Buried Lysine, But Not Arginine, Titrates and Alters Transmembrane Helix Tilt

- The ionization of amino acid residues influence membrane protein structure and function.
- The basic residues lysine (Lys) and arginine (Arg) in membrane proteins are enriched at the interfacial region and are believed to assist in anchoring the transmembrane orientations .
- In dioleoyl-phosphatidylcholine (DOPC) bilayer membranes, buried charged lysine, in fashion similar to arginine, modulates helix orientation to optimize access to the aqueous interface, or if occluded by aromatic rings, may cause a transmembrane helix to exit the lipid bilayer.
- Interestingly, the influence of neutral lysine (vis-à-vis leucine) upon helix orientation also depends upon its aqueous access.
- Results suggest that changes in the ionization states of particular residues will regulate membrane protein function and furthermore illustrate the subtle complexity of ionization behavior with respect to the detailed lipid and protein environment.

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Buried lysine, but not arginine, titrates and alters transmembrane helix tilt

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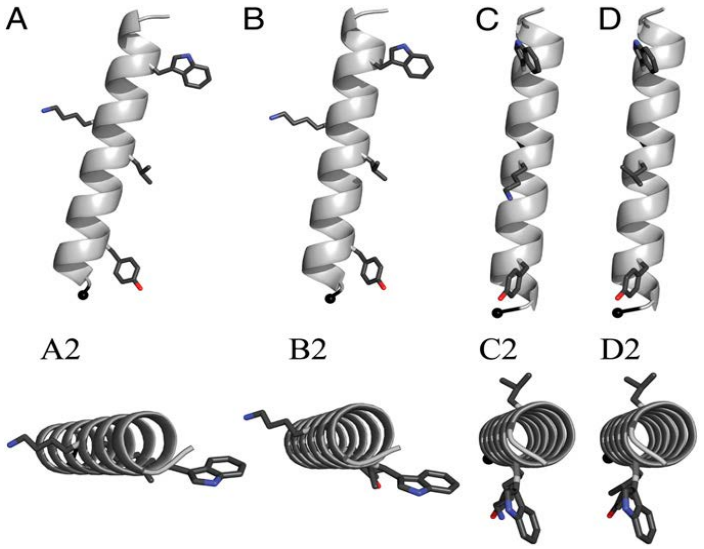

Models to show peptide helix transmembrane orientations in DOPC bilayers as function of lysine residue position and ionization state. (A) Y5GWALP23-K+14. (B) Y5GWALP23-K014. (C) Y5GWALP23-K012. (D) Y5GWALP23 itself, with no ionizable residue. See text for the peptide sequences. The side chain of residue 12 is shown as sticks for either leucine (A, B, and D) or lysine (C). [Note that Y5GWALP23-K+12 exhibits multistate behavior (as does GWALP23-R+12 (17)) and would not have a single orientation.] The peptide GWALP23-R+14 (17) orients similarly to Y5GWALP23-K+14, shown in (A). Note that Y5GWALP23-K012 (C) orients similarly to Y5GWALP23 itself (D). An alternate perspective (top view) is shown in (A2–D2).