

UC SANTA BARBARA

# THE *Current*

March 8, 2012

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## **UCSB Associate Professor Receives \$750,000 NSF Research Award**

Songi Han, associate professor in the Department of Chemistry & Biochemistry at UC Santa Barbara, has received a \$750,000 award from the National Science Foundation for her research, "IDBR: Novel Electron-Nuclear Dual Resonance Instrument with Arbitrary Microwave Pulse Shaping to Advance the Structure and Dynamics Study of Biological Systems."

The project aims to enhance the sensitivity of pulsed electron paramagnetic resonance (EPR) instruments, spectroscopic tools that offer important analysis and diagnostic information in the chemical and biomedical fields. While currently not as highly developed and widely disseminated as sister technologies, such as Nuclear Magnetic Resonance (NMR) and Magnetic Resonance Imaging (MRI), EPR technology offers the opportunity to dissect the structures and functions of large and complex biological systems that often escape the limits of NMR and MRI diagnosis.

NMR gives the most detailed information of a biomolecule at the atomic level.

But, the level of detail is both its strength and its detriment. Objects under scrutiny -- proteins, for instance -- have to be well-defined, not too large, and "well-behaved," according to Han.

"More often than not, in biology, proteins are part of a messy system," said Han, adding that they often interact with one another and with other structures. The real

strength of EPR, she said, is its ability to give an overview of large and complex biological systems, where the tight, close-up focus of NMR and MRI can't provide useful information on structure and dynamics.

Take, for example, the early and soluble protein aggregates that are thought to be toxic species, which eventually form amyloid fibrils found in the brain of Alzheimer's sufferers. These soluble protein oligomers and aggregates are already too big to be viewed easily by NMR spectroscopy, too ill-defined to be viewed by X-ray crystallography and too small to be seen by transmission electron microscopy, said Han. With the degree of control being developed by Han and her colleagues to refine EPR spectroscopy, these hard-to-see proteins can be analyzed not just for structure, but also for their interactions in the larger system, in water, and as a function of environmental factors and time.

The key to accuracy is to control the shapes of the EPR spectroscope's pulses, which are used to excite the electron spin probes that report on the host molecule's local structure and their environment. Current technology provides little control over these pulses, which often result in less-than-accurate control over the readings.

By manipulating the input, said Han, it's possible to overcome the shortcomings of conventional pulsed EPR measurements.

"In order for me to account for the imperfection of my hardware, I need to shape my pulses with arbitrary pulse forms," said Han. It would also be possible to measure very fast-decaying (short-lived) signals of the electron spins of the biomolecular samples that currently can't be read due to the much slower reacting artifact originating from the slow pulse response of the conventional EPR spectroscope. Han's development will potentially push EPR to be a more mainstream analytical tool, by offering higher sensitivity, higher time resolution and the need for smaller sample quantities.

The funding from the NSF instrumentation development grant will go toward the development and applications of the EPR pulse shaping technology, which will include building, trials and troubleshooting, said Han. She and her group, which also includes co-principal investigators Mark Sherwin and John Martinis, professors of physics, are among the few researchers in the world offering unique microwave technologies essential for this development.

"We think this technology is so sought after and relevant that it has the potential to be commercialized within the next three years," said Han.

Han, who joined the UCSB faculty in 2004, received her doctoral degree in the natural sciences from Aachen University of Technology in Germany. She completed postdoctoral studies at UC Berkeley with the Feodor Lynen Fellowship of the Humboldt Foundation.

She is the recipient of numerous honors and awards, including the 2011 NIH New Innovator Award, the 2010 Dreyfus Teacher-Scholar Award; the 2008 Packard Fellowship for Science and Engineering; the 2007 National Science Foundation Early Career Development Award; and the 2004 Camille and Henry Dreyfus New Faculty Award.

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