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Message from the President

At Virginia Tech, we believe that collaborative research and discovery advance knowledge and deliver innovation to individuals and communities. By working to break down traditional barriers between research disciplines, we increase creativity and the likelihood of new scientific breakthroughs that will make a real difference to society.

When the Virginia Bioinformatics Institute (VBI) first opened its doors in 2000, our intentions were clear. We wanted to create an environment where collaborative research would become a role model for future initiatives and create an institute that would be able to assume a major role in supporting Virginia Tech's strategy to become one of the leading research universities in the country. These ambitious goals reflected our willingness to take on new challenges and adopt an entrepreneurial approach to life science research.

I am pleased to report that 2007 was a milestone year for VBI. While it is commendable to have ambitious objectives, we need to confirm that we are on-track with our plans, vision and goals. In June 2007, the time was therefore right for the University to conduct an independent scientific review of the institute. We wanted an independent mechanism to evaluate the quality and direction of the research carried out at VBI. We also wanted to explore future opportunities for scientific research, provide an assessment of the institute's ability to compete nationally and internationally, and look closely at VBI's organizational structure in relation to the broader university community.

Four internationally known experts in the fields of biology, bioinformatics, high-performance computing and nanotechnology/engineering and a committee chairperson participated in an extensive review of the institute. On July 2nd, the initial deliberations of the panel were submitted to me, the provost of Virginia Tech and Dr. Bruno Sobral, executive and scientific director of VBI; they have since been formally documented. The panel's findings were persuasive and indicated that VBI has developed strong capabilities and remarkable visibility in a very short time. Different metrics revealed that VBI has demonstrated high quality research and services and successful efforts in talent development. The panel members concluded that VBI is a competitive transdisciplinary research institute that has considerable growth potential within a strong national and international network.

VBI has come a long way in a short time. It is helping Virginia Tech to move forward with its commitment to teaching and learning, research and discovery, and outreach and engagement. We will be working side-by-side with VBI to ensure that this "success story" is given ample opportunities and the right framework to realize its full potential.

Charles W. Steger

Charles W. Steger, Ph.D.
President; Virginia Polytechnic Institute and State University

VirginiaTech
Invent the Future

Letter from the Director

The Virginia Bioinformatics Institute (VBI) was founded in 2000 with the goal of tapping into the convergence of computing and the life sciences. VBI was conceived as an institute where the contributions of scientists from different disciplines would be valued, nurtured and used to develop knowledge in the life sciences as well as deliver new technologies and products that benefit society. In seven years, we have made considerable progress towards these goals and I believe we are building a robust scientific program that focuses on the desired culture of collaborative research.

In June 2007, VBI underwent an extensive, independent scientific review of our research programs. The outcome highlighted the high quality, competitiveness, and significant potential of our research initiatives in bioinformatics, systems biology, high-performance computing and related computational science and information technology. This bodes well for the future of VBI as we use and refine the solid foundation we have established to meet the challenges that lie ahead in the next phase of development.

The past year has seen many healthy advances in our science and research programs. The scientific community is deploying new models, tools and cyberinfrastructure arising from work at VBI in bioinformatics-related research efforts. Our strengths in the study of cellular components, cellular networks and systems biology are helping to build comprehensive models of the ways in which complex biological systems operate at different scales and in different organisms. In complexity science, we are building a portfolio of projects that spans infectious disease epidemiology, public health informatics, social networks, decision-making and computational behavioral economics.

In May 2007, VBI's Core Laboratory Facility completed the largest ever Affymetrix GeneChip® microarray study for a plant experimental system in an academic research setting. Researchers at VBI and other institutions are now probing the massive data sets generated in these experiments in search of crucial information that may help to protect commercially valuable soybean crop from infection and disease. This is one example of how research teams and resources contribute to scientific advances at VBI. You will find more examples in this annual report.

Team-based science is the theme of this year's annual report. It is one of the guiding principles behind the way we do science and provides an ideal opportunity to showcase some of the many exciting research initiatives underway at VBI. I hope it gives you a sense of the breadth and scope of our research undertakings. I would like to thank everyone connected to the institute, past and present, for their contributions to the success of VBI. We can look with confidence towards the future and anticipate further exciting breakthroughs arising from our team-science initiatives.

Bruno Sobral, Ph.D.
Executive and Scientific Director; Virginia Bioinformatics Institute at Virginia Tech

VIRGINIA BIOINFORMATICS INSTITUTE AT VIRGINIA TECH VBI

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2006

July

Computational model simulates AZT metabolism in mitochondria

Guy Cormier named Chief Information Officer at VBI

August

Sequences reveal benign origin of deadly plant pathogens

Faculty member introduces Stress Systems Biology research program at VBI

September

VBI researchers develop disposable, disease-screening microchip

Computer modelers of pandemic flu converge on Blacksburg, Va.

VBI unveils new facility in National Capital Region

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Bluefield State College students and professors receive hands-on training at VBI

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Nobel Laureate keynotes 9th Annual Computational Genomics Conference

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Fungal gene impacts viability of destructive pathogen

Stefan Hoops named SBML Editor

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Potential route to diabetes therapeutics

First Roche GS-FLX™ installed

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Uniform language for describing genes of pathogenic and beneficial microbes

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Rickettsia felis, a cat-flea-borne pathogen, sheds light on Rickettsial evolution

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VBI researchers contribute to new museum exhibit

VBI and the Department of Biological Sciences at Virginia Tech unveil new plant growth facility

May

VBI completes largest ever Affymetrix Gene Chip® plant experiment

Third Security sponsors Virginia Tech iGEM team

VBI and Mayo Clinic awarded $2.4 million from NIH to study chronic rhinosinusitis

June

Galileo Magnet High School students learn about cyberinfrastructure at VBI

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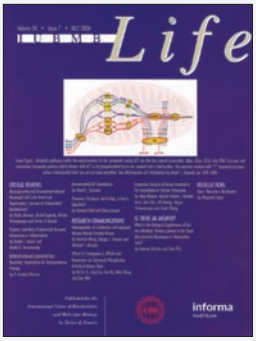


Assistant Professor **David Samuels** and VBI researchers develop a computational model that allows scientists to better understand the metabolism and toxicity of the HIV/AIDS drug zidovudine (azidothymidine, AZT).

Guy Cormier named chief information officer at VBI

Guy Cormier joins VBI as a member of the senior management team with direct responsibility for operations, resources and strategic development of the Core Computational Facility as well as Information Technology support.

August

Faculty member introduces Stress Systems Biology program at Virginia Bioinformatics Institute

Dr. **Andy Pereira** joins the Virginia Bioinformatics Institute. Dr. Pereira's research at VBI looks at how plants respond to environmental stress in particular identifying the genes and mechanisms involved in this often complex relationship. Pereira's work at VBI provides valuable information on how different plant species adapt to cope with severe, external influences, such as drought and disease.

Sequences reveal benign origin of deadly plant pathogens

An international team of researchers publishes the draft genome sequences of two deadly plant pathogens, *Phytophthora ramorum* and *Phytophthora sojae*. *P. sojae* causes severe damage in soybean crops and results in $1–2 million in annual losses for commercial farmers in the United States. *P. ramorum*, which causes sudden oak death, has attacked and killed tens of thousands of oak trees in California and Oregon.

September

VBI researchers develop disposable, disease-screening microchip

Researchers at VBI develop a disposable microchip that replaces space-consuming instrumentation with fast, cost-effective, lab-on-a-chip technology. The microfluidic device is suitable for large-scale screening of disease-related biomarkers. Protein biomarkers are useful as "molecular indicators" for a wide range of diseases including breast cancer.

Computer modelers of pandemic flu converge on Blacksburg, VA

MIDAS Models of Infectious Disease Agent Study

VBI hosted a workshop on modeling emerging infectious diseases as part of the **Models of Infectious Disease Agent Study** (MIDAS) project. The workshop brought together leading experts and decision makers from academia, national laboratories, and governmental agencies. MIDAS is a research partnership with a mandate to develop computational models to assist policy makers, public health workers and other researchers in making better-informed decisions about natural or intentionally caused disease outbreaks.

VBI unveils new facility in National Capital Region

VBI opens a new office complex in the **National Capital Region**. The new Facility, which is located in Virginia Tech's National Capital Region offices on King Street, Alexandria, Va., is the first step in a strategic move to build a larger presence in the greater Washington, D.C. area. The offices and resources expand the research, development and outreach activities of the institute.

October

Bluefield State College students and professors receive hands-on training at Virginia Bioinformatics Institute

Professors and students from **Bluefield State College's** introductory cyberinfrastructure course visit VBI as part of a field trip designed to give the students an opportunity to learn more about cyberinfrastructure environments and the Institute's commitment to team science. The four professors for the class, along with seven students, were given a tour of VBI facilities, an overview of the Institute from VBI's Executive and Scientific Director Bruno Sobral, and a chance to interact with VBI scientists while participating in several cyberinfrastructure team modules.

November

Nobel Laureate keynotes 9th Annual Computational Genomics Conference

Barry Marshall, 2005 Nobel Laureate, is the keynote speaker at the Ninth Annual Computational Genomics Conference in Baltimore, Md. At the conference, an international group of scientists came together to discuss some of the latest cutting-edge developments in computational biology and bioinformatics. VBI Deputy Director João Setubal and Executive and Scientific Director Bruno Sobral chaired the conference, which included 122 attendees and featured 24 oral presentations and 60 poster presentations. The conference was sponsored by VBI, The Jackson Laboratory, The Institute for Genomic Research, the National Human Genome Research Institute, the National Science Foundation, and Virginia Tech.

December

Fungal gene impacts viability of destructive pathogen

Scientists at VBI and Duke University Medical Center have pinpointed a fungal gene that appears to play an important role in the development and virulence of *Alternaria brassicicola*. *A. brassicicola*, a destructive fungal pathogen that causes black spot disease on most cultivated Brassica crops worldwide, results in considerable leaf loss in many economically important crops including canola, cabbage and broccoli. Sensitivity to spores of *Alternaria* species is also clinically associated with human respiratory disorders such as allergy, asthma and chronic sinusitis.

Stefan Hoops named SBML Editor

Stefan Hoops, computational systems biologist at VBI, is named an SBML (Systems Biology Markup Language) Editor by the SBML community. In this position, Hoops helps manage the overall SBML development process, which leads to new editions of the language. SBML is a computer-readable format for describing qualitative and quantitative models of biochemical reaction networks. It can also be used to express gene regulatory networks and other phenomena of interest in systems biology.

Highlights

2007

January

Potential route to diabetes therapeutics

Work in the laboratory of VBI Assistant Professor **Biswarup Mukhopadhyay** provides important information for researchers designing drugs for type 2 diabetics. The research, which was published in the *Journal of Biological Chemistry**, should in time help researchers to identify potential targets for docking inhibitors that will slow down, but not fully eliminate, the body's overproduction of glucose.

** Christopher L. Case, Edward M. Concar, Kristin L. Boswell, & Biswarup Mukhopadhyay (2006) Roles of Asp[75], Asp[78], and Glu[83] of GTP-dependent phosphoenolpyruvate carboxykinase from Mycobacterium smegmatis. Journal of Biological Chemistry 281(51): 39 262–39 272.*

First Roche GS-FLX™ installed at VBI Core Laboratory Facility

VBI announces the first **Roche GS-FLX™** installation at its Core Laboratory Facility on the Virginia Tech campus. The Roche GS-FLX™ is a next-generation genome sequencing system that takes advantage of 454 Life Sciences™ revolutionary sequencing technology and allows researchers to go from genome to sequence in record time.

February

Uniform language for describing genes of pathogenic and beneficial microbes

An international group of scientists announces a major expansion of a lingua franca used to describe the activities of genes in living organisms. The expansion provides terms that scientists can use to describe the complex events that occur when a pathogenic or beneficial microbe encounters its host. Understanding these events is crucial for developing new interventions for preventing infections by disease-causing microbes while preserving or encouraging the presence of beneficial microbes.

March

Rickettsia felis, a cat-flea-borne pathogen, sheds light on Rickettsial evolution

VBI researchers in collaboration with scientists from the University of Maryland School of Medicine create a new classification system for rickettsia bacteria that may assist researchers in the way they approach the development of diagnostics and vaccines for the virulent rickettsial pathogens. Some species of *Rickettsia* are known to cause harmful diseases in humans, such as epidemic typhus (*R. prowazekii*) and Rocky Mountain spotted fever (*R. rickettsii*), while others have been identified as emerging pathogens and critical agents for the development of bioweapons.

April

VBI researchers contribute to new museum exhibit

Stephen Eubank, deputy director of the Network Dynamics and Simulation Science Laboratory (NDSSL) at VBI, and **Bryan Lewis**, NDSSL graduate student, contribute to the development

of a visualization display for a new museum exhibit that focuses on infectious diseases. The display was on show to the general public at the Marian Koshland Science Museum of the National Academy of Sciences in Washington, D.C.

VBI and the Department of Biological Sciences at Virginia Tech unveil new plant growth facility

VBI, in collaboration with the Department of Biological Sciences at Virginia Tech, announces the opening of the Biological Sciences-VBI Plant Growth Facility. The 3,240-square-foot plant growth facility has been designed as a university service center and will operate on a cost recovery basis.

May

VBI completes largest ever Affymetrix GeneChip® plant experiment

VBI completes the largest ever **Affymetrix GeneChip®** microarray study for a plant experimental system in an academic research setting. The 2600-chip experiment explores the counter-play of plant and pathogen genes during infection of soybean with the root-rot pathogen *Phytophthora sojae*, with a focus on mechanisms of long-lasting disease resistance. *P. sojae* causes severe damage in soybean crops and results in $100-200 million annually in losses for commercial farmers in the United States alone.

Third Security sponsors Virginia Tech iGEM team

THIRD SECURITY, LLC

Third Security, LLC, a private equity and venture capital firm, sponsors a team of Virginia Tech students taking part in the 2007 **International Genetically Engineered Machines** (iGEM) competition. The funds provided by Third Security help support laboratory work by Virginia Tech's team of undergraduate students, as well as their participation in iGEM's annual jamboree.

VBI and Mayo Clinic awarded $2.4 million from NIH to study chronic rhinosinusitis

VBI and Department of Biological Sciences Associate Professor **Chris Lawrence** teams up with Mayo Clinic on a $2.4 million project funded by the National Institute of Allergy and Infectious Diseases (NIAID), a division of the National Institutes of Health (NIH). The work could help researchers develop treatments, diagnostic tools, and preventative measures for patients suffering from chronic rhinosinusitis (CRS). CRS is a debilitating chronic airway disease that results in up to 18–22 million clinical cases per year and at least 30 million courses of antibiotic treatment (National Center for Health Statistics).

June

Galileo Magnet High School students learn about cyberinfrastructure at Virginia Bioinformatics Institute

Students enrolled in **Galileo Magnet High School's Microbial Genomics** course visit VBI with their instructors to learn more about the institute's cyberinfrastructure work and present findings from their final exam projects.

Focus on Team Science

- Reverse Engineering Yeast
- Partnering With Clinical Researchers

Over the years, the Virginia Bioinformatics Institute has performed according to the visions and goals that were put in place when the institute was founded in 2000. VBI continues to make major contributions to the scientific community and society at large based on credible research initiatives and sound science. The Institute's emphasis on team science allows researchers to go beyond their own disciplines and expertise in search of new organizational structures. This flexible, team-based approach to science brings unforeseen benefits, drives innovation and helps to deliver real breakthroughs that improve the quality of human life.

"Transdisciplinary research is the foundation of the Virginia Bioinformatics Institute. Our achievements arise from a collaborative culture geared to stimulate creativity and generate innovation. It is this culture that allows us to make significant contributions to the development of life science knowledge, technologies and useful products aimed at society's needs."

Bruno Sobral,
Executive and Scientific Director

in focus

Team Science

Reverse Engineering Yeast

For such a large-scale project, you need a team science approach to do this right, where each member of the team is involved in the experimental design and implementation from day one

In 2003 VBI Yeast Systems Biologist Ana Martins joined a small collaborative research team at VBI to investigate the effects of oxidative stress on *Saccharomyces cerevisiae*, or baker's yeast, a common model system that may be used to study human disease. Over the past three years, Martins has watched the team evolve and the work progress, as three of the Institute's research groups worked together to uncover the impact of oxidative stress on biological systems.

Reactive oxygen species (ROS) are a byproduct of the metabolism of oxygen. When exposed to environmental stress, ROS levels in organisms increase, leading to cell damage. This is oxidative stress, a process that has been linked to Parkinson's and Alzheimer's diseases and which seems to also play a role in the aging process.

VBI Professor Reinhard Laubenbacher, Associate Professor Pedro Mendes, and Associate Professor Vladimir Shulaev are using a systems biology approach to study the oxidative stress response in yeast. The group uses yeast because its mechanisms of protection against the damaging effects of ROS are very similar to those used by the human body. Their goal is to build a systems level picture of the response of yeast to perturbations (stress) and to infer how the system is organized internally, a process known as "reverse-engineering". This is achieved by developing new experimental techniques, generating large data sets and creating mathematical models that can describe the behavior of the system.

Harvesting Data: OMICS style

Data are needed before models can be developed, however. The three groups at VBI—Laubenbacher's Applied Discrete Mathematics Research Group, Mendes' Biochemical Networks Modeling Group, and Shulaev's Biochemical Profiling Group—worked together to design experiments that would generate genomic, proteomic, and metabolomic data sets to uncover critical information about the yeast regulatory network involved in the oxidative stress response. The use of mathematical and computational methods to help design the experiments was an important characteristic of the systems biology approach to the project. Martins worked with all of the research groups to help coordinate efforts and knew that the first steps were some of the most important.

"Designing the experiments was key," she explained. "The input of biologists, statisticians, and computer modelers was crucial at the beginning of the project to make sure that the experiments were set up properly. For such a large-scale project, you need a team science approach to do this right, where each member of the team is involved in the experimental design and implementation from day one."

Martins was responsible for overseeing the sample collection process once the experimental design was complete. With meticulous measurements needed - some being taken every three minutes—she knew she needed help from several people. Some members of the team that typically weren't involved in lab work, such as mathematicians from Laubenbacher's group, volunteered to help with the process.

After sample collection was finished, metabolomics profiling was performed by Shulaev's group using mass spectrometry technologies. VBI's Core Laboratory Facility (CLF) completed gene expression profiling on the samples and is working with Leepika Tuli, a Ph.D. student in Shulaev's group, on the proteomics profiling using two-dimensional gel electrophoresis.

"Not only did we have all the project's team members under the same roof, but we were able to use VBI's CLF to generate our data," said Martins. "Not many researchers can just walk down the hall to drop off samples or check on the progress of their microarrays. We have that convenience here thanks to our Core Lab Facility."

Wei Sha, a former VBI Ph.D. student who worked on the project, handled the statistical analysis of the microarray data generated from the CLF, while Martins focused on analyzing the data from a biological perspective. One invaluable tool used for this work was DOME, a relational database system developed by the Mendes research group that provides a way to link data from molecular profiling and allows statistical analyses across various data types.

After seeing the project evolve from experimental design to data analysis, Martins is pleased with the direction the team's work is headed. "I think the work offers a whole new resource to the scientific community interested in oxidative stress and its link to disease," she explained. "Yeast is a model organism where you can extrapolate to many human genes, proteins and metabolites and it's well suited to systems biology. We're only at the beginning of understanding the impact of stress conditions on human disease but this work provides a useful framework that will be built upon by other scientists down the line."

The Team

Three research teams at VBI are working together to investigate the effects of oxidative stress on *Saccharomyces cerevisiae*, or baker's yeast, a common model system that may be used to study human disease

Dr. Vladimir Shulaev, Biochemical Networks Modeling Group

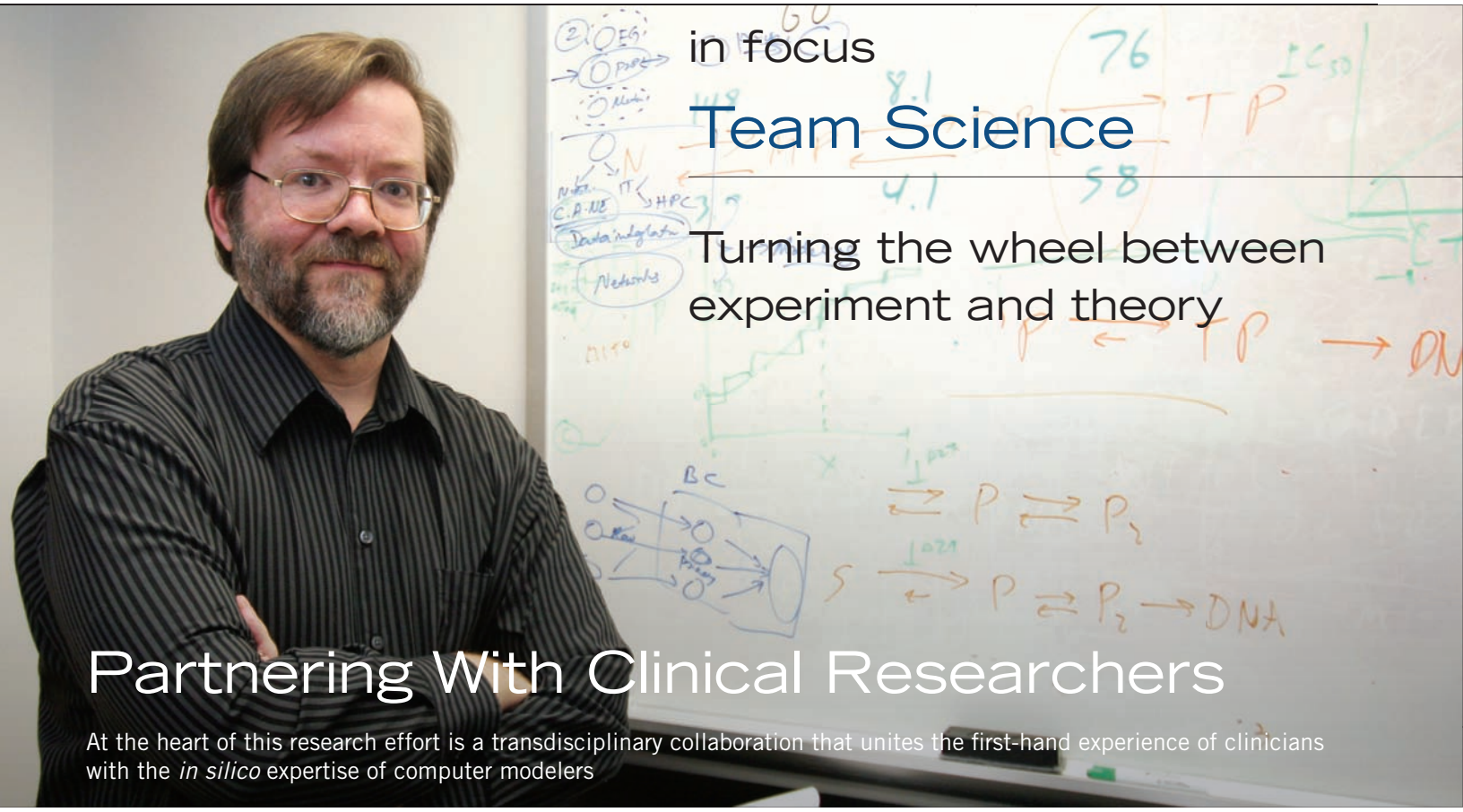
Develops metabolomics technology and applies high-throughput metabolite profiling to study the oxidative stress response in plants and yeast and other microrganisms, specifically using mass spectrometry-based analytical techniques

Dr. Pedro Mendes, Biochemical Networks Modeling Group

Develops computational tools to study biochemical networks. Biochemical networks are central to biological function and computer modeling helps to understand how these networks operate

Dr. Reinhard Laubenbacher, Applied Discrete Mathematics Research Group

Develops methods to create top-down models of biological systems using discrete mathematics. Applies mathematical models to genomics, proteomics, and metabolomics data



in focus

Team Science

Turning the wheel between experiment and theory

Partnering With Clinical Researchers

At the heart of this research effort is a transdisciplinary collaboration that unites the first-hand experience of clinicians with the *in silico* expertise of computer modelers

For Dr. David Samuels' research group, turning the wheel between experiment and theory depends on having a very close-knit collaboration between clinicians and computational biologists. "We build theoretical models based on clinical data, use the modeling results to design and carry out new experiments, and apply the information gleaned to refine our models and make further scientific discoveries. It's a fully integrated process that demands a close working relationship between experimentalists on the one hand and those making the computational models on the other." He adds: "In one of our research projects, we are using this type of approach to dissect some of the key metabolic events in mitochondria. When mitochondrial metabolism goes off course, the results can be devastating with severe clinical repercussions."

Mitochondrial Dysfunction

Mitochondria are the "engines" present in each cell that produce adenosine triphosphate (ATP), the key energy currency that drives metabolism. Mitochondria also have their own DNA (mitochondrial or mtDNA) that encodes a small but essential number of proteins required for energy production in cells. The synthesis of mtDNA is carried out by a series of reactions that take place in the mitochondria. However, the enzymes that support these reactions are all encoded in the nuclear DNA. When these nuclear genes are disrupted, the results can be devastating and lead to either the depletion or enhanced mutation of mtDNA. These molecular changes result in loss of cell function or cell death, which in turn may lead to several debilitating neuromuscular diseases (see box, page 15).

Dr. Samuels comments: "*POLG*, for example, is a nuclear gene that codes for the polymerase gamma enzyme. Mutations in the *POLG* gene have recently been identified as a major cause of neuromuscular disease. They cause the loss of mtDNA or result in multiple secondary mutations of mtDNA. Secondary mutations include either changes in a single base or the removal of a large segment of the mtDNA. The net result of these mutations is that the mitochondria's ability to produce ATP is undermined, leading to cellular dysfunction and cell death."

Some of the genetic diseases that result from mitochondrial dysfunction are often fatal in early childhood. The metabolism supporting mtDNA replication is also altered in ischemia and cancer, two health problems that have a wider impact in the general population. Dr. Samuels and collaborators are developing computational models that can be applied to these genetic diseases. The computational models will allow the researchers to more easily navigate between experimentation, data acquisition, analysis and the generation of new hypotheses.

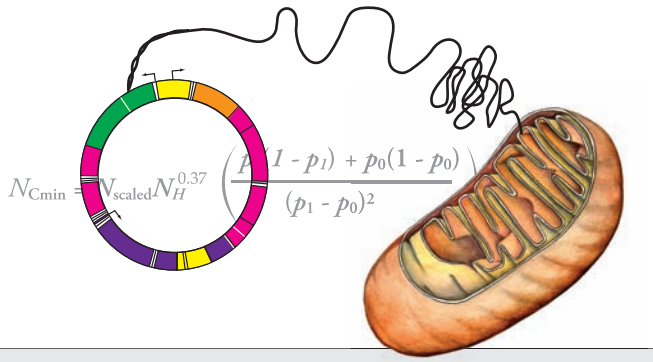
Transdisciplinary Team

At the heart of this research effort is a transdisciplinary collaboration that unites the first-hand experience of clinicians with the *in silico* expertise of computer modelers. Patrick Chinnery, Wellcome Senior Fellow in Clinical Science and Professor of Neurogenetics at the University of Newcastle in the United Kingdom, leads the project's effort to provide experimental clinical data. "These diseases affect at least 1 in 5000, which means over 50 000 patients in the United States alone. At present we have no effective treatment, so we desperately need to understand the underlying disease mechanisms." He adds: "Mitochondrial biology is complex, making it very difficult to see the wood for the trees - especially when it comes to biochemical and genetic data collected from patients around the world. The computational approach developed by Dr Samuels and colleagues has helped us to see patterns where previously we saw noise. This has guided experimental work in new directions, and together we are starting to solve some of the major issues that face the field. I believe that this work will have a major impact on clinical practice in the near future."

Members of the international community of clinicians and research scientists interested in polymerase gamma and mitochondrial DNA replication met in September 2007 for an international workshop in Naarden, The Netherlands. The 154th European Neuromuscular Centre Workshop entitled "Disorders of mitochondrial DNA synthesis: understanding the complex relationship between genotype and phenotype" brought together 23 physicians and scientists to develop new collaborations and report on the current status of efforts to understand the underlying disease mechanisms. The group hopes to establish a gold-standard on-line mutation database, a control sequence database, as well as a patient register for future clinical trials. The goal of this initiative is to improve the diagnosis and treatment of patients who carry *POLG* mutations.

Participants at the 154th European Neuromuscular Centre Workshop, Naarden, The Netherlands

For treatments to be developed, researchers will have to understand in greater detail the molecular events that lead to the different forms of neurological disease. By closing the gap between experiment and theory, the work of Dr. Samuels and colleagues should allow researchers to design new experiments that investigate how these diseases arise and progress. An increased understanding of pathogenesis should in time deliver benefits to researchers, clinicians and their patients.



Disorders of mitochondrial DNA synthesis. Several distinct diseases of mitochondrial dysfunction have been identified that are linked to changes in mitochondrial DNA. These diseases, which have different symptoms, appear to have different causes at the molecular level. The precise disease mechanisms remain to be established.

Mitochondrial DNA depletion syndromes

- Slow, progressive mitochondrial disorders that start in childhood and are associated with reduced cellular levels of mitochondrial DNA
- Often presents itself in infancy with kidney failure, myopathy (muscle weakness), decreased muscle tone, hypoglycemia (low glucose levels), and lactic acidosis (accumulation of lactic acid) as symptoms
- In severe cases lead to early death in infants

Autosomal dominant and recessive progressive external opthalmoplegia

- Progressive external opthalmoplegia are characterized by multiple mitochondrial DNA deletions in skeletal muscle
- The most common clinical features include adult onset of weakness of the external eye muscles and exercise intolerance. Additional symptoms may include, but are not limited to, cataracts and hearing loss
- Both autosomal dominant and autosomal recessive inheritance can occur

Mitochondrial neurogastrointestinal encephalomyopathy

- Rare autosomal recessive neurologic disorder characterised by multiple mitochondrial DNA deletions
- Recurrent nausea, vomiting, or diarrhea amongst the symptoms

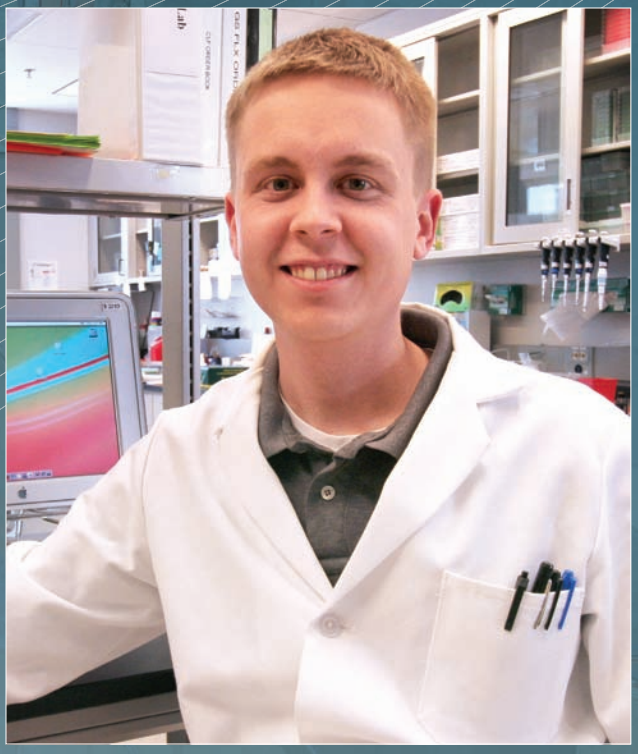
Resources and People

- Core Facilities
- Administration and Finance
- Public Relations
- Education and Outreach
- Science In Focus

The Virginia Bioinformatics Institute offers essential key services for clients at universities, institutions, and private sector companies around the globe. The Institute's resources are a unique feature of VBI's infrastructure. By integrating multi-user resources, VBI's core facilities combine high-throughput data generation from the Core Laboratory Facility with the data analysis capabilities of the Core Computational Facility. Resources and people are combined in a team-based approach to deliver the highest possible quality of service.

"At VBI, we offer a full range of core resources that are designed to enable collaborative, team-based science. VBI's Core Laboratory Facility, for example, caters to the development and application of a wide range of high throughput technologies that represent state-of-the-art approaches to life science research."

Adam Jerauld, Genomics Specialist,
Core Laboratory Facility



Core Laboratory Facility

The Core Laboratory Facility functions as a multi-user resource dedicated to the development and application of high-throughput technologies

The Core Laboratory Facility (CLF) at the Virginia Bioinformatics Institute (VBI) functions as a multi-user resource dedicated to the development and application of various high-throughput technologies that aid in the discovery and analysis of biological macromolecules. Over the past year, the Core Laboratory Facility (CLF) at VBI continued to develop and expand the range of high-throughput technologies it offers to customers in the global life science community (see box on page 19).

First GS-FLX™ installed at VBI

In January 2007, the CLF announced that the first Roche GS-FLX™ was installed in its laboratory on the Virginia Tech campus. The Roche GS-FLX is a next-generation genome sequencing system that takes advantage of 454 Life Sciences™ revolutionary sequencing technology and allows researchers to go from genome to sequence in record time. The sequence of a typical bacterial genome can be obtained in days with one person and one instrument without the need for cloning and colony picking.

The Roche GS-FLX brings a new dimension to VBI's large-scale DNA sequencing capabilities. The addition of the Roche GS-FLX allows researchers to accurately sequence more than 100 megabases (million bases) per 7-hour run and achieve read lengths of 200 base pairs or greater. This translates into a cost-effective, high-performance solution with many applications. Beyond genome sequencing, the GS-FLX will also offer applications such as the sequencing of transcriptomes, clinical samples, paired-end amplicon sequencing, and other cutting-edge uses of the technology and services.

Acquisition of the equipment was made possible through Virginia's Commonwealth Research Initiative. The Commonwealth Research Initiative has been put in place to help universities build their research capacities and stimulate economic development.

Largest ever Affymetrix GeneChip® microarray plant study

In May 2007, the CLF completed the largest ever Affymetrix GeneChip® microarray study for a plant experimental system in an academic research setting. The 2600-chip experiment explores the counter-play of plant and pathogen genes during infection of soybean with the root-rot pathogen *Phytophthora sojae*, with a focus on mechanisms of long-lasting disease resistance.

P. sojae causes severe damage in soybean crops and results in $100-200 million annually in losses for commercial farmers in the United States alone. The GeneChip experiment is part of a project aimed at understanding and improving a more long-lasting form of disease resistance called quantitative or multigenic resistance.

The CLF was able to successfully complete the data generation stage for this 2600-chip experiment within a six-month period. This was possible due to a highly effective collaboration between the research scientists and the ability of the team to scale-up its array processing capabilities. The Affymetrix GeneChip® microarrays used in the study comprised probes for 38 000 soybean genes and 15 800 *P.sojae* genes. The productivity of the CLF's Affymetrix processing was increased four-fold to accommodate the scale of the project.

The Affymetrix microarray experiment combines two approaches, transcriptional profiling and quantitative trait locus (QTL) mapping. These approaches are well suited for dissecting complex biological processes that involve the interactions of many genes. The information obtained from this study will be valuable for understanding how legumes may be protected from a wide variety of pathogens, and how many hosts may be protected against oomycete pathogens. With the massive data set from the CLF now in hand, the data-analysis phase of the project has begun.

The project is supported by cooperative agreement DBI-0211863 from the National Science Foundation Plant Genome Research Program. The project is a multidisciplinary collaboration involving Brett Tyler (VBI), Saghai Maroof (Department of Crop and Soil Environmental Sciences, Virginia Tech), Ina Hoeschele (VBI), Anne Dorrance (Ohio State University) and Steve St. Martin (Ohio State University).

Services available at the Core Laboratory Facility.

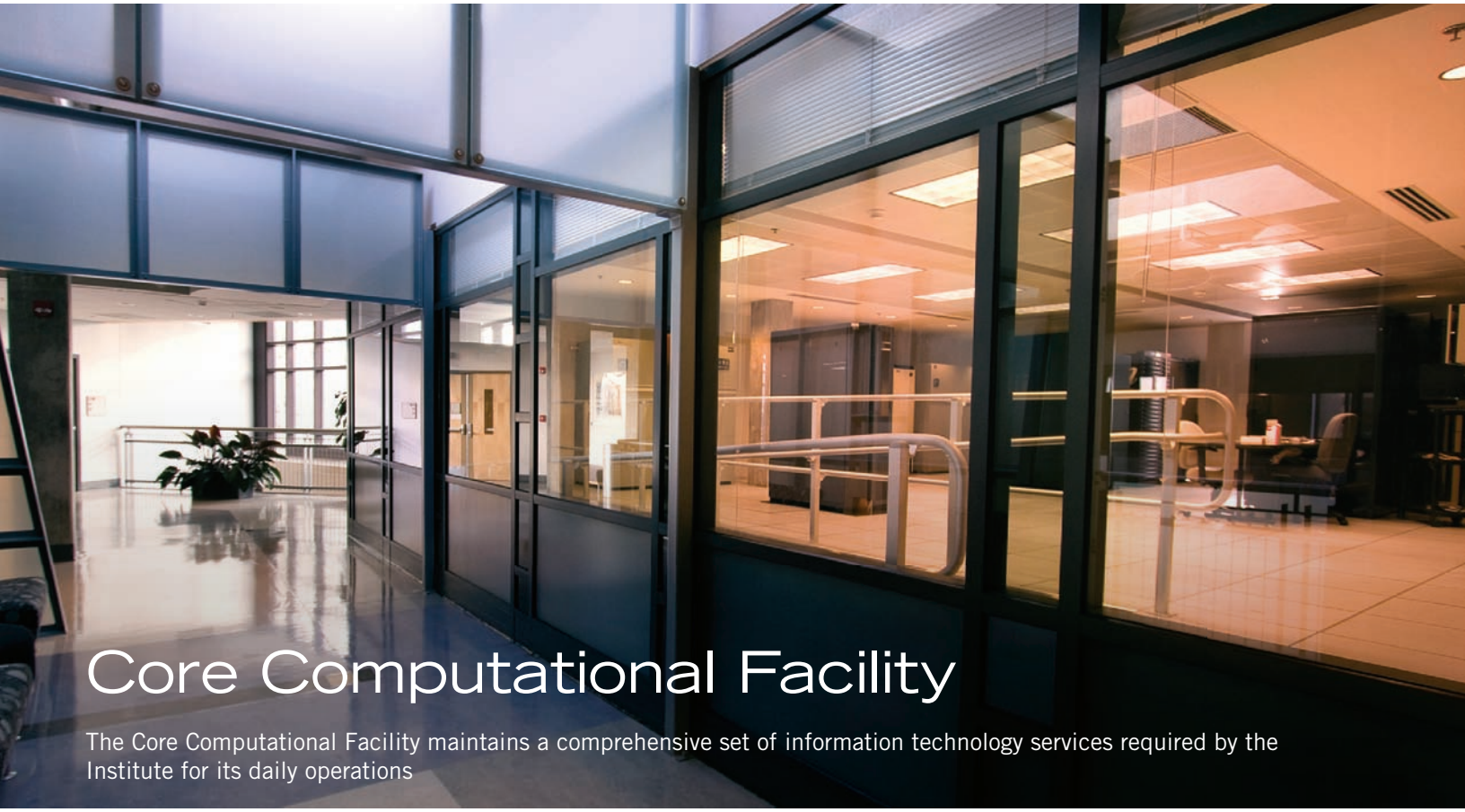
VBI's Core Laboratory Facility (CLF) currently provides analysis platforms for DNA (sequencing and genotyping), RNA (gene expression analysis) and proteins (proteomics). It also offers a selection of molecular biology applications (colony picking, cloning, DNA/RNA isolations). The CLF is supported by a custom Laboratory Information Management System (LIMS), designed and built by GraphLogic, Inc. of Branford, Connecticut, that provides an easy-to-use, secure interface for sample submission and data retrieval. The CLF is also actively engaged in the development and testing of new technologies as needed.

Currently available services include:

- DNA Sequencing
- GS-FLX Sequencing
- Robotics
- Molecular Biology
- Genotyping
- Gene Expression Analysis
- Proteomics

Details and additional information are available at https://www.vbi.vt.edu/core_laboratory_facility

Left to right: Roderick Jensen, Kristin Lee, Adam Jerauld, Kristal Cooper, Megan Ferringer Blauvelt, Clive Evans



Core Computational Facility

The Core Computational Facility maintains a comprehensive set of information technology services required by the Institute for its daily operations

Information Technology at VBI is omnipresent and supports all aspects of the research and administrative enterprises. The Information Technology Group at VBI is charged with defining, maintaining, and improving information technology services and the underlying infrastructure using an efficient, secure and sound approach. The infrastructure is built to be scalable and adaptable, enabling the many applications required to meet VBI's research and business needs. The Core Computational Facility (CCF) is an integral part of these undertakings, comprising a cost-recovery service center providing access to computational services and infrastructure that sustain the scientific projects conducted at VBI.

Information technology services and support

The Information Technology Group maintains a comprehensive set of information technology services required by the Institute for its daily operations. These services include the hosting of the Institute's websites (for example www.vbi.vt.edu), email and calendaring systems, instant messaging environment, and an enterprise wiki, amongst others. All desktop platforms are fully supported and a helpdesk is available that ensures quality services are provided and strong customer relationships are formed and maintained.

VBI's Core Computational Facility (CCF) mission is to:

- Provide, support and facilitate access to research computing and communications resources that enhance the productivity and competitive advantage of researchers at VBI
- Enable VBI researchers to accelerate the rate of scientific breakthroughs
- Enable transdisciplinary and collaborative research between VBI researchers and their peers at other research institutions
- Facilitate the efficient use of information technologies by providing training, outreach, and consulting in the use of computational hardware and software resources.

Videoconferencing – Access and InSors Grid

The videoconferencing resources at VBI's main facility in Blacksburg, Va., and its satellite office space in Alexandria, Va. (National Capital Region location), provide videoconferencing capabilities for VBI's research community. The resources can be used to view or broadcast presentations and conduct real-time conferencing between two or more sites. Providing flexibility, convenience and speed of communication across distances, the Access and InSors technologies are critical enabling factors within the VBI facility. The Access Grid room at VBI can accommodate the multimedia viewing and conferencing needs of individuals or groups. The installed technologies offer the flexibility to adapt the environment to serve a wide variety of remote site connectivity requirements. Accompanied by a professional and knowledgeable staff, the VBI Access Grid facility delivers efficiency, progress, and productivity for the research and business needs of its clients.

VBI's videoconferencing resources

The Core Computational Facility

The CCF is the data management and analysis machine of VBI. The CCF provides high-performance and high-throughput computing resources to support computational sciences, data mining, and access to a wide range of biological applications. The services currently offered by the CCF include computational processing, compound services (scientific analysis applications via webservices, website hosting), database and system administration, as well as data storage and archiving. These services are designed to assist researchers in the study of large-scale biological systems involving genes, proteins, and their interactions, as well as metabolic networks (systems biology).

Two large multiprocessor servers are at the center of the CCF's computational processing capabilities – a Sun Enterprise 15000 and an IBM Power 4 cluster. Comprehensive data backup and recovery systems guarantee the integrity and availability of CCF services. An IBM Storage Area Network (SAN) provides over 35 terabytes of combined disk and tape storage, including an off-site copy for added security.

The CCF uses gigabit Ethernet as its communication backbone and has a dedicated, scalable, and high-speed connection to the Internet, Internet2 and the National Lambda-Rail networks. Recent additions to the CCF continue to strengthen the Core Facility's best-in-class capabilities. Currently, the principal database platform supported by the CCF is Oracle, but access to MySQL and PostgreSQL are also supported. The CCF also provides production hosting of servers, websites and web-based applications.

The Team

A professional team of information technology specialists and managers provides timely and knowledgeable support and services. The team, which supports the research and administrative missions of the Institute, is divided into three sections: System Administration; Desktop Support; and Application Development. Two experienced managers, the Chief Information Officer and the Information Technology Production Lead, guide the group. There is significant overlap between the three sections which ensures that communication channels are open and that the right expertise is applied quickly to all information technology-related projects. Security is a major focus within the team to protect the Institute's information technology infrastructure and ensure the integrity of information. This work is carried out in collaboration with peers at Virginia Tech and other organizations such as the SANS Institute, Internet2 and Educause.

Left to right, back row: Willie Shank, Dominik Borkowski, Jeremy Johnson, David Bynum, Doug McMaster, Mark DiFilippo, Guy Cormier
Front row: Sally Waldon, Clark Gaylord, Dustan Yates, Zeb Bowden, Anthony Robinson, Rik Obiso

Administration and Finance Team

The groups that comprise VBI's Administration and Finance Team internally support the research mission of the Institute by providing administrative support, business services, financial reporting, facilities services, human resources, and grants and contracts management.

Administration

VBI's Administrative Team provides a solid infrastructure for the Institute's dynamic research environment, allowing for continued growth and success. The team maintains a strong foundation for the Institute, overseeing a wide variety of functions central to the operation of the Institute. The members of the team provide general support for VBI faculty and their research groups and apply their expertise to many areas, including administrative assistance, financial management, and human resources.

Left to right, back row: Emily Berisford, Jim Walke, Shannon Worringham, Lauren Coble, Renee Nester, Jodi Lewis
Front row: Betsy Williams, Kim Borkowski, Bruno Sobral, Otto Folkerts, Joyce Randall

not pictured: Carol Volker, Jodi Lewis

Facilities	Finance	Grants and Contracts	Human Resources
Space configuration	Financial and support services	Research and identify funding opportunities	Staff recruitment
Design, construction, renovation, operation, and maintenance of facilities	Accounting	Secure funding for VBI research projects	Employee relations
	Financial reporting	Writing, editorial and graphic design support	Resource planning
	Purchasing	Financial reporting and coordination services	
	Invoice processing	Post-award reporting and coordination	
	Account reconciliation		

Facilities

Left to right: Eric Sheppard, Linda Correll, Wilson Barnes, Susan Huckle, Sheryl Locascio, David Gibbs

Finance

Left to right, back row: Kelly O'Rourke, Mary Smith, Alesha Johnson, Deb Williams, Stacey Walton, Shelana Ryan

Grants and Contracts

Left to right, back row: Darleen Baker, Lauren Coble, Megan Frair, Deborah Wray, June Mullins Front row: Sharon Lawson, Mary Wells

Human Resources

Left to right, back row: Lynn Byrd, Lauren Matsko
Front row: Kimberlyn McDonald, Alyssa Needham

Public Relations

Left to right: Ivan Morozov, Susan Bland, Barry Whyte, June Mullins

The Public Relations team at VBI identifies key audiences for the Institute and delivers a research-driven communication program to ensure information about VBI reaches its target groups. Managing the information flow for the Institute to both internal and external audiences is one of the primary responsibilities of this service-oriented group.

Publications

The group produced VBI's third annual scientific report, which showcases the latest accomplishments of VBI's research faculty during the fiscal year. The report highlights the work of the Institute's researchers and the use of team-based science to implement new innovations and discoveries in many scientific areas including bioinformatics and systems biology.

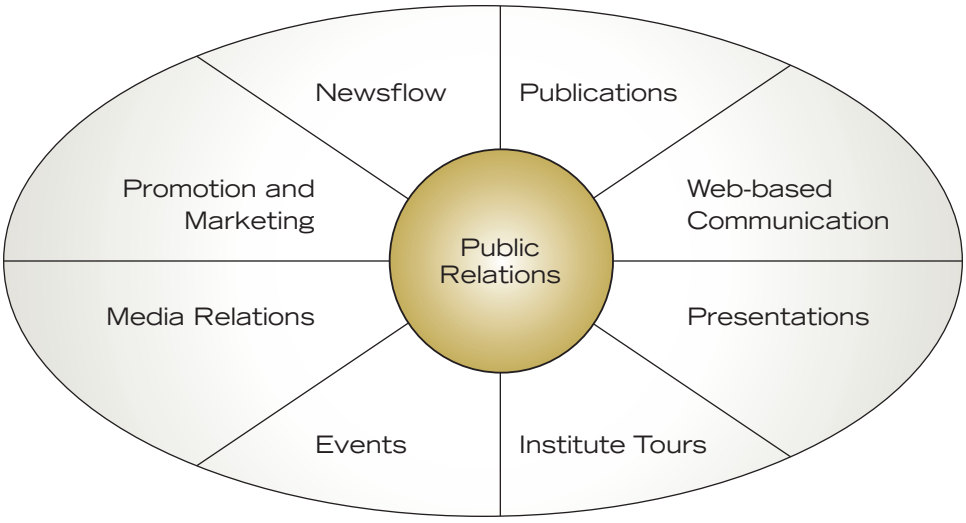
The PR team continues to produce VBI e_Connections, VBI's quarterly electronic newsletter. The electronic source provides valuable information for VBI's audiences and includes feature articles, technology updates, a review of recent news, as well as a section featuring interviews with individuals connected to the life sciences, such as researchers, authors, faculty, and students. Over the course of the past fiscal year, the newsletter has included articles about the Ninth Annual Computational Genomics Conference, as well as interviews with VBI's Core Lab Facility Manager about the installation of the Roche GS-FLX™ sequencing system and Athel Cornish-Bowden, Directeur de Recherche at the Centre National de la Recherche Scientifique, Marseilles, France.

Website

The team launched VBI's new website in March, 2007. Highlighted by a simple design and navigational layout, the site features improved search capabilities, a stronger visual identity, an events calendar, a searchable staff directory, and RSS feeds. The site is designed to showcase the science at VBI and to accommodate the Institute's growth and development (See article, page 66).

Media Coverage

In the past fiscal year, VBI's communication program resulted in coverage in the following media outlets: Affymetrix Update Newsletter, Bio-Inform newsletter, Bio-IT World, Blue Ridge Business Journal, Business Wire, Carolina Newswire, Clinica, Medical Technology News, The Collegiate Times, Genetic Engineering News, Genome Technology, GenomeWeb Daily News, The Indianapolis Star, In Sequence newsletter, Laboratorytalk, Nanotechnology.com, The Roanoke Times, ScienceDaily.com, TechJournal South, and United Press International. Some of VBI's news has been featured in on-line publications from around the world including Canada, India, and the United Kingdom.



Education and Outreach

VBI's Education and Outreach group is committed to building and maintaining strong relationships with the Institute's external audiences, as well as developing education programs designed to foster interest in scientific research for students of all ages. The group promotes VBI's involvement in a wide variety of educational programs to the Virginia Tech community and beyond.

Conferences

The Education and Outreach team hosted the Ninth Annual Computational Genomics Conference in Baltimore, Md. on October 28-31, 2006. The event, which featured 2005 Nobel Laureate Barry Marshall as the keynote speaker, included a wide range of talks describing the latest advances in computational methods for analysis of genome sequences, high-throughput automated genome annotation, the use of bioinformatics for the study of biological networks and infectious disease research, as well as other topics. The conference was sponsored by VBI, The Jackson Laboratory, The Institute for Genomic Research (TIGR), the National Human Genome Research Institute, the National Science Foundation, and Virginia Tech.

Educational Opportunities

Students enrolled in Galileo Magnet High School's Microbial Genomics course visited VBI with their instructors on May 30, 2007 to learn more about the institute's cyberinfrastructure work and present findings from their final exam projects. The students were given an overview of VBI's cyberinfrastructure program and participated in several cyberinfrastructure team modules, incorporating pathogen information from several ongoing projects into realistic scenarios. The visit was part of VBI's National Science Foundation-funded partnership with Galileo Magnet High School and Bluefield State College to support education in cyberinfrastructure.

Left to right: Daphne Rainey, Lea Hamblin, Susan Faulkner, Morgan Maurer

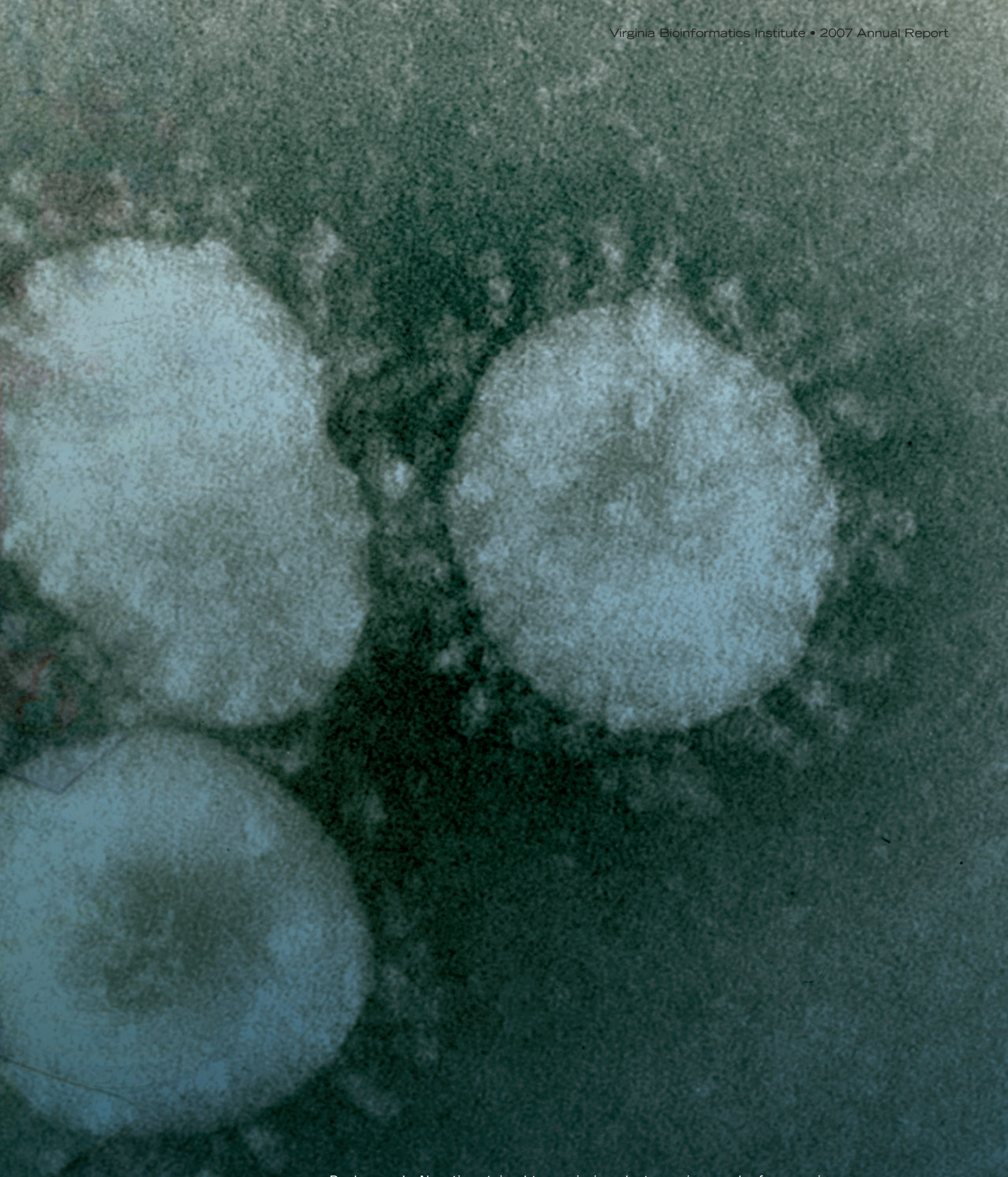
The team coordinates VBI's participation in the Bioengineering and Bioinformatics Summer Institute (BBSI), which is a summer program designed for junior or senior undergraduates who are interested in attending graduate school in biomedical engineering and/or bioinformatics. With funding from the National Science Foundation/National Institutes of Health BBSI program, Summer Institute for Quantitative and Integrative Bioengineering (SIQIB) students are provided with a 10-week educational and research experience. The objectives for BBSI are to provide students with quantitative and integrated bioengineering/bioinformatics related educational and research experiences and motivate these students to pursue graduate degrees and careers in biomedical engineering and bioinformatics-related fields. The Virginia Tech-Wake Forest University School of Biomedical Engineering and Science (SBES) is the driving force behind the program.

The year ahead

During the summer of 2008, several researchers at VBI will offer workshops, jamborees, and seminars in an effort to share their expertise with other scientists, postdoctoral students, and graduate students. VBI's Summer Institute will span six weeks in June and July and will take place at VBI or another location. While each participating researcher at VBI designs the program, the Education and Outreach Group will work with Continuing and Professional Education at Virginia Tech to provide the infrastructure for the Summer Institute.

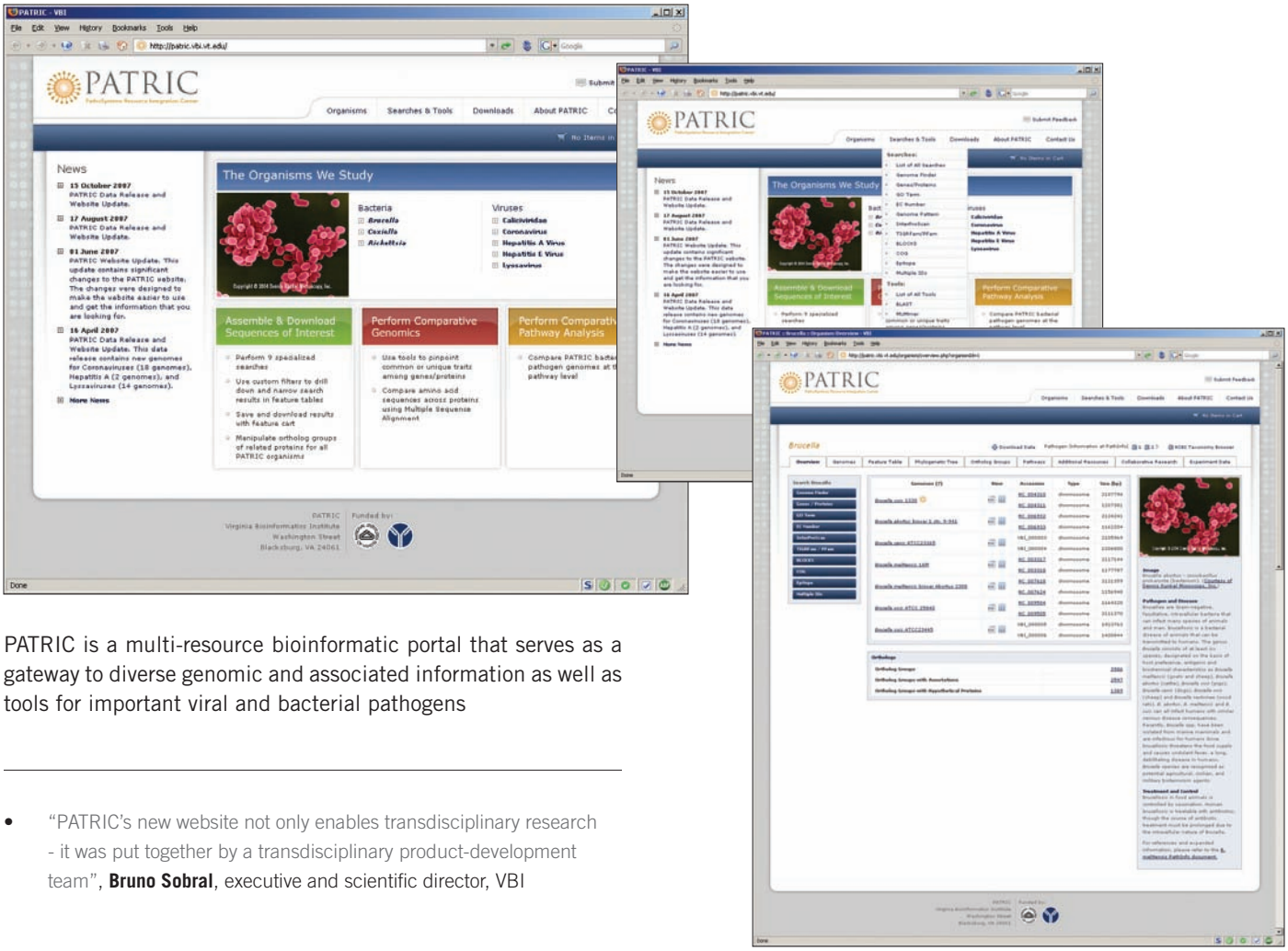
Research Feature Articles

- PATRIC launches new web site
- Undergraduates reveal enzyme's secrets



Background: Negative-stained transmission electron micrograph of coronaviruses
Adapted from the CDC Public Health Image Library. Credit Dr. Fred Murphy

PATRIC launches new web site



PATRIC is a multi-resource bioinformatic portal that serves as a gateway to diverse genomic and associated information as well as tools for important viral and bacterial pathogens

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- "PATRIC's new website not only enables transdisciplinary research - it was put together by a transdisciplinary product-development team", **Bruno Sobral**, executive and scientific director, VBI

PATRIC, the PathoSystems Resource Integration Center project, unveiled its new-look web site on June 1, 2007. The new website, which is accessible at http://patric.vbi.vt.edu, was significantly re-engineered by the PATRIC team and the Department of Computer Science at Virginia Tech to improve usability based on an extensive survey of user needs. In addition to new tools, the site also has a completely new visual identity developed in collaboration with New City Media of Blacksburg, Va.

PATRIC is a multi-resource bioinformatic portal that serves as a gateway to diverse genomic and associated information as well as tools for important viral and bacterial pathogens. It is funded by the National Institute of Allergy and Infectious Diseases (NIAID).

Design team

The project brought together the Department of Computer Science's user interface design expertise, New City Media's design skills and VBI's extensive domain knowledge to create a user-friendly, easily accessible and informative resource. The new site incorporates tools identified by PATRIC users as capabilities that would make the site more user-friendly. New organization and navigation make it easier to move among website areas, while specific search, comparison, and collection functions have been expanded and upgraded. Beyond the new navigation, organization and user interface, the PATRIC site now provides additional support for comparative genomics, a suite of new searches and filtering options, as well as enhanced features for collecting related gene and protein sequences of interest.

Users can now perform a multiple sequence alignment across members of an ortholog group and arrange members onscreen based on phylogeny. A full list of the search capabilities, including the new additions, is available at http://patric.vbi.vt.edu/searches/index.php.

Collecting related sequences of interest is made easier with an improved feature cart that allows you to collect items of interest as you browse. Large sets of features from organism feature tables, ortholog group pages, search result tables, and individual feature tables can be collected with this powerful tool and then exported as FASTA DNA or FASTA protein sequences.

The new features and re-alignment of the PATRIC web site will serve the significant growth in user requirements anticipated in the years ahead.

About PATRIC

In June 2004, Drs. Bruno Sobral (Principal Investigator) and João Setubal (Co-Principal Investigator) from VBI were awarded a five-year $10.3 million contract from the National Institute of Allergy and Infectious Diseases (NIAID) to establish a multi-organism relational database for infectious disease research that focuses on biodefense and emerging infectious diseases.

The PathoSystems Resource Integration Center (PATRIC), under development in Dr. Sobral's Cyberinfrastructure Group, is a comprehensive web-based resource for genomic and associated information on important viral and bacterial pathogens. PATRIC is one of eight Bioinformatics Resource Centers (BRC) in the United States established with the support of the NIAID.

The BRCs were created to facilitate a research community that would collect and share information vital to the development of new diagnostics, drugs, and vaccines. PATRIC is funded through NIAID contract HHSN266200400035C.

Scanning and Analyzing Multiple Genomes

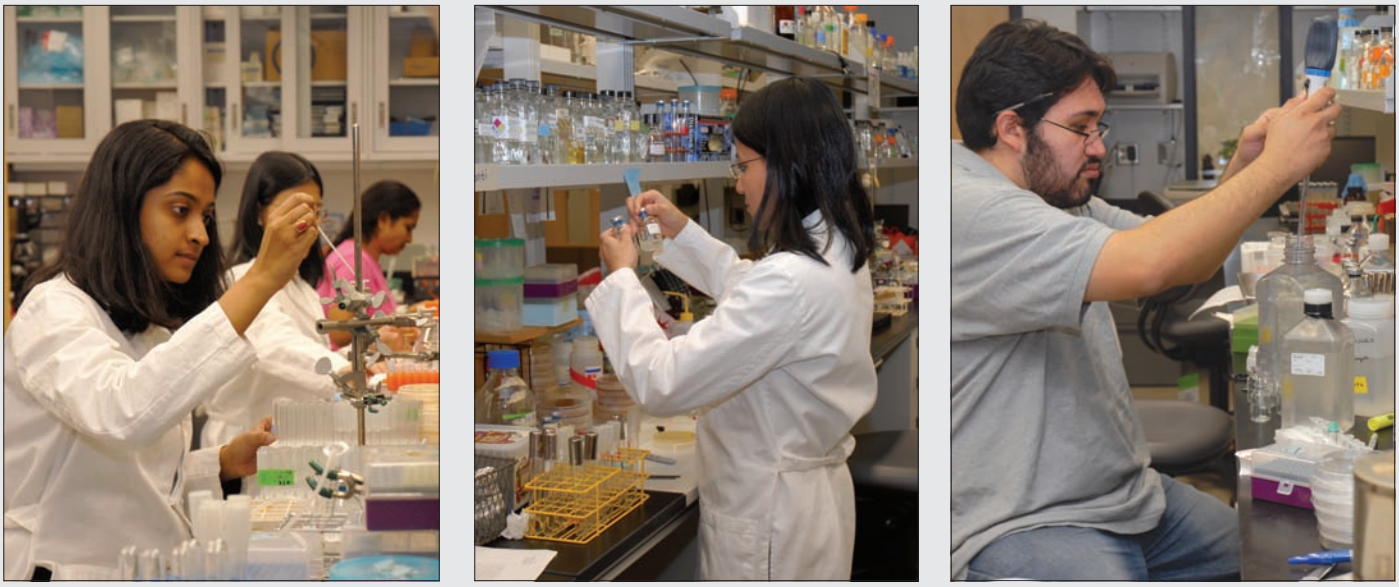
- Dr. Robert Heinzen is section head of the *Coxiella* Pathogenesis Section Laboratory of Intracellular Parasites at Rocky Mountain Laboratories, a National Institutes of Health biomedical research facility located in Hamilton, MT. Dr. Heinzen commented: "PATRIC's new web site is a valuable resource for the biodefense research community. The PATRIC group has organized an immense amount of genome data into a user-friendly interface. The bioinformatics resources available through PATRIC are especially relevant for obligate intracellular bacterial pathogens such as *Coxiella* and *Rickettsia*, which currently lack robust methods of genetic manipulation. Consequently, functional studies of their putative virulence genes are frequently conducted using expression in heterologous hosts. The identification of target genes is aided considerably by the PATRIC interface that allows one to easily scan and analyze multiple genomes of a given pathogen.

PATRIC's organisms	Associated Disease(s)
Brucella	Brucellosis
Coxiella	Q Fever
Rickettsia	Rocky Mountain Spotted Fever, Epidemic Typhus
Caliciviridae	Foodborne Gastroenteritis
Coronaviruses	SARS
Hepatitis A viruses	Viral Hepatitis
Hepatitis E viruses	Viral Hepatitis
Lyssaviruses	Rabies

newcitymedia

PATRIC
PathoSystems Resource Integration Center

Undergraduates reveal enzyme's secrets



Researchers in VBI Associate Professor Biswarup Mukhopadhyay's laboratory

While there are no traditional classrooms inside the Hokie stone-clad walls of the Virginia Bioinformatics Institute (VBI), learning is certainly happening. On a typical day you can find a student meeting with a faculty member about an ongoing research project, giving a research overview in the conference center, or using advanced microfluidic technologies to detect cancer biomarkers in cellular extracts. Students are an integral part of VBI. And it's not just graduate students working at the institute. Many of VBI's research groups and administrative units have undergraduate and high school students on their teams, some of which play a very active role in scientific research.

"I think the earlier you can get someone to think like a researcher, the better off everyone is," says Christopher Case, a former undergraduate research assistant at VBI. "The student benefits by participating in research at an early stage in their academic career. Since undergraduates with appropriate training can perform excellent scientific research, the students' research advisers, the scientific community, and the general public also benefit. It does take a certain kind of research faculty member to provide such an opportunity."

VBI Associate Professor Biswarup Mukhopadhyay is certainly that kind of researcher. He has always made an effort to integrate student contributions into his programs. Case worked for Mukhopadhyay's research group at VBI for three years while completing his undergraduate degree in Biochemistry at Virginia Tech. Not only did Case perform work in the lab, but he, along with two other undergraduate research students, co-authored a paper with Mukhopadhyay that appeared in the *Journal of Biological Chemistry*. "Roles of Asp^{75}, Asp^{78}, and Glu^{83} of GTP-dependent phosphoenolpyruvate carboxykinase from *Mycobacterium smegmatis*" (see box, page 31) also featured work from undergraduate students Kristen Boswell and Edward Concar. Boswell worked with Mukhopadhyay as an undergraduate biochemistry student at Virginia Tech, while Concar studied microbiology at the University of Illinois at Urbana-Champaign, where Mukhopadhyay worked as a postdoctoral researcher in the laboratory of Dr. Ralph Wolfe. His work with Concar at the University of Illinois resulted in an earlier published paper and the beginnings of the work continued at VBI by Boswell and Case.

"The students not only got their training here, but also contributed to the success of the laboratory," Mukhopadhyay explained. "Eddy started the work, Kristin moved it further and then Chris picked it up and did a lot of work to generate some definitive conclusions. It is a joy to see that even in their short stays in the lab they made major contributions and had fun doing it."

The students that have worked in Mukhopadhyay's lab appreciate the commitment he has made to their learning experiences, providing his expertise and guidance for those with no prior knowledge of lab techniques, as well as assistance in preparing undergraduate research grants and thesis work.

According to Concar, "Dr. Mukhopadhyay has the ability to see scientific potential in students, regardless of their status and experience. He is also very generous with his time and expertise in helping students develop their research and analytical skills. This publication is a good example that through his teaching and guidance, undergraduate students with a drive for science can have their hard worked published in a scientific journal."

Scientific credentials

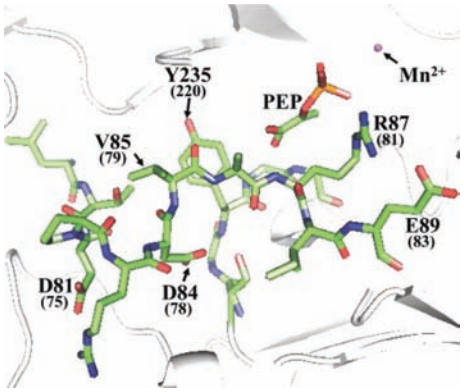
The students' undergraduate research experiences have certainly had an impact on their professional and academic careers. Boswell is currently a biochemistry graduate students at the University of Wisconsin, while Concar credits the work for helping him establish what he calls his "science credentials", leading to a research associate position in the biochemistry department of Genencor Inc., which is a leading industrial biotechnology company. Case is currently pursuing a Ph.D. in Microbiology from the Yale University School of Medicine's Biological and Biomedical Sciences program. He is confident that his undergraduate experiences at VBI helped him gain acceptance into the graduate program and ease his transition from undergraduate to graduate research.

"I am better prepared to learn new techniques, plan experiments, and write scientific papers—three very important aspects of graduate and post-graduate research," he says. "My observations of the training of undergraduate and high school students have also prepared me to one day take on a teaching role, both in academia and research."

Case CL, Concar EM, Boswell KL, Mukhopadhyay B (2006) Roles of Asp^{75}, Asp^{78}, and Glu^{83} of GTP-dependent phosphoenolpyruvate carboxykinase from *Mycobacterium smegmatis*. *J. Biol. Chem.* 281: 39262-39272

- The paper investigates ways to control the activity of phosphoenolpyruvate carboxykinase (PEPCK) – a key enzyme involved in the metabolic pathway used by the human body to produce glucose, which helps control blood sugar levels during fasting. An overproduction of this enzyme, among other things, leads to type 2 diabetes. The researchers identified three key amino acid residues of PEPCK and examined how changing each residue affected the enzyme's properties.

- The work helps provide a better understanding of the mechanisms of PEPCK and, therefore, a more complete picture of the chemistries involved in diabetes. Mukhopadhyay and his team found that it is possible to influence the activity of the enzyme from a site distinct from where the reaction takes place and, by manipulating the various PEPCK residues, they found a way to slow down but not fully eliminate the activity of PEPCK in humans. Researchers can use this information to develop therapeutics that help type 2 diabetics achieve normal blood glucose levels.



The structure of the phosphoenolpyruvate-binding site of human cytosolic phosphoenolpyruvate carboxykinase

Research Groups

Dr. Christopher Barrett
Dr. Allan Dickerman
Dr. Ina Hoeschele
Dr. Reinhard Laubenbacher
Dr. Christopher Lawrence
Dr. Iuliana Lazar
Dr. Pedro Mendes
Dr. Biswarup Mukhopadhyay
Dr. Jean Peccoud
Dr. Andy Pereira
Dr. Dharmendar Rathore
Dr. David Samuels
Dr. João Setubal
Dr. Vladimir Shulaev
Dr. Bruno Sobral
Dr. Brett Tyler

Dr. C. Barrett

Network Dynamics and Simulation Science Laboratory

Left to right, back row: Christopher Barrett, Sanket Badare, Henning Mortveit, Bryan Lewis, Matt Macauley, Xizhou Feng, Ashwin Aji, Steve Harris, Stephen Eubank, Andrea Apolloni
Front row: Madhav Marathe, Annette Feng, Anil Vullikanti, Kofi Adasi, Deepti Chafekar, Ginger Hansen, Paula Stretz, Achla Marathe, Yard Kidane, Joyce Randall

not pictured: Madhav Marathe

The need for simulations is derived from questions posed by scientists, policy makers, and planners involved with very large complex systems

The Network Dynamics and Simulation Science Laboratory (NDSSL) designs, develops and implements simulation tools to understand large biological, information, social, and technological systems. The need for simulations is derived from questions posed by scientists, policy makers, and planners involved with very large complex systems. Extremely detailed, multi-scale computer simulations allow formal and experimental investigation of large-scale systems. By enabling individuals to explore the potential impact of different interventions or strategies on the course of a disease outbreak or a specific transportation scenario, for example, important information can be prioritized as to the potential merits of different interventions.

NDSSL has established funded programs of at least $15 million over three years in the area of complex systems, including programs with the National Institutes of Health, the Centers for Disease Control and Prevention, the Defense Threat Reduction Agency and the National Science Foundation. The group recently established a presence in the National Capital Region, which is located in Virginia Tech's National Capital Region offices near Washington, DC, and plays a leading role in the institutional initiative in Policy Informatics for Complex Systems.

NDSSL is pursuing new programs in communication networks, commodity markets and high performance computing, and continues to develop diverse tools for reasoning about complex systems. Simulation performance is also being studied on TeraGrid architectures. These tools have been used to support policy planning for pandemics through several stakeholder-designed studies. The United States Department of Health and Human Services has used these studies to create the Community Strategy for Pandemic Influenza Mitigation. The environments that NDSSL creates will also be used in a new Centers for Disease Control and Prevention Public Health Informatics program. The group is developing a new understanding of the dynamics of reaction-diffusion systems over large, irregular, but structured, networks. Both the tools and their theoretical underpinnings will be leveraged as part of a large new multi-year research program devoted to building a national comprehensive incident management system.

Research Interests

- Simulation of very large systems
- Theoretical foundations of simulation
- Interaction-based systems, computing, dynamical systems
- Computational and systems biology
- Computational problems in epidemiology
- Cognitive science and computationally aided reasoning
- Computational economics
- Infrastructure simulation

Selected Recent Publications

Kumar VSA, Marathe MV, Parthasarathy S, Srinivasan A (2007) Scheduling on unrelated machines under tree-like precedence constraints, *Algorithmica,* 2007.

Atkins K, Barrett CL, Beckman RE, Bissett K, Chen J, Eubank S, Anil Kumar VS, Lewis B, Macauley M, Marathe A, Marathe MV, Mortveit HS, Stretz P (2006) Simulated pandemic influenza outbreaks in Chicago: NIH DHHS Study Final report. *NDSSL Internal Report No. 06-023,* 2006.

Atkins K, Barrett C, Beckman R, Bisset K, Chen J, Eubank S, Anil Kumar VS, Lewis B, Marathe A, Marathe M, Mortveit H, Stretz P (2006) DTRA Alabama National Guard Study Capability Demonstration. *NDSSL Internal Report No. 06-060*, 2006.

Barrett C, Hunt H III, Marathe M, Ravi SS, Rosenkrantz D, Stearns R, Thakur M (2006) Complexity of reachability problems for finite discrete dynamical systems. *Journal of Computer and System Sciences* **72**(8): 1317-1345.

Eubank S, Anil Kumar VS, Marathe MV, Srinivasan A, Wang N (2006) Structure of social contact networks and their impact on epidemics. In *AMS-DIMACS Special Volume on Epidemiology* Vol. 70, pp. 181-213.

Dr. A. Dickerman

Phylogenomics Research Group

Left to right: Eric Nordberg, Allan Dickerman, Elena Shulaeva

By analyzing and describing the diversity of phylogenetic patterns that characterize the different components of organisms' genomes, the group is uncovering important information about their lineage

Research Interests

- Phylogenetic approaches to comparative genomics
- Gene expression programs in *Arabidopsis* embryogenesis
- Pathogen identification by microarrays of rRNA probes

Selected Recent Publications

Tyler BM, Tripathy S, Zhang XM et al (53 authors) (2006) *Phytophthora* genome sequences uncover evolutionary origins and mechanisms of pathogenesis. *Science* **313**: 1261-1266.

Snyder EE, Kampanya N, Lu J, Nordberg EK, Karur HR, Shukla M, Soneja J, TianY, Xue T, Yoo H, Zhang F, Dharmanolla C, Dongre NV, Gillespie JJ, Hamelius J, Hance M, Huntington KI, Jukneliene D, Koziski J, Mackasmiel L, Mane SP, Nguyen V, Purkayastha A, Shallom J, Yu G, Guo Y, Gabbard J, Hix D, Azad AF, Baker SC, Boyle SM, Khudyakov Y, Meng XJ, Rupprecht C, Vinje J, Crasta OR, Czar MJ, Dickerman A, Eckart JD, Kenyon R, Will R, Setubal JC, Sobral BWS (2007) PATRIC: The VBI PathoSystems Resource Integration Center. *Nucleic Acids Research* **35**: D401-D406.

Tian YY, Dickerman AW (2007) GeneTrees: a phylogenomics resource for prokaryotes. *Nucleic Acids Research* **35**: D328-D331.

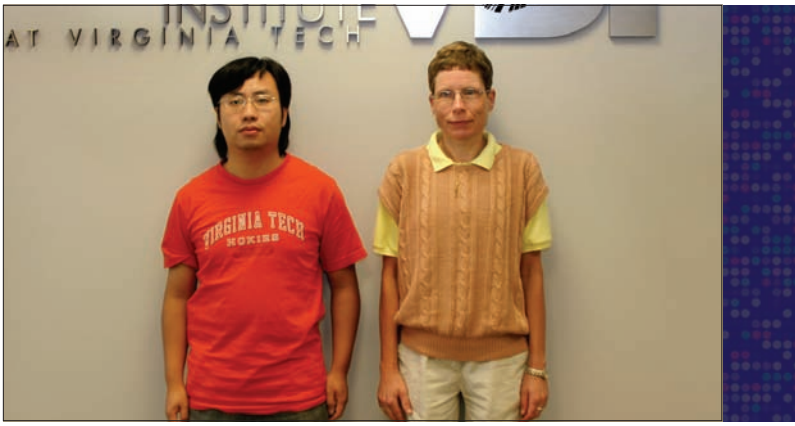
Williams KP, Sobral BW, Dickerman AW (2007) A Robust Species Tree for the Alphaproteobacteria. *J Bacteriol* **189**: 4578-4586.

Phylogenomics is an important tool used by researchers to better understand the similarities and differences of species in an evolutionary context. Phylogenetic models can be used to identify patterns of diversification in gene sequences related to changes in function. Dr. Allan Dickerman's research group creates analysis tools needed to construct the history of common ancestry for all of the components of genomes within a particular area of interest. By analyzing and describing the diversity of phylogenetic patterns that characterize the different components of organisms' genomes, the group is uncovering important information about their lineage. The group uses this information to fully define a supported phylogenetic tree model. Making comparisons to this dominant tree model can reveal genes that exhibit alternative patterns of ancestry. The groups' findings are available through the "GeneTrees" database (genetrees.vbi.vt.edu), which was made public in December, 2006, as a way to provide this kind of information and analysis methodology to scientists and the public.

The complex genomic patterns generated by evolution reflect population dynamics of organisms in their environments, which can impact human interests in many ways. Dr. Dickerman's group is involved in different kinds of environmental surveys of microbes, largely using ribosomal RNA, but with different detection methods. Dr. Marc Fisher, a recent Ph.D. from Virginia Tech's Department of Entomology, analyzed diversity of bacterial endosymbionts in termite guts, doing much of his molecular work in Dickerman's lab with related work continuing. Group members are also sampling for microbial diversity in the atmosphere, working with Dr. David Schmale of Virginia Tech's Department of Plant Pathology, Physiology and Weed Science who gathers samples using remote-controlled aircraft. Another major effort for the group is a United States Department of Agriculture-funded project to develop a microarray strategy for identifying plant pathogens from infected tissue, which involves using Affymetrix microarray design for rRNA. In addition, the group provides bioinformatics support to outside collaborators on several projects focusing on functional genomics and systems biology in the plants *Arabidopsis* and *Populus*.

Dr. I. Hoeschele

Statistical Genetics Research Group



Left to right: Lei Bao, Ina Hoeschele

The common theme of research in the Statistical Genetics Research Group is the use of data from systems genetics experiments to understand how the joint action and interaction of multiple genes determines complex phenotypes

Statistical genetics provides a way to understand how the joint action and interaction of many genes determines complex traits and diseases in animal, human and plant populations. The common theme of research in the Statistical Genetics Research Group is the use of data from systems genetics experiments to further the understanding of how the joint action and interaction of multiple genes determines complex diseases or phenotypes at the organism level. The group has evaluated and continues to evaluate different methods for high-dimensional mapping of expression quantitative trait loci. Researchers in the group have implemented a structural equation modeling analysis based on maximum likelihood inference and a genetic algorithm that can reconstruct networks consisting of several hundred gene and expression Quantitative Trait Loci nodes. This method is based on genetical genomics or systems genetics experiments that provide causal inference and strong constraints on network topology. The Statistical Genetics Research Group has analyzed several microarray expression and proteomic profiling experiments comparing different models and methods for differential expression analysis.

The statistical and computational methods developed by the group are currently being applied to a genetical genomics experiment conducted in the laboratory of Professor Brett Tyler at VBI in collaboration with Virginia Tech and The Ohio State University researchers, in which a soybean recombinant inbred line population infected with the pathogen *Phytophthora sojae* is phenotyped for quantitative disease resistance, genotyped for genetic markers, and expression profiled using an Affymetrix GeneChip® containing comprehensive probe sets for soybean and *P. sojae*. Another application is a mouse model of human lung cancer developed by researchers in the Department of Cancer Biology at Wake Forest University. The group has also performed some efficiency enhancing modifications to its deterministic method for haplotype reconstruction in complex human pedigrees and a review paper has been prepared on this topic.

Research Interests

- Quantitative and statistical genetics
- Joint linkage and linkage disequilibrium gene mapping
- Genetic parameter estimation
- (Co)variance component estimation
- Generalized linear mixed models
- Nonadditive genetic models
- Design and analysis of microarray transcription profiling experiments

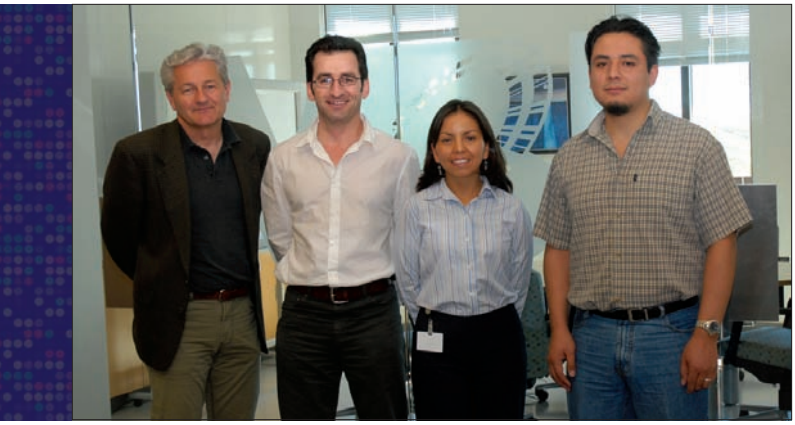
Selected Recent Publications

Betthauser JM, Pfister-Genskow M, Xu H, Gouleke PJ, Lacson JC, Koopang RW, Liu B, Hoeschele I, Eilertsen KJ, Leno GH (2006) Nucleoplasmin facilitates reprogramming and *in vivo* development of bovine nuclear transfer embryos. *Molecular Reproduction and Development* **73**:977-986.

Stock KF, Distl O, Hoeschele I (2007) Influence of priors in Bayesian estimation of genetic parameters for multivariate threshold models using Gibbs sampling. *Genetics, Selection, Evolution* **39**:123-137.

Gao G, Hoeschele, I (2007) A note on a haplotyping method in pedigrees. *Genetics, Selection, Evolution*. In press.

Hoeschele I (2007) Mapping quantitative trait loci in outbred pedigrees. In *Handbook of Statistical Genetics*, Balding DJ, Bishop M, Cannings C (eds) pp 477-525. Wiley. In press.



Dr. R. Laubenbacher

Applied Discrete Mathematics Research Group

Left to right: Reinhard Laubenbacher, Abdul Salam Jarrah, Paola Vera-Licona, Alan Veliz-Cuba

The Applied Discrete Mathematics Research Group focuses on the development and application of algorithms and software to reverse-engineer biochemical networks from large-scale system measurements

Research Interests

- Mathematical biology
- Applied discrete mathematics
- Symbolic computation
- Systems biology

Selected Recent Publications

Choi V, Huang Y, Lam V, Potter D, Laubenbacher R, Duca K (2006) Using formal concept analysis for microarray data comparison. *5th Asia-Pacific Biocomputing Conference.*

Colon-Reyes O, Jarrah A, Laubenbacher R, Sturmfels B (2006) Monomial dynamical systems over finite fields. *Complex Systems* **4**(16): 333-342.

Castiglione F, Duca KA, Jarrah A, Laubenbacher R, Hochberg D, Thorley-Lawson DA (2007) Simulating Epstein-Barr Virus Infection with C-ImmSim. *Bioinformatics* **23:** 1371-1377.

Choi V, Huang Y, Lam V, Potter D, Laubenbacher R, Duca K (2007) Using formal concept analysis for microarray data comparison. *Journal of Bioinformatics and Computational Biology* **6**(1): 57-66.

Jarrah A, Laubenbacher R (2007) Discrete models of biochemical networks: The toric variety of nested canalyzing functions. *Proceedings of the Second International Conference on Algebraic Biology.*

One of the central problems in systems biology is to infer biochemical networks from system-wide experimental measurements, including gene regulatory, metabolic, and signaling networks. The goal of this "top-down" modeling approach is to create a comprehensive overview of these networks. Over the past year, Dr. Reinhard Laubenbacher's Applied Discrete Mathematics Group has made several theoretical and applied advances toward the development of mathematical tools to solve this complex problem. More specifically, the group has focused on the development and application of algorithms and software to reverse-engineer biochemical networks from large-scale system measurements such as DNA microarray data.

The group uses techniques from discrete mathematics and symbolic computation, implemented in open-source symbolic computation software. The techniques are being tested on both simulated and published data sets, as well as a data set generated as part of a yeast systems biology project in collaboration with Drs. Pedro Mendes and Vladimir Shulaev at VBI. For this project, Dr. Laubenbacher's group is developing computation methods to reverse-engineer biochemical networks, which are then applied to genomic, proteomic, and metabolomic data with a specific focus on the oxidative stress network in the yeast *Saccharomyces cerevisiae.* For their work, the group has selected the modeling paradigm of time-discrete dynamical systems of finite state sets, including Boolean networks, which have a long history of serving as models of gene regulatory and other biochemical networks. Group members hope to release software allowing novice users to reverse-engineer networks based on their experimental data. The model for this software is COPASI (Complex Pathway Simulator), a biochemical network simulator developed by Dr. Pedro Mendes' Biochemical Networks Modeling Group at VBI that is accessible to a broad audience of users without a modeling background.

Dr. C. Lawrence

Research Group

Left to right: Kwang-Hyung Kim, Chris Lawrence, Graciela Santopietro, Mauricio La Rota, Amanda Cronin, Mihaela Babiceanu, Ashley Wilkinson

not pictured: Yangrae Cho

By closely studying interactions of fungi with plants and humans, the group hopes to significantly advance the current level of understanding of host-pathogen interactions and open up new opportunities for biomedical and agricultural research

Dr. Chris Lawrence's Research Group studies the ways in which fungi lead to plant and human disease. Many pathological relationships have developed between ubiquitous airborne fungi (molds) and prospective hosts across kingdoms. Fungi cause devastating diseases of plants, animals, humans and even other fungi. In some cases, the co-evolution of host and potential pathogen has resulted in the selective tailoring of the innate immune system of plants, animals and other eukaryotes to recognize, respond to and persevere against attempted invasive infection. Even though the innate human immune system is very effective at detecting and thwarting attempted infection by fungi, many chronic airway diseases such as allergy, asthma and various forms of sinusitis are the result of both deleterious alterations in airway functionality and overzealous innate and adaptive immune responses leading to chronic inflammation. Most often these immune system defects significantly affect an individual's daily quality of life and productivity. By closely studying interactions of fungi with plants and humans, the group hopes to significantly advance the current level of host-pathogen interactions and open up new opportunities for biomedical and agricultural research.

In Dr. Lawrence's laboratory, the majority of group members' research thus far has been focused on pathogenomics of the ubiquitous fungus *Alternaria*. Besides being an important genus of necrotrophic fungi causing economically important plant diseases, *Alternaria* has long been clinically associated with chronic respiratory diseases such as IgE-dependent mold allergy, life-threatening forms of asthma, chronic sinusitis and other allergic airway disorders. The group has continued to develop a new model pathosystem for plant-fungal genomics research (The *Alternaria brassicicola-Brassicaceae* interaction). Functional genomic methods are used to dissect the molecular events involved in infection, identify fungal genes involved in pathogenesis, and determine the plant genes involved in disease susceptibility and resistance. The group has also developed a new model fungal genomics system for chronic airway disorder research centered upon the more clinically relevant species, *Alternaria alternata*.

Research Interests

- The *Alternaria-Brassicaceae* pathosystem as a model for necrotrophic fungal-plant interactions
- The genome sequence of the model nectrophic fungus *Alternaria brassicicola*
- The role of *Alternaria* in chronic respiratory disorders
- Fungal biotechnology

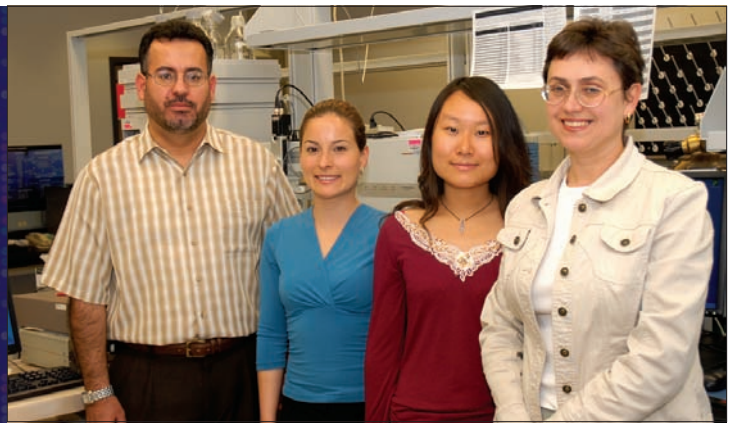
Selected Recent Publications

Cho Y, Davis JW, Kim K, Wang J, Sun Q, Cramer RA, Lawrence CB (2006) A high throughput targeted gene disruption method for *Alternaria brassicicola* functional genomics using Linear Minimal Element (LME) constructs. *Molecular Plant-Microbe Interact.***19**: 7-15.

Cramer RA, Thon M, Cho Y, Craven KD, Knudson DL, Mitchell TK, Lawrence CB (2006) Bioinformatic analysis of expressed sequence tags derived from a compatible *Alternaria brassicocola—Brassica oleracea* interaction. *Molecular Plant Pathology* **7**: 113-124.

Cho Y, Cramer RC, Kim K, Pryor BM, Lawrence CB (2007) The Amk1 Map Kinase Regulates Virulence Factors in *Alternaria brassicicola. Fungal Genetics and Biology* **44**:543-553.

Kim K, Cho Y, Cramer RC, Lawrence CB (2007) Functional analysis of the *Alternaria brassicicola* non-ribosomal peptide synthetase gene AbNPS2 reveals a role in conidial cell wall construction. *Molecular Plant Pathology* **8**: 23-29.



Dr. I. Lazar

Research Group

Left to right: Abdulilah Dawoud, Jenny Armenta, Xu Yang, Iuliana Lazar

The development of novel technologies and bioanalytical strategies for fast proteomic profiling of cancerous cells and tissues is essential for speeding up the discovery process of early disease biomarkers

Research Interests

- 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

Selected Recent Publications

Lazar IM, Trisiripisal P, Sarvaiya HA (2006) Microfluidic liquid chromatography system for proteomic applications and biomarker screening. *Anal. Chem.* **78**(15): 5513-5524.

Sarvaiya HA, Yoon JH, Lazar IM (2006) Proteome profile of the MCF7 cancer cell line: a mass spectrometric evaluation. *Rapid Commun. Mass Spectrom.* **20**: 3039-3055.

Bissel P, Geherin S, Igarashi K, Gandour RD, Lazar IM, Castagnoli N Jr (2006) Mass spectrometric studies on 4-aryl-1-cyclopropyl-1,2-dihydropyridinyl derivatives: an examination of a novel fragmentation pathway. *J. Mass Spectrom.* **41**(12): 1643-1653.

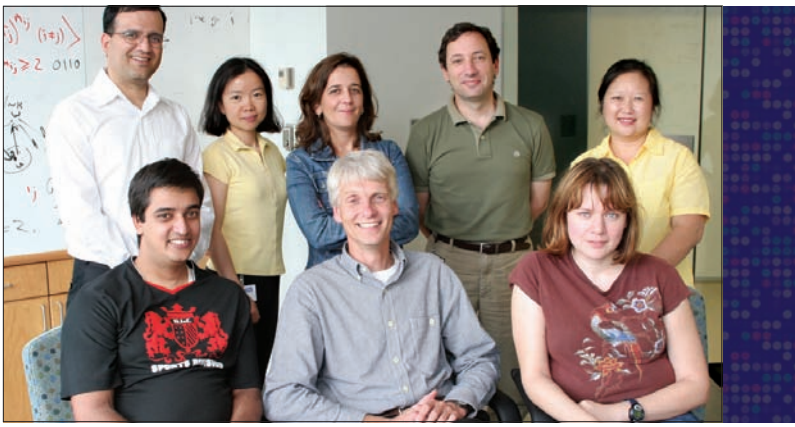
Mass spectrometry has evolved into an essential tool in peptide/protein sample analysis. The challenges associated with a "proteomic" sample are numerous: complexity (thousands of proteins/sample), wide range of concentrations, low level expression for certain components (less than 1000 copies/cell), dynamic composition (different sets of proteins are expressed in various stages of cell development), and availability. Moreover, for one single starting protein mix, the final stage of mass spectrometry analysis involves the investigation of ten to hundreds of peptide fractions.

Microfabrication is emerging to be one of the most significant trends in analytical chemistry instrumentation in the next decades. Microfluidic devices present unique opportunities for integration, multiplexing and capability of handling small sample quantities, and represent an optimal platform for proteomic applications. Progressively smaller, faster, and "smarter" devices with integrated complex detection systems will be designed to accommodate the accelerating demand for information-producing, high-throughput instrumentation.

The development of novel technologies and bioanalytical strategies for fast proteomic profiling of cancerous cells and tissues is essential for speeding up the discovery process of early disease biomarkers. Moreover, the perfection of such technologies can lead to their ultimate implementation for fast, large-scale population screening applications. To date, Dr. Iuliana Lazar's research group has developed bioanalytical protocols that have enabled the confident identification of ~2600 proteins (P<0.001) from only ~40 µg of cellular extracts. Over 200 of these proteins were correlated with cellular processes relevant to cancer, and more than 25 were previously reported as putative cancer biomarkers. The long-term objective of the group is focused on transferring this technology onto high-throughput microfluidic platforms for the detection of protein co-expression patterns. The reliable quantitation of all protein components and the identification of post-translationally modified proteins, in particular phosphoproteins, are the major topics that are being pursued.

Dr. P. Mendes

Biochemical Networks Modeling Group



Left to right, back row: Bharat Mehrotra, Hui Cheng, Anna Martins, Pedro Mendes, Xing Jing Li. Front row: Aejaaz Kamal, Stefan Hoops, Revonda Pokrzywa

The Biochemical Networks Modeling Group develops computational methods to study biochemical networks using data from experimental observations

Systems biology brings together modeling, simulation and quantitative experiments, allowing researchers to use the data of one of these approaches to repeatedly define the framework of the other approaches. Biochemical networks are central to biological function, while computer modeling provides a particularly useful way to understand their workings. Biochemical models are the ideal means to design and predict the effect of interventions such as curing diseases, improving crop yields, and designing biotechnology. Dr. Pedro Mendes is chair in Computational Systems Biology at the University of Manchester, England, and leads the Biochemical Networks Modeling Group at VBI. The main goal of the Biochemical Networks Modeling Group is to develop computational methods for studying biochemical networks using data from experimental observations.

The group has been pursing two separate strategies for building biochemical models. "Bottom-up" modeling uses *in vitro* kinetic properties of enzymes in the network to form a model of the entire pathway. "Top-down" modeling is based on reverse-engineering the pathway dynamics using measurements of the system's response to environmental or genetic perturbations. The group has completed work in both of these areas recently, and has developed software infrastructure for both. A common component of the two modeling strategies is that both require the simulation of the behavior of the system through a mathematical model. Dr. Mendes' group has been involved in this work through the development of the simulator COPASI (Complex Pathway Simulator) in collaboration with the Kummer group that recently moved from EML Research to the University of Heidelberg. This year, a commercial licensing scheme has been established for the use of the software by for-profit corporations for a small fee (non-profit use is free) and two versions have been released. The group has continued its collaboration with VBI faculty members Drs. Reinhard Laubenbacher and Vladimir Shulaev, developing a method to characterize every isoenzyme of an important pathway in yeast that plays a major role in metabolism and the response of yeast to various stresses, particularly oxidative stress. This work will help the group build a comprehensive model of the pentose-phosphate pathway.

Research Interests

- Modeling and simulation of biochemical systems
- Global optimization and inverse problems
- Management and analysis of systems biology data sets
- Oxidative stress and its cellular regulation
- Reverse-engineering of biochemical networks

Selected Recent Publications

Camacho D, Vera-Licona P, Mendes P, Laubenbacher R (2007) Comparison of reverse-engineering methods using an *in silico* network. *Annals of the New York Academy of Sciences*. In press.

Henriques ID, Aga DS, Mendes P, O'Connor SK, Love NG (2007) Metabolic footprinting: a new approach to identify physiological changes in complex microbial communities upon exposure to toxic chemicals. *Environ. Sci. Technol.* **41**: 3945-3951.

Hoops S, Sahle S, Gauges R, Lee C, Pahle J, Simus N, Singhal M, Xu L, Mendes P, Kummer U (2006) COPASI - a COmplex PAthway SImulator. *Bioinformatics* **22**: 3067-3074.

Martins AM, Sha W, Evans C, Martino-Catt S, Mendes P, Shulaev V (2007) Comparison of sampling techniques for parallel analysis of transcript and metabolite levels in *Saccharomyces cerevisiae*. *Yeast*. **24**: 181-188.

Mendes P (2006) Metabolomics and the challenges ahead. *Brief. Bioinform.* **7**: 127.

Sansone SA, Fan T, Goodacre R, Griffin JL, Hardy NW, Kaddurah-Daouk R, Kristal BS, Lindon J, Mendes P, Morrison N, Nikolau B, Robertson D, Sumner LW, Taylor C, van der Werf M, van Ommen B, Fiehn O (2007) The metabolomics standards initiative. *Nature Biotechnol.* **25**: 846-848.

Dr. B. Mukhopadhyay

Research Group

Left to right, back row: Eric Johnson, Ban Wang, Biswarup Mukhopadhyay, Karla Piedl, Sean Fanning
Front row: Dwi Susanti, Jennifer Stieber, Deanna Colton, Endang Purwantini, Lakshmi Dharmarajan

Dr. Biswarup Mukhopadhyay's research group studies the biochemical mechanisms used by microorganisms to survive under extreme conditions

Research Interests

- Proteomics-based functional genomics study of extreme condition microbiology
- Remnants of ancient metabolism in methanogenic archaea
- Coal bioconversion to methane and mitigation of methane-induced mine explosion
- Tuberculosis – metabolism of the mycobacteria
- Type 2 diabetes – structure function studies of pyruvate carboxylase and phosphoenolpyruvate carboxykinase
- Structure function studies of a novel phosphoenolpyruvate carboxylase

Selected Recent Publications

Johnson EF, Mukhopadhyay B (2007) A novel coenzyme F_{420}-dependent sulfite reductase and a small size sulfite reductase in methanogenic archaea. In *Proceedings of the International Symposium on Microbial Sulfur Metabolism,* Dahl C & Friedrich CG (eds), Springer, New York, N.Y. In press.

Case CL, Concar EM, Boswell KL, Mukhopadhyay B (2006) Roles of Asp^{75}, Asp^{78}, and Glu^{83} of GTP-dependent phosphoenolpyruvate carboxykinase from *Mycobacterium smegmatis*. *J. Biol. Chem*. **281**: 39262-39272.

Lai H, Kraszewski JL, Purwantini E, Mukhopadhyay B (2006) Identification of the pyruvate carboxylase genes in *Pseudomonas aeruginosa* PA01 and development of a *P. aeruginosa*-based over-expression system for a_4- and a_4b_4-type pyruvate carboxylases. *Appl. Environ. Microbiol.* **72**: 7785-7792.

Seleem MN, Ali M, Boyle SM, Mukhopadhyay B, Witonsky SG, Schurig GG, Sriranganathan N (2006) Establishment of gene expression system in *Ochrobactrum anthropi*. *Appl. Environ. Microbiol*. **72**: 6833-6836.

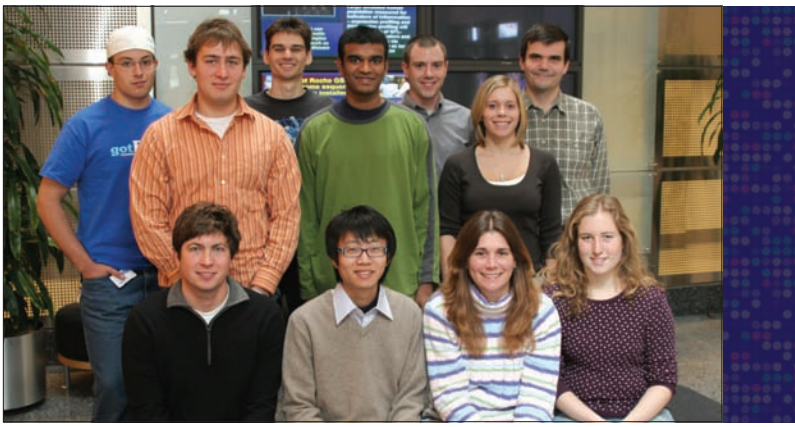
Dr. Biswarup Mukhopadhyay's research group works on extreme condition microbiology and enzymology. Researchers in Dr. Mukhopadhyay's laboratory are interested in providing a better understanding of how metabolic reactions and pathways arose and evolved from inorganic reactions as well as determining how microorganisms survive or thrive in extreme environments. They are also interested in developing therapeutics for the treatment of tuberculosis (TB) and diabetes and are using several approaches to investigate new energy production processes.

The group uses microbiology, bioinformatics, proteomics, protein structure modeling, protein and small molecule biochemistry, enzymology and enzyme kinetics to support its research initiatives. Phosphoenolpyruvate carboxykinase plays a major role in the development of type 2 diabetes and attainment and maintenance of dormancy by *Mycobacterium tuberculosis* (the causative agent of TB) in the human body. Research has shown that the activity of phosphoenolpyruvate carboxykinase can be controlled by interfering with amino acid residues that are distant from the active site but which are connected to the active site via long-range interactions. This observation can be used to develop therapeutics that will help maintain blood glucose level in type 2 diabetics at an optimal level and will allow for the development of drugs for treating tuberculosis.

Work in Dr. Mukhopadhyay's laboratory on the mycobacteria has identified a protein that is involved in cell envelope synthesis. This protein is being investigated as a possible target for the development of TB drugs. Clinical strains of *M. tuberculosis* from Indonesia are also being investigated to understand the mechanism for the development of more virulent and drug-resistant tuberculosis. Work on *Methanocaldococcus jannaschii*, a hyperthermophilic archaeon that lives in deep-sea hydrothermal vents, has allowed the group to develop a hypothesis on the evolution of methanogenesis, sulfate reduction and anaerobic methane oxidation. Microorganisms with interesting and useful metabolic properties have also been isolated for work on the conversion of coal and paraffin to methane to increase natural gas production.

Dr. J. Peccoud

Synthetic Biology Research Group



Left to right, back row: Matthew Sweede, Matthew Lux, Christopher Villareal, Nalin Palapitiya, David Ball, Emily Delalla, Jean Peccoud. Front row: Brian Hartnett, Yizhi (Patrick) Cai, Jodi Lewis, Blair Lyons

The Synthetic Biology Group develops software applications, computational methods, molecular toolboxes, and high-throughput instruments to make possible the computer-assisted design of synthetic genetic systems

The Synthetic Biology Group at VBI streamlines the design and fabrication of artificial gene networks. Computer-assisted design of genetic systems is poised to bring significant benefits to the biomedical community and the biotechnology industry. However, the lack of calibrated genetic parts remains a major limitation. The Synthetic Biology Group, which is led by Dr. Jean Peccoud, develops software, computational tools and high throughput data acquisition processes that allow researchers to calibrate genetic components used to design synthetic genetic systems.

The group is developing software tools that can guide users through the design of new DNA molecules or help them verify previously designed molecules. GenoCAD (www.genocad.org) is an experimental web site allowing non-specialists to design and validate large-scale genetic systems for use in basic biological research or product development programs. GenoCAD relies on a computer science theory used to develop programming languages and also includes a database of previously characterized genetic parts that users can integrate in the design of their own constructs.

The group is also developing high-throughput data acquisition processes and corresponding data analysis methods to calibrate genetic parts. After reaching the conclusion that no commercial instrument meets the requirements of this approach, the Synthetic Biology Group has initiated the development of a customized optical tracker to monitor the expression of multiple genes in single cells. This approach will complement the current use of flow cytometry data to characterize genetic parts for synthetic biology applications. The integration of experimental designs, custom data acquisition platforms, and data analysis algorithms leveraging the power of high-performance computing architectures contributes to the development of a superior technology that will make it possible to predict the behavior of very large-scale genetic systems.

The Synthetic Biology Group at VBI also participates in the International Genetically Engineered Machines (iGEM) competition, an annual event organized by the Massachusetts Institute of Technology (MIT) that gives undergraduate students the opportunity to design and build an engineered biological system using standard DNA parts.

Research Interests

- Computer Assisted Design of synthetic genetic systems
- Calibration of genetic parts
- Modularity of artificial gene networks
- Portability of artificial gene networks across biological species

Selected Recent Publications

Griffith M, Courtney T, Peccoud J, Sanders WH (2006) Dynamic partitioning for hybrid simulation of the bistable HIV-1 transactivation network. *Bioinformatics* **22**: 2782-2789.

Dr. A. Pereira

Research Group

Left to right, back row: Madana M. Ambavaram, Andy Pereira, Peter Wittich. Front row: Amal Harb, Utlwang Batlang, Arjun Krishnan

The interaction and adaptation of plants to environmental signals and stresses need to be analyzed in a network model using a systems biology approach

Research Interests

- Plant responses to external stress including drought, salinity and disease
- Development of gain-of-function transposon mutagenesis in *Arabidopsis*, rice and tomato
- Analysis of genetic networks underlying the pathways involved in abiotic stress using various -omics tools
- Comparative functional genomics between model plants *Arabidopsis* and rice

Selected Recent Publications

Marsch-Martinez N, Greco R, Becker JD, Dixit S, Bergervoet JHW, Karaba A, de Folter S, Pereira A (2006) BOLITA, an Arabidopsis AP2/ERF-like transcription factor that affects cell expansion and proliferation/differentiation pathways. *Plant Mol. Biol.* **62**: 825-843.

Salentijn EMJ, Pereira A, Angenent GC, van der Linden CG, Krens F, Smulders MJM, Vosman B (2007) Plant translational genomics: from model species to crops. *Mol. Breeding* **20**: 1-13.

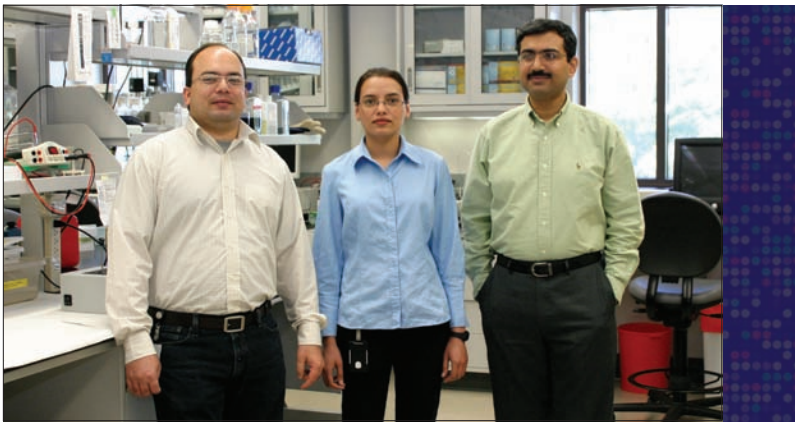
Karaba A, Dixit S, Greco R, Aharoni A, Trijatmiko KR, Marsch-Martinez N, Krishnan A, Nataraja KN, Udayakumar M, Pereira A (2007) Improvement of water use efficiency in rice by expression of HARDY, an Arabidopsis drought and salt tolerance gene. *Proc. Natl Acad. Sci. USA.* **104**: 15270-15275.

Environmental factors such as heat, cold, drought, nutrient deficiencies or toxicities cause major global crop losses every year. Uncovering ways to help plants survive in unfavorable environments can have a huge impact on agricultural productivity. The interaction and adaptation of plants to environmental signals and stresses are complex and need to be analyzed in a network model using a systems biology approach. The focus of the work in Dr. Andy Pereira's research group is to examine how plants respond to environmental stresses, in particular identifying the genes and mechanisms involved in these processes. By using a "genome biology" approach to look at genes that have retained similar functions over time in different plant species, the group's work provides valuable information on how different plant species have adapted to cope with severe, external influences. In addition, research is helping to uncover more details regarding the cross-talk between a plant's adaptive responses to different physical and biological stresses that are commonly encountered in the environment.

Group members have initiated studies using transcription factor genes that have been identified from *Arabidopsis* and which provide abiotic (drought and salt) stress resistance when expressed in *Arabidopsis* and rice. The stress-resistant genotypes provide genetic perturbations that help uncover the downstream-regulated network of genes that probably have a cellular role in abiotic stress resistance. When compared to the altered transcriptome in engineered stress-resistant genotypes, the drought transcriptome reveals distinct subsets of genes represented in Gene Ontology (GO) functional categories that overlap and which are unique to specific drought-resistance mechanisms. By using the completely sequenced *Arabidopsis* and rice plant genomes as experimental systems, members of Dr. Pereira's group can develop a network model conserved between plant species. This network model can be linked to other gene/protein interaction information that is being generated. These studies will help identify the cellular network that determines a phenotype across plant species.

Dr. D. Rathore

Research Group



Left to right: Rana Nagarkatti, Dewal Jani, Dharmendar Rathore

Dr. Rathore's research group is working to identify parasite factors that lead to malaria infection in humans and which can be developed as a vaccine or drug target

Malaria, a devastating disease caused by *Plasmodium* parasites, is responsible for 10% of all the disease-associated mortality in children under the age of five. The majority of these fatalities are caused by an infection of *Plasmodium falciparum*, the most lethal form of the human malaria parasite. Dr. Rathore's research group is actively pursuing a genomics approach towards the identification of parasite factors that lead to the successful onset and sustenance of malaria infection in its human host and which can be developed either as a vaccine or a drug target.

While malaria infection begins with the invasion of hepatocytes by *Plasmodium* sporozoites inoculated by an infected mosquito, clinical symptoms of malaria, which include high fever, chills and anemia, are due to the subsequent infection and rapid multiplication of the parasite inside red blood cells. To sustain its rapid pace of development, the parasite cannibalizes hemoglobin. This process releases heme, which is toxic to the parasite. To protect itself, the parasite uses a unique, yet poorly understood parasite-specific mechanism to convert heme into a non-toxic and insoluble material called hemozoin. Dr. Rathore's group has recently identified a novel *Plasmodium* protein that is responsible for this activity and researchers in the group have named it Heme Detoxification Protein or HDP. They have found that Heme Detoxification Protein is essential for the parasite, is highly conserved and follows an unusual trafficking route to the food vacuole, which is the site of hemozoin formation. To date, this trafficking route has never been observed for any of the known Plasmodial proteins.

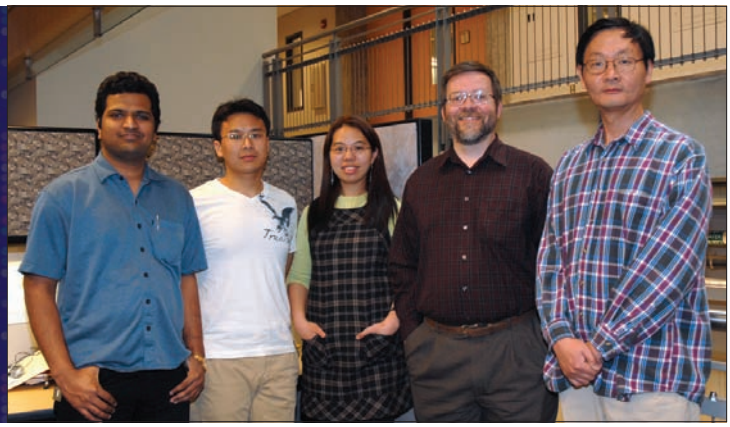
As blocking the activity of this protein could potentially translate into the inhibition of parasite development in the host cells, researchers in Dr. Rathore's group have recently conducted a high throughput screening of 80,000 drug-like molecules and have identified several compounds that not only block the interaction of this protein with heme but which also show potent anti-malarial activity on *P. falciparum* parasites in culture.

Research Interests

- Malaria pathogenesis
- Malaria therapeutics

Selected Recent Publications

Rathore D (2007) American Society of Tropical Medicine and Hygiene – 55th Annual Meeting. 12–16 November 2006, Atlanta, GA, USA. *IDrugs* **10**(2): 93-95.



Dr. D. Samuels

Research Group

Left to right: Harsha Rajasimha, Zhuo Song, Passorn Wonnapinij, David Samuels, Jonghoon Kang

Dr. Samuels' research group uses bioinformatics and computational biology to study diseases involving the function of mitochondria

Research Interests

- Toxicity of nucleoside analogs, such as AZT, used as antiviral drugs
- Metabolism of DNA precursors in mitochondria
- Physical properties of DNA and mutation mechanisms
- The role of mitochondria in aging
- The interaction of pathogens with the host mitochondria

Selected Recent Publications

Samuels DC, Carothers AD, Horton R, Chinnery PF (2006) The power to detect disease associations with mitochondrial DNA haplogroups. *The American Journal of Human Genetics* **78**(4): 713-720.

Durham SE, Samuels DC, Chinnery PF (2006) Is selection required for the accumulation of somatic mitochondrial DNA mutations in post-mitotic cells? *Neuromuscular Disorders* **16**(6): 381-386.

Samuels DC (2006) Mitochondrial AZT metabolism. *IUBMB Life* **58**(7): 403-408.

Samuels DC (2007) Computational models of antiviral toxicity. *Current Opinion in Drug Discovery & Development* **10**(1): 43-48.

Pyle A, Taylor RW, Durham SE, Deschauer M, Schaefer AM, Samuels DC, Chinnery PF (2007) Depletion of mitochondrial DNA in leucocytes harbouring the 3243A -> G mtDNA mutation. *Journal of Medical Genetics* **44**(1): 69-74.

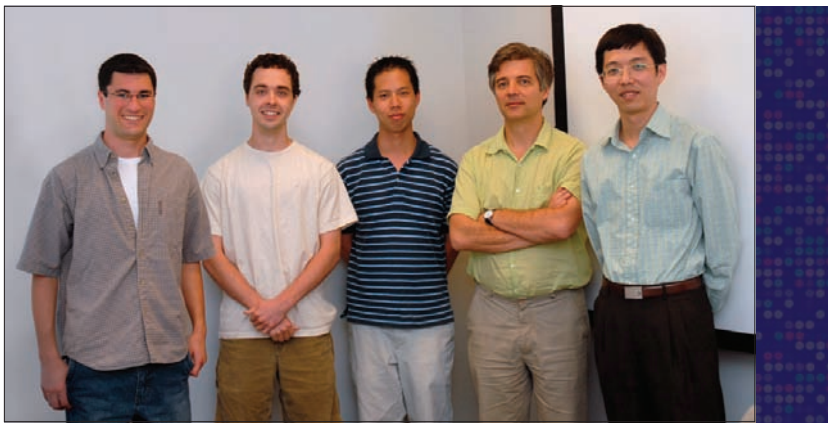
Dr. Samuels' research group works closely with clinical and wet-lab researchers to apply computational techniques to biomedical research involving mitochondrial dysfunction. Mitochondria possess their own genome that is distinct from the nuclear genome. Mutations within the mitochondrial genome may lead to a loss of energy within a cell and, in turn, the loss of cell function. This loss of function may have severe clinical repercussions and contribute to different neurodegenerative diseases. The accumulation of mutations in mitochondrial DNA may also be linked to the decrease in the ability of a cell to function as an organism ages.

Work published in the past year has concentrated on two areas: the toxicity mechanisms of antiviral drugs and the dynamics of pathogenic mitochondrial DNA (mtDNA) mutations. In modeling the toxicity mechanisms of antiviral drugs such as AZT (azidothymidine, zidovudine), researchers in the group have been developing new computational models of the metabolism of these drugs. This has involved the development of a detailed computational model of the mitochondrial DNA polymerase and its interaction with the activated antiviral drugs. This DNA polymerase model may be generalized in the future to build a model of viral DNA polymerases (reverse transcriptases in most cases).

Over the past year, the modeling of pathogenic mtDNA mutations has focused on the analysis of new clinical data that have been derived from experiments designed to test the groups mathematical models. The predictions of the models have been confirmed in the new data, and new unexpected behavior has also been found in these experiments. The group is now in the process of developing new hypotheses based on these new clinical data, which will be incorporated into the next generation of models.

Dr. J. Setubal

Research Group



Left to right: Chris Lasher, Andrew Warren, Tsai-Tien Tseng, João Setubal, Jian Sun

Dr. Setubal's research group develops bioinformatics infrastructure for the genomic analysis of multiple microorganisms

The Setubal research group works primarily on bioinformatics for bacterial genome annotation and sequence analysis. New bacterial genomes continue to become available at an exponential rate thanks to new sequencing technologies. Comparative genomics is one of the main beneficiaries of the surge in sequencing since it has become cheap enough to sequence several strains of the same species as well as species from phylogenetically under-represented groups. This presents exciting opportunities for the Setubal research group.

In addition to specific genome analyses (which currently cover the genera *Agrobacterium, Brucella, Rickettsia* [alpha-proteobacteria], *Azotobacter, Coxiella, Pseudomonas, and Xanthomonas* [alpha-proteobacteria]), current topics of interest include automated genome annotation, web-based infrastructure for genome annotation and analysis, and exploitation of ortholog groupings for comparative studies.

During this reporting period significant advances were achieved for the PATRIC (PathoSystems Resource Integration Center) project. PATRIC is a comprehensive web-based resource for genomic and associated information on important viral and bacterial pathogens. It is one of eight Bioinformatics Resource Centers (BRC) in the United States established with the support of the National Institute of Allergy and Infectious Diseases. The BRCs were created to facilitate a research community that would collect and share information vital to the development of new diagnostics, drugs, and vaccines. The advances in PATRIC in the past year were exemplified by the first published description of PATRIC in the 2007 database issue of *Nucleic Acids Research* and the release and publication of PATRIC's first genomics analysis tool, GenVar.

In other projects, progress was also made, notably in the generation of hundreds of new Gene Ontology (GO) terms for plant-associated microbes in the Plant-Associated Microbe Gene Ontology (PAMGO) project. PAMGO is an established interest group of the worldwide Gene Ontology Consortium. The GO Consortium has been working since 2000 to develop a common language of terms that can be used to describe how individual genes function in diverse organisms.

Research Interests

- Bioinformatics infrastructure for genome annotation
- Algorithms for genome analysis
- Automated annotation of bacterial genomes
- Bacterial plant pathogens
- Bacterial genome evolution

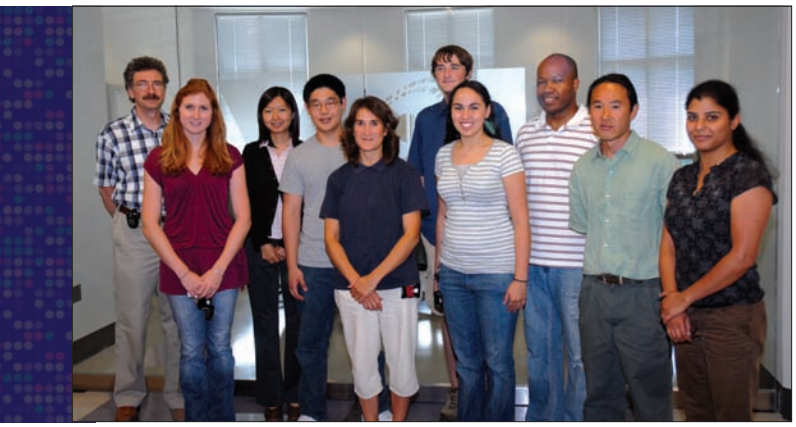
Selected Recent Publications

Slater S, Goodner B, Setubal J, Goldman B, Wood D, Nester E (2007) The *Agrobacterium tumefaciens* C58 genome. In *Agrobacterium*, Tzfira T, Citovsky V (eds), Springer, New York. In press.

Snyder EE, Kampanya N, Lu J, Nordberg EK, Karur HR, Shukla M, Soneja J, Tian Y, Xue T, Yoo H, Zhang F, Dharmanolla C, Dongre NV, Gillespie JJ, Hamelius J, Hance M, Huntington KI, Jukneliene D, Koziski J, Mackasmiel L, Mane SP, Nguyen V, Purkayastha A, Shallom J, Yu G, Guo Y, Gabbard J, Hix D, Azad AF, Baker SC, Boyle SM, Khudyakov Y, Meng XJ, Rupprecht C, Vinje J, Crasta OR, Czar MJ, Dickerman A, Eckart JD, Kenyon R, Will R, Setubal JC, Sobral BWS (2007) PATRIC: The VBI PathoSystems Resource Integration Center. *Nucleic Acids Research* **35**: D401-D406.

Yu G, Snyder E, Boyle S, Crasta O, Czar M, Mane S, Purkayastha A, Sobral B, Setubal JC (2007) A Versatile Computational Pipeline for Bacterial Genome Annotation Improvement and Comparative Analysis, with Brucella as a Use Case. *Nucleic Acids Research* **35**(12):3953-3962.

Baker SC, Jukneliene D, Purkayastha A, Snyder EE, Crasta OR, Czar MJ, Setubal JC, Sobral BW (2006) Developing bioinformatic resources for coronaviruses. *Advances in Experimental Medicine and Biology* **581**:395-398.



Dr. V. Shulaev

Biochemical Profiling Research Group

Left to right: Vladimir Shulaev, Sarah Holt, Wei Sha, Chao Zang, Debby Reed, Matthew Reed, Stephanie Baptiste, Diego Cortes, Joel Shuman, Leepika Tuli

Metabolomics is a powerful tool that complements large-scale genomic and proteomic technologies

Research Interests

- Applications of metabolomics to systems biology and functional genomics
- Metabolomics and yeast systems biology
- Metabolomics and cancer
- Metabolomics of *Plasmodium falciparum*
- Application of metabolomics to study gene function in *Arabidopsis*
- Woodland strawberry (*Fragaria vesca*) as a model for fruit functional genomics

Selected Recent Publications

Bajad S, Shulaev V (2007) Highly-parallel metabolomics approaches using LC-MS^2 for pharmaceutical and environmental analysis. *Trends in Analytical Chemistry* **26**: 625-636.

Coutu1 J, Shulaev V, Mittler, R (2007) Reactive oxygen signaling in plants. In *Annual plant reviews*: *intracellular signaling in plants*. Zhenbiao Yang (ed), Blackwell Publishing. In press.

Martins AM, Sha W, Evans C, Martino-Catt S, Mendes P, Shulaev V (2007) Comparison of sampling techniques for parallel analysis of transcript and metabolite levels in *Saccharomyces cerevisiae*. *Yeast* **24**: 181-188.

Pisciotta JM, Coppens I, Tripathi AK, Scholl PF, Shuman J, Bajad S, Shulaev V, Sullivan DJ (2007) The role of neutral lipid nanospheres in *Plasmodium falciparum* heme crystallization. *Biochem J.* **402**: 197-204.

Varbanova M, Yamaguchi S, Yang Y, McKelvey K, Hanada A, Borochov R, Yu F, Jikumaru Y, Ross J, Cortes D, Je Ma C, Noel JP, Mander L, Shulaev V, Kamiya Y, Rodermel S, Weiss D, Pichersky E (2007) Methylation of gibberellins by *Arabidopsis* GAMT1 and GAMT2. *Plant Cell.* **19**: 32-45.

Metabolomics involves the global analysis of all cellular metabolites, which are small-molecule products of the chemical processes occurring in living organisms. This type of analysis is becoming more popular in genomics research, complementing other commonly used techniques to look at genes and proteins on a large scale. Although metabolomics has emerged as a powerful tool for functional genomics, it is now being applied to other areas. For example, metabolomics is being used by researchers to study mutant phenotypes, evaluate responses to environmental stress, further drug discovery work and conduct human disease and nutrition research. Metabolomics is also being applied as a systems biology tool.

The Biochemical Profiling Group at the Virginia Bioinformatics Institute is developing a high-throughput metabolomics platform for metabolic biomarker discovery, gene function elucidation and as a tool for systems biology. This platform is based on a combination of untargeted metabolite profiling, targeted analysis, and metabolic fingerprinting. For sample analysis, researchers in the group employ mass spectrometry-based analytical techniques due to their high sensitivity and wide range of covered metabolites. The platform has been successfully used in collaborative systems biology projects to study oxidative stress response in the yeast *Saccharomyces cerevisiae*, to identify unique metabolic signatures associated with the progression of malignancy in human breast epithelium cells, as well as in the response to various drugs by the malaria parasite *Plasmodium falciparum* and to elucidate early metabolic responses to abiotic stress in plants.

Dr. B. Tyler

Research Group

Left to right, back row: Marcus Chibucos, Trudy Torto-Alalibo, Lachelle Waller, Bryndan Durham, Nick Galloway, Daolong Dou, Lecong Zhou. *Front row:* Konstantinos Krampis, Regina Hanlon, Brett Tyler, Felipe Arredondo

The Tyler group is identifying and characterizing the genes and biological mechanisms that enable pathogens to recognize and overcome the defense systems of their plant hosts

The genus *Phytophthora* includes a group of belligerent plant pathogens that cause widespread devastation in crop plants and forest ecosystems. The pathogen *Phytophthora infestans* was responsible for the potato famine in Ireland in the mid-1800s. Together with other economic, political and social factors, this famine decimated the country's population and is reported to have resulted in around 1 million deaths. *Phytophthora ramorum* is a newly emerged species attacking trees and shrubs of coastal oak forests in California. *Phytophthora sojae* causes serious losses to the United States soybean crop.

Phytophthora pathogens (oomycetes) resemble fungi but belong to a kingdom of life called Stramenopiles. The Tyler group is looking at ways to delineate the host-pathogen-environment relationships that help *Phytophthora* recognize and infect its hosts.

The host and pathogen are engaged in an ongoing co-evolutionary battle spanning interconnected genetic regulatory networks. Researchers in Dr. Brett Tyler's group are building data collections and tool sets that will allow them to dissect in detail these host-pathogen genetic networks. The available data and tools will allow the compilation of an extensive parts list for the organisms, help to build a picture of the dynamics of how the pathogen and plant genes interact, and allow the researchers to infer genetic regulatory networks from the data acquired by experiment.

The Tyler group and collaborators have sequenced the genomes of the oomycetes *P. sojae, P. ramorum* and *Hyaloperonospora parasitica*, as well as the fungus *Alternaria brassicicola.* A comparison of these genome sequences has revealed that many genes are evolving unusually rapidly, including a large, diverse set of genes that encode virulence proteins that can enter plant cells. Standardized Gene Ontology terms have been created for describing the functions of the plant pathogen genes. The group recently completed the large-scale gene expression profiling of soybean and its pathogen *P. sojae* using Affymetrix GeneChip® microarrays. A genetical genomics approach is being used to infer genetic regulatory networks from these data.

Research Interests

- Comparative and functional genomics of oomycete plant pathogens
- Molecular analysis of oomycete virulence proteins
- Functional genomics of quantitative disease resistance and infection responses in plants
- Computational prediction of gene functions
- Mathematical modeling of complex cellular responses

Selected Recent Publications

Jiang RHY, Tyler BM, Govers F (2006) Comparative analysis of *Phytophthora* genes encoding secreted proteins reveals conserved synteny and lineage-specific gene duplications and deletions. *Molecular Plant-Microbe Interactions* **19:** 1311-1321.

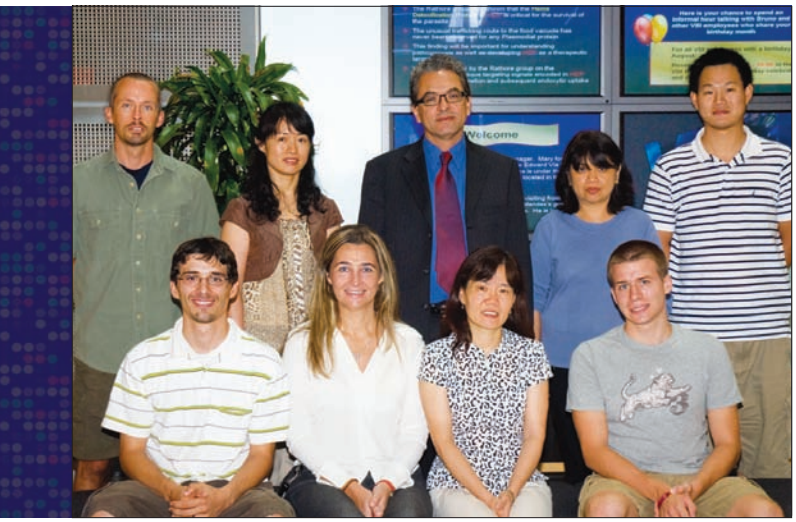
Krampis K, Tyler BM, Boore JL (2006) Extensive variation in nuclear mitochondrial DNA content between the genomes of *Phytophthora sojae* and *Phytophthora ramorum*. *Molecular Plant-Microbe Interactions* **19:** 1329-1336.

Tyler BM, Tripathy S, Zhang XM et al. (53 authors) (2006) *Phytophthora* genome sequences uncover evolutionary origins and mechanisms of pathogenesis. *Science* **313:** 1261-1266.

Zhang X, Scheuring C, Tripathy S, et al. (2006) An integrated BAC and genome sequence physical map of *Phytophthora sojae*. *Molecular Plant-Microbe Interactions* **19:** 1302-1310.

Torto-Alalibo T, Tripathy S, Smith BM, et al. (2007) Expressed sequence tags from *Phytophthora sojae* reveal genes specific to development and infection. *Molecular Plant-Microbe Interactions* **20**: 781-793.

Tyler BM (2007) *Phytophthora sojae*: root rot pathogen of soybean and model oomycete. *Molecular Plant Pathology* **8:** 1-8.



Dr. B. Sobral

PathoSystems Biology Research Group

Left to right, back row: Timothy Driscoll, Chunhong Mao, Bruno Sobral, Endang Purwantini, Shenghua Li
Front row: Matt Dyer, Isabel Da Fonseca, Chunxia Wang, James Lester

The PathoSystems Biology Group focuses on understanding and reverse engineering host-pathogen-environment interactions

Research Interests

- Alpha-proteobacteria, using the *Sinorhizobium meliloti-Medicago truncatula* symbiosis as a model system, and their strategies and success as intracellular bacteria
- Comparative biology of intra- and extracellular forms of alpha-proteobacteria
- Comparative genomics, especially of alpha-proteobacteria, focused on evolution and dynamics of intracellular lifestyles across multiple bacterial-host systems

Selected Recent Publications

Dyer MD, Murali TM, Sobral BWS (2007) Computational prediction of host-pathogen protein-protein interactions. *Bioinformatics* **23**(13): i159-i166.

Nene V, Wortman JR, Lawson D, and 92 other authors (2007) Genome sequence of *Aedes aegypti*, a major arbovirus vector. *Science* **316**(5832): 1718-1723.

Wang C, Saldanha M, Sheng X, Shelswell KJ, Walsh KY, Sobral BWS, Charles TC (2007) Roles of poly-3-hydroxybutyrate (PHB) and glycogen in symbiosis of *Sinorhizobium meliloti* with *Medicago sp. Microbiology* **153**: 388-398.

Wang C, Sobral BWS, Williams KP (2007) Loss of a universal tRNA feature. *Journal of Bacteriology* **189**: 1954-1962.

Williams KP, Sobral BWS, Dickerman AW (2007) A robust species tree for the Alphaproteobacteria. *Journal of Bacteriology* **189**(13): 4578-4586.

The primary focus of the PathoSystems Biology Group is to look in detail at the alpha-proteobacterial genomes from the bias of the Rhizobiales. Rhizobiales is a sub-division of the alpha-proteobacteria that includes many bacteria living in close association with plants.

The PathoSystems Biology Research Group is engaged in functional genomic studies of key genes for carbon metabolite and nodulation/nitrogen fixation in *Sinorhizobium meliloti.* They are also making comparisons of Rhizobia with other alpha-proteobacteria and participating in the genome sequencing project of *Aedes aegypti*. Researchers in the group have also performed genome-wide analyses of the ExoS/ChvI two-component regulatory system in *S. meliloti,* investigated the influence of the polyhydroxybutyrate granule-associated proteins on polyhydroxybutyrate accumulation and symbiotic nitrogen fixation in *S. meliloti* Rm1021, and carried out comparative modeling of the cell cycle (from *Caulobacter crescentus* to *S. meliloti*).

Two resources for the research community - the Rhizobiales Bioinformatics Resource Center and the NodMutDB Nodulation Mutant Database - are under active development. Research in the group has also identified a novel small non-coding RNA in *S. meliloti,* probed the regulation of transcription during infection and nodulation, and helped to identify enzymes using Open Reading Frame screening. The group has also identified a tRNA unique to the alpha-proteobacteria, constructed a robust species tree for the alpha-proteobacteria, and continues to work on the computational prediction of host-pathogen protein-protein interactions. The PathoSystems Biology Research Group also collaborates with Dr. John Tyson's research group (Department of Biological Sciences, Virginia Tech) on a project to model the cell division cycle in alpha-proteobacteria. This is an extension of the Tyson group's research on the cell division cycle of *Caulobacter crescentus*, a bacterium that inhabits freshwater, seawater and soils.

Dr. B. Sobral

CyberInfrastructure Research Group

Left to right, back row: Bruno Sobral, Yan Zhang, Oswald Crasta, Bruce Sharp, Dan Sullivan, Eric Nordberg, Mark Scott, Rebecca Wattam, Eric Snyder, Herman Formadi, Lucas Mackasmiel, Jeetendra Soneja. *Middle row:* Shamira Shallom, Tian Xue, Dan Liu, Wei Sun, Saroj Mohapatra, Rebecca Will, Chengdong Zhang, Stephen Cammer, Qiang Yu, Shrinivasrao Mane. *Front row:* Daphne Rainey, Joshua Shallom, Ron Kenyon, Mike Czar, Maulik Shukla, Nishant Vaghela

The approach used for research in the Cyberinfrastructure Group is transdisciplinary, uniting diverse initiatives to address some of the key challenges in the biomedical, environmental and agricultural sciences

The Cyberinfrastructure Group applies the principles of cyberinfrastructure to integrate data, computational infrastructure and people for the purpose of scientific discovery, primarily in the area of infectious diseases. The group curates genomic, microarray, proteomic and literature data from various infectious disease systems and designs and implements the databases required to support and disseminate them. The Cyberinfrastructure Group also develops tools for analysis and visualization of the data across its systems.

The Cyberinfrastructure Group is bringing all of these resources together through a common portal architecture for acquiring, storing, accessing, analyzing and portraying the data, enhancing the capability for knowledge discovery and facilitating collaboration among researchers. Through its education and outreach activities, the Cyberinfrastructure Group is developing sessions for and collaborations with external researchers, resulting in discoveries and publications. Cyberinfrastructure Group resources include the following: genome curation, storage, and portrayal infrastructure; genome and proteome curation protocols for bacterial and viral systems; high quality curated genome, proteome and literature data for select biodefense and emerging infectious disease pathosystems; storage, analysis, visualization and portrayal tools for gene expression microarray and diverse protein profiles. The Cyberinfrastructure Group also offers Collaborative Research Team resources for the collaborative design and analysis of experiments and the discovery of new knowledge, user-centered software design and development, and bioinformatics training materials and session deployment focused on research goals and data.

Research Interests

- Development and deployment of cyberinfrastructure supporting infectious disease research
- Transdisciplinary partnerships aimed at supporting the development of vaccines, diagnostics and therapeutics against infectious agents

Selected Recent Publications

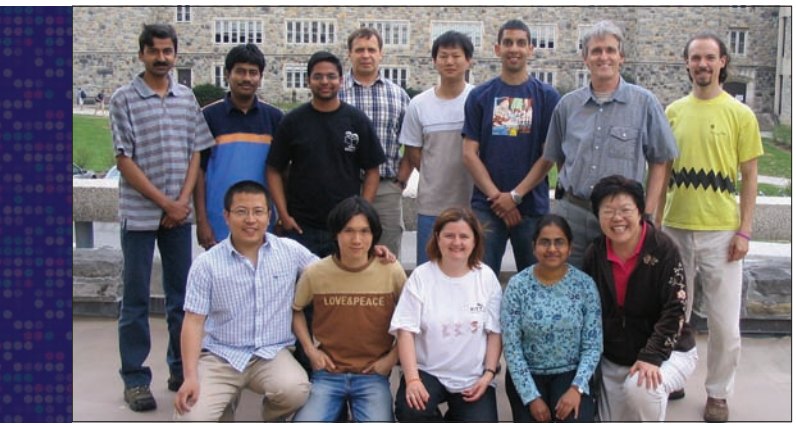
Gilchrist CA, Houpt E, Trapaidze N, Fei Z, Crasta O, Asgharpour A, Evans C, Martino-Catt S, Baba DJ, Stroup S, Hamano S, Ehrenkaufer G, Okada M, Singh U, Nozaki T, Mann BJ, Petri WA Jr (2006) Impact of intestinal colonization and invasion on the *E. histolytica* transcriptome. *Molecular and Biochemical Parasitology* **147**:163-176.

Gillespie JJ, Beier MS, Rahman MS, Ammerman NC, Shallom JM, Purkayastha A, Sobral BS, Azad AF (2007) Plasmids and *Rickettsial* Evolution: Insight from *Rickettsia felis*. *PLoS ONE* **2**(3): e266. doi:10.1371/journal.pone.0000266

Snyder EE, Kampanya N, Lu J, et al. (2007) PATRIC: The VBI PathoSystems Resource Integration Center. *Nucleic Acids Research* **35:** D401-D406 (Database issue).

Wang C, Sobral BW, Williams KP (2007) Loss of a universal tRNA feature. *J. Bacteriol.* **189**(5): 1954-1962.

Williams KP, Sobral BW, Dickerman AW (2007) A robust species tree for the Alphaproteobacteria. *J. Bacteriol.* **189**: 4578-4586.



Dr. J. Tyson

VBI Faculty Fellow

Left to right, back row: Debashis Barik, Sandip Kar, Rajat Singhania, Paul Brazhnik, Shenghua Li, Ranjit Randhawa, John Tyson, Jason Zwolak. Front row: Tongli Zhang, Teeraphan Laomettachit, Elife Zerrin Bagci, Janani Ravi, Kathy Chen

Dr. John Tyson's Research Group is converting network diagrams into dynamical models and exploring the models using analytical and computational methods

Research Interests

- Spatial and temporal organization of biological systems Network dynamics and systems biology
- Cell division cycle in bacteria and yeast
- Bifurcation analysis, stochastic modeling and parameter estimation

Selected Recent Publications

Csikasz-Nagy A, Battogtokh D, Chen KC, Novak B, Tyson JJ (2006) Analysis of a generic model of eukaryotic cell cycle regulation. *Biophys. J.* **90**(12): 4361-4379.

Ciliberto A, Capuani F, Tyson JJ (2007) Modeling networks of coupled enzymatic reactions using the total quasi-steady state approximation. *PLoS Comp. Biol.* **3**(3): e45.

Csikasz-Nagy A, Gyorffy B, Kapuy O, Tyson JJ, Novak B (2007) Modeling the septation initiation network (SIN) in fission yeast cells. *Curr. Genet.* **51**(4): 245-255.

Zhang T, Brazhnik P, Tyson JJ (2007) Exploring mechanisms of the DNA damage response: p53 pulses and their possible relevance to apoptosis. *Cell Cycle* **6**(1): 85-94.

The fundamental goal of molecular cell biology is to understand how the information encoded in a genome is used to direct a cell's complex physiological response to its environment. One major achievement in molecular biology has been the identification and characterization of the molecular components of a living organism; the complete sequencing of the human genome is one notable example. The grand challenge of post-genomic cellular biology is to assemble a working model of a living cell, a model that gives a reliable account of how the physiological properties of a cell derive from its underlying molecular machinery. Complex networks of interacting proteins control the physiological properties of a cell, including metabolism, reproduction, motility and signaling. Diagrams of these networks can be useful in classifying the results of the hundreds or more of observations that occur during experiments, but one difficulty is developing tools that will help researchers understand the dynamics of such control systems.

Using basic principles of biochemical kinetics, Dr. John Tyson's Research Group is converting network diagrams into dynamical models and exploring the models using analytical and computational methods. Of particular interest to group members are the mechanisms that control cell growth, division and death in eukaryotes, such as yeasts, plants, insects and vertebrates. The group has recently published a mathematical model of the protein interaction network (PIN) that is thought to direct DNA synthesis and nuclear division in all eukaryotic cells. By numerical simulations and theoretical analysis, Dr. Tyson's group showed that this model successfully accounts for the properties of cell growth and division in many types of cells. A second paper from the group investigated the cell's response to DNA damage and how the decision is made to attempt repair or to trigger cell death. Improvements of the mathematical representation of PINs was the topic for a third paper from group members.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Finance and Administration

"My contribution to team science at VBI is to work closely with the faculty and their research teams in putting together high quality proposals. For me, team science is about developing new ideas, facilitating collaborations, fostering new partnerships, and collaboratively using new tools to understand highly complex systems."

Sharon Lawson,
Senior Grants and Contracts Manager

The theme of this year's annual report highlights the importance of teams in the success of the Virginia Bioinformatics Institute (VBI). A team-based approach to scientific initiatives and institute-wide resources is at the center of the purpose and values of VBI. We continue to see the direct benefits of this collaborative approach reflected in the progress of the Institute.

VBI continued to show growth in total active awards and number of employees for the fiscal year ending June 30, 2007. Total active awards by sponsor reached $63 million and the Institute employed 232 personnel by the end of the 2006-2007 fiscal year. Three federal sponsors support the extramural research program of VBI: the National Institutes of Health (36%), the National Science Foundation (33.3%) and the United States Department of Defense (21.5%). Other leading federal agencies and academic institutions represent the balance of our funding. Collectively, the diversity of all sponsors ensures a stable platform from which to grow.

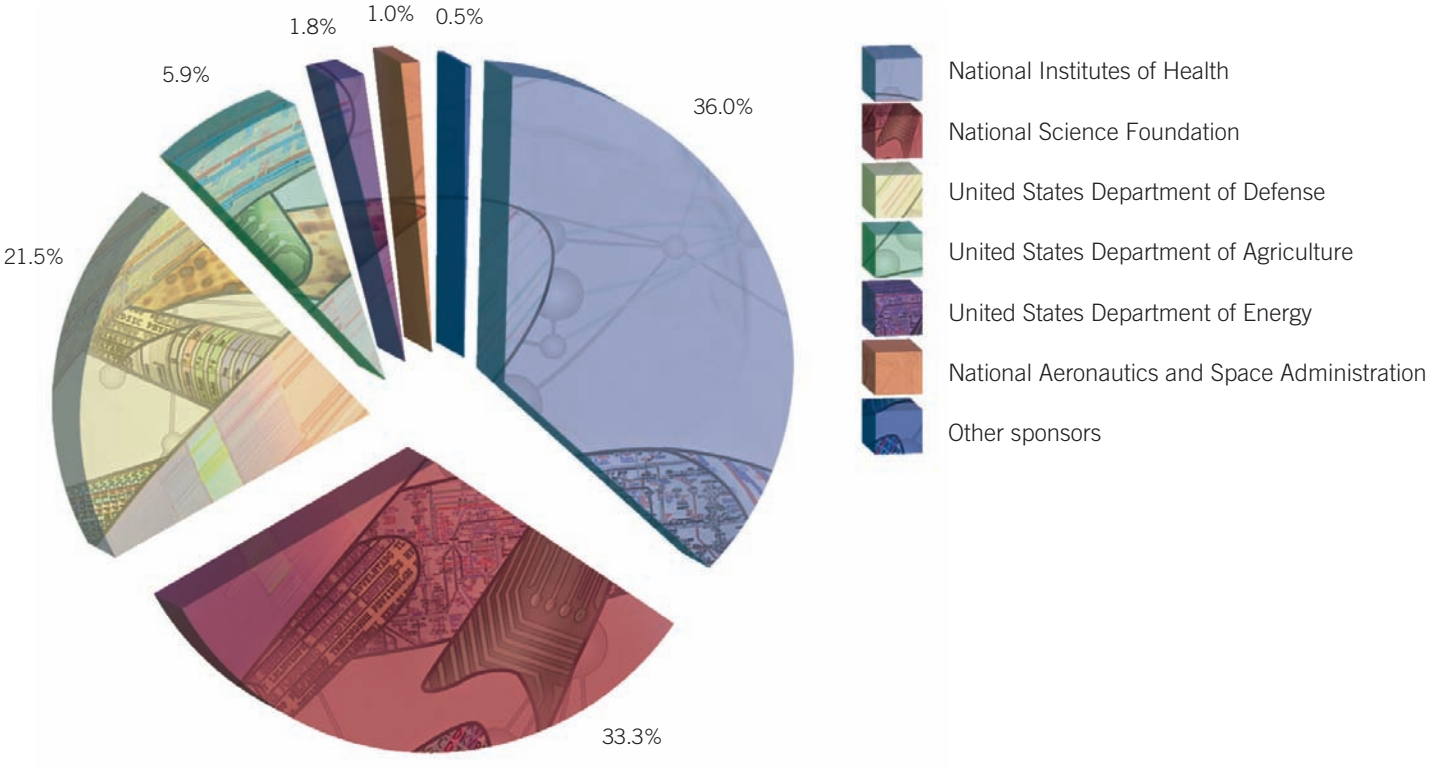
VBI also participated in the Commonwealth Research Initiative in the past fiscal year, which supported the purchase of the GS-FLX™ genome sequencer from Roche. The GS-FLX™ allows researchers to go from genome to sequence in record time. This new genome-sequencing platform will continue to provide a competitive edge to researchers at VBI, Virginia Tech, across the Commonwealth of Virginia and beyond, as genomes can be sequenced in the fraction of the time required by more traditional methods. This support from the Commonwealth Research Initiative allows VBI to continue its role as a shared resource for the wider research community.

We would like to thank all employees of the Institute, past and present, for their contribution to the success of VBI. The Institute's team-based approach to the life sciences allows us to look forward to many exciting new developments in the years ahead.

Sincerely,

Lauren Coble
Associate Director, Administration and Finance

Active Research Grants and Contracts
as of June 30, 2007

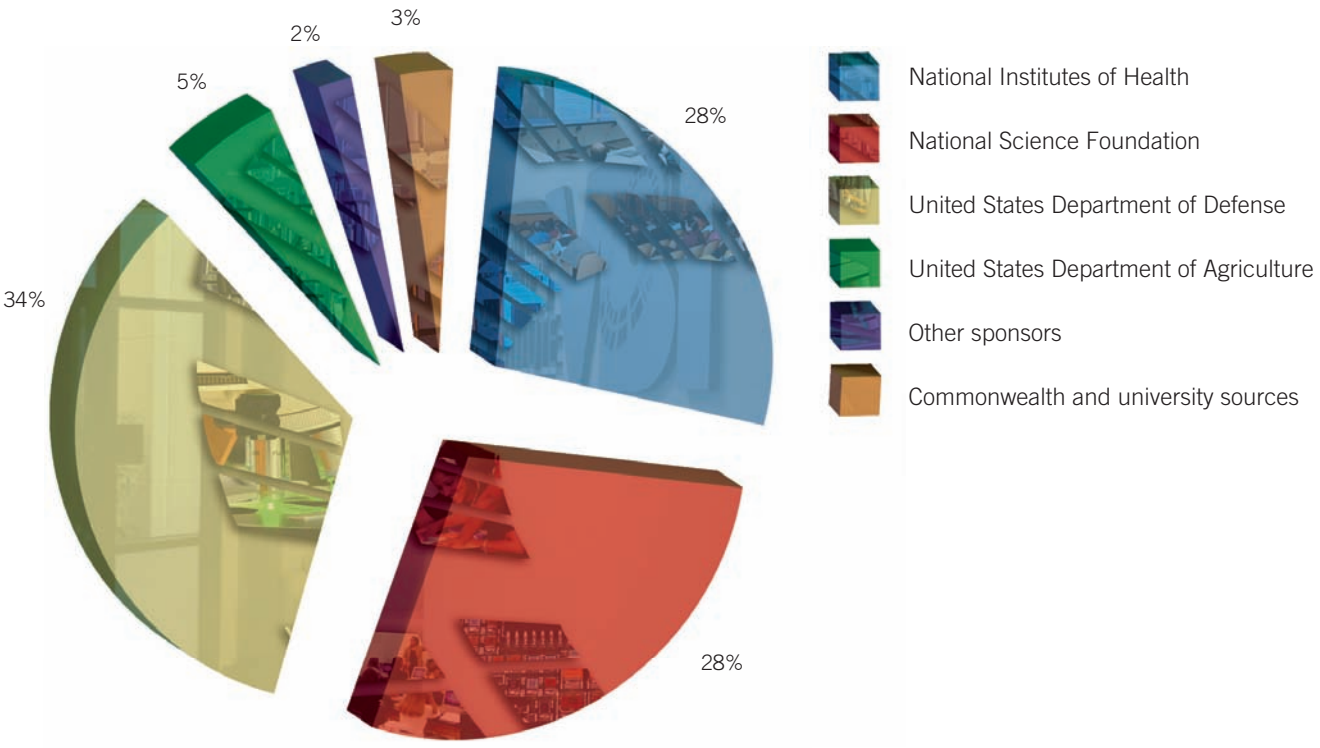


Total Active Awards by Sponsor
as of June 30, 2007

National Institutes of Health	$ 23,171,068
National Science Foundation	20,336,367
United States Department of Defense	13,114,915
United States Department of Agriculture	4,331,731
United States Department of Energy	1,046,190
National Aeronautics and Space Administration	595,153
Other sponsors	314,454
Total active awards	$ 62,909,878

2007 Research Expenditures by Sponsor
as of June 30, 2007

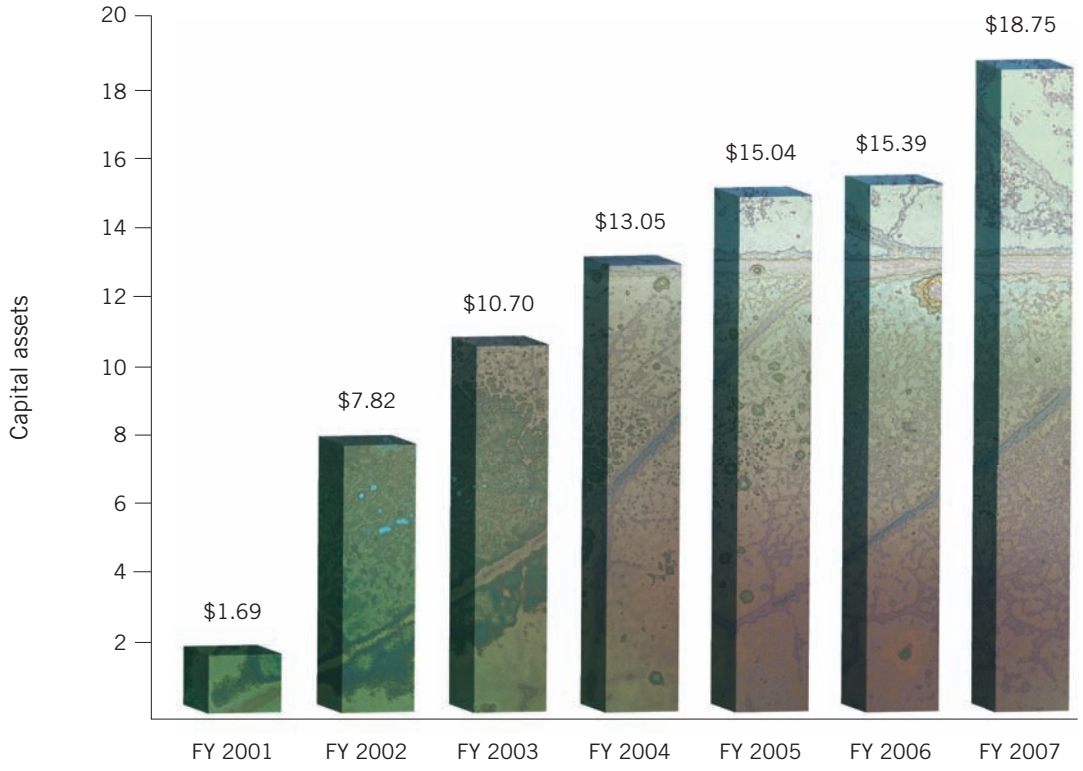
National Institutes of Health	$ 4,071,867
National Science Foundation	4,148,426
United States Department of Defense	4,995,905
United States Department of Agriculture	760,610
Other sponsors	290,701
Commonwealth and university sources	507,683
Total extramural expenses	$ 14,775,192



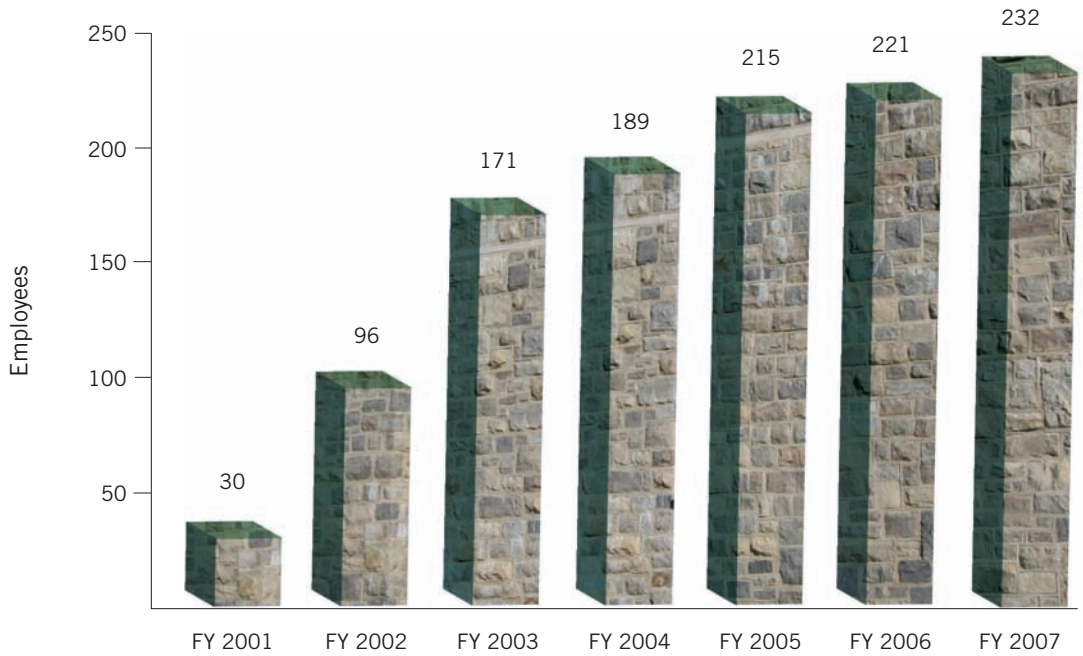
Financial Operating Activity
for the years ended June 30, 2007 and 2006

Revenues	FY 2007	FY 2006
Grants and contracts		
National Science Foundation	$ 4,743,485	$ 3,115,413
United States Department of Defense	4,763,084	4,123,852
National Institutes of Health	4,517,213	5,539,237
United States Department of Agriculture	801,101	1,147,850
United States Department of Energy	207,906	388,097
United States Department of Transportation	45,844	126,924
Foundations	1,346	24,424
National Aeronautics and Space Administration	52,823	6,029
Industry	11,042	4,810
Other federal sources	–	10,169
Total grants and contracts	15,143,844	14,486,805
Commonwealth and university sources	3,049,078	3,111,826
Total operating revenue	18,192,922	17,598,631
Expenses		
Personnel expenses	14,994,014	14,602,596
Operating expenses		
Contractual services	1,116,220	941,619
Information technology	1,030,803	634,856
Travel and other	687,885	617,214
Supplies and materials	2,160,960	1,750,613
Building and other rentals	790,144	58,856
Subcontracts	925,962	1,752,777
Equipment	1,613,555	580,623
Total operating expenses	8,325,529	6,336,558
Indirect expenses	4,351,070	4,096,187
Total expenses	27,670,613	25,035,341
Non-operating sources		
University support	9,425,808	8,509,015
Commonwealth Research Initiative	1,503,000	
Total Non-Operating Sources	10,928,808	8,509,015
Gain in net assets	$ 1,451,117	$ 1,072,305

Capital assets
for fiscal years 2001-2007 (all dollars in millions)



Personnel
for fiscal years 2001-2007



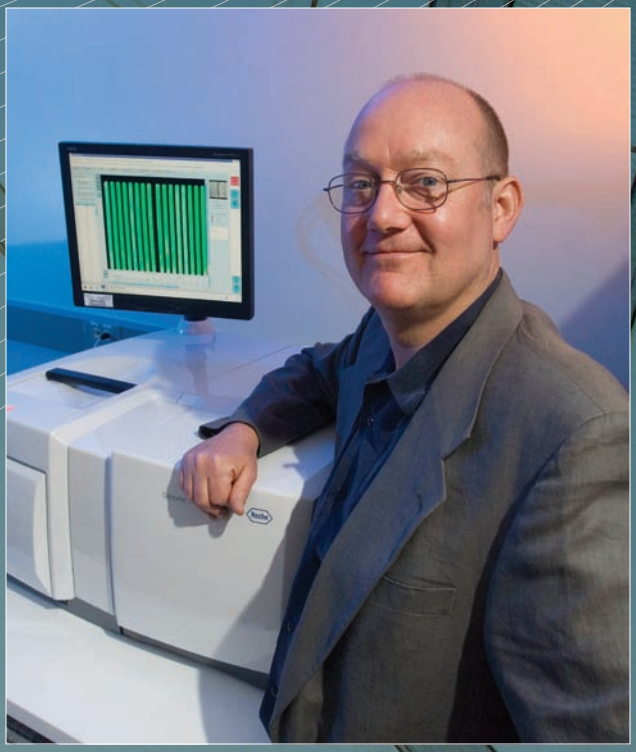
Building the Future

- Technology
- Outreach and Engagement
- Communications

Building the future requires commitment and endeavor. Whether it's channeling innovation into technology development, training the next generation of undergraduates or introducing new communication resources that link collaborators closer together, a team-based approach maximizes the chances for success. At VBI, institutional resources in business development, outreach and engagement and public relations are available to assist institute-wide research initiatives as well as education and training projects. In this way, transdisciplinary or collaborative research at VBI is given ample opportunity to deliver real benefits to the life science community.

"The Virginia Bioinformatics Institute's team-based research is a source of innovation that can lead to the development of new products, technologies and services. My role at VBI is to identify new discoveries, technology, know-how and intellectual property that have commercial potential and to identify partners who can assist and support commercial development."

Otto Folkerts,
Associate Director Technology Development



Technology Development

VBI continually strives to identify new technologies and protect its intellectual property. As a research center with a significant critical mass in basic and applied research, innovation gives rise to the development of new products, technologies and services. The Institute works closely with the appropriate individuals at Virginia Tech, and in partnership with Virginia Tech Intellectual Properties, Inc. and outside law firms, to secure its intellectual property portfolio. In the past year six Invention Disclosures, four Provisional Patent Applications, three US Utility Applications and one International Patent Application were filed (see Table).

The Technology Development Continuum

- Identify new discoveries, technology, know-how, and intellectual property that have commercial potential
- Protect intellectual property by filing invention disclosures with the university, and patent applications with the US Patent and Trademark Office
- Identify opportunities and hurdles for product or technology development, and determine which enabling technologies or critical path activities are necessary
- Find partners who can assist in and fund commercial development, or in select cases determine the potential to start new business ventures around technology

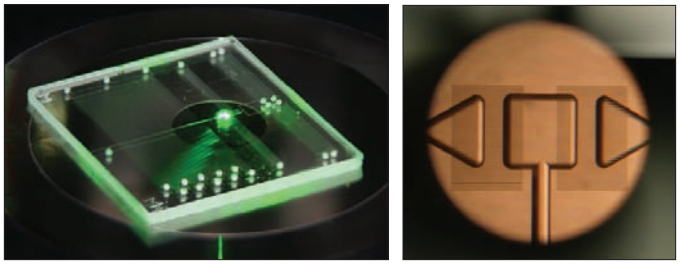
Case study: Microfluidic devices for cancer biomarker discovery

Cancer is a leading cause of disease and death worldwide. More than a million new cases are diagnosed annually, resulting in more than half a million mortalities, and over US$ 200 billion in direct medical costs or indirect costs are associated with loss of productivity due to illness or death. Much of the individual suffering and cost to society can be mitigated by accurate and early diagnosis and treatment. This is driving the need for new cancer diagnostic platforms, assays and tests.

Dr. Iuliana Lazar's research program aims to develop fully integrated microfluidic liquid chromatography and mass spectrometry devices that will enable high-throughput analysis of protein extracts from cancer cells. Through differential expression analysis, biomarker discovery and screening of cancer tissues or serum from cancer patients and healthy individuals, it is hoped that devices and methods for clinical diagnostics and large-scale population screening can be developed, tested and ultimately marketed to clinical laboratories and diagnostic companies for use in routine screening and diagnosis.

The microfluidic device under development by Dr. Lazar is suitable for large-scale screening of disease-related biomarkers. Protein biomarkers are useful as "molecular indicators" for a wide range of diseases including breast cancer. The lab-on-a-chip integrates a pump, valve, separation column, and detection interface onto a small glass microchip and delivers a performance to match benchtop instrumentation typically occupying a few square feet of lab space.

Microfluidic devices have emerged as powerful and reliable analysis platforms for proteomic applications and biomarker screening. The new diagnostic devices being developed by Dr. Lazar are versatile, fully integrated systems that fit on a versatile glass microchip. The miniature format as well as the ability to manipulate small amounts of sample result in short analysis times (approximately 30 minutes), use of smaller volumes of reagent and significant reductions in cost.



The microfluidic chips are expected to perform better than bench-top systems in two areas. As a result of simultaneous micro-arraying capability they are expected to be up to 10 times faster, and have ten to one hundred times greater sensitivity in comparison with conventional mass spectrometry systems. Because of their small size they can be manufactured at significantly reduced costs.

To date Dr. Lazar has developed and tested a number of prototypes for different applications. Mass spectrometry analysis of MCF7 breast cancer cell protein extracts separated on the microfluidic chip, demonstrated that a number of known proteins and putative breast cancer biomarkers could be detected with high statistical significance. Five putative cancer biomarkers have been identified.

Funding and industry partners are being sought for further development and extensive testing of the microfluidic chip mass spectrometry interface, and optimizing the chip and assays for detection of specific cancer biomarkers.

Invention disclosures, provisional patent applications, US utility applications, and international patent applications in the fiscal year ended June 30, 2007, at VBI

VT Disclosure Number	Principal Investigator	Filing Date	Title
Invention Disclosures			
06.074	Dharmendar Rathore	07/07/06	HDP: a novel heme detoxification protein in *Plasmodium falciparum* malaria
06.090	Pedro Mendes	08/17/06	COPASI
06.135	Bruno Sobral	12/12/06	*Brucella abortus* genes and proteins encoding virulence factors
07.020	Jean Peccoud	02/23/07	Software for design and verification of synthetic gene constructs
07.048	Bruno Sobral	05/02/07	Method of using probiotic bacteria to treat or prevent obesity and type 2 diabetes
07.051	Brett Tyler	05/04/07	Double-Shot: a double barreled device for biolistic transformation of living tissues
Provisional Applications			
06.135	Bruno Sobral	11/24/06	*Brucella abortus* genome sequencing and virulence factors
07.020	Jean Peccoud	03/30/07	Software for design and verification of synthetic gene constructs
07.048	Bruno Sobral	06/08/07	Method of using probiotic bacteria to treat or prevent obesity and type 2 diabetes
07.051	Brett Tyler	06/07/07	Double-Shot: a double barreled device for biolistic transformation of living tissue
US Utility Applications			
06.057	Iuliana Lazar	08/24/06	Microfluidic devices and methods facilitating high-throughput, on chip detection and separation techniques
06.059	Chris Lawrence	10/13/06	Fungus-induced inflammation and eosinophil degranulation
06.026	Chris Lawrence	03/14/07	Targeted and non-targeted gene insertion using linear minimal element constructs
International Patent Applications			
05.062	Dharmendar Rathore	10/13/06	A novel therapeutic target for protozoal diseases

Outreach and Engagement

Virginia Tech's first iGEM team competes in international event

"Boston or bust" was the motto for Virginia Tech's first ever International Genetically Engineered Machines (iGEM) team. Boston, MA, was the location for the 2007 iGEM jamboree, an annual competition organized by the Massachusetts Institute of Technology (MIT) that gives undergraduate students the opportunity to design and build an engineered biological system using standard DNA parts. Getting to Boston, however, was going to take a lot of hard work for students with schedules already full of class meetings, exams, homework, and part-time jobs.

Left to right: Matthew Lux, Nalin Pilapitiya, Susan Faulkner, Matthew Sweede, Jean Peccoud, Emily DeLalla, David Ball, Blair Lyons, Bill Baumann, Rebecca Shelton, Jodi Lewis, Yizhi (Patrick) Cai, Otto Folkerts

Getting the parts in place

In the fall of 2006, VBI Associate Professor Jean Peccoud spearheaded the effort to create an iGEM team at Virginia Tech. This involved recruiting members, coordinating meetings, and helping to secure sponsorship. By January, five undergraduate students had joined the team and started meeting on a regular basis. According to Peccoud, "The team met twice a week, once at a journal club to discuss scientific papers on synthetic biology and also at a lab meeting, where the students discussed work plans and met with researchers in my lab." Peccoud leads VBI's Synthetic Biology Research Group, whose projects focus on artificial gene networks and synthetic biology. In addition to Peccoud, the team worked closely with Bill Baumann, associate professor of Electrical and Computer Engineering in Virginia Tech's College of Engineering.

"At VBI, we try to foster creative learning environments that allow students to come into direct contact with some of the latest developments in scientific research," said VBI Executive and Scientific Director Bruno Sobral. "The iGEM project is a great example of how we can promote interaction between research faculty and their scientific teams on the one hand and undergraduate students who are just starting on their career path on the other."

As the iGEM team continued to work, Peccoud worked hand-in-hand with VBI's management team to find a team sponsor. In May, it was announced that Third Security, LLC, a private equity and venture capital firm, would sponsor the Virginia Tech team. The funds provided by the firm helped support laboratory work as well as the students' participation in the competition's jamboree in Boston. DNA 2.0, a California-based company providing synthetic genes, also stepped up to the plate as sponsors in July.

Sizing up the competition

After spending many hours over the summer working on their project, the Virginia Tech team hosted two other regional iGEM teams – the University of Virginia and Davidson and Missouri Western teams – at VBI. The meeting gave the students an opportunity to share experiences and ongoing work for the national competition and acclimatize them to the competitive nature of iGEM. It was here that the teams unveiled ideas for their projects and discussed specific issues they encountered throughout the process, including how they decided on a particular project, the different approaches that have been considered, and what the end results of the projects could be.

Using *Escherichia coli* and bacteriophage lambda as a model population, the Virginia Tech team's primary project focused on engineering disease epidemics. They examined the development of an epidemic within and between populations, creating a population interaction model that could be related to the spread of infection between groups of people. The team designed a network for the spread of infection and created models, which they verified experimentally.

Bringing home gold

On November 3-4, the Virginia Tech iGEM team's hard work paid off, as they made the trip to Boston for the university's first appearance in the national iGEM competition. The two-day event included a team presentation of the project as well as a poster presentation, both of which were evaluated by competition judges. The judges also looked at the team's website that described the project and its history throughout the year. The judges awarded the team a gold medal in recognition of the work performed to sequence all of the BioBricks in the iGEM Registry. BioBricks are the standard interchangeable biological parts used by the participants in the annual iGEM competition to produce systems that work as molecules inside living organisms. Having these sequences available will be very useful for future iGEM teams.

"In addition to the work by Virginia Tech's iGEM team, sequencing the Registry required the contributions of many people in VBI's Core Laboratory Facility, Core Computational Facility, Cyberinfrastructure Group, and Synthetic Biology Group," Peccoud said. "This is an excellent example of the project-oriented and collaborative approach to biological research for which VBI is known. All contributors worked very hard to release the first set of data in time for the iGEM Jamboree."

According to Blair Lyons, a freshman in General Engineering and Biochemistry, "Being a part of Virginia Tech's first ever iGEM team has been an invaluable experience. Not only did we gain research and laboratory experience, but we learned how to combine mathematical modeling, engineering methods, and genetic engineering tools that could one day have an impact on human health.

iGEM Timeline 2007

February	Virginia Tech's first IGEM team announced
March	Team meets twice a week at journal club and lab meetings (March - April)
April	
May	Third Security provides sponsorship for the team
June	Students work over the summer on their project (June - July)
July	Virginia Tech team hosts regional teams at VBI
August	Final preparation completed before national competition (August - October)
September	
October	
November	Team wins gold medal in national iGEM competition in Boston

New VBI web site launched

Free to the public and used all over the world, Joomla!™ is led by a team of project managers from a variety of backgrounds and disciplines working in 11 different countries.

After months of preparation and behind the scenes work, VBI unveiled its new website in March, 2007. VBI Webmaster Ivan Morozov, along with Strategic and Research Communications Officer Barry Whyte, worked closely with the Institute's management, faculty, and staff to create an online presence that reflects the visual identity, priorities, and future direction of the Institute.

Whyte remarked: "Early in the project we needed a good idea of what the new site map might look like. We therefore started a dialog with users of the existing web site and conducted a structured survey which was useful in assessing the strengths and weaknesses of what we had." After pinpointing what VBI needed from its website, Morozov, Whyte, and members of the Information Technology staff had to determine the best way to meet these needs, which included the review of approximately 20 Content Management Systems (CMSs). Joomla!™, an open-source CMS, was chosen to handle the site's content. Free to the public and used all over the world, Joomla!™ is led by a team of project managers from a variety of backgrounds and disciplines working in 11 different countries. The system was designed for use by both experts and non-technical users and accommodates multiple administrators. For VBI, this means that users from different areas of the Institute can oversee the content of their own sections of the site without having to rely on assistance from web administrators.

"Joomla!™ had most of the things we were looking for in a CMS," said Morozov. "Separate program areas at VBI can manage their pages on the site. For example, individual faculty members can update information about their research and publications, so the site features the most current content. We've been rolling out the training for this since the launch of the site. Also, the CMS gives us a dynamic site, which means it automatically updates the content on the site's front page without using a lot of resources. There's also plenty of scope for introducing new features and functionality – including multimedia."

After choosing Joomla!™ as the new CMS for the site, there was the daunting task of moving all of the site's content into the new system. "This was a big undertaking," Morozov explained. "All of the data had to be physically transferred and arranged, so older information that people may have bookmarked can still be accessed in the same way. VBI's Core Computational Facility team played a key part in ensuring that this transition went smoothly."

The navigation has also been simplified for the new site and more efficient search capabilities have been integrated, making it easier for visitors to find exactly what they're looking for. Several other new functionalities have been integrated, such as a searchable staff directory, a new-look employment section, as well as an event calendar, which is managed by VBI's Education and Outreach group and provides detailed information about seminars at the Institute and other special events. An RSS feed is also included, providing interested users with updates when new content is added. Whyte commented: "Web technologies change quickly and you need to implement a flexible solution to stay ahead of the curve. With Joomla!™ we've introduced a web site that we can evolve over the years ahead."

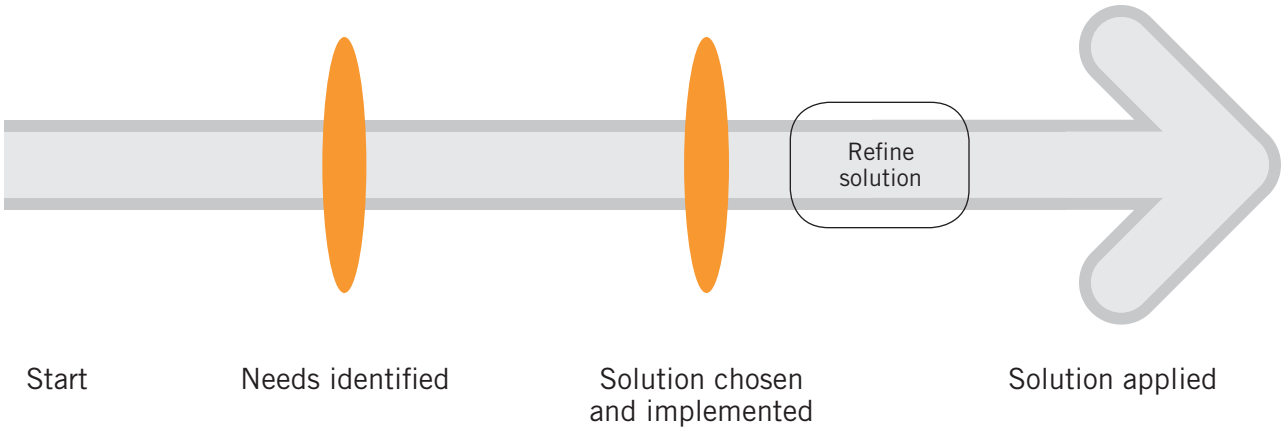
Joomla!™ at a glance

- Access to RSS feeds
- Business or organizational directories
- User forums and discussion groups
- Calendars
- Blogs
- Email newsletters
- Dynamic form builders
- Document management
- Data collection and reporting tools
- Image and multimedia galleries

Joomla!™

- Simplified navigation
- Better search capabilities
- Higher priority to science

- Stronger visual identity
- RSS feeds, event calendar, searchable jobs and staff directory, and other new functionality
- Designed for growth and development



VBI's Policy Advisory Board

The Policy Advisory Board of the Virginia Bioinformatics Institute was established in 2000 by a Board of Visitors' resolution to help guide the Institute in its efforts to produce economically beneficial research to the Commonwealth of Virginia and beyond. The Policy Advisory Board exercises its authority principally in policy-making and oversight, serving in an advisory role to the university administration and the Institute's director, and helping develop, secure, and enhance resources for the Institute. The role of the Policy Advisory Board is instrumental in helping to advance the economic development components of the Institute's mission.

Members of the Board of Visitors

George C. Nolen, Chair
Ben J. Davenport, Jr.

At-large (Recommended by the University)

Mr. John Alderson
Dr. Robert Walters
Mr. Lawrence H. Framme, III
The Honorable Thomas D. Rust

Representative from the Tobacco Indemnification and Community Revitalization Commission

Mr. Clarence D. Bryant, III

Recommended by the Governor

Dr. Christoph von Arb
Mr. Buddy G. Beck
Mr. R.J. Kirk

Ex-officio

Dr. Charles Steger
Mr. James A. Hyatt
Dr. Mark McNamee
Dr. Bruno Sobral

Others/Senior Staff

Mr. M. Dwight Shelton, Jr.
Mr. Ralph M. Byers
Ms. Lauren Coble
Dr. Otto Folkerts
Dr. João Setubal