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Protein Dynamics in an RNA Binding Protein[1]

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Using ^{15}N NMR relaxation measurements, analyzed with the Lipari-Szabo formalism, we have found that the human U1A RNA binding protein has ps-ns motions in those loops that make contact with RNA. Specific mutations can alter the extent and pattern of motions, and those proteins inevitably lose RNA binding affinity. Proteins with enhanced mobility of loops and termini presumably lose affinity due to increased conformational sampling by those parts of the protein that interact directly with RNA. There is an entropic penalty associated with locking down those elements upon RNA binding, in addition to a loss of binding efficiency caused by the increased number of conformations adopted by the protein. However, in addition to local conformational heterogeneity, analysis of molecular dynamics trajectories by Reorientational Eigenmode Dynamics reveals that loops of the wild type protein undergo correlated motions that link distal sites across the binding surface. Mutations that disrupt correlated motions result in weaker RNA binding, implying that there is a network of interactions across the surface of the protein. (KBH was a Postdoctoral Fellow with Al Redfield from 1985-1990). This work was supported by the NIH (to KBH) and NSF (SAS).

[1]In collaboration with James Kranz, Johnson & Johnson; and Scott Showalter, Florida State University.