Characterizing the interaction between EG_6-coated AuNPs and cyt *c* using molecular dynamics

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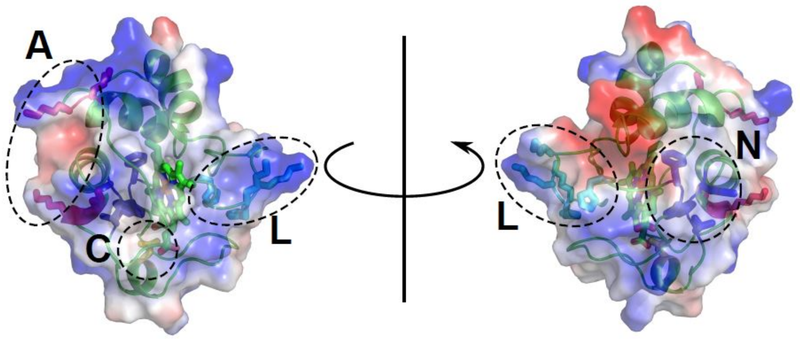
Motivation and Objectives

EG_6-coated gold nanoparticles (AuNPs) are being considered as candidates for biologically benign nanoparticles.



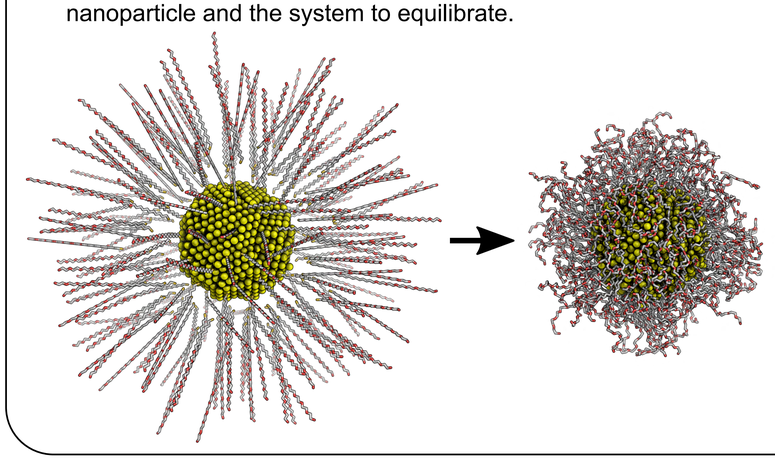
- Cyt c is a peripheral membrane protein found in the mitochondria[1].
- Experiments have shown that AuNPs can bind and interact with cyt *c* when it is attached to a bilayer[2], creating a potential hazard.
- The nanoparticle's coating significantly impacts its interaction with the protein. EG_6-coated AuNP show weak adherence to bilayers in the presence of cyt *c*[1].

Simulation Methods

The simulation to construct the nanoparticle is done using LAMMPS[3] with explicit TIP3P[4] solvent. For the subsequent simulations, the protein (PDB 1akk)[5] is placed so that its nearest atom is 4.5 nm away from the center of the nanoparticle in each of the starting configurations. The systems are solvated and ionized in VMD[6]. Each configuration undergoes an energy minimization along with *NPT* and *NVT* equilibrations before 50.0 ns production simulation. These simulations are preformed using NAMD[7] on the MARCC supercomputer. Trajectories are analyzed using VMD[6].

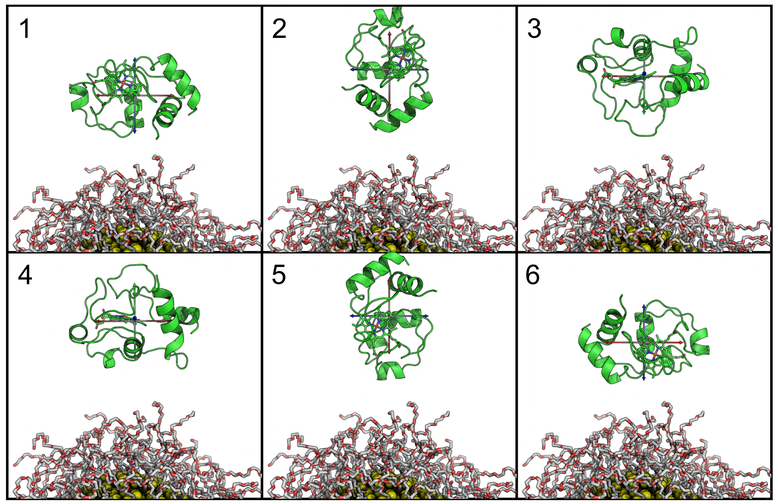
Nanoparticle Preparation

- 200 EG_6 molecules are placed around a 4.0 nm diameter gold core.
- A 4.0 ns simulation is conducted to allow the ligands to attach to the nanoparticle and the system to equilibrate.



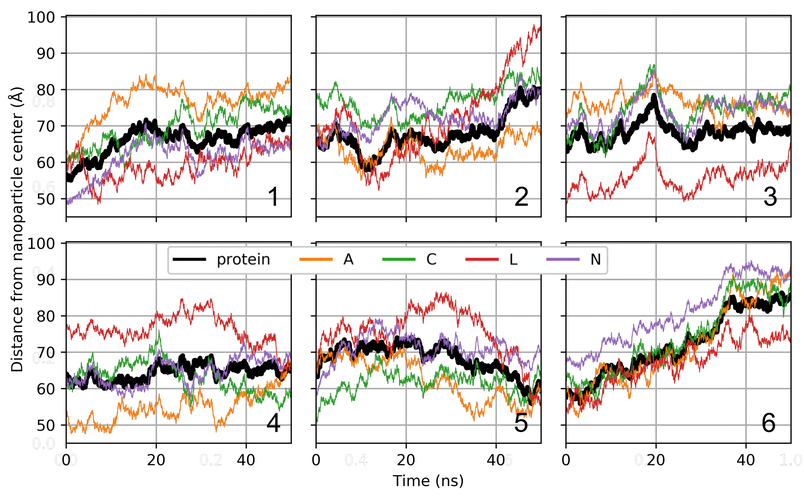
Summary of Starting Orientations

Six different starting orientations are chosen so as to provide adequate sampling of the entire protein surface.



- Six systems are prepared where the protein is arranged in different starting orientations according to its principal axes.
- A constant distance is maintained between the edge of the protein and the nanoparticle.
- 50 nanosecond simulations are conducted on each system, and the results are analyzed.

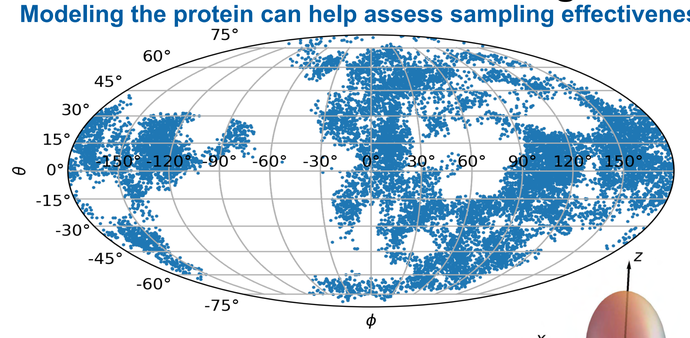
Tracking Protein Dynamics



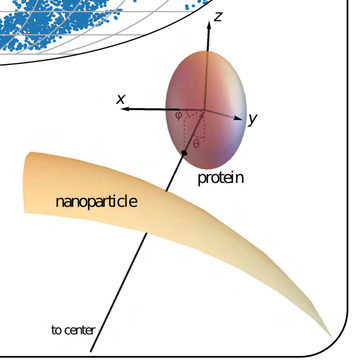
- The distance between the center of mass of the nanoparticle and various locations on the protein report on protein motion
- Helps identify how close individual binding sites are to the nanoparticle, as well as the protein as a whole
- In comparison to another ligand previously studied, the EG_6-AuNPs show little affinity for cyt *c* during these simulations[1], agreeing with experimental evidence, although more sampling is needed.

Protein Surface Coverage

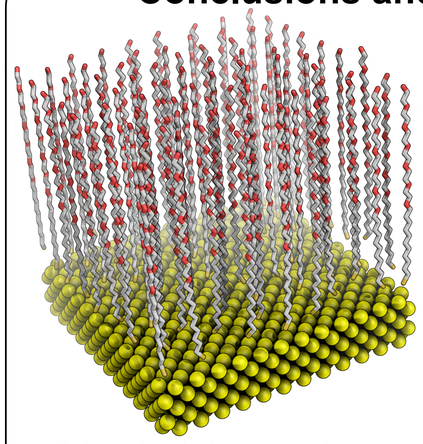
Modeling the protein can help assess sampling effectiveness.



- Investigating the locations on the protein that are aligned towards the nanoparticle during the simulations highlights the level of surface coverage.
- Provides data to assess whether starting orientations are sufficient.



Conclusions and Future Work



- Simulations confirm previously gathered experimental data showing little affinity between EG_6-coated AuNPs and cyt *c*.
- Ongoing work aims to enhance simulation sampling as well as investigate the effects of nanoparticle curvature.
- Future simulations will combine gold nanoparticle, protein, and bilayer into one system.

Using simulations, we aim to uncover the interaction between EG_6-coated AuNPs and cyt *c*–a membrane binding protein–so as to control and limit their insertion and possible toxicity.

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