

The Architecture of Inactivated SARS-CoV-2 with Postfusion Spikes Revealed by Cryo-EM and Cryo-ET

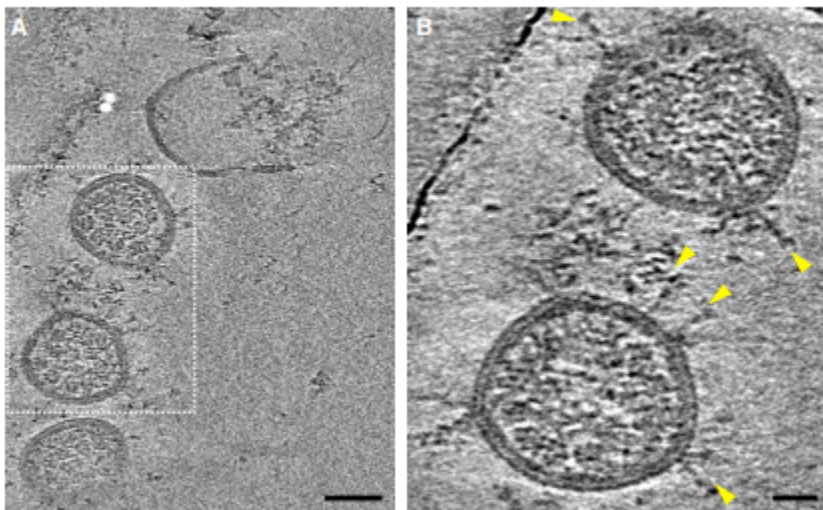
-----Work in Progress-----

Coronaviruses are enveloped single-stranded positive-RNA viruses, roughly 80–120 nm in diameter. The viral RNA is intimately associated with the viral nucleocapsid protein (N), forming large viral ribonucleoprotein complexes. The viral envelope is derived from the host cell and decorated with viral surface proteins: spike (S), membrane (M), and envelope (E).

The 3D nature of cryo-ET allows analysis of features that would normally be obstructed in cryo-EM projection images

The prefusion conformations of SARS-CoV-2 spike were determined alone and in complex with the cell surface receptor ACE-2 or a neutralizing antibody

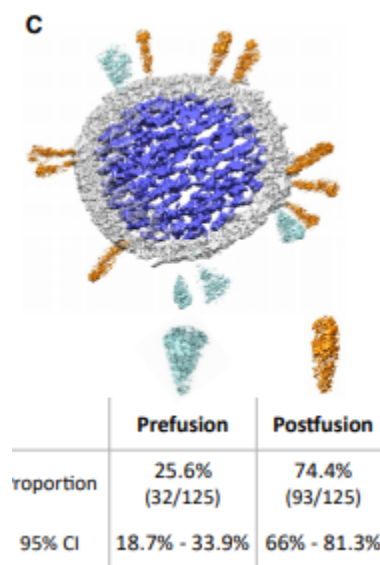
The spikes in the tomograms confirmed the findings from negative staining and cryo-EM, showing that the spikes adopt a conformation consistent with the postfusion state of the S2 protein (Figures A and B).



Frequently, the spikes were arranged in clusters .

To obtain an in situ 3D structure of the postfusion SARS-CoV-2 spike on the native virion, we carried out cryoET and subtomogram alignment and averaging

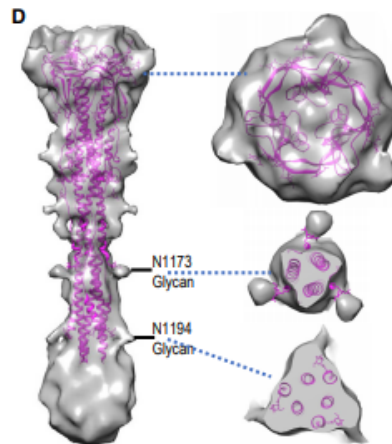
Among 125 spikes from 19 virus particles analyzed from high defocused tomograms, we observed 32 prefusion and 93 postfusion spikes from which S1 had dissociated. The postfusion spikes account for 74% of total spikes in the b-propiolactone-treated SARS-CoV-2 particles (Figure C).



Virus tomograms also showed the ribonucleoprotein complexes organized inside the viruses .

Despite the determination of many structures of prefusion SARS-CoV-2 spike alone and in complex with its receptor and antibodies, the structure of the postfusion SARS-CoV-2 spike is still lacking.

Density map of the postfusion SARS-CoV-2 spike fitted with a SARS-CoV mode :



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