

Abstract

In the application of saturation transfer difference (STD) experiments to the study of protein-ligand interactions, the relaxation of the ligand is one of the major influences on the experimentally observed STD factors, making interpretation difficult when attempting to define a group epitope map (GEM). In this work, an approximation of the relaxation matrix is described named “group epitope mapping considering relaxation of the ligand” (GEM-CRL), resulting in a simplified equation reflecting the directly transferred magnetisation rate from the protein onto the ligand. In this, the relaxation of the ligand is accounted for implicitly by inclusion of the experimentally determined longitudinal relaxation rates.

Additional to the analysis of STD spectra, application of these experiments for two systems are shown. In the first application the binding kinetics of disaccharides trehalose and trehalose-6-phosphat to repressor protein TreR of *E. coli* have been determined using STD NMR and shed light on the contrasting biological roles of these two sugars. The second application of STD experiments revealed lead structures for the development of inhibitors for CK2, a target protein in cancer research. Under the new ligands for CK2 important metabolites such as Serotonine were found.

In the second part of this work, NMR investigation of a chiral Co(III) salen catalyst, important for enantioselective hydrolytic kinetic resolution (HKR), revealed the coordination behavior of the paramagnetic, active species of this complex. Combined with quantum chemical DFT calculations, the paramagnetic chemical shifts were used to determine the salen ligand conformation, resulting in a mechanistic proposal for the enantioselective step in catalysis.