Molecular Basis of Encapsulation of Positively Supercharged Species by Ferritin

Penn Master of Chemical Sciences

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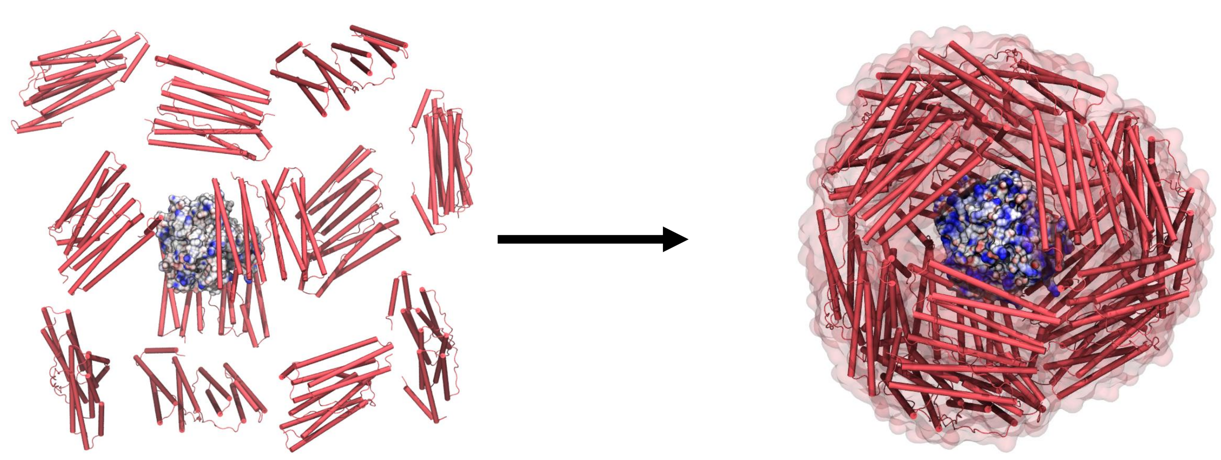
Purpose

- Protein-protein host guest systems have a broad range of applications including chemical sensing, separations, materials science, catalysis, and pharmaceutics[1]. Ferritin with its self-assembling, high-biocompatibility, and negatively charged inner core is an attractive host system for positively charged species. It's been shown to encapsulated positively charged species such as GFP (green fluorescent protein), carbonic anhydrase II, and gold nanoparticles[2]. We now aim to understand the mechanisms behind encapsulation of positively charged proteins inside the core of ferritin by generating an ensemble of configurations using molecular dynamics.

Background

- Ferritin, a ubiquitous protein across all domains of life, is responsible for maintaining the levels of iron within cells by oxidizing iron into mineralize iron that can be store within its hollow core for release later.
- Ferritin is composed of 24 subunit of a tetrahelical bundle with a short fifth helix.
- Aftn is the only known ferritin to be able to dissociate into its subunits and reform back to a spherical cage by tuning the salt concentration of the solution. This opens a milder pathway to induce encapsulation



Ffigure 1.
Dissassemble ferritin subunits on the left surrounding gust complex. Fully assemble ferritin cage around gust complex on the right

Experimental Design

Crystal Structures

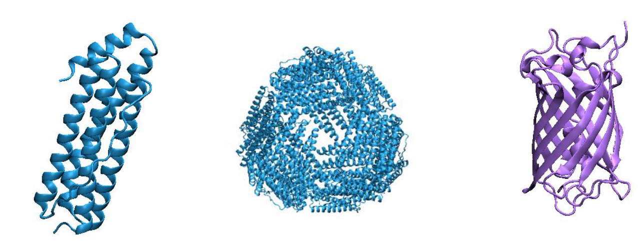


Figure 2.
Crystal Structure of a subunit of ferritin, fully assemble ferritin, and GFP +36

- Figure on left is a subunit of ferritin, PDB ID: 1SQ3
- Middle Figure is ferritin in its fully assemble state
- Right figure is GFP+36 PDB ID:2B3P

Simulation Parameters

- NPT Ensemble (constant number of molecules, pressure, and temperature)
- Immerse with explicit water molecules in a water box
- Temperature: 300K
- Pressure: 1atm
- Minimized for 1000steps
- Equilibration time: 40ns

Methodology/ Preliminary Results

1) Find time region where GFP docks onto Ferritin

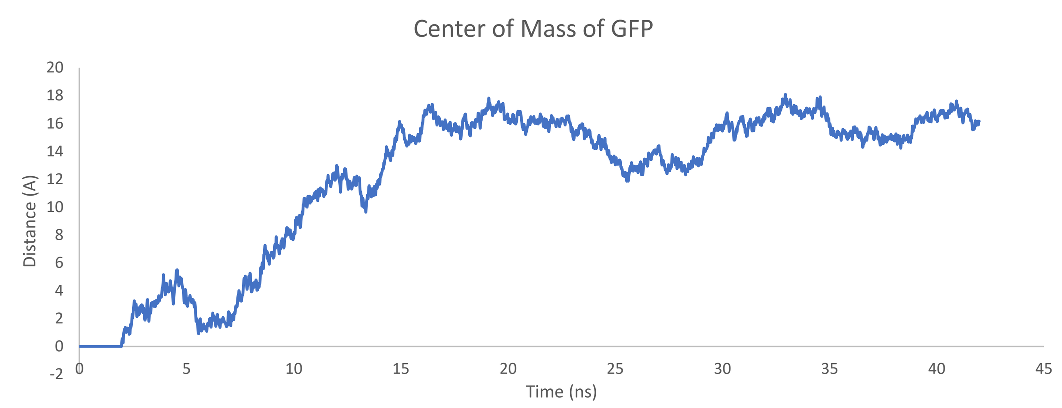


Figure 3

3) Construct a graph to show length of time pairs of residues are in contact

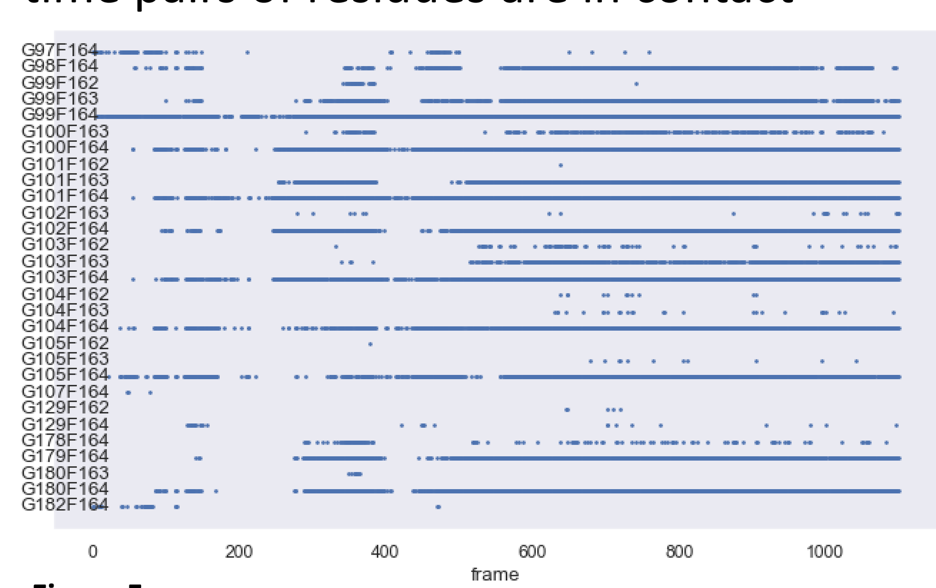


Figure 5

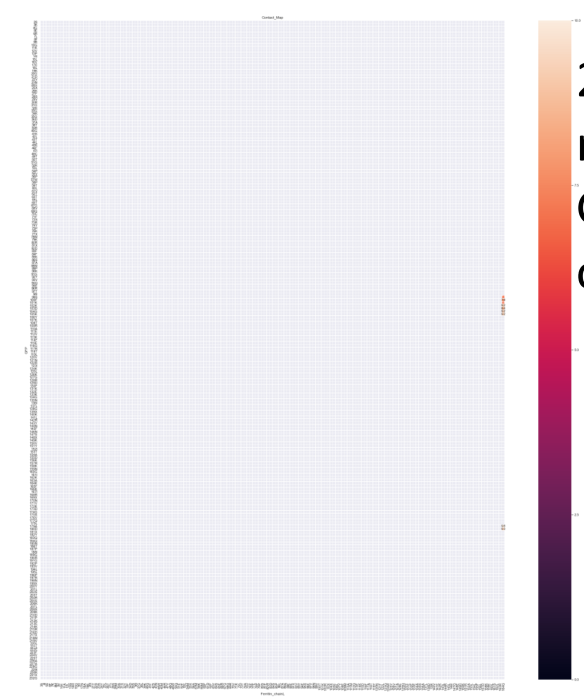


Figure 4

2) Construct an average contact map between the residues on GFP against residues on ferritin over the trajectory

3) Visually Inspect the Residue Pairs

Table 1.List of Residues in contact

	GFP	Ferritin	Distance between CA
Chain G	96R	164Q	7.1
	97T	164Q	7.8
	98I	164Q	6.9
	99S	164Q	9.2
	100F	164Q	8.4
	101K	164Q	9.2
	102K	164Q	9.2
	176V	164Q	9.8
	177Q	164Q	9.3

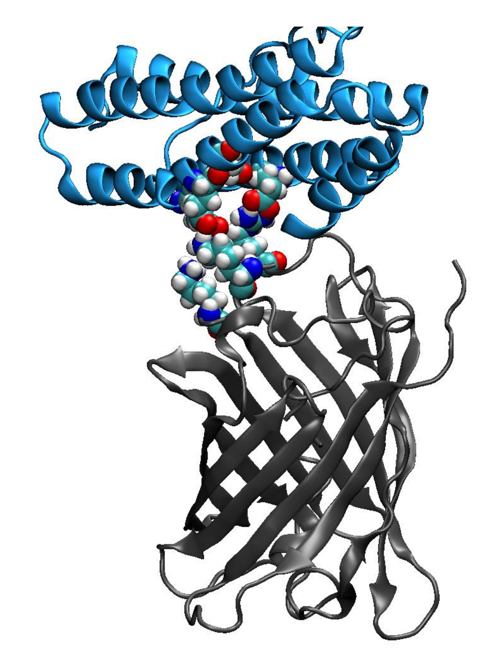


Figure 6

References

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