Membrane Dynamics & Bilayer Probes II

2185-Pos Board B204
Surfactants Alter Nanoparticle - Model Cell Membrane Interactions
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Due to their small size, nanoparticles (NPs) have the ability to penetrate pulmonary and vascular tissue, and as a result, are classified as potential human carcinogens. On the other hand, nanoparticle insertion into targeted cells can play a key role in drug delivery and gene therapy applications, prompting a need to more thoroughly characterize nanoparticle/membrane interactions. Polystyrene nanoparticles with modifications in surface functionalization and detergent conditions were introduced to a Langmuir phospholipid monolayer, a cell membrane outer leaflet model. Negatively charged (COO^- functionalized) detergent free nanoparticles solubilized a zwitterionic 1,2-dimyristoyl-*sn*-glycero-3-phosphocholine (DMPC) monolayer held at constant, physiological pressure, removing material from the air/water interface to a greater extent than did positively charged (NH_3^+ functionalized) nanoparticles. To determine the role of lipid charge in nanoparticle/membrane interactions, negatively charged 1,2-dilauroyl-*sn*-glycero-3-phospho-(1'-*rac*-glycerol) (DLPG) and positively charged 1,2-dimyristoyl-3-trimethylammonium-propane (DMTAP) lipid monolayers were used. Nanoparticles of opposite charge than the membrane removed a larger percentage of the monolayer compared to like-charged particle/phospholipid systems. Vesicle leakage assays were run to determine applicability of these results to a more physiologically relevant bilayer system.
Ionic and non-ionic surfactants, typically present in nanoparticle solutions to limit aggregation, all showed significant surface activity and monolayer insertion which can be directly correlated to surfactant hydrophobicity. Adding surfactant to detergent-free nanoparticle solutions decreased the magnitude of monolayer solubilization compared to nanoparticles alone. To better understand nanoparticle-detergent-membrane interactions, either nanoparticles or detergents were introduced to the monolayer, and following a time lapse, the other component was introduced. Under various surfactant and salt conditions, dynamic light scattering and zeta potential measurements were used to estimate the amount of particle associated detergent and determine particle size and extent of aggregation. A model of detergent sequestration by the polystyrene nanoparticles explains these results.

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Size-Dependent Interaction between Gold Nanoparticles and Lipid Bilayer Membranes
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Metal nanoparticles, in particular gold nanoparticles (AuNPs) are of great interest in biomedical research, such as in diagnosis and therapeutics[1]. Recent studies indicate the size-dependent cytotoxicity of the AuNPs[2], however the means of membrane association and interaction are currently unknown. To better understand and optimize these novel compounds, their interactions with biological membranes need to be investigated. We used AuNPs stabilized by triphenylphosphine derivatives ranging in size from 1.4 to 15 nm size in bilayer experiments [3]. We observe size-dependent membrane association: AuNPs of 15 nm diameter generate ion-selective currents while smaller 1.4 nm particles show no such effects. We therefore presently examine intermediate AuNP sizes to find the size-limitation for these effects.
[1] Tiwari, P.M. et al. Functionalized Gold Nanoparticles and their Biomedical Applications. Nanomaterials 2011, 1, 31-63.
[2] Pan, Y. et al. Size-Dependent Cytotoxicity of Gold Nanoparticles. small 2007, 3, No.11, 1941-1949.
[3] Benz, R. et al. Formation of large, ion-permeable membrane channels by the matrix protein (porin) of Escherichia coli. Biochim Biophys Acta 1978, 511: 305-319.

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Study of Nanoparticle-Lipid Bilayer Interactions: Insights from Coarse-Grained Molecular Dynamics Simulations
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One of the main aims in the design of engineered nanomaterials with applications in medicine, such as diagnostic and therapeutic nanoparticles (NPs), is the ability of these materials to translocate across the human cells without damaging essential tissues. The entry point of a NP to a cell is the plasma membrane. Thus, the first step into assessing the NP cytotoxicity requires a thorough understanding of the NP-membrane interaction mechanism. Extensive Molecular Dynamics (MD) simulations and free-energy calculations were employed, providing insights into the significance of NP surface chemistry and cholesterol concentration of the membrane in the NP-membrane interplay. The MARTINI coarse-grained force-field as implemented in the GROMACS simulation package was employed to model NPs and investigate their interaction with a model lipid bilayer. NPs with a diameter of 3 nm and a surface comprising different patterns of hydrophobic and hydrophilic groups were designed. MD equilibrium simulations were carried out in order to gain insight into the mechanism of NP-membrane interaction. To evaluate the molecular energetics of this interaction, Potential of Mean Force (PMF) calculations, using the Umbrella Sampling technique, were also performed. Our results demonstrate that certain surface patterns, such as an ordered distribution of hydrophilic groups, alter the interaction mechanisms and change the molecular energetics of the NP-membrane interactions. Moreover, PMF calculations showed that an increase in the cholesterol concentration of the membrane leads to a higher energy barrier of NP translocation across the membrane. The results from the present study provide valuable information on possible links between NP surface characteristics and cholesterol concentration with specific interaction types with the cell membrane, and provide insights into the design of NPs with tailored functionalities, for example direct cellular entry.

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How Instantaneous Lipid Flows Influence Membrane Protein Diffusion
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Instantaneous lipid flows have previously been shown to exist within pure lipid bilayers using molecular dynamics simulations. The role of lipid flows and implications for membrane dynamics over a larger scale is yet to be explored. using HPC resources we capture the behaviour of ''crowded'' bacterial membranes by simulating large arrays (up to 256) of outer membrane proteins (OMP) in a 120nmx120nm patch of bilayer. We use a POPE:POPG 3:1 lipid mix and five different OMPs. Correlated lipid movement stretches over 10s of nanometres and is a function of system size which has important implications for simulations attempting to capture protein clustering. We show that these short lived correlated lipid movements are not suppressed by the addition of outer membrane proteins and play a role in both the rotational and translational diffusion of the proteins.

2189-Pos Board B208
Diffusion Effects in Cross-Linked Bilayers
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We investigate peptide interactions with model membranes and how they affect phase dynamics and mobility. Previously, we have studied lipid phase rearrangement due to cross-linking lipids in the headgroup position. Clustering and possible subanomalous diffusion inhibit domain coalescence and alter the conformation energy minimum. Building on this, our current efforts investigate peptide perturbations in lipid bilayers. We cross-link transmembrane peptides on the surface of lipid vesicles to examine the interactions between the helices, mimicking B cell receptor clustering. We conduct these studies by modifying the transmembrane portion of the mIgM receptor and incorporating the resulting peptide into the bilayer. We analyze these associations using microscopy, FRAP, FRET and CD spectroscopy.

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Measuring Lipid Membrane Viscosity using Rotational and Translational Particle Diffusion
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The two-dimensional fluidity of lipid bilayers enables the motion of membrane-bound macromolecules and is therefore crucial to biological function. However, lipid bilayer viscosity remains poorly quantified, largely due to the difficulty of relating the diffusion coefficients of membrane-associated tracer particles to the viscosity of the underlying membrane. We address this with a new technique for measuring lipid bilayer viscosity, in which determination of both the rotational and translational diffusion coefficients of tracer particles enables quantification of viscosity as well as the effective size of the tracers. Surprisingly, we find a wide distribution of effective tracer sizes, due