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New technique boosts protein NMR imaging speeds

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Solid-state nuclear magnetic resonance, or SSNMR, is a valuable tool to image and analyze the chemical makeup of proteins and other biomolecules. But the imaging process is time-consuming and requires large amounts of costly isotope-labeled sample for study.

Yoshitaka Ishii, associate professor of chemistry at the University of Illinois at Chicago, believes he has found a quicker and more efficient approach to using SSNMR called paramagnetic relaxation-assisted condensed data collection, or PACC. Details of the approach are reported in the March issue of *Nature Methods* (online Feb. 8.)

Ishii and his associates found a way of increasing sensitivity of SSNMR by doping samples at varying concentrations with the paramagnetic copper-acid solution Cu-EDTA, a chemical used in many industrial applications. That made the study samples more active transponders, providing strong signals and detailed spectral information with minimal downtime.

"With SSNMR, we collect the signal responses but then have to wait for the SSNMR system to recycle, which takes up to three seconds," said Ishii. "You have to do this hundreds of times. And during most of that time, you're basically doing nothing. By our approach, we've reduced that waiting period by up to 20 times."

Ishii said the slow process of gathering spectral signal information has been the "de facto standard for over 20 years." He found it shocking how

much time is spent just waiting for results using traditional SSNMR.

The chemists also boosted the SSNMR efficiency by using a spinning speed of 40 kilohertz, instead of the usual 10 kHz, and doing a fast recycling of low radio frequency field power sequences, which minimizes the amount of irradiation heat surrounding the study sample.

"The radio frequency irradiation process typically increases temperature, but we worked it so we could get a signal without strong irradiation, which could fry out a protein," said Ishii.

Ishii and his group studied various types of molecules using this new approach, including the amyloid fibrils often associated with Alzheimer's disease, larger globular proteins and cytoskeleton proteins. The new approach worked well with each type.

The doping solution they added to enhance the sensitivity of samples did not change the chemical structure of proteins studied. Ishii said the approach also enabled his group to get useful spectral signals using much smaller samples.

"We often need samples as large as 10 microliters, but with this approach we can use as little as one microliter or less," he said. "With protein structure work, preparing samples is a major bottleneck, which limits our ability to analyze it. This approach opens up the possibility for more difficult structure determination work."

Ishii hopes the PACC approach may be enhanced to achieve even greater SSNMR sensitivity, but notes the technique, as presently tested, should allow study of molecular structural features that are currently difficult to obtain using other laboratory methods.

Source: University of Illinois at Chicago