Understanding the Mechanisms of Decorated Nanoparticle Aggregation In Lipid Membranes

Jahmal Ennis[1], Jesse Sandberg[1], Ezry St.Iago-McRae[1], Julianne Griepenburg[1,2], and Grace Brannigan[1,2]
[1]Center for Computational and Integrative Biology and [2]Department of Physics, Rutgers University, Camden, NJ

Abstract

Gold nanoparticles are a ubiquitous photosensitizer with a broad range of applications in microscopy and targeted drug delivery. Vesicles photosensitized with gold nanoparticles are promising as targeted drug delivery vehicles due to their non-invasive rupture mechanism. Controlling the vesicle properties increases control of the spatial-temporal release of cargo and drug dosage. The aggregation of gold nanoparticles affects the photoporation of these vesicles by interfering with peak SPR wavelengths. Current well known coarse-grained models do not fully capture the gold-gold interaction that drive gold to both aggregate with themselves and adsorb other molecules to their surface. To study the mechanism of gold nanoparticle aggregation in lipid membranes, an accurate coarse-grained model is necessary. We develop a more robust coarse-grained model of ligand coated gold nanoparticles, the polar core model, and test our model against the standard model and the spica model. We used coarse-grained molecular dynamics simulation via the MARTINI forcefield to simulate simple spherical nanoparticles with a decorated ligand exterior. We find that both the core parameters and ligand length contribute to gold nanoparticle aggregation, only the polar nanoparticle model replicates the non-monotonic behavior observed in experimental studies.

Polar Nanoparticles are more Hydrated at Short Ligand Lengths

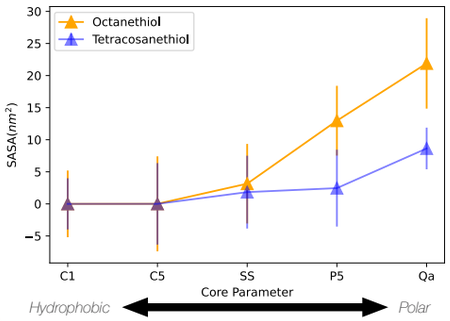


Fig 2. Solvent accessible surface area as a function of varying gold core parameters. Each systems contains a single 2 nm gold nanoparticle embedded in a POPC membrane. Systems were simulated for 20 microseconds, only the final 5 μs were analyzed. Cores that are more hydrophobic have a smaller solvent accessible surface area than their polar counter parts. This trend is enhanced at short ligand lengths.

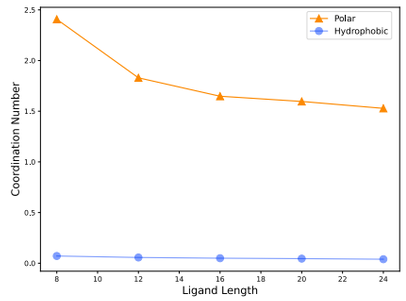


Fig 3. Water Coordination number for nanoparticles with varying core parameters. Each systems contains a single 2 nm gold nanoparticle embedded in a POPC membrane. Systems were simulated for 20 microseconds, only the final 5 μs were analyzed. The nanoparticles with hydrophobic cores have near 0 coordination as expected. Polar nanoparticles show a downward monotonic trend as ligand length increases.

Summary

- Nanoparticles with polar cores have increased solvent accessible solvent area, readily exposing their cores to water
- Short ligands with polar cores are increasingly hydrated compared to their longer ligand counterparts.
- Core exposure increases largest aggregate fraction overall until ligand lengths that cover exposed regions of the nanoparticle .

Background

- Ligand coated nanoparticles (NPs, Figure 1) are multipurpose tools used in biosensing, biolabelling, and controlled drug delivery[1]
- Martini is a biological force-field, therefore, parameters for metals have not yet been developed
- Phenomena such as lipid interactions with gold NP's and gold NP aggregation in lipid bilayers cannot be fully understood with current gold Martini models

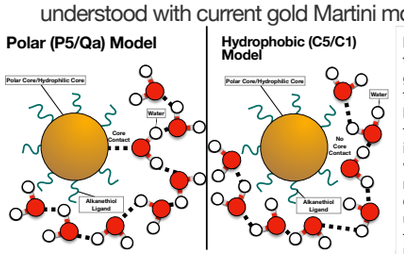
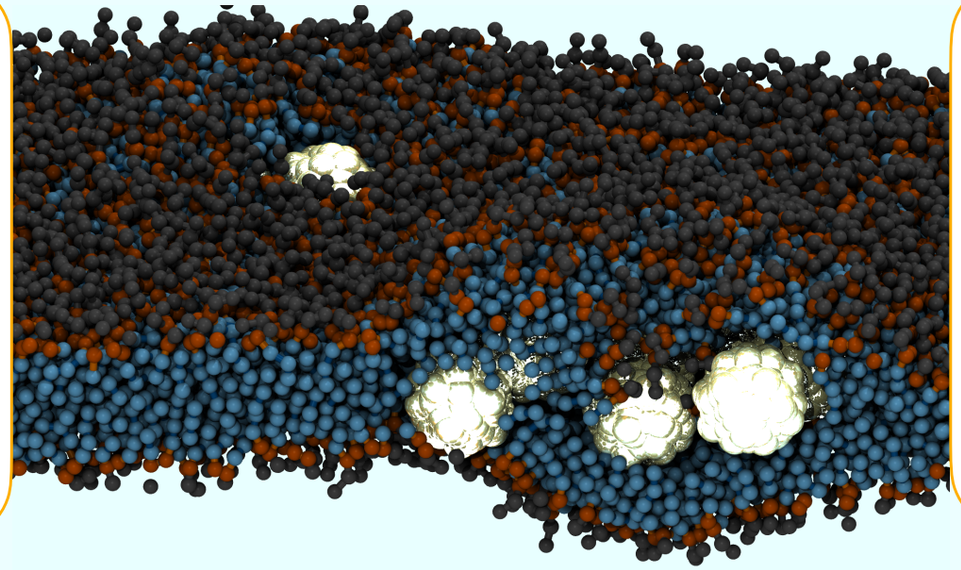


Fig 1. Illustration of two types of Martini gold core models. On the right is the model our lab designed to account for the strong interaction's gold has with itself and water. The model on the left is the current martini model used for mainly studying fully ligand coated gold NP's in solution.



Polar nanoparticles exhibit increased aggregation behavior at short lengths

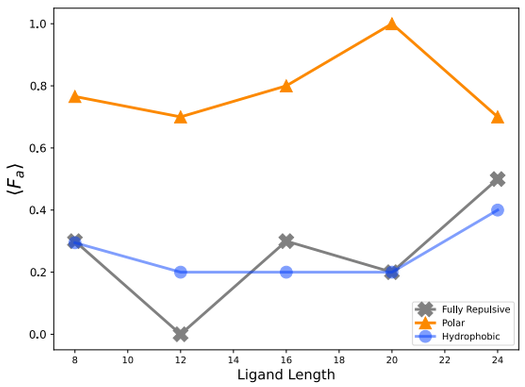


Fig 4. Fraction of nanoparticles in the largest aggregate in the largest aggregate in systems of varying ligand length. Each systems contains a set of 10, 2 nm gold nanoparticles embedded in a POPC membrane. Systems were simulated for 5 μs, only the final 1 μs was analyzed. The two model core's prevalent in the literature are the hydrophobic, standard model and the fully repulsive spica model. The polar model was designed in the Brannigan lab. We observe both high aggregation at short ligand lengths and a non-monotonic behavior similar to experimental systems.

Research Questions

1. Do interactions between the nanoparticle and the surrounding environment change depending on the core parameter's?
2. What is the primary mechanism of aggregation of nanoparticles with polar and hydrophobic cores in phosphatidylcholine membranes?
3. How do polar interactions affect nanoparticle aggregation?

Methods

- Simulation software: Gromacs 2016[3], Force Field: Martini 2.2[2]
- POPC Membranes were constructed using the insane.py tool[4]
- # of NP's in largest aggregate (n)
- Total # of nanoparticles in the system (n_{tot})
- Total number of single nanoparticle in the system (n_s)

Largest Aggregate Fraction

$$F_a = \frac{n}{n_{tot}}$$

Approach

- CG-MD simulations of hydrophobic and polar nanoparticles.
- Simulating single nanoparticles with 5 different core types to understand the impact of core parameters on core exposure.
- Simulating nanoparticles at 5 different ligand length to understand the role of ligand length in aggregate formation.

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