FTDMP: A FRAMEWORK FOR PROTEIN-PROTEIN, PROTEIN-DNA AND PROTEIN-RNA DOCKING AND SCORING

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Knowledge of the 3D structure of protein-protein and protein-nucleic acid complexes is crucial for understanding the molecular mechanisms that govern essential cellular processes. Experimental methods such as X-ray crystallography, NMR, and CryoEM provide high-quality structures, but are expensive and time consuming. Thus, there is a need for computational structure prediction. While the AI-based method AlphaFold has revolutionized single chain protein structure prediction, challenges remain, particularly in modeling antibody-antigen interactions, protein-nucleic acid complexes, and proteins lacking close homologs. In these cases, docking can be employed to generate structure models. As a result, effective methods for selection of the most accurate models are necessary.

Here we present FTDMP, a newly developed framework for protein-protein and protein-nucleic acid docking and scoring. The framework can be used in two ways: to perform docking and subsequent scoring, or to evaluate and rank user provided models coming from various sources (AlphaFold, RoseTTAFold, docking, etc.). The full FTDMP docking and scoring framework was tested on protein-protein, protein-DNA, and protein-RNA docking benchmarks [1-3]. Compared to currently available docking systems, FTDMP demonstrated improved results of the free unbound-unbound docking when the top-ranked model was considered, and very high rates for bound-bound docking (up to 83% for the top prediction). The ranking in FTDMP is done by a newly developed method, VoroIF-jury [4]. The protocol based on this method obtained top results in the community-wide CASP15-CAPRI scoring experiment [5]. FTDMP can be used not only with the built-in, but also with external scoring methods. Thus, the framework can be employed for fast and straightforward evaluation of new scoring functions.

FTDMP, docking benchmarks and docking results are available at https://github.com/kliment-olechnovic/ftdmp.

[1] van Dijk, M., Bonvin, A.M. (2008). A protein-DNA docking benchmark. Nucleic Acids Res, 36, e88.
[2] Guest, J. D., et al. (2021). An expanded benchmark for antibody-antigen docking and affinity prediction reveals insights into antibody recognition determinants. Structure, 29(6), 606-621.e5.
[3] Zheng, J., et al. (2020). P3DOCK: a protein-RNA docking webserver based on template-based and template-free docking. Bioinformatics, 36(1), 96-103.
[4] Olechnovič, K., et al. (2023). Prediction of protein assemblies by structure sampling followed by interface-focused scoring. Proteins, 91(12), 1724-1733.
[5] Lensink, M.F., et al. (2023). Impact of AlphaFold on structure prediction of protein complexes: The CASP15-CAPRI experiment. Proteins, 91(12), 1658-1683.