Biophysical insight into the SARS-CoV2 spike-ACE2 interaction and its modulation by hepcidin through a multifaceted computational approach

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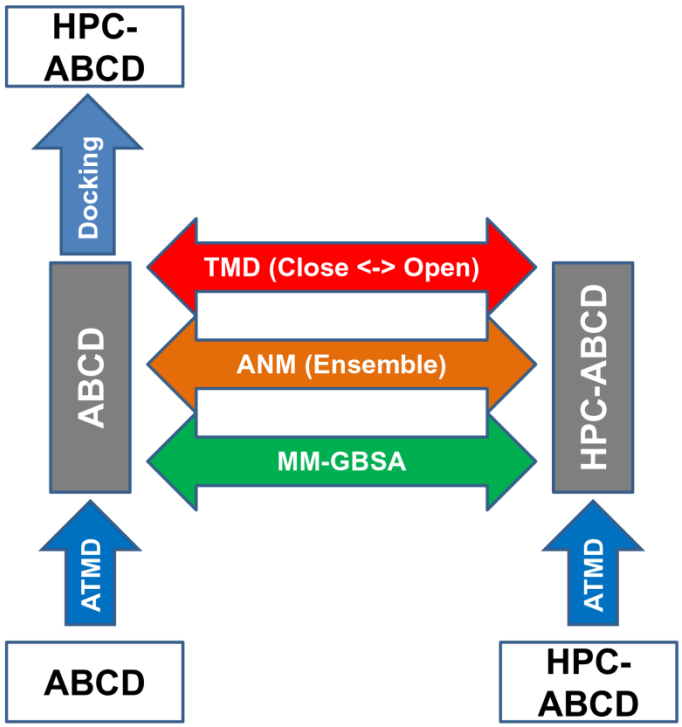
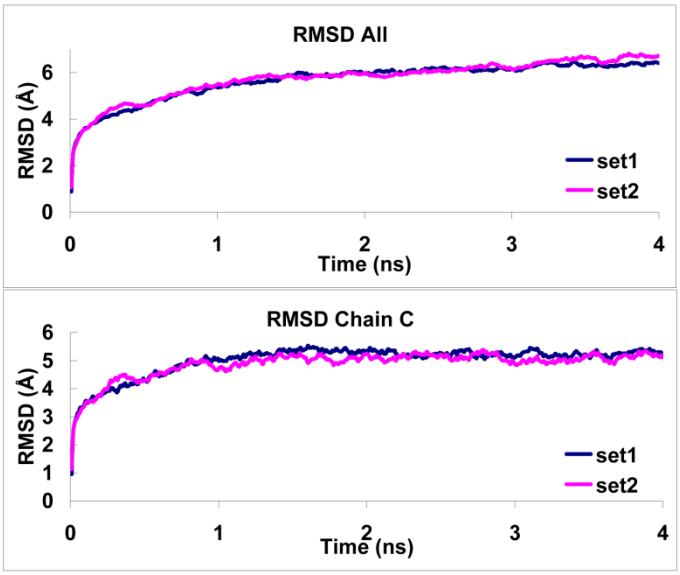
Figure S1. The brief of the performed simulations is presented

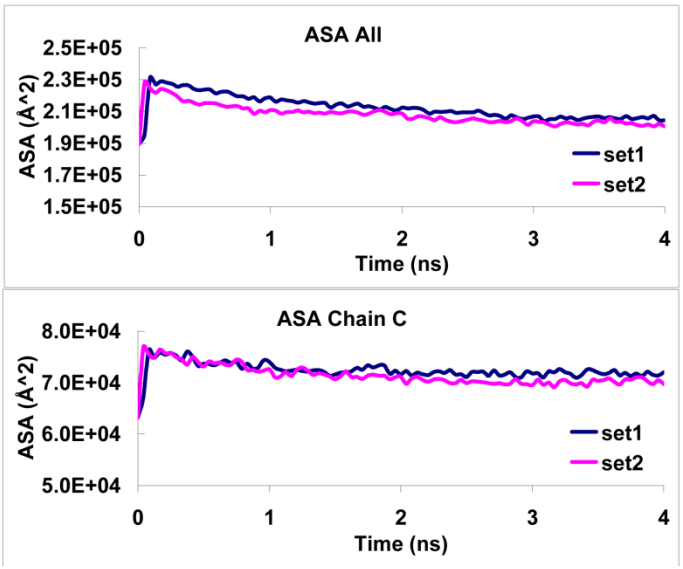


Here, the trimeric spike is presented by “ABC”, ACE2 subunit by “D” and hepcidin by “HPC”. The adaptive tempering all atom MD (AT-MD, for 4 ns accelerated MD) is performed to optimized the primary complexes. The sampling efficiency of ATMD reaches to 10 fold greater than regular MD [Zhang, C.; Ma, J., Enhanced sampling and applications in protein folding in explicit solvent. The Journal of Chemical Physics 2010, 132, 244101].Anisotropic network model (ANM) is performed to generate rich structural ensembles around ground state of the complexes. Targeted MD (TMD) simulation is utilized to simulate the transition pathway from close to open and vice versa transition of the chain C (which binds to ACE2 and HPC in AMR).

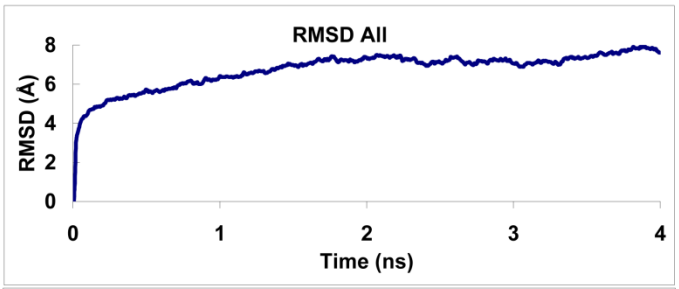
Figure S2. RMSD values and accessible surface area (ASA) as stability indicators of the AT-MD trajectories are presented.

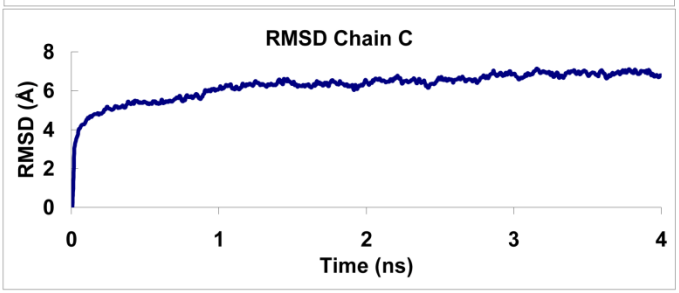


a. The changes of RMSD value as an indicator of the trajectory stability is presented for hepcidin free ABCD complex and for chain C. Chain C binds to ACE2.

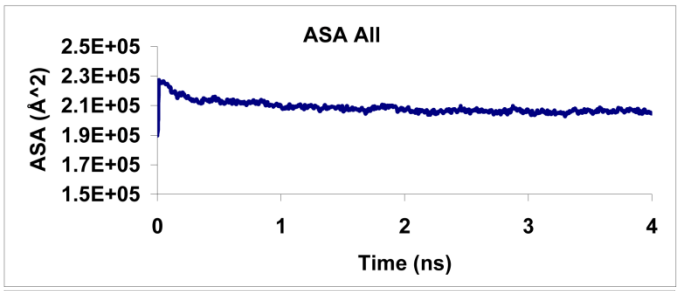


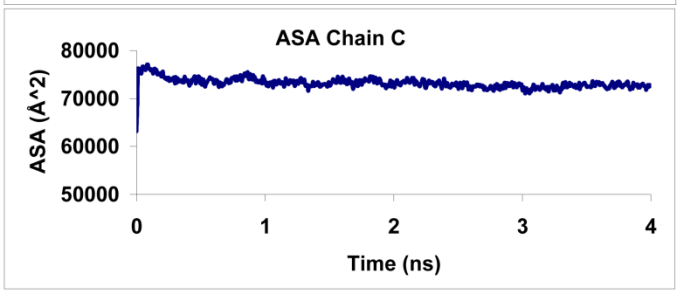
b. The ASA value as an indicator of the trajectory stability is presented for hepcidin free ABCD complex and for chain C. Chain C binds to ACE2.





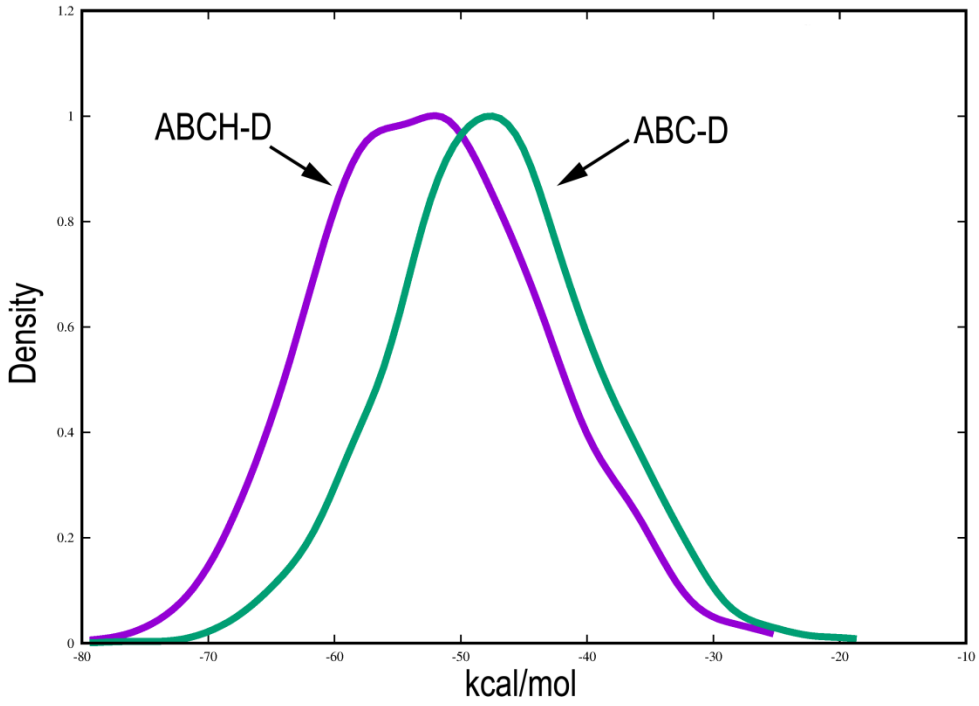
c. The changes of RMSD value as an indicator of the trajectory stability is presented for ABCD-HPC complex and for chain C. Chain C binds to ACE2 and HPC.





d. The ASA value as an indicator of the trajectory stability is presented for ABCD-HPC complex and for chain C. Chain C binds to ACE2 and HPC.

Figure S3. The density of MM-GBSA predicted affinity is presented.



The affinity of ACE2 (chain D) to spike trimer (ABC) in the presence (ABCH-D) and the absence of hepcidin (ABC-D) is defined using MM-GBSA approach.