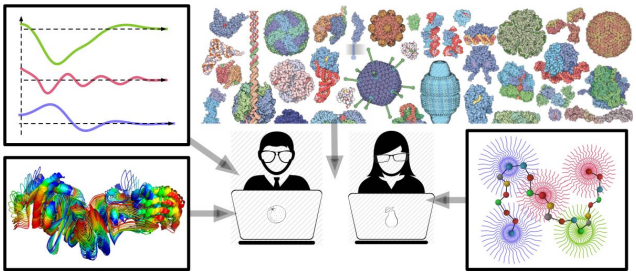

Contribution ID: **24** Type: **Talk**

Asymmetric hydrophobic mismatch in assembly of ATP synthase rotor ring

Tuesday, 13 February 2024 11:35 (25 minutes)

Rotary ATPases are multisubunit enzyme complexes that couple synthesis or hydrolysis of ATP molecules with transport of ions across a membrane. Their transmembrane part includes a homo- or a heterooligomer of *c* subunits called a *c*-ring, with a patch of several lipids confined inside it. Little is known about this patch; it is usually not well resolved in experimental structures, but it is clear that the lipids in it are displaced relative to the surrounding membrane. Here, we show that a protocol involving coarse-grained and atomistic molecular dynamics simulations can be used to obtain a model of the rotor ring protein-lipid assembly that fits well the experimental densities. We then study the mechanism of self-assembly of tetradecameric spinach chloroplast ATP synthase *c*-ring and demonstrate that *c* subunits display unusual asymmetric hydrophobic mismatch. Monomers and partially assembled oligomers cause a deformation of the surrounding membrane, which results in their mutual attraction. Because of asymmetry in the deformation, the subunits assume a relative orientation that favors correct assembly of higher-order oligomers and, eventually, of the whole ring. We estimate the binding energies of different oligomers and build a model for the complete assembly process of a *c*-ring starting from individual protomers. Presented modeling process and biophysical considerations are likely generalizable to assembly of other membrane protein complexes with high-order rotational symmetry.

Submitting to:

Integrative Computational Biology workshop

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Session Classification: Computational Methods and Deep Learning