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Complete Relaxation and Conformational Exchange Matrix (CORCEMA) Analysis of Saturation Transfer Difference (STD) NMR Spectra of Ligand-Protein Complexes

N. Rama Krishna and V. Jayalakshmi

Department of Biochemistry & Molecular Genetics
University of Alabama at Birmingham Birmingham, AL 35294-2041

An interesting recent application of intermolecular NOE experiment is the saturation transfer difference NMR (STD-NMR) method that is useful in screening compound libraries to identify bio-active ligands. This technique also identifies the group epitopes of the bound ligand in a reversibly forming protein-ligand complex. We present here a complete relaxation and conformational exchange matrix (CORCEMA) theory (Moseley et al., *J. Magn. Reson.*, **B108**, 243-261 (1995)) applicable for the STD-NMR experiment. Using some ideal model systems we have analyzed the factors that influence the STD intensity changes in the ligand proton NMR spectrum when the resonances from some protons on the receptor protein are saturated. These factors will be discussed and some examples of its application in some model systems will be presented. This CORCEMA theory for STD-NMR and the associated algorithm are useful in a quantitative interpretation of the STD-NMR effects, and are likely to be useful in structure-based drug design efforts. They are also useful in a quantitative characterization of protein-protein (or protein-nucleic acid) contact surfaces from an intermolecular cross-saturation NMR experiment.