Supplementary Material

Distinctive features of the XBB.1.5 and XBB.1.16 Spike Protein RBDs and their roles in conformational changes and ACE2 binding

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Table S1. List of all molecular systems used in this work. The WT, delta and omicron simulations of the RBD-only, RBD-hACE2, and WT and Omicron RBD-down Trimer systems are from earlier work (indicated by one *) and all others are new simulations.

System	Variant/ (PDB ID)	# Water	Ion Conc.	# Atoms (total)	Box Size (Å)^3	Time (ns)
RBD Only	XBB.1.5 (Mutated on 7T9L)	28,360	0.15 M	835,23	96x96x96	1000
	XBB.1.16 (Mutated on 7T9L)	24,765	0.15 M	72,749	92x92x92	1000 *
RBD-hACE2	Delta* (7W9I)	75,956	0.15 M	242,060	138x138x138	200
	Omicron* (7T9L)	70,801	0.15 M	226,700	134x134x134	200
	XBB.1.5 (Mutated on 7T9L)	82,424	0.15 M	242,286	137x137x137	300
	XBB.1.5 Run 2**	82,424	0.15 M	242,286	137x137x137	100
	XBB.1.16 (Mutated on 7T9L)	77,837	0.15 M	247,015	144x144x144	300
	XBB.1.16 Run 2**	77,140	0.15 M	246,725	144x144x144	100
	XBB.1.16 Run 3**	77,155	0.15 M	246,205	141x141x141	100
RBD-down	XBB.1.5/XBB.1.16*** RBD-down Trimer	89,355	0.15 M	261,559	141x141x141	100

Simulations extended from 100 to 200ns from ref. Hossen, M.L., et al. *PCCP* **24**, 9123-9129 (2022).

** Rerun from the last frame of 200 ns of XBB.1.5 (mutated on 7T9L).

***Residues in the truncated systems: Chain A (330-530); Chain B (30-530, 968-1000); Chain C (330-530, 968-1000).

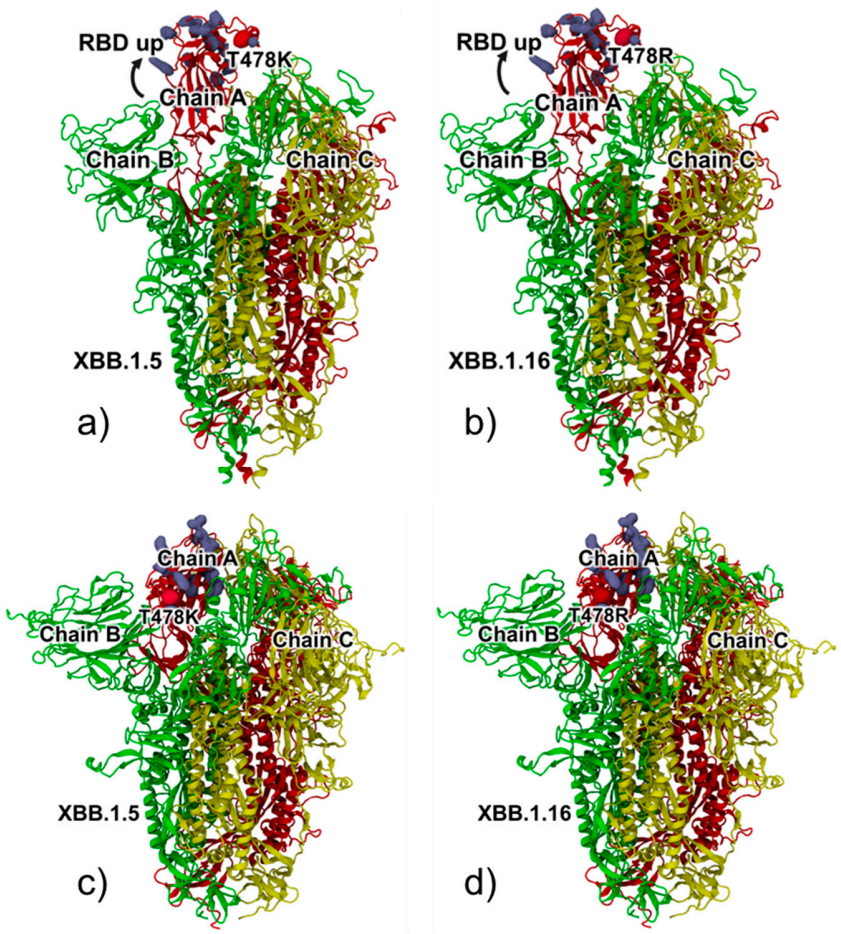

Figure S1. The RBD-up conformation for the spike trimer, showing the mutations in the RBD of chain A of a) XBB.1.5 and b) XBB.1.16. The RBD-down conformation for c) XBB.1.5 and d) XBB.1.16, showing the same mutations as in a-b. The T478K/R mutations highlighted in red surface.

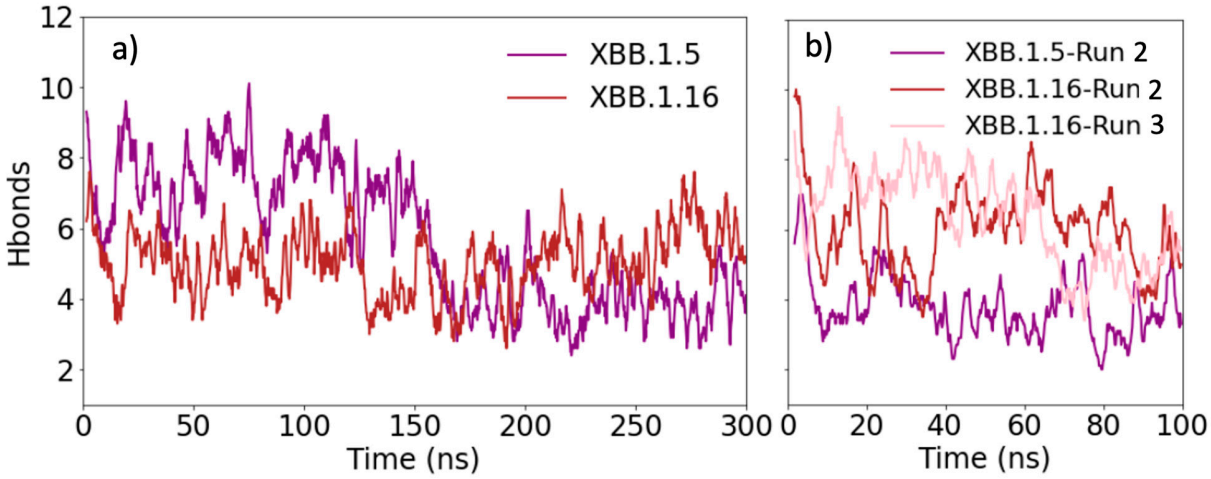

Figure S2. Number of hydrogen bonds between RBD and ACE2 for XBB.1.5 and XBB.1.16 as a function of time. a) For both XBB.1.5 and XBB.1.16, mutations were introduced to omicron RBD. Therefore, the simulations started from the structure of the omicron RBD-ACE2 complex. b) Reruns of XBB.1.5 and XBB.1.16, starting from the frame extracted at 200-ns of the XBB.1.5 of a). Even though both reruns of XBB.1.16 were started from the XBB.1.5 structure, hydrogen bonds were restored, whereas the number of hydrogen bonds remained lower in the rerun of XBB.1.5.

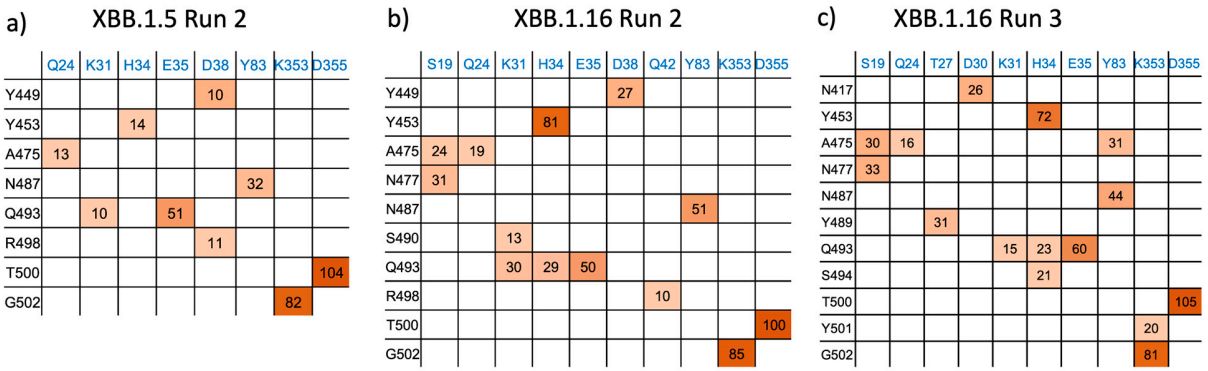

Figure S3. Hydrogen bond occupancies for the interacting residue pairs of RBD and ACE2 for the reruns of Fig. S2. a) XBB.1.5 run 2 a) XBB.1.16 run 2 c) XBB.1.16 run 3.

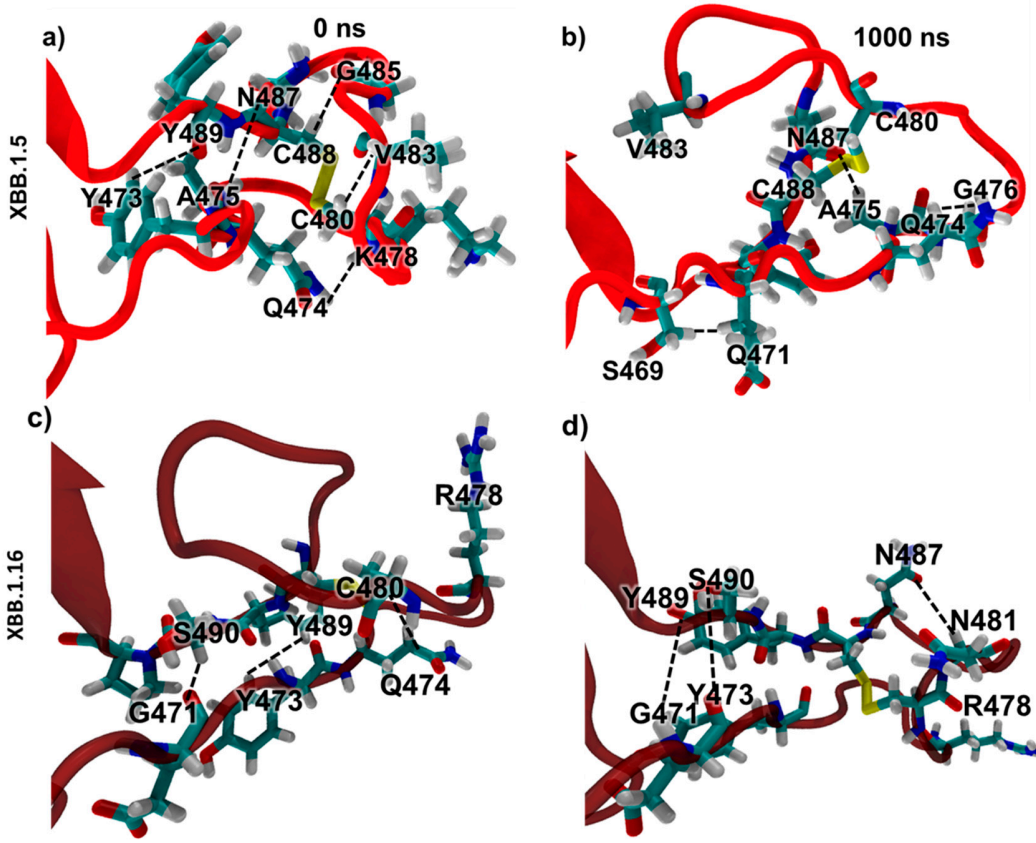

Figure S4. Representative conformations of the a,b) XBB.1.5 and c,d) XBB.1.16 variants displaying hydrogen bonding within the loop residues. The analysis was carried out for the first 20 ns and last 20 ns of a 1000 ns simulation. The initial configuration used for XBB.1.5 was the same as the omicron structure, whereas the initial configuration used for XBB.1.16 was the final configuration from the XBB.1.5 simulation.

Video S1. Conformational dynamics of the Spike protein RBD of XBB.1.5 from a 1000 ns simulation trajectory of the RBD-only system.

Video S2. Conformational dynamics of the Spike protein RBD of XBB.1.16 from a 1000 ns simulation trajectory of the RBD-only system.