

Biomedical Informatics

Edward H. Shortliffe • James J. Cimino

Editors

Michael F. Chiang

Co-Editor

Biomedical Informatics

Computer Applications in Health Care
and Biomedicine

5th Edition

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Editors

Edward H. Shortliffe
Biomedical Informatics
Columbia University
New York, NY, USA

James J. Cimino
Informatics Institute
University of Alabama at
Birmingham
Birmingham, AL, USA

Co-Editor

Michael F. Chiang
National Eye Institute
National Institutes of Health
Bethesda, MD, USA

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This volume is dedicated to AMIA, the principal professional association for the editors. Born as the American Medical Informatics Association in 1990, AMIA is now preferentially known simply by its acronym and has grown to include some 5500 members who are dedicated to all aspects of biomedical informatics. AMIA and this textbook have evolved in parallel for four decades, and we thank the organization and its members for all they have done for the field and for health care and biomedicine. May both AMIA and this volume evolve and prosper in parallel for years to come.

Foreword

Health and biomedicine are in the midst of revolutionary change. Health care, mental health, and public health are converging as discovery science reveals these traditional “silos” share biologic pathways and collaborative management demonstrates better outcomes. Health care reimbursement is increasingly framed in terms of paying for outcomes achieved through value-based purchasing and population health management. Individuals are more engaged in their health and wellness decisions, using personal biomedical monitoring devices and testing services and engaging in citizen science. Systems biology is revealing the complex interactions among a person’s genome, microbiome, immune system, neurologic system, social factors, and environment. Novel biomarkers and therapeutics exploit these interactions.

These advances are fueled by digitization and generation of data at an unprecedented scale. The volume of health care data has multiplied 8 times since 2013 and is projected to grow at a compound annual rate of 36% between 2018 and 2025¹. The rate of growth of biomedical research data is comparable². When you consider recent estimates that socioeconomic, health behaviors, and environment—factors outside of the domain of health care and biomedicine—contribute as much as 80% to health outcomes³, the variety and scale of health-related data are breathtaking.

Biomedical informatics provides the scientific basis for making sense of these data—methods and tools to structure, mine, visualize, and reason with data and information. Biomedical informatics also provides the scientific basis for incorporating data and information into effective workflows—techniques to link people, process, and technology into systems; methods to evaluate systems and technology components; and methods to facilitate system-level change.

Biomedical informatics grew out of efforts to understand biomedical reasoning⁴, such as artificial intelligence; to develop medical systems, such as multiphasic screening⁵; and to write computer programs to solve clinical problems, such as diagnosis and treatment of acid-base disorders⁶. By the late 1970s, “medical informatics” was used interchangeably with “computer applications in medical care”. As computer programs were written for various allied health disciplines, nursing informatics, dental informatics, and public health informatics emerged. The 1980s saw the emergence of computational biology for applications such as scientific visualization and bioinformatics to support tasks such as DNA sequence analysis.

Biomedical Informatics: Computer Applications in Health Care and Biomedicine provided the first comprehensive guide to the field with its first edition in 1990. That edition and the subsequent three have served as the core syllabus for introductory courses in informatics and as a reference source for those seeking advanced training or working in the field. The fifth edition carries on the tradition with new topics, comprehensive glossary, reading lists, and citations.

I encourage people who are considering formal education in biomedical informatics to use this book to sample the field. The book's framework provides a guide for educators from junior high to graduate school as they design introductory courses in biomedical informatics. It is the basic text for students entering the field.

With digitization and data driving change across the health and biomedicine ecosystem, everyone in the ecosystem will benefit from reading *Biomedical Informatics* and using it as a handbook to guide their work. The following is a sample of questions readers can turn to the book to explore:

- **Practicing health professionals**—How do I recognize an information need? How do I quickly scan and filter information to answer a question? How do I sense the fitness of the information to answer my question? How do I configure my electronic health record to focus my attention and save time? How do I recognize when to override decision support? How do I analyze data from my practice to identify learning and improvement opportunities? How do I engage with patients outside of face-to-face encounters?
- **Quality improvement teams**—How might we detect if the outcome we are trying to improve is changing in the desired direction? Are data available in our operational systems that are fit for that purpose? What combination of pattern detection algorithm, workflow process, decision support, and training might work together to change the outcome? How can we adapt operational processes and systems to test the change and to scale if it proves effective?
- **Discovery science teams**—How do data about biological systems differ from data about physical systems? How do we decide when to use integrative analytic approaches and when to use reductionist approaches? How much context do we need to keep about data we create and how do we structure the metadata? How do we optimize compute and storage platforms? How might we leverage electronic health record-derived phenotype to generate hypotheses?
- **Artificial intelligence researchers or health “app” developers**—What health outcome am I trying to change? Do I need a detection, prediction, or classification algorithm? What sources of data might be fit for that purpose? What type of intervention might change the outcome? Who would be the best target for the intervention? What is the best place in their workflow to incorporate the intervention?
- **Health system leaders**—How do we restructure team roles and electronic health record workflows to reduce clinician burnout and improve care quality? How do we take advantage of technology-enabled self-management and virtual visits to increase adherence and close gaps in care? How do we continuously evaluate evidence and implement or de-implement guidelines and decision support across our system? How do we leverage technology to deploy context-sensitive just-in-time learning across our system?
- **Health policy makers**—How might we enhance health information privacy and security and reduce barriers to using data for population

health, health care quality improvement, and discovery? To what degree is de-identification a safeguard? What combination of legislative mandate, executive action, and industry-driven innovation will accelerate health data interoperability and business agility? How might federal and state governments enable communities to access small area data to inform their collective action to improve community health and well-being?

You have taken the first step in exploring these frontiers by picking up this book. Enjoy!

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William W. Stead, MD, FACMI

Chief Strategy Officer, Vanderbilt University Medical Center,
McKesson Foundation Professor, Department of Biomedical
Informatics, Professor, Department of Medicine, Vanderbilt University
Nashville, TN, USA
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Preface to the Fifth Edition

The world of biomedical research and health care has changed remarkably in the 30 years since the first edition of this book was published. So too has the world of computing and communications and thus the underlying scientific issues that sit at the intersections among biomedical science, patient care, public health, and information technology. It is no longer necessary to argue that it has become impossible to practice modern medicine, or to conduct modern biological research, without information technologies. Since the initiation of the Human Genome Project three decades ago, life scientists have been generating data at a rate that defies traditional methods for information management and data analysis.

Health professionals also are constantly reminded that a large percentage of their activities relates to information management—for example, obtaining and recording information about patients, consulting colleagues, reading and assessing the scientific literature, planning diagnostic procedures, devising strategies for patient care, interpreting results of laboratory and radiologic studies, or conducting case-based and population-based research. Artificial intelligence, “big data,” and data science are having unprecedented impact on the world, with the biomedical field a particularly active and visible component of such activity.

It is complexity and uncertainty, plus society’s overriding concern for patient well-being, and the resulting need for optimal decision making, that set medicine and health apart from many other information-intensive fields. Our desire to provide the best possible health and health care for our society gives a special significance to the effective organization and management of the huge bodies of data with which health professionals and biomedical researchers must deal. It also suggests the need for specialized approaches and for skilled scientists who are knowledgeable about human biology, clinical care, information technologies, and the scientific issues that drive the effective use of such technologies in the biomedical context.

Information Management in Biomedicine

The clinical and research influence of biomedical-computing systems is remarkably broad. Clinical information systems, which provide communication and information-management functions, are now installed in essentially all health care institutions. Physicians can search entire drug indexes in a few seconds, using the information provided by a computer program to anticipate harmful side effects or drug interactions. Electrocardiograms (ECGs) are typically analyzed initially by computer programs, and similar techniques are being applied for interpretation of pulmonary-function tests and a variety of laboratory and radiologic abnormalities. Devices with embedded processors routinely monitor patients and provide warnings in critical-care settings, such as the

intensive-care unit (ICU) or the operating room. Both biomedical researchers and clinicians regularly use computer programs to search the medical literature, and modern clinical research would be severely hampered without computer-based data-storage techniques and statistical analysis systems. Machine learning methods and artificial intelligence are generating remarkable results in medical settings. These have attracted attention not only from the news media, patients, and clinicians but also from health system leaders and from major corporations and startup companies that are offering new approaches to patient care and health information management. Advanced decision-support tools also are emerging from research laboratories, are being integrated with patient-care systems, and are beginning to have a profound effect on the way medicine is practiced.

Despite this extensive use of computers in health care settings and biomedical research, and a resulting expansion of interest in learning more about biomedical computing, many life scientists, health-science students, and professionals have found it difficult to obtain a comprehensive and rigorous, but nontechnical, overview of the field. Both practitioners and basic scientists are recognizing that thorough preparation for their professional futures requires that they gain an understanding of the state of the art in biomedical computing, of the current and future capabilities *and* limitations of the technology, and of the way in which such developments fit within the scientific, social, and financial context of biomedicine and our health care system. In turn, the future of the biomedical-computing field will be largely determined by how well health professionals and biomedical scientists are prepared to guide and to capitalize upon the discipline's development.

This book is intended to meet this growing need for such well-equipped professionals. The first edition appeared in 1990 (published by Addison-Wesley) and was used extensively in courses on medical informatics throughout the world (in some cases with translations to other languages). It was updated with a second edition (published by Springer) in 2000, responding to the remarkable changes that occurred during the 1990s, most notably the Human Genome Project and the introduction of the World Wide Web with its impact on adoption and acceptance of the Internet. The third edition (again published by Springer) appeared in 2006, reflecting the ongoing rapid evolution of both technology and health- and biomedically related applications, plus the emerging government recognition of the key role that health information technology would need to play in promoting quality, safety, and efficiency in patient care. With that edition the title of the book was changed from *Medical Informatics* to *Biomedical Informatics*, reflecting (as is discussed in ► Chap. 1) both the increasing breadth of the basic discipline and the evolving new name for academic units, societies, research programs, and publications in the field. The fourth edition (published by Springer in 2014) followed the same conceptual framework for learning about the science that underlies applications of computing and communications technology in biomedicine and health care, for understanding the state of the art in computer applications in clinical care and biology, for critiquing existing systems, and for anticipating future directions that the field may take.

In many respects, the fourth edition was very different from its predecessors, however. Most importantly, it reflected the remarkable changes in computing and communications that continued to occur, most notably in communications, networking, and health information technology policy, and the exploding interest in the role that information technology must play in systems integration and the melding of genomics with innovations in clinical practice and treatment. Several new chapters were introduced and most of the remaining ones underwent extensive revision.

In this fifth edition, we have found that two previous single-chapter topics have expanded to warrant two complementary chapters, specifically Cognitive Science (split into *Cognitive Informatics* and *Human-Computer Interaction, Usability, and Workflow*) and Consumer Health Informatics and Personal Health Records (split into *Personal Health Informatics* and *mHealth and Applications*). There is a new chapter on precision medicine, which has emerged in the past 6 years as a unique area of special interest. Those readers who are familiar with the first four editions will find that the organization and philosophy are essentially unchanged (although bioinformatics, as a set of methodologies, is now considered a “recurrent theme” rather than an “application”), but the content is either new or extensively updated.¹

This book differs from other introductions to the field in its broad coverage and in its emphasis on the field’s conceptual underpinnings rather than on technical details. Our book presumes no health- or computer-science background, but it does assume that you are interested in a comprehensive domain summary that stresses the underlying concepts and that introduces technical details only to the extent that they are necessary to meet the principal goal. Recent specialized texts are available to cover the technical underpinnings of many topics in this book; many are cited as suggested readings throughout the book, or are cited in the text for those who wish to pursue a more technical exposure to a topic.

Overview and Guide to Use of This Book

This book is written as a text so that it can be used in formal courses, but we have adopted a broad view of the population for whom it is intended. Thus, it may be used not only by students of medicine and of the other health professions but also as an introductory text by future biomedical informatics professionals, as well as for self-study and for reference by practitioners, including those who are pursuing formal board certification in clinical informatics (as is discussed in more detail later in this

¹ As with the first four editions, this book has tended to draw both its examples and its contributors from North America. There is excellent work in other parts of the world as well, although variations in health care systems, and especially financing, do tend to change the way in which systems evolve from one country to the next. The basic concepts are identical, however, so the book is intended to be useful in educational programs in other parts of the world as well.

“Preface”). The book is probably too detailed for use in a 2- or 3-day continuing-education course, although it could be introduced as a reference for further independent study.

Our principal goal in writing this text is to teach *concepts* in biomedical informatics—the study of biomedical information and its use in decision making—and to illustrate them in the context of descriptions of representative systems that are in use today or that taught us lessons in the past. As you will see, biomedical informatics is more than the study of computers in biomedicine, and we have organized the book to emphasize that point. ► Chapter 1 first sets the stage for the rest of the book by providing a glimpse of the future, defining important terms and concepts, describing the content of the field, explaining the connections between biomedical informatics and related disciplines, and discussing the forces that have influenced research in biomedical informatics and its integration into clinical practice and biological research.

Broad issues regarding the nature of data, information, and knowledge pervade all areas of application, as do concepts related to optimal decision making. ► Chapters 2 and 3 focus on these topics but mention computers only in passing. They serve as the foundation for all that follows. ► Chapters 4 and 5 on cognitive science issues enhance the discussions in ► Chaps. 2 and 3, pointing out that decision making and behavior are deeply rooted in the ways in which information is processed by the human mind. Key concepts underlying system design, human-computer interaction, patient safety, educational technology, and decision making are introduced in these chapters.

► Chapter 6 introduces the central notions of software engineering that are important for understanding the applications described later. We have dropped a chapter from previous editions that dealt broadly with system architectures, networking, and computer-system design. This topic is more about engineering than informatics, it changes rapidly, and there are excellent books on this subject to which students can turn if they need more information on these topics.

► Chapter 7 summarizes the issues of standards development, focusing in particular on data exchange and issues related to sharing of clinical data. This important and rapidly evolving topic warrants inclusion given the evolution of the health information exchange, institutional system integration challenges, federal government directives, and the increasingly central role of standards in enabling clinical systems to have their desired influence on health care practices.

► Chapter 8 addresses a topic of increasing practical relevance in both the clinical and biological worlds: natural language understanding and the processing of biomedical texts. The importance of these methods is clear when one considers the amount of information contained in free-text notes or reports (either dictated and transcribed or increasingly created using speech-understanding systems) or in the published biomedical literature. Even with efforts to encourage structured data entry in clinical systems, there will likely always be an important role for techniques that allow computer systems to extract meaning from natural language documents.

► Chapter 9 recognizes that bioinformatics is not just an application area but rather a fundamental area of study. The chapter introduces

many of the concepts and analytical tools that underlie modern computational approaches to the management of human biological data, especially in areas such as genomics and proteomics. Applications of bioinformatics related to human health and disease later appear in a chapter on “Translational Bioinformatics” (► Chap. 26).

► Chapter 10 is a comprehensive introduction to the conceptual underpinnings of biomedical and clinical image capture, analysis, interpretation, and use. This overview of the basic issues and imaging modalities serves as background for ► Chap. 22, which deals with imaging applications issues, highlighted in the world of radiological imaging and image management (e.g., in picture archiving and communication systems).

► Chapter 11 considers personal health informatics not as a set of applications (which are covered in ► Chap. 19), but as introductory concepts that relate to this topic, such as notions of the digital self and the digital divide, patient-generated health data, and how a focus on the patient (or on healthy individuals) affects both the person and the field of biomedical informatics.

► Chapter 12 addresses the key legal and ethical issues that have arisen when health information systems are considered. Then, in ► Chap. 13, the challenges associated with technology assessment and with the evaluation of clinical information systems are introduced.

► Chapters 14–28 (which include two new chapters in this edition, including one on mHealth and another on precision medicine) survey many of the key biomedical areas in which informatics methods are being used. Each chapter explains the conceptual and organizational issues in building that type of system, reviews the pertinent history, and examines the barriers to successful implementations.

► Chapter 29 reprises and updates a chapter that was new in the fourth edition, providing a summary of the rapidly evolving policy issues related to health information technology. Although the emphasis is on US government policy, there is some discussion of issues that clearly generalize both to states (in the USA) and to other countries.

The book concludes in ► Chap. 30 with a look to the future—a vision of how informatics concepts, computers, and advanced communication devices one day may pervade every aspect of biomedical research and clinical practice. Rather than offering a single point of view developed by a group of forward thinkers, as was offered in the fourth edition, we have invited seven prominent and innovative thinkers to contribute their own views. We integrate these seven future perspectives (representing clinical medicine, nursing, health policy, translational bioinformatics, academic informatics, the information technology industry, and the federal government) into a chapter where the editors have synthesized the seven perspectives after building on how an analysis of the past helps to inform the future of this dynamic field.

The Study of Computer Applications in Biomedicine

The actual and potential uses of computers in health care and biomedicine form a remarkably broad and complex topic. However, just as you do not need to understand how a telephone or an ATM machine works

to make good use of it and to tell when it is functioning poorly, we believe that technical biomedical-computing skills are not needed by health workers and life scientists who wish simply to become effective users of evolving information technologies. On the other hand, such technical skills are of course necessary for individuals with career commitment to developing information systems for biomedical and health environments. Thus, this book will neither teach you to be a programmer nor show you how to fix a broken computer (although it might motivate you to learn how to do both). It also will not tell you about every important biomedical-computing system or application; we shall use an extensive bibliography included with each chapter to direct you to a wealth of literature where review articles and individual project reports can be found. We describe specific systems only as examples that can provide you with an understanding of the conceptual and organizational issues to be addressed in building systems for such uses. Examples also help to reveal the remaining barriers to successful implementations. Some of the application systems described in the book are well established, even in the commercial marketplace. Others are just beginning to be used broadly in biomedical settings. Several are still largely confined to the research laboratory.

Because we wish to emphasize the concepts underlying this field, we generally limit the discussion of technical implementation details. The computer-science issues can be learned from other courses and other textbooks. One exception, however, is our emphasis on the details of decision science as they relate to biomedical problem solving (► Chaps. 3 and 24). These topics generally are not presented in computer-science courses, yet they play a central role in the intelligent use of biomedical data and knowledge. Sections on medical decision making and computer-assisted decision support accordingly include more technical detail than you will find in other chapters.

All chapters include an annotated list of “Suggested Readings” to which you can turn if you have a particular interest in a topic, and there is a comprehensive set of references with each chapter. We use **boldface** print to indicate the key terms of each chapter; the definitions of these terms are included in the “Glossary” at the end of the book. Because many of the issues in biomedical informatics are conceptual, we have included “Questions for Discussion” at the end of each chapter. You will quickly discover that most of these questions do not have “right” answers. They are intended to illuminate key issues in the field and to motivate you to examine additional readings and new areas of research.

It is inherently limiting to learn about computer applications solely by reading about them. We accordingly encourage you to complement your studies by seeing real systems in use—ideally by using them yourself. Your understanding of system limitations and of what *you* would do to improve a biomedical-computing system will be greatly enhanced if you have had personal experience with representative applications. Be aggressive in seeking opportunities to observe and use working systems.

In a field that is changing as rapidly as biomedical informatics is, it is difficult ever to feel that you have knowledge that is completely current.

However, the conceptual basis for study changes much more slowly than do the detailed technological issues. Thus, the lessons you learn from this volume will provide you with a foundation on which you can continue to build in the years ahead.

The Need for a Course in Biomedical Informatics

A suggestion that new courses are needed in the curricula for students of the health professions is generally not met with enthusiasm. If anything, educators and students have been clamoring for *reduced* lecture time, for more emphasis on small group sessions, and for more free time for problem solving and reflection. Yet, in recent decades, many studies and reports have specifically identified biomedical informatics, including computer applications, as an area in which new educational opportunities need to be developed so that physicians and other health professionals will be better prepared for clinical practice. As early as 1984, the Association of American Medical Colleges (AAMC) recommended the formation of new academic units in biomedical informatics in our medical schools, and subsequent studies and reports have continued to stress the importance of the field and the need for its inclusion in the educational environments of health professionals.

The reason for this strong recommendation is clear: *The practice of medicine is inextricably entwined with the management of information.* In the past, practitioners handled medical information through resources such as the nearest hospital or medical-school library; personal collections of books, journals, and reprints; files of patient records; consultation with colleagues; manual office bookkeeping; and (all-too-often flawed) memorization. Although these techniques continue to be variably valuable, information technology is offering new methods for finding, filing, and sorting information: online bibliographic retrieval systems, including full-text publications; personal computers, laptops, tablets, and smart phones, with database software to maintain personal information and commonly used references; office-practice and clinical information systems and EHRs to capture, communicate, and preserve key elements of the health record; information retrieval and consultation systems to provide assistance when an answer to a question is needed rapidly; practice-management systems to integrate billing and receivable functions with other aspects of office or clinic organization; and other online information resources that help to reduce the pressure to memorize in a field that defies total mastery of all but its narrowest aspects. With such a pervasive and inevitable role for computers in clinical practice, and with a growing failure of traditional techniques to deal with the rapidly increasing information-management needs of practitioners, it has become obvious to many people that an essential topic has emerged for study in schools and clinical training programs (such as residencies) that train medical and other health professionals.

What is less clear is how the subject should be taught in medical schools or other health professional degree programs, and to what extent it should be left for postgraduate education. We believe that top-

ics in biomedical informatics are best taught and learned in the context of health-science training, which allows concepts from both the health sciences and informatics science to be integrated. Biomedical-computing novices are likely to have only limited opportunities for intensive study of the material once their health-professional training has been completed, although elective opportunities for informatics rotations are now offered to residents in many academic medical centers.

The format of biomedical informatics education has evolved as faculty members have been hired to carry out informatics research and to develop courses at more health-science schools, and as the emphasis on lectures as the primary teaching method continues to diminish. Computers will be used increasingly as teaching tools and as devices for communication, problem solving, and data sharing among students and faculty. Indeed, the recent COVID-19 pandemic has moved many traditional medical teaching experiences from the classroom to online teaching environments using video conferencing and on-demand access to course materials. Such experiences do not teach informatics (unless that is the topic of the course), but they have rapidly engaged both faculty and students in technology-intensive teaching and learning experiences. The acceptance of computing, and dependence upon it, has already influenced faculty, trainees, and curriculum committees. This book is designed to be used in a traditional introductory course, whether taught online or in a classroom, although the “Questions for Discussion” also could be used to focus conversation in small seminars and working groups. Integration of biomedical informatics topics into clinical experiences has also become more common. The goal is increasingly to provide instruction in biomedical informatics whenever this field is most relevant to the topic the student is studying. This aim requires educational opportunities throughout the years of formal training, supplemented by continuing-education programs after graduation.

The goal of integrating biomedicine and biomedical informatics is to provide a mechanism for increasing the sophistication of health professionals, so that they know and understand the available resources. They also should be familiar with biomedical computing’s successes and failures, its research frontiers, and its limitations, so that they can avoid repeating the mistakes of the past. Study of biomedical informatics also should improve their skills in information management and problem solving. With a suitable integration of hands-on computer experience, computer-mediated learning, courses in clinical problem solving, and study of the material in this volume, health-science students will be well prepared to make effective use of computational tools and information management in health care delivery.

The Need for Specialists in Biomedical Informatics

As mentioned, this book also is intended to be used as an introductory text in programs of study for people who intend to make their professional careers in biomedical informatics. If we have persuaded you that a course in biomedical informatics is needed, then the requirement for

trained faculty to teach the courses will be obvious. Some people might argue, however, that a course on this subject could be taught by a computer scientist who had an interest in biomedical computing, or by a physician or biologist who had taken a few computing courses. Indeed, in the past, most teaching—and research—has been undertaken by faculty trained primarily in one of the fields and later drawn to the other. Today, however, schools have come to realize the need for professionals trained specifically at the interfaces among biomedicine, biomedical informatics, and related disciplines such as computer science, statistics, cognitive science, health economics, and medical ethics.

This book outlines a first course for students training for careers in the biomedical informatics field. We specifically address the need for an educational experience in which computing and information-science concepts are synthesized with biomedical issues regarding research, training, and clinical practice. It is the *integration* of the related disciplines that originally was lacking in the educational opportunities available to students with career interests in biomedical informatics. Schools are establishing such courses and training programs in growing numbers, but their efforts have been constrained by a lack of faculty who have a broad familiarity with the field and who can develop curricula for students of the health professions as well as of informatics itself.

The increasing introduction of computing techniques into biomedical environments requires that well-trained individuals be available not only to teach students but also to design, develop, select, and manage the biomedical-computing systems of tomorrow. There is a wide range of context-dependent computing issues that people can appreciate only by working on problems defined by the health care setting and its constraints. The field's development has been hampered because there are relatively few trained personnel to design research programs, to carry out the experimental and developmental activities, and to provide academic leadership in biomedical informatics. A frequently cited problem is the difficulty a health professional (or a biologist) and a technically trained computer scientist experience when they try to communicate with one another. The vocabularies of the two fields are complex and have little overlap, and there is a process of acculturation to biomedicine that is difficult for computer scientists to appreciate through distant observation. Thus, interdisciplinary research and development projects are more likely to be successful when they are led by people who can effectively bridge the biomedical and computing fields. Such professionals often can facilitate sensitive communication among program personnel whose backgrounds and training differ substantially.

Hospitals and health systems have begun to learn that they need such individuals, especially with the increasing implementation of, and dependence upon, EHRs and related clinical systems. The creation of a *Chief Medical Information Officer* (CMIO) has now become a common innovation. As the concept became popular, however, questions arose about how to identify and evaluate candidates for such key institutional roles. The need for some kind of suitable certification process became clear—one that would require individuals to demonstrate both formal training and the broad skills and knowledge that were required. Thus,

the American Medical Informatics Association (AMIA) and its members began to develop plans for a formal certification program. For physicians, the most meaningful approach was to create a formal medical subspecialty in clinical informatics. Working with the American Board of Preventive Medicine and the parent organization, the American Board of Medical Specialties (ABMS), AMIA helped to obtain approval for a subspecialty board that would allow medical specialists, with board certification in any ABMS specialty (such as pediatrics, internal medicine, radiology, pathology, preventive medicine) to pursue subspecialty board certification in clinical informatics. This proposal was ultimately approved by the ABMS in 2011, and the board examination was first administered in 2013². After a period during which currently active clinical informatics physician experts could sit for their clinical informatics boards, board eligibility now requires a formal fellowship in clinical informatics. This is similar to the fellowship requirement for other subspecialties such as cardiology, nephrology, and the like. Many health care institutions now offer formal clinical informatics fellowships for physicians who have completed a residency in one of the almost 30 ABMS specialties. These individuals are now often turning to this volume as a resource to help them to prepare for their board examinations.

It is exciting to be working in a field that is maturing and that is having a beneficial effect on society. There is ample opportunity remaining for innovation as new technologies evolve and fundamental computing problems succumb to the creativity and hard work of our colleagues. In light of the increasing sophistication and specialization required in computer science in general, it is hardly surprising that a new discipline should arise at that field's interface with biomedicine. This book is dedicated to clarifying the definition and to nurturing the effectiveness of that discipline: biomedical informatics.

Edward H. Shortliffe

New York, NY, USA

James J. Cimino

Birmingham, AL, USA

Michael F. Chiang

Bethesda, MD, USA

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2 AMIA is currently developing a Health Informatics Certification program (AHIC) for individuals who seek professional certification in health-related informatics but are not physicians or are otherwise not eligible to take the ABMS board certification exam. ► <https://www.amia.org/ahic> (Accessed June 10, 2020).

Acknowledgments

In the 1980s, when I was based at Stanford University, I conferred with colleagues Larry Fagan and Gio Wiederhold, and we decided to compile the first comprehensive textbook on what was then called medical informatics. As it turned out, none of us predicted the enormity of the task we were about to undertake. Our challenge was to create a multiauthored textbook that captured the collective expertise of leaders in the field yet was cohesive in content and style. The concept for the book was first developed in 1982. We had begun to teach a course on computer applications in health care at Stanford's School of Medicine and had quickly determined that there was no comprehensive introductory text on the subject. Despite several published collections of research descriptions and subject reviews, none had been developed to meet the needs of a rigorous introductory course. The thought of writing a textbook was daunting due to the diversity of topics. None of us felt that he was sufficiently expert in the full range of important subjects for us to write the book ourselves. Yet we wanted to avoid putting together a collection of disconnected chapters containing assorted subject reviews. Thus, we decided to solicit contributions from leaders in the pertinent fields but to provide organizational guidelines in advance for each chapter. We also urged contributors to avoid writing subject reviews but, instead, to focus on the key conceptual topics in their field and to pick a handful of examples to illustrate their didactic points.

As the draft chapters began to come in, we realized that major editing would be required if we were to achieve our goals of cohesiveness and a uniform orientation across all the chapters. We were thus delighted when, in 1987, Leslie Perreault, a graduate of our informatics training program, assumed responsibility for reworking the individual chapters to make an integral whole and for bringing the project to completion. The final product, published in 1990, was the result of many compromises, heavy editing, detailed rewriting, and numerous iterations. We were gratified by the positive response to the book when it finally appeared, and especially by the students of biomedical informatics who have often come to us at scientific meetings and told us about their appreciation of the book.

As the 1990s progressed, however, we began to realize that, despite our emphasis on basic concepts in the field (rather than a survey of existing systems), the volume was beginning to show its age. A great deal had changed since the initial chapters were written, and it became clear that a new edition would be required. The original editors discussed the project and decided that we should redesign the book, solicit updated chapters, and publish a new edition. Leslie Perreault by this time was a busy Director at First Consulting Group in New York City and would not have as much time to devote to the project as she had when we did the first edition. With trepidation, in light of our knowledge of the work that would be involved, we embarked on the new project.

As before, the chapter authors did a marvelous job, trying to meet our deadlines, putting up with editing changes that were designed to

bring a uniform style to the book, and contributing excellent chapters that nicely reflected the changes in the field during the preceding decade.

No sooner had the second edition appeared in print in 2000 than we started to get inquiries about when the next update would appear. We began to realize that the maintenance of a textbook in a field such as biomedical informatics was nearly a constant, ongoing process. By this time I had moved to Columbia University and the initial group of editors had largely disbanded to take on other responsibilities, with Leslie Perreault no longer available. Accordingly, as plans for a third edition began to take shape, my Columbia colleague Jim Cimino joined me as the new associate editor, whereas Drs. Fagan, Wiederhold, and Perreault continued to be involved as chapter authors. Once again the authors did their best to try to meet our deadlines as the third edition took shape. This time we added several chapters, attempting to cover additional key topics that readers and authors had identified as being necessary enhancements to the earlier editions. We were once again extremely appreciative of all the authors' commitment and for the excellence of their work on behalf of the book and the field.

Predictably, it was only a short time after the publication of the third edition in 2006 that we began to get queries about a fourth edition. We resisted for a year or two, but it became clear that the third edition was becoming rapidly stale in some key areas and that there were new topics that were not in the book and needed to be added. With that in mind we, in consultation with Grant Weston from Springer's offices in London, agreed to embark on a fourth edition. Progress was slowed by my professional moves (to Phoenix, Arizona, then Houston, Texas, and then back to New York) with a very busy 3-year stint as President and CEO of the American Medical Informatics Association. Similarly, Jim Cimino left Columbia to assume new responsibilities at the NIH Clinical Center in Bethesda, MD. With several new chapters in mind, and the need to change authors of some of the existing chapters due to retirements (this too will happen, even in a young field like informatics), we began working on the fourth edition, finally completing the effort with publication in early 2014.

Now, seven years later, we are completing the fifth edition of the volume. It was not long after the publication of the fourth edition that we began to get requests for a new edition that would include many of the new and emerging topics that had not made it into the 2014 publication. With the introduction of new chapters, major revisions to previous chapters, and some reordering of authors or introduction of new ones, we have attempted to assure that this new edition will fill the necessary gaps and engage our readers with its currency and relevance. As Jim Cimino (now directing the Informatics Institute at the University of Alabama in Birmingham) and I considered the development of this edition, we realized that we were not getting any younger and it would be wise to craft a succession plan so that others could handle the inevitable requests for a sixth and subsequent editions. We were delighted when Michael Chiang agreed to join us as an associate editor, coauthoring three chapters and becoming fully involved in the book's philosophy and the editing tasks involved. Michael was a postdoctoral informatics

trainee at Columbia when we were both there on the faculty. A well-known pediatric ophthalmologist, he is now balancing his clinical career with an active set of research and academic activities in biomedical informatics. We believe that Michael will be a perfect person to carry the book into the future as Jim and I (both of whom view the book as a significant component of our professional life's work) phase out our own involvement after this edition. I should add that, in mid-2020, Michael was named director of the National Eye Institute at NIH, which offers further evidence of his accomplishments as a ophthalmologist, researcher, and informatician.

For this edition we owe particular gratitude to Elektra McDermott, our developmental editor, whose rigorous attention to detail has been crucial given the size and the complexity of the undertaking. At Springer we have been delighted to work once again with Grant Weston, Executive Editor in their Medicine and Life Sciences division, who has been extremely supportive despite our missed deadlines. And I want to offer my sincere personal thanks to Jim Cimino, who has been a superb and talented collaborator in this effort for the last three editions. Without his hard work and expertise, we would still be struggling to complete the massive editing job associated with this now very long manuscript.

Edward H. Shortliffe

New York, NY, USA

December 2020

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Editors

Edward H. Shortliffe, MD, PhD, MACP, FACMI Biomedical Informatics, Columbia University, Arizona State University, and Weill Cornell Medical College, New York, NY, USA

Columbia University, New York, NY, USA

Arizona State University, Phoenix, AZ, USA

Weill Cornell Medical College, New York, NY, USA

ted@shortliffe.net

James J. Cimino, MD, FACP, FACMI Informatics Institute, University of Alabama at Birmingham, Birmingham, AL, USA

jamescimino@uabmc.edu

Associate Editor

Michael F. Chiang, MD, MA, FACMI National Eye Institute, National Institutes of Health, Bethesda, MD, USA

michael.chiang@nih.gov

Contributors

Russ B. Altman, MD, PhD, FACMI Departments of Bioengineering, Genetics and Medicine, Stanford University, Stanford, CA, USA

russ.altman@stanford.edu

Suzanne Bakken, RN, PhD, FAAN, FACMI, FIAHSI Department of Biomedical Informatics, Vagelos College of Physicians and Surgeons, School of Nursing, and Data Science Institute, Columbia University, New York, NY, USA

sbh22@cumc.columbia.edu

David W. Bates, MD, MSc, FACMI Division of General Internal, Medicine and Primary Care, Department of Medicine, Brigham and Women's Hospital, Boston, MA, USA

dbates@partners.org

David Blumenthal, MD, MPP Commonwealth Fund, New York, NY, USA

db@cmwf.org

Patricia Flatley Brennan, RN, PhD, FACMI National Library of Medicine, National Institutes of Health, Bethesda, MD, USA

patti.brennan@nih.gov

Eun Kyoung Choe, PhD College of Information Studies, University of Maryland, College Park, College Park, MD, USA
choe@umd.edu

Terry P. Clemmer, MD Pulmonary – Critical Care Medicine, Intermountain Healthcare (Retired), Salt Lake City, UT, USA
terry.clemmer@imail.org

Sarah Collins Rossetti, PhD, RN, FACMI Department of Biomedical Informatics, School of Nursing, Columbia University Medical Center, New York, NY, USA
sac2125@cumc.columbia.edu

Todd Cooper Trusted Solutions Foundry, Inc., San Diego, CA, USA

Robert M. Cronin, MD, MS, MEng Department of Biomedical Informatics, Vanderbilt University, Nashville, TN, USA
The Department of Internal Medicine, The Ohio State University, Columbus, OH, USA
robert.cronin@vumc.org

George Demiris, PhD, FACMI Department of Biostatistics, Epidemiology and Informatics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA
gdemiris@nursing.upenn.edu

Dina Demner-Fushman, MD, PhD, FACMI National Library of Medicine, Lister Hill National Center for Biomedical Communications, Bethesda, MD, USA
ddemner@mail.nih.gov

Joshua C. Denny, MD, MS, FACMI All of Us Research Program, National Institutes of Health, Bethesda, MD, USA
josh.denny@vumc.org

Parvati Dev, PhD, FACMI SimTabs, Los Altos Hills, CA, USA
parvati@parvatidev.org

Patricia C. Dykes, PhD, MA, RN, FAAN, FACMI Center for Patient Safety Research & Practice, Brigham and Women's Hospital, Boston, MA, USA
pdynes@bwh.harvard.edu

Noémie Elhadad, PhD, FACMI Department of Biomedical Informatics, Columbia University, New York, NY, USA
noemie.elhadad@columbia.edu

Peter J. Embi, MD, MS, FACMI Regenstrief Institute and Indiana University School of Medicine, Indianapolis, IN, USA

Bradley J. Erickson, MD, PhD Department of Radiology, Mayo Clinic, Rochester, MN, USA
bje@mayo.edu

Carol Friedman, PhD, FACMI Department of Biomedical Informatics, Columbia University, New York, NY, USA

Charles P. Friedman, PhD, FACMI, FIAHSI Department of Learning Health Sciences, University of Michigan Medical School, Ann Arbor, MI, USA
cpfried@umich.edu

Mark Frisse, MD, MS, MBA, FACMI Biomedical Informatics, Vanderbilt University, Nashville, TN, USA
mark.frisse@vanderbilt.edu

Jeremy D. Goldhaber-Fiebert, PhD Center for Primary Care and Outcomes Research/Center for Health Policy, Stanford University, Stanford, CA, USA
jeremygf@stanford.edu

Kenneth W. Goodman, PhD, FACMI Institute for Bioethics and Health Policy, University of Miami Miller School of Medicine, Miami, FL, USA
kgoodman@med.miami.edu

Robert A. Greenes, MD, PhD, FACMI Department of Biomedical Informatics, Arizona State University, Mayo Clinic, Scottsdale, AZ, USA

Hayit Greenspan, PhD Tel Aviv University, Tel Aviv, Israel

W. Edward Hammond, PhD, FACMI Duke Center for Health Informatics, Duke University Medical Center, Durham, NC, USA

Vitaly Herasevich, MD, PhD Department of Anesthesiology and Perioperative Medicine, Mayo Clinic, Rochester, MN, USA
vitaly@mayo.edu

William Hersh, MD, FACP, FACMI, FAMIA, FIAHSI Department of Medical Informatics & Clinical Epidemiology, School of Medicine, Oregon Health & Science University, Portland, OR, USA
hersh@ohsu.edu

Assaf Hoogi, PhD Computer Science Department, Ariel University, Israel, Ariel, Israel

Eric Horvitz, MD, PhD, FACMI Microsoft, Redmond, WA, USA
horvitz@microsoft.com

George Hripcsak, MD, MS, FACMI Department of Biomedical Informatics, Columbia University Medical Center, New York, NY, USA
hripcsak@columbia.edu

Charles Jaffe, MD, PhD, FACMI Health Level Seven International, Ann Arbor, MI, USA
cjaffe@hl7.org

Holly Jimison, PhD, FACMI Khoury College of Computer Sciences & Bouve College of Health Sciences, Northeastern University, Boston, MA, USA
h.jimison@northeastern.edu

Kevin B. Johnson, MD, MS, FACMI Department of Biomedical Informatics, Vanderbilt University, Nashville, TN, USA
kevin.johnson@vumc.org

Thomas Kannampallil, PhD Institute for Informatics, Washington University School of Medicine, St Louis, MO, USA
thomas.k@wustl.edu

David R. Kaufman, PhD, FACMI Medical Informatics, SUNY Downstate Medical Center, Brooklyn, NY, USA
david.kaufman@downstate.edu

Kensaku Kawamoto, MD, PhD, MHS, FACMI University of Utah, Salt Lake City, UT, USA

Predrag Klasnja, PhD School of Information, University of Michigan, Ann Arbor, MI, USA
klasnja@umich.edu

Wayne R. Kubick, BA, MBA Health Level 7 International, Ann Arbor, MI, USA

Martin LaVenture, MPH, PhD, FACMI Informatics Savvy Advisors, Edina, MN, USA
 Institute for Health Informatics (IHI), University of Minnesota, Minneapolis, MN, USA
marty@umn.edu

Russell B. Leftwich, MD InterSystems, Cambridge, MA, USA
 Vanderbilt University Medical Center, Department of Biomedical Informatics, Nashville, TN, USA

Roger G. Mark, MD, PhD Department of Electrical Engineering and Computer Science (EECS), Institute of Medical Engineering and Science, Massachusetts Institute of Technology, Cambridge, MA, USA
rgmark@mit.edu

Clement J. McDonald, MD, MS, FACMI Lister Hill National Center for Biomedical Communications, National Library of Medicine, National Institutes of Health, Bethesda, MD, USA
clemmcdonald@mail.nih.gov; CJMcDona@Regenstrief.org

Genevieve B. Melton, MD, PhD, FACMI Department of Surgery and Institute for Health Informatics, University of Minnesota, Minneapolis, MN, USA
gmelton@umn.edu

Blackford Middleton, MD, MPH, MSc, FACMI Apervita, Inc, Chicago, IL, USA

Matt Might, PhD UAB Hugh Kaul Precision Medicine Institute, University of Alabama at Birmingham, Birmingham, AL, USA
might@uab.edu

Randolph A. Miller, MD, FACMI Department of Biomedical Informatics, Vanderbilt University Medical Center, Nashville, TN, USA
randolph.a.miller@vanderbilt.edu

Sean D. Mooney, PhD, FACMI Department of Biomedical Informatics and Medical Education, University of Washington, Seattle, WA, USA
sdmooney@uw.edu

Judy Murphy, RN, FACMI, LFHIMSS, FAAN IBM Global Healthcare, Armonk, NY, USA
judy.murphy29@gmail.com

Mark A. Musen, MD, PhD, FACMI Stanford Center for Biomedical Informatics Research, Stanford University, Stanford, CA, USA
musen@stanford.edu

Viet Nguyen, MD Stratametrics LLC, Salt Lake City, UT, USA

Douglas K. Owens, MD, MS Center for Primary Care and Outcomes Research/Center for Health Policy, Stanford University, Stanford, CA, USA
owens@stanford.edu

Judy G. Ozbolt, PhD, RN(Ret), FAAN, FACMI Department of Organizational Systems and Adult Health, University of Maryland School of Nursing, Baltimore, MD, USA
judy.ozbolt@gmail.com

Vimla L. Patel, PhD, DSc, FACMI Center for Cognitive Studies in Medicine and Public Health, The New York Academy of Medicine, New York, NY, USA
vpatel@nyam.org

Philip R. O. Payne, PhD, FACMI Institute for Informatics, Washington University School of Medicine in St. Louis, St. Louis, MO, USA
prpayne@wustl.edu

Brian W. Pickering, MB, BCH Department of Anesthesiology and Perioperative Medicine, Mayo Clinic, Rochester, MN, USA
pickering.brian@mayo.edu

Wanda Pratt, PhD, FACMI Information School, University of Washington, Seattle, WA, USA
wpratt@uw.edu

William C. Reed, MS, PhD Huntzinger Management Group, Inc, Moosic, PA, USA
wcreed@huntzingergroup.com

David A. Ross, DSc Task Force for Global Health, Decatur, GA, USA
dross@taskforce.org

Daniel L. Rubin, MD, MS, FSIIM, FACMI Departments of Biomedical Data Science, Radiology, and Medicine, Stanford University, Stanford, CA, USA
dlrubin@stanford.edu

Robert S. Rudin, PhD RAND Healthcare, RAND Corporation, Boston, MA, USA
rrudin@rand.org

Titus Schleyer, DMD, PhD, FAMIA, FACMI Department of Medicine, Division of General Internal Medicine and Geriatrics, Indiana University School of Medicine, Indianapolis, IN, USA
schleyer@regenstrief.org

Nigam H. Shah, MBBS, PhD, FACMI Department of Medicine, Stanford University, Stanford, CA, USA
nigam@stanford.edu

Harold C. Sox, MD, MACP Patient-Centered Outcomes Research Institute, Washington, DC, USA
Geisel School of Medicine at Dartmouth, Dartmouth College, Hanover, NH, USA
hsox@comcast.net

Catherine Staes, PhD, MPH, RN, FACMI Nursing Informatics Program, College of Nursing, University of Utah, Lake City, UT, USA
Catherine.Staes@hsc.utah.edu

Justin B. Starren, MD, PhD Division of Health and Biomedical Informatics, Departments of Preventive Medicine and Medical Social Sciences, Northwestern University Feinberg School of Medicine, Chicago, IL, USA
Justin.Starren@northwestern.edu

Paul C. Tang, MD, MS, FACMI Clinical Excellence Research Center, Stanford University, Stanford, CA, USA
paultang@stanford.edu

Peter Tarczy-Horoch, MD, FACMI Biomedical Informatics and Medical Education, University of Washington, Seattle, WA, USA
pth@uw.edu

Jessica D. Tenenbaum, PhD, FACMI Department of Biostatistics & Bioinformatics, Duke University, Durham, NC, USA
jessie.tenenbaum@duke.edu

David K. Vawdrey, PhD, FACMI Geisinger, Danville, PA, USA

Lynn Harold Vogel, AB, AM, PhD LH Vogel Consulting, LLC, Ridgewood, NJ, USA

lynn@lhvogelconsulting.com

Robert M. Wachter, MD Department of Medicine, University of California, San Francisco, San Francisco, CA, USA

Robert.Wachter@ucsf.edu

Adam B. Wilcox, MD, PhD, FACMI University of Washington, Seattle, WA, USA

abwilcox@uw.edu

Jeremy C. Wyatt, MBBS, FRCP, FACMI, FFCI Wessex Institute of Health Research, Faculty of Medicine, University of Southampton, Southampton, UK

j.c.wyatt@soton.ac.uk

William A. Yasnoff, MD, PhD, FACMI National Health Information Infrastructure Advisors, Portland, OR, USA

Division of Health Sciences Informatics, Johns Hopkins University, Portland, OR, USA

National Health Information Infrastructure (NHII) Advisors and Johns Hopkins University, Portland, OR, USA

william.yasnoff@nhiiadvisors.com

About the Future Perspective Authors (Chapter 30)

David Blumenthal, MD, MPP

became President and CEO of the Commonwealth Fund, a national health care philanthropy based in New York City, in January, 2013. Previously, he served as Chief Health Information and Innovation Officer at Partners Health System in Boston, MA, and was Samuel O. Thier Professor of Medicine and Professor of Health Care Policy at Massachusetts General Hospital/ Harvard Medical School. From 2009 to 2011, Dr. Blumenthal was the National Coordinator for Health Information Technology under President Barack Obama. In this role he was charged with building an interoperable, private and secure nationwide health information system and supporting the widespread, meaningful use of health IT. Prior to that, Dr. Blumenthal was a practicing primary care physician, director of the Institute for Health Policy, and professor of medicine and health policy at Massachusetts General Hospital/Partners Healthcare System and Harvard Medical School. As a renowned health services researcher and national authority on health IT adoption, Dr. Blumenthal has authored over 300 scholarly publications, including the seminal studies on the adoption and use of health information technology in the United States. Dr. Blumenthal received his undergraduate, medical, and public policy degrees from Harvard University and completed his residency in internal medicine at Massachusetts General Hospital.

Patricia Flatley Brennan, RN, PhD, FAAN, FACMI

is the Director of the National Library of Medicine (NLM) and Adjunct Investigator in the National Institute of Nursing Research's Advanced Visualization Branch at the National Institutes of Health (NIH). As the world's largest biomedical library, NLM produces digital information resources used by scientists, health professionals, and members of the public. A leader in research in computational health informatics, NLM plays a pivotal role in translating research into practice. NLM's research and information services support scientific discovery, health care, and public health. Prior to joining

NLM, Dr. Brennan was the Lillian L. Moehlman Bascom Professor at the School of Nursing and College of Engineering at the University of Wisconsin–Madison. Dr. Brennan is a pioneer in the development of innovative information systems and services such as ComputerLink, an electronic network designed to reduce isolation and improve self-care among home care patients. She directed HeartCare, a web-based information and communication service that helps home-dwelling cardiac patients recover faster and with fewer symptoms, and also directed Project HealthDesign, an initiative designed to stimulate the next generation of personal health records. Her professional accomplishments reflect her background, which unites engineering, information technology, and clinical care to improve public health and ensure the best possible experience in patient care. A past president of the American Medical Informatics Association, Dr. Brennan was elected to the National Academy of Medicine in 2001. She is a fellow of the American Academy of Nursing, the American College of Medical Informatics, and the New York Academy of Medicine. In 2020, Dr. Brennan was inducted into the American Institute for Medical and Biological Engineering (AIMBE). The AIMBE College of Fellows is among the highest professional distinctions accorded to a medical and biological engineer.

Mark Frisse, MD, MS, MBA

is an Emeritus Professor in the Department of Biomedical Informatics at Vanderbilt University Medical Center. Until July 2020, he held the Accenture Endowed Chair within the Department. His interests are directed toward the potential contribution to economically sustainable health care through more effective use of informatics and information technology. In addition to his teaching and research responsibilities at the Vanderbilt Medical School, he also directed the Masters of Management in Health Care graduate program at Vanderbilt's Owen Graduate School of Management and led a health information technology course for the executive Masters of Health Care Delivery Science program at Tuck School of Business, Dartmouth College. Previously, Dr. Frisse has held leadership positions at Washington University, Express Scripts, and the First Consulting Group.

At Express Scripts, he was Chief Medical Officer and was responsible for their Practice Patterns Science division and helped found RxHub. At First Consulting, he led engagements in vendor selection, quality governance, physician information technology leadership development, and clinician governance. A board-certified internist with fellowship training in medical oncology, he obtained his bachelor's degree from the University of Notre Dame in 1974 and his MD from Washington University in 1978. He received a master's degree in medical information science from Stanford University in 1987 and an MBA from Washington University in 1997. He is a fellow of the American College of Physicians, the American College of Medical Informatics, and the New York Academy of Medicine. He is an elected member of the National Academy of Medicine.

Eric Horvitz

is a technical fellow at Microsoft, where he serves as the company's first Chief Scientific Officer. He previously served as director of Microsoft Research Labs. He has pursued principles and applications of AI with contributions in machine learning, perception, natural language understanding, and decision making. His research centers on challenges with uses of AI amidst the complexities of the open world, including uses of probabilistic and decision-theoretic representations for reasoning and action, models of bounded rationality, and human-AI complementarity and coordination. His efforts and collaborations have led to fielded systems in healthcare, transportation, ecommerce, operating systems, and aerospace. He received the Feigenbaum Prize and the Allen Newell Prize for contributions to AI. He was inducted into the CHI Academy for contributions at the intersection of AI and human-computer interaction. He has been elected fellow of the American College of Medical Informatics (ACMI), National Academy of Engineering (NAE), Association of Computing Machinery (ACM), Association for the Advancement of AI (AAAI), the American Association for the Advancement of Science (AAAS), the American Academy of Arts and Sciences, and the American Philosophical Society. He has served as president of the AAAI, and on advisory commit-

tees for the NSF, NIH, and the U.S. Department of Defense. He currently serves on the Board of Regents of the National Library of Medicine and on the scientific advisory board of the Allen Institute for AI. He earned his Bachelors in biophysics at Binghamton University and a PhD in biomedical informatics and his MD at Stanford University.

Judy Murphy, RN, FACMI, FHIMSS, FAAN

is a nursing executive with a long history in health informatics. She was Chief Nursing Officer for IBM Global Healthcare, where she was strategic advisor regarding provider IT solutions to achieve the quadruple aim. Prior to working at IBM, she was Deputy National Coordinator for Programs and Policy at the ONC in Washington D.C. where she led federal efforts to assist healthcare providers in adopting health IT to improve care and to promote consumers' understanding and use of health IT for their own health. She came to ONC with 25 years of health informatics experience at Aurora Health Care in Wisconsin, a large integrated delivery network. As Vice President-EHR Applications, she led their EHR program since 1995, when Aurora was an early adopter of technology. She publishes and lectures nationally and internationally. She served on the AMIA and HIMSS Board of Directors and is a Fellow in the American Academy of Nursing, the American College of Medical Informatics and HIMSS. She has received numerous awards, including the HIMSS 2018 Most Influential Women in Health IT, the AMIA 2014 Don Eugene Detmer Award for Health Policy Contributions in Informatics, the HIMSS 2014 Federal Health IT Leadership Award, and the HIMSS 2006 Nursing Informatics Leadership Award.

Peter Tarczy-Hornoch, MD

is Professor and Chair of the Department of Biomedical Informatics and Medical Education at the University of Washington (UW). His background includes computer science, bioengineering, biomedical informatics, medicine (Pediatrics and Neonatology) with undergraduate and medical degrees from Stanford, Residency at the University of Minnesota, Fellowship at the University of Washington. He has played a key role in establishing and growing the biomedical informatics research, teaching and practice activities at UW

for over two decades. The unifying theme of his research has been data integration of electronic biomedical data (clinical and genomic) both for a) knowledge discovery and b) in order to integrate this knowledge with clinical data at the point of care for decision support. His current research focuses on a) secondary use of electronic medical record (EMR) for translational research including outcomes research, learning healthcare systems, patient accrual and biospecimen acquisition based on complex phenotypic eligibility criteria, b) the use of EMR systems for cross institutional comparative effectiveness research, and c) integration of genomic data into the EMR for clinical decision support. Key past research has included data integration and knowledge base creation for genomic testing. He has served in a number of national leadership roles including founding chair of the AMIA Genomics (now Genomics and Translational Bioinformatics) working group.

Robert M. Wachter, MD

is Professor and Chair of the Department of Medicine at the University of California, San Francisco. He is author of 300 articles and 6 books and is a frequent contributor to the *New York Times* and *Wall Street Journal*. He coined the term “hospitalist” in 1996 and is often considered the “father” of the hospitalist field, the fastest growing specialty in the history of modern medicine. He is past president of the Society of Hospital Medicine and past chair of the American Board of Internal Medicine. In the safety and quality arenas, his book, *Understanding Patient Safety*, is the world’s top selling safety primer. In 2004, he received the John M. Eisenberg Award, the nation’s top honor in patient safety. Twelve times, *Modern Healthcare* magazine has ranked him as one of the 50 most influential physician-executives in the U.S.; he was #1 on the list in 2015. His 2015 book, *The Digital Doctor: Hope, Hype and Harm at the Dawn of Medicine’s Computer Age*, was a *New York Times* science best-seller. In 2016, he chaired a blue-ribbon commission advising England’s National Health Service on its digital strategy. He is an elected member of the National Academy of Medicine.

About the Editors



Edward H. Shortliffe

is Chair Emeritus and Adjunct Professor in the Department of Biomedical Informatics at Columbia University's Vagelos College of Physicians and Surgeons. Previously he served as President and CEO of the American Medical Informatics Association. He was Professor of Biomedical Informatics at the University of Texas Health Science Center in Houston and at Arizona State University. A board-certified internist, he was Founding Dean of the University of Arizona College of Medicine – Phoenix and served as Professor of Biomedical Informatics and of Medicine at Columbia University. Before that he was Professor of Medicine and of Computer Science at Stanford University. Honors include his election to membership in the National Academy of Medicine (where he served on the executive council for 6 years and has chaired the membership committee) and in the American Society for Clinical Investigation. He has also been elected to fellowship in the American College of Medical Informatics and the American Association for Artificial Intelligence. A Master of the American College of Physicians (ACP), he held a position for 6 years on that organization's Board of Regents. He is Editor Emeritus of the *Journal of Biomedical Informatics* and has served on the editorial boards for several other biomedical informatics publications. In the early 1980s, he was recipient of a research career development award from the National Library of Medicine. In addition, he received the Grace Murray Hopper Award of the Association for Computing Machinery in 1976, the Morris F. Collen Award of the American College of Medical Informatics in 2006, and was a Henry J. Kaiser Family Foundation Faculty Scholar in General Internal Medicine. He has served on the oversight committee for the Division on Engineering and Physical Sciences (National Academy of Sciences), the National Committee on Vital and Health Statistics (NCVHS), and on the President's Information Technology Advisory Committee (PITAC). Dr. Shortliffe has authored over 350 articles and books in the fields of biomedical computing and artificial intelligence.



James J. Cimino

is a board-certified internist who completed a National Library of Medicine informatics fellowship at the Massachusetts General Hospital and Harvard University and then went on to an academic position at Columbia University College of Physicians and Surgeons and the Presbyterian Hospital in New York. He spent 20 years at Columbia, carrying out clinical informatics research, building clinical information systems, teaching medical informatics and medicine, and caring for patients, rising to the rank of full professor in both Biomedical Informatics and Medicine. His principal research areas there included desiderata for controlled terminologies, mobile and Web-based clinical information systems for clinicians and patients, and a context-aware form of clinical decision support called “infobuttons.” In 2008, he moved to the National Institutes of Health, where he was the Chief of the Laboratory for Informatics Development and a Tenured Investigator at the NIH Clinical Center and the National Library of Medicine. His principal project involved the development of the Biomedical Translational Research Information System (BTRIS), an NIH-wide clinical research data resource. In 2015, he left the NIH to be the inaugural Director of the Informatics Institute at the University of Alabama at Birmingham. The Institute is charged with improving informatics research, education, and service across the University, supporting the Personalized Medicine Institute, the Center for Genomic Medicine, and the University Health System Foundation, including improvement of and access to electronic health records. He holds the rank of Tenured Professor in Medicine and is the Chief for the Informatics Section in the Division of General Internal Medicine. He continues to conduct research in clinical informatics and clinical research informatics, he was Director of the NLM’s weeklong Biomedical Informatics course for 16 years, and teaches at Columbia University and Georgetown University as an Adjunct Professor. He is an Associate Editor of the *Journal of Biomedical Informatics*. His honors include Fellowships of the American College of Physicians, the New York Academy of Medicine and the American College of Medical Informatics (Past President), the Priscilla Mayden Award from the University of Utah, the Donald A.B. Lindberg Award for Innovation in Informatics and the President’s Award, both from the American Medical

Informatics Association, the Morris F. Collen Award of the American College of Medical Informatics, the Medal of Honor from New York Medical College, the NIH Clinical Center Director's Award (twice), and induction into the National Academy of Medicine (formerly the Institute of Medicine).



Michael F. Chiang

is Director of the National Eye Institute, at the National Institutes of Health in Bethesda, Maryland. His clinical practice focuses on pediatric ophthalmology, and he is board-certified in clinical informatics. His research develops and applies biomedical informatics methods to clinical ophthalmology in areas such as retinopathy of prematurity (ROP), telehealth, artificial intelligence, clinical information systems, genotype-phenotype correlation, and data analytics. His group has published over 200 peer-reviewed papers, and has developed an assistive artificial intelligence system for ROP that received breakthrough status from the US Food and Drug Administration. He received a BS in Electrical Engineering and Biology from Stanford University, an MD from the Harvard-MIT Division of Health Sciences and Technology, and an MA in Biomedical Informatics from Columbia University. He completed clinical training at the Johns Hopkins Wilmer Eye Institute. Between 2001 and 2010, he worked at Columbia University, where he was Anne S. Cohen Associate Professor of Ophthalmology & Biomedical Informatics, director of medical student education in ophthalmology, and director of the introductory graduate student course in biomedical informatics. From 2010 to 2020, he was Knowles Professor of Ophthalmology & Medical Informatics and Clinical Epidemiology, and Associate Director of the Casey Eye Institute, at the Oregon Health & Science University (OHSU) Casey Eye Institute. He has served as a member of the American Academy of Ophthalmology (AAO) Board of Trustees, Chair of the AAO IRIS Registry Data Analytics Committee, Chair of the AAO Task Force on Artificial Intelligence, Chair of the AAO Medical Information Technology Committee, and on numerous other national and local committees. He currently serves as an Associate Editor for *JAMIA*, and is on the Editorial Board for *Ophthalmology* and the *Asia-Pacific Journal of Ophthalmology*.