Development of a transferable coarse-grained model of heparan sulfate and heparin to investigate their interactions with viral proteins in complex biomolecular systems

Heparan sulfate (HS) and heparin (HP) are complex sugar molecules present in most animals, including humans. HS occurs on the surface of cells and in the environment that surrounds cells in tissues, while HP is mainly stored in special immune cells called mast cells and released during inflammation. By interacting with many different proteins, HS and HP help regulate a wide range of biological processes, including communication between cells, control of signaling pathways, and immune responses. HS and HP also play important roles in many diseases. HS regulates growth factors that influence how cells grow and move, processes closely linked to cancer development. HS is also involved in viral infections, as many viruses use it as an initial attachment factor to enter cells. HP, in turn, is essential for the regulation of blood clotting and is widely used in medicine as an anticoagulant drug.

Despite their importance, understanding how these molecules interact with proteins remains very challenging. HS and HP chains vary widely in length and chemical composition, creating many different structural variants. These molecules are also highly flexible and can interact with several proteins at the same time. Because of this complexity, many aspects of their behavior are difficult to study directly using experimental methods.

This project aims to develop computational models that will make it possible to study long HS and HP chains and their interactions with proteins in large biological systems at the molecular level. The models will use a computational approach known as coarse-grained molecular simulations, which simplifies the representation of molecules and makes it possible to simulate much larger biological systems and processes occurring over longer periods of time than models that represent every atom in a molecule. As a result, it will become possible to investigate how long HS and HP chains interact with proteins in realistic biological systems.

The new models will allow exploration of how the structure of HS and HP influences the way these molecules bind to proteins, including how factors such as chain length and chemical composition affect these interactions. In the long term, this knowledge may help better understand the mechanisms of viral infections, blood coagulation, cancer progression, and other processes involving HS and HP, which could in turn support the development of new biomedical strategies and therapeutic approaches.