Membrane Physical Chemistry III

2477-Pos

Lipid Mediated Interaction of Transmembrane Helices as Studied by a Mesoscopic Model

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The role transmembrane helices (TMH) play in biological systems includes creating ion transport pathways, cell signaling and facilitating photon absorption in photosynthetic complexes. The packing and spatial organization of those helices was found to be important for their functional properties. It was shown (Walters & DeGrado, PNAS (2006); 13, 37) that despite the large number of available conformations, experimentally observed helix-helix interactions can be classified into very few interaction clusters. This suggests that a basic, universal set of interactions might govern the helix packing. Using a coarse-grained model we investigate the interaction of helical peptides in a lipid bilayer using the dissipative particle dynamics (DPD) simulation technique. We incorporate in our model basic hydrophobic-hydrophilic interactions without referencing a specific TMH, thereby studying the common motifs in lipid mediated protein interactions. Our model successfully reproduces the effect of hydrophobic mismatch on peptides in a lipid bilayer (de Meyer, Venturoli & Smit, Biophys. J (2008); 95, 4) and predicts a selective aggregation pattern. A more detailed representation of a helix further reveals the characteristics of the helix-helix interactions

2478-Pos

The Interaction of Curcumin with Phospholipid Model Membranes. a Study using Differential Scanning Calorimetry, NMR, X-Ray Diffraction and Infrared Spectroscopy

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Curcumin is a polyphenol present in turmeric, widely used in Asian traditional medicine and cooking, which has many and diverse biological effects and is found incorporated in membranes. We have studied the mode in which curcumin modulates the physical properties of 1, 2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC) multilamellar membranes and 1, 2-dielaidoyl-sn-glycero-3-phosphoetnanolamine (DEPE). Curcumin disordered DPPC membranes at temperatures below Tc as seen through DSC, FT-IR, 2H-NMR, WAXD and SAXD. The decrease induced in Tc, suggests that curcumin is oriented in the bilayer with its main axis parallel to the acyl chains. Above Tc curcumin also introduced disordering as seen by FT-IR. FT-IR also showed that curcumin alters the conformation of the polar group of DPPC, increasing the percentage of unhydrated C=O groups, but however it does not form hydrogen bonds with neither the C=O group nor the phosphate group of DPPC. SAXD showed a remarkable increase in the repeating spacings by the presence of curcumin probably indicating the formation of a ripple phase. A partial phase diagram was built, which suggest the formation of a phospholipid/curcumin complex given place to immiscibilities in both the fluid and the rigid states, between curcumin and DPPC. Additionally DEPE was used to test the effect of curcumin on its polymorphism, and it was found that the temperature at which HII phase is formed was decreased, indicating that curcumin favours negative curvature of the membrane, which may be important to explain its effect on membrane dynamics and on membrane proteins or on proteins which may be activated through membrane insertion.

2479-Pos

Assesment of the Biophysical Parameters of Platelet Membrane in Leukemic Patients

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The clinical history of myeloproliferative and myelodysplastic disorders is often complicated by thromboembolic or hemorrhagic events. The mechanisms of these major and life threatening complications remain unclear.
Membrane organization influences many of the unique cellular functions and is strongly correlated (among other factors) to the membrane lipid composition; it may be evaluated by following up the membrane fluidity and aggregation properties of the cell. In our work, we try to correlate changes in platelets membrane fluidity and aggregation parameters with the clinical status of the patient disease.
Membrane fluidity and aggregation properties of platelets collected from 176 patients suffering of various entities of myeloid malignancies as well as from 34 healthy controls were monitored along one to 6 month in the attempt to establish a correlation between membrane organization changes and alterations of the platelet function which accompany the disease.
Membrane fluidity was assessed by fluorescence anisotropy measurements. The platelet membrane shows to be more rigid compared with controls/normal regardless of the clinical type of myeloproliferative disorder. However patients with severe clinical status due to acute myeloid leukemia have a more fluid membrane compared to the same patients found previously in a better state.
Aggregation was assessed by optical methods (Chronolog Aggregometer). The lag phase amplitude and duration, the slope, amplitude and secretion phase of the aggregation curve were monitored revealing that the leukemic platelet response is reduced for all agonist reagents (ADP, epinephrine, collagen and risocetin). The reduction of the epinephrine response is more pronounced comparatively to the response to other reagents. These results suggest the possible mechanisms of platelets disorders induced by the disease.

2480-Pos

Characterization of a Homologous Series of Fluorescent Fatty Amines. Photophysics, Aqueous Solubility and Binding to Albumin and to POPC Bilayers

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The *7-nitrobenz-2-oxa-1,3-diazol-4-yl (*NBD) is a small and very polar group whose fluorescence quantum yield strongly depends on the polarity of its environment. When bound to the polar headgroup of lipid molecules it allows the characterization of the structure and dynamics of lipid bilayers. The solvent dependence of its fluorescence has been exploited by this research group to characterize the kinetics and thermodynamics of the interaction of different amphiphiles with lipid bilayers and proteins.
In this work we report on the synthesis and characterization of a homologous series of fluorescent fatty amines (NBD-Cn; n=4, 6, 8, 10, 12, 14 and 16). At 25°C and pH=7.4, the critical aggregation concentration (CAC) in aqueous media range from $2x10^{-4}$ M for NBD-C_4 to $4x10^{-9}$ M for NBD-C_{12}. The partition coefficient to lipid bilayers prepared from *1-palmitoyl-2-oleoyl phosphatidylcholine* (POPC) was also measured for the amphiphiles with a CAC>20 nM (NBD-C_4 to NBD-C_{10}) and ranged from $9.5x10^2$ to $3.6x10^5$, with a $\Delta\Delta G$=-4.9 ± 0.5 kJ/mol *per* ethyl group. The amphiphiles interacted efficiently with Bovine Serum Albumin (K_B=$1.7x10^4$ and $7.9x10^6$ M^{-1} for NBD-C_4 and NBD-C_{10} respectively) and this was inhibited by fatty acids indicating that binding occurs essentially in the same binding site.
Some photophysical properties of the amphiphiles in POPC bilayers were also measured and we found no significant variation along the series indicating that the NBD group is located in a region with the same properties regardless of the length of the non-polar group. An exception was noted for the case of NBD-C_{14} that showed somewhat smaller fluorescence anisotropy. The amphiphiles lifetime decay observed was mono-exponential in water or methanol but when inserted in POPC bilayers a bi-exponential law was required.

2481-Pos

New Method for the Measurement of Binding Constants for Amphiphiles with a Very Small Solubility in Aqueous Media

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The aqueous solubility of the monomeric form of most amphiphiles is relatively small and above a certain concentration, the critical aggregation concentration (CAC), they tend to form aggregates where the contact between their non-polar moieties and water is minimized. The affinity of the amphiphiles to hydrophobic environments, such as proteins or lipid bilayers, may be obtained by equilibrium titration with the binding agent but its correct evaluation requires the use of amphiphile concentrations below their CAC which, at times, can be extremely low.
In this work we develop a method where the partition of amphiphiles between water and lipid bilayers may be accurately measured for amphiphiles with a CAC in the sub-nanomolar range. The method is based on the physical