Inter-Domain Dynamics in a Two-Domain Protein Studied by NMR YAROSLAV RYABOV, University of Maryland at College Park, DAVID FUSHMAN — Domain orientation and dynamics often play an important role in regulation of multidomain proteins function. Here we consider a two-domain system, Lys48-linked di-ubiquitin (Ub$_2$), which is the simplest model of the polyubiquitin chain involved in the ubiquitin-proteasome pathway. Under physiological conditions Ub$_2$ adopts a compact conformation, in which the functionally important hydrophobic residues are sequestered at the interface between the two Ub$_2$ domains. Here we present a dynamic model that combines the anisotropic overall rotational diffusion with intra- and interdomain dynamics. This model describes the interdomain motion as a transition between two distinct conformational states. The model is applied to experimental $^{15}$N relaxation data for Lys48-linked Ub$_2$ acquired at neutral (pH 6.8) and acidic (pH 4.5) conditions. The model provides complete picture of Ub$_2$ domain mobility including domain orientations, time scales of domain motions, and occupation probabilities for both states of Ub$_2$. The obtained results are consistent with independent data on chemical shift perturbation mapping and spin labeling.