A sense of structure

The two main methods for determining protein structure—NMR spectroscopy and X-ray crystallography—each have distinct limitations and benefits. To determine whether one method is preferable to the other or whether the two can serve complementary purposes, two groups involved in the Northeast Structural Genomics Consortium screened >400 proteins by both methods.

The researchers produced $^{1}H–^{15}N$ heteronuclear single-quantum correlation (HSQC) spectra of each protein, believing that well-resolved HSQC spectra indicated folded proteins that were amenable to NMR spectroscopy. They then categorized the results as excellent, good, promising, or poor and/or unfolded on the basis of parameters such as spectral dispersion, line widths, and number of resolved peaks. Similarly, they screened each protein for its ability to produce diffraction-quality crystals and, when possible, they determined 3-D structures.

Of the 420 proteins studied, the researchers could determine the structures of only a handful by both methods. Furthermore, although good HSQC spectra did indicate how well a protein was folded, the spectra were poor indicators of whether the protein could form crystals or whether its structure could be determined by X-ray crystallography.

At the same time, although each method was applicable to only a subset of the proteins studied, the researchers found that a concerted approach with both methods increased the likelihood of a 3-D structure being calculated for a given protein. Thus, the groups recommend that a parallel approach with both NMR spectroscopy and X-ray crystallography be pursued to maximize the success rate of any large-scale structural study. (*J. Am. Chem. Soc.* **2005**, *127*, 16,505–16,511; 16,512–16,517)