Supporting Information

pH-Dependent Molecular Dynamics of Vesicular Stomatitis Virus Glycoprotein G

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Table S1 Protonation states of titratable amino acids in VSV-G at pH7 and pH5, as determined from a Monte-Carlo pH titration.

	protonation state at pH7	protonation state at pH5
lysine 47	ζ-deprotonated	ζ-protonated
histidine 132	ε-protonated	δ- and ε-protonated
histidine 162	ε-protonated	δ-protonated
glutamate 286	γ-carboxy-deprotonated (subunit C)	γ-carboxy-protonated
histidine 389	ε-protonated	δ- and ε-protonated
histidine 397	ε-protonated	δ- and ε-protonated
histidine 407	ε-protonated	δ- and ε-protonated

A

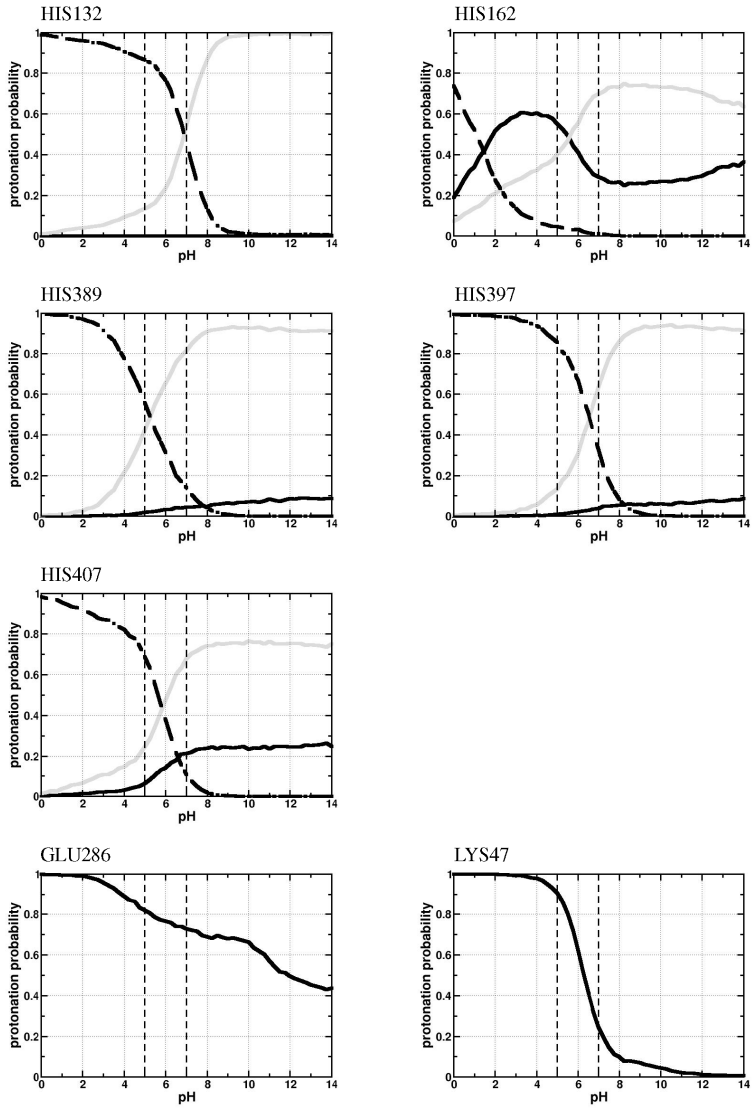


Figure S1: (A) Titration curves for differentially protonated residues in VSV-G simulations. For histidine residues, the probabilities for double protonation (black dotted curve), δ-protonation (black curve), and ε-protonation (grey curve) are shown, for E286 and K47 the probability of side chain protonation is given. The protonation probabilities are calculated for the prefusion conformation (PDB: 2J6J). The simulation systems were protonated according to the titration results. The side chains of E286 of the three protomers point to each other with a CD-CD distance of 4.96 Å. As the protonation probability at pH 7 is 0.7 in all three chains, E286 was protonated in chains A and B, but deprotonated in chain C at this pH value. At pH 5, all three E286 side chains were protonated.

B

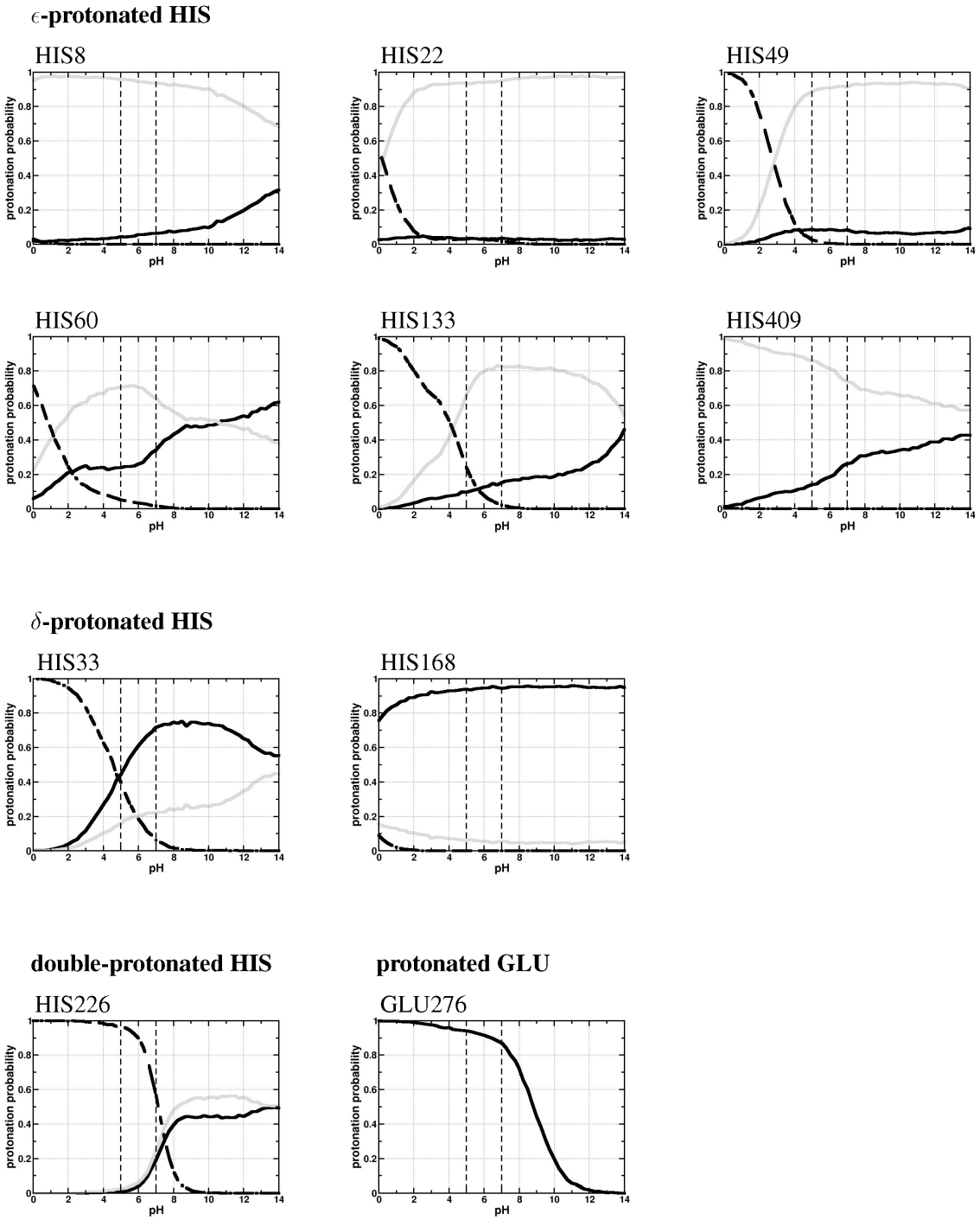


Figure S1 (continued): (B) Titration curves for all histidines, which do not change their protonation state between pH5 and pH7, and for Glu276. For all residues not listed in (A) or (B), standard protonation states were adopted in both simulations.

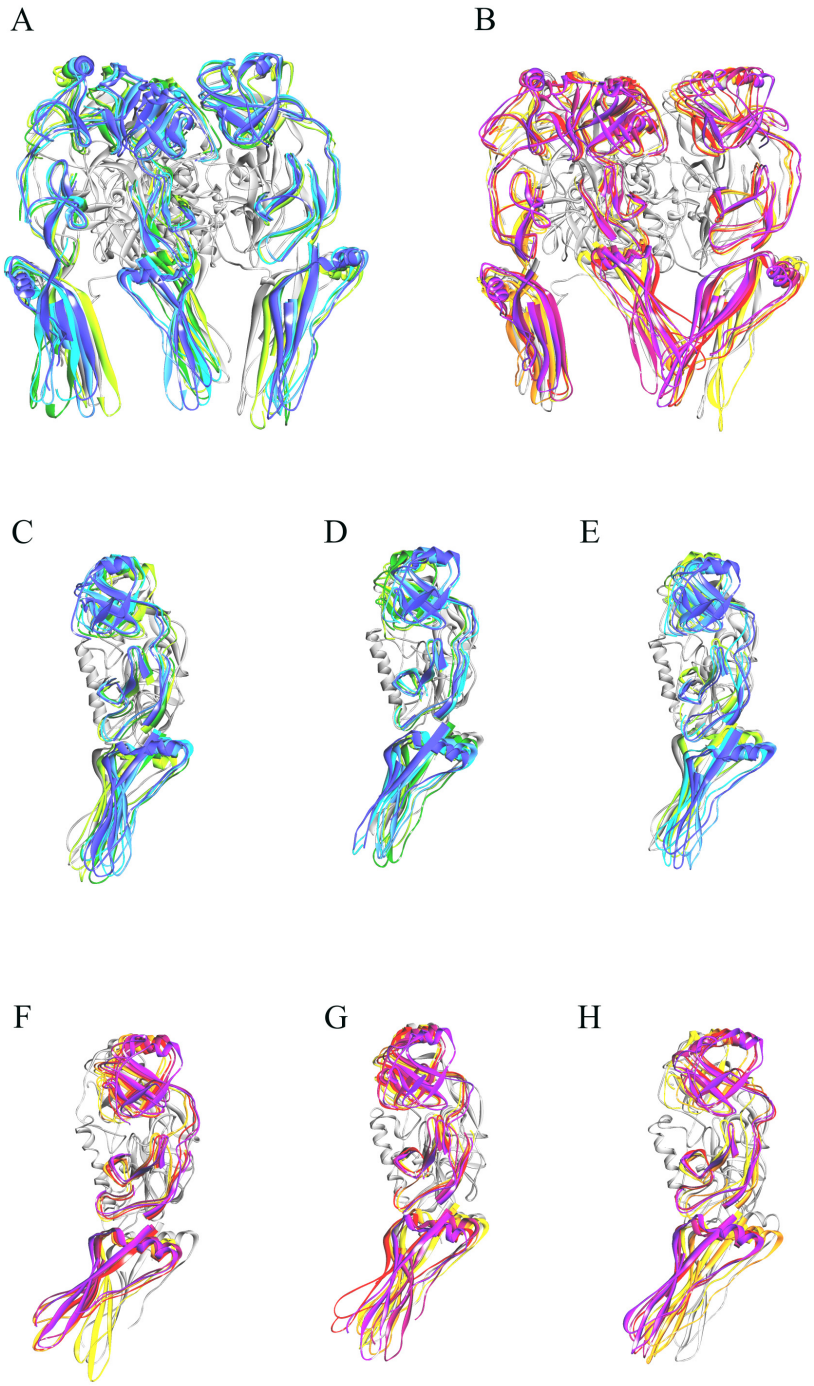


Figure S2 Overlay of VSV-G trimers and monomers at pH7 (A, C. D, and E) and pH5 (B, F, G, and H) after 10, 20, 30, 40 and 50 ns of simulation with their respective minimized starting structure (grey) minimization (only domains I and IV are colored). Coloring of pH7 structures: 10 ns (light green), 20 ns (green), 30 ns (cyan), 40 ns (light blue), 50 ns (blue). Coloring of pH5 structures: 10 ns (yellow), 20 ns (orange), 30 ns (red), 40 ns (magenta), 50 ns (purple).

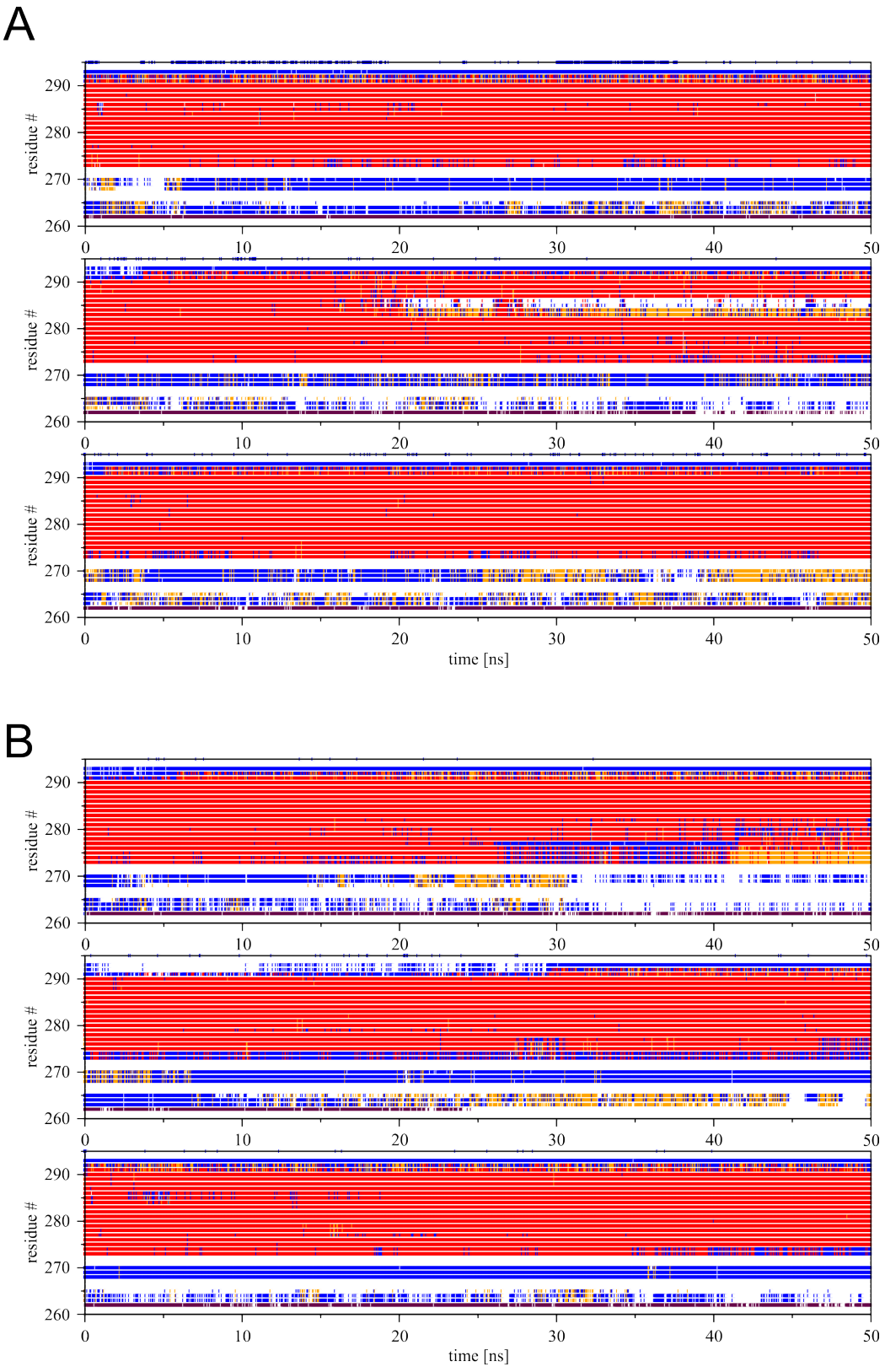


Figure S3 Secondary structure analysis of the central helix bundle over 50 ns of simulation. A) System VSV-G7, B) system VSV-G5. Secondary structure elements are colour coded: α-helix (red), antiparallel β-sheet (blue), 3_{10}-helix (orange), turn/disordered (white).

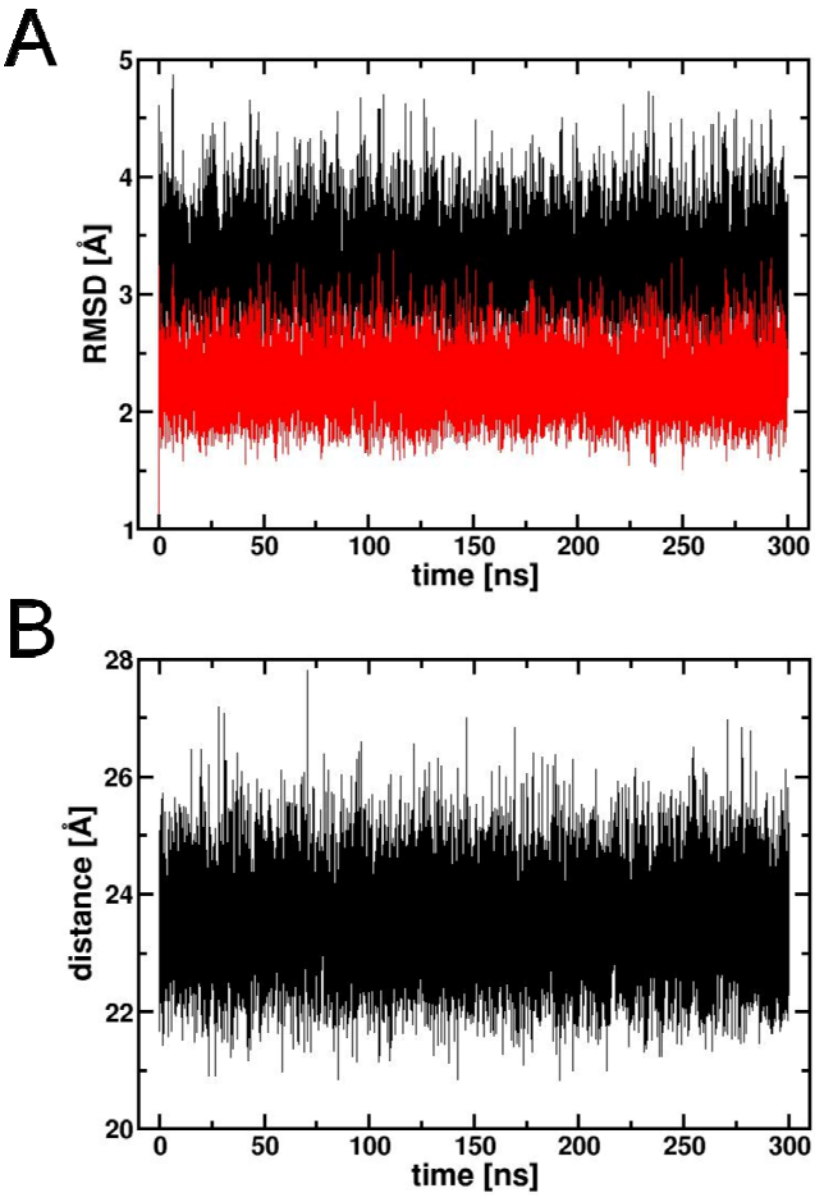


Figure S4 Fluctuations detected in the coarse-grained RedMD simulation. A) RMSD deviation for the Cα-atoms from the starting structure detected for the full-length VSV trimer (black) and after omission of domain IV (red). B) T265-R292 distance used to monitor a putative helix elongation in domain II. The distance remains close to the value detected in the prefusion structure indicating that no major changes in secondary structure occur.

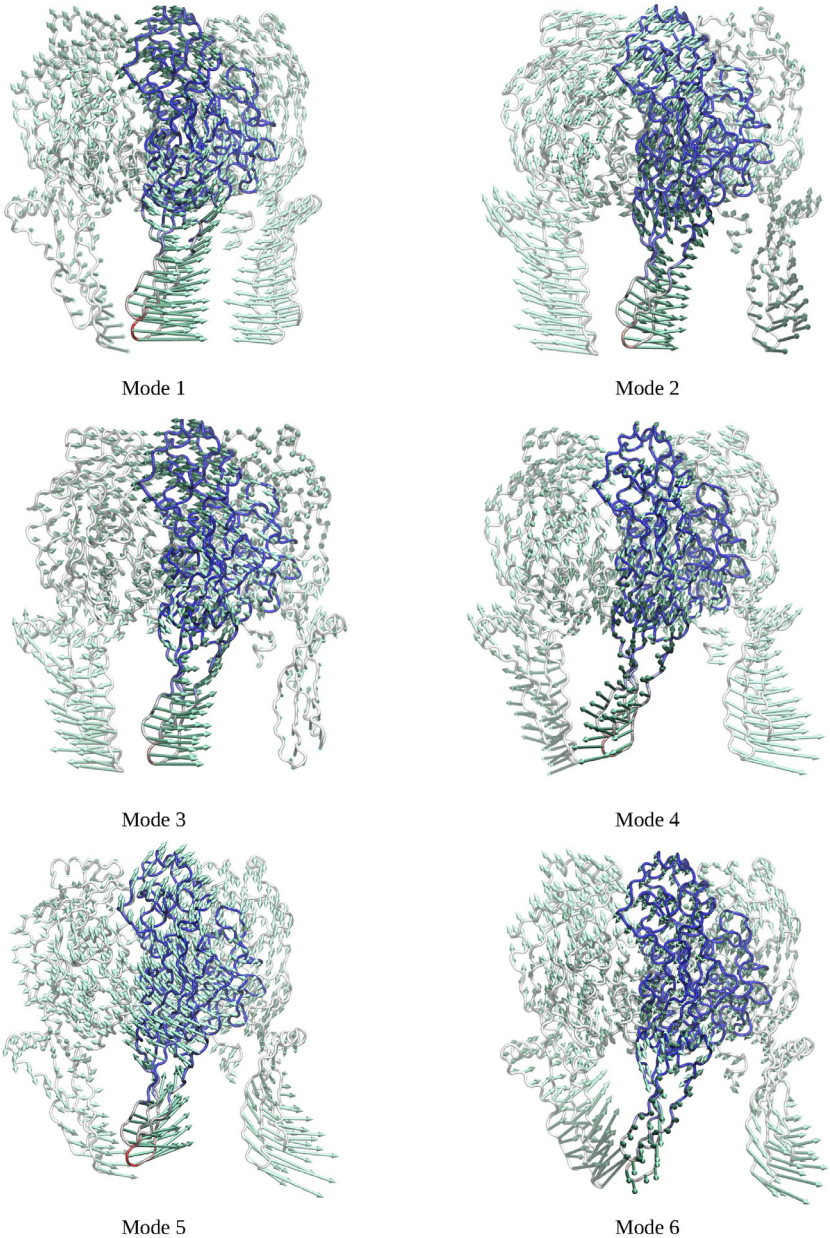


Figure S5 Structure of VSV-G indicating the six principal modes with the highest eigenvalues (vector presentation) deduced from the coarse-grained RedMD simulation. For clarity each mode is shown as separate panel, and arrows are only drawn in one direction. The arrow lengths and the color of the residues of subunit A show the mobility along the displayed mode (red: high mobility, blue: low mobility).

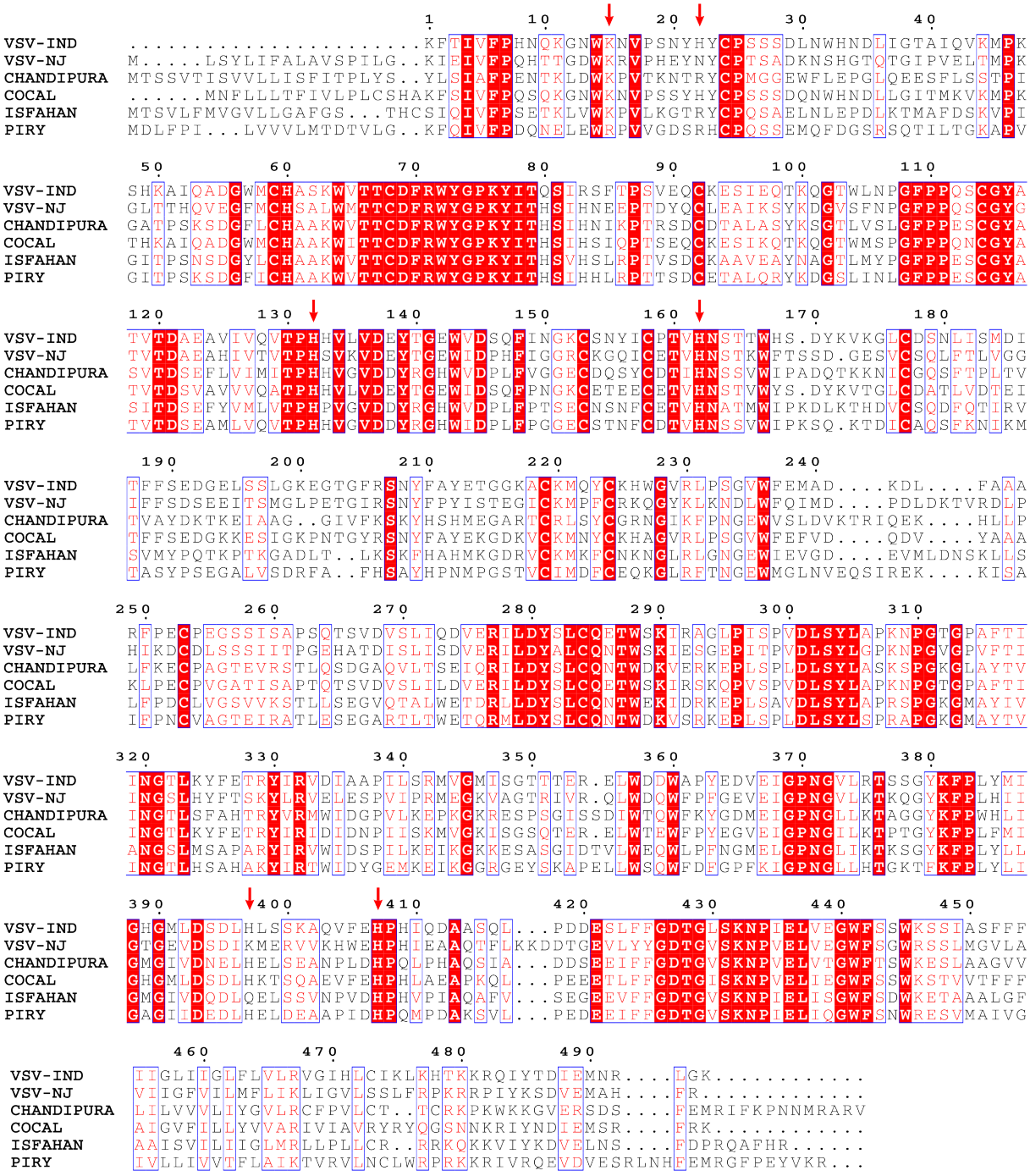
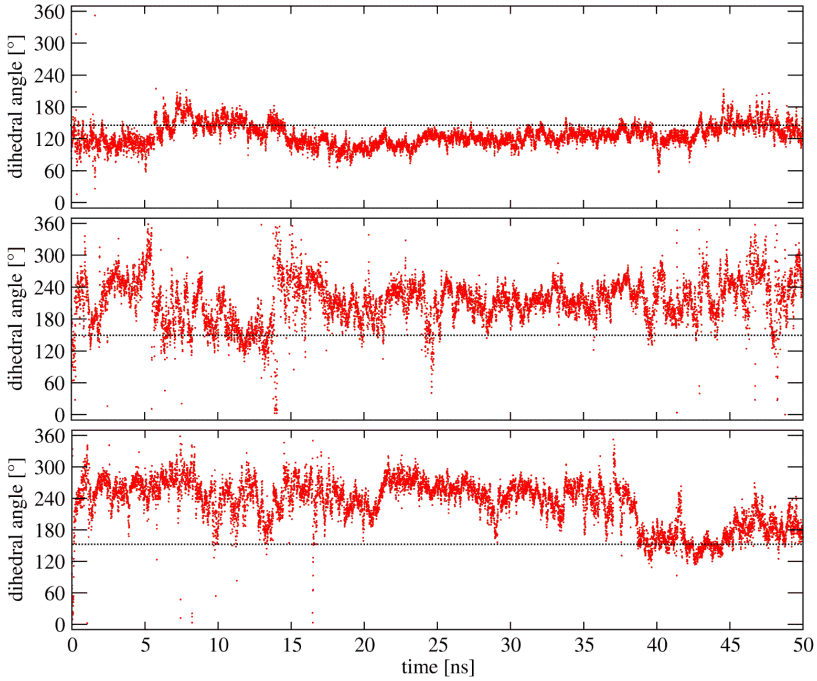


Figure S6 Sequence alignment of VSV Indiana strain (VSV-IND, as crystallized in PDB: 2J6J) and closely related members of the rhabdovirus family: VSV New Jersey strain (VSV-NJ), Chandipura virus (CHANDIPURA), cocal virus (COCAL), Isfahan virus (ISFAHAN) and piry virus (PIRY). Structurally important conserved residues referred to in the text are marked by red arrows.

A



B

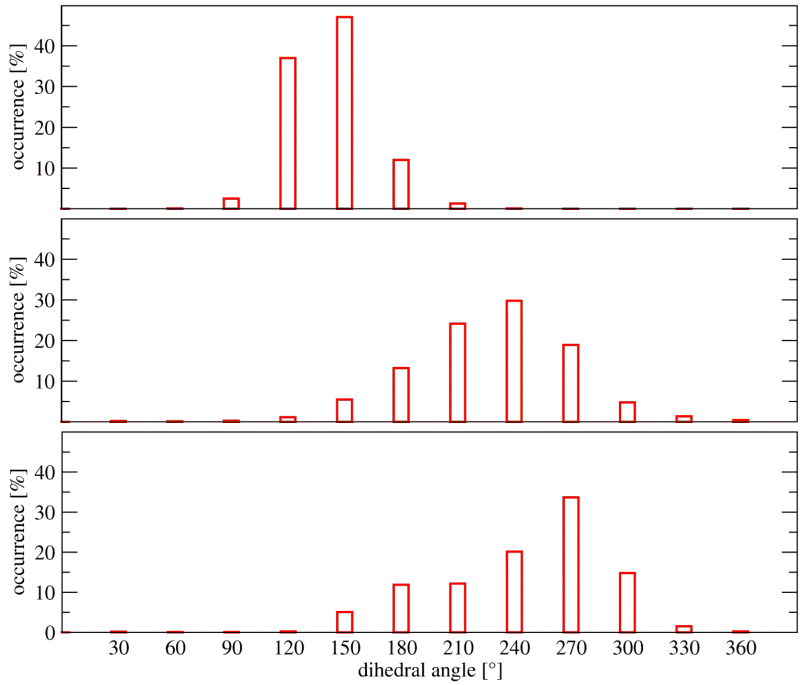
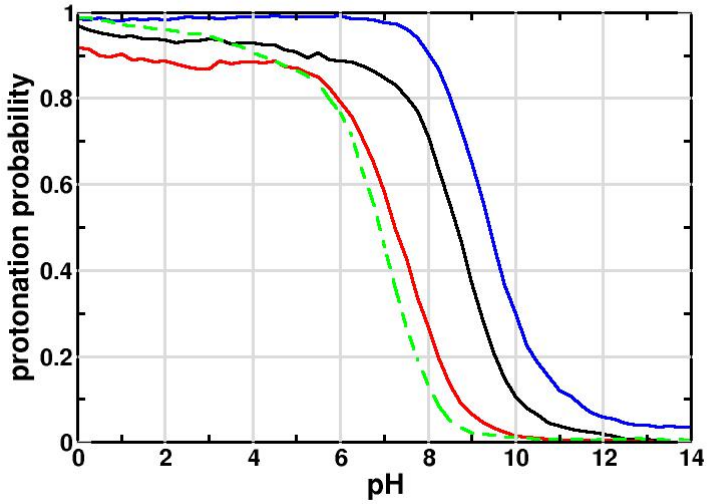


Figure S7: Sampling of domain IV in a pH5 control simulation at 298K. A) Plot of the dihedral angle between Cα-atoms of C219, C224, C158, and Y73 over simulation time for each subunit: Subunit A (upper panel), subunit B (middle panel) and subunit C (lower panel). The angle of 156° present in the crystal starting structure is indicated by a dotted line B) Histogram presentation of the dihedral angles sampled over the simulation time. Subunit A (upper panel), subunit B (middle panel) and subunit C (lower panel).

A



B

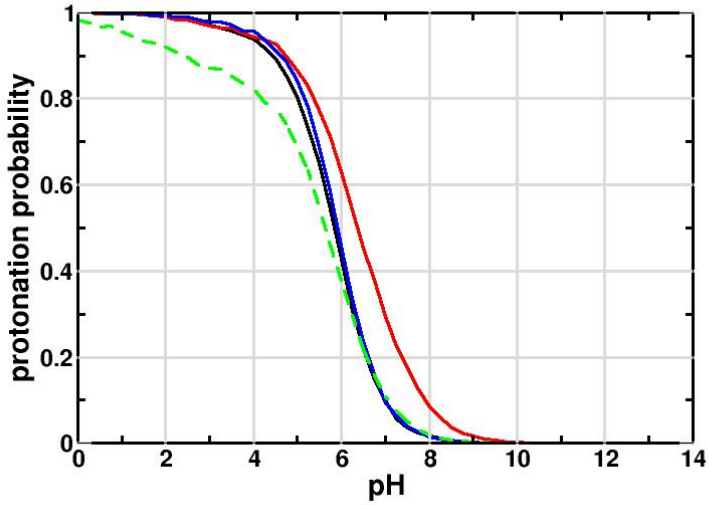


Figure S8: Titration curves for His132 (A) and His407 (B) in the VSV-G pH5 simulation at 310K. The probabilities for double protonation in the starting structure are shown as green dotted line (The starting crystal structure 2J6J is a symmetric homotrimer. Therefore, the same titration behaviour is present in all subunits.). The titration curves for the three subunits after 50 ns of MD simulation are shown in red, blue, and black.