

Abstract Submitted
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Molecular Dynamics Simulations of Phosphatidylinositol Bisphosphate (PIP₂) DAVID SLOCHOWER, PAUL JANMEY, University of Pennsylvania — We are interested in the dynamics of membranes containing the highly charged phospholipid phosphatidylinositol bisphosphate (PIP₂ or PtdInsP₂). We performed a geometry optimization at the Hartree-Fock 6-31+G* level of theory to determine the biological conformation of the phospholipid headgroup in the presence of water and partial charge distribution. The angle between the headgroup and the acyl chains that form an anchor in the membrane is 94°, indicating that the inositol ring may lie flat along the surface of the inner plasma membrane. Next, we employed hybrid quantum mechanics/molecular mechanics simulations to investigate the protonation state of PIP₂ and its interactions with physiological divalent cations such as magnesium and calcium. Based on preliminary data, we propose that the binding of magnesium to PIP₂ is mediated by a water molecule that is absent when calcium binds. These results may explain the ability of calcium to induce the formation of PIP₂ clusters and phase separation from other phospholipids.

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