Supplementary Information

Computational simulations reveal the binding dynamics between human ACE2 and the receptor binding domain of SARS-CoV-2 spike protein

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Table S1. The structure comparison. Root-Mean-Square-Deviation (RMSD) are calculated pairwisely, with unit in Angstrom (Å).

RMSD for ACE2 subunit	***DE Shaw (10μs)***	***DE Shaw (500ns)***	***Trajectory 1***	***Trajectory 2***	***Trajectory 3***	***6LZG.B***
DE Shaw (10μs)	0.00	3.92	4.15	3.90	3.90	3.47
DE Shaw (500ns)	3.92	0.00	3.14	2.88	4.12	2.83
Trajectory 1	4.15	3.14	0..00	2.56	4.04	2.93
Trajectory 2	3.90	2.88	256	0.00	3.71	2.62
Trajectory 3	3.90	4.12	4.04	3.71	0.00	3.65
6LZG.A	3.47	2.83	2.93	2.62	3.65	0.00

RMSD for RBD subunit	***DE Shaw (10μs)***	***DE Shaw (500ns)***	***Trajectory 1***	***Trajectory 2***	***Trajectory 3***	***6LZG.B***
DE Shaw (10μs)	0.00	2.98	4.41	2.80	2.83	2.51
DE Shaw (500ns)	2.98	0.00	4.51	3.15	3.05	2.79
Trajectory 1	4.41	4.51	0..00	4.50	4.06	4.58
Trajectory 2	2.80	3.51	4.50	0.00	2.25	2.39
Trajectory 3	2.83	3.05	4.06	2.25	0.00	2.50
6LZG.B	2.51	2.79	4.58	2.39	2.50	0.00

RMSD for ACE2/RBD complex	***DE Shaw (10μs)***	***DE Shaw (500ns)***	***Trajectory 1***	***Trajectory 2***	***Trajectory 3***	***6LZG.B***
DE Shaw (10μs)	0.00	5.09	6.01	5.23	4.04	3.60
DE Shaw (500ns)	5.09	0.00	3.67	3.47	5.26	3.38

Trajectory 1	6.01	3.67	0.00	3.93	5.86	4.42
Trajectory 2	5.23	3.47	3.93	0.00	4.73	3.27
Trajectory 3	4.04	5.26	5.86	4.73	0.00	3.79
6LZG	3.60	3.38	4.42	3.27	3.79	0.00

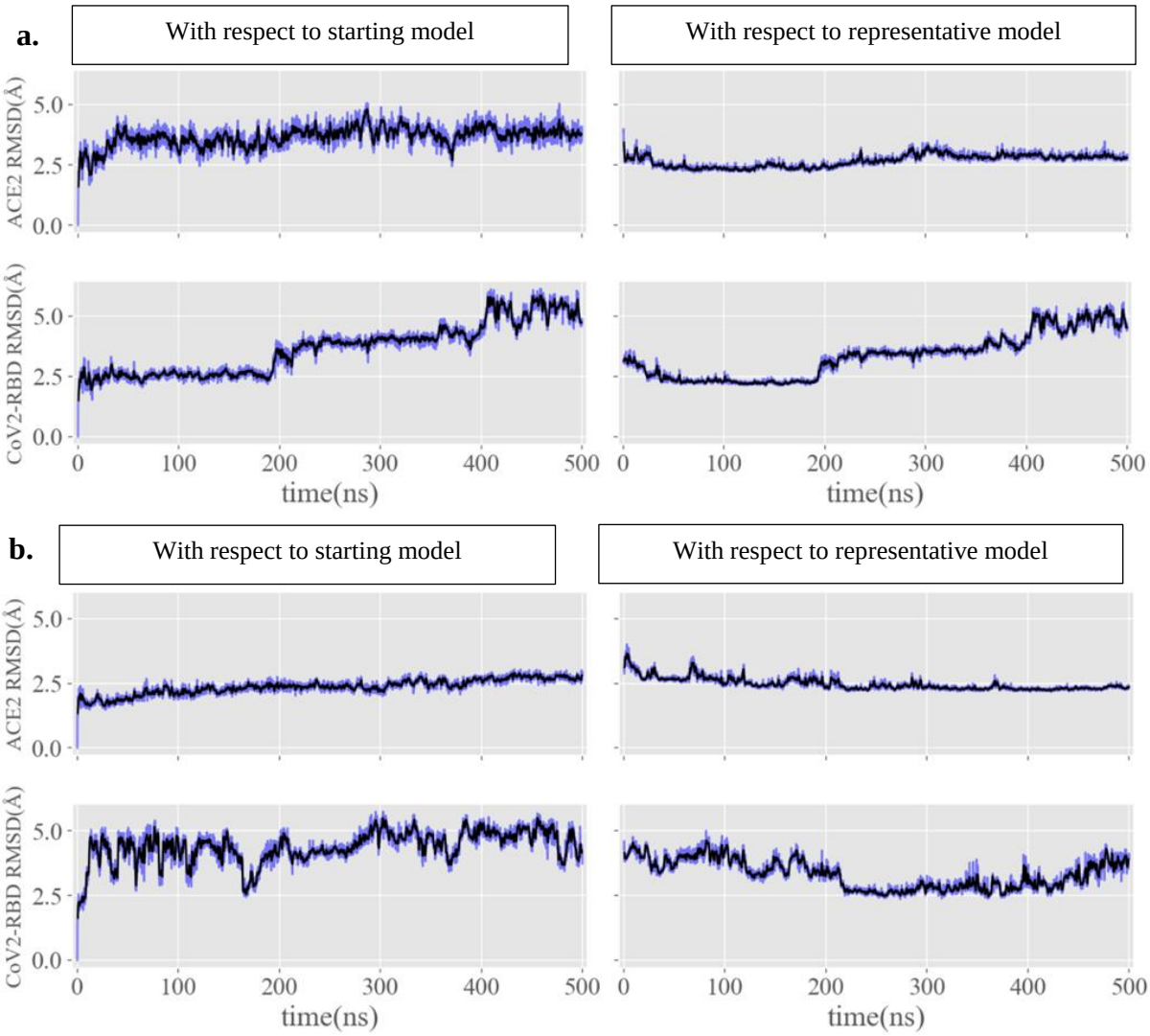

Figure S1. The structure difference compared to the starting and representative models. (**a**) simulation trajectory #2; (**b**) simulation trajectory #3.

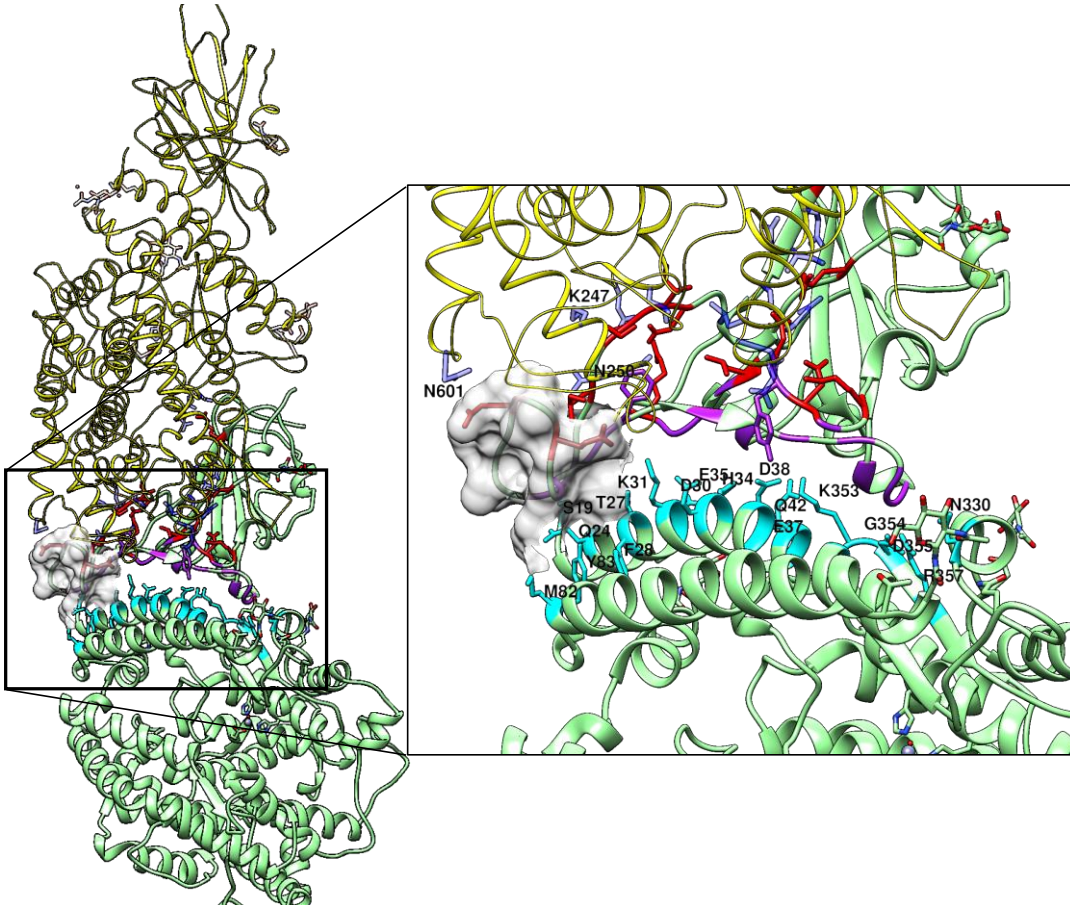

Figure S2. The contacts between CoV2-RBD and the ACE2 in crystal. Two copies of the CoV2-RBD/ACE2 complex (asymmetric unit) are shown in green and yellow color. The loop region between β6 and β7 of the CoV2-RBD is highlighted with the surface representation. This region interacts with two ACE2 molecules: one at the binding site (green), and the other one (yellow) is due to the crystal packing. The cyan color highlights the contacting residues of ACE2.

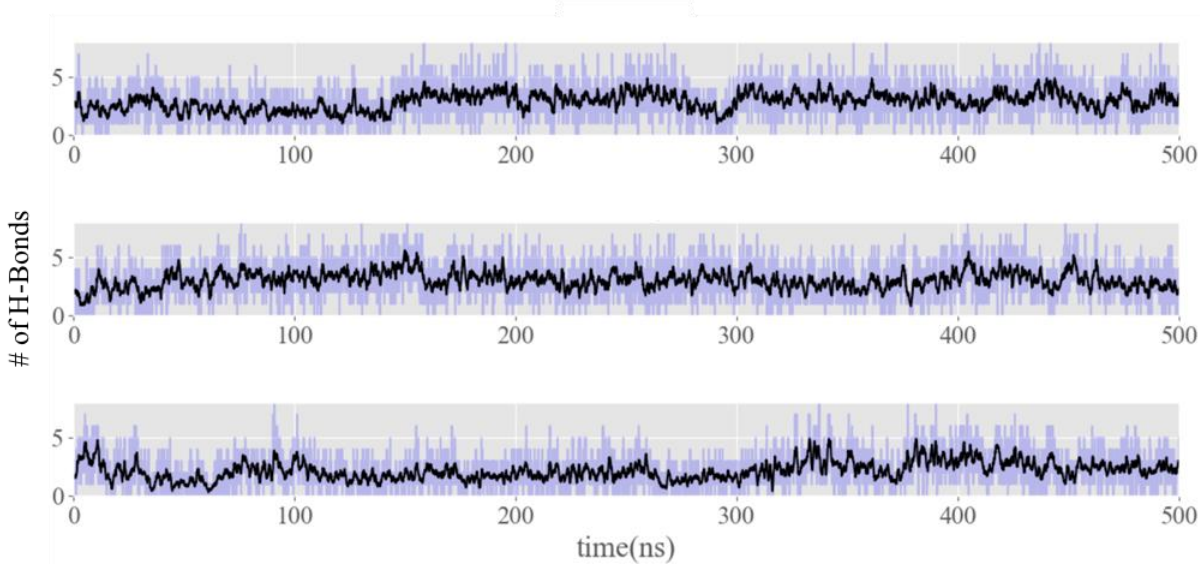

Figure S3. Number of hydrogen bonds at the complex interface using the default donor-receptor distance cutoff=3.0 Å.

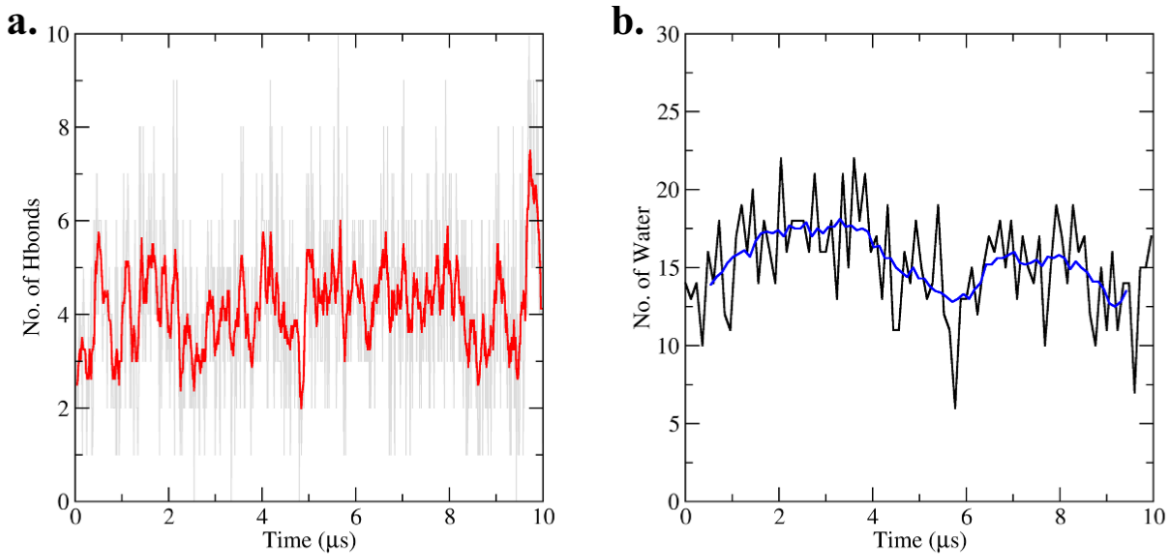

Figure S4. Statistics of hydrogen bonds and water molecules at the complex interface as observed in the 10 microsecond trajectory simulated by DE Shaw research. (a) The hydrogen bonds are between ACE2 and RBD, excluding the water mediated interactions. (b) The water molecules within 2.5 Å of both ACE2 and RBD simultaneously were considered as residing at the complex interface.

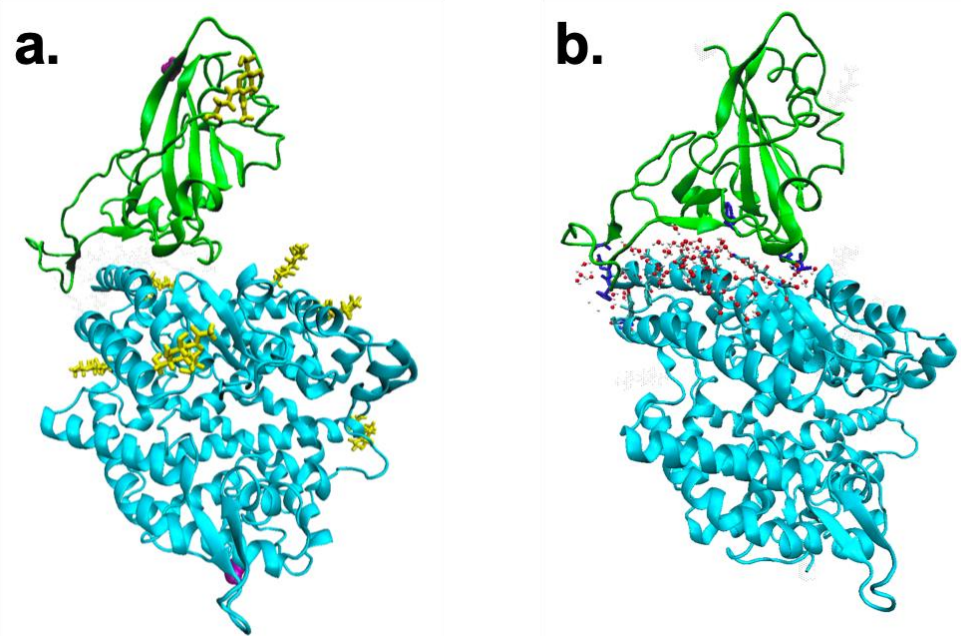

Figure S5. Representative structures from the 10 μs simulation data by DE Shaw Research. (**a**) the glycosylation sites are shown in the yellow stick form. (**b**) water molecules are observed within the interface of RBD and ACE2.

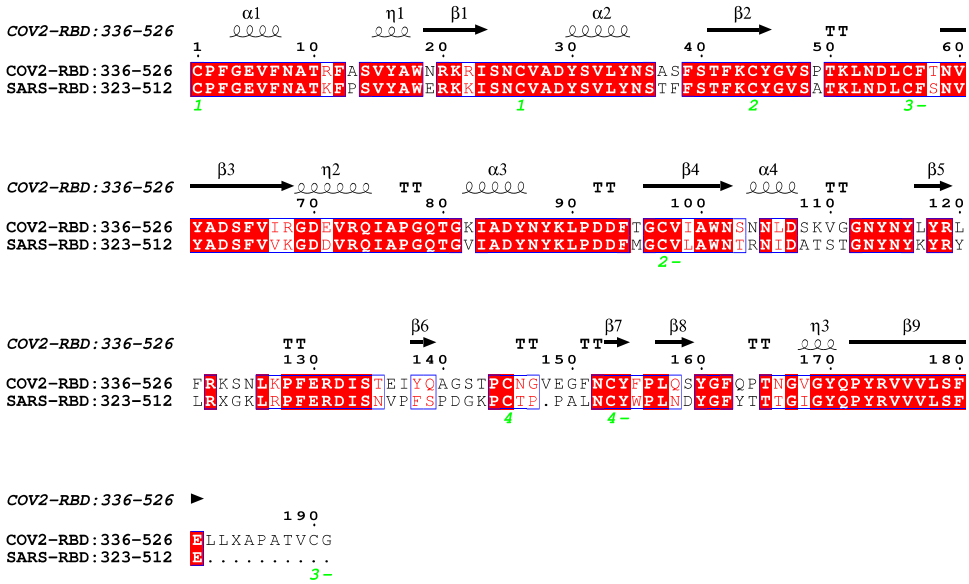

Figure S6. The sequence alignment of receptor binding domain (RBD) for SARS-COV-2 and SARS-COV.

Figure S7. The multiple sequence alignment (MSA) for the ACE2 proteins from multiple animals.