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**Effect of Lipid Bilayer on Human Islet Amyloid Polypeptide Self Assembly** CHI-CHENG CHIU, SADANAND SINGH, JUAN J. DE PABLO, University of Wisconsin-Madison — Aggregates of human islet amyloid polypeptides (hIAPP, also known as human amylin) are commonly found in the pancreatic $\beta$-cells of type II diabetes patients. Experimental studies have shown that small aggregates of hIAPP, that arise during the assembly process, lead to membrane leakage and are highly cytotoxic. Due to the fast assembly kinetics, it is difficult to study the early aggregation of hIAPP experimentally. In this work, we use molecular simulation with a coarse grained (CG) model to investigate the oligomerization of hIAPP with and without the presence of lipid bilayers. We develop a CG protein model that reproduces the three thremodynamically stable structures of hIAPP, namely $\alpha$-helix, $\beta$-hairpin, and unstructured coil, and the corresponding free energy differences calculated by atomistic molecular simulations. The aggregated structure of hIAPP also agrees with that proposed by NMR experiments. We further investigate the assembly of hIAPP in the presence of a lipid bilayer and its effect on the membrane leakage. Comparing our results with the mechanism proposed based on experimental data provides a better understanding of the origins of hIAPP self assembly and its toxicity.

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