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**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 ( $\text{Ub}_2$ ), which is the simplest model of the polyubiquitin chain involved in the ubiquitin-proteasome pathway. Under physiological conditions  $\text{Ub}_2$  adopts a compact conformation, in which the functionally important hydrophobic residues are sequestered at the interface between the two  $\text{Ub}_2$  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  $^{15}\text{N}$  relaxation data for Lys48-linked  $\text{Ub}_2$  acquired at neutral (pH 6.8) and acidic (pH 4.5) conditions. The model provides complete picture of  $\text{Ub}_2$  domain mobility including domain orientations, time scales of domain motions, and occupation probabilities for both states of  $\text{Ub}_2$ . The obtained results are consistent with independent data on chemical shift perturbation mapping and spin labeling.

Yaroslav Ryabov  
University of Maryland at College Park

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