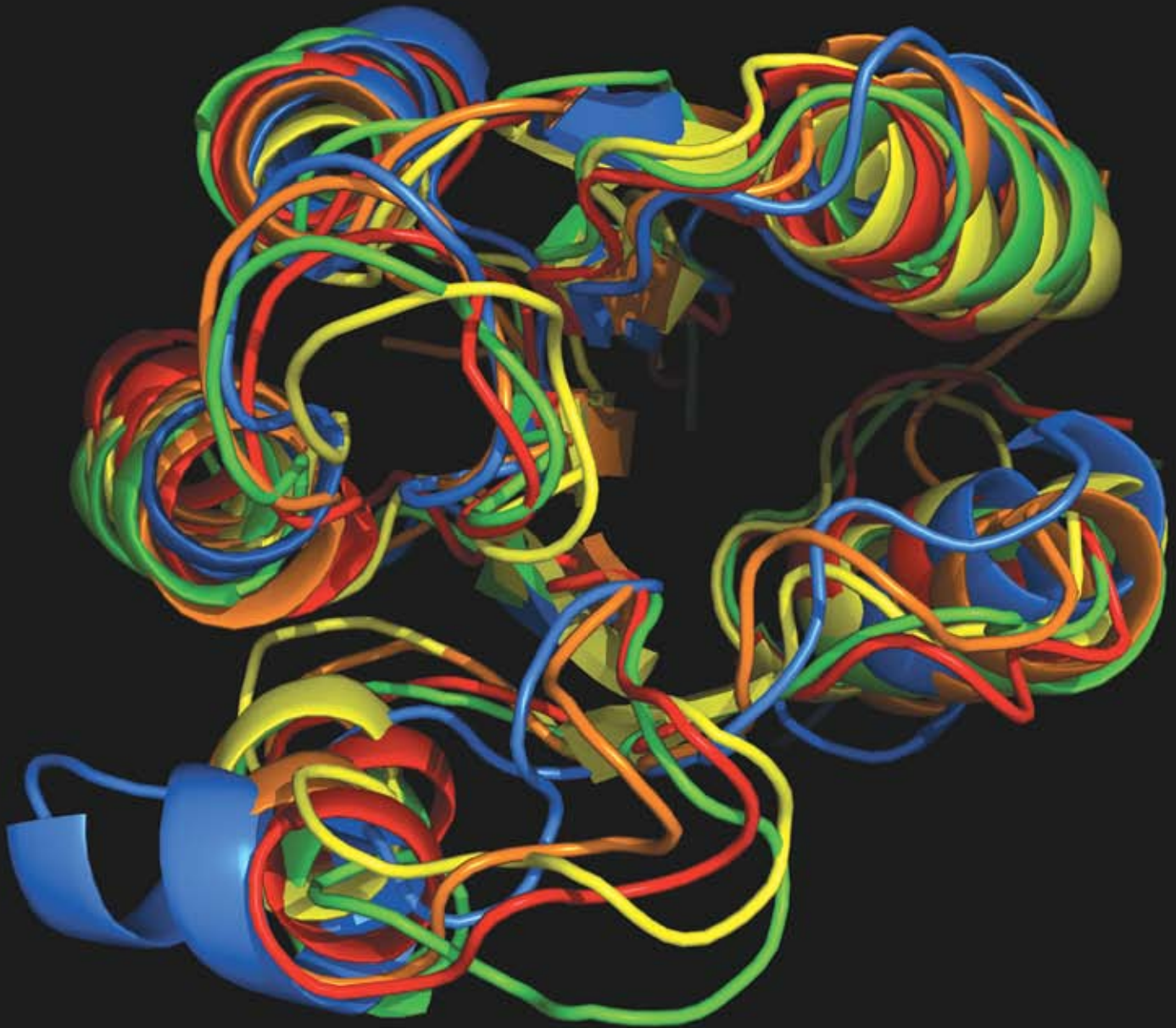


NC STATE UNIVERSITY

Volume VII Number 2  
Summer 2007

# results.

Research and Graduate Studies at North Carolina State University



**SYSTEMS BIOLOGY**  
Insights on the  
Irreducible Sum of the Parts

# results.

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## The Systems Approach: Synergies of Integration and Interaction

**In the beginning, there were biology, chemistry, and physics.** The basic sciences helped answer questions about humans and the world around them for centuries. Then, the discovery of the structure of DNA more than 50 years ago pushed science into the realm of molecular genetics, while the sequencing of the human genome in the past decade opened the door to a slate of “-omics” sciences: proteomics, metabolomics, and transcriptomics. Researchers worked with increasingly smaller bits of nature, hoping to unlock larger secrets about plant and human health, disease, and physical traits.

Out of a fear that science was losing the forest for the trees, a new movement has sprung up in recent years to reintegrate the “-omics” sciences into a more holistic approach so researchers can get a better picture of living organisms and how they operate. The effort, known as *systems biology*, studies the interactions of molecular and cellular components, using experiments and mathematical models to determine how they impact an overall organism and its function. The field is so new and is evolving so quickly that few people can agree on exactly what “systems biology” means.

### “It’s not a science; it’s a process.”

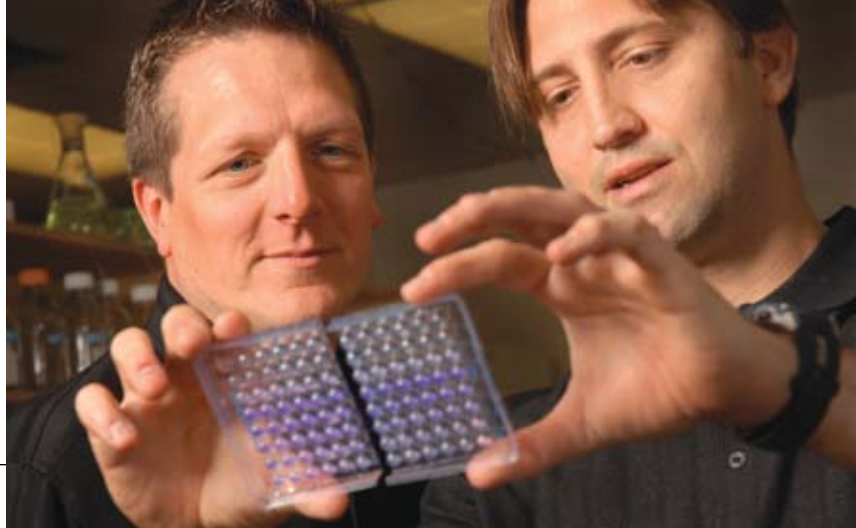
Dr. John Cavanagh, a biochemistry professor who has proposed a Center for Systems Biology at NC State, compares it to an automobile. Scientists have been doing the equivalent of studying the exhaust system or the drive train or the engine by themselves. A systems approach would consolidate the efforts so they could see how changes in one area affect the others as they try to optimize overall performance. “It’s not a science; it’s a process of looking at the sum of the parts,” Cavanagh says. “We use all of our tools and arrange the modules as needed to examine a problem.”

The interdisciplinary, applied nature of systems biology fits well with NC State’s strengths, Vice Chancellor of Research and Graduate Studies John Gilligan says. With a solid reputation in life sciences and engineering—looking at a system instead of individual parts is an established practice in engineering—and decades of experience in solving real-world problems, the University is well positioned to become an early leader in the field, Gilligan says. “Systems biology is very engineering-oriented, and because people from different disciplines are working together, it offers a bigger view of the world than single-investigator projects.”

This issue of RESULTS showcases the projects of several systems biology teams at NC State, as well as individual scientists working with government laboratories and other universities.

**On the cover:** Overlay of NMR structures of mutant response regulator proteins involved in bacterial protection. Such comparative structural and dynamics studies allow systems biology teams to delineate critical intra-protein communication pathways that link protein regions over large distances and provide targets for therapeutic intervention. Illustration courtesy of laboratory of Dr. John Cavanagh, NC State University.

# Fishing for Superbug and Seafood Safety



Drs. John Cavanagh and Christian Melander analyze results of an anti-biofilm screening test.

If you have been avoiding shellfish since that brutal attack of gastroenteritis after eating oysters on the halfshell, you may be assuming you are allergic to the tasty delicacies. More likely, you experienced an attack of *Vibrio parahaemolyticus*, a bacterial infection that is the leading cause of seafood gastroenteritis in the U.S. Alternatively, it may have been its cousin, *Vibrio vulnificus*, which causes severe septicemia, has a hospitalization rate of 91%, and is responsible for 95% of U.S. seafood deaths.

“These compounds appear to be effective against not only *Vibrio*, but also several other drug- and immunity-resistant bacteria.”

*Vibrio* species in the U.S. cause a minimum of 41,000 illnesses yearly, increasing during natural disasters involving flooding. Following Hurricane Katrina, 17 cases of *Vibrio vulnificus* were seen—five of them fatal.

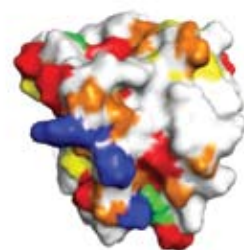
Dr. John Cavanagh, professor of molecular and structural biochemistry, and Dr. Christian Melander, assistant professor of chemistry, are leading a project taking a systems biology approach to stopping *Vibrio* infections. “The project’s strengths come from integrating high-throughput comparative genomics methods, state-of-the-art structural biology, computational studies, and drug design strategies,” says Cavanagh. Comparative genomics efforts at the National Oceanic and Atmospheric Administration’s Hollings Marine Laboratory will provide information about which gene signal pathways are responsible for *Vibrio* virulence,

persistence, and adaptability. Cavanagh’s structural biology studies will then examine those pathways in detail, providing therapeutic targets for Melander’s team of drug synthetic chemists to exploit.

The virulence and persistence of *Vibrio* are due to its ability to form biofilms—communities of bacteria that respond differently than a single bacterium to ensure survival in hostile and shifting environments. In the biofilm form, *Vibrio* can be up to 10,000 times more resistant to antibiotics, as well as inherently resistant to immune response.

Melander’s research group has discovered a class of chemical compounds that inhibit biofilm formation. “These compounds appear to be effective against not only *Vibrio*, but also several other drug- and immunity-resistant bacteria,” says Melander. Such “superbugs” include: *Haemophilus influenzae* (ear, eye, and respiratory tract infections); *Bordetella pertussis* (whooping cough); *Acinetobacter baumannii* (frequently found in hospitals, infecting patients through open wounds, catheters, and breathing tubes); and *Pseudomonas aeruginosa* (opportunistic infections of immuno-compromised individuals, including cancer and cystic fibrosis patients).

Melander and Cavanagh have a patent pending on the compounds and their uses, and have incorporated Agile Sciences, Inc. With angel investor backing, the start-up company will further develop the product, recruit drug company partners, and advance products to clinical trials. The eventual products will treat surfaces where the target bacteria lurk, including hospitals, medical devices, ships, seafood processing equipment—and maybe even that oyster bar you’ve been avoiding.

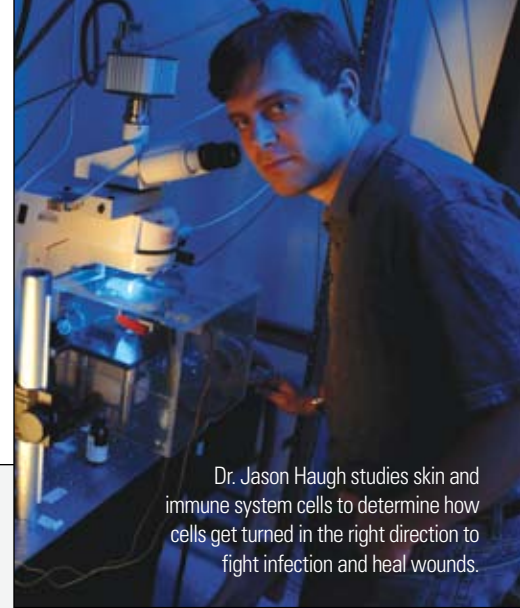


*Vibrio* bacteria



Gram staining protocol showing amount of biofilms remaining after treating with antibiofilm compounds. Light purple color in lower right indicates almost total elimination of biofilm.

# Unlocking Cell Migration



Dr. Jason Haugh studies skin and immune system cells to determine how cells get turned in the right direction to fight infection and heal wounds.

**When someone is injured or sick**, the body springs into action, clotting blood, and fighting infection. These protection mechanisms involve a flurry of activity within the body. Chemical signals are sent through nerves and other cells like a 911 call to warn of a problem. Platelets and white blood cells then act as first responders, migrating to the wound or source of the infection to handle the emergency.

Scientists understand the signaling part of the process but are trying to get a better handle on the cell migration part. So the National Institute of General Medical Studies has funded a 10-year, \$80 million effort known as the Cell Migration Consortium (CMC) to study cell movement through a systems biology approach. "In almost any physiological process, cells have to get from one place to another," says Dr. Jason Haugh, an associate professor in the Department of Chemical and Biomolecular Engineering. Haugh is designing computer models for CMC to determine how cells organize themselves to begin their journeys.

When a cell receives a signal that it's time to go, it assumes a polarity, Haugh says. One region of the cell takes the lead, and the rest follows behind in an almost inchworm-like motion. In his simulations, Haugh is studying skin cells known as fibroblasts, as well as cells involved in the immune response, all of which play important roles in wound healing. A video of a fibroblast experiment and the corresponding simulation show the cell lighting up with fluorescence as enzymes inside are activated by chemical receptors picking up the warning signals being sent through the body. "Without a signal to direct the cell, it migrates slowly and follows a random path," he says. "That is an ineffective strategy if the cell is to arrive at a specific location."

Haugh is studying pathways in the cell that he thinks are responsible for establishing polarity. But he says more research is needed to learn how a cell establishes its front and back ends. "The right combination of molecular

components is needed to form a new leading edge, and these molecules interact dynamically with respect to location and time," he says. Other members of the CMC research team will build on Haugh's findings as they study how cells gain traction and momentum in their movement. "All sorts of physical forces are in play, as well as the biochemistry regulating it," he says. "It's a complex problem that we're trying to approach from different angles."

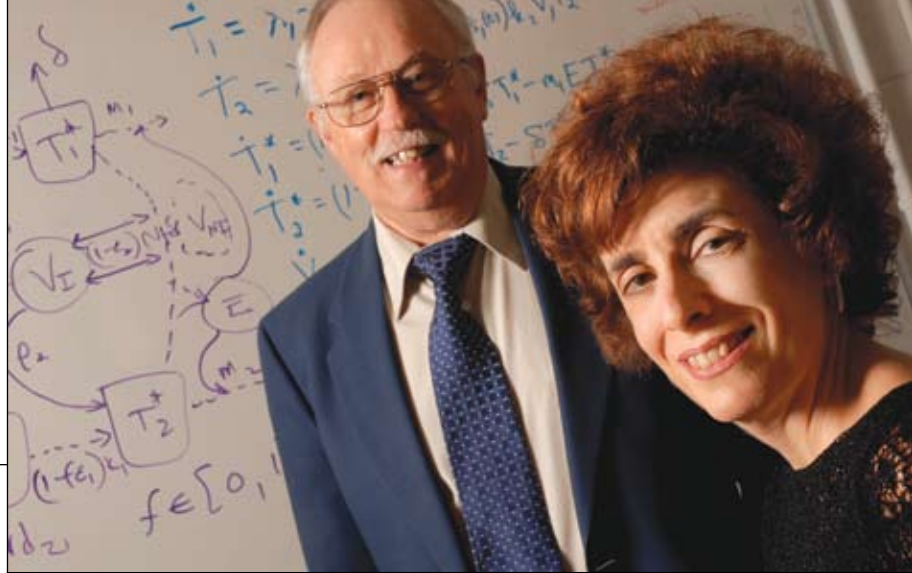


Mouse fibroblasts light up with green fluorescence as they respond to the presence of platelet-derived growth factor (red).

“When a cell receives a signal that it’s time to move, it assumes a polarity. One area takes the lead, and the rest follows behind in an almost inchworm-like motion.”



# New Math for HIV Patients



## After years of being viewed as a certain death

sentence, the human immunodeficiency virus (HIV) is now considered a chronic health problem that can be managed with medication. But the virus' ability to mutate and become resistant to drugs makes charting a course of treatment tricky, so physicians disagree on the benefit of early and continuous intervention.

To determine how best to treat patients whose HIV has been diagnosed early, Drexel Professor of Mathematics H. Thomas Banks and William Neal Reynolds Professor of Statistics Marie Davidian have developed a model to predict how the virus progresses in people. "The model shows numerically the battle raging within people between the virus and their immune systems," Davidian says. After infection, most HIV patients achieve a natural plateau at which their bodies control the amount of virus in their systems. Those with higher plateaus develop AIDS quickly, while those with low viral loads can live for years without the disease. That has led some physicians to advocate "drug holidays" for patients. Pulling patients off treatment from time to time would give them a break from the physical and financial cost of taking a mix of antiviral drugs, Banks says. Yet, others maintain fighting HIV early and often is the best way to control the virus.

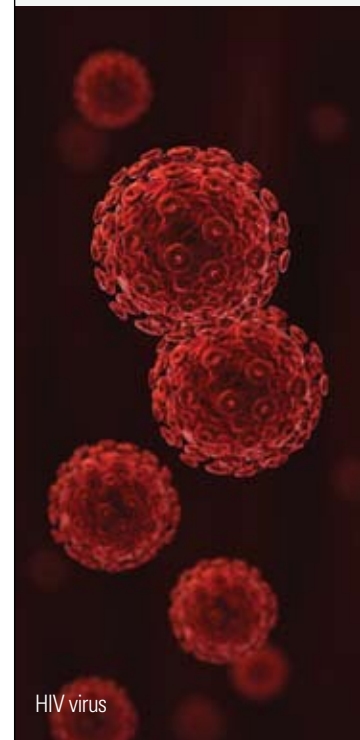
"More precise targeting of populations and treatments has the promise to produce improved drugs and more effective uses."

Banks and Davidian validated the model—a series of differential equations involving parameters to describe

"The model shows numerically the battle raging within people between the virus and their immune systems."

the disease—using five years of data from scores of HIV patients at Massachusetts General Hospital in Boston. They then created a probability distribution for the parameters to characterize how various populations react to infections and to treatment cycles that begin and end at different intervals. "This model has sophisticated math and sophisticated statistics," Banks says. "Neither would have worked without the other."

With a \$3.5 million grant from the National Institute of Allergy and Infectious Disease, the College of Physical and Mathematical Sciences professors have teamed with Mass General on a four-year clinical trial. With a systems approach, the model determined three treatment cycles to study. Some HIV patients will receive no medication, while others will stop taking their drugs after three or eight months. Data will be collected during the trial, scheduled to start this fall, to refine the model. The goal, Davidian says, is to get as close to personalized medical treatment as possible. An even larger aim is to change the way drug trials are run, Banks says. "Mathematical models are a useful tool to design clinical trials," he says. "More precise targeting of populations and treatments has the promise to produce improved drugs and more effective uses."



HIV virus

# The Buzz on Nature and Nurture



Forty strains of *Drosophila melanogaster* have been inbred to produce genetically identical insects for research. (Photo courtesy of Richard Lyman)

**Inside a lab in Gardner Hall**, they are getting drunk, beating up on one another, and getting poked in the eyes. It's not an instance of out-of-control students, only scores of fruit flies taking part in an international genetics research effort. NC State's Drs. Trudy Mackay and Robert Anholt are teaming with the Baylor University College of Medicine and scientists in a half-dozen foreign countries in a systems approach to determine how physical and behavioral traits are effected by genes and the environment.

Mackay is the William Neal Reynolds Distinguished Professor and Distinguished University Professor of Genetics. She is also the 2007 winner of the O. Max Gardner Award, the UNC Board of Governors' highest faculty honor. Anholt is a professor of zoology and genetics, and the director of the W. M. Keck Center for Behavioral Biology.

Mackay spent a year inbreeding 40 strains of *Drosophila melanogaster* captured at the State Farmers Market in Raleigh. Twenty generations later, the insects in each line are genetically identical, allowing scientists to note any variation in traits caused by environmental differences. Once the genome of each strain is sequenced at Baylor, researchers will be able to look at how genetic differences are expressed. "We're interested in the traits in and of themselves," Mackay says. "We want to see how genes work together. We don't know how many genes affect each complex trait."



Drs. Trudy Mackay and Robert Anholt hope to use findings from studies on fruit flies to determine the genetic basis for human physical and behavioral traits.

“This could open up a new view for looking at population variation and help achieve the goal of individualized medicine.”

Because the same genes are recognizable across species, scientists hope to correlate their findings to humans. “We can accumulate large amounts of data quickly using flies,” Anholt says, “and it’s statistically valid since we are able to control their environment and genetic background.” Already, the husband and wife researchers in the College of Agriculture and Life Sciences have measured how quickly different fruit fly strains become intoxicated on ethanol vapors to zero in on a few genes that seem to form a metabolic pathway related to alcohol sensitivity. They are translating their results from flies to humans by using longitudinal data collected on 1,700 participants in the 60-year-old Framingham Heart Study.

Similarly, Mackay and Anholt are studying the genetic basis of aggressive behavior in the flies by observing how they fight over food. They also have developed a fly model for ocular hypertension—a common risk factor for glaucoma—and are checking the insects’ olfactory function. Using the same fruit fly lines, their international partners are studying traits like development and learning and memory. As the studies progress, the researchers will move beyond genes into protein and metabolic impacts on traits. “This could open up a new view for looking at population variation,” Mackay says, “and help achieve the goal of individualized medicine.”

# Stacking the Systems Bio Building Blocks



**From Polk Hall on NC State's main campus** to a biotechnology research campus being sculpted in the clay of Cabarrus County, University administrators are building toward the future with an eye on the growth of systems biology research.

The Structural and Integrative Biosciences Laboratory (SIBL), expected to open in October 2007, is part of a \$15 million overhaul of Polk Hall. The lab will be equipped so students can attack complex problems, such as cancer or Alzheimer's, using a variety of sciences, from chemistry to molecular biology to genetics. "In the past, we've taken a very reductionist approach to teaching science, with everyone focused on his or her own discipline. But science doesn't work like that in the real world," says Dr. John Cavanagh, a biochemistry professor and SIBL director. Faculty from different science departments will work with students in SIBL, but the students will spend most of their time as teams in the lab. "We're teaching process, not fundamentals," Cavanagh says. "They don't need to be experts in everything, but they need to understand the connections between chemistry and biology and biology and physics and be able to work across disciplines to see how components interact."

That interdisciplinary philosophy is also in play on the North Carolina Research Campus in Kannapolis. The \$1 billion project will combine the research talents of NC State and six other North Carolina universities to improve the nutritional value of produce from the field to the table. "Rather than working with a few plant breeders, we're taking a systems approach," says Dr. Steven Leath, associate dean for research in the College of Agriculture and Life Sciences. "We'll have plant biologists working with genetics folks and biochemists

working with people in food science." Researchers from other universities will work with NC State's Institute of Advanced Fruit and Vegetable Science, providing input on human health, nutrition enhancements, and food processing and packaging.

**"We will have the critical mass needed to tackle a systems biology approach because we'll have the strengths of several universities and the best equipment in the world in one location."**

The 350-acre campus, the brainchild of Dole Food Company, Inc., owner David Murdock, will feature state-of-the-art technology, such as a 950-megahertz nuclear magnetic resonance imager—the world's largest—for studying complex proteins. Thirteen NC State faculty members will be based in Kannapolis, while short-term housing on site will allow other researchers to commute from Raleigh to take advantage of the scientific equipment and participate in projects. "We will have the critical mass needed to tackle a systems biology approach," Leath says, "because we'll have the strengths of several universities and the best equipment in the world in one location."

Addition to Polk Hall (above) will include the Structural and Integrative Biosciences Laboratory when renovations are completed this fall.



Rendering of NC State's Institute for Advanced Fruit and Vegetable Science at the North Carolina Research Campus in Kannapolis, NC.



Dr. Steven Leath examines designs for NC State's 45,000-square-foot greenhouse/headhouse complex (left) to be built in Kannapolis.



# Hens' Histories Hint at Ovarian Cancer Biomarker



Blood work collected by Dr. Jim Pettite from scores of hens gives scientists a look at physiological changes as they develop ovarian cancer.

**Rather than ponder the ages-old question** of the chicken and the egg, a group of NC State researchers is using egg-laying chickens and systems biology to answer a more pressing issue: What comes first, ovarian cancer or detectable physiological changes related to the cancer?

“If we can find a true biomarker, we will be able to save countless lives.”



Ovarian cancer is particularly deadly, with less than half of the women contracting it surviving five years. “It’s such a horrible disease, and it’s usually diagnosed too late,” says Dr. Jon Horowitz, associate professor of molecular biomedical sciences in the College of Veterinary Medicine (CVM). The belated diagnosis means scientists don’t know if there are any telltale signs, or biomarkers, in a woman’s physiology that could serve as an early warning, similar to the increase in prostate-specific antigen (PSA) in men that signals the potential for prostate cancer.

Researchers at the Mayo Clinic in Minnesota began collecting blood samples from every female patient several years ago and have, over time, amassed more than 100 samples from women with early-stage ovarian cancer. But the samples provide only a single snapshot for each woman, says Dr. Dave Muddiman, who formerly worked at the Mayo Clinic and now heads up the W.M. Keck FT-ICR Mass Spectrometry Laboratory in the College of Physical and Mathematical Sciences at NC State. That makes it difficult to identify any potential biomarkers.

Through the CVM’s Center for Comparative Medicine and Translational Research, which links human and animal research efforts across NC State, Muddiman joined forces with Horowitz and poultry science professors Jim

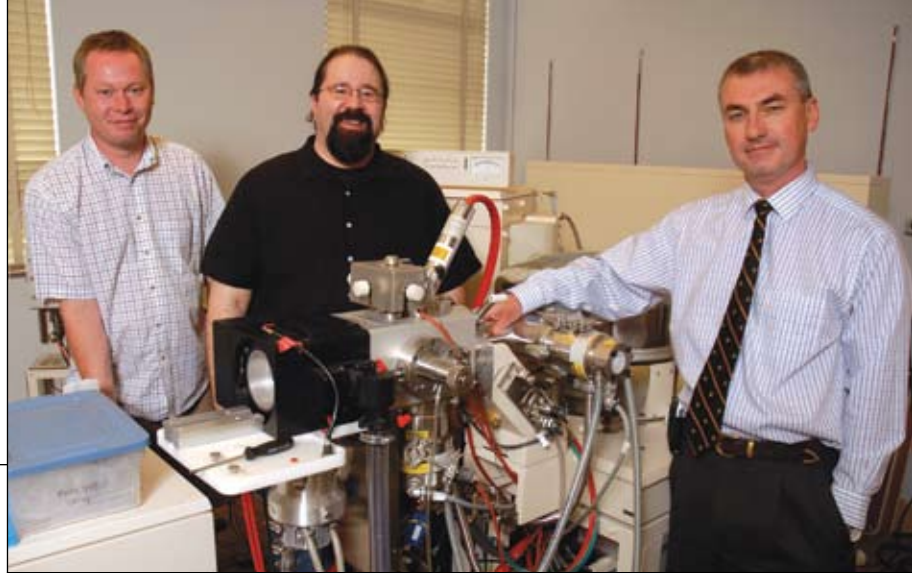
Pettite, Paul Mozdziak, and Ken Anderson. Because 10 to 25 percent of hens develop ovarian cancer after about two years of steady egg production, the poultry science group has collected blood samples and other data on about 250 hens before and after their cancers. That data can be beneficial to studying human cancer, Pettite says, because of similarities between chicken and human cells. “We have what amounts to a medical history on these hens,” Muddiman says, “We can see how their systems changed over time.”

Muddiman’s research team is running extensive tests on the hen blood samples to catalog molecular changes. Once they find some potential targets, Horowitz will conduct a more in-depth protein and genetic analysis. He will also compare the findings with the human samples at the Mayo Clinic to see if a common biomarker can be found. “We have to figure out which molecular changes are real and which are red herrings,” he says. “If we can find a true biomarker, we will be able to save countless lives.”



At right, Drs. Dave Muddiman (left) and Jon Horowitz will conduct an in-depth analysis of the hen blood samples for clues that could lead to a diagnostic test for ovarian cancer.

# Rooting Out Nematodes



**Nematodes are pretty sneaky.** The parasitic worms destroy about \$100 billion in crops worldwide every year, but many of them do their damage only after somehow conning their way into plant root systems. So a multidisciplinary group of NC State researchers is using various approaches to outsmart nematodes, learning how they find their way inside plants and, more importantly, how to slam the door on them for good.

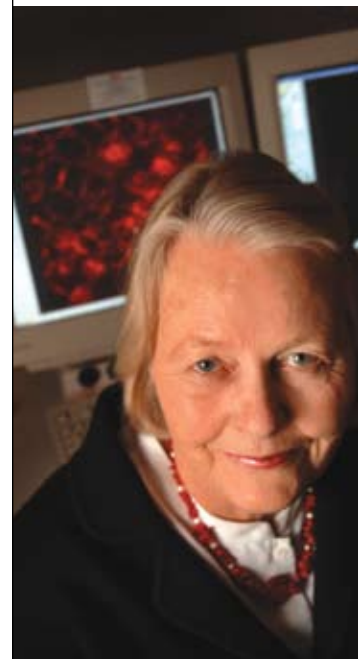
To get a better idea of how to attack nematodes, plant pathology professors David Bird and Charles Opperman, co-directors of the Center for the Biology of Nematode Parasitism in the College of Agriculture and Life Sciences, have been sequencing its genome for several years. But it was a bit of serendipity that unlocked the secret of the nematode's trickery. Plant biology professor Nina Allen's research team was working on another project when they noticed plant root hairs behaving the same way around nematodes as they do with Nodulation factor, signal molecules produced by beneficial bacteria that help plants take in nutrients. Roots and bacteria swap chemical signals through the soil so they can find each other, so Allen and Bird surmised that nematodes must have the ability to not only sense the signal from the roots, but also secrete their own chemical signal to fake out the plants and gain access to the roots.

Knowing the chemical composition of Nod factor, Bird enlisted the help of Dr. Nigel Deighton, director of NC State's Metabolomics and Proteomics Lab, to use a mass spectrometer to isolate a similar molecule in nematodes. "Instead of having me look for a needle in a haystack, they've given me a pin and said to find something that looks like it," Deighton says. Likewise, Dr. Michael B. Goshe, an assistant professor of biochemistry, is using mass spectrometry to examine the protein changes within a nematode when it reacts to plants. "They really wake up when they sense plants are near," Goshe says. "It's like they've had a cup of coffee."

"There are so many interactions going on between the plant and the nematode. It's a true systems ecology within which we're trying to work."

Attacking the nematode problem on a molecular, genetic, and proteomic level is producing reams of data, so Dr. Dahlia Nielsen of the Bioinformatics Research Center is crunching those numbers. In addition to helping the team find ways to shut the nematodes down, she hopes to find metabolic pathways that could be used to make plants resistant to the parasites. "There are so many interactions going on between the plant and the nematode," Allen says. "It's a true systems ecology within which we're trying to work."

Drs. Nigel Deighton, Michael Goshe, and David Bird (l.to r.) are studying nematodes on genetic, molecular, and proteomic levels to find the best way to control the parasitic worms.



Imaging by Dr. Nina Allen's research team unlocked a clue to the success of a nematode (diagram at left) at infiltrating plant roots.



# Breeding Better Biofuels

**Nature's design for trees works perfectly for** photosynthesis, but not so well for biofuel production. The same stiffness in the wood cells that allows a tree to stand tall and catch as much sunlight as possible means extra processing steps to convert wood into ethanol—steps that add both cost and environmental risk. So Drs. Vincent Chiang and Ron Sederoff, co-directors of the Forest Biotechnology Group in the College of Natural Resources, are using a combination of genomics, bioinformatics, and biochemistry to design trees that are green in more ways than one.

“We really don't need to create a strong tree for fuel as long as the tree can survive.”

Lignin, the glue-like polymer that makes wood stiff and strong, is the main obstacle to biofuel processing since, unlike the cellulose in wood, it doesn't break down easily. Chemical pretreatments can filter out lignin, but they leave processors with a messy cleanup problem. Chiang studied the problem for two decades—first for the paper industry and now for the Department of Energy—and has identified the genes that control lignin production in fast-growing poplar trees. By manipulating these genes, he can produce poplars with up to 50 percent less lignin. Chiang says a 10 to 20 percent reduction would be an appropriate balance for producing biofuel without harming the tree. “We really don't need to create a strong tree for fuel as long as the tree can survive.”

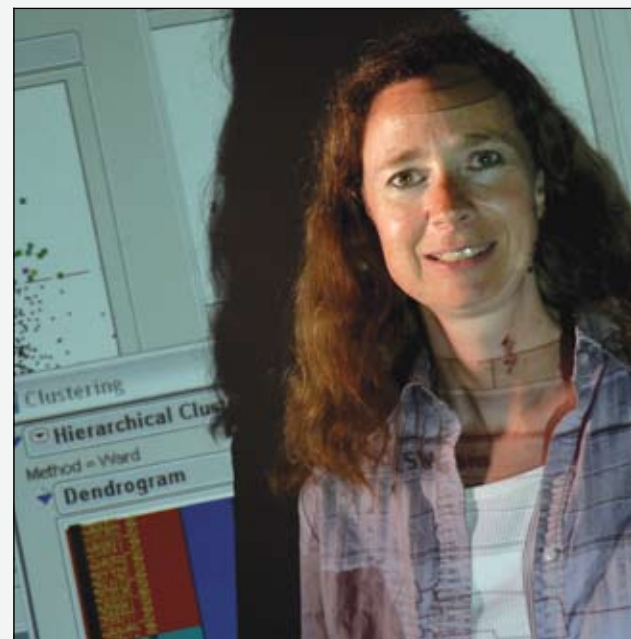
But consistently achieving that perfect blend of lignin and cellulose is a trickier matter. The Forest Biotechnology Group is experimenting with other genes, proteins, and metabolic pathways to learn more about how wood is



Drs. Ron Sederoff (left) and Vincent Chiang are devising ways to alter the production of lignin in poplar trees to make biofuel processing easier.

formed and, in turn, how to get a better handle on lignin. “There's a system of things regulating each other,” Sederoff says. “We're looking at processes in a context larger than simple gene expression.” Rather than limit the lignin production, one such effort would change the chemical composition of the lignin that trees produce to make it easier to decompose.

Chiang and Sederoff are coordinating their research with Dr. Hou-min Chang of the Department of Wood & Paper Science to ensure the trees they're creating work for biofuel production. They also have enlisted Dr. Dahlia Nielsen of the Bioinformatics Research Center to use their data to develop quantitative methods for breeding easily processed poplars. “Tree breeders don't look at just one tree; they look at thousands,” Sederoff says. “We need to be able to harvest enough modified trees to make an impact in bioenergy.”



Dr. Dahlia Nielsen (right) analyzes the data produced by numerous research projects to develop quantitative methods for finding solutions.



# Genes May Imprint Birth Stats



Dr. Jorge Piedrahita and CVM Assistant Research Scientist Lauren Gast discuss their research efforts.

**While cloning cows at Texas A&M** several years ago, Dr. Jorge Piedrahita noticed that very few of the cloned animals could later reproduce. Cloning somehow disrupts the normal development of the placenta, says Piedrahita, now a professor of molecular biomedical sciences at NC State's College of Veterinary Medicine. That discovery spawned his fascination with placental function and the critical role a tiny subset of genes, called *imprinted genes*, plays in animal and human development.

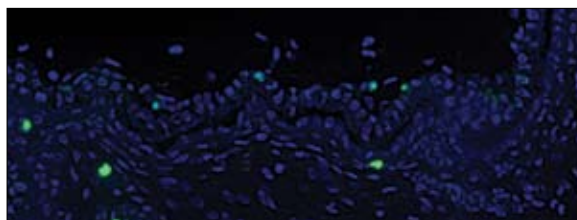
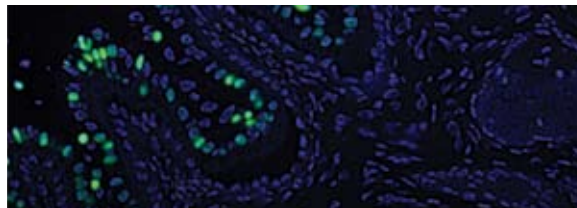
Researchers have identified fewer than 100 imprinted genes in humans, but they have been implicated in a range of illnesses, from diabetes to Alzheimer's to alcoholism.

Found only in placental mammals, imprinted genes are expressed differently in the paternal and maternal DNA handed down to offspring. Also, unlike other genes that rely mostly on the DNA sequence to function, they are regulated by conformation, or how tightly packed the genetic material is within cells. Researchers have identified fewer than 100 imprinted genes in humans, but they have been implicated in a range of illnesses, from diabetes to Alzheimer's to alcoholism.

As part of a five-year National Institutes of Health grant, Piedrahita is working with OB-GYNs at Duke University Medical Center to monitor women during at-risk pregnancies and collect samples from their placentas after birth for study. Babies whose birth weight is in the eighth percentile or lower have been shown to be at higher risk for diseases as

adults. So he is conducting genomic analyses on the tissue samples, while Dr. Dahlia Nielsen in the Bioinformatics Research Center does a quantitative study to correlate imprinted genes, clinical data from the mother during pregnancy—factors like age, diet and exposure to chemicals—and fetal development and birth weight. "You have to go beyond the genes responsible for growth to a systems focus because the effects of imprinted genes are so complex," Piedrahita says. "Too many factors can cause a baby to be small. You can't just say, 'This is it.'"

In animals, imprinted genes may affect the size of litters. Working with the USDA Meat and Animal Research Center, Piedrahita is providing a genetic analysis of placentas in two breeds of pigs. He has determined that a key metabolic pathway is regulated differently in the placentas of an Asian breed and a commercial breed. That allows the Asian breed to produce 14 to 16 piglets in a litter, compared to 9 to 12 for the commercial breed. But he still is figuring out how imprinted genes regulate that pathway. "These genes play such an important role in human disease and agriculture production," he says, "They will provide a research challenge for the rest of my life."



(Top) Green cells indicate normal process of apoptosis (cell death) and development in a normal pig placenta. (Bottom) Placental cells from pig with abnormally imprinted genes show a lack of or delay in apoptosis.

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As it enters its seventh year, Results has a new look to go with its features of new research and graduate studies programs at NC State. We're eager to know what you think about the fascinating research programs that enhance NC State's educational programs and contributions to a better future for our state and the world. Our thanks to designer Tyler Bergholz of NC State Creative Services.

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Research and Graduate Studies at North Carolina State University

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