

Investigating biological structures at the atomic scale enables a deeper understanding of protein structures and complex biological process, thereby facilitating the development of novel biomolecules with improved functionalities. In this thesis, I present two distinct research projects that serves as a foundation for constructing novel structures using protein engineering and synthetic structural biology techniques.

Using modeller 9v21 and deep learning tools (AlphaFold2 and ESMFold), the first part of this thesis focused on predicting the three-dimensional structure of the NinH protein, which is a member of the family of nucleoid-associated proteins. By integrating experimental data and *in silico* tools, we deciphered the relationship between the conformation of the NinH protein and its functional properties. Our findings shed the light on the structure of the NinH protein and its similarity with the Fis protein.

In the second part, we employed coarse-grained molecular simulations to investigate the dynamic process of the bacteriorhodopsin-nanodisc fusion with the lipid bilayer for potential cargo delivery. By modelling the interaction between the nanodisc and lipid membrane I provided detailed understanding of the mechanism and the key factors driving this fusion. This included the Ca^{2+} ions interaction with negatively charged lipid membrane, inverted micelle formation and membrane scaffold protein interaction with lipids. Our results provide valuable information for building a biological system delivering cargo to the lipid bilayers using nanodisc as a carrier, with implications for producing GUVs with membrane protein.

My research on the NinH protein structure not only deepens our understanding of the nucleoid-associated protein family but also provides a valuable insight for engineering these proteins with enhanced functions. Similarly, the elucidated mechanism of nanodisc-membrane fusion opens doors for designing optimized nanodiscs as efficient cargo delivery systems. As such,

both projects lay a crucial foundation for building novel biomolecules with tailored properties within the exciting new field of synthetic structural biology.