NIH/NIGMS Funding Opportunity and Trainee Forum

Chair:

Professor May D. Wang
Georgia Institute of Technology and Emory University

Co-Chair:

Professor Greg Gibson
Georgia Institute of Technology

Schedule

Time	Speaker	Title
10:00 – 10:40am	**Dr. Greg Gibson**	Genetic and Transcriptional Risk Scores across Environments
10:40 – 11:00am	**Peter Audano**	Alignment-free variant analysis in pathogen surveillance
11:00 – 11:20am	**Ryan Hoffman**	Challenges and Quality When Using Big Data from the Neonatal ICU
11:20 – 11:40am	**Ariel Kniss**	Frequency Response Analysis Approach for Studying Intracellular T Cell Signaling
11:40 – 12:00pm	**Robert Chen**	Computational Phenotyping from Electronic Health Records
12:00 – 12:30pm	**Dr. Veerasamy "Ravi" Ravichandran**	NIH/NIGMS Funding Opportunities In Computational Sciences

Genetic and Transcriptional Risk Scores across Environments

Greg Gibson

Professor, School of Biology, Georgia Institute of Technology

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ABSTRACT

Genome-wide association studies and RNAseq analysis have revolutionized the way we approach the genetics of disease in the past five years. As databases of genetic associations accumulate, genetic risk score (GRS) profiles are being developed in an effort to predict which diseases individuals are at risk for. However, predictive value is constrained by low disease prevalence and environmental modification, so we have become interested in the question of how genetic variants that modify gene expression (eQTL) contribute to pathology and therapeutic response. The notion of a transcriptional risk score (TRS) holds promise, particularly for autoimmune and inflammatory diseases, since RNA profiling of immune cell types is relatively straight forward. I will discuss how GRS and TRS might be used to classify individuals with heterogeneous genetic contributions to disease, modified by lifestyle and environment.

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BIOGRAPHY

Greg Gibson has been Professor of Biology and Director of the Center for Integrative Genomics at Georgia Tech since 2009. After 15 years developing genomic tools for the study of complex traits in Drosophila, his lab now focuses on transcriptomic applications in understanding disease risk. He is the author of two text books of Genomics and Human Genetics, and Section Editor for Natural Variation at PLoS Genetics.

Alignment-free variant analysis in pathogen surveillance

Peter Audano

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ABSTRACT

Modern variant-calling pipelines for next generation sequencing (NGS) data first align sequence reads to a reference. For some bacterial species, hyper-variable regions associated with drug resistance cause alignments to fail, and so variant calling often misses these critical mutations. We are developing a novel alignment-free approach that can find variants in heavily mutated genes as well as identify large insertions or deletions. To date, alignment-free approaches offer only limited variant calling ability, so this work represents a significant leap forward in alignment-free inference. Because it is fast and robust, this software is also being used to replace other alignment-based algorithms and enable rapid bacterial strain-typing. This approach is being developed to support surveillance efforts at the Centers for Disease Control and Prevention (CDC).

BIOGRAPHY

Peter graduated Southern Polytechnic State University in 2008 with a BS in computer science. As a student, he worked full time for Earthlink, Internet Security Systems, and IBM. After graduating from the bioinformatics MS program at The Georgia Institute of Technology, he transitioned to a PhD track. Today, he a bioinformatics PhD candidate under the supervision of Dr. Fredrik Vannberg. Peter is interested in advancing science through bioinformatics and advancing bioinformatics through software engineering. He believes that tools are limited by their ease of use, documentation, and ability to generate meaningful error messages. He hopes to improve the field by setting an example and by creating flexible programs other engineers can utilize to solve new problems of their own.

Challenges and Quality When Using Big Data from the Neonatal ICU

Ryan Hoffman

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ABSTRACT

Health informatics and big data tools and technologies have the potential to revolutionize healthcare practices. Neonatal pain and distress are areas of specific clinical interest and high impact. In adult patients, a self-report is the gold standard of pain assessment. In neonatal patients such a report is not possible, and various pain approximation and scoring systems have been developed to fill this need. These scoring systems are fundamentally subjective, making it desirable to develop systems that can objectively approximate pain and distress. This talk outlines some of the quality control considerations and issues encountered in investigating these data sets, and validating their accuracy for future research reuse.

BIOGRAPHY

Ryan Hoffman is a graduate student in Dr. May Wang's Biomedical Informatics and Bioimaging Laboratory at Georgia Tech. He joined the lab in 2013 after graduating from Georgia Tech with a B.S. in Biomedical Engineering. Since joining the lab, his work has focused on histopathological image processing techniques and critical care health informatics. In the summer of 2014 he interned with Children's Healthcare of Atlanta, gaining experience with the tools, technologies, and challenges of healthcare-related big data at enterprise scale.

Frequency Response Analysis Approach for Studying Intracellular T Cell Signaling

Ariel S. Kniss

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ABSTRACT

T cells, a key component of the adaptive immune response, undergo intracellular Ca^{2+} signaling upon activation with an antigen presenting cell. This Ca^{2+} signaling has been shown to oscillate, with the downstream response dependent on the frequency of signaling[1]. Frequency response analysis, developed in control engineering, is an approach that has been shown useful for understanding other dynamic biological systems[2], but has been previously difficult to apply to suspension T cells. Here we present the use of a microfluidic device[3] for probing intracellular T cell signaling with a range of input frequencies to drive Ca^{2+} signaling, providing a more systematic view of the multifaceted signaling dynamics. Spectral analysis performed on single cell traces[4] reveals heterogeneity in response upon stimulation of Jurkat T cells with 25 μM H_2O_2 at varying frequencies. Specifically, we observe attenuation of T cell signaling with periods below 2 minutes and an optimal gain at the 6 min oscillatory condition. Interestingly, there is also variability within a given experimental condition. Through a frequency response analysis approach, we are able to demonstrate filtering characteristics of intracellular Ca^{2+} signaling in immune T cells. Combined with computational modeling, we aim to extract dominant feedback mechanisms in the complex underlying regulatory circuit.

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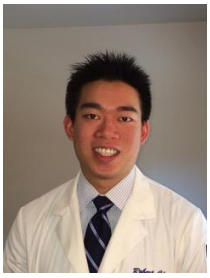
BIOGRAPHY

Ariel S. Kniss graduated from Bucknell University in 2011 with undergraduate degrees in Mathematics and Biology. She is currently working toward her PhD in Biomedical Engineering at Georgia Tech and Emory University in the labs of Dr. Melissa Kemp and Dr. Hang Lu. Her research interests lie in using quantitative analysis methods to interrogate and model biological systems, with the ultimate goal of gaining a more complete view of the underlying network topology. Outside of lab, she enjoys running, hiking, and her newfound hobby, sewing.

References: [1]Dolmetsch R.E., *et al*., *Nature*, (1998). [2]Mettetal, J.T., *et al*., *Science,* (2008). [3]Chingozha, L., *et al.*, *Analytical Chemistry*, (2014). [4]Uhlen, P., *Scence Signaling*, (2004).



Computational Phenotyping from Electronic Health Records

Robert Chen

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ABSTRACT

Phenotyping algorithms describe how to map patients' electronic health records to meaningful clinical concepts. Current phenotyping algorithms are often rule-based, require significant amounts of human supervision, and are difficult to scale. We address these problems by developing automated phenotyping algorithms based upon higher order tensor factorization. We employ various methods to evaluate the meaningfulness and usefulness of these phenotypes via physician surveys and predictive modeling strategies. Further, we develop analytic pipelines and augmented phenotypng methods that allow us to capture important characteristics such as temporal event sequences in patient phenotypes. Finally, we have an ongoing goal of improving the usability of phenotyping algorithms. To this end, we developed automated, cloud-based pipelines that allow clinical researchers and others without extensive programming experience to input data and extract phenotypes and predictive modeling results quickly.

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BIOGRAPHY

Robert Chen is an MD/PhD candidate, working on an MD at Emory University and a PhD in Computer Science at the Georgia Institute of Technology. He earned a BS in Mathematics from the Massachusetts Institute of Technology. He has published several research papers in top venues including Nature Genetics, Nature Protocols, and KDD.

NIH/NIGMS Funding Opportunities in Computational Sciences

Veerasamy "Ravi" Ravichandran, Ph.D.

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BIOGRAPHY

Veerasamy "Ravi" Ravichandran, Ph.D., is a program director in the Division of Biomedical Technology, Bioinformatics, and Computational Biology. He manages research, resource and training grants in the areas of biomedical technology, bioinformatics and computational biology. Ravichandran is also involved in facilitating and coordinating trans-NIH activities related to big data. Earlier in his career, he was a staff scientist at the National Institute of Neurological Disorders and Stroke, a research scientist at the National Institute of Standards and Technology, and an associate research scientist at Yale University School of Medicine and the University of Pennsylvania. Ravichandran conducted postdoctoral research as an IRTA fellow in the NCI Laboratory of Pathology and Experimental Immunology Branch. He earned a bachelor's degree in chemistry, master's degrees in biochemistry and philosophy/clinical biochemistry, and a Ph.D. in biochemistry from the University of Madras in India. Ravichandran also earned a master's degree in computer science and bioinformatics from John Hopkins University and a certificate degree in database development from George Washington University.