Toward the elucidation of structure and dynamics of membrane protein complexes by NMR

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Membrane protein complexes regulate a myriad of cellular functions, including ion transport, signal transduction etc. We present the application of both solution and solid-state NMR techniques to the elucidation of the interactions between Ca-ATPase (or SERCA, Sarco(endo)plasmic Ca-ATPase) and its endogenous inhibitor, phospholamban (PLB). The SERCA/PLB complex is central to the regulation of heart muscle contraction and relaxation cycle. Naturally occurring mutations disrupt SERCA/PLB interactions, impairing heart function. Solution NMR studies reveal a conformational switch of PLB from lipid-bound to enzyme bound state. In addition, 2D PISEMA and CPMAS experiments carried out on the SERCA/PLB complex reconstituted in mechanically oriented lipid bilayers show that substantial topological changes occur upon portein-protein interactions. These results pave the way for the application of these techniques to study other large membrane protein assemblies.