Using a method called called GFT-NMR (G-matrix Fourier Transform-Nuclear Magnetic Resonance), a team of structural genomics scientists presented a paper on how they determined the structures of eight proteins in just 10 to 20 days per protein.

The team, led by Thomas Szyperski, PhD, professor of chemistry, University at Buffalo, N.Y., demonstrate their method in the current issue of the *Proceedings of the National Academy of Sciences* [Liu, et al., vol 102, pp 10487-10492 (2005)]. The GFT-NMR method, they say, is applicable to proteins with 200 amino acid residues or more, including membrane proteins.

Researchers typically need an average of six to 12 months to solve a single protein using conventional NMR methods. "Structure determination nowadays can be accelerated by using highly sensitive spectrometers equipped with cryogenic probes," the authors write. The idea of the cryogenic probe is to cool the RF coil, which is picking up the NMR signal," says Szyperski. "This reduces the thermal noise in the RF coil and, therefore, the signal-to-noise ratio is increased about three-fold in comparison to a conventional NMR probe. A three-fold increase in signal-to-noise corresponds to reduced measurement times by about an order of magnitude because the signal-to-noise scales with the square root of the measurement time."

Measurement times can be reduced from two days to five hours, says Szyperski. The GFT-NMR approach then focuses on reducing data sampling time in order to take full advantage of the high signal-to-noise ratio. "It's a better way to acquire multidimensional NMR information," says Szyperski.

"If the signal-to-noise ratio is tremendously high you want to get your data very rapidly," he says. "This is what we call the 'NMR sampling problem,' which is related to the very long minimal measurement time associated with very high dimensionality. GFT-NMR is a projection technique where you project the higher dimensional NMR spectrum in a lower dimensional space."

"With highly sensitive instrumentation, this protocol can lead to data acquisition in the 'sampling limited' regime, in which a large fraction (or even most) of the spectrometer time is invested to sample indirect dimensions and not for achieving sufficient signal-to-noise ratios," the authors write. The GFT-NMR approach offers a solution to this problem, they say, by joint sampling of several indirect dimensions.

The paper's authors are supported by the National Institutes of Health-funded Northeast Structural Genomics Consortium (NESG), part of the Protein Structure Initiative (PSI). Szyperski is director of the NESG's NMR division, which is the only large-scale center funded by the PSI with a strong NMR component. NESG is starting to operate as an NMR branch for the other structural genomics consortia that are focused exclusively on crystallography, including the New York Center on Membrane Protein Structure.

Szyperski expects his lab to solve between 12 and 15 structures per year using GFT-NMR.

By Elizabeth Tolchin