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Supplemental Information: Neuropilin-1 Assists SARS-CoV-2 Infection by Stimulating the Separation of Spike Protein Domains S1 and S2

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Table S1: Simulation Systems.

Models	Simulated systems	Methods	Atomic number	Simulation time
Model 1 to model 7	Spike protein; Nrp1 a2-b1-b2	Explicit solvent model; conventional MD	~530,000 atoms (with solvent)	20 ns
Model 1 to model 7	Spike protein; ACE2; one Nrp1 a2-b1-b2	Implicit solvent model; Steered MD	71,386 atoms	20 ns
Model 1	Spike protein; ACE2; three Nrp1 a2-b1-b2	Implicit solvent model; Steered MD	85,206 atoms	20 ns

Figure S1: Instances of excluded models. a) Clash with Spike trimer – most of the Nrp1 would be buried on top of S2;; b) no extra space for a1 domain addition; c) merge of similar models; d) models that place b2 domain too far (distal) from the membrane.

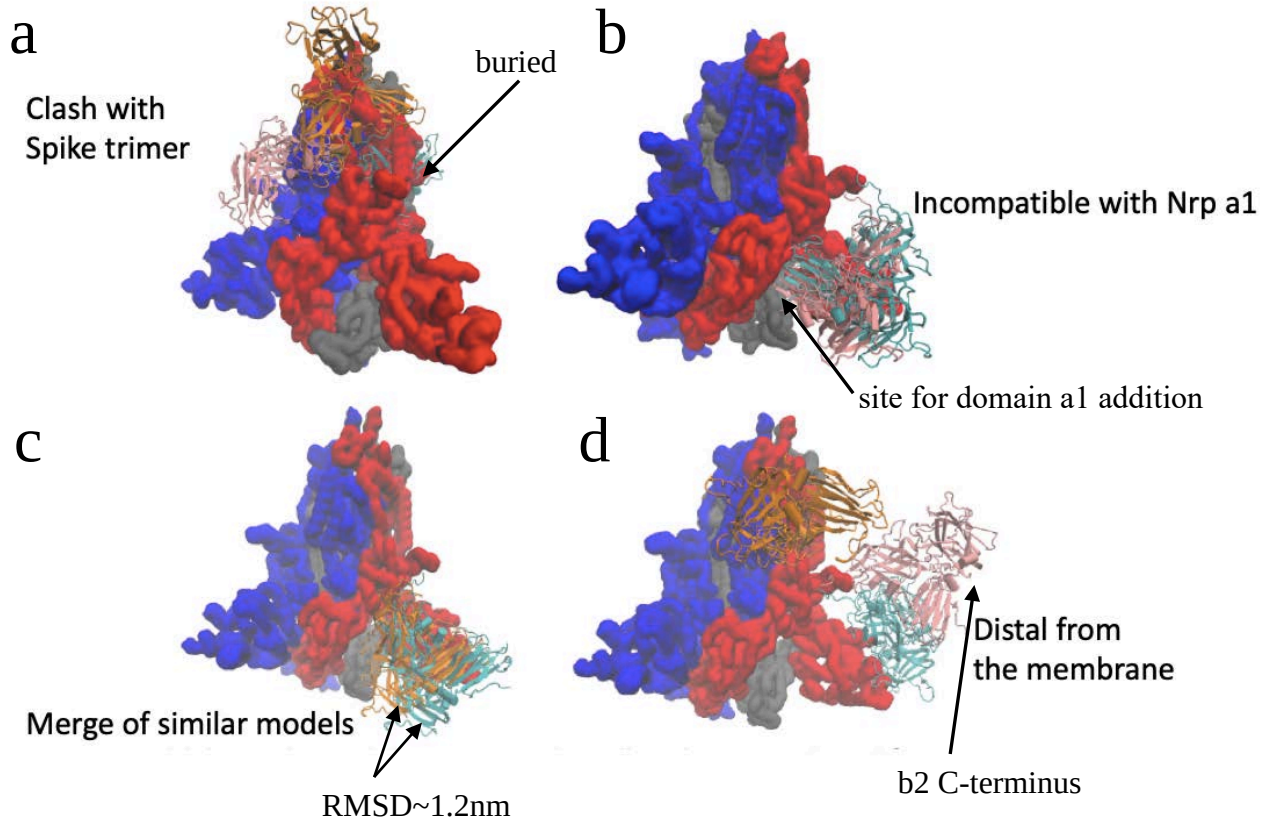

Figure S2: Time evolution of RMSD of the 7 models of Nrp1: Spike complex.

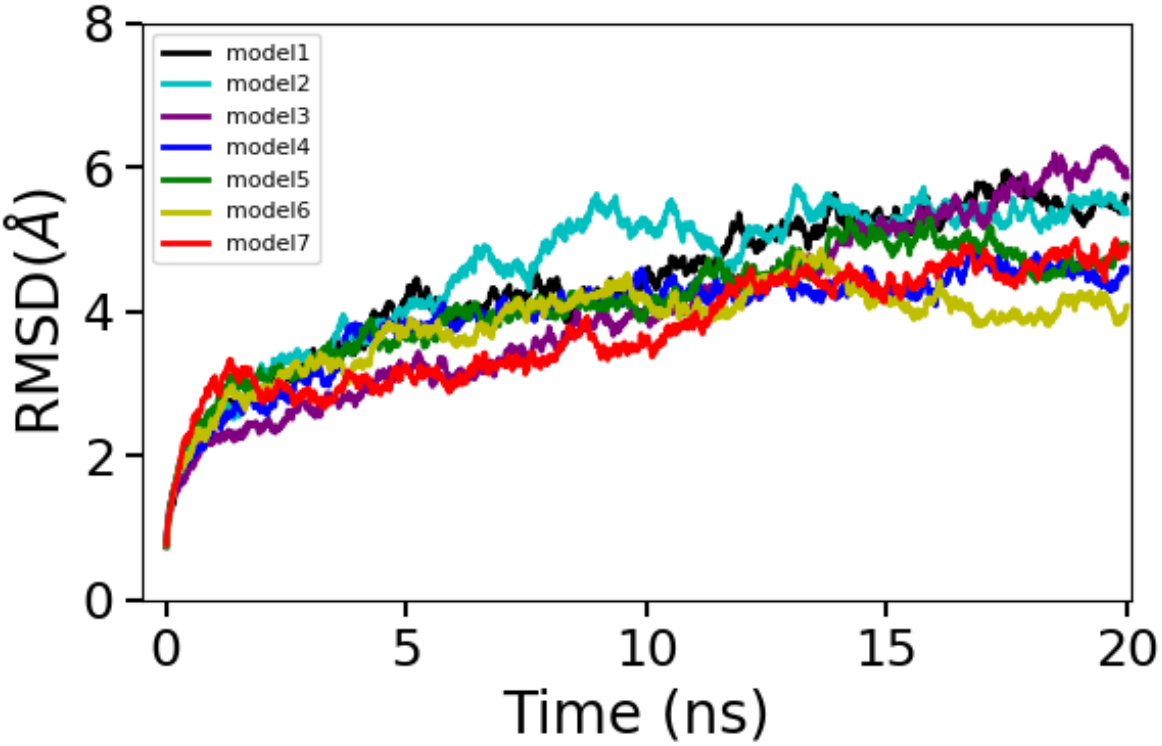

Figure S3: Residues identified as wider interface (> 30% occupancy and less than 0.6 nm distant to the other protein). Typically, a cut-off of 0.4 nm used to judge the interaction between two amino acids (Table in Fig. 2b). In order to include the neighboring residues at the Nrp1: Spike interfaces, we also used a cut-off of 0.6nm, yielding interface residues shown pictorially in aligned sequence segment bars for the two proteins.
Nrp1 domains: a2: res. 27-141, b1: res. 147-265, b2: res. 275-424.
Spike protein S1: N1: res. 1-19, N2: res 20-38, N3: res. 58-90, N4: res. 210-220, N5: res. 293-318, RBD^N: res. 318-330, RBD^C: res. 525-541, C1: res. 602-610, C2: res. 621-626, C3: res. 631-644, C: res. 682-685, $S2^N$: res. 689-691

	Nrp1 domains	Spike protein S1
Model 1	b1, b2	N2, C2, C3, C
Model 2	a2, b1	N1, N2, N4, C
Model 3	a2, b1	N1, N2, N3, N4, RBD^N, RBD^C, C2, C, $S2^N$
Model 4	a2, b1, b2	N1, N2, N3, N4, C3, C
Model 5	b1	N3, N4, N5, C1, C, $S2^N$
Model 6	a2, b1	N2, N3, N4, RBD^C, C1,C2, C3, C, $S2^N$
Model 7	b1, b2	N1, N2, N3, C2, C3, C

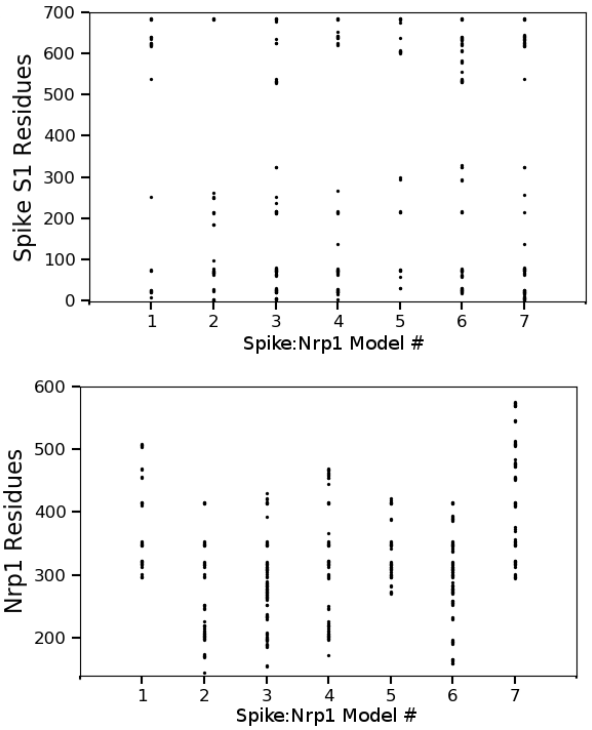

Figure S4: Glycosylation sites (N17, N74, N323, N616, shown as small spheres to Chain C in red) may alter the affinity for Nrp1 binding.

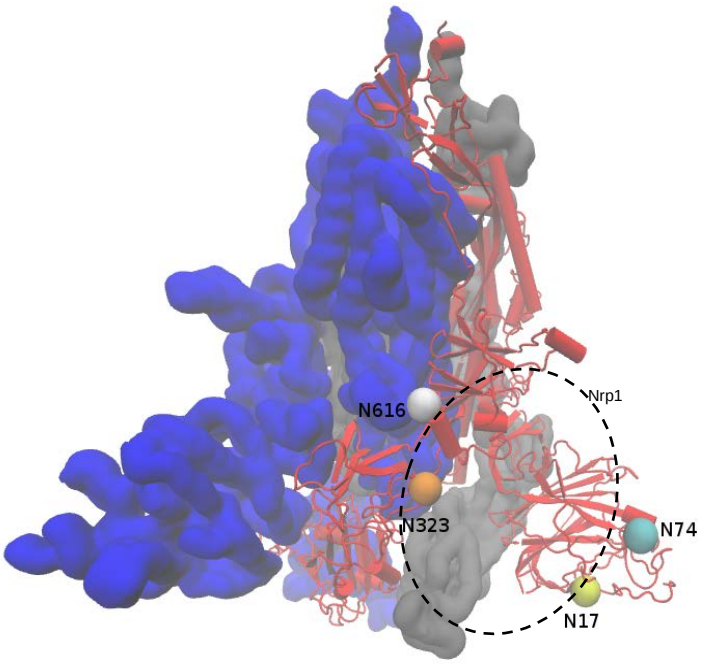

Figure S5: Force-Displacement curves for the simulation of the 7 model structures. Black for ACE2-S1: S2 and red for ACE2-S1-Nrp1: S2 separation.