

**Table S1. Omicron spike trimer interface analysis by PDBePISA****a Overall interface comparison between Omicron and G614 S trimer**

	Protomer1			Protomer2			interface area, Å <sup>2</sup>	ΔiG kcal/mol	ΔiG P-value	#HB	#SB
	iNat	iNres	Surface Å <sup>2</sup>	iNat	iNres	Surface Å <sup>2</sup>					
Omicron	660	188	59124	714	191	58896	6397.6	-60.4	0.092	56	14
G614	623	176	56231	670	181	56824	6017.4	-59.6	0.056	46	10

Note:

iNat: the number of interfacing atoms.

iNres: the number of interfacing residues.

ΔiG: Solvation energy effect, kcal/mol

HB: Hydrogen bond

SB: Salt bridge

**b Unique hydrophilic interaction contributed by Omicron mutations**

Protomer 1	Hydrogen bonds		Salt bridges	
	Dist. [Å]	Protomer 2	Protomer 1	Protomer 2
A:ASN 317[ OD1]	3.79	B:LYS 764[ NZ ]	A:ASP 568[ OD2]	B:LYS 856[ NZ ]
A:ASP 568[ OD2]	2.80	B:LYS 856[ NZ ]		
A:THR 572[ OG1]	2.79	B:LYS 856[ NZ ]		

**c Individual interface contact contributed by Omicron mutations**

	HSDC	ASA	BSA	ΔiG
A:ASN 417		55.99	8.14	-0.12
A:LYS 547		117.56	65.99	0.31
A:GLY 614	H	75.10	57.25	0.04
A:LYS 969	H	95.26	26.12	0.29
B:LYS 764	H	77.78	11.22	-0.41
B:TYR 796	H	192.06	50.52	0.24
B:PHE 981		124.99	44.63	0.41

ASA: Accessible Surface Area, Å<sup>2</sup>

BSA: Buried Surface Area, Å<sup>2</sup>

ΔiG: Solvation energy effect, kcal/mol

|||: Buried area percentage, one bar per 10%