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.

Gold Core Hydrophobicity Decreases Interactions with Solvent

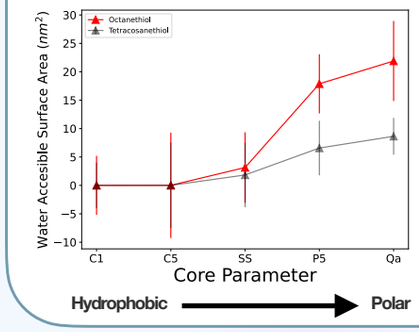


Fig 2. The Water Accessible Surface Area with varying core parameters for the gold core model.

GNP Core Parameters And Ligand Length Influence Aggregation

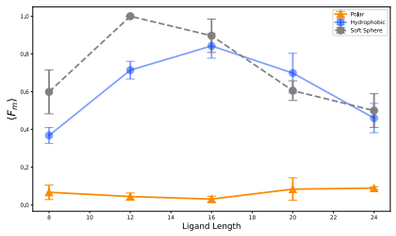


Fig 3. Fraction of GNP monomers in systems with varying NP diameters.

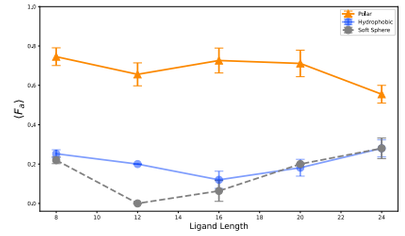


Fig 4. Fraction of nanoparticles in the largest aggregate in systems of varying ligand length.

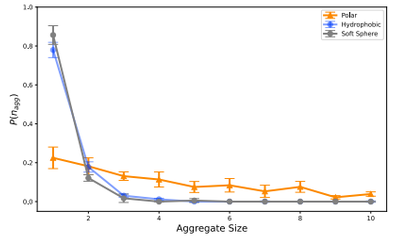


Fig 5. Probability Distribution of GNP cluster sizes for varying core types.

Background

- Ligand-coated gold nanoparticles (GNPs, Figure 1) are multipurpose tools used in biosensing, biolabelling, and controlled drug delivery[1]
- Three main CG GNP models are commonly used: polar bead, hydrophobic bead, and soft sphere[4,5,6]
- MARTINI gold core models have not been systematically validated in non polar solvent
- Experimentally, GNP aggregation has a complex relationship with ligand length
- We qualitatively compare coarse-grained GNP aggregation with experimental results

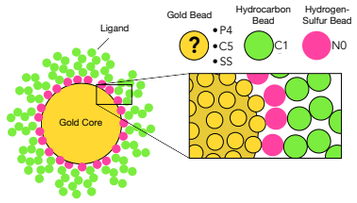
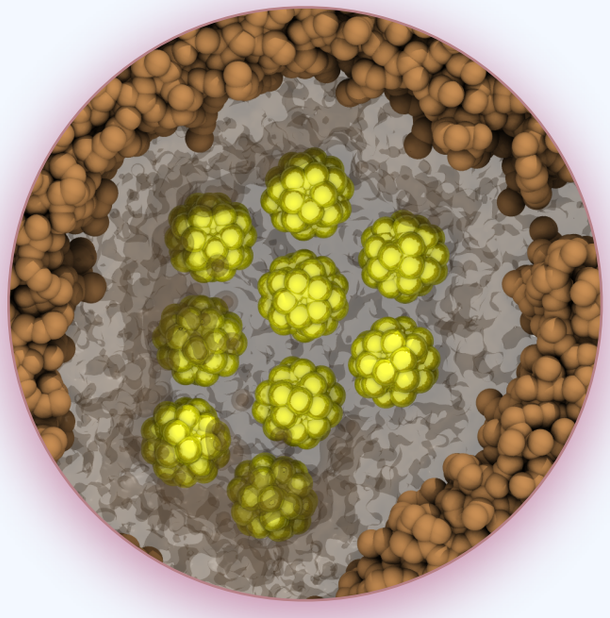


Fig 1. Representation of gold nanoparticle model core and assigned bead types



Polar Core Gold Nanoparticle Dimerization Is Driven By Short Range Interactions

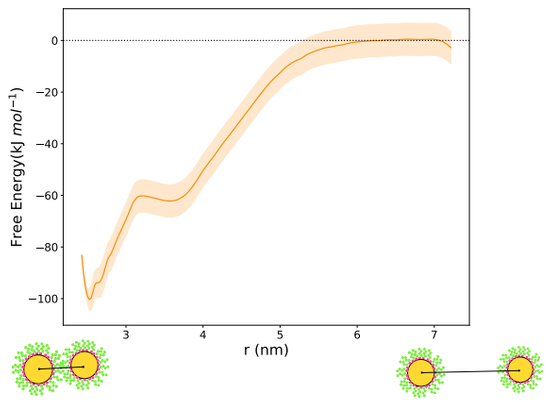


Fig 6. Free energy of dimerization profiles of GNPs with polar core in lipid membranes.

Summary

- GNP interactions with solvent decrease with gold core hydrophobicity
- Hydrophobic GNP aggregation is a non-monotonic function of ligand length with a peak at a 12 carbon ligand length
- The propensity of GNPs to aggregate into large multimeric assemblies in the polar bead model agrees qualitatively with experimental GNP aggregation[7,8]
- We are currently developing a gold model with the MARTINI team.

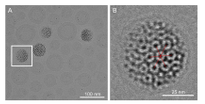


Fig 7. Cryo-TEM images of GNPs aggregating in polymersomes[8]

Research Questions

1. Does GNP core exposure affect interaction with surrounding solvent?
2. Does large scale GNP aggregation depend on the gold core parameter?
3. Does ligand length affect gold nanoparticle aggregation?

Approach

- Measure Water ASA to evaluate the effect of core and ligand parameters on gold surface exposure
- Measure PDF of GNP cluster sizes to understand how core parameters affect aggregation
- Measure aggregate fraction (F_a) using $F_a = \frac{n}{n_{tot}}$
- 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

Methods

- Simulation software: Gromacs 2016[3]
- Force Field: Martini 2.2[2]
- Free energy profiles calculated using umbrella sampling with GMX Wham
- Aggregate fraction and probability distribution systems contain 10 GNPs

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