

The Zarivach lab

Magnetosome formation and iron biomineralization in Magnetotactic bacteria

Background: The term biomineralization describes processes of mineral deposition, within or outside a cell that are aided and controlled by a bioorganic matrix. Such processes – which take place in all kingdoms of life – include the formation of bones, skeletons and shells, the uptake and storage of minerals, and the inhibition of mineral crystallization in supersaturated mineral environments. Biomineralization events can be controlled by proteins, which pump the specific metals and initiate the mineral nucleation event and control the growth phase, the crystal size and the localization of the biominerals.

Iron biomineralization is a process involving proteins that control the properties of magnetic nanoparticles. One of the main constituents of these magnetic nanoparticles, magnetite (magnetic iron oxide, Fe_3O_4), is found in a large variety of living organisms, from prokaryotes to eukaryotes including humans. Magnetite is involved in a wide range of biological functions, for each of which a unique particle property is required. Alongside their role in nature, magnetite nanoparticles are becoming increasingly important for their applications in the fields of nano- and biotechnology, with different types of magnetic nanoparticles being used in catalysis, magnetic recording media, and biomedical applications, such as the treatment of some cancers and the detection and separation of biomolecules. One of the simplest magnetic biomineralization systems is that found in the magnetosome of magnetotactic bacteria, where magnetic nanoparticles are produced in a controlled manner by a set of specialized biomineralization proteins.

Magnetotactic bacteria comprise a diverse group of aquatic microorganisms, which have the unique ability to navigate along geomagnetic fields, behaviour that is believed to simplify their search for low-oxygen environments. The magnetic orientation abilities of magnetotactic bacteria are dependent on the integrity of the magnetosome, a specialized subcellular organelle, assembled from a chain of lipid invaginations, each able to biomineralize and enclose a single ~50 nm crystal of magnetite or its sulfide analog, greigite (Fe_3S_4). During the biomineralization event, the bacterium absorbs iron ions from its surroundings, pumps them into the magnetosome, and controls the way in which the iron is crystallized as a magnetite crystal with a precise size and shape. At present, the exact mechanisms of magnetosome formation and iron biomineralization and the structure-function relationship of magnetosome associated proteins (MAPs) are unknown. What is known, however, is that there are several types of MAPs, all localized in a genomic island common to all magnetotactic bacteria. These proteins include: (i) a set of incorporated membrane proteins that are believed to facilitate vesicle formation, vesicle localization and iron transport, (ii) a set of proteins that affect magnetite formation and size, (iii) a set of chain-forming proteins, and (iv) a large set of unknown proteins, assumed to be involved in magnetosome formation and in protein-protein interactions.

Aims: The overall goal of the work in my lab is to understand the structure-function relationships of protein-mineral interactions and organelle-associated functions via the study of the proteins involved in magnetite biomineralization. An understanding of structure-function relationships of biomineralizing proteins (MAPs in this case) will provide insights into the fundamental processes of iron biomineralization, protein-mineral interactions and organelle formation, which are currently not well understood. To achieve this overall goal, my lab combines several approaches focusing on MAPs structure-function studies at the prediction level *in silico*, at the secondary structure level in the interaction with magnetite, and at the atomic level (via new structural biology methodologies). To

assess the results and to verify the proposed models, my team test MAPs for their abilities to affect magnetite in vitro. The research directions that are studied in my lab are: 1) to develop and exploit the expression and purification of MAPs and MAP-scaffold protein chimeras (MAPs and their conjugates are used to study the ability of different magnetotactic bacteria to affect the size and shape of magnetite nanoparticles); 2) to develop methodologies for the crystallization of MAPs and MAP-conjugates in the presence and absence of minerals, and 3) to determine and analyze the 3D structures of MAPs involved in magnetite biomineralization.

This research is innovative in that it uses rational engineering of biological components, based on their atomic structures, for the crystallization and structure determination (using X-ray crystallography) of biomineralization proteins interacting with minerals. Such a system, together with in vitro biochemical and biophysical analysis, allow the determination of the structure-function relationships of biomineralizing proteins.

Overall my lab is focused on biochemical and structural studies of proteins and as such I am also involved in many projects raised from different groups within BGU including health sciences and engineering faculties.