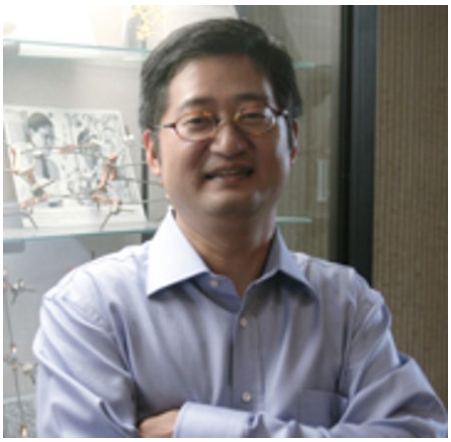
JOSEPH F. FOSTER MEMORIAL
CHEMICAL BIOLOGY AND BIOCHEMISTRY SEMINAR

Monday, November 27, 2023
3:30 PM, BRWN 4102



"Membrane Protein Folding: What Lipids Do"

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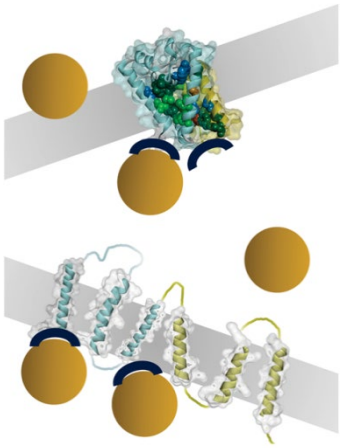
Abstract:

My talk addresses two unresolved questions regarding how the lipid bilayer in cells mediates folding and function of membrane proteins: *1)* Is the lipid bilayer a good solvent for the denatured states of membrane proteins? *2)* What is the role of lipid solvation in the stability and cooperativity of membrane proteins? In the past decade, we have developed an array of methods to delineate thermodynamic stability, conformational features of the denatured states, and residue interaction network of membrane proteins. The methods are based on the steric trapping strategy, which couples spontaneous denaturation of a doubly biotinylated protein to the simultaneous binding of bulky monovalent streptavidin. Using the intramembrane protease GlpG of *E. coli* as a model, we find that the bilayer *1)* contracts the denatured state ensemble of GlpG, *2)* enhances the stability of the protein by facilitating the residue burial in the protein interior, and *3)* strengthens the residue-interaction network so that the whole residue-packed regions act as a single cooperative unit. These results shed light and cast shadows in the folding and function of membrane proteins. The enhanced stability and cooperativity indicate that the bilayer is an adequate medium for stabilizing membrane proteins and transmitting local stimuli across the protein, which benefits function. However, the contraction of the denatured states and facilitation of residue burial point to the lipophopic effect, increasing the chance of nonspecific collapse of polypeptide chains in the crowded cell membranes. Furthermore, the enhanced cooperativity renders the conformational integrity of membrane proteins vulnerable to missense mutations.



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Department of Chemistry