# Scanning the Issue

## Special Issue on Bioinformatics, Part I: Advances and Challenges

Biomedical informatics is an emerging discipline that coalesces the health sciences, including medicine, dentistry, pharmacology, nursing, radiology, and biological sciences with computer science, mathematics, statistics, engineering, information technologies, and management. Biomedical informatics recently has evolved to focus on the molecular basis of genomic data by identifying and quantifying gene and gene products.

The objective of this two-part special issue is to provide the theoretical foundations and the current applications of biomedical informatics in medicine and biology. We focus on structures and algorithms to analyze genomics data and develop computational solutions to produce new knowledge and understanding and interpretation of diseases such as cancer and, in terms of gene identification, for use in diagnostic and therapeutic target design. Therefore, to highlight this emerging discipline, we devoted this special issue (Part I) to advances and challenges in genomics and proteomic-related research papers.

The first paper, "Rapid development of nucleic acid diagnostics," by Fitch *et al.*, deals with an important result of the human genome project that has yielded a significant increase in the availability of nucleic sequence information for both viruses and bacteria. This work has important public health implications and the signatures developed are targeted for widely available instruments. This paper discusses the computational and engineering aspects of converting this raw nucleic sequence data into pathogen-specific and instrument-ready assays including those for the foot-and-mouth-disease virus, the Venezuelan encephalitis virus, and the human deficiency virus. This paper includes some tutorial background information on the biology involved to help the reader more fully understand this important topic.

The second paper, "Functional bioinformatics of microarray data: From expression to regulation," by Moreau *et al.*, discusses a new technique using microarrays to monitor the expression of thousands of genes in a single experiment, and, through a series of such experiments, enables one to identify the mechanisms that govern the activation of genes in any organism. This identification process represents a major goal of molecular biology.

The third paper, "Classifying gene expression data of cancer using classifier ensemble with mutually exclusive

features," by Cho and Ryu, discusses a new framework which combines a set of gene expression data classifiers trained with mutually exclusive features. The feature selection was based on the nonoverlapping correlation to learn different aspects of training data and search a reasonable solution in a large solution space. Experimental results show that the classifier ensemble combination produces higher recognition accuracy than conventional classifiers.

The fourth paper, "Complex life science multi-database queries," by Miled *et al.*, presents a framework that associates the integration of life science web databases applying the techniques used in the Biological and Chemical Integration Information System (BACIIS) to address these challenges. The confederation of widely distributed life science databases is a critical scientific problem because these databases have been organized around disciplinary interests, various subject areas or in other ways for institutional convenience. This paper proposes an approach that may overcome the current limitations of the query capabilities of each individual life science web database in the proposed system.

The fifth paper, "*In silico* radiation oncology: Combining novel simulation algorithms with current visualization techniques," by Stamatakos *et al.*, reviews the experimental, mathematical, and three-dimensional (3-D) computer simulation models of tumor growth and response to radiation therapy as well as the development and radiation responses of tumors. It describes novel Monte Carlo simulation algorithms of tumor growth and response to irradiation, specific applications of the algorithms, and 3-D visualization of the predicted outcome. The paper concludes with a critical evaluation of the presented paradigms and suggestions for additional research.
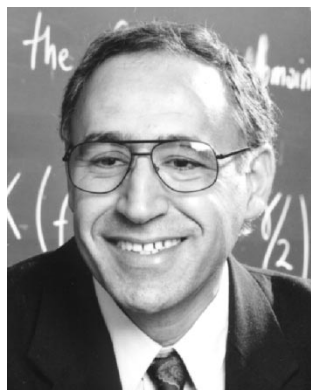
The sixth paper, "From Boolean to probabilistic Boolean networks as models of genetic regulatory networks," by Shmulevich *et al.*, deals with the importance of mathematical and computational modeling of genetic regulatory networks, which promises to uncover the fundamental principles governing biological systems. This paper discusses the use of the probabilistic Boolean algorithm to model complex, large-scale, and dynamical regulatory genetic networks as well as the target identification problem for therapeutic intervention using several computational algorithms and tools. The inference of Boolean networks from real gene expression data is considered from the viewpoints of computational learning theory and nonlinear signal processing, touching on the computational complexity of learning and robustness.

The seventh paper, "Visualizing metabolic pathways: Comparative genomics and expression analysis," by Lindroos and Andersson, presents the two currently used and integrated databases of metabolic pathways and genomes to determine gene functions. The analysis of metabolic pathways from different species facilitates delineation of their evolutionary relationships and identification of suitable targets in the design of novel antimicrobial drugs.

The last paper, "Genomewide motif identification using a dictionary model," by Sabatti and Lange gives an extensive summary of models and algorithms for identifying binding sites in noncoding regions of DNA. Binding sites control the transcription of genes into messenger RNA in preparation for translation into proteins. The paper then presents a unified model based on the integration of the main features of the existing algorithm. These algorithms rely on recursive formulas and the maximization/minorization principle. Finally, it concludes with a prospectus of future data analyses and theoretical research.

It is clear that only through cross-disciplinary cooperation and the application of powerful tools and techniques can science, engineering, and medicine unlock and apply molecular biology to serve all of humankind. In Part II of this special issue, which will be published in December, we will examine some additional topics that are having an impact on this rapidly emerging field.

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**Metin Akay** (Senior Member, IEEE) received the B.S. and M.S. degrees in electrical engineering from the Bogazici University, Istanbul, Turkey, in 1981 and 1984, respectively, and the Ph.D. degree from Rutgers University, New Brunswick, NJ, in 1990.

He is currently Associate Professor of Engineering, Psychology and Brain Sciences, and Computer Science at Dartmouth University, Hanover, NJ. He has played a key role in promoting the biomedical education in the world by writing several prestigious books and editing the *IEEE Biomedical Engineering Book Series* (New York: Wiley/IEEE Press), sponsored by the IEEE Engineering in Medicine and Biology Society (EMBS). He is the author or coauthor of 12 books, including *Theory and Design of Biomedical Instruments* (New York: Academic, 1991), *Biomedical Signal Processing* (New York: Academic, 1994), *Detection Estimation of Biomedical Signals* (New York: Academic, 1996), *Time-Frequency and Wavelets in BME* (New York: Wiley/IEEE Press, 1997), *Nonlinear Biomedical Signal Processing* (New York: Wiley/IEEE Press, 2000), *Information Technology in Medicine* (New York: Wiley, 2000). He gave 30 keynote and plenary talks and several invited talks at the international meetings including the ICAP'94, IFSA'95, the DSP applications and Exhibition Conference '96, the Satellite Symposium of the IEEE EMBS'98 in China, the 12th Annual Conference of Japanese Society of Medical Electronics and Biomedical Engineering, and the first and second Latin-American Conference on Biomedical Engineering in 1998 and 2001. His Neural Engineering and Informatics Lab is interested in investigating the respiratory somatosensory (RSS) responses of patients with obstructive sleep apnea syndrome (OSAS) and the effect of developmental abnormalities and maturation on the dynamics of respiration.

Prof. Akay is a recipient of the IEEE EMBS Career Service "for his outstanding contributions to the advancement of the scientific stature and visibility of IEEE-EMBS and extraordinary dedication to the promotion of biomedical engineering education in the world." He is also a recipient of the IEEE Third Millennium Medal for "his contributions to biomedical engineering research and education." He served as the invited Guest Editor for 12 special issues of *IEEE Engineering in Medicine and Biology* magazine, *Annals of BME*, and *Journal of BME* in the areas of cardiovascular engineering, virtual reality in medicine, advances in biomedical signal processing, and fuzzy logic in medicine. He is also the invited Guest Editor for PROCEEDINGS OF THE IEEE (Special Issue on Neural Engineering). He is also the Guest Editor for the two special issues of PROCEEDINGS OF THE IEEE on Functional Genomics, which will be published in 2002. He was the Chair of the IEEE EMBS Summer School in 1997, 2001, and 2002. He was also the Program Chair of the Annual IEEE EMBS Conference in 2001. These activities were sponsored by the National Science Foundation and largely attended by women and minorities. He is a strong supporter of women and minorities in engineering, medicine, and science in the world. He is also the IEEE Distinguished Lecturer in Bioengineering. He received the IEEE Engineering in Medicine and Biology Society Early Career Achievement Award in 1997 "for outstanding contributions in the detection of coronary artery disease, in understanding of early human development, and leadership and contributions in biomedical engineering education." He received the Young Investigator Award of the Sigma Xi Society, Northeast Region in 1998 and 2000 for "his outstanding research activity and the ability to communicate the importance of his research to the general public." He is a Member of Eta Kappa, Sigma Xi, Tau Beta Pi, The American Heart Association, and The New York Academy of Science. He also serves on the advisory board of several international journals including the IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING, IEEE TRANSACATION ON INFORMATION TECHNOLOGY IN BIOMEDICINE, and the National Institutes of Health Bioengineering partnership study session and several NSF review panels.