vesiculation in the RBC membrane. We investigate vesiculation induced by the spontaneous curvature of the membrane domain and vesiculation induced by a stiffened cytoskeleton causing compression on the lipid bilayer. In addition, we model vesiculation in RBCs from patients suffering from the blood disorders of hereditary spherocytosis (HS) and elliptocytosis (HE). Our simulation results show that the spontaneous curvature of a membrane domain induces vesicles with a diameter less than 50 nm. We also found that compression on the membrane can cause the formation of vesicles having heterogeneous composition with a size similar to the size of the cytoskeleton corral. When both effects are taken into consideration, the compression on the membrane can facilitate the formation of vesicles originated from the membrane domain with the same spontaneous curvature. While the size of the vesicles induced by the compression in the normal RBC membrane is similar to the cytoskeleton corral size, the vesicle sizes become more diverse in HS RBCs because the constrain from the cytoskeleton on the lipid bilayer is reduced. When the vertical connectivity between the lipid bilayer and the cytoskeleton is elevated, multiple vesicles, with sizes similar to the cytoskeleton corral dimension, are generated from the compressed membrane. However, membrane with low vertical connectivity tends to produce larger vesicles under the same compression ratio as above. In HE RBCs, the reduced cytoskeleton connectivity facilitates the membrane vesiculation. It is noted that vesicles released from the HE RBCs could contain spectrin filaments while vesicles released from the HS RBCs are depleted of cytoskeleton components.

1227-Pos Board B178

Modeling and Simulations of Glycosphingolipids Determining A, B, and O Blood Groups

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Glycosphingolipids are the biological recognition sites in determining human A, B, and O blood groups. They are composed of the long-chain amino alcohol sphingosine, a long-chain fatty acid, and an oligosaccharide polar head group that is joined by a glyosidic linkage. These oligosaccharide sequences that determine human A, B, and O blood groups are almost identical except one terminal sugar (galactose). To understand the structural function and dynamics of the A, B, and H glycoshingolipids and how they act as receptors on the red blood cell to determine the A, B, and O blood groups, we performed molecular dynamics simulations for all three blood type antigens in a membrane bilayer environment. Using CHARMM-GUI (www.charmm-gui.org), we built a membrane bilayer and put one Blood Type A antigen in the upper leaflet and one in the bottom leaflet, and simulated it three times. This was done for Blood Type B antigen and Blood Type H antigen. Future work involves gaining a deeper understanding of the glycosphingolipids' structure and dynamics, which will help lead to a better functional understanding of the human glycome.

1228-Pos Board B179

Advanced Modeling of the Human Skin Barrier

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The first line of defense of the human body against harmful agents such as toxic chemicals, viruses and bacteria is the stratum corneum (SC), the skin's outer layer. A simple ''brick and mortar'' analogy is often used to describe how the lipid matrix (the ''mortar'') of the stratum corneum holds together keratin-rich and largely impenetrable corneocytes (the ''bricks''). Primarily due to uncertainty in the molecular structure of the lipid matrix, the pathways of permeation of toxic chemicals or drugs administered transdermally are not completely understood. We've used molecular dynamics to simulate a multi-lamellae 30-nm cross-section of the lipid matrix, totaling nearly 1 million atoms, under varying conditions of acidity and salt concentration for more than two microseconds. During our simulations, the skin's lipids form spontaneously a multilamellar structure where small pockets of water are separated by regions of partial fusion between the lamellae. The simulations suggest a potential assembly mechanism of the SC having a delicate balance between the lipid, water and salinity contents, which we've interrogated further using our recently developed coarse grain parameters for ceramides and cholesterol. In addition to visualizing a key event in the assembly of the largest human organ, our results further clarify the criteria to develop new delivery vehicles for pharmaceutical treatment.

1229-Pos Board B180

Dehydration of Multilamellar Fatty Acid Membranes: Towards a Computational Model of the Stratum Corneum

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The level of hydration controls the cohesion between apposed lamellae of saturated free fatty acids found in the lipid matrix of stratum corneum, the outermost layer of mammalian skin. This multilamellar lipid matrix is highly impermeable to water and ions, so that the local hydration shell of its fatty acids may not always be in equilibrium with the acidity and relative humidity, which significantly changes skin growth over a course of days. The homeostasis of the stratum corneum at each moment of its growth likely requires a balance between two factors, which affect in opposite ways the diffusion of hydrophilic species through the stratum corneum: (i) an increase in water order as the lipid lamellae come in closer contact, and (ii) a decrease in water order as the fraction of charged fatty acids is lowered by pH. We employed molecular dynamics simulations to estimate the impact of both effects on water molecules confined between lamellae of fatty acids. Under conditions where membrane undulations are energetically favorable, the charged fatty acids are able to sequester cations around points of contact between lamellae that are fully dehydrated, while essentially maintaining a multilamellar structure for the entire system. This observation suggests that the undulations of the fatty acid lamellae control the diffusion of hydrophilic species through the water phase by altering the positional and rotational order of water molecules in the embedded/occluded ''droplets''.

1230-Pos Board B181

Quantifying Molecular Transport through Lipid Electropores Induced by Nanosecond Pulsed Electric Fields

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High amplitude, nanosecond-duration, pulsed electric fields (nsPEFs) induce the formation of nanometer-diameter pores in cell membranes. These transient lipid electropores facilitate the transport of normally impermeant ions and small molecules across the membrane. Quantitative measurements of molecular transport through lipid electropores are essential for the validation of electroporation models and for optimizing the nsPEF dose for application-specific responses. We calibrated the fluorescence intensity of the membrane integrity marker dye YO-PRO-1 in dense cell lysates using a fast confocal microscope in order to quantify the time-dependent molecular influx of YO-PRO-1 into living cells after nsPEF exposure. Using this method we were able to measure the number of YO-PRO-1 molecules that enter U-937 human histiocytic lymphoma cells following electropermeabilization by a single 6 ns, 20 MV/m pulse.

1231-Pos Board B182

Concentration Effect on the Hydrogen-Bond Strength between Small Molecules at the Oil/Water Interface: Application to Coarse-Grained Model Development

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Oil-water interface are ubiquitous in nature and are particularly important in biology as a simplified model for the membrane-water system. This model is used to study the transfer of biological molecules across the membrane. We are interested in the thermodynamic behavior across the bulk oil, oil/water interface and the bulk water at varying alcohol concentrations. In addition to all atom simulations, we also performed coarse-grain simulations using the SDK model. In oil/water interface, the alcohols behaves differently at different concentration. Lower concentrations of alcohol prefers associative behavior but at higher concentration it becomes less associative. All of the simulations and free energy calculations were carried out with NAMD version 2.9 and for coarse-grain we used LAMMPS. System were described with the CHARMM27 force field. The TIP3P model was used for water. The results we obtained are compared with the existing theoretical and experimental findings.