

PROMOTION RECOMMENDATION
THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF COMPUTATIONAL MEDICINE AND BIOINFORMATICS
COLLEGE OF LITERATURE, SCIENCE, AND THE ARTS
DEPARTMENT OF MATHEMATICS

Indika Rajapakse Ph.D., assistant professor of computational medicine and bioinformatics, Department of Computational Medicine and Bioinformatics, Medical School, and assistant professor of mathematics, Department of Mathematics, College of Literature, Science, and the Arts, is recommended for promotion to associate professor of computational medicine and bioinformatics, with tenure, Department of Computational Medicine and Bioinformatics, Medical School, and associate professor of mathematics, without tenure, Department of Mathematics, College of Literature, Science, and the Arts.

Academic Degrees:

Ph.D.	2004	Washington State University
B.Sc.	1997	University of Moratuwa, Sri Lanka

Professional Record:

2014-present	Assistant Professor of Mathematics, University of Michigan
2013-present	Assistant Professor of Computational Medicine and Bioinformatics, University of Michigan

Summary of Evaluation:

Teaching: Dr. Rajapakse designed a new course since his arrival - Bioinformatics 540 (Mathematics 540). He has been the sole instructor each fall since 2015 and now has over 30 students per class. He also teaches in Mathematics 547 (Bioinformatics 547 and Statistics 547), "Probabilistic Modeling in Bioinformatics" along with Professor Daniel Burns in the Department of Mathematics. This class is taught annually in the Winter Semester and has, on average, 20 students. In addition, Dr. Rajapakse jointly organized the department's journal club in 2014-2015, and has actively participated in running the department's seminar series since his arrival at Michigan. Dr. Rajapakse is in the process of developing a new textbook, *Mathematics of Biological Networks*, to be published in summer 2018 by Springer Verlag. This textbook will be used for his 540 course. He has also instructed many labs on use of chromosome conformation capture (Hi-C) technology, as well as 3D genome imaging.

Dr. Rajapaske is the advisor of two active Ph.D. students, and had one student successfully defend her thesis recently and move immediately to a scientist position at Draper Labs in Cambridge, Massachusetts. He has also jointly supervised three Ph.D. candidates. In addition, he has mentored five post-doctoral fellows, one currently, one joined his lab as a senior scientist, two are now in industry positions, and one is now an assistant professor at Northwestern Polytechnical University, Xi'an, China. He has mentored four undergraduate students since his arrival at Michigan; of which two have entered Ph.D. programs here, and are pursuing research under his supervision. He has served on nine Ph.D. dissertation committees (two in Bioinformatics, one in Human Genetics, three in Mathematics, one in Biomedical Engineering, one in Mechanical Engineering, and one in a joint program between the University of Maryland and NCI) and has served on four preliminary exam committees in Bioinformatics.

Research: Dr. Rajapakse was recruited as one of the first University of Michigan Network Biology Cluster faculty, an initiative of former University of Michigan President Mary Sue Coleman. This program was initiated to establish collaborations by connecting them with researchers that have similar interests across campus. This has been successful in his collaborations with Dr. Anthony Bloch in the Department of Mathematics, regarding how to bring network controllability ideas to nonlinear control theory; and he also worked with Dr. Mercedes Pascual, prior to her leaving Michigan. This work was in the network dynamics of ecological communities. He has also connected through this program with the Center for the Study of Complex Systems. Dr. Rajapakse's area of research is the study the dynamics of genome organization in human cells, with emphasis on gaining a deeper understanding of how the cell cycle guides cell fate decisions. Using a theme of data-guided mathematics to gain an understanding of the dynamical form-function relationships in the human genome, he hopes to develop strategies for direct reprogramming of normal and abnormal cells. His lab has been built with the particular focus of integrating genomics technologies, including genome-wide chromosome conformation capture (Hi-C) and RNA-seq, high-resolution imaging, genome editing, and quantitative methods to understand the genome as a dynamical system in 3D, i.e. a 4D system with time [1-7f]. Having both cell biology and mathematical expertise within his laboratory allows them to collect, analyze, and interpret all genomics data on-site. These novel and powerful methodological contributions have put Dr. Rajapakse in a leadership status in the emerging field of the "4D Nucleome" in bioinformatics, computational biology, and its sister field of mathematical biology. Dr. Rajapakse has published 28 papers, one book and has two papers currently under revision.

Dr. Rajapakse has just had an exciting new paper accepted for publication in Proceedings of the National Academy of Sciences USA. Dr. Rajapakse is the corresponding and senior author, designed, and directed the research for this paper. This paper introduces a new data-guided mathematical framework that predicts top candidate transcription factors for direct reprogramming of any cell type into any target cell type. The algorithm successfully identified several factors previously validated for reprogramming. This work lays a foundation for improved direct reprogramming strategies by considering conversion efficiency, timing, and optimality, and predicting several novel factors and combinations of factors as candidates for reprogramming. These strategies are applicable to cell replacement therapies, regenerative medicine, and improving control over biological processes. Dr. Rajapakse has secured funding from the Department of Defense (Defense Advanced Research Projects Agency (DARPA) and Air Force Office of Scientific Research (AFOSR). He is building additional expertise in quantitative approaches to fundamental problems in genome organization by establishing collaborations with Dr. Stephen Smale, a mathematician and Fields Medalist, and Dr. Thomas Ried at the National Cancer Institute (NCI), a pioneer in molecular cytogenetics. He has also been involved in the initial stages of the NIH Common Fund 4D Nucleome (4DN) initiative with Dr. Ried, who conceived the 4DN. Interestingly, DARPA is utilizing Dr. Rajapakse's work on the 4DN as a partial basis for developing of a new computational paradigm called "reservoir computing."

Dr. Rajapakse has given presentations at the following: The Institute of Molecular Biology (University of Mainz, Germany); DARPA Biochronicity Program, AFOSR/DARPA/NCI Strategic Workshop on the Convergence of Physical Sciences for Biomedical Applications, DARPA; Beijing Genomics Institute (China); Draper Labs, (Cambridge, MA); Department of Mathematics and Physics (University of Houston); Indiana University Network Science Institute; and the Viterbi School of Engineering (University of Southern California). He was also a visiting professor for the month of November 2015 in Mathematics at the City University of Hong Kong (CUHK), and will be returning for July 2017.

Recent and Significant Publications:

Chen H, Chen J, Muir L, Ronquist S, Meixner W, Ried T, Smale S, Rajapakse I: Functional organization of the human genome in space and time. *Proceedings of the National Academy of Sciences* 112:8002-8007, 2015.

Chen J, Hero A, Rajapakse: Spectral identification of topological domains. *Bioinformatics* 32: 2151-2158, 2016.

Rajapakse I, Smale S: Mathematics of the genome. *Foundations of Computational Mathematics*, DOI 10.1007/s10208-016-9316-x, 2016. Published online

Seaman L, Chen H, Brown M, Wangsa D, Patterson G, Camps J, Omenn G, Ried T, Rajapakse I: Nucleome analysis reveals structure-function relationships for colon cancer. *Molecular Cancer Research* 10.1158/1541-7786.MCR-16-0374, 2017. Published online

Rajapakse I, Smale S: Emergence of function from coordinated cells in a tissue. *Proceedings of the National Academy of Science*, 114:1462-1467, 2017.

Service: Internationally, Dr. Rajapakse has been a Workshop Organizer for Gene Dynamics and Chromosomes for the City University of Hong Kong (CUHK); and for Computational Mathematical Biology with Emphasis on the Genome workshop at Foundations of Computational Mathematics conference in Barcelona, Spain. Nationally, Dr. Rajapakse will be the organizer of the DARPA “Deep Purposeful Learning (Deep Purple) and Fundamental of Complex Collectives” meeting in 2017-18. He is a member of the Smale Institute, and serves on the Editorial Board of *Frontiers in Biophysics*. He is an ad hoc journal reviewer for *Proceedings of the National Academy of Sciences*, *Nucleus*, *Bioinformatics*, *Journal of Mathematical Biology*, *PLOS Computational Biology and Methods*. Dr. Rajapakse is a member of the Sri Lanka Association of Advancement of Science (lifetime member); and of the Society for Industrial and Applied Mathematics (SIAM). Locally, Dr. Rajapakse is developing the “The Science of Me” program in the Ann Arbor Public Schools to provide middle school science students an engaging, motivating and authentic experience of science. This program will begin in the summer of 2018.

External Reviewers:

Reviewer A: “Re quality: I can say it is quite different from what others are doing in the field (which I applaud - especially during times when it is becoming increasingly difficult to do different things). Re quantity: from his publication list, he has obviously published a great amount. Re focus: again - clearly focused. Re scholarly impact: he is the only pure mathematician I know that has made any impact on my field.”

Reviewer B: “I have never met an electrical engineer trained in mathematics with Indika’s interest in, and profound knowledge of, nuclear biology. He is a man driven by scientific curiosity....I am convinced that his standing as an international leader in the field will become more and more obvious in the future, when his research concept bears even more fruits.”

Reviewer C: “I want to emphasize that the research of Dr. Rajapakse is extremely significant to a large scientific community....understanding how the genome folds, and how this can be determined by integrating imaging and genomic data is widely believed to be very significant for understanding ow


the genome works in normal and disease states. The work of Dr. Rajapakse makes important contributions to this field and I fully expect that he and his team will continue their very successful trajectory.”

Reviewer D: “Indika has a very challenging research program in that he is working on results in basic mathematics, as well as running a wetlab that does high throughput cell molecular biology. I am very impressed that he can do this, and that he has academically prepared himself to do this. Also obtaining the funding to run such a lab is very challenging, and he has managed so far. He has a solid publishing record in that his publication record since 2015, he has been quality senior author papers in both biology and mathematics venues. This is a solid record considering he started his faculty position in 2013.”

Reviewer E: “With my view from afar, Dr. Rajapakse seems to be rather successful, with a diverse set of publications, including many in top journals. These publications include both theoretical ones and ones focused on data analysis...The diversity of Dr. Rajapakse’s papers and broad range from theory to applications are a major strength.”

Summary of Recommendation:

Dr. Rajapakse’s research is novel, interdisciplinary and growing; it will have a transformative impact on our understanding of the dynamic 3D organization of the nucleus and its connection to biological function. In addition, he is performing groundbreaking mathematical modeling of genome structure and function relationships which promises to shed light on basic developmental and pathophysiological processes. We wholeheartedly recommend Indika Rajapakse Ph.D. for promotion to associate professor of computational medicine and bioinformatics, with tenure, Department of Computational Medicine and Bioinformatics, Medical School, and associate professor of mathematics, without tenure, Department of Mathematics, College of Literature, Science, and the Arts.



Marschall S. Runge, M.D., Ph.D.
Executive Vice President for Medical Affairs
Dean, Medical School

Andrew D. Martin, Dean
Professor of Political Science and Statistics
College of Literature, Science, and the Arts

May 2018