SFB1565 Seminar

Prof. Dr. Gabriel A. Frank

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Symmetry-driven allocation of protein functional subunits revealed by cryo-EM and graph theory

Gabriel A. Frank's lecture sheds light on the fascinating world of bacterioferritins. Through the skilful combination of cryo-EM and graph theory, he and his team identified four dominant configurations of the two subunits, which enable iron transfer and iron uptake through their specific arrangement and that this restriction of possible configurations is caused by mutations. The lecture promises to provide exciting insights into symmetry-driven protein organization and its evolutionary significance.

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Physics Department Building
Lecture Hall HS5

Hosted by Prof. Dr. Jörg Enderlein

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Iron transfer into and out of bacterioferritins requires the simultaneous positioning of the two subunit types around the pseudo-C3 symmetric pores of the nanocages. However, it is unclear how the two subunit types are distributed in hetero-ferritins, and the forces driving their organization are unknown. Answering these questions requires the structural and functional classification of the quaternary configuration of pseudo-symmetric oligomers. However, the octahedral geometry of ferritin leads to ~700,000 such configurations, which renders the determination of specific configurations meaningless.

We solved this problem by combining cryo-EM with graph theory. Using this strategy, we found that only four configurations dominate the ensemble of the quaternary organizations of hetero-oligomeric bacterioferritin. The limited diversity of quaternary organizations results from mutations in the subunit-type interfaces that disfavor the formation of specific subunit-type associations. When combined with the interconnected architecture of ferritin, these localized assembly rules lead to the formation of highly functional oligomers. In these oligomers, the number of pseudo-C3 symmetric pores composed of the two subunit types is maximal.

The mutations responsible for these preferential assembly patterns have a clear evolutionary signal that emerges upon the subunits' specialization events. This assembly mechanism represents a negative design strategy that prevents the formation of arrangements with reduced functionality and can mitigate the impact of random variations in the composition of the nanocage subunits.

Biographical sketch

Gabriel Frank is a senior lecturer of Structural Biology at the Department of Life Sciences at Ben Gurion University of the Negev (BGU). Gabriel began his academic career at the Technion-Israel Institute of Technology, studying Physics and Material Science. In 2003, Gabriel received a master's in Material Engineering from BGU. During his MSc studies, he became interested in the complexity and intricacies of molecular structures produced by living organisms. Following his interest, Gabriel switched fields to Biophysics during his Ph.D. at the Weizman Institute of Science (2004-2010), under the mentorship of Profs. Amnon Horovitz and Gilad Haran, where he studied the dynamics of molecular machines at a single molecule level, focusing on GroEL.

Before being accepted to BGU (in 2016), Dr. Frank took a postdoctoral research position at the National Institutes of Health in Bethesda, MD, USA, where he continued his research on molecular machines using Cryo-Electron Microscopy (Cryo-EM). Gabriel's lab at BGU aims to understand the diversity of structural mechanisms enabling proteins to sense, integrate, and respond to cues from their environment, using Cryo-EM, functional and spectroscopic assays. In parallel to his research and teaching obligations Gabriel spearheaded the adaptation of macromolecular structure determination using Cryo-EM, making BGU the national leader in this field.