2009-2010 University Research Professors

Gang Cao: Spinning, But Keeping His Balance

By David Wheeler

Gang Cao believes in balance. A physics professor in the College of Arts and Sciences, Cao enjoys curling up on the couch after a hard day's work, glass of wine in hand, classical music on the stereo. "There are so many fascinating, exciting things going on in the world," says Cao, whose parents are comparative literature professors in China. "As an intellectual, as a human being, you should know more than simply what you are doing at work."

Before explaining his research, Cao places his hands on his tidy desk. The sleeves on his crisp white shirt are rolled up evenly.

His belief in balance extends to physics—and specifically to an emphasis on both the study and creation of materials used in science. His pioneering approach has attracted a $4.5 million National Science Foundation grant for UK's Center for Advanced Materials. "Our unique niche is that we are going to focus on novel materials synthesis and characterization—both the creation and investigation of materials. And this approach is still largely missing in the United States.

"There is this biased view that making materials is a low-level job, so scientists don't need to do it," he says, leaning back in his chair. "But if you want to be a good materials scientist, the first thing you need to know is how to *make* materials."

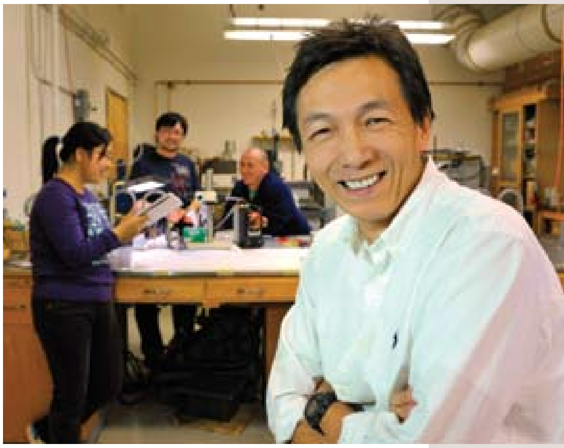
Take, for example, "spin valves"—a nano-level technology that is part of a $100-billion industry called spintronics. Spin valves, which control the direction of an electric current through magnetism, are used as magnetic sensors in devices such as computers and iPods. Spin valves can be created in artificial thin films, but they can also occur naturally in crystal formations. Cao not only creates spin valves synthetically, but also studies them in laboratory-grown crystals.

The process of synthetically manufacturing a spin valve is complicated and costly though, requiring expensive equipment, powerful vacuums, and nanoscale patterning of artificial thin films. And after all that trouble, the performance of the resulting valves is sometimes difficult to control.

Responding to this problem, Cao made two important discoveries about spin valves that were published in 2008 in *Physical Review Letters*. First, he bypassed the complicated synthetic manufacturing process with his team's discovery of naturally manufactured single crystals that demonstrated the properties of spin valves. He calls it "the bulk spin valve effect." Second, Cao found through research in his lab that these crystals were cheaper and easier to make, and had a stronger spin valve effect than synthetically produced spin valves.

When discussing his research, Cao, who came to UK in 2002, makes sure to credit colleagues with whom he has collaborated, including Lance DeLong, Joseph Brill, Sean Parkin, and Kwok-Wai Ng. "I am also very fortunate right now to also have four excellent graduate students and strong departmental support," he says.

Discoveries such as the bulk spin valve effect could help this country regain its footing in materials research. "Whoever controls the development of new materials controls science and technology," Cao says with a confident smile. "If you can develop better materials, then you can make better iPods, better computers, better cameras."



Cao's scientific ambition springs from the strong obligation he feels toward his parents. "They expected me to be successful in science," he says. After earning a bachelor's degree at Wuhan University in China, Cao came to the United States to study physics at Temple University. "I studied so hard," he says. "For the first couple of years, it was for my parents. I didn't want to let them down. Then, when you really get into physics, you just want to spend every minute in the lab."

But now Cao doesn't tie himself to the lab, because of a "major, wonderful" change in his life. "We have three sons—the youngest two years old—so I have to put my work in a different perspective these days," he says with a laugh. ■

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.

Subba Reddy Palli: Big Discoveries from Tiny Creatures

Subba Reddy Palli grew up in a small village in India. After school, he would often go to the family farm to help his father as he tackled the challenges of farming. In talking with his father, Palli learned that insects are the farmer's major nemesis, and even at a young age envisioned himself studying insect control to help his father and other farmers.

As an entomology professor in UK's College of Agriculture for the past seven years, Palli has made significant strides toward increasing the power of insecticides. However, farmers aren't the only people Palli is potentially helping. What started out as an idea to kill bugs in the field of his native India may also save cancer patients' lives.

Cancer treatments such as chemotherapy kill cancer cells but also harm healthy cells in the process. With $800,000 in funding from Rheogene, DowAgrosciences, and the Kentucky Tobacco Research and Development Center, Palli developed "gene switch" technology, which triggers protein production only in the cancer cells to kill them so they can't proliferate and form a tumor. "Using the receptors I cloned from insects, it works just like a light switch," he says. "We can control when this gene is turned on and off." So in the future, a patient with a small tumor could get a drug injection that flips a switch and releases a protein to kill the cancer cells. The drug, a chemical ligand, would be injected directly into a tumor.

Eventually, this same technology may also have applications in treating diabetes. For diabetic patients, the chemical might be administered in the form of a pill, instead of an injection, to help control insulin production.

As for the research you are more likely to expect from an entomologist, Palli figured out a way to fight insect pests that often develop resistance to the insecticides most commonly used to kill them. Over time, the insect's body increased the production of enzymes that improved their ability to "detoxify"—metabolize and excrete—the insecticide.

Palli discovered that this problem can be solved with a new technology called RNA interference. RNA stands for ribonucleic acid, a molecule with numerous functions. "We can take small double-stranded RNAs, mix them with the insecticides, and feed them to insects," he says, leaning away from his glowing computer screen. "That prevents the increase of these enzymes, so the insects won't be able to degrade insecticides. Therefore, they will die from the same insecticides to which they are resistant right now." Palli has already shown that this strategy works in red flour beetles, who love stored grain products. He is testing the strategy on other insect pests such as the Colorado potato beetle and bed bugs.

Palli's research was made possible by $3.8 million in funding from the NIH, NSF and USDA. Palli is thrilled by this support, but admits he couldn't have accomplished what he has without his talented lab team, including 10 postdoctoral fellows, five graduate students, and eight undergraduate students.

Though the general public is likely to be most excited about the human health applications of his research, Palli is especially enthusiastic about the promise of helping farmers like his father. "The technologies we're developing at UK can be adapted by scientists all over the world to kill insect pests. When I visit different countries, I give seminars and talk to people. They know what we are doing, and they understand the value of our work here. If our work can one day help reduce hunger in the world by increasing food production, I will be very pleased." ■

Kevin Sarge: "Sumo" Wrestling with Alzheimer's Disease

Kevin Sarge is exactly what an interviewer hopes for. He answers questions precisely and after careful reflection. No question is too simplistic or off-target. When he talks about his research, he puts you at ease: Sarge, a professor of molecular and cellular biochemistry in the College of Medicine, is a patient man.

That patient approach to his work is part of what makes him a good scientist. Sarge describes the scientific process as requiring much hard work, but adds that if scientists persevere, their work can definitely pay off. Sarge's research has been funded by the NIH, published in prestigious journals such as *Science and Nature*, and is now officially recognized at UK by a University Research Professorship. When he was notified of this award, Sarge says he was both surprised and honored. "I know there are many outstanding researchers here at UK who have made really important discoveries and are very worthy of being recognized for their accomplishments."

Sarge attended Penn State in the early 1980s, followed by graduate school at North Carolina State before taking a postdoctoral fellowship at Northwestern. Since coming to UK in 1993, he has conducted research that holds promise in the fight against Alzheimer's disease. "I like studying disease processes at the level of what is going wrong with the proteins and other biomolecules involved," he says. "Because if you find protein differences in the disease state, then you can envision straightforward approaches that could compensate for the difference and perhaps correct the disease."

Knowing his Alzheimer's research is complicated, especially for a non-scientist, he walks over to a dry-erase board to create a visual aid for what he's about to discuss. Sarge draws a horizontal rectangle about the size of a ruler, which he labels "APP"—amyloid precursor protein—something all of us have in our body. "APP starts off as one protein," he says. However, certain enzymes sometimes come along and clip the protein into pieces, creating different proteins from the original APP.

To visualize this, imagine APP as a ruler. Now imagine someone cutting the ruler at the 8-inch mark and the 9-inch mark. In scientific terms, this is called "cleaving." Sarge explains: "It's like taking a pair of molecular scissors and getting the little piece out of the whole protein." Enzymes are generally known for their role as catalysts, and two particular enzymes, γ γsecretase and β-secretase, cleave the APP, essentially cutting out a section of the "ruler."

In this case, the "little piece," the section between the 8- and 9-inch marks on our imaginary ruler, is called the Aβ peptide. Because many scientists believe that this peptide causes Alzheimer's disease, any discovery of a way to block or delay the cleavage events that lead to the creation of Aβ peptide is welcomed. That's what Sarge hopes his research will do. His team discovered a particular protein, called a SUMO protein, which appears to block β-secretase from cleaving, effectively stopping the creation of the Aβ peptide. This SUMO protein is attached to APP by a bonding event called sumoylation that regulates many aspects of normal protein function.

"If we could find a way to increase SUMO protein attachment to APP, this could conceivably delay the onset of Alzheimer's."

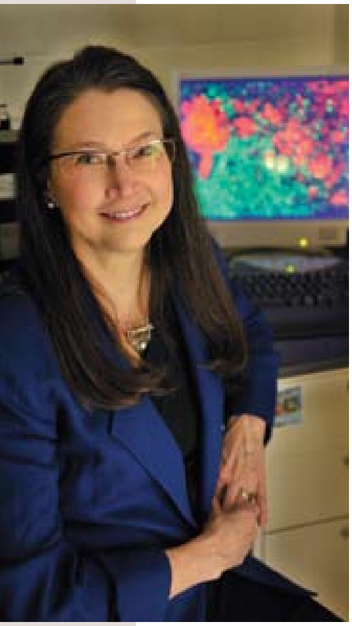
For Sarge, the most difficult and the most rewarding aspects of his research go hand in hand—in the form of articles written for peer-reviewed scientific journals. He describes the process as often being long and complicated, with many back-and-forth revisions. But when he was notified by email that he had an article accepted in the journal *Science*, he says, "I felt like I was floating."

Because it's difficult to know which scientific experiment will lead to a solution to which problem, Sarge stresses the importance of general science in the quest to cure diseases. "We can't just be doing disease-specific research," he says. "You've got to take a more general approach, because, you never know, your findings may be hugely important in the battle against many different diseases. You never know where the next big result is going to come from." ■

Karin Westlund High: Progress in the War against Pain

Painfully shy as a ninth grader, Karin Westlund High stepped on the stage, pulled out her note cards, and presented her science fair project—a comparison between pharmaceutical-grade penicillin and the mold growing on an orange. This was at the regional science competition in Austin, Texas, and the room was packed with students and teachers.

"I'd been on the stage since I was three years old, doing ballet, tap and jazz," says High, still soft-spoken even now that she is a professor in the UK College of Medicine's Department of Physiology. "But when you are on a ballet stage, the lights blind you to the audience—you can't see any faces. The regional science fair was different: I could see a hundred or so unfamiliar faces judging my every word."



But she won this competition, and then the Ford Future Scientists Award in 1967. She knew she was meant to be a scientist. Today, High is a highly regarded researcher in the field of pain studies. In fact, she has made so much progress in the field that she received the American Pain Society's Lifetime Achievement Award last May. "I was very gratified by the award, but I'd like to think I have quite a few more years of work left to offer," she says with a quiet laugh.

High's first major discovery was a cure without any side effects for the debilitating pain of abdominal cancers. Using an animal model, her team discovered that a pinpoint lesion made by a microscalpel on the spinal cord eradicates abdominal cancer pain. The discovery was published in the 1999 *Proceedings of the National Academy of Science*. Since then, in 44 case reports around the world, doctors have documented successful performance of this procedure on patients.

The procedure, which has not yet been widely adopted in the United States, is considered to be radical because it involves making a cut on the spinal cord—something that cannot be undone. The medical establishment in the United States is uncomfortable with curing pain in this way and prefers to prescribe drugs instead, High says. Previously, pain has returned after cuts were made in other places in the spinal cord. This, however, has not happened in patients with this abdominal surgery, some living for up to three years after the procedure.

High's second major discovery involves gene therapy. Her laboratory used an animal's natural ability to make proteins to overproduce an opiate at the location of the pain. Her experiment involved injecting a harmless, inactive herpes virus into lab rats suffering from pancreatitis. High not only demonstrated that the animals had less pain after the procedure, but she also encountered a surprise finding.

"The opiate repaired the damaged tissue, which was totally unexpected," says High. She published different aspects of this experiment in four research journals: *Molecular Pain*, *Molecular Therapy*, *Gene Therapy*, and *The European Journal of Neuroscience.* High says it is too early to use this experimental treatment with patients, but the procedure is being studied in a Phase I clinical trial. David Fink, chief of neurology at the University of Michigan and lead investigator of this clinical trial, says, "Very interesting results so far."

High's most recent discovery shares certain characteristics with the nicotine patch. In cooperation with a Lexington biotechnology company called AllTranz, Inc., a pharmaceutical company founded in 2004 by UK's Audra Stinchcomb and based in Lexington, High created a transdermal patch containing a chemical that can stop pancreatitis pain. The chemical comes from the marijuana plant, but is non-addictive and non-psychotropic.

"It's a practical approach to reducing pain," says High. Unlike her first two major discoveries, the patch has a good chance of catching on in the United States for two reasons: it's a pharmaceutical approach, which the American medical community prefers, and the public is already accustomed to the idea of a transdermal patch, thanks to the nicotine patch.

When High looks back on her career, she can't help but think about the junior high science teacher—Linda Baines—who pushed her to excel when she was a shy teenager. And one further goal of High's is to inspire the next generation of scientists. One of her former students, Kathleen Sluka, is now a professor at University of Iowa's medical school and directs the pain laboratory there. "It's very rewarding to see Kathleen become a major research player in the field of pain," High says. ■