Size dependent disruption of tethered lipid bilayers by carboxylate-modified polystyrene nanoparticles

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Engineered nanomaterials (ENM) are increasingly being used in commercial products and biomedical interventions, thereby increasing human exposure to ENM. A comprehensive understanding of molecular interactions between ENM and cell membranes is needed to understand ENM toxicity. Tethered bilayer lipid membranes (tBLM) are robust biomimetic interfaces, whose enhanced stability over unsupported BLM makes them well suited to study biomembrane phenomena. The goal of this study was to characterize interactions between carboxyl-functionalized polystyrene ENM and a tBLM. Electrochemical impedance spectroscopy (EIS) was used to monitor changes in the tBLM's electrical resistance (R_m) following ENM exposure. The methods's ability to distinguish between two different particle sizes (20 and 100 nm) was assessed.

The tBLM were fabricated on ultra smooth gold electrode by chemical absorption of a lower tBLM leaflet followed by rupture of liposomes to deposit the upper leaflet. EIS was used to measure the tBLM's R_m as a function of time following exposure to carboxylated polystyrene ENM 20 nm or 100 nm in diameter for five hours (Fig. 1). The R_m values were stable in the absence of ENM, but decreased significantly at a rate that varied with the ENM's particle size (Figs. 2 and 3). An exponential decay model was fitted to the data, and statistical analysis of the resulting model parameters was analyzed using hierarchical analysis. The resulting dendrogram (Fig. 4) indicated that the method could distinguish between ENM having different particle sizes.

Results of this study show that method provided sufficient resolution, sensitivity, and reproducibility to characterize ENM-BLM interactions. The information-rich R_m vs. time profiles may provide insight into fundamental mechanisms by which ENM interact with biomembranes. Moreover, the hierarchical analysis allowed ENM having different properties (e.g., size) to be classified according to the potency for tBLM disruption. The tBLM method is suitable for miniaturization and adaptation to microelectrode arrays for high-throughput screening of ENM libraries. The method thus holds potential as an aid in developing ENM that are both safe and effective for a wide range of applications.

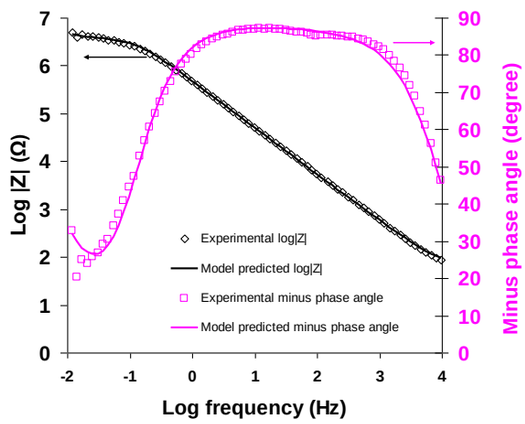

Figure 1. Experimental and model-predicted EIS spectra of a 0.45 cm^2 tBLM formed on gold in 10 mM KCl. Extracted membrane resistance and capacitance were 1.2 $M\Omega cm^2$ and 0.8 $\mu F/cm^2$, respectively.

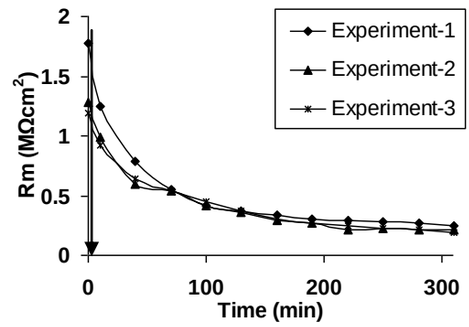

Figure 2. Triplicate R_m vs. time profiles showing tBLM interactions with 100 µg/ml of 20 nm carboxyl-functionalized polystyrene ENMs in 10 mM KCl. The arrow indicates the time of ENM addition

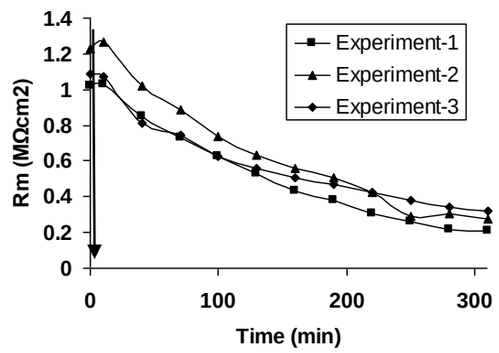

Figure 3. Triplicate R_m vs. time profiles showing tBLM interactions with 100 µg/ml of 100 nm carboxyl-functionalized polystyrene ENMs in 10 mM KCl. The arrow indicates the time of ENM addition.

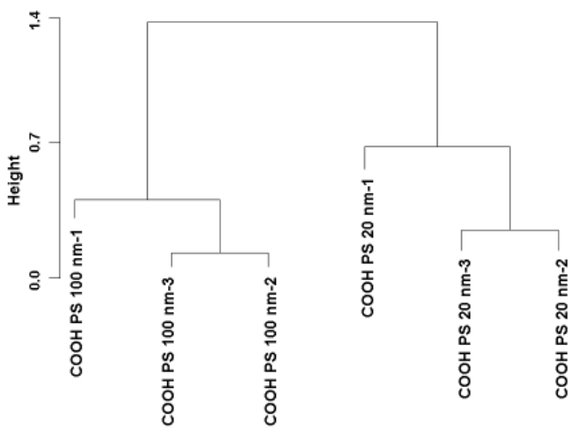

Figure 4. (A) Hierarchical clustering dendrogram for interactions of 100 nm and 20 nm carboxyl-functionalized polystyrene ENM with tBLM.