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Integrative modeling of protein oligomers using Heligeom

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Protein oligomers can modify their overall architecture in response to changes in the environment, such as ion concentration and composition, the presence of small ligands or mechanic stress. These changes may involve small variations in the subunit-subunit interface which can lead to important changes in the overall shape due to multiplication effect. They may also involve large interface variations and lead to alternative assembly modes. These characteristics pose specific problems for the integrative modeling of oligomeric assemblies. For example, characterizing different oligomerization states in solution from SAXS experiments may be tricky. Theoretical approaches were developed in the past to directly relate peaks of the SAXS profiles to quantities such as pitch or number of monomers per turn. Although these approaches benefit from periodicity, the analytic treatment only holds as long as the repeated subunit has a simple, well-defined geometric form such as a sphere. I will present a strategy to handle more complex protein shapes based on the combination of interface sampling, screw construction (Heligeom [1]) and SAXS profile reconstruction (FoxS [2]) and I will illustrate this approach in the case of the polymorphic RecA filament of homologous recombination.

In addition to establishing the correspondence between interface geometry at the dimer level and helical properties of the oligomer, our python module Heligeom allows comparative analyses of oligomeric assemblies. It also includes a cyclic adjustment tool which enables generating assemblies with desired ring sizes with interfaces as close as possible to a predicted interface, where the predicted interface may come from docking [3] or from deep-learning calculations. Heligeom will soon be made available as a web server, making its functionalities available to researchers interested in helical or ring protein assemblies.

1. B. Boyer, J. Ezelin, P. Poulain, A. Saladin, M. Zacharias, C. H. Robert and C. Prévost (2015). An integrative approach to the study of filamentous oligomeric assemblies, with application to RecA. PLoS ONE 10 (3): e0116414 — doi: 10.1371/journal.pone.0116414

2. Schneidman-Duhovny D, Hammel M, Tainer JA, Sali A. FoXS, FoXSDock and MultiFoXS: Single-state and multi-state structural modeling of proteins and their complexes based on SAXS profiles. Nucleic Acids Res. 2016 Jul 8;44(W1):W424-9 — doi: 10.1093/nar/gkw389

3. L. Tran, N. Basdevant, C. Prévost and T. Ha-Duong (2016) Structure of ring-shaped Aβ42 oligomers determined by conformational selection. Scientific Reports 6, 21429 — doi: 10.1038/srep21429

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