Developing a Martini gold model for use in biological contexts

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Abstract

The success of the Martini force field is largely due to its ability to reproduce experimental phenomena, its extensive library of biological molecules, and the abundance of tools available to further develop models of small molecules. However, many inorganic materials cannot be investigated in Martini because they have no direct correspondence to a Martini bead type. One such material is gold, making it infeasible to investigate gold-protein interactions, ligand-coated gold nanoparticle aggregation, and small molecule binding to gold surfaces in Martini. To bridge this gap, we present Martini Gold: a gold model and strategy for parameterizing metals in the Martini force field. We use atomistic simulations as a foundation for the Martini gold model. Our goal was to maintain gold cluster size, stability, and interaction energy between the coarse-grained and atomistic systems. To achieve this goal we determined the number of gold atoms that corresponds to a Martini S-bead, matched atomistic and coarse-grained gold-gold dimerization free energies in oil and water, and matched atomistic and coarse-grained small molecule adsorption free energies to gold surfaces. We demonstrate the model's accuracy by comparing coarse-grained simulations of gold nanoparticle aggregation in lipid membranes with experimental data. Based on the gold parameterization scheme, we designed a workflow to parameterize new metals in Martini.

Approach

- Match dimerization free energies between varying size atomistic force field gold clusters and Martini bead s
- Overlay Martini bead with an adjustable virtual site
- Match atomistic force field gold-gold dimerization free energies in different solvents to Martini bead with virtual site
- Match atomistic force-field adsorption free energies between amino acids and gold slab to amino acids and Martini slab

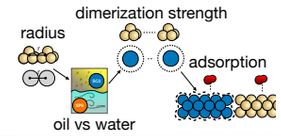


Fig 2. Parameterization roadmap for gold

Methods

- Simulation software: Gromacs 2024[2]
- Force Field: CHARMM[3] with Interface[4], Martini 3[5]
- System Building Tools: Charmm-gui[7,8], COBY[9], Insane[6]
- Free energy profiles were obtained with COLVARS[10]
- All atomistic systems were equilibrated for 20 ns and production is 200 ns
- All coarse-grained systems were equilibrated for 200 ns and production is 2 μs

Self-Interaction potentials

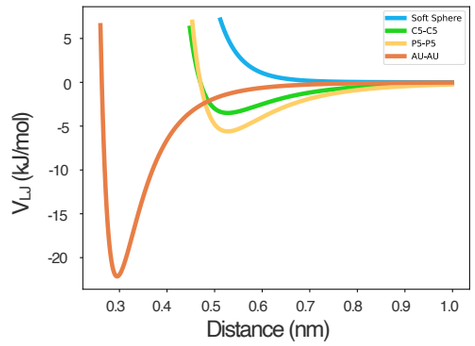


Fig 3. Lennard Jones self interaction potentials for atomistic gold or Martini beads that are typically chosen to represent gold. Atomistic in orange, soft sphere in blue, C5 in green, and P5 in yellow.

Background

- Gold (GNPs, Figure 1) is used in biosensing, biolabelling, and controlled drug delivery[1]
- In these applications, gold interacts with biological molecules.
- The Interface force field[4] is an additive inorganic force field that can accurately capture metal-biomolecule interactions.
- The ability to capture metal-biological molecule interactions in Martini is currently not possible
- Researchers have used adhoc polar bead, hydrophobic bead, and soft sphere Gold models that do not fully capture golds behavior

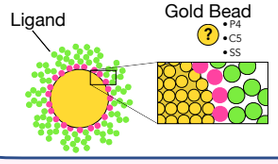


Fig 1. Representation of existing martini gold nanoparticle model core and assigned bead types

Bead size determination

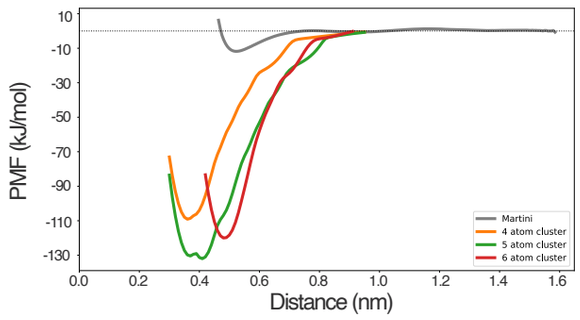
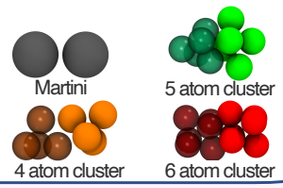


Fig 4. Dimerization free energy profiles between martini S beads (grey), or atomistic gold cluster of varying sizes: 4 atom cluster (orange), 5 atom cluster (green), 6 atom cluster (red). Representative images of clusters are colored as above.



Gold-Gold dimerization free energies

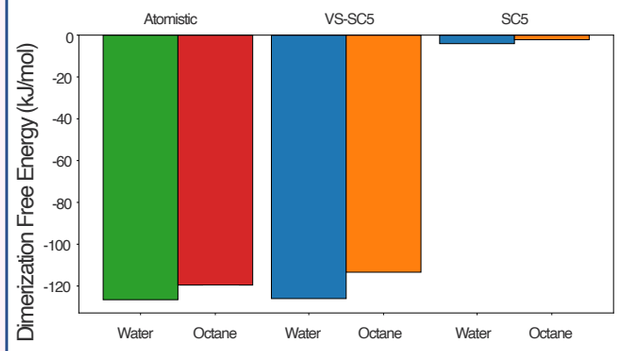


Fig 5. Dimerization free energy between gold clusters (6 atom), Martini beads overlayed with virtual sites (vs-SC5), or non-virtual site Martini beads (SC5). Dimerization free energies were calculated under water solvent or octane solvent conditions.

Summary

- Here we have developed the first Martini gold model that captures gold-gold and gold-biomolecule interactions.
- We determined that a single Martini bead best represents a 6 atom gold cluster.
- We developed a bead that has significantly larger self-interactions than any current Martini bead, better representing gold.
- We match small molecule adsorption free energies to gold surfaces.
- We tested the model by building a gold nanoparticle system and observed strong gold nanoparticle dimerization, which is expected.

Model Goals

Develop a Martini gold model that accurately captures gold-gold and gold-biomolecule interactions

1. What is the best mapping between a gold cluster and a Martini Bead?
2. Can we reproduce the dimerization free energies of atomistic gold clusters ?
3. Can we reproduce the interaction free energies between gold surfaces and small molecules in aqueous environments?

Validation of gold model using lipid membrane embedded gold nanoparticles

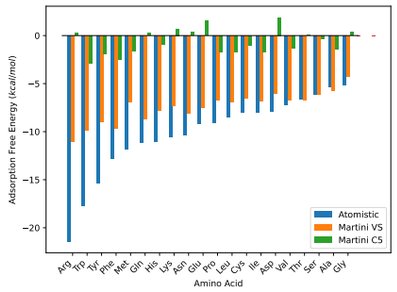


Fig 6. Adsorption free energy of the 20 amino acids to a slab of: atomistic gold (blue), Martini bead overlayed with virtual site tuned to newly specified potentials for Martini gold (orange), or Martini C5 beads (green)

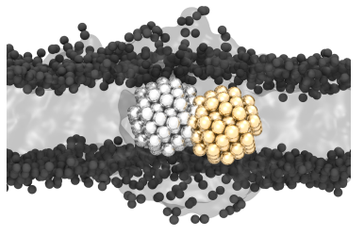


Fig 7. Representative image of gold nanoparticle model built with the adjusted Martini virtual site gold potentials.

References

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