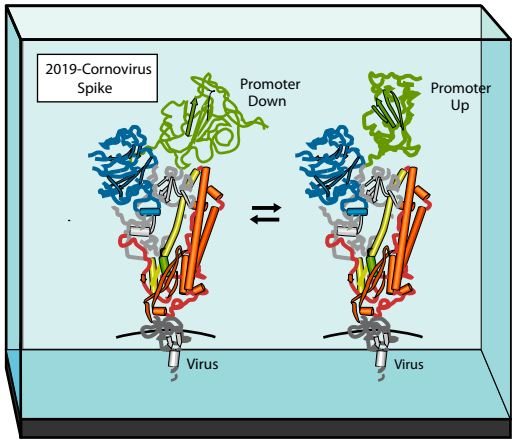
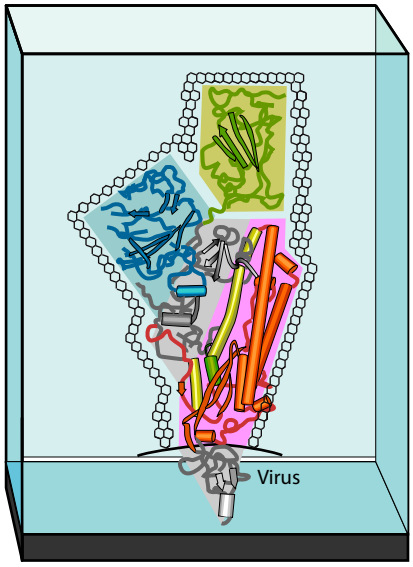
The Omicron Virus Spike and ACE2 Enzyme Binding

Since the coronavirus pandemic has produced major advances in our understanding of the structure and binding properties of virus,[1,2] it seemed to be the right time to test the Transient Linear Hydration (TLH) hypothesis.[3]



First of all, the spikes have a triangular shape composed of a number of protein units, which have different shapes and proportions of coils, linear and filamentous segments. At the top of the spike is a "promoter protein" which can adopt two conformations: one at an angle and one vertical. As the spike approaches the ACE2 (angiotensin converting enzyme) on a target cell, the promoter rotates into the up-position.[1]

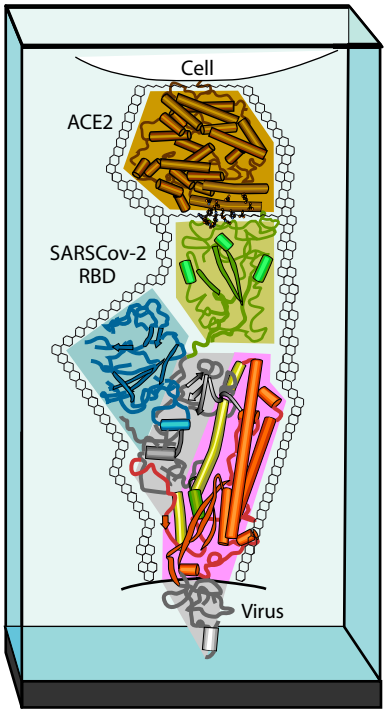


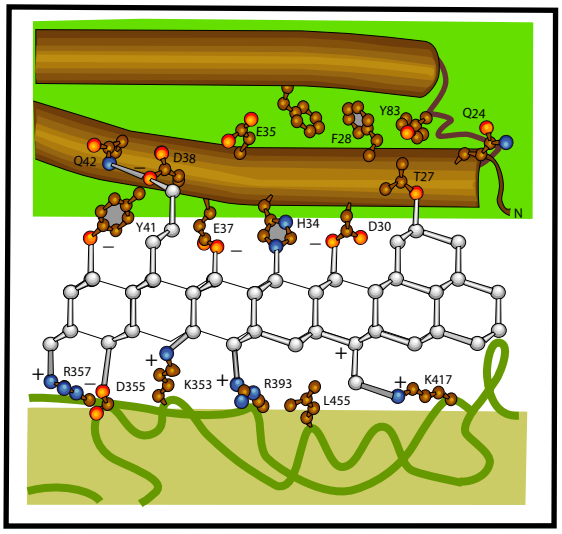
Although, only limited information is available on the detailed structure of the spike, it can be seen in this orientation that the outer surface, as well as some intersecting surfaces of the protein units, correspond to cubic hydration patterning.[3] This does not mean that the outer surface of the spike is covered completely by exposed polypeptides, but rather, that it reflects the hydration patterning which occurred in the formation of the anhydrous cores of the proteins. In fact, much of the outer surface is coated with polysaccharides to disrupt hydration order and increase stability and solubility. Peptides are exposed on binding surfaces.

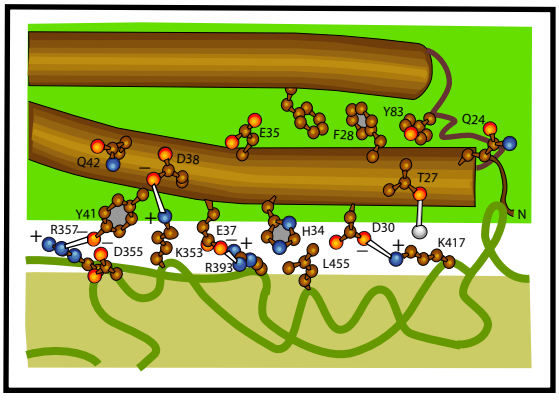
Again, as proposed in the TLH hypothesis,[3] both patterning and binding are believed to be directed and driven primarily by the extremely-rapid (10^{-11} second) formation of ice-like linear elements water molecules in cubic forms on lipid surfaces and between ions. Then, as attachments occur and ordered water molecules move back into the liquid state, energy is withdrawn from binding units and they move toward order. Propagation of cubic patterning is so rapid on outer surfaces, relative to molecular motion, that it is as if they are in a hydration cage with the quantized distance of 2.76 Angstroms between the water molecules (the same as in cubic ice).[4]

As illustrated above, the viral spike is composed of a number of separate proteins; each produced by RNA codes stored in the viral body. Once bound to surfacec of cells in the hoste's body, enzymes released from the virus dissolve the spike, permit the virus to enter the cell and use the cells machinery to produce more virus and destroy the cell. Now, let us look at the binding between the spike, the ACE2 enzyme and the cell.

Instead of binding directly to cells, the covid virus binds to blood-pressure-control ACE2-enzymes on surfaces of cells. Notice that the ACE2 enzyme is composed, almost entirely, of coils. Long helical coils in the lower protein provide linear strength to the spike, but central proteins are composed primarily of folded linear segments. Whether composed of coils or linear segments, the central cores of all protein units are anhydrous with the ordered water, which directed their formation no longer there.[3] The orientation of the ACE2 enzyme, as shown, is not quite the same as the spike, but it conforms with the same cubic patterning as the spike, with two coils at the bottom of the ACE2 unit, as shown below, providing the binding groups for the upper surface of the spike.[2]







As the viral spike approaches the lower surface of the ACE2 enzyme, as shown on the left, ice-like transient linear elements of hydration continually form between the oppositely-charged ions on the surfaces to draw them together in a quantized, coordinated manner. Notice that the peptides on the surface of the ACE2 enzyme are all relatively ridged and primarily anionic while those on the upper surface of the stem are cationic and attached to more mobile linear segments on the ends of lysine and arginine peptides with longer side-chains.

Prior to binding, cations on the upper surface of the spike most likely have more freedom to adopt alternate conformations than those attached to ACE2. However, as unstable ordered water leaves and moves spontaneously into the higher-energy liquid-bonding state, peptide bonding must become more-ordered and ridged, with loss of entropy. Although more accurate computer simulations will be required to provide validation of the interpretations given above, it appears that the TLH hypothesis provides a viable and rational interpretation of structure and process.

References

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