## **Supporting Information**

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Figure SI1: The RMSD between successive running average structures for the dileucine simulation (panel A) and rhodopsin (panel B). This is the RMSD between the average structure for t = 0 to t = i and the average structure for t = 0 to t = i + 1. All non-hydrogen atoms were used for the dileucine RMSD while only transmembrane  $\alpha$ -carbons were used for the rhodopsin RMSD.



Figure SI2: The RMSD between each frame of the rhodopsin trajectory and the starting crystal structure using only transmembrane  $\alpha$ -carbons.



Figure SI3: All-to-all RMSD for the dileucine simulation (panel A) and CB2 (panel B). All nonhydrogen atoms are used for the dileucine RMSD and only transmembrane  $\alpha$ -carbons are used for the CB2 RMSD. 4