Characterizing Loop Dynamics and Ligand Recognition in Human- and Avian-type Influenza Neuraminidases via Generalized Born Molecular Dynamics and End-point Free Energy Calculations

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Supporting Information

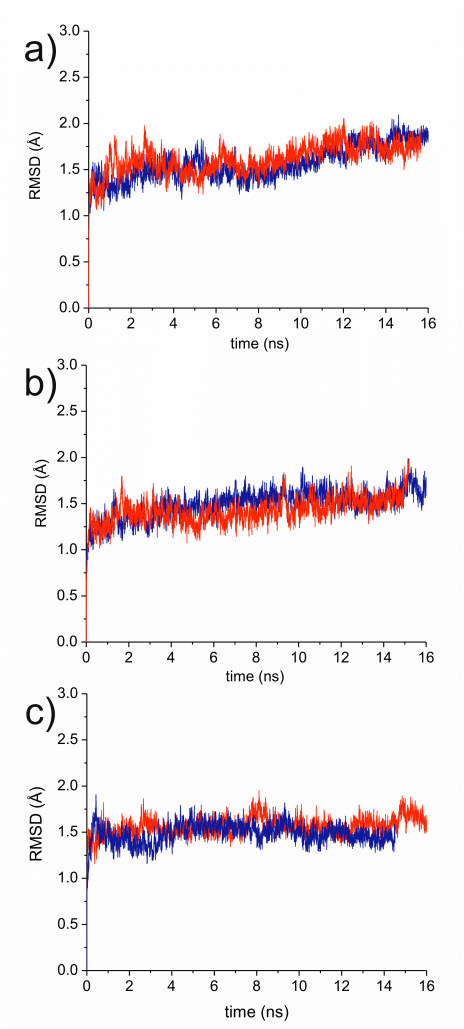

Figure S1: Overall RMSD for all backbone atoms. Overall root-mean-square deviations of the backbone atoms for the N1-closed (a), the N9-closed (b) and the N1-open (c) systems. Blue lines correspond to the apo simulations while red lines correspond to the oseltamivir-bound systems.

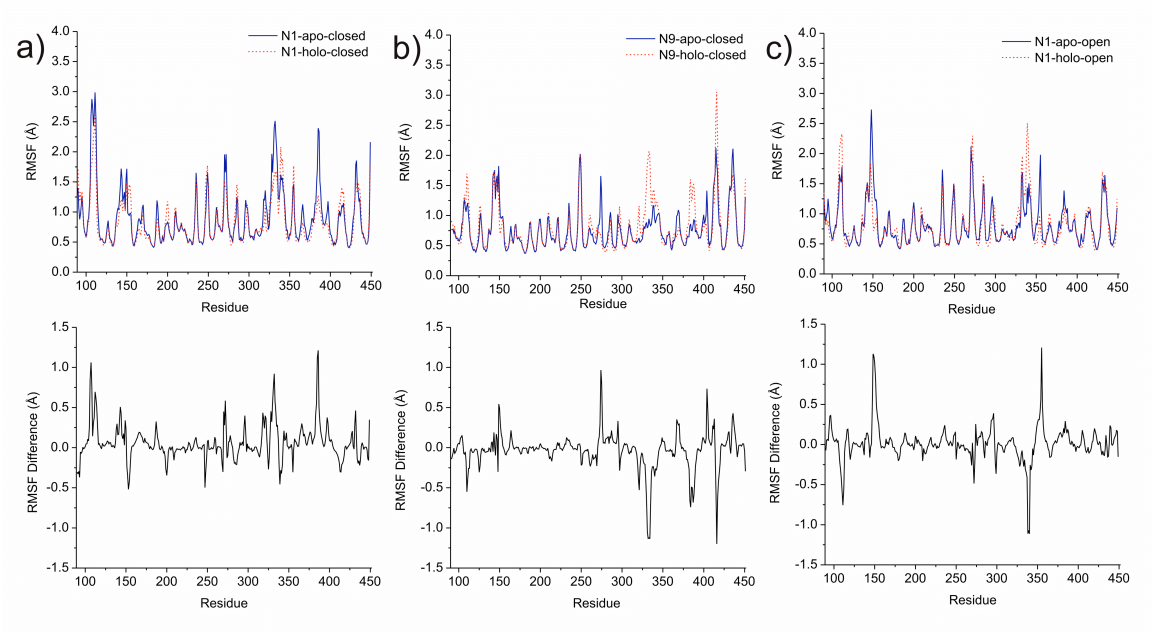

Figure S2: Root-mean-square fluctuation (RMSF) analysis. RMSFs per residue (top panels) for the N1-closed (a), the N9-closed (b) and the N1-open (c) systems are shown with solid blue lines representing the apo simulations and dotted red lines representing the oseltamivir-bound systems. The bottom panels represent the corresponding RMSF Differences for the three systems (apo subtracted from holo).

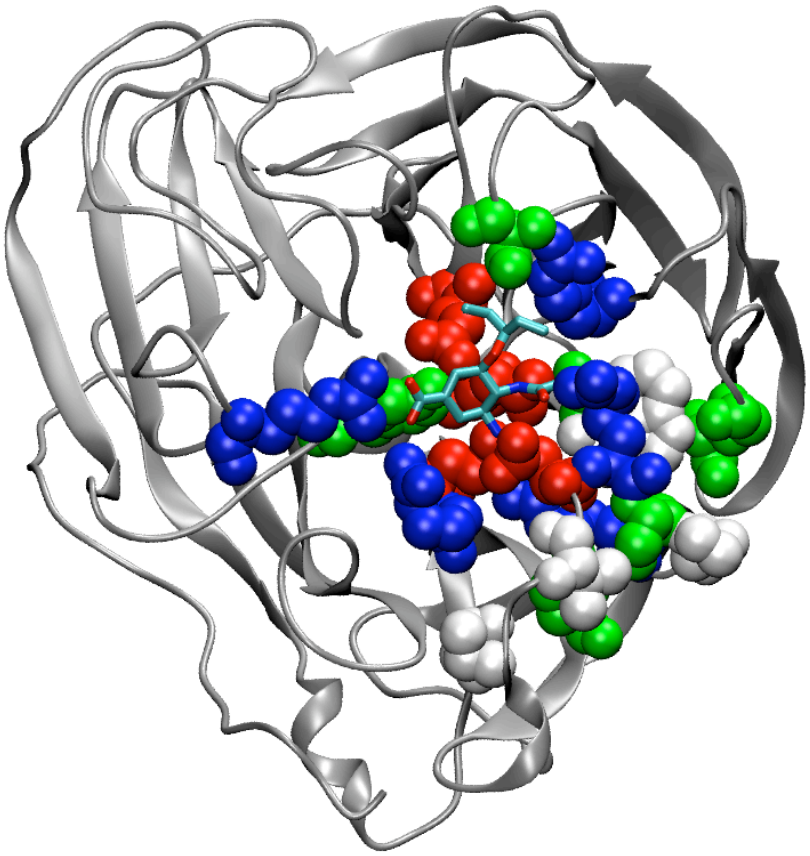

Figure S3: N1 Sialic acid and 150-loop hot spot residues. The hot spot residues in the sialic acid region (residues 118, 119, 224, 227, 246, 277, 371, 406) and 150-loop region (residues 116, 136, 149, 151, 152, 153, 154, 156, 178, 179, 195, 196) of N1 are shown in space filling and colored by residue type (green: polar, white: hydrophobic, red: acidic, blue: basic). The N1 backbone is shown in grey cartoon and oseltamivir is shown in licorice (carbons: cyan, oxygens: red, nitrogens: navy blue; for clarity no hydrogens are displayed).

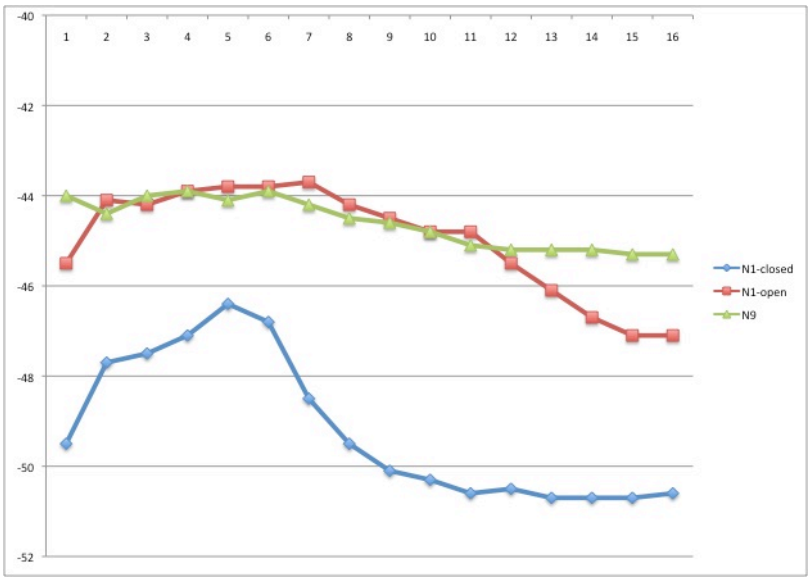

Figure S4: Convergence of the MM-GBSA Calculations. The MM-GBSA binding free energies for the N1-closed (blue square), N1-open (red circle), and N9 (green triangle) systems are shown as a function of simulation length in 1 ns increments. Energies are plotted in kcal/mol.

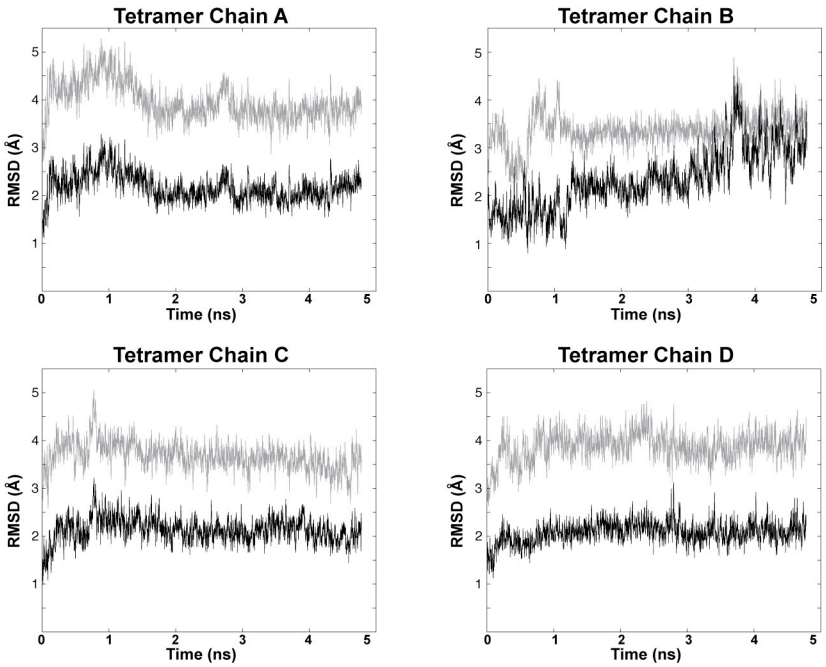

Figure S5: Tetramer Open/Close Loop Transitions. Root-mean-square deviation (RMSD) of the 150-loop (comprising residues N146-R152) from the MD with respect to the open (grey) and closed (black) crystal structures are shown for the N1-oseltamivir-bound-closed tetramer simulations.

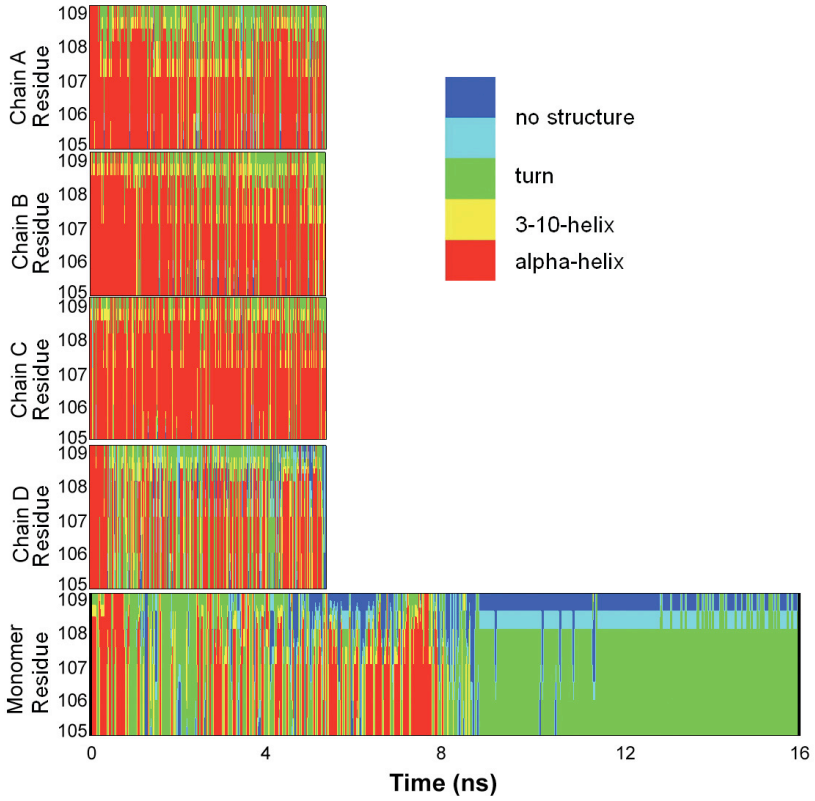

Figure S6: Secondary Structure Character of the 110-Helix. Secondary structure characterization of the core of the 110-helix (residues 105 to 109), shown as a function of time. The four chains extracted from the tetramer simulation are shown in the top four panels and the 16 ns monomer simulation is shown on the bottom.

Complete reference 9:

9) Itzstein, M. v.; Wu, W.-Y.; Kok, G. B.; Pegg, M. S.; Dyason, J. C.; Jin, B.; Phan, T. V.; Smythe, M. L.; White, H. F.; Oliver, S. W.; Colman, P. M.; Varghese, J. N.; Ryan, D. M.; Woods, J. M.; Bethell, R. C.; Hotham, V. J.; Cameron, J. M.; Penn, C. R. *Nature* **1993**, *363*, 418-423.