Activation of nanoscale allosteric protein domain motion revealed by neutron spin echo spectroscopy\(^1\) ZIMEI BU, City College of New York, BELA FARAGO, Intitut Laue Langevin, DAVID CALLAWAY, City College of New York — NHERF1 is a multi-domain scaffolding protein that assembles the signaling complexes, and regulates the cell surface expression and endocytic recycling of a variety of membrane proteins. The ability of the two PDZ domains in NHERF1 to assemble protein complexes is allosterically modulated by a membrane-cytoskeleton linker protein ezrin, whose binding site is located as far as 110 angstroms away from the PDZ domains. Here, using neutron spin echo (NSE) spectroscopy, selective deuterium labeling, and theoretical analyses, we reveal the activation of inter-domain motion in NHERF1 on nanometer length scales and on sub-microsecond time scales upon forming a complex with ezrin. We show that a much simplified coarse-grained model is sufficient to describe inter-domain motion of a multi-domain protein or protein complex. We expect that future NSE experiments will benefit by exploiting our approach of selective deuteration to resolve the specific domain motions of interest from a plethora of global translational and rotational motions. The results demonstrate that propagation of allosteric signals to distal sites involves the activation of long-range coupled domain motions on submicrosecond time scales, and that these coupled motions can be distinguished and characterized by NSE.

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