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SPECTROSCOPY

SPEED DEMON

New computational method leads to better NMR structures faster

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SPEEDSTERS
Szyperski (left) and students with 600-MHz NMR spectrometer.

A new technique uses mathematical calculations to increase the speed and precision of multidimensional nuclear magnetic resonance (NMR) spectroscopy. G-matrix Fourier transform (GFT) NMR could help make NMR more competitive with X-ray crystallography for biomolecular structure determinations.

The method was developed by associate professor of chemistry and biochemistry Thomas Szyperski and postdoc Seho Kim of the State University of New York, Buffalo [*J. Am. Chem. Soc.*, **125**, 1385 (2003)].

NMR solution structures are obtained with multidimensional NMR, in which measurement time increases exponentially with number of dimensions. GFT NMR will potentially improve data collection speed by orders of magnitude. In the JACS study, "the gain was a factor of 250, while we increased the precision of the frequency measurements three- to fourfold," Szyperski notes. The technique uses linear equations (G-matrices) and Fourier transforms to calculate and correlate resonance frequencies from data obtained in large numbers of low-dimensional NMR experiments.

Its goal is similar to that of ultrafast multidimensional NMR, developed by chemistry professor Lucio Frydman's group at Weizmann Institute of Science, Rehovot, Israel--a technique that speeds things up by using magnetic field gradients to acquire each multidimensional NMR spectrum in a single scan [*Proc. Natl. Acad. Sci. USA*, **99**, 15858 (2002); *C&EN*, Dec. 23, 2002, page 7]. Chemistry professor Ray Freeman of Cambridge University and Eriks Kupce of Varian, Walton-on-Thames, England, are also "coming up with a very nice accelerated 2-D NMR method," Frydman says, adding that, like California's 1848 gold frenzy, "it seems we're about to face a new 'NMR rush.' "

The GFT approach "has many promising features," comments biochemistry professor John L. Markley of the University of Wisconsin, Madison. "It offers the means of collecting multidimensional NMR data much more quickly, enabling the practical collection of 4-D and 5-D data sets for biological macromolecules. On the flip side, considerably more data processing and analysis are involved. The present demonstration was with a small protein where the answers--chemical shift assignments--were known," he says. "The next step needed will be to show that the method can support the assignment of NMR signals from a larger protein with unknown assignments."

Chemistry professor David E. Wemmer of the University of California, Berkeley, says, "The idea looks powerful and might be quite significant in terms of increasing information content and accelerating multidimensional experiments."

And professor of molecular biology and biochemistry Gaetano T. Montelione of Rutgers University, Piscataway, N.J.--whose group is collaborating with Szyperski's on GFT software development--says, "The value and impact of NMR, both for proteomics and more traditional structural biology, are greatly enhanced by GFT and related methods."

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