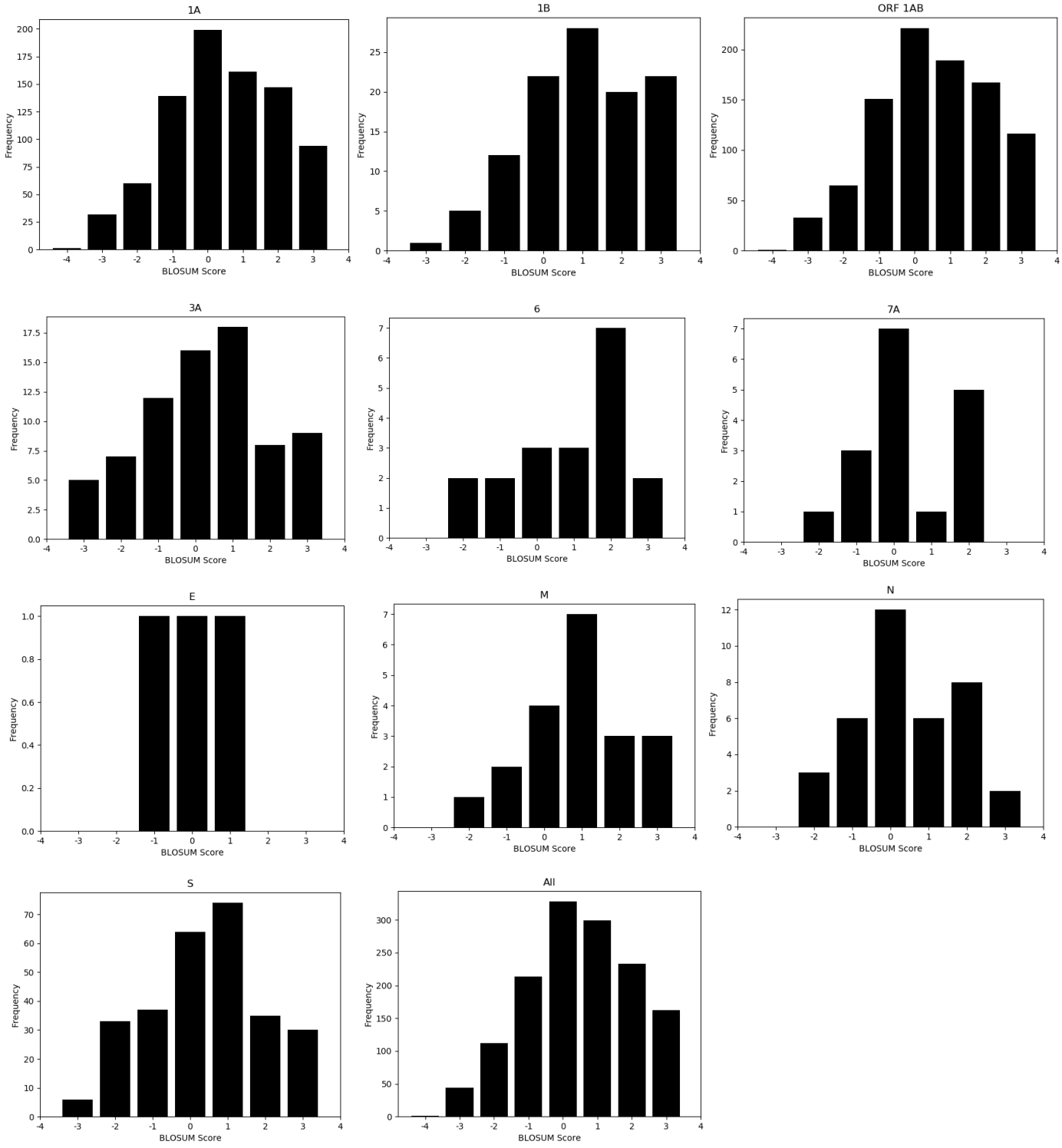
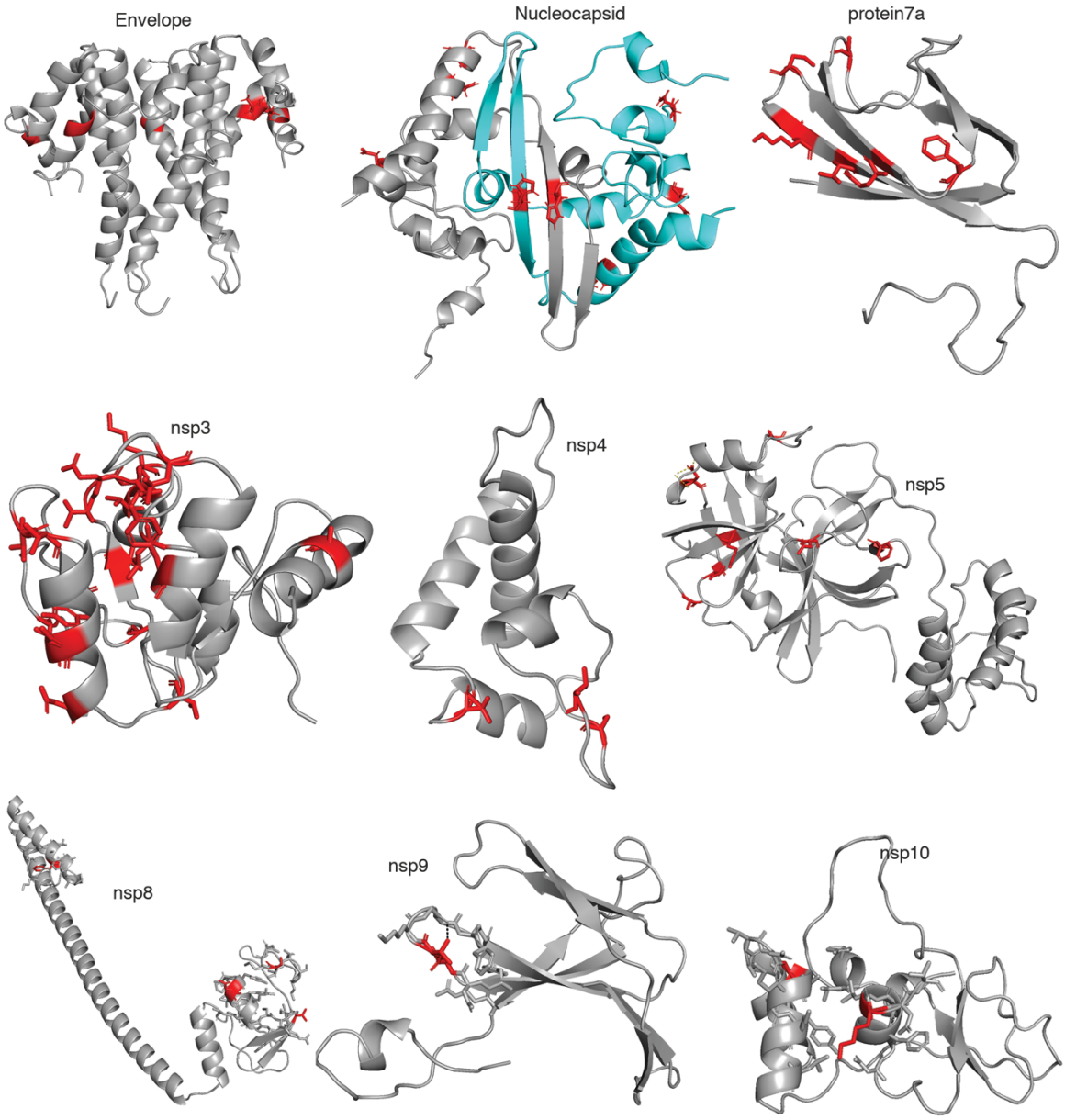


Supplementary Figure 1. The BLOSUM scores for the amino acid substitutions present in the SDPs. A graph is plotted that combines all of the proteins and one for each of the individual proteins that were analysed.



Supplementary Figure 2. Overview of modelled DCPs.

Supplementary Table 2 - Analysis of DCPs present in the SARS-CoV and SARS-CoV-2 Spike protein interface with human ACE2.

SDP	SARS-CoV structural analysis	SARS-CoV-2 structural analysis	Effect?
V404=K417	V404 is not in the interface	K417 is in the interface and could form a salt bridge with ACE-2 D30	Likely – new polar interaction within interface
R426=N439	Loss of hydrogen bond to ACE2 Gln325 due to shorter sidechain. N would still be able to form hydrogen bonds	N439 is located away from the interface site and so does not form a hydrogen bond with ACE2. Instead forms a hydrogen bond with S443 (also a DCP – A430=S443) which is likely to stabilise the loop they are both part of.	Likely – Loss of interface hydrogen bond.
Y442=L455	Y422 forms hydrogen bond to backbone of W476 – loss could result in conformational change. The sidechain also contacts the backbone of ACE2 D30 and K31	L455 remains in interface and contacts ACE2 D30 and H34.	Likely – loss of intramolecular hydrogen bond
F460=Y473	Conservative change.	Introduction of OH group that can form hydrogen bonds. Y473 forms hydrogen bond with backbone of R457 and is closer to ACE2 T27 so potential to form hydrogen bond in interface.	Possible – introduction of hydrogen bond (could be with ACE2)
P462=A475	Located in a loop, could affect this conformation – many DCPs in this loop	Loop has different conformation.	Possible – Conformational change of loop
N479=Q493	Interface hydrogen bond formed with ACE2 H34 backbone. With a shorter sidechain this this may be lost in SARS-CoV-2.	Q493 forms a hydrogen bond with ACE2 E35 in this complex. So hydrogen bond is maintained but also different.	Possible – hydrogen bond with ACE2 retained but to different residue.
Y484=Q498	Y484 can form hydrogen bonds with ACE2 Gln42 (sidechain) and intramolecular H bonds with T433 (backbone), Y436 (sidechain).	Q498 maintains hydrogen bonds with ACE2 Gln42	Possible – change in residue forming hydrogen bonds with ACE2.
T485=P499	Sidechain points away from interface, loss of hydrogen bond with R426 (also a	Loop conformation similar as for SARS-CoV structure but not coordinated with other loop	Likely - loss of intramolecular hydrogen bond

	DCP) backbone in adjacent loop. This hydrogen bond is likely to coordinate the structure between these two loops. There are multiple DCPs present in both loops		
I489=V503	Conservative change I489 in direct contact with ACE2 Q325	slightly smaller sidechain is further away from ACE2 Q325.	Unlikely.