Assessing The Effects Of Coarse-Grained Models For Gold On The Aggregation Of Nanoparticles In Lipid Bilayers

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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 several applications, GNPs interact with the periphery of the lipid bilayer or embed between the leaflets, causing deformations to the membrane. Many interactions between lipids and nanoparticles occur over long timescales; therefore, coarse-grained (CG) molecular dynamics simulations are necessary to study GNP-Lipid systems further. Several conflicting CG models for gold have been proposed, differing in chemical nature and resolution. Many studies rely on a hydrophobic bead for the gold core, while others use polar beads or soft spheres. It is frequently presumed that aggregation behavior is dominated by the ligands that functionalize the GNP, and that systematic parameterization of the gold core itself is unnecessary. Furthermore, GNP models that have been validated in the aqueous phase are rarely retested in a membrane. Here, we compare the aggregation behavior of nanoparticles with gold cores composed of three different types of beads: polar beads, hydrophobic beads, or soft sphere beads. We use aggregation as a metric to compare the models to each other and experimental data. We find a pronounced dependence on the choice of model beads, particularly for gold nanoparticles with shorter ligands, and we observe large-scale aggregation in nanoparticles composed of polar beads that correspond most closely with experimental results. These results suggest that interactions of the GNP cores help drive gold nanoparticle interactions, particularly for shorter ligand lengths, and that a polar core model may be more suitable than a hydrophobic model for studying GNPs in hydrophobic environments.

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

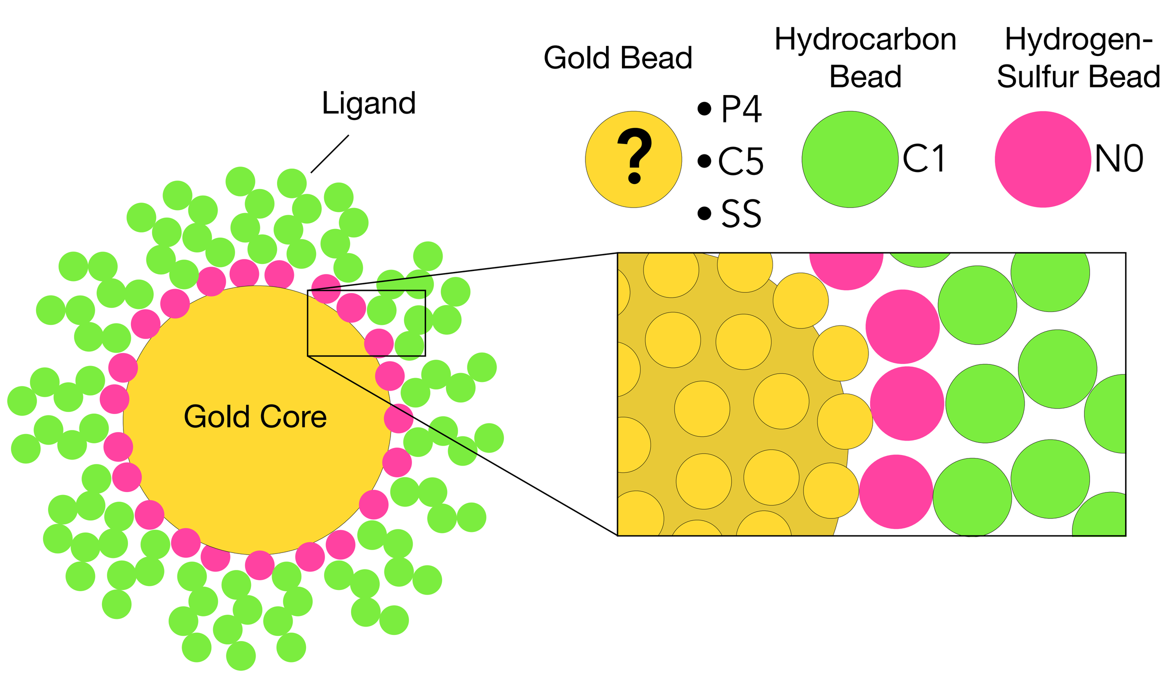

Fig 1. Representation of gold nanoparticle model core and assigned bead types

Research Question

1. Does large scale GNP aggregation depend on the gold core parameter?
2. Does ligand length affect gold nanoparticle aggregation?
3. Does ligand length affect the amount of exposed gold surface?

Results

Aggregation of Polar-Bead GNPs Qualitative Matches Experiments

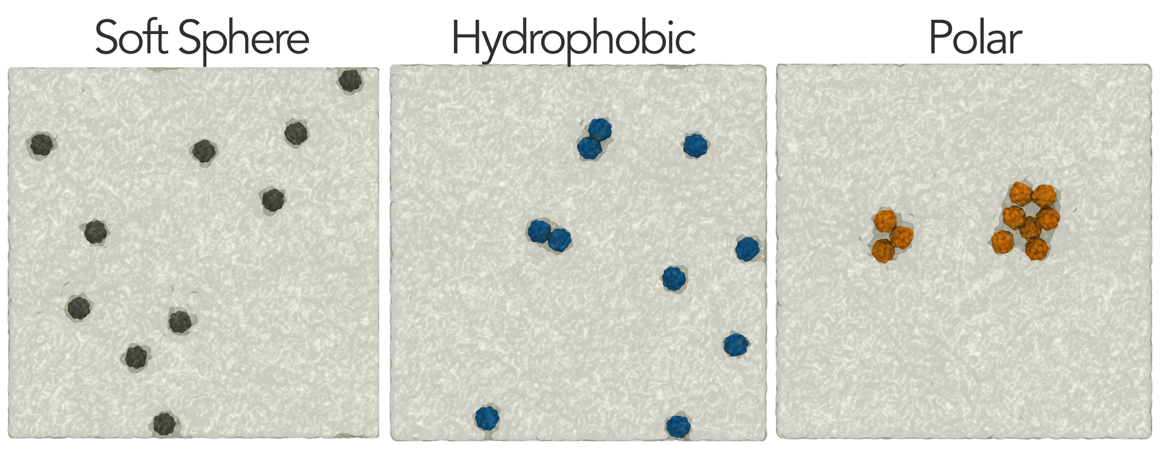

Fig 2. Representative image of GNPs aggregation in various core types (Soft Sphere, Hydrophobic, or Polar).

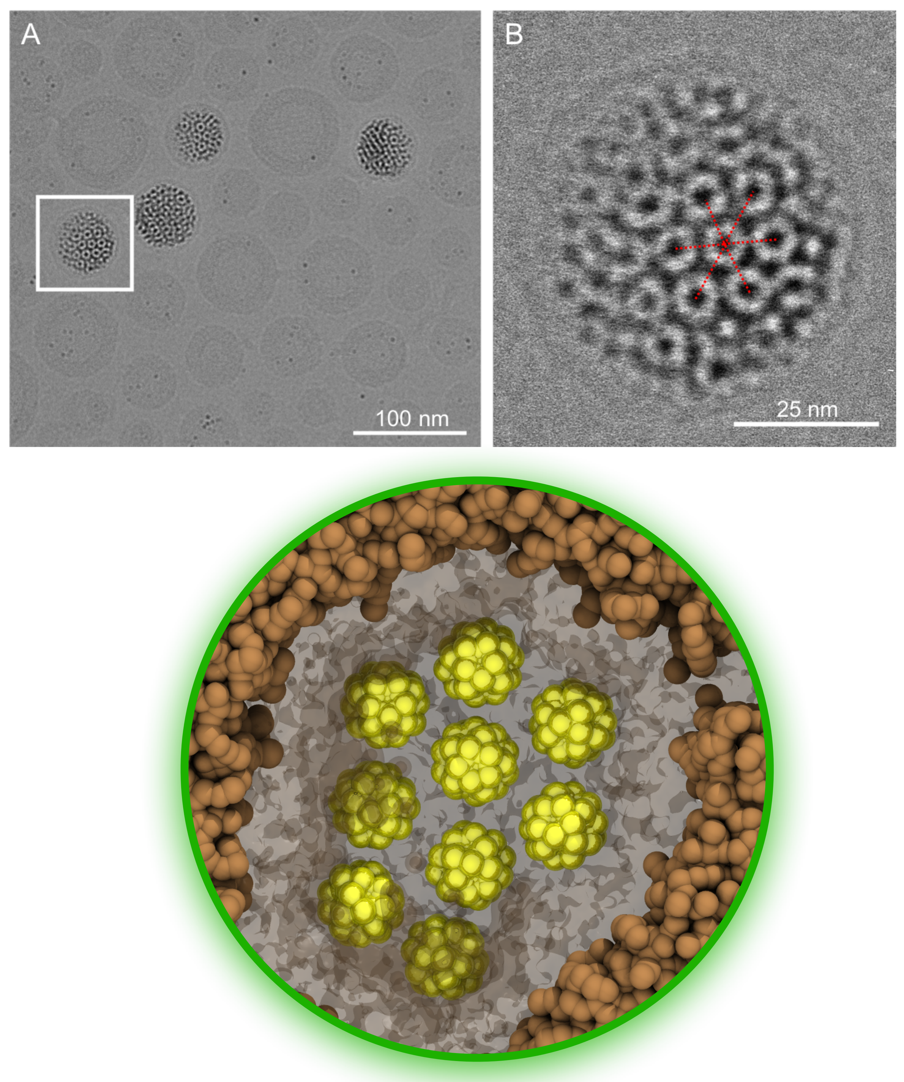

Fig 6. Top: Cryo-TEM images of GNPs aggregating in polymersomes[8]. Bottom: Representative image of aggregated dodecanthiol coated GNPs. GNPs in yellow and lipids in orange

GNP Core Parameters And Ligand Length Influence Aggregation

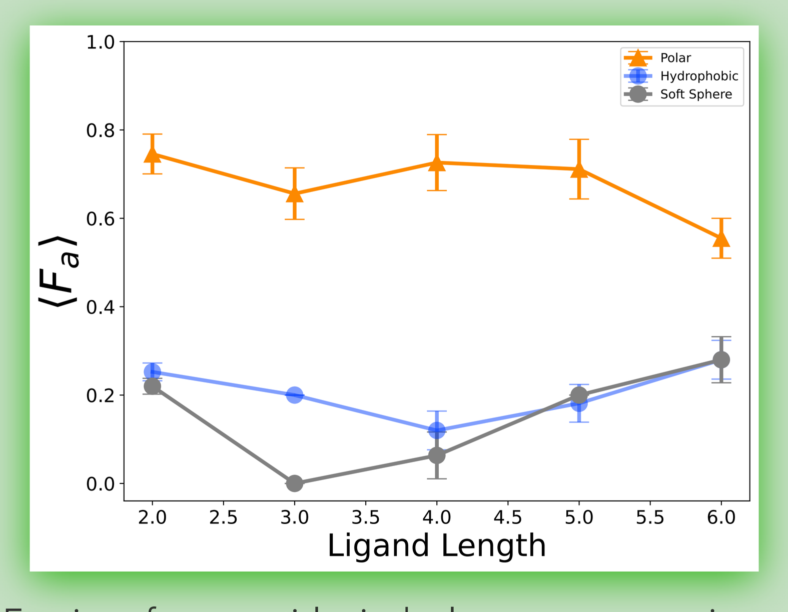

Fig 3. Fraction of nanoparticles in the largest aggregate in systems of varying ligand length.

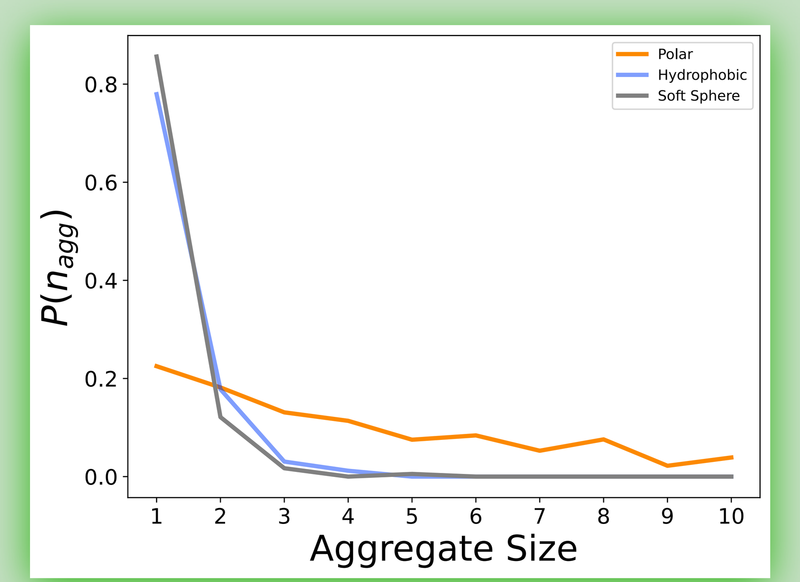

Fig 4. Probability Distribution of GNP cluster sizes for varying core types.

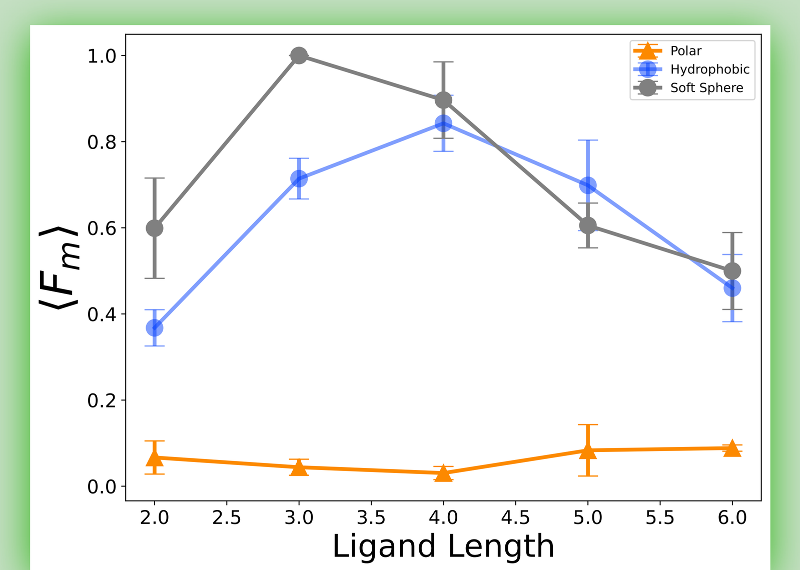

Fig 5. Fraction of GNP monomers in systems with varying NP diameters.

Ligand Length Determines GNP Core Exposure

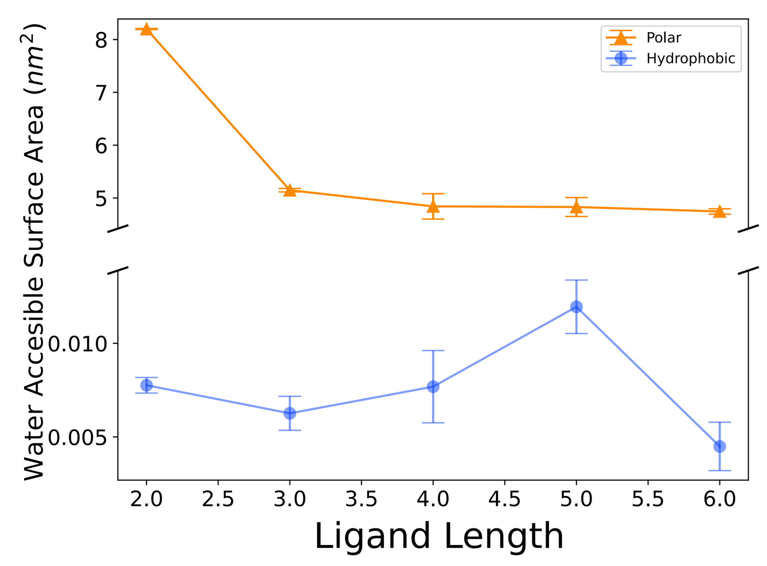

Fig 7. The SASA of GNP cores as a function of ligand length.

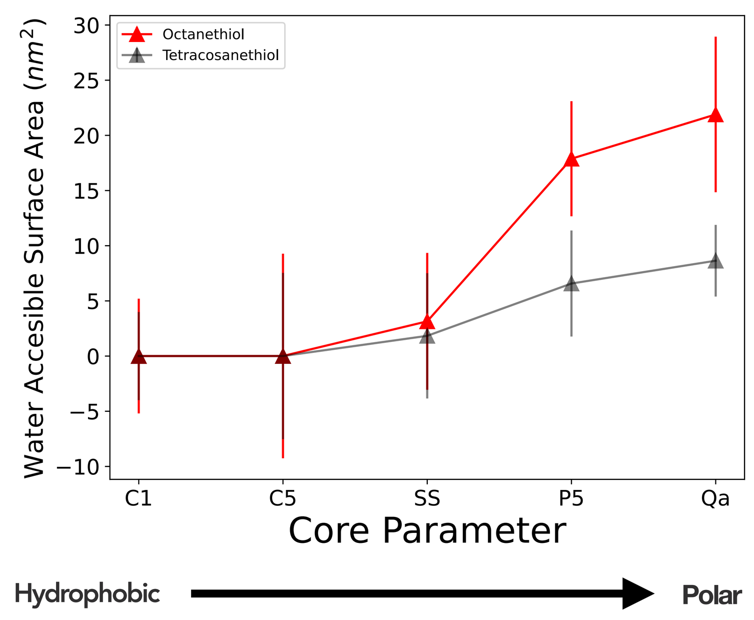

Fig 8. The SASA with varying core parameters for the gold core model.

Methods & 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_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

- Simulation software: Gromacs 2016[3]
- Force Field: Martini 2.2[2]
- Simulation Time: 5 μs
- Aggregate fraction and PDFs systems contain 10 GNPs

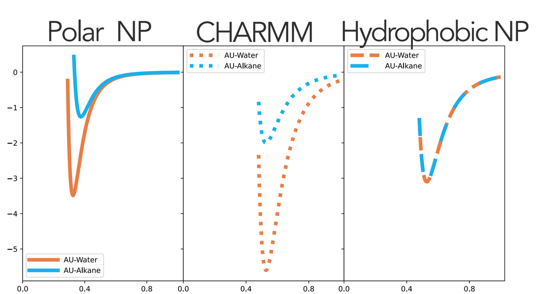

Fig 9. Lennard Jones interactions of gold (P5, AU, C5) with water (P4, O, P4) or Carbons (C5, C, C5)

Summary

- Single GNP core 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]

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