The functional roles of proteins are manifested in the variety of sub-states that they sample on defined timescales. One goal of structural biology is to describe these sub-states and their motions in atomic detail. The timescales of motions can range from fast (picoseconds) to much slower global processes on the order of milliseconds to seconds. Many techniques are available to study these timescales including NMR spectroscopy, X-ray diffraction, SAX, and WAX. The measurements from these techniques can be combined with structure generation protocols to determine ensembles of structures that accurately describe protein motions. The comparison of ensembles generated using NMR relaxation measurements with those determined from multi conformer fits combinations of molecular dynamics, NMR spectroscopy and X-ray crystallography to uncover the sub-states that are sampled by dihydrofolate reductase prior to catalysis and during product release as well as for the third IgG-binding domain of Protein G. The application of these methods enables the biological implications of the motions to be understood.