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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 interdomain 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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