

# Guest Editors' Introduction to the Special Issue

**T**HIS special issue includes a selection of papers presenting recent advances in computational nanobioscience. A number of 34 papers were submitted in response to the call for papers, of which, following a rigorous review process, 10 papers were selected for publication. Selected papers illustrate the variety of applications that computational methods find in the field of nanobioscience, ranging from computational modeling of molecular processes and bioassay design all the way to integrative data analysis methods and system level simulation. Furthermore, selected papers convincingly demonstrate the central role played by computational methods in contemporary nanobioscience research – a role that is bound only to increase in the future.

The first four of the selected papers fall in the area of computational modeling and design of molecular systems. This is currently a very active area of research, with rapid-paced progress driven by emerging biomedical applications that require ever growing accuracy and throughput.

- The paper by Avihoo et al. addresses the problem of designing artificial RNA switches, which may find future applications in gene therapy. Inspired by the modularity observed in natural riboswitches, the authors propose design methods based on assembling smaller building blocks. Switching is achieved by ensuring that the designed RNAs can fold into two highly stable conformations that are energetically close to each other but are separated by a high energy barrier.
- The paper by Balla and Rajasekaran addresses the problem of selecting degenerate primers for multiplex PCR reactions. The authors combine methodologies from the area of biosequence motif discovery with a simple iterative technique to obtain primer selection algorithms that significantly outperform previous methods.
- The paper by Rose et al. presents a coupled equilibrium model for predicting the error response of tag-antitag systems when the temperature and input concentrations are varied. This model has been implemented in the *NucleicPark* software package for *in silico* analysis of tag-antitag systems.
- The paper by Măndoiu and Prăjescu proposes a new Single Nucleotide Polymorphism (SNP) genotyping assay architecture that combines multiplexed solution-phase single-base extension (SBE) reactions with sequencing by hybridization (SBH) using universal DNA arrays. The authors propose efficient algorithms for decoding the results of SBE/SBH experiments, as well as practical heuristics for partitioning large sets of SNPs into minimum number of SBE/SBH assays.

The next four papers address problems in the area of high-throughput biomolecular data analysis. Extracting biologically meaningful insights from high-throughput datasets

and integrating data from heterogeneous sources rise numerous challenges that require advanced computational techniques for their solution.

- The paper by Merschmann and Plastino proposes a data mining technique based on Bayes' theorem, called Highest Subset Probability (HiSP), for predicting the functional family of a protein from its motif composition. Experiments on datasets extracted from the Prosite protein family database show that HiSP outperforms other known methods, and performs well on imbalanced datasets known to hinder the performance of standard classifiers.
- The paper by Pei and Zhang introduces a novel “seed-refine” approach for detecting protein complexes from high-throughput protein-protein interaction (PPI) data. The proposed approach combines a probabilistic subgraph scoring function with a local optimization procedure that seeks to identify a set of (possibly overlapping) high-scoring subgraphs in the PPI network.
- The paper by Sanfilippo et al. presents a novel methodology, called Cross-Ontological Analytics, for estimating semantic similarity between pairs of genes based on Gene Ontology annotations. The proposed methodology captures both intra- and inter-hierarchy relations, and can further integrate textual information extracted from biomedical literature.
- The paper by He and Zelikovsky addresses a key problem in large-scale disease association studies, namely the tag SNP selection problem. The authors demonstrate the close interdependence between tag SNP selection and prediction methods used to reconstruct missing SNP genotypes from tag SNP genotypes. They give two SNP prediction methods based on multiple linear regression and support vector machines and propose greedy and local optimization procedures for tag SNP selection.

The final two papers fall within the realm of biological system modeling and simulation. Studies in this area are becoming increasingly important as we seek to develop insights into the high-level workings of large molecular or cellular systems.

- The paper by Qiu and Lane models the impact of transitive RNA interference mismatch and off-target knock-down on transcriptome stability. Simulations based on the proposed model are used to obtain a theoretical upper limit of 6 nucleotides on the number of hybridization mismatches that can be tolerated between short interfering RNAs and their targets.
- The paper by Maheswaran et al. proposes a model for a stratified epithelium, featuring multiple cell types and capturing biological processes such as cell division, differentiation, adhesion, and death. The authors use the

model to study the role of differential adhesion and cell division in the maintenance of the ordered structure of epithelial tissue.

We would like to thank all authors for their high-quality submissions, and the anonymous reviewers for volunteering their time and expertise in evaluating the scientific merits of submitted papers. We would also like to thank the Editor-in-Chief, Prof. Dr. C. Ruggiero, for providing us the opportunity to showcase in this special issue a sampling of the exciting research currently being conducted in computational nanobioscience. We hope that, by making a number of important nanobioscience problems accessible to a wider Computer Science audience and by bringing some fundamental computational techniques to the attention of more nanobioscience researchers, the special issue will foster further collaborations between these two communities.

#### GUEST EDITORS

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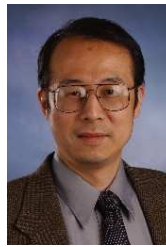
**Ion I. Măndoiu** received the M.S. degree from Bucharest University in 1992 and the Ph.D. degree from Georgia Institute of Technology in 2000, both in Computer Science.

Between 2000 and 2003 he was a post-doctoral researcher and then Research Scientist at the University of California at Los Angeles and at San Diego. He is currently an Assistant Professor with the Computer Science and Engineering Department at the University of Connecticut, Storrs. He is the author of 60 papers in international journals and

refereed conference proceedings. His main research interest is in the design and analysis of approximation algorithms for NP-hard optimization problems, particularly in the areas of bioinformatics, design automation, and ad-hoc wireless networks.

Dr. Măndoiu is a member of the Association for Computing Machinery and of the International Society for Computational Biology. He is founding co-chair of the ACIS International Workshop on Self-Assembling Wireless Networks (SAWN), Program Committee co-chair of the 2007 International Symposium on Bioinformatics Research and Applications (ISBRA), and Program Committee Chair of the 2007 System Level Interconnect Prediction Workshop (SLIP 2007). He also serves on the editorial board of the *International Journal of Bioinformatics Research and Applications*, and is a guest editor for *IEEE/ACM Transactions on Computational Biology and Bioinformatics*, *International Journal of Wireless and Mobile Computing*, and the *Journal of Universal Computer Science*.

Dr. Măndoiu received the best paper award at the joint Asia-South Pacific Design Automation/VLSI Design Conferences in 2003, and the best poster award at the Annual BACUS Symposium on Photomask Technology in 2005. He is a 2006 recipient of the NSF Faculty Early Career Development Award.



**Yi Pan** is the chair and a professor in the Department of Computer Science and a professor in the Department of Computer Information Systems at Georgia State University. Dr. Pan received his B.Eng. and M.Eng. degrees in computer engineering from Tsinghua University, China, in 1982 and 1984, respectively, and his Ph.D. degree in computer science from the University of Pittsburgh, USA, in 1991.

Dr. Pan's research interests include parallel and distributed computing, optical networks, wireless networks, and bioinformatics. Dr. Pan has published more than 100 journal papers with over 30 papers published in various IEEE journals. In addition, he has published over 100 papers in refereed conferences (including IPDPS, ICPP, ICDCS, INFOCOM, and GLOBECOM). He has also co-edited 24 books (including proceedings) and contributed several book chapters. His pioneer work on computing using reconfigurable optical buses has inspired extensive subsequent work by many researchers, and his research results have been cited by more than 100 researchers worldwide in books, theses, journal and conference papers. He is a co-inventor of three U.S. patents (pending) and 5 provisional patents, and has received many awards from agencies such as NSF, AFOSR, JSPS, IISF and Mellon Foundation. His recent research has been supported by NSF, NIH, NSFC, AFOSR, AFRL, JSPS, IISF and the states of Georgia and Ohio. He has served as a reviewer/panelist for many research foundations/agencies such as the U.S. National Science Foundation, the Natural Sciences and Engineering Research Council of Canada, the Australian Research Council, and the Hong Kong Research Grants Council. Dr. Pan has served as an editor-in-chief or editorial board member for 15 journals including 5 IEEE Transactions and a guest editor for 10 journals including IEEE/ACM Transactions on Computational Biology and Bioinformatics and IEEE Transactions on NanoBioscience. He has organized several international conferences and workshops and has also served as a program committee member for several major international conferences such as INFOCOM, GLOBECOM, ICC, IPDPS, and ICPP.

Dr. Pan has delivered over 10 keynote speeches at many international conferences. Dr. Pan is an IEEE Distinguished Speaker (2000-2002), a Yamacraw Distinguished Speaker (2002), a Shell Oil Colloquium Speaker (2002), and a senior member of IEEE. He is listed in Men of Achievement, Who's Who in Midwest, Who's Who in America, Who's Who in American Education, Who's Who in Computational Science and Engineering, and Who's Who of Asian Americans.



**Alexander Zelikovsky** received the Ph.D. degree in Computer Science from the Institute of Mathematics of the Belorussian Academy of Sciences in Minsk (Belarus) in 1989 and worked at the Institute of Mathematics in Kishinev (Moldova) (1989-1995). Between 1992 and 1995 he visited Bonn University and the Institut für Informatik in Saarbrücken (Germany). Dr. Zelikovsky was a Research Scientist at University of Virginia (1995-1997) and a Post-doctoral Scholar at UCLA (1997-1998). He is an Associate Professor at Computer Science Department of Georgia State University which he joined in 1999. He is the author of more than 130 refereed publications. Dr. Zelikovsky's research interests include bioinformatics, discrete and approximation algorithms, combinatorial optimization, VLSI physical layout design, and ad-hoc wireless networks.

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