



e_Connections

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interview

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Barrett gives talk at international symposium

Many challenges in the area of public policy can be attributed to the complexity of large systems such as transportation systems, electric power markets and grids, the Internet, and public health. These systems consist of many interacting physical, technological, and societal components and the number and variety of parts within these systems makes the evaluation process very difficult. High performance computing capabilities, however, can help researchers better understand these systems and explore the potential impact of different scenarios, which can aid policy makers in their decision-making processes.

According to Barrett, the informatic support needed to better understand these systems must be able to provide:

- representations of the situation
- comparisons to current information
- possible action assessments across possible configurations
- inclusion of multiple stakeholders
- direction for research in both the engineered and natural systems involved
- decision support for policy and operations



Chris Barrett

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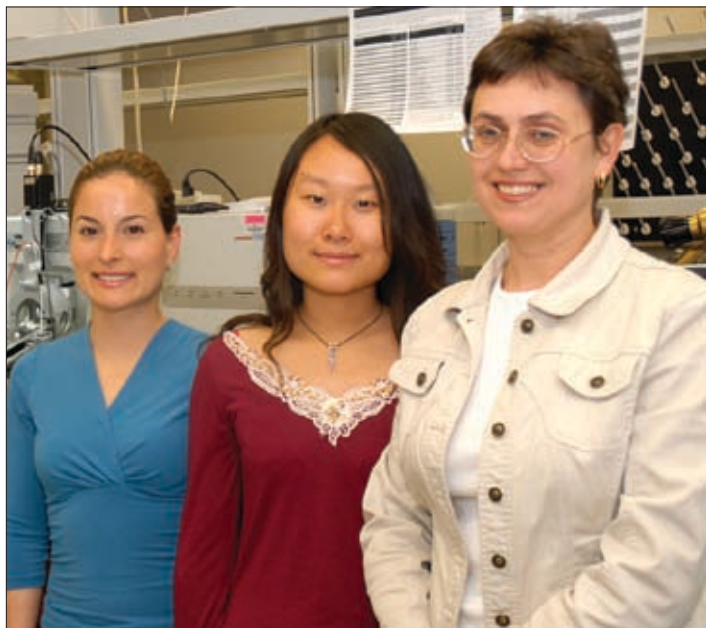
Chris Barrett, professor at VBI and director of the institute's Network Dynamics and Simulation Science Laboratory (NDSSL), outlined an interaction-based approach to the behavioral analysis of some of these large complex systems during a plenary lecture for the Eighteenth International Symposium on Mathematical Theory of Networks and Systems (MTNS 2008) on August 1 on the Virginia Tech campus. In his talk, "Contagion as a Practical Example of Informatic Support of the Analysis of Complex Interdependent Systems," Barrett discussed how computer simulation tools can be used to study these systems and how recent changes in high performance computing have created new ways in which resources can be made available to policy and decision makers to facilitate their work.

Characterizing these systems is very difficult, he explained, because they are highly asymmetric, heterogeneous, and very large. This makes some of the traditional approaches used to examine large systems ineffective. For example, reduced-order modeling tries to break large-scale models into approximate, smaller models that faithfully preserve essential properties of the larger systems. However, this top-down approach can struggle to deal with the complexity of very large systems like countrywide social networks of individuals, the Internet or transportation networks. The size of the systems also warrants a large amount of computation.

Barrett discussed the group's work in infectious disease epidemiology and public health policy to illustrate how high-performance computing is used to analyze complex interdependent systems. He explained the group's process, which begins with activity-based analysis to examine individual-level activities and motives. This allows the group to determine who is where, as well as when and why, which helps in building highly detailed social networks from the bottom up. They first gather information from census data about people in the network, including age, income, and occupation, to determine the composition of different families. Based on these data, the group then creates a synthetic population and uses information from travel surveys to assign motives to members of the population. Once family characteristics and motives have been established, daily itineraries can be created for each synthetic person and NDSSL group members can begin moving them around from place to place.

"This process leads to the creation of social networks and you end up with contact graphs that can be used to measure the structural properties of these networks," Barrett explains. "What we can deliver to policy and decision makers through high performance computing are practicable tools that allow them to test different scenarios and look at potential outcomes."

Invitrogen Spectrometer Donation Helps Student Training



Left to right: Jenny Armenta; Xu Yang; Iuliana Lazar

VBI and Department of Biological Sciences Assistant Professor Iuliana Lazar recently received an equipment donation from Invitrogen to help train undergraduate and graduate students at Virginia Tech, and advance the work of her research group.

The group is setting up the Matrix-Assisted Laser Desorption Ionization - Time of Flight (MALDI-TOF) mass spectrometer, manufactured by Bruker, for the fast analysis of peptide/protein samples. In addition, the MALDI-TOF will aid the implementation of advanced mass spectrometer detection technologies on high-throughput microfluidic chips. Lazar plans to use the donated equipment as a training tool for undergraduate and graduate students in her lab who want to become familiar with the use of mass spectrometry techniques. "Once up and running, this equipment will be a welcome addition to our lab," said Lazar. "Not only will it complement our high-throughput proteomic investigations, but it will serve as a teaching tool, allowing students at Virginia Tech to gain hands-on mass spectrometry experience."

There are many challenges involved in peptide/protein sample analysis, including the complexity of the sample, as well as the wide range of concentrations, low level expression of certain components, dynamic content, and often low availability of final sample for analysis. The sensitivity of measurement offered by mass spectrometry makes it an essential tool in proteomic investigations. Dr. Lazar's research group is interested in developing fully integrated, stand-alone microfluidic devices with mass spectrometry detection for high-

throughput proteomic investigations, as well as bioanalytical strategies for global proteomic profiling of cancer cells and tissues, and microfluidic-mass spectrometric platforms for cancer biomarker discovery and screening.

Kirk Kocan from Invitrogen, added: "Invitrogen Corporation provides products and services that support academic and government research institutions and pharmaceutical and biotech companies worldwide in their efforts to improve the human condition. The company provides essential life science technologies for disease research, drug discovery, and commercial bioproduction."

Invitrogen's research and development efforts are focused on breakthrough innovation in all major areas of biological discovery including functional genomics, proteomics, bioinformatics and cell biology — placing Invitrogen's products in nearly every major laboratory in the world. Founded in 1987, Invitrogen is headquartered in Carlsbad, California, and conducts business in more than 70 countries around the world.

Research Interests of Lazar Group

- Development of fully integrated, stand-alone microfluidic devices with mass spectrometry (MS) detection for high-throughput proteomic investigations
- Development of bioanalytical strategies for global proteomic profiling of cancer cells and tissues: qualitative profiling, differential protein expression analysis, and characterization of post-translational modifications
- Development of microfluidic-mass spectrometric platforms for cancer biomarker discovery and screening

VBI e_Connections

VBI e_Connections is a quarterly publication of the Virginia Bioinformatics Institute produced by the Public Relations team. The newsletter includes feature articles, technology updates as well as interviews that may be of interest to VBI's audiences. Contributions are welcomed.

Please direct submissions to newsletter-editor@vbi.vt.edu
 Newsletter team: Susan Bland: Editor; Barry Whyte: Editor; June Mullins: Graphic design.

For further information, please contact:
 Barry Whyte at Tel: 540-231-1767, email: whyte@vbi.vt.edu
 Website: www.vbi.vt.edu

VBI Study Finds Mitochondrial Mutations More Common Than Expected

NEW YORK (GenomeWeb News) – Mutations in mitochondrial DNA are more common in the general population than previously imagined, according to new research.

In a paper appearing in the latest issue of the *American Journal of Human Genetics*, researchers from the UK and the US looked at the prevalence of ten potentially pathogenic mitochondrial mutations in some three thousand British babies. Their work revealed a larger than anticipated pool of mitochondrial mutations — at least one in every 200 European infants tested carried disease-linked mutations. Now, researchers say, more needs to be done to understand and prevent the transmission of mitochondrial disease.

Mitochondrial diseases, caused by mutations in mitochondrial DNA, can lead to muscle weakness, diabetes, heart disease, stroke, or epilepsy. The symptoms and severity of these diseases vary widely from one individual to the next. Even individuals from the same family, who presumably share mutations, can have different forms of the disease. In addition, the amount of mutated mitochondrial DNA can differ from one cell to the next.

“There’s a lot of variation in how these diseases show up,” co-author David Samuels, a researcher at Virginia Tech’s Virginia Bioinformatics Institute, told GenomeWeb Daily News.

Based on epidemiology and pedigree analyses, researchers previously estimated that roughly one in every 5,000 people has mitochondrial disease. However, this is likely an underestimate, Samuels explained, because the diseases can manifest themselves in so many different ways and the link to mitochondria may not be detected.

Source: GenomeWeb News, August 14, 2008

Peccoud attends DTRA workshop, presents tutorial at systems biology conference



Jean Peccoud

VBI Associate Professor Jean Peccoud attended a workshop organized by the Defense Threat Reduction Agency (DTRA) on August 19 and 20 at the California Institute for Telecommunication and Information Technology (Calit2) at the University of California San Diego (UCSD). “Transdisciplinary Science & Technology for Chem Bio Defense” is part of the NBIC Convergence (NBICC) initiative, which reflects the areas of nanotechnology,

biosciences, information technology and cognitive sciences. The underlying philosophy is that it is within the convergence

of these and other disciplines (transdisciplinary) where radical advances in knowledge will be made. The purpose of the workshop, which was by invitation only and limited to a select group of approximately 40 scientists and engineers, was to assist the NBICC with the development of its Strategic Science Roadmap.

On August 23, Peccoud presented a tutorial on GenoCAD at the 9th International Conference on Systems Biology (ICSB) in Göteborg, Sweden. The tutorial, “Linguistic methods to design and verify synthetic genetic constructs,” gave a short introduction to the theory of formal languages, reviewed common architectures of genetic constructs, and explored a number of issues associated with the development of new grammars for developing genetic constructs for various biological applications. Attendees were also given the opportunity to design new constructs using the user-friendly GenoCAD environment.

VBI Scientific Publications

Characterization of an *Entamoeba histolytica* High-Mobility-Group Box Protein Induced during Intestinal Infection

Abhyankar MM, Hochreiter AE, Hershey J, Evans C, Zhang Y, Crasta O, Sobral BW, Mann BJ, Petri WA Jr, Gilchrist CA

Eukaryotic Cell 2008 July 25 Epub ahead of print PMID: 18658254

The unicellular eukaryote *Entamoeba histolytica* is a human parasite that causes amebic dysentery and liver abscess. Researchers from the University of Virginia and the Virginia Bioinformatics Institute have identified an up-regulated transcript that encodes a putative high-mobility-group box (HMGB) protein, EhHMGB1, by performing a genome-wide analysis of gene expression modulated by intestinal colonization and invasion. The researchers tested if EhHMGB1 encoded a functional HMGB protein, and determined its role in control of parasite gene expression. The study showed that EhHMGB1 is a bona fide HMGB protein with the capacity to recapitulate part of the modulation of parasite gene expression observed during adaptation to the host intestine.



Diego Cortes

Cortes makes the transition from research assistant to postdoctoral work

Diego Cortes, a former graduate student in Virginia Tech's interdisciplinary Ph.D. program in Genetics, Bioinformatics, and Computational Biology (GBCB), is now a postdoctoral researcher in VBI's Biochemical Profiling Research Group.

"At VBI, there are many opportunities to get involved in projects that cross disciplinary boundaries, and to interact on a daily basis with people of different areas of expertise, who can provide valuable input to your research"

The Virginia Bioinformatics Institute's involvement with Virginia Tech's interdisciplinary Ph.D. program in Genetics, Bioinformatics, and Computational Biology (GBCB) has established a very productive relationship between VBI faculty and GBCB students. Through this mutually beneficial relationship, faculty members can connect with students looking for real-life research experiences that complement their academic interests.

This was the path followed by Diego Cortes, who started the GBCB program in 2003 and also became a graduate research assistant for VBI's Biochemical Profiling Research Group. Headed by VBI Associate Professor Vladimir Shulaev, the group uses metabolomics tools based on mass spectrometry as the platform for its research, applying it to functional genomics and systems biology studies. The approach involves the global analysis of all cellular metabolites, which are small-molecule products of the chemical processes occurring in living organisms, and can provide a holistic view of a biological system when combined with gene and protein expression profiling and mathematical modeling. After working in the group for five years and receiving his Ph.D., Cortes decided to stay at VBI to continue his postdoctoral work.

"Only in a few academic institutions in the United States and around the world will someone have the privilege to work with a group of people with such a wide variety of expertise in the life sciences,"

Cortes says when explaining why he decided to continue his professional career at the institute. "Also, I am very excited about the research project I will be working on."

As a postdoctoral researcher in the group, Cortes' work will focus on examining the progression of cancer in human breast epithelial cells to identify the unique metabolic characteristics that differentiate the early stages of malignant cell transformation associated with the progression of malignancy.

"This project is very appealing to me because it combines different areas of knowledge from basic biology, mathematics, and analytical chemistry to medicine and computational biology, and in the long run, drug development and disease treatment," he explains.

This research project differs from his work as a graduate research assistant, which involved characterizing the function of a family of enzymes in *Arabidopsis* at the gene expression and metabolic levels. Specifically, Cortes looked at the SABATH family of methyltransferases, which are responsible for a chemical modification of plant hormones called phytohormones. Phytohormones regulate key processes in plants related to normal growth, development, reproduction, and defense response mechanisms against diseases and other stresses, which highlights the importance of studying this group of enzymes and their effects. While the focus is on *Arabidopsis*, a popular model organism

in plant biology and the first plant to have its genome sequenced, the results will be useful for other plant species with similar processes regulated by phytohormones. Although he is taking on a new project, Cortes will continue this work, which he hopes will help to provide a better understanding of the physiological role of this family of enzymes, further insights into secondary plant metabolism, and more extensive knowledge of the consequences of modulating the expression of SABATH methyltransferases.

According to Cortes, the most important preparation for his current position was the combination of experiences as a student of the GBCB program and as a research assistant at VBI.

"I had the opportunity to interact with students from backgrounds other than molecular biology and genomics, which are my primary areas of training and expertise. While completing my academic coursework in GBCB, I got to exchange ideas, participate in small research projects, and receive input from students and faculty from other areas within the life sciences, and also from computer science, mathematics, and statistics—from many different departments across the campus," he said. "At VBI, there are many opportunities to get involved in projects that cross disciplinary boundaries, and to interact on a daily basis with people of different areas of expertise, who can provide valuable input to your research."