




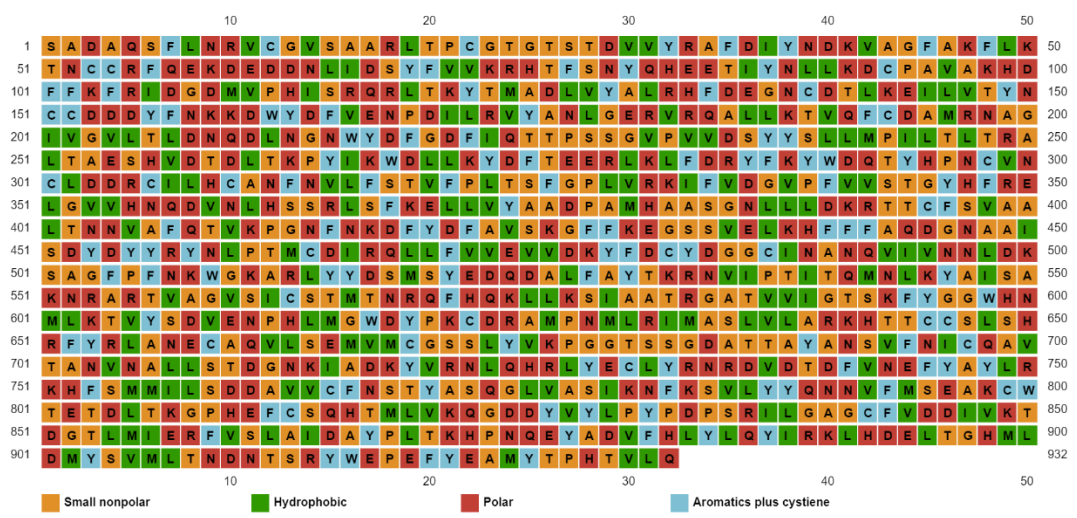
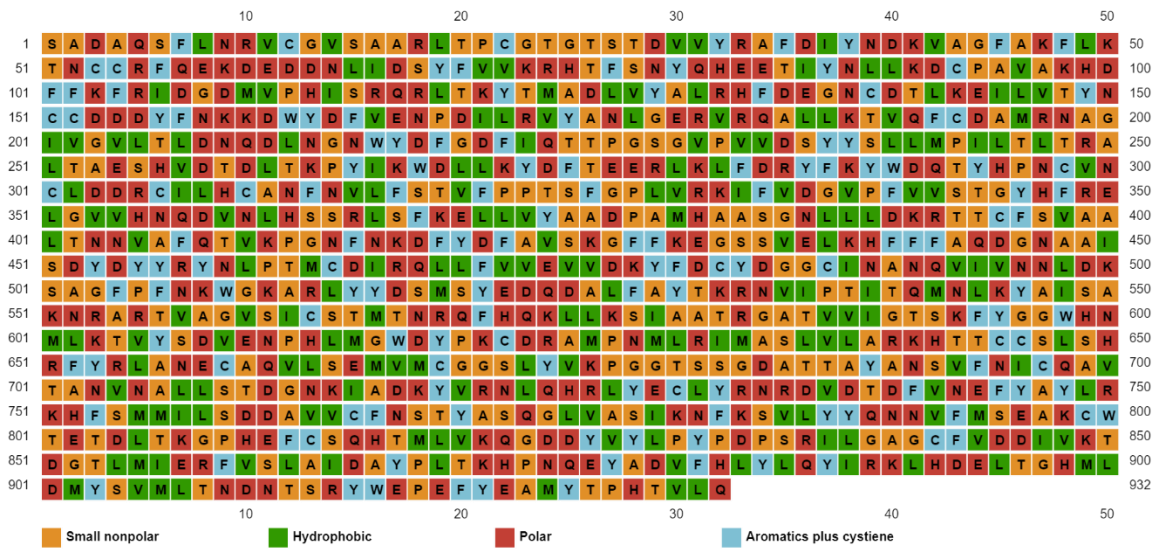
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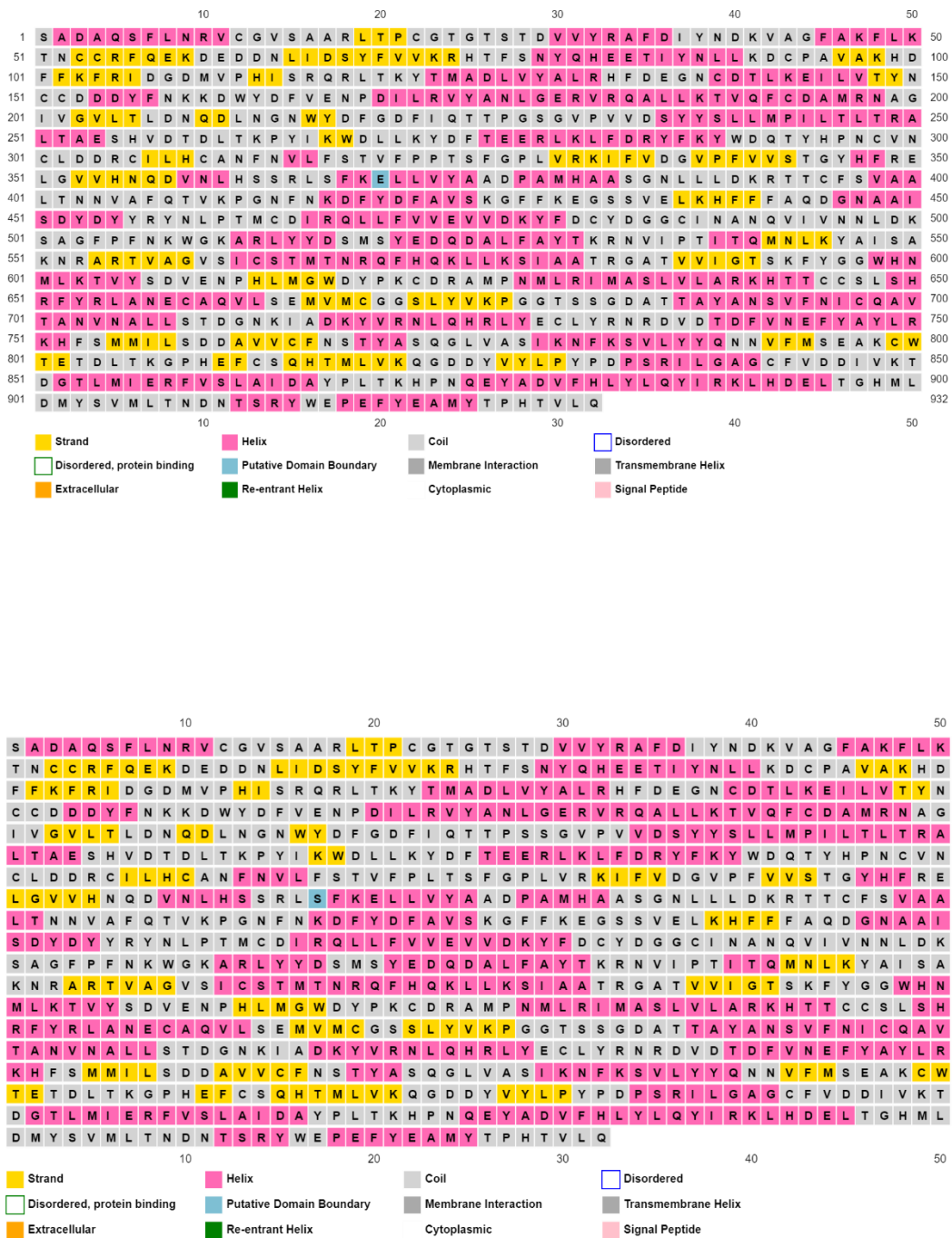
		
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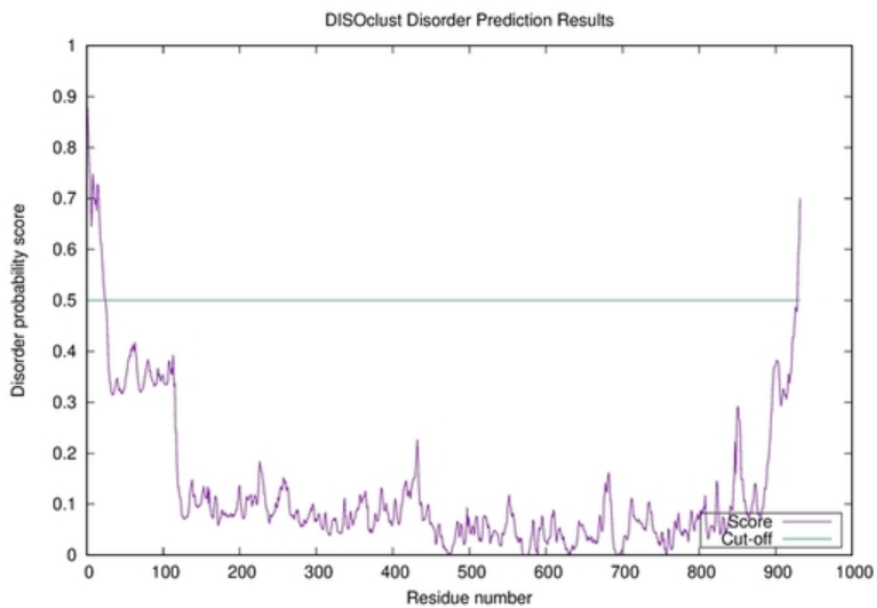
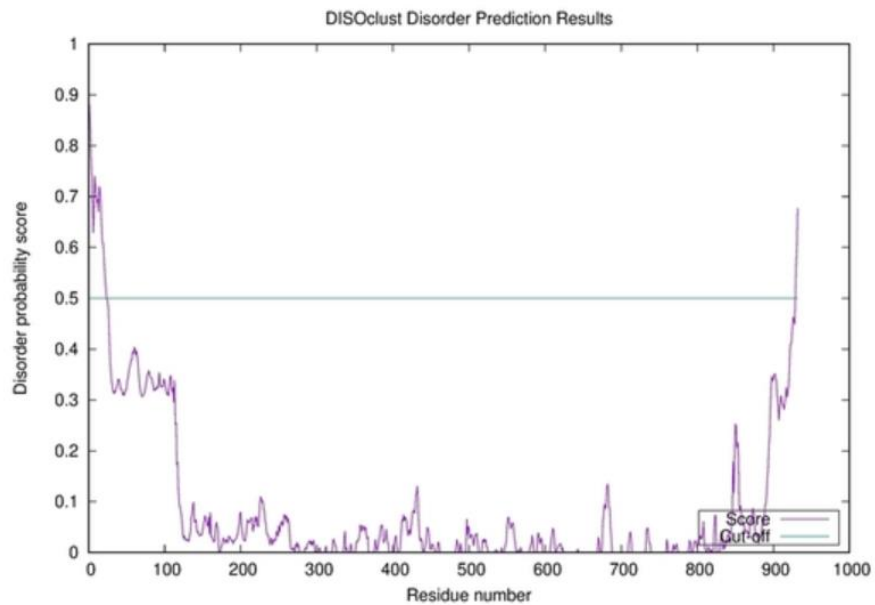
		

Supplementary Figure 1: Clustal omega analysis of RNA dependent RNA polymerase sequences between SARS CoV-2 wild type and delta variant. * Represents the match while the gap denotes the mismatch.





Supplementary Figure 2: Distribution of non-polar and polar residues and predicted secondary structures retrieved from PSIPRED. (a) SARS CoV-2 wild type and (b) SARS CoV-2 delta variant. Small non-polar residues are indicated by orange colour, polar residues by red and green symbolizes hydrophobic residues. Alpha helixes are indicated by pink, beta sheets by yellow and blue symbolizes for putative domain boundary



Supplementary Figure 3: The image shows a plot of the probability of disorder (on the y axis) for each numbered amino acid in the sequence (on the x axis). The disorder/order probability threshold is shown as a dashed line on the plot.

(a) SARS CoV-2 wild type and (b) SARS CoV-2 delta variant.

365 - 932: score = 314.272

RLSFKELLVYAADPAMHAASGNLLDKRRTTCFSVAALTNVAFQTVKPGNFNKDFYDFAV
 SKGFFKEGSSVELKHFFFAQDGNAAISDYDYRYRNLPTMCDIRQLLFVVEVVDKYFDCYD
 GGCINANQIVNNLDKSAGFPFNKKGKARLYYDSMSYEDQDALFAYTKRNVIPITITQMNL
 KYAISAKNRARTVAGVSICTMTNRQFHQKLLKLSIAATRGATVVIIGTSKFYGGWVHMLKT
 VYSDVENPHLMGWDYPKCDRAMPNMLRIMASLVLARKHTTCCSLSHRFYRLANCAQVLS
 EMVMCGGSLYVKPGGTSSGDATTAYANSVFNICQAVTANVNALLSTDGNKIADKYVRNLQ
 HRLYECLYRNRDVTDFVNEFYAYLRKHFMMILSDAVVCFNSTYASQGLVASIKNFKS
 VLYYQNNVFMSEAKCWTEIDLTKGPHEFCQHTMLVKQGGDYVYLPYPDPSRIILGAGCFV
 DDIVKTDGTLMIERFVSLAIDAYPLTKHPNQEYADVFLYLYQYIRKLHDEL TGHMLDMYS
 VMLTNDNTRSYWEPEFEAMYTPHTVLQ

Predicted features:

DOMAIN	365	932	Nsp12 RNA-dependent RNA polymerase	[condition: none]	
ACT_SITE	759			[condition: S]	[group: 1]
ACT_SITE	760			[condition: D]	[group: 1]
ACT_SITE	761			[condition: D]	[group: 1]

Supplementary Figure 4: Active site residues of SARS CoV-2 delta variant from PROSITE.

Tables

Supplementary Table 1: Observed structural differences in SARS CoV-2 wild type and delta variant through PSIPRED.

Parameters	Wild Type	Delta Variant
Non-polar	27.14%	27.03%
Polar	33.36%	33.36%
Helixes	38	38
Strands	30	30
Putative domain boundary	1 – E [370]	1 – S [367]

Supplementary Table 2: Analysis of the structures of c-beta deviations from Ramachandran Plot through RaptorX.

(a) SARS CoV-2 wild type and (b) SARS CoV-2 delta variant.

(a)

SARS CoV-2 Wild Type	
Amino acid with c-beta deviations	Structures
A759 SER	Overlap
A26 THR	Coiled
A259 THR	Coiled
A523 ASP	Alpha helix
A760 ASP	Coiled
A336 ASP	Beta sheet
A154 ASP	Overlap
A894 GLU	Alpha helix
A315 VAL	Alpha helix
A377 ASP	Coiled
A608 ASP	overlap

(b)

SARS CoV-2 Delta Variant	
Amino acid with c-beta deviations	Structures
A759 SER	Overlap
A26 THR	Coiled
A259 THR	Coiled
A523 ASP	Alpha helix
A760 ASP	Coiled
A336 ASP	Beta sheet
A154 ASP	Overlap
A894 GLU	Alpha helix
A315 VAL	Alpha helix
A608 ASP	overlap

Supplementary Table 3: Available ligand binding pockets in SARS CoV-2 delta variant retrieved from DogSiteScorer

Pocket ID	No. of sub pockets	DrugScore
P_0	5	0.796744
P_1	6	0.807282
P_2	4	0.810032
P_3	4	0.804645
P_4	3	0.805271
P_5	0	0.797945
P_6	2	0.787926
P_7	2	0.833644
P_8	3	0.775354
P_9	2	0.714024
P_10	2	0.802264
P_11	3	0.628391
P_12	0	0.415845
P_13	2	0.491249

P_14	0	0.385506
P_15	0	0.37231
P_16	0	0.433427
P_17	0	0.349045
P_18	2	0.517213
P_19	0	0.318026
P_20	2	0.328814
P_21	2	0.290505
P_22	0	0.249207
P_23	0	0.216916
P_24	0	0.199898
P_25	0	0.19103
P_26	0	0.223314
P_27	0	0.191765
P_28	0	0.16414
P_29	0	0.195384
P_30	0	0.166527
P_31	0	0.151884
P_32	0	0.175731
P_33	0	0.172151
P_34	0	0.199087

P_35	0	0.224526
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