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Computational Design of A/ß Propeller Building Blocks for Protein Assemblies

Yueyan Wu [1], Aurora Pierucci [1], Arnout Voet [1]

[1] KU Leuven, Leuven, Belgium

Protein assemblies hold great potential in diverse applications, but perfect symmetry, which is the impetus in artificial protein assembly design but lacking in natural proteins, poses a challenge. Using computational protein design approaches, our lab has developed perfectly symmetric artificial β propeller proteins, some of which serve as building blocks for protein assemblies by metal or ligand binding strategies. However, their assembly into larger particles remains challenging. Here, we tried to introduce α helices into the β propeller proteins, aiming to promote self-assemblies through coiled-coil-like protein-protein interactions.

The preliminary α/β propeller building blocks were designed with a combination of knowledge-based methods and advanced deep-learning methods which were successfully validated by biochemical experiments and X-ray diffractions. Based on these, new building blocks will be designed, and future work will explore the design of protein assemblies, especially 2D arrays and 3D cages, for applications in enzyme scaffolds, biosensors, and drug delivery.