Many biological processes derive from the interplay of two or more proteins. This interplay often is driven by allosteric and dynamic changes within one or more of the proteins. NMR (structure and dynamics) combined with other structural (X-ray, SAXS) and biophysical techniques is unique in the ability to dissect these interactions. Our recent work has focused on the ubiquitin-conjugating enzymes (E2s) interacting with ubiquitin ligases (E3s) to create the post-translational modification of ubiquitination (Mol. Cell 2009, 2013; Structure 2012; EMBO J. 2014), which is critical to protein regulation in ERAD. RING finger proteins constitute the large majority of E3s and function by interacting with E2s charged with ubiquitin. How low-affinity RING:E2 interactions result in highly processive substrate ubiquitination remains largely unknown. The RING E3, gp78, represents an excellent model to study this process. gp78 includes a high-affinity secondary binding region for its cognate E2, Ube2g2, the G2BR. Structural analyses reveal two allosteric events that are critical to the recognition, ubiquitin-transfer, and release of these proteins. These processes suggest a role for conformational dynamics in this biological machine; however, recent attempts to apply CPMG techniques