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Combining partial NMR data and protein threading for protein structure prediction

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Protein threading provides an effective method for fold recognition and backbone structure prediction. But its application is currently limited due to its level of prediction accuracy and scope of applicability. One way to significantly improve its usefulness is through the incorporation of underconstrained (or partial) NMR data. It is well known that the NMR method for protein structure determination applies only to small proteins and that its effectiveness decreases rapidly as the protein mass increases beyond about 30 kD. Here, we present a computational framework for applying underconstrained NMR data (that alone are insufficient for structure determination) as constraints in protein threading and also in all-atom model construction. In this study, we consider both secondary structure assignments from chemical shifts and NOE distance restraints. Our results have shown that both secondary structure assignments and a small number of long-range NOEs can significantly improve the threading quality in both fold recognition and threading-alignment accuracy, and can possibly extend threading's scope of applicability from homologs to analogs. An accurate backbone structure generated by NMR-constrained threading can then provide a great amount of structural information, equivalent to that provided by many NMR data; and hence can help reduce the number of NMR data typically required for an accurate structure determination. This new technique can potentially accelerate current NMR structure determination processes and possibly expand NMR's capability to larger proteins.

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