



connecting to the future

# innovation

## 2005 Annual Report

VIRGINIA  
BIOINFORMATICS  
INSTITUTE  
AT VIRGINIA TECH



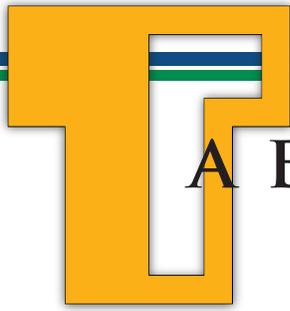


VIRGINIA  
BIOINFORMATICS  
INSTITUTE  
AT VIRGINIA TECH



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# MESSAGE FROM THE PRESIDENT



As developments in science and technology continue to advance, organizations and academic institutions must create, distribute, and benefit from new knowledge to thrive in the global community. Virginia Tech recognizes these needs and is building on its heritage as a land-grant university where the focus has always been to link excellence in research and education to societal needs. The Virginia Bioinformatics Institute at Virginia Tech is an important part of this undertaking as it strives to balance the discovery, dissemination, and application of new knowledge.

Since the Institute began in 2000, VBI's dedicated faculty and staff have made multidisciplinary research and collaboration a primary focus. The Institute brings together a wide variety of academic disciplines in an effort to answer questions that impact all areas of life. With the Institute's innovative and multidisciplinary approach to research, VBI has seen significant increases in its funded research projects and scholarly output. These successes are helping Virginia Tech and VBI achieve even greater distinction and international prominence in the scientific community.

Virginia Tech has always maintained its strong commitment to education. This means retaining as well as enhancing teaching methods that have proven to be successful, while at the same time actively pursuing alternative approaches to the university learning experience. We understand that the model of traditional classroom-based instruction is changing and that learning occurs on multiple levels. VBI exemplifies one of the ways students can benefit from instruction outside the classroom. Although VBI is a research institute, a wide variety of learning opportunities for graduate and undergraduate students exist. Many students at VBI regularly work side by side with faculty in their laboratories and make valuable contributions to research projects. This first-hand experience of doing team-based research is a crucial part of today's scientific education.

Innovation is the backbone of our economy and initiatives like VBI must be strongly encouraged. In the years ahead, it will be exciting to watch VBI build on its strengths in education and multidisciplinary research as it explores different mechanisms for transferring technologies and competencies to the private sector. The Institute has shown substantial progress in its first five years of operation and we are confident that this success will contribute to significant economic development for the Commonwealth of Virginia. We are excited about VBI's future and are confident that the Institute's contributions to research, technology, and education will continue to flourish.

Dr. Charles Steger  
President  
Virginia Polytechnic Institute and State University

## LETTER FROM THE DIRECTOR

Innovation or the way in which we bring new methods, ideas and approaches to the life sciences is the theme of this year's annual report from the Virginia Bioinformatics Institute (VBI). Progress in science is equally dependent on the skills of innovation and the application of invention to the specific needs of society. By successfully channeling innovation into transdisciplinary approaches combining information technology and biology, researchers at VBI are addressing some of today's key challenges in the biomedical, environmental and plant sciences.

Over the past five years, VBI has grown into a transdisciplinary research institute with over 200 employees. Today, the Institute has 18 faculty using diverse methods and tools including, for example, simulation and modeling, statistical genetics, computational systems biology as well as large-scale comparative genomics and microfluidic bioanalytical studies. At the heart of this significant pace of development is our ability to transform innovation into meaningful and productive advances in science and technology.

Success in research and innovation drives the development of our Institute and we believe it is essential to communicate achievements and challenges to the public. With this in mind, we hope in future years to provide annual reports that will explore some of the key themes of biology in the 21st century and show how research at VBI fits into the bigger picture of unmet societal needs. For example, we hope to look in detail at the importance of studying biological and other networks, emerging fields like systems biology as well as the very latest developments in informatics relevant to the work of VBI. These scientific explorations will help to explain VBI's unique approach to team-based, transdisciplinary research.

Recently, we have taken great strides in our outreach activities at VBI. These efforts are designed to engage our wider public — from high school students interested in science to web developers looking for the latest advances in computation tools and software. Education is a key component of our efforts at VBI and we will be making every effort to continue the momentum we are building in our outreach activities.

Looking to the future, we will be placing considerable emphasis on supporting the transfer of technologies and competencies from the Institute's academic research to commercial undertakings. By harnessing our growth in innovation, knowledge and scientific discoveries, VBI is poised to make substantial contributions to societal needs in the years to come.



A handwritten signature in black ink, which appears to read 'Bruno Sobral'.

Dr. Bruno Sobral  
Executive and Scientific Director  
Virginia Bioinformatics Institute at Virginia Tech



# ACHIEVEMENTS

## 2004\*

### ■ JULY

Institute recognizes three distinguished contributors

NIAID awards VBI \$2.89 million as part of \$8.74 million contract with SSS

### ■ AUGUST

*Journal of Theoretical Biology* publishes computational method

Workshop teaches students about mathematical biology

### ■ SEPTEMBER

Computer science professor receives Faculty Fellowship

### ■ OCTOBER

Pathogen Portal project receives additional \$4.9 million in funding

Symposium held on Information Visualization

Student research assistants receive awards

### ■ DECEMBER

Cutting edge program features research professor

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\* additional details are available on subsequent pages



The Virginia Bioinformatics Institute (VBI) at Virginia Tech integrates experimental and computational research to increase the understanding of host, pathogen, and environment interactions, collectively known as the “disease triangle.” At VBI, researchers collaborate to increase the understanding of molecular, cellular, and environmental interactions that affect human health, agricultural systems, and the environment.

The Institute’s research groups specialize in the life sciences, biophysics, biochemistry, mathematics, modeling, computer science, statistics, and economics. These groups are developing new experimental techniques, applying existing and novel approaches to biological problems, and creating analytic and theoretical tools to convert biological data into useful knowledge.

# 2005\*

## ■ FEBRUARY

*Bioinformatics* journal features new application

## ■ MARCH

Researcher serves on National Institutes of Health study section

## ■ APRIL

Researcher receives NSF CAREER award

## ■ MAY

*Science* features Executive and Scientific Director

VBI honors Spring graduates

VBI student receives poster award

Institute hosts BRC and IOWG meetings

Respected VT alumni visit facilities

VBI hosts web services international symposium

## ■ JUNE

CLF unveils new LIMS systems

Institute holds NIAID proteomics meeting

\* additional details are available on subsequent pages

## ACHIEVEMENTS HIGHLIGHTS OF THE YEAR

### JULY 2004

#### Institute recognizes three distinguished contributors

VBI recognizes Minnis E. Ridenour, David E. Sebring, and Tracy D. Wilkins for their service and dedication to VBI at the Institute's annual picnic/birthday celebration. These special guests were instrumental in the development of the Institute and continue to support VBI as valued advisors.



Left to right:  
Bruno Sobral, Dave Sebring, Minnis Ridenour, Louise Ridenour, Tracy Wilkins, and Sarah Wilkins

#### NIAID awards VBI \$2.89 million as part of \$8.74 million contract with SSS



The National Institute of Allergy and Infectious Diseases (NIAID) awards VBI \$2.89 million as part of an \$8.74 million contract with Social & Scientific Systems, Inc. (SSS) to establish an Administrative Resource for Biodefense Proteomic Research Centers. VBI will lead efforts to design and implement an integrated Data Management System to collect, store, view, and query proteomics data from all NIAID-funded Proteomics Research Centers.

### AUGUST 2004

#### *Journal of Theoretical Biology* publishes computational method

The *Journal of Theoretical Biology* publishes an article by VBI Research Professor Reinhard Laubenbacher and Brandilyn Stigler, VBI graduate research assistant, describing a computational approach to study gene regulatory networks.



ELSEVIER

Major advances in biology and other life sciences have resulted in the generation of large amounts of information by scientists. This data is not very useful if it cannot be analyzed or if it is too complex and vast to be manually interpreted. Scientists need effective ways to manage information, which is where bioinformatics steps in.

Bioinformatics weds biology with information technology, providing scientists with ways to organize, manage, and analyze large biological databases. Data produced by researchers all over the world are collected and organized in a variety of databases created for different subject areas. To be useful for scientists, these databases must be easily accessible and provide a way to extract only needed information.

The process doesn't end with the organization of data, however. Bioinformatics also involves the development of computational tools to efficiently analyze the data and interpret the results. Another important component of bioinformatics is the use of mathematical formulas and statistics to assess relationships among large sets of data.

Bioinformatics leads to advances in the understanding of basic biological processes and includes tasks such as mapping an organism's genome and deciphering the raw data with computer science tools. The products of bioinformatics research yield useful information to combat infectious diseases in humans, plants, and animals.

## ACHIEVEMENTS HIGHLIGHTS OF THE YEAR

### Workshop teaches students about mathematical biology

The Virginia Department of Mathematics, Averett University, the Institute for Advanced Learning and Research, and VBI sponsor a workshop for Danville-area secondary mathematics teachers and high school students. VBI graduate students Brandilyn Stigler and Olgamary Rivera-Marrero direct the program using mathematical modeling software to teach students how to model biological systems and solve problems.

### SEPTEMBER 2004

#### Computer science professor receives Faculty Fellowship

Virginia Tech's College of Engineering (COE) and VBI award VBI's Faculty Fellowship to Dr. T.M. Murali, assistant professor in the department of computer science. In this role, Murali is carrying out theoretical and computational research to extend and refine the functional annotation framework he has developed over the last two years to predict gene function.

### OCTOBER 2004

#### Pathogen Portal project receives additional \$4.9 million in funding



VBI receives \$4.9 million in additional funding from the United States Department of Defense (DoD) to continue the development of the PathPort (Pathogen Portal) project.

Using its high-performance computational infrastructure and a world-class team of biologists and computer technologists, the VBI Cyberinfrastructure Group will continue to develop PathPort as a key to unlock the door to the acquisition of more powerful knowledge for infectious disease research.

### Symposium on Information Visualization

VBI Research Assistant Professor Karen Duca, graduate research assistant Purvi Saraiya, and Virginia Tech Computer Science Assistant Professor Chris North present a paper at the IEEE Symposium on Information Visualization. The work may help guide biologists in selecting the best tool for their data, and computer scientists in developing and evaluating visualizations.



### Student research assistants receive awards

Elena Dimitrova, a graduate research assistant in VBI Research Professor Reinhard Laubenbacher's research group, wins "Best Graduate Student Oral Presentation in Mathematics and Physics" at the Society for Advancement of Chicanos and Native Americans in Science (SACNAS) National Conference. Christopher Case, an undergraduate research assistant in VBI



Research Assistant Professor Biswarup Mukhopadhyay's research group, receives a fellowship from the Fralin Biotechnology Center of Virginia Tech, as well as two awards from Virginia Tech's Department of Biochemistry.

### DECEMBER 2004

#### Cutting edge program features research professor

VBI and the Institute for Advanced Learning and Research conduct a program on bioinformatics for teachers. Keynote speaker and VBI Research Professor Brett Tyler introduces the teachers to bioinformatics and its relevance to the sequence of DNA bases, biochemical pathways and growth and provides examples of classroom activities to incorporate bioinformatics concepts within the curriculum.

## ACHIEVEMENTS HIGHLIGHTS OF THE YEAR

### FEBRUARY 2005

#### *Bioinformatics* features new application

The journal *Bioinformatics* features a new application developed by the Cyberinfrastructure Group at VBI. Authored by VBI research associate Eric Nordberg, “YODA: Selecting Signature Oligonucleotides” describes a stand-alone application for the rapid design of microarray probe sets. YODA (Yet-another Oligonucleotide Design Application) will assist biological researchers in selecting signature sequences.

### MARCH 2005

#### Researcher serves on National Institutes of Health study section



VBI Research Associate Professor Pedro Mendes accepts an invitation to serve on the Modeling and Analysis of Biological Systems study section for the National Institutes of Health’s (NIH) Center for Scientific Review (CSR), which evaluates the majority of the research grant applications sent to NIH.

### APRIL 2005

#### Researcher receives NSF CAREER award

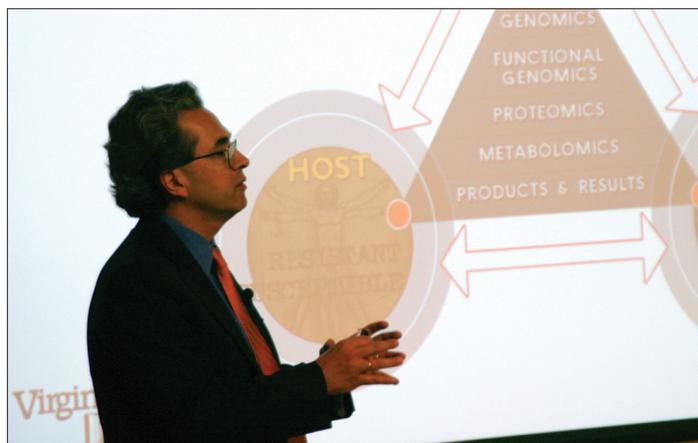
Iuliana Lazar, a research assistant professor at VBI, receives a five-year National Science Foundation (NSF) Faculty Early Career Development Award of \$400,000 for research on the development of microfluidic devices with mass spectrometric detection for proteomic applications.



### MAY 2005

#### *Science* features executive and scientific director

The publication *Science* features Bruno Sobral, VBI executive and scientific director, in the article “Informatics: The Evolution of Computation.” The article focuses on the growth of bioinformatics, specifically highlighting career opportunities and the future of the field.



Dr. Bruno Sobral

#### VBI honors spring graduates

VBI honors its graduating student employees at a special event. These student employees work in a variety of research and administrative positions within the Institute.

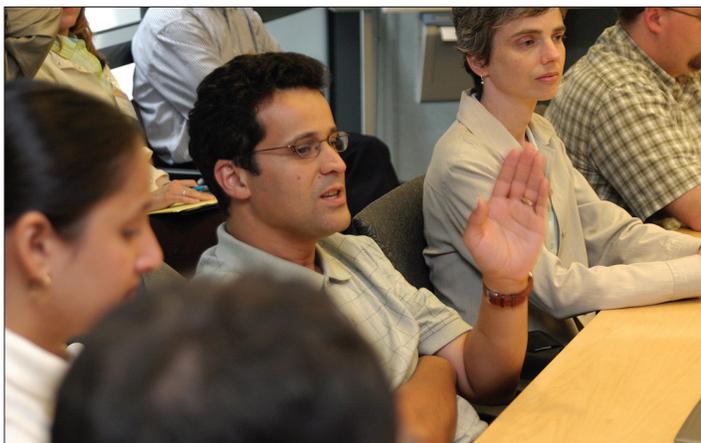
#### VBI student receives poster award

Biomedical Engineering student Hetal Sarvaiya, who works with Research Assistant Professor Iuliana Lazar at VBI, is honored at The Virginia Tech/Wake Forest School of Biomedical Engineering and Sciences 4th Student Research Symposium. She receives an award for her poster presentation entitled “Identification of Potential Biomarkers for Breast Cancer Using Proteomics and Mass Spectrometry.”

## ACHIEVEMENTS HIGHLIGHTS OF THE YEAR

### Institute hosts BRC and IOWG meetings

VBI hosts the second Bioinformatics Resource Centers (BRC) and Interoperability Working Group (IOWG) meeting. The BRC2 meeting addresses strategies and software tools for genome sequence annotation, comparative genomics, and sequence polymorphism identification, while the IOWG meeting addresses interoperation of BRCs.



*Discussion session during BRC meeting*

### Respected VT alumni visit facilities

Over 200 members of the Old Guard, an organization of individuals who have been Virginia Tech alumni for 50 years or more, visit VBI's facilities as part of a two-day event, which includes special reunion activities for the graduating classes of 1935, 1940, 1945, and 1960.



### VBI hosts web services international symposium

VBI hosts the International Symposium on Web Services for Computational Biology and Bioinformatics, where researchers present cutting edge web service applications such as BioMoby, caBIG, and myGrid. The symposium highlights topics ranging from web service architecture and technical issues, to the use of web service-based applications for obtaining scientific results.

### JUNE 2005

#### CLF unveils new LIMS systems

VBI's Core Laboratory Facility (CLF) hosts an open house to unveil its new Laboratory Information Management System (LIMS), which is designed to track submissions to the lab and data generated from those samples, making the sample submission and data retrieval process more efficient for the lab and its clients.



*VBI CLF presentation during LIMS meeting*

### Institute holds NIAID proteomics meeting

VBI hosts the NIAID BPRC 2nd Programmatic meeting. Each Proteomics Research Center, as well as the Administrative Center, updates the other groups on their research and participants ask questions about the NIAID Biodefense & Emerging Infections Research Resources Repository.



# HISTORY OF VBI

Growth and Expansion

VBI Today

Looking to the Future



## Seeds of Innovation

In 1998, a paper by Dave Sebring, VBI's associate director of corporate and government relations, and Dr. Gary Evans, director of the Natural Resources Institute at the United States Department of Agriculture, found its way into the hands of Virginia Governor Jim Gilmore. The paper asserted that biotechnology would become the new economic engine of growth in the 21st century. It also explicitly argued that regions supporting entrepreneurial activities arising from leading university research in this emerging field were poised to reap major benefits in the years ahead.

Convinced by the arguments about the considerable potential of biotechnology, Gilmore sent the paper to several Virginia colleges. After reading the document, Virginia Tech President Charles Steger believed that opening a bioinformatics center could contribute in a major way to Virginia Tech's advancement of biotechnology research.

Virginia Tech had already established leading colleges of agriculture and life sciences as well as engineering, which made the creation of a bioinformatics center a natural progression for the university. Virginia Tech began making plans to secure state funding in 1999. The Tobacco Indemnification and Community Revitalization Commission approved \$12.3 million from the state to help fund the development of the Virginia Bioinformatics Institute at Virginia Tech. This was the only funding given to the Institute before its opening.

*VBI opened its doors in July 2000 in the Virginia Tech Corporate Research Center with only five employees, including Sebring and VBI Executive and Scientific Director Bruno Sobral.*

## THE HISTORY OF VBI

### Growth and Expansion

By 2003, VBI had reached a point in its development where it was ready to occupy new premises on the Virginia Tech campus. The first phase of the move to the new facility began in December 2003 when approximately 100 of the Institute's employees were relocated from Research Building XV at the Corporate Research Center to a new building on Virginia Tech's campus.

In January 2005, VBI completed its two-phase move onto Virginia Tech's campus, occupying more than 130,000 square feet on the corner of Washington Street and Duck Pond Drive, while still maintaining a presence at the Virginia Tech Corporate Research Center.

#### First-class infrastructure and resources

- 130,000 square feet of working space
- Building and resources conceived for flexibility
- Highly trained, multinational personnel engaged in transdisciplinary research projects
- In-built, amenable infrastructure to support easy access to computer and other communication networks
- Access to cutting-edge computing and core laboratory facilities for high throughput applications in genomics, gene expression, and proteomics
- Built to support innovation and future growth



## VBI today

Since its inception, VBI has focused on the study of the biological sciences. The research platform of VBI is primarily centered on the “disease triangle” of host-pathogen-environment interactions. By using bioinformatics, which combines interdisciplinary approaches to information technology and biology, researchers at VBI interpret and apply vast amounts of biological data generated from basic research to some of the key challenges in the biomedical and plant sciences. Today, high performance computing methods being used by faculty are also finding applications in areas like telecommunications, internet economics, and social networks.

VBI researchers are working to find new treatments and cures for the many diseases that affect humans, animals, and crops. They are also investigating ways to create high-yield, insect- and disease-resistant crops. VBI scientists develop bioinformatics information and tools to support further scientific discoveries. For this purpose, work at VBI involves collaboration in diverse disciplines such as mathematics, computer science, biology, plant pathology, biochemistry, statistics, and economics. These collaborations may involve far-reaching, transdisciplinary research projects combining innovation and discoveries in the areas of bioinformatics and systems biology. Over its five-year history, VBI has achieved many milestones. The Institute currently has over 200 employees and around \$45 million in extramural funding.



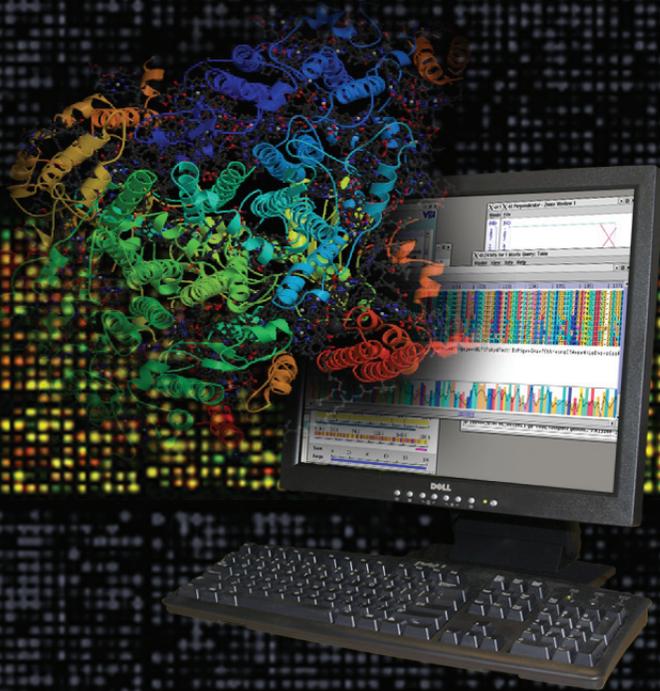
## Looking to the future

VBI continues to grow at a considerable pace as it pursues its research goals and development path. The objectives remain to foster excellence in fundamental and applied academic research by addressing far-reaching scientific projects through transdisciplinary approaches to research. Employees at VBI are also looking at ways to strengthen the exchange of information and results between life scientists as well as to promote new contacts and projects between collaborators in both the academic and private sectors. In the years ahead, VBI will closely explore innovative ways to transfer technologies and competencies from academic to industrial settings. This will in the long term serve to stimulate business development and promote new employment opportunities.

VBI is poised for further growth to support its research efforts in biomedicine, agriculture, and bioinformatics. All of these initiatives are designed to drive growth in knowledge, innovation, and scientific discoveries.



# INNOVATION AND THE LIFE SCIENCES



*“Biology is set to become highly quantitative in the 21st century. It will become a computer-intensive discipline.”*

*Denis Noble, Science, March 1, 2002*



## A history of innovation

Over the years, many scientific achievements have enabled a notable revolution in the development of the life sciences. Examples include the discovery of the structure of DNA by Watson and Crick in 1953, the development of monoclonal antibodies by Köhler and Milstein in 1975, as well as the many contributions from international groups to the sequencing of genomes from different organisms.

Biotechnology, in the industrial sense, started some 25 years ago with the intention of exploiting the technology platforms of genetic engineering and gene transfer. Biotechnology landmarks in the early- to mid-1970s, which included the discovery of restriction enzymes, the first transfer of genetic material and the development of early DNA sequencing methods, have been followed by the invention of polymerase chain reaction for copying and amplifying segments of DNA by Kary Mullis and coworkers in 1983, and the completion of genome sequences for organisms as diverse as *Drosophila* (fruit fly), humans, rat, and the much used model plant *Arabidopsis*.

Some recent highlights in the life sciences include the cloning of the first mammal from adult DNA (Dolly the sheep), the sequencing of the human genome by Celera and the Human Genome Project, and the production of the first gene chip containing the full complement of human genes by Affymetrix.

## INNOVATION AND THE LIFE SCIENCES

### Bioinformatic milestones

Bioinformatics is the field of science uniting biology, computer science, and information technology in a single discipline. Some sources cite the first use of the term bioinformatics in the scientific literature as 1991. However, the use of computers in biological research goes back many years. For example, the Needleman-Wunsch algorithm, which is used to align biological sequence information for comparison purposes, was first published in 1970.

When biologists refer to bioinformatics, they are usually thinking about the use of computers to store, compare, retrieve, analyze, or predict the composition or structure of biological molecules. More recently, simulation is becoming part of this landscape as the performance capabilities of computers and computer grid networks make further advances.

In the post-genomic era, bioinformatics also encompasses comparative and functional genomics, proteomics, structural genomics as well as medical informatics projects looking at the management of biomedical data associated with particular molecules or patients.

Today, bioinformatics is a cornerstone of efforts to understand large-scale biological systems and networks (systems biology) as well as studying genome sequences and determining the structures of proteins. In time, it should play a large role in designing new therapeutics with reduced side effects and selecting optimal drug treatments for different patients (personalized medicine).

### Significant challenges for global health

By 2025, more than one billion people worldwide will be over 60 years of age (World Health Organization). At the same time, a large increase in degenerative diseases and morbidity closely linked to aging populations is anticipated.

Chronic diseases now account for more than 50% of all deaths worldwide and infectious diseases like tuberculosis are re-emerging as a burden to public health. According to the European Association for Bioindustries (EuropaBio), only one third of the 30,000 known diseases have available treatments.

New disease epidemics, the risk of pandemics, and the threat of bioterrorism mean that society has to intensify

### Selected Milestones in Bioinformatics

Milestone	Contributor	Timeline
Protein Sequence Database (now part of the Protein Information Resource) initiated	Margaret Dayhoff	Early 1970s
Practical Extraction Report Language (PERL) (for scanning and extraction of information) released	Larry Wall	1987
National Center for Biotechnology Innovation (NCBI) created		1988
FASTA program for sequence comparison released	Lipman and Pearson	1988
BLAST tool for sequence comparison introduced National Center for Biotechnology Innovation	Based on work by Samuel Karlin and Steven Altschul	1990



## INNOVATION AND THE LIFE SCIENCES



its research efforts in biomedical science to develop new vaccines, diagnostics, and therapeutics. Society must also explore new approaches to prevent the onset of disease and find a way to feed the world's growing population. Bioinformatics and biotechnologies have a key role to play in meeting these global challenges.

### New ways to tackle disease

Technologies that may support major advances in tackling disease in the future might include RNAi (RNA interference approaches), stem cells, organ modelling/regeneration, smarter vaccines, systems biological approaches for drug discovery, computer modelling for drug design, and rapid whole genome sequencing.

New genes and their functions appear to be discovered on an almost daily basis in areas as diverse as cancer, obesity, memory, and longevity. This should also lead to many exciting new discoveries in the years ahead. The establishment of the human genome nucleotide sequence was a landmark achievement in transdisciplinary science.

Understanding the human genome will eventually allow the molecular basis of diseases to be unravelled in a systematic way. Pharmacogenomics is set to impact personalized drug treatments by improving drug efficacy, enabling individualized drug treatments and reducing adverse drug reactions.

Further developments are providing safer vaccines, new model organisms for studying the progress and treatment of disease (e.g. "humanized mice"), and novel genetically modified crops. Transgenic animals are being developed for the production of biologicals (Biopharming). In time, the re-engineering of metabolic pathways of microorganisms should be possible to provide, for example, novel antibiotics.

### Innovation at VBI

Researchers at VBI are involved in a wide range of activities that integrate biology, computer science and information technology. These projects are being used to tackle many of the unmet medical and agricultural needs facing society today. Further details of these innovative research projects are outlined on pages 32-51 of this annual report.



# RESOURCES AND PEOPLE

Core Facilities

Administration and Finance Team

Public Relations & Outreach and Education

Feature Articles

VBI Faculty

VBI Faculty Fellows





## VBI CORE FACILITIES

### VBI Core Facility

In addition to VBI's strengths in academic research, the Institute offers essential key services for clientele working at Virginia Tech as well as other universities, institutions, and private sector companies. The Institute's Core Facilities are a unique feature of VBI's infrastructure. By integrating multi-user resources, the Core Facilities combine high-throughput data generation from the Core Laboratory Facility (CLF) with the data analysis capabilities of the Core Computational Facility (CCF).

Industrial-scale biotechnologies and computational technologies are too expensive for most laboratories to acquire and maintain. VBI's Core Facilities provide researchers with access to the latest technology platforms for the generation of data, as well as the computational tools needed for extensive data analysis on a cost-recovery basis.



*Left to right:*

*Dustin Machi, Clive Evans, Dominik Borkowski, Mark DiFilippo, David Bynum, Susan Martino-Catt, Adam Jerauld, Don Shaw, Doug McMaster, Tina Lawrence, Ryan Chase, Stephanie Conrad, Chris Umberger, Sally Waldon, Kristin Lee, and Megan Ferring Blauvelt.*

## VBI CORE FACILITIES CORE LABORATORY FACILITY

The Core Laboratory Facility (CLF) is the data generation machine of the VBI's Core Facilities. The CLF functions as a multi-user resource, dedicated to the development and application of various high-throughput technologies used in the analysis of DNA, RNA, and proteins. The CLF offers a "one stop shop" for these technologies, providing researchers access to its tools and experienced staff. The main goal of the CLF is to provide high quality data in a timely fashion and, at the same time, deliver excellent customer service in a collaborative environment.

In addition to its ongoing application of existing technologies, the CLF is actively engaged in the development and testing of new technologies. It is this combination of application and development that allows the CLF to be a leader in partnering with

researchers to enable a complete systems biology approach to their science. The CLF continually upgrades its equipment, processes, and software and expands its staff requirements to meet the growing demands for offered services. This ensures high quality production and workflow capabilities, as well as the availability of dedicated professionals to assist users in the successful application of technologies.

### The services currently offered by the Core Laboratory Facility include

- DNA Sequence Analysis
- Gene Expression Analysis
- Proteomics
- Genotyping
- Robotics



### Laboratory Information Management System (LIMS)

The CLF uses a custom-designed Laboratory Information Management System (LIMS) (designed and built by GraphLogic, Inc., Branford, CT) as a secure, web-based interface to facilitate customer sample submission and data retrieval. Behind the scenes, the LIMS supports the CLF production environment with its ability to store, retrieve, and manage information related to projects, clients, workflows, samples, equipment, reagents, inventory, and associated costs.

The LIMS is fully supported by the Core Computational Facility (CCF) to ensure secure and efficient data storage and retrieval capabilities. The seamless link between the CLF and the CCF provides our clientele with a simple and effective connection between data generation and data analysis.

## VBI CORE FACILITIES

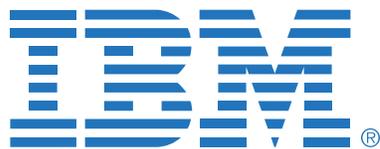
### CORE COMPUTATIONAL FACILITY

The Core Computational Facility (CCF) is the data management and analysis machine of the VBI's Core Facilities. The CCF provides high performance computing resources to support data visualization, data mining, and a wide range of biological applications. A team of dedicated information technology professionals guarantees that the CCF remains a state-of-the-art facility.

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).

#### Services Offered By the Core Computational Facility

- Computational Processing
- Compound Services (web applications, analysis webservice)
- Database and System Administration
- Data Storage and Backup



## VBI CORE FACILITIES CORE COMPUTATIONAL FACILITY



Powerful supercomputers, including a Sun Enterprise I5000 and an IBM Power 4, are at the center of the CCF's computational processing, providing resources that can be used for a wide variety of applications. 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.

Generating huge amounts of data is getting easier to do each day, making it even more critical to have a solid computational infrastructure in place. Recent additions to the CCF continue to strengthen the Core Facilities' best-in-class capabilities.

The CCF's newest cluster, an IBM Power 4, has an extensive set of tools and applications for biologists, all available via webservices and the CCF website. These services are available through simple website tools or through other analysis tools that communicate via webservices.

The CCF, working in collaboration with VBI bioinformaticians and faculty, is evaluating a system that will allow researchers to graphically design analysis pipelines and then execute them on large datasets. The data and analyzed results are stored on a variety of disc arrays that attach directly to any of the CCF's high performance machines. Additionally, the CCF also provides production hosting of websites and web-based applications.

## ADMINISTRATION AND FINANCE TEAMS

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. The team provides a solid infrastructure for the Institute's dynamic research environment, allowing for continued growth and success.



### ADMINISTRATION

VBI's Administrative 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. With such a wide range of roles, the team includes a very diverse group of professionals with extensive backgrounds and experience.

*Left to right:*

*Shannon Worryingham, Julia Paul, Jana Carden, Kim Borkowski, Dave Sebring, Bruno Sobral, Cory Byrd, Lauren Coble, Sharon Lawson, David Martin, Kimberly Smith, Lynn Byrd, Margaret Gabler, and Barbara Waller.*

*Not pictured: Jim Walke.*



## ADMINISTRATION AND FINANCE TEAMS

### FACILITIES

VBI's Facilities Team is an integral part of the continued growth and evolution of the Institute. The team is actively involved with faculty and staff members at VBI, handling space configurations and facilities operations. In addition, the team coordinates with various external authorities and departments in the design, construction, renovation, operation, and maintenance of VBI's facilities. The members of the Facilities Team support all aspects of the Institute's daily functions and are closely involved in all long-term planning.



*Left to right:  
Linda Correll, Sheryl Locascio, Jonathan Schremp,  
Dawn Maxey, Jennifer Uerz, and David Gibbs.*

### FINANCE

The Finance Team at VBI serves as an important component in the overall financial management of the Institute. Members of the team provide a wide variety of professional financial and support services, including accounting, financial reporting, purchasing, invoice processing, and account reconciliations. The team is comprised of business professionals dedicated to administering sound business and financial management practices to ensure the continued overall success and growth of VBI.



*Left to right:  
Stacey Lyons, Deb Williams, Shelana Ryan, and Tina  
Lawrence*

### GRANTS and CONTRACTS

VBI's Grants and Contracts Team plays an important role in securing funding for the Institute's transdisciplinary research projects. The team administers guidance and assistance throughout the entire process, beginning with researching and identifying funding opportunities from both federal and private agencies. The team works closely with the Institute's faculty members to provide technical writing, editing, and graphic design assistance, as well as financial reporting and coordination services. Post-award reporting and coordination is also handled by VBI's Grants and Contracts Team, completing this comprehensive support system for the funding process.



*Left to right:  
June Mullins, Sharon Lawson, and Darleen Baker*



## PUBLIC RELATIONS & EDUCATION AND OUTREACH



Left to right:  
Rachel Judy, June Mullins, Susan Bland,  
Susan Faulkner, Ivan Morozov, Valencia  
Person, Alana Manzini, Erika Allen, and  
Lea Hamblin.

### PUBLIC RELATIONS

The goal of VBI's Public Relations group is to identify key audiences and design effective communication strategies in an effort to provide these groups with timely information about VBI and its activities. The group is dedicated to managing the information flow for VBI, while serving as a crucial channel between the Institute and its internal and external publics.

#### Publications

The Public Relations group develops several publications and marketing pieces throughout the year to help promote VBI and its research. The group created and distributed the Institute's 2004 annual report, which highlighted VBI's research and financial achievements for the fiscal year. An information kit, which contains interchangeable and customizable documents that can be used to target more specific audiences, was created by the group. This packet includes key information about the Institute, such as fact sheets and articles highlighting recent accomplishments. The group also developed a flier showcasing VBI's Core Facilities. The one-page promotional piece provides a brief overview of the Institute and highlights the services offered by the Core Computational and Laboratory Facilities.

#### Media Relations

Writing and distributing press releases on VBI's activities is another responsibility of the group. These releases focus on newsworthy achievements of the Institute, including funding awards, the publication of journal articles, research accomplishments, education and outreach activities, and personnel highlights. The group distributes this information to the media and serves as a contact for any requests for additional information.

The group also serves as a liaison between reporters and VBI faculty members, coordinating interviews and other promotional opportunities. These efforts have resulted in coverage of VBI by many popular media outlets, including The Washington Post, The New York Times, ABC News, The Free Lance-Star, Richmond Times-Dispatch, The Roanoke Times, The Kansas City Star, Medical News Today, Science magazine, as well as a variety of publications produced by Virginia Tech.

#### Website

An informative website is an essential information dissemination tool for research-based organizations. The Public Relations group is responsible for the development, coordination, and maintenance of VBI's website from both a technical and creative standpoint. More specifically, the group oversees the design and organization, and also develops content for the various sections of the site. VBI news items are posted to the site in a timely manner, and information about each of the Institute's research groups is included. Sites created to publicize and provide more information for specific events, such as conferences and meetings, are also developed by the group.

#### Visual Communication

The group assists VBI personnel in the creation of presentations for a variety of audiences, and also develops graphical elements, including logos for specific VBI research projects and illustrations and graphics for articles, grant submissions, and project-specific websites. The group develops slide shows for several plasma screens within the Institute, which serve as a communication tool for both VBI employees and

## PUBLIC RELATIONS & EDUCATION AND OUTREACH

visitors. The screens highlight VBI's upcoming events and news items, and provide information about ongoing research activities. Each month, a different VBI research group is featured on the screens.

In the years ahead, the Public Relations group will be building further its research-driven communication program to assist VBI with its many activities in education, research, and business development.

### EDUCATION AND OUTREACH

Building strong connections with external audiences and developing educational programs are important components of a research institution's success. VBI's Education and Outreach group is dedicated to sharing bioinformatics research and information with the Virginia Tech community and beyond through a variety of programs, events, and other outreach efforts.

#### Educational opportunities for students and teachers

The scientists and researchers of tomorrow are the students currently enrolled in elementary, middle, and high schools. VBI's Education and Outreach group has developed and integrated various programs to encourage the interest of these students in bioinformatics. VBI participates in Montgomery County Public Schools' High School/High Tech program, which is designed for students with various types of disabilities from high schools in Blacksburg, Virginia and surrounding areas. The program provides these students with opportunities to explore careers in science, mathematics, and technology, and incorporates features such as preparatory experiences, connecting activities, work-based experience, and development and leadership activities. Over the past year, VBI has provided two High School/High Tech students with hands-on work experiences at the Institute. In addition, VBI's Education and Outreach Coordinator Susan Faulkner serves on the program's board of directors.

The group has also worked with the Institute for Advanced Learning and Research in Danville, Virginia to provide a bioinformatics educational program for elementary, middle, high school, and community college teachers. VBI Research Professor Brett Tyler introduced the teachers to bioinformatics concepts and provided examples of classroom activities that could help incorporate bioinformatics concepts into their curriculums.

#### Student recruitment for educational programs and internships

VBI is also involved with national programs designed to enhance students' educational experiences. Several VBI researchers have participated in the Multicultural Academic Opportunities Program (MAOP). Virginia Tech's MAOP program recruits undergraduate students from around the nation to work in a summer research institute program involving various academic disciplines. The purpose of the program is to promote the diversification of Virginia Tech's student body. VBI researchers have welcomed MAOP students into their research groups, providing them with personal guidance and research learning opportunities.

#### Meetings and Conferences

VBI welcomes collaborators, partners, and researchers from around the world, and strives to provide an exemplary environment for the sharing of scientific information. The Education and Outreach group has coordinated several scientific meetings at VBI, including:

- Models of Infectious Disease Agent Study (MIDAS)
- Bioinformatics Resource Centers (BRC), Interoperability Working Group (IOWG), and Scientific Working Group (SWG)
- Administrative Resource for Biodefense Proteomics Research Centers

VBI also hosted "Web Services for Computational Biology and Bioinformatics," an international symposium with 85 attendees from across the world. During the three-day event, researchers presented cutting-edge web services applications and discussed topics ranging from web services architecture and technical issues, to the use of web service-based applications for obtaining scientific results.

#### Outreach within VBI

As VBI continues to grow, fostering a strong sense of community within the walls of the Institute becomes more challenging. The Education and Outreach group offers Institute-wide activities designed to create an atmosphere of connectedness and kinship. The group sponsors a coffee social each morning and helps organize a weekly social event that is sponsored by a different research group at VBI. These events provide opportunities for VBI faculty and staff to meet new employees and connect with coworkers they may not interact with on a regular basis. In addition, the group developed and coordinated VBI's First Annual Retreat. This event brought together research faculty and their group members to share scientific discoveries and ongoing work with each research group at VBI.

FEATURE STORY / PEOPLE IN THE SPOTLIGHT  
VBI RESEARCH FACULTY

## Sequencing Deadly Genomes From a Distant Kingdom



*Phytophthora ramorum* is an insidious, “fungal-like” pathogen that has attacked and killed thousands of oak trees in California and Oregon

Understanding the host-pathogen-environment triangle requires knowing in intimate detail the genomic make-up that helps this pathogen recognize and infect oak trees

For Brett Tyler’s research group and collaborators, 2004/2005 has been a vintage year for decoding the genomes of some of nature’s deadliest plant pathogens. By successfully mapping the genome of the pathogen *Phytophthora ramorum*, researchers in Tyler’s group at the Virginia Bioinformatics Institute (VBI) are one step closer to developing ways to track and control sudden oak death disease.

*P. ramorum* is an insidious, “fungal-like” pathogen that has attacked and killed thousands of oak trees in California and Oregon. Because of the conditions it thrives in, namely cool and moist air, *P. ramorum* also threatens red and pin oak forests found in the Eastern region of the United States. If it were to take hold in these

populations, it could have devastating effects on many of the forests throughout the Appalachian highlands.

Tyler says: “To tackle sudden oak death disease, we have taken a close look at *P. ramorum*’s genome. Understanding the host—pathogen—environment triangle requires knowing in intimate detail the genomic make-up that helps this pathogen recognize and infect oak trees, cut off the food supply to the plant, and spread from one tree to another.”

He adds: “The completion of the genome sequence of *P. ramorum* is a significant step forward in our efforts to combat this devastating disease. It makes it much easier to find the key genes involved in propagating



sudden oak death disease. By having the complete list of components for *Phytophthora*, a lot of the guesswork is removed from future research.”

In 2002, the United States Department of Agriculture and the National Science Foundation jointly awarded \$2.3 million to VBI to start work on sequencing the genome. The assembly of the raw DNA sequence data was carried out in collaboration with the United States Department of Energy Joint Genome Institute, which also contributed \$1.1 million towards the project. The sequencing of the genome in 2004 represents the fastest recorded time between the identification of a complex pathogen (in 2000) and the completion of its genome.

Scientists can now do more research to determine the function of key genes and determine how these genes may influence some of the known disease-causing features of this organism. In time, this will allow them to develop novel diagnostic methods to rapidly identify sudden oak death disease. It may also enable the development of interventions for specific, defined targets involved in the disease process, whether it is a step in host recognition or disease propagation.

## A GENOMIC TREASURE TROVE

The *P. ramorum* sequence contains approximately 200,000 single nucleotide polymorphisms or SNPs, single base differences found along the sequence of nucleotides that make up the pathogen’s genetic sequence. Tyler’s group is using these small differences to “fingerprint” isolates from different disease outbreaks. So far, his team has identified three major invasions of *P. ramorum* into California based on these fingerprinting results.

The *P. ramorum* genome contains around 16,000 genes, about half the number found in humans, but around three times as many as simple fungi like yeast. Many of the extra genes show evidence of rapid changes expected as a pathogen adapts to the challenges of defeating the defense systems of its host. As many as 6000 of these genes may be involved in attacking the many plant species that *P. ramorum* can infect. Tyler’s group is currently measuring the activities of each of these genes during infection to determine their function.

## FAMILY TIES

The sequence also gives important clues as to the evolutionary origins of *P. ramorum*. Tyler notes: “Although it resembles fungi, *P. ramorum* in fact belongs to a group known as the Stramenopiles. These organisms

## About Sudden Oak Disease

- First reported in 1995 in central coastal California
- Pathogen invades susceptible trees through the bark, killing portions of the tree
- Spread by infected woody shrubs in the forest understory and in ornamental planting
- In the US, sudden oak death is known to occur only along the west coast
- Has attacked and killed thousands of oak trees in California and Oregon
- Potential to infect oaks, other trees and shrubs elsewhere in the United States

are more closely related to algae such as kelp and diatoms, which means that conventional fungal-control mechanisms are unlikely to be effective against these pathogens. The sequence information has provided a unique family ‘snap-shot’ of the Stramenopiles. This will be useful as we develop strategies for counteracting the far-reaching effects of these organisms.”

*P. ramorum* was not the only genome to be sequenced in this short time-frame. Tyler and colleagues also elucidated the genome sequence of a related pathogen, *Phytophthora sojae*, which causes severe disease in soybean crops amounting to \$1-2 million in losses annually. Tyler’s group has been investigating *P. sojae* for over 18 years as an easily studied “model” *Phytophthora* species. Much of the information learnt from the *P. ramorum* genome was obtained by comparing its genome to that of the better understood *P. sojae*. Tyler concludes: “Both sequencing projects generated synergies. We have used the sequence of *P. sojae* as a kind of ‘Rosetta Stone’ to better understand *P. ramorum*’s genetic makeup. This is a win-win situation for studying both of these deadly pathogens and their intriguing biological heritage.”

## FEATURE STORY / PEOPLE IN THE SPOTLIGHT

### VBI RESEARCH STUDENT

# Bridging The Gap Between Mathematics And Computational Biology



After completing her post-doctorate work, Stigler would like to help bridge the gap that exists between mathematics and computational biology at other universities

**B**randy Stigler wasn't sure of what she would encounter when she came to VBI; she just knew it would be something new and different. After coming to the Institute from New Mexico in 2002, Stigler is now working at Ohio State University's Mathematical Biosciences Institute. She credits experiences at VBI for preparing her both for this new position and future endeavors.

Stigler came to VBI as a graduate research assistant in 1999, working with Dr. Reinhard Laubenbacher, a VBI research professor and professor of mathematics at Virginia Tech. Laubenbacher was her master's program advisor at New Mexico State University when he decided to accept a research position at VBI. He invited all of his students to come with him to Virginia, and Stigler admitted that she blindly made the choice to come.

"I knew that somehow math was involved...so I just took a chance," she explained. "I really had no idea,

and it turned out to be one of the best decisions I've made."

After arriving at VBI, Stigler began learning about bioinformatics and how it integrates a variety of disciplines for one purpose. The main focus of her research was on the development of mathematical modeling tools to be used for genetic regulatory networks. She published several papers in scientific journals and presented her research findings at various conferences across the nation.

Stigler was a member of Laubenbacher's Applied Discrete Mathematics Group at VBI. Applying discrete mathematical methods, the group uses bioinformatics tools to model various biological networks. Currently the group is involved in several projects, including the development of computer models of immune responses to pathogens and the creation of computer simulations to aid in the study of biological networks.



One of Stigler's most memorable experiences was in August 2004, when she participated in a biomathematical workshop at Virginia Tech's Institute of Advanced Learning and Research in Danville, Va. VBI sponsored the workshop for Danville-area high school students and teachers. Stigler and another VBI graduate researcher directed the program, which used mathematical modeling software to teach students how to solve biological problems.

According to Stigler, her relationships with VBI faculty have helped her mature not only in the mathematical field, but in every aspect that relates to being a good research scientist. Laubenbacher is a "fantastic" advisor, she said, and has challenged her to push herself when solving problems. During her time at VBI, she felt that Laubenbacher embraced her and other group members as colleagues, instead of just a group of students. Laubenbacher is confident in the skills that Stigler has developed while working with him, and believes that she has a promising future ahead of her.

"One of Brandy's biggest assets is her tremendous curiosity and openness to new ideas. This is crucial for somebody working in a team science environment," Laubenbacher said. "She is not afraid to ask questions-also crucial in an environment in which one is constantly confronted with unfamiliar scientific territory. With these skills, as well as extraordinary scientific talent, I am confident that Brandy will have a very successful professional career."

One of VBI's greatest strengths, according to Stigler, is that all of the faculty members at VBI are open, cooperative people. Through her work with VBI research associate professors Pedro Mendes and Vladimir Shulaev, she has been able to experience being a part of a bioinformatics community.

"It's not that each person does their work and every now and then, you work together. It's very much a cooperation between people and VBI faculty understand that," she explained.

Stigler also appreciates the respect the faculty have for other faculty and researchers within the Institute, despite their expertise in different disciplines. She

always felt comfortable asking questions when she didn't understand something, and also pointed out that the faculty had no problem coming to her if they had questions.

"If I didn't understand something about mathematical modeling, I could go ask Pedro, and it's no big deal," she said. "They opened their doors and said, 'Yeah, come on in. Let's learn.'"

After completing her post-doctorate work at Ohio State University, Stigler would like to help bridge the gap that exists between mathematics and computational biology at other universities. She has learned that many departments are looking to make that connection,



*Dr. Reinhard Laubenbacher (left) and Brandy Stigler*

but either don't know how, or don't have the proper resources. There's no doubt in her mind, though, that VBI has been instrumental in her future in mathematical biology.

"This has been such a fantastic experience. I've been so spoiled," Stigler said. "At VBI, it seems that all parties involved want to bring their skills to the table, but they also want to learn from the other side as well. So I think that's wonderful. I've had the chance to learn in a very friendly environment."

# RESEARCH GROUPS AT VBI

DR. C. BARRETT  
DR. A. DICKERMAN  
DR. K. DUCA  
DR. I. HOESCHELE  
DR. R. LAUBENBACHER  
DR. C. LAWRENCE  
DR. I. LAZAR  
DR. P. MENDES  
DR. B. MUKHOPADHYAY  
DR. D. RATHORE  
DR. D. SAMUELS  
DR. J. SETUBAL  
DR. V. SHULAEV  
DR. B. SOBRAL  
DR. B. TYLER

VBI faculty collaborate to bring together diverse disciplines such as mathematics, computer science, biology, plant pathology, biochemistry, statistics and economics.

Collaborative work of VBI faculty helps link seemingly unrelated fields in an effort to develop and implement new innovations and discoveries in the areas of bioinformatics and systems biology.

Researchers focus on specific processes, such as interactions in cells, advance proteomic investigations, microbial genomics, metabolomics, functional interactions among pathogen and host genes, and the molecular basis for the onset and progression of infectious diseases.



# NETWORK DYNAMICS AND SIMULATION SCIENCE LABORATORY

## DR. C. BARRETT

Left to right:

Paula Stretz, Christopher Barrett, Julia Paul, Henning Mortveit, Madhav Marathe, Kevin Allen, Subodh Lele, Aseem Deshpande, Keith Bisset

Not pictured: Karla Atkins, Richard Beckman, Stephen Eubank, Achla Marathe, Anil Vullikanti

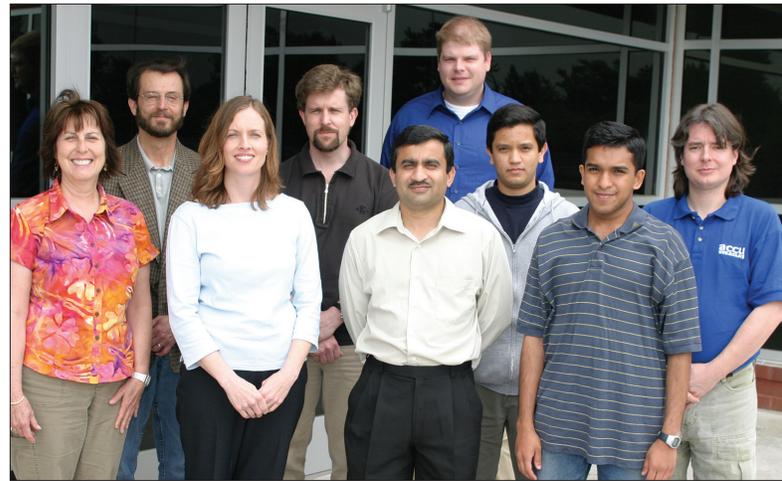
**D**r. Chris Barrett's Network Dynamics and Simulation Science Laboratory group is pursuing an advanced research and development program to understand large biological, information, social, and technological systems. This program incorporates interaction-based modeling, simulation, and associated analysis, experimental design, and decision support tools. Extremely detailed, multi-scale computer simulations allow formal and experimental investigation of these large-scale systems.

The need for such simulations is derived from questions posed by scientists, policy makers, and planners involved with very large complex systems. The simulation applications are underwritten by a theoretical program in discrete mathematics and theoretical computer science that is sustained by more than a decade of experience with the interplay of research and application.

The group is currently pursuing projects in five programmatic areas. TRANSIMS is one part of the multi-track Travel Model Improvement Program sponsored by the U.S. Department of Transportation, Environmental Protection Agency, and Department of Energy. Its purpose is to develop new, integrated transportation and air quality forecasting procedures necessary to satisfy the Intermodal Surface Transportation Efficiency Act and the Clean Air Act and its amendments.

The Epidemiological Simulation System or EpiSims has been developed with support from the U.S. Departments of Energy, Homeland Security, and Health and Human Services for epidemiological work and the study of the spread of infectious diseases. The purpose of EpiSims is to provide an experimental test bed for analyzing proposed responses to natural or intentionally caused disease outbreaks.

For population dynamic studies, critical information about people falls into two categories: (1) static information that does not change over the course of a



The Network Dynamics and Simulation Science Laboratory group is pursuing an advanced research and development program to understand large biological, information, social, and technological systems.

simulation, including age, income, communication device ownership, and home location; and (2) time-dependent information, such as an individual's location, type of activity, and health status. The group's population and transportation simulation system can represent every individual and their network in an extended urban region, including areas spanning hundreds of square miles and municipalities, at a spatial resolution of meters and a temporal resolution of one second or less.

For telecommunications, research is being conducted to develop an end-to-end simulation environment for representing and analyzing extremely large, complex telecommunication networks that are made up of cellular networks, public switched telephone networks, Internet networks, and ad hoc mesh networks.

Commodity markets are sensitive indicators of infrastructure disruptions and are often used to gauge public mood and awareness in crisis situations. The group has recently designed and constructed a detailed agent-based analysis tool for the simulation of large commodity markets and the interdependencies with a physical infrastructure using a synthetic urban population mobility data set. This tool is suitable for the study of Internet economics and commodity markets.

In addition, the group is exploring ways of using its approach of combining network and data analysis with simulation-based dynamic analysis to investigate molecular, system, and ecological biology problems.

## PHYLOGENOMICS RESEARCH GROUP

DR. A. DICKERMAN



Left to right:

Allan Dickerman, Elena Shulaeva, Johanna Craig, Yuying Tian

By using phylogenetic models, it is possible to describe interesting patterns of conservation and diversification in gene sequences relative to changes in function.

**D**r. Dickerman's Phylogenomics Group develops functional interpretation of genomic data using comparative methods. This combines phylogenetic evolutionary modeling with high-throughput functional data such as gene expression levels. By using phylogenetic models, the group is able to describe interesting patterns of conservation and diversification in the gene sequence relative to changes in function. Phylogenetics exploits the principle that today's genetically encoded systems are products of descent with modification from ancestral systems deeper in the past. This analysis method can describe species as well as components within a single genome, which allows for the study of the similarities and differences among species in an explicitly evolutionary context.

An outcome of their work in this area is a database and software system built to query, visualize, and investigate large sets of pre-computed gene phylogenies. Web and Java interfaces are also available providing similar functionality. A key function of this system is the comparison of gene phylogeny structure to an estimate of the "species phylogeny" as represented by a tree based on small-subunit ribosomal RNA (SSU rRNA). This enables researchers to estimate which branches of the gene phylogeny represent gene duplication events and which reflect simple species divergences. Horizontal transfer is another phenomenon that can be inferred from this approach. This system is currently supporting large databases of fully sequenced bacterial genomes and viruses, as well as smaller databases for *Arabidopsis* and strawberry sequences. A larger

database is being constructed for all fully sequenced genomes.

The group is collaborating with Dr. David Meinke at Oklahoma State University in another research area, namely the bioinformatic and functional analysis of genes active in the early development of plant seeds. This work uses *Arabidopsis thaliana*, or mouse-eared cress, which is a small flowering plant used widely as a model organism in plant biology. In an effort to contribute to the identification of the functions of all genes in this model plant, Dickerman's group is also working to identify and study every *Arabidopsis* gene essential for seed development. This research coordinates the collection, analysis, and presentation of information on essential genes that results in a severe seed phenotype when disrupted by mutation. The ongoing results of this work are published on the "SeedGenes" website hosted by the Dickerman group ([www.seedgenes.org](http://www.seedgenes.org)).

In collaboration with VBI researcher Dr. Vladimir Shulaev, Dickerman's group is studying the wild strawberry as a model to determine which fruit genes produce economically important traits, such as disease resistance. By profiling wild strawberry, they hope to identify useful compounds in plants, as well as the genes that produce them. Research efforts in this area of agricultural production will allow scientists to begin improving the dietary value of certain foods and identifying compounds that may have medicinal properties. This technology will have a positive impact on the widespread problems of malnutrition and disease.

Dr. Dickerman's group collaborates with Dr. Eric Beers in Virginia Tech's Department of Horticulture to measure messenger RNA levels in xylem (complex vascular system tissue of higher plants that carries water and dissolved minerals) and phloem (vascular system tissue that carries soluble material through the plant, as well as assists in support and storage). This research is revealing new information about the biology of wood formation.

## BIOMEDICAL SIMULATION RESEARCH GROUP

### DR. K. DUCA

Left to right,  
front row: Dustin Potter, Mike Shapiro, Nicholas Polys  
back row: Kichol Lee, Karen Duca, Vy Lam

Not pictured: Purvi Saraiya



The goal of the Biomedical Simulation Research Group is to understand the initial response to viral infections across diverse systems.

While great strides have been made in treating infectious diseases of bacterial origin, researchers and clinicians have not been as successful controlling many viral diseases. The classic approach to preventing infections has been with vaccines, yet many viruses evade vaccine-induced immunity due to their genetic lability or weak antigenicity. Living in a world where almost 40 million people are infected with human immunodeficiency virus (HIV) and one in which the threat of bioterrorism is perhaps growing, it is important to be prepared to cope with pathogens for which no vaccines are available and to treat patients post infection. New biotechnology tools create opportunities to dissect the entire viral infection process from both the host and pathogen side, revealing potential therapeutic interventions that were previously inaccessible.

Dr. Karen Duca's research group is centered on understanding, detecting, and treating infectious diseases caused by viral infections, especially influenza and corona viruses. Scientists are generally aware of the methods that a virus uses to invade cells, but the very early defensive strategies that the cells use against the invaders are not quite as clear. The human immune system, while complex in itself, is part of a larger network of physiological systems. The goal of Duca's group is to understand the initial response to viral infections across these diverse systems.

In collaboration with Dr. Reinhard Laubenbacher at VBI and Dr. David Thorley-Lawson at Tufts Medical College, the group has developed a computer simulation that aids in studying the dynamics of Epstein-Barr virus infection of its human host. The tool is comprised of a 3D virtual environment of a human being and a back-end simulation engine, complete with controllable representations of the events happening in the infected tissue. More specifically, this simulation tool permits visualization and analysis of how a virus spreads from

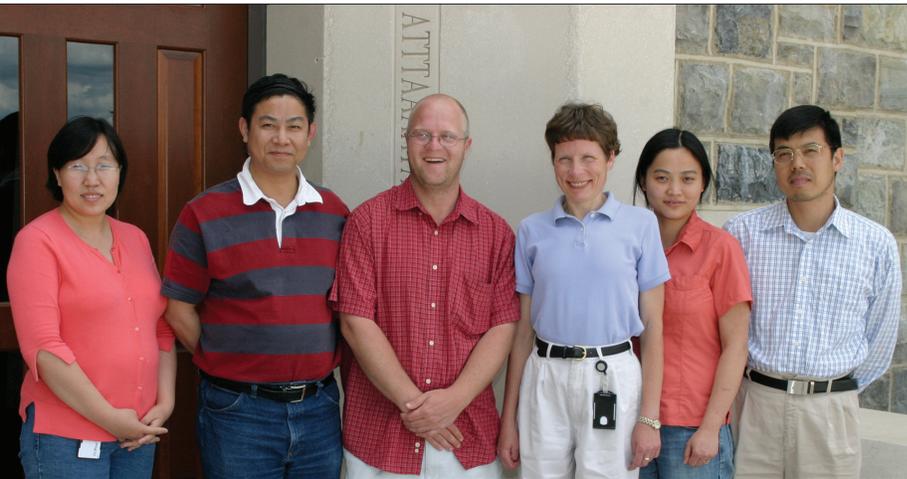
its initial point of infection, as well as the resultant immune response. While the simulation is currently restricted to one pathogen, the group's goal is to create a collection of tools that scientists can use to examine a whole variety of infections, such as influenza, Severe Acute Respiratory Syndrome (SARS), and HIV, and the corresponding immune responses. The tools will eventually become mechanisms for new drug discovery.

The group is also devoting its time to other projects. They are working with computer scientists at Virginia Tech and beyond to develop quality visualizations and new approaches for bioinformatics software. In addition to software, the group is developing new *in vitro* imaging methods with Dr. Amy Bell in Virginia Tech's College of Engineering. In collaboration with Drs. Rosa Gualano and Gary Anderson at the University of Melbourne, the group is exploring the impact of smoking on respiratory infections such as influenza. Of particular interest are the cellular pathways damaged by smoking that impact the body's early immune response to influenza infections. These important studies will help determine how lung perturbing agents undermine human health when acting individually or together.

Along with those specifically mentioned, Duca's group collaborates with investigators at the Via College of Osteopathic Medicine, the University of Virginia, and Virginia Tech's College of Engineering.

## STATISTICAL GENETICS RESEARCH GROUP

DR. I. HOESCHELE



Left to right:

Hua Li, Yongcai Mao, Alberto de la Fuente, Ina Hoeschele, Bing Liu, Guimin Gao

Research in Dr. Hoeschele's group focuses on learning which genes and gene networks affect complex traits in animal, human, and plant populations.

Recent scientific and technological advances have contributed to a tremendous increase in genetic data. Statistical genetics involves the study of these ever-increasing amounts of data. Researchers turn the data into mathematical models, simulations, and visualization tools that allow them to better understand the disease triangle (host, pathogen, and environment) and develop predictive disease models. Informatics and modeling research helps in the reorganization of biological research and education, leading to the development of better quality drugs, vaccines, and cures for infectious diseases.

Dr. Ina Hoeschele's statistical genetics research group is focused on learning which genes and gene networks affect complex traits in animal, human, and plant populations. The group develops statistical methods to locate unknown genes and identify gene networks affecting complex traits. These research findings will lead to an understanding of the genetic architectures of complex and quantitative traits such as heart disease, cancer, diabetes, obesity, and arthritis.

The group's research in this area includes statistical design and basic analysis of gene expression experiments, reconstruction of gene regulatory and protein signaling networks, and joint linkage and linkage disequilibrium mapping of quantitative trait loci (QTL) in complex pedigrees using efficient haplotyping methods.

The practical applications of their research include improving mammalian cloning efficiency which can then be applied to areas of biopharmaceutical production and

the development of animal models for human disease. Additionally, a better understanding of the molecular basis of lung tumors will lead to the development of cancer prevention treatments.

Hoeschele's group's findings will also contribute to the development of new agricultural technologies that will save farmers and consumers billions of dollars in annual losses, as well as improve productivity, health, nutrition, and food safety in breeding.

The group collaborates with Wake Forest University Medical School, the Pennington Biomedical Center (Louisiana), and the Monsanto Company.

## APPLIED DISCRETE MATHEMATICS RESEARCH GROUP

### DR. R. LAUBENBACHER

Left to right:

Miguel Colon-Velez, Edgar Delgado-Eckert, Paola Vera-Licona, Reinhard Laubenbacher, Abdul Jarrah, Omar Colón-Reyes, Elena Dimitrova, Steve Buck, John McGee, Brandilyn Stigler



**D**r. Reinhard Laubenbacher leads the Applied Discrete Mathematics Group at VBI. The group develops mathematical models that can be integrated into computational methods for the modeling and simulation of biological and other systems. This work involves the development and application of bioinformatics tools using discrete mathematics, dynamical systems theory, and symbolic computation. Mathematical methods suitable for this type of approach include computational polynomial algebra, combinatorial topology, as well as combinatorics.

The group focuses on the development of mathematical models for gene regulatory networks, the development of computer models of immune response to viral pathogens, the development of theory and applications of computer simulation to the study of networks, and the topological analysis of interaction patterns in networks.

Large-scale computer simulations are becoming an increasingly important tool in the analysis of highly complex natural and technological systems composed of many interacting entities. Examples of such systems include networks of cells in an organism, such as the immune system, or people in a city transmitting an infectious pathogen. New mathematical tools are needed to design and analyze simulations with large numbers of entities. In collaboration with several collaborators, including Karen Duca at VBI, Laubenbacher's group has developed a multi-scale computer simulation of the immune response that occurs in humans after infection with respiratory pathogens. The simulation is based on a mathematical specification that provides the foundation for a built-in control theory for modeling the immune system. The project currently focuses on the Epstein-Barr and influenza viruses, but is also suitable for applications in other systems such as, for example, transportation and communication networks.

Large-scale computer simulations are becoming an increasingly important tool in the analysis of highly complex natural and technological systems.

The systems are represented as dynamical networks that can be studied with tools from dynamical systems theory, graph theory, and computational algebra.

The group is also working with VBI researchers Vladimir Shulaev and Pedro Mendes to generate a mathematical model describing the biochemical network responsible for the cellular responses to oxidative stress using baker's yeast. Baker's yeast is a common model system for human diseases. Oxygen generates reactive and dangerous molecules, known as reactive oxygen species (ROS). ROS molecules, which are highly toxic, are responsible for cellular stress due to their strong reactive behavior and several human diseases, such as Alzheimer's and Parkinson's, may be related to ROS. The model being developed by the group will further researchers' knowledge of the oxidative stress process and provide insight into new ways to combat related diseases.

Laubenbacher's group has also developed Discrete Visualizer of Dynamics (DVD), a tool for the visualization of the dynamics of multi-state discrete models of biological networks. The multi-state discrete models that can be viewed by DVD are polynomial systems over finite fields.

The Applied Discrete Mathematics Group collaborates with several colleges and universities, including Tufts University Medical School, and the math departments of Cornell University; East Tennessee State University; University of California, Berkeley; and University of Munich, Germany.

## RESEARCH GROUP

DR. C. LAWRENCE



Left to right:

Graciela Santopietro, Qihong Sun, Kwang-Hyung Kim, Chris Lawrence, Violeta Macioszek, Derrick Scott, Michaela Babiceanu, Yangrae Cho, Carlos Mauricio La Rota

Although they represent just four percent of fungal diversity, rots can cause up to 80 percent of foliar fungal losses in some parts of the world.

**D**r. Christopher Lawrence's research group studies the interactions of fungi with plants and humans. One project funded by the National Science Foundation (NSF) Plant Genome Program aims to characterize the defense responses of resistant and susceptible plant hosts when they are attacked by destructive necrotrophic fungi. Necrotrophs, the so called "rots", represent the largest class of fungal plant pathogens, yet our understanding of host-parasite interactions comprising this class of pathogens is extremely limited.

Although they represent just four percent of fungal diversity, rots can cause up to 80 percent of foliar fungal losses in some parts of the world. The group is using the necrotrophic fungus *Alternaria brassicicola*, the model flowering plant *Arabidopsis*, and the closely related Brassica crops in their studies.

Lawrence and colleagues received a grant from the NSF-USDA Interagency Microbial Genome Sequencing Program in 2004 to determine the sequence of and annotate the *Alternaria brassicicola* genome using bioinformatics. His group is now utilizing the genome information from both *Alternaria* and *Arabidopsis* to help unravel the complexities of the interaction at the molecular level. The data generated from these studies may provide insight into the design and implementation of new strategies for controlling necrotrophic pathogens in economically important crops.

Humans are constantly exposed to *Alternaria* and other airborne fungi. Mounting evidence clearly shows that these fungi play a critical role in the development of chronic airway diseases such as asthma, allergy, and chronic rhinosinusitis (CRS). CRS alone affects over 30 million people in the United States annually with a direct cost of the illness exceeding \$5.6 billion per year.

The fungus that appears to be most strongly associated with this phenomenon is *Alternaria*. Lawrence has established a consortium with researchers at the Mayo Clinic in Rochester, Minnesota, to investigate the role of fungi in CRS and asthma. Lawrence and his group have been using the set of predicted proteins obtained from the *Alternaria* genome sequence and other technologies developed at VBI to aid researchers at Mayo in identifying fungal proteins that have a profound effect on the human immune system.

The collective goal of this research is to aid in the understanding of the role of fungi in modulating immune responses in humans and the design and discovery of novel therapeutics for treating fungal-associated conditions.

The Lawrence group collaborates with colleagues at Colorado State University, the Mayo Clinic, SUNY-Buffalo Medical School, North Carolina State University, Washington University Genome Sequencing Center, University of Arizona, University of Delaware, University of Minnesota, Wageningen University-the Netherlands and the Center for Necrotrophic Fungal Pathogens-Perth, Australia.

RESEARCH GROUP  
DR. I. LAZAR

Left to right:

Iuliana Lazar, Hetal Sarvaiya, Nileshwari Vaghela, Phichet Trisiripisal



**D**r. Iuliana Lazar's research group focuses on the development of microfluidic devices with mass spectrometric detection for a variety of bioanalytical applications, as well as the development of mass spectrometric methods and protocols for qualitative and quantitative mapping of protein components in cancerous cells and tissues. The routine implementation of powerful, miniaturized bioanalysis platforms in everyday research will significantly increase the capability to identify disease biomarkers relevant to early diagnosis, prognosis, and treatment response.

Proteomics is an area of research that is focused on the analysis of the protein content of cells, tissues, and microorganisms. Mass spectrometric detection has become an irreplaceable tool in proteomic investigations due to its sensitivity, specificity, and high resolving power. Microfluidic devices provide the optimum analytical platform for fast, sensitive, and parallel handling of minute amounts of samples.

In the biotechnological arena, progressively smaller and faster devices can accommodate the ever-increasing demand for information-producing, high-throughput instrumentation. The integration of these two cutting-edge technologies will assist in bridging the gaps between technology and biology and help establish novel approaches for the investigation of biological systems.

The group has performed extensive research to identify specific biomarkers in cancer cell lines. Thus far, these efforts have resulted in the high-confidence identification of over 1,900 proteins and more than 20 potential disease biomarkers.

Recently, Lazar was awarded a National Science Foundation Faculty Early Career Development Award for her research on the development of microfluidic

Mass spectrometric detection has become an irreplaceable tool in proteomic investigations due to its sensitivity, specificity, and high resolution.

devices with mass spectrometric detection. By addressing technological limitations that slow down proteomic investigations, the development of micro-analytical systems and detection strategies will impact practically any field of biological, biomedical, pharmaceutical, and biodefense research.



## BIOCHEMICAL NETWORKS MODELING GROUP

DR. P. MENDES



Left to right,  
front row: Aejaaz Kamal, Revonda Pokrzywa, Wei Sha,  
Hui Cheng, Christine Lee, Ana Martins, Xing Jing Li,  
Pedro Mendes  
back row: Anurag Srivastava, Bharat Mehrotra, Kimberly  
Heard, Diogo Camacho, Sameer Tupe, Jessica Caldwell,  
Stefan Hoops

The Biochemical Networks Modeling Group is developing methods to reveal the structure of gene networks.

**D**r. Pedro Mendes and his Biochemical Networks Modeling Group focus on computer simulation and analysis of biochemical networks, an area that has recently become known as systems biology. Their research comprises three major areas: development of simulation software, construction and analysis of dynamic models of biochemical networks, and bioinformatics support for functional genomics. Mendes' group collectively has experience in various fields including biochemistry, computer science, biology, genetics, and mathematics. Together, they research how cells work at the biochemical level using computer programs that simulate the dynamics of biochemical systems.

There are currently not many real, well-known gene networks and only portions of the gene networks of cells are available. Many scientific questions, however, depend on the particular details of gene networks. The Biochemical Networks Modeling Group is developing methods to help uncover the structure of gene networks. To determine if these methods work, the group tests them with simulated experiments on artificial gene networks, which are useful for generating data sets to test inference methods and other gene expression analyses, and for gaining an understanding of the underlying factors involved in gene expression dynamics.

The group is also working with VBI researchers Reinhard Laubenbacher and Vladimir Shulaev to generate methods based on nonlinear dynamics to create top-down models describing the biochemical network responsible for the cellular responses to

oxidative stress using baker's yeast, which is a common model system for human diseases.

Oxidative stress affects most organisms that require oxygen to survive. Oxygen generates reactive and dangerous molecules, known as reactive oxygen species (ROS). Highly toxic, ROS are responsible for cellular stress due to their highly reactive behavior and a number of human diseases, such as Alzheimer's and Parkinson's, seem to be related to ROS.

The methods generated by the group are being developed with simulated data and the results of yeast systems biology experiments conducted at VBI. In addition to research on baker's yeast, the group also conducts research involving other model organisms, such as the *Arabidopsis thaliana* plant, the forage legume *Medicago truncatula* (a relative of alfalfa), *Vitis vinifera* (the common grapevine), and *Plasmodium falciparum* (the malaria parasite).

Many of the group's projects are done in collaboration with other schools and organizations, as well as other departments at Virginia Tech. Some current collaborators are the Free University of Amsterdam, the University of Stellenbosch, the European Media Laboratory, the Marine Research Institute (Vigo, Spain), University of Nevada, Reno, the S.R. Noble Foundation, and Southeastern Oklahoma State University.

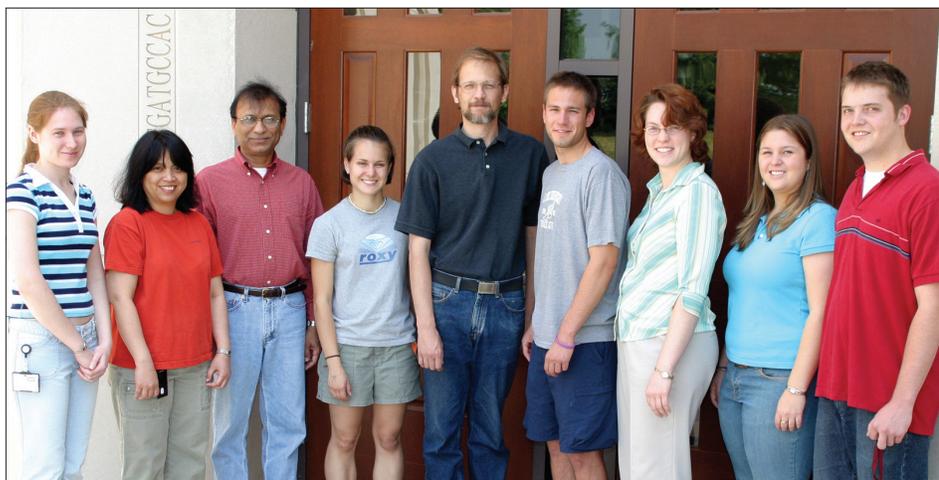
## RESEARCH GROUP

### DR. B. MUKHOPADHYAY

Left to right:

Ashley Hoffman, Endang Purwantini, Biswarup Mukhopadhyay, Deanna Colton, Eric Johnson, Robert Solberg, Jessica Kraszewski, Ashley Shifflett, Christopher Case.

Not pictured: Jennifer Stieber, Shiv Kale, Hannah Glasson, Kimberly Haynie, Lakshmi Dharmarajan



**D**r. Biswarup Mukhopadhyay's research group investigates biology under extreme conditions. Research focuses on the biochemical mechanisms employed by microorganisms to thrive in deep-sea floor hydrothermal vents, to live and produce gas in coal beds, and to combat the oxidative challenge mounted by the human body. The group, which includes high school, undergraduate, and graduate students, uses microbiology, biochemistry, microbial genetics, enzymology, proteomics, biochemical engineering, and bioinformatics techniques.

Organisms in deep-sea hydrothermal vents grow at temperatures as high as 121°C and hold clues to the development of modern cells like those found in humans today. Many produce methane, which is both an energy source and a green house gas, and belong to the domain of life called the archaea. One example is *Methanocaldococcus jannaschii*, which grows at temperatures up to 94°C and uses hydrogen exclusively as an energy source. The group is investigating how this organism deals with toxic compounds such as sulfite and extreme changes in the availability of hydrogen that occur within the vents. In another archaeon, the group has discovered a new type of phosphoenolpyruvate carboxylase. The newly discovered archaeal enzyme may have a role in the efficient operation of the carbon cycle. The enzyme may also determine the pathogenicity of *Clostridium perfringens* and the efficacy of different bacteria in cheese and wine production.

In collaboration with Altuda Energy Corporation in San Antonio, Texas, the group is investigating the use of indigenous microbes to enhance the production of methane in coal beds and to eliminate toxic hydrogen sulfide and potentially explosive methane in coalmines.

In collaboration with the Department of Pharmacy, Institut Teknologi Bandung (ITB), Rotinsulu Pulmonary

Research in Dr. Mukhopadhyay's research group focuses on the biochemical mechanisms employed by microorganisms to thrive in deep-sea floor hydrothermal vents, to live and produce gas in coal beds, and to combat the oxidative challenge mounted by the human body.

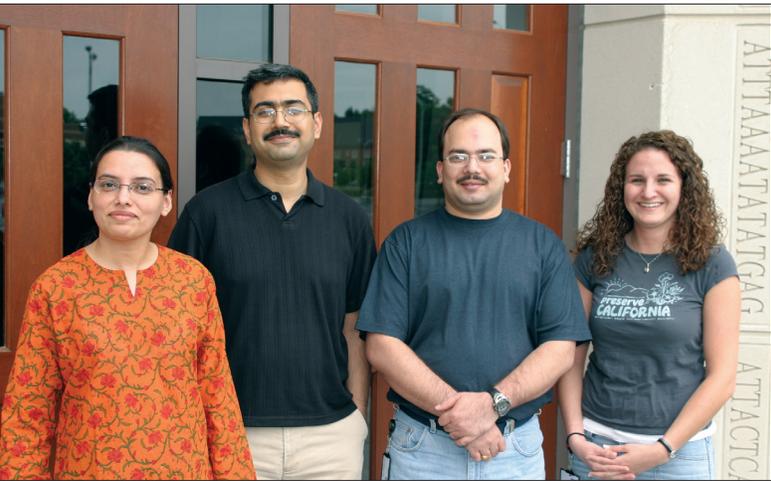
Hospital (Bandung, Indonesia), the Center for Tuberculosis at Johns Hopkins University (Baltimore, MD), and the Sam Houston University (Huntsville, TX), the group works on diagnostics, vaccines, and therapeutics for tuberculosis. Group member Dr. Endang Purwantini leads the team for this project. Several clinical isolates of *Mycobacterium tuberculosis* from two endemic areas in Bandung, Indonesia, are being investigated for potential vaccines and diagnostics. For therapeutic interventions, research focuses on the mechanisms that *M. tuberculosis* uses to combat oxidative stress mounted by the human body as well as its ability to lie dormant in an infected host.

Phosphoenolpyruvate carboxykinase is a key enzyme for glucose production by the liver. In type 2 diabetes, the enzyme causes an overproduction of glucose. The group is identifying target sites on this enzyme for the development of therapeutic agents that will lower but not eliminate its activity, thereby preventing excessive glucose levels in the blood.

Research in the laboratory is supported by the National Aeronautics and Space Administration (NASA), the Department of Energy (DOE), VBI-JHU Collaborative Research Initiative on Infectious Diseases, Virginia Tech Institute for Biomedical and Public Health Sciences (IBPHS), and the Virginia Bioinformatics Institute. The tuberculosis collaboration is also supported by the Government of Indonesia.

## RESEARCH GROUP

DR. D. RATHORE



Left to right:

Dewal Jani, Dharmendar Rathore, Rana Nagarkatti, Kristal Cooper

Using cutting-edge technologies, researchers in Dr. Rathore's laboratory have identified and characterized several malaria parasite antigens that play a role in initiating malarial infection.

**D**r. Dharmendar Rathore's laboratory investigates the mechanisms of infection of two major parasitic diseases, malaria and cryptosporidiosis, at the molecular level. Both are important human diseases affecting the world population.

Malaria, a blood-borne infection caused by *Plasmodium* parasites, is a major health issue in the tropics. Between 300 and 500 million clinical episodes of the disease occur each year, resulting in the death of more than one million people, mainly children under the age of five. In malaria-endemic areas, the prevalence of this disease creates a serious economic burden. It is estimated that without the development of effective intervention strategies, the number of worldwide malaria cases will double in the next 20 years, which creates an urgent need to understand the basic biology of the parasite in order to develop new vaccines, drugs, and insecticides. Similarly, cryptosporidiosis, a water-borne infection caused by *Cryptosporidium* parasites, is life-threatening in AIDS patients and other immunocompromised individuals. The parasite is resistant to water disinfection processes, which makes the infection a major public health concern. Large-scale outbreaks of cryptosporidiosis in the United States have been associated with contamination of community drinking water. There is no known cure for this disease.

In the pursuit to develop new treatments for these diseases, the biggest stumbling block has been the limited understanding of the biology of the infection process. By understanding the mechanism that leads to a successful infection, new strategies can be developed that will prevent the pathogen from establishing an infection, resulting in its control.

The genomes of the organisms causing malaria and cryptosporidiosis have recently been sequenced and Rathore's group's research is focused on exploiting these genetic blueprints of *Plasmodium falciparum* and *Cryptosporidium* parasites in an effort to better understand the molecular basis of the pathogens' onset and sustenance of infection.

Using cutting-edge technologies, researchers in Rathore's laboratory have identified and characterized several malaria parasite antigens that play a role in initiating the infection. Recently, their laboratory has identified a novel malaria parasite protein that is involved in neutralizing toxic heme, a byproduct of hemoglobin degradation, which could serve as a drug target. Similarly, they have developed a cell-based assay system to study proteins from *Cryptosporidium* parasites that could be involved in pathogenesis. This assay system will be utilized for the identification of parasite proteins involved in disease pathogenesis.

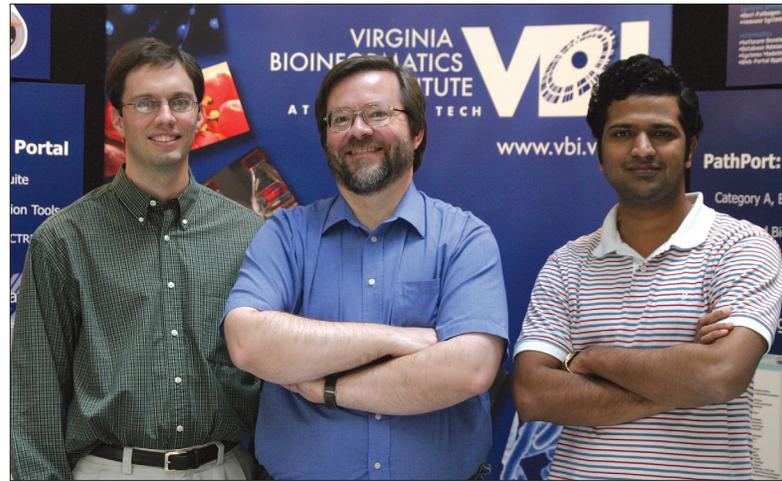
These investigations will contribute towards the development of new approaches to control the infection.

## MODELING RESEARCH GROUP

### DR. D. SAMUELS

Left to right:

Patrick Bradshaw, David Samuels, Harsha Rajasimha



Dr. David Samuels' research group focuses on cell biology modeling for applications in biomedicine.

Mitochondria contain the genes for parts of the proteins that are responsible for the vast majority of the energy production in the cell. Mutation of a cell's mitochondria can lead to loss of cell function. If enough cells stop functioning, a person will develop a mitochondrial disease, which particularly affects nerve and muscle tissue. Mitochondrial mutations begin to appear in every person at noticeable levels in late middle age and become steadily more prevalent as the aging process continues.

The strong relationship between advancing age and mitochondrial mutations is one of the possible explanations for the decrease in a cell's ability to function as a person grows older.

Dr. David Samuels' research group focuses on cell biology modeling with a biomedical emphasis. The group creates computational and mathematical models of mitochondria to study the effects of mitochondrial mutations over the human lifespan. Mutations in the DNA of mitochondria lead to loss of energy in the cell, and ultimately the loss of cell function. The problem is most apparent in cells with high energy requirements, such as neurons and muscle cells. It can take many years, sometimes even decades, for mutations of mitochondrial DNA to build up levels high enough to cause loss of cellular function. Because of these long time scales, these mutations are often associated with slowly developing neurodegenerative diseases, such as Alzheimer's, Lou Gehrig's, and others.

The Samuels group's research uses simulations to understand the development of mitochondrial DNA mutations over the course of a human's lifetime. Their goal is to identify the metabolic pathways responsible for the majority of the damage to mitochondria and determine how to minimize or completely eliminate the damage.

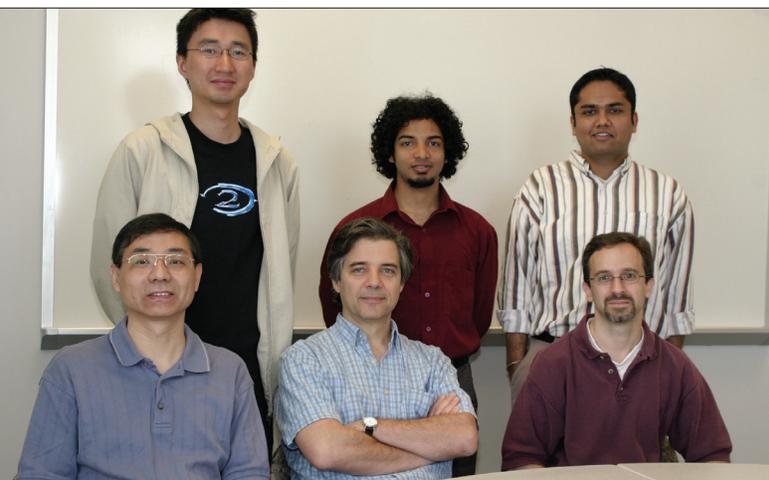
Samuels' group is also developing models of the HIV treatment cocktail, highly active anti-retroviral therapy (HAART), and studying its effects on the patient's mitochondria. These drugs get into the patient's mitochondria and can affect the small, but critical amount of DNA in the mitochondria. Many anti-AIDS drugs that seemed promising in the lab have been found in clinical trials to have serious and sometimes fatal complications because of their effects on the patient's mitochondrial DNA.

The HAART treatment does not remove the HIV virus, but it does keep it under control, which means the therapy must continue for the rest of the patient's life. HAART drugs passed clinical trials, but they were only tested for short-term effects. Now that advances in science and technology are helping AIDS patients to live longer, there is a concern about the damaging effects that HAART has on mitochondria.

Samuels' group is working to identify the metabolic pathways responsible for the majority of the damage to mitochondrial DNA and to determine whether the toxic side effects of HAART can eventually be minimized or eliminated.

## RESEARCH GROUP

DR. J. SETUBAL



Left to right,  
front row: Jian Lu, João Setubal, Michael Czar  
back row: Wenjie Zheng, Lokesh Das, Jinal Jhaveri

Dr. Setubal's research group is developing bioinformatics infrastructure for the genomic analysis of multiple microbial organisms.

The exponential growth of available genetic information over the last decade has created exciting challenges for computational biologists like Dr. João Setubal. Simply managing this information is a daunting task because of the volume of data that exists. In addition, extracting useful information from this data requires sophisticated computational tools and environments to analyze, compare, and combine different kinds of genomic information. It is at this level that Setubal's research group concentrates its efforts. The group is developing a single bioinformatics infrastructure for the genomic analysis of multiple microbial organisms and creating new genomics analysis tools and effective algorithms for solving problems derived from genomic research.

The Setubal group plays a key role in VBI's Bioinformatics Resource Center (BRC). To effectively address threats posed by infectious diseases in the 21st century, there is a need to develop and use molecular biological data as integrated, interacting systems rather than as independent pathogen (disease) and host (human) data sets. An information system to access, integrate, share, manipulate, and analyze these data is necessary. Called the PathoSystems Resource Integration Center (PATRIC), VBI's BRC retains high quality curated data on select pathogens and provides relevant tools to enable and facilitate researchers' analytical and visualization needs.

Researchers can store, view, display, query, annotate, and analyze genomic and related data and bibliographic information. PATRIC is a multi-organism relational database for infectious disease research focusing on biodefense and emerging infectious diseases.

The center is one of eight BRC facilities around the United States established to integrate genomic and post-sequence data from several priority pathogens such as *Brucella* (causes Brucellosis in cattle, pigs, and humans), calciviruses (causes many of the viral dysenteries on cruise ships), hepatitis A, *Coxiella burnetii/Rickettsia* spp. (which cause Q fever, Rocky Mountain spotted fever, and typhus), coronaviruses (e.g. Severe Acute Respiratory System or SARS), and rabies virus. The BRC initiative creates a community of scientists from a variety of disciplines who collect and share information to formulate scientific hypotheses that will generate new targets for diagnostics, drugs, and vaccines.

The Setubal group is also researching *Agrobacterium* biovars (subsets of the bacterial species) and sequencing two new biovars to gain insight into the evolutionary history and plant disease mechanisms of the genus *Agrobacterium*. Much progress in plant molecular biology, genetics, and agricultural biotechnology is attributed to this genus because of its ability to transfer certain genes into the nuclear genome of a variety of plant species, fungi, algae, and even animal cell lines. Because genetic engineering of plants depends on this natural transfer mechanism, *Agrobacterium* has become a crucial part of plant molecular biology and genetics research over the last two decades.

The Setubal group collaborates with the University of Washington and the Monsanto Corporation.

## RESEARCH GROUP

### DR. V. SHULAEV

Left to right,  
front row: Leepika Tuli, Joel Shuman, Ana Martins, Autumn Clapp  
back row: Teruko Oosumi, Diego Cortes, Vladimir Shulaev, Vladimir Polejaev, Hope Cruzewski



Dr. Vladimir Shulaev's Research Laboratory's work focuses on plant response mechanisms to stresses like disease, drought, high salinity, and temperature. Stresses on crops have reduced the agricultural industry's productivity. Past attempts to improve plant stress tolerance through traditional methods (breeding, genetic engineering) have failed partially because of a limited understanding of the mechanisms underlying the plant's responses to stress. A better understanding will help determine the best method for future crop breeding.

The group's research focuses on metabolic profiling of plant-derived chemicals involved in the stress response process; the profiling of these chemicals helps identify novel metabolites that can be used to improve human health and nutrition. Plants respond to stress by producing chemical compounds, many of which are needed to protect cells and organisms from extreme environmental conditions and pathogens. Many of these compounds are also used in pharmaceuticals, insecticides, and antioxidants, and have other uses within the health, food, and cosmetic industries.

Shulaev's group studies biological systems including plants, malaria, and modeling of oxidative stress in yeast. *Arabidopsis thaliana* is a particularly useful model system for metabolomics studies. It may be used to better understand the mechanisms of plant adaptation to osmotic and oxidative stress (abiotic stress) and to investigate early events in the fungal pathogenesis of *Arabidopsis*, which is very important in determining the specificity of responses to different pathogens.

A platform for comprehensive genomics has not yet been developed in *Arabidopsis*. Limitations exist in transferring gene functions discovered in *Arabidopsis* to phylogenetically distant plant species. Consequently, plant scientists have concentrated on new model

Research in Dr. Shulaev's group focuses on the mechanisms of a plant's response to certain kinds of stresses such as disease, drought, high salinity, and temperature.

organisms more closely related to groups of important crops. No comprehensive genomics platform has been developed for fruit crops, despite their significant economic importance and their indispensable role in human nutrition and disease prevention. The group is working together with Dr. Allan Dickerman at VBI, as well as Dr. Richard Veilleux from Virginia Tech's department of horticulture, in developing a functional genomics platform for fruit crops using *Fragaria vesca* as a model plant species. Wild strawberry's fleshy fruit makes it an ideal model for fruit functional genomics research. This allows for the study of the molecular mechanisms involved in fruit development and ripening, as well as the detailed biochemical study of the fruit's profile at the metabolic level.

The laboratory also collaborates with Drs. Reinhard Laubenbacher and Pedro Mendes at VBI. This work involves the metabolic profiling of baker's yeast, a common model system for human diseases. The group focuses on the oxidative stress response and gathers data obtained by simultaneous measurements of mRNA, proteins, and metabolites.

Shulaev's group also collaborates with the Department of Molecular, Cellular, and Developmental Biology at the University of Michigan, the Structural Biology Laboratory at the Salk Institute for Biological Studies, and Johns Hopkins University's Bloomberg School of Public Health.

## RESEARCH GROUP

DR. B. TYLER



Left to right,  
 front row: Rajat Singhania, Dianjing Guo, Sucheta Tripathy, Samantha Chandrasekar, Regina Hanlon, Lisa McCoig, Angela Ko, Brett Tyler, Xia Wang  
 middle row: Nikolaus Galloway, Yinghui Dan, Lecong Zhou, Varun Pandey, Daolong Dou  
 back row: Xuemin Zhang, Konstantinos Krampis, Trudy Torto-Alalibo, Felipe Arredondo, Lachelle Waller, Brian Smith, Nathan Bruce, Andrew Kincaid  
 not pictured: Ken Tian, Tejal Kharkhanis, Venkat Srinivasan, Shomir Wilson

Research in Dr. Tyler's group focuses on identification and characterization of the genes in *Phytophthora* species that enable these pathogens to recognize and overcome the defenses of their plant hosts.

Much of Dr. Brett Tyler's group's research is focused on identifying and characterizing the signals exchanged between plant pathogens and the plant species they attack. *Phytophthora* pathogens are fungus-like organisms called oomycetes that include the pathogen responsible for the Irish potato famine in the 19th century. These pathogens resemble fungi, but belong to a kingdom of life called Stramenopiles, which are more closely related to algae. Because of this identity crisis, conventional fungus control measures often fail against these pathogens.

Tyler's group is identifying and characterizing the genes in *Phytophthora* species that enable these pathogens to recognize and overcome the defenses of their plant hosts. They are also trying to determine what mechanisms are used to overcome the defenses. The group is using genome-wide approaches, namely utilizing a combination of high-throughput experimental methods and bioinformatics approaches to identify pathogen and host genes involved in the interaction, and to predict the functional interactions among the products of those genes that determine the outcome of infection.

*P. sojae*, a member of the *Phytophthora* genus that is responsible for between \$1 and \$2 million in damage to soybean crops annually, has been used for many basic studies of *Phytophthora* because it is easy to manipulate genetically. Tyler's group has recently completed the draft genome sequence for *P. sojae* and *P. ramorum*. *P. ramorum* causes sudden oak death, a disease that has

killed thousands of trees in California and Oregon and poses a large threat to trees and plants in East coast states, including Virginia. Having the complete genome sequence of an organism provides an excellent starting point for identifying genes that cause disease and aids researchers in developing genetic tools for detecting and tracking the pathogen.

The group's long-term goal is to understand the signals and responses exchanged in the environment of a variety of plants that allow plant pathogens to recognize susceptible plant species. A better understanding of this process will eventually allow scientists to safeguard crops against *Phytophthora* pathogens and develop more sustainable agricultural systems.

Tyler has collaborated with other researchers at VBI to create a web-based bioinformatics annotation system for the raw DNA sequence data that has been produced at the Department of Energy Joint Genome Institute. The system will allow *Phytophthora* experts around the world to interpret the DNA sequence. Tyler is also working with VBI researcher Dr. Allan Dickerman and Virginia Tech computer science researcher Dr. T.M. Murali to develop methods for transferring information about gene functions from species in different kingdoms.

Tyler's group collaborates with colleagues at the University of California Riverside, North Carolina State University, Ohio State University, the Joint Genome Institute, the National Center for Genome Resources, and The Institute for Genome Research.

## PATHOSYSTEMS BIOLOGY RESEARCH GROUP

DR. B. SOBRAL

Left to right,  
Endang Purwantini, Chunhong Mao, Bruno Sobral, Yongqun He, Jing Qiu, Chunxia Wang, Xiaoyan Sheng

The PathoSystems Biology Group's research is centered on understanding and comparing host-pathogen-environment interactions. These interactions, sometimes referred to as the "disease triangle", help researchers better understand evolutionary and developmental processes of a diverse array of organisms. When pathogens and hosts interact with each other in a specific environment, they display interwoven communication strategies that disturb genetic, regulatory, and biochemical networks. Understanding this kind of interaction requires both an integration of reductionist molecular data, and an integrated, comparative view of the interaction itself.

Microorganisms perform all known biological nitrogen-fixation processes. In particular, Rhizobiaceae bacteria inhabit the root nodules of leguminous plants (e.g., beans, alfalfa, and soybean). These bacteria and legumes have developed a symbiotic relationship, which allow legumes the net benefit of fixing atmospheric dinitrogen, while the bacteria gain photosynthate from the plant. Understanding this biological process is of great interest from an evolutionary and developmental standpoint. In addition, chemical nitrogen fertilizers are costly and can lead to eutrophication, which can provide an economic and environmental incentive for research. The Pathosystems Biology group focuses on understanding how rhizobia-legume symbioses are established and maintained.

By comparing genes, proteins, and metabolites of the legume-rhizobial symbioses, the research team aims to pinpoint the similarities and differences within networks, genes, proteins, and metabolites affected during nodule development. This work will increase researchers' understanding of intracellular bacteria, the information required to determine how other plants (non-legumes) might be developed so they too can fix nitrogen in symbiosis. This, in turn, will decrease reliability on chemical fertilizers and substantially benefit the environment, agriculture, and health care.

The group's *Brucella* research is focused on studying *Brucella*-host interaction by using technologies such as microarrays and bioinformatical data analysis. *Brucella* species are bacteria that cause brucellosis in humans and animals. *B. melitensis*, *B. suis*, *B. abortus*, and *B. canis* are pathogenic to humans and have been identified as priority agents amenable for use in biological warfare and bioterrorism. To date, there is no safe, effective



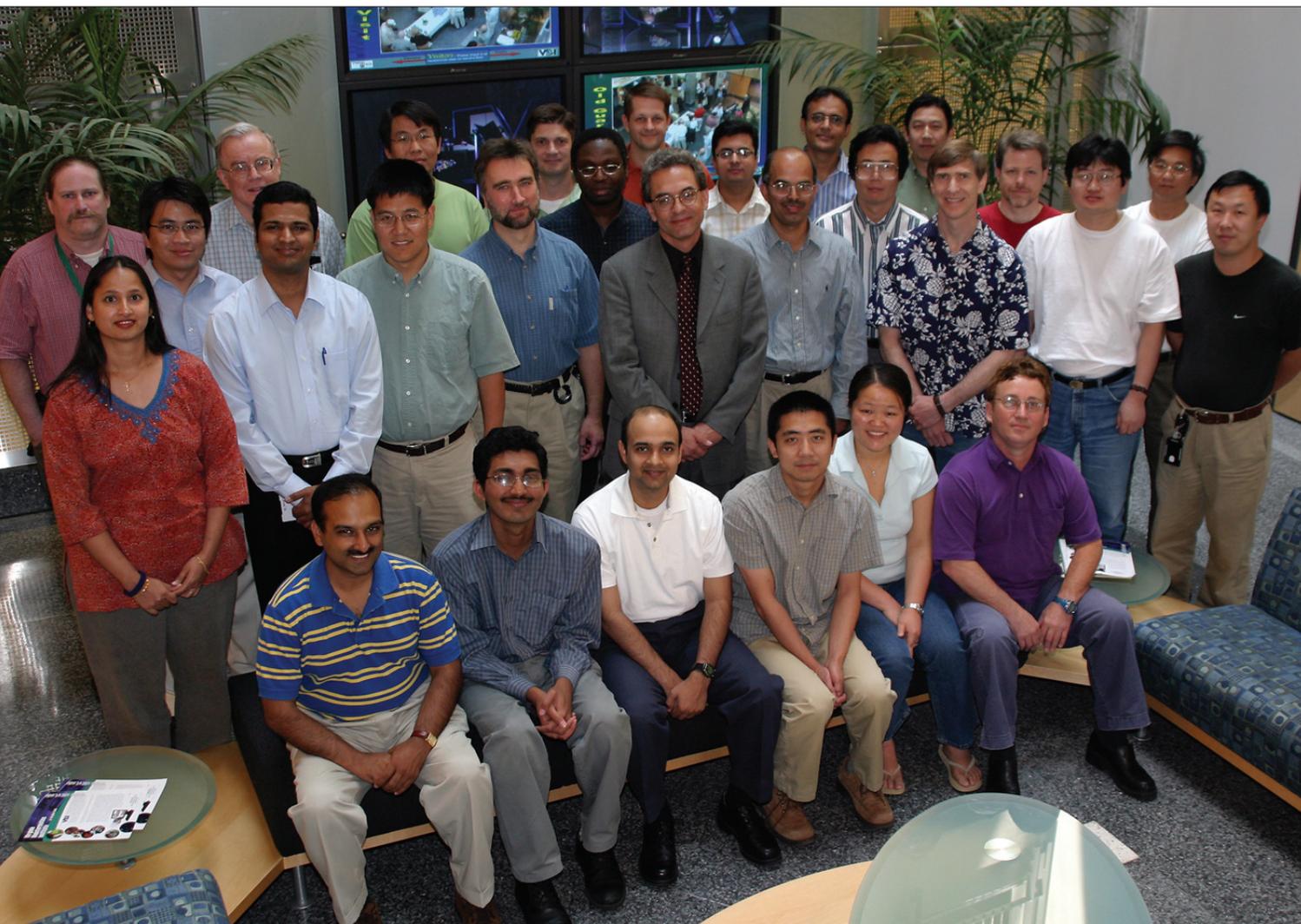
When pathogens and hosts interact with each other in a specific environment, they display interwoven communication strategies that disturb genetic, regulatory, and biochemical networks.

*Brucella* vaccine available for human use; the vaccine strains used in animals are considered to be too virulent or unsafe in humans. Novel vaccines that are non-infectious to humans, but effective in stimulating a broad protective immune response in them are needed. However, the exact mechanism of *Brucella* pathogenesis and host protective immunity remains unclear and requires further study. Many current technologies offer an unparalleled opportunity to understand *Brucella* pathogenesis and host immune mechanism and further improve vaccine development by analyzing a broad range of molecules at the same time. *Brucella* can also be used as a model to study other intracellular pathogens such as *Mycobacterium tuberculosis*.

Tuberculosis (TB) is one of the most common infectious diseases in the world today and *M. tuberculosis*, the causative agent, is another focus of the PathoSystems Biology Group. TB is an infection generally associated with the lungs, but it can also affect bones, joints, and the central nervous system. Despite the effectiveness of current anti-TB drugs, multi-drug resistant organisms are becoming a growing problem, and the mortality rate caused by TB remains high, especially in developing countries. The PathoSystems Biology Group is working with Dr. B. Mukhopadhyay at VBI to develop technology to study genome-wide gene expression patterns of the *Mycobacterium tuberculosis* strains at different stages of infection. They are also analyzing changes in the gene expression profile of the TB organism in response to drug treatments in the hopes of finding new targets for intervention.

## CYBERINFRASTRUCTURE RESEARCH GROUP

DR. B. SOBRAL



The Cyberinfrastructure research group is building PathPort as a set of web services to consolidate, annotate, validate, disseminate, and analyze available pathogen data from different sources through a life sciences framework.

*Left to right,*  
*front row: Ranjan Jha, Kiran Indukuri, Nishant Vaghela, Qiang Yu, Hui Liu, George Abramochkin*  
*middle row: Susan Baker, Harsha Rajasimha, Jian Li, Darius Dziuda, Bruno Sobral, Oswald Crasta, Dana Eckart, Zhangjun Fei, Yan Zhang*  
*back row: Eric Snyder, Nithiwat Kampanya, Bruce Sharp, Yongjian Guo, Ron Kenyon, Herman Formadi, Bryan Lewis, Maulik Shukla, Pradhuman Jhala, Jeff Chen, Tony Zhang, Stephen Cammer, Chendong Zhang*

**D**r. Bruno Sobral's Cyberinfrastructure group is focused on engineering open frameworks for data and tool interoperability and integration for the life sciences. The group aims to bring together data, software programs, and scientific expertise with computational methods and hardware to transform experimental data into knowledge that can be used to advance agricultural, environmental, and biomedical research.

PathPort, which is short for Pathogen Portal, is an interoperability open framework developed by the group that combines information about pathogens with powerful analysis and visualization tools. The analysis capabilities that this tool provides will aid in the detection and identification of high-priority pathogens, which include organisms that cause infectious diseases or could potentially be used as biological weapons. This work has opened the door for scientists, government officials, and emergency responders to more effectively combat infectious diseases by providing access to

## CYBERINFRASTRUCTURE RESEARCH GROUP

DR. B. SOBRAL

relevant data sets and tools. The Cyberinfrastructure group is building PathPort as a set of web services to consolidate, annotate, validate, disseminate, and analyze available pathogen data from different sources through a life sciences framework.

PathPort is supported by ToolBus, the client-side software that allows researchers to access web-services from all over the world through a single user interface. Researchers can also analyze data and examine the results using ToolBus' visualization tools.

Expressed Sequence Tag (EST) projects are empowering the scientific community to discover and study gene functions. Scientists use phenotypes of cells to better understand cell biology and help compare diseased and healthy cells. EST analysis projects lead to the discovery of the latest gene functions, and allow scientists to study them more thoroughly. However, EST projects require the sequencing of thousands of ESTs at a time, which makes these undertakings difficult to manage.

As a result, the Cyberinfrastructure group has developed the EST Analysis Pipeline (ESTAP), an automated system for the analysis of EST data. A database handles the data and results, analyzing all of the information quickly and consistently. This is achieved by using an analysis pipeline, which is a set of computer programs that moves data from one program to the next without human intervention. Researchers using ESTAP can quickly analyze and annotate ESTs, making the discovery of genes and gene functions an easier process.

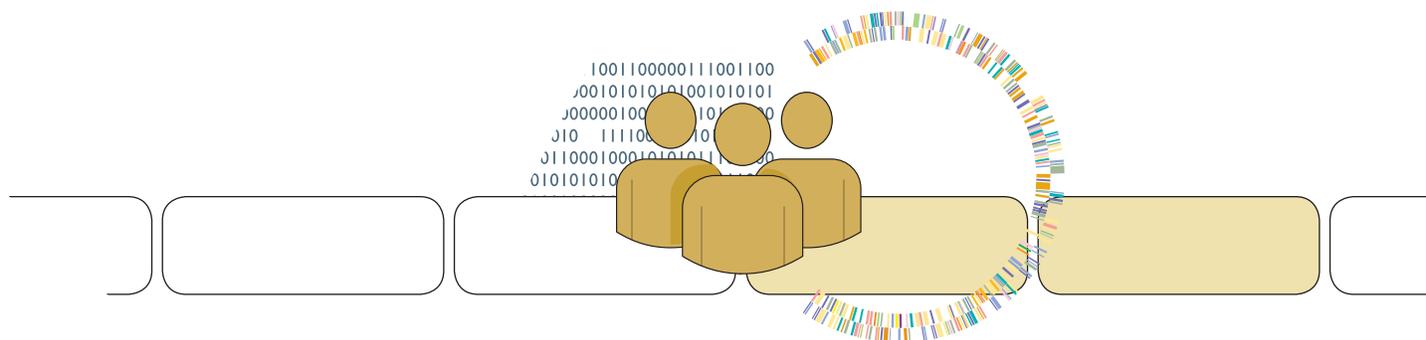
The group also plays an important role in the Middle Atlantic Regional Center for Excellence for Biodefense and Emerging Infectious Diseases (MARCE). This research is focused on enabling rapid defense against bioterrorism and emerging infectious diseases and involves 14 universities, seven government partners, and 10 corporate partners working together to improve the nation's public health response system.

VBI serves at the Bioinformatics and Genomics Research CORE (BGRC) for the MARCE, providing data generation, processing, and storage services through its Core Laboratory Facility (CLF) and Core Computational Facility (CCF). The Cyberinfrastructure group provides computational software for the project through its PathPort software system, as well as bioinformatics training and workshops for participating researchers.

The Cyberinfrastructure group also helps support VBI as one of eight national Bioinformatics Resource Centers (BRC). VBI's BRC retains high quality curated data on select pathogens and provides relevant tools to enable and facilitate researchers' analytical and visualization needs. The center is one of eight BRC facilities throughout the United States established to integrate genomic and post-sequence data from several priority pathogens. The BRC initiative creates a community of scientists from a variety of disciplines who collect and share information to formulate scientific hypotheses that will generate new targets for diagnostics, drugs, and vaccines.

In addition, the group is designing and implementing an integrated National Proteomics Biodefense Database System to help support six Biodefense Proteomic Research Centers that are applying proteomics technologies to characterize pathogen and/or host cell proteomes. The Cyberinfrastructure group's system will be used to collect, store, view, and query proteomics data, including source data, experimental protocols, and novel technologies supplied by the centers.

The goal of the program is to identify candidate targets for the next generation of vaccines, therapeutics, and diagnostics, and perform early stage validation of these targets.



**VBI FACULTY FELLOW****DR. A. BELL****Imaging how viral and host cells interact**

VBI Faculty Fellow and Virginia Tech Electrical and Computer Engineering Associate Professor Amy Bell is applying image processing techniques to wide-field, epi-fluorescent microscope images in an effort to understand how viral and host cells interact. Bell works with Vy Lam, a VBI Postdoctoral Associate, and VBI Research Assistant Professor Karen Duca. The team has developed a model—rooted in the physics of fluorescence microscopy—that significantly improves the noise mitigation in the images over previously established techniques. The ultimate goal is to transform the denoised images into a quantitative description of the viral propagation and host-virus interaction with signal processing techniques. Bell and Duca are also working on ways to identify new signal processing methods for characterizing complex phenotypes in host-virus interactions, which could help researchers answer important questions about the human body's responses to viruses.

In the future, Bell will focus on investigating signal processing techniques for developing a characteristic profile of any unknown host-virus system, and identifying and investigating significant problems in the development of microdevices for understanding and characterizing viral propagation.

**VBI FACULTY FELLOW****DR. T. M. MURALI****Predicting gene function**

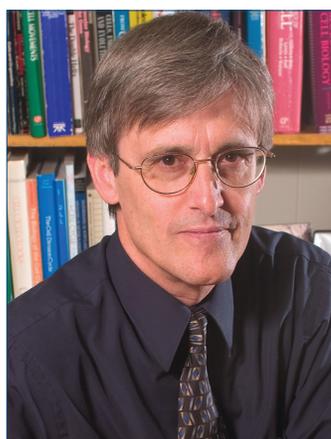
The complete genome sequences of more than 250 organisms are now available and the genomes of an additional 1,200 organisms are in the process of being sequenced. Unfortunately, the biological functions of as many as 60 percent of the genes in sequenced genomes are unknown or poorly understood. Many genes of unknown function might support important cellular functions. Discovering the functions of these genes will provide critical insights into the biology of many organisms and improve our ability to annotate any genomes that are sequenced in the future.

VBI Faculty Fellow and Virginia Tech Assistant Professor of Computer Science T.M. Murali is pioneering the use of functional linkage networks (FLNs) as a mechanism for predicting gene function. Nodes in an FLN are genes, while edges in an FLN represent functional associations between genes of unknown function and genes with known biological roles. Dr. Murali and his colleagues have developed the GAIN system for systematically and robustly propagating functional information in an FLN, while also taking into account both the global structure of the FLN and the local constraints imposed by it.

At VBI, Murali collaborates closely with Brett Tyler and Allan Dickerman on constructing FLNs from a diverse variety of biological data sets and also on applying GAIN to predict gene function in a diverse variety of organisms. In addition, he collaborates with Madhav Marathe, Henning Mortveit, and Anil Vullikanti from VBI's Network Dynamics and Simulation Science Laboratory on the mathematical and algorithmic foundations of GAIN and on new techniques to assist in the study of properties of biological networks. In the second year of his VBI fellowship, Murali plans to explore new collaborations with VBI researchers on novel applications of GAIN.

## VBI FACULTY FELLOW

DR. J. TYSON



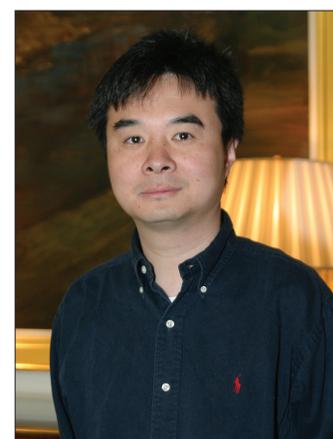
### Building mathematical models of biological cells

VBI Faculty Fellow and Virginia Tech University Distinguished Professor of Biology John Tyson is dedicating one day of each week during the academic year to work on projects of direct relevance to VBI's research platforms. He is leading efforts to explore opportunities for funded projects, one of which involves experimental cell biologists, modelers, mathematicians, and computer scientists from VBI, Virginia Tech, and five other universities. This work has led to the formation of collaborations both inside and outside of VBI. Tyson was also one of 800 nominees for the National Institutes of Health Director's Pioneer Award and, although he did not receive the award, was selected to proceed to the second phase of the award process, which consisted of just 250 candidates.

Tyson has also worked on a mathematical model of the regulation of cell division in a group of bacteria called *Caulobacter*. These bacteria are closely related to economically important microorganisms such as *Rhizobium*, *Brucella*, and *Rickettsia*, which are of particular interest to researchers at VBI and the Virginia-Maryland College of Veterinary Medicine. He and VBI Executive and Scientific Director Bruno Sobral are jointly supporting a student in Virginia Tech's Genetics, Bioinformatics, and Computational Biology (GBCB) Ph.D. program, who is continuing this work in collaboration with Dr. Paul Brazhnik in Virginia Tech's department of biological sciences. In addition, Tyson teaches a weekly, informal seminar class at VBI focused on advanced topics in the areas of network dynamics and cell physiology.

## VBI FACULTY FELLOW

DR. E. WANG



### Biofluidics in microscale devices

VBI Fellow and Aerospace and Ocean Engineering Associate Professor Dr. Joseph Wang is working with VBI's Dr. Iuliana Lazar to develop stand-alone microfluidic analysis platforms with mass spectrometric detection for bioanalytical applications. Wang's research has focused on biofluidics in microscale devices. In such devices, the continuum fluid assumption may break down; the flow dynamics is dominated by electrokinetic forces, energy dissipation, and surface interactions; and there are no effective experimental means to diagnose the processes. Wang has been developing first-principle based, hybrid fluid-particle simulation models on parallel computers to support experimental research and to explore design options for microfluidic systems.

As an example, Wang and his student recently applied computational fluid dynamics and particle-in-cell methods to simulate the dynamics of bio-particles in an aqueous electrolyte solution in a microchannel with an electrode array. In such a device, the fluid flow is driven by the electroosmotic pumping effect and the bio-particle motion is controlled by the dielectrophoretic force and the fluid drag force. Wang's investigation revealed the effects of particle shape and particle electric properties on particle dynamics. Currently, Wang is extending his simulation model to study detailed DNA-fluid interactions and is exploring new design concepts for bio-analytical devices for DNA handling and sampling.



# FINANCE AND ADMINISTRATION

Financial Diversity

Diversity of VBI Personnel

Policy Board



The Virginia Bioinformatics Institute (VBI) has diverse financial support, from the Virginia Tech community to a worldwide sponsor base. The Institute's sponsors include private foundations and industrial leaders as well as support from prominent federal and state government institutions. In the fiscal year 2005, the Institute was second in overhead earned per dollar of university research support and comprised 10% of all research awards received within the university.<sup>(1)</sup>

VBI continues to be a research leader for Virginia Tech. The Office of the Vice President for Research publishes all awards greater than \$1 million awarded within the university community. Of these top new awards for the fiscal year that ended June 30, 2005, VBI had more within the university than any other single center (over 23% of the total top awards). More than \$19 million in new awards were received within the fiscal year.

With its overall financial results for the fiscal year, the Institute is in an ideal position to continue its commitment to research excellence. Thanks to continued commonwealth and university support, VBI experienced an overall gain in net assets for the fiscal year. Strong performance on grants and contracts brought more than \$9 million in revenue to the university.

The diverse mix of grants and contract sponsors promises a bright future for the Institute and should ensure exciting new opportunities for further growth.

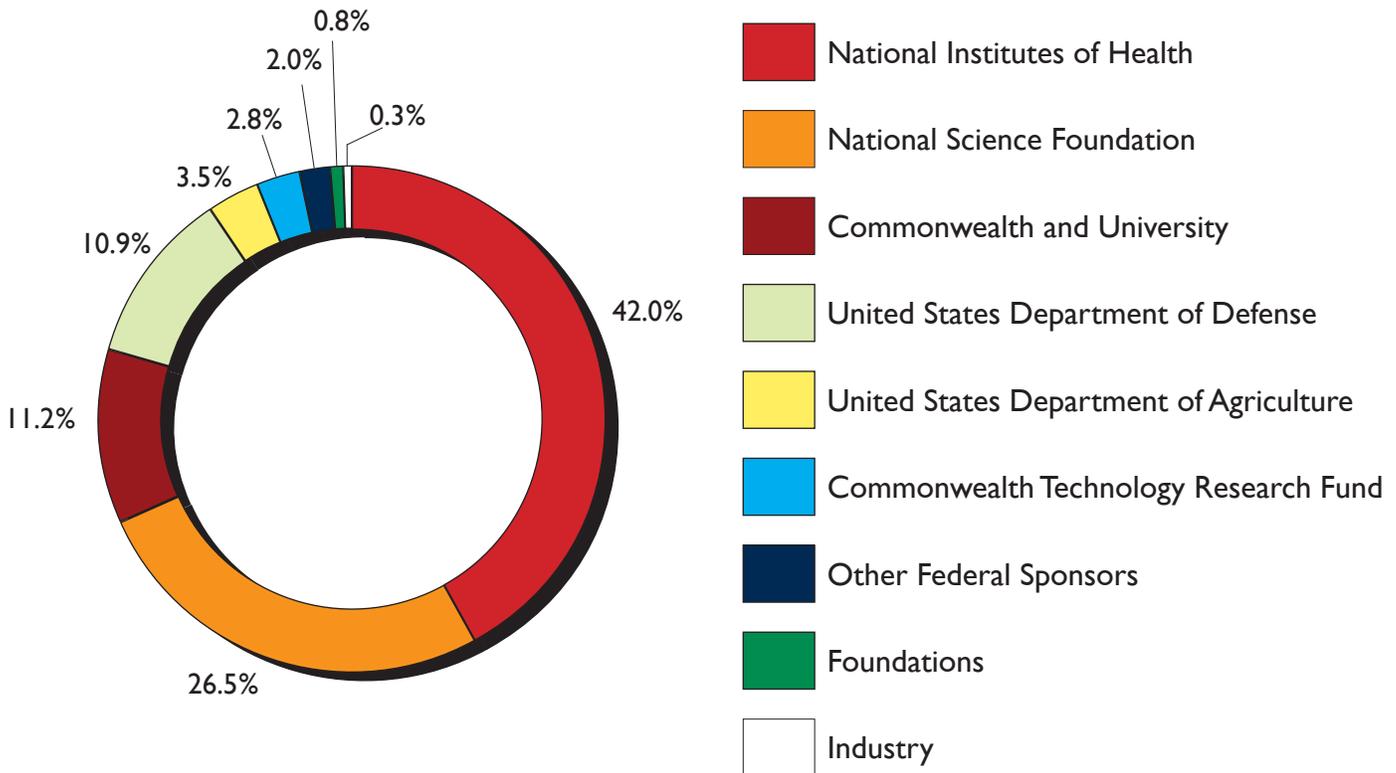
(1) Source: "Progress of Sponsored Programs", a report published quarterly by the Office of the Vice President for Research, final report for the full 2005 fiscal year.

## FINANCIAL DIVERSITY

### TOTAL RESEARCH GRANTS AND CONTRACTS FOR FY 2005

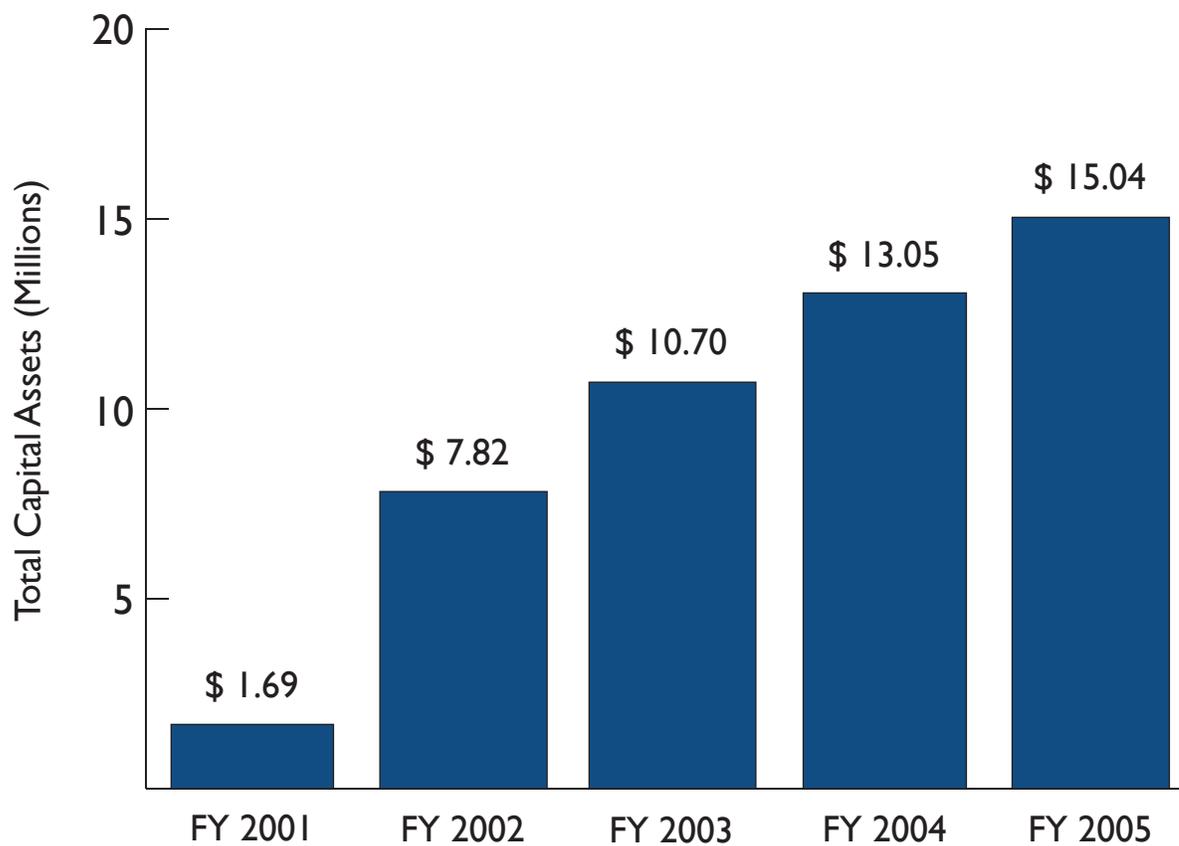
#### SPONSORS

National Institutes of Health	\$ 19,220,505
National Science Foundation	12,103,173
Commonwealth and University	5,120,419
United States Department of Defense	4,989,467
United States Department of Agriculture	1,614,404
Commonwealth Technology Research Fund	1,270,058
Other Federal Sponsors	897,559
Foundations	375,000
Industry	156,263
<b>TOTAL</b>	<b>\$ 45,746,848</b>



## FINANCIAL DIVERSITY

### TOTAL CAPITAL ASSETS FOR FY 2001-2005



FISCAL YEAR	Total Capital Assets
2005	\$ 15,041,139
2004	\$ 13,052,308
2003	\$ 10,702,247
2002	\$ 7,819,501
2001	\$ 1,684,745

## FINANCIAL DIVERSITY

### FINANCIAL OPERATING ACTIVITY FOR FY 2005

#### REVENUES

##### GRANTS AND CONTRACTS

National Science Foundation	\$ 3,252,492
United States Department of Defense	2,605,195
National Institutes of Health	2,267,910
Other Federal Sources	734,255
Industry	284,628
Foundations	60,648
<b>TOTAL GRANTS AND CONTRACTS</b>	<u>9,205,128</u>

Commonwealth and University Sources	3,167,004
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<b>TOTAL REVENUES</b>	<u>12,372,132</u>
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#### EXPENSES

Personnel Expenses	<u>12,037,942</u>
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##### OPERATING EXPENSES

Contractual Services	815,176
Information Technology	317,919
Travel and Awards	595,814
Supply and Materials	1,321,426
Building and Other Rentals	1,005,595
Subcontracts	1,474,891
Equipment	220,536
<b>TOTAL OPERATING EXPENSES</b>	<u>5,751,357</u>

Indirect Expenses	2,574,144
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<b>TOTAL EXPENSES</b>	<u>20,363,443</u>
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#### NON-OPERATING SOURCES

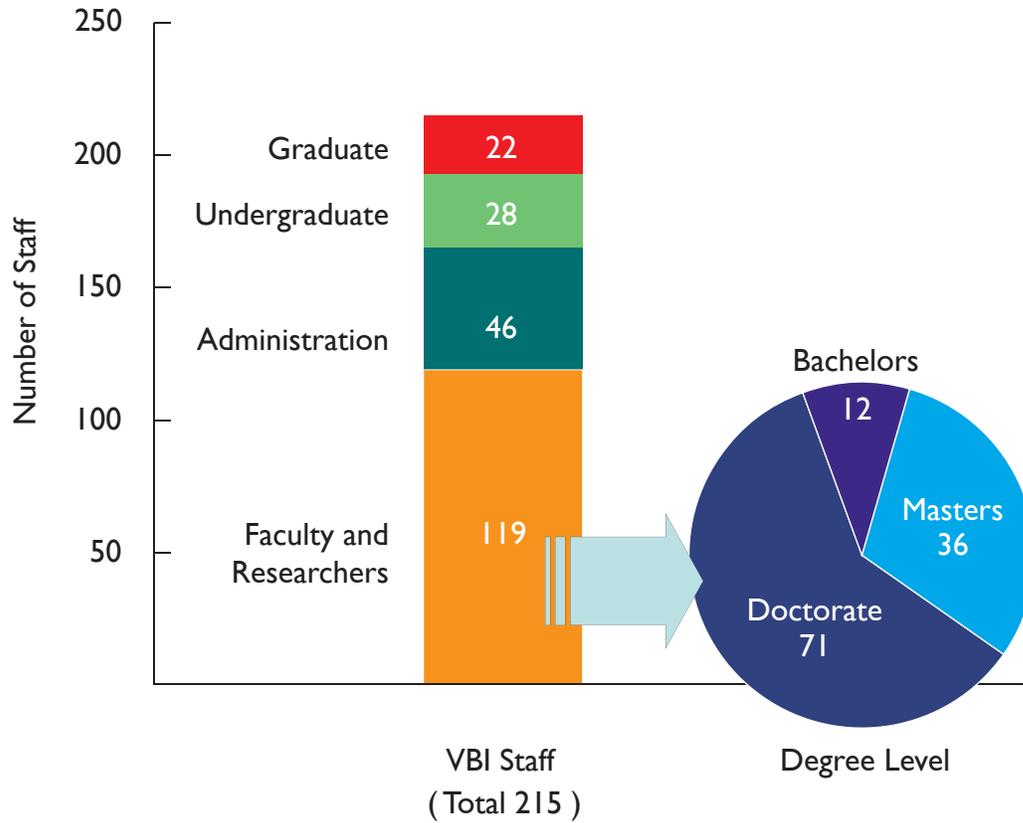
University Support	<u>8,349,457</u>
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<b>GAIN IN NET ASSETS</b>	<u>\$ 358,146</u>
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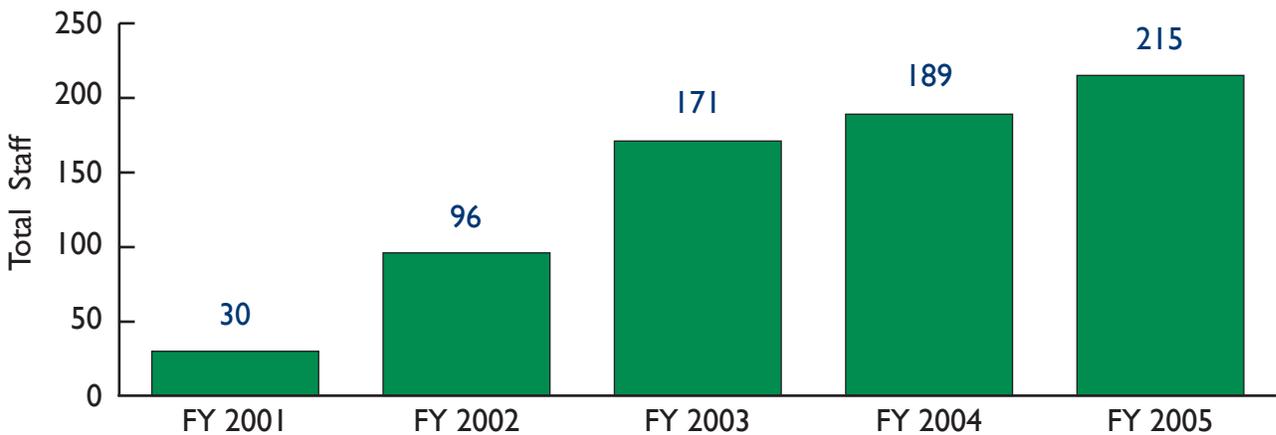


## DIVERSITY OF VBI PERSONNEL VBI PERSONNEL COMPOSITION

Staff and faculty composition as of the fiscal year ended June 30, 2005

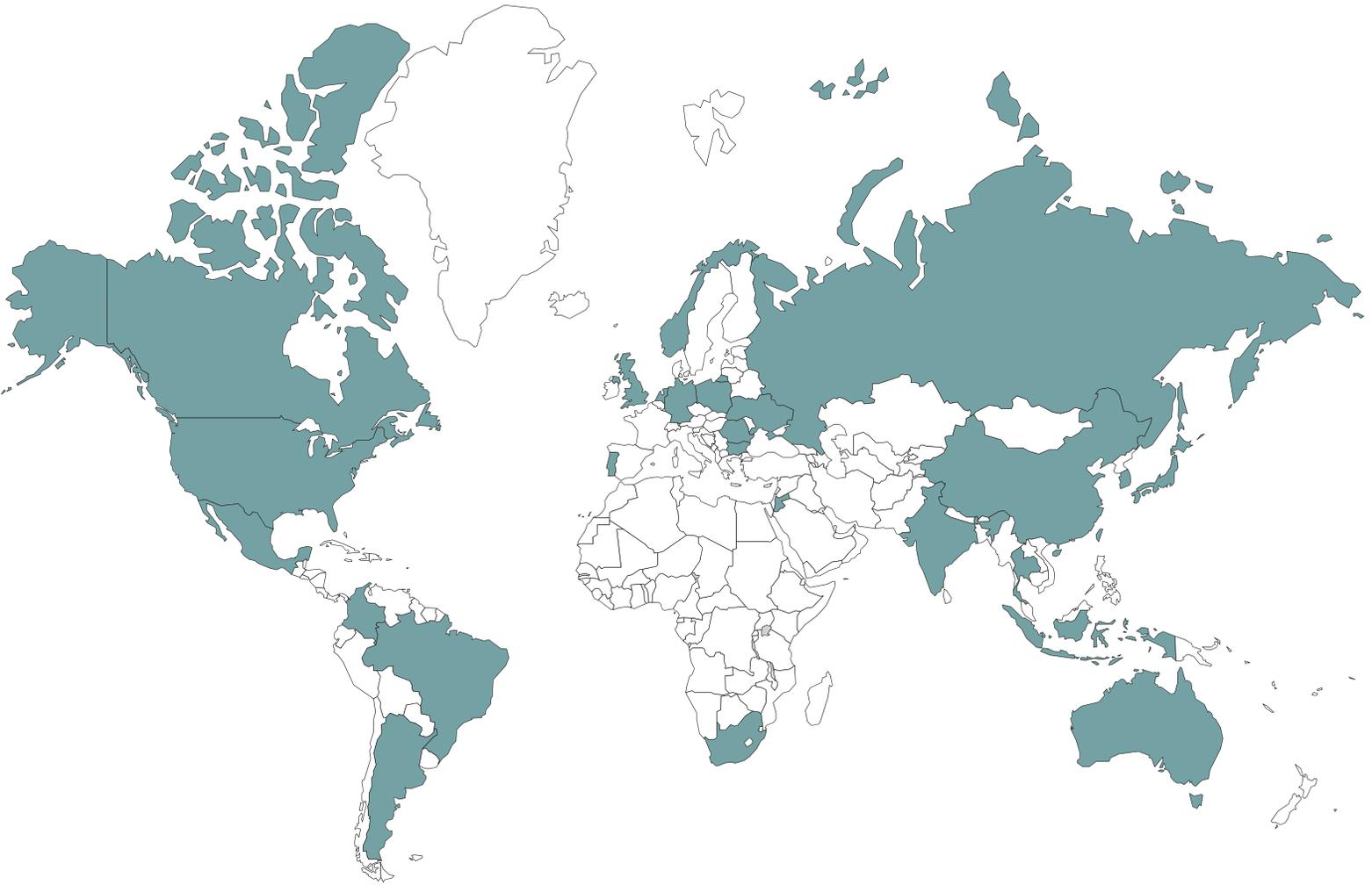


The total staff numbers for the fiscal years ended June 30, 2001 - 2005



## DIVERSITY OF VBI PERSONNEL

### GLOBAL ORIGIN OF VBI PERSONNEL



#### International personnel at a glance:

- 215 employees
- 26 countries
- Highly qualified employees
- Transdisciplinary, team-based science

#### An internationally diverse team supports:

- Excellence in fundamental and applied academic research
- Exchange of information and results between life scientists
- Global contacts between academic and private sectors
- Growth in knowledge and scientific discoveries



## Connecting to a Global Future

Today's scientific initiatives cross global borders. VBI's research not only spans international borders, it also transcends conventional disciplinary boundaries. The Institute's unique approach to science combines computational and biological studies.

VBI is fully committed to fulfilling its mandate of team-based science by developing an internationally diverse employee base. The Institute supports Virginia Tech's resolve to provide scientists and researchers to the global community by training and educating the workers of tomorrow. These efforts will ensure the vitality of global research and innovation in the years ahead.

### GLOBAL PERSONNEL DIVERSITY

	ARGENTINA		INDONESIA		RUSSIA
	AUSTRALIA		JAPAN		SOUTH AFRICA
	BRAZIL		JORDAN		SOUTH KOREA
	BULGARIA		MEXICO		TAIWAN
	CANADA		NETHERLANDS		THAILAND
	CHINA		NORWAY		UKRAINE
	COLOMBIA		POLAND		UNITED KINGDOM
	GERMANY		PORTUGAL		UNITED STATES
	INDIA		ROMANIA		

## VBI POLICY BOARD



The Policy Board of the Virginia Bioinformatics Institute was established in 2000 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 helping develop, secure, and enhance resources for the Institute. The role of the policy advisory board is instrumental to advance the economic development components of the Institute's mission.

### Members of the Board of Visitors

Mr. Jacob Andrew Lutz, III, Chair  
Dr. Hemant Kanakia

### At-large

#### Recommended by the University

Mr. John Alderson  
Mr. Lawrence H. Framme, III  
The Honorable Thomas D. Rust  
Mr. Gary P. Clisham

#### 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

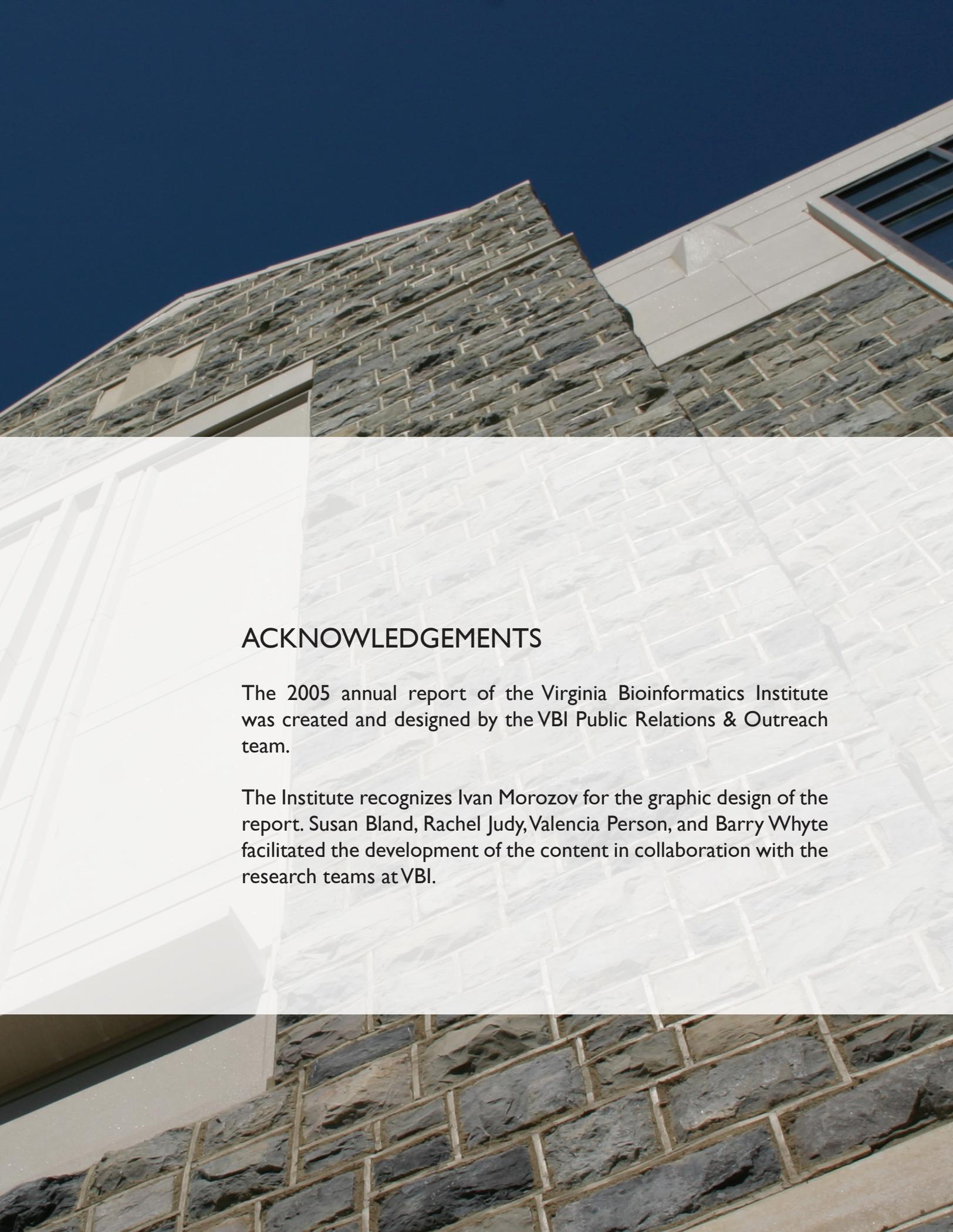
### Ex-officio

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

### Senior Staff Members

Mr. M. Dwight Shelton, Jr.  
Mr. Ralph M. Byers  
Mr. Dave Sebring  
Ms. Lauren Coble  
Dr. Susan Faulkner





## ACKNOWLEDGEMENTS

The 2005 annual report of the Virginia Bioinformatics Institute was created and designed by the VBI Public Relations & Outreach team.

The Institute recognizes Ivan Morozov for the graphic design of the report. Susan Bland, Rachel Judy, Valencia Person, and Barry Whyte facilitated the development of the content in collaboration with the research teams at VBI.

[www.vbi.vt.edu](http://www.vbi.vt.edu)

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