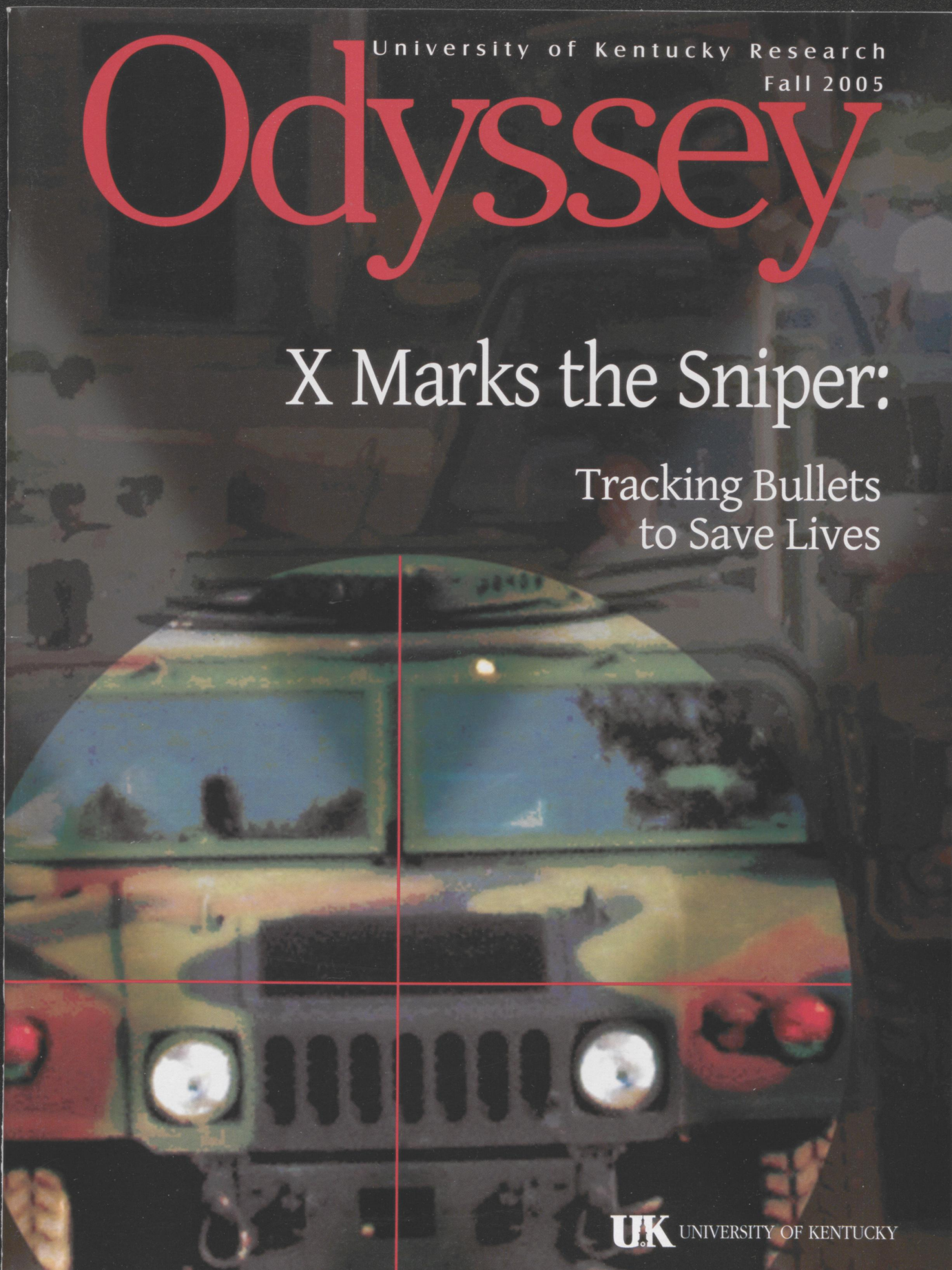


The background of the cover is a dark, grainy photograph of a military vehicle, possibly an armored car or tank, with a red crosshair overlay. The vehicle's headlights and front grille are visible. The text is overlaid on this image.

University of Kentucky Research
Fall 2005

Odyssey

X Marks the Sniper:

Tracking Bullets
to Save Lives

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Cover Story

X Marks the Sniper: Tracking Bullets to Save Lives



UK and high-tech defense contractor M2 Technologies are partners on the Anti-Sniper Infrared Targeting System (ASITS). This patent-pending technology unites off-the-

shelf infrared cameras, video processors and computers with software developed at UK to track the heat signature of a bullet. One day ASITS may protect military convoys and school playgrounds from gunfire. And if M2's plan is realized, this technology may soon become a key Kentucky industry.

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The results of a massive, five-year breast-cancer trial focused on a drug called Herceptin are in, and the news is good for women with a particularly aggressive type of breast cancer—HER-2. UK's Edward Romond calls this "the single biggest advance in the treatment of breast cancer in decades."

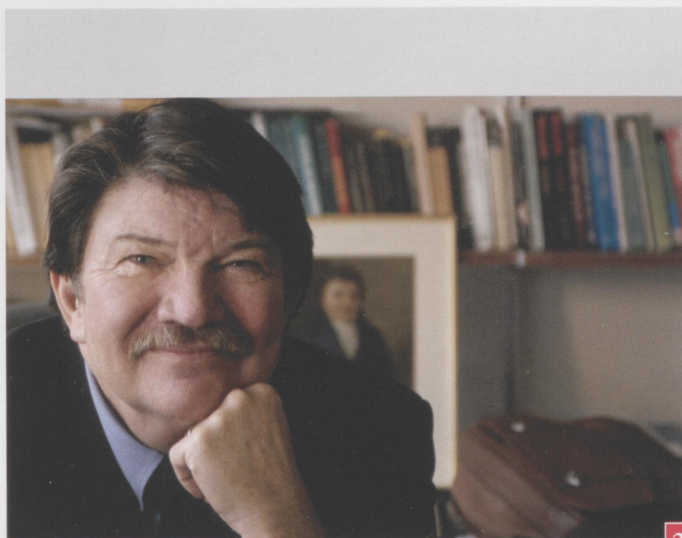
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X Marks the Sniper:

Right: ASITS program manager Steve Robinson, who served four and a half years in the Army Corp of Engineers and was a colonel in the U.S. Army Reserves, aims through the triangular opening of the chronograph, which measures the speed of the bullet.

Written by Alicia P. Gregory

Two months ago in Iraq, a group of Americans were pinned down by a sniper," Janet Morris tells me, as we sit at her dining room table. Her husband Chris adds, "One hundred and fifty U.S. soldiers held down for an entire day because they didn't know where the gunfire was coming from."

Janet continues: "The sniper was moving back and forth in a group of connected buildings, staying far enough inside that the Americans couldn't see the muzzle flash from his rifle. That's why we've spent 10 years pushing for this technology."

Janet Morris is president and CEO of M2 Technologies, a high-tech defense contractor with 25 employees in three states. The company is developing the Anti-Sniper Infrared Targeting System (ASITS). This patent-pending technology unites off-the-shelf infrared cameras, video processors and computers with software developed at the University of Kentucky to track the heat signature of a bullet. One day ASITS may protect military convoys and school playgrounds from gunfire. And if the Morrises' plan is realized, ASITS may soon become a key Kentucky industry.

M2's Anti-Sniper Infrared Targeting System (ASITS) is patent-pending technology that unites off-the-shelf infrared cameras, video processors and computers with software developed at the University of Kentucky to track the heat signature of a bullet.

Tracking Bullets to Save Lives



"For a long time the government bred the Morgan horse to be a war machine—capable of pulling cannon, charging into battle and being on parade," Chris says. Chris and Janet Morris have raised Morgans for 10 years and in 2003 moved their company, M2 Technologies, and their farm, Paradise Morgans, from Massachusetts to Versailles, Kentucky.

Forward Thinking on the Farm

"Humans have been settling arguments by chucking rocks at each other for thousands of years—it's a guy thing," Janet says emphatically.

I've come to Paradise Morgans, the Morris's breeding and wellness horse farm off a quiet back road in Versailles, to learn how their bullet-tracking technology began. A gray and white Maine Coon cat rubs against my legs as Janet adds, "Projectile weapons are just fancier, better rocks."

This woman entrepreneur knows a thing or two about "guy things." She's faced off against a number of generals in her years as a strategic planner for the U.S. government. Janet and Chris tell me they got into strategic planning when they attended a seminar by former CIA director Ray Cline on doing business with the intelligence community. They were doing research for a novel, one of 47 books they've co-written, some under pseudonyms.

"If you write a spy novel, you better know how the system works," Chris says softly, but with no less passion than is conveyed by his wife's ebullience.

"We were interested in international security before Tom Clancy was, and we were trying to check ourselves to see whether we had the wiring right for our stories," she says.



One thing led to another, and soon the Morrises were research directors at the U.S. Global Strategy Council in Washington, D.C. This long-term strategic planning think tank, started by Cline, is comprised of 400 former intelligence officers.

"As part of our work there we came up with 'Non-Lethality: A Global Strategy,'" Janet explains. The goal: to be less lethal than, but prevail over the enemy. "It's very hard to win a war if you don't want to lose your own people, and you don't want to kill the enemy, but the enemy is happy to die and wants to kill you."

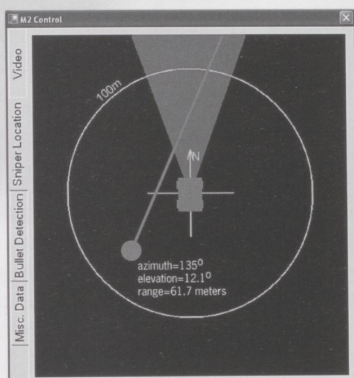
In 1996 the Morrises' plan turned into the Joint Non-Lethal Weapons Program, which covers weapons in three broad areas: counter-personnel (clearing facilities/structures of personnel, controlling crowds, incapacitating the enemy), counter-material (disabling equipment, denying access to vehicles and aircraft), and counter-capability (disabling or neutralizing facilities and systems, denying use of weapons of mass destruction).

"But we're getting off track," Janet says, after delving into the policy side of things. "Back to projectile weapons. Anytime you shoot something through the air, the projectile gets hot. Our technology will find the shooter, even if it can't see the spot he fired from, because it tracks the heat from that bullet's passage through the air and gives us a precise track back to the source in less than a second. He can't drop that gun and step out of the way before we find him."

"But what happens then?" I ask.

Chris responds: "The question is: Do you hook this up to a machine gun and put it on automatic shoot back, or do you have a man in the loop to

Daniel Lau explains the ASITS computer display: "The big dot indicates the position of the sniper relative to the camera, shown mounted on what looks like the overhead profile of a military Humvee [rectangle in center]. The line coming out from the dot indicates the bullet's path."



decide whether or not to fire or call for reinforcements?"

"But if you were the United Nations, you wouldn't want to do either of those," Janet says firmly. "You'd simply want the system to fax back a photo of the shooter to your office to document the incident."

Chris, vice president and board chairman of M2 Technologies since the company started in 1995, adds, "Police chiefs in Los Angeles and Washington, D.C., have already offered to test our system in locations where they know every one or two weeks there will be a shooting. That is a step toward passive surveillance of a community."

Janet says, "It has no Big Brother aspect ..."

"Because it doesn't become active until someone shoots," Chris says, finishing her sentence.

"And if you're shooting in an urban environment," Janet states, "you're either police or a bad guy. This technology will make guns an unattractive choice for criminals."

"You're going to want this system if you're a policeman, a security guard, own a chain of gas stations, handle an inner-city school or playground in a

continued on p. 6



The Advanced Science and Technology Commercialization Center (ASTeCC) in the heart of the UK campus is home to Daniel Lau, UK electrical engineering assistant professor, and to M2 Technologies, a high-tech defense contractor—partners on ASITS. Lau says, "The collaboration with M2 is every professor's dream. M2 has completely assumed the responsibility of seeking funding for this project, and that fact has totally freed me to focus on the continued improvement and refinement of ASITS."

"Our technology will find the shooter, even if it can't see the spot he fired from, because it tracks the heat from that bullet's passage through the air and gives us a precise track back to the source in less than a second. He can't drop that gun and step out of the way before we find him."

—Janet Morris

drug dealer's neighborhood. You're going to want this if you're in a military convoy, if you're Secret Service for VIP protection, if you're a pilot of a domestic airplane. We can develop different products for all of those applications from this one technology."

Bullet Tracking in the Bluegrass

The ASITS concept began with a project at Lawrence Livermore National Laboratory in California in the mid '90s. Janet and Chris were consultants on a system known as Lifeguard that could detect a bullet in flight. And it just so happened that an undergraduate named Daniel Lau was working on that project—but more on him later.

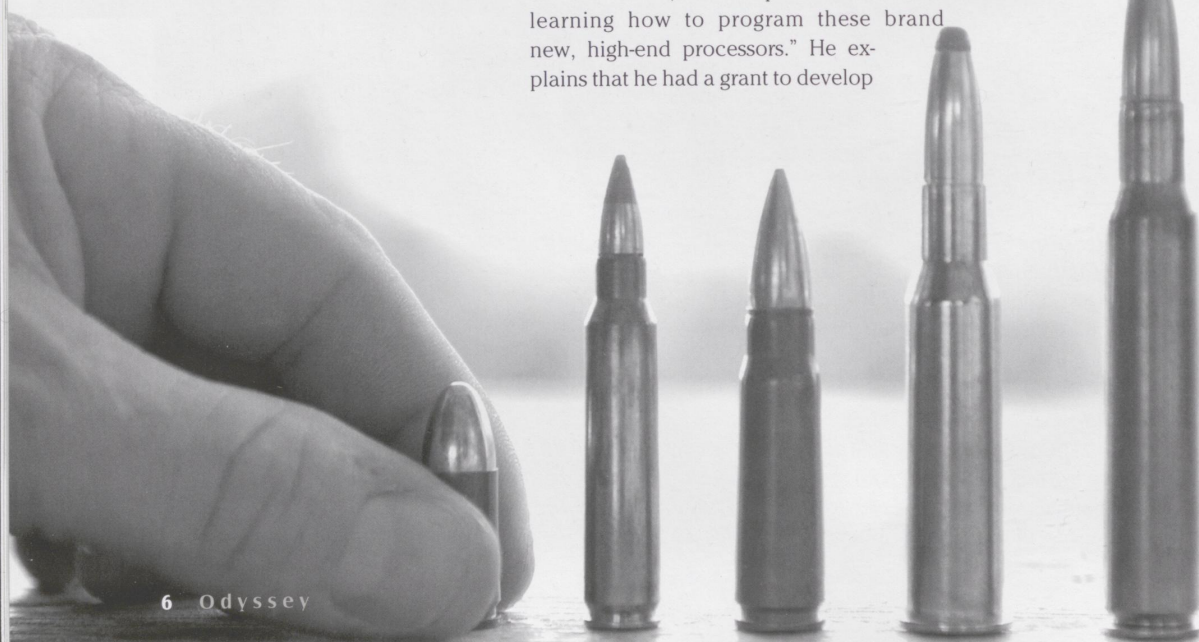
"The timing wasn't right," Janet says, stroking the cat, which is now curled up on her lap. "The technology wasn't there to do it quick enough, cheap enough and small enough to get this system into the hands of the people who needed it."

Fast forward to 2003. The Morrisses moved M2 Technologies and Paradise Morgans to Kentucky from Massachusetts, to be closer to horse experts and veterinarians. "I thought I was in Kentucky for one reason [her prize Morgan horses], and it turns out I'm here for another [collaborating with UK]," Janet says.

Shortly after moving here, the Morrisses got in touch with Eric Grulke, the UK College of Engineering's Associate Dean for Research and Graduate Studies. "We said to Eric, 'The thing we'd most like to do with you is this bullet tracker project. Here's how far we got, and here's what's left to do.' And as it happened, they had exactly the talent that we needed for this project," says Janet.

That talent being Daniel Lau, a Pittsburgh native who since his undergraduate stint at Livermore earned a bachelor's degree from Purdue University and a Ph.D. from the University of Delaware, both in electrical engineering. He joined UK as an assistant professor in 2001 and has worked on digital halftoning and 3-D face recognition. He joined the M2 team to develop ASITS and helped them pitch the project in Washington, D.C., to defense department officials and to Senator Jim Bunning, R-Ky.

Daniel points out that the UK/M2 partnership came at exactly the right time. "Huay Khoo, an undergrad in my lab at the time, had spent six or seven months learning how to program these brand new, high-end processors." He explains that he had a grant to develop



a training tool for minimally invasive surgery.

"Doctors had been training by performing really simple tasks with their surgical tools, like tying shoelaces, in the equivalent of a shoebox. We developed a system with a desktop PC and three video cameras that could track their tools in 3-D space inside that box." The mathematic principles behind that 3-D, real-time tracking were precisely the same principles they would use to track bullets. "We had a leg up," he says with a smile.

Not long after Daniel signed on, Lexington-native Steve Robinson, who Janet and Chris say has exactly the right mix of military chops and engineering know-how, was hired as program manager.

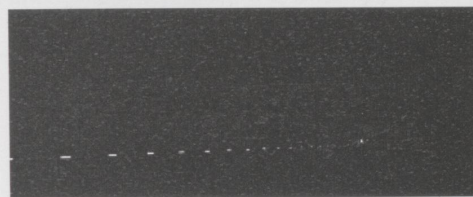
"Steve, like many of our people, has an operational background in the military and is comfortable with ballistics—something that's key for ASITS," Chris explains. Robinson had four and a half years of active-duty service in the Army Corp of Engineers and served as a colonel in the U.S. Army Reserves. He also spent 20 years in medical device research and development, and worked full-time as a defense contractor before sending M2 his resume based on their newspaper ad.

"Many in academia really don't understand the military or what its needs are, and, likewise, the military is somewhat suspicious of white-coat academia. Steve is very effective as a translator between these two worlds," Chris says.

Nuts, Bolts & Bullets

BANG ... BANG ... BANG ... BANG ... BANG.

Five shots echo off the wood shelter above us and the concrete below. Behind the target at 300 meters, a cloud of dirt billows into the air. The scent of gunpowder lingers as



The infrared camera captures the path of a bullet—a series of dashes and dots that show the bullet slowing down. Using the size, shape, spacing, and brightness of these spots, the ASITS software can track the bullet back to determine the position of the sniper.

The infrared camera captures the unmistakable muzzle flash from a 30.06 M1 rifle. Other commercial systems use infrared cameras to detect muzzle flash, but snipers can use low-tech means like a pillow or a potato to hide the flash. ASITS doesn't need muzzle flash. It only needs a bullet to pass through the field of view of the camera in order to track it back to the sniper.

Steve Robinson lays down the AK-47—the gun of choice for Iraqi insurgents, he tells me as he wipes the sweat off his brow with a paper towel. It's 10:30 a.m. and feels like 95 degrees in the shade.

"Look," Steve says, "2399 feet per second," gesturing toward Daniel, who is taking a morning away from his UK lab for one of many field trips in the past few months to test ASITS. Steve points to the digital readout from the chronograph, an odd-looking contraption on a tripod two yards in front of where he's shooting. It measures the speed of the bullet as it passes through two triangular openings.

"How far could that bullet go?" I ask, sipping water to combat the August heat.

"The effective range is about 500 meters," Steve says.

"And it's hot," Daniel adds quickly, kicking a still-warm bullet casing from the concrete to the grass. "The bullet is over 800 degrees Celsius coming out of the gun—eight times the temperature of boiling water—and that's what we capitalize on.

"Because the bullet is so hot, we use what's called a midwave infrared camera. It sees thermal energy, on the 3- to 5-micron range." A micron is one millionth of a meter. Okay, that's tiny. "When you're operating in this range, the camera actually has to be cooled down, and the electronic cooling system bumps up the price of the camera. One camera costs \$80,000," Daniel says, opening a rugged black case to show me the 10" by 6" boxy camera.

"These are the same cameras that are mounted under fighter jets for their targeting systems. The sensitivity is insane," he says, giving an example: "U.S. pilots have taken pictures of enemy airfields, and these photos reveal a group of planes and you can see that two planes beside them must have recently taken off, simply by the temperature difference of the concrete."

Every piece of hardware in ASITS (infrared camera, PC with monitor, and high-end processors) is available off the shelf, albeit with a hefty price tag. "In addition to the camera, we use a Matrox Odyssey X-pro, a 12-inch board that's

basically an entire computer itself." At \$7,500 a pop, the ASITS prototype will use four of these processors.

"Right now we're using a single processor," Daniel says. He points to first-year grad student Brent Sundheimer, who sits with the computer in the back seat of Steve's SUV, analyzing the images from the last barrage of bullets. "Brent is working on linking multiple processors together, so once we get the money to buy more, we'll be ready. These processors take the video in, at a rate of 200 frames per second. Then they send out what we call 'bullet spots' to the PC for display."

You have only five milliseconds to process each frame of video with one of these Matrox boards, he tells me. "So if that's not enough time, you need to add more boards. More processors mean faster, real-time sniper location, and that's our end goal."

Two months before we came to the Bluegrass Sportsmen's League in Wilmore for this firsthand demonstration of ASITS, I was sitting in Daniel's third-floor office in the Advanced Science and Technology Commercialization Center (ASTeCC) in the heart of the UK campus. Just below us, in the ASTeCC basement, was M2's ASITS office.

"The unique part of ASITS is the software that runs it," Daniel told me, leaning back in his chair. The first version of this software was written by Huay Khoo, then a grad student in Daniel's lab, who has since earned her master's in electrical engineering and left UK.

In July Michael Shaw took on software development responsibilities, along with Brent Sundheimer, as the newest member of the ASITS team. Michael, who has a Ph.D. from the University of Alabama, tells me for eight years he's been teaching part-time in the UK math department, and he's worked on 3-D projects at UK's Center for Visualization and Virtual Environments and the Center for Minimally Invasive Surgery. "Michael's background allowed him to hit the ground running to enhance our bullet-tracking software," Daniel says.

Using the size, shape, spacing, and brightness of the spots that form the path of the bullet, the software can track the bullet back to determine the relative position of the sniper in terms of both the line-of-sight and range from the infrared camera.

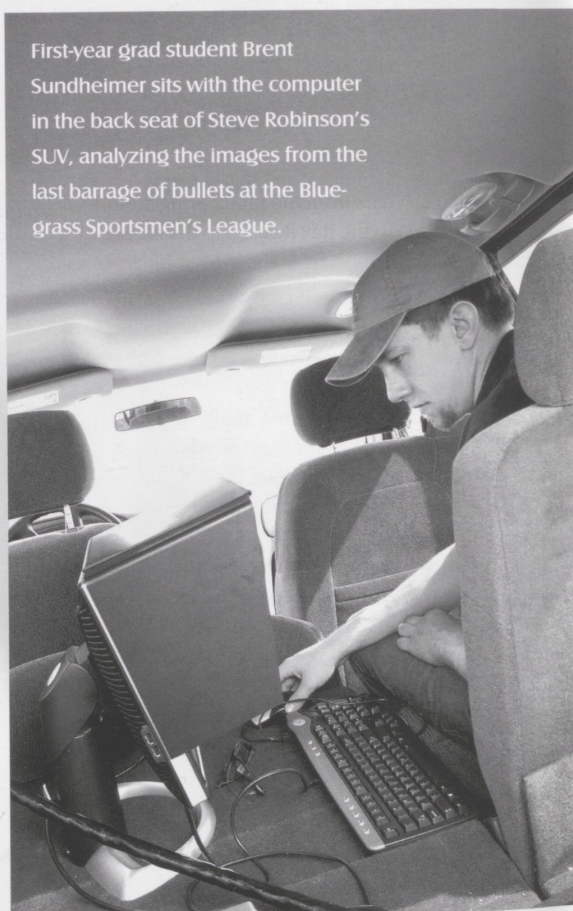
These cameras have a 40-degree field of view, and all Daniel needs is for the bullet to pass through that field. "Tracking the bullet is pretty easy. The hard part is, based on those spots, trying to figure out the position of the sniper," he says about his part of the project.

"It involves ballistic models, meaning, if I know the speed of the bullet, and if I look at the physical spacing between the bullet spots over several frames, from that alone I can estimate a 3-D trajectory. Also, I can look at the brightness of the spot and figure out how hot the bullet is." He reminds me that the bullet is sizzling at roughly

860 degrees when it comes out of the muzzle of the rifle. "As it travels it's cooling off, in other words decreasing in brightness, and it's also slowing down. The more spots that show up in the camera's view, the better my 3-D estimate will be."

The science of sniper pinpointing requires hours and hours at the shooting range, Daniel says. "We've got to do bullet characterization and temperature profiling—shoot the same rifle over and over to measure variations in speed and temperature. We'll

First-year grad student Brent Sundheimer sits with the computer in the back seat of Steve Robinson's SUV, analyzing the images from the last barrage of bullets at the Bluegrass Sportsmen's League.



be setting the camera up at 100 meters, 200 meters and 300 meters, and controlling it remotely. At each distance we'll measure the temperature of the bullet.

"So far we know we can see the bullet out to 100 meters," he says, adding that military personnel have told him that beyond 300 meters, Iraqi insurgents aren't as effective because they typically have access to only subpar weapons. "So our military doesn't consider insurgents at 300 meters to be a serious threat."

"We want to get ASITS to American soldiers in Iraq as soon as possible," Janet says. "M2's goal for any technology is to get it out in less than five years." That's light years faster than the development cycle for the big three defense contractors. "It takes them more like 25 years from the time I bring them my idea to the day it gets into the hands of the guy who needs it. UK has helped me cut down the development time significantly."

Daniel says right now M2 is seeking funds to build three prototypes. "We'll buy three pieces of hardware, put our software on it, and then deploy the three systems with the Marines so they can test them in the field. I could have the prototypes assembled and ready to go in three months."

Competing in Quantico

A U.S. Marine sniper takes his position at a third-story window in a stark concrete-block building. In the crosshairs of his rifle site, a target 200 meters away. BANG. Below, there is a flurry of activity as clusters of people check monitors to see if they located the sniper.

It was early June at the Marine Corp base in Quantico, Virginia, and an

In the first round of experiments at the Marine Corp base in Quantico, Virginia, a Marine sniper at one end of the open field was shooting at a Humvee on the other. The ASITS infrared camera and computer shown here were set up right next to the sniper.



international event was under way. "There were systems from France, Israel, Canada, and the United States." And Steve says with pride, "We were invited by the U.S. Marine Corps Warfighting Laboratory to come because they wanted to see our system—'we' being M2 Technologies and UK."

Janet adds, "It was really fun to go up against systems that had a 10-year and multi-million-dollar jump on us and have ASITS favorably compete with them."

The purpose of the weeklong Quantico event was to officially evaluate acoustic sniper detection systems. Daniel explains, "The Marines were planning to purchase a handful of different acoustic systems to send out to Iraq in August for testing purposes. The Marines in Iraq won't rely on those systems; they're just supposed to see how well the technology improves their regular operations and then give feedback to the manufacturers."

What the Marines did was set up a series of experiments. The first had a sniper on one end of an open field shooting at a Humvee on the other. ("Humvee" comes from the pronunciation of this vehicle's abbreviated military title: High-Mobility Multipurpose Wheeled Vehicle, HMMWV). The acoustic systems, clusters of microphones on the Humvee that were wirelessly linked to the operators in a tent on the sidelines, had no trouble picking up the whistle of the bullet when it got close enough to the Humvee.

"The people with infrared systems were invited to come and observe, and we were allowed to collect as much data as we wanted," Daniel says. "There were other systems using infrared cameras, but we were the only bullet tracker."

The primary difference between ASITS and other infrared and acoustic systems is that ASITS doesn't need line-of-sight to the shooter. Daniel tells me that other systems need to see the muzzle flash—the burning powder that shoots out the barrel of the gun with the bullet—or hear the muzzle blast. The need for sight



A Marine sniper takes aim at a target from a second-story window in Quantico's concrete-block mock town, used to train soldiers for urban combat.

and sound put these systems at a clear disadvantage during the second round of experiments at Quantico.

"MOUT is an acronym for Military Operations on Urban Terrain," Steve explains. "A mock town was built at Quantico just to train soldiers to fight in cities. It has a dozen buildings made of concrete block, some several stories high. We had Marine snipers shooting through alleys, down streets and from windows at multiple elevations.

"And we were the only ones that didn't need to be downrange from the bullet. We actually set up in a room on the first floor, when the snipers were shooting up on the third, and tracked bullets as they crossed in front of us."

In urban combat the very nature of sound waves confounds an acoustic system, Janet says, offering an everyday analogy. "When you drive down the road next to a kid with his radio cranked up, the car is vibrating and those huge bass waves bounce off everything." Likewise, the blast of a rifle will reflect off walls and windows of tall buildings, repeating the sound and masking its origin.

"What we found out at Quantico," Daniel explains, "is that because of echoes, these systems hear the initial shot, have a window of so many milli-

seconds, and then they actually turn off. I thought that some intelligent way to figure out which sounds were reflections—you'd assume they'd be less intense—would be built into the system, but instead it just shuts off. So if you have two snipers shooting at you at the same time, the acoustic system doesn't catch the second sniper." And that's exactly what happened, he tells me. "Two Marine snipers counted down and shot at the same time. We were standing in the tent watching, and all of the acoustic systems recorded only the first person to shoot.

"ASITS had no trouble tracking multiple bullets," says Daniel.

The infrared muzzle flash detectors had their own problems at Quantico, namely the intuition of a shooter. In real combat, the main goal of the sniper is to conceal his location by disguising the flash from his gun. And there are a number of low-tech ways to mask muzzle flash. "A pillow, a potato," says Janet with a laugh. "A silencer or hanging cheesecloth in front of them and shooting through it," Steve says, adding that the Marine snipers told him that their best possible scenario would be to blast a tiny hole in the wall and shoot through that hole. Second best: crawl into a

closet, way in the back of the room, or climb into the rafters and aim through the window.

"We heard the radio communication, and the guys doing infrared muzzle detection were asking the Marine captain in charge, 'Can you ask the snipers to scoot out the window a little farther? We're not picking anything up.'" Steve says with a smile, "Not exactly a realistic battle scenario."

"The Marine snipers loved our system," Daniel says. "They told us the others were completely impractical for urban combat."

Where Do We Go from Here?

"We're hoping to manufacture this technology in Kentucky, because we think it's an industry," Janet says. And the Morrisses are looking at Somerset. "Southern Kentucky Economic Development Corporation is one of the most forward-looking organizations of its sort that we've come across," she says.

"Hal Rogers [R-Ky.] has done a good job at getting genuine interest in enhancing the local economy by recruiting various high-tech ventures. For a small company like ours, the tax incentives make it very attractive for us to manufacture there."

The project received its first round of funding from the U.S. Marine Corps in October 2004, and Steve estimates ASITS could be ready for production in the next 12 to 18 months. "But there are plenty of things to work on in the meantime." He puts on his R&D hat and offers an analogy: "If the customer wants to buy a Chevrolet, don't try to sell him a Cadillac. He can't afford a Cadillac. He doesn't want a Cadillac. Give him a Chevy. The key is

knowing the customer's requirements and then developing a product that meets those exact requirements.

"This concept relates to this project in that we need to experiment with lower-cost solutions."

Daniel tells me the most efficient way to reduce the cost of ASITS would be to use multiple lower-priced cameras. He has palm-sized, \$7,500 cameras and will be testing them to see if a group of these less sensitive cameras can capture enough bullet spots to track a sniper. These cameras operate at 30 frames per second, "and we'll be lucky if they capture one bullet spot; whereas, we're picking up five, six, seven, eight spots with the more expensive one. But if I can have several of these inexpensive cameras, and if each one is positioned at a different viewpoint and could see one spot, I could get a 3-D trajectory and do everything that I'm doing with an \$80,000 camera."

"So one challenge we have is to lower the cost of the system," Steve says. "Then we need to look at delivering ASITS in multiple product configurations—on top of a weapon like a rifle scope, on a console in a Humvee or other manned vehicle, on a handheld device like a PDA, on an unmanned robot operated by joystick, or on an unmanned aircraft." There are many possible configurations, but M2's first goal is to manufacture a system for a Humvee with a camera mounted above the vehicle.

"In addition, we're working on a sister technology called the Anti-Projectile Infrared Targeting System (APITS)."

Daniel explains: "It's the same idea except we're going to track mortars, artillery shells and rocket-propelled grenades, and it will have a response

capability. We'll track projectiles using ASITS, then we'll use a steerable laser to actually put a spot on the projectile. And then we're going to use a .50 caliber weapon to launch an interceptor that will automatically steer itself into the laser spot and take out the projectile.

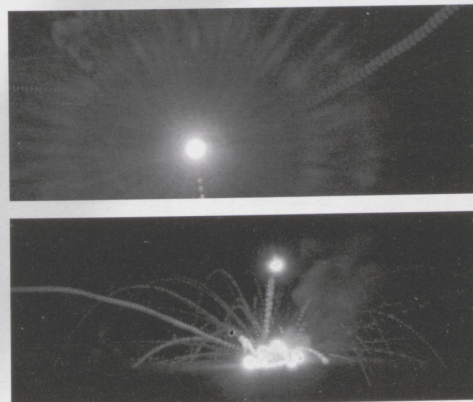
"A mortar shell travels between 200 and 300 meters per second. The .50 caliber weapon will launch our interceptor at over 850 meters per second," Daniel says, rattling off these numbers as he adjusts his glasses. "We could destroy an incoming projectile 2 kilometers away in 2.5 seconds." He adds that the Army is working on a radar-based system to do the same thing but is facing problems.

"This radar system came from the Navy—when there's an incoming cruise missile, they have these monster machines that launch 300 bullets to try to take it out. The Army has been able to miniaturize the radar to work for mortars, but the 300 rounds are the problem. In reality, 299 rounds miss and there's too much collateral damage to use this in an urban environment. Our APITS system would be a much more effective and elegant solution."

Daniel says ASITS is quickly becoming the defining project of his career, and he's glad. "The collaboration with M2 is every professor's dream. Typically, a professor has to teach, find money to do research, and then do the research related to funded projects. M2 has completely assumed the responsibility of seeking funding for this project, and that fact has totally freed me to focus on the continued improvement and refinement of ASITS, as well as to expand the focus of ASITS to a wider array of applications like projectile tracking."

Janet says she's proud of her UK-based team. "You want to work with people who get things done, not people who stretch the process out, and that's what's so refreshing about UK. Everybody's been super creative, and the quality of the talent at UK is incredible. They're in the top three of any school we've worked with.

"We like it here and my horses like it here," Janet says with a smile. "And if we keep finding people of this quality, the limit to what we can do here is going to be set only by how much teaming with us the university wants to do."



The infrared camera captured these two images during an ASITS test using fireworks to simulate rocket fire. A sister technology called the Anti-Projectile Infrared Targeting System (APITS) is being developed to track and intercept mortars, artillery shells, and rocket-propelled grenades.

Written by Robin Roenker

Edward Romond stepped to the podium last May at the Orlando, Florida, convention center to address an army of doctors united by a common enemy: cancer.

Five thousand of the nation's premier clinical oncologists at this hastily called symposium at the annual American Society of Clinical Oncology meeting sat waiting for what they had heard was extremely good news. What Romond, a professor of medicine in the UK College of Medicine, didn't know at the time was that 3,000 more people watched eagerly on video screens in overflow rooms nearby.

Romond was there to talk about the results of a massive, five-year clinical trial focused on a drug called Herceptin, research sponsored by the National Cancer Institute (NCI) that was published last October in *The*



Breast cancer is the most commonly diagnosed cancer in women and the second leading cause of cancer-related death in women in this country.

Breast Cancer Breakthrough

New England Journal of Medicine. At issue was the drug's effectiveness in reducing the spread of cancer in patients with a particularly aggressive form of breast cancer.

Romond began his presentation not with talk of trial methodology, molecular makeup of receptor proteins, or statistical P-values of the data obtained, but with a focus on the patients themselves.

"On behalf of the 3,351 women who participated in this clinical trial," Romond began, "I have the privilege of presenting these results to you." Recalling that opening months later, Romond pauses and glances out of his office window. His soft-spoken voice cracks and gets



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Edward Romond has been involved in clinical trials in cancer research since he came to the University of Kentucky 22 years ago. He says that because of molecular biology and targeted therapies, the progress in breast cancer treatment in the next 10 years will be even much greater than in recent years.



even softer. "It's very important to emphasize the courage of these women," he says. "It was ...," he pauses again, "pretty emotional."

When Romond had finished his 15-minute presentation of what he calls "the single biggest advance in the treatment of breast cancer in decades," the response was amazing, he says. Applause rang out for minutes. Colleagues told him later that members of breast cancer advocacy groups in the audience were in tears.

Tears and applause, to greet the news that in Herceptin may lie the power to—in Romond's words—"change one of the deadliest types of breast cancer into something we can treat successfully." In short, Herceptin can save lives.

The Herceptin Story

The extremely aggressive form of cancer on trial is called HER-2 positive breast cancer. Compared to other types of breast cancer, HER-2 is more likely to spread to other organs—even in spite of chemotherapy—and to recur more often after treatment.

Of the more than 211,000 women who will be diagnosed with breast cancer this year, around 20 to 25 percent will get the bad news that they have HER-2 positive breast cancer, according to estimates by the National Institutes of Health. Their risk of dying from cancer has been significantly higher than women with other types of breast cancer. But because of Herceptin, that possible death sentence may soon be lifted.

Developed in the 1990s as an antibody to block the HER-2 protein, Herceptin—the prescription name for trastuzumab—has been FDA approved since 1998 for treatment of patients with advanced HER-2 positive breast cancer that has spread to outlying organs such as the bones, lungs or liver.

So while physicians knew of Herceptin's potential to prolong life and shrink tumors for patients whose cancer had spread, researchers wanted to test whether administering the drug just after diagnosis might prevent the spread of the disease in its early stages to other organs.

Answering that question through the clinical trial, which featured over 500 testing sites throughout the United States and Canada, was the objective of Romond and the other cancer researchers involved. Early last January, his study merged with a similar NCI-sponsored national clinical trial that sought to answer essentially

"This trial heralds the single biggest advance in the treatment of breast cancer in decades."

—Edward Romond

the same question. The merger of the two trials provided researchers with a much larger dataset for analysis—3,351 women—which allowed for statistically significant results much sooner than either study would have yielded separately.

Both trials enrolled women whose HER-2 cancer had not yet spread to other organs, but whose cancer did show a tendency to spread, as evidenced by its presence in at least one lymph node. Half of the patients received chemotherapy only, while half received Herceptin along with chemotherapy. Those who got Herceptin were given the drug intravenously once a week during a three-month chemo regimen, and then weekly for nine months after chemo.

The results were straightforward and incredibly encouraging: The trials showed that the number of cases of recurrent breast cancer was 52 percent less in the women who received Herceptin along with their chemotherapy, compared to those who received chemotherapy alone. "It was absolutely incontrovertible that this benefit is real," Romond says, his tone an exclamation point.

Citing the 52 percent reduced risk of cancer recurrence and a 33 percent improvement in survival rate, Gabriel Hortobagyi, president-elect of the American Society of Clinical Oncology and chair of the breast medical oncology department at the University of Texas M.D. Anderson Cancer Center, says, "In oncology, we get excited about improvements of 2 percent to 4 percent. We haven't seen anything of this magnitude in breast cancer research in 30 years."

"One of the striking things in the data is when you get three or four years out from when the cancer is diagnosed, 90 percent of the women who received Herceptin have no detectable cancer anywhere else in their body," Romond says. "And these are women whose prognosis of having cancer spread with chemotherapy alone was worse than a 50-50 chance."

The health of the 3,351 women in the study will be monitored for the rest of their lives, but neither study is accepting new patients. Here's why: When presented with the initial study data in mid-April of 2005, monitoring committees told Romond and his colleagues to immediately stop both trials. "They said unequivocally—and I'm happy to echo their words—"The question is

answered. Herceptin is overwhelmingly beneficial," says Romond.

Since the results of the trials were released, Herceptin has also been offered to members of the control group who were within one year of their cancer diagnosis.

To make the drug available to recently diagnosed HER-2 positive breast cancer patients everywhere in America, all that's left is FDA approval. It's a status Romond believes might be granted even before the end of this year, given the compelling results of the clinical trials—and the potential of the drug to save lives.

A Death Sentence No More

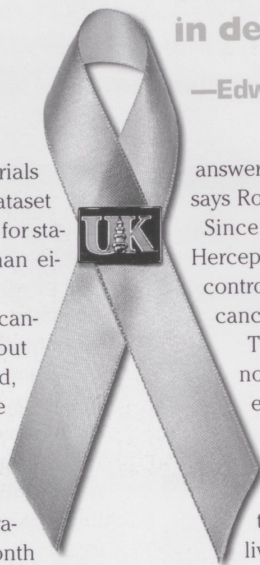
Romond has seen the drug's success stories firsthand, and the numbers aren't mere statistics to him. When he talks about this trial, it's clear he's thinking of the names and faces of his own patients—patients who are alive today because they received Herceptin.

He tells of a young woman from near London, Kentucky, who was in her early 30s with two young children at the time of her breast cancer diagnosis three years ago.

"When I talked to her about it, I said, 'This is really bad breast cancer, I have to be honest with you,'" Romond recalls. He recommended that she enter the clinical trial in hope of receiving Herceptin. But the woman said she doubted whether she could join the study, since the car she owned wasn't reliable enough to get her back and forth to Lexington, a 150-mile round trip, for weekly treatments.

The next day, though, the woman called Romond to tell him her father, who lived in Texas, had bought her a car so she could participate in the trial. "She got randomized to receive Herceptin, and she finished it two years ago. I saw her yesterday, and she's fine," Romond says. "Perfectly fine. Cancer-free." One life saved.

It's easy to see when you talk with him that as wonderful as the statistics are, for Romond the lingering impact of the study is in Herceptin's potential to save the lives of his patients. "It's rewarding to me because of my patients," he says. "They're right there in front of me. And I know the difference it's made in their lives." ■



Miles Osland

Packing a Mean Sax

Written by Jeff Worley

When you hear the word “research,” you might imagine a man in a university greenhouse, clipping small samples from soybean plants to study under a microscope.

You might imagine a woman in a darkened lab, watching a green rain of particles in a laser-scattering device to determine their physical and chemical makeup.

What you almost surely wouldn't imagine is Miles Osland. A professor of saxophone and director of jazz studies at UK, this cool sax man was the recipient last year of a \$24,000 UK Research Support Grant. Osland used this grant to commission three works by major international composers who have proven themselves to be “technically adventurous,” he says, and last year he traveled to Sweden, Brazil and England to work with them. All three works are being performed this year at UK and will be released along with many other newly commissioned





In his office in UK's Fine Arts building, Osland works with David Harper, a junior music major from Hopkinsville, Kentucky. Harper is this year's Lewis Award winner, a College of Fine Arts scholarship worth \$10,000 over four years.

works on a two-CD set titled "Commission Impossible" on the Sea Breeze label (California) in early 2006.

But what does any of this have to do with research?

"Yeah," says Osland, who seems to like talking about music almost as much as playing it, "usually this kind of money goes to fund projects in medicine or the hard sciences, but my project, titled 'Development, Documentation and Dissemination of New Works for Saxophone,' is fully in keeping with the stated goals in the university's strategic plan of expanding knowledge through research, scholarship and creative activity."

Last May at UK, Osland was the featured soloist in the last of the three commissioned performances outlined in his grant proposal. "The Concerto for Alto Saxophone and Wind Orchestra," by English composer Mike Mower, was premiered by the UK Wind Ensemble at the Singletary Center for the Arts. The other works resulting from the research project include "MOSAX Overdrive for Saxofonquartett" by Sweden's Anders Åstrand and "Four Miniatures from Brazil" by Brazilian composer Hudson Nogueira. These two works are for saxophone quartet.

Saxophone Research

Leaning back slightly in his desk chair, talking about jazz and other musical influences, his fingers testing the keys of a favorite alto sax on his lap, Osland strikes you as the real deal. His black hair is combed straight back and cinched in a ponytail. Through his small, wire-rimmed glasses his eyes are alive with the intensity of a man happily lost in his subject. And the room's accoutrements bear witness. A considerable library of neatly shelved jazz CDs lines one wall. A full set of drums anchors a corner. A larger-than-life Duke Ellington beams down from a timeworn poster, and next to the Duke is a blown-up photo of contemporary saxman Michael Brecker, who, Osland says, is technically "an absolute wonder." And on another wall you can't miss the two Kentucky personalized license plates that trailed Osland around the state for years: UK JAZZ and MOSAX. This is Music World, and the man is clearly into it.

And when asked exactly how a sax man does research, he is quick and to the point: "Learning and

continued on p. 18

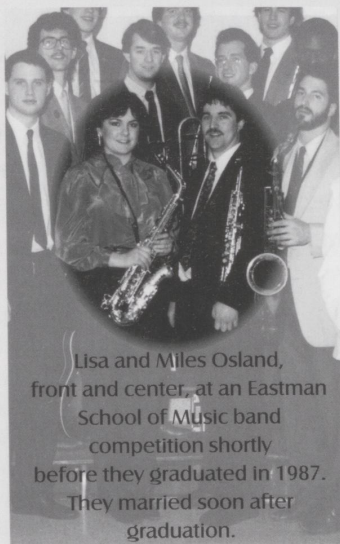
Miles and Miles

It's a natural question: With a name like Miles, wasn't Osland destined to become a jazz musician?

"Well, it's interesting," he says, laying the sax aside for the moment. "I'm adopted, and the story goes that my adopted father saw Miles Davis in San Francisco a couple months before he and my adopted mother received me, and he was so inspired by seeing Davis that he named me Miles. So, yes, I guess I *had* to become a jazz musician. Neither of my parents had any musical background whatsoever. I have a secret fantasy that I'm the product of some great jazz musician's one-night-stand," Osland laughs.

He adds that when he was growing up in Escondido, 30 minutes north of San Diego, his mother played the bigger role in sparking his interest in jazz. "My mother, a lover of the '60s West Coast Cool School of Jazz, was listening to Dave Brubeck all day on phonograph. When I was 10 years old, we sat down and had a serious talk about what instrument I should play. She put on 'Take Five,' and I listened to the Paul Desmond alto saxophone solo on that. Then she put on a Pete Fountain/Al Hirt recording, and I listened to the clarinet on that, and then there was a Herbie Mann recording on flute. I ended up choosing flute because of that recording."

But there was just something about the sax that called out to him. Osland listened and listened again to his mother's Duke Ellington albums, featuring Johnny Hodges on sax, and to Cannonball Adderley. "I took up the sax at age 12 and haven't put it down since. Probably of all the instruments I play, the sax is the most versatile.



Lisa and Miles Osland, front and center, at an Eastman School of Music band competition shortly before they graduated in 1987. They married soon after graduation.

Maybe one appeal, especially of the tenor sax, is that it's so close to the range of the human male voice."

Along with flute and saxophone, Osland also plays clarinet, piano and drums. And he says that he "can get around on the guitar a little bit," too. "In high school, I was in a rock and roll garage band. It was great fun, but thankfully there are no recordings that exist from that musical chapter of my life."



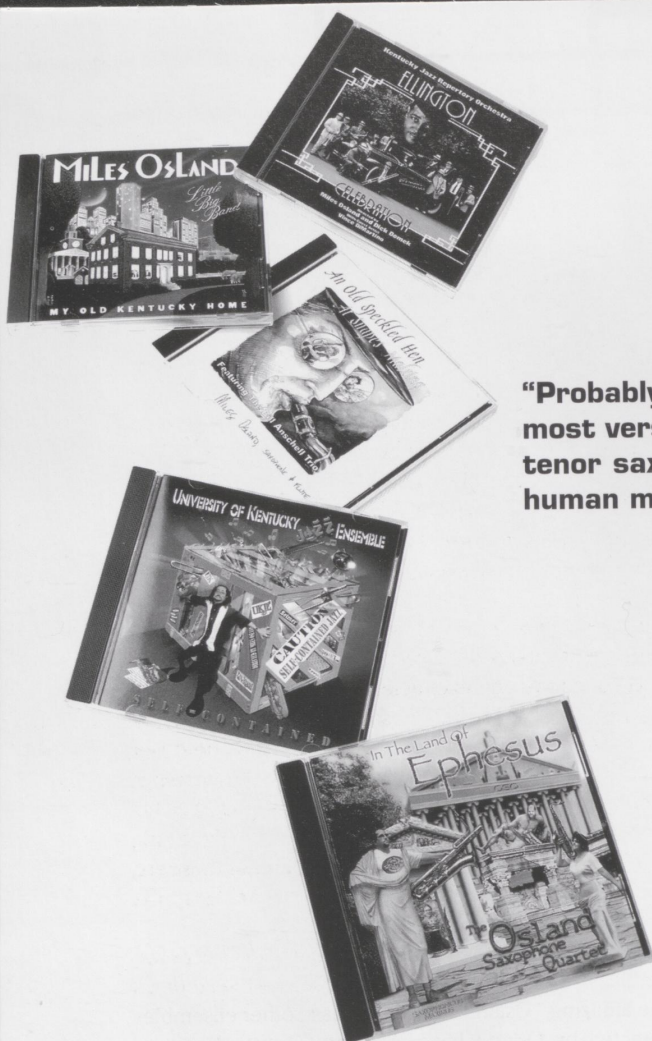
After receiving a bachelor of music degree at California State University, Northridge in 1985, Osland decided to go cross-country for his master's degree, to the Eastman School of Music in Rochester, New York. At that time Eastman boasted perhaps the best teacher of saxophone in the country, Osland says—Ramon Ricker. Eastman and Ricker didn't disappoint: Miles was very happy there and wound up in 1987 with a master of music degree in performance, jazz studies and con-

temporary media, with an emphasis in saxophone.

His days at Eastman were rich with music, and his personal life took an up-tempo swing as well. He met another student, named Lisa, who was just as serious about the saxophone as he was. Then they got serious about each other and were married shortly after they graduated. "Ray Ricker, the man who brought us together in the first place, was the best man at our wedding," Osland says.

Miles also met someone at Eastman who would turn out to be instrumental in his career path. Osland was a member of a summer session orchestra at Eastman and met a trumpet player named Vince DiMartino, at the time a professor of music at the University of Kentucky. DiMartino was an Eastman School grad, and he and Osland really loved each other's playing. DiMartino at the time was lobbying to get a sax professor at UK, and someone who could also take over the jazz ensemble he'd been heading up for 17 years.

"I got the job and have been directing the jazz ensemble and heading up jazz studies and saxophone studio ever since," Osland says. "It was this connection that got me here." And although DiMartino left UK in 1993 to become the first distinguished artist-in-residence at Centre College in Danville, Kentucky, he and Osland still cook up some hot jazz together. "We've had a Big Band together ever since I've been here—going on 16 years now. We play the last Monday of every month at Comedy Off Broadway, out at Lexington Green. It's a real fine ensemble of musicians, all from Central Kentucky."



"Probably of all the instruments I play, the sax is the most versatile. Maybe one appeal, especially of the tenor sax, is that it's so close to the range of the human male voice."

normal range. "A few bars of altissimo can be used as a surprising, melodic statement.

"Mower follows this with what's known as 'slap-tongue.' Listen." Osland surrounds the mouthpiece and reed with his lips, then sends a series of staccato bursts of air into the sax. The instrument emits a few explosive slaps; for a few seconds, it becomes a pitched pop gun. "It's a neat technique," says Osland, laughing. "It introduces the element of surprise and also adds a percussive touch to the music."

After a few bars of slap-tongue, Mower introduces a passage that calls for fast alternate fingerings. "This lets you do some up-tempo stuff and add a rippling sound." To demonstrate, Osland plays a few measures at a slower tempo, then says, "Here's what this sounds like as written." His fingers fly up and down the keys, the notes cascading wildly, as if in free fall. This sound gives way then to trilling between two notes (one of the major techniques used by blues sax players) and adding some note-bending. "Bending is done with the embouchure—but you have to keep your airstream steady," Osland explains.

The final technique in this cadenza enables a sax player to, paradoxically, hit a lower note than the sax can play, below B-flat. "The lowest note on a sax is B-flat. But if you stick your knee in the bell, you get a half-step lower."

Stick your knee in the bell?

Osland laughs. "It's a cool technique that I've never seen written in any classical piece—watch this." He plays down a scale, note by note, until low B-flat sounds. Then he lifts his left knee and inserts it halfway into the bell of the sax. B-flat wobbles a bit, then falls lower.

"Mower masses quite a few techniques here, but he doesn't do it to just show off the technique of the performer. They're appropriate to what's come before in the concerto; everything in this final cadenza makes good musical and harmonic sense." And when Osland premiered this piece last April at UK's Singletary Center, the audience obviously thought so, too. The 300 or so

playing new music in a performance *is* our research. Let me show you."

On his black metal music stand, he opens Mower's concerto to the final cadenza in the third movement, some 20 minutes into the composition. Hundreds of tiny notes, like arranged buckshot, bounce across and down the two pages. "Our research can focus on developing and using new techniques in our performances, and combining these techniques in musically exciting ways," Osland explains, tightening a reed onto the mouthpiece of the sax and letting his fingers run through a silent drill on the keys.

"The first technique Mower inserts here is what's called 'altissimo,'" says Osland. "It's a way to get an octave or two above what's thought to be the highest range of the saxophone." Using an advanced method of "voicing" the embouchure—the positioning and use of the lips, tongue and bottom jaw pressure—along with unique fingerings, Osland launches a ripple of notes skyward. It's a technique with attitude and altitude. It's music that flies high. Then he lands back in a more

listeners stood and gave him—and the Wind Ensemble—a long and hearty standing ovation.

"This concerto is probably the most demanding piece of music I've ever attempted—the hardest to research, develop, practice, and perform," says Osland, his eyes suddenly a bit weary from the memory of that exhausting performance. "But one way I think about the experience is, all the new ways I went about practicing and learning the piece will be reflected now in how I teach. So my students will be the ultimate beneficiaries."

 Since he's been at the University of Kentucky, Osland hasn't let much (blue)grass grow under his feet. He's published five compositions—for jazz orchestra, jazz ensemble, for little big band, and for saxophone ensemble—with a company in Los Angeles. He has made eight commercial recordings as a leader or co-leader, the most recent titled "In the Land of Ephesus." And five of his recordings have been submitted for Grammy nominations by Sea Breeze Jazz Records, a well-respected label in jazz.

Osland has made 20 educational recordings, 11 of these resulting from an annual four-week summer session at UK called May Band. "For the past 11 years, the students end this session by recording a CD of new music for a publishing company to distribute for demonstration; some of this music is written by the students, although most of it is from West Coast composers already in the publisher's catalog." This CD goes out to some 1,500 jazz band directors in middle schools, high schools and universities around the country. "This instructional recording includes two- to three-minute excerpts of each tune, so it's a sampler of sorts. And it's got UK's name on it."

In addition to his current \$24,000 UK Research Support Grant, he has garnered awards and fellowships from the Lexington Arts & Cultural Council, the Kentucky Arts Council, and the National Endowment for the Arts.

And then there's Miles Osland the author. He has also found time to publish six books, the most recent titled *The Music of Eddie Daniels* (published by Warner Brothers), and has published over 75 articles and reviews on

saxophone technique and jazz improvisation. This work can be found in the country's leading music publications, including *Downbeat*, *Saxophone Journal* and *Jazz Educators Journal*.

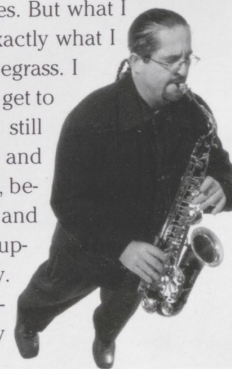
But outside of performing, nothing seems to give Osland as much satisfaction as teaching. "I love working with students and seeing them improve, sometimes immensely, in just a semester. There have been a couple this past semester that just took off—wow!—and sometimes the students don't see it as easily as the teacher."

He adds that the excitement of seeing a student improve is magnified in an ensemble setting. One of the most notable, Osland says, was the 2003 student jazz ensemble, which under his direction won top awards at the 36th Annual Elmhurst College Jazz Festival in Illinois. Out of the 36 ensembles to perform, only six big bands received an outstanding rating, and of those six, UK was the only ensemble invited to perform during the awards concert.

"I can honestly say that our ensembles, year after year, are truly among the best in the country—the students are amazing," Osland says. In the past, other ensembles directed by Osland have won the "Outstanding Jazz Ensemble" award at the Elmhurst and Notre Dame jazz festivals nine times, and five of their recordings have received four-star reviews from *Downbeat* and were submitted for Grammy nominations.

Deflecting "too much credit" for the excellence of these student groups, he underscores the importance of a "very special" colleague in the School of Music—his wife Lisa. "She directs the sax quartets and also teaches students one-on-one in the studio."

"I always thought that I would end up on one of the coasts—New York or Los Angeles. But what I have learned is that I can do exactly what I want to do right here in the Bluegrass. I am in a very fortunate position: I get to satisfy my 'teaching habit,' yet still advance myself as a recording and performing artist. And, of course, being the recipient of fellowships and grants such as the UK Research Support Grant has helped immensely. It's really tough for a musician-scholar to find funding, so I really appreciate the support." ■



Odyssey onlineexclusive

The summer 2005 issue of Odyssey (www.research.uky.edu/odyssey/exclusive) highlights how the university's massive computational power and rapid-fire network capabilities equip 15 research teams at UK in their diverse projects. This work ranges from gossamer solar-sailed spacecraft to ultracold atomic collisions; fungal genomes to DNA repair. The common denominator of all these projects is UK faculty researchers, postdocs, grad students, and undergraduates using supercomputers in the common cause of discovery. The articles on George Huang, and Brad Anderson and Tian-Xiang Xiang are reprinted here.

—JW

George Huang: Making Air Flow Work for Industry

George Huang, a professor of mechanical engineering, specializes in using Computational Fluid Dynamics (CFD) techniques to analyze air flow patterns in an array of industry applications. Huang began his career at NASA, studying air flow as it applied to aerospace design. When he came to UK in 1996, one of his goals was to utilize his expertise to assist local companies.

"Basically, if we look at air flow over an airplane, it's the same as the air flow inside of a printer, for example. It's the same flow, only the geometry is different," Huang explains.

"I believe as engineers, we have a responsibility to do not only fundamental research for publication, but to make sure that our work is connected to industry. And part of my mission is to connect my work with reality."

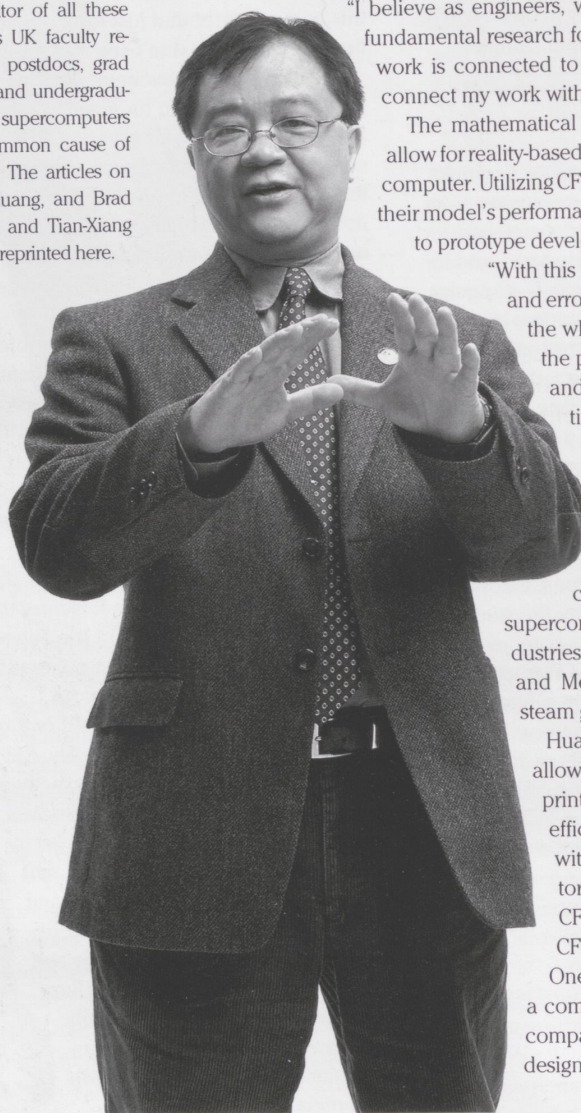
The mathematical CFD codes that Huang has developed allow for reality-based modeling of industry design concepts via computer. Utilizing CFD, industries can computationally predict their model's performance, acoustics, stability, and control prior to prototype development—saving both time and money.

"With this technology, you can actually do the trial and error on the computer. It's cheaper, and that's the whole point," Huang says. "You can do all the pre-design experiments on the computer, and then you can select only the most effective ones to go to prototype development."

The CFD codes themselves are computationally intensive, requiring the power of a 200-node parallel computer cluster, which Huang has designed with his team in the lab. Utilizing both his own computer cluster and the university's supercomputer, Huang has assisted Kentucky industries like Vogt Power International, Lexmark, and MedVenture to optimize their designs for steam generators, printers and hand dryers.

Huang's collaboration with Lexmark engineers allowed them to manipulate air flow within their printers to make the ink-drying process more efficient and to reduce noise. And his work with Vogt in designing more efficient generators has led the company to develop its own CFD branch, which, in turn, now provides CFD consulting services to other industries.

One of Huang's long-term goals is to establish a computational center at UK to formally assist companies in using CFD to maximize industrial design.



Brad Anderson & Tian-Xiang Xiang:

Streamlining Drug Design

The high cost of prescription drugs is a hot-button issue today. Patients protest that their medications are unaffordable, while pharmaceutical companies insist that the cost of years of research—and hundreds of failed drugs along the way—must be factored into prescription prices.

One means of easing the debate may ultimately lie in computer-assisted drug design. Its premise: initially narrow the field of potential new drugs computationally, allowing only the most promising ones to enter laboratory testing. It's a process that could vastly streamline drug development, thereby lowering the cost to produce—and potentially, to buy—new prescription medications.

Since the early 1990s, professors of pharmaceutical sciences Brad Anderson and Tian-Xiang Xiang have collaborated in utilizing computers to predict the developability and delivery properties of drugs. The computational methods being employed by these researchers can assist in the design of new molecules and in testing existing compounds for their efficacy and potential to be developed into marketable drugs.

Anderson and Xiang have been particularly interested in studying membrane transport—the process by which a molecule gains entrance to a cell through its membrane—as a measure of its delivery potential. After all, unless the drug can successfully cross membranes, it will never be absorbed into the bloodstream after a patient ingests a tablet, nor will the drug enter the targeted cells.

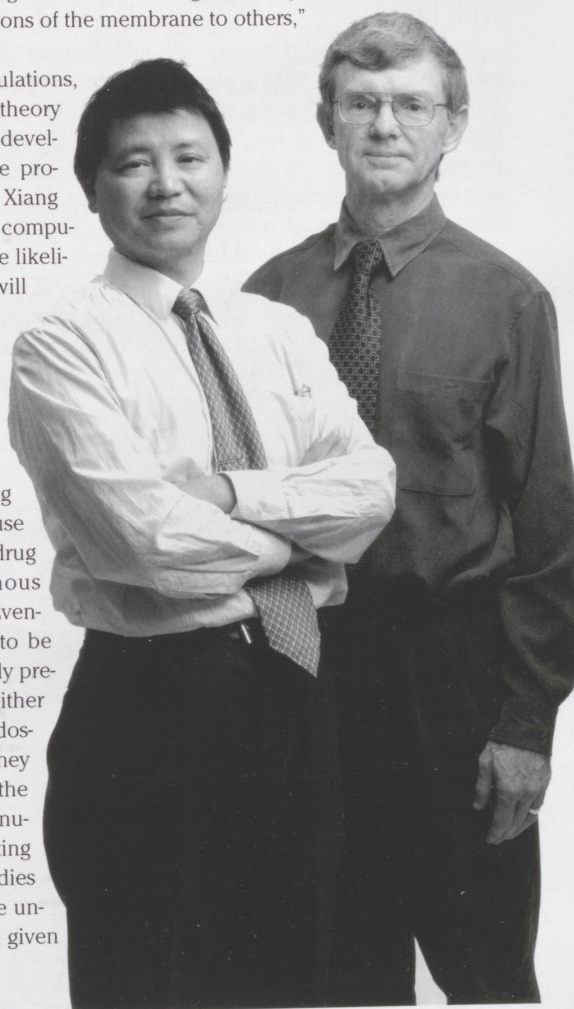
Yet the inner workings of the membrane transport mechanism are some-

what mysterious, since experimental observations do not allow one to directly observe the molecules moving within the membrane. "All we see in a transport experiment is what we have on one side of the membrane, and the rate at which it gets to the other side," Anderson says. But by utilizing molecular dynamics simulation, driven by many hours of computation on the university's supercomputer, Anderson and Xiang have been able to simulate a rare, albeit virtual, peek at how membrane transport works.

"Even though a membrane is very thin, only 30 or 40 angstroms thick, it is a very complex barrier, consisting of multiple domains. The molecular dynamics simulation allows us to watch the molecules as they partition into the membrane and diffuse through these various regions. They tumble. They rotate. They prefer certain regions of the membrane to others," explains Anderson.

Informed by their simulations, as well as specialized theory and equations they've developed to describe these processes, Anderson and Xiang are making progress in computationally predicting the likelihood that a given drug will effectively transport across a membrane. Those drugs that can cross within a desirable time frame may warrant further lab testing.

Anderson and Xiang are also exploring the use of simulation to test drug stability in "amorphous solid-state matrices." Eventually the pair hopes to be able to computationally predict a drug's stability either in tablets or other solid dosage forms. In doing so, they may be able to avoid the lengthy process of manufacturing and conducting long-term stability studies of compounds that are unlikely to be stable in a given formulation. ■



Rethinking a Major German Thinker

Written by Jeff Worley

"He had a big chip on his shoulder. He was always very radical in his political and religious views; in fact, he lost his job at Jena University because he was accused of being an atheist. He was self-righteous and extremely irascible. Someone once said of him, 'He had a hard time putting up with life.'"

Dan Breazeale, who seems, well, quite comfortable with life himself, is talking about the German thinker Johann Gottlieb Fichte, the philosopher who has most intrigued him during his 34-year career at UK. And Breazeale, professor of philosophy and this year's College of Arts & Sciences Distinguished Professor, puts the blame for his intense interest in Fichte (1762-1814) squarely on the shoulders of Bertrand Russell.

"When I was 17 or 18, I read Russell's *History of Modern Philosophy*, and Russell says something to the effect that of all the great philosophers, Fichte carries subjectivism to the point of insanity. I mean, Russell really slandered this guy—one of the major figures in German philosophy," says Breazeale, an extremely engaging man who laughs easily and often. "And maybe because I have a strong contrarian streak, I thought, 'C'mon, Fichte can't be *that* bad.' And I started reading his work."

When Breazeale traveled to West Germany on a Humboldt Fellowship in 1976, five years after he came to UK from Yale University, he began an intense study of the philosopher. But he ran into a serious problem.

"The more I read Fichte, the more I realized I had ideas to work out. The way most philosophers do this is to talk to other philosophers, but there was nobody I could talk to in my own language;

so I decided to translate a small selection of Fichte's more important early writings. Then I'd publish them and have a basis for conversation, so these translations were meant to be a means to an end. That was the plan anyway."

Well, Breazeale says, one thing led to another. "Here it is nearly 30 years later, and I've translated four big fat volumes of Fichte and I've just started on another one—I didn't mean to!—and somewhere along the way I also founded a very active scholarly association called the North American Fichte Society and became intensely involved in international Fichte research, which has



"The greatest benefit I have derived from my lifelong engagement with a few of the great philosophers of the past is that this study has helped me think through many of my own perplexities."

meant frequent travel to conferences in Europe and elsewhere. Fichte," he adds, "has been very, very good to me."

So what was this man's philosophy all about?

"He spent his entire life working on a system he called the *Wissenschaftslehre*, which means a theory of science or scientific knowledge," Breazeale explains. The primary task of Fichte's system was to explain how human beings who believe they are moral, responsible and free can at the same time feel integrated into a world that works on the directly opposite scientific principles of cause and effect, tenets that certainly appear to have nothing to do with morality, responsibility or freedom.

"He tried to resolve this tension between spirit (or free self-consciousness) and nature (or the objective world of which we are conscious) by *starting* with the former and then proceeding to the latter, understood now as a set of limitations that are conditions for the very possibility of freedom and intellect."

Any understanding Breazeale has of Fichte's writings has been hard-won, he says.

"This guy gave some of the most abstract philosophical lectures that have ever been given. His lectures are pitiless in their level of total abstraction—page after page of soul-trying abstraction."

But Fichte could also come down to earth, Breazeale says. He enjoyed giving popular lectures on the vocation of the scholar, on nationalism and other topics of general interest. "He even gave lectures about the importance of universities abolishing fraternities so that students could live a

more upstanding, serious kind of life," he adds with a chuckle.

Despite his evident commitment to pure scholarly labor, Breazeale maintains that intensely studying any philosopher is only a means to an end—being better able to examine one's own life. "I believe, as Socrates did, that the unexamined life is not worth living, and, when all has been said and done, the greatest benefit I have derived from my lifelong engagement with a few of the great philosophers of the past is that this has helped me think through many of my own perplexities."

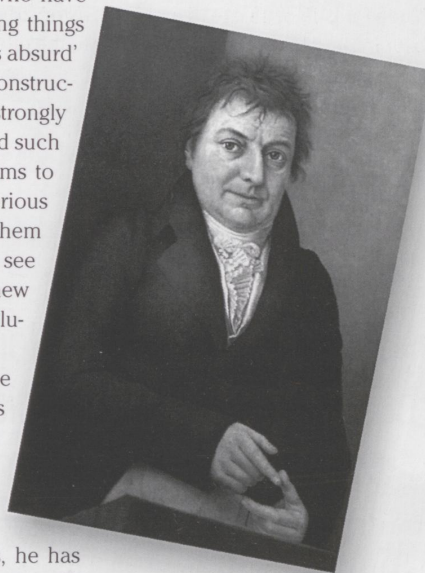
Through the years the philosophers Breazeale has been most attracted to are those who have challenged common-sense intuitions about reality and value. "Philosophers who have made a big splash by saying things like, 'God is dead' or 'Life is absurd' or 'The world is merely a construction of the mind' have most strongly attracted my attention. I find such apparently outrageous claims to be the most worthy of serious reflection. When you take them seriously, you may come to see the everyday world in a new and startling—and often illuminating—way."

Breazeale is proud of the fact that largely through his translations of Fichte, the state of Fichte scholarship is "robust" compared to what it was 30 years ago. In addition to the translations, he has written and published more than 50 essays, research papers and book chapters on Fichte and his contemporaries, and has given scores of invited lectures and presentations at professional conferences in the

United States and abroad. And recently, he's been contacted by Oxford University Press and asked to assemble 24 of his published articles on Fichte in book form.

One of the things that Breazeale says he's most proud of is his graduate students through the years. He has taught a dozen different graduate seminars and has directed as many dissertations.

"Most of my graduate students are interested in the same questions I am, and my own research has benefited as much from the contributions and criticisms of my students as, I hope, theirs has benefited from mine. I take a great deal of personal pleasure in the careers and successes of these students." ■



Johann Gottlieb Fichte is one of the major figures in German philosophy in the period between Immanuel Kant and Georg Wilhelm Friedrich Hegel.

Breathing Easier

in the Bluegrass

Written by Jeff Worley

UK College of Nursing Plays Major Role in Smoke-free Lexington

Here's Ellen Hahn, talking about an encounter that dramatically changed the focus of her professional life:

"I had just come to UK—this was 1993—and was driving near downtown Lexington. I looked over and saw a woman walking with her four- or five-year-old son. She was smoking. She'd take a puff, bend down, and give him a puff. I stopped my car and said out loud, 'Surely not.' But then they walked past me, and she continued to share her cigarette with her child. She was teaching him how to smoke."

When Hahn saw this, she realized that in Kentucky there were larger issues than drunk driving, her primary research focus when she got her doctorate in health policy and community health at the Indiana University School of Nursing just a few months earlier. So she began a full-court press to educate Kentuckians about the dangers of smoking to their health and to the health of those around them. In the Lexington area, Hahn, a professor in UK's College of Nursing, has become known

as a crusader for smoke-free public places.

"Secondhand smoke, also known as environmental tobacco smoke, is a mixture of the smoke given off by the burning end of a cigarette, pipe or cigar, and the smoke exhaled from the lungs of smokers," explains Hahn, who, when she talks about the smoking issue, manages to be intense and affable at the same time. "It's involuntarily inhaled by nonsmokers, lingers in the air hours after cigarettes have been extinguished, and can cause or worsen a wide range of health problems, including cancer, respiratory infections and asthma."



The EPA has classified secondhand smoke as a known cause of cancer in humans. It causes approximately 3,000 lung cancer deaths and 35,000 heart disease deaths in adult nonsmokers in the United States each year. A study published in *The New England Journal of Medicine* in 1999 found that nonsmokers exposed to environmental smoke were 25 percent more likely to have coronary heart diseases compared to nonsmokers not exposed to smoke. And a 2002 U.S. Department of Health and Human Services report on carcinogens found that nonsmokers exposed to secondhand smoke at work are at elevated risk for adverse health effects.

Almost everyone believes that secondhand smoke is bad for us. But how bad? And what can be done about it? These were the key questions Hahn set out to answer in four recent studies, all of which are now completed. And the early data she and her colleagues collected set the stage for a once-unimaginable policy shift in Lexington. In the heart of tobacco country, a smoke-free law went into effect in April 2004 in all public establishments in Lexington-Fayette County, including restaurants and bars.

Building the Research Base

In September 2003 Hahn and several of her staff, backed in part by a \$75,000 Robert Wood Foundation grant, did some field research, measuring the air quality in 10 Lexington businesses—restaurants, bars, night clubs, and bowling alleys—where smoking was common. The researchers, wearing backpacks, went into these establishments during three Friday and Saturday evenings. In each backpack was a MetOne photometer, which can detect and measure the level of fine-particle air pollution.

"We measured the room, counted the number of people who were smoking at the beginning, middle and end of the evening, and collected all sorts of data," Hahn explains. Specifically, her group wanted to measure particulate matter, very fine particles you can't see with the naked eye. After their visits, the researchers downloaded the information for computer analysis.

"We found that all venues tested were heavily polluted and dangerously above the federal standards for outdoor air quality," Hahn says.

Then, exactly one year later, after Lexington's smoke-



Ellen Hahn, a professor in UK's College of Nursing, has become known in Kentucky as a crusader for smoke-free public places.

"Smoke-free laws act as a vaccine to protect workers and the public from heart disease, cancer and other respiratory diseases caused or worsened by secondhand tobacco smoke."

—Ellen Hahn

How do you go smoke-free in the heart of tobacco country?

In the spring of 2001, Ellen Hahn was invited to talk to a group called Lexington Health United. This group included Emery Wilson, former UK dean of the medical school, and Douglas Scutchfield, the former head of the university's School of Public Health. Representatives from Lexington hospitals and health insurers were also there.

"Todd Warnick, the former tobacco use prevention coordinator from the Lexington-Fayette County Health Department, and I were asked to suggest the most effective way to fight smoking in the Bluegrass," says Hahn. "Todd and I agreed that the most effective policy would be to pass a smoke-free law in Lexington, so this was our message to the group."

Given that the city is in the heart of tobacco country, that Kentucky has three times the number of tobacco farms of any other state, and that Kentucky leads the country in adult smoking, Hahn wasn't optimistic about this suggestion taking root. "But they liked idea and asked us to put together a strategic plan on how to do this. So we did."

Hahn says the next two and a half years were the "education phase" of the smoke-free initiative. The work she and her colleagues did was made easier by the fact that the Health Department had already distributed pamphlets about the benefits of smoke-free environments to area restaurants. "Half of the food establishments in Lexington were already voluntarily smoke-free when we started, though there were no smoke-free bars."

In 2001, Hahn helped organize a two-day clean-air forum at the University of Kentucky. Experts on smoking cessation came from around the country. "Also, Dr. [David] Stevens was there the whole time, and he became a champion for this initiative," she

says. Stevens, a retired orthopedic surgeon and former chief of staff at Shriners Hospital for Children, serves as an at-large member of the Lexington-Fayette Urban County Council and asked then Vice Mayor Isabel Yates to appoint a task force to study the smoke-free issue.

"To get input, Isabel assembled a huge group from the community—bar and restaurant owners, burley coop folks, health professionals, farmers, police, fire, and council members. Everyone agreed that secondhand smoke harmed people. There was also consensus that a smoke-free law wouldn't hurt the farmers financially."

In November 2002, the council members began to discuss and debate the issue. Hahn made frequent appearances on radio talk shows during this time and wrote op-ed pieces for the *Lexington Herald-Leader* to try to keep the issue on the front burner. Finally, on July 1, 2003, the city council passed the law.

"It was just a couple days before July 4, and I was quoted in the *Herald-Leader* as saying, 'What a great way to celebrate our Independence Day,'" Hahn recalls. The new ordinance, which was supposed to take effect in late September, didn't sail easily into the law books, however. The Lexington Food and Beverage Association filed a suit to block the law. The suit failed; in April 2004 the Kentucky Supreme Court ruled in favor of the law, and it went into effect that month.

"If somebody had asked me when I first came to UK in '93 what the odds were of Lexington passing such a law a little over a decade later, I would have said zero," she says. "But the time was right for this. It was all about getting the facts, educating people, and about political will."

continued from p. 25

free law went into effect, this study was repeated.

"We went into the same places at the same times of night and took readings," says Kiyoun Lee, UK College of Public Health assistant professor and co-principal investigator in the study. "Fine particle air pollution was 11 times lower after the smoke-free law was enforced." Hahn adds that during this second visit, one of the sites wasn't enforcing the new law, and the readings were "enlightening."

"In that bar, we saw particulate matter that was sky high. What's interesting about this kind of monitoring is, some people think that if you don't smell the secondhand smoke, it's not there; in actuality those toxins are still in the air. Ventilation systems can reduce the smell and the odor, but they don't take the toxins away."

• • •

A second study, conducted by UK's Survey Research Center during the same time as the air-quality study, sought out public opinion about a smoke-free law in Lexington. Over 1,000 Fayette County adults (Lexington is in Fayette County), selected randomly, were asked how a smoke-free law would alter their various social practices.

Almost seven of 10 said they would go to restaurants and other public places either more often or about as often when the smoke-free law went into effect; and overall, 57 percent of those surveyed expressed support for the new smoke-free law.

"The results were similar to what we find in other smoke-free communities around the country, that these laws are a 'win' for public health and

a 'win' for business," says Hahn.

Two-thirds of those surveyed believed their risk of a heart attack or developing cancer would be higher if they lived or worked in a place that allowed smoking. This finding didn't surprise Hahn at all: "Smoke-free laws act as a vaccine to protect workers and the public from heart disease, cancer and other respiratory diseases caused or worsened by second-hand tobacco smoke."

After Lexington's smoke-free law was in effect for about six months, this survey was repeated. "We found a significant jump in support of the new law—64 percent were in favor compared to 57 percent support prior to the law going into effect," says Hahn.

An additional benefit of the ordinance is that it helps smokers who want to quit. "Smokers who work and live in smoke-free environments are more likely to quit compared to those who are permitted to smoke indoors," says Hahn. "Our survey showed that of the people who were already trying to quit before the law took effect, 44 percent quit smoking altogether after its implementation."

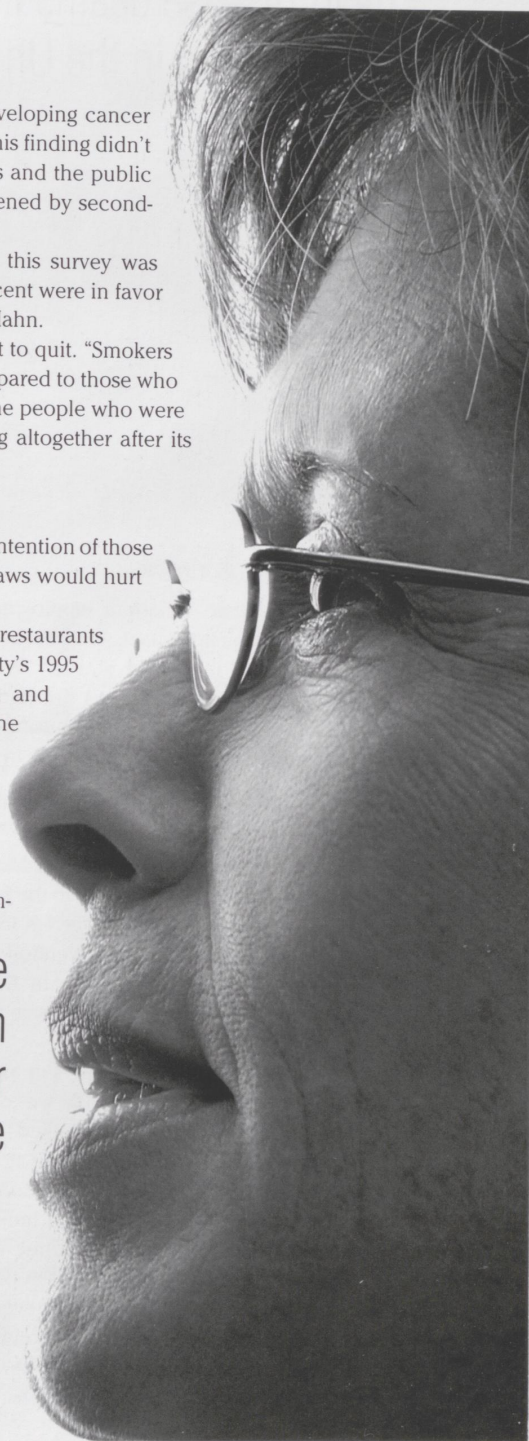
In this smoke-free process, Hahn did encounter some detractors. A major contention of those in the business community who opposed smoke-free laws was that such laws would hurt business.

It's a common argument, Hahn says, but findings from other cities where restaurants and bars have gone smoke-free don't support the contention. New York City's 1995 Smoke-free Air Act had no adverse effects on restaurant employment, and restaurant employment growth was three times higher than in the rest of the state from 1993 to 1997. Gross restaurant sales in Flagstaff, Arizona, increased 16 percent one year after a smoke-free ordinance.

But what about Lexington? To find out whether Lexington's bars and restaurants had been hit in the wallet by the city's smoke-free ordinance, Hahn brought in two economic experts and pulled in data from July 2000 through February 2005 from the Kentucky Workforce Cabinet, the Lexington-

"If somebody had asked me when I first came to UK in '93 what the odds were of Lexington passing a smoke-free ordinance a little over a decade later, I would have said zero. But the time was right for this."

—Ellen Hahn



Secondhand smoke causes approximately 3,000 lung cancer deaths and 35,000 heart disease deaths in adult nonsmokers in the United States each year.

Fayette Urban County Government Department of Revenue, and the Lexington-Fayette County Health Department.

One top economist who joined the study was Donald Mullineaux, a professor in UK's Gatton College of Business and Economics. "We used separate econometric models that included data over time on restaurant and bar employment, wages and business closures," says Mullineaux, who also serves as the duPont Endowed Chair in Banking. "We controlled for population size, seasonality, tourism, and local labor market conditions." Working with him in this statistical analysis was Eric Thompson, an economist from the University of Nebraska-Lincoln.

They found that restaurant employment increased since the law went into effect, while the average number of bar workers remained stable. "We found that Lexington's smoke-free law has not had a significant impact on overall employment, business closures or openings, or payroll withholding taxes in the restaurant or bar industries," says Thompson.

A fourth study, which was reported last July, segued from the economic health impact to the personal health of restaurant and bar workers. The UK College of Nursing collaborated with the UK Prevention Research Center to examine nicotine deposits in the hair of 106 employees at nearly 50 randomly selected Lexington bars and restaurants.

"We went to the owners in person and asked if we could recruit workers. Everybody we asked was helpful," Hahn explains. Her team asked the employees some questions about their smoking history, their health status, and their daily exposure to secondhand smoke.

Hair samples were analyzed four months before the ordinance took effect and then three months after it became law. Lower nicotine levels in the hair samples were found after the law took effect even among workers who smoked. Also, workers got fewer colds and sinus infections after the law went into effect (84 percent pre-law; 49 percent at three months; and 50 percent at six months).

"Food service workers are disproportionately affected by secondhand smoke when compared to white collar workers, and Lexington's law is helping to change that," Hahn says emphatically.



In becoming the first municipality in Kentucky to enact a comprehensive smoke-free law, Lexington joins a long list of cities to do so. "Over 1,900 municipalities in the United States have some sort of smoke-free laws," Hahn says. "And about 400 communities have what are called 100 percent comprehensive smoke-free laws. We can be proud to say we're one of them."

At the time Lexington's law went into effect, Kentucky's largest metropolitan area, Louisville, and one of its rural towns, Georgetown, were involved in smoke-free debates. Using resources at the UK College of Nursing's Center for Smoke-free Policy, which Hahn directs, she sent up-to-the-minute data on the effects of secondhand smoke on restaurant and bar employees to proponents of the smoke-free ordinance in both Louisville and Georgetown.

"I provided testimony, at the request of the city councils, about Lexington's experience, and I helped the people leading the smoke-free ordinance to strategize, based on our experience here," says Hahn. Louisville and Georgetown followed Lexington's lead. Georgetown passed a more comprehensive ordinance than Lexington's (it covers all workplaces as well as buildings open to the public), and it took effect October 1, 2005. Though not as strong as Lexington's, Louisville's ordinance (smoking in bars is permitted), was voted in, and it took effect last November. ■

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Sylvia Daunert:

Fabricating "Smart Pills" with Genetically Engineered Proteins

Sylvia Daunert is visualizing a "smart pill" for diabetes. But it's not the kind you swallow. Instead it's a matchstick-sized device implanted in the abdomen that automatically releases medication to combat each dangerous surge in blood glucose.

Why is a chemistry professor focused on diabetes? "I'm interested in all kinds of medical uses for my protein-based biosensors," says Daunert, a native of Barcelona, Spain, who is the UK Gill Eminent Professor of Analytical and Biological Chemistry. "I love to see that basic science has real applications."

Her smart-pill technology unites 11 years of research on biosensors (made from genetically engineered proteins) with drug delivery and nanotechnology. Daunert's research has been supported by NIH, the National Institute of Environmental Health Sciences, NSF, DOE, NASA, and the Army.

"I've been developing new photoproteins—bacteria that are genetically engineered to glow and emit different colors when they detect key substances." This bioluminescence is created by altering the same proteins that make jellyfish glow.

The first application for Daunert's proteins was detection of environmental pollutants like arsenic, and she developed different types of field tools,

including paper strips and CDs. These CDs are discs with a number of tiny wells (depressions) that can hold water samples. "We put the CD in an instrument—which can be miniaturized to look like a music CD player—that analyzes all of these samples at the same time to detect target pollutants. We also use this CD technology in clinical diagnosis to detect biomolecules in the human body," she explains, adding that these CDs are fabricated by her collaborator Marc Madou at the University of California-Irvine, who is also fashioning her smart pills.

"The smart pill technology is 'smart' because it delivers only the amount of drug that is needed at each particular time. The proteins will detect the concentration of the target biomolecule and respond accordingly, by opening up vials to release more or less of the drug. Marc's group fabricates these tiny vials with lids."

Most of the vials are filled with drugs, but others house Daunert's proteins and, she says, because the protein vials open for only a short time,

the proteins have a long lifespan inside the smart pill.

But nano-vials aren't her only means of drug delivery. In April 2005, Madou, Daunert and her husband Leonidas Bachas (also a professor in the UK chemistry department) published a paper in the journal *Nature Materials* that describes a method of using hydrogels to deliver drugs inside a smart pill.

"Hydrogels look like a spongy material that swells and shrinks. Have you ever seen those toys: 'Grow a Dinosaur?' Those are hydrogels. You put them in water and they expand." Daunert and her team can control this swelling and shrinking in order to sense concentrations and release drugs.

Daunert has formed two Lexington-based companies since 2000: ChipRx and SenseOmics. "ChipRx is developing the smart pills to treat many different kinds of diseases. Although we're advancing the technology by leaps and bounds, it's one thing to do it in the lab, and another to test it in animals, and then go through FDA approval.



We're talking 10 years," Daunert says, but adds with a smile, "SenseOmics is now. It markets the proteins that we're developing in the lab for all kinds of applications: smart pills, environmental sensors, medical imaging, and disease management."

This last application holds special meaning for Daunert. "My daughter has Crohn's disease. That's how I met Dr. H. R. Shashidhar in the UK pediatric gastroenterology department. He knew about my research and suggested I help him develop some new methods to help patients manage their disease." Daunert has already made some progress tailoring her bioluminescent proteins for this purpose, with funding from the NSF.

She explains that in Crohn's disease, an inflammatory bowel disease that affects the small intestine, flare-ups are caused by a higher concentration of pathogenic bacteria than of normal bacteria. And what she's looking at are the signaling molecules bacteria use to communicate with each other. "What we're trying to do is analyze the saliva of Crohn's patients to detect the concentration of these signaling molecules in order to predict if the patient is heading toward a flare-up. We could then treat a patient aggressively before the flare-up starts."

Daunert plans to use her University Research Professorship funds to organize a series of workshops for students and faculty from diverse fields to learn about medical applications for nanodevices, and for pursuing collaborations with researchers at UK's Institute for Molecular Medicine.

—Alicia P. Gregory



Linda Dwoskin:

Creating New Treatments for Nicotine and Methamphetamine Abuse

Linda Dwoskin is looking for a few good molecules. In two related projects—one focused on nicotine and the other on methamphetamine—she is trying to find small molecules that block receptors and transporter proteins responsible for the "reward" associated with nicotine and methamphetamine use. These molecules might serve as novel therapeutic agents to help those "hooked" on the drugs, Dwoskin says, and enable them to stop using. In both of these projects, she is teaming up with UK colleagues—Peter Crooks (pharmacy) and Michael Bardo (psychology).

"The first project is focused on discovering small molecules that block nicotine receptors, proteins located in neuronal membranes in the brain. We chemically modify these molecules. Then, we see how the new molecules interact with specific nicotine receptors and determine their ability to block the rewarding effects of nicotine," says Dwoskin, a professor of pharmaceutical sciences.

The most promising compounds are tested in animals, in this case rats. "Our best candidate small molecules are administered to rats that are conditioned to press a lever to get IV nicotine," Dwoskin explains. "We determine

which of our compounds is most effective in stopping the rewarding effects of nicotine and, perhaps, the craving for nicotine."

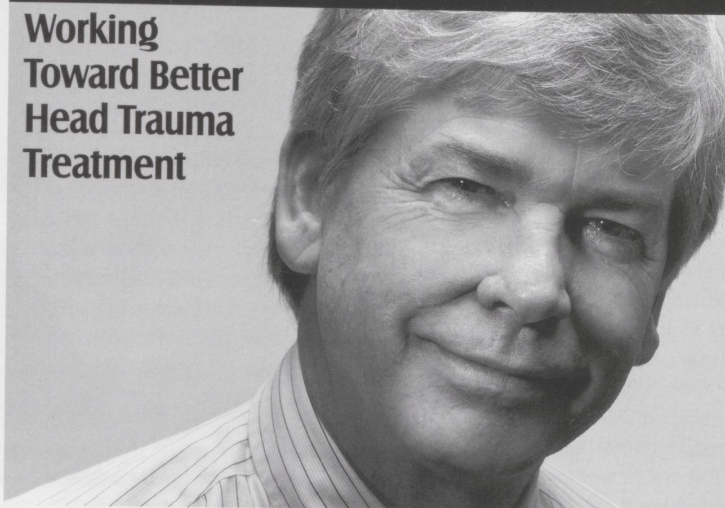
Dwoskin likens nicotine to a skeleton key. "Nicotine fits into all of these different types of nicotine receptors," she explains. "By making different chinks in the key, we should be able to focus in on one particular lock, providing an exact fit to the specific lock responsible for nicotine's rewarding effect and in this way obtain a compound with a nicotine-blocking action."

She believes this work may lead to drugs that help people stop smoking, and the National Institutes of Health obviously agrees: Two years ago the NIH awarded her a grant of more than \$6 million to continue the work. This was the largest single grant ever received by the College of Pharmacy.

In a second project, which Dwoskin says is much further along, she is continuing work that could lead to new treatments for methamphetamine abuse. For the past 10 years, Dwoskin, Crooks and Bardo have been focusing on a compound called lobeline, an alkaloid from American Indian tobacco. Backed with NIH funding, their methamphetamine work uses a process similar to that of the nicotine

Stephen Scheff:

Working Toward Better Head Trauma Treatment



study. "Lobeline is a much more complicated molecule than nicotine, so there's more you can do to alter its structure," Dwoskin says.

"After determining that lobeline blocked the neurochemical effects of methamphetamine, we found that when rats that press levers to obtain IV methamphetamine are given lobeline, they don't want the drug anymore. Even when the rats were offered larger doses of methamphetamine, they still would not work to obtain the drug. This was very encouraging evidence from animal studies," Dwoskin says.

This was such good news, in fact, that the researchers patented lobeline as a methamphetamine-blocking agent, and Crooks and Dwoskin began working with investors in 2002 to form a company to further develop and market it. The result was Yaupon Therapeutics Inc., a specialty pharmaceutical company that develops small molecule pharmaceuticals licensed from academic laboratories.

"Lobeline, with support from the National Institute on Drug Abuse, has now passed Phase I clinical trials with flying colors," Dwoskin says. "In human subjects given the drug, it was shown to be safe; there were no adverse effects."

Dwoskin says she is pleased to be named as a University Research Professor for 2005-2006 and she is using this award to support a postdoc from Belarus, Russia, to work on these projects. "She comes very highly recommended and will make a great addition to our lab."

—Jeff Worley

You can count on Stephen Scheff, a professor of anatomy and neurobiology at the University of Kentucky, to be exuberant and at least a little unpredictable, so his response to a question about brain injury after head trauma was almost unsurprising.

"You want to talk about some things we know about head trauma? Well, why don't we start with what happens on the football field?"

Then Scheff, who's been teaching brain anatomy in the UK College of Medicine for nearly 24 years, explains. "It's well known among football players that creatine monohydrate, a dietary supplement, helps their muscles respond better and recoup faster after, say, running 40 yards at top speed then being tackled and piled on by a few 300-pound men. With creatine, the guy's ready to go again in a couple minutes."

Although it's unlikely, Scheff adds, that professional athletes use creatine specifically to lessen the severity of head trauma, that is one of its possible ef-

fects. "It's commercially available and has been found to be very neuroprotective in experimental head trauma studies."

But what doesn't exist yet, and this is the focus of Scheff's current research, is a substance that is neuroprotective *after* brain injury.

Using brain tissue from rats and mice with induced neurotrauma, Scheff is working to understand why certain cells in the brain respond the way they do to injury. "There's a big push now to look at the genetic make-up of those cells," says Scheff, who has also worked diligently on various facets of Alzheimer's disease over the years. "We're trying to discover what kind of proteins and genes those cells express, and what happens in those cells under different conditions following an injury."

Working at UK's Sanders-Brown Center on Aging, Scheff and his research team—two graduate students and three technicians—take brain tissue from rats

with induced injuries and examine select neurons with a technique called laser capture microdissection. These selected cells can then be subjected to a number of scientific analyses.

In this process a plastic cap is put on the tissue and a laser is pulsed at the target cells. The cap, with a piece of plastic inside, "soaks up" the cells, is removed, and the RNA and DNA can then be extracted and analyzed.

"What we can do is identify the genes that are 'upregulated,' which means, in this case, an increase in activity in response to injury. We hope that some of these are genes that play a role in protecting the cell. The next step is to try to find ways to regulate precisely those particular genes after trauma."

Currently, Scheff says, there is no therapeutic intervention following head trauma that's very successful. "But we're working right now on a substance that looks very promising—cyclosporin." With Pat Sullivan, an assistant professor of anatomy and neurobiology at UK, Scheff has published several articles in the past half dozen years on the use of cyclosporin as a neuroprotective agent following injury.

"Ah! Now! Think about it! We've got a compound we know works when given prior to the injury, and have something we know works—at least in animal models—after the injury. The question is, Are the same type of genes upregulated or downregulated when affected by these two substances? And what can we do to enhance this?"

In his work on brain injury, Scheff's lab will "benefit nicely," he says, from the funding that goes along with his University Research Professorship. He plans to use the money to travel to Washington, D.C., for advanced training in laser capture microdissection and to purchase newer and better equipment for his lab.

"Our findings in the months ahead just might give us a real breakthrough in how we deal with head trauma."

—Jeff Worley

Isaac Shlosman:

Building Galaxies in His Basement

The birth, life and death of a hundred billion stars plays out in silence. But this galactic drama isn't in the heavens. Instead, it's down two flights of stairs from Isaac Shlosman's office.

In the cool, dim basement of the Chemistry-Physics building at UK, Shlosman's own personal galaxies pulse on a cluster of computers. Created by software written by Shlosman and his team, this 3-D, animated model may one day help scientists grasp the formation and evolution of galaxies.

Shlosman, a professor in the physics and astronomy department, was born in Russia and grew up in Israel. He begins with a lesson in the relative size of the celestial bodies he studies. From largest to smallest are universe, galaxy and solar system. "Galaxies are the building blocks of this universe, and inside each galaxy there is the part we can see—ordi-

nary luminous matter like stars—and the part we can't see, so-called dark matter."

Scientists measure dark matter by the gravity it produces. "After the Big Bang, the universe was perfectly uniform and homogenous—like an even spread of butter on toast," he says with a chuckle. But gravity stepped in. "Because the universe is relatively young, less than 14 billion years old, gravity was only partially successful in clumping the matter. Ordinary luminous matter falls into traps prepared by dark matter, so it clumps together with the dark matter."

This clumping forms two types of galaxies: disks (circles with spiral arms) and ellipsoids (3-D ovals). "How does the universe decide which kind to form? That's the question we're trying to answer with our computer models."

Shlosman's models start with young galaxies. "We let gravity operate vir-

2005-2006 University Research Professors

University Research Professors

tually to clump the matter and see what kind of products we get. We form stars, and our stars age and explode and disperse energy and matter." These simulations are rooted in reality: the latest observations from world-class telescopes across the globe "and above it," Shlosman adds, are used to test the models.

His 14 years at UK have been peppered with stints at Lawrence Livermore National Laboratory, Cal Tech, the University of Colorado at Boulder, the Canary Islands (the location of the largest European telescope) and Hawaii (Canada-France-Hawaii telescope). Time spent with observers, combined with analysis of images from the Hubble Space Telescope, allow him to "see how the individual galaxies behave, and we use that as an advantage to form them and test them virtually."

But a huge part of this, Shlosman notes with excitement, involves the most bizarre objects in the universe: black holes. "Our universe is infested with black holes. In the last few years we've learned that they sit at the center of most galaxies—including our Milky Way. Black holes are the size of a solar system, a small fraction of a light year across, but they have a billion times more material squeezed into them than a solar system."

A lot of junk is flying around in space, and black holes are galactic trash cans, but, Shlosman adds, this trash doesn't just fall into a black hole. "It's like a bathtub full of water. You want to empty the tub, so you pull the stopper. The water doesn't rush straight down. It goes in spiraling." Because of this, the space junk which closes in on a black hole forms

a rapidly spinning disk. As it gets closer and closer it is squeezed by the black hole's gravity and it heats up to hundreds of millions of degrees.

Heat makes light. "This material emits every possible color of visual light, and infrared, X-ray and gamma rays. This is the most luminous stuff in the universe." The assembly of this superheated space junk is called accretion, and its motion around a black hole is what scientists call an accretion disk.

In 1989 Shlosman says he was contemplating this question: What is the source of gas in accretion disks around black holes? The prevailing theory was that the gas had a local origin—"Say, deposited by stars in the vicinity of the black hole. I took a different view—that the gas is supplied to the black holes from large distances, basically from the whole body of the host galaxy and beyond. My point was that there is a causal connection between the evolution of the galaxy and the evolution of the black holes in their very centers." Shlosman and two colleagues published this theory in *Nature* magazine in 1989 and then a commissioned review article on the same subject in 1990.

"Ten years later new data started

to come in, and it seems there is a tight correlation between the masses of black holes and the velocities of stars 3,000 light years away from them."

Much more can be learned about black holes, Shlosman says. He is recruiting a new postdoc, funded by the University Research Professorship, to tackle this subject as part of his team. ■

—Alicia P. Gregory

The UK Board of Trustees first awarded University Research Professorships in 1977. The goal of these \$35,000, one-year professorships is to enhance scholarly research and awareness of UK's research mission by recognizing outstanding faculty.

UK Continues Study of Blood Substitute for Trauma Patients

The University of Kentucky is taking part in a national clinical research trial, with at least 22 other trauma centers across the country, to evaluate the ability of a blood substitute to reduce death rates among trauma patients. About two million Americans suffer trauma-related injuries each year, and trauma is the leading cause of death among those under 45 years old.

The blood substitute, PolyHeme®, is produced from and carries oxygen in the same way as human blood. Polyheme is universally compatible with all blood types, can restore lost blood volume and can be rapidly and massively infused.

The study investigates whether PolyHeme increases survival of critically injured patients. Since last May, the blood substitute has been carried on most emergency medical helicopters in Kentucky and ambulances in some Central Kentucky counties.

Andrew Bernard, a trauma surgeon at the UK Hospital and assistant professor of surgery in the College of Medicine, is leading UK's contribution to this trial. Under the current standard of care, trauma patients receive saline solution for hydration in the field, and then their blood is typed and matched for transfusion at the hospital. Trauma patients who have lost massive amounts of blood display dangerously low blood pressure and are at risk of organ failure and death due to oxygen deprivation.

"The potential benefits of using the oxygen-bearing blood substitute in the pre-hospital setting is to boost oxygen levels earlier in treatment, which could protect major organs and improve patient survival rates," Bernard says.

Northfield Laboratories in Evanston, Illinois, which manufactures the blood substitute, hopes to enroll 720 patients in the nationwide, one-year study. Bernard

expects to enroll 40 to 50 patients at UK.

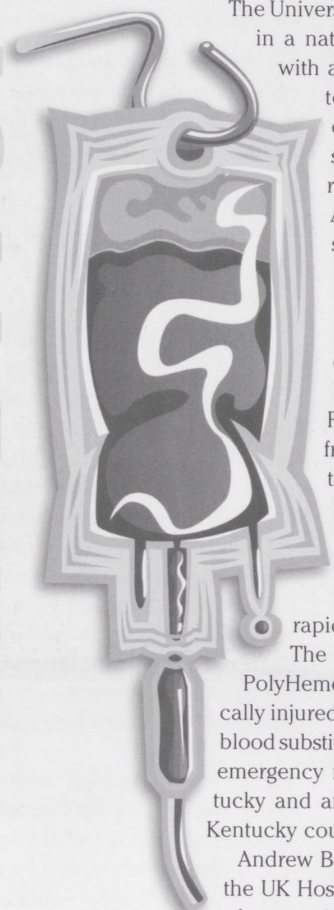
Due to the extent and nature of their injuries, it is unlikely the patients eligible for this research study will be able to provide informed consent. So the study is being conducted under a federal regulation that allows such research an exemption from the informed consent requirement at the time of enrollment in certain emergent, life-threatening situations.

Trauma victims who are transported by emergency medical services in Kentucky to the UK Hospital Trauma Center, who are at least 18 years old and who have low blood pressure within normal limits can be included in the study. While in route to the hospital, they receive either the usual saline solution to boost blood pressure (control group) or PolyHeme.

Once at the hospital, control group patients receive saline for hydration and blood transfusions as needed to boost oxygen levels. Those on PolyHeme receive saline for hydration and up to six units of the blood substitute during the first 12 hours to boost oxygen levels. Blood transfusions are given after that. Patients who receive PolyHeme may require less donated blood which, in large volumes, can suppress immunity. PolyHeme has not been shown to suppress patients' immune systems in some of the same ways as donated blood.

Efforts are made to notify family members of the patient's enrollment in the study. When notified, they are offered the choice of allowing the patient to continue in the study or to withdraw. In either case, the patient continues to receive the best medical care available.

In mid-November, Northfield Laboratories announced results from the first 500 patients. The trial's data analysis committee reviewed the data, identified no significant differences between the two groups, and recommended that the trial continue without modification.



Fighting Back against Fibromyalgia

University of Kentucky physician Leslie Crofford, a professor of rheumatology in the College of Medicine, has recently published results from a study of a drug that reduces the pain of fibromyalgia and improves sleep. The article appeared last spring in the journal *Arthritis & Rheumatism*.

Fibromyalgia is characterized by widespread musculoskeletal pain, fatigue and sleep problems. It's hard to treat, and most patients continue to have persistent symptoms even after pain management interventions. The cause of fibromyalgia is unknown.

"Fibromyalgia is a debilitating condition affecting as many as six million Americans, yet there is no approved treatment that relieves its core symptoms," says Crofford, the Gloria W. Singletary Chair and director of the Center for the Advancement of Women's Health. "This is the first study suggesting that the drug Lyrica may be effective in reducing the pain of fibromyalgia and improve some of its other symptoms such as sleep problems and fatigue."

The benefit with Lyrica was demonstrated as early as the first week of treatment. Overall, a significantly greater number of patients receiving Lyrica (450 mg per day) rather than a placebo experienced a reduction of pain, significant improvement in the quality of sleep and reduced fatigue. The eight-week trial included 529 patients with fibromyalgia.



Leslie Crofford

Research Team Earns Largest NIH Grant in College of Ag History

The National Institutes of Health has awarded a grant of more than \$6.6 million to the UK College of Agriculture to study the toxicity of environmental pollutants with a focus on nutrition, health and disease. It is the largest single NIH grant ever received by the college. The grant will support the employment of over 50 UK faculty, research scientists and students.

Under the leadership of Bernhard Hennig (nutrition and toxicology) and Leonidas Bachas (chemistry), this fund-

ing is the latest to support the work of UK's Superfund Basic Research Program (SBRP), an interdisciplinary group formed in 1997. The SBRP examines the potential links between various diseases and contaminants found at Superfund sites, including chlorinated pollutants such as PCBs (polychlorinated biphenyls).

"Kentucky has some of the worst health statistics in the United States, with a high incidence of age-related diseases such as atherosclerosis, cancer, obesity,

hypertension, and diabetes, and poor dietary habits such as high intake of processed foods," says Hennig. "The state also has numerous Superfund sites, identified by the federal government as specific areas containing high levels of toxic pollutants, which could markedly contribute to the pathology of age-related diseases."

For more information, visit www.uky.edu/research/superfund.

—Laura Skillman and Carl Nathe

The Joy of Soy

The labels in the snack food aisle make lots of big promises: low-fat, no-fat, low-cal and low-carb tasty treats. But what really makes a food healthy? And should we believe the commercial hype about soy products and our health?

Renowned nutrition, weight-loss expert and UK physician James Anderson addressed the issue of soy in two articles in last June's *Journal of the American College of Nutrition*. One article was a report on his study of soy in adult weight loss.

Meal replacements, including powders, drinks and energy bars, are popular weight-loss tools. Anderson tested two commercially available meal replacements—one soy-based and one milk-based—in a group of obese adults for 12 weeks. Both groups lost weight, but the soy-based group lost slightly more weight in any given week and displayed lower cholesterol levels. Soy intake also produced small but significant reductions in serum glucose. This evidence suggests that soy may be valuable in maintaining overall health, lowering cholesterol, and even slowing the development of diabetes. "Soy is an excellent source of high-quality protein," Anderson concludes.

In the companion article, "Snack Foods: Comparing Nutrition Values of Excellent Choices and 'Junk Foods,'" Anderson tabulated the nutrition value of about 100 snack foods and rated them on their nutrient and calorie content.

Anderson wants manufacturers and government to make the nutritional value of snack foods more readily available to consumers. "Labels should clearly identify excellent food choices and junk foods," says Anderson. "The government should also consider options such as taxing junk foods, subsidizing healthy foods, and pro-

hibiting junk food advertisements in media targeted to children, especially advertising in schools."

As a physician, Anderson regularly treats young people who are trying to control their weight. He believes stemming the American obesity epidemic is a task shared by all.

"Communities, schools, legislative bodies, movies, television, and food companies should partner in promoting healthful food choices. Where childhood obesity is concerned, we are all responsible," Anderson says.

Anderson, an endocrinologist in the UK College of Medicine and director of the UK Metabolic Research Group, is also the director of the Obesity Research Network, a nationwide network of physicians and scientists recognized for their work in the treatment of obesity. He also is medical director of the HMR® Program for Weight Management in conjunction with the University of Kentucky. For more information, visit www.mc.uky.edu/nutritionresearch.

—Allison Elliott



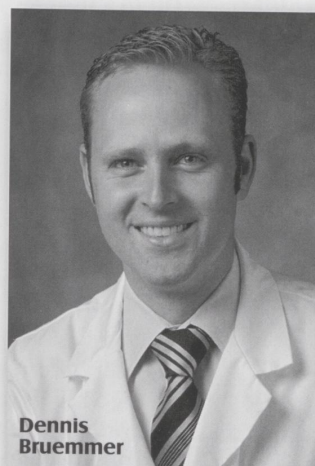
Gill Institute Researcher Wins Prestigious Award

UK researcher Dennis Bruemmer has received the 2005 Irvine Page Award for Young Investigators from the American Heart Association. An assistant professor of medicine in the Division of Endocrinology and Molecular Medicine, Bruemmer came to the University of Kentucky from the University of California, Los Angeles, and is also a faculty member of the UK Gill Heart Institute Cardiovascular Research Center.

His current research is focused on understanding the mechanisms leading to diabetic vascular complications. "In my lab, we are focused on characterizing how specific proteins in the nucleus of the cell regulate cell functions and thereby prevent the development of cardiovascular disease

in diabetes," Bruemmer explains. "Understanding these mechanisms is important because the nuclear receptors involved can be activated by drugs already clinically used to treat insulin-resistance in patients with type 2 diabetes, a common cardiovascular risk factor."

Cardiovascular disease is the leading cause of death in the nation, accounting for nearly half of all deaths. Diabetes is associated with significantly accelerated rates of cardiovascular complications. According to the Center for Disease Control and Prevention, over 18.3 percent of all Americans 60 or older had diabetes in 2002 and an estimated 65 percent of patients with diabetes ultimately die from cardiovascular causes.



Dennis Bruemmer

Preventing Shingles

A painful, blistering rash, shingles attacks an estimated one million Americans each year. Also known as herpes zoster, shingles is caused by the chicken pox virus and can develop in anyone who has had chicken pox. The chicken pox virus remains dormant in nerve root cells of the body. Ten percent of people who had chicken pox as children get shingles as adults, usually after age 60.

UK professor of internal medicine Richard Greenberg was one of several researchers nationwide whose work on an experimental vaccine to prevent outbreaks of shingles was featured in *The New York Times* last June. The researchers reported that the vaccine can reduce incidence and severity of shingles by more than half, and that the development of this drug could spare hundreds of thousands of older Americans from this painful disease. Results of the five-and-a-half-year study were published in *The New England Journal of Medicine*.

This unusually large clinical trial involved more than 38,500 people over age 60. The study was conducted by Veterans Affairs hospitals across the country. At UK, 1,167 subjects were enrolled, says Greenberg, who has a joint appointment with UK and the Lexington Veterans Administration.

Michael Oxman, an infectious disease specialist in San Diego who headed up the study, says widespread use of the vaccine in that age group could prevent 250,000 cases of shingles a year. Merck, developer of the vaccine, has applied for FDA approval.

"The Shingles Prevention Study was a significant breakthrough for everyone who looks forward to retirement and many years of 'postponed' fun, enjoyment, travel, and family," Greenberg says. "Without the vaccine, the pain and suffering caused by shingles can last the remainder of their lives."

UK's Newest College Off to a Healthy Start

To Stephen Wyatt, the reason the University of Kentucky needed a College of Public Health is self-evident.

"It's because Kentucky is number 1, or close to the top, in many health behaviors that lead to disease or death: tobacco use, childhood and adolescent obesity, and physical inactivity, among others," says Wyatt, UK's first dean of the College of Public Health.

For Wyatt, a professor of preventive medicine and environmental health, the college has a dual mission: to fight the state's health problems and to create solutions that are efficient, cost-effective and well-targeted to individual Kentucky communities.

One highly visible program supported by the College of Public Health is the Cooper-Clayton method to stop smoking. This program was developed in the early '80s by Thomas Cooper, a Lexington dentist, and Richard Clayton, an expert on drug addiction and currently associate dean for research in the new college.

"The Cooper-Clayton method combines nicotine replacement therapy with a comprehensive smoking-cessation support program that helps smokers change the behavior patterns that accompany smoking," Wyatt explains. Working with the Kentucky Cancer Program and the Kentucky Department for Public Health and local health departments, Clayton and Cooper have given hundreds of classes across the state. "Kentucky leads the country in the percentage of adults who smoke, and this program is a direct response to that problem," Wyatt adds.

The new dean was happily surprised by the fact that the college received full accreditation, for five years, from the Council on Education in Public Health last June. The college received this honor on its first try, which, he says, is an



Stephen Wyatt

extremely rare feat. "Attaining this status will clearly strengthen our efforts in education, research and service to make Kentucky a healthier place to live," says Wyatt. Grant awards since July 2005 to faculty associated with the college total nearly \$5,500,000.

The college currently has 36 faculty and 250 graduate students, and Wyatt believes these numbers will increase since there are currently huge career opportunities in public health. "Between 1976 and 1984, a huge number of folks came into the state and federal public health system, and these people are now at the end of their careers, so the opportunities for new university grads are out there. In fact, numerous reports indicate that as high as 30 percent of the federal public health workforce is eligible to retire over the next five years.

—JW

UK Researchers Attract Record Amount in FY 2005

University of Kentucky faculty researchers brought in a record \$274 million in grants and contracts in FY 2005. That's a 15 percent increase over last year and the fourth year in a row that UK has exceeded \$200 million.

"Securing grants and contracts is an extremely competitive and arduous process," says Wendy Baldwin, UK's executive vice president for research. "The achievement of UK faculty is even more remarkable when you consider how slow the growth has been for research budgets at the federal level in recent years."

Baldwin cited the importance of research at UK in meeting challenges that confront the state.

"From early intervention efforts on behalf of children with disabilities to the development of new pharmaceuticals and therapies," Baldwin says, "our research is making a difference in the lives of Kentuckians."

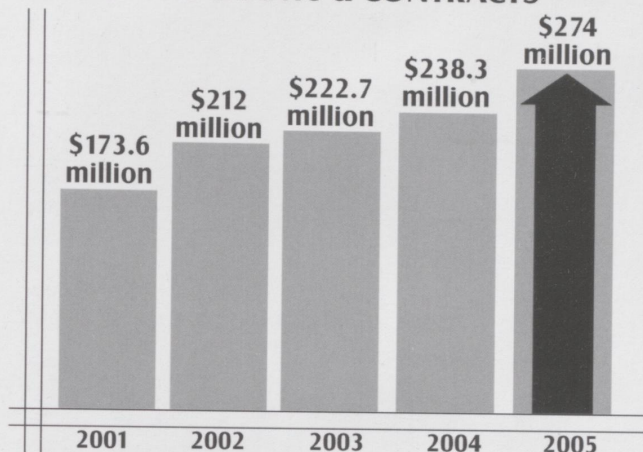
FY 05 Selected Research Highlights

UK began a \$2 million NSF project to recruit, retain and graduate Appalachian and minority science, technology, engineering, and mathematics (STEM) majors. The STEM project is under the direction of Robert Tannenbaum (undergraduate education), Carl Eberhart (mathematics) and Jeffrey Osborn (biology).

Working with scientists at Ohio State University, Russell Mumper, associate director of UK's Center for Pharmaceutical Science & Technology, has developed freeze-dried black raspberry gels for oral and topical cancer chemo-prevention. In a new study, 20 patients with oral lesions will receive treatment with the gels to see if the berries inhibit cancer growth.

Peter Nagy, a professor of plant pathology currently backed by grants from both NSF and NIH, is using Tombusviruses, RNA viruses of plants, to identify the

UNIVERSITY OF KENTUCKY RESEARCH GRANTS & CONTRACTS



players and unravel the mechanism of virus replication. RNA replication is the central process in viral infections and leads to the production of millions of progeny viruses in infected cells. Better understanding of virus replication will lead to improved antiviral strategies and enhanced resistance against viral diseases in plants.

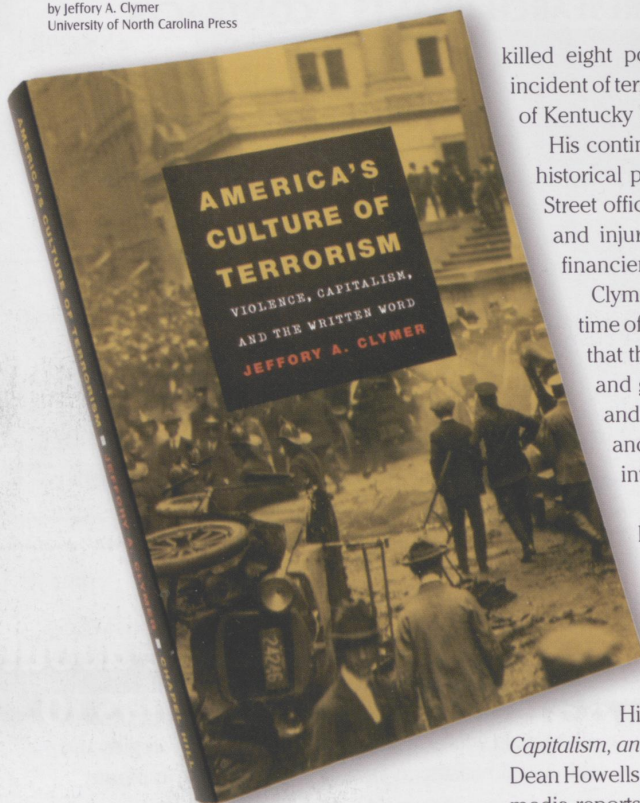
Two UK colleges were awarded over \$20 million in Center of Biomedical Research Excellence (COBRE) grants from NIH, which will enable the university to be more competitive in seeking future research funding and attracting top faculty and graduate students. Jeffrey Ebersole will oversee the College of Dentistry COBRE and the researchers who will investigate how oral diseases affect other health problems, including HIV, atherosclerosis and gestational diabetes. Louis Hersh, COBRE program director for the College of Medicine, will work with researchers in molecular and cellular biochemistry on diabetes, cancer and Alzheimer's disease projects.

For more on UK's FY 2005 sponsored project awards, go to www.research.uky.edu/numbers. ■

Book End

Terrorism on American Soil through the Lens of Literature

America's Culture of Terrorism: Violence, Capitalism, and the Written Word
by Jeffery A. Clymer
University of North Carolina Press



As a scholar of literature, Jeffery Clymer, an associate professor of English at UK, is obsessed with words and how individuals struggle to define the events of their day. An Illinois native with a longstanding interest in the history of labor issues and class struggle, Clymer's dissertation topic—terrorism in American literature and culture—began to come into focus after he read accounts of an 1886 bombing at a workers' rally in Chicago's Haymarket Square.

The workers were on strike for an eight-hour workday. A few days into the strike, anarchists and labor radicals organized a rally to draw the city's attention to the conflict. At the protest, someone—who was never identified—threw a bomb that

killed eight policemen. "Newspapers reported Haymarket as the first incident of terrorism on U.S. soil," says Clymer, who came to the University of Kentucky last fall from Saint Louis University.

His continued reading about violence on American soil during this historical period led him to the 1920 bombing of J.P. Morgan's Wall Street office in New York, in which a still-unknown bomber killed 38 and injured hundreds. The multimillionaire Morgan was a major financier and banker.

Clymer happened to be reading these accounts at around the time of the 1995 Oklahoma City bombing and was struck by the fact that the targets of all three bombings were symbols of capitalism and governmental authority. Other similarities between historic and contemporary acts of terrorism—the attendant media frenzy and violence without a claim of responsibility—deepened his interest in the subject of terrorism on American soil.

Clymer began examining how 19th-century writers used language to name, explain and make sense of these acts of violence. Clymer focused his research on the period of American history between Haymarket and the J.P. Morgan Wall Street bombing, and was particularly interested in the ways in which acts of violence are connected to the growth of industry and capitalism.

His resulting book, *America's Culture of Terrorism: Violence, Capitalism, and the Written Word*, examines works by Henry James, William Dean Howells, Jack London, and Ida B. Wells, as well as trial transcripts and media reports to show how emerging ideas about terrorism were, in part, shaped by how these writers and transcripts portrayed various terrorist acts on U.S. soil.

Clymer becomes animated when discussing the social value of literature and says it's his prerogative as a professor of English to delve into territory that is more commonly reserved for historians and social scientists.

"I'm a literature professor, but I see literature as being deeply enmeshed in the culture," he explains. "Imaginative literature is a genre where real and intractable social problems are articulated, described and processed. We comprehend events through language, and literature is one of culture's important sites where we establish—and fight over—our terms, ideas, and ways of talking about or understanding life."

Clymer had completed the manuscript for *America's Culture of Terrorism* before September 11, 2001. However, the magnitude of the events of that day led him to add an epilogue that reflects the difficulty in making sense of such a catastrophic occurrence. He found that as with previous examples of terrorism in our history, 9/11 compelled Americans "to attempt to regain our mental balance by groping toward" a collective understanding of terrible events. ■

—Laura Sutton

Odyssey
Fall 2005

Parting Shots

I don't know anything about music. In my line you don't have to.

—ELVIS PRESLEY

Everybody should be able to make some music...That's the cosmic dance!

—MAUDE (RUTH GORDON),
FROM "HAROLD & MAUDE"

Music is the only language in which you cannot say a mean or sarcastic thing.

—JOHN ERSKINE

Never look at the trombones.

You'll only encourage them.

—RICHARD STRAUSS, ON CONDUCTING

Without music, life would be a mistake.

—FRIEDRICH NIETZSCHE

The best music... is essentially there to provide you something to face the world with.

—BRUCE SPRINGSTEEN

Music is nothing separate from me. It is me. You'd have to remove the music surgically.

—RAY CHARLES

There's nothing remarkable about it. All one has to do is hit the right keys at the right time and the instrument plays itself.

—JOHANN SEBASTIAN BACH

Too many pieces of music finish too long after the end.

—IGOR STRAVINSKY

Music is the art of thinking with sounds.

—JULES COMBARIEU

Odyssey

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Breathing Easier in the Bluegrass, p. 24

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