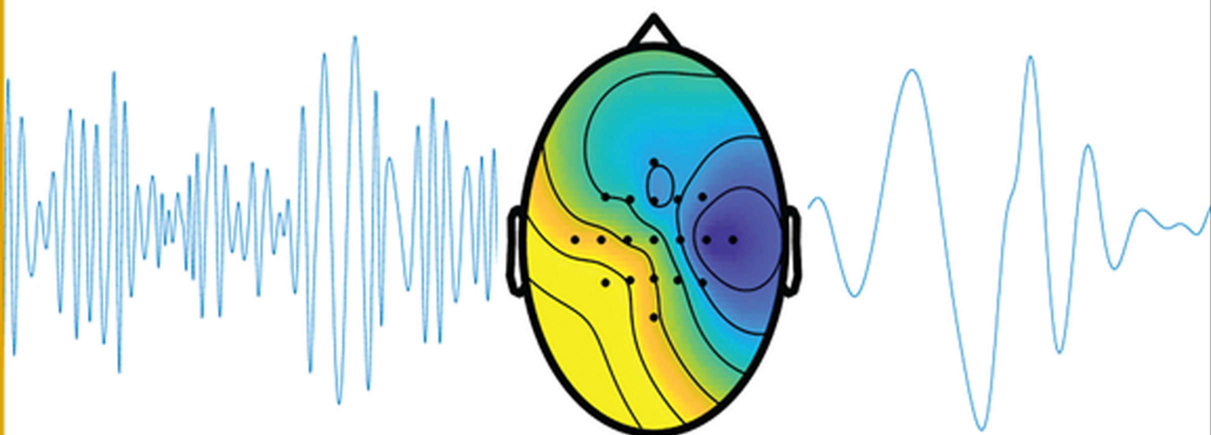
Biomedical Signal Analysis

RANGARAJ M. RANGAYYAN
SRIDHAR KRISHNAN

Third Edition



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Third Edition

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DEDICATION

Mátr dévô bhava
Pitr dévô bhava
Áchárya dévô bhava

Look upon your mother as your God
Look upon your father as your God
Look upon your teacher as your God

— from the sacred Vedic hymns of the *Taittireeya Upanishad* of India.

This book is dedicated to the fond memory of
my mother Srimati Padma Srinivasan Rangayyan
and my father Sri Srinivasan Mandayam Rangayyan,
and to all of my teachers,
in particular, Professor Ivaturi Surya Narayana Murthy.
Rangaraj

This book is dedicated to
my parents, mentors, students,
and my wife Mahitha,
and to our children Sibi and Sarvi.
Sridhar

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ABOUT THE AUTHORS

Photo credit: Skogen Photography
for the University of Calgary.

Rangaraj M. Rangayyan is Professor Emeritus of Electrical and Computer Engineering, University of Calgary, Calgary, Alberta, Canada. He received the Bachelor of Engineering degree in Electronics and Communication Engineering in 1976 from the University of Mysore at the People's Education Society College of Engineering, Mandya, Karnataka, India, and the Ph.D. in Electrical Engineering from the Indian Institute of Science, Bangalore, Karnataka, India, in 1980. He served the University of Manitoba, Winnipeg, Manitoba, Canada and the University of Calgary in research, academic, and administrative positions from 1981 to 2016. His research interests are in digital signal and image processing, biomedical signal and image analysis, and computer-aided diagnosis.

Dr. Rangayyan has published more than 170 papers in journals and 270 papers in proceedings of conferences. According to Google Scholar, Dr. Rangayyan's publications have attracted $>$ 18,000 citations with an h-index $>$ 66. He has supervised or cosupervised 27 Master's theses, 17 Doctoral theses, and more than 50 researchers at various levels. He has been recognized with the 1997 and 2001 Research Excellence Awards of the Department of Electrical and Computer Engineering, the 1997 Research Award of the Faculty of Engineering, appointment as "University Professor" (2003 to 2013) at the University of Calgary, and Outstanding Teaching Performance Award of the Schulich School of Engineering (2016). He is the author of two textbooks: "Biomedical Signal Analysis" (IEEE/ Wiley, 2002, 2015) and "Biomedical Image Analysis" (CRC, 2005). He has coauthored and coedited several books, including "Color Image Processing with Biomedical

Applications” (SPIE, 2011). He was recognized with the 2013 IEEE Canada Outstanding Engineer Medal, the IEEE Third Millennium Medal (2000), and elected as Fellow, IEEE (2001); Fellow, Engineering Institute of Canada (2002); Fellow, American Institute for Medical and Biological Engineering (2003); Fellow, SPIE (2003); Fellow, Society for Imaging Informatics in Medicine (2007); Fellow, Canadian Medical and Biological Engineering Society (2007); Fellow, Canadian Academy of Engineering (2009); and Fellow, Royal Society of Canada (2016).

Dr. Rangayyan’s research has been featured in many newsletters, magazines, and newspapers, as well as in several radio and television interviews. He has been invited to present lectures in more than 20 countries and has held Visiting or Honorary Professorships with the University of Liverpool, Liverpool, UK; Tampere University of Technology, Tampere, Finland; Universitatea Politehnica Bucureşti, Bucharest, Romania; Universidade de São Paulo, São Paulo, Brasil; Universidade Estadual Paulista, Sorocaba, São Paulo, Brasil; Cleveland Clinic Foundation, Cleveland, OH, USA; Indian Institute of Science, Bangalore, Karnataka, India; Indian Institute of Technology, Kharagpur, West Bengal, India; Manipal Institute of Technology, Manipal, Karnataka, India; Amity University, Noida, India; Beijing University of Posts and Telecommunications, Beijing, China; Xiamen University, Xiamen, Fujian, China; Kyushu University, Fukuoka, Japan; University of Rome Tor Vergata, Rome, Italy; and École Nationale Supérieure des Télécommunications de Bretagne, Brest, France. He has been recognized as a Distinguished Lecturer by the IEEE Engineering in Medicine and Biology Society (EMBS), the University of Toronto, and the Hong Kong Institution of Engineers.

For further details, please visit his website `https://rangayyan.ca`

Sridhar Krishnan received the B.E. degree in Electronics and Communication Engineering from the College of Engineering, Guindy, Anna University, India, in 1993, and the M.Sc. and Ph.D. degrees in Electrical and Computer Engineering from the University of Calgary, Calgary, Alberta, Canada, in 1996 and 1999, respectively. He joined the Department of Electrical, Computer, and Biomedical Engineering, Toronto Metropolitan University — TMU (formerly Ryerson University), Toronto, Ontario, Canada, in July 1999, and currently, he is a Professor in the Department. He was TMU’s Founding Program Director of the Undergraduate Biomedical Engineering Program, and also the Founding Co-Director of the Institute for Biomedical Engineering, Science and Technology (iBEST). Dr. Krishnan is an Affiliate Scientist with the University Health Network and the Keenan Research Centre, St. Michael’s Hospital, Toronto. He held the Canada Research Chair position (2007–2017) in Biomedical Signal Analysis. He has published 405 papers in refereed journals and conference proceedings, and filed/obtained 16 patents/invention disclosures. He is currently serving as a scientific advisor to six technological start-ups in the areas of digital health, wearables, and AI.

Dr. Krishnan is a recipient of the Outstanding Canadian Biomedical Engineer Award from the Canadian Medical and Biological Engineering Society, Achievement in Innovation Award from Innovate Calgary, Sarwan Sahota Distinguished Scholar Award from TMU, Young Engineer Achievement Award from Engineers Canada, New Pioneers Award in Science and Technology from Skills for Change, and Exemplary Service Award from IEEE Toronto Section. He is a Fellow of the Canadian Academy of Engineering and a registered professional engineer in the Province of Ontario.

For further details, please visit his website
`https://www.ecb.torontomu.ca/people/Krishnan.html`

FOREWORD BY PROF. WILLIS J. TOMPKINS

I have known Raj Rangayyan for more than 30 years. Our research and teaching careers in our respective universities both focused on the acquisition and analysis of signals from the human body. In 1993, I published a textbook called "Biomedical Digital Signal Processing" that I had developed to support the courses that I taught. Subsequently, about a decade later, in 2002, Raj published the first edition of his seminal book, "Biomedical Signal Analysis."

In my book, I had focused mostly on the analysis of a single physiological signal, the electrocardiogram. However, the human body produces a myriad of signals, not just electrical but also thermal, acoustical, pressure, vibratory, and others. In his first edition, Raj summarized time and frequency domain tools to analyze many human biological signals from basic action potentials in myocytes to the diversity of signals produced by the physiological subsystems of the human body.

When I read the first edition, it was clear to me that Raj had produced the most complete work, both in breadth and depth, on the analysis of signals that are generated by the human body. His second edition was greatly expanded, adding new topics and analyses, growing from the first edition's 512 pages to 672 pages.

Now, the third edition, written with the help of coauthor, Sridhar Krishnan, provides revisions of some of the early chapters but also adds substantial new material in the later chapters. At the end of chapters, the book also includes comprehensive sets of study questions, problems, laboratory exercises, and projects to facilitate and enhance learning. This book is an excellent resource for teaching courses on biomedical signal analysis to senior-level and graduate-level engineering students with good background in signals and systems.

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July, 2023

FOREWORD BY PROF. ALAN V. OPPENHEIM

I'm delighted to have this opportunity to express my thoughts about the Third Edition of Biomedical Signal Analysis and more broadly about the field of signal processing. When asked, I was totally unfamiliar with the previous editions of the book and had only a cursory familiarity with biomedical signals and issues related to that specific application of signal processing. My entire academic career as a researcher and teacher, spanning about seven decades, has been primarily focused on the theoretical aspects of signal processing and the applications to speech, radar, communications, and image analysis and processing. Being invited to write a foreword for this edition has been an opportunity for me to delve more deeply into how signal processing has been and can be used for the analysis and processing of biomedical signals and data. More broadly, it also offers me the opportunity to comment on the audience that I see this book as being best matched to and to also express some personal thoughts and comments about the field of signal processing.

Biomedical signal analysis, either formally or informally, has a long and rich history going back centuries and even millennia. Listening to acoustic signals from the heart and lungs and introducing and analyzing echoes from acoustic and higher frequency signals penetrating the body have long been well-established noninvasive diagnostic methodologies. And over many centuries, these techniques have been significantly enhanced by the invention of various transducer and sensor technologies, such as the stethoscope, X-ray and ultrasound imaging, and the MRI. With modern technology, an increasing number of highly sophisticated transducers and sensors are being developed and introduced to generate and capture biomedical signals and data for analysis on-line (that is, in real time) or off-line for screening and diagnostic purposes. As transducer, sensor, and signal processing algorithms advance, there are an increasing number of low-cost sophisticated devices for home and personal use. Overall, the field of biomedical signal analysis has become an increasingly important application area for utilizing sophisticated signal processing methods and tools and for the development of new signal processing methodologies with applications beyond this specific class of signals.

In the preface to the previous editions and this new edition, the authors indicate, as the intended audience, engineering students in their final year of undergraduate studies; specifically, that

> "Electrical Engineering students with a good background in Signals and Systems will be well prepared for the material in this book. A course on Digital Signal Processing or Digital Filters would form a useful link to the material in the present book, but a capable student without this background should be able to gain a basic understanding of the subject matter."

From my perspective, I see great value and potential hazards for some audiences. As the authors point out, for students and practitioners with a strong background in signal processing and who are just becoming involved with this application area, this book provides an excellent high-level introduction to a wide variety of biomedical signals as well as an overview of a wide variety of signal processing methodologies with rich examples of how these might be or are being applied to this class of signals. It does not nor does it claim to present these methodologies in any depth. It assumes that the reader either has the necessary background or is capable of acquiring it. Students with the background of a previous undergraduate course in signals and systems will likely be equipped to understand the signal processing terminology in the earlier chapters of this book. Signal processing concepts such as Wiener filtering, time–frequency analysis, and wavelets are more typically discussed in more advanced courses. Many of the signal processing concepts referred to in this book can easily appear simple and familiar on the surface, but their effective use ultimately depends on a relatively sophisticated understanding of the techniques, the underlying assumptions, and their limitations.

Many of the basic tools of signal processing are developed from a mathematical formulation of the objectives of the processing. While signal processing technology is firmly grounded in mathematical analysis, its effective use in practical environments is an art. An important component of the art of signal processing is in understanding the objectives, the assumptions in the development of the tools, and the tradeoffs involved. There now exist a variety of signal processing toolboxes that are more or less "plug and play," that is, relatively straightforward to apply to a data set. The art is in choosing which to use, how to set the parameters, and how to interpret the results. For example, filtering, as discussed in Chapter 3, is one of the fundamental sets of techniques in signal processing. The most typically used digital filter designs (Butterworth, Chebychev, elliptic IIR filters, data truncation and windowing, Parks–McClellan, and Savitzky–Golay FIR filters) are all "optimum" designs for filtering and data smoothing, but with different optimality criteria and different assumptions about the data and about the objectives of the processing. Each introduces different trade-offs between time-domain and frequency-domain characteristics. Consequently, in utilizing any filter design package, it is essential for the user to understand carefully the assumptions and trade-offs associated with the various filter designs. As I often like to comment:

> *"anything's optimum if you pick the error criterion correctly. And just because it's optimum doesn't mean it's good."*

Another basic set of tools in signal processing is directed at or based on characterizing the frequency content in signals, that is spectral analysis as discussed in Chapter 6 and illustrated in a number of other chapters. There are many available software packages for use in spectral analysis of biomedical signals, but here again, they are developed based on underlying assumptions and objectives. Some level of stationarity in the data is, of course, one of them, and trade-offs and assumptions about the length of the data record and the underlying spectral content is another. Here again, spectral analysis of data has a long history, with many of the standard procedures more or less optimum under different formulations of optimality. For example, there is a significant difference in how one should approach spectral analysis of a data set in attempting to identify a narrowband signal in a data set versus characterizing the spectral content in a broadband signal in the presence of noise.

For data that is nonstationary in the underlying assumptions, adaptive and time–frequency analysis methods are an important part of the signal processing toolset. Many of these are discussed or mentioned in the latter chapters of the book (for example, Chapters 7, 8, and 9), but again, the reader is cautioned to understand carefully the basis for and the underlying assumptions of these methods before applying them from a readily available toolbox to their particular data sets. In a purely theoretical sense, we can choose to characterize a signal in either the time domain or, through the Fourier transform, the frequency domain. While intuitively we can refer to a signal as having "time-varying frequency content," a precise description of what we mean by that is often elusive. Theoretically, you're either in the time domain or in the frequency domain, not wandering somewhere in between. While appropriately many biomedical signals are best characterized through some notion of "time-varying frequency content," considerable care is required in interpreting what is meant by that and which tools are appropriate in a given context.

In summary, I see this book as a wonderful resource for students and practitioners who have a relatively strong signal processing background and who are working or are beginning to work with biomedical signals. I would also emphasize the cautionary note that the effective use of signal processing techniques and toolboxes is an art, and having a solid understanding of these tools is essential for their effective use. Creatively and artfully applying the tools, and perhaps modifying them, require a good understanding of the theory and mathematics behind them.

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PREFACE

From the Second to the Third Edition

The field of biomedical signal analysis has been advancing rapidly over the past few years. More and more techniques are being developed to analyze not only the well-known signals from the previous century, but new types of biomedical signals are being explored, acquired, studied, and analyzed for various novel applications. Courses on biomedical instrumentation and signal analysis are increasingly common and popular elements in engineering curricula.

The previous editions of the book were adopted for study by several students, teachers, and researchers around the world. Keeping in mind the appreciative comments received, we have maintained the first six chapters of the book with minimal change. We have also maintained the style and spirit of the original book.

The minor modifications in the new edition include the following: additional discussions and illustrations related to the neuron, action potential, and photoplethysmography (Chapter 1); the discrete Fourier transform, frequency response, pole–zero plots, and the relationships between various representations of signals, systems, and transforms (Chapter 3); and turning points, zero-crossings, and turns count (Chapter 5). Several equations and figures have been revised and reformatted for improved comprehension. A few sections have been relocated and revised for improved connection to related sections.

The major changes in the Third Edition are present in the last four chapters, which represent thoroughly revised, expanded, updated, and reorganized versions of the last three chapters in the Second Edition. Substantial new material has been added on modeling and analysis of nonstationary and multicomponent signals as well as pattern recognition and diagnostic decision. Detailed discussions have been added on the Kalman filter, dictionary learning, electrophysiological modeling, detection of epileptic seizures, analysis of ventricular fibrillation, and diagnosis of Parkinson's disease. Additional discussions on the strengths and limitations of computer-aided diagnosis are provided at the end of Chapter 10.

The following list describes some of the new topics, techniques, and applications presented in the Third Edition:

- Mathematical and electrophysiological modeling of the heart at the cellular, tissue, and organ levels.
- The Kalman filter and dictionary-learning methods for sophisticated analysis of nonstationary, multicomponent, and multisource signals.
- Detection of ventricular fibrillation and wavelet analysis for studies on cardiopulmonary resuscitation.
- Neural decoding for control of prostheses using the Kalman filter.
- Techniques for adaptive decomposition of multicomponent and multisource signals, including dictionary learning, nonnegative matrix decomposition, and decomposition-based adaptive time–frequency distributions.
- Detection of epileptic seizures using dictionary learning.
- Detection of T-wave alternans in ECG signals.
- Extraction of the fetal ECG from single-channel maternal ECG.
- EEG analysis for brain–computer interfaces.
- Detection of sleep apnea.
- Monitoring Parkinson's disease using multimodal signal analysis.

References appear at the end of each chapter to facilitate chapter-by-chapter access to pdf files through digital libraries. The pdf files include hyperlinks to sections, figures, equations, references, and websites cited for efficient navigation.

In order to control and limit the number of pages in the book, the page size has been increased. This change has facilitated improved formatting and layout of the text and figures. In spite of the addition of substantial new material, the number of pages in the Third Edition is almost the same as that in the Second Edition.

Expanded and improved teaching and learning resources are available at the companion website: `www.wiley.com/go/rangayyan3e`, and also at `https://github.com/srikrishnan1972/Biomedical-Signal-Analysis`

The Intended Audience

As with the previous editions, the Third Edition is directed at engineering students in their final (senior) year of undergraduate studies or in their graduate studies. Electrical Engineering students with a good background in signals and systems will be well prepared for the material in the book. Students in other engineering disciplines, or in computer science, physics, mathematics, or geosciences, should also be able to appreciate the material in the book. A course on digital signal processing or digital filters would form a useful link to the material in the present book, but a capable student without this background should be able to gain a basic understanding of the subject matter. The introductory materials on systems, filters, and transforms provided in Chapter 3 should assist the reader without formal training on the same topics. Practicing engineers, computer scientists, information technologists, medical physicists, and specialists in machine learning, artificial intelligence, and data processing working in diverse areas such as telecommunications, seismic and geophysical applications, biomedical applications, and hospital information systems may find the book useful in their quest to learn advanced techniques for signal analysis. They could draw inspiration from other applications of signal processing or analysis, and satisfy their curiosity regarding computer applications in medicine, digital healthcare, and computer-aided medical diagnosis.

Teaching and Learning Plans

The book starts with an illustrated introduction to biomedical signals in Chapter 1. Chapter 2 continues the introduction, with emphasis on the analysis of multiple channels of correlated signals.

Chapter 3 deals exclusively with filtering of signals for removal of artifacts as an important step before signal analysis. The basic properties of systems and transforms as well as signal processing techniques are reviewed and described where required. The chapter is written as a mix of theory and application so as to facilitate easy comprehension of the basics of signals, systems, and transforms. The emphasis is on the application of filters to particular problems in biomedical signal analysis. A large number of illustrations are included to provide a visual representation of the problem and the effectiveness of the various filtering methods described.

Chapter 4 presents techniques that are particularly useful in the detection of events in biomedical signals. Analysis of waveshape and waveform complexity of events and components of signals is the focus of Chapter 5. Techniques for frequency-domain characterization of biomedical signals and systems are presented in Chapter 6. A number of diverse examples are provided in all of the chapters. Attention is directed to the characteristics of the problems that are encountered when analyzing and interpreting biomedical signals, rather than to any specific diagnostic application with particular signals.

The material in the book up to and including Chapter 6 provides more than adequate material for a one-semester (13-week) course at the senior (fourth-year) engineering level. Our own teaching experience indicates that this material will require about $36 - -40$ hours of lectures. It would be desirable to augment the lectures with about 12 hours of tutorials (problem-solving sessions) and 10 laboratory sessions.

Modeling biomedical signal-generating processes and systems for parametric representation and analysis is the subject of Chapter 7. Chapters 8 and 9 deal with adaptive analysis of nonstationary, multicomponent, and multisource signals. The topics in these chapters are of high mathematical complexity and are not suitable for undergraduate courses. Some sections may be selected and included in a first course on biomedical signal analysis if there is particular interest in these topics. Otherwise, the three chapters could be left for self-study by those in need of the techniques, or included in an advanced course.

Chapter 10 presents the final aspect of biomedical signal analysis, and provides an introduction to pattern classification, diagnostic decision-making, computer-aided diagnosis, and computer-aided healthcare. Although this topic is advanced in nature and could form a graduate-level course on its own, the material is introduced so as to draw the entire exercise of biomedical signal analysis to its concluding stage of diagnostic decision and healthcare. It is recommended that a few sections from this chapter be included even in a first course on biomedical signal analysis so as to give the students a flavor of the end result.

Each chapter includes a number of study questions and problems to facilitate preparation for tests and examinations. A number of laboratory exercises are also provided at the end of each chapter, which could be used to formulate hands-on exercises with real-life signals. Data files related to the problems and exercises at the end of each chapter are available at the site

`https://github.com/srikrishnan1972/Biomedical-Signal-Analysis`

It is strongly recommended that the first one or two laboratory sessions in the course include visits to a local hospital, health sciences center, or clinical laboratory to view and experience procedures related to biomedical signal acquisition and analysis in a practical (clinical) setting. Signals acquired from fellow students and instructors could form interesting and motivating material for laboratory exercises, and may be used to supplement the data files provided. A few workshops by physiologists, neuroscientists, and cardiologists should also be included in the course so as to provide the students with a nonengineering perspective on the subject.

Practical experience with real-life signals is a key element in understanding and appreciating biomedical signal analysis. This aspect could be difficult and frustrating at times, but provides professional satisfaction and educational fun!

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SRIDHAR KRISHNAN

Toronto, Ontario, Canada
November, 2023

Excerpts from the Preface to the Second Edition

The first edition of this book has been received very well around the world. Professors at several universities across North America, Europe, Asia, and other regions of the world are using the book as a textbook. A low-cost paperback edition for selected regions of the world and a Russian edition have been published. I have received several messages and comments from many students, professors, and researchers via mail and at conferences with positive feedback about the book. I am grateful to IEEE and Wiley for publishing and promoting the book and to the many users of the book for their support and feedback.

I have myself used the book to teach my course ENEL 563 Biomedical Signal Analysis at the University of Calgary. In addition to positive responses, I have received suggestions from students and professors on revising the book to provide additional examples and including advanced topics and discussions on recent developments in the book. I also made notes identifying parts of the book that could be improved for clarity, augmented with details for improved comprehension, and expanded with additional examples for better illustrations of application. I have also identified a few new developments, novel applications, and advanced techniques for inclusion in the second edition to make the book more interesting and appealing to a wider readership.

New Material in the Second Edition

In view of the success of the first edition, I have not made any major change in the organization and style of the book. Notwithstanding a tighter format to reduce white space and control the total number of pages, the second edition of the book remains similar to the first edition in terms of organization and style of presentation. New material has been inserted into the same chapters as before, thereby expanding the book. The new topics have been chosen with care not only to fit with the structure and organization of the book but also to provide additional support material and advanced topics that can be assimilated and appreciated in a first course or an advanced study of the subject area.

Some of the substantial and important additions made to the book deal with the following topics:

- analysis of the variation of parameters of the electromyogram with force;
- illustrations of the electroencephalogram with application to sleep analysis and prediction of epileptic seizures;
- details on the theory of linear systems and numerical examples related to convolution;
- details on the z-transform and the Fourier transform along with additional examples of Fourier spectra and spectral analysis of biomedical signals;
- details on linear filters and their characteristics, such as the impulse response, transfer function, and pole–zero diagrams;
- description and demonstration of nonlinear order-statistic filters;

- derivation of the matched filter;
- derivations related to the complex cepstrum;
- details on random processes and their properties;
- wavelets and the wavelet transform with biomedical applications;
- fractal analysis with biomedical applications;
- time–frequency distributions and analysis of nonstationary signals with biomedical applications;
- principal component analysis, independent component analysis, and blind source separation with biomedical applications;
- monitoring of sleep apnea;
- analysis of various types of bioacoustic signals that could bear diagnostic information; and
- methods for pattern analysis and classification with illustrations of application to biomedical signals.

Discussions related to the topics listed above are spread throughout the book with several new references added to assist the reader in further studies. Many more problems and projects have been added at the ends of the chapters.

The first edition of the book (2002) has 516 pages (plus xxxv pages of front matter) with nine chapters, 538 numbered equations (with many more equations not numbered but as parts of procedures), 232 numbered figures (many with multiple subfigures), and 265 references. The second edition (2015) has 672 pages (plus xliii pages of front matter) in a more compact layout than the first edition, with nine chapters, 814 numbered equations (and many more equations not numbered but as parts of procedures), 370 numbered figures (many with multiple subfigures), and 505 references. The discussions on some of the new topics added were kept brief in order to control the size of the book; regardless, the second edition is approximately 50% larger than the first edition in several aspects.

RANGARAJ MANDAYAM RANGAYYAN

Calgary, Alberta, Canada
February, 2015

Excerpts from the Preface to the First Edition: Background and Motivation

The establishment of the clinical electrocardiograph (ECG) by the Dutch physician Willem Einthoven in 1903 marked the beginning of a new era in medical diagnostic techniques, including the entry of electronics into healthcare. Since then, electronics, and subsequently computers, have become integral components of biomedical signal analysis systems, performing a variety of tasks from data acquisition and preprocessing for removal of artifacts to feature extraction and interpretation. Electronic instrumentation and computers have been applied to investigate a host of biological and physiological systems and phenomena, such as the electrical activity of the cardiovascular system, the brain, the neuromuscular system, and the gastric system; pressure variations in the cardiovascular system; sound and vibration signals from the cardiovascular, the musculoskeletal, and the respiratory systems; and magnetic fields of the brain, to name a few.

The primary step in investigations of physiological systems requires the development of appropriate sensors and instrumentation to transduce the phenomenon of interest into a measurable electrical signal. The next step of analysis of the signals, however, is not always an easy task for a physician or life-sciences specialist. The clinically relevant information in the signal is often masked by noise and interference, and the signal features may not be readily comprehensible by the visual or auditory systems of a human observer. Heart sounds, for example, have most of their energy at or below the threshold of auditory perception of most humans; the interference patterns of a surface electromyographic signal are too complex to permit visual analysis. Some repetitious or attention-demanding tasks, such as on-line monitoring of the ECG of a critically ill patient with cardiac rhythm problems, could be uninteresting and tiring for a human observer. Furthermore, the variability present in a given type of signal from one subject to another, and the interobserver variability inherent in subjective analysis performed by physicians or analysts make consistent understanding or evaluation of any phenomenon difficult, if not impossible. These factors created the need not only for improved instrumentation, but also for the development of methods for objective analysis via signal processing algorithms implemented in electronic hardware or on computers.

Processing of biomedical signals, until a few years ago, was mainly directed toward filtering for removal of noise and power-line interference; spectral analysis to understand the frequency characteristics of signals; and modeling for feature representation and parameterization. Recent trends have been toward quantitative or objective analysis of physiological systems and phenomena via signal analysis. The field of biomedical signal analysis has advanced to the stage of practical application of signal processing and pattern analysis techniques for efficient and improved noninvasive diagnosis, on-line monitoring of critically ill patients, and rehabilitation and sensory aids for the handicapped. Techniques developed by engineers are gaining wider acceptance by practicing clinicians, and the role of engineering in diagnosis and treatment is gaining much-deserved respect.

The major strength in the application of computers in biomedical signal analysis lies in the potential use of signal processing and modeling techniques for quantitative or objective analysis. Analysis of signals by human observers is almost always accompanied by perceptual limitations, interpersonal variations, errors caused by fatigue, errors caused by the very low rate of incidence of a certain sign of abnormality, environmental distractions, and so on. The interpretation of a signal by an expert bears the weight of the experience and expertise of the analyst; however, such analysis is almost always subjective. Computer analysis of biomedical signals, if performed with the appropriate logic, has the potential to add objective strength to the interpretation of the expert. It thus becomes possible to improve the diagnostic confidence or accuracy of even an expert with many years of experience. This approach to improved healthcare could be labeled as *computer-aided diagnosis*.

Developing an algorithm for biomedical signal analysis, however, is not an easy task; quite often, it might not even be a straightforward process. The engineer or computer analyst is often bewildered by the variability of features in biomedical signals and systems, which is far higher than that encountered in physical systems or observations. Benign diseases often mimic the features of malignant diseases; malignancies may exhibit a characteristic pattern, which, however, is not always guaranteed to appear. Handling all of the possibilities and degrees of freedom in a biomedical system is a major challenge in most applications. Techniques proven to work well with a certain system or set of signals may not work in another seemingly similar situation.

The Problem-solving Approach

The approach I have taken in presenting material in this book is primarily that of development of algorithms for problem solving. Engineers are often said to be (with admiration, I believe) problem solvers. However, the development of a problem statement and gaining of a good understanding of the problem could require a significant amount of preparatory work. I have selected a logical series of problems, from the many case studies I have encountered in my research work, for presentation in the book. Each chapter deals with a certain type of a problem with biomedical signals. Each chapter begins with a statement of the problem, followed immediately with a few illustrations of the problem with real-life case studies and the associated signals. Signal processing, modeling, or analysis techniques are then presented, starting with relatively simple "textbook" methods, followed by more sophisticated research approaches directed at the specific problem. Each chapter concludes with one or more applications to significant and practical problems. The book is illustrated copiously with real-life biomedical signals and their derivatives.

The methods presented in the book are at a fairly high level of technical sophistication. A good background in signal and system analysis as well as probability, random variables, and stochastic processes is required in order to follow the procedures and analysis. Familiarity with systems theory and transforms such as the Laplace and Fourier, the latter in both continuous and discrete versions, will be assumed. We will not be getting into details of the transducers and instrumentation techniques essential for biomedical signal acquisition; instead, we will be studying the problems present in the signals after they have been acquired, concentrating on how to solve the problems. Concurrent or prior study of the physiological phenomena associated with the signals of specific interest, with a clinical textbook, is strongly recommended.

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September, 2001

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Acknowledgments: Third Edition

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