Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supporting Information

Frustration-Driven Allosteric Regulation and Signal Transmission in the SARS-CoV-2 Spike Omicron Trimer Structures: A Crosstalk of the Omicron Mutation Sites Allosterically Regulates Tradeoffs of Protein Stability and Conformational Adaptability

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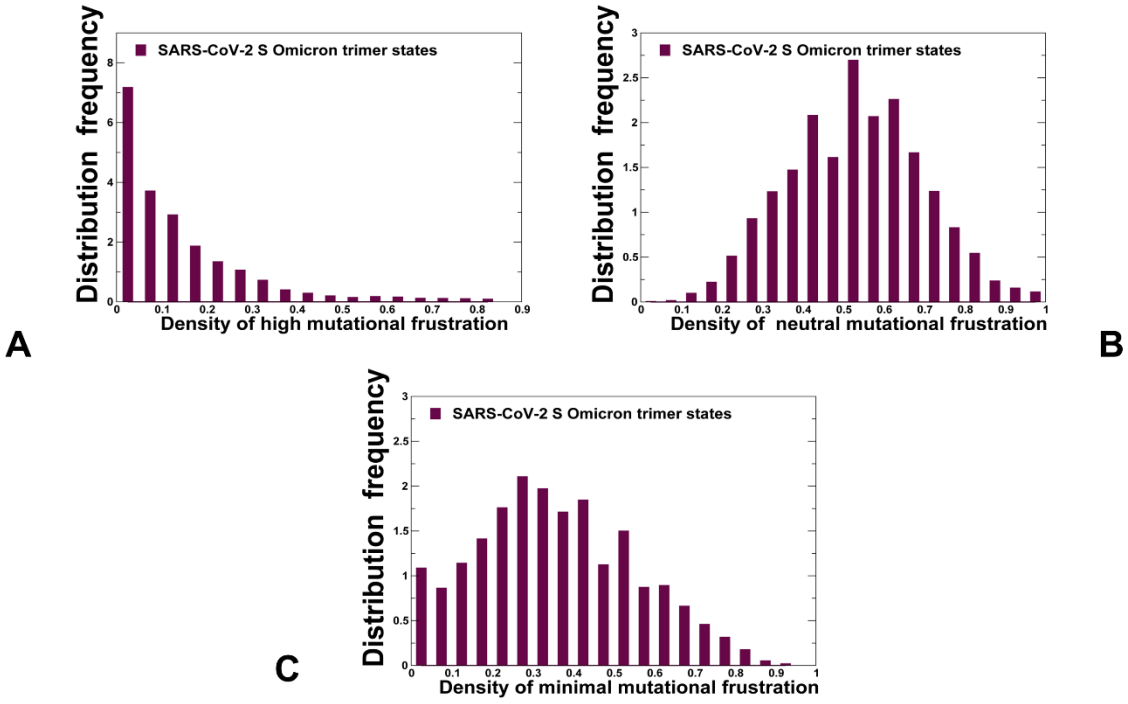

Figure S1. The distribution of local mutational frustration in the closed and open forms of the SARS-CoV-2 S Omicron structures. The relative density of highly frustrated contacts (A), neutrally frustrated contracts (B) and minimally frustrated contacts (C) in the S Omicron closed and open trimer structures. The distributions were constructed by averaging computations for the closed S Omicron trimer states (pdb ids 7TF8, 7WK2, and 7TNW) and open S Omicron trimers (pdb ids 7TEI, 7WK3, and 7TO4).

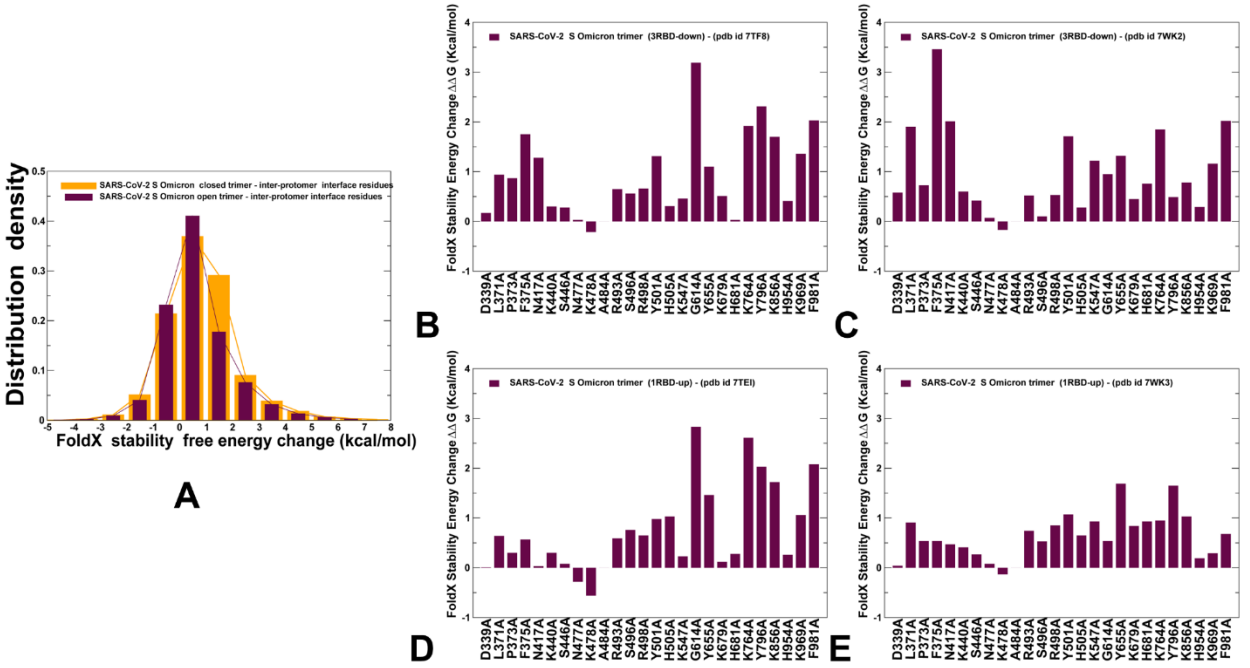

Figure S2. Mutational sensitivity analysis of the inter-protomer residues and alanine scanning of the Omicron sites in the S Omicron closed and open structures. (A) The distribution density of FoldX protein stability changes upon alanine mutations for the inter-protomer contact residues in the S Omicron structures. The stability change density obtained from alanine scanning of the closed S Omicron structures (pdb id 7TF8, 7WK2, 7TNW) is shown in orange bars, and the density obtained from mutational scanning of the 1RBD-up open S Omicron structures (pdb id 7TEI, 7WK3, 7TO4) is shown in maroon bars. The ensemble-based alanine scanning of the Omicron sites in the closed S Omicron structures pdb id 7TF8 (B) and pdb id 7WK2 (C). The ensemble-based alanine scanning of the Omicron sites in the open S Omicron structures pdb id 7TEI (D) and pdb id 7WK3 (E).The protein stability changes are shown in maroon-colored filled bars.

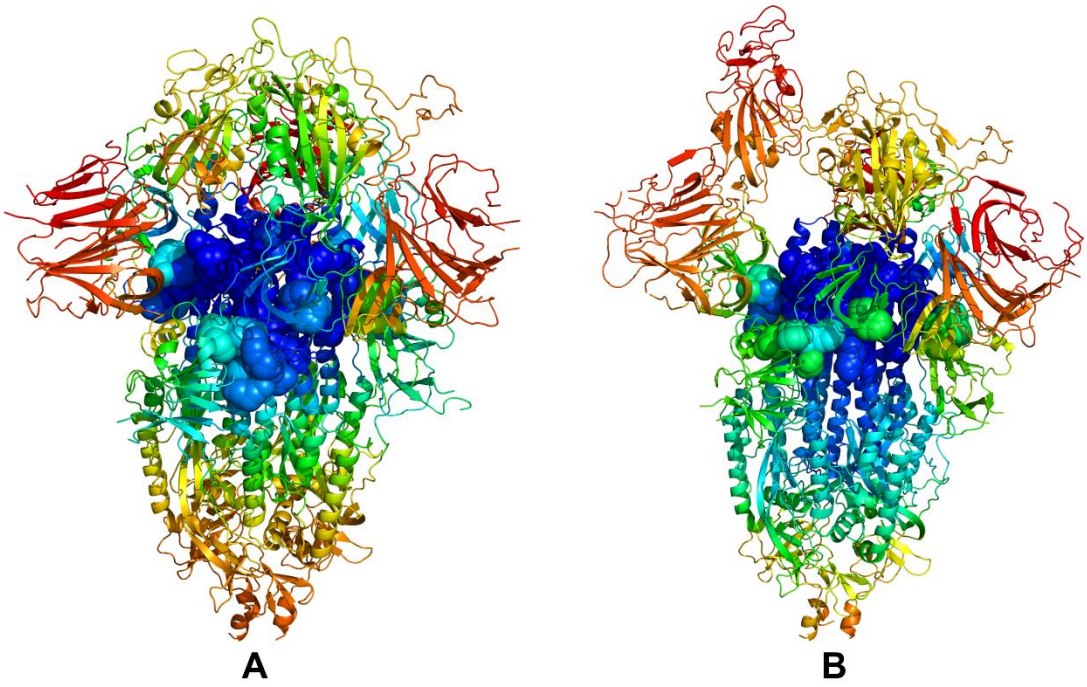

Figure S3. Structural mapping of local interaction clusters anchored by the hinge sites F318, A570, T572, F592, D614G, N764K, N856K, Q954H, and N969K. The structural mapping of the slow mode mobility profiles projected onto the cryo-EM structure of the closed S Omicron trimer (pdb id 7TF8) (A) and the cryo-EM structure of the open S Omicron trimer (pdb id 7TEI). The collective dynamics maps are colored according based on the rigidity-flexibility scale with the most rigid regions colored in blue and most flexible regions colored in red.

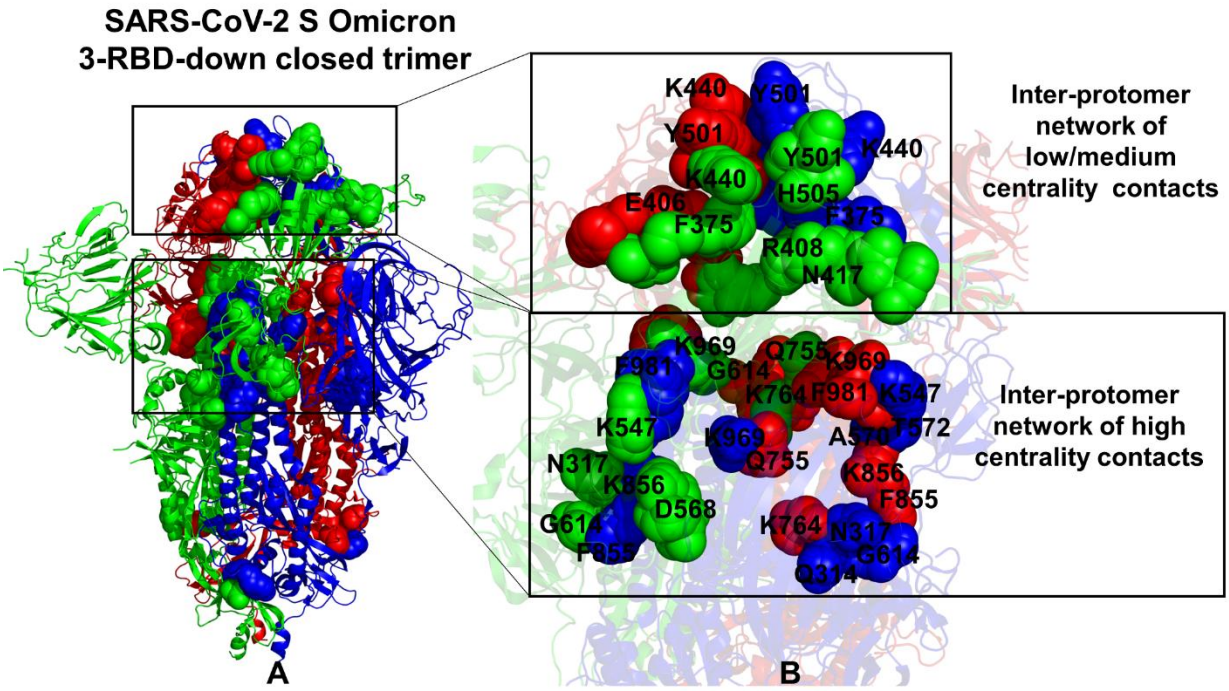

Figure S4. Structural mapping of the inter-protomer network bridges in the 3-RBD down closed S Omicron trimer structures (A) The overall view of the major inter-protomer network bridges. The closed S Omicron trimer is shown in ribbons with the protomers A,B,C in green, red and blue respectively. The inter-protomer bridges are shown in spheres. (B) A close up of the inter-protomer RBD-RBD network is formed by low centrality residues. (top of panel B). The inter-protomer network of high centrality bridging sites (bottom of panel B). The residues that form the inter-protomer network are shown in spheres colored according to the respective protomer and annotated.

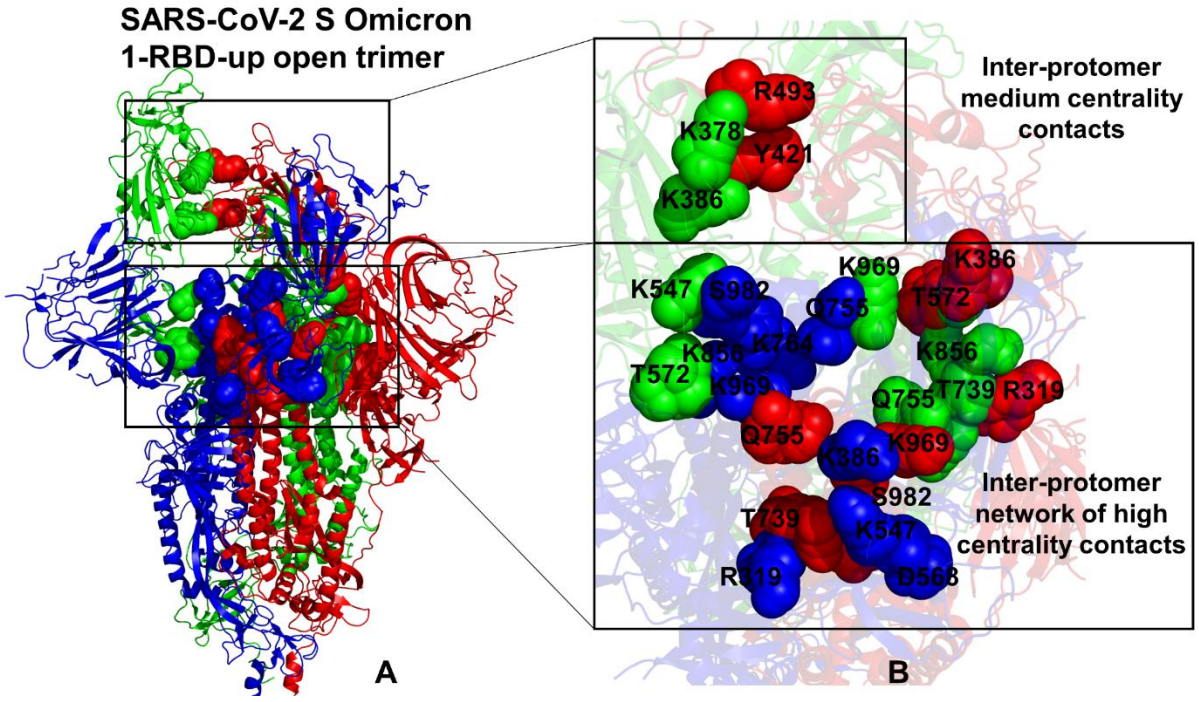

Figure S5. Structural mapping of the inter-protomer network bridges in the 1RBD-up open S Omicron trimer structures (A) The overall view of the major inter-protomer network bridges. The open S Omicron trimer is shown in ribbons with the protomers A,B,C in green, red and blue respectively. The inter-protomer bridges are shown in spheres. (B) A close up of the inter-protomer RBD contacts is formed by low centrality residues (top of panel B). The inter-protomer network of high centrality bridging sites(bottom of panel B). The residues that form the inter-protomer network are shown in spheres colored according to the respective protomer and annotated.