[P17] Analytical Symmetry in Large Macromolecular Assemblies

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Many protein complexes in the Protein Data Bank (PDB) are symmetric homo-oligomers. Indeed, it appears that large symmetrical protein structures have evolved in many organisms because they carry specific morphological and functional advantages compared to small individual protein molecules [1,2]. There is therefore considerable interest in studying and modelling the structures of these large bio-molecular complexes. Recently we have proposed a novel ab-initio protein docking algorithm for protein complexes with arbitrary point group symmetry [3] that can assemble protein complexes with any type of point-group symmetry including those of high order (tetrahedral, octahedral, and icosahedral). However, the inverse problem is even more interesting. Below we report on a very fast analytical method for the analysis of symmetric protein assemblies [4,5].

Analytical methods that perform the best structural superposition between different structures are very well known, however this structural alignment cannot be, generally, used to determine symmetries in protein assemblies. This is because of two underlying problems. First of all, to determine the best set of rotation axes for symmetrical assemblies (corresponding to cyclic, dihedral, tetrahedral, octahedral and icosahedral assemblies), in addition to the correspondence between the atoms in different subunits, a correspondence between subunits (or protein chains) is also required. Brute-force approaches will be prohibitively expensive for high-order symmetries in this case. Second, given the correspondence between the atoms and the subunits, a very fast method to estimate the quality of symmetry, or, more generally, to compute the symmetry-aware penalty function is needed.

We addressed these two challenges and developed computational tools that first find the correspondence between the subunits for all types of point-groups symmetries, and second = analytically compute the best symmetry group that minimizes the symmetry-aware root-mean-square deviation (RMSD) over transformation operators (rotations) in this group. More precisely, our tools automatically determine the axes of symmetry for a given symmetry group by analytically minimizing the RMSD-based penalty function. Exhaustive analysis of symmetric structures in the Protein Data Bank revealed that (1) There is no clear assembly stability preference for a particular type of symmetry group; (2) There is no dependence of quality of assembly packing on the size of the assembly; (3) However, for the dihedral symmetries, assemblies with the even orders are more stable compared to the ones with the odd orders.

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