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Lecture title:

"Unveiling the structure of macromolecular assemblies using integrative dynamic modeling"

Abstract:

Proteins often assemble in large macromolecular complexes to achieve a specific biological task. Unfortunately, owing to their size and complexity, these structures are difficult to determine at atomistic resolution, preventing thus a complete understanding of their mechanism of action.

To predict the structure and function of these large biological assemblies we developed a new approach that uses swarm intelligence optimization guided by experimental-based restraints to characterize quaternary protein structure accounting for native dynamics.

Using this integrative strategy we were able to reveal the assembly mechanism of aerolysin (a bacterial pore-forming toxin that produces heptameric pores at the target membrane), and the basal body structure of Yersinia type III secretion system.

The native dynamics of individual components emerges as the key determinant to define the architecture and understand the function of these large multi-protein complexes. Therefore, the ability of our approach to integrate protein dynamics with sparse experimental data looks as a promising step toward the molecular characterization of large systems.