

Supplementary Information

Interface design of SARS-CoV-2 symmetrical nsp7 dimer and machine learning-guided nsp7 sequence prediction reveals physicochemical properties and hotspots for nsp7 stability, adaptation, and therapeutic design

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Table S1. Sequences of ML-predicted nsp7 affinity-enhancing designs used in Table 7 of the main manuscript.

S. No.	ML-predicted nsp7 affinity enhancing design sequences
1.	STMAEVQRISFLMFLVLKQLRVDATPELGAQCLQLRIDQLAKDTTEACQKTLISLVS SISM
2.	STMAEVRRASIESITVLLQLRVKTTPELGAQCLQLNIDIMLAKDTTEACAKTLISLVS MVSM
3.	SQMAEVIWASFLVSLVLKQLRVDATPELGAQCDQLQKDISLAKDTTEACQKLLSLVS VSVSM
4.	STMAEVRRASEESSTVLRQLRVDTTPELGAQCAQLQKDIQLAKDTTEACQKTLISLIS VSFSM

Table S2. Sequences of ML-predicted nsp7 affinity-reducing designs used in Table 8 of the main manuscript.

S. No.	ML-predicted nsp7 affinity reducing design sequences
1.	STMTEVIRASIIISFLVLLQLRVQATPELLAQCEQLNKDIILAKDTTEASQK LISLVSQSSM
2.	STMTAVIRASILVFLVLLQLRVDTTPELGAQCLQLNIDIILAKDTTEASQK LASLVSQMSM
3.	SQMAEVQWASFIILVLLQLRVKATPELGAQCLQLNKDIILAKDTTEACQ KTLSSSVSFSM
4.	STMTEVIRISILSFLVLKQLRVDTTPELGAQCEQLNKDIVLAKDTTEASQ KTLSSSVSMSM

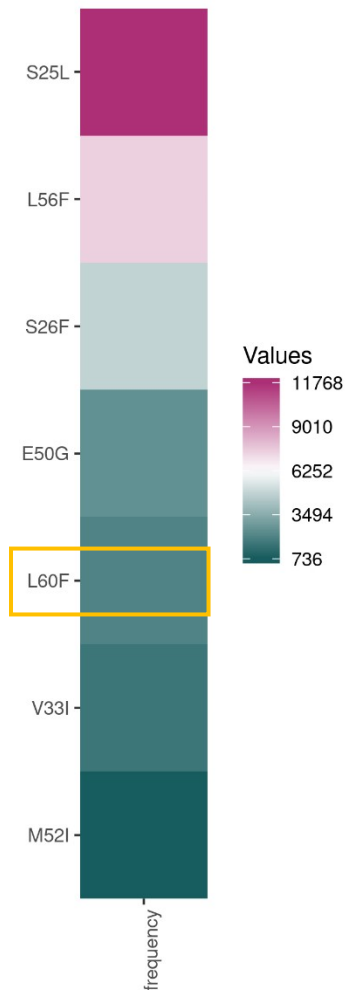


Figure S1. The Heat map displaying nsp7 mutations and their frequencies at the dimeric nsp7 interface, derived from the CoV-GLUE database. The SARS-CoV-2 nsp7 mutations derived from the CoV-GLUE database are shown. In this illustration, the frequencies of the mutations among COVID-19 patients ranging from low to high numbers, are represented using pine green-to-white-to-dark pink colours. The mutations that strengthened the dimeric nsp7 and that are derived from the CPD-approach are represented with a box adjacent to the mutants. 1 mutation out of 7 (with MinProp cut-off of 0.0001) was predicted to be adaptive and positively selected to form stable nsp7 dimers in our design computations, thereby resulting in ~14.28% correlation and matching with the clinically available data.

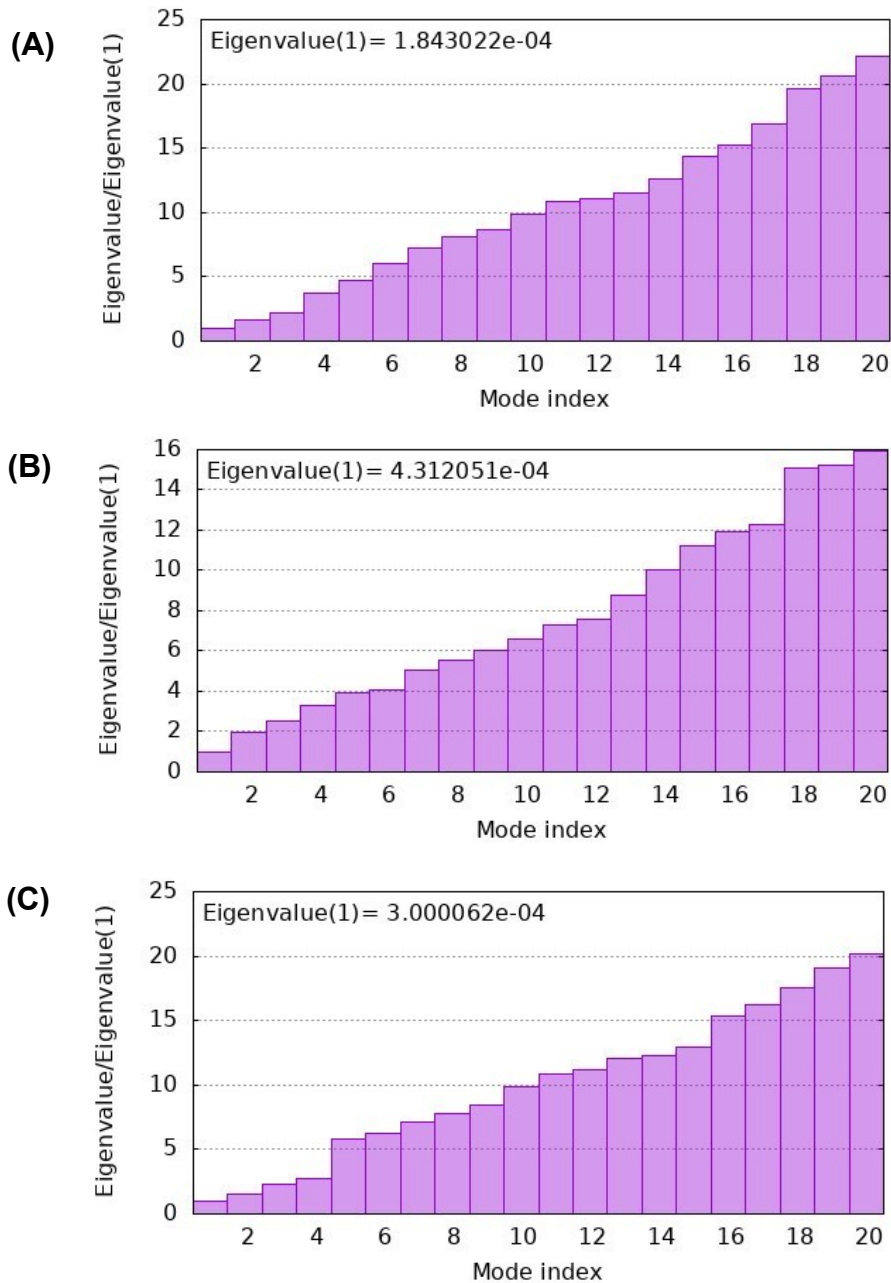


Figure S2. Eigenvalue plots of dimeric structures of wild-type nsp7, affinity-enhancing, and affinity-reducing design are shown obtained from the Normal Mode Analysis (NMA) conducted via the iMODS server. Plots (A to C) compare eigenvalues versus the mode index for the dimeric structures of wild-type nsp7, affinity-enhancing design, and affinity-reducing design, respectively.