

Abstract Submitted  
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**Role of Transbilayer Distribution of Lipid Molecules on the Structure and Protein-Lipid Interaction of an Amyloidogenic Protein on the Membrane Surface**<sup>1</sup> KWAN CHENG, Texas Tech University and Trinity University, SARA CHENG, University of Texas at Austin — We used molecular dynamics simulations to examine the effects of transbilayer distribution of lipid molecules, particularly anionic lipids with negatively charged headgroups, on the structure and binding kinetics of an amyloidogenic protein on the membrane surface and subsequent protein-induced structural disruption of the membrane. Our systems consisted of a model beta-sheet rich dimeric protein absorbed on asymmetric bilayers with neutral and anionic lipids and symmetric bilayers with neutral lipids. We observed larger folding, domain aggregation, and tilt angle of the absorbed protein on the asymmetric bilayer surfaces. We also detected more focused bilayer thinning in the asymmetric bilayer due to weak lipid-protein interactions. Our results support the mechanism that the higher lipid packing in the protein-contacting lipid leaflet promotes stronger protein-protein but weaker protein-lipid interactions of an amyloidogenic protein on the membrane surface. We speculate that the observed surface-induced structural and protein-lipid interaction of our model amyloidogenic protein may play a role in the early membrane-associated amyloid cascade pathway that leads to membrane structural damage of neurons in Alzheimer's disease.

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Kwan Cheng  
Texas Tech University and Trinity University

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