

Abstract Submitted
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Divalent cation-induced cluster formation by polyphosphoinositides in model membranes¹ YU-HSIU WANG, PAUL JANMEY, University of Pennsylvania — Phosphatidylinositol-(4,5)-bisphosphate (PI4,5P2) binds with variable levels of specificity to hundreds of intracellular proteins in vitro. Such restricted targeting of proteins to PIP2 in cell membranes is thought to result in part from the formation of spatially distinct PIP2 pools. The hypothesis that PIP2 forms nanodomains in the membrane by electrostatic interactions with divalent cations is tested using lipid monolayer and bilayer model membranes. Competitive binding between Ca²⁺ and Mg²⁺ to PIP2 is quantified by surface pressure measurements and analyzed by a Langmuir competitive adsorption model. Addition of Ca²⁺, but not Mg²⁺, Zn²⁺ or polyamines to PIP2-coating monolayers induces surface pressure drops coincident with the formation of PIP2 nanodomains visualized by fluorescence, atomic force and electronic microscopy. Studies of bilayer membranes using probe-partitioning fluorescence resonance energy transfer (FRET) and fluorescence correlation spectroscopy (FCS) also reveal Ca²⁺-induced domain formation or diffusion retardation which follows the trends: Ca²⁺ \gg Mg²⁺ $>$ Zn²⁺, while polyamines have minimal effects. These results suggest that divalent metal ions have substantial effects on PIP2 lateral organization under their physiological concentrations.

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