Doctoral School of Information and Biomedical Technologies Polish Academy of Sciences

Subject

Targeting biological time scales in molecular simulation for the study of protein complexes: The stability of SARS-CoV-2

Supervisors, contact, place of research

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Project Description

Molecular simulations of large biological systems, such as entire viral capsids, remains a challenging endeavour from the computational point of view and a priori molecular assessment of the infecting capability is not yet possible [1]. On one hand, the increasing availability of high-performance computing to carry out large-scale all-atom molecular dynamics (AA-MD) simulation and the employment of several enhanced sampling methods attempt to overcome the free energy barriers associated to sampling of large conformational changes in protein complexes. Those methods have a potential for delivering molecular structures and underlying infectious mechanism of the biological systems at the microsecond time-scales at most. On the other hand, efficient coarse-grained (CG) models can be 10-fold faster than MD and due to soft energy landscape they are able to capture the essential picture of the entire viral capsid at the biological scale (i.e. milisecond time-scale). Here, we plan to develop the computational mode using GoMartini [2] approach for the sampling the large conformational changes from the close to open conformation due to the interaction between the COVID-19 Spike protein and the human angiotensin converting enzyme 2 (ACE2) receptor. Such process can be of great help to devise potential new drugs [3] or test the efficacy during the cell recognition, limiting the activity of the virus. We plan to conduct research in COVID-19 and distribute tasks e.g. model development, parametrisation of GoMartini model, bioinformatic analysis, molecular simulation which wiill allow relevant publications in high impact journals.

Bibliography

[1] Martinez M, Cooper CD, Poma AB, Guzman HV, *Free* Energies of the Disassembly of Viral Capsids from a Multiscale Molecular Simulation Approach*. J. Chem. Inf. Model.* 2020, 60, 2, 974-981
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[3] Boopathi S, Poma AB, Kolandaivel P (2020) Novel 2019 Coronavirus Structure, Mechanism of Action, Antiviral drug promises and rule out against its treatment, *J. Biomol. Struct. Dyn.* DOI: 10.1080/07391102.2020.1758788