

The evolutionary conserved Tyr169 stabilizes the $\beta 2$ - $\alpha 2$ loop of the prion protein

Supplementary Informations

D. Huang^{a*}, and A. Caflisch^{a*}

^aDepartment of Biochemistry
University of Zürich, Winterthurerstrasse 190
CH-8057 Zürich, Switzerland
Phone: (+41 44) 635 55 68, FAX: (+41 44) 635 68 62
email: dhuang@bioc.uzh.ch
email: caflisch@bioc.uzh.ch

*Corresponding authors

keywords: molecular dynamics, prion, PrP^C, $\beta 2$ - $\alpha 2$ loop

References

- [1] Blöchliger, N.; Vitalis, A.; Caffisch, A. *Computer Physics Communications*, **2013**, *184*(11), 2446–2453.

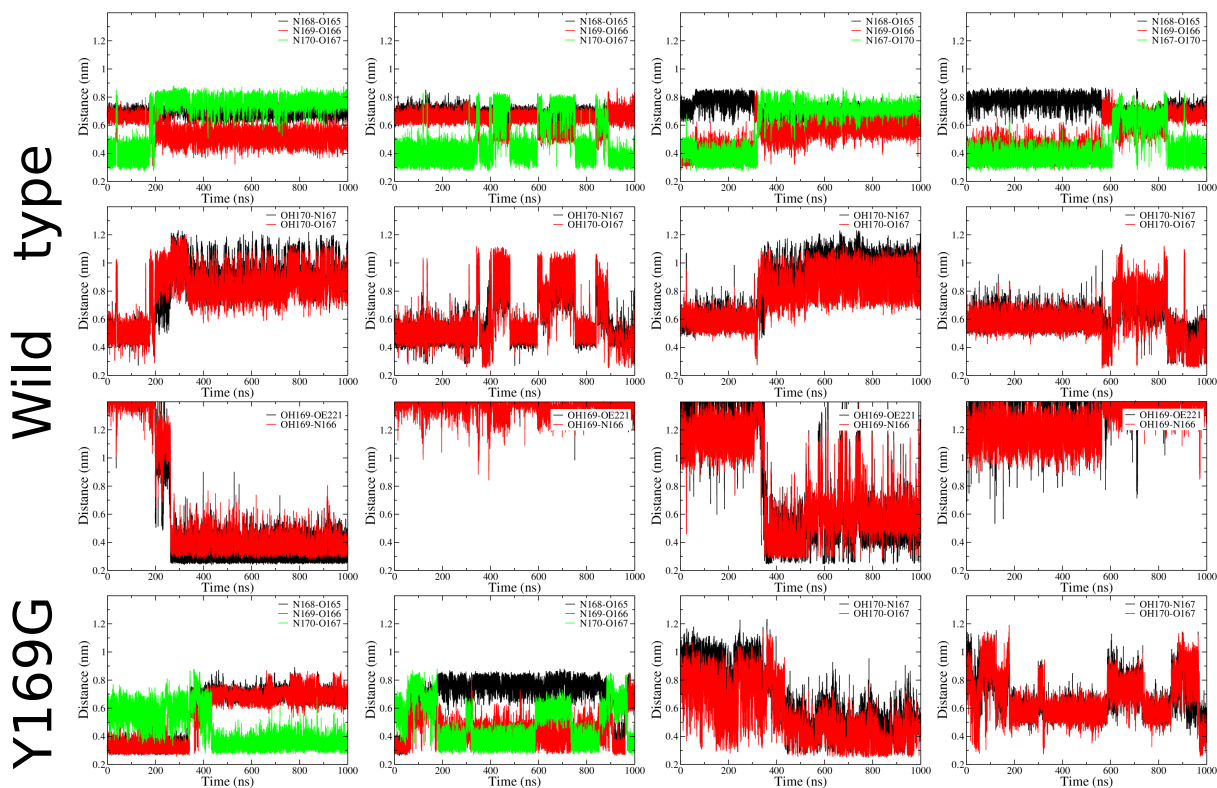


Figure S1: Time series of distances. For the wild type simulations, the first and last two columns refer to the simulation starting from two different β turn substates of the $\beta 2$ - $\alpha 2$ loop, respectively.

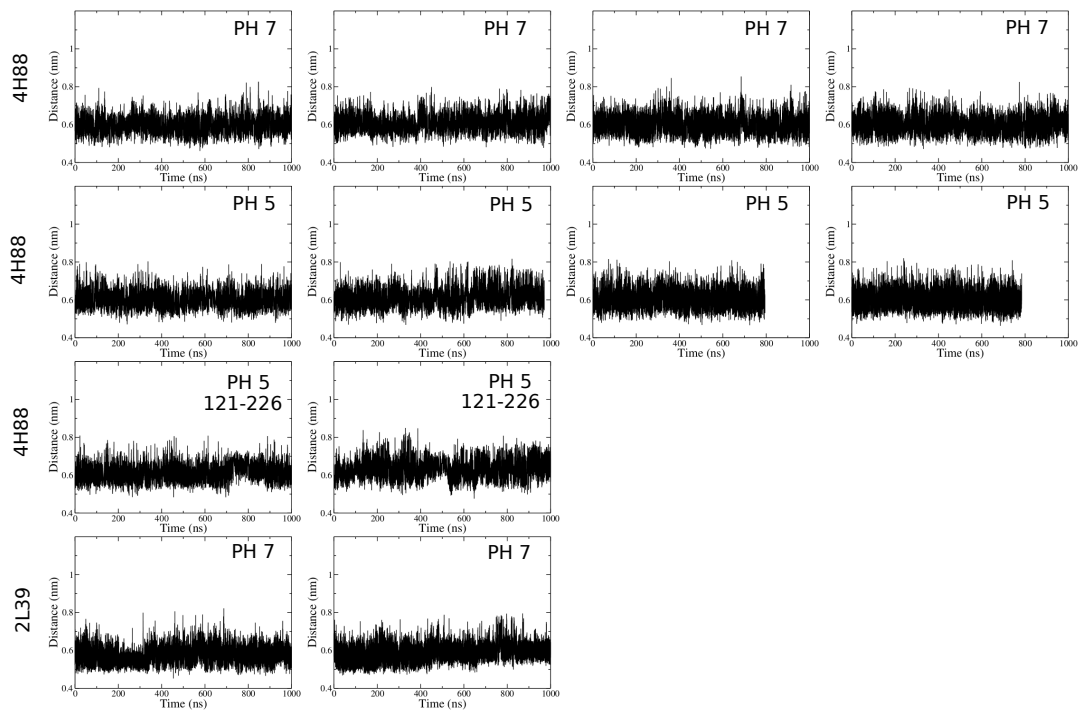


Figure S2: Time series of the distance between $C\alpha$ atoms of P165 and N188 in the wild type simulations. No transition is observed.

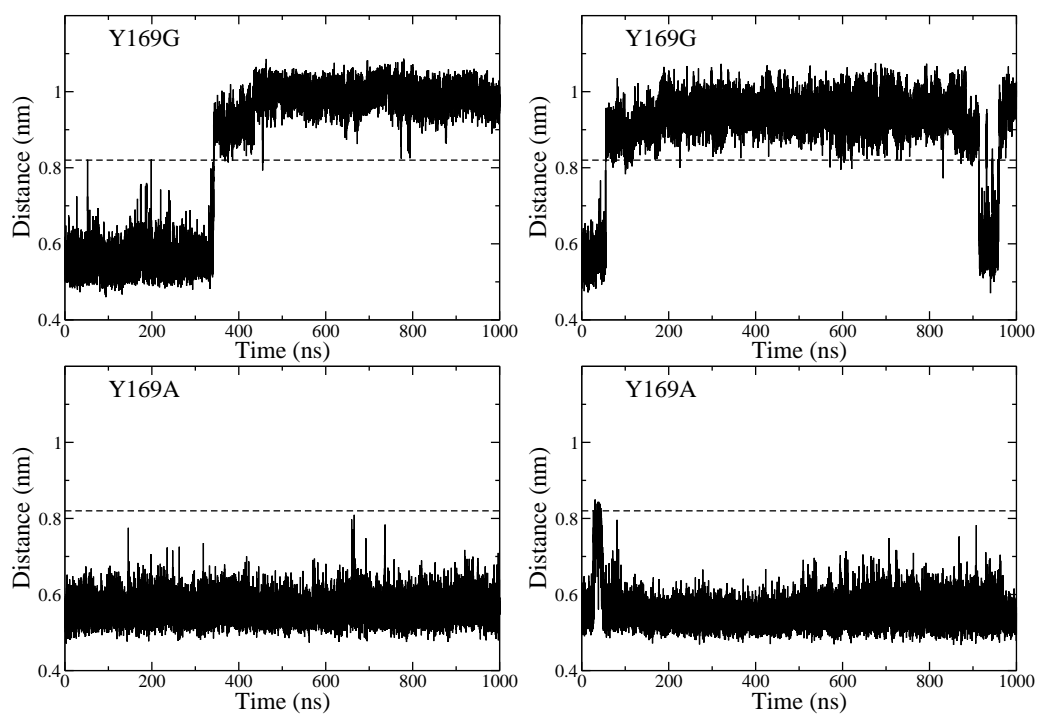


Figure S3: Time series of the distance between $C\alpha$ atoms of P165 and N168 in simulations of the single-point mutants Y169G (top) and Y169A (bottom). No transition is observed for Y169A.

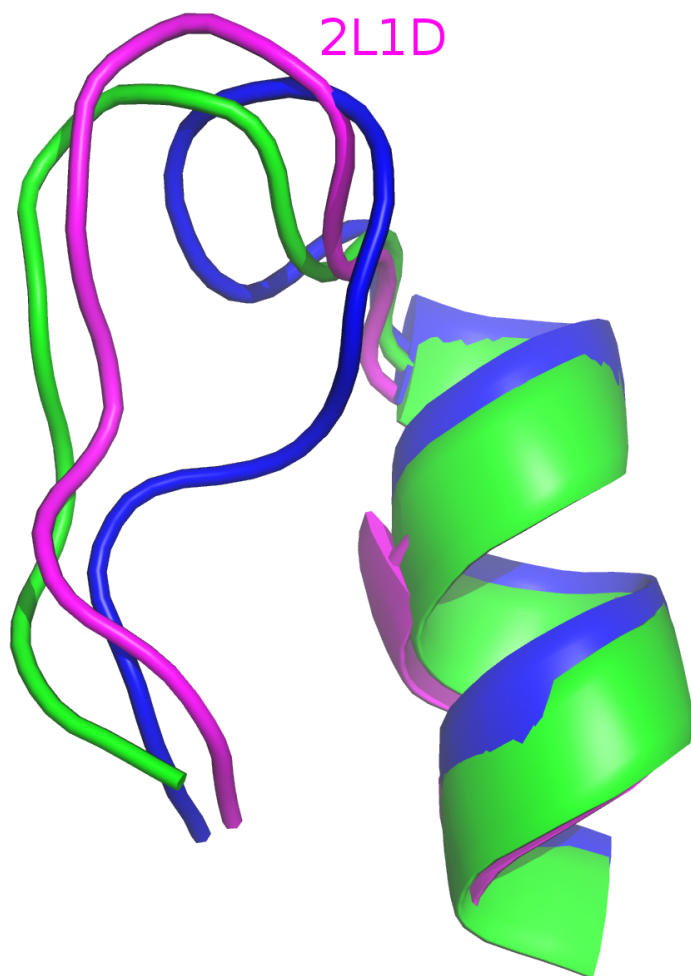


Figure S4: One of the two β turn conformations (green) of Y169G sampled in the MD simulations is structurally similar to the NMR conformation (magenta, PDB code 2L1D). The other conformation (blue) shows differences in the segment next to helix 2. The C_{α} atoms of helix 2 were used for the structural overlap.

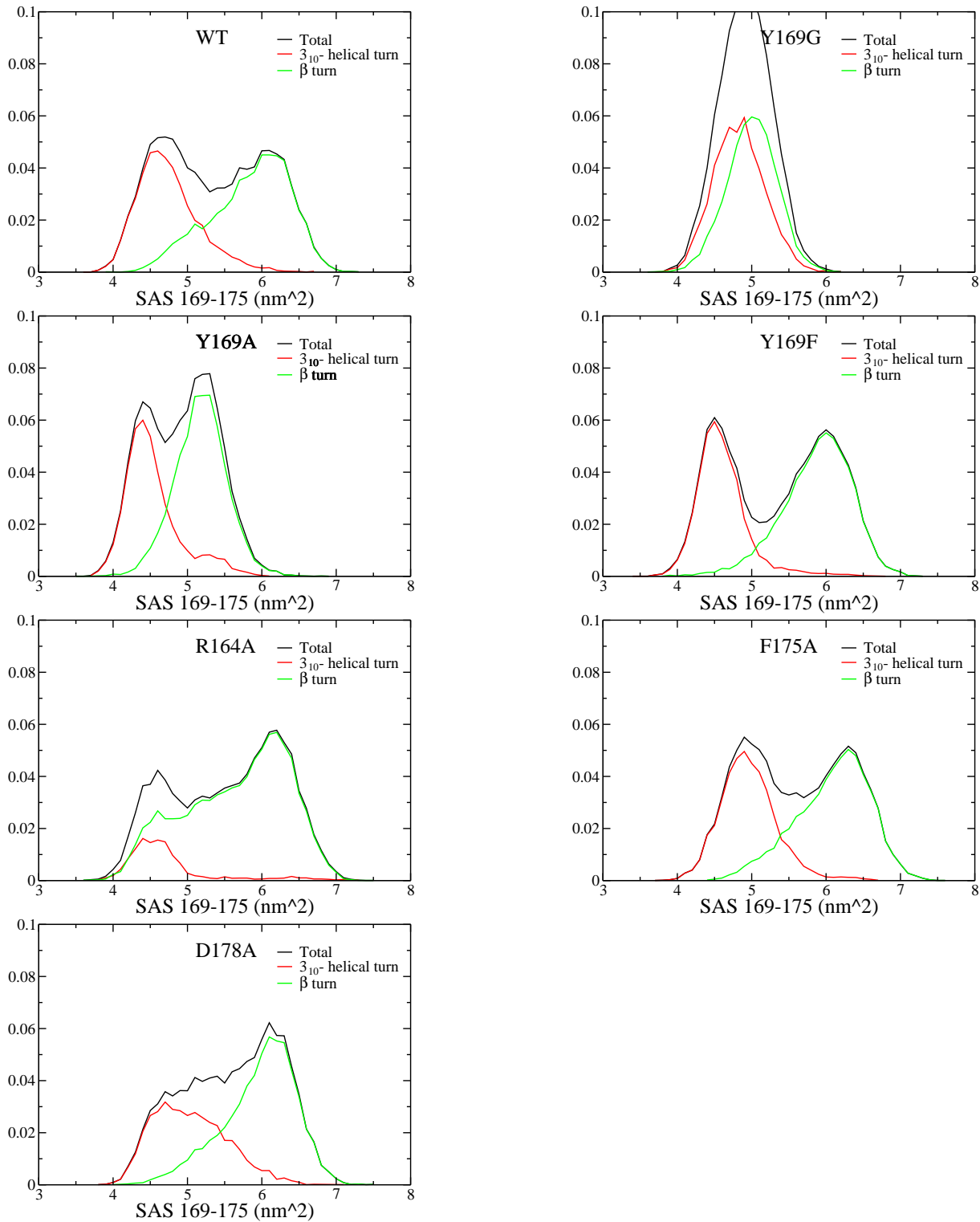


Figure S5: Distribution of solvent accessible surface for residues 169 to 175. The umbrella sampling was used for these plots. A threshold in the PMF distance, i.e., the distance between the C_{α} atoms of residues 165 and 168, was used to assign individual snapshots to the 3_{10} -helical turn (red) or β turn (green).

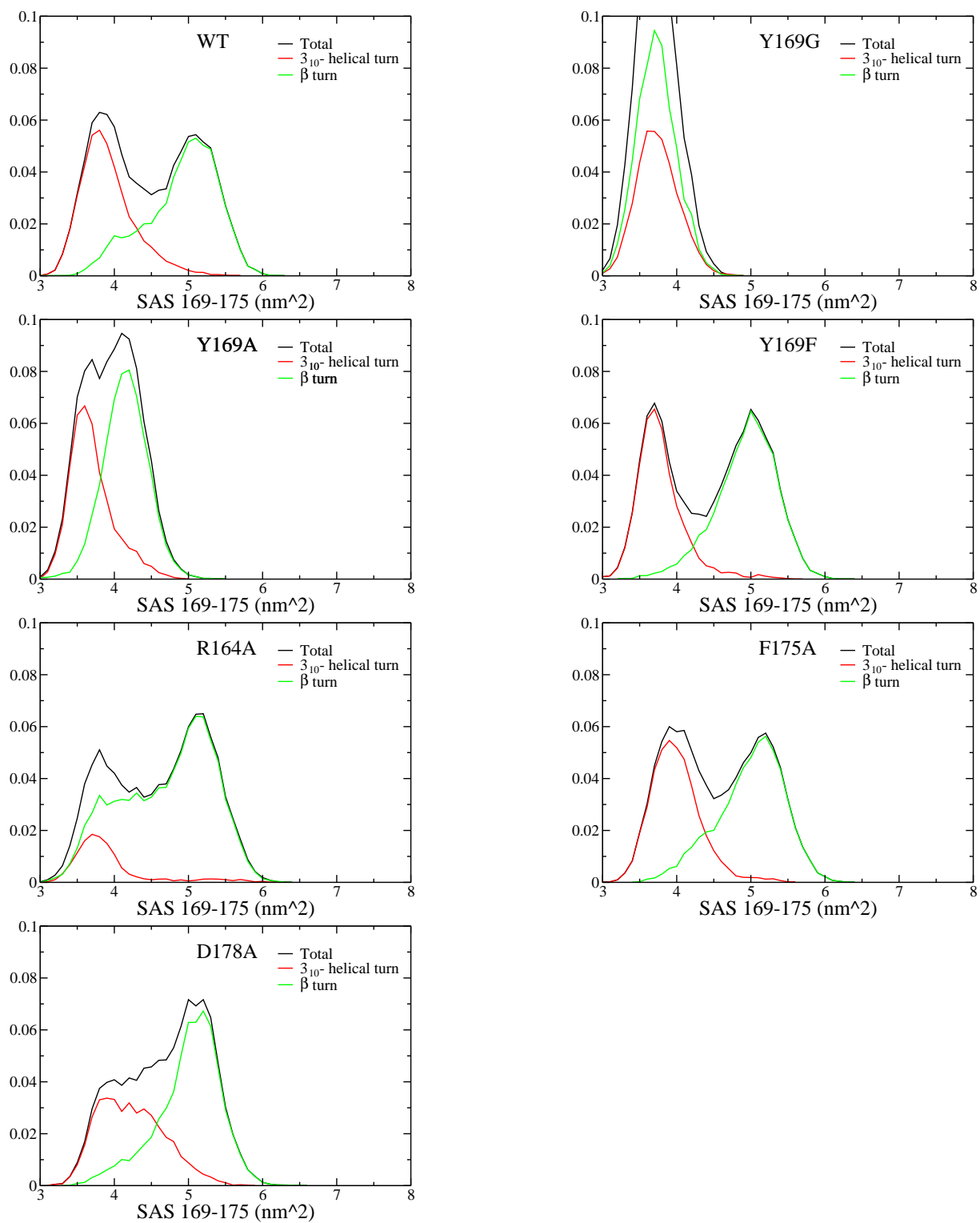


Figure S6: Same as Figure SI5 for the side chain atoms only

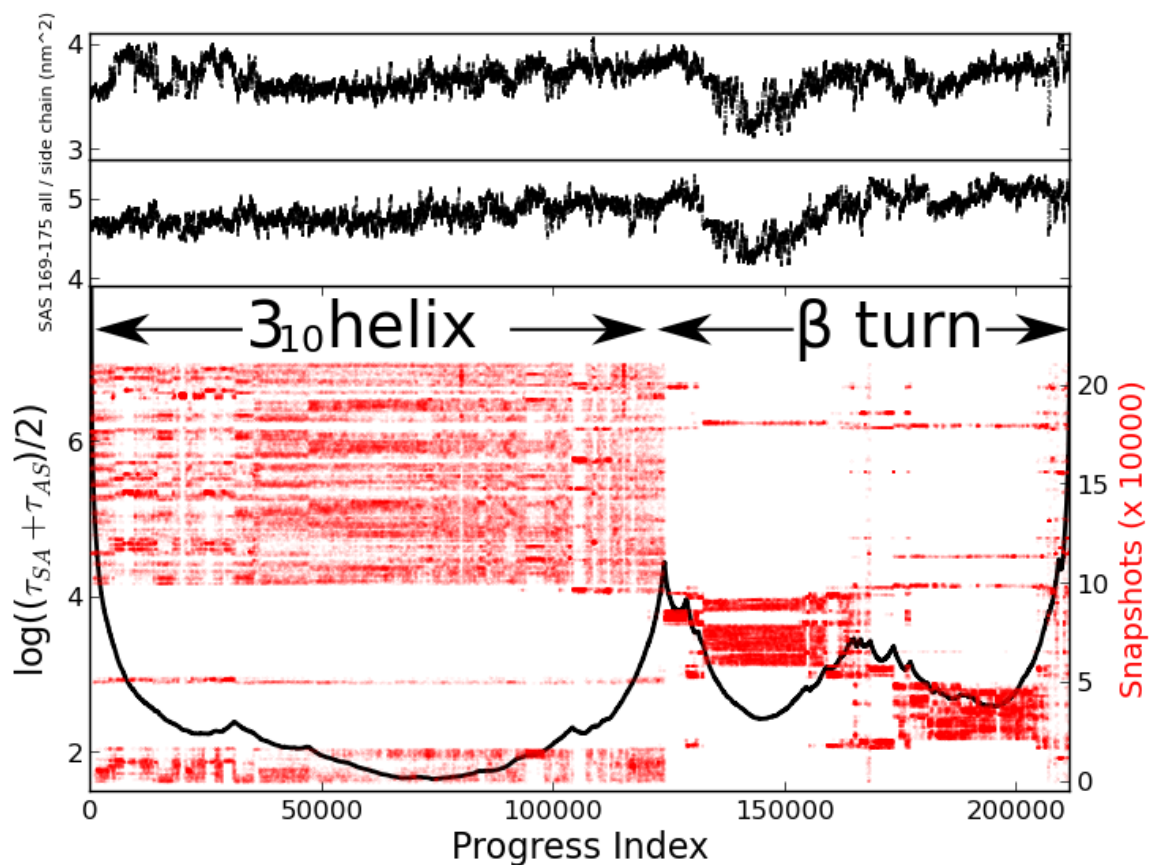


Figure S7: SAPPHIRE plot¹ for Y169G mouse PrP^C. The progress index, of 210000 snapshots originating from about 4.2 μ s of MD data, is annotated (from bottom panel to top) with cut-based profile (black curve, left y-axis), dynamical trace (red dots, right y-axis), and solvent accessible surface area of residues 169-175 all atoms and side chains.

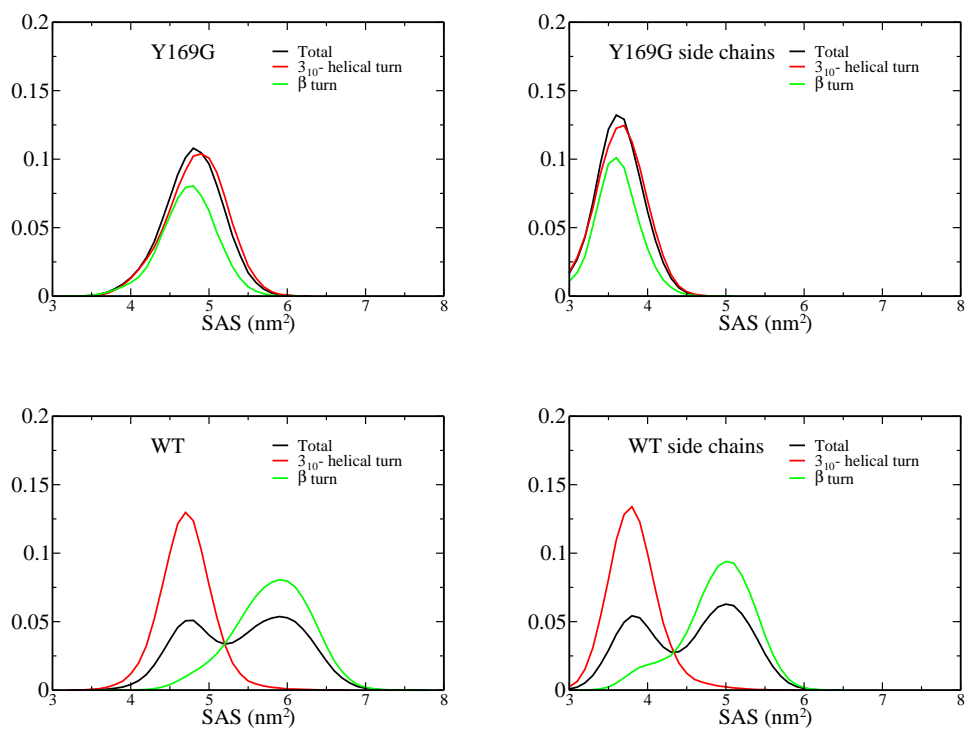


Figure S8: Distribution of solvent accessible surface for residues 169 to 175. The unbiased sampling was used for these plots. Individual snapshots of the wild type were assigned to the 3_{10} -helical turn or β turn according to the SAPPHERE plot progress index smaller or larger than 250000, respectively. For the Y169G the threshold in the progress index was 125000.

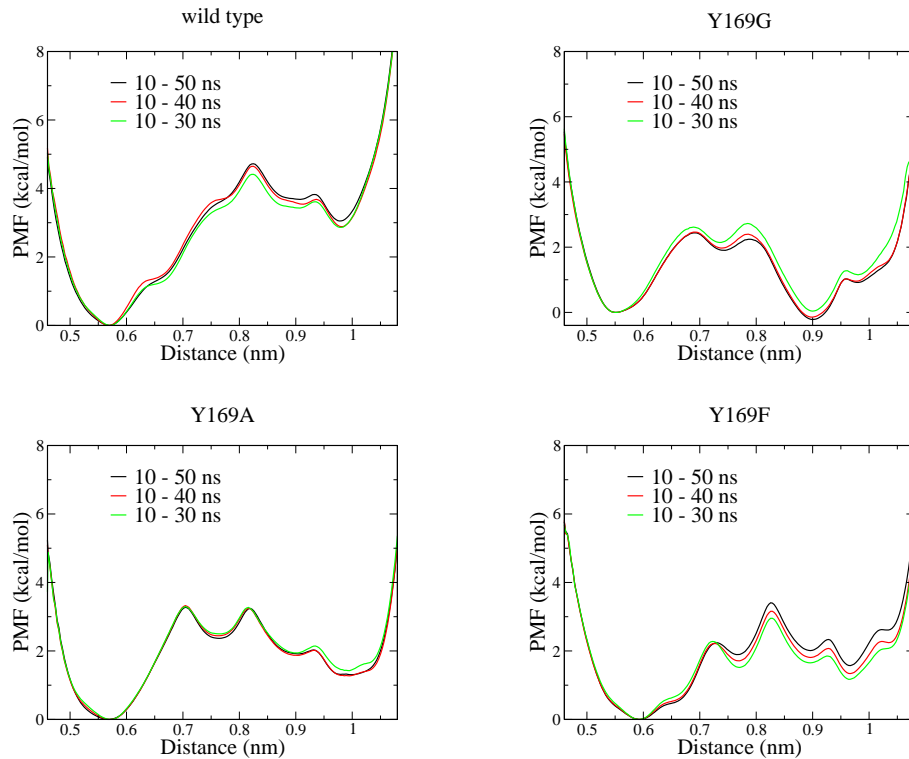


Figure S9: PMF calculations using different temporal lengths of the individual windows in umbrella sampling. The similar profiles indicate that convergence was reached.

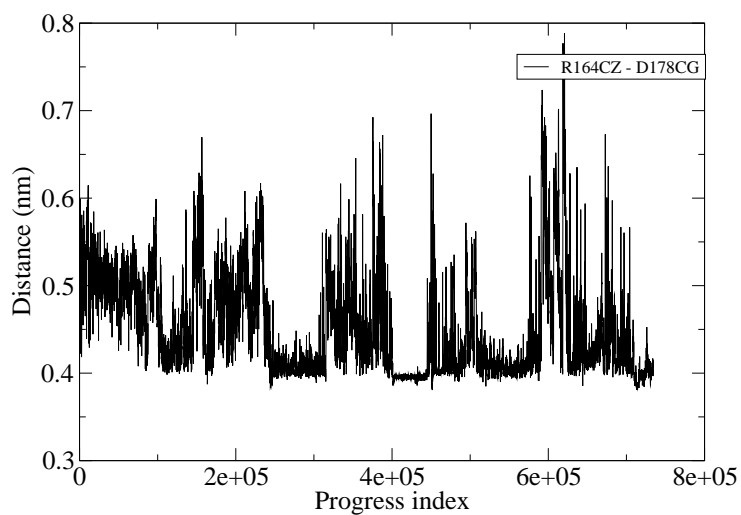


Figure S10: Distance of R164 CZ to D178 CG in the wild type simulations. This time series shows that the ionic interaction between the side chains of R164 and D178 is either direct or bridged by one to two water molecules.

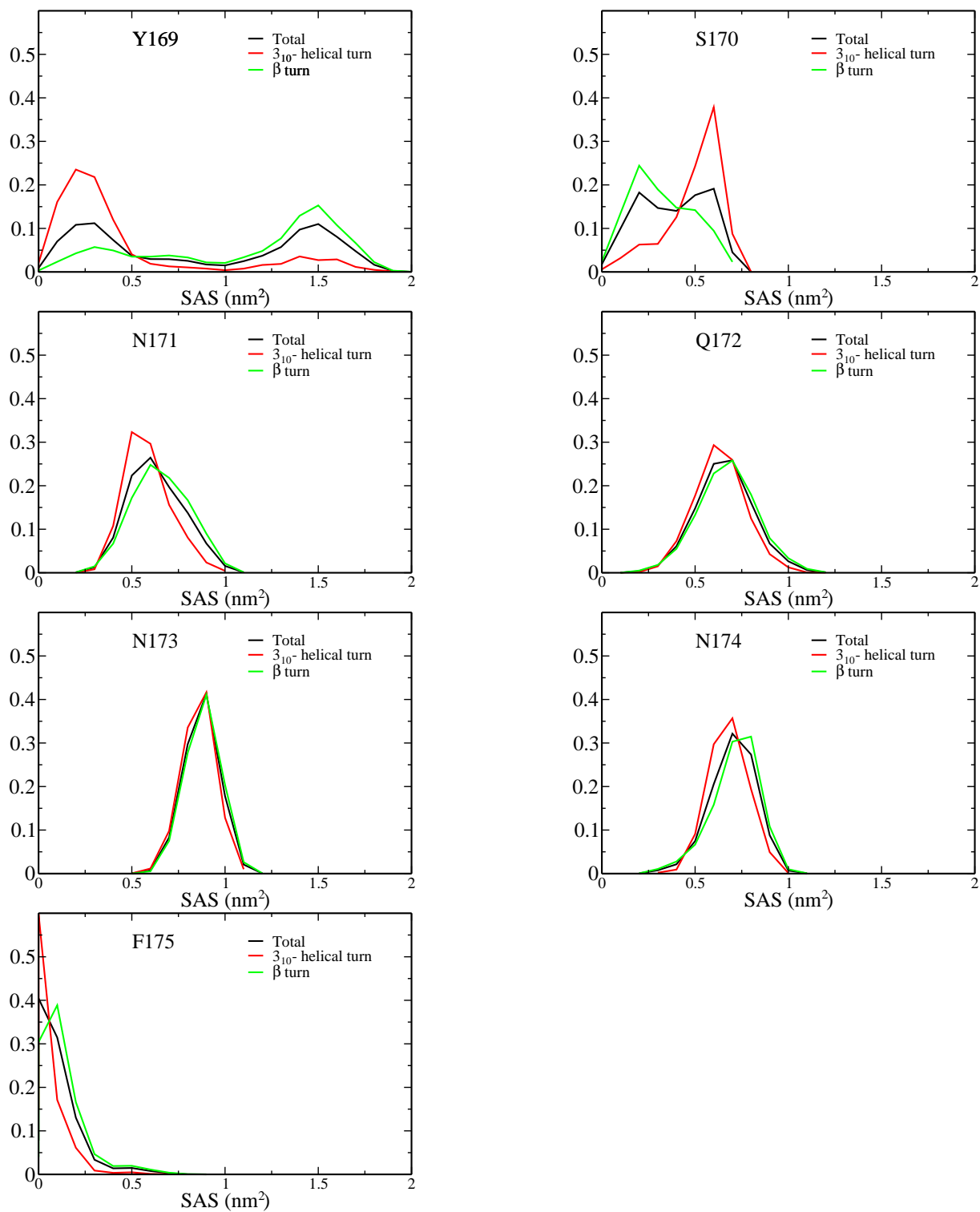


Figure S11: Distribution of solvent accessible surface for individual residues in the unbiased sampling of wild type. Individual snapshots were assigned to the 3₁₀-helical turn or β turn according to the SAPHIRE plot progress index smaller or larger than 250000, respectively.