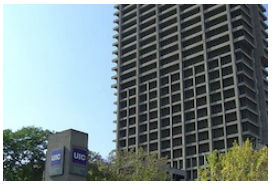

X-Ray Reflectivity Studies of Membrane-Bound Configurations of PKCα-C2 and KIF16B-PX Domains

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Title:	X-Ray Reflectivity Studies of Membrane-Bound Configurations of PKCα-C2 and KIF16B-PX Domains
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Abstract:	Upon cellular stimulation, a large number of cellular proteins reversibly translocate to their proper membrane surfaces to form complex arrays of protein-

	protein and lipid-protein molecular interactions. These proteins are collectively known as peripheral proteins (or amphitrophic proteins) that interact with and penetrate only one leaflet of the membrane bilayer. Understanding the membrane binding mechanism utilized by peripheral proteins is essential to reveal how they efficiently execute their biological functions by cooperating with their biological molecular partners. In this work, synchrotron X-ray reflectivity is used to investigate the penetration and orientation of membrane-bound for protein kinase Calpha-C2 domain (PKCα-C2) and kinesin family protein KIF16B-PX domains. X-ray reflectivity measurements are carried out to determine the configuration of the C2 domain of PKCα-C2 bound to a lipid monolayer of a 7:3 mixture of SOPC and SOPS supported on a buffered aqueous solution. The reflectivity was analyzed in terms of the known crystallographic structure of PKCα-C2 and a slab model representation of the lipid layer. The configuration of lipid-bound PKCα-C2 is characterized by two angles that define its orientation, θ =35° ± 10°and φ =210° ± 30°, and a penetration depth (PEN = 7.5 ± 2 Å) into the lipid layer. In this structure the longest β-sheet of PKCα-C2 are nearly perpendicular to the lipid layer and the domain penetrates into the headgroup region of the lipid layer, but not into the tailgroup region. The membrane-bound configuration of KIF16B-PX domain to this monolayer is quantitatively characterized by θ=30°(±10°) and φ=20°(+15°/–35°), with ~17± 2Å penetration depth into SOPC/SOPS/PtdIns(3)P mixed monolayer by X-ray reflectivity measurements. The configuration suggests that the binding mechanism was initiated by electrostatic interactions between anionic PtdIns(3)P headgroup and two conserved basic motifs of the PX domain, and then proceeded by hydrophobic insertion to further enhance the binding affinity. The binding configuration of KIF16B-PX also suggests a spatiotemporal model for the mechanism of transport of cargo by KIF16B.
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