Membrane Physical Chemistry I

1782-Pos Board B692
Quantifying the Effect of Detergent on Interactions between Nanoparticles and a Model Cell Membrane
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Due to their small size, nanoparticles (NPs) have the ability to penetrate cell membranes, and are therefore classified as potential human carcinogens. NP insertion into targeted cells also proves beneficial for drug delivery and gene therapy applications, prompting a need to more thoroughly characterize NP/membrane interactions. Polystyrene NPs with modifications in size, surface functionalization and detergent conditions were introduced to a Langmuir lipid monolayer of 1,2-dimyristoyl-*sn*-glycero-3-phosphocholine (DMPC), a model of the outer leaflet of the cell membrane. At bilayer equivalent pressure, aminated and carboxylated NPs showed appreciable monolayer insertion whereas plain NPs solubilized the phospholipid layer, removing it from the air/water interface.
Detergent added to a NP solution typically prevents particle aggregation, but the amphiphilic character of surfactant may also affect cell membrane interactions. Detergent-free NP solutions interact differently compared to those containing detergent, resulting in monolayer destruction. To examine the role of charged detergents, sodium dodecyl sulfate (SDS) and dodecyl trimethyl ammonium bromide (DTAB) surfactants were introduced. Solutions composed of surfactant and NP functionalized with groups of the same charge showed appreciable interactions with the monolayer. Solutions of NPs and surfactants with opposing functional group charge aggregated, preventing authentic interactions. NP solutions with a higher concentration (1 wt%) of detergent initially showed increased insertion into the monolayer, suggesting cooperative behavior between NP and surfactant. The behavior of these NPs with the monolayer has two distinct regimes - an initial insertion event followed by monolayer destruction which is suggestive of interplay between kinetic and thermodynamic control.

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Nanomechanical Stability of Phase-Segregated Multicomponent Lipid Bilayers Enhanced by Pluronics
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Lipid-polymer/peptide systems have been used as platforms to understand various cellular components, functions, and processes such as the cell glycocalyx, the hydrophobic mismatch, and interaction of specific peptides with lipid bilayers. In this study, we used AFM-based force mapping to quantify by means of breakthrough forces the nanomechanical stability of raft-forming lipid bilayers consisting of dioleoylphosphatidylcholine, sphingomyelin, and cholesterol (DEC) in the presence of diblock copolymers comprised of polystyrene(PS) and polyethylene oxide(PEO). Varying molecular weights of PS-b-PEO (Pluronics-mimics): PS(3.6)-b-PEO(25), PS(3.6)-b-PEO(16.6), PS(3.8)-b-PEO (6.5), PS(19)-b-PEO(6.4) were used in the experiments. The presence of the polymer led to a significant increase in the breakthrough forces when compared to a pure DEC bilayer. Bilayers with greater proportion of PS exhibited the highest breakthrough force hence is the most mechanically stable. Based on the results, we proposed the incorporation of the PS moiety into the bilayer core as the main mechanism of the enhanced stability. Our force mapping results provide a direct measurement of the effect of Pluronics on the stability of phase-separated multicomponent lipid bilayers that mimic biological membrane. In addition, the lipid bilayer-Pluronic-mimics systems presented in this study pose as an attractive platform for obtaining fundamental understanding on the role of Pluronics in drug delivery application as well as being a biological response modifier.

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Formation of Tethered Bilayer Lipid Membranes(TBLM) from Mixed Lipid-Detergent Micelles
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tBLMs are solid-supported lipid bilayers separated by a ~ 2 nm thick hydration layer from the substrate. Compared to cell membranes, they are simpler in their chemical composition and can therefore be quantitatively studied with a variety of experimental techniques. Compared to free-standing or vesicle membranes, they are more long-term stable even though their in-plane fluidity equals that of free bilayers.1 tBLMs can be formed by rapid solvent exchange (RSE),2,3 which leads to highly electrically insulating, defect-free bilayers, or by vesicle fusion. Here we develop an alternative way of forming tBLMs by fusing mixed lipid-detergent micelles. Self-assembled monolayers (SAMs) of tether lipid are formed on gold surface and incubated with mixed lipid-detergent micelles. At this point, the mixed micelles are stable and lipid will not interact with the SAM. However, upon dilution with buffer to a detergent concentration smaller than the CMC, micelles disintegrate. Because the CMC of phospholipids is high, they deposit on the SAM while detergent molecules dissolve as monomers in solution. The deposition process is simultaneously monitored by surface plasmon resonance (SPR) and electrochemical impedance spectroscopy (EIS). EIS reveals that the resistances of resulting tBLM are comparable to that of tBLMs formed by RSE or vesicle fusion. To demonstrate the general applicability of this method, we studied the formation of tBLMs from mixed micelles of DPhyPC + CHAPS, DOPC + CHAPS and DPhyPC + decylmaltoside. Formation of tBLM by this method could be used to incorporate integral membranes protein into tBLMs in which the use of detergent is unavoidable.
1. Shenoy et al, Soft Matter, 2010, 6, 1263.
2. McGillivray DJ et al, Biointerphases, 2007, 2, 21.
3. Heinrich F et al, Langmuir, 2009, 25, 4219.

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Effect of Octylglucoside on the Disk Phase of Bicelles
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Atomically resolved membrane protein structures provide information on the protein's function. To obtain atomically resolved structures of membrane proteins, high quality protein crystals are required. Membrane proteins are not straightforward to crystallize; only ~150 membrane proteins structures are known as compared to ~20,000 for soluble proteins. Their importance is highlighted by the fact that at least one third of genes in yeast and multicellular organisms encode membrane proteins. To both extract membrane proteins from their native environment as well as stabilize monomeric dispersions of the proteins in water it is necessary to use detergents. Octylglucoside (OG) and maltoside, with sugar-based headgroups, have proven to be most effective in membrane protein purification and stabilization. Yet treatment of membrane proteins with these surfactants does not ensure that the protein will retain its native structure. Furthermore, it is then not trivial to find a protocol that will lead to the crystallization of the proteins. Many hit- and miss trials are employed, with most trials being unsuccessful.
A system that can provide a membrane-like environment and which enables nucleation and growth of protein crystals is the bicelle system [1]. However, how this system promotes protein crystallization and growth is unknown. For crystallization, purified membrane proteins are mixed with bicelles, which means that the purifying detergent (commonly OG) is mixed with the bicelle. Obtaining the effect of OG on bicelles will reveal the true lipidic scaffold enabling protein crystallization. In the present work we report the effect of OG on the disk phase of the bicelle system using Small Angle Neutron and X-Ray Scattering (SANS and SAXS).
1. Faham, S. and J.U. Bowie, Bicelle crystallization: a new method for crystallizing membrane proteins yields a monomeric bacteriorhodopsin structure. Journal of Molecular Biology, 2002. 316(1): p. 1-6.

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Unusual Stability of Archaeal Tetraether Liposomes Against Surfactants
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Bipolar tetraether liposomes (BTL) hold great promise for technological applications and serve as an excellent model for studying the plasma membrane of the crenarchaeota, which can thrive in a variety of extreme environments. Physical properties of BTL have thus evolved as an important research subject. In this study, using dynamic light scattering, we have examined the effect of surfactant n-tetradecyl-β-D-maltoside (TDM) on unilamellar vesicles composed of POPC (a monopolar diester hybrid lipid) and the polar lipid fraction E (PLFE, one kind of archaeal bipolar tetraether lipids) isolated from the thermoacidophile Sulfolobus acidocaldarius (growth temperature 72oC; growth pH 2.5) at 25oC. POPC and PLFE differ considerably in their structure; therefore, they were expected to behave differently when exposed to TDM. We found that TDM disrupts the POPC/cholesterol vesicles effectively; however, higher concentrations of TDM were required to disrupt PLFE/POPC vesicles. As the TDM concentration was increased, the size of liposomes reduced. For a given liposome system, the particle size drops abruptly at a specific TDM concentration. The TDM concentration where the vesicle size is reduced to half its original value was designated as C1/2. For PLPF/POPC mixtures with [total lipid] = 0.2 mM, C1/2 changes little with the amount of PLFE until 70 mol%, above which C1/2 undergoes a dramatic increase. According to the C1/2 values, PLFE unilamellar vesicles are ~14 times more stable against the surfactant TDM than POPC unilamellar vesicles. A surprising result is that, for 100 mol% PLFE, C1/2 is increased as the vesicle diameter is reduced, probably due to a change in transmembrane asymmetry. Tests on the stability of PLFE-based liposomes against other surfactants such as bile salts are being carried out. (supported by NSF DMR 0706410).