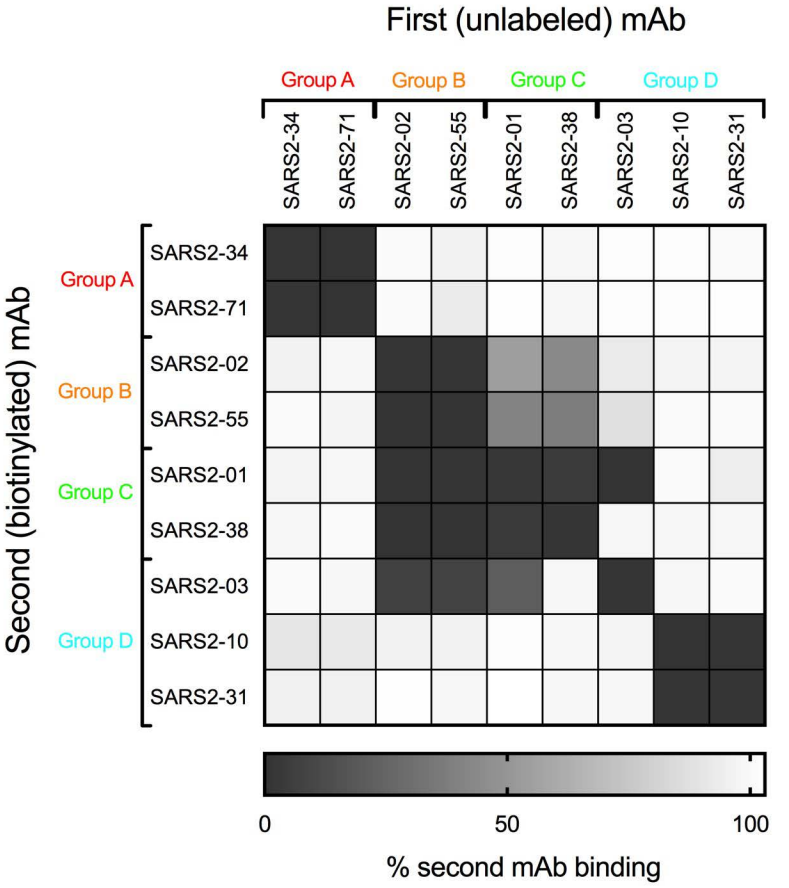

First (unlabeled) mAb
Group A
Group B
Group C
Group D
SARS2-34
SARS2-71
SARS2-02
SARS2-55
SARS2-01
SARS2-38
SARS2-03
SARS2-10
SARS2-31
Second (biotinylated) mAb
0
50
100
% second mAb binding

Figure S1

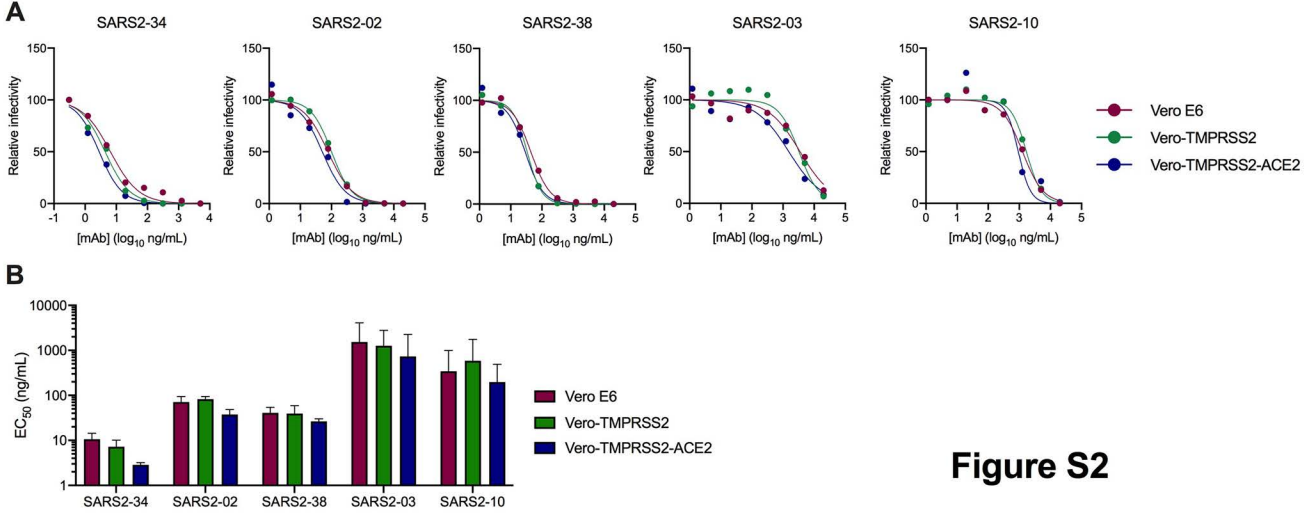
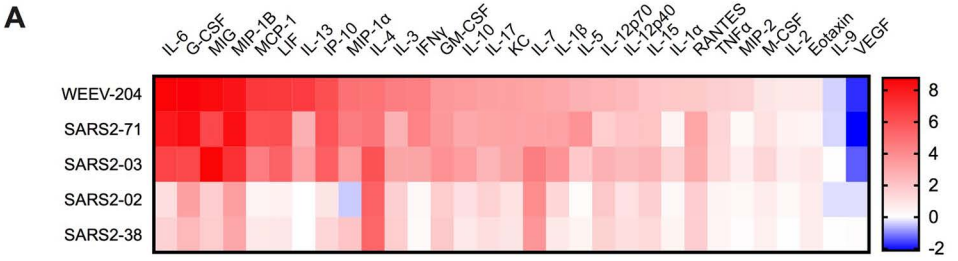

A
SARS2-34
SARS2-02
SARS2-38
SARS2-03
SARS2-10
Relative infectivity
[mAb] (log10 ng/mL)
Vero E6
Vero-TMPRSS2
Vero-TMPRSS2-ACE2
B
EC50 (ng/mL)
SARS2-34
SARS2-02
SARS2-38
SARS2-03
SARS2-10
Vero E6
Vero-TMPRSS2
Vero-TMPRSS2-ACE2

Figure S2


A
IL-6
G-CSF
MIG
MIP-1B
MCP-1
LIF
IL-13
IP-10
MIP-1α
IL-4
IL-3
IFNγ
GM-CSF
IL-10
IL-17
KC
IL-7
IL-1β
IL-5
IL-12p70
IL-12p40
IL-15
IL-1α
RANTES
TNFα
MIP-2
M-CSF
IL-2
Eotaxin
IL-9
VEGF
WEEV-204
SARS2-71
SARS2-02
SARS2-38
SARS2-03
8
6
4
2
0
-2

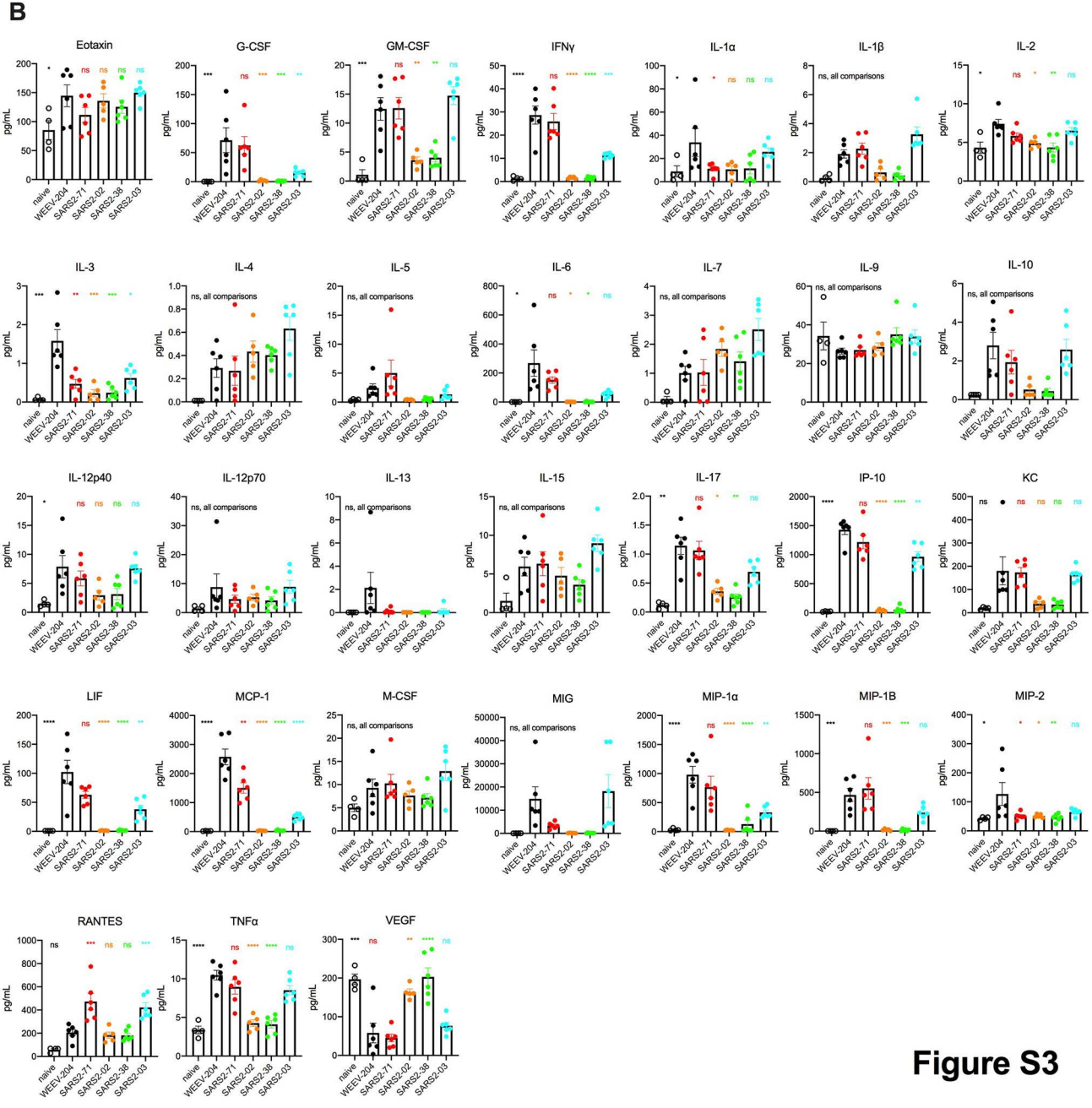
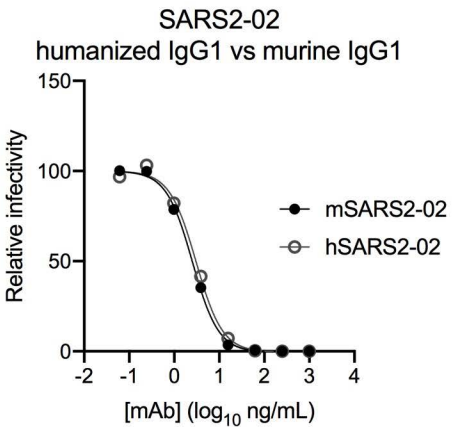

B
Eotaxin
G-CSF
GM-CSF
IFNγ
IL-1α
IL-1β
IL-2
IL-3
IL-4
IL-5
IL-6
IL-7
IL-9
IL-10
IL-12p40
IL-12p70
IL-13
IL-15
IL-17
IP-10
KC
LIF
MCP-1
M-CSF
MIG
MIP-1α
MIP-1B
MIP-2
RANTES
TNFα
VEGF
pg/mL
ns, all comparisons
naive
WEEV-204
SARS2-71
SARS2-02
SARS2-38
SARS2-03

Figure S3


SARS2-02
humanized IgG1 vs murine IgG1
Relative infectivity
150
100
50
0
-2
-1
0
1
2
3
4
[mAb] (log10 ng/mL)
mSARS2-02
hSARS2-02

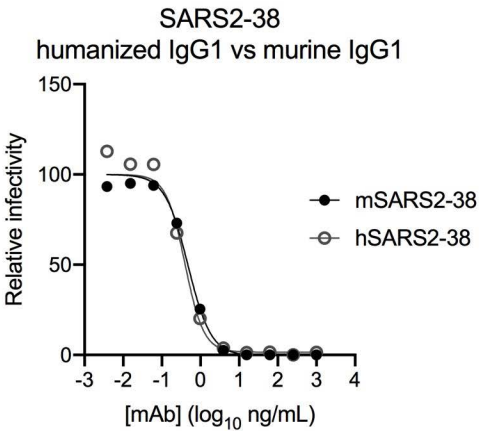
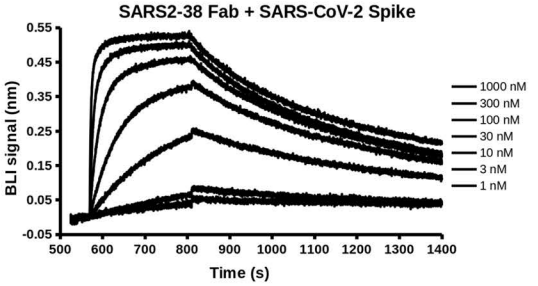
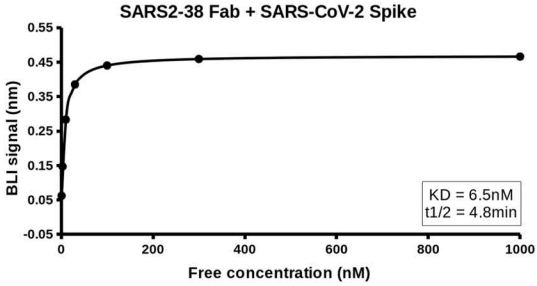

SARS2-38
humanized IgG1 vs murine IgG1
Relative infectivity
150
100
50
0
-3
-2
-1
0
1
2
3
4
[mAb] (log10 ng/mL)
mSARS2-38
hSARS2-38

Figure S4

A


SARS2-38 Fab + SARS-CoV-2 Spike
BLI signal (nm)
Time (s)
1000 nM
300 nM
100 nM
30 nM
10 nM
3 nM
1 nM


SARS2-38 Fab + SARS-CoV-2 Spike
BLI signal (nm)
Free concentration (nM)
KD = 6.5nM
t1/2 = 4.8min

B

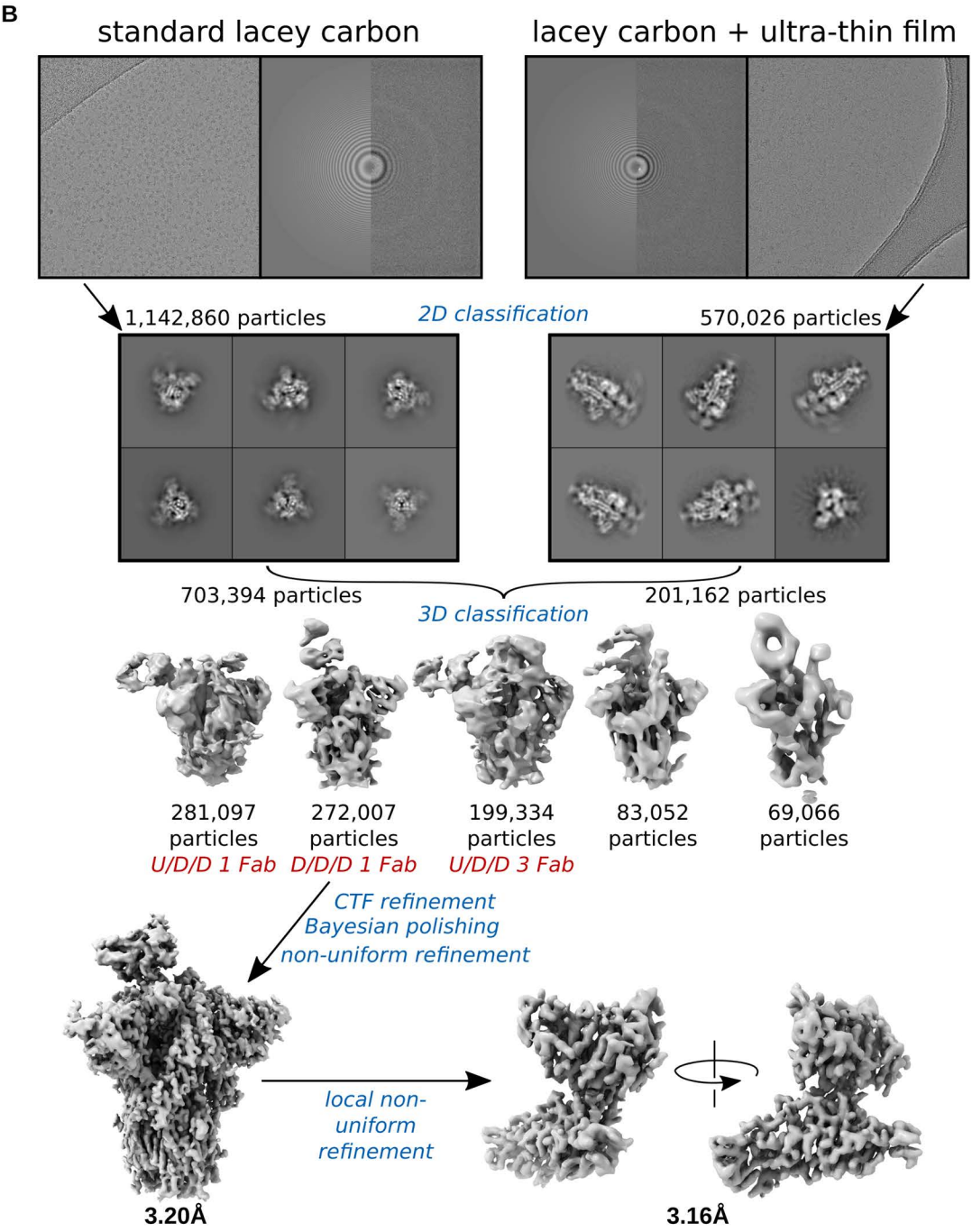
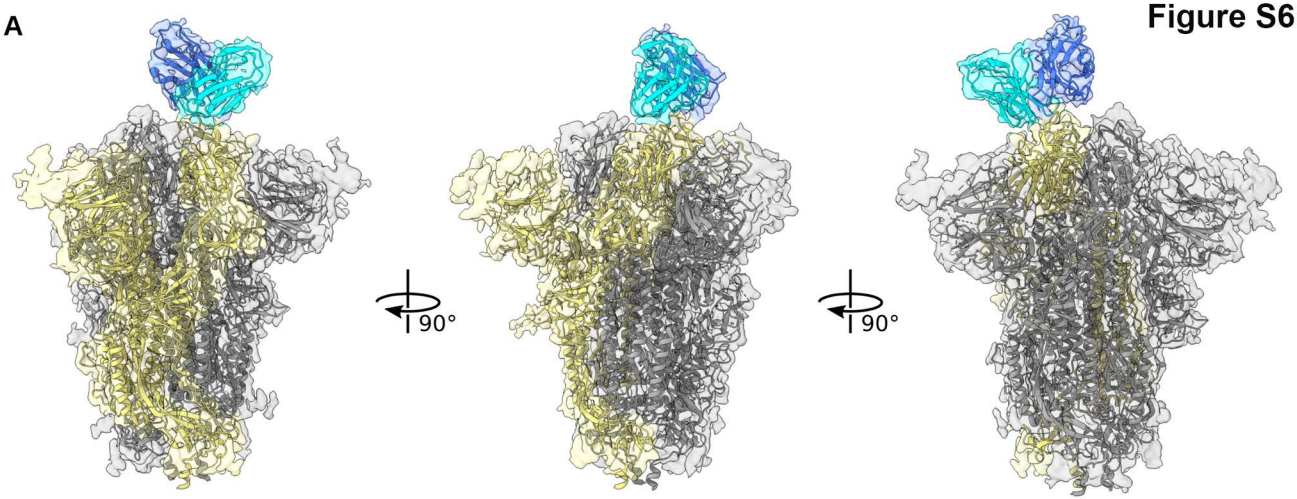
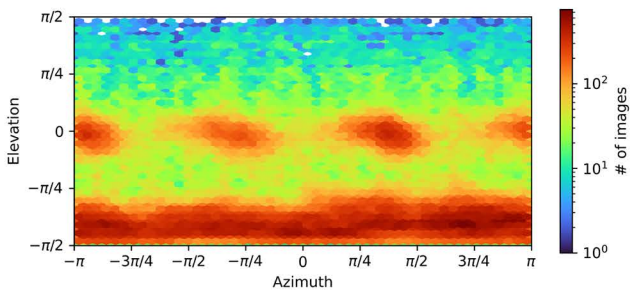
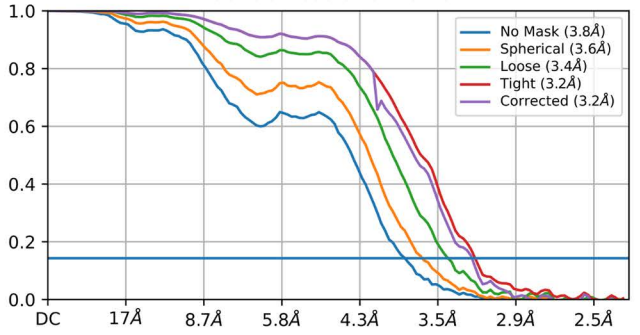
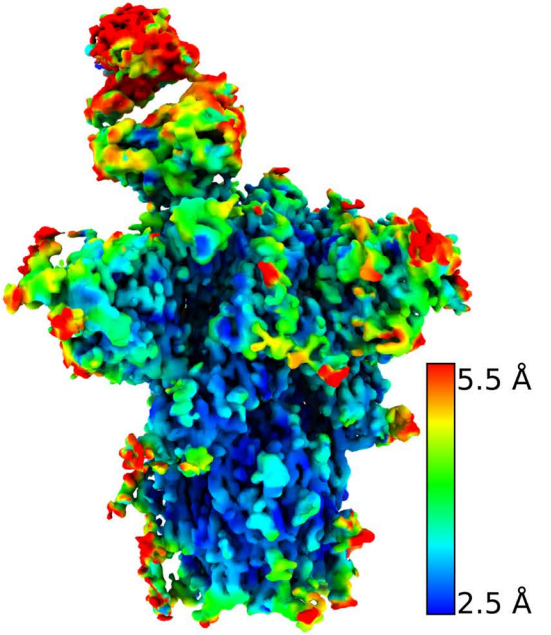

standard lacey carbon
lacey carbon + ultra-thin film
1,142,860 particles
2D classification
570,026 particles
703,394 particles
3D classification
201,162 particles
281,097 particles
U/D/D 1 Fab
272,007 particles
D/D/D 1 Fab
199,334 particles
U/D/D 3 Fab
83,052 particles
69,066 particles
CTF refinement
Bayesian polishing
non-uniform refinement
local non-uniform refinement
3.20Å
3.16Å

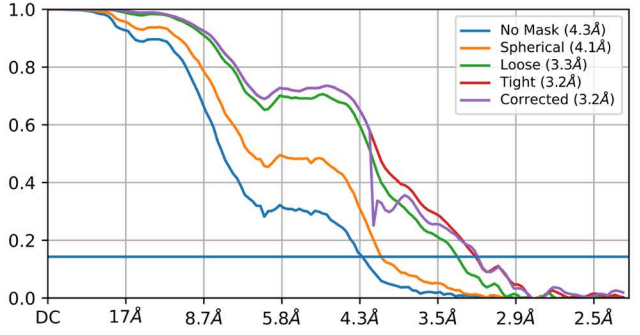
Figure S6


A
90°
90°


B
Elevation
Azimuth
# of images


C
GSFSC Resolution: 3.20Å
No Mask (3.8Å)
Spherical (3.6Å)
Loose (3.4Å)
Tight (3.2Å)
Corrected (3.2Å)
DC
17Å
8.7Å
5.8Å
4.3Å
3.5Å
2.9Å
2.5Å


D
5.5 Å
2.5 Å


E
GSFSC Resolution: 3.16Å
No Mask (4.3Å)
Spherical (4.1Å)
Loose (3.3Å)
Tight (3.2Å)
Corrected (3.2Å)
DC
17Å
8.7Å
5.8Å
4.3Å
3.5Å
2.9Å
2.5Å

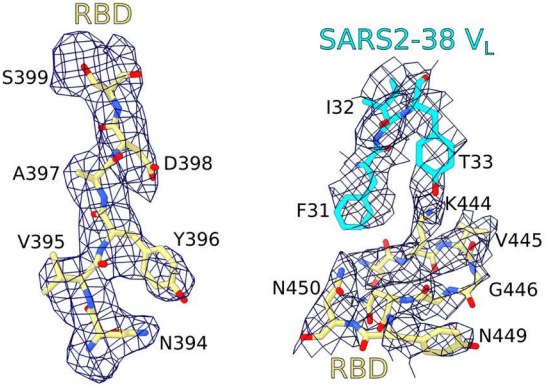

F
RBD
S399
A397
D398
V395
Y396
N394
SARS2-38 V_L
I32
T33
F31
K444
V445
N450
G446
N449
RBD

Table S1

Cryo-EM data collection, processing, and model refinement statistics		
	SARS-CoV-2 spike + Fab SARS2-38 (global) PDB 7MKL EMD-23898	SARS-CoV-2 spike + Fab SARS2-38 (local) PDB 7MKM EMD-23899
Data collection		
Magnification	59,000x	59,000x
Exposure ($e^-/Å^2$)	50	50
Defocus range (μm)	0.8-2.3	0.8-2.3
Pixel size (Å/pixel)	1.16	1.16
Data processing		
Initial particles (no.)	1,712,886	1,712,886
Final particles (no.)	272,007	272,007
Nominal resolution (Å)	3.20	3.16
FSC threshold	0.143	0.143
Model refinement		
Adapted PDB models	6M0J, 1KIQ, 5XJM, 6VXX	6M0J, 1KIQ, 5XJM
Model resolution (Å)	4.1	4.2
FSC threshold	0.5	0.5
Model composition		
Non-hydrogen atoms	25,597	3,192
Residues	3,164	406
Ligands	63	1
B-factors ($Å^2$)		
Residues	102.17	76.19
Ligands (glycans)	122.20	81.01
Bonds (RMSD)		
Length (Å)	0.004	0.003
Angles (°)	0.816	0.797
Validation		
Molprobity score	1.69	1.51
Clash score	10.10	8.33
Rotamer outliers (%)	0.00	0.00
Ramachandran		
Favored (%)	97.09	97.75
Allowed (%)	2.91	2.25
Outliers (%)	0.0	0.0