CONTENTS 2008

Message from the President

When the Virginia Bioinformatics Institute started operations in 2000, the university embarked on a groundbreaking initiative to foster collaborative research in the life sciences. Today, VBI employs more than 230 highly qualified people and plays a key role in helping Virginia Tech become an internationally renowned research university, one that contributes to the scientific and economic development of the Commonwealth of Virginia and beyond.

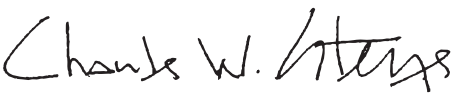
Over the past eight years, VBI has played a pivotal role in helping the university advance discovery, learning, and engagement. The recent implementation of a new research program structure to facilitate transdisciplinary science marks an exciting step in the evolution of VBI. The institute should be commended for not resting on its achievements but for choosing to pursue a bold course of change intended to sustain VBI in its next stage of growth and development.

The past year has seen further significant advances in the scientific output of VBI. In 2008, VBI researchers used powerful computers to simulate a pandemic influenza outbreak in the city of Chicago, modeling the spread of influenza through a population of more than 8.6 million. This type of innovative research is having a major impact on the work of policy- and decision-makers around the country. It is but one example from the past 12 months of internationally competitive VBI research that has been published in high-impact scientific journals.

Virginia Tech's commitment to research, technology development, and education continues to generate impressive results for the university. According to recent data from the National Science Foundation, a 14 percent growth in sponsored research activity allowed Virginia Tech to rise from 54th to 42nd in the NSF's ranking for fiscal year 2007. For universities without a medical school, Virginia Tech ranked ninth in the nation. Behind these achievements are collaborative research and discovery initiatives, like those underway at VBI, that are leading to innovation and new scientific breakthroughs.

The current financial market environment is a reality with which we are all dealing. The recent slowdown in the global economy is adding to the challenges posed by budget reductions. These are challenging times, but Virginia Tech has prevailed through other demanding periods in its history. I am confident that we will maintain excellence in our academic enterprise and continue to provide the high-quality research that our peers recognize as a hallmark of Virginia Tech.

Managing the university through the current, uncertain financial market conditions will remain a priority in 2009. We will continue to find ways to support innovation at the university. Our success depends on it.



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

VirginiaTech
Invent the Future

Letter from the Director

The Virginia Bioinformatics Institute (VBI) has achieved remarkable results in its first eight years. With a focus on infectious disease research, scientific education, economic development and public policy, VBI has created a distinctive culture that promotes transdisciplinary, team-based research. Our scientific achievements have been recognized by the wider scientific community, and VBI has continued to grow and prosper.

We are proud of our accomplishments, but we also recognize that we have a unique opportunity to do even better. To achieve a higher level of performance, in 2007-2008 VBI began a major transition that included refining our Mission, Vision and Values – the foundation upon which VBI is built. Our Mission is to solve society's most important problems in the life sciences through transdisciplinary research and education. Our Vision is to be a world leader in transdisciplinary life science research and education. And our Values – the principles that guide us – are excellence, integrity, valuing people, teamwork and prosperity.

In undertaking this transition, VBI also restructured the Institute to enhance teamwork and collaboration – the hallmarks of transdisciplinary science. Our new structure brings researchers together in teams in the areas of informatics, biosystems and technical infrastructure. These teams support our current research projects, and position us to develop new research programs in other promising areas.

As part of our commitment to grow, VBI is on the cusp of an exciting expansion. Plans are in development for the construction of a new 50,000-square-foot addition to our main building on the Virginia Tech campus. The additional space will enable VBI's Network Dynamics and Simulation Science Laboratory to relocate from the university's Corporate Research Center to VBI's main facility, and support the expansion of the Cyberinfrastructure Group and other research groups. VBI also intends to grow in the nation's capital, in concert with Virginia Tech's plans to build a major research center in Arlington, VA, near Washington, D.C. VBI's strengths in Policy and Decision Informatics will play a key role in defining the research programs of the new facility, and we will be working hand-in-hand with Virginia Tech to promote the university's objectives.

As VBI grows, the Institute will benefit from a new state-of-the-art Intranet that was developed during the year. The Intranet will serve as the information "nerve center" of VBI, enhancing Institute-wide collaboration.

Our achievements are possible because of the dedication, talent and vision of an exceptional group of employees, collaborators and sponsors. I would like to thank you all for your continued support as we pursue the next exciting phase of VBI's future.

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

VIRGINIA BIOINFORMATICS INSTITUTE AT VIRGINIA TECH VBI

OUR MISSION IS TO SOLVE SOCIETY'S MOST IMPORTANT PROBLEMS IN THE LIFE SCIENCES THROUGH TRANSDISCIPLINARY RESEARCH AND EDUCATION.

Our Vision

VBI will be a world leader in transdisciplinary life science research and education. In practice this means:

- We make transformative discoveries.
- We solve important problems.
- We develop the next generation of transdisciplinary researchers.
- We influence public policy.
- We transition scientific research into use.

EXCELLENCE

INTEGRITY

VALUE PEOPLE

TEAMWORK

PROSPERITY

Kristal Cooper, GS-FLX™ and Affymetrix Specialist in the Virginia Bioinformatics Institute's Core Laboratory Facility, is VBI's first Mission, Vision and Values (MV&V) Champion. The MV&V Champion award recognizes individuals or teams at VBI who have made outstanding contributions to the team science environment in a way that exemplifies VBI's MV&V. Kristal received her award from VBI Executive and Scientific Director Bruno Sobral on November 21, 2008. He remarked: "Kristal contributes to the Mission, Vision, and Values of VBI through her excellence and teamwork. She exceeds expectations, promotes innovation, and exudes an entrepreneurial spirit in her work. It is a pleasure to recognize her contribution to VBI in this way."

Highlights

2007

July

VBI launches genome sequencing services on the Roche GS-FLX™

Montgomery County high school students attend week-long program at VBI

August

VBI hosts genome annotation workshop series

September

HARDY rice: less water, more food

VBI hosts 2nd annual research symposium

October

VBI Executive and Scientific Director speaks to BIO IT Coalition

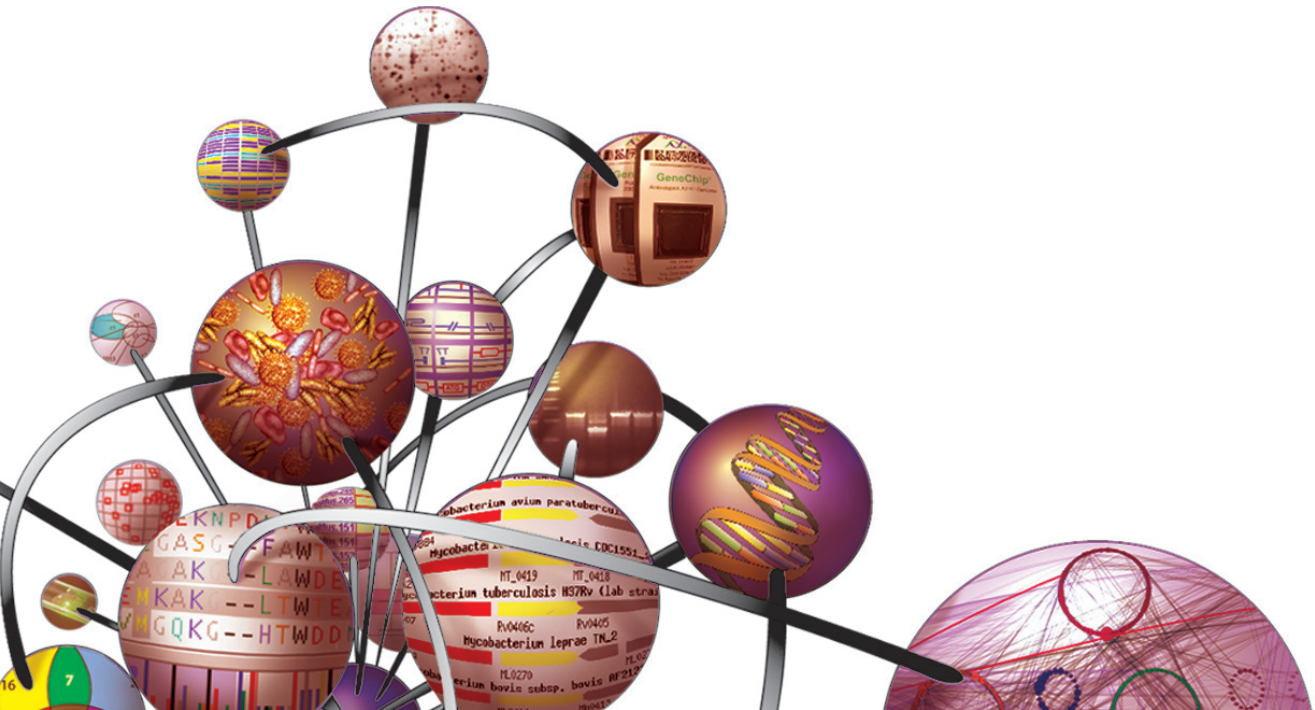
November

Virginia Tech's iGEM team receives gold medal in national competition

Swiss Ambassador visits VBI

December

VBI appoints Scientific Advisory Board



2008

January

New faculty member investigates impact of nutrition on human health

In silico modeling helps predict severity of mitochondrial disease

February

Researchers unveil landscape of human-pathogen protein interactions

VBI and Mayo Clinic investigate link between fungal proteins, innate immunity and asthma

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Jeanne Forbis named VBI's chief of staff and executive communications officer

Huge virulence gene superfamily responsible for devastating plant diseases

Stephen Eubank featured in ASM video podcast

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April (continued)

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May

NSF awards $918,000 for cyberinfrastructure education and outreach project

VBI laboratory manager receives Virginia Tech Staff Leadership Award

VBI holds Summer Research Institute

Tyler receives Noel T. Keen award for research excellence in molecular plant pathology

June

Brucella abortus S19 genome sequenced; points toward virulence genes

Highlights

2007

July

VBI launches genome sequencing services on the Roche GS-FLX

VBI announces the official launch of its genome sequencing services for the Roche GS-FLX™. The launch coincides with the successful completion of pilot projects and the availability of approved service costs for shotgun genome sequencing on the Roche GS-FLX™. The Roche GS-FLX™ is a next-generation genome sequencing system that takes advantage of 454 Life Sciences™ revolutionary sequencing technology and allows researchers to go from genome to sequence in record time.

Montgomery County high school students attend week-long program at VBI

VBI hosts 11 students from Montgomery County high schools in a week-long summer program designed to encourage students' interest in scientific research. The program offered instruction in bioinformatics, biotechnology, and genomics and included a discussion/lecture series and eight research activity labs.

August

VBI hosts genome annotation workshop series

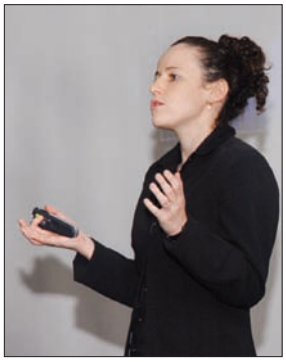
VBI hosts a series of bioinformatics workshops centered on the theme of microbial gene sequence annotation. The VBI Genome Annotation Workshop Series included three workshops: Plant-Associated Microbe Gene Ontology (PAMGO) training, Oomycete Bioinformatics Resources training, and the *Hyaloperonospora parasitica* Genome Sequence Annotation Jamboree.

September

HARDY rice: less water, more food

An international team of scientists produces a new type of rice that grows better and uses water more efficiently than other rice crops. VBI Professor **Andy Pereira** has been working with colleagues to identify, characterize and make use of a gene known as *HARDY* that improves key features of this important grain crop. The research shows that *HARDY* contributes to more efficient water use in rice, a primary source of food for more than half of the world's population.

VBI hosts 2nd annual research symposium



With a goal of sharing scientific ideas and research, as well as promoting collaborative work across the Institute, VBI hosts its second annual research symposium. The event consisted of presentations from students, post-graduates and other scientists working at VBI. **Olga Troyanskaya**, assistant professor in Princeton University's Department of Computer Science and head of the Laboratory for Bioinformatics and Functional Genomics at the Lewis-Sigler Institute for Integrative Genomics, NJ, served as the keynote speaker.

October

VBI Executive and Scientific Director speaks to BIO IT Coalition

VBI Executive and Scientific Director Bruno Sobral is the featured speaker at the BIO IT Coalition's September luncheon meeting. Sobral's talk, titled "VBI: A Transdisciplinary Scientific Collaborative in Life Sciences", highlighted VBI's vision to create a collaborative transdisciplinary research culture conducive to the development of new life science technologies and knowledge.

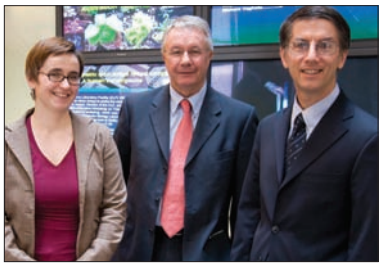
2008

November

Virginia Tech's iGEM team receives gold medal in national competition

Virginia Tech's **iGEM team** makes a successful first appearance at the 2007 national iGEM competition in Boston, MA, and receives a gold medal from competition judges for their efforts. The two-day competition included oral presentations by each participating team as well as poster presentations. The judges awarded the Virginia Tech team a gold medal in recognition of the work performed to sequence all of the BioBricks in the iGEM Registry. Having these sequences available will be very useful for future iGEM teams.

Swiss Ambassador visits VBI



The **Swiss Ambassador** to the United States visits VBI as part of a two-day visit to Virginia Tech. Swiss Ambassador Urs Ziswiler and Dora Fitzli, Counselor for Science and Technology at the Swiss Embassy in Washington, DC, were given an overview of the activities of the Institute and a tour of VBI's building by Professor Brett Tyler and Strategic and Research Communications Officer Barry Whyte.

December

VBI appoints Scientific Advisory Board

VBI announces the appointment of six members to its newly formed Scientific Advisory Board. Members of the board, which include scientific leaders in fields such as high-performance computing, biology, bioinformatics, and nanotechnology/ engineering, serve as scientific advisors for the Institute, providing regular external reviews of research strengths as well as guidance on new strategic scientific initiatives and funding opportunities.

2008

January

New faculty member investigates impact of nutrition on human health

VBI welcomes its newest faculty member, **Josep Bassaganya-Riera**. The long-term goal of Bassaganya-Riera's research at VBI is to better understand how nutrition affects human health. More specifically, he is examining the cellular and molecular mechanisms by which dietary lipids and phytochemicals regulate inflammation and metabolism, and prevent chronic diseases. His work focuses on three research areas: nutritional immunology, gastrointestinal health, and obesity and its accompanying complications, such as type 2 diabetes and cardiovascular disease.

In silico modeling helps predict severity of mitochondrial disease

A team of researchers in Australia, the United Kingdom and the United States, including VBI Assistant Professor David Samuels, reveals how mitochondrial diseases are passed from the mother to the next generation in a mouse model system. The study shows for the first time how mitochondrial diseases that cause muscle weakness, diabetes, stroke, heart failure and epilepsy are passed from mother to offspring.

February

Researchers unveil landscape of human-pathogen protein interactions

Researchers at VBI and the Department of Computer Science at Virginia Tech provide the first global analysis of human proteins interacting with viral proteins and proteins in other pathogens. The scientists examined publicly available experimental data for 190 different pathogens that comprise 10 477 interactions between human and pathogen proteins. This approach provides a highly detailed network map of human proteins interfacing with proteins in different pathogens. The network of interactions reveals possible key intervention points for the future development of therapeutics against infectious diseases.

Highlights

2008

VBI and Mayo Clinic investigate link between fungal proteins, innate immunity and asthma

Researchers at Mayo Clinic and VBI receive a second grant from the National Institute of Allergy and Infectious Diseases (NIAID) to advance understanding of the role of environmental fungi in chronic airway disorders. NIAID awarded the researchers a further $1.8 million for these studies over a five-year period to investigate how the environmental fungus *Alternaria* triggers airway inflammation and bronchial asthma.

March

NDSSL conducts training for Defense Threat Reduction Agency

The Network Dynamics and Simulation Science Laboratory (NDSSL) at VBI conducts a training session for analysts from the Defense Threat Reduction Agency (DTRA). The workshop prepared DTRA analysts for initial use of a new prototype application of the Comprehensive National Incident Management System (CNIMS). The CNIMS provides those involved in disaster management in the United States military with essential operational information about the populations being affected by a possible crisis.

Scientists simulate pandemic influenza outbreak in Chicago

By using computer simulations and modeling, an international group of researchers including scientists from VBI's Network Dynamics and Simulation Science Laboratory (NDSSL) determines how a pandemic influenza outbreak might travel through a city similar in size to Chicago, Ill. This information helped them to determine the preferred intervention strategy to contain a potential flu pandemic, including what people should do to decrease the likelihood of disease transmission.

April

Jeanne Forbis named VBI's Chief of Staff and Executive Communications Officer

VBI names **Jeanne Forbis** as its chief of staff and executive communications officer. Forbis serves as a key advisor to VBI Executive and Scientific Director Bruno Sobral and will play a key role in shaping the institute's collaborative culture in the years ahead. A communications and managerial leader with more than 20 years experience, Forbis comes to VBI from medical device manufacturer Medtronic, where she served as vice president of global public and media relations.

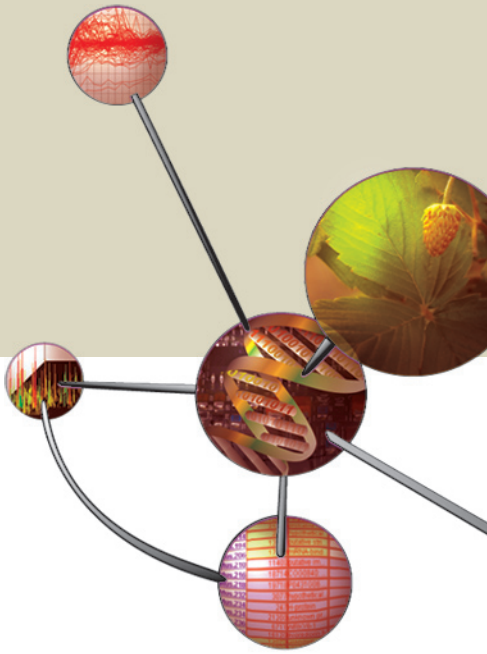
Huge virulence gene superfamily responsible for devastating plant diseases

A research team from VBI identifies an enormous superfamily of pathogen genes involved in the infection of plants. The *Avh* superfamily comprises genes found in the plant pathogens *Phytophthora ramorum* and *Phytophthora sojae*. The pathogen genes produce effector proteins that manipulate how plant cells work in such a way as to make the plant hosts more susceptible to infection. The results suggest that a single gene from a common ancestor of both pathogen species has spawned hundreds of very different, fast-evolving genes that encode for these highly damaging effector proteins.

Stephen Eubank featured in ASM video podcast

A video podcast produced by the American Society for Microbiology (ASM) features VBI Professor and Deputy Director of the Network Dynamics and Simulation Science Laboratory (NDSSL) **Stephen Eubank**. "Modern Transportation and Infectious Disease" explores the impact of air and mass transit travel on the spread of infectious disease. Eubank discusses how the NDSSL models the way people move around cities, which is an important tool when determining how a disease may travel through a population.

2008



VBI graduate research assistants receive outstanding student awards

(left to right: LaChelle Waller, Karen DePauw, and Konstantinos Krampis)

Two graduate research assistants at VBI receive outstanding student awards from the Virginia Tech Graduate School. **LaChelle Waller**, a student in Virginia Tech's Genetics, Bioinformatics, and Computational Biology (GBCB) Ph.D. program was named Graduate Woman of the Year at Virginia Tech. GBCB student **Konstantinos Krampis** was recognized as the university's Outstanding Interdisciplinary Program Student.

NDSSL demonstrates research in Technology Forum for Senate Armed Services Committee

The Network Dynamics and Simulation Science Laboratory (NDSSL) at VBI presents its Comprehensive National Incident Management System (CNIMS), which is being developed for the Defense Threat Reduction Agency (DTRA), at a technology forum for the Senate Armed Services Committee (SASC). The CNIMS provides those involved in disaster management in the United States military with essential detailed operational information about the populations being affected by a possible crisis.

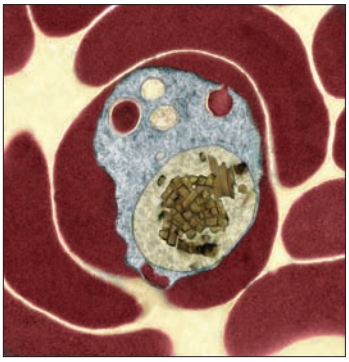
Barrett gives keynote lecture at HiCOMB 2008

VBI Professor and Network Dynamics and Simulation Science Laboratory (NDSSL) Director **Chris Barrett** presents the keynote address at High Performance Computational Biology (HiCOMB) 2008, the seventh annual Institute of Electrical and Electronics Engineers (IEE) international workshop on high performance computational biology. In his talk, "HPC-based Policy Informatics: A Public Health Epidemiology Example," Barrett outlined how the NDSSL uses high performance computing to look in detail at policy informatics and the behavioral analysis of large complex systems.

Pathogen virulence proteins suppress plant immunity

Researchers from VBI and their colleagues identify a key function of a large family of virulence proteins that play an important role in the production of infectious disease by the plant pathogen *Phytophthora sojae*. VBI Professor Brett Tyler and others examined the function of the virulence (or effector) protein Avr1b in *P. sojae* and discovered that Avr1b is capable of suppressing an important process in plant immunity called programmed cell death. Programmed cell death is an in-built suicide mechanism that kills infected plant tissue and fills it with toxins so the pathogen can no longer feed on it.

Elusive protein protects malaria parasite from heme



VBI researchers and their colleagues identify Heme Detoxification Protein (HDP), a unique protein encoded in the malaria genome that represents a potential target for developing new malaria drugs. The team has characterized HDP and demonstrated that it plays a major role in protecting *Plasmodium* as the pathogen pursues infection of its host.

Highlights

2008

April (continued)

Scientists reveal evolutionary intricacies of *Rickettsia* pathogens

UNIVERSITY OF MARYLAND
SCHOOL OF MEDICINE

Scientists from VBI and the University of Maryland School of Medicine unveil some of the evolutionary intricacies of rickettsial pathogens by analyzing over a decade's worth of genomic data. Some species of *Rickettsia* are known to cause harmful diseases in humans, such as epidemic typhus (*R. prowazekii*) and Rocky Mountain spotted fever (*R. rickettsii*), while others have been identified as emerging pathogens and organisms that might possibly be used for the development of biological weapons. The new data open up exciting new possibilities for future research.

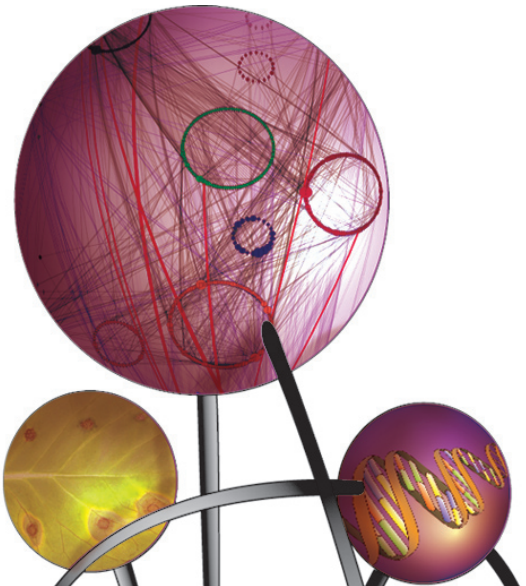
VBI graduate assistant awarded prestigious scholarship from Virginia Tech College of Science

Kwang-Hyung Kim, a graduate research assistant at VBI and Ph.D. student in Virginia Tech's Department of Biological Sciences, receives the College of Science's Roundtable "Make-a-Difference" Scholarship for Graduate Study. The scholarship was established to recognize graduate students who will make a significant difference to the college and the world outside of the university.

May

NSF awards $918,000 for cyberinfrastructure education and outreach project

The National Science Foundation (NSF) awards VBI $918,000 to expand its education and outreach program in Cyberinfrastructure - Training, Education, Advancement and Mentoring (CI-TEAM). VBI will collaborate with scientific researchers and educators of high school and undergraduate students from several institutions nationwide to build its educational program for the next generation of computer-savvy biologists.



2008

VBI laboratory manager receives Virginia Tech Staff Leadership Award

In recognition of her strong leadership qualities, **Linda Correll**, lab facilities and resource manager at VBI, receives the Virginia Tech Staff Leadership Award at the 2008 McComas Staff Leadership Seminar. Correll directs VBI's Shared Laboratory Facilities program for the institute's multi-user environment.

VBI holds Summer Research Institute

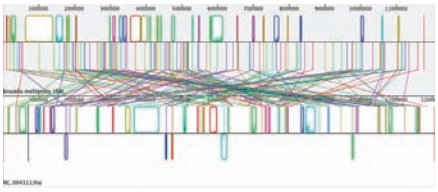
As part of an exciting new education and outreach initiative, VBI designs five summer professional development programs for the 2008 VBI Summer Institute. The purpose of the VBI Summer Institute is to provide professionals and undergraduate and graduate students with workshop and professional development opportunities that allow for direct interaction with VBI faculty.

Tyler receives Noel T. Keen award for research excellence in molecular plant pathology

Brett Tyler, professor at VBI and in the Department of Plant Pathology, Physiology and Weed Science at Virginia Tech, receives the 2008 Noel T. Keen award for research excellence in molecular plant pathology. The annual award recognizes members of the American Phytopathological Society who have made outstanding contributions and demonstrated sustained excellence and leadership in molecular plant pathology research.

June

Brucella abortus S19 genome sequenced; points toward virulence genes

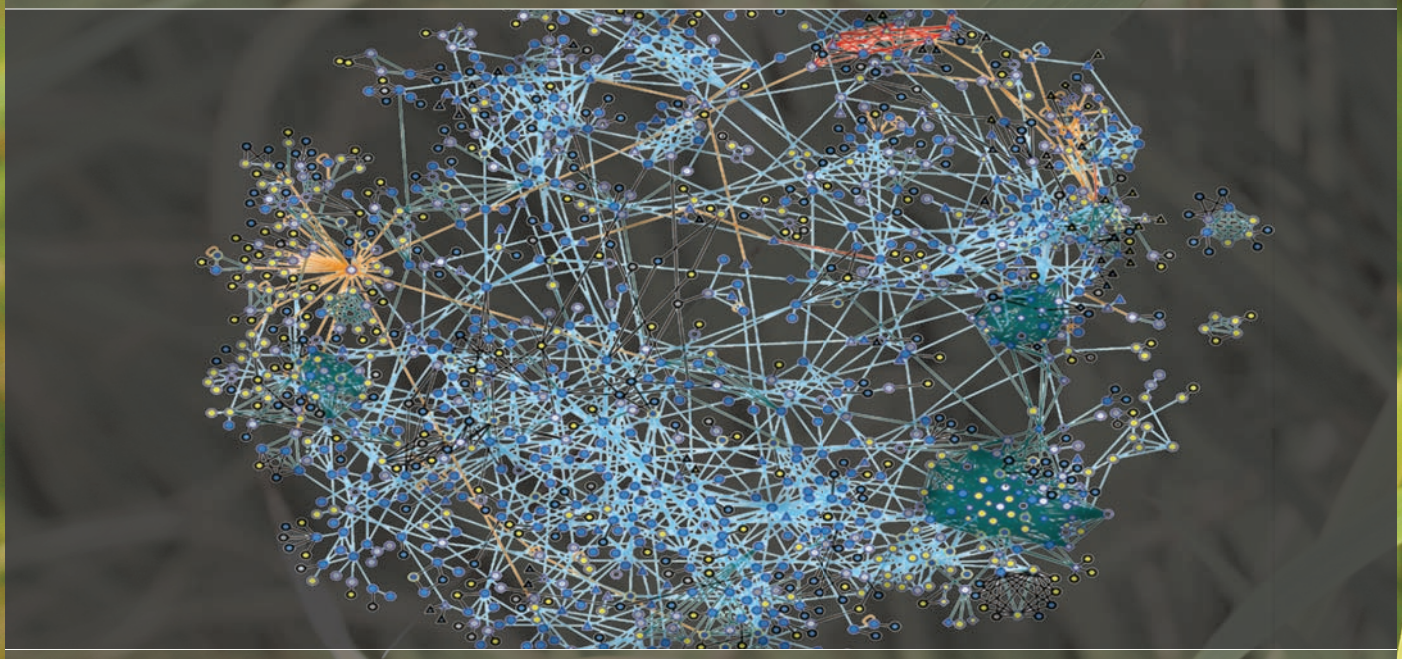


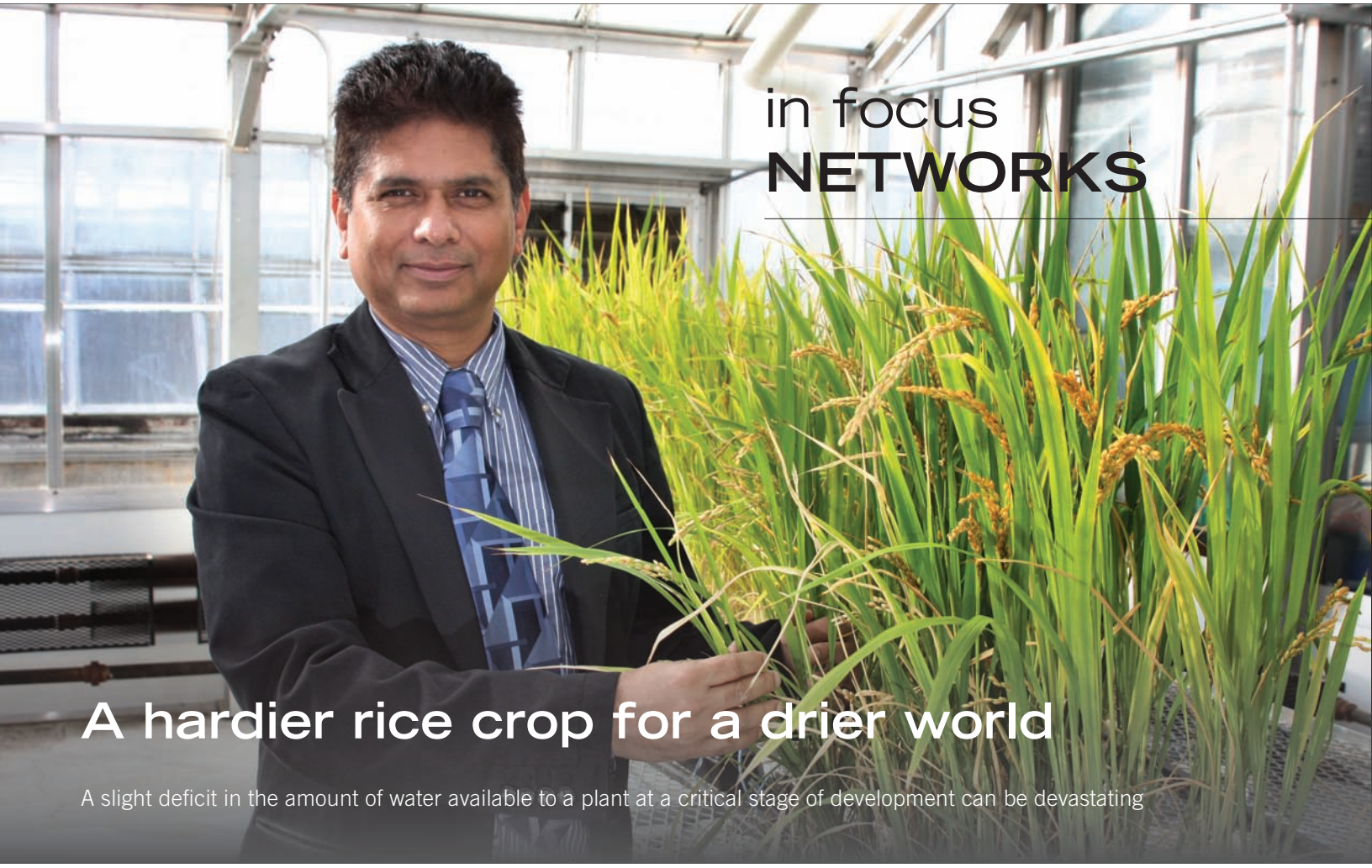
Researchers at VBI and collaborators sequence the genome of *Brucella abortus* strain S19. Scientists have long wanted to know what genetic features make strain S19 suitable for use as a vaccine in cattle because it may hold the secret as to why other *Brucella* strains cause disease and trigger the abortion of developing embryos in livestock. The researchers have discovered a group of 24 genes that are linked to virulence by making comparisons of the newly available S19 genome sequence to previously sequenced genomes of two virulent strains of *B. abortus*.

Focus on Networks

A hardier rice crop for a drier world

Environmental factors such as climate change and a growing global population create challenges for the world's agricultural production systems. VBI Professor Andy Pereira and his research group are developing network models to create a more complete perspective of the effects external stresses have on plants. This "big picture" approach paves the way for the development of improved crop production methods.





in focus
NETWORKS

A hardier rice crop for a drier world

A slight deficit in the amount of water available to a plant at a critical stage of development can be devastating

Emerging climate change and a rapidly growing global population place tremendous stresses on water sources. When there is not enough water to meet demands, an area is said to be experiencing a drought. While droughts can last for several years, even an intense drought occurring over a short period of time can cause significant damage, especially to agricultural production.

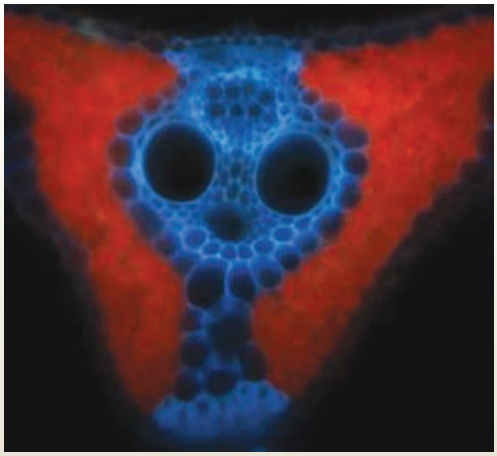
Rice is one crop that is particularly vulnerable to drought conditions. A staple food crop across the globe that feeds more than half of the world's population, rice is also a water guzzler when compared to other crops. It typically uses up to three times more water than maize or wheat and consumes 30% of the fresh water used for crops worldwide. Last year, VBI Professor Andy Pereira's research group and a team of international collaborators uncovered a way to combat the effects drought have on this important crop. The group has produced a new type of rice that grows better in drought conditions and uses water more efficiently than other rice crops. Pereira's group, along with colleagues in India, Indonesia, Israel, Italy, Mexico, and The Netherlands, identified and characterized a gene that improves drought response in rice.

Identifying *HARDY*

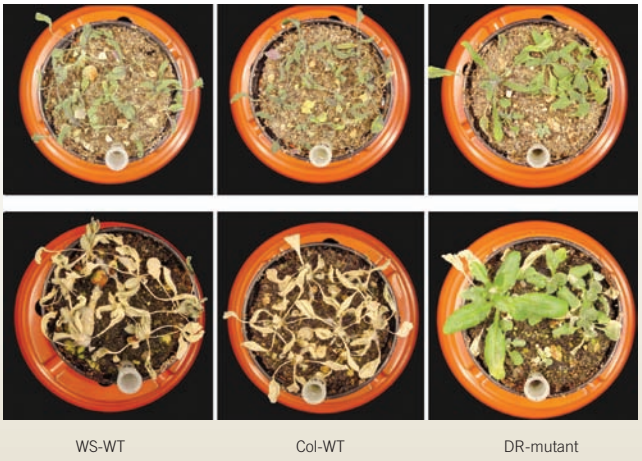
By using a powerful screening technique to examine a large number of *Arabidopsis* plants with possible drought-resistant capabilities, the team identified a gene known as *HARDY* that improved water-use efficiency in the plant. The group then introduced the *HARDY* gene into rice and discovered that it contributed to improved water-use efficiency and higher biomass (plant tissue). Further studies demonstrated that *HARDY* significantly enhanced the capacity of rice to photosynthesize and reduce water loss.

According to Pereira, "Drought conditions do not have to be significant to affect crop yield. A slight deficit in the amount of water available to a plant at a critical reproductive stage can be devastating. In conditions where water is scarce, it is important for crops to be able to efficiently generate biomass using limited amounts of water."

HARDY rice has shown a significant increase in biomass under both drought and non-drought conditions. The researchers found that the biomass of *HARDY* rice increased by around 50% under drought conditions compared to an unmodified version of the same type of rice. The scientists were able



HARDY leaf cross section. Reproduced with permission from Proceedings of the National Academy of Sciences



Rehydrate → Assess Recovery → Drought Resistant

to connect these water-use efficiency improvements to a specific type of protein, also known as a transcription factor, encoded by the *HARDY* gene that binds to DNA and controls gene expression. While team members are still unsure of the exact function of this protein in *HARDY*, they do know that the identification of the gene will lead to improved water-use efficiency and drought resistance in rice and possibly other grain and seed crops.

While efforts like the discovery of the *HARDY* gene focus on one of the ways plants respond to drought conditions– with a change in biomass – a more systematic method is needed to identify comprehensive patterns of response, which is why the Pereira group is currently using a systems biology approach to examine plant-environment interactions.

Piecing together the drought-resistance puzzle

"Dissecting drought is an extremely complicated process because there are so many factors of response involved," explains Pereira. "Drought can affect a plant's reproductive process, its root system, or even its leaves. These are just a few of the many different pieces of the drought resistance puzzle. This cannot be seen as simple and must be examined from a complex system perspective. The most effective way to better understand these complexities is by developing network models to examine all of these factors simultaneously."

"This approach helps us to see the big picture of drought responses in plants, specifically resistance and tolerance," Pereira says. "More importantly, we are able to identify how certain genes in the plant regulate other genes."

Using transcriptome analysis of *Arabidopsis*, the group has been able to identify common regulated gene pathways and genes following exposure to drought-like conditions. The group used this information to construct an *Arabidopsis* drought gene interaction network. Since plants' perception and resistance to drought has evolved through some common conserved mechanisms, the group can use this network to analyze comparative gene functions between *Arabidopsis* and other plants. For example, this strategy has allowed the group to identify 1,400 genes common in both *Arabidopsis* and rice that could possibly contribute to improved drought resistance.

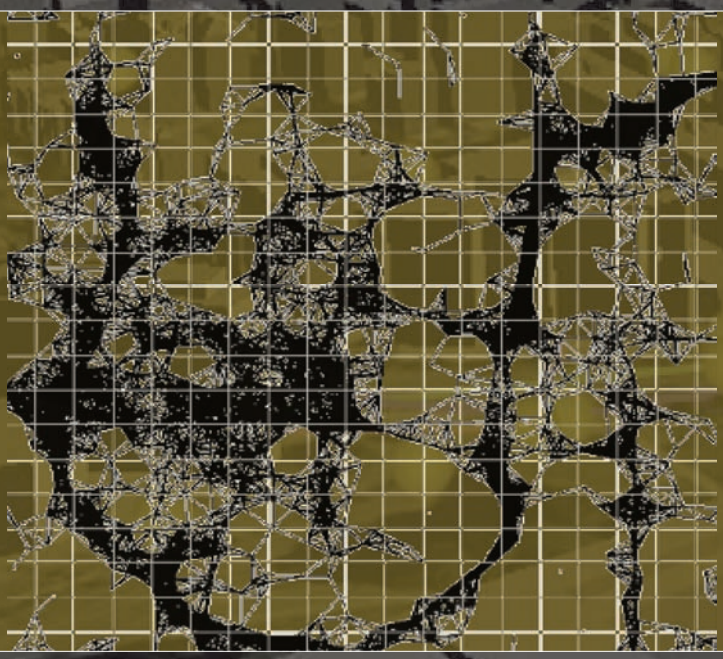
"The gene interaction network helps us to identify key regulatory genes that are worthy of further study and which may be critical for improving drought resistance. This is done by first calculating the probabilities for each gene in the network from statistical tests for differential expression. The use of an algorithm then allows us to identify groups of genes and their networks that show significant differential expression. This combined bioinformatic and systems biology approach is a powerful way to find those genes that may be modified in some way to improve crop viability," Pereira says.

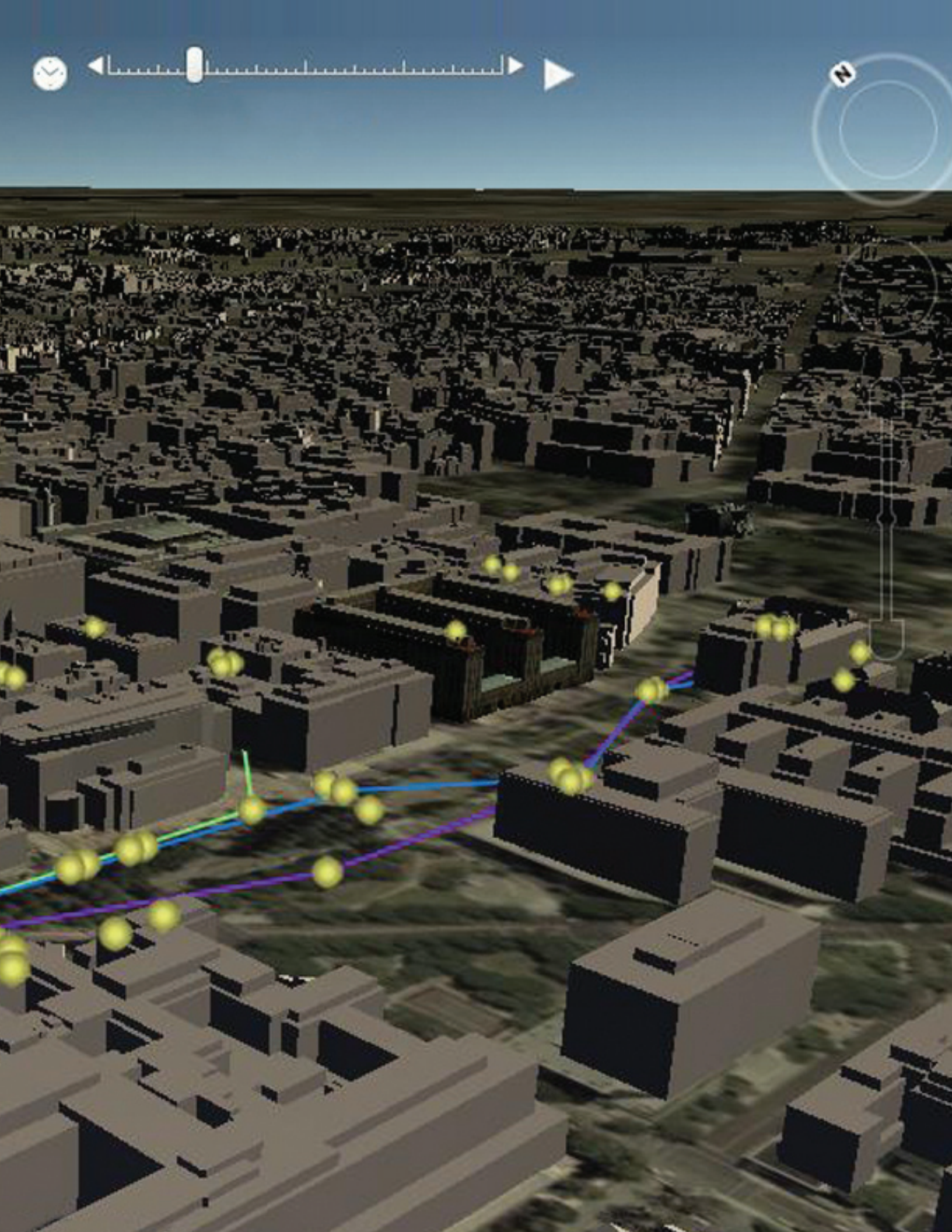
Pereira's group aims to uncover much more information about the interactions between plants and the environment. In addition to drought, the group is examining the ways plants respond to external influences, such as heat, cold, and nutrient deficiencies or toxicities. Plants respond to these environmental factors in a variety of ways, ranging from quick, short-term signals and transcriptional responses to longer-term, metabolic and developmental responses that help avoid and resist the imposed stress. Many of these responses take energy away from plants, which detracts from their ability to survive. Environmental challenges are going to grow significantly as the human population increases and the demand for food widens. Research on biological systems and networks offers hope that new, innovative solutions can be found to strengthen plant viability and increase agricultural output.

Focus on Networks

Artificial markets for wireless networks

The Network Dynamics and Simulation Science Laboratory at VBI develops and implements informatics-oriented methods to help improve the understanding, design, and control of a wide range of complex systems. Wireless communication is one complex system where informatics can impact the design of future wireless networks. Artificial spectrum markets can bring profound technical and economic benefits as they allow researchers to develop more efficient ways to share wireless spectrum.

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in focus
NETWORKS

Artificial markets for wireless networks

Artificial markets allow researchers to develop more efficient ways to share wireless spectrum

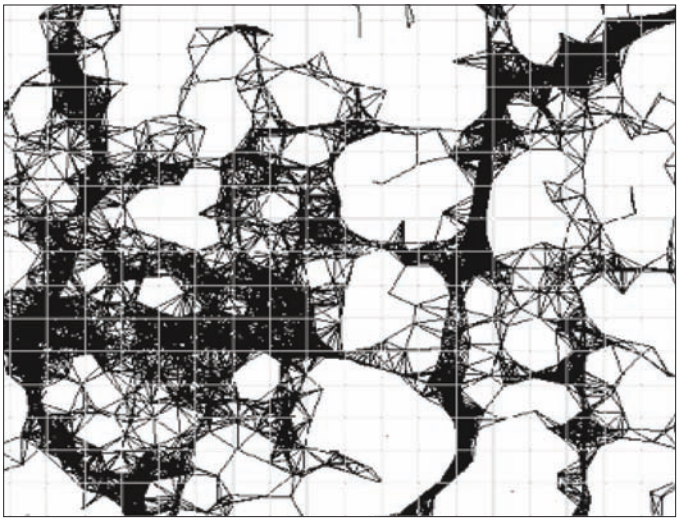
In the not too distant past, an analog telephone would interfere with a neighboring device unless a free communication channel was available for use. Then came the digital telephone. Smart digital technologies allow modern phones to share the same spectrum frequencies in much the same way as the Internet is able to use and re-use different "channels" to transfer information. But there are limits. The growing demand for wireless communications has placed a strain on the available spectrum while at the same time many licensed spectrum bands have been left under-utilized. Researchers are therefore investing considerable time and energy in efforts to come up with optimal designs for spectrum markets that can ultimately lead to efficient allocation of this precious resource.

DSA anybody?

Dynamic Spectrum Access (DSA) is one type of radio technology that promises to increase spectrum sharing and overcome the lack of available spectrum for new communication services. Anil Vullikanti, senior research associate in the Network Dynamics and Simulation Science Laboratory (NDSSL) at VBI, comments: "DSA allows new types of spectrum sharing. For example, transmission can take place at times when primary users of a band are inactive or real-time trading of access rights to spectrum can be permitted." Spectrum access rights can be traded on what is known as a secondary market, secondary in the sense that it follows the primary assignment of spectrum use by regulatory or government bodies. Policy- and decision-makers are very interested in understanding how to design these secondary markets and institute these designs in practice so as to obtain better cost-benefit ratios.

Says Vullikanti: "Our goal is to develop market-driven DSA architecture for cellular networks using computational models. This architecture will allow us to investigate what the optimal design for spectrum markets ought to look like. We want to be able to develop such tools that are accessible and useable by policy- and decision makers so they can understand the cause of market successes and failures. This fits nicely with our goal to develop high-performance computing models of complex networks and web-service-based architectures to support public policy."

Market-driven design of future wireless networks has the potential to bring profound technical and economic benefits



Team effort

At the center of this research effort is a transdisciplinary collaboration that spans the fields of wireless networking, social sciences, algorithmics and economics. Researchers in the NDSSL group are working with collaborators at the State University of New York at Stony Brook and Alcatel-Lucent Bell Labs to develop practical modeling tools for the market-driven design of future wireless networks. Says Madhav Marathe, deputy director of the NDSSL, "This work requires knowing which radio frequencies can be reused concurrently over spatial regions without causing signal degradation, understanding the social network that generates the temporal and spatial demand patterns, and having a handle on the market mechanisms that control admission to, and distribution through, the communication network. In other words, we need to understand the coupled social network that creates the demand and supply, the market that allocates resources, and the communication network that ultimately carries the traffic."

The team will build an artificial market that will encompass efficient methods to study detailed agent-based market mechanisms. The market will include models that look at the mobility and calling patterns of agents, such as the user, at a very high level of detail - right down to individuals within large synthetic populations. Users of the artificial market will be able to test the impact of different market clearing mechanisms in order to determine the best practices for serving the spectrum needs of a large population of wireless users. They will also be able to look at various bidding strategies, the effects of different types of demand, and investigate the impact of changing levels of resources such as power levels or frequency bands. This will provide a powerful tool to look at how excess supply and demand are eventually resolved in the wireless communication market.

Economic sense

"It makes sound economic sense to design spectrum markets with the utmost of care," says Achla Marathe, lead economist at NDSSL. "In the past, poor market designs have led to market inefficiencies. Evidence from the restructured electricity markets in California and elsewhere demonstrated that flawed market designs can lead to adverse economic outcomes. We are offering a platform that permits testing of the economic viability of different market mechanisms via a computational experimental market for dynamic market sharing. We want to see increased spectrum availability and improved liquidity in the secondary spectrum markets. Increased efficiencies will translate into lower costs and increased customer demand - all the prerequisites of an effective, healthy wireless spectrum market."

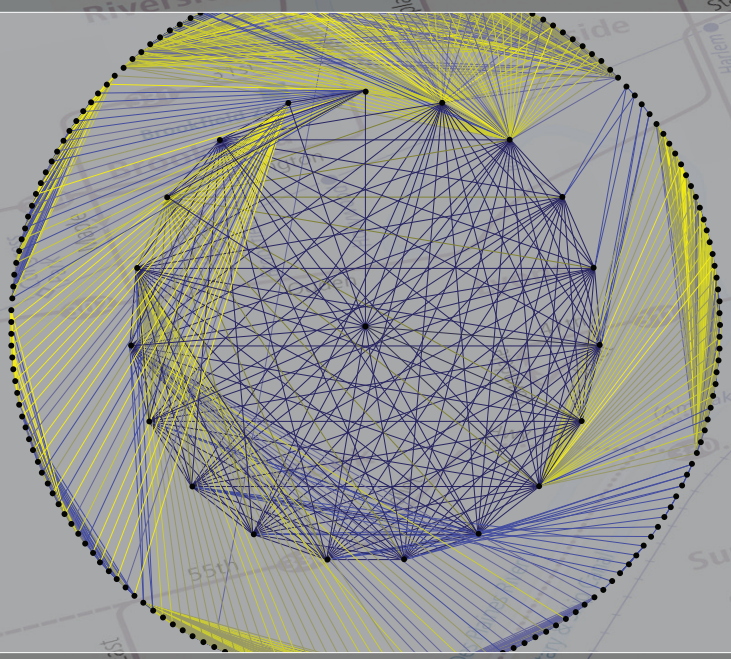
Some of the benefits of dynamic spectrum sharing

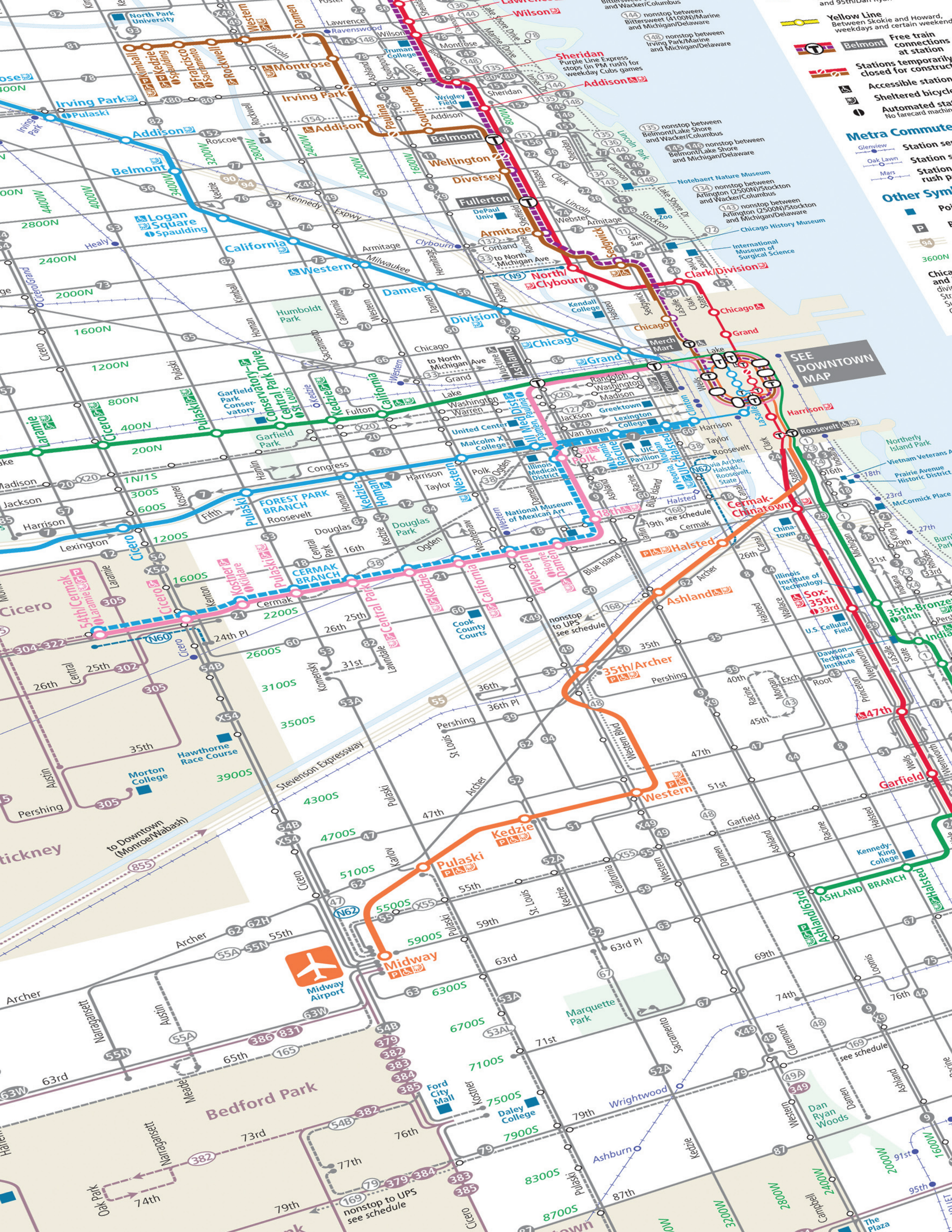
- Greater spectrum sharing
- Decreased spectrum costs
- Increased competition
- Increased innovation by operators
- Active secondary spectrum market
- Feasible small-scale market entry
- Faster business and technology lifecycles
- More use of innovative technologies
- Better spectrum management

Focus on Networks

Being ready for pandemic influenza

Most experts agree that it is only a matter of time before a human flu pandemic grips the world. A novel flu strain that can transmit easily between humans could trigger a disease pandemic that kills tens of millions of people worldwide. Researchers at the Virginia Bioinformatics Institute at Virginia Tech are using high-performance computer simulations to show how diseases like flu spread through large populations. They want to provide policy makers, decision makers and public health experts with a way to test health interventions that will help to put the brakes on the spread of a deadly influenza outbreak.




Yellow Line
Between Skokie and Howard, weekdays and certain weekends
Belmont
Free train connections at station
Stations temporarily closed for construction
Accessible station
Sheltered bicycle
Automated station
No farecard machine
Metra Commuter
Station serves
Station
Station rush
Glenview
Oak Lawn
Mars
Other Symbols
Point
144 nonstop between Bittersweet (4100N)/Marine and Michigan/Delaware
148 nonstop between Irving Park/Marine and Michigan/Delaware
Sheridan
Purple Line Express stops (in PM rush) for weekday Cubs games
135 nonstop between Belmont/Lake Shore and Wacker/Columbus
145 146 nonstop between Belmont/Lake Shore and Michigan/Delaware
Notebaert Nature Museum
134 nonstop between Arlington (2500N)/Stockton and Wacker/Columbus
143 nonstop between Arlington (2500N)/Stockton and Michigan/Delaware
Chicago History Museum
International Museum of Surgical Science
Lawrence
Wilson
Addison
Wrigley Field
Wellington
Diversey
Fullerton
DePaul Univ
Armitage
North/Clybourn
Sedgwick
Clark/Division
Chicago
Grand
Merch Mart
SEE DOWNTOWN MAP
Harrison
Roosevelt
Northerly Island Park
Vineyard Veterans
Prairie Avenue Historic District
McCormick Place
Cermak-Chinatown
Chinatown
Illinois Institute of Technology
Sox-35th
U.S. Cellular Field
Dawson Technical Institute
35th-Bronzeville-IIT
Indiana
47th
Garfield
Kennedy-King College
ASHLAND BRANCH
Halsted
Ashland/63rd
North Park University
Kimball
Kedzie
Spaulding
Francisco
Sacramento
Rockwell
Western
Damen
Montrose
Irving Park
Paulina
Southport
Addison
Belmont
Truman College
Ravenswood
Irving Park
Pulaski
Addison
Belmont
Logan Square
Spaulding
California
Western
Damen
Division
Chicago
Grand
Clinton
UIC-Halsted
Racine
Illinois Medical District
Western
Kedzie-Homan
Pulaski
Cicero
FOREST PARK BRANCH
Humboldt Park
Garfield Park Conservatory
Conservatory-Central Park Drive
Kedzie
California
Ashland
Laramie
Cicero
Pulaski
Garfield Park
Polk
18th
Damen
Western
California
Kedzie
Central Park
Pulaski
Kostner
Cicero
54th/Cermak
CERMAK BRANCH
National Museum of Mexican Art
Douglas Park
Cook County Courts
Malcolm X College
United Center
Greektown
Lexington College
Halsted
Ashland
35th/Archer
Western
Kedzie
Pulaski
Midway
Midway Airport
Hawthorne Race Course
Morton College
Stevenson Expressway
Cicero
Stickney
to Downtown (Monroe/Wabash)
Bedford Park
Ford City Mall
Daley College
Marquette Park
Dan Ryan Woods
Wrightwood
Ashburn
Healy
Cicero/Grand
nonstop to UPS see schedule
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2000N
1600N
1200N
800N
400N
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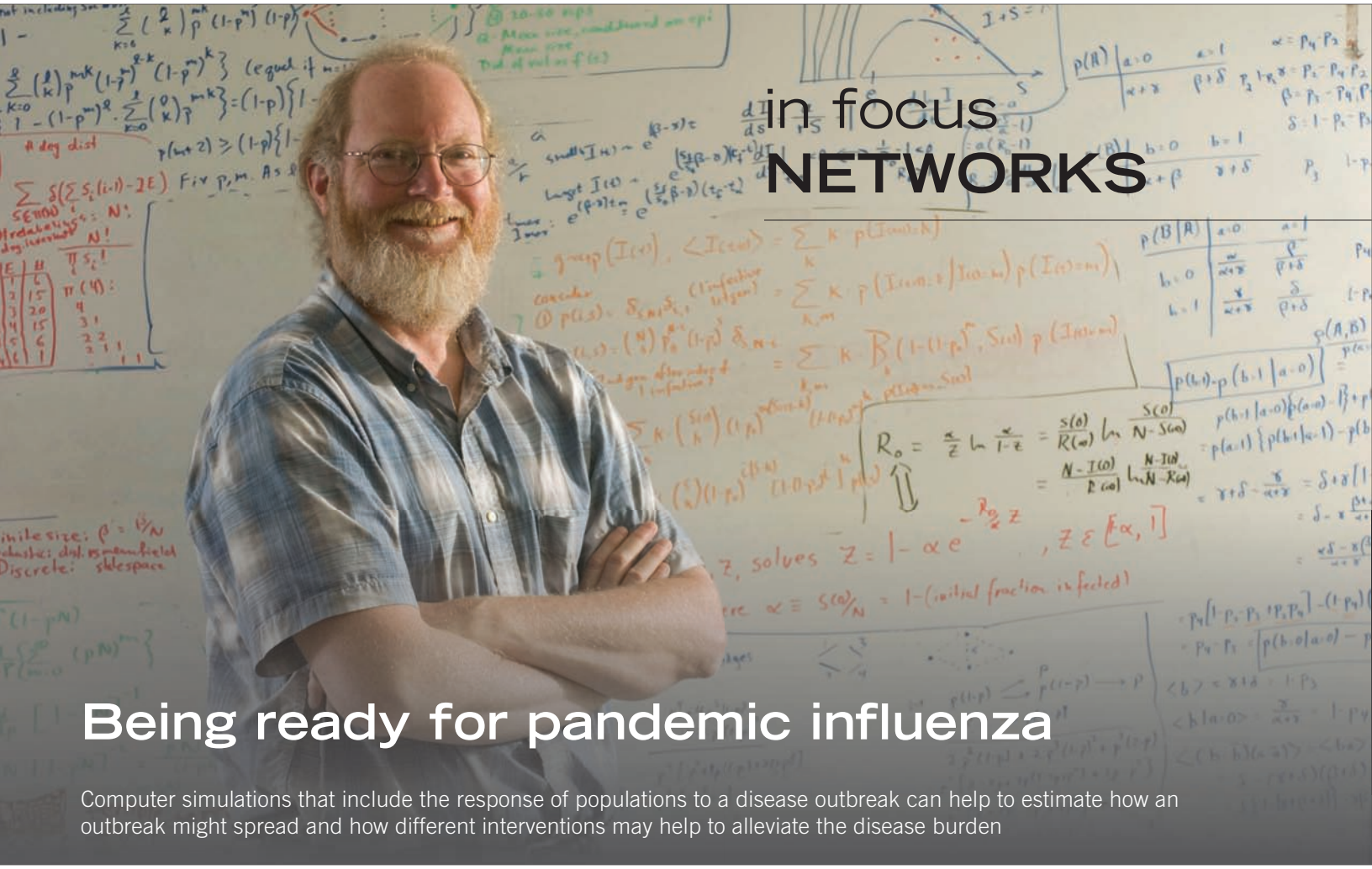


in focus
NETWORKS

Being ready for pandemic influenza

Computer simulations that include the response of populations to a disease outbreak can help to estimate how an outbreak might spread and how different interventions may help to alleviate the disease burden

The Network Dynamics and Simulation Science Laboratory (NDSSL) at the Virginia Bioinformatics Institute (VBI) at Virginia Tech is using computer simulations of mathematical models to investigate how infectious diseases like influenza emerge and spread through large populations of people. These simulations allow experts to test the impact of different public health interventions on the spread of infectious agents like viruses through large populations.

Policy makers and other experts need to know in advance what is the optimal combination of measures to stop the spread of a disease outbreak. They need to know how effective it will be, for example, to isolate those infected with the virus and how to optimize the use of limited resources like antiviral treatments. Powerful computer simulations provide valuable lessons and allow for better informed decisions before a real outbreak takes place.

"The global epidemic of avian influenza in bird populations, as well as the risk of a virulent form of the bird flu virus being transferred to humans, has helped to increase awareness of the very real threat posed by an influenza pandemic," says Stephen Eubank, deputy director of the Network Dynamics and Simulation Science Laboratory at VBI. "Countries around the globe want to be as ready as possible if a flu pandemic were to be unleashed on the world. Our research team tries to help in this forward planning by creating virtual cities, populating them with synthetic people, and looking at the impact of social contacts on the spread of a disease pandemic in an urban environment."

Eubank and colleagues at VBI have been working as part of the MIDAS (Models of Infectious Disease Agent Study) group, a network that comprises principal investigators, scientific collaborators, software engineers, data and computer experts, as well as students from research and informatics groups across the globe.

Modeling flu in the United States

"MIDAS recently completed a set of simulations for the city of Chicago for the United States Department of Health and Human Services that were published in the Proceedings of the National Academy of Sciences*," says Eubank. "For the study, a high-performance cluster of 100 'blades', with four processors each, spent about 24 hours modeling the spread of pandemic influenza through the city. A blade is a modular unit of powerful computer hardware that is designed for easy integration into rack computer systems. The simulations run on these machines showed that the behavior of individuals can have a very large impact on how quickly a disease will spread through a city like Chicago, which has a population of more than 8.6 million people."

To model Chicago at the level of detail needed the researchers typically start with census information, public surveys, and transportation data. This gives them a realistic picture of the daily activities of the synthetic people built into the models and leads to detailed estimates of social contacts in an urban environment. A realistic picture is built of how social mixing patterns change under different interventions, such as closing schools or workplaces. On top of the social network, the researchers add important information on the influenza virus, such as how it spreads, how fast, and how deadly it is. The researchers use the model to suggest the best mix of intervention strategies in a variety of scenarios, taking factors like these into account.

Says Eubank, "For Chicago, we were able to determine how a pandemic influenza outbreak might travel through the city. All of the simulations suggested that the combination of providing households with antiviral treatments in advance and minimizing social contact could play a major role in reducing the spread of illness. The timely initiation of these interventions and school closure were important contributory factors to putting the brakes on a pandemic."

Experts believe that the world is closer to another flu pandemic than at any time since 1968, when the most recent pandemic took place. For now, the World Health Organization says that the world is on phase 3 alert. This means that a new influenza virus subtype, the avian H5N1 bird flu virus, is causing disease in people but is not yet spreading quickly among humans. If efficient and sustained human-to-human transmission were to materialize, a phase 6 alert would be issued. Computer modeling and simulations like those performed by VBI researchers allow researchers to enact phase 6 scenarios today. The hope is that by identifying the best possible combination of interventions lives can be saved when the next influenza pandemic strikes.

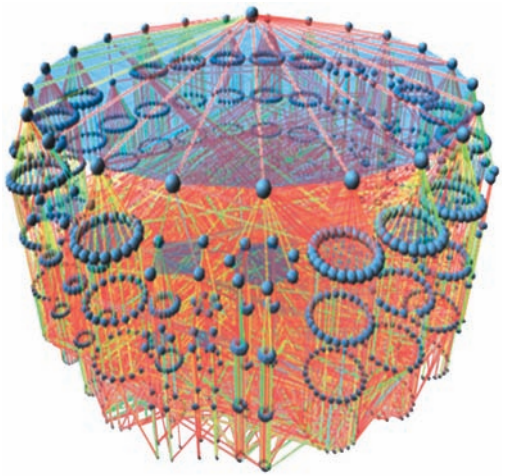
* M. E Halloran et al (2008) Modeling targeted layered containment of an influenza pandemic in the United States. Proceedings of the National Academy of Sciences. 105 (12):4639-4644.

Ten things you need to know about pandemic influenza

- Pandemic influenza is different from avian influenza
- Influenza pandemics are recurring events
- The world may be on the brink of another pandemic
- All countries will be affected
- Widespread illness will occur
- Medical supplies will be inadequate
- Large numbers of deaths will occur
- Economic and social disruption will be great
- Every country must be prepared
- The World Health Organization will alert the world when the pandemic threat increases

Adapted from the World Health Organization

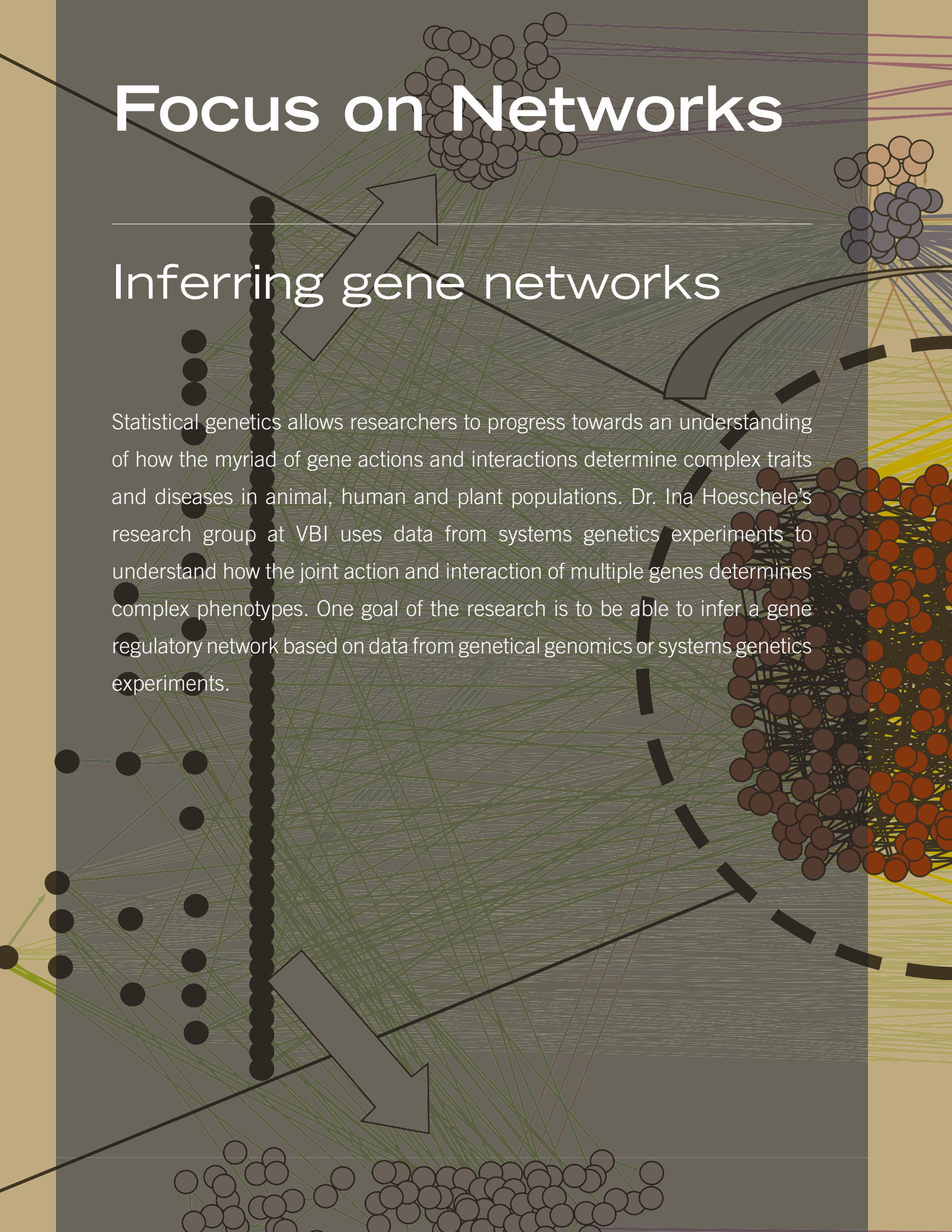
http://www.who.int/csr/disease/influenza/pandemic10things/en/index.html

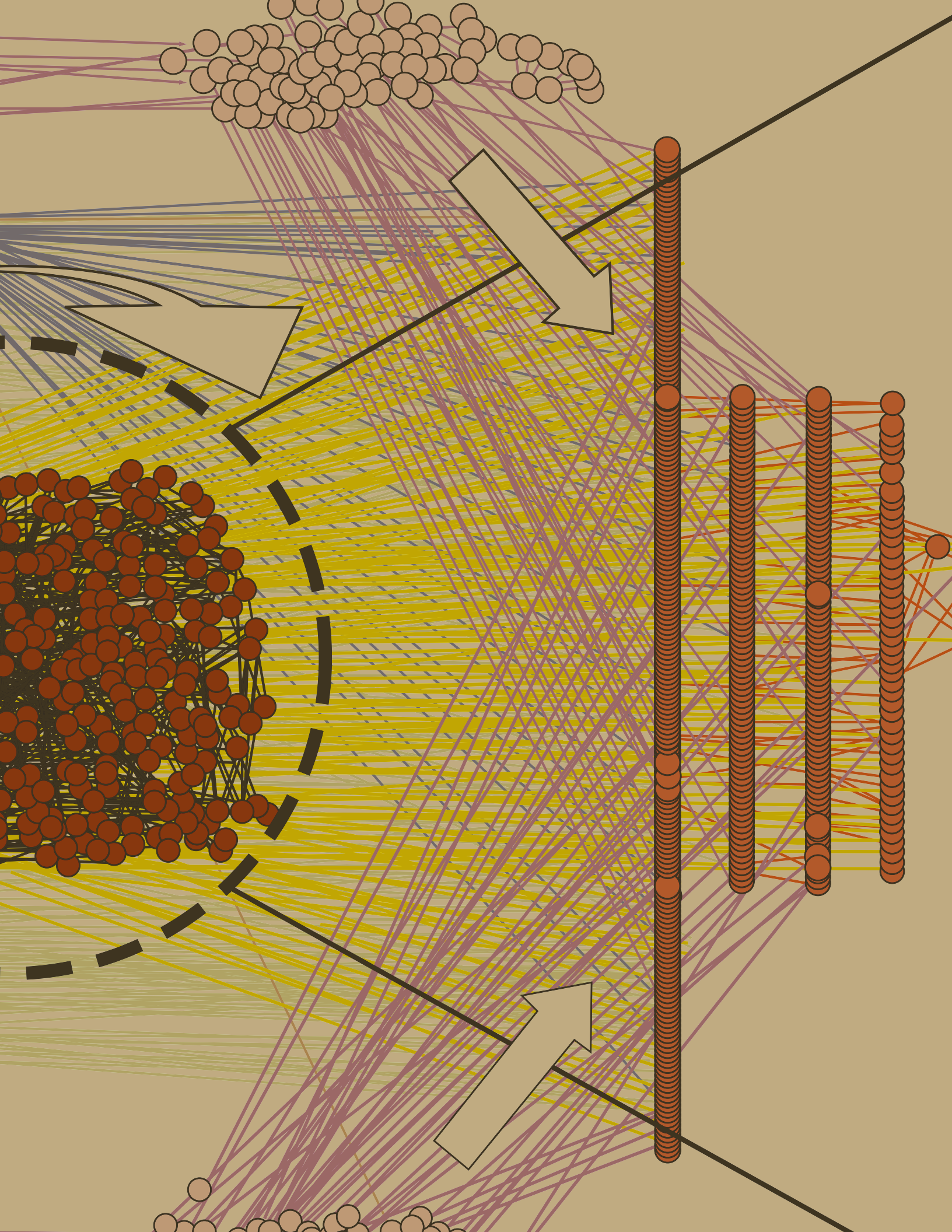


Focus on Networks

Inferring gene networks

Statistical genetics allows researchers to progress towards an understanding of how the myriad of gene actions and interactions determine complex traits and diseases in animal, human and plant populations. Dr. Ina Hoeschele's research group at VBI uses data from systems genetics experiments to understand how the joint action and interaction of multiple genes determines complex phenotypes. One goal of the research is to be able to infer a gene regulatory network based on data from genetical genomics or systems genetics experiments.





in focus
NETWORKS

Inferring gene networks

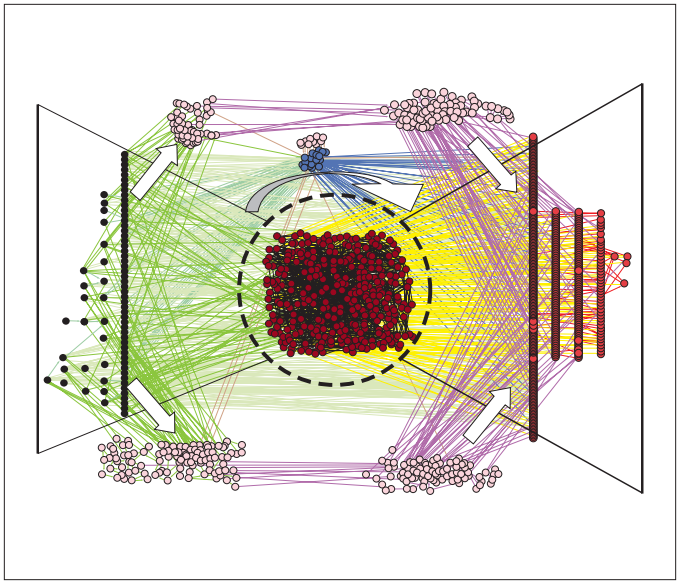
Being able to infer a causal network, including DNA markers, expressed genes, and disease or other phenotypes, would help complex trait geneticists and other biologists significantly in understanding the genetic architecture of complex traits

Inferring the gene network

Ina Hoeschele, Alberto de la Fuente and Bing Liu at VBI recently took a step towards inferring a larger gene network from experimental data by developing a new method for genetical genomics or systems genetic experiments. They wanted a method that was better suited to some of the cyclical relationships that genes exhibit in real life. They also wanted to go beyond some of the smaller sized gene networks that were being generated by existing approaches.

Said Hoeschele, professor at VBI: "We wanted to develop an algorithm that would allow us to construct networks of several hundreds of genes and their Expression Quantitative Trait Loci. This was an order of magnitude above what was published in the current literature. We were particularly interested in reconstructing cyclic networks since that this is the type of network that arises when the entire collection of regulatory processes occurring in the cell are projected onto the gene space."

To meet this goal, a new method was devised and published in the journal Genetics in 2008.* Hoeschele remarked: "We came up with a three-step method that can be applied to any organism for which DNA sequence information, gene expression data, and marker genotyping data are available. First, we map the expression Quantitative Trait Loci, which represent 'natural' perturbations that allow us to infer regulatory relationships among genes rather than just correlations. Secondly, we identify pairs of regulator and target genes to obtain what we call an encompassing directed network. Finally, we identify a set of sparser networks within the encompassing network using an approach known as structural equation modeling."



The three steps in inferring the gene network

- Expression Quantitative Trait Locus (eQTL) analysis to produce lists of:
  - *cis*-regulations
  - *cis-trans*-regulations
  - *trans*-regulations
- Generation of an encompassing (maximal) directed network
- Identification of sparser networks within the encompassing network using Structural Equation Modeling

Testing the method on yeast data

With the method in place, the next step was to apply it to real data. For this purpose, the researchers selected a publicly available genetical genomics data set for yeast (*Saccharomyces cerevisiae*) containing genome-wide gene expression profiles and marker genotype profiles on a genetically randomized population resulting from a cross between a laboratory and a wild-type strain. After performing expression Quantitative Trait Loci (QTL) mapping on this population, an encompassing directed network was constructed from the identified 28,609 regulator-target pairs. This gene network comprised 4274 gene nodes, of which 4116 genes were targets having at least one regulator, and 2118 genes were regulators of at least one target. A total of 1960 genes were both regulator and target genes, and there were 135 cases of reciprocal regulation.

Hoeschele said: "Known regulator genes in yeast were confirmed to be among the top regulators in our encompassing network. Because the encompassing network was assembled from individual regulator-target pairs that were evaluated only in a local context and not in the context of the entire network, it contains regulations that are actually not present. Therefore, to further examine a densely connected, cyclic sub-network of the encompassing network, we performed network sparsification by structural equation modeling on this sub-network with 265 gene nodes and 241 expression QTL nodes. We then examined biological function enrichment of the sparsified sub-network. Multiple biological functions were significantly enriched. In particular, about 41.6% of the genes were involved in enzyme-catalyzed chemical transformations (catalytic activities). Approximately 18% were linked to hydrolase activities, reactions that involved water molecules and the breaking of a chemical bond in a substrate." Hoeschele added: "Our network represents the whole of cellular regulation which goes beyond transcriptional regulatory networks that are based on physical binding of transcription factors to regulatory sequences. Other cases of regulation involve metabolism and signal transduction, which is supported by the strong enrichment of catalytic activity in our network."

Future directions

Said Hoeschele: "Our structural equation modeling implementation for gene network inference allowed us to take two steps beyond the current methodology for building gene networks. Existing software for gene network inference based on structural equation modeling was limited to the analysis of a small number of gene expression traits or e-traits. In our first step, we therefore pushed the boundary from at most 20 e-traits to several hundred that were considered in our network." She added: "Prior network inference in genetical genomics has relied on Bayesian network analysis, a graphical type of modeling related to structural equation modeling. This method has been limited to networks that are not cyclic yet cycles or feedback loops are thought to be pervasive in genetic networks representing the whole of cellular regulation. Our structural equation modeling method permits inference of cyclic networks with several hundred gene and expression QTL nodes, which is in the same order as the size of networks evaluated by Bayesian network analysis."

Much more work lies ahead. The team has focused on using structural equation modeling to infer gene regulatory networks only using gene expression traits. Current work focuses on including disease phenotypes and other 'omics' data such as metabolomic and epigenomic data.

* Liu B, de la Fuente A, Hoeschele I (2008) Gene network inference via structural equation modeling in genetical genomics experiments. Genetics 178: 1763-1776.

Resources and People

- Core Facilities
- Administration and Finance
- Public Relations
- Education and Outreach

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

The Core Laboratory Facility

The Core Laboratory Facility is a dedicated multi-user resource for the development and application of state-of-the-art high-throughput technologies

The mission of the Core Laboratory Facility (CLF) at the Virginia Bioinformatics Institute (VBI) is to provide life science customers worldwide with access to best-in-class technologies for the discovery and analysis of biological macromolecules. In the past year, the CLF has continued to develop and expand its impressive portfolio of high-throughput technologies for diverse clients in the global life science community.

Genome sequencing goes from strength to strength

The availability of the Roche GS-FLX™ genome sequencer at the CLF has created unique opportunities for researchers to use next-generation sequencing systems in their projects. It is also helping VBI establish new scientific collaborations and consortia. The revolutionary sequencing technology offered by the GS-FLX™ allows researchers to go from genome to sequence in record time. The CLF's GS-FLX™ sequencing facility has been open on a fee-for-service basis for shotgun genome sequencing since June 1, 2007. More than 50 sequencing projects for customers have been completed, generating more than 90 Gbp (90 billion base pairs) of data. Acquisition of the equipment was made possible through Virginia's Commonwealth Research Initiative.

The GS-FLX™ has been used in a wide range of national and international research projects that include the sequencing of ten pathogenic bacterial genomes, investigation of the soil bacterium *Rhizobium meliloti*, and the characterization of microRNAs in prostate cancer cell lines. The CLF at VBI has also integrated the recently launched Titanium sequencing plates and chemistry into its GS-FLX™ system, which has allowed a 5-fold increase in sequence data output per run (to 500 Mbp).

Cross-project team science

Work at the CLF is leveraged across many projects at the Institute. In June 2008, VBI, the National Ames Disease Center, Ames, IA, and collaborators at 454 Life Sciences, Branford, CT, announced that they had sequenced the genome of *Brucella abortus* strain S19. Scientists have long wanted to know what genetic features make strain S19 suitable for use as a vaccine in cattle because it may hold the secret as to why other *Brucella* strains cause disease and trigger the abortion of developing embryos in livestock. A group of 24 genes were discovered that is linked to virulence by making comparisons of the newly available S19 genome sequence to previously sequenced genomes of two virulent strains of

Left to right: (front row) Shamira Shallom, Kris Lee, Carmine Graniello; (back row) Don Shaw , Bob Settlage, Megan Frair, Onyi Freeman, Kristal Cooper, Clive Evans

B. abortus. The CLF provided extensive sequencing support for this project through its high-throughput technologies. The paper "Genome sequence of *Brucella abortus* vaccine strain S19 compared to virulent strains yields candidate virulence genes" was published in PLoS One (May 2008, Volume 3, Issue 5, e2193).

Professor Andy Pereira at VBI is using the Roche GS-FLX™ and maize Affymetrix GeneChips® for transcriptome sequencing. This research effort will help to identify and measure the expression of drought-resistant genes in maize. The objective is to look for sustainable ways to maintain high crop yields under conditions of limited water availability. Associate Professor Vladimir Shulaev of VBI is leading an international consortium that is sequencing the full genome of the woodland strawberry (*Fragaria vesca*) on the Roche GS-FLX™. The genome sequence will be an invaluable resource for the scientific community for this economically important plant species. It will offer scientists a way to identify genes linked to nutritional benefits and allow them to investigate ways for crop improvement. The genome sequence will be assembled and annotated by the Rosaceae scientific community.

Full range of services available at the CLF

Genome sequencing is one part of a wider portfolio of services offered by the CLF. Researchers from the University of Virginia, led by Dr William Petri, and the Virginia Bioinformatics Institute have been using the CLF's Affymetrix GeneChip® services, for example, to perform genome-wide analysis of gene expression during intestinal colonization and invasion by *Entamoeba histolytica*. The unicellular eukaryote *Entamoeba histolytica* is a human parasite that causes amebic dysentery and liver abscess. The study confirmed that a particular protein, EhHMGB1, has the capacity to affect parasite gene expression observed during adaptation of the parasite to the host intestine.

Services available at the Core Laboratory Facility

At the CLF, a wide range of technology platforms is available for the study of DNA (sequencing and genotyping), RNA (gene expression analysis) and proteins (proteomics). The CLF also offers a selection of molecular biology applications. The CLF is supported by a custom Laboratory Information Management System (LIMS), designed and built by GraphLogic, Inc. of Branford, Connecticut, that provides an easy-to-use, secure interface for sample submission and data retrieval. The CLF is also actively engaged in the development and testing of new technologies as needed.

Currently available services include the following:

- DNA Sequencing
- GS-FLX™ Sequencing
- Robotics
- Molecular Biology
- Genotyping (including Affymetrix SNP chips)
- Gene Expression Analysis
- Proteomics

Further details are available at https://www.vbi.vt.edu/core_laboratory_facility

The Core Computational Facility

The Core Computational Facility is the data management and analysis machine of VBI's core infrastructure

The Core Computational Facility (CCF) at VBI defines, maintains, and improves information technology services and the underlying infrastructure that supports the daily operations of the Institute. CCF resources are built to be scalable and adaptable, enabling the many applications required to meet VBI's research and business needs. The CCF is an integral part of these undertakings, comprising a cost-recovery service center providing access to computational services and infrastructure that sustain the scientific projects conducted at VBI.

More performance, more capacity

In early 2008, the CCF announced a new addition to its resources – a new platform designed to improve computational performance and capacity while reducing storage costs for the Institute and its customers. The Axiom 500 from Pillar Data Systems is an application-aware storage platform that combines two different storage environments into a single system that can be managed from one location. The system features both network-attached storage and storage area network functionalities. VBI's storage area network infrastructure is primarily used to support the various research databases used at the Institute, featuring management systems such as Oracle, MySQL, and PostgreSQL. It also supports the large storage needs of specific groups at VBI, such as VBI's Core Laboratory Facility (CLF), which generates large amounts of data through its Roche GS-FLX™ genome sequencing system and other cutting-edge high-throughput technologies (see page 32). The CCF's network-attached storage services provide high-capacity access to personal and group file systems.

The Axiom 500 tripled the Institute's storage capacity to 60 terabytes of data, which is roughly three times the amount of text-only information housed at the United States Library of Congress. While increasing the amount of computational storage space at VBI, the new system is actually more cost-effective, resulting in a decrease in service fees for CCF customers. The additional storage space also makes file duplication easier, strengthening the Institute's data back-up capabilities.

The Axiom 500 houses all of VBI's shared drives – network locations where employees can share large files and work groups can save and share important information – and provides more storage space for each faculty and staff member's home drive, where personal work data can be saved.

"The decision to add the Pillar Data System to our Core Computational Facility resources was an easy one," explained VBI's Chief Information Officer Guy Cormier. "After looking at several systems, we found the Axiom 500 offers us more

Left to right: (front row) Xing Jing, Sally Waldon, Dom Borkowski, Dustan Yates; (middle row) Jeremy Johnson, Scott Cover, Mandy Wilson, Guy Cormier, Jason Decker, Anthony Robinson, David Bynum, Kathy Laskowski, Russel Hertzberg; (back Row)Jim Stoll, Zeb Bowden, Bahaa Al-amood

expansion capabilities and, most importantly, flexibility. The system doesn't require us to change our protocols. We can configure it to fit our needs."

Information Technology Services and Support

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

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

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

The Core Computational Facility

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

Two large multiprocessor servers are at the center of the CCF's computational processing capabilities – a Sun Enterprise 15000 and an IBM Power 4 cluster. Comprehensive data backup and recovery systems guarantee the integrity and availability of CCF services. An IBM Storage Area Network (SAN) and Axiom 500 together provide over 60 terabytes of combined disk and tape storage, including an off-site copy for added security. The CCF uses gigabit Ethernet as its communication backbone and has a dedicated, scalable, and high-speed connection to the Internet, Internet2 and the National Lambda-Rail networks. Recent additions to the CCF continue to strengthen the Core Facility's best-in-class capabilities. Currently, the principal database platform supported by the CCF is Oracle, but access to MySQL and PostgreSQL are also supported. The CCF also provides production hosting of servers, websites and web-based applications.

Administration and Finance Team

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

Administration

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

Left to right:
(front row) Jodi Lewis, Jeanne Forbis, Betsy Williams, Kim Borkowski, Traci Roberts, Joyce Randall;

(back row) Sharon Smyth, Teresa Jewell, Lisa Gunderman, Bruno Sobral, Emily Alberts, Otto Folkerts, Shannon Worringham, Lauren Coble, Brian Gittens, Renee Nester

Finance

Left to right: (front row) Kristin Collins, Deb Williams, Alesha Johnson; (back row) Stacey Walton, Richard Webb, Katim Faal, Adeel Khan, Shelana Ryan

Human Resources

Left to right: Alyssa Needham, Lynn Byrd, Brian Gittens, Erin Cassidy, David Martin

Facilities

Left to right: Susan Huckle, David Gibbs, Sheryl Locascio, Mark DiFilippo, Barbara Waller, Linda Correll, Wilson Barnes

Grants and Contracts

Left to right: Jim Walke, Sharon Lawson, Carol Volker, Deborah Wray

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

Public Relations

The Public Relations team at VBI identifies key audiences for the Institute and delivers a research-driven communication program to those audiences. The group ensures that information about VBI reaches its public via web-based communication, promotional materials, specialty publications, media outlets, and presentations. Managing the information flow for the Institute to both internal and external audiences is one of the primary responsibilities of this service-oriented group.

Left to right: Barry Whyte, June Mullins, Aimee Drysdale, Darleen Baker, Susan Bland, Ivan Morozov

Publications

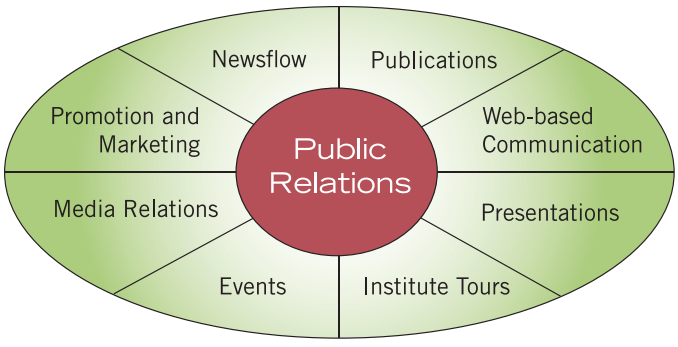
The group produced VBI's fourth scientific annual report, which showcases some of the exciting scientific achievements from VBI research groups during the 2008 fiscal year. The research presented in the report highlights VBI researchers' involvement in a wide range of transdisciplinary research projects that bring together diverse disciplines such as mathematics, computer science, plant pathology, biochemistry, systems biology, statistics, economics, and synthetic biology.

The Public Relations team also produces VBI e_Connections, the Institute's quarterly electronic newsletter. VBI e_Connections provides valuable information for those interested in news from the Institute and includes feature articles highlighting important events, technology updates, recent news, as well as a section featuring interviews with individuals involved in the life sciences, such as researchers, authors, faculty, and students.

Over the past fiscal year, the electronic newsletter has included articles about the keynote talk at the VBI Second Annual Research Symposium, a presentation by the director of the National Visualization and Analytics Center, and the efforts of a VBI faculty member to uncover previously unrecognized work by a 19th century French mathematician that had been completed almost 200 years ago. The newsletter also included an article written by a VBI graduate research assistant on the latest developments in applications for semantic web technologies.

Media Coverage

The Public Relations team's media relations' efforts have resulted in coverage in several prominent national and international media outlets. A news release about a collaborative project to develop a new type of rice that grows better and uses water more efficiently than other rice crops garnered coverage by the United Kingdom's The Daily Telegraph, Asian News International, and CBC Canada, while a release highlighting work by VBI's Network Dynamics and Simulation Science Laboratory to determine how a pandemic influenza outbreak might travel through a city similar in size to Chicago, Ill., led to coverage by USA Today and Reuters news service. Several media outlets have also featured other VBI news. They include the Bioinform newsletter (GenomeWeb News), Genetic Engineering and Biotechnology News, Genome Technology, GenomeWeb Daily News, The Roanoke Times, ScienceDaily.com, United Press International, and The Virginia Engineer, as well as various online publications from around the world, including India, China and Australia.



Education and Outreach

VBI's Education and Outreach group is committed to developing educational programs designed to foster interest in scientific research for students of all ages. The team strives to build and maintain strong relationships with the Institute's external audiences, promoting VBI's involvement in a wide variety of educational programs in the Virginia Tech community and beyond.

Left to right: Reinhard Laubenbacher, Susan Faulkner, Kristy DiVittorio, Betsy Williams

Educational Opportunities

Over the course of the fiscal year, VBI's Education and Outreach team partnered with other centers and colleges at Virginia Tech to offer unique research opportunities for undergraduate students. VBI and Virginia Tech's College of Agriculture and Life Sciences each established one Systems Biology Fellowship that provided outstanding undergraduate students with an opportunity to spend ten weeks in the summer of 2008 participating in an ongoing systems biology research project.

The team also collaborated with the Virginia Tech-Wake Forest University School of Biomedical Engineering and Science to coordinate the Institute's participation in the Bioengineering and Bioinformatics Summer Institute (BBSI). The program, which is designed for junior or senior undergraduates interested in attending graduate school in biomedical engineering and/or bioinformatics, emphasized four major research areas: Computational Systems Biology, Computational Bio-Imaging, Computation Physiology, and Mathematics. In addition, the group's efforts resulted in a partnership between VBI and the Interdisciplinary Center for Applied Mathematics (ICAM) at Virginia Tech to develop Research Experience for Undergraduate Site: Modeling and Simulation in Systems Biology. The scientific focus of this program for rising juniors and seniors was the modeling and simulation of biological networks through the study of the spread of epidemics in social networks.

Professional Development

The Education and Outreach team coordinated the 2008 VBI Summer Institute, which was designed to provide professionals and undergraduate and graduate students with workshop and professional development opportunities. Five summer courses, which were taught by VBI faculty members, were offered exploring topics such as how simulations are used in public health epidemiology work and how oomycete molecular genetics researchers use available bioinformatic and genomic resources.

The Year Ahead

The team will continue its efforts to cultivate student interest in scientific research. In collaboration with Virginia Tech's Ph.D. program in Genetics, Bioinformatics, and Computational Biology (GBCB), VBI will offer fellowships to support graduate work in transdisciplinary team science, covering the costs of the students' first two years in the GBCB program, plus tuition and fees. The group is also developing Kids' Tech University (KTU), a semester-long educational research program designed to encourage children's interest in science, technology, engineering, and mathematics. The program will feature lectures by university researchers, hands-on activities, and virtual labs to reinforce the lecture concepts.

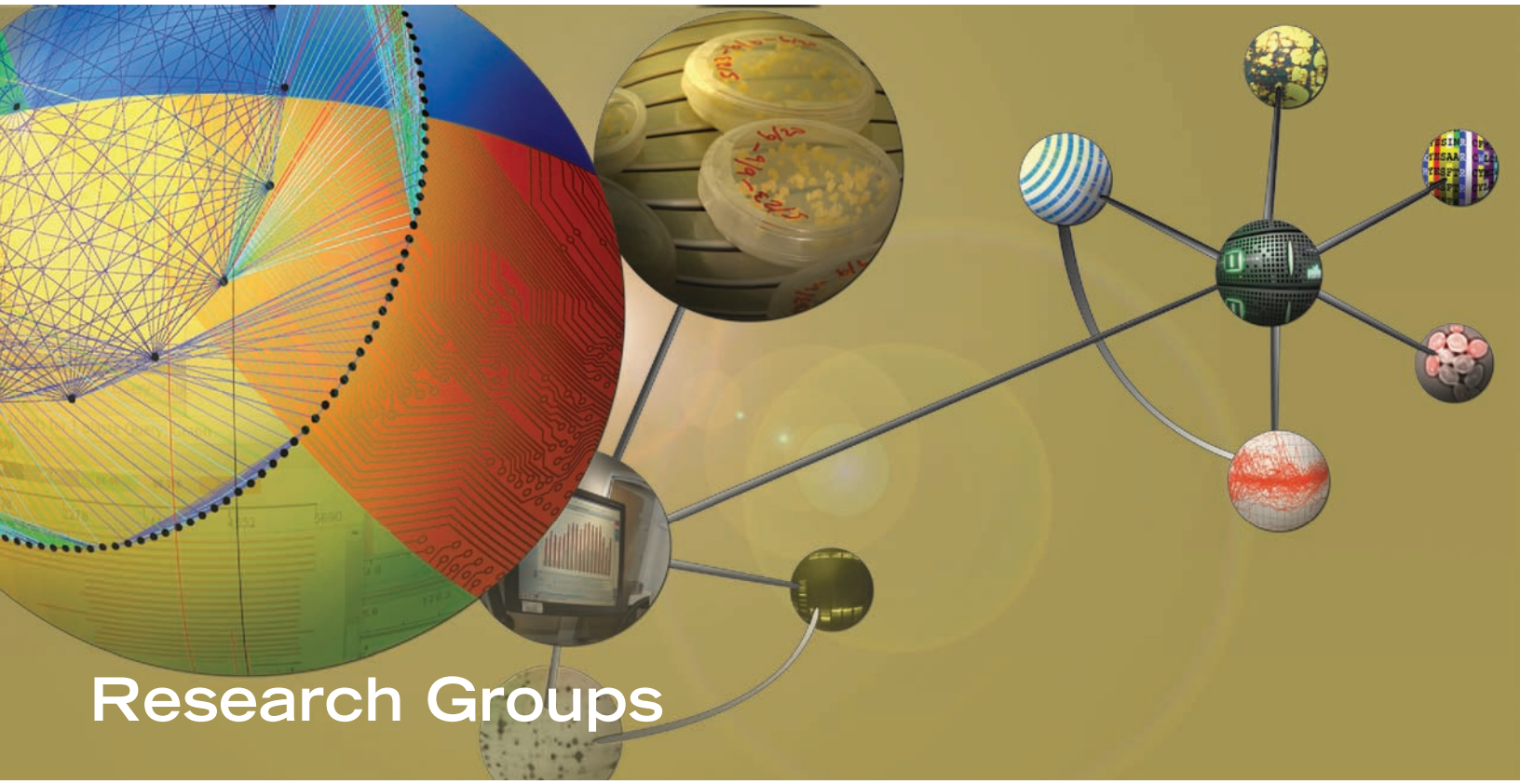
VBI Education and Outreach funded projects (fiscal year 2007-2008)	
Undergraduate research opportunities	**Funding agency**
Bioengineering/Bioinformatics Summer Institute (BBSI)	NSF / NIH
CI-TEAM Implementation for Biological Researchers, Educators and Developers (CIBRED)	NSF
Research Experiences for Undergraduates Site: Modeling and Simulation in Systems Biology (MSSB)	NSF
Systems Biology Fellowships	VBI
Graduate research opportunitiess	**Funding agency**
RETs: Bioengineering/Bioinformatics Research Experiences for Teachers	NSF / NIH (via BBSI project)

Our mission is to solve society's most important problems in the life sciences through transdisciplinary research and education.

Our Vision

VBI will be a world leader in transdisciplinary life science research and education. In practice this means:

We make transformative discoveries.
We solve important problems.
We develop the next generation of transdisciplinary researchers.
We influence public policy.
We transition scientific research into use.



Research Groups

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

Dr. Chris Barrett

The Network Dynamics and Simulation Science Laboratory

Left to right:
(back row) Richard Beckman, Gabriel Mateescu, Bryan Lewis, Stephen Eubank, Sharon Smyth, Jonathan Leidig, Zhifeng Sun, Tridib Dutta, Chris Kuhlman, Xizhou Feng, Chris Barrett; (middle row) Henning Mortveit, Anil Vullikanti, Keith Bisset, Joyce Randall, Paula Stretz, Kofi Adasi, Shrirang Yardi, Elaine Nsoesie, Achla Marathe; (front row) Ginger Hansen, Maleq Khan, Annette Feng, Madhav Marathe, Karthik Channakeshava, Lisa Durbeck

The Comprehensive National Incident Management System (CNIMS) integrates surveillance, simulation-assisted hypothesis testing, and decision support for use in situational awareness and planning in complex systems

Research Interests

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

Selected Recent Publications

Atkins K, Barrett C, Beckman R, Bisset K, Chen J, Eubank S, Lewis B, Marathe A, Marathe M, Mortveit H, Stretz P, Vullikanti A (2007) An analysis of layered public health interventions at Ft. Lewis and Ft. Hood during a pandemic influenza event. *NDSSL Technical Report No. 07-019*.

Barrett C, Hunt H III, Marathe M, Ravi S, Rosenkrantz D, Stearns R, Thakur MR (2007) Predecessor existence problems for finite discrete dynamical systems. *Theoretical Computer Science* **386**(1-2): 3-37.

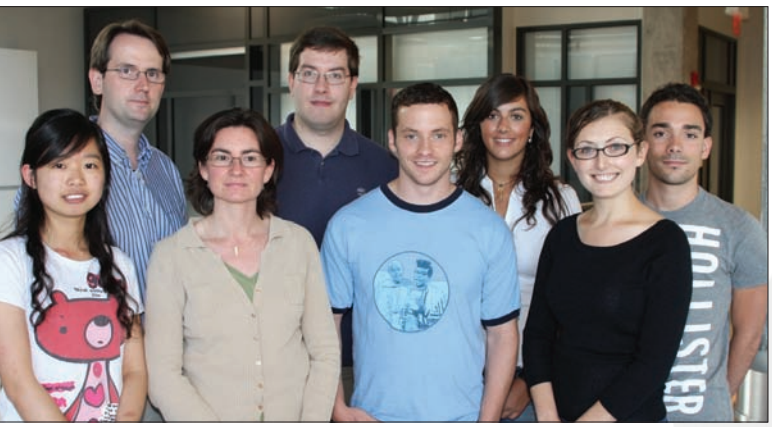
Mozumder P, Marathe A (2007) Role of information and communication networks in malaria survival. *Malaria Journal* **6**:136.

Halloran M, Ferguson N, Eubank S, Longini Jr I, Cummings D, Lewis B, Xu S, Fraser C, Vullikanti A, Germann T, Wagener D, Beckman R, Kadau K, Barrett C, Macken C, Burke D, Cooley P (2008) Modeling targeted layered containment of an influenza pandemic in the United States. *Proceedings of the National Academy of Sciences. USA* **105**(12): 4639-4644.

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

NDSSL has established funded programs of more than $15 million in the past three years in the area of complex systems, including programs with the National Institutes of Health, the Centers for Disease Control and Prevention, the Department of Defense and the National Science Foundation. The group has established a presence in the National Capital Region that plays a leading role in a new institutional initiative in Policy Informatics for Complex Systems.

NDSSL is pursuing new programs in wireless networks, commodity markets and high performance computing, and continues to develop diverse tools for reasoning about complex systems. These tools have been used in several stakeholder-designed studies supporting policy planning for disease pandemics. Two large studies to support pandemic planning for military preparedness have been completed for Defense Threat Reduction Agency (DTRA) using the Department of Defense's prototype system built by NDSSL - the Comprehensive National Incident Management System (CNIMS). CNIMS integrates surveillance, simulation-assisted hypothesis testing, and decision support for use in situational awareness and planning in complex systems. NDSSL continues to develop highly efficient algorithms for several combinatorial and dynamical problems arising from the study of complex networks.



Dr. Josep Bassaganya-Riera

The Nutritional Immunology Research Group

Left to right: (back row) Josep Bassaganya-Riera, Chris Moore, Sandra Sanchez, Anibal de Horna; (front row) Rong Song, Raquel Hontecillas, Amir Guri, Sarah Misyak

Group members not in the picture: Ashlee Carter, Nick Evans, William Horne

The central integrative theme of research in the Nutritional Immunology Research Group is the study of inflammatory and immunological processes at the molecular, cellular and whole organism levels

The Nutritional Immunology Research Group is engaged in research programs in the areas of nutraceutical discovery, intestinal health, and the prevention of obesity-related inflammation. The central integrative theme connecting these research areas is the study of inflammatory and immunological processes at the molecular, cellular and whole organism levels.

In the area of nutritional immunology, the group is identifying novel, bioactive and naturally occurring modulators of inflammation (for example dietary lipids such as conjugated linoleic acid) and analyzing the relation between nutraceutical targets and disease-gene products. The team is also investigating the mechanisms of immune modulation by naturally occurring agonists of nuclear receptors and identifying their molecular targets in immunological networks.

In the area of intestinal health, the Nutritional Immunology Research Group is developing novel therapies against Crohn's disease and ulcerative colitis. These two clinical manifestations of inflammatory bowel disease afflict more than 1 million people in North America and 4 million people worldwide. The research group has shown that conjugated linoleic acid can ameliorate gut inflammation in a pig model and has proposed that this dietary lipid may have beneficial effects on mucosal immune responses that are mediated by epithelial and immune cell peroxisome proliferator-activated receptor gamma.

According to recent estimates from the Centers for Disease Control and Prevention, 30% of the United States population is obese and 65% is overweight. In the area of obesity-related inflammation, the Nutritional Immunology Research Group is characterizing the mechanisms of obesity-related inflammation at the cellular and molecular levels and discovering novel therapies for uncoupling obesity from its co-morbidities (i.e., type 2 diabetes, heart disease, stroke). Abscisic acid is being used as a proof-of-concept to establish a solid pipeline of immune regulatory compounds for the prevention of chronic disease.

Research Interests

- Nutritional Immunology
- Gastrointestinal health
- Type 2 diabetes, cardiovascular disease and obesity

Selected Recent Publications

Bassaganya-Riera J, Guri AJ, Noble AM, Reynolds KA, King J, Wood C, Ashby M, Rai D, Hontecillas R (2007) Docosahexaenoic and arachidonic acid-enriched infant formulas modulate antigen-specific T cell responses to influenza virus in neonatal piglets. *American Journal of Clinical Nutrition* **85**: 824-836.

Guri AJ, Hontecillas R, Si H, Liu D, Bassaganya-Riera J (2007) Abscisic acid ameliorates glucose tolerance and obesity-related inflammation in db/db mice fed high fat diets. *Clinical Nutrition* **26**: 107-116.

Hontecillas R, Bassaganya-Riera J (2007) Peroxisome proliferator-activated receptor γ is required for regulatory $CD4^+$ T cell-mediated protection against colitis. *Journal of Immunology* **178**: 2940-2949.

Guri AJ, Hontecillas R, Ferrer G, Casagran O, Wankhade U, Noble AM, Eizirik D, Ortis F, Cnop M, Liu D, Si H, Bassaganya-Riera J (2008) The loss of PPAR γ in immune cells abrogates the ability of abscisic acid to improve insulin sensitivity through a mechanism involving suppression of MCP-1 expression and macrophage infiltration into white adipose tissue. *Journal of Nutritional Biochemistry* **19**: 216-228.

Guri AJ, Hontecillas R, Bassaganya-Riera J (2008) Dietary modulators of PPARs: Implications for the prevention and treatment of metabolic syndrome. *Nutrigenetics and Nutrigenomics* **1**: 126-135.

Dr. Allan Dickerman

Phylogenomics Research Group

Left to right:
Allan Dickerman, Elena Shulaeva, Kelly Williams

Phylogenomics offers researchers a way to better understand the evolutionary similarities and differences of species

Research Interests

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

Selected Recent Publications

Fisher M, Miller D, Brewster C, Husseneder C, Dickerman A (2007) Diversity of gut bacteria of *Reticulitermes flavipes* as examined by 16S rRNA gene sequencing and amplified rDNA restriction analysis. *Current Microbiology* **55**(3): 254-259.

Muralla R, Chen E, Sweeney C, Gray JA, Dickerman A, Nikolau BJ, Meinke D (2008) A bifunctional locus (BIO3-BIO1) required for biotin biosynthesis in *Arabidopsis. Plant Physiology* **146**(1): 60-73.

Williams KP (2008) Strong mimicry of an rRNA binding site for two proteins by the mRNA encoding both proteins. *RNA Biology* **5**(3): 145-148.

The Phylogenomics Research Group is collaborating with Chris Lawrence of the Virginia Bioinformatics Institute and Stephen Goodwin of Purdue University on a project to design and validate an Affymetrix microarray that comprises probes for a variety of bacterial and eukaryotic plant pathogens. The final chip design contains 31,405 probes and targets 7930 taxa in 97 pathogen genera and 11 plant species. Affymetrix has synthesized the chip and experiments to test the validation and sensitivity of the chip are underway.

Dickerman's group is identifying important protein interaction patterns relevant to wood development in poplar in collaboration with Eric Beers in Virginia Tech's Department of Horticulture and Amy Brunner in the Department of Forestry. The identification of protein-protein interaction networks associated with biomass production in the woody tissues of poplar, a model biomass crop, will lead to a more detailed understanding of the molecular biology and genomics of plant biomass production, and ultimately contribute to strategies for biomass crop improvement. The Dickerman group has also been working with the VBI Cyberinfrastructure Group to prepare a robust phylogenetic tree to resolve the evolutionary history of the α-proteobacteria. The phylogenetic tree will provide important insights into the evolution of this large and important group of bacteria.

Dr. Kelly Williams joined the Dickerman group in the fall of 2007. He has developed a project describing an instance of genes coding for RNA-binding proteins that develop binding sites for their own products. The results were recently published in *RNA Biology*.

Dr. Ina Hoeschele

Statistical Genetics Research Group

Left to right:
Lei Bao, Ina Hoeschele

Statistical genetics provides a way to understand how the joint action and interaction of many genes determines complex traits and diseases in animal, human and plant populations

The Statistical Genetics Research Group uses data from systems genetics experiments to investigate how the joint action and interaction of multiple genes determines complex diseases or phenotypes of plants, animals and humans. The group is currently developing, implementing and evaluating methods for very high-dimensional Quantitative Trait Locus (QTL) mapping and global gene regulatory network inference in systems genetics experiments. For this purpose, the research team focuses on Bayesian variable selection using parametric and nonparametric approaches that are performed with and without dimension reduction.

As part of its research program, the Statistical Genetics Research Group is analyzing a large systems genetics experiment to investigate the genetic basis of disease resistance to a major pathogen in soybean. This work is being conducted in collaboration with VBI Professor Brett Tyler at VBI and researchers at Virginia Tech and The Ohio State University. A recombinant inbred line population of soybean infected with the pathogen *Phytophthora sojae* has been phenotyped for quantitative disease resistance, genotyped for genetic markers, and analyzed using an Affymetrix GeneChip® containing probe sets for soybean and *P. sojae*. In this project, researchers are interested in evaluating the effects of multiple factors and their interactions on the expression of 37,420 soybean genes. The goal is to infer genetic regulatory networks from these data that will be useful in building a picture of how pathogen and plant genes interact during infection.

Research Interests

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

Selected Recent Publications

Gao G, Hoeschele I (2007) A note on a haplotyping method in pedigrees. *Genetics, Selection, Evolution* **40**: 25-36.

Liu B, de la Fuente A, Hoeschele I (2008) Gene network inference via structural equation modeling in genetical genomics experiments. *Genetics* **178**: 1763-1776.

Stock KF, Hoeschele I, Distl O (2007) Bayesian estimation of genetic parameters for multivariate threshold and continuous phenotypes and molecular genetic data in simulated horse populations using Gibbs sampling. *BMC Genetics* **8**: 19.

Stock KF, Hoeschele I, Distl O (2007) Estimation of genetic parameters and prediction of breeding values for multivariate threshold and continuous data in a simulated horse population using Gibbs sampling and residual maximum likelihood. *Journal of Animal Breeding and Genetics* **124**: 308-319.

Dr. Reinhard Laubenbacher

Applied Discrete Mathematics Research Group

Left to right:
Reinhard Laubenbacher, Katherine Swett, Franziska Hinkelmann, David Murrugarra, Abdul Salam Jarrah, Shamira Shallom, Alan Aldo Veliz-Cuba

The goal of mathematical systems biology is to understand complex biological networks through the use of mathematical models and data analysis techniques

Research Interests

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

Selected Recent Publications

Camacho D, Vera-Licona P, Mendes P, Laubenbacher R (2007) Comparison of reverse engineering methods using an in silico network. *Annals of the New York Academy of Sciences* **1115**: 73-89.

Choi V, Huang Y, Lam V, Potter D, Laubenbacher R, Duca K (2008) Using formal concept analysis for microarray data comparison. *Journal of Bioinformatics and Computational Biology* **6**(1): 65-75.

Duca KA, Shapiro M, Delgado-Eckert E, Hadinoto V, Jarrah A, Laubenbacher R, Thorley-Lawson DA (2007) A virtual look at Epstein–Barr virus infection: biological interpretations. *PLoS Pathogens* **3**(10): 1388-1400.

Jarrah A, Laubenbacher R, Stigler B, Stillman M (2007) Reverse-engineering polynomial dynamical systems. *Advances in Applied Mathematics* **39**: 477–489.

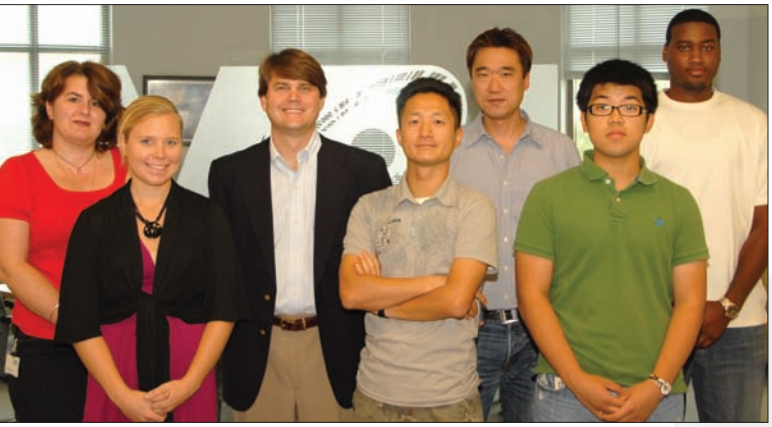
Jarrah A, Raposa B, Laubenbacher R (2007) Nested canalyzing, unate cascade, and polynomial functions. *Physica D: Nonlinear* **233**(2): 167-174.

Stigler B, Jarrah A, Stillman M, Laubenbacher R (2007) Reverse engineering of dynamic networks. *Annals of the New York Academy of Sciences* **1115**: 168-177.

One of the central problems of systems biology is to infer biochemical networks from system-wide experimental measurements, including gene regulatory, metabolic, and signaling networks. The goal of mathematical systems biology is to understand complex biological networks through the use of mathematical models and data analysis techniques. Dr. Reinhard Laubenbacher's Applied Discrete Mathematics Group is working on the development and application of mathematical techniques to reverse-engineer biochemical networks from large-scale system measurements such as DNA and protein sequence data.

The group is using a framework of finite dynamical systems for its work and is developing algebraic tools for analysis. The group is currently collaborating with Drs. Pedro Mendes and Vladimir Shulaev at VBI on two projects. To provide a more complete understanding of the oxidative stress response network in yeast, the Applied Discrete Mathematics Research Group is carrying out a research program to develop further the mathematical foundation for this family of dynamical systems. The second systems biology project, which also features a partnership with Wake Forest University Comprehensive Cancer Center, involves the use of metabolomics to identify metabolic markers for breast cancer diagnosis.

Metabolomics is useful in identifying overall metabolic changes associated with breast cancer development, as well as the most affected metabolites and metabolic networks. In combination with metabolic fingerprinting, the group is developing these molecular markers using mathematical, statistical, and machine learning algorithms.



Dr. Christopher B. Lawrence

Research Group

Left to right:
Mihaela Babiceanu, Amanda Cronin, Chris Lawrence, Kwang-Hyung Kim, Sang-Wook Park, Jinki Cho, Derrick Scott

The genus Alternaria contains many economically important fungal species that impact plant and human health

Dr. Chris Lawrence's Research Group studies the ways in which fungi cause diseases of plants and humans. The group is using the *Alternaria brassicicola*-Brassicaceae interaction as a system to study fungal pathogenesis and defense responses in plants. The species *Alternaria alternata*, which is clinically linked to human airway disorders such as allergy, severe asthma and chronic rhinosinusitis (CRS), is the focus of their biomedical research. Moreover, the Lawrence laboratory has been the lead group involved in the *A. brassicicola* genome-sequencing project. Bioinformatic analyses of the genome were carried out at the Virginia Bioinformatics Institute. In order to study fungal pathogenesis of plants, more than a hundred genes have been functionally analyzed through gene knockout and overexpression experiments, making *A. brassicicola* the species of choice for functional genomics research to understand the disease mechanisms for this important genus of fungi. The *A. alternata* genome sequencing project is also now underway in the Lawrence laboratory and will prove to be an invaluable resource for human airway health-related research.

The Lawrence laboratory is part of a National Institutes of Health-funded consortium that involves researchers at the Allergic Diseases Research Laboratory at Mayo Clinic in Rochester, MN. One project in this collaboration is directed towards further understanding of the pathogenesis of CRS and the role of Alternaria proteins in airway inflammation in humans. The other project is centered on understanding how secreted Alternaria proteins influence the innate and adaptive immune systems in a mouse model of allergic airway inflammation. Lastly, the Lawrence group is exploring the use of fungi and other microorganisms as sources of novel therapeutics and for biotechnology and bio-based material applications.

Research Interests

- The *Alternaria-Brassicicola* genome sequencing project
- Fungal pathogenesis of plants and humans
- Alternaria pathogenomics and human airway disorders
- Fungal biotechnology and bio-based materials

Selected Recent Publications

Cho Y, Cramer RC, Kim K-H, Pryor BM, Mitchell TK, Lawrence CB (2007) The Amk1 map kinase regulates hydrolytic enzyme gene expression in *Alternaria brassicicola*. *Fungal Genetics and Biology* **44**: 543-553.

Craven K, Valez H, Cho Y, Lawrence CB, Mitchell TK (2008) Anastomosis is required for pathogenicity of the fungal necrotroph *Alternaria brassicicola*. *Eukaryotic Cell* **7**: 675-683.

Kim K-H, Cho Y, La Rota CM, Cramer RC, Lawrence CB (2007) Functional analysis of the *Alternaria brassicicola* non-ribosomal peptide synthetase gene *AbNRPS2* reveals a role in conidial cell wall construction. *Molecular Plant Pathology* **8**: 23-29.

Lawrence CB, Mitchell TK, Cramer RC, Craven KD, Cho Y, Kim K-H (2008) At death's door: Alternaria pathogenicity mechanisms. *The Plant Pathology Journal* **24**: 101-111.

Yoon J, Ponikau JU, Lawrence CB, Kita H (2008) Innate anti-fungal immunity of human eosinophils mediated by a β2-integrin, CD11b. *Journal of Immunology* **181**(4): 2907-2915.

Dr. Iuliana M. Lazar

Research Group

Left to right:
Iuliana Lazar, Debby Reed, Jenny Armenta, Xu Yang, Milagros Perez

The discovery of novel-diagnostic protein patterns and therapeutic targets could have a tremendous impact on public health

Research Interests

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

Selected Recent Publications

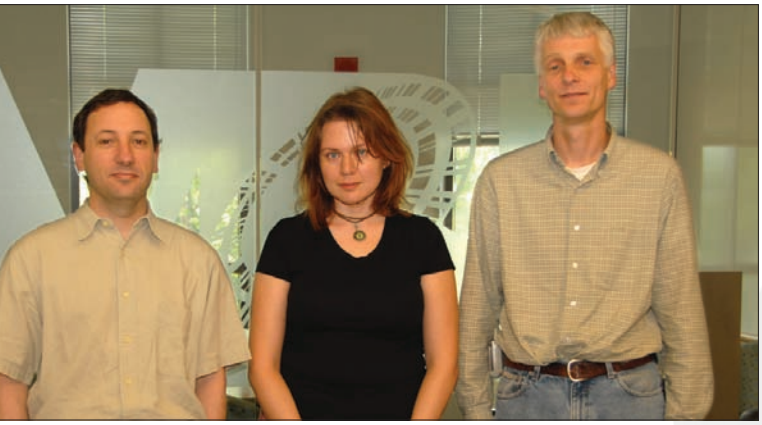
Dawoud AA, Sarvaiya HA, Lazar IM (2007) Microfluidic platform with mass spectrometry detection for the analysis of phosphoproteins. *Electrophoresis* **28**: 4645-4660.

Lazar IM (2007) Microfluidic devices with mass spectrometry detection. In *Handbook of Capillary and Microchip Electrophoresis and Associated Microtechniques*. Landers JP (ed), CRC Press, 3rd edition, 1459-1506.

Monitoring quantitative changes in the cellular proteome in response to stress-inducing conditions is essential for helping researchers better understand complex signaling pathways. The discovery of novel-diagnostic protein patterns and therapeutic targets could have a tremendous impact on public health. For example, breast cancer is the most common type of cancer among women worldwide, which emphasizes the need to elucidate the pathways that lead to its development.

The sensitivity of measurement offered by mass spectrometry makes it an essential tool in proteomic investigations. Dr. Iuliana Lazar's research group is interested in developing fully integrated, stand-alone microfluidic devices with mass spectrometry detection for high-throughput proteomic investigations, as well as bioanalytical strategies for global proteomic profiling of cancer cells and tissues, and microfluidic-mass spectrometric platforms for cancer biomarker discovery and screening.

The group has developed and implemented two methods based on stable isotope labeling and spectral counting for protein differential expression using both conventional and microfluidic platforms. MCF-7 breast cancer cell extracts were cultured in the presence of estradiol, the most abundant circulating estrogen in humans, and tamoxifen, a non-steroidal drug commonly prescribed in hormonal breast cancer therapy. Over 500 proteins ($P<0.001$) were identified in the two extracts – approximately 255 proteins were matched by two peptides and 16 proteins exhibited a greater than two-fold change in expression level as a result of estrogen stimulation or tamoxifen inhibition of cell proliferation. The stand-alone microfluidic liquid chromatography system has enabled the identification of ~50 proteins, along with several previously reported biomarkers. In future work, the group plans to compare the label-free approach with the stable isotope labeling method, and the differential protein expression pattern will be evaluated for biological relevance.



Dr. Pedro Mendes

Biochemical Networks Modeling Group

Left to right:
Pedro Mendes, Revonda Pokrzywa, Stefan Hoops

Biochemical models are the ideal means to design and predict the effect of interventions such as treating diseases, improving crop yields, and designing biotechnology

Systems biology brings together modeling, simulation and quantitative experiments, allowing researchers to use the data from one of these approaches to repeatedly define the framework of the other approaches. Biochemical networks are central to biological function, but are very complex in nature. Computer modeling and simulation of biochemical networks provide useful ways to describe and understand their functions. Biochemical models are the ideal means to design and predict the effect of interventions such as treating diseases, improving crop yields, and designing biotechnology.

Dr. Pedro Mendes is chair of Computational Systems Biology at the University of Manchester, England, and leads the Biochemical Networks Modeling Group at VBI. The main goal of the Biochemical Networks Modeling Group is to develop computational methods for studying biochemical networks using data from experimental observations. One tool that continues to be developed by the group to aid in the modeling and simulation of biochemical networks is COPASI (Complex Pathway Simulator). COPASI is an open-source software package that allows users with limited knowledge of mathematics to construct kinetic models. An additional tool developed by the group is B-Net, a database schema that can organize background knowledge about the biochemical networks before models and simulations are created. B-net is being adapted for use in projects such as whole-genome network reconstruction and the creation of a consensus model of the metabolic network of baker's yeast. The group has also continued its involvement in the establishment of community standards for systems biology that play a formal role in the definition of the Systems Biology Markup Language (SBML). SBML is an application-independent file format to specify systems biology models and has served as a catalyst for new developments in the area of systems biology. The Biochemical Networks Modeling Group has been involved with the SMBL effort since its inception.

Research Interests

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

Selected Recent Publications

Camacho D, Vera Licona P, Mendes P, Laubenbacher R (2007) Comparison of reverse-engineering methods using an *in silico* network. *Annals of the New York Academy of Sciences* **1115**: 73-89.

Kell DB, Mendes P (2007) The markup is the model: Reasoning about systems biology models in the Semantic Web era. *Journal of Theoretical Biology* **252**: 538-543.

Bandara AB, Contreras A, Contreras-Rodriguez A, Martins AM, Dobrean V, Poff-Reichow S, Rajasekaran P, Sriranganathan N, Schurig GG, Boyle SM (2007) *Brucella suis* urease encoded by *ure1* but not *ure2* is necessary for intestinal infection of BALB/c mice. *BMC Microbiology* **7**: 57.

Dr. Biswarup Mukhopadhyay

Research Group

Left to right:
(back row) Ban Wang, Eric Johnson, Jeremiah Hicks, Jason Rodriguez, Lakshmi Dharmarajan; (front row) Dwi Susanti Endang Purwantini, Karla Piedl, Biswarup Mukhopadhyay, Usha Loganathan , Jennifer Downs

Research in the Mukhopadhyay laboratory focuses on methanogenic archaea, tuberculosis, type 2 diabetes and coalbed methane

Research Interests

- Sulfite metabolism in methanogenic archaea
- Coal bioconversion to methane and mitigation of methane-induced mine explosion
- Structure function studies of phospho*enol*pyruvate carboxykinase – Type 2 diabetes
- Structure function studies of an archaeal-type phospho*enol*pyruvate carboxylase
- Tuberculosis – metabolism of the mycobacteria

Selected Recent Publications

Case CL, Mukhopadhyay B (2007) Kinetic characterization of recombinant human cytosolic phosphoenolpyruvate carboxykinase with and without a His_{10}-tag. *Biochimica Biophysica Acta* **1770**: 1576-1584.

Staples CR, Lahiri S, Raymond J, Von Herbulis L, Mukhophadhyay B, Blankenship RE (2007) The expression and association of group IV nitrogenase NifD and NifH homologs in the non-nitrogen fixing archaeon *Methanocaldococcus jannaschii*. *Journal of Bacteriology* **89**: 7392-7398.

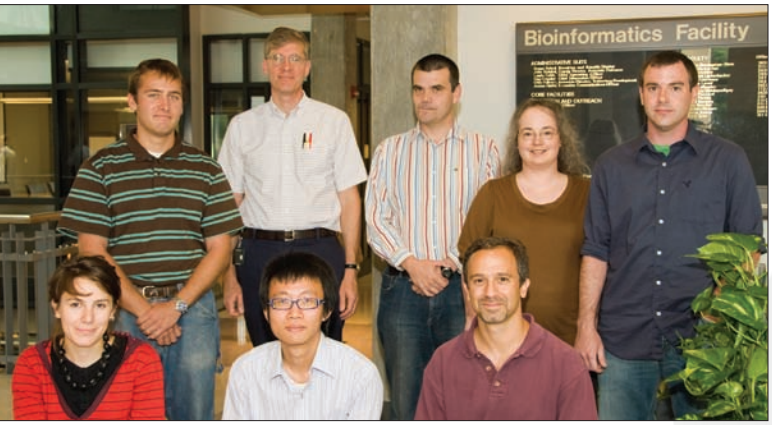
Anderson I, Rodriguez J, Susanti D, Porat I, Reich C, Ulrich LE, Elkins JG, Mavromatis K, Lykidis A, Kim E, Thompson LS, Nolan M, Land M, Copeland A, Lapidus A, Lucas S, Detter C, Zhulin IB, Olsen GJ, Whitman W, Mukhopadhyay B, Bristow J, Kyrpides N (2008) Genome sequence of *Thermofilum pendens* reveals an exceptional loss of biosynthetic pathways without genome reduction. *Journal of Bacteriology* **190**: 2957-2965.

Dr. Mukhopadhyay's laboratory is interested in providing a better understanding of how metabolic reactions and pathways arose and evolved from inorganic reactions and determining how microorganisms survive in extreme environments. The team is also interested in developing therapeutics and diagnostics for the treatment of tuberculosis and diabetes and using several approaches to investigate new energy production processes.

Methanocaldococcus jannaschii is a methane-producing organism found in submarine hydrothermal vents. The Mukhopadhyay research group has discovered that *M. jannaschii* possesses a new type of sulfite reductase, which represents an ancient detoxification system. Unlike other methanogens, methane production and sulfite reduction have been shown not to be mutually exclusive processes in this organism. The Mukhopadhyay research group is also exploring the use of microbial organisms to convert coal to methane and reduce the risk of methane-induced mine explosion.

The group is studying the structure-function relationships in GTP-dependent phospho*enol*pyruvate carboxykinase (GTP-PEPCK). The gluconeogenic activity of this enzyme is most likely required for attainment and maintenance of dormancy or latency of *Mycobacterium tuberculosis*, which causes tuberculosis in humans. An untimely and unusually high activity of GTP-PEPCK also contributes to the development of obesity and type 2 diabetes. An agent that will lower the activity of this enzyme would be useful in the treatment of these diseases.

The Mukhopadhyay laboratory is investigating Coenzyme F_{420} metabolism of the mycobacteria and MDR/XDR strains of *Mycobacterium tuberculosis* for the development of therapeutics for tuberculosis. The latter investigation is in collaboration with the Rotinsulu Pulmonary Hospital and the Institut Teknologi Bandung, Bandung, Indonesia.



Dr. Jean Peccoud

Synthetic Biology Research Group

Left to right:
(back row) Matt Lux, William Baumann, Jean Peccoud, Julie Marchand, David Ball; (front row) Laura Adam, Patrick Cai, Michael Czar

Now that it is possible to synthesize the entire genome of a bacterium, it is time to develop a way to represent this object in a more compact and meaningful form than the 582,970 bases of its DNA sequence

The Synthetic Biology Group at VBI combines experimental and computational methods to crack the code of life. The group is developing new computer languages to represent complex phenotypes that are encoded in long DNA sequences composed of multiple functional blocks. This transformative approach is validated on a small scale using libraries of related artificial gene networks derived from a small number of functional blocks.

This computational effort is complemented by efforts to collect better data to characterize the dynamics of the gene networks encoded in artificial gene networks. Bacterial or yeast cells are grown under a microscope for extended periods of time during which images are collected every few minutes. Custom imaging software has been developed to reduce tens of thousands of images typically collected in such experiments to a smaller data set describing the time evolution of regulatory processes in individual cells. In collaboration with Dr. John Tyson's research group, this approach is being applied to the network controlling the cell cycle in yeast. Its application to single cells and time resolution capabilities give a new insight into the mechanisms controlling this important biological process.

Research arising from the Synthetic Biology Group directly translates into biomedical and biotechnology applications that leverage the potential of chemical DNA synthesis. The group released GenoCAD, a web-based application that can be regarded as the first Computer Assisted Design system for synthetic DNA sequences. GenoCAD provides a sequence builder function that guides users through the process of designing a new genetic construct from a database of standard genetic parts. It also includes a sequence verification tool that can be used to ensure that DNA sequences are consistent with a set of predefined design guidelines. The Synthetic Biology Group is pursuing targeted efforts to develop high-quality libraries of biological parts that maximize the value of GenoCAD to its users.

Research Interests

- Linguistic models of DNA sequences
- High-throughput imaging
- Design automation of synthetic genetic systems

Selected Recent Publications

Cai Y, Hartnett B, Gustafsson C, Peccoud J (2007) A syntactic model to design and verify synthetic genetic constructs derived from standard biological parts. *Bioinformatics* **23**: 2760-2767.

Peccoud J, Coulombel L (2007) A competition of synthetic biology or how to create the "water of *E. coli*" and nano-barbies. *MS-Medecine Sciences* **23**: 551-552.

Peccoud J, Courtney T, Sanders WH (2007) Möbius: an integrated discrete-event modeling environment. *Bioinformatics* **23**: 3412-3414.

Dr. Andy Pereira

Research Group

Left to right:
(back row) Batlang Utlwang, Arjun Krishnan, Andy Pereira, Madana Ambavaram, Bryan Moretz, Peter Wittich; (front row) Amal Harb, Marcella Welch, Michelle Harlow, Alicia Foremant

Uncovering ways to help plants survive in unfavorable environments can have a huge impact on agricultural productivity

Research Interests

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

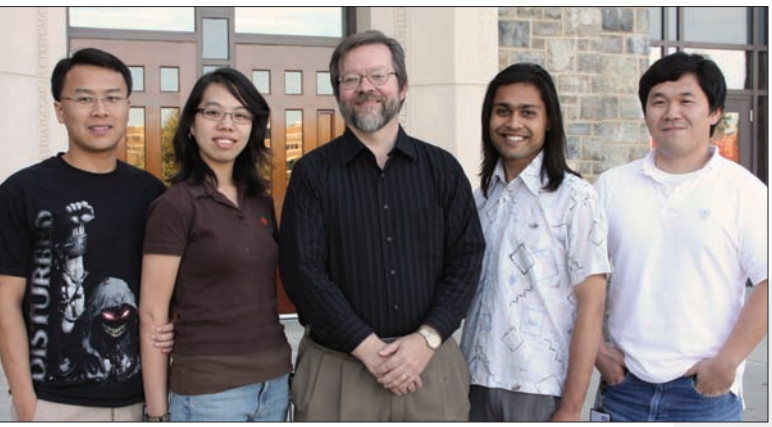
Selected Recent Publications

Karaba A, Dixit S, Greco R, Aharoni A, Trijatmiko K, Marsch-Martinez N, Krishnan A, Nataraja K, Udayakumar M, Pereira A (2007) Improvement of water use efficiency in rice by expression of *HARDY*, an *Arabidopsis* drought and salt tolerance gene. *Proceedings of the National Academy of Sciences USA* **104**(39): 15270-15275.

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

Plants respond to environmental factors such as heat, cold, drought, nutrient deficiencies or toxicities in a variety of ways. Many of these responses take needed energy away from the plant, resulting in major global crop losses each year. Uncovering ways to help plants survive in unfavorable environments can have a huge impact on agricultural productivity. The interaction and adaptation of plants to environmental signals and stresses are complex and need to be analyzed in a network model using a systems biology approach. The focus of the work in Dr. Andy Pereira's research group is to examine plant-environment interaction as a system involving plant perception of and response and resistance to environmental stress. By using a "genome biology" approach to look at genes that have retained similar functions over time in different plant species, the group's work provides valuable information on how different plant species have adapted to cope with severe, external influences. Drought, specifically, has become a serious global problem due to climate change and the increasing needs of the world population. The response and resistance of plants to drought is complex, however, making it difficult to identify the causal traits using traditional approaches.

Members of the Pereira research group are using comparative analysis of *Arabidopsis* and rice to better understand the conserved pathways involved in drought stress. By integrating *Arabidopsis* gene interaction networks with rice ortholog information, the group can analyze comparative gene functions of the plant, which can be used as a model for other plants. Using transcriptome analysis, common regulated pathways and genes have been revealed in *Arabidopsis* and rice when the plants are exposed to drought-like conditions. In addition, the group is identifying genes that contribute to improved drought resistance. The goal of the work is to determine the network of gene actions in *Arabidopsis* and rice to provide insights for future crop improvement measures.



Dr. David C. Samuels

Research Group

Left to right:
Zhuo Song, Passorn Wonnapinij, David Samuels, Vishal Gandhi, Saangho Lee

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

Research in Dr. Samuels' group involves the application of computational and mathematical tools to research problems in cell biology and medicine. Current projects underway in the group are concerned with mitochondrial diseases and mitochondrial metabolism. These projects arise from research of genetic diseases that are caused by mutations in either nuclear or mitochondrial genes, and from research on the toxicity of nucleoside analogs used as antiviral agents in the treatment of Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS).

Work published in the past year has focused on simulations of mammalian embryogenesis, hematopoietic stem cells, and the enzyme kinetics of small molecule carriers. Some of this work involves experimental tests of hypotheses that are based on computer simulation models developed by the group. Other aspects of this research have led to new hypotheses that may be tested in future experiments.

In a recent paper published in the *American Journal of Human Genetics* (**83**(2): 254-260), Dr Samuels' group and collaborators in the United Kingdom have shown that mutations in mitochondrial DNA are more common in the general population than previously thought. Clinical analysis of blood samples from almost 3,000 infants born in north Cumbria, England, showed that at least 1 in 200 individuals in the general public harbor mitochondrial DNA mutations that may lead to disease. Mutations in mitochondrial DNA inherited from the mother may cause mitochondrial diseases that include muscle weakness, diabetes, stroke, heart failure, or epilepsy. The findings emphasize the pressing need to develop effective ways to interrupt the transmission of these mutations to the next generation.

Research Interests

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

Selected Recent Publications

Durham Steve E, Samuels David C, Cree Lynsey M, Chinnery Patrick F (2007) Normal levels of wild-type mitochondrial DNA maintain cytochrome *c* oxidase activity for two pathogenic mitochondrial DNA mutations but not for m.3243A -> G. *American Journal of Human Genetics* **81**(1): 189-195.

Cree Lynsey M, Samuels David C, Chuva de Sousa-Lopes Susana, Rajasimha Harsha K, Wonnapinij Passorn, Mann Jeffrey R, Dahl Hans-Henrik M, Chinnery Patrick F (2008) A reduction of mitochondrial DNA molecules during embryogenesis explains the rapid segregation of genotypes. *Nature Genetics* **40**(2): 249-254.

Krishnan Kim J, Reeve Amy K, Samuels David C, Chinnery Patrick F, Blackwood John K, Taylor Robert W, Wanrooij Sjoerd, Spelbrink Johannes N, Lightowlers Robert N, Turnbull Doug M (2008) What causes mitochondrial DNA deletions in human cells? *Nature Genetics* **40**(3): 275-279.

Rajasimha Harsha K, Chinnery Patrick F, Samuels David C (2008) Selection against pathogenic mtDNA mutations in a stem cell population leads to the loss of the 3243A -> G mutation in blood. *American Journal of Human Genetics* **82**(2): 333-343.

Dr. João C. Setubal

Research Group

Left to right:
João Setubal, Andrew Warren, Nalvo De Almeida Jr., Chris Lasher, Kuan Yang

Comparative genomics has greatly benefited from the surge in the number of bacterial genomes available through new sequencing technologies

Research Interests

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

Selected Recent Publications

Setubal JC, Wood D, Burr T, Farrand S, Goldman B, Goodner B, Otten L, Slater S (2009) The Genomics of Agrobacterium: Insights into Pathogenicity, Biocontrol, and Evolution. In R. Jackson (ed.), *Plant Pathogenic Bacteria: Genomics and Molecular Biology*, pp. 91-112. Horizon Press, 2009.

Setubal JC (2008) Similarity Search (theory), chapter A05. In *Bioinformatics in Tropical Disease Research: A Practical and Case-Study Approach*, Gruber A, Durham AM, Huynhtop C, del Portillo H (eds), Bethesda, M.D., National Library of Medicine, National Center for Biotechnology Information.

Yan S, Liu H, Mohr TJ, Jenrette J, Chiodini R, Zaccardelli M, Setubal JC, Vinatzer B (2008) The role of recombination in the evolution of the model plant pathogen *Pseudomonas syringae* pv. *tomato* DC3000, a very atypical tomato strain. *Applied Environmental Microbiology* **74**(10): 3171-3181.

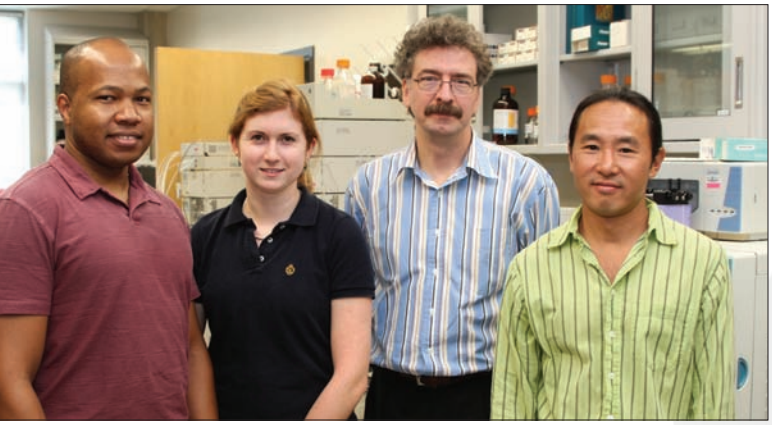
Gillespie JJ, Williams K, Snyder EE, Nordberg E, Ceraul SM, Dharmanolla C, Rainey D, Soneja J, Shallom JM, Shukla M, Vishnubhat ND, Wattam R, Purkayastha A, Czar M, Crasta O, Setubal JC, Azad AF, Sobral BW (2008) *Rickettsia* phylogenomics: Unwinding the intricacies of obligate intracellular life. *PLoS ONE*, **3**(4): e2018 doi:10.1371/journal.pone.0002018.

Dr. João Setubal's research group works primarily on bioinformatics for bacterial genome annotation and sequence analysis. The group participates in several genome projects, providing a community genome annotation system in addition to various computational analyses. Three of these projects are: *Agrobacterium* biovars with the Agrobacterium Consortium; *Azotobacter vinelandii* with the Azotobacter consortium; and *Pseudomonas syringae* with the Boris Vinatzer laboratory at Virginia Tech.

The goal of the *Agrobacterium* project is to better understand molecular microbe-plant interactions and the evolution of *Agrobacterium* species through genome comparisons. *Azotobacter vinelandii,* a free-living α-proteobacterium species that has nitrogen-fixation capabilities, is a well-known model for biochemistry studies. The goal is to obtain a detailed view of *A. vinelandii*'s genome and couple that with the extensive existing knowledge of its biochemical properties. *Pseudomonas syringae* is a plant pathogen. The numerous strains of *P. syringae* have a variety of host-plant specificities. Many of these strains impact important agricultural crops, such as tomato. The goal of this project is to study the genomes of several strains and gain insights about the interplay between pathogen evolution and the early stages of human agriculture, which is an idea advanced by Boris Vinatzer.

The group is also part of the National Institutes of Health/National Institute of Allergy and Infectious Diseases-funded PathoSystems Resource Integration Center (PATRIC) that manages a bioinformatics resource for genomic and other related information on human bacterial and viral pathogens.

In addition to work related to specific genomes, other topics of activity include the development of a graph-based approach for uncovering conserved blocks of genes in related bacterial genomes and DNA/peptide sequence analysis in phage display cancer data.



Dr. Vladimir Shulaev

Biochemical Profiling Research Group

Left to right:
Diego Cortes, Sarah Holt, Vladimir Shulaev, Joel Shuman

The Biochemical Profiling Group develops and applies state-of-the-art metabolomics technologies to biological systems

Metabolomics is a powerful tool that complements large-scale genomic and proteomic technologies. A high-throughput metabolomics platform is needed as a tool to understand systems biology, discover metabolic biomarkers, and elucidate gene function. The Biochemical Profiling Group at the Virginia Bioinformatics Institute is building a high-throughput metabolomics platform that combines untargeted metabolite profiling, metabolic fingerprinting, and targeted analysis.

Analytical techniques like mass spectrometry provide sample analysis for a wide range of metabolites at high sensitivity. This platform has been successfully used to elucidate early metabolic responses to abiotic stress in plants, identify unique metabolic signatures associated with the progression of malignancy in human breast epithelium cells, study the infection of red blood cells by the malaria parasite *Plasmodium falciparum*, investigate the impact of drug treatment on malaria infection, and, in a collaborative systems biology project, study the oxidative stress response in the yeast *Saccharomyces cerevisiae*.

The Biochemical Profiling Group is a key member of the Rosaceae scientific community. Rosaceae is an economically important group of plants that comprises more than 3000 species including strawberry, apple, peach and pear. The Biochemical Profiling Group is part of the International Consortium that is sequencing the full genome of the woodland strawberry (*Fragaria vesca*) using the Roche GS-FLX™ technology. The sequencing of the woodland strawberry genome will provide an invaluable resource to the wider plant research community.

Research Interests

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

Selected Recent Publications

Tuli L, Martins A, Sha W, Mendes P, Shulaev V (2007) Proteome analysis of oxidative stress response to cumene hydroperoxide in *Saccharomyces cerevisiae*. *Molecular & Cellular Proteomics* **6**: 46-46.

Miller G, Shulaev V, Mittler R (2008) Reactive oxygen signaling and abiotic stress. *Physiologia Plantarum* **133**: 481-489.

Shulaev V, Cortes D, Miller G, Mittler R (2008) Metabolomics for plant stress response. *Physiologia Plantarum* **132**: 199-208.

Shulaev V, Korban KS, Sosinski B, Abbott AG, Aldwinckle HS, Folta KM, Iezzoni A, Main D, Arús P, Dandekar AM, Lewers K, Brown SK, Davis TM, Gardiner SE, Potter D, Veilleux RE (2008) Multiple models for Rosaceae genomics. *Plant Physiology* **147**(3): 985-1003.

Suzuki N, Bajad S, Shuman J, Shulaev V, Mittler R (2008) The transcriptional co-activator MBF1c is a key regulator of thermotolerance in *Arabidopsis thaliana*. *Journal of Biological Chemistry* **283**: 9269-9275.

Dr. Bruno W. S. Sobral

CyberInfrastructure Research Group

Left to right:
(back row) Derren Rosbach, Eric Nordberg, Mane Shrinivasrao, Mark Scott, Ron Kenyon; (middle row) Isabel Da Fonseca, Herman Formadi, Joshua Shallom, Emily Alberts, Eric Snyder, Harry Yoo, Rebecca Wattam, Dan Liu, Bruno Sobral; (front row) Chunhong Mao, Chunxia Wang, Yan Zhang, Chengdong Zhang, Maulik Shukla, Oswald Crasta, Nirali Vaghela, Rebecca Will

The Cyberinfrastructure Group applies the principles of cyberinfrastructure to enable transformative scientific discoveries

Research Interests

- Development and deployment of cyberinfrastructure
- Infectious disease research
- Host-pathogen-environment interactions

Selected Recent Publications

Gillespie JJ, Beier MS, Rahman S, et al. (2007) Plasmids and rickettsial evolution: Insight from *Rickettsia felis*. *PLoS One* **2**(3): e266.

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

Yu GX, Snyder EE, Boyle SM, et al. (2007) A versatile computational pipeline for bacterial genome annotation improvement and comparative analysis, with *Brucella* as a use case. *Nucleic Acids Research* **35**(12): 3953-3962.

Crasta OR, Folkerts O, Fei Z, et al. (2008) Genome sequence of *Brucella abortus* vaccine strain S19 compared to virulent strains yields candidate virulence genes. *PLoS ONE* **3**(5): e2193. doi:10.1371/journal.pone.0002193.

Dyer MD, Murali TM, Sobral BWS (2008) The landscape of human proteins targeted by viruses and other pathogens. *PLoS Pathogens* **4**(2): e32.

Zhang C, Crasta O, Cammer S, et al. (2008) An emerging cyberinfrastructure for biodefense pathogen and pathogen:host data. *Nucleic Acids Research* **36**(Database issue): D884-891.

The Cyberinfrastructure Group develops methods, infrastructure, and resources to help enable scientific discoveries in infectious disease research and other fields by applying the principles of cyberinfrastructure to integrate data, computational infrastructure, and people. The group has developed many public resources for curated, diverse molecular and literature data from various infectious disease systems, and implemented the processes, systems, and databases required to support them. It also conducts research applying its methods and data to make new discoveries of its own.

The Cyberinfrastructure Group participates in education and outreach activities that facilitate collaborations with external researchers, resulting in scientific discoveries and publications and an outreach program involving the development of a project-centric cyberinfrastructure course for educators from high schools and undergraduate institutions as well as graduates and postgraduates. The group also studies intracellular symbiotic systems, in particular the interactions of the nitrogen-fixing bacterium *Sinorhizobium meliloti* with the legume *Medicago*.

In the past year, key accomplishments included publication of the *Brucella abortus* S19 genome, deployment of a pipeline to improve genome annotations, publication of an extensive global analysis of human protein interactions with viral and other proteins, phylogenomic analysis of ten rickettsial genomes, publication of an Alphaproteobacteria phylogenetic tree, development of a program to generate oligonucleotide sequences from whole genome sequences, continuing progress in numerous collaborative research projects, and development of an online self-guided bioinformatics tutorial.

Dr. Brett M. Tyler

Research Group

Left to right:
(back row) Grace Martin, Konstantinos Krampis, Lachelle Waller, Lee Falin, Lecong Zhou, Trudy Torto-Alalibo, Felipe Arredondo, Biao Gu; (front row) Regina Hanlon, Brett Tyler, Shiv Kale

By using a genetical genomics approach, the Tyler group hopes to better understand the host-pathogen genetic networks that control oomycete infection of plants

Oomycetes are fungal-like organisms related to marine algae that cause tens of billions of dollars of losses to agriculture, forestry, and natural ecosystems every year. The oomycete *Phytophthora infestans* was responsible for the potato famine in Ireland in the mid-1800s, while *Phytophthora ramorum* is attacking trees and shrubs of coastal oak forests in California and *Phytophthora sojae* is causing serious losses to the United States soybean crop.

Dr. Brett Tyler's research group is building data collections and tool sets that will allow the team to dissect in detail the host-pathogen genetic networks that control infection of plants by oomycete pathogens. Understanding the structure of these networks will aid in the development of disease prevention and control measures. The Tyler group and collaborators have sequenced the genomes of the oomycetes *P. sojae*, *P. ramorum*, and *Hyaloperonospora parasitica*, as well as the fungus *Alternaria brassicicola*. A comparison of these genome sequences has revealed that many genes are evolving unusually rapidly, including a large, diverse set of genes that encode virulence proteins that can enter plant cells to suppress defense reactions. To determine the dynamics of how the pathogen and plant genes interact, the group is conducting gene expression profiling of soybean and its pathogen *P. sojae* using Affymetrix GeneChip® microarrays. This work includes the construction of a very high-density genetic map of soybean. A genetical genomics approach is being used to infer genetic regulatory networks from these data.

Research Interests

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

Selected Recent Publications

Dou D, Kale SD, Wang XL, Chen Y, Wang Q, Wang X, Jiang RHY, Arredondo FD, Anderson RG, Thakur PB, McDowell JM, Wang YC, Tyler BM (2008) Conserved C-terminal motifs required for avirulence and suppression of cell death by *Phytophthora sojae* effector Avr1b. *Plant Cell* **20**(4): 1118-1133.

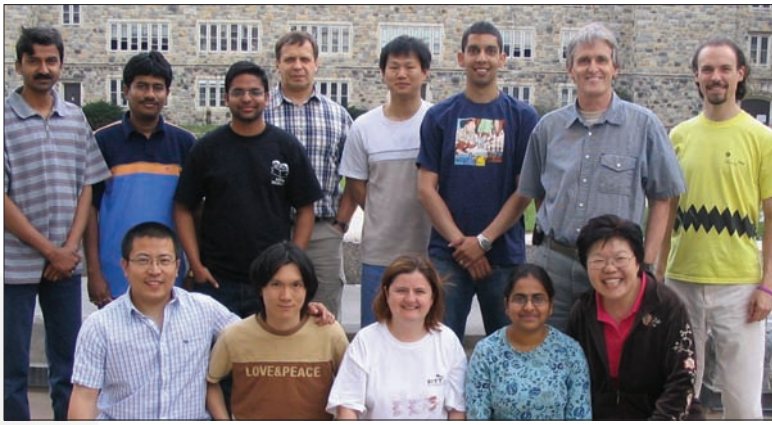
Jiang RHY, Tripathy S, Govers F, Tyler BM (2008) RXLR effector reservoir in two *Phytophthora* species is dominated by a single rapidly evolving super-family with more than 700 members. *Proceedings of the National Academy of Sciences USA* **105**(12): 4874-4879.

Tyler BM (2008) Genomics of fungal- and oomycete-soybean interactions. In *Genetics and genomics of soybean.* Stacey G (ed), Springer, New York, 243-268.

Tyler BM, Jiang RHY, Zhou L, Tripathy S, Dou D, Torto-Alalibo T, Li H, Mao Y, Liu B, Vega-Sanchez M, Mideros SX, Hanlon R, Smith BM, Krampis K, Ye K, Martin SS, Dorrance AE, Hoeschele I, Maroof MAS (2008) Functional genomics and bioinformatics of the *Phytophthora sojae*-soybean interaction. In *The Genomics of Disease*. Gustafson P, Stacey G, Taylor J (eds), Kluwer Academic/Plenum Publisher, New York, 67-78.

Dr. John J. Tyson

VBI Faculty Fellow



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

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

Research Interests

- Spatial and temporal organization of biological systems
- Network dynamics and systems biology
- Bifurcation analysis, stochastic modeling and parameter estimation

Selected Recent Publications

Calzone L, Thieffry D, Tyson JJ, Novak B (2007) Dynamical modeling of syncytial mitotic cycles in *Drosophila* embryos. *Molecular Systems Biology* **3**:131.

Novak B, Tyson JJ, Gyorffy B, Csikasz-Nagy A (2007) Irreversible cell-cycle transitions are due to systems-level feedback. *Nature Cell Biology* **9**: 724-728.

Csikasz-Nagy A, Gyorffy B, Alt W, Tyson JJ, Novak B (2008) Spatial controls for growth zone formation during the fission yeast cell cycle. *Yeast* **25**: 59-69.

Li S, Brazhnik P, Sobral B, Tyson JJ (2008) A quantitative study of the division cycle of *Caulobacter crescentus* stalked cells. *PLoS Computational Biology* **4**: e9.

Sabouri-Ghomi M, Ciliberto A, Novak B, Tyson JJ (2008) Antagonism and bistability in protein interaction networks. *Journal of Theoretical Biology* **250**: 209-218.

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

Dr. John Tyson's Research Group is converting network diagrams into sets of nonlinear ordinary differential equations (chemical rate equations) using the principles of biochemical kinetics and exploring the models by analytical and computational methods. Of particular interest are the mechanisms that control cell division in prokaryotes (bacteria) and eukaryotes (yeasts, plants, insects, vertebrates).

The group has recently published a comprehensive model of the genetic regulatory network that controls DNA synthesis, division and differentiation in a class of bacterial cells. A second paper from the group explored the mechanisms controlling nuclear division during the earliest stage of development of fruit fly embryos. A third paper modeled spatial patterns of growth in fission yeast cells.

Finance and Administration

- Awards by Sponsor
- Expenses by Sponsor
- Capital Assets
- Personnel

The Virginia Bioinformatics Institute is commited to solving society's most important problems through transdisciplinary research.

The theme of this year's annual report from the Virginia Bioinformatics Institute is networks. In this report you will find several examples of how researchers at VBI are looking in detail at the networks that make up biological systems. People are also part of networks and it is the personal interactions between the employees of VBI that help to build the collaborative culture of our Institute. We continue to see the direct benefits of these relationships reflected in our accomplishments.

VBI continued to show growth in total active awards and number of employees for the fiscal year ending June 30, 2008. Total active awards by sponsor reached $97 million and the Institute employed 239 personnel by the end of the 2007-2008 fiscal year. While our three primary federal sponsors remained the same, support, in terms of funding from the United States Department of Defense, increased from 21.5% in 2007 to 32.8% in 2008. Notably, this reflects the efforts of our Network Dynamics and Simulation Science Laboratory with the award of a $20.6 million contract from the Defense Threat Reduction Agency. This funding is being used to develop the Comprehensive National Incident Management System (CNIMS), an integrated informatics capability that supports analyses of very large and complex crisis events on a national scale.

In summary, three federal sponsors support the extramural research program of VBI: the National Institutes of Health (34.7%), the United States Department of Defense (32.8%), and the National Science Foundation (21.4%). Other leading federal agencies and academic institutions represent the balance of our funding. VBI's focus on large-scale research continues to positively impact our progress and ensures a stable platform through which we continue to grow.

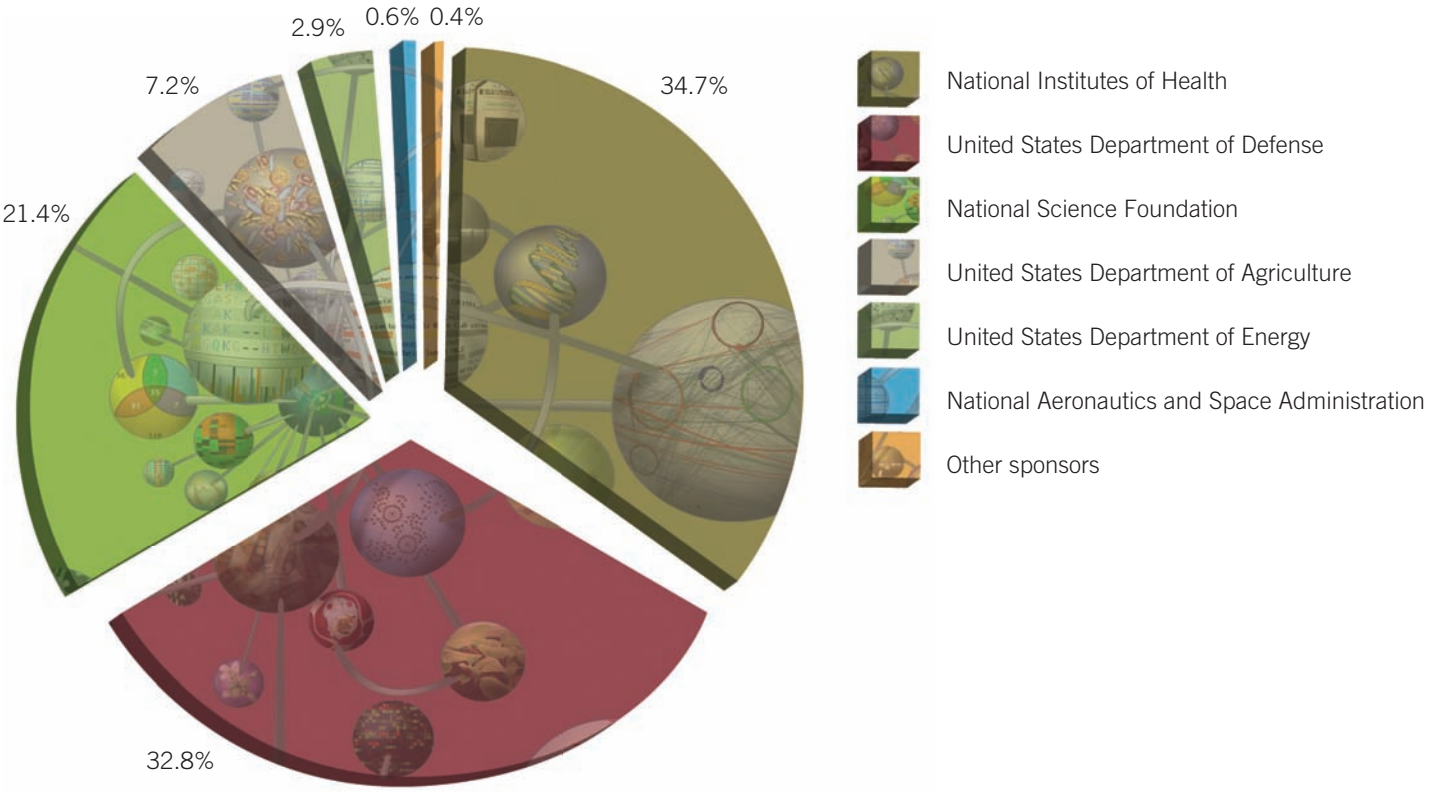
We would like to thank everyone at VBI for the commitment they have shown in making the many achievements of the Institute possible and we look forward to further exciting opportunities in the years ahead.

Lauren Coble
Chief Operating Officer


Activation Lab Students
Fitness Welcome

2008 Active Awards by Sponsor

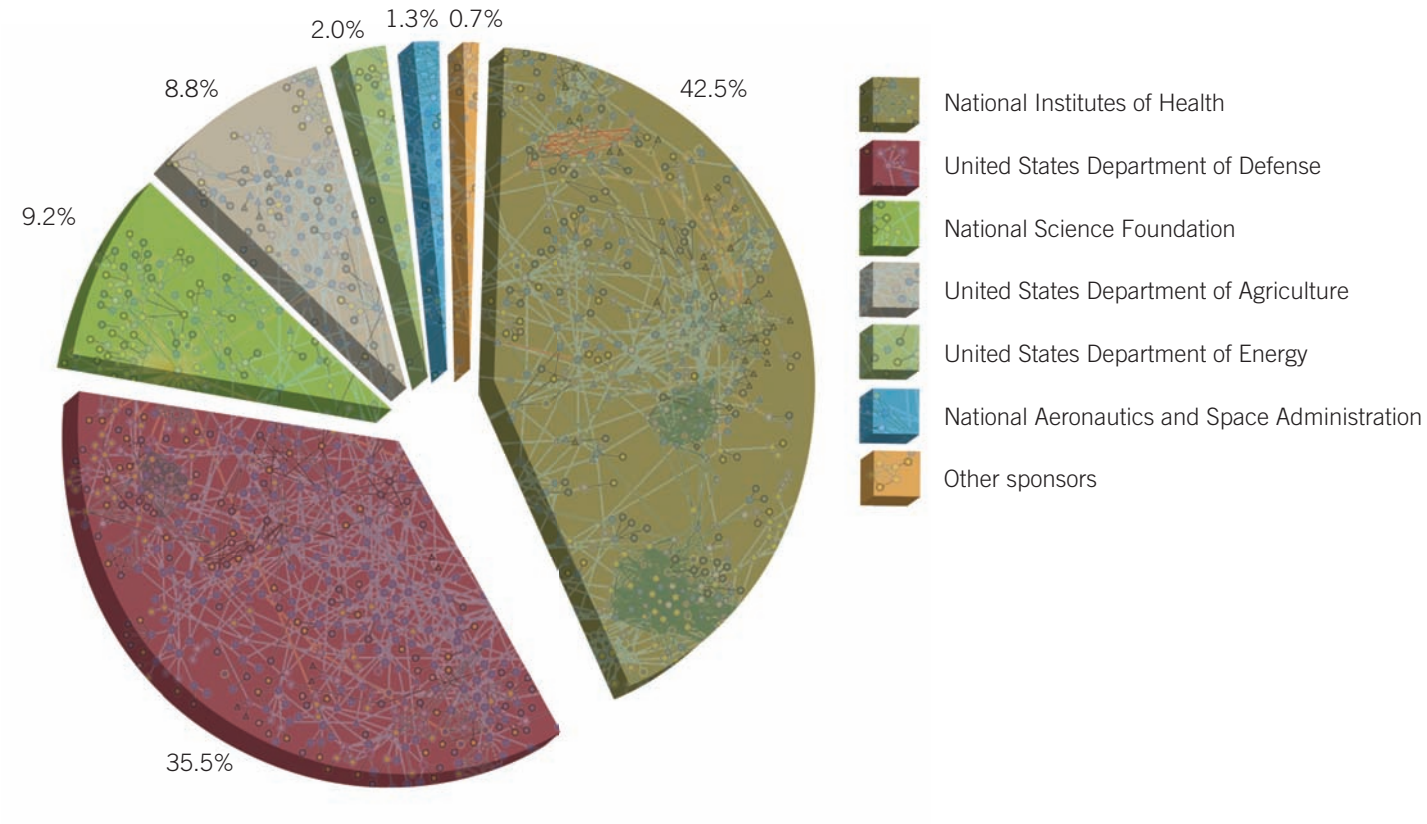
for the year ended June 30, 2008



Awards	FY 2008
National Institutes of Health	$ 33,701,420
United States Department of Defense	31,911,537
National Science Foundation	20,803,650
United States Department of Agriculture	7,020,324
United States Department of Energy	2,780,659
National Aeronautics and Space Administration	595,153
Other sponsors	397,064
Total active awards	$ 97,209,807

2008 Extramural Research Expenses by Sponsor

for the year ended June 30, 2008



Expenses	FY 2008
National Institutes of Health	$ 5,955,766
United States Department of Defense	4,977,507
National Science Foundation	1,286,216
United States Department of Agriculture	1,225,228
United States Department of Energy	278,597
National Aeronautics and Space Administration	184,993
Other sponsors	100,997
Total expenses	$ 14,009,304

Financial Highlights

for the year ended June 30, 2008

Expenses

Total expenses	$ 27,090,119
Total extramural research expenses	$ 14,009,304

Capital assets

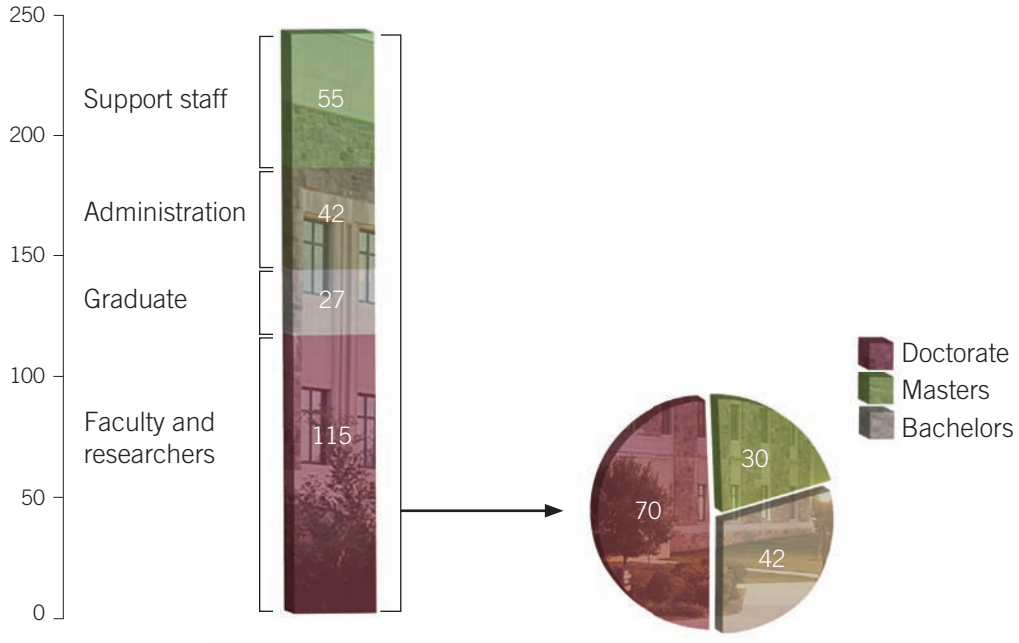
$ 19,452,459

Grants and contracts

Number of awards received	33
Value of awards received	$ 17,827,085
Value of active awards outstanding	$ 97,209,807

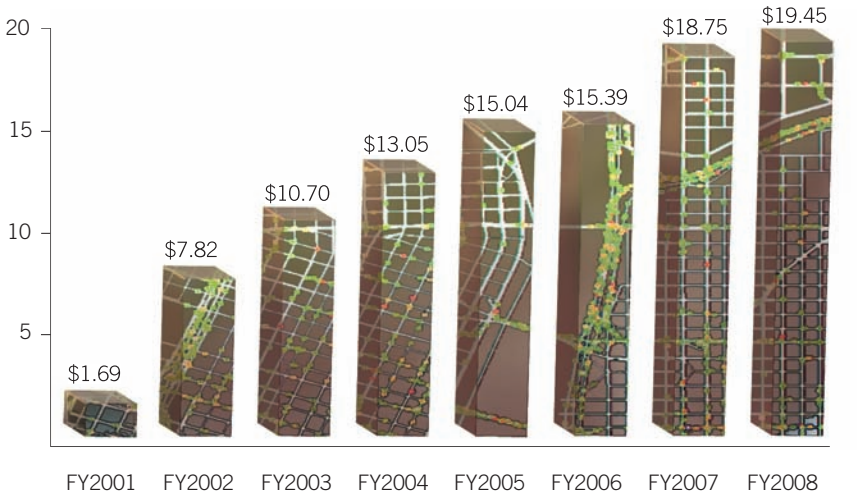
Staff and faculty composition

for the year ended June 30, 2008



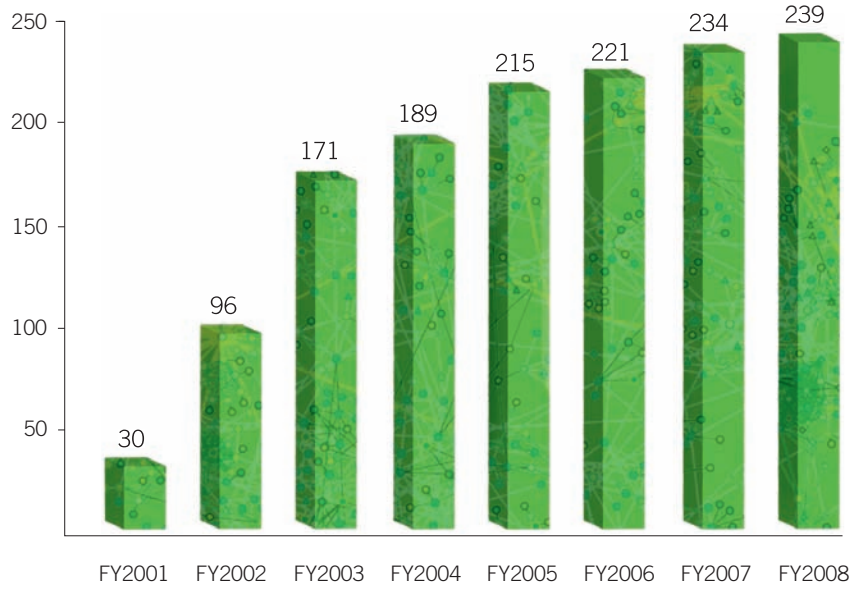
Capital Assets

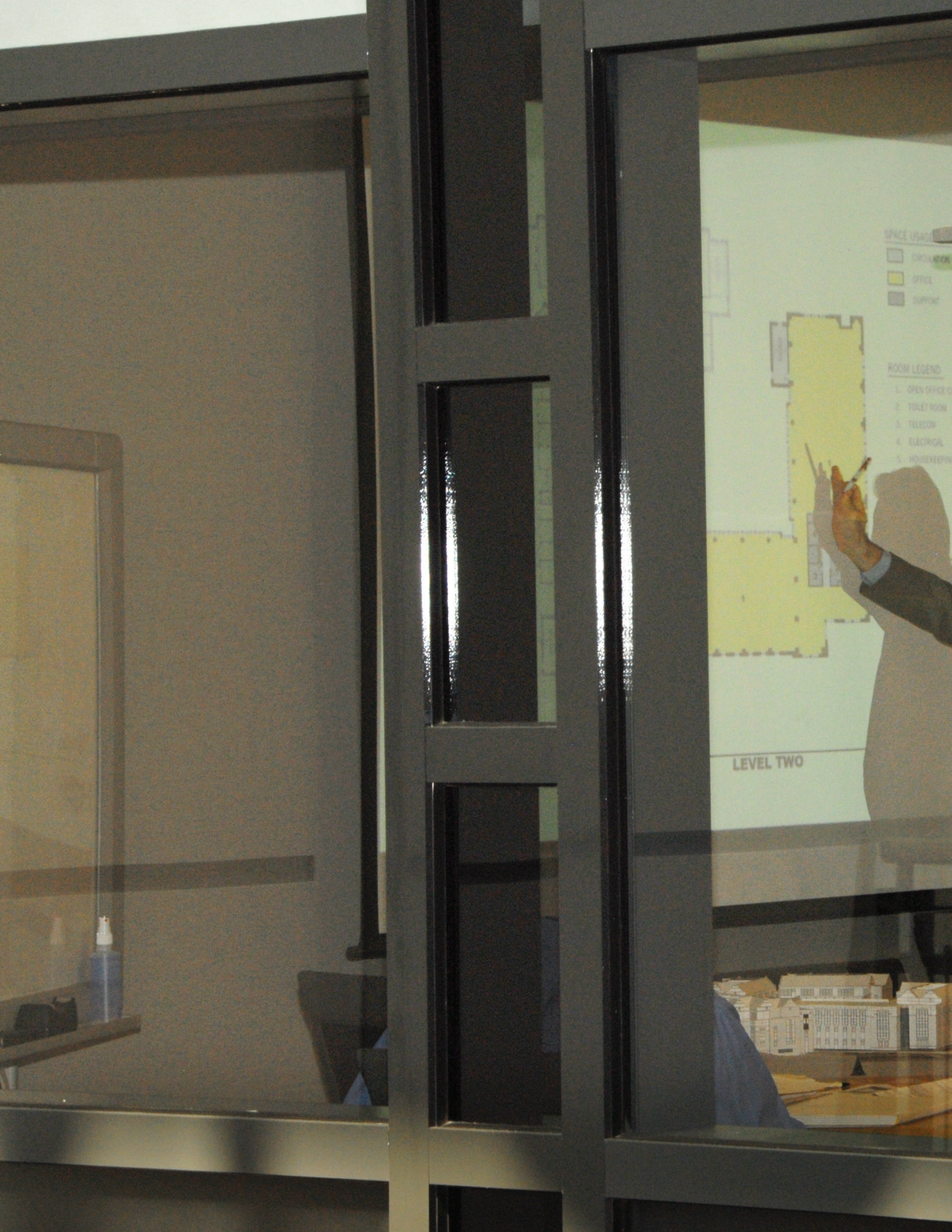
for fiscal years 2001-2008 (all dollars in millions)



Personnel

for fiscal years 2001-2008




SPACE USAGE
ROOM LEGEND
LEVEL TWO

Inventing the Future

- Technology Development
- VBI Research Projects
- Education and Outreach

Organizations must look to the future to ensure a strong position in an ever-changing world. This is especially true in the area of cutting-edge scientific research. VBI's transdisciplinary research environment encourages the development of new technologies, discoveries, and intellectual property that have commercial value and which will benefit future research. In addition, the Institute continues to expand its education and outreach program and strives to effectively prepare the next generation of computational scientists to help solve society's most complex problems. VBI is committed to advancing discovery and innovation in the life sciences for many years to come.

Technology Development

The Virginia Bioinformatics Institute is a research center with a significant critical mass in basic and applied research. The innovation behind this research enables the development of new products, technologies and services. The institute works closely with Virginia Tech Intellectual Properties, Inc. to secure its intellectual property portfolio. In the past year, 31 Invention Disclosures, 5 Provisional Patent Applications, 2 US Utility Applications and 1 International Patent Application were filed (see Table pages 70 and 71).

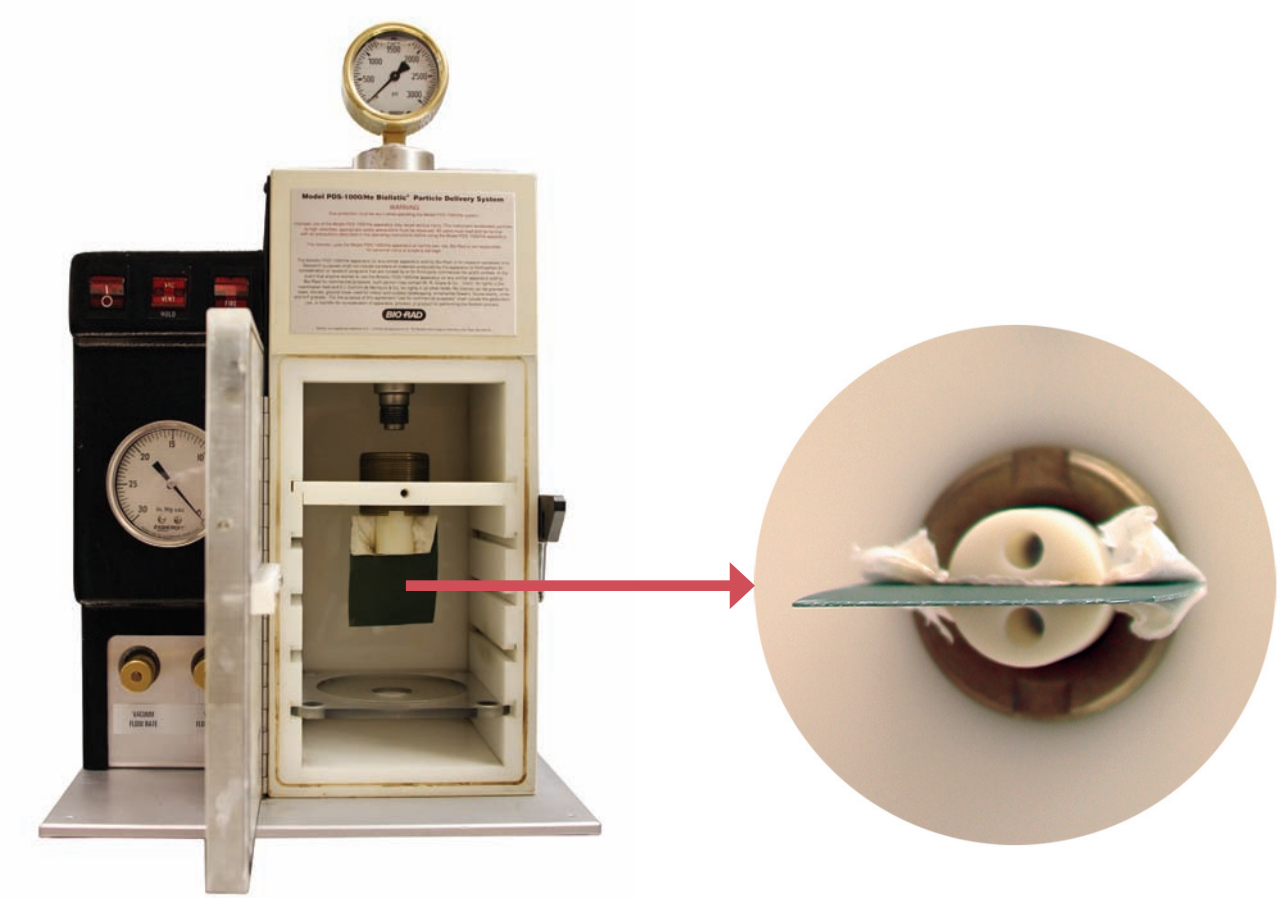
Case study: The DoubleShot Device

For 20 years or more, scientists have used a mechanical device known as a gene gun for the biolistic transformation of living tissue. The gene gun is capable of firing metal particles coated with DNA into plant or animal tissues. In the process, it can allow for the integration of new genes, and the information they code for, into different types of cells. This innovation has been a key technology supporting molecular biology research in laboratories around the globe.

In a new twist to this technology, Shiv Kale, a research assistant at VBI, and Professor Brett Tyler, have invented a new double-barreled device by a simple modification of the conventional gene gun apparatus. DoubleShot is a modification part that fits on a conventional gene gun and allows simultaneous application of control and test DNA from a single shot of helium, the gas used to deliver the projectile into the tissue. This innovation not only saves time but also significantly reduces experimental variation that occurs when successive shots from a single gene gun are used. The use of DoubleShot means that the speed and penetration of the DNA-coated projectiles can be better matched and the precision of the delivery is enhanced due to side-by-side arrival of the particles in the plant tissue.

Kale invented the device when he was an undergraduate in Dr Tyler's research team. The scientists have used the technology to study how virulence proteins from plant pathogens enter their soybean host and allow infection to progress. In 2008, Tyler and his group identified the region of a large family of virulence proteins in oomycete plant pathogens that enable these virulence proteins to enter the cells of their hosts.* The protein region contains the amino acid sequence motifs RXLR and dEER and has the ability to carry the virulence proteins across the membrane that surrounds plant cells. This transport can take place without any additional machinery from the pathogen.

Close-up of the The DoubleShot device attached to the Gene Gun



The DoubleShot device is not just applicable to the delivery of DNA to plant tissues. It is likely to work for biolistic transformation of any tissue or in vitro culture that can be presented as thin layers or monolayers. An additional bonus is that the device allows quantitative comparisons to be made. For example, dose-response titers of gene expression are possible as well as comparisons of a series of mutations to a promoter or gene of interest.

Funding and industry partners are being sought for further development of the DoubleShot device from a prototype to a fully-fledged commercial product. The invention has been disclosed to Virginia Tech Intellectual Properties who have filed a US utility patent application (see Table).

[*] Dou et al (2008) The Plant Cell 20:1930-1947.

The technology development continuum

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

Invention disclosures, provisional patent applications, US utility applications, and international patent applications in the fiscal year ended June 30, 2008, at VBI

VT Disclosure No.	Principal Investigator	Filing Date	Title
Invention Disclosures			
07.076	Scott,Mark (Sobral)	07/02/07	An efficient method for computing all genome subsets which share common oligonucleotide sequences of a fixed length
07.103	Peccoud, Jean	09/17/07	Adaptive 5D optical tracker for closed loop acquisition of gene network dynamics
08.004	Peccoud, Jean	01/04/08	Software for converting DNA sequence into chemical equations representing the gene network encoded in the sequence
08.005	Peccoud, Jean	01/04/08	Software for calibrating genetic parts
08.006	Peccoud, Jean	01/04/08	A calibrated library of genetic parts for *Escherichia coli*
08.007	Peccoud, Jean	01/04/08	A calibrated library of genetic parts for *Saccharomyces cerevisiae*
08.008	Peccoud, Jean	01/04/08	A calibrated library of genetic parts for human cells
08.009	Peccoud, Jean	01/04/08	A calibrated library of genetic parts for *Arabidopsis thaliana*
08.010	Peccoud, Jean	01/04/08	A calibrated library of genetic parts for filamentous fungi
08.011	Peccoud, Jean	01/04/08	A calibrated library of genetic parts for *Bacillus subtilus*
08.012	Peccoud, Jean	01/04/08	A calibrated library of genetic parts for insect cells
08.013	Peccoud, Jean	01/04/08	A calibrated library of genetic parts for *in vitro* expression
08.014	Peccoud, Jean	01/04/08	An automated process to assemble generic constructs derived from standardized genetic parts
08.030	Peccoud, Jean	02/13/08	Design automation of synthetic genetic systems
08.031	Peccoud, Jean	02/13/08	Computer assisted design of aptamers
08.032	Peccoud, Jean	03/19/08	Constrained stochastic optimization algorithm to identify gene network models
08.049	Christopher, Barrett	03/19/08	Complex situation analysis and support system (COSAS)
08.050	Christopher, Barrett	03/19/08	Simfrastructure
08.051	Christopher, Barrett	03/19/08	Wireless network modeling techniques
08.052	Christopher, Barrett	03/19/08	Power/energy market modeling techniques
08.053	Christopher, Barrett	03/19/08	FastDiffuse & Dynamic FastDiffuse methods
08.054	Christopher, Barrett	03/19/08	Sequestration sizing tool
08.055	Christopher, Barrett	03/19/08	EpiSimdemics
08.056	Christopher, Barrett	03/19/08	GaLib
08.057	Christopher, Barrett	03/19/08	Integrated data management tools
08.058	Christopher, Barrett	03/19/08	Simulation of generic markets (Sigma)
08.081	Lawrence, Christopher	05/05/08	Fungal genes for production of small molecule with histone deacetylation (HDAC) inhibition activity
08.090	Lazar, Iuliana; Hoeschele, Ina	05/05/08	Protein differential expression analysis of breast cancer cells
08.091	Mukhopadhyay, Biswarup	05/08/08	Application of coenzyme F-420-dependent sulfite reductase (Fsr) and Fsr containing methanogen in bioprocessing

VT Disclosure No.	Principal Investigator	Filing Date	Title
Invention Disclosures (continued)			
08.094	Bassaganya-Riera, Josep	05/27/08	Method of using nutraceuticals for ameliorating hypertension and vascular inflammation
08.101	Tyler, Brett	05/27/08	Method to block entry of RXLR-dEER motif containing virulence proteins into host cells
United States Provisional Patent Applications			
07.103	Peccoud, Jean	10/10/07	Adaptive 5D optical tracker for closed loop acquisition of gene network dynamics
07.076	Scott, Mark (Sobral)	10/17/07	An efficient method for computing all genome subsets which share common oligonucleotide sequences of a fixed length
08.049	Barrett, Christopher	04/14/08	Complex situation analysis and support system (COSAS)
08.090	Lazar, Iuliana	05/21/08	Methods and compositions for proteomic profiling
08.101	Tyler, Brett	05/19/08	Method to block entry of RXLR-dEER motif containing virulence proteins into host cells
United States Utility Patent Applications			
08.101	Tyler, Brett	06/06/08	Double-Shot: a double barreled device for biolistic transformation of living tissues
07.020	Peccoud, Jean	03/30/08	Software for design and verification of synthetic gene constructs
International Utility Patent Applications			
06.057	Lazar, Iuliana	08/23/07	Microfluidic devices and methods facilitating high-throughput, on chip detection and separation techniques

VBI research projects

https://www.vbi.vt.edu/projects

OMGN
Oomycete Molecular Genetics Research Collaboration Network

Rhizobiales BRC
Rhizobiales Bioinformatics Resource Center

Applied Discrete Mathematics

Dissecting Soybean Resistance to *Phytophthora*

SeedGenes Project
Essential Genes in Arabidopsis Development

Resource Center for Biodefense Proteomics Research

Biochemical Networks Modeling Group

GenoCAD™

Yeast Systems Biology Mathematical Modeling and Yeast Oxidative Stress Project

PATRIC
PathoSystems Resource Integration Center

COPASI
Complex Pathway Simulator

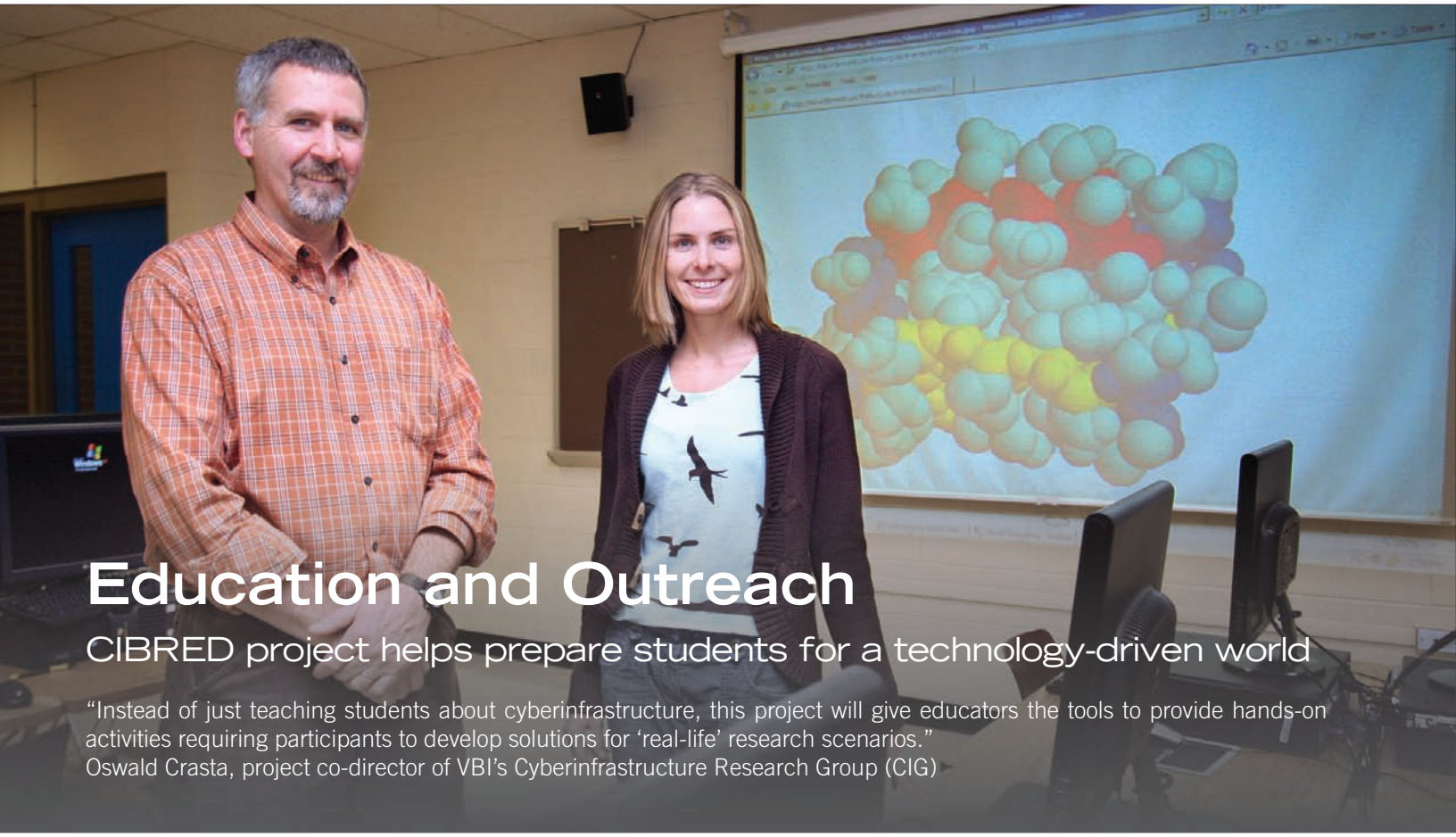
MARCE
The Middle Atlantic Regional Center of Excellence for Biodefense and Emerging Infectious Diseases

PAMGO
Plant-Associated Microbe Gene Ontology

NDSSL
Network Dynamics and Simulation Science Laboratory

VBI MICROBIAL DATABASE

NodMutDB
A Database of Nodule Mutants



Education and Outreach

CIBRED project helps prepare students for a technology-driven world

"Instead of just teaching students about cyberinfrastructure, this project will give educators the tools to provide hands-on activities requiring participants to develop solutions for 'real-life' research scenarios."
Oswald Crasta, project co-director of VBI's Cyberinfrastructure Research Group (CIG)

When Blacksburg High School Principal Michael Hurst was approached with the opportunity to partner with the Virginia Bioinformatics Institute (VBI) at Virginia Tech on a cyberinfrastructure education and outreach project, he immediately began contacting teachers at the school to gauge their interest. Hurst is committed to increasing partnerships with the high school's neighboring university to help strengthen teachers' grant proposal experience, contribute to staff development, and provide additional educational opportunities for students. He used these reasons to persuade Steve Hulburt, head of the school's science department, to join the project.

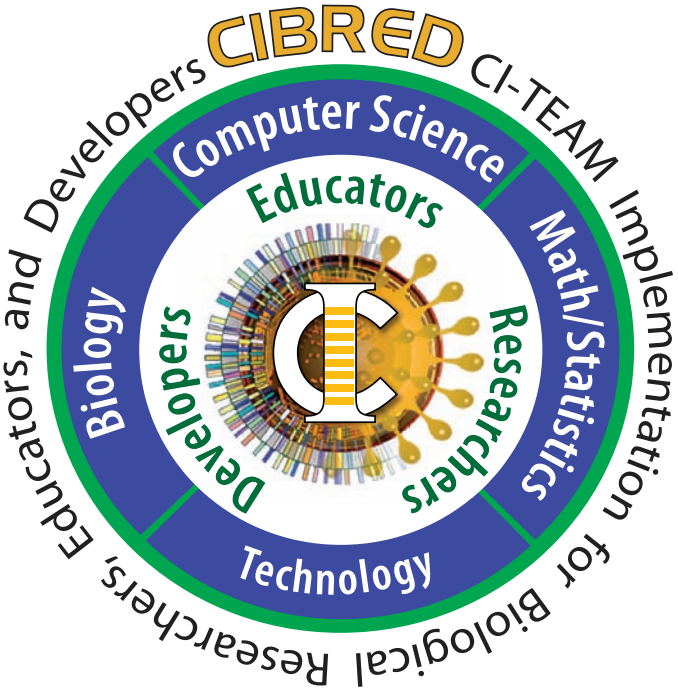
"There was one problem, however," Hulburt explained. "No one really understood what cyberinfrastructure was." Hulburt recruited second-year biology teacher Katie Renga to join him on the project and together they began learning more about cyberinfrastructure and the possible opportunities their involvement in the project could bring to Blacksburg High School and its students. Both teachers visited VBI in June for the first CIBRED collaborator workshop, where they met with other educators involved with the project and learned more about the goals of CIBRED.

Building on a proven model

The project, "CI-TEAM Implementation for Biological Researchers, Educators and Developers" (CIBRED), is designed to expand VBI's education and outreach program in cyberinfrastructure, also known as CI-TEAM (Cyberinfrastructure – Training, Education, Advancement and Mentoring). Cyberinfrastructure, a research environment that combines high performance computational resources with scientific work, has become an important tool for researchers working on projects involving large amounts of data. Supported by a $918,000 grant from the National Science Foundation (NSF) for the years 2008 through 2010, CIBRED has allowed VBI to form collaborations with researchers from different scientific disciplines, as well as high school and college educators from several institutions nationwide, to build an educational program for the next generation of scientific researchers. The scientists and educators involved in CIBRED are creating a collection of educational modules that will help instructors teach students how to use bioinformatics tools to better understand specific scientific problems in an environment that removes the boundaries between different research disciplines. CIBRED will build upon the CI-TEAM Demonstration Project that was developed in collaboration with Galileo Magnet High School and Bluefield State College. The project was funded through a $287,000 grant from NSF in 2006 and 2007.

"The success of the previous demonstration project showed us that this kind of cyberinfrastructure-related coursework is something high schools and colleges want and need for their students," said Oswald Crasta, project co-director of VBI's Cyberinfrastructure Group (CIG) and principal investigator of the CIBRED project. "Our goal is to build on this success with CIBRED. Instead of just teaching students about cyberinfrastructure, this project will give educators the tools to provide hands-on activities requiring participants to develop solutions for 'real-life' research scenarios. These activities will provide students with the information and skills they will need to obtain cutting-edge, technology-oriented careers in the years ahead."

Crasta and CIBRED co-principal investigators Stephen Cammer and Daphne Rainey, also of VBI, are collaborating with educators from National University Research Institute, Hampton University, Howard University, Virginia Tech, and several high schools in Virginia and California, including Hulburt and Renga from Blacksburg High School, to coordinate curriculum design efforts.



A commitment to educational opportunities for students

Hulburt and Renga are hopeful about the possibilities CIBRED will offer their students. They point to increasing funding restrictions for high school science curriculums as a reason why the school's involvement as a partnering institution is so important. The goal of the project is not to create a new course for high schools and colleges, which would require additional financial resources and personnel, but, rather, to design a series of topic-specific modules that complement various subjects. This flexible curriculum can be integrated into different high school and college environments with varying educational requirements.

"We won't be starting a new class," Hulburt explained. "Instead, we are developing modules centered on a specific subject area that can be used in a variety of classes. It's like a virtual packet of lesson plans. Teachers can look at their existing curriculum to see how the modules might fit in."

"These modules will be more extensive and interactive than our usual class activities," Renga added. "This new approach will take traditional class activities a step further, giving the students a specific problem and the tools to find a solution. This integrates a more project-centered approach that follows through an entire process."

One obstacle the teachers foresee, however, involves resources. The high school has only three classrooms with computers, including one mobile classroom, that are shared by all of the school's teachers. The modules being developed for CIBRED require extensive computer work, which means a great deal of planning will be needed to ensure the proper resources are available. Hulburt and Renga hope to use some of the modules during the 2008-2009 academic year as a trial run before fully integrating them into classes the following year, which should help identify any possible scheduling problems. An additional concern is the advanced level of science involved and the extensive amount of work required. Regardless of the challenges, Hulburt and Renga are committed to providing their students with the educational opportunities available through the CIBRED project.

"These modules involve long-term lab work, which requires a major commitment by the students, but we certainly have students that are interested about being involved in this level of science. I know students here are capable of doing this and we see enormous opportunities in leading students toward a more complete understanding of informatics-based science. It will give them an advantage when they enter their first year of college," Hulburt said.

"More than anything, I'm excited about getting the students excited."

VBI's Policy Advisory Board

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

Members of the Board of Visitors

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

Representative from the Tobacco Indemnification and Community Revitalization Commission

Mr. Clarence D. Bryant, III

At-large (Recommended by the University)

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

Ex-officio

Dr. Charles Steger
Dr. Mark McNamee
Dr. Bruno Sobral

Other Senior Staff

Mr. Ralph M. Byers
Ms. Lauren Coble
Ms. Jeanne Forbis
Dr. Chris Barrett
Mr. M. Dwight Shelton, Jr.

Scientific Advisory Board

Members of the Scientific Advisory Board of the Virginia Bioinformatics Institute, which include scientific leaders in high-performance computing, biology, bioinformatics, and nanotechnology/engineering, serve as scientific advisors for the Institute. They provide regular external reviews of research strengths as well as guidance on new strategic scientific initiatives and funding opportunities.

Stephan Bieri, Chair
William J. Feiereisen
William Gelbart
Paul Keim
Richard W. Siegel
Bob Walters