

## SUPPLEMENTARY MATERIALS

### **Conformational Plasticity-Rigidity Axis of the Coagulation Factor VII Zymogen Elucidated by Atomistic Simulations of the N-Terminally Truncated Factor VIIa Protease Domain**

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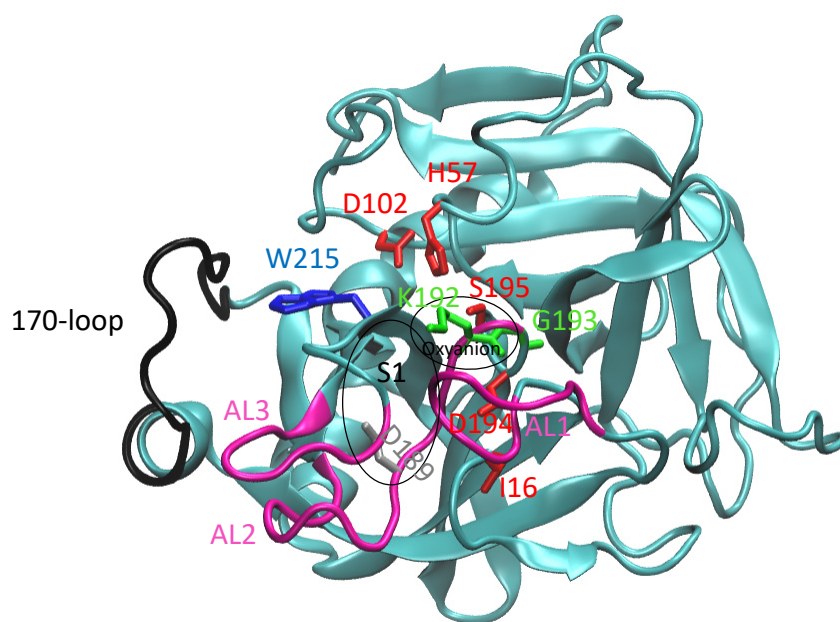
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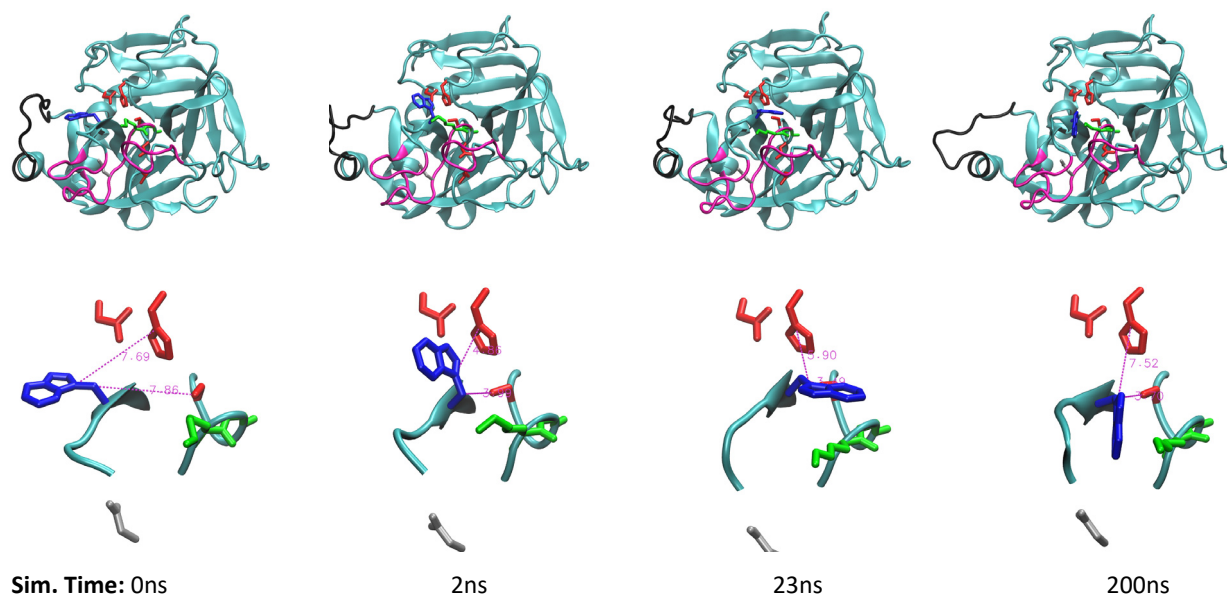
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$C_{\alpha}$ – RMSD (Å)											
$\langle \text{FVIIa} \rangle_{\text{MD}}$	0										
$\langle \text{FVIIa-desIVG} \rangle_{\text{MD}}$	0.936	0									
$\langle \text{FVIIa}_{\text{VYT}} \rangle_{\text{MD}}$	1.860	1.955	0								
$\langle \text{FVIIa}_{\text{VYT}}\text{-desIVG} \rangle_{\text{MD}}$	1.962	1.891	0.544	0							
$\langle \text{Trypsin} \rangle_{\text{MD}}$	2.405	2.530	2.328	2.435	0						
$\langle \text{Trypsin-desIVG} \rangle_{\text{MD}}$	2.495	2.491	2.368	2.368	0.775	0					
$\langle \text{Trypsinogen} \rangle_{\text{MD}}$	3.111	3.003	2.578	2.410	1.276	0.637	0				
$\text{FVIIa}^{\text{Xtal}}$	2.198	2.320	1.483	1.628	2.860	2.953	3.104	0			
$\text{FVIIa}_{\text{VYT}}^{\text{Xtal}}$	1.937	2.118	0.802	1.063	2.447	2.548	2.762	1.341	0		
$\text{Trypsin}^{\text{Xtal}}$	2.980	3.128	2.371	2.492	0.735	1.186	1.464	2.798	2.404	0	
$\text{Trypsinogen}^{\text{Xtal}}$	3.225	3.146	2.678	2.519	1.437	1.210	1.288	3.072	2.738	1.290	0

**Table S1:** RMSD values from MD trajectories are reported with reference to the averaged structure over the whole trajectory. RMSD is calculated by the align command in PyMOL without outlier rejection.

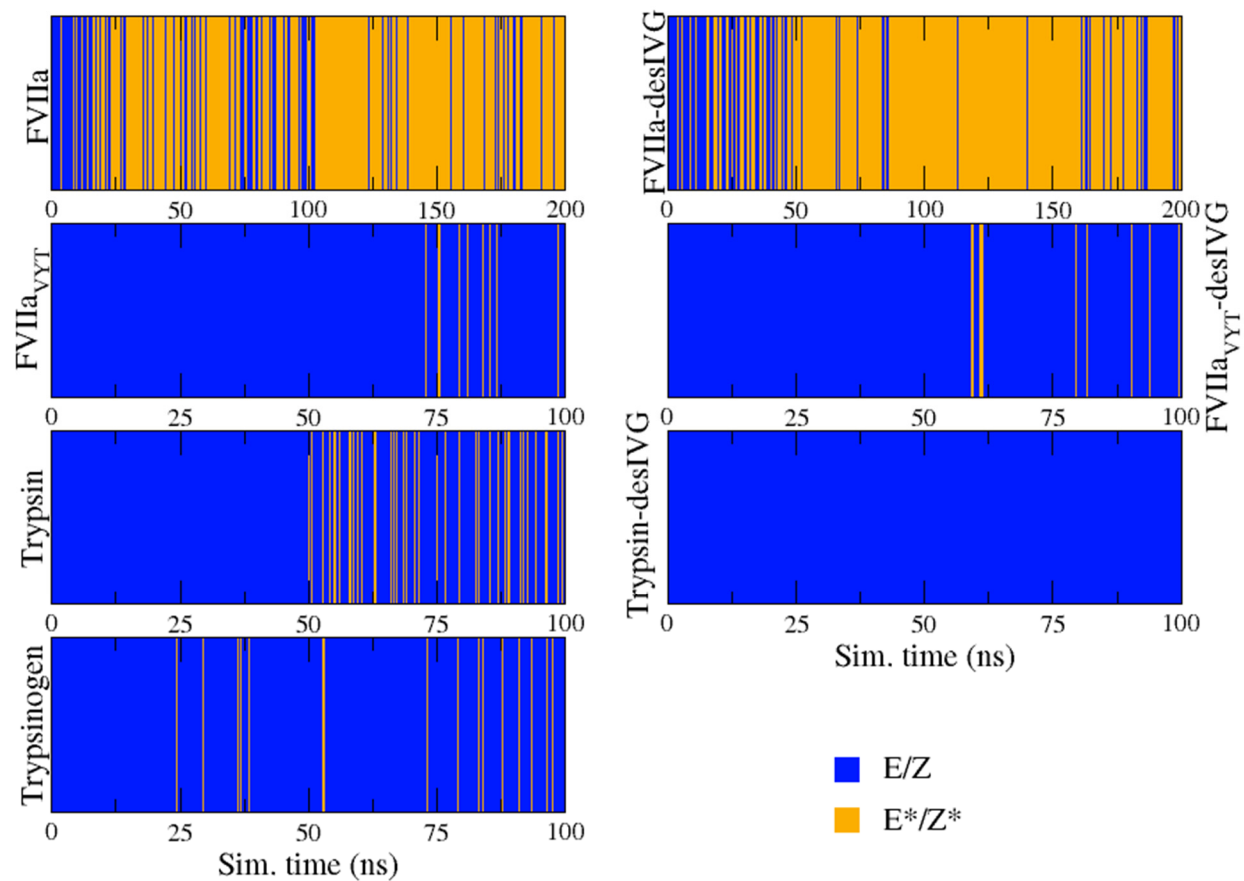


**Figure S1:** FVIIa (PDB ID: 1dan\_H) shown as ribbon diagram with certain key loops (170-loop, AL1-3) and amino acids marked with colored labels. The active site triad consists of D102, H57 and S195 (red). The oxyanion hole consists of K192 and G193 (green). The E/Z-E\*/Z\* conformation is determined by W215 through its distance to H57. The S1 pocket is indicated by the gray circle with D189 placed at the bottom of the pocket.

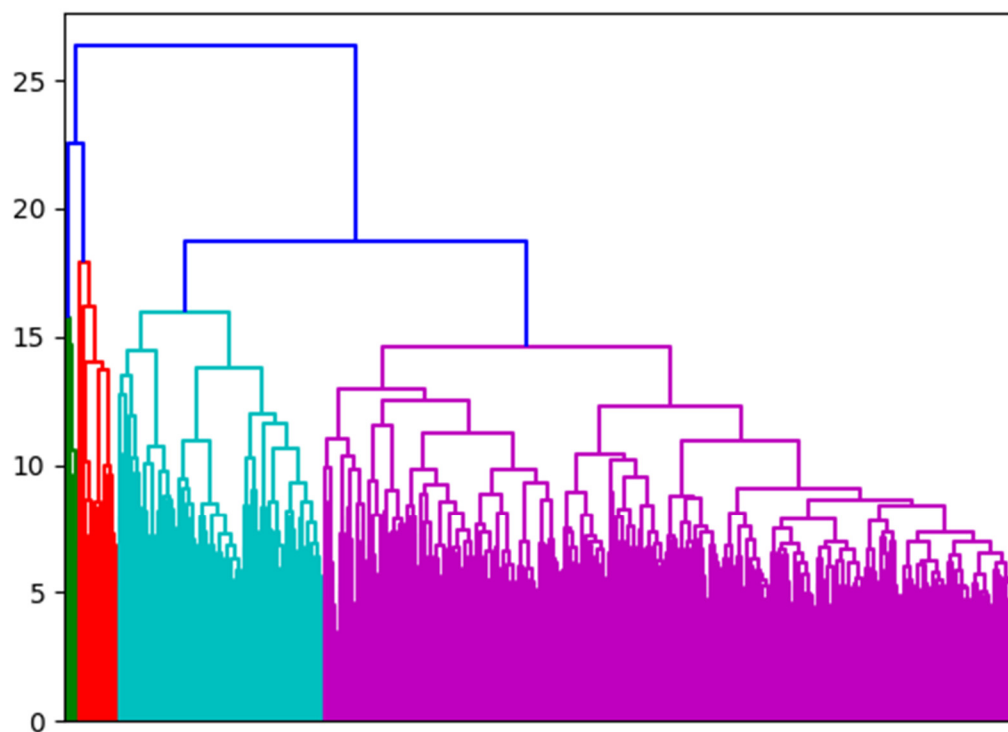


**Figure S2:** Structure of FVIIa (top panels) and a closeup view of the region determining the E/Z-E\*/Z\* conformation (bottom panels) at different stages during the simulation. The graphical details including coloring are consistent with the definition shown in Figure S2.

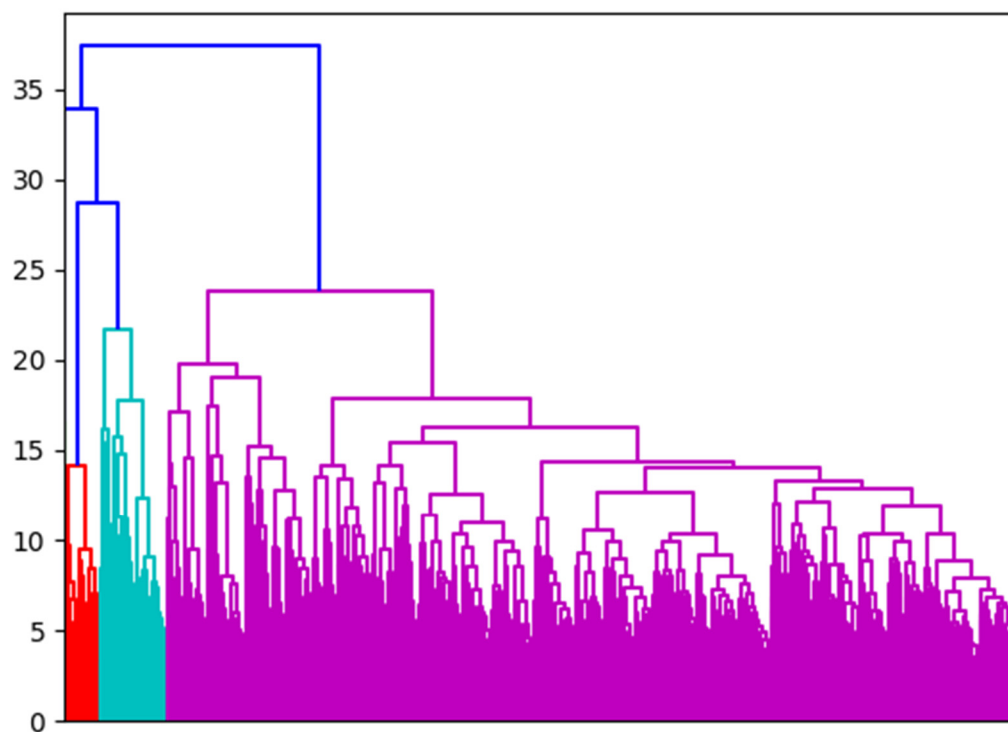




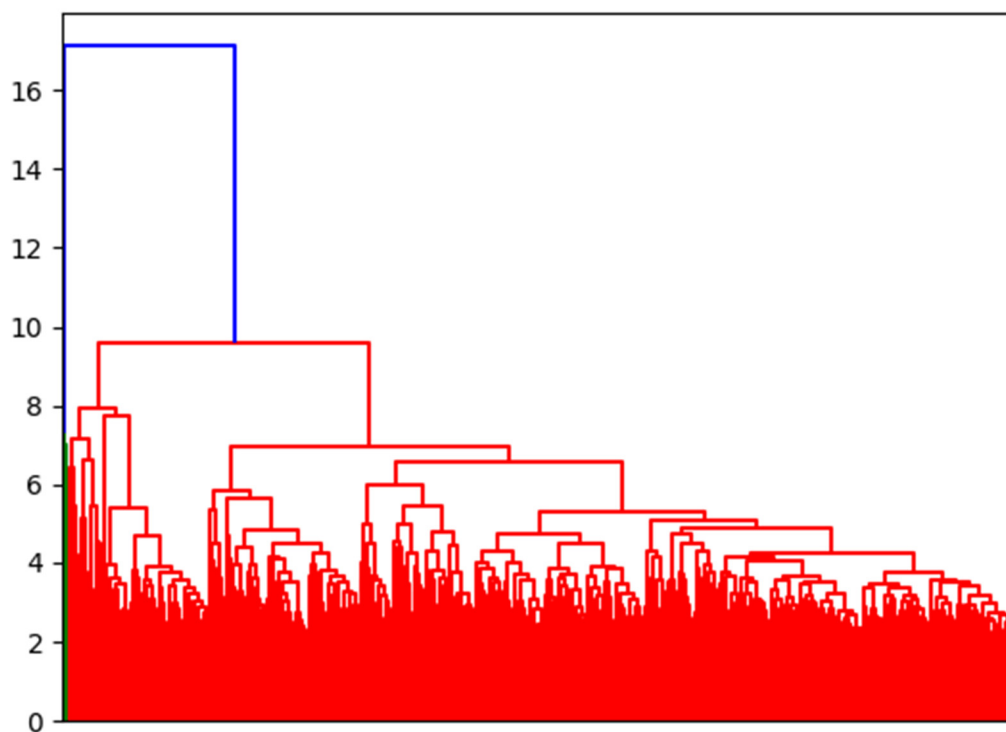
**Figure S3:** Time evolution of E/Z-E\*/Z\* conformational transitions during the simulations.



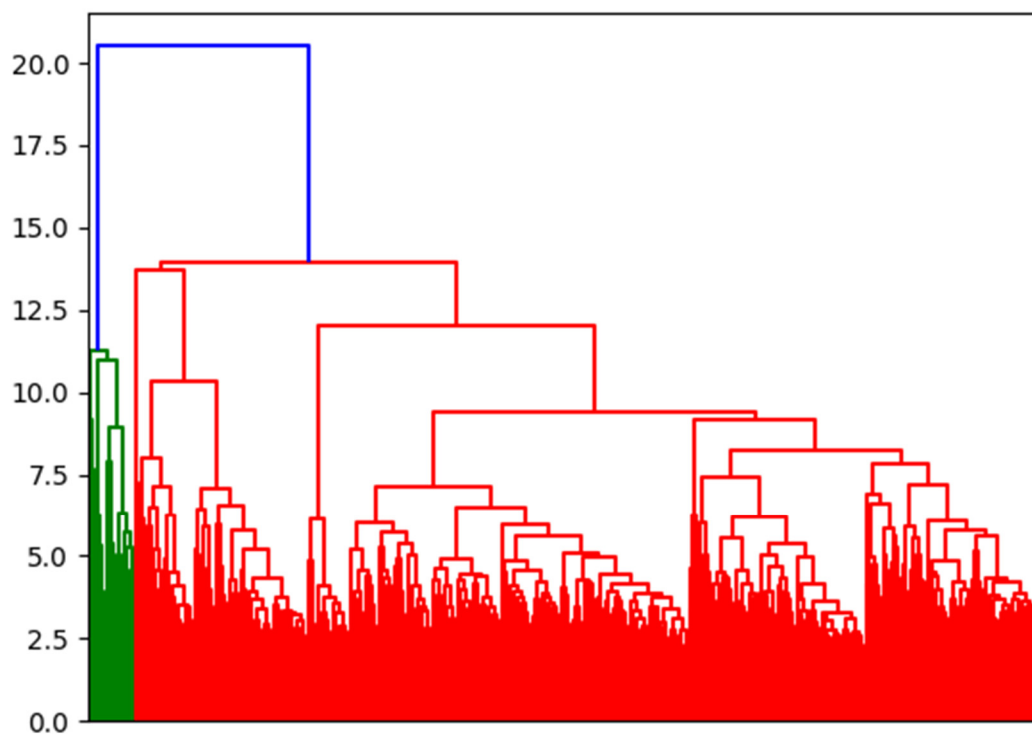
**Figure S4:** Dendrogram of RMSD-based hierarchical clusters from the simulated ensemble of FVIIa. Agglomeration is performed using the average/UPGMA linkage approach.



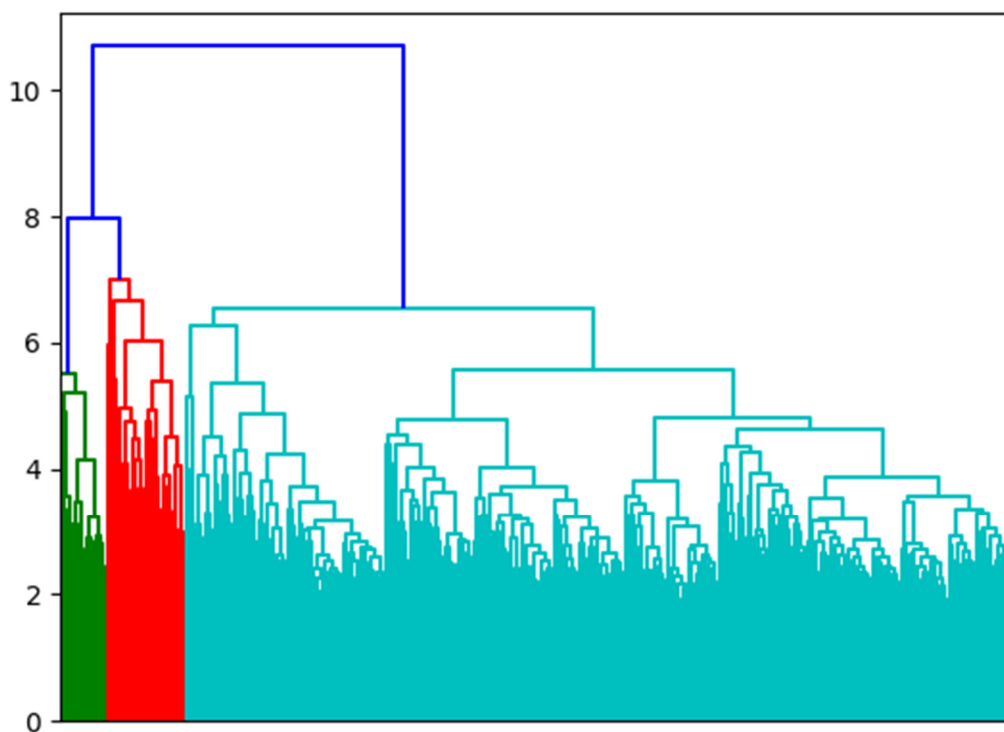
**Figure S5:** Dendrogram of RMSD-based hierarchical clusters from the simulated ensemble of FVIIa-desIVG. Agglomeration is performed using the average/UPGMA linkage approach.



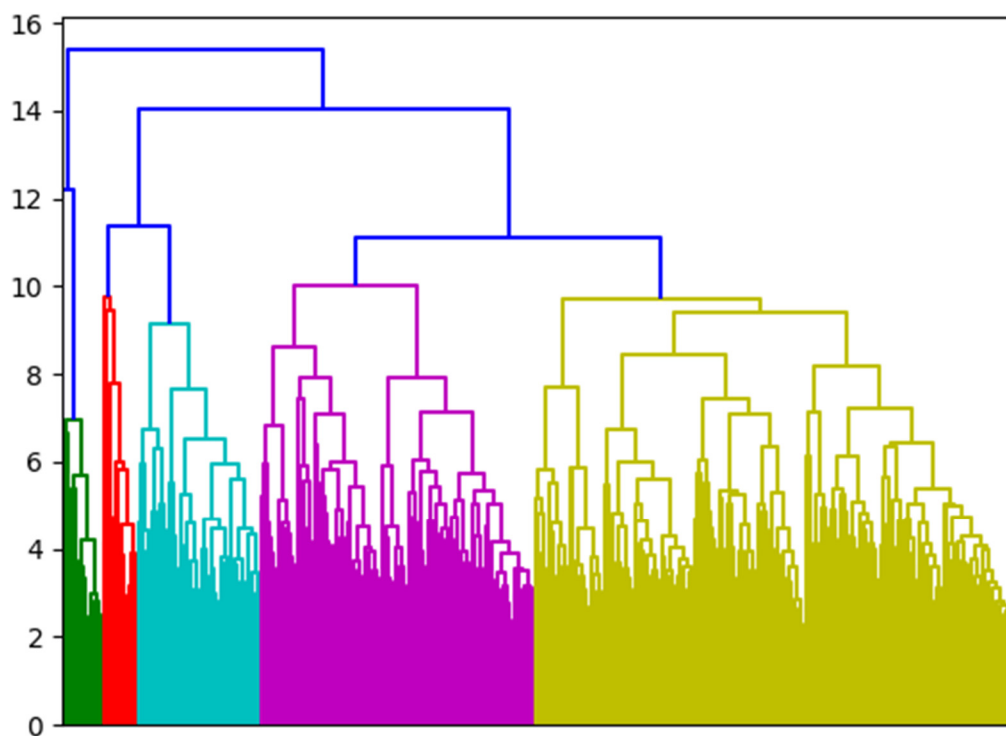
**Figure S6:** Dendrogram of RMSD-based hierarchical clusters from the simulated ensemble of FVIIa<sub>VYT</sub>. Agglomeration is performed using the average/UPGMA linkage approach.



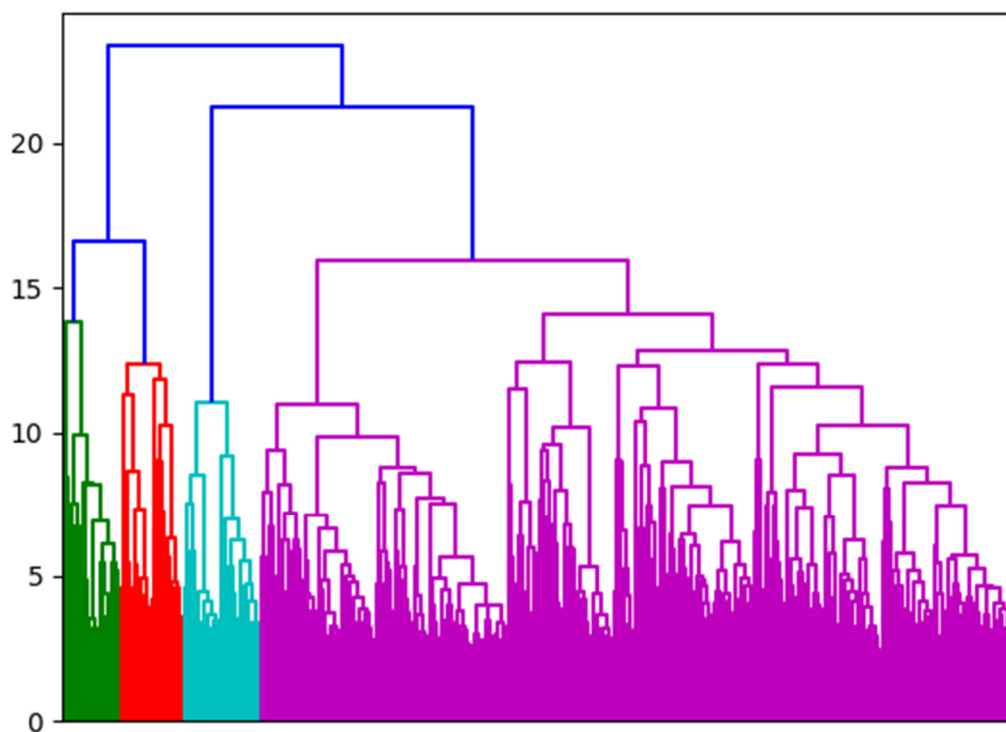
**Figure S7:** Dendrogram of RMSD-based hierarchical clusters from the simulated ensemble of FVIIa<sub>VYT</sub>-desIVG. Agglomeration is performed using the average/UPGMA linkage approach.



**Figure S8:** Dendrogram of RMSD-based hierarchical clusters from the simulated ensemble of trypsin. Agglomeration is performed using the average/UPGMA linkage approach.

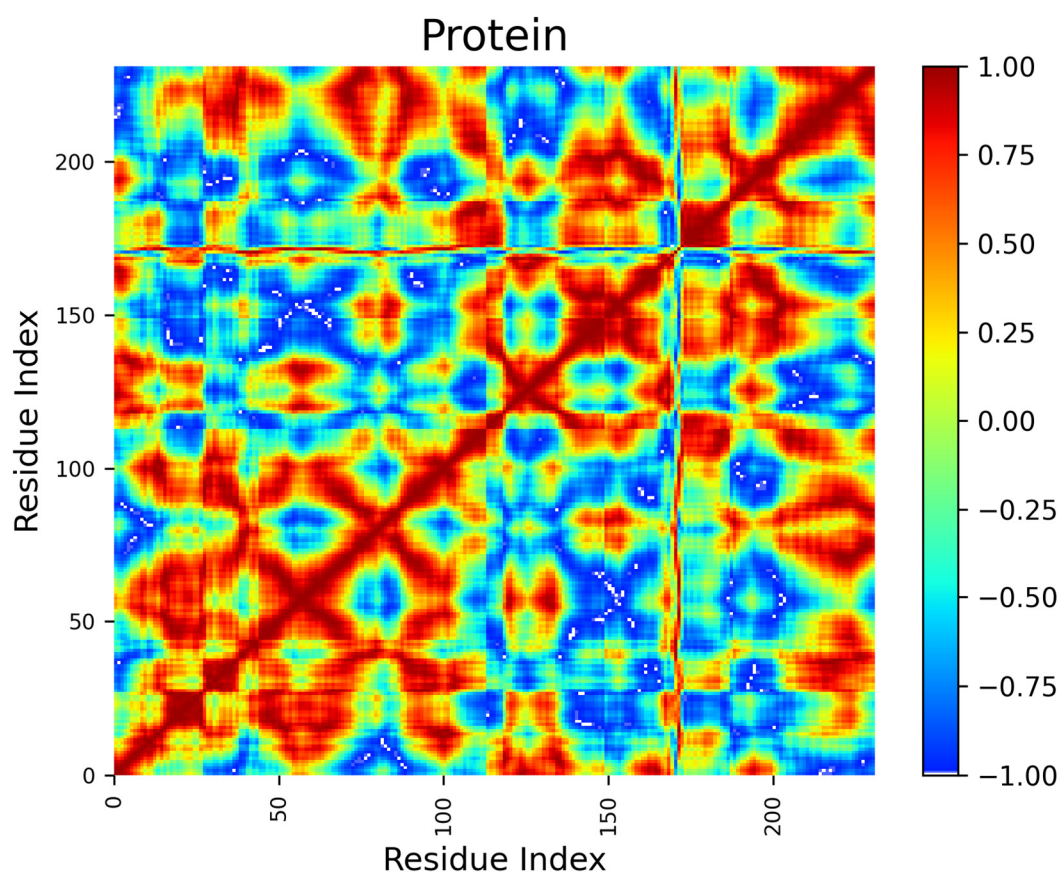


**Figure S9:** Dendrogram of RMSD-based hierarchical clusters from the simulated ensemble of trypsin-desIVG. Agglomeration is performed using the average/UPGMA linkage approach.

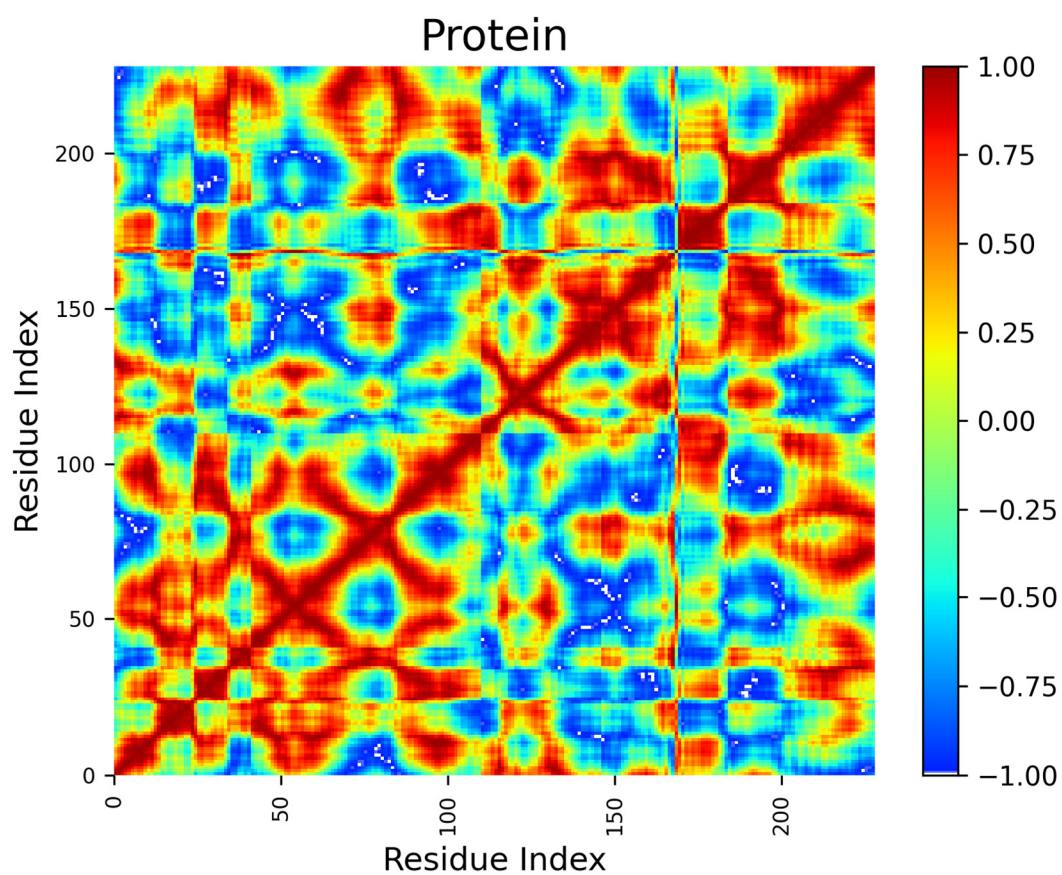


**Figure S10:** Dendrogram of RMSD-based hierarchical clusters from the simulated ensemble of trypsinogen. Agglomeration is performed using the average/UPGMA linkage approach.

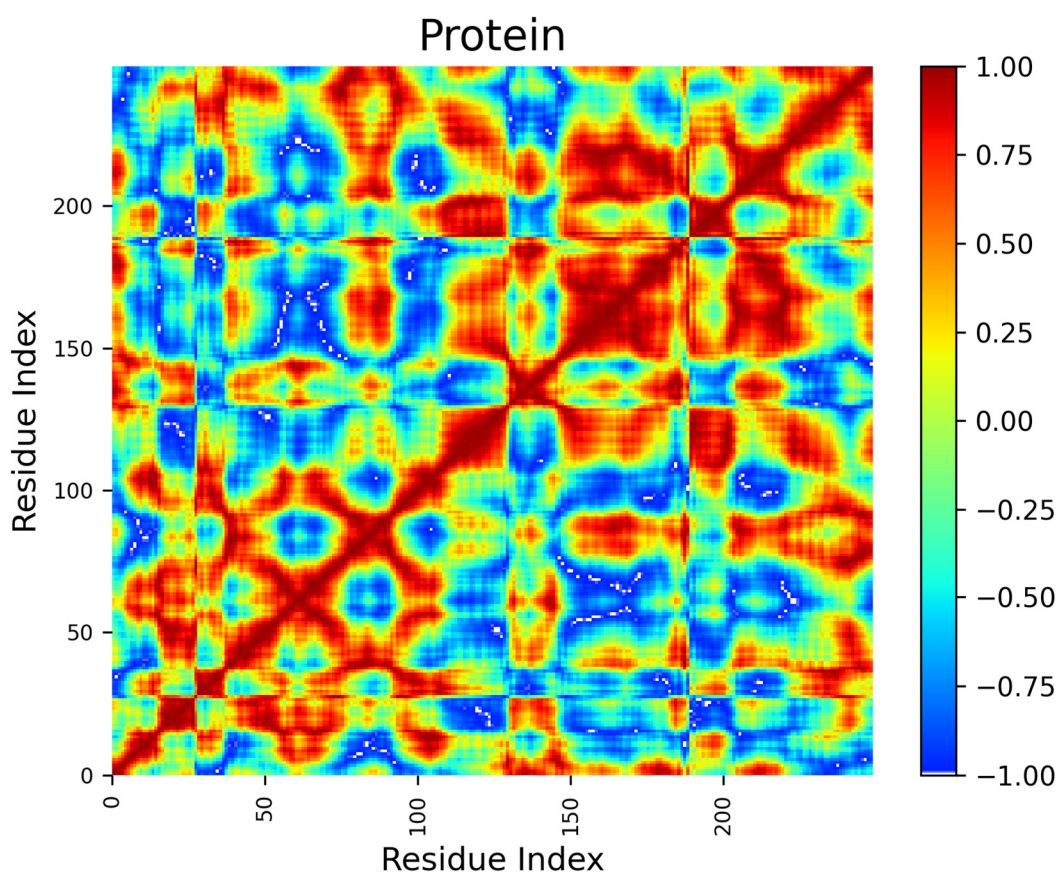




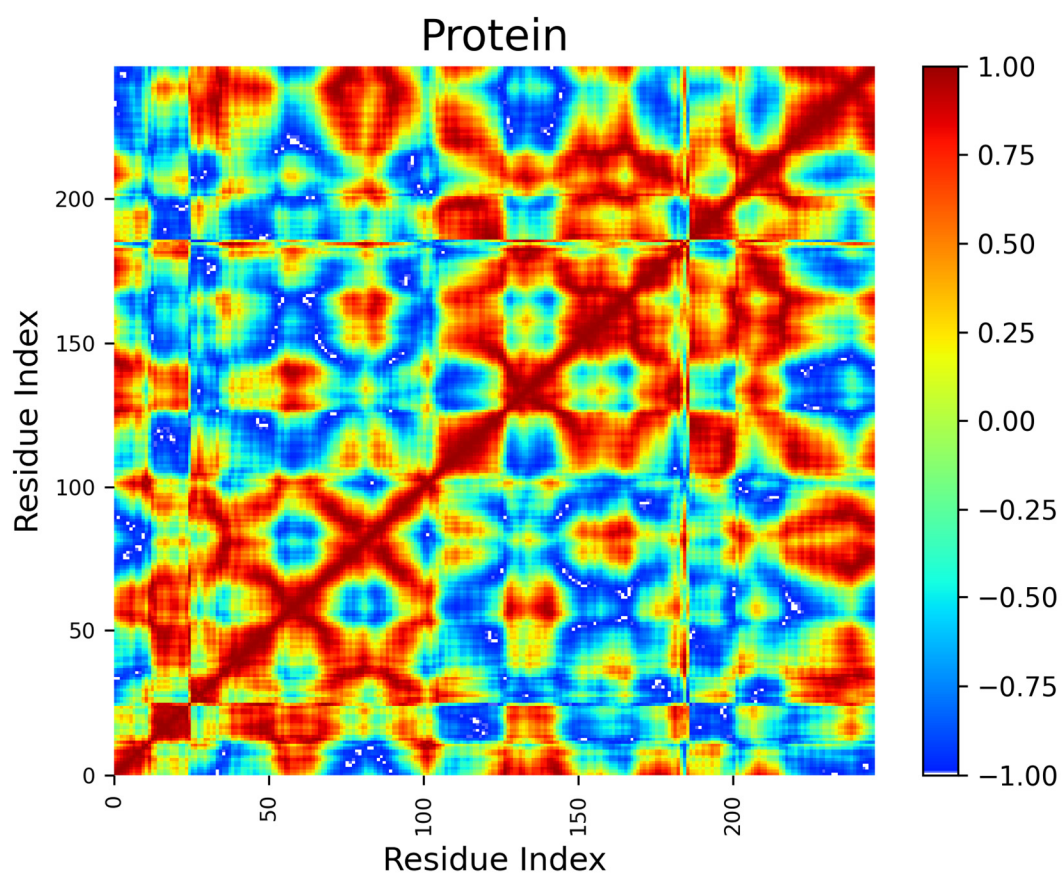
**Figure S11:** Heatmap of per-residue dynamic cross-correlations over the simulated trajectory of FVIIa.



**Figure S12:** Heatmap of per-residue dynamic cross-correlations over the simulated trajectory of FVIIa-desIVG.

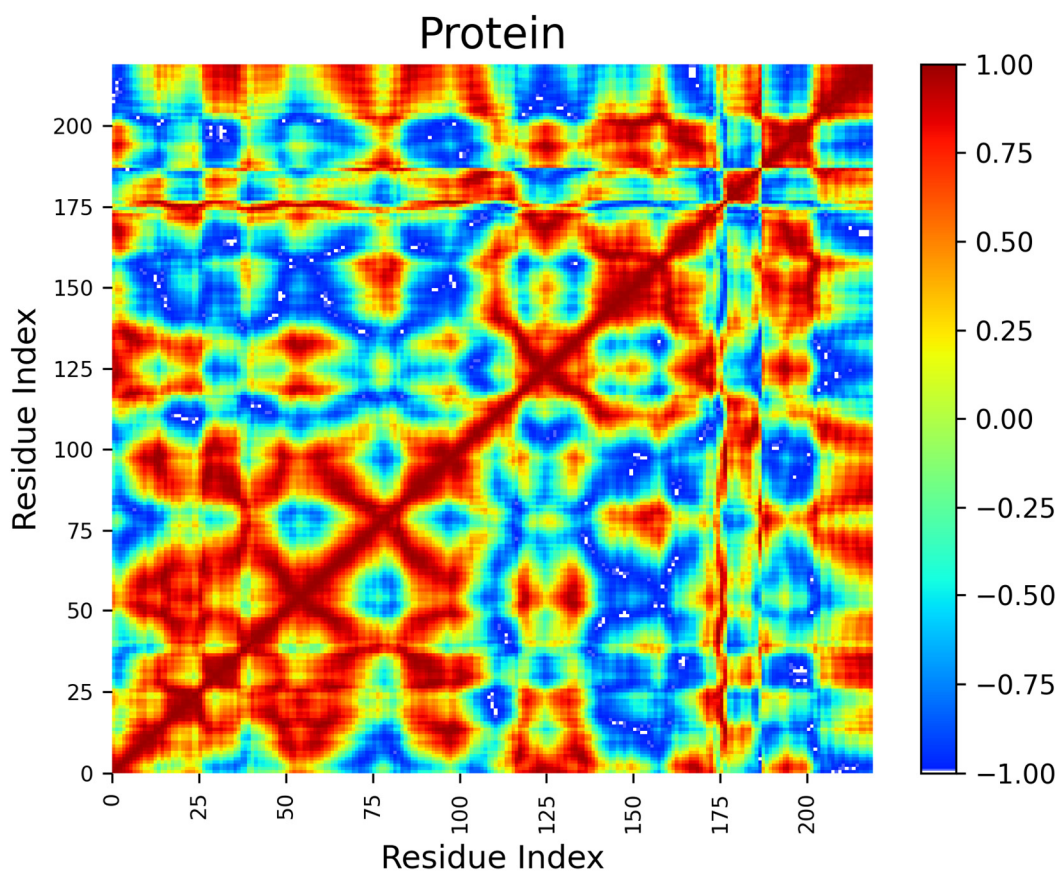


**Figure S13:** Heatmap of per-residue dynamic cross-correlations over the simulated trajectory of FVIIa<sub>vyt</sub>.

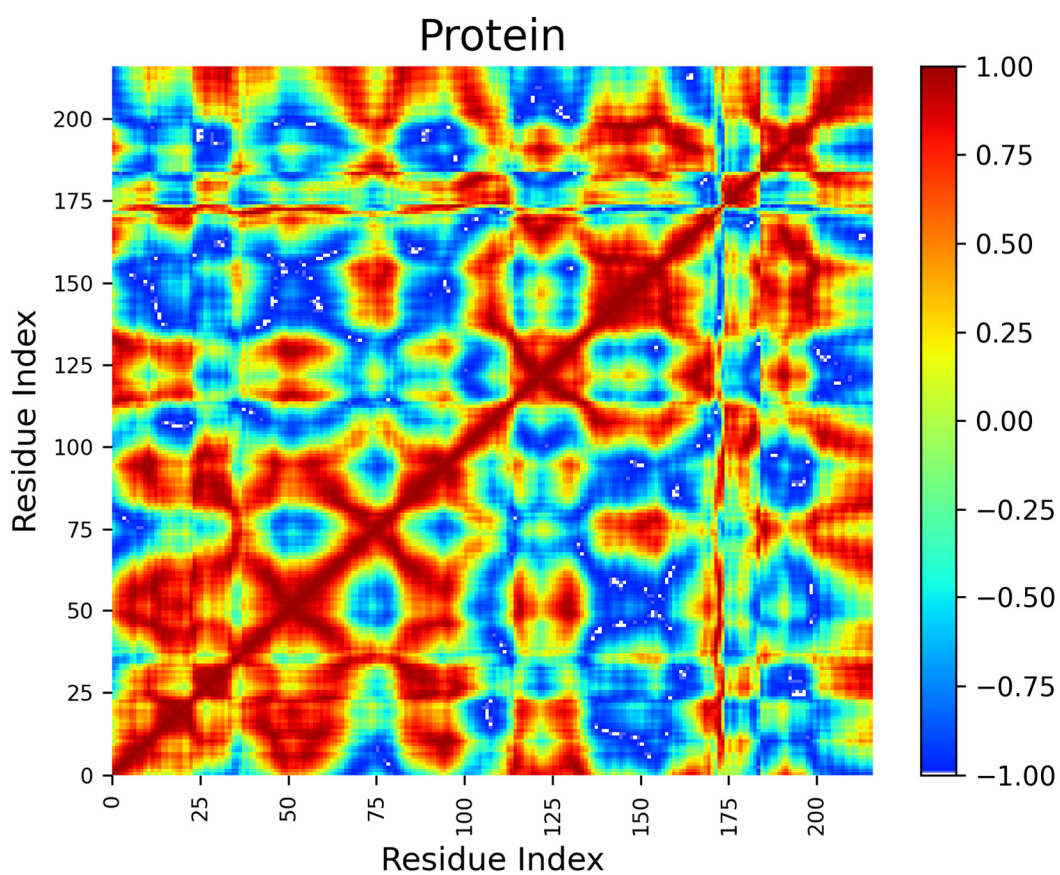


**Figure S14:** Heatmap of per-residue dynamic cross-correlations over the simulated trajectory of FVIIa<sub>VYT</sub>-desIVG.

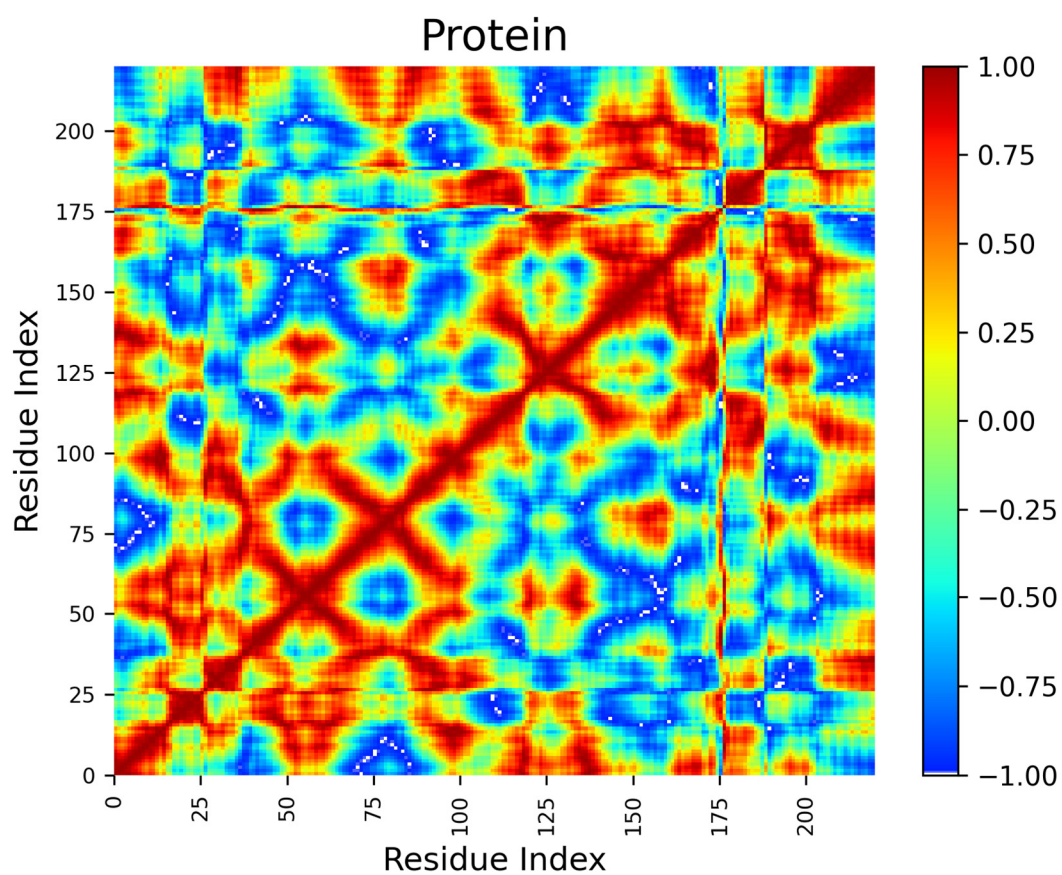




**Figure S15:** Heatmap of per-residue dynamic cross-correlations over the simulated trajectory of trypsin.



**Figure S16:** Heatmap of per-residue dynamic cross-correlations over the simulated trajectory of trypsin-desIVG.



**Figure S17:** Heatmap of per-residue dynamic cross-correlations over the simulated trajectory of trypsinogen.