

Supplementary Data

Insights from In Silico Study of Receptor Energetics of SARS-CoV-2 Variants

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Table S1: Mutations in the receptor binding domain (RBD) of Beta, Delta, Kappa, and Delta Plus variants.

Variants	Mutations
Beta	LYS417 → ASN417, GLU484 → LYS484, ASN501 → TYR501
Delta	LEU452 → ARG452, THR478 → LYS478
Kappa	LEU452 → ARG452, GLU484 → GLN484
Delta Plus	LYS417 → ASN417, THR478 → LYS478, LEU452 → ARG452

Table S2: Mutations in the receptor binding domain (RBD) the Omicron variant.

Variants	Mutations
Omicron	LYS417 → ASN417, GLY446 → SER446, GLU484 → ALA484, GLN493 → ARG493, GLY496 → SER496, GLN498 → ARG498, ASN501 → TYR501, TYR505 → HSD505, SER477 → ASN477, GLY339 → ASP339, SER371 → LEU371, SER373 → PRO373, SER375 → PHE375, ASN440 → LYS440, THR478 → LYS478

Table S3: Details of system preparation of SARS-CoV-2 variants for harmonically restrained MD simulation in umbrella sampling.

Variants	System Size (\AA^3)	Ions Added (0.15 M Conc.)	Total Atoms
Beta	$250 \times 90 \times 90$	192 Na^+ and 168 Cl^-	189,275
Delta	$250 \times 90 \times 90$	191 Na^+ and 168 Cl^-	189,254
Omicron	$250 \times 90 \times 90$	190 Na^+ and 168 Cl^-	189,368
Kappa	$250 \times 90 \times 90$	191 Na^+ and 167 Cl^-	188,882
Delta Plus	$250 \times 90 \times 90$	192 Na^+ and 168 Cl^-	189,391

Table S4: Details of system preparation of SARS-CoV-2 variants for unrestrained MD simulation.

Variants	System Size (\AA^3)	Ions Added (0.15 M Conc.)	Total Atoms
Beta	$133 \times 133 \times 133$	219 Na^+ and 197 Cl^-	222,749
Delta	$133 \times 133 \times 133$	222 Na^+ and 119 Cl^-	222,758
Omicron	$133 \times 133 \times 133$	224 Na^+ and 202 Cl^-	227,029
Kappa	$137 \times 137 \times 137$	241 Na^+ and 217 Cl^-	242,409
Delta Plus	$133 \times 133 \times 133$	221 Na^+ and 197 Cl^-	222,719

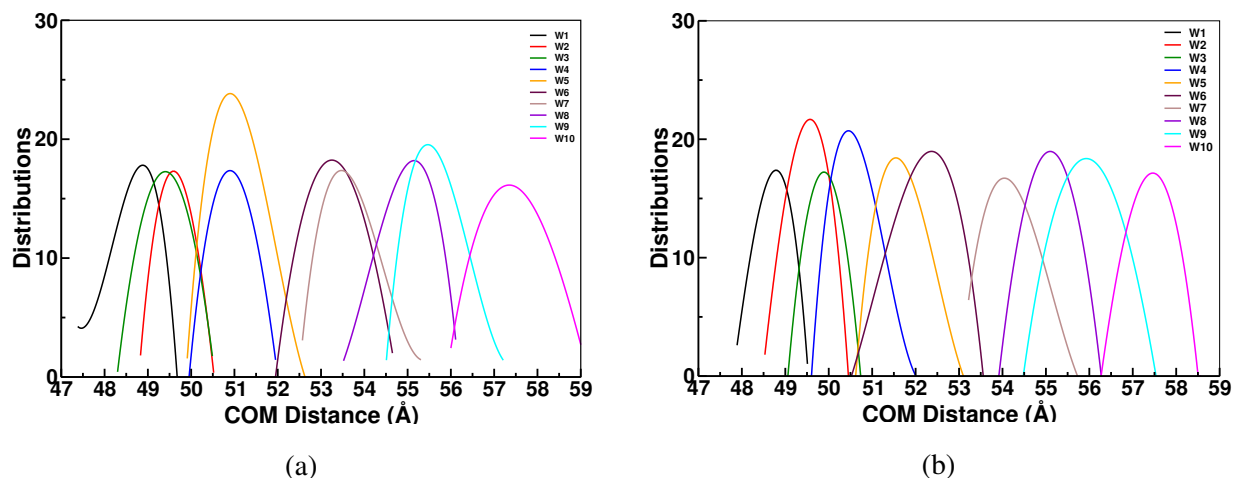
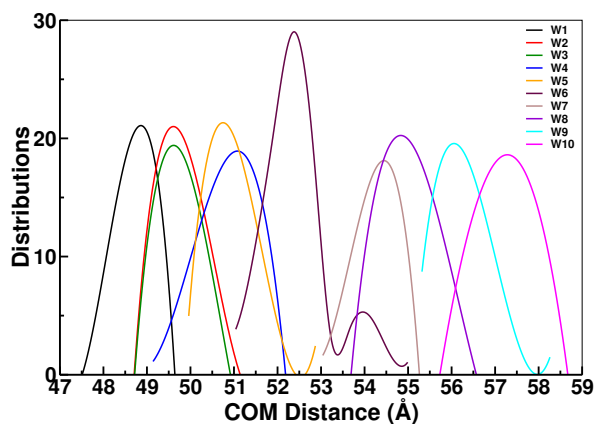
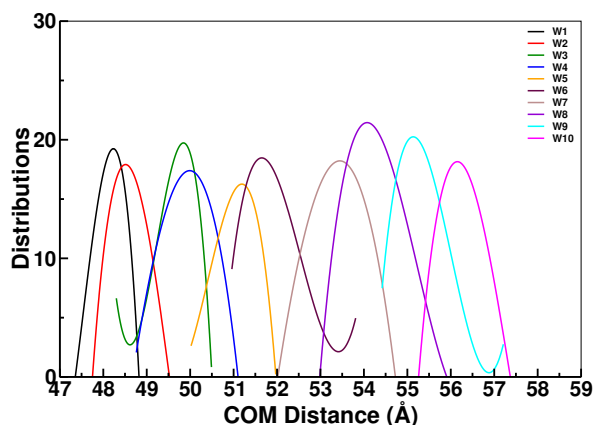


Figure S1: Distribution versus COM distance in (a) Delta (b) Delta Plus to ensure the overlapping of umbrella windows.



(a)



(b)

Figure S2: Distribution versus COM distance in (a) Beta (b) Kappa to ensure the overlapping of umbrella windows.

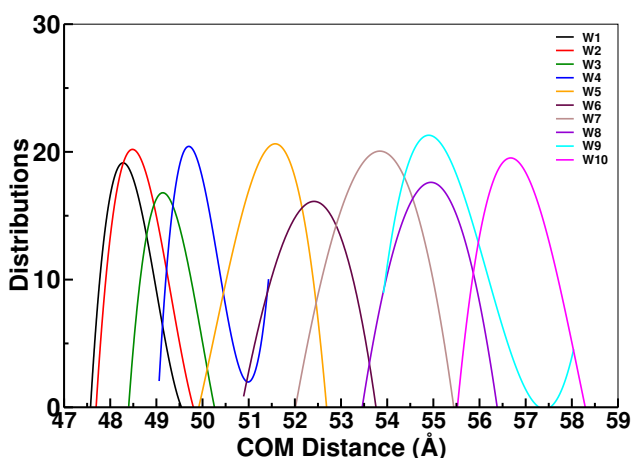
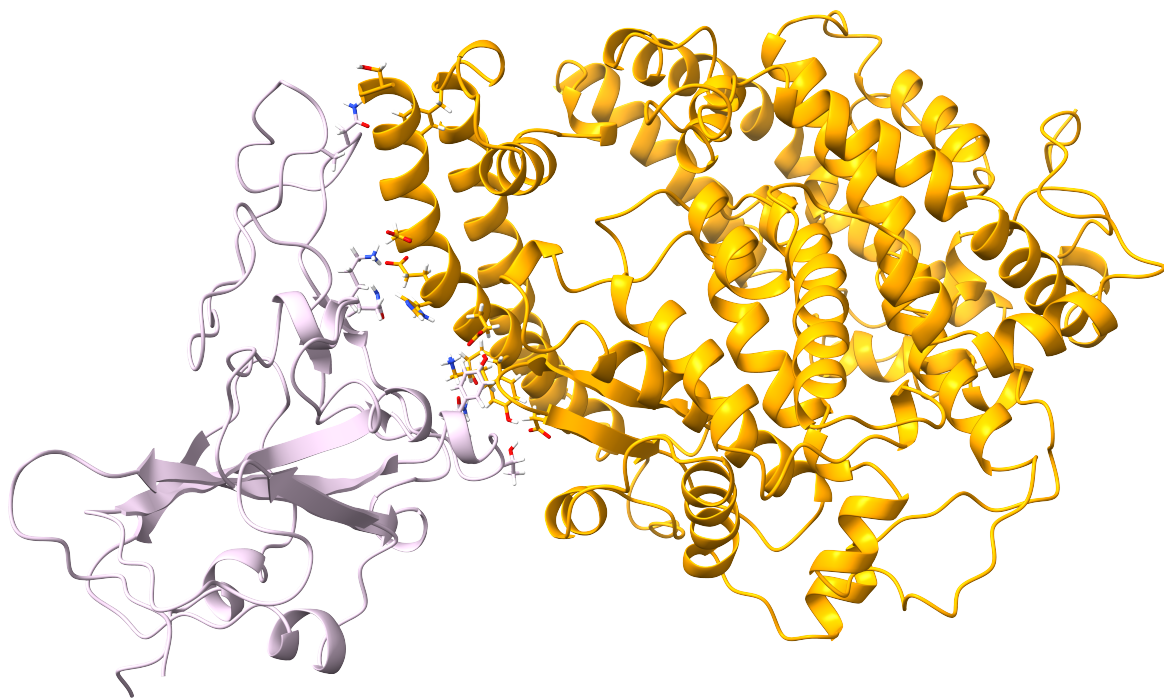
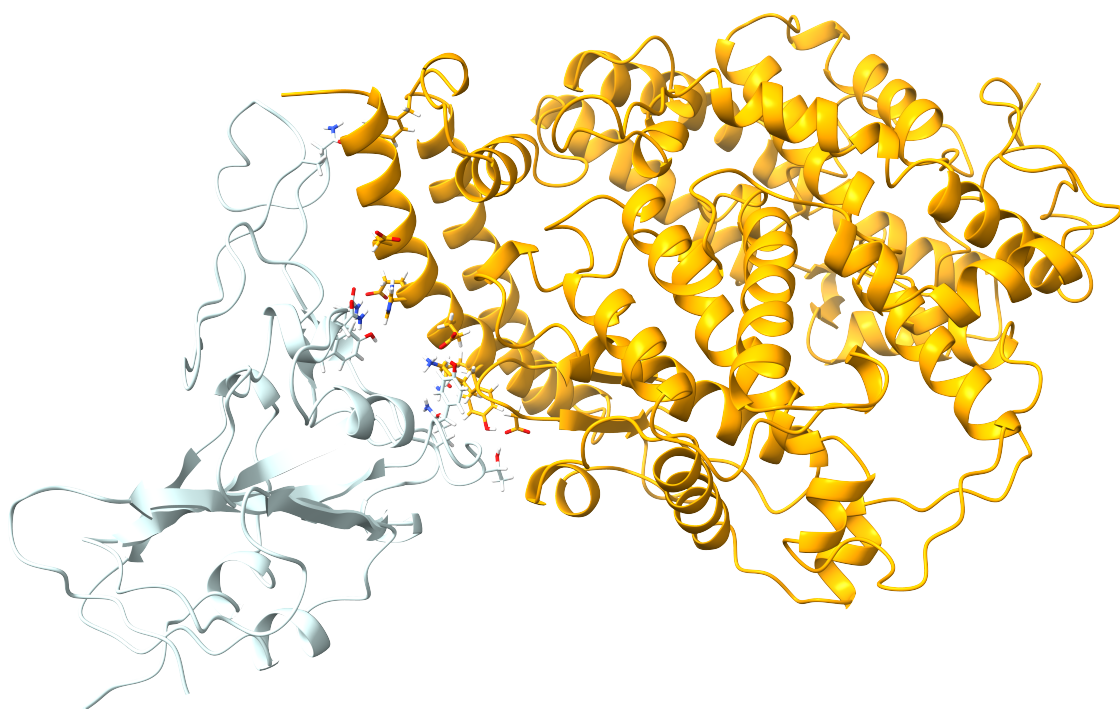


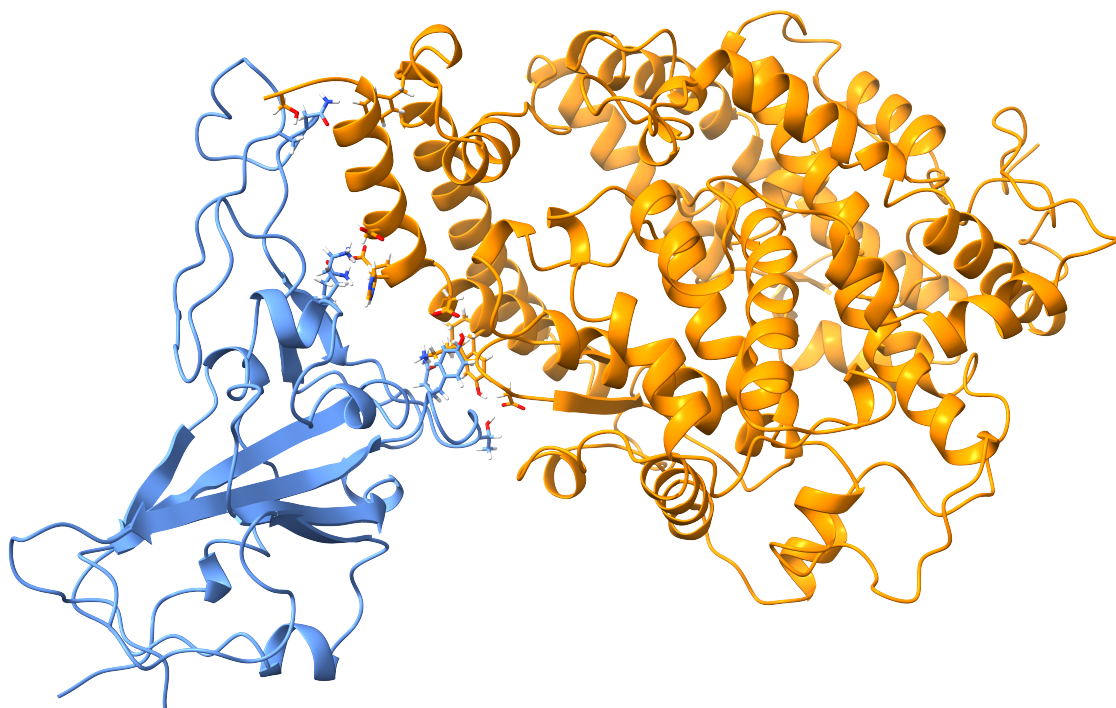
Figure S3: Distribution versus COM distance in Omicron to ensure the overlapping of umbrella windows.



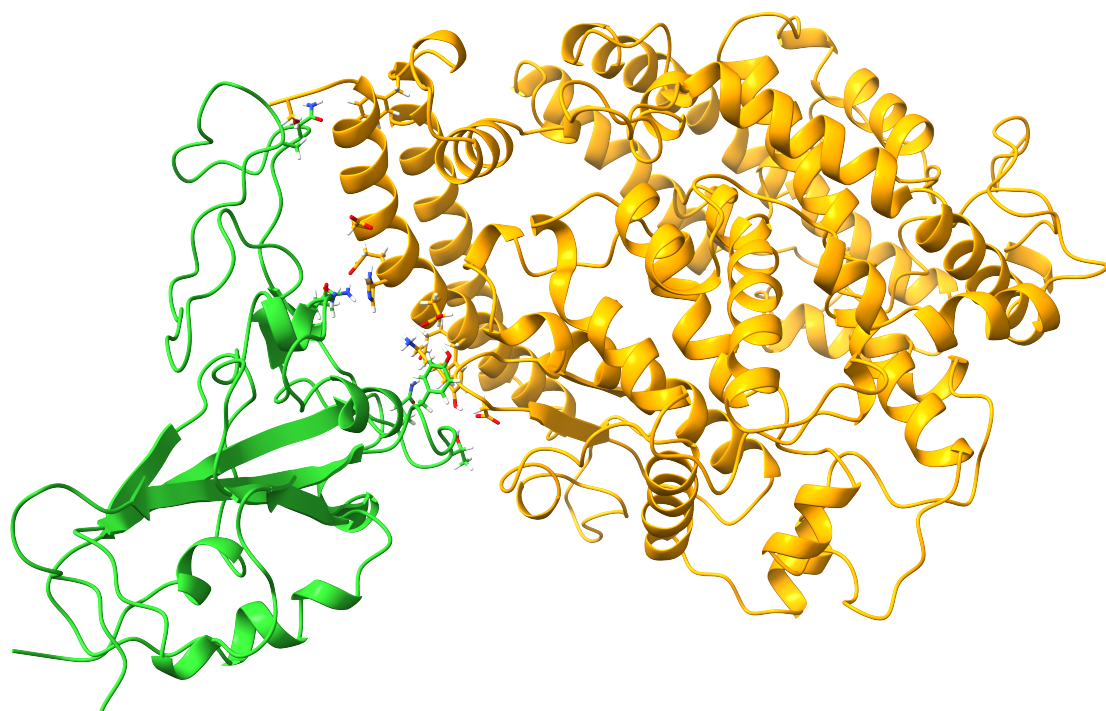
(a)



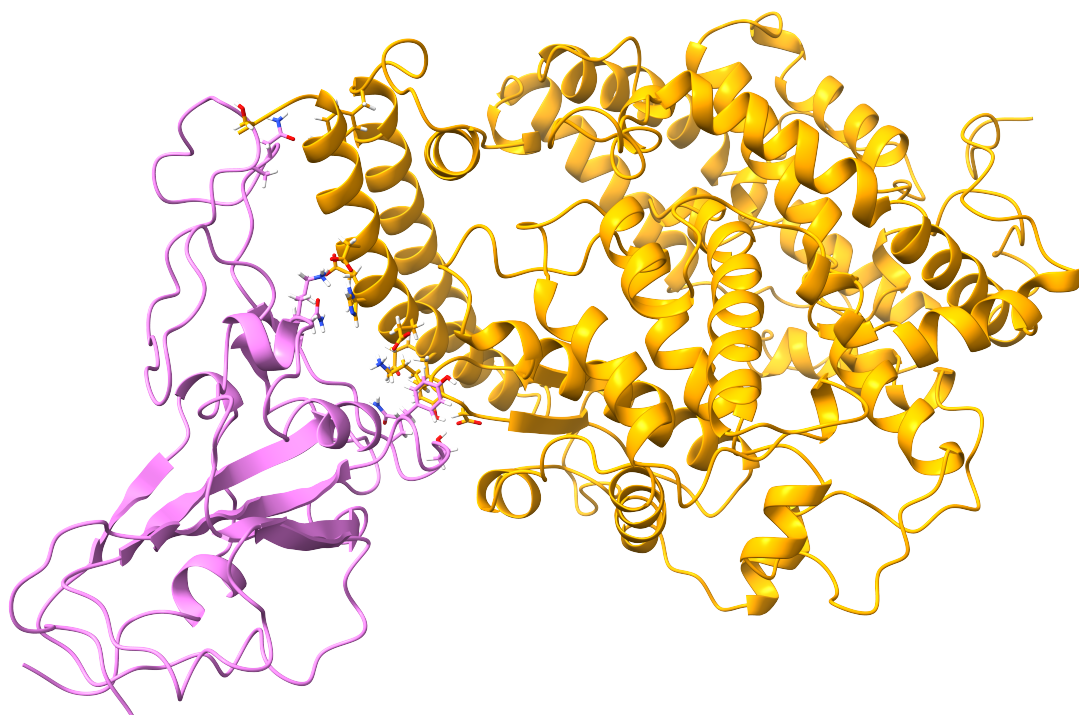
(b)



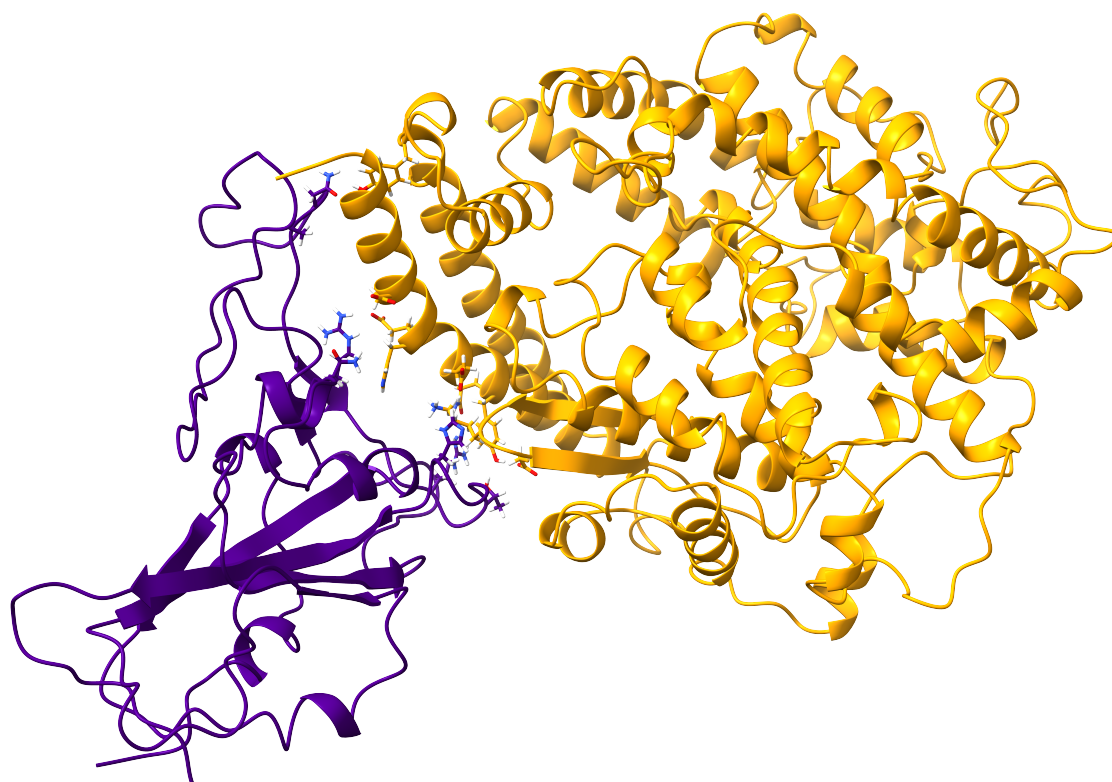
(c)



(d)



(e)



(f)

Figure S4: Structural images of the protein-protein complexes, including key residues, in their most stable minima obtained from umbrella sampling simulations (a) Delta, (b) Delta Plus, (c) Wild-type, (d) Beta, (e) Kappa, and (f) Omicron.

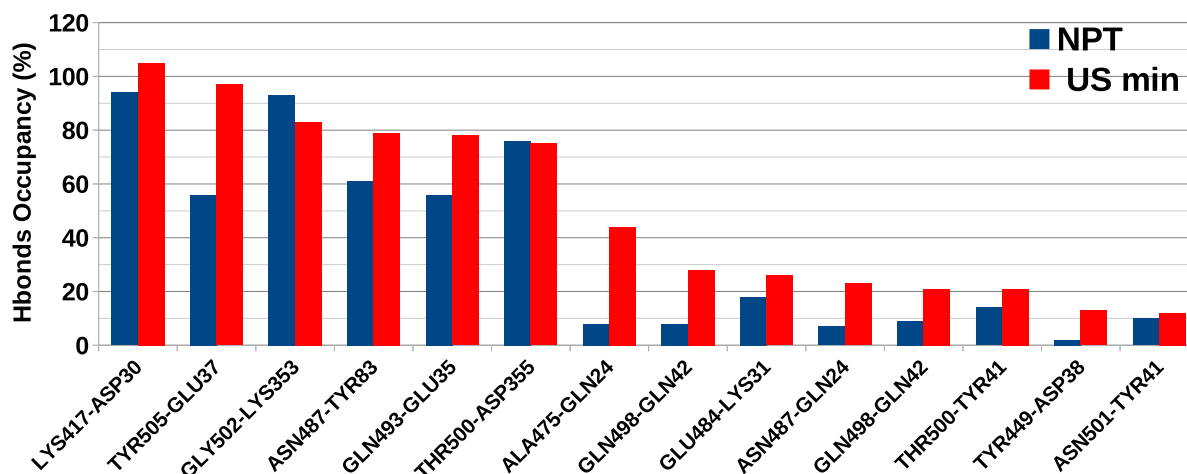


Figure S5: Comparison of occupancy of Hbonds of umbrella windows corresponding to free energy minimum (US min) and initial configuration (NPT) in the Delta variant.

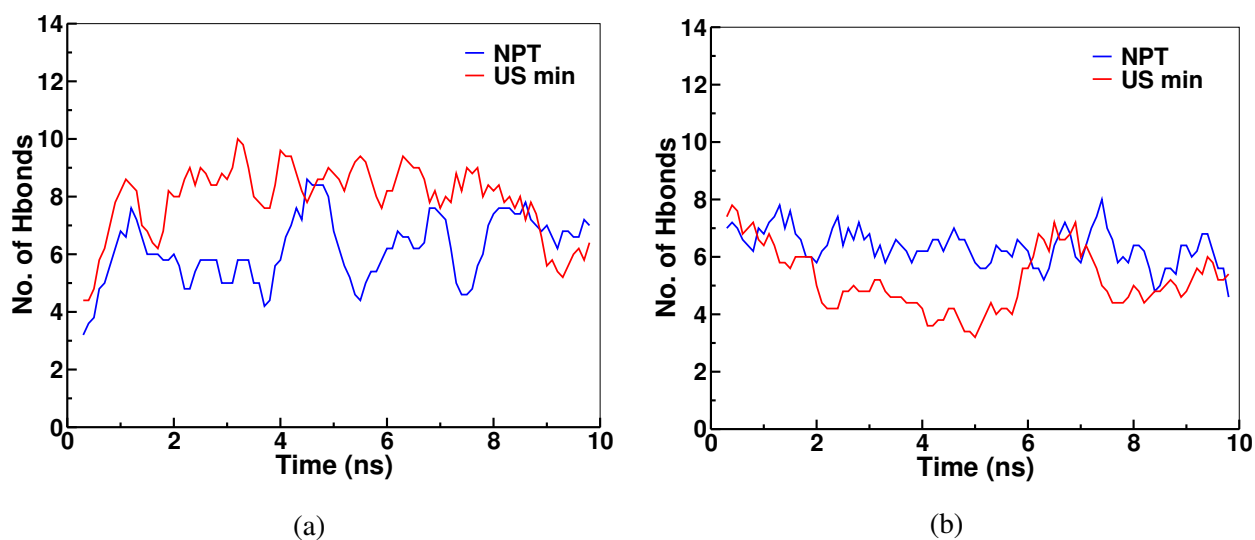


Figure S6: Comparison of time evolution of Hbonds of umbrella windows corresponding to free energy minimum (US min) and initial configuration (NPT) in (a) Delta (b) Delta Plus variants.

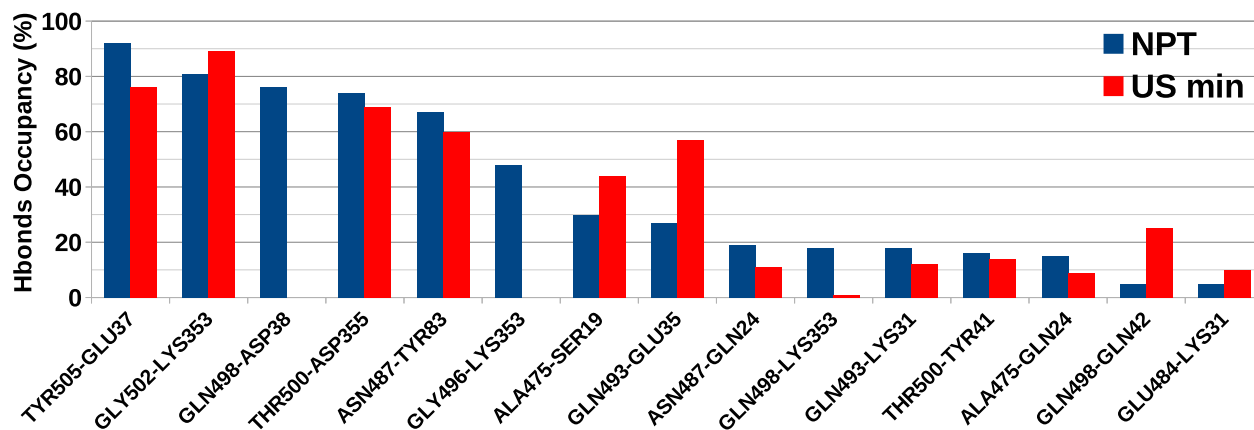


Figure S7: Comparison of occupancy of Hbonds of umbrella windows corresponding to free energy minimum (US min) and initial configuration (NPT) in the Delta Plus variant..

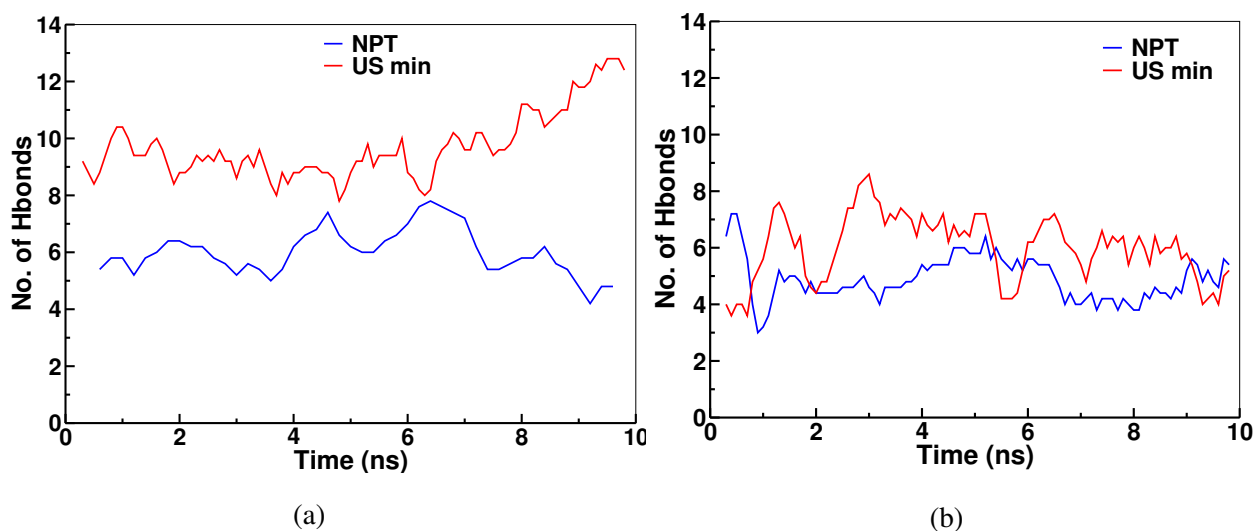


Figure S8: Comparison of time evolution of Hbonds of umbrella windows corresponding to free energy minimum (US min) and initial configuration (NPT) in (a) WT (b) Beta variants.

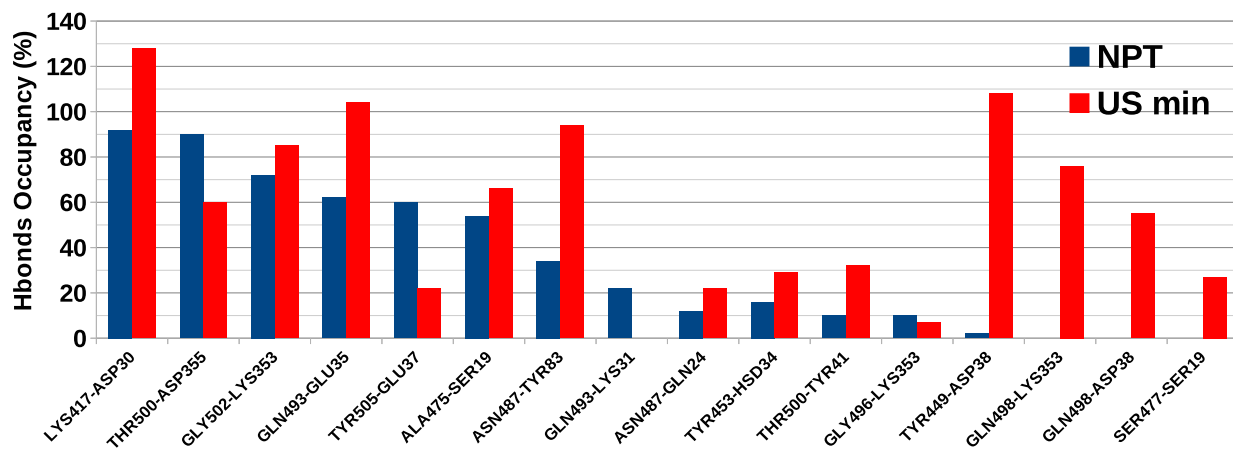


Figure S9: Comparison of occupancy of Hbonds of umbrella windows corresponding to free energy minimum (US min) and initial configuration (NPT) in the WT.

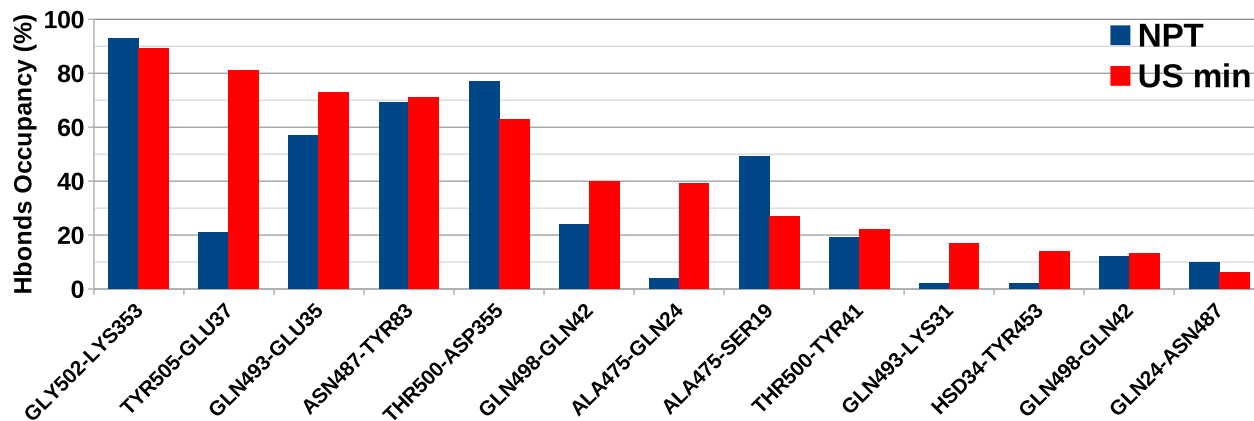


Figure S10: Comparison of occupancy of Hbonds of umbrella windows corresponding to free energy minimum (US min) and initial configuration (NPT) in the Beta variant.

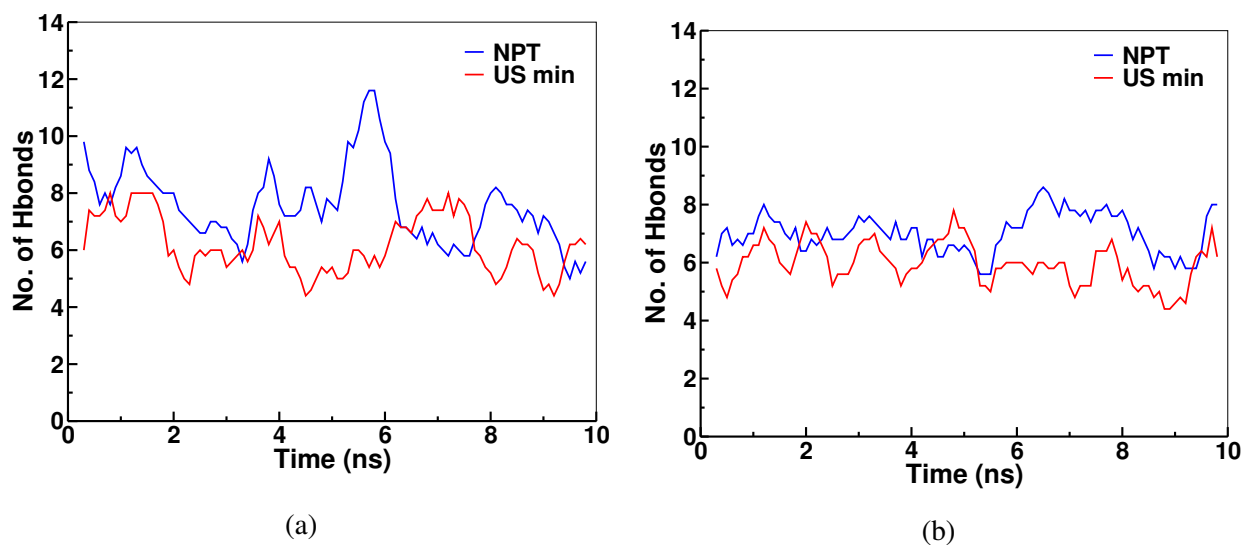


Figure S11: Comparison of time evolution of Hbonds of umbrella windows corresponding to free energy minimum (US min) and initial configuration (NPT) in (a) Kappa (b) Omicron variants.

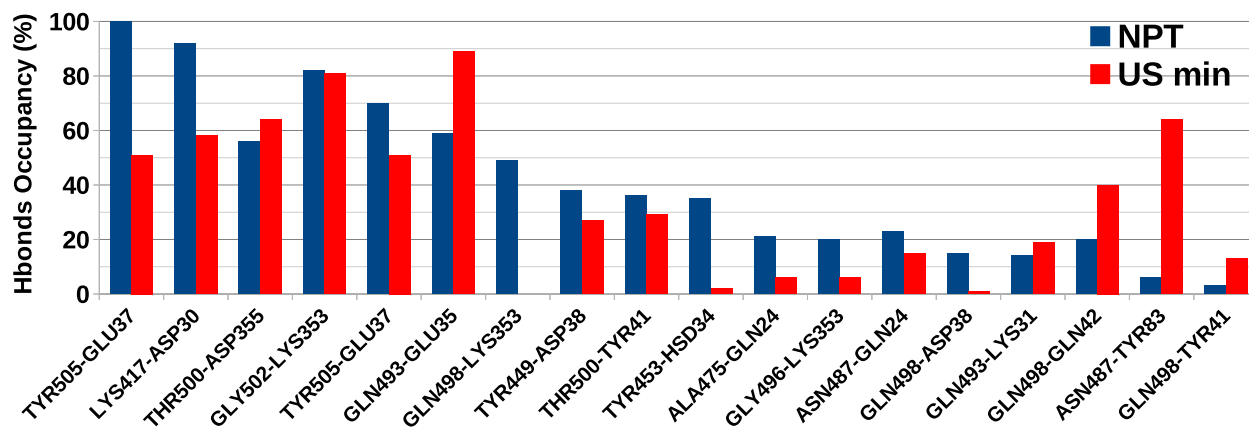


Figure S12: Comparison of occupancy of Hbonds of umbrella windows corresponding to free energy minimum (US min) and initial configuration (NPT) in the Kappa variant.

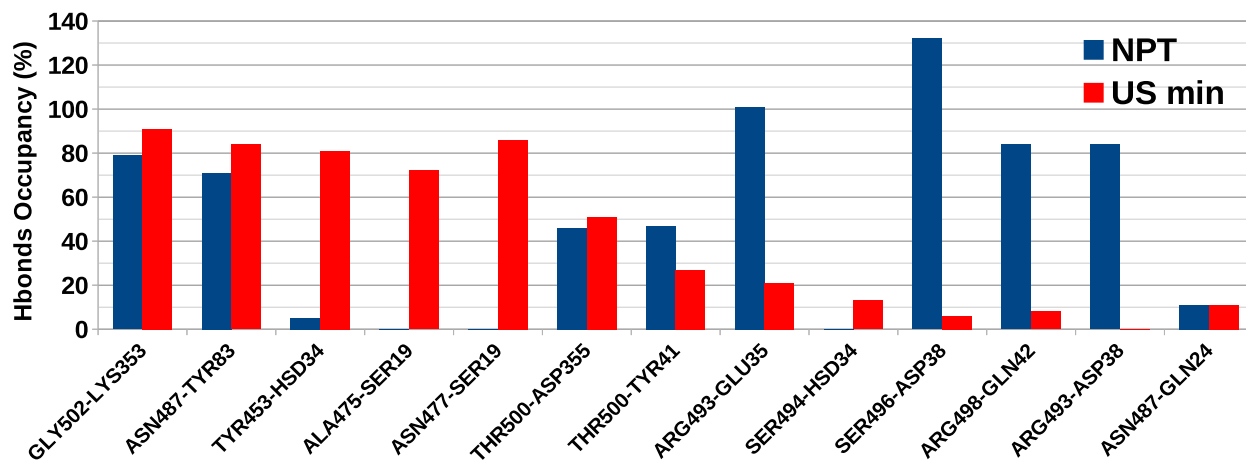


Figure S13: Comparison of occupancy of Hbonds of umbrella windows corresponding to free energy minimum (US min) and initial configuration (NPT) in the Omicron variant.

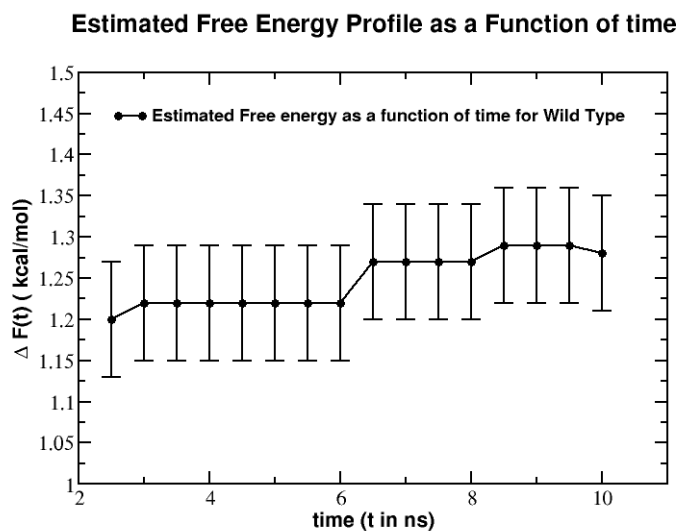


Figure S14: Time evolution of free energy obtained from the umbrella windows corresponding to the lowest free energy in the Wild-type.