Exploring the Dynamics of Endothelial Glycocalyx Under Flow Shear Stress via Large-Scale Molecular Dynamics Simulations

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Introduction

Many cardiovascular diseases, like atherosclerosis [1], are associated with the dynamics of the endothelial glycocalyx under flow shear stresses, as glycocalyx plays a prominent role in orchestrating multiple biological processes occurring at the plasma membrane. Reliable prediction of the dynamics of the glycocalyx under blood flow is of great importance for understanding the pathodology of cardiovascular diseases, helping to form therapeutic strategies. However, detailed mechanisms behind the interactions between blood flow and the glycocalyx at the molecular level are still poorly understood, despite numerous studies via classical theoretical or experimental methods.

Methods

In this research, large-scale molecular dynamics (MD) simulations are conducted on the UK's national supercomputing service, ARCHER, to study the interactions between the flow and glycocalyx. An all-atom flow/glycocalyx system (Fig.1) is adopted [2] with the bulk flow velocity set in the realistic physiological range. The system is simulated by MD using ~ 6 million atoms.

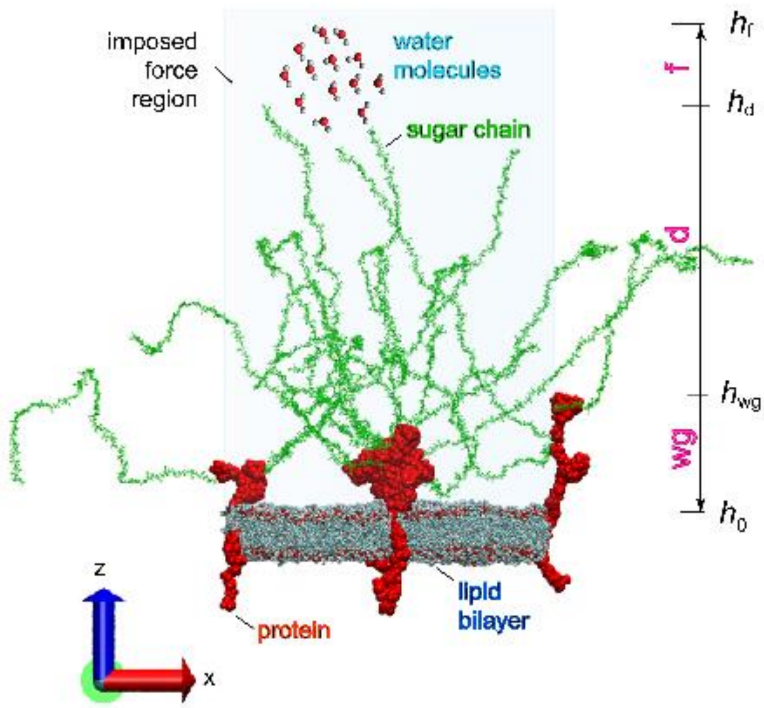

Fig.1 An all-atom glycocalyx/flow system containing ~ 6 million atoms.

Results and Discussion

The simulation results include detailed velocity distribution and time evolution as well as the dynamics of the glycocalyx constituents under the flow shear stresses. Comprehensive analysis leads to a new model for predicting the glycocalyx behaviours. The model reconciles a longstanding debate about the force transmisson mode via the glycocalyx. Furthermore, the biological significance behind the coupled dynamics between the flow and the bio-complex is discussed in order to further understand the mechanisms for mechanotransduction of the endothelial glycocalyx.

Conclusions

For the first time, flow in the physiologically relevant range is realized in the most detailed atomistic model of the glycocalyx. The intricate dynamics of the glycocalyx biomolecules revealed have potential applications in the pathologies of glycocalyx-related diseases, for example in renal or cardiovascular conditions.

Acknowledgement

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References

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[2] X.Z. Jiang, H. Gong, K.H. Luo, Y. Ventikos, Journal of The Royal Society Interface, 14 (2017).