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## Investigating the dynamics of protein-protein interfaces in well structured and fuzzy complexes

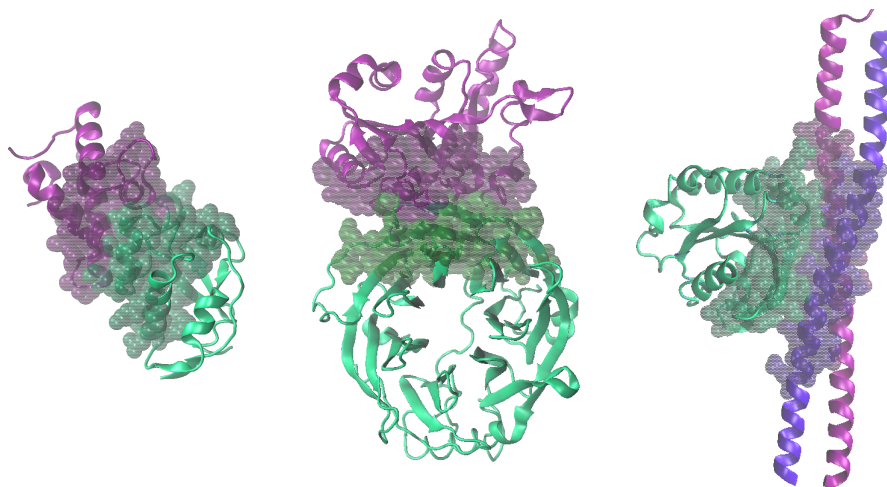
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The modeling of protein assemblies at the atomic level remains a central issue in structural biology, as protein interactions play a key role in numerous cellular processes. Over the recent years our group started focusing on the dynamic properties of the protein/protein interface using classical modeling tools such as Molecular Dynamics simulations (1).

For globular proteins, predicting the structure of the assembly is traditionally addressed using docking tools, where the quality of the models is based on their similarity to a single reference experimental structure. However, using a static reference does not take into account the dynamic quality of the protein interface. Using all-atom classical MD simulations, we investigate the stability of the reference interface, and of models of various accuracies, for three complexes that previously served as targets in the CAPRI competition. To assess the quality of the models from a dynamic perspective, we set up new criteria which take into account the stability of the reference experimental protein interface (2). We show that, when the protein interfaces are allowed to evolve along time, the original ranking based on the static CAPRI criteria no longer holds.



For IDPs and proteins comprising disordered fragment the issue of dynamics is even more crucial as the protein-protein interface is likely to undergo important conformational changes along time. Here we present the case of the fuzzy complex formed by tubulin and the tau IDP. In particular we highlight the part play by the disordered tubulin C-terminal tails in stabilizing the assembly (3).

[1] E. Karaca, C. Prévost and S. Sacquin-Mora, *Molecules*, **2022**, 27, 1841

[2] C. Prévost and S. Sacquin-Mora, *Proteins*, **2021**, 89, 1315-1323

[3] J. Marien, C. Prévost, and S Sacquin-Mora, *Biochemistry*, **2023**, 62, 2492–2502