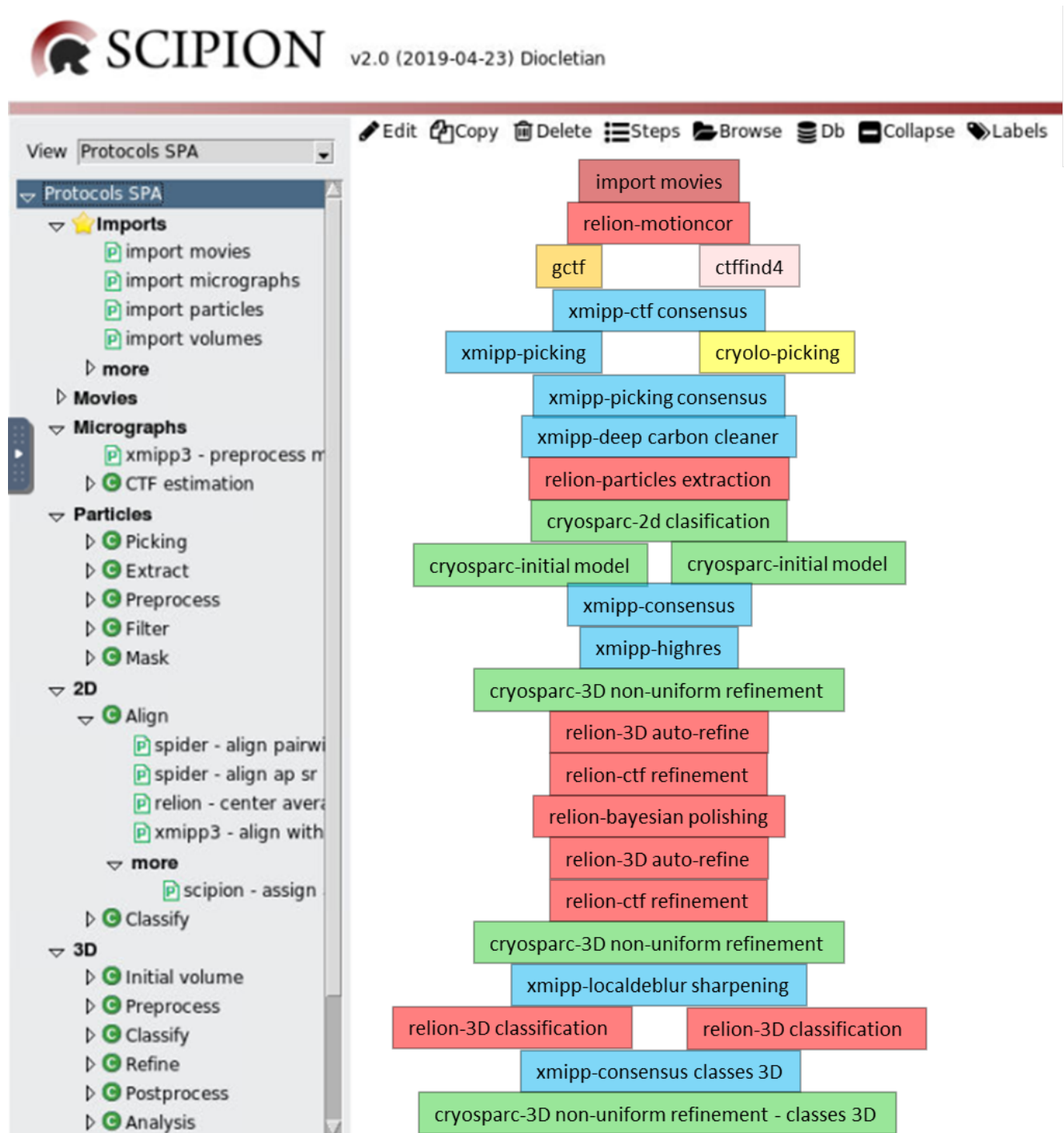
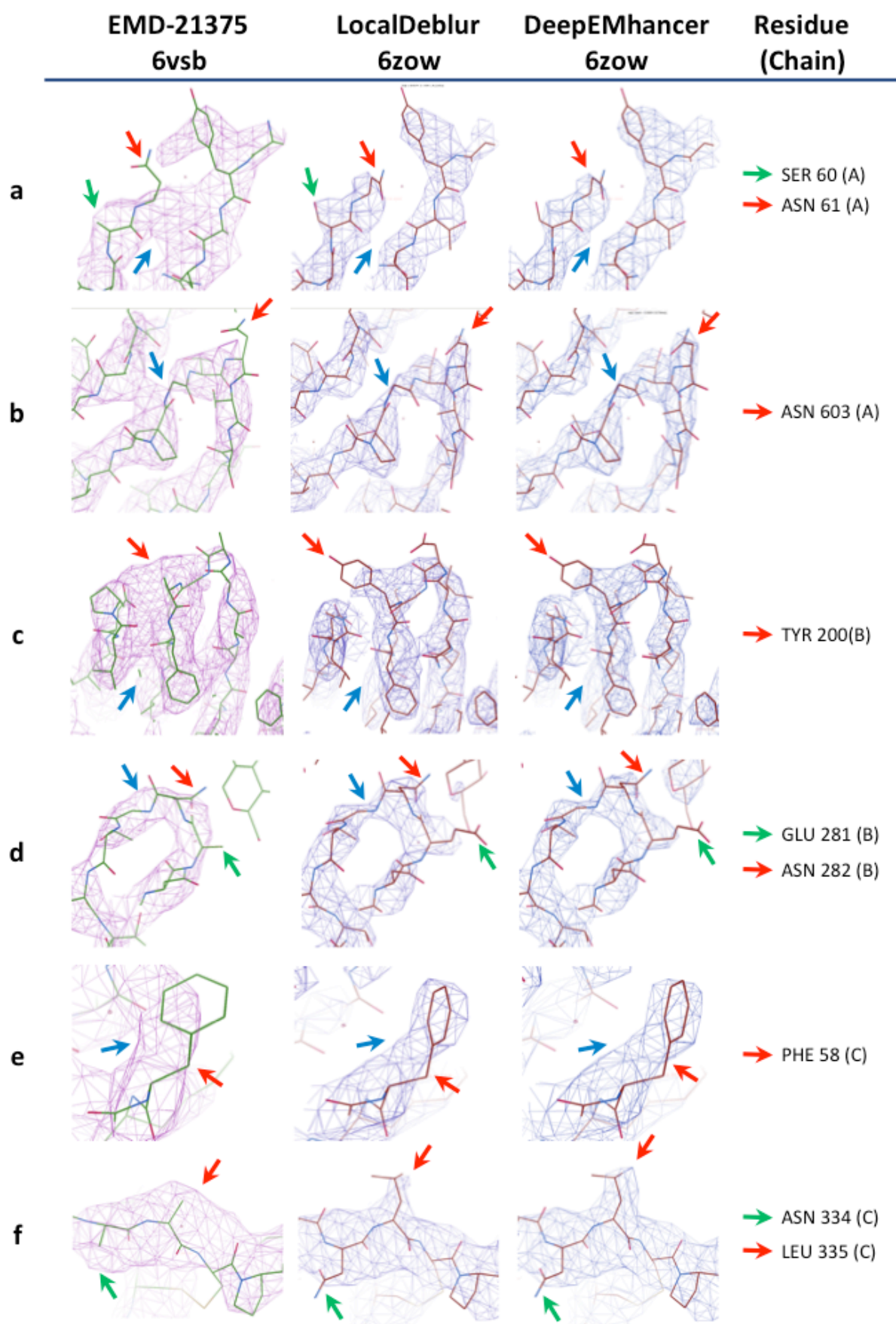


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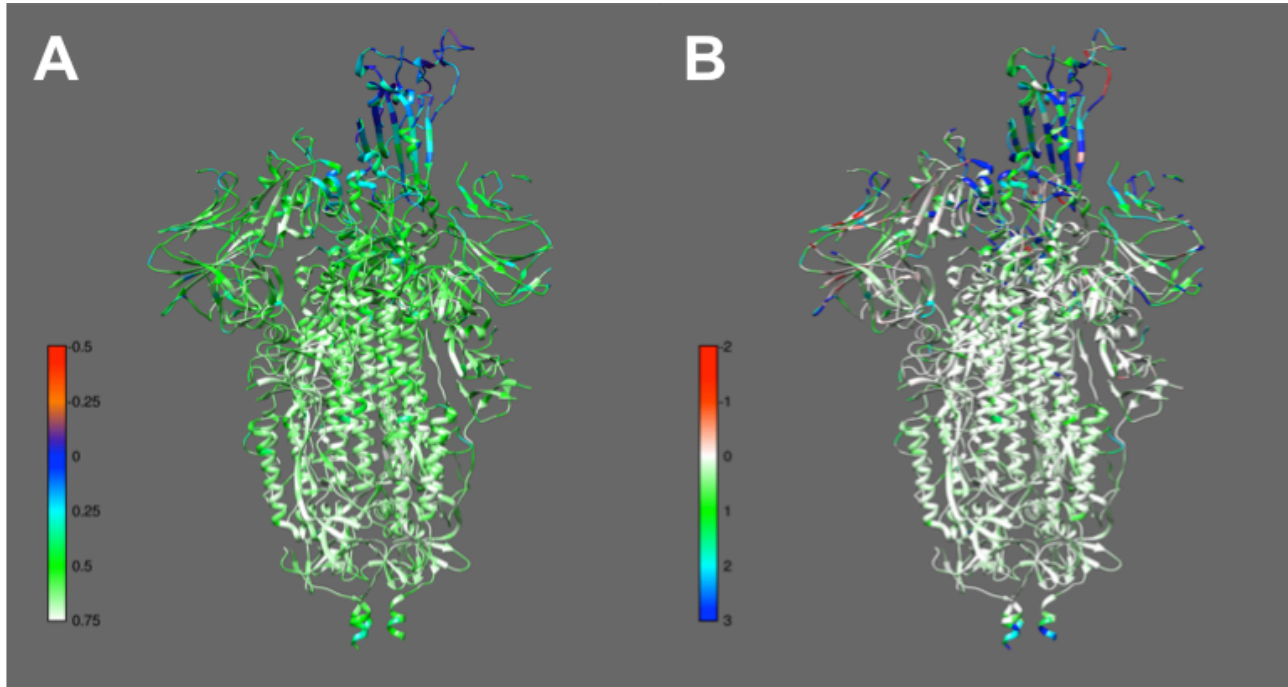
Supplementary Material Figure 1. Graphical representation of the processing workflow in Scipion. The workflow is also accessible at Scipion Workflow Repository at <http://workflows.scipion.i2pc.es/>.



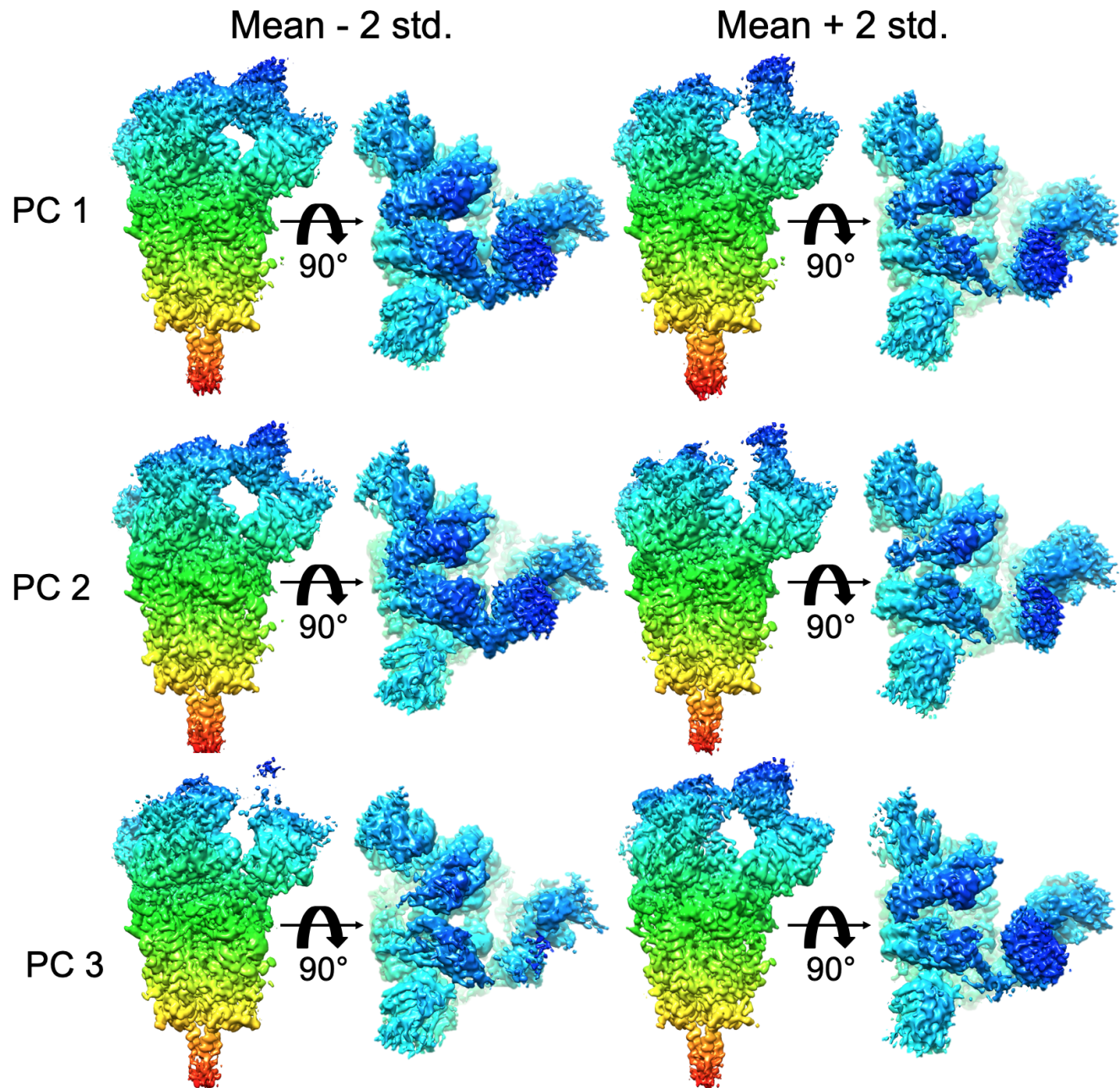
Supplementary Material Figure SM2. Comparison of the ability to trace the atomic structure between the original cryo-EM map (EMD-21375) and the two sharpened maps derived from the new reconstructed ensemble map. Six representative 3D map areas (a-f) illustrate the fitting between map and atomic structure. The red arrows detail aminoacid side chains fitted to better defined densities in the sharpened map compared to the original map. These side chains could have been modeled (a, b, d, e) or being absent (c, f) in the original map. The green arrows indicate other additional residues whose side chains have been modeled only in the sharpened maps, while they were absent in the original one. The blue arrows point at densities that make it difficult to follow the carbon skeleton shape or discriminate among different chains in the original map, whereas they appear better resolved in the sharpened maps.



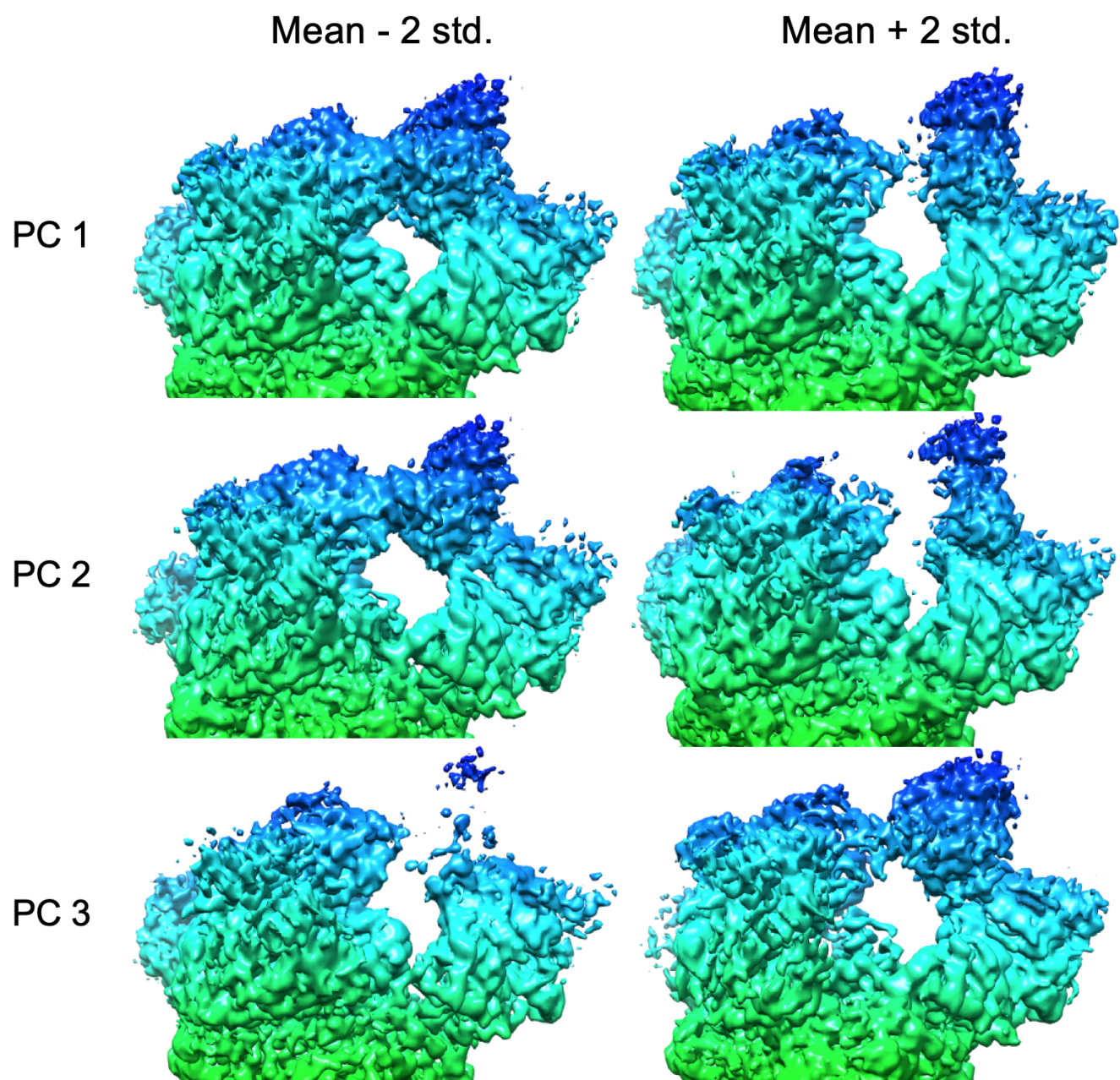
Supplementary Material Figure SM3. Map-to-Model quality measures for the ensemble map. A) Q-score values represented on each amino acid of the new ensemble atomic model. Q-scores close to 1 indicate better resolvability of the residue. B) FSC-Q values are represented for each residue. Values close to zero indicate a good map-to-model fit, while values far from zero indicate areas where the model loses support with respect to the map signal.



Supplementary Material Figure SM4. Principal Component Analysis. Side and top views of mean volume ± 2 std for the three principal components. Coloring indicates z-depth of the structure, and is added to assist visualization of the top view.



Supplementary Material Figure SM5. Principal Component Analysis. Enlarged top half of the side views showing details of the density changes captured by the principal components. Coloring indicates z-depth of the structure, and is added to assist visualization of the top view.



Supplementary Table SM1. Validation scores of the new atomic structure PDB 6ZOW

Validation scores	Whole structure¹	Modeled structure²
EMRinger	2.66	2.73
CC(mask)	0.75	0.76
Ramachandran outliers (Goal: < 0.2%)	0.00	0.00
Ramachandran favored (Goal: > 98%)	97.06	97.28
Rotamer outliers (Goal: < 1%)	0.52	0.17
C-beta outliers	0	0
Clashscore	12.06	12.43
MolProbity overall score	1.76	1.74
Q-Score	0.55	0.58
FSC-Q	0.73	0.58

¹ Chains A, a, B, C

² Excluding the chain a (RBD, added by rigid fitting)

Supplementary Table SM2. Number of sequons and size of their respective glycan chains.

Subunit	Size of N-linked glycan chain	6VSB		6ZOW	
		Number of sequons	Number of glycans	Number of sequons	Number of glycans
S1	1	26	26	18	18
	2	0	0	7	14
	3	0	0	2	6
	Subtotal	26	26	27	38
S2	1	1	1	0	0
	2	17	34	9	18
	3	0	0	5	15
	4	0	0	2	8
	5	0	0	2	10
	Subtotal	18	35	18	51
TOTAL		44	61	45	89

Supplementary Material Movie 1. Movie presenting the morphing between the two algorithmically stable classes described in the main text, spanning Principal Component Axis 1.