Title:	Interpretation of spectroscopic data using molecular simulations for the secondary active transporter BetP
Authors:	Sharma, Monika (/jspui/browse?type=author&value=Sharma%2C+Monika)
Keywords:	Mechanistic Dynamic membrane Proteins
Issue Date:	2019
Publisher:	Rockefeller University Press
Citation:	Journal of General Physiology, 151(3),pp. 381-394.
Abstract:	Mechanistic understanding of dynamic membrane proteins such as transporters, receptors, and channels requires accurate depictions of conformational ensembles, and the manner in which they interchange as a function of environmental factors including substrates, lipids, and inhibitors. Spectroscopic techniques such as electron spin resonance (ESR) pulsed electron–electron double resonance (PELDOR), also known as double electron–electron resonance (DEER), provide a complement to atomistic structures obtained from x-ray crystallography or cryo-EM, since spectroscopic data reflect an ensemble and can be measured in more native solvents, unperturbed by a crystal lattice. However, attempts to interpret DEER data are frequently stymied by discrepancies with the structural data, which may arise due to differences in conditions, the dynamics of the protein, or the flexibility of the attached paramagnetic spin labels. Recently, molecular simulation techniques such as EBMetaD have been developed that create a conformational ensemble matching an experimental distance distribution while applying the minimal possible bias. Moreover, it has been proposed that the work required during an EBMetaD simulation to match an experimentally determined distribution could be used as a metric with which to assign conformational states to a given measurement. Here, we demonstrate the application of this concept for a sodium-coupled transport protein, BetP. Because the probe, protein, and lipid bilayer are all represented in atomic detail, the different contributions to the work, such as the extent of protein backbone movements, can be separated. This work therefore illustrates how ranking simulations based on EBMetaD can help to bridge the gap between structural and biophysical data and thereby enhance our understanding of membrane protein conformational mechanisms.
Description:	Only IISERM authors are available in the record.
URI:	https://rupress.org/jgp/article/151/3/381/124249/Interpretation-of-spectroscopic-data-using (https://rupress.org/jgp/article/151/3/381/124249/Interpretation-of-spectroscopic-data-using) http://hdl.handle.net/123456789/2199 (http://hdl.handle.net/123456789/2199)
Appears in Collections:	Research Articles (/jspui/handle/123456789/9)

Need to add pdf.odt (/jspui/bitstream/123456789/2199/1/Need%20to%20add%20pdf.odt)	8.63 kB	OpenDocument Text	View/Open (/jspui/bitstream/12345

Show full item record (/jspui/handle/123456789/2199?mode=full)

(/jspui/handle/123456789/2199/statistics)