Understanding ferritin biomineralization by high-resolution cryo-electron microscopy

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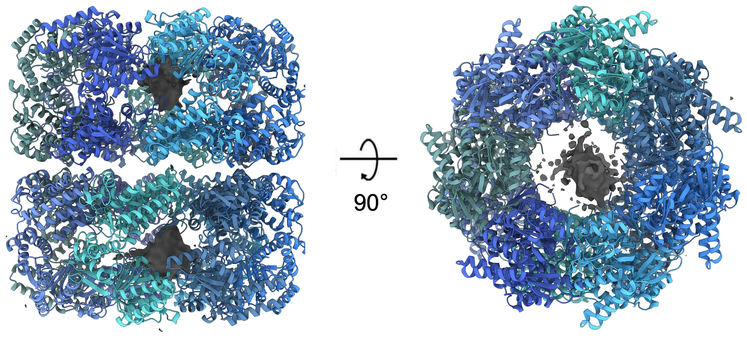
Overview

Biological molecules are capable of interacting with inorganic materials, giving rise to highly controlled material synthesis and the creation of new bio-inorganic materials with unique function and properties. However, little is known about the molecular interactions between the biological molecules with inorganic materials. This knowledge gap represents one of the biggest hurdles to the rational design of biomolecules for novel, highly controlled nanostructure synthesis. The focus of our work is to extend the powerful methods of single-particle cryo-electron microscopy (cryo-EM) to study protein and inorganic nanoparticle (NP) interactions, with a concentration on ferritin-NP complexes. Our goals are to ultimately make significant contributions to the understanding of biomineralization in ferritin, as well as elucidating the general fundamental molecular interactions of biomolecules with nanomaterials.

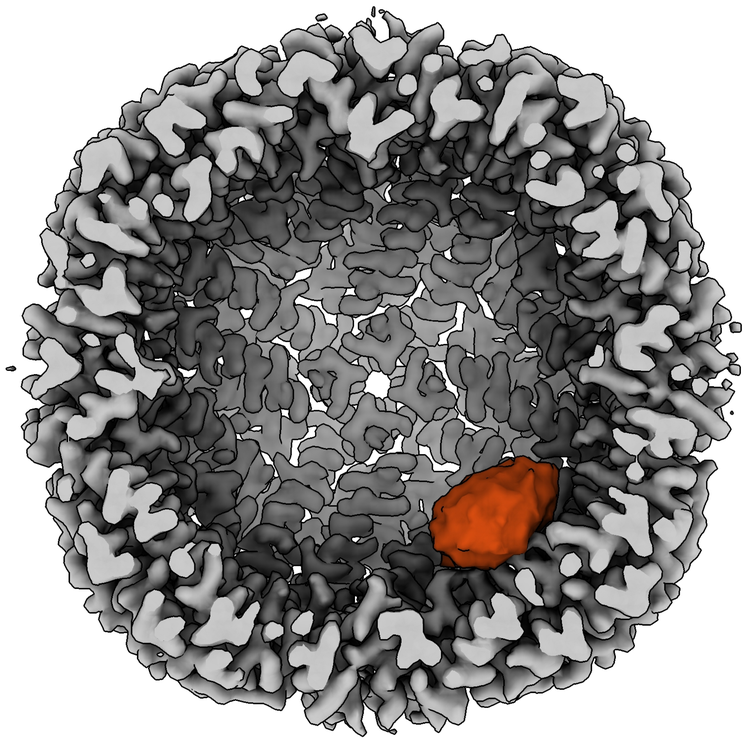
GroEL-NP structure



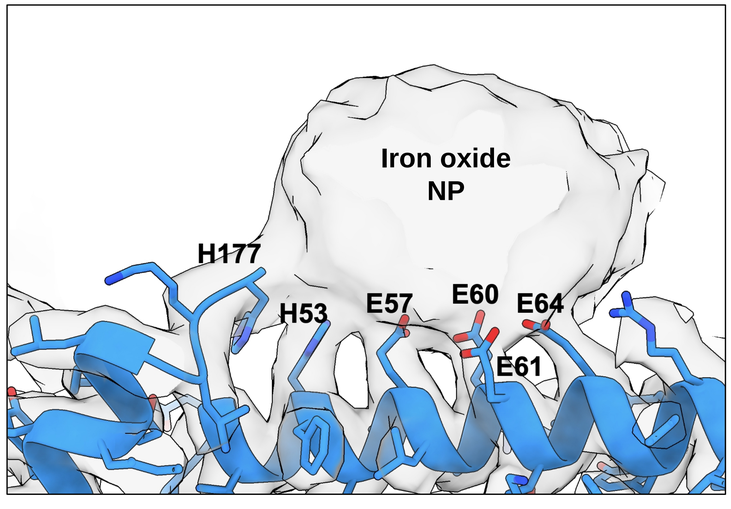
Our first demonstration of single particle cryo-EM on a protein nanoparticle complex was on GroEL bound to platinum NPs. The final resolution was 3.93 Å and the platinum NPs can be seen in the central cavity of GroEL. This study set the stage for future work on ferritin complexes with NPs.

Ferritin-NP structure

Sample preparation and data processing methods were optimized to yield a 2.87 Å structure of Ferritin bound to an iron oxide NP.

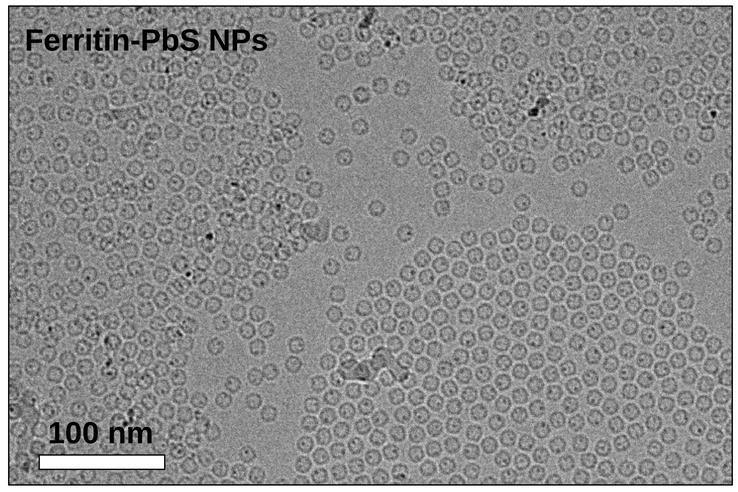


The high-resolution map allowed the direct visualization of the interaction of the protein with the iron oxide NP. A New interaction of the ferritin C-terminus with the NP was found. This represents the first time these details have been seen in ferritin.



Current work

We are currently focused on improving cryo-EM data quality and quantity to enhance the resolution of the Ferritin-NP 3D reconstruction. The goal is to further improve the details and map features at the protein-NP interface.



Additionally, we are exploring the structure of new Ferritin-NP complexes, such as ferritin bound PbS NPs (see above).

Areas for Collaboration

- Other ferritin-based nanoparticle systems and materials
- Studying mechanisms of new Protein-based nanomaterials syntheses
- High-resolution structural studies by cryo-EM and Microcrystal electron diffraction (MicroED)

References

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- F. Banihashemi, G. Bu, A. Thaker, D. Williams, J.Y.S. Lin, and B.L. Nannenga. **Beam-sensitive metal-organic framework structure determination by microcrystal electron diffraction**. *Ultramicroscopy* **2020** 216, 113048