

Supporting Information

Diverse Effects on the Native β -Sheet of the Human Prion Protein due to Disease- Associated Mutations

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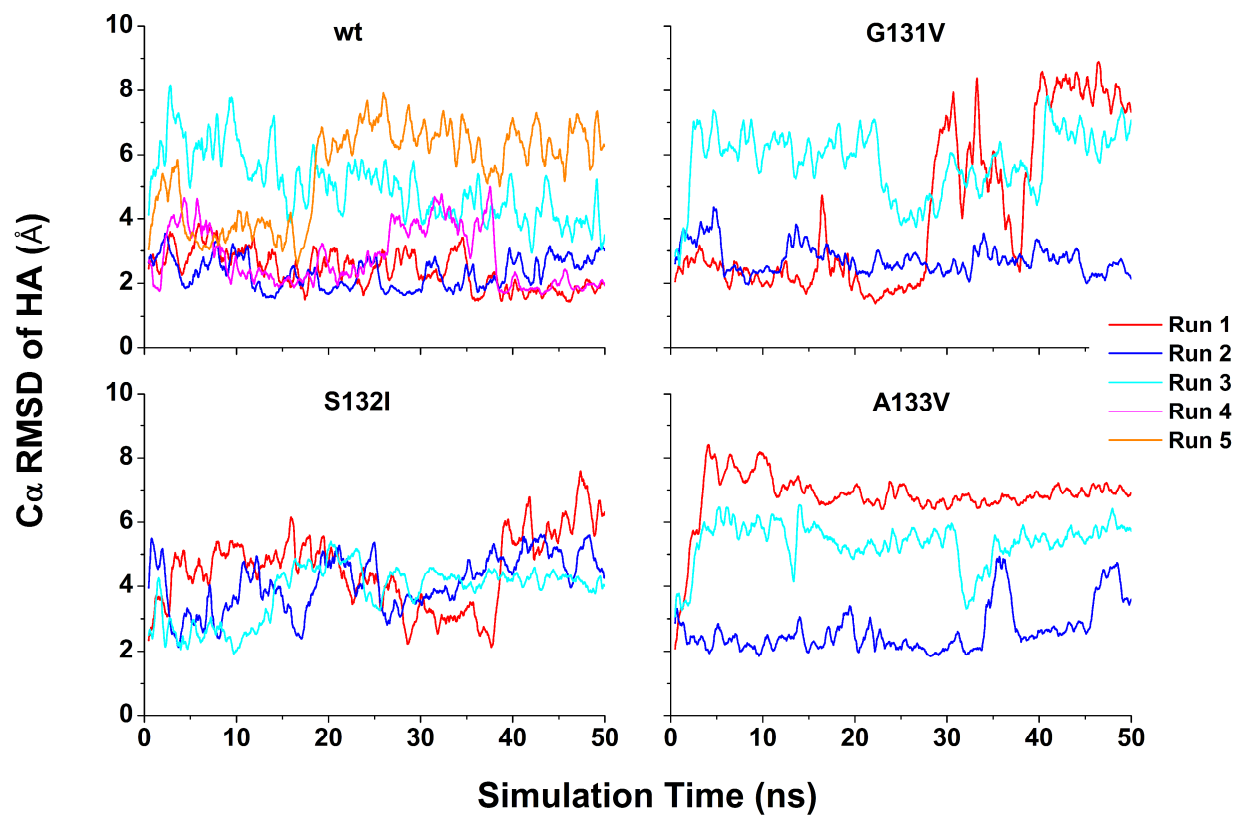


FIGURE S1: $C\alpha$ RMSD of HA in MD simulations. Structures were aligned on the $C\alpha$ atoms of the core region (residues 174-186 and 200 to 219) before RMSD measurements. The results of both wt and mutants are shown. For clarity, a running average over 500 ps is shown.

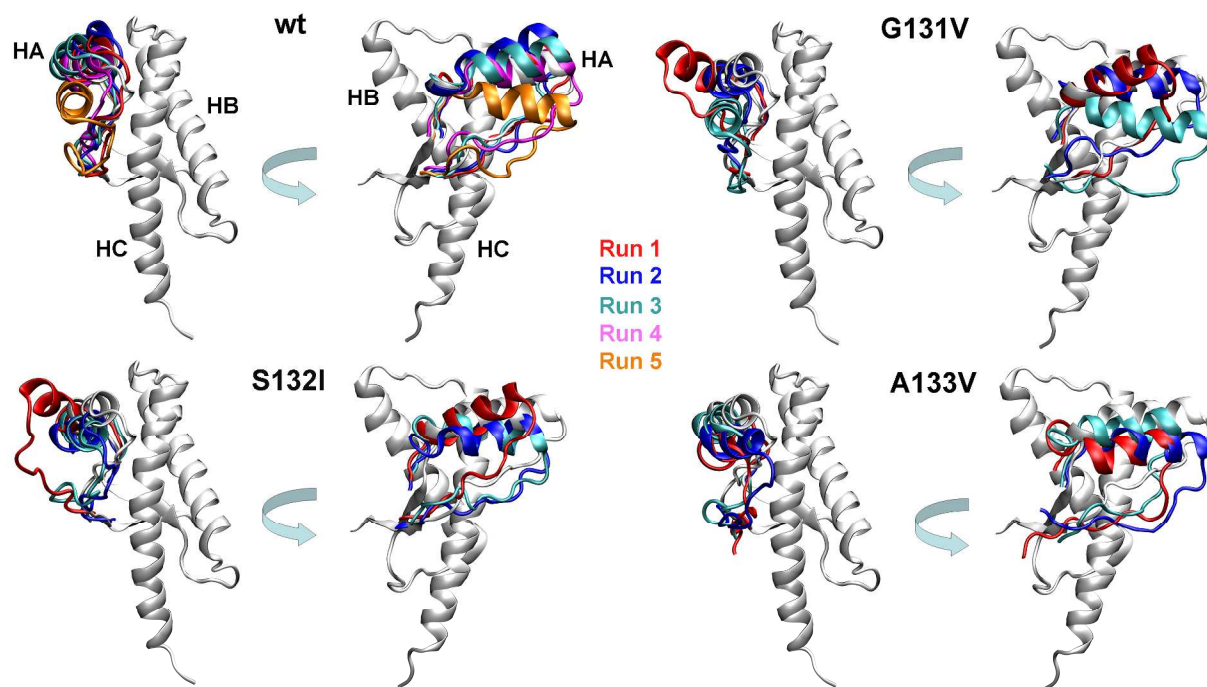


FIGURE S2: HA movements in MD simulations. Structures were aligned on the C α atoms of the core region (residues 174-186 and 200 to 219). The starting structures are gray while the final structures, only HA and the loop before HA are shown for clarity, at the end of the simulations are colored.

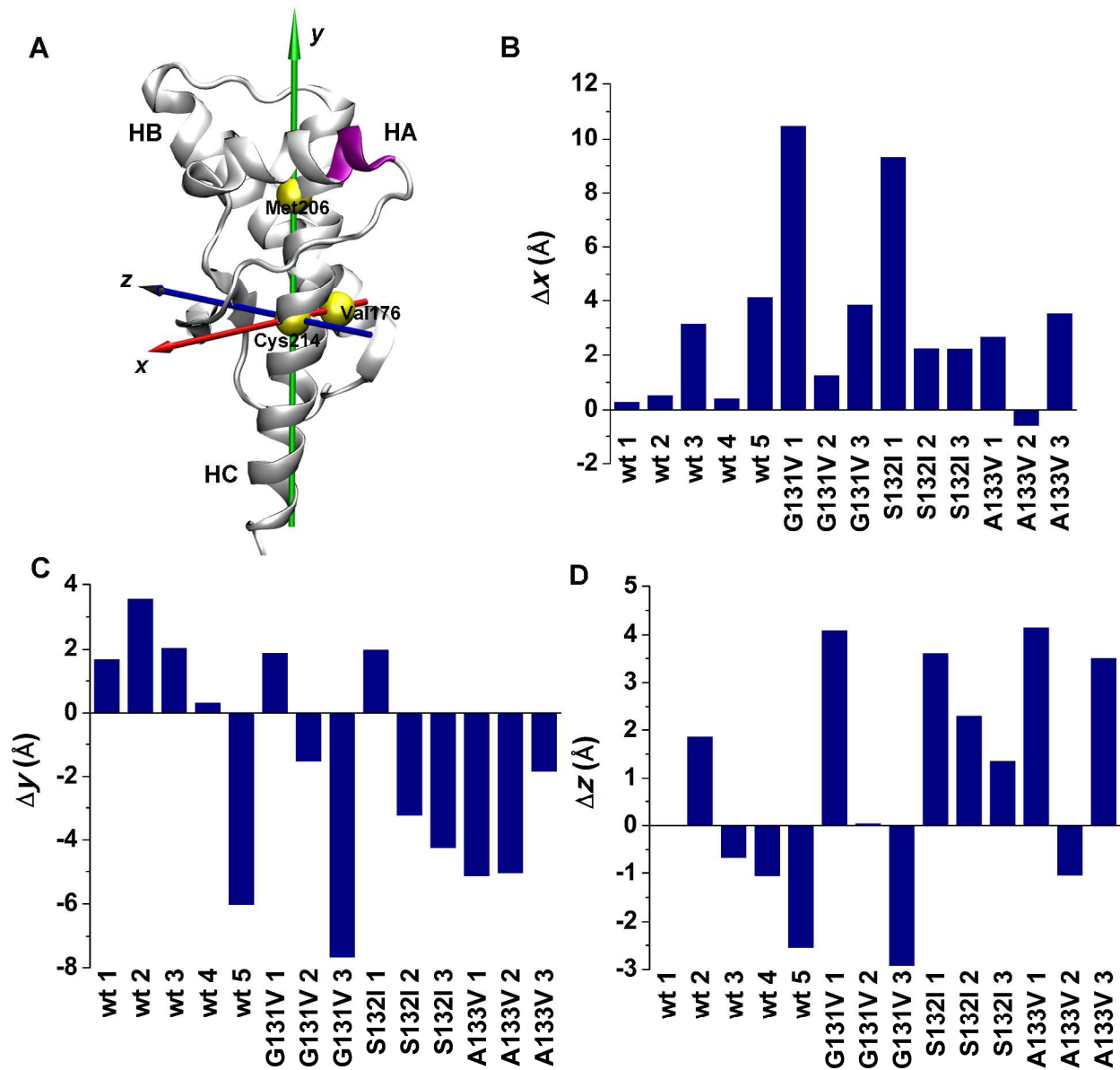


FIGURE S3: Movements of the HA N-terminus. The moving vectors of the HA N-terminus ($C\alpha$ atoms of residues 144-147, colored in purple) relative to its starting position at the end of the simulations were calculated in a defined coordinate system (A): $C\alpha$ of Cys214 in HC is at the origin, x axis goes through $C\alpha$ of Val176 in HB, and y axis goes through $C\alpha$ of Met206 in HC. The three $C\alpha$ atoms are shown as yellow spheres. Movements along x , y , and z are shown in B, C, and D, respectively.

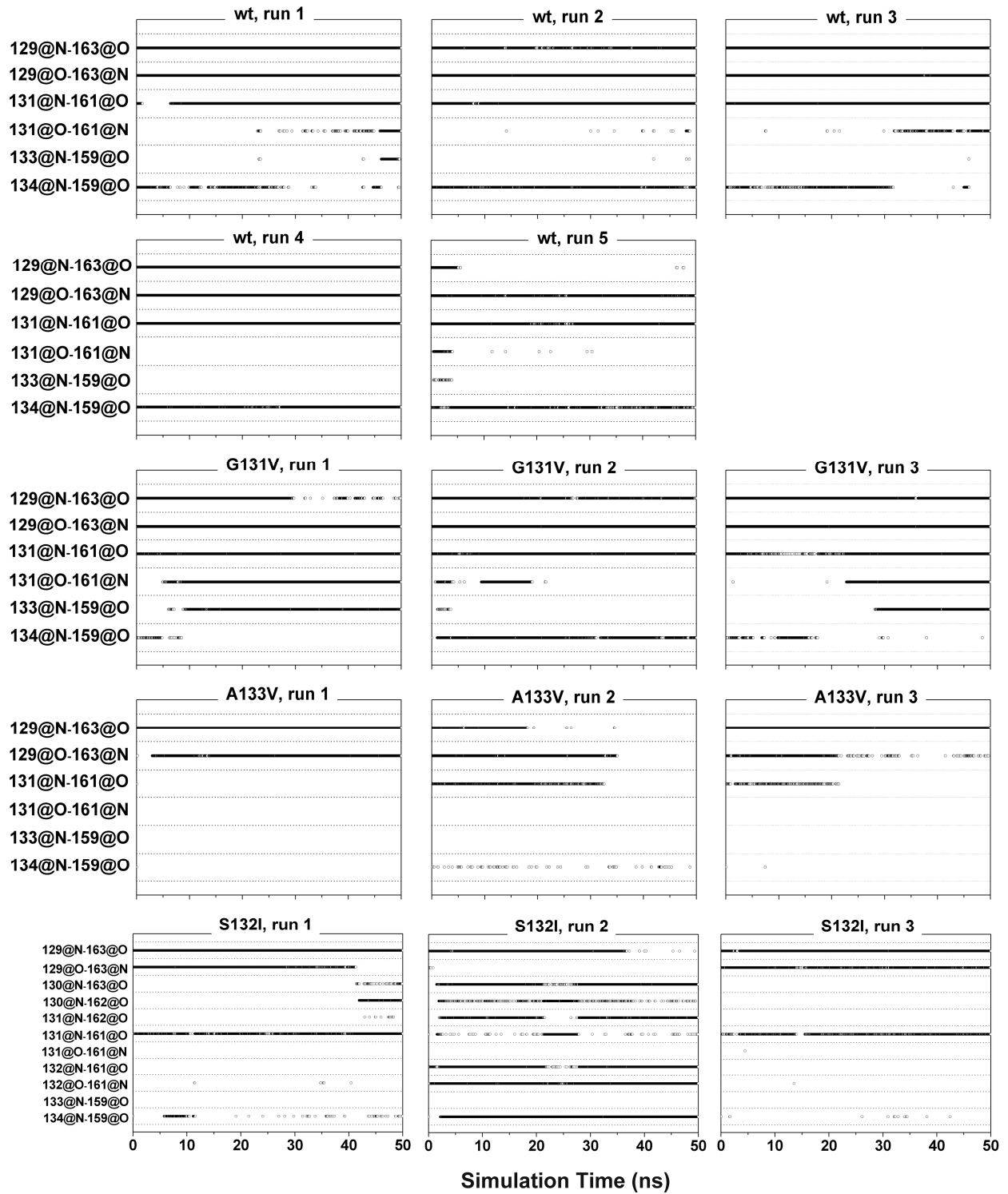


FIGURE S4: Time course of main-chain hydrogen bonds between the S1 and S2 strands in MD simulations. The results of all runs of wt and mutants are shown.

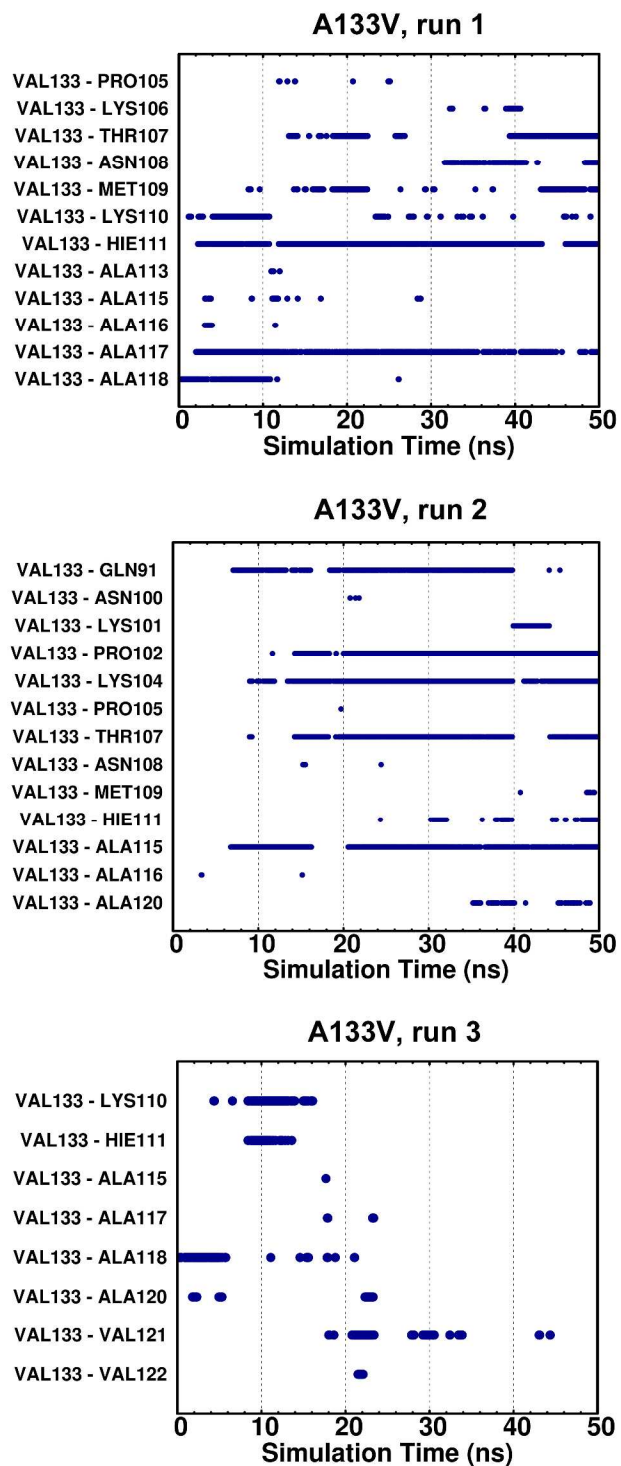


FIGURE S5: Time course of hydrophobic side chain-side chain contacts between V133 and residues of the N-terminal region. The results of all three runs are shown.

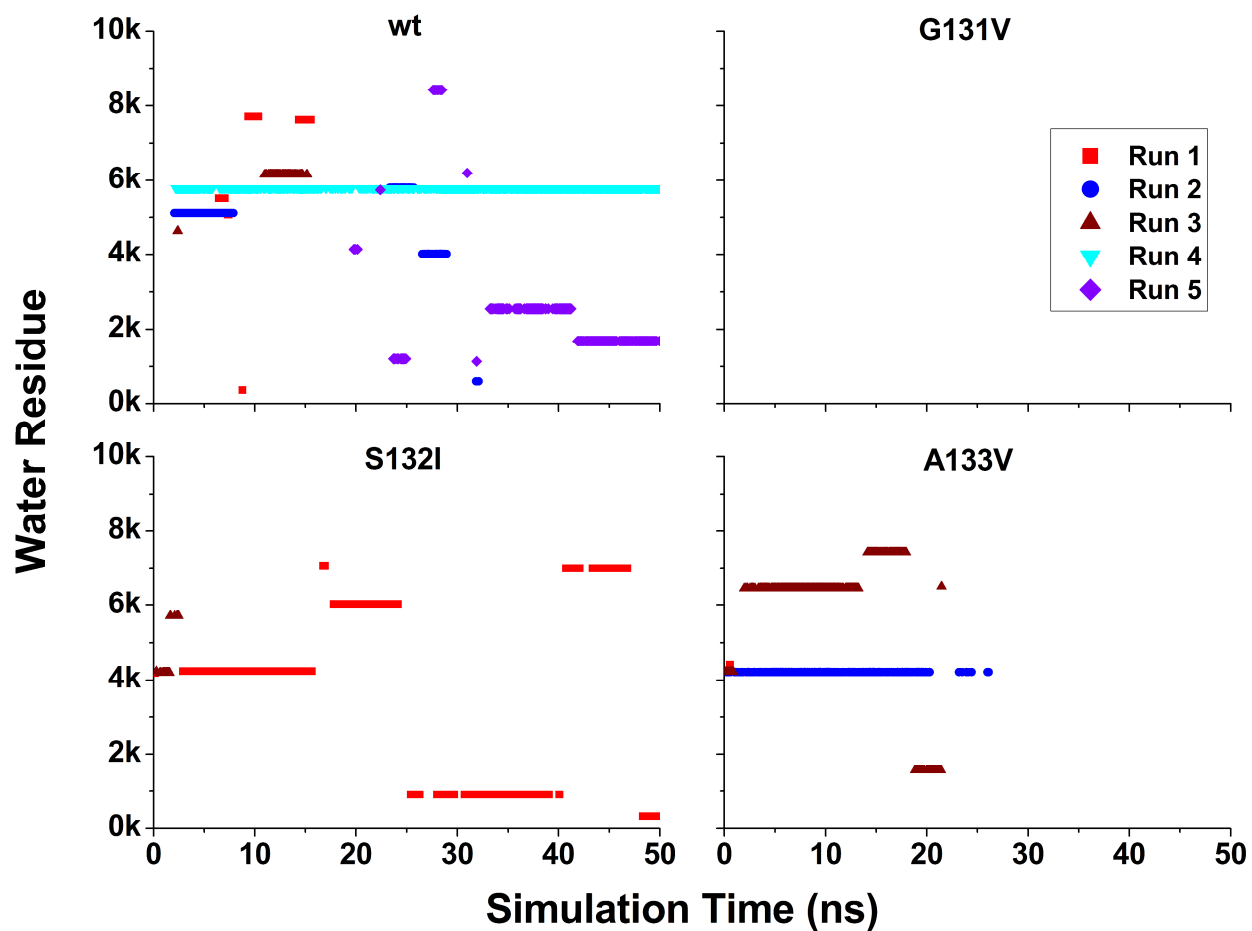


FIGURE S6: Time course of water molecules residing in the conserved water site at the native β -sheet. A coordinating water molecule is defined when it simultaneously hydrogen bonding with S1, S2, and HC. The results of all runs of wt and mutants are shown. y axis indicates the identity number of water molecules.

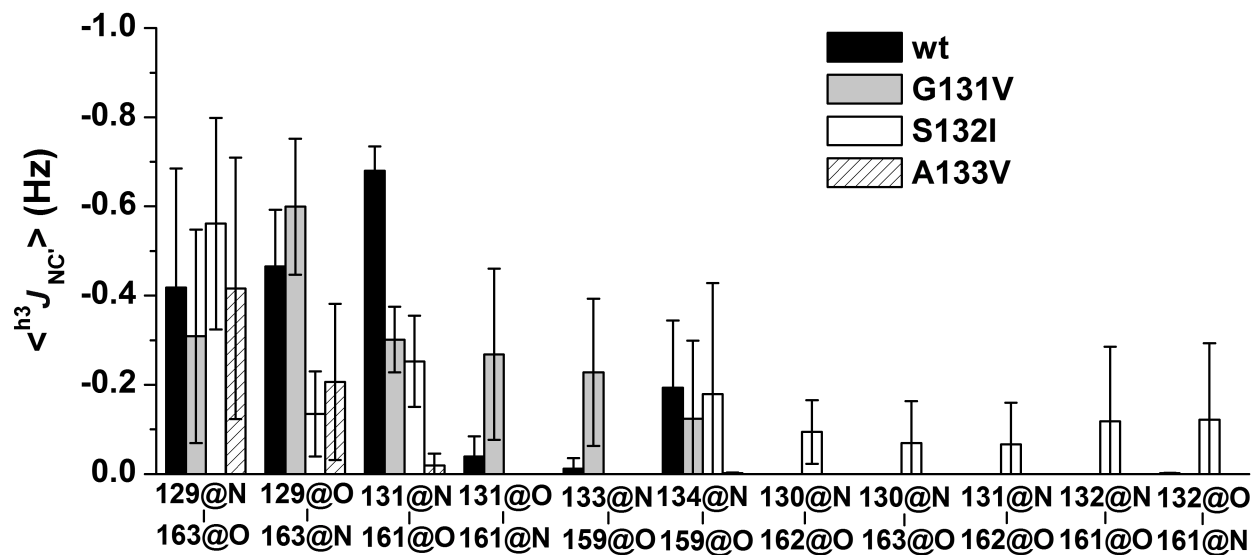


FIGURE S7: Predicted hydrogen bond scalar couplings (${}^{\text{h}3}J_{\text{NC}'}$) for hydrogen bonds between S1 and S2. Structures used for the calculations of ${}^{\text{h}3}J_{\text{NC}'}$ were extracted from the last 25 ns of MD trajectories in 100 ps intervals. ${}^{\text{h}3}J_{\text{NC}'}$ was calculated according to a simple geometric formula: ${}^{\text{h}3}J_{\text{NC}'} = -357 \text{ Hz} \exp(-3.2 r_{\text{HO}}) \cos^2 \theta$, where r_{HO} is the $\text{H}\cdots\text{O}$ distance and θ is the $\text{H}\cdots\text{O}=\text{C}$ angle. Error bars represent standard deviations over all runs. These are predicted coupling constants and it remains to be seen whether they are large and distinct enough to distinguish between the different proteins.