Exhaustive mapping of methyl assignments in large proteins

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The use of methyl probes has opened new avenues for the application of NMR methods to study large molecular machines. However, in the absence of previously established backbone assignments, deriving confident assignments for methyl resonances remains a challenge. Here, we describe a fully automated method which makes use of 2 NOE peak lists and a known crystal structure (or homology-based model), to exhaustively map the set of all possible consistent assignments using algorithms from the theory of exact computing. We present results from a benchmark set of 10 protein targets spanning a range of sizes from 20-45 kDa, which show that our method can deliver 100% correct, unambiguous assignments for up to 80% of methyl-bearing residues in the system. Finally, we discuss the use of our method to model the domain structure of larger proteins, guided by methyl NOEs