SUPPLEMENTARY MATERIAL

The pH dependence of flavivirus envelope protein structure: insights from molecular dynamics simulations

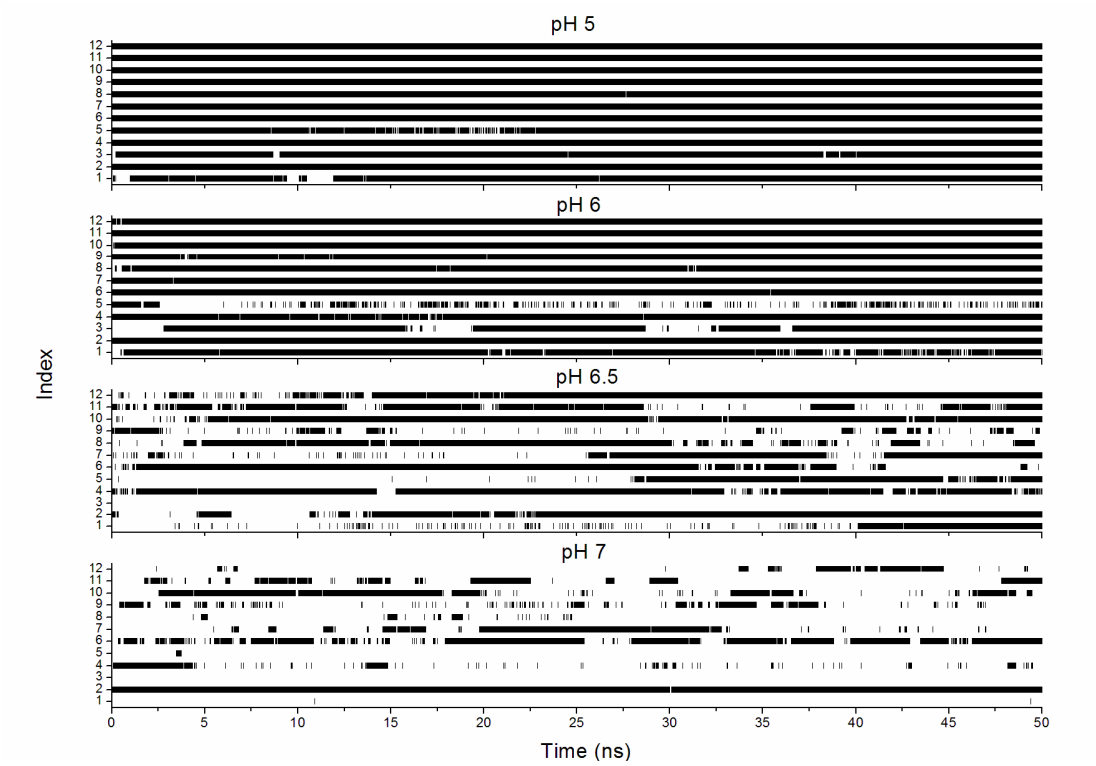

Figure S1. Protonation maps for His and N-terminus in function of the time for each pH excluding the data for pH 8, which do not suffer from protonation. The index number and related His residue are (1)His27, (2)His94, (3)His144, (4)His149, (5)His158, (6)His209, (7)His244, (8)His261, (9)His282, (10)His317, (11)His346, and (12)N-terminus.

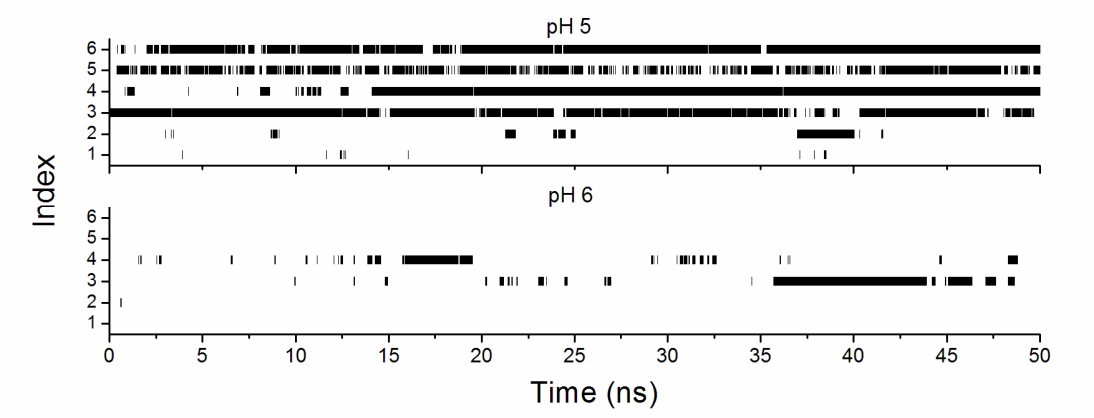

Figure S2. Protonation maps for Asp and Glu in function of the time for pH 5 and 6. The index number and related Asp and Glu are (1)Asp10, (2)Asp42, (3)Glu44, (4)Glu147, (5)Glu338, and (6)Glu370.

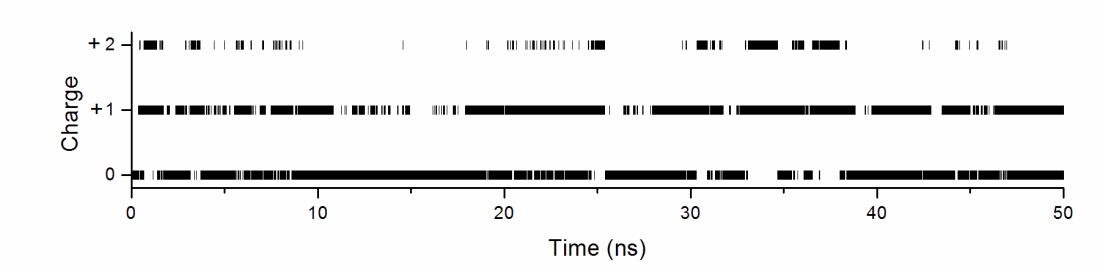

Figure S3. Existence map of the sum of the charges of His209 and His282 during the simulation at pH 7.

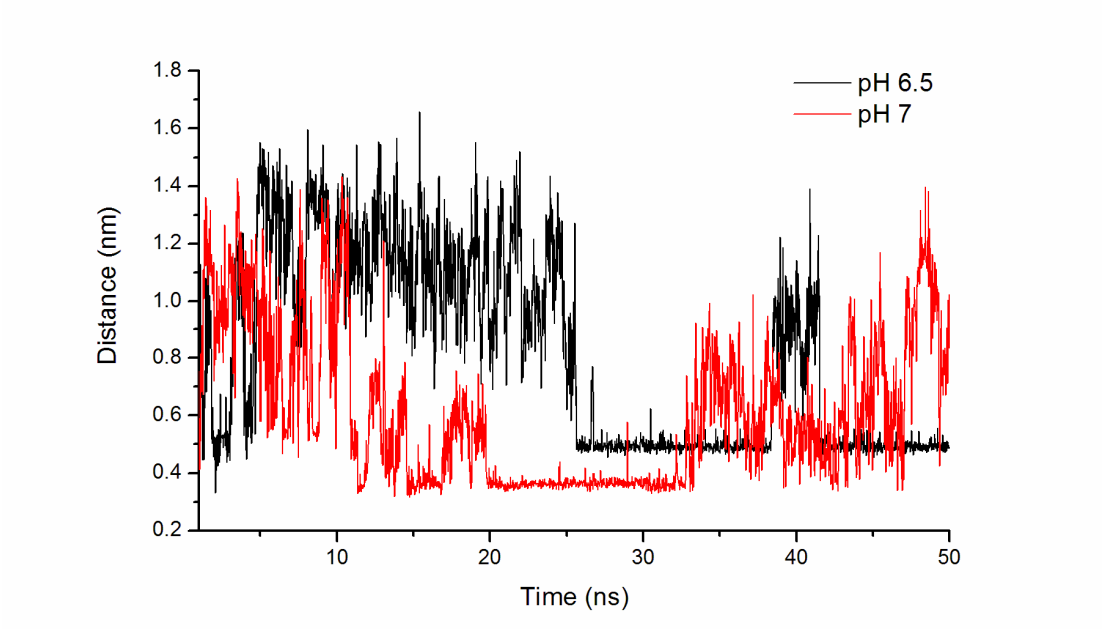

Figure S4. Distance between the center of mass of the side chains of His244 and Asp98 showing the formation of a salt bridge when His244 is double protonated.

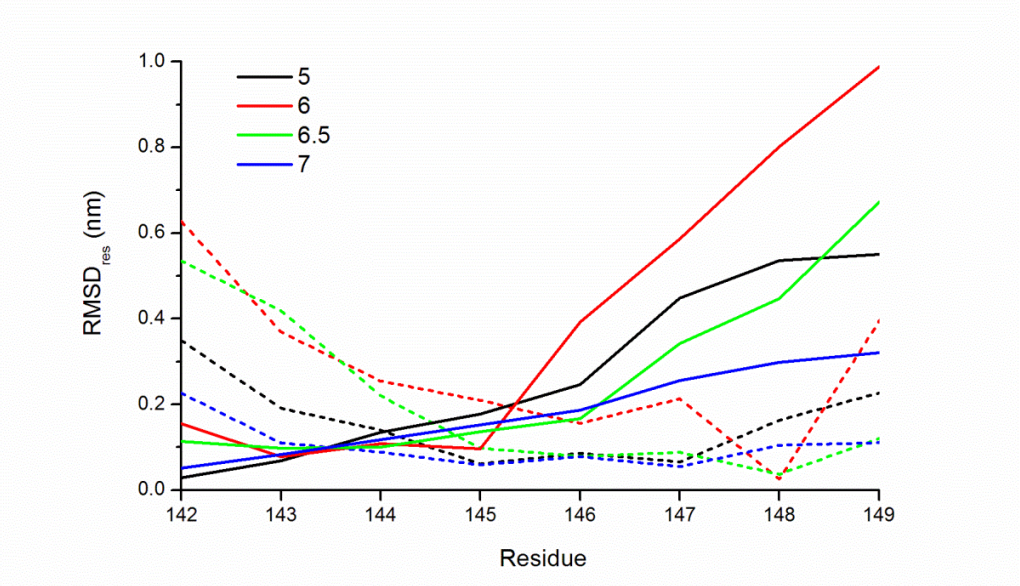

Figure S5. $RMSD_{res}$ in the DI Thr142-His149 segment obtained by the fit, relatively to the averaged pH 8 structure, of DIII (dashed lines) and DI (solid lines) in the averaged structures. The $RMSD_{res}$ are small along the Thr142-Ser145 region while they are larger in the Gly146-

Glu148 segment by the fit of DI, thereby proving that the residues His144-Ser145 perform the function of a hinge. This conclusion is in agreement with the rotation of DIII (Figure 6) where the reference residues of the center of the rotation (Thr353, Val354, and Val367) are close to residues His144 and Ser145.

Table S1. Protonated fraction of the N-terminus group. The predicted pK_a is 6.72

pH 5	**pH 6**	**pH 6.5**	**pH 7**	**pH 8**
1.00	1.00	0.80	0.16	0.01

Table S2. Protonated fraction of Glu and Asp residues at pH 5 and 6. For pHs higher than 6, they are not protonated

pH	**Asp42**	**Glu44**	**Glu147**	**Glu338**	**Glu370**
5	0.10	0.85	0.76	0.64	0.88
6	0	0.24	0.13	0	0