have demonstrated some of the effects of monovalent ions on phospholipid bilayers, including decreased area per lipid, higher ordering in head group vertical orientations, and decreased lateral lipid mobility [1-4]. MD simulations of porated membranes have also shown that the binding of monovalent cations to phospholipids can increase pore line tension, which leads to a decrease in pore lifetime [5]. In this work we employ MD simulations to systematically study the effects of varying the concentration of Na^+, K^+, and Cl^- in POPC lipid bilayer systems during different stages of electropore formation.

1.Gurtovenko, A.A. and I. Vattulainen, J Phys Chem B, 2008. 112(7): p. 1953-62.
2.Vacha, R., et al., Journal of Physical Chemistry A, 2009. 113(26): p. 7235-7243.
3.Vacha, R., et al., J Phys Chem B, 2010. 114(29): p. 9504-9.
4.Jurkiewicz, P., et al., Biochim Biophys Acta, 2012. 1818(3): p. 609-16.
5.Leontiadou, H., A.E. Mark, and S.J. Marrink, Biophys J, 2007. 92(12): p. 4209-15.

886-Pos Board B655

Conduction and Selectivity of Ions through a Sodium Channel

Leticia Stock[1], Lucie Delemotte[2], Vincenzo Carnevale[2], Werner Treptow[1,2], Michael L. Klein[2].
[1]Universidade de Brasilia, Brasilia, Brazil, [2]Temple University, Philadelphia, PA, USA.

The NavAb (a bacterial voltage-gated Na^+ channel) atomic structure has been recently resolved. Because NavAb is a possible ancestor of the vertebrate Nav and Cav - voltage dependent Na^+ and Ca^{++} channels, respectively - such a structure provides a unique opportunity to deepen our understanding on these closely related channels. Strikingly, the NavAb structure displays a selectivity filter much wider than the one observed in the well characterized K^+ channels, and therefore raises relevant questions concerning the conduction and selectivity mechanism in this channel. We follow from an ongoing project aiming at studying the conduction mechanism and selectivity on sodium channels. For that purpose, the Free-Energy surface (FES) of the permeation events of two Na^+ ions was assessed by means of a 180 ns long metadynamics calculation. In such method, two reaction coordinates are defined for each ion: the axial distance (z) along the pore axis and the radial distance (x, y) plane. The resulting four-dimensional FES is employed to retrieve the minimum energy pathway covered by the ions. In order to investigate channel selectivity, the present work extends the above mentioned studies to the two-ions constructs: sodium-potassium and potassium-potassium. Our findings point to a dynamical process in which ions transit between favorable interaction sites. Also, subtle differences in the process free-energy landscape may lead to significantly altered permeation rates. Taken together, these results are likely to provide a rationalization for selectivity.

887-Pos Board B656

The Electric Fingerprint of Membrane Voltage Sensor Domains

Cristiano Amaral, Caio S. Souza, Letícia L. Stock, Werner Treptow.
Universidade de Brasilia, Brasilia, Brazil.

Voltage-sensor domains (VSDs) are electrically-charged constructs controlling the voltage-dependent activity of ion channels in excitable cells. Four packed transmembrane (TM) helices, S1 through S4, form the domain in which S4 contains 4 to 7 positively charged basic amino acids, mostly arginines. VSDs operate essentially by transferring the S4 charges across the transmembrane electric field (**E**), giving rise to the observable Q, the so-called ''gating charge''. Mostly supported by structure-function studies on voltage-gated potassium (Kv) channels, a focused **E** has been identified as one key electric property of the VSD machinery. The recent increasing availability of other VSD-containing ion channel structures, including the x-ray structures for the NavAb and NavRh voltage-gated Na^+ channels, provides us with the opportunity to extend the structure-based investigation of the domain electrostatic properties over a larger set of distinct conformations and isoforms. Using all-atom MD simulations in combination with electrostatic calculations, founded on an energetic formalism, we show that, over the entire set of available VSD structures, a specific hydration of the voltage sensor focuses **E** over a narrow TM region across the domain, at the vicinity of the so-called catalytic center. Furthermore, its focalization and shape is largely preserved over distinct conformations of the construct. Our results support that a focused and conformation-independent TM field is a robust electric feature of the VSD machinery, despite sequence variations or local structural modifications of the domain. This electric fingerprint seems to favor a highly conserved sensing mechanism for VSDs over the large family of voltage-gated cation channels.

888-Pos Board B657

Skeletal Calsequestrin - Calcium Interaction: Role of Acidic C-Terminus

Naresh C. Bal[1], Amit Kumar[2], Harapriya Chakravarty[3], Tuniki Balaraju[3], Chandralata Bal[3], Nivedita Jena[1], Ashoke Sharon[3], Muthu Periasamy[1].
[1]The Ohio State University, Columbus, OH, USA, [2]Science and Technology Park, Pula, Italy, [3]Birla Institute of Technology, Ranchi, India.

Skeletal isoform of calsequestrin (CASQ1) is expressed primarily in fast twitch skeletal muscles in all vertebrates and buffers Ca^{2+} inside the sarcoendoplasmic reticulum (SR), the intracellular Ca^{2+} store. CASQ1 has a very unique C-terminus composed sole of aspartic acid residues. Presence of more than 10 consecutive aspartic acid residues in a protein sequence [referred as consecutive aspartate stretch (CAS)] is a very rare feature that is found only in about 20 proteins in the human genome. However, the role of CAS in CASQ1 function has not been investigated. Here we applied computational approach to understand the role of CAS in Ca^{2+}-binding. The recent structure of CASQ1 has resolved the structure of its whole protein except for the CAS. We prepared the model by adding the CAS residues and performed molecular dynamics simulations for 50 nanoseconds in the presence of various Ca^{2+} concentrations. Our study shows that the CAS assumes a compact structure at higher Ca^{2+} concentrations and indicates that the CAS might work as a metal sensor. We found that the CAS undergoes maximal Ca^{2+}-binding before the rest of the surface is saturated. The study revealed various Ca^{2+}-binding sites with differing affinities and geometry. Interestingly, some sites are Ca^{2+}-concentrations dependent while some others are independent of Ca^{2+} concentration. The low affinity sites of CASQ1 bind Ca^{2+} transiently that is mediated by water molecules and can dissociate quickly to support Ca^{2+}-release during contraction. These studies collectively indicate the CAS works as a Ca^{2+}-sensor that may be a novel metal sensing motif. We propose the term ''D_n-motif'' for CAS.

Single Molecule Techniques I

889-Pos Board B658

Single-Molecule DNA Curtains Reveals the Details of KOPS Targeting, Translocation, and Collision with Protein Roadblocks of DNA Translocase FtsK

Ja Yil Lee[1], Ilya J. Finkelstein[1,2], Estelle Crozat[3,4], David J. Sherratt[3], Eric C. Greene[1,5].
[1]Department of Biochemistry and Molecular Biophysics Columbia University, New York, NY, USA, [2]Department of Chemistry and Biochemistry, Austin, TX, USA, [3]Department of Biochemistry, University of Oxford, Oxford, United Kingdom, [4]Institut de Genetique Microbienne, Universite Paris Sud 11, Orsay, France, [5]Howard Hughes Medical Institute Columbia University, New York, NY, USA.

In E coli cell division, two daughter chromosomes often form a dimer, which impedes a proper segregation of chromosomes. The chromosome dimer can be resolved by XerCD-mediated site specific recombination at dif site. The alignment of two dif sites and activation of XerCD require FtsK translocation, which is directed by a short DNA sequence called KOPS (FtsK Orienting Polar Sequences). KOPS targeting and translocation activities of FtsK were examined using single-molecule DNA curtains, which enables to visualize the protein-DNA interaction in real time. We show that FtsK preferentially locates KOPS through 3D collision within our resolution and non-hydrolysable nucleotides enhance the FtsK loading on KOPS. We also reveal that KOPS determines the orientation of FtsK translocation, but only upon initial binding to KOPS. During the translocation, FtsK abruptly pauses and/or changes its direction independently of KOPS, suggesting that FtsK cannot identify KOPS once it begins to translocate. Next we investigated the collision of FtsK with various protein roadblocks including XerCD through two-color labeling in DNA curtains. Interestingly, the FtsK, which has a hexameric ring structure, changes its direction and bypasses the roadblocks, and can also push them along the DNA. Our single-molecule results help reveal how FtsK might function in the crowded environments expected to be found in physiological settings.

890-Pos Board B659

Single-Molecule Dissection of KRas and EGFR Signaling Dynamics in Individual Cancers

Hong-Won Lee[1], Min Kwon Cha[1], Seung-Hyo Lee[2], Tea-young Yoon[1].
[1]Department of Physics, KAIST, 335 Gwahak-ro, Yuseong-gu, Daejeon, Korea, Republic of, [2]Graduate School of Medical Science and Engineering, KAIST, 335 Gwahak-ro, Yuseong-gu, Daejeon, Korea, Republic of.

At the molecule level, individual cancers are driven by their own sets of dysregulated protein-protein interactions. Due to the lack of PCR technique for