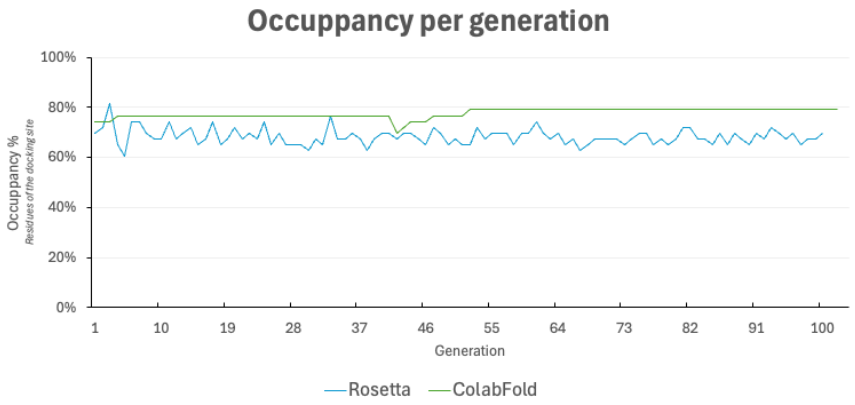
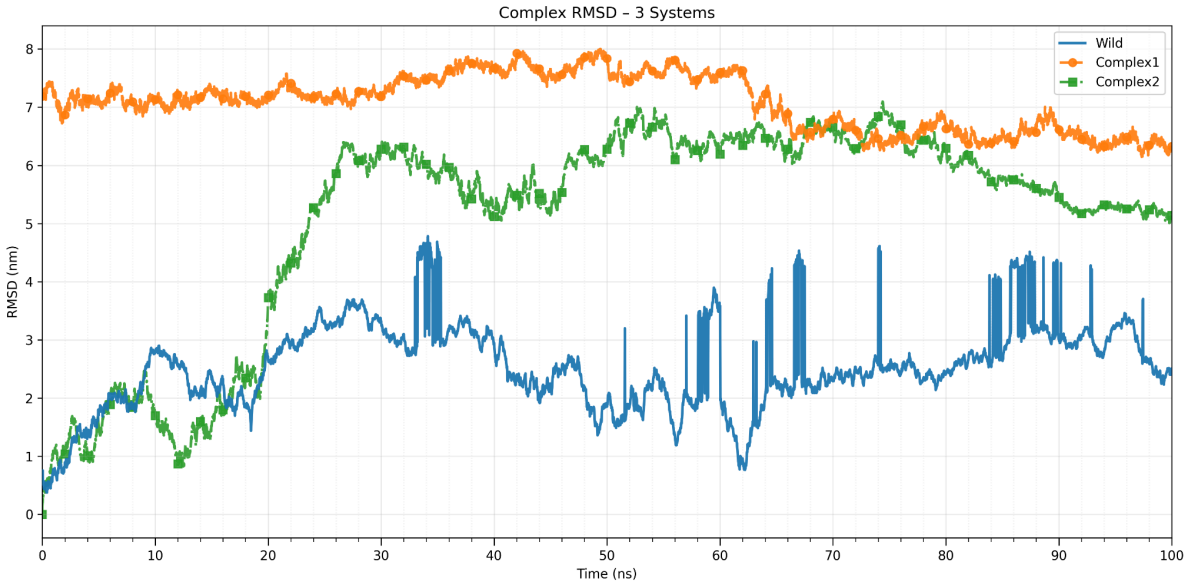
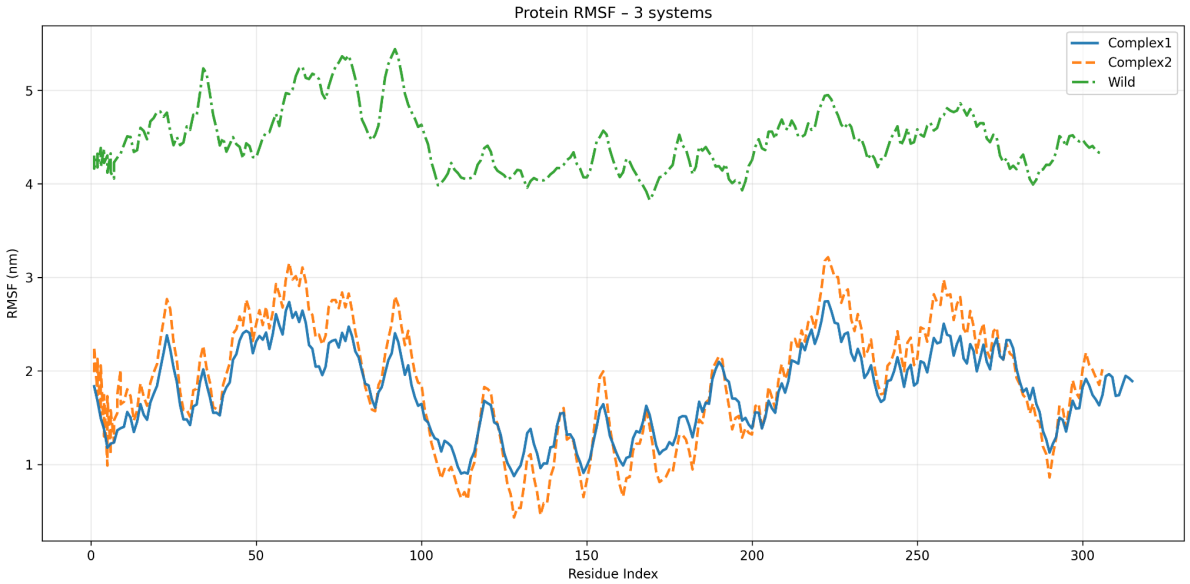
Supplementary material



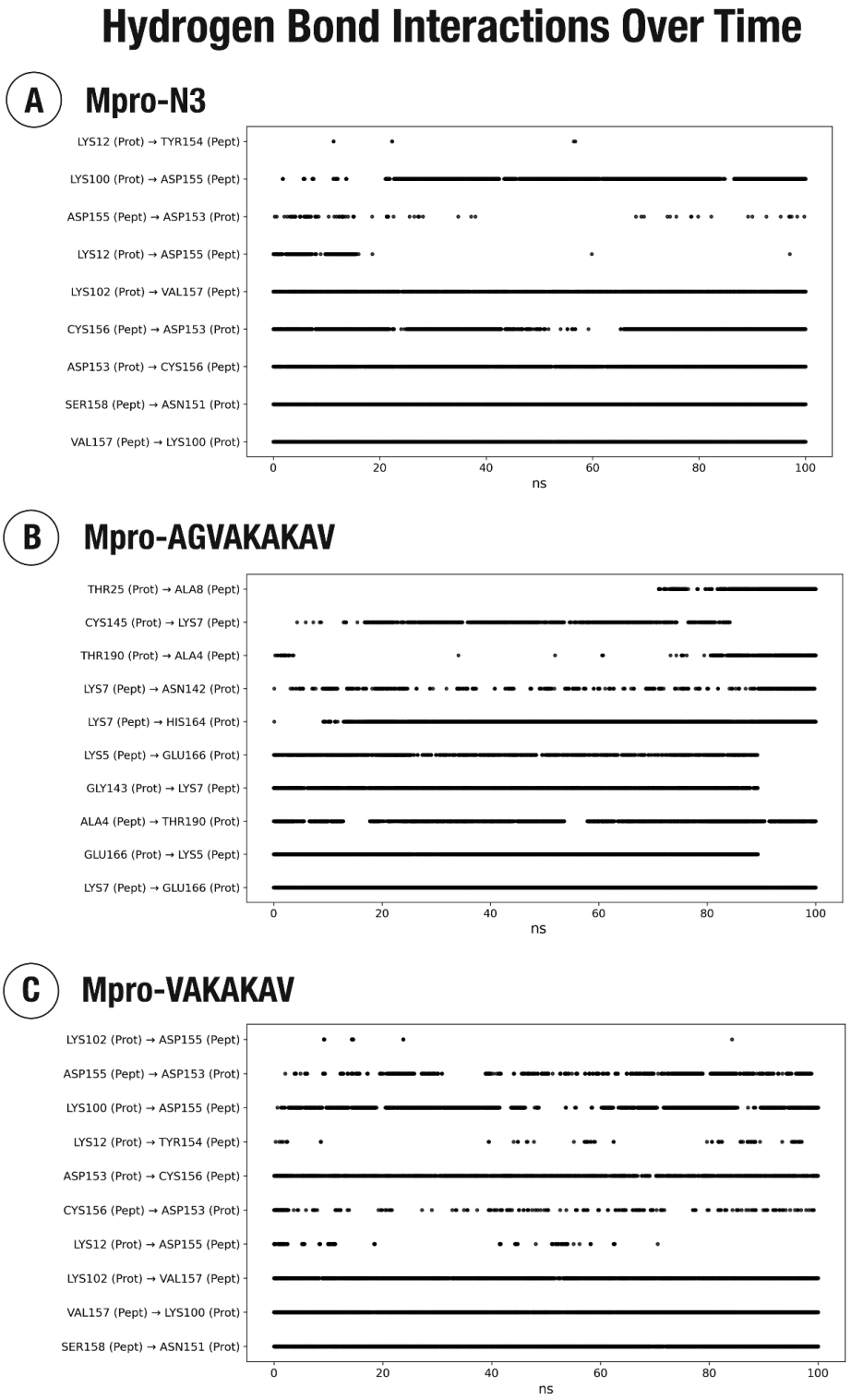
Supplementary Figure S1. Occupancy obtained by the best peptide of each of the 100 generations.



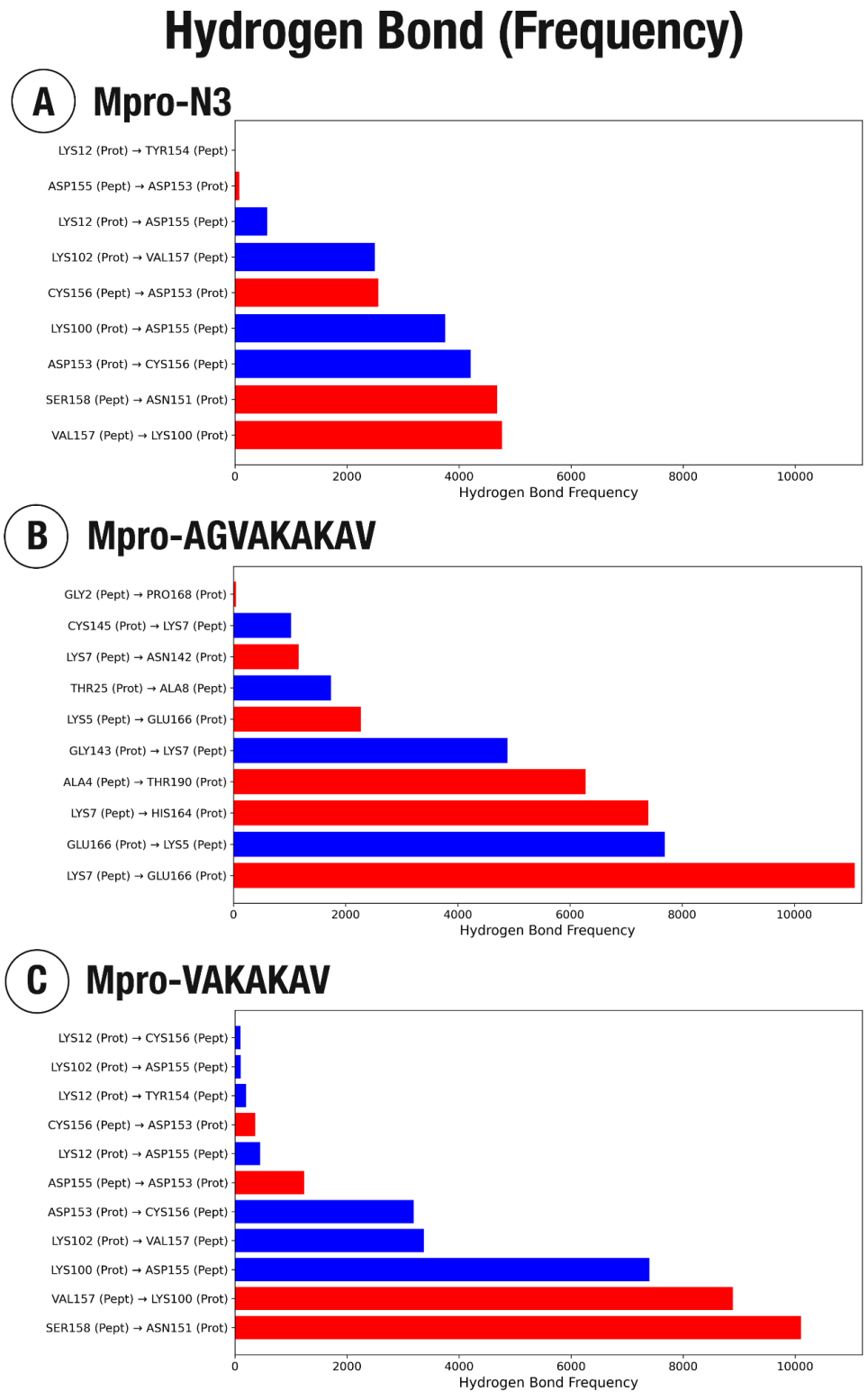
Supplementary Figure S2. RMSD of the three simulated systems – Mpro-N3 (Wild), Mpro-AGVAKAKAV (Complex1), and Mpro-VAKAKAV (Complex2) – over 100 ns of molecular dynamics.



Supplementary Figure S3. RMSF of Mpro in complexes with different ligands – Mpro-N3 (Wild), Complex1 (Mpro-AGVAKAKAV), and Complex2 (Mpro-VAKAKAV) – over 100 ns of molecular dynamics simulation.



Supplementary Figure S4. Hydrogen bonding interactions over 100 ns of molecular dynamics of MPRO with different ligands. Each point represents a frame in which the donor→acceptor pair meets the geometric H-bond criterion (distance H…A ≤ 3.5 Å; angle D–H···A ≥ 135°). Dense bands indicate persistent (high occupancy) bonds, while gaps indicate intermittent contacts. The labels on the y-axis show the binding direction (Protein → Peptide or Peptide → Protein).



Supplementary Figure S5. Cumulative hydrogen bond frequencies across 100 ns molecular dynamics simulations of the reference system (Mpro-N3), Mpro-AGVAKAKAV, and Mpro-VAKAKAV. Interactions directed from Protein to Peptide are represented in blue, while those from Peptide to Protein are shown in red.