

Simultaneous detection of up to seven different ion species, including secondary electrons, allowed generation of ion ratio images whose signal intensity could be correlated to composition through the use of calibration curves from standard samples.

### 223-Plat

#### Lipid Bilayer Structure and Dynamics Studied with Molecular Dynamics Simulations and NMR Measurements

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We apply novel NMR experiments and molecular dynamics simulations to extract information about dynamics and structure of phosphatidylcholine lipid bilayers. We have developed a method to quantitatively measure rotational dynamics of hydrocarbon groups by using NMR relaxation measurements. The results from this method can be used to directly compare dynamics between simulations and experiments, which has not been possible previously. We apply this technique to phosphatidylcholine bilayers with and without cholesterol. In addition, we have measured order parameters for all hydrocarbon segments in phosphatidylcholine bilayer with and without cholesterol, and compared those to the simulation results [1]. The results reveal how cholesterol affects the molecular structure and dynamics of phosphatidylcholine glycerol and headgroup regions. The quality of simulation models will be critically discussed emphasizing the headgroup and glycerol regions.

[1] Ferreira et al. PCCP 15, 1976 (2013)

### 224-Plat

#### Understanding the Membrane Permeability of Hydrogen Sulfide through Molecular Dynamics Simulations using a Polarizable Force Field

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Hydrogen sulfide (H<sub>2</sub>S) is an acutely toxic gas, with a threshold toxicity of 200 ppm. It is also a gas transmitter, acting through the S-sulphydration of cysteine side chains [1]. Despite being chemically analogous to water, H<sub>2</sub>S can permeate biological membranes without a facilitator [1]. To examine this process, we used molecular dynamics simulations to calculate the potential of mean force (PMF) of H<sub>2</sub>S crossing a model lipid bilayer. As H<sub>2</sub>S is a highly polarizable molecule, we used the Drude polarizable force field for H<sub>2</sub>S developed in our group [2], in conjunction with a polarizable model for DPPC lipid bilayers [3]. Our computed PMFs show that H<sub>2</sub>S is sparingly soluble in bulk water and partitions readily into the interior of the membrane. Free energies are lowest when H<sub>2</sub>S is in the tail region of the lipids and the barriers corresponding to H<sub>2</sub>S crossing the water/lipid interface are small. This is in contrast the high free energies that occur when water molecules enter the membrane interior. Induced polarization plays a secondary role in H<sub>2</sub>S permeation, with H<sub>2</sub>S being most strongly polarized in the bulk solvent and near the lipid head groups, but having a dipole moment near the gas phase value of 0.98 D in the membrane interior. Despite a significant dipole moment and large polarizability, H<sub>2</sub>S is solvated and permeates membranes like a hydrophobic solute.

[1] Gadalla, Snyder, *J. Neurochem.* 2010, **113**, 14.

[2] Mathai et al. *PNAS* 2009, **106**, 16633.

[3] Riahi, Rowley, *J. Phys. Chem. B* 2013, **117**, 5222.

[4] Chowdhary et al. *J. Phys. Chem. B*, 2013, **117**, 9142.

### 225-Plat

#### The Interaction of Resveratrol with DPPC Bilayers - a Biophysical Contribution on the Mediterranean Diet

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Resveratrol, contained in the skin of grape and accordingly in red wine, exhibits a wide range of health effects such as cardioprotection and anti-oxidation. Biophysical studies on the unspecific interaction of resveratrol with lipid membranes are rare so far. Here we present results from a series of investigations on the interaction of resveratrol with DPPC model membranes, combining structural (neutron reflectometry) and thermodynamic methods (measurement of partition coefficient, Langmuir isotherm and differential scanning calorimetry (DSC)).

The details of the partitioning and the neutron experiments report on the localization of resveratrol within the membrane headgroup layer, close to the inter-

face between the hydrophilic headgroup region and the hydrophobic core. Its presence decreases the tilt angle of the headgroups with respect to the membrane surface normal, as compared to the control (pure DPPC). At the same time, the projected area per headgroup drops, and the bilayer is more condensed.

The analysis of the thermograms confirms these findings. DSC measurements on SUVs of pure DPPC (0.05°C/min) exhibit a complex characteristics of the main transition, revealing three peaks. We attribute them to a contribution of the headgroups and a bending dependent contribution of the chains, different for the two leaflets. With resveratrol, the headgroup transition exhibits a freezing point depression together with a loss in cooperativity. The chain condensation makes the corresponding transition more uniform. We conjecture a compensating effect of resveratrol: extrusion allows for an asymmetric distribution among the two leaflets that partially counteracts the curvature induced packing gradient in the core region.

The findings in summary yield a more comprehensive view on the passive impact of resveratrol in model membranes that will hopefully contribute to a better understanding of the biophysical mechanisms behind the Mediterranean diet.

### 226-Plat

#### DMPC: A Remarkable Exception to the Tocopherol's Membrane Presence

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There are many conflicting results in the literature regarding  $\alpha$ -tocopherol's (aToc) biological function. To a great extent, this ambiguity regarding aToc's physiological role has been perpetuated because of the lack of conclusive, and sometimes conflicting, experimental data.

Dimyristoyl phosphatidylcholine (DMPC, di-14:0PC) is one of the most common model systems for examining the location, behavior, and antioxidant properties of aToc in membranes. For decades, biophysicists have used DMPC bilayers as biological mimics. For the most part, DMPC's popularity as a model membrane system can be attributed to the fact that it is stable, inexpensive, and easy to obtain. Importantly, the bilayers that it forms have physical properties not dissimilar to those found in biological membranes (e.g., liquid crystalline order, hydrophobic thickness, etc.).

Using different physical techniques (i.e., neutron diffraction, NMR and UV spectroscopy), we obtained structural data that rationalize much of the previously conflicting and inexplicable data regarding aToc behavior in DMPC bilayers. Our neutron, 2H NMR and oxidation assays data unambiguously locate aToc's active chromanol moiety deep in the hydrophobic core of DMPC bilayers, a location that is in stark contrast to what was previously observed in other PC bilayers. Our results clearly demonstrate the importance of lipid species diversity found in biological membranes, and strongly suggest that measurements regarding aToc's oxidation kinetics and its by-products in DMPC bilayers should be revisited taking into consideration its proposed location in these bilayers.

### 227-Plat

#### Lipid Mediated Heterogeneity in Cisplatin Resistance in Cancer Cell Lines

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Cisplatin is a classic chemotherapeutic agent used for treating several forms of cancer. However, cells develop resistance to the drug in some patients and the mechanism of resistance to cisplatin is currently unknown. We hypothesize that some aspects leading to resistance of cells to cisplatin have their origin in the mixing properties of plasma membrane lipids. These changes in the plasma membrane could augment or suppress cisplatin induced signaling events in a way that infers resistance to cisplatin. Here, we present experimental results linking the resistance of cisplatin to the effects that cisplatin has on the mixing properties of plasma membranes. We have accomplished this by measuring how cisplatin treatment alters miscibility critical temperatures in giant plasma membrane vesicles isolated from cancer cells with varying resistance to this drug. In addition, we have monitored cellular responses to cisplatin treatment in the presence of biochemical modulators of membrane physical properties. We conclude that membrane physical properties play a role in cancer cells developing resistance to this chemotherapeutic drug. Further understanding of the molecular mechanisms through which membrane physical properties impact this process will enable in better understanding for developing therapies for battling cancer.