



Investigating The Effect Of The Martini Gold Core Model On Gold Nanoparticle Aggregation In Lipid Membranes

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Abstract

Gold nanoparticles (GNPs) are ubiquitous photosensitizers with a broad range of applications spanning from microscopy to targeted drug delivery. In a number of applications, GNPs interact with the periphery of the lipid bilayer or embed between the leaflets causing deformations to the membrane. Here we investigate the mechanism of GNP aggregation using coarse-grained molecular dynamics via the MARTINI force field. The MARTINI forcefield, while widely used, was developed primarily for organic molecules. Metals do not have a straightforward correspondence with any of the fundamental MARTINI components (beads), and the most appropriate bead assignment depends upon the surrounding environment. Current MARTINI GNP models were designed to reproduce gold self-interaction in aqueous environments. Here we present a new MARTINI model for the gold core, designed to reproduce the aggregation behavior of gold in various hydrophobic environments. We simulate multi-nanoparticle systems in lipid membranes of varying ligand length, and we find that this model yields a complex ligand length dependence that more closely matches experimental results than a widely used GNP model parameterized in water. We observe that large-scale nanoparticle aggregation is sensitive to both ligand chain length and gold core parameters. These results suggest that gold nanoparticle aggregation is partly driven by interactions between the GNP cores and by microscopic perturbations to lipid packing due to the functional groups.

Atomistic Gold LJ Potentials Provide Insight for CG Modeling

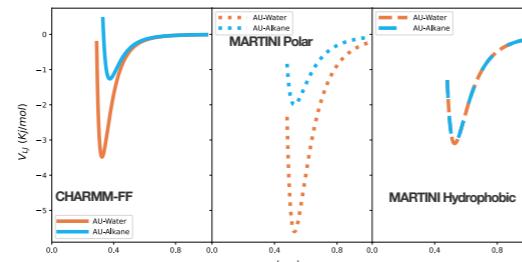


Fig 2. Water-gold and water-alkane Lennard Jones potentials for three different gold models. Panel 1 is the CHARMM model, panel 2 is the MARTINI polar bead model, and panel 3 is the MARTINI hydrophobic bead model.

GNP Core Parameters And Ligand Length Influence Aggregation Dynamics

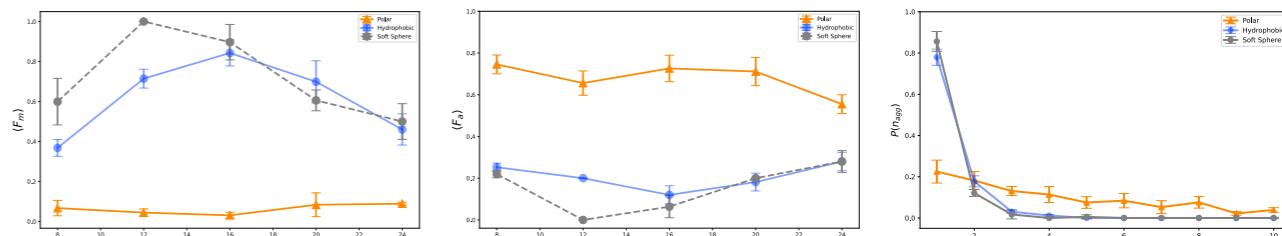


Fig 3. Fraction of GNP monomers in systems with varying NP diameters.

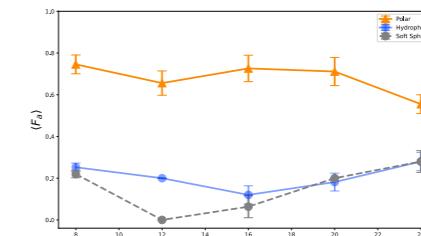


Fig 4. Fraction of nanoparticles in the largest aggregate in systems of varying ligand length.

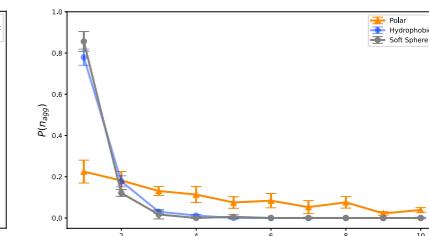


Fig 5. Probability Distribution of GNP cluster sizes for varying core types.

Background

- Ligand-coated gold nanoparticles (GNPs, Figure 1) are multipurpose tools used in biosensing, biolabelling, and controlled drug delivery¹
- Three main CG GNP models are commonly used: polar bead, hydrophobic bead, and soft sphere^{4,5,6}
- No MARTINI gold core model has been systematically validated
- Experimentally, GNP aggregation has a complex relationship with ligand length
- We qualitatively compare coarse-grained GNP aggregation with experimental results

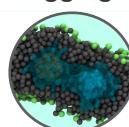
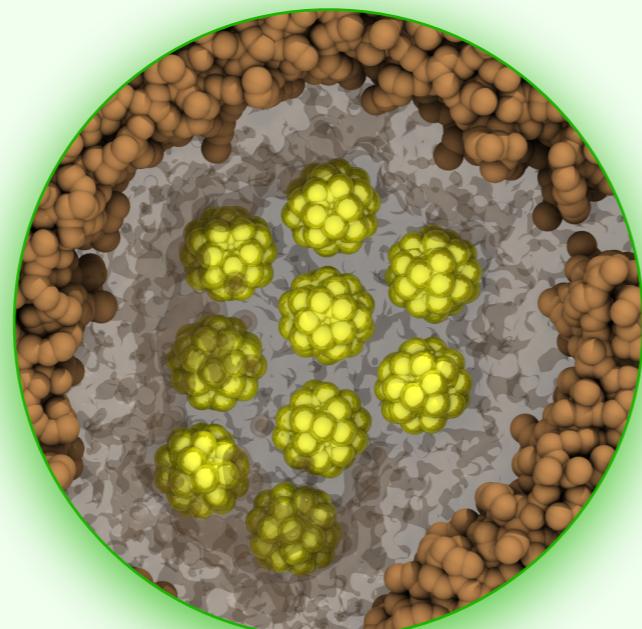


Fig 1. Visualization of 2 nm polar nanoparticles aggregating. Ligands in blue, nanoparticles in ochre and blue, lipid heads in green, lipid tails are in grey.



Research Questions

- Does ligand length affect the amount of exposed gold surface?
- Does ligand length affect gold nanoparticle aggregation?
- Does the gold core parameter affect GNP aggregation?

Approach

- Measure SASA to evaluate the effect of core and ligand parameters on gold surface exposure
- Measure probability distribution to understand how core parameter affects aggregation
- Measure aggregate fraction (F_d) using $F_d = \frac{n}{n_{tot}}$
- Measure aggregate fraction (F_m) using $F_m = \frac{n_s}{n_{tot}}$

○ n is the number of GNPs in the largest aggregate
○ n_s is the number of single GNPs
○ n_{tot} are the total number of GNPs

Ligand Length Determines GNP Core Exposure

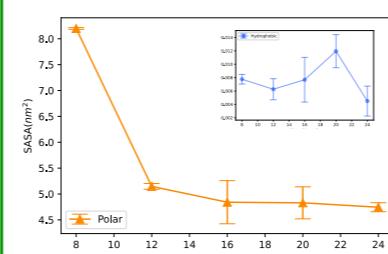


Fig 6. The solvent-accessible surface area of GNP cores as a function of ligand length. Inset shows hydrophobic cores

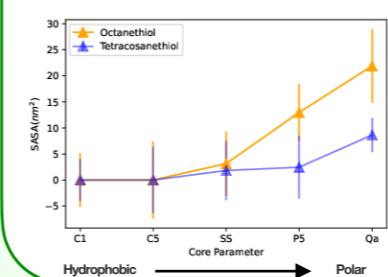


Fig 7. Shows the SASA with varying Lennard Jones parameters for the gold core model. 24 (blue) and 8 (orange) carbon ligands.

Summary

- GNP exposure to solvent is dependent on gold core parameters and ligand length
- Here we show that aggregation is dependent on GNP core parameterization.
- Nanoparticles composed of polar beads form larger aggregates than their hydrophobic counterparts
- The propensity of GNPs to aggregate into large multimeric assemblies in the polar bead model agrees qualitatively with experimental GNP aggregation^{7,8}

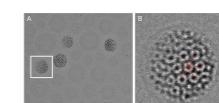


Fig 8. Cryo-TEM images of GNPs aggregating in polymersomes⁸

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