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Assessing the stability of protein complexes within large assemblies

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Structural genomics projects exploiting Tandem Affinity Purification (TAP) or similar data have revealed remarkable features of proteomes [G06]. While these insights are essentially of combinatorial nature—selected proteins are known to interact within a complex, leveraging this information requires building three dimensional models of these complexes. Such an endeavour has recently been completed for the Nuclear Pore Complex (NPC), for which plausible reconstructions have been computed from different experimental data, including TAP data [A07a-b]. Yet, a full synergy between TAP data and the reconstruction is not at play for two reasons. First, the models built are qualitative. Second, the reconstruction does not elucidate the precise connexion between the model and TAP data. In particular, deciding whether proteins seen in a TAP experiment correspond to a single complex or a mixture of complexes within the NPC is not addressed.

This talk will present a method addressing these limitations. First, we shall introduce toleranced models to inherently model uncertain shapes. A toleranced model is a one-parameter family of shapes (a continuum of geometries) representing an uncertain shape, which can be used to investigate stable complexes amidst the continuum. Second, for models reconstructed from TAP data, we shall explain how toleranced models and their built-in geometric statistics can be used to infer stable contacts, and also to investigate protein complexes associated to specific protein types. Illustrations will be provided
on NPC models derived from the density maps presented in [A07a-b].

Bibliography

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