Interdomain Twists of Human Thymidine Phosphorylase and its Active-Inactive Conformations: Binding of 5-FU and its Analogues to hTP *vs.* DPD

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SUPPLEMENTARY INFOMATION

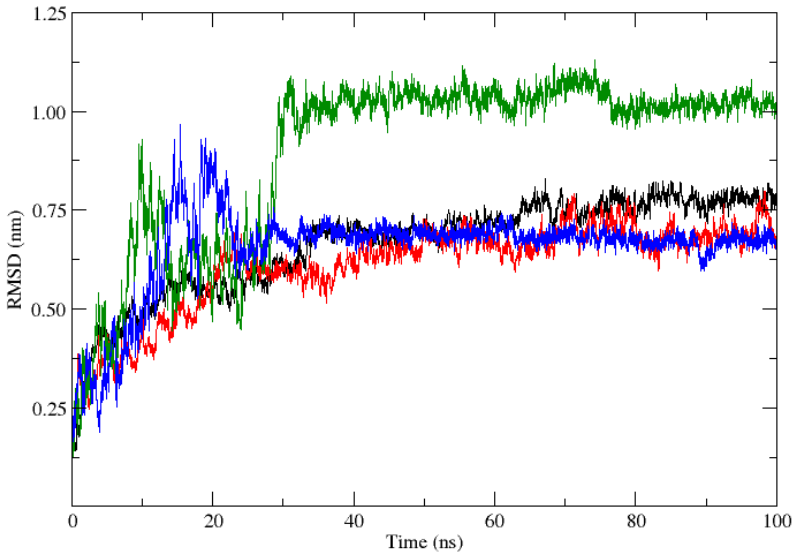

Figure S1: Root Mean Square Deviation (RMSD) plots of the backbone atoms of unliganded monomer (black), unliganded dimer (red), monomer complexed with neutral 5-FU (green) and monomer complexed with protonated 5-FU MD simulations over 100 ns.

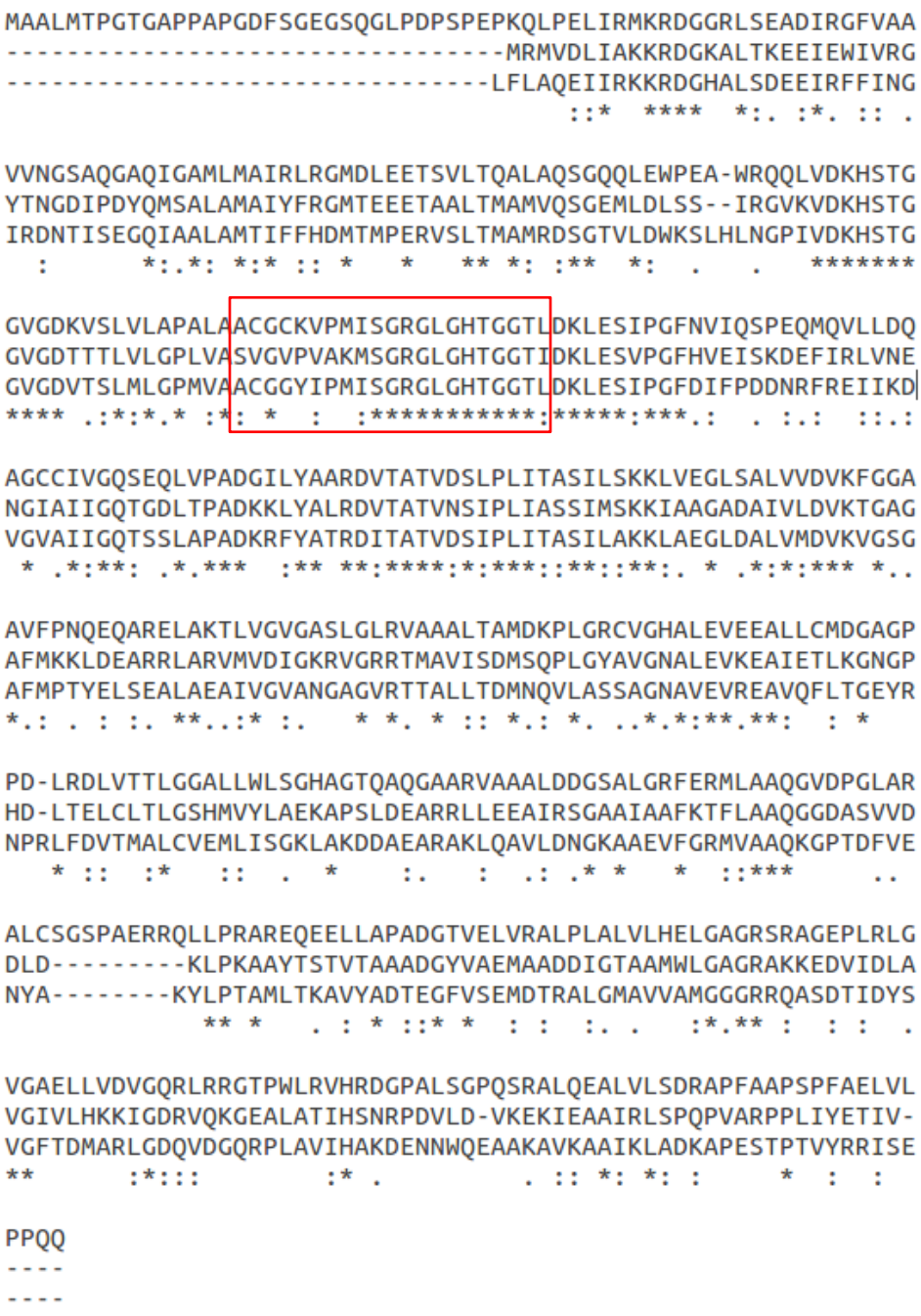

Figure S2: Sequence alignment of human thymidine phosphorylase (hTP) (2WK6), *Geobacillus sterothemophilus* pyrimidine nucleoside phosphorylase (BsPyNP) (1BRW), and *Escherichia coli* thymidine phosphorylase (EcTP) (1AZY) in respective order; the glycine rich area (in red square); each row includes maximum of 60 residues.

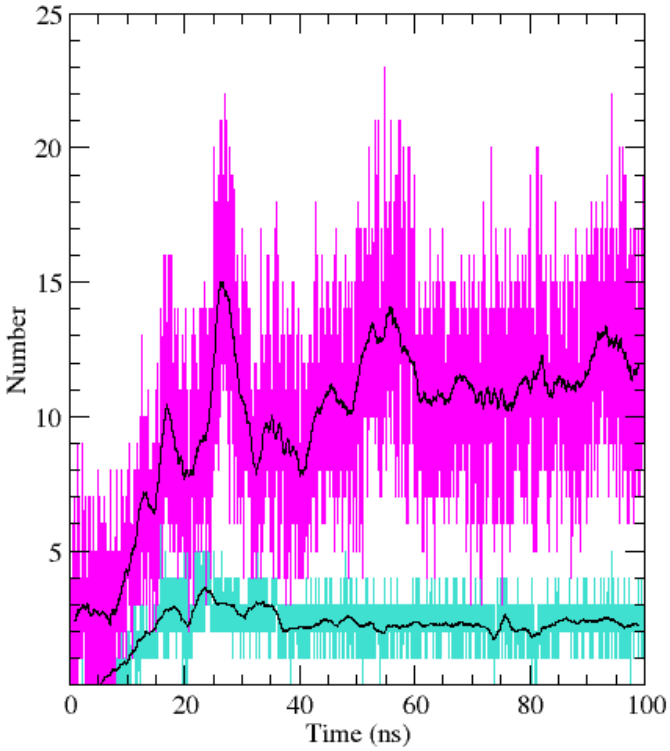

Figure S3: Number of hydrogen bonds between 5-FU and water in the monomer complex with protonated 5-FU. Number of hydrogen bonds is shown in cyan and number of pairs within 0.35 nm is shown in magenta; running averages of each are in black. Each running average single point was generated by averaging 100 frames.

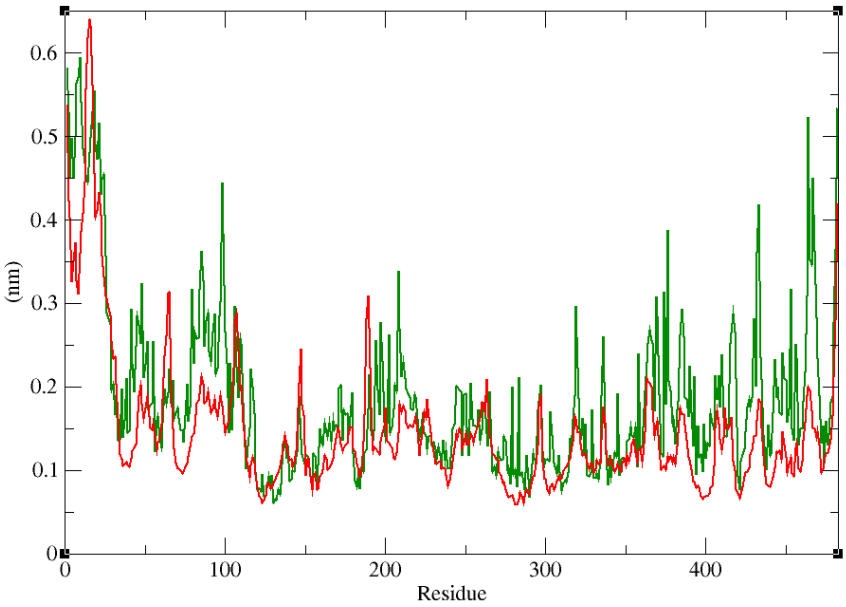

Figure S4: RMSF of the dimer bound to neutral ligands (green) and unliganded dimer (red)

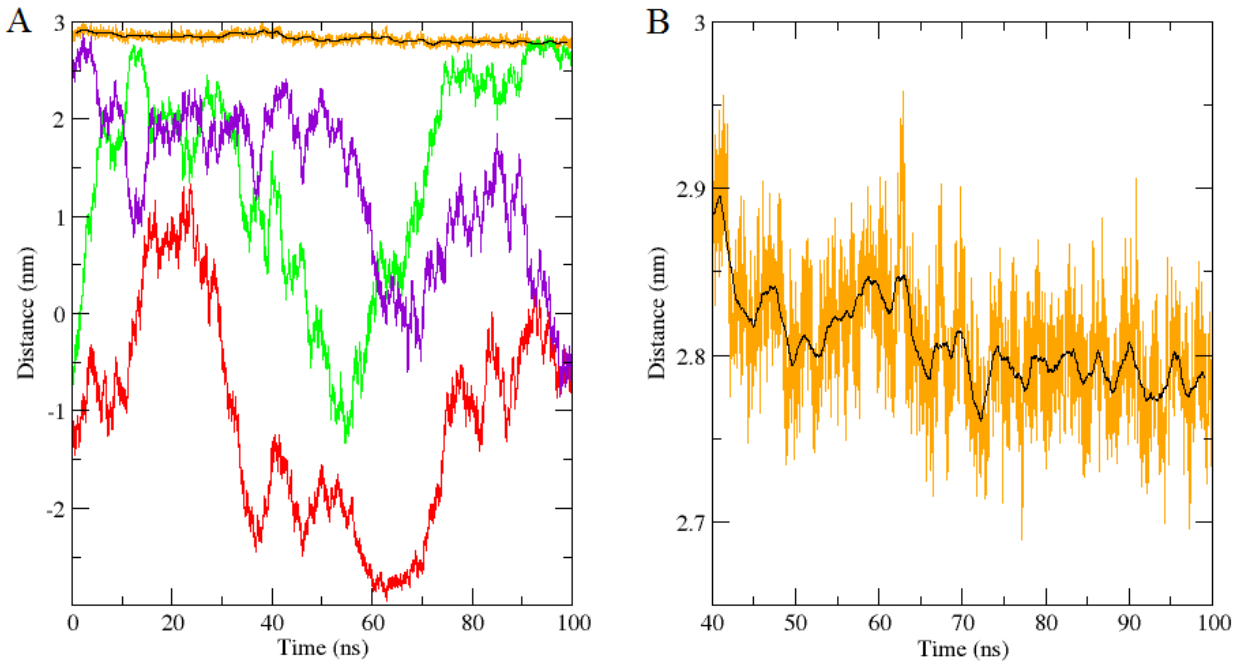

Figure S5: Plots of distance between the centre of mass of α-domain part A and α/β-domain part A of the unliganded monomer. Distance in x direction (red), y direction (green), z direction (purple) and absolute distance (orange) with running average (black). Each running average single point was generated by averaging 100 frames.

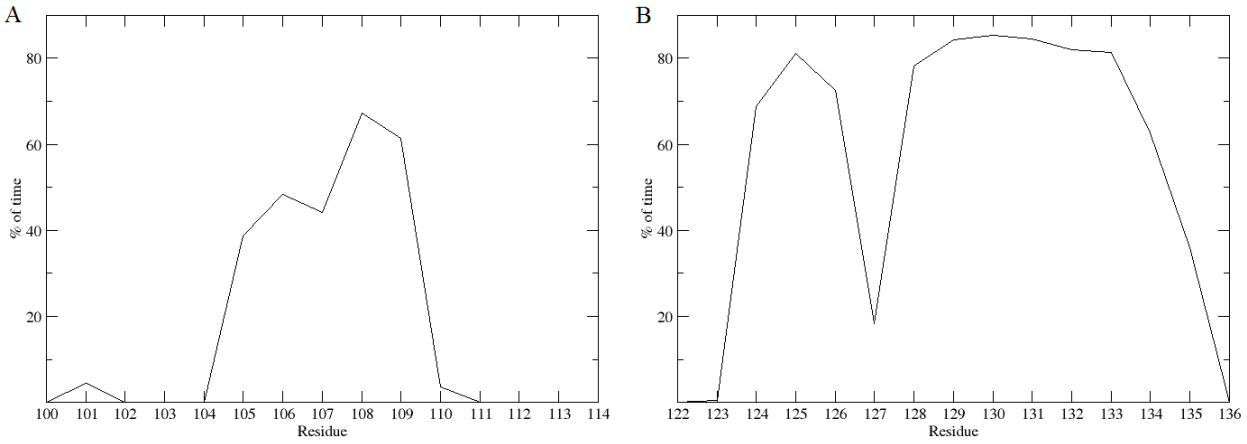

Figure S6: Helicity of A) a new small helix in hinge 1 and B) helix 5 in the unliganded monomer after convergence to 100 ns.

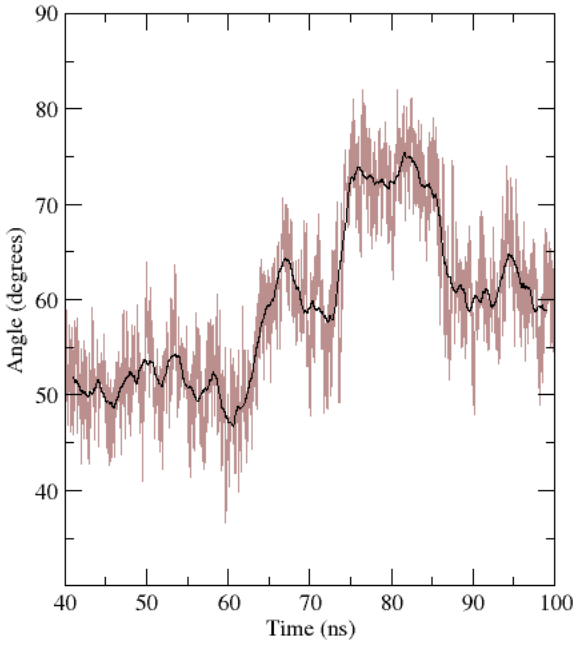

Figure S7: Angle between two planes of α-domain part A and α/β-domain part A (brown) with running average (black) in the unliganded monomer. Each running average single point was generated by averaging 100 frames.

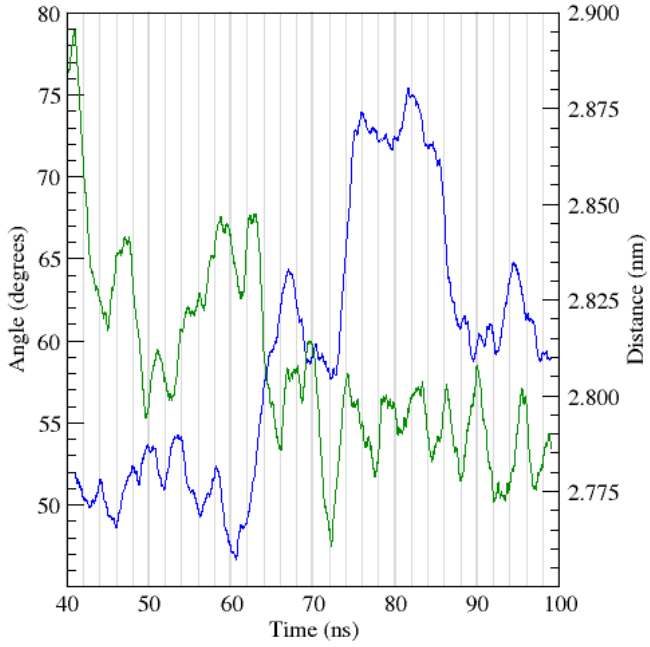

Figure S8: The running average angle between two planes (blue) and average distance between two centres of mass (green) of α-domain part A and α/β-domain part A of the unliganded monomer. Each running average single point was generated by averaging 100 frames.

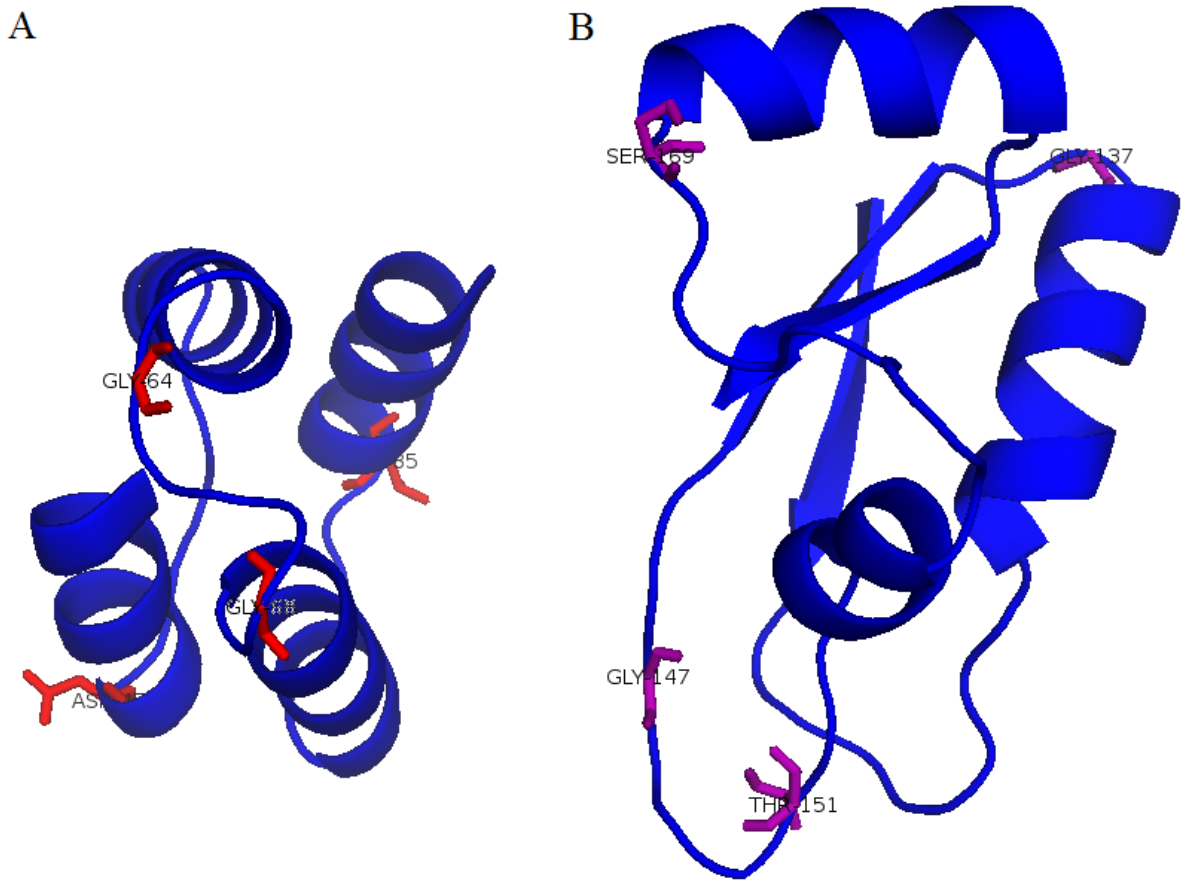

Figure S9: Residues with increased fluctuation of A) α-domain part A and B) α/β-domain part A (in red and purple respectively) in the unliganded monomer.

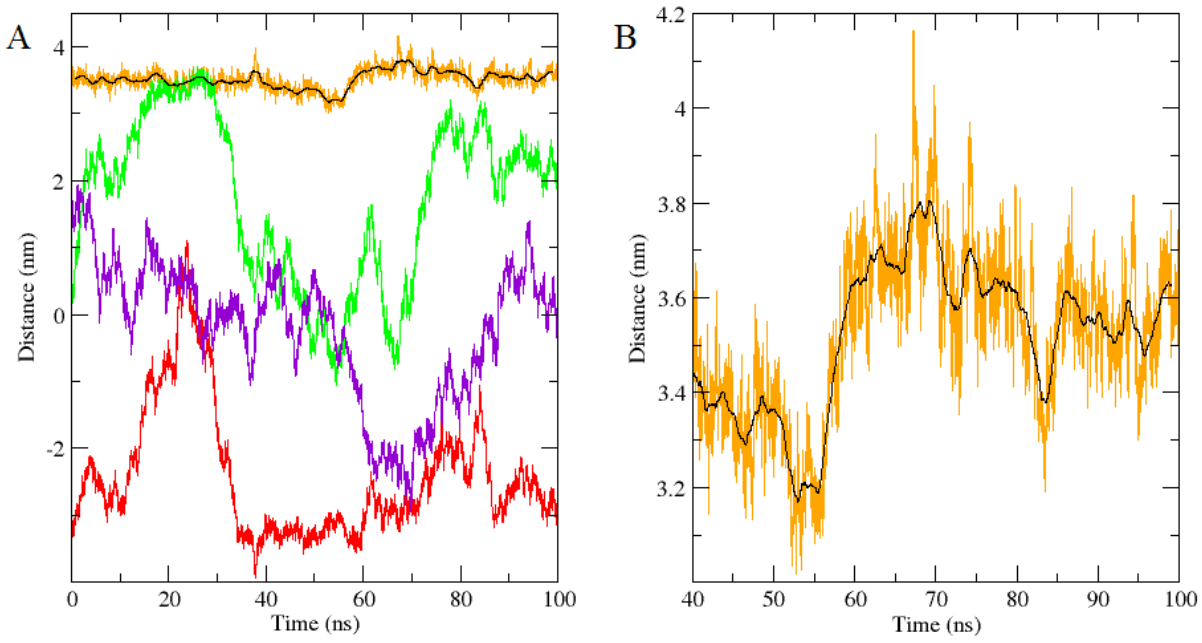

Figure S10: Plots of distance between the centre of mass of α-domain part B and α/β-domain part B of the unliganded monomer. Distance in x direction (red), y direction (green), z direction (purple) and absolute distance (orange) with running average (black). Each running average single point was generated by averaging 100 frames.

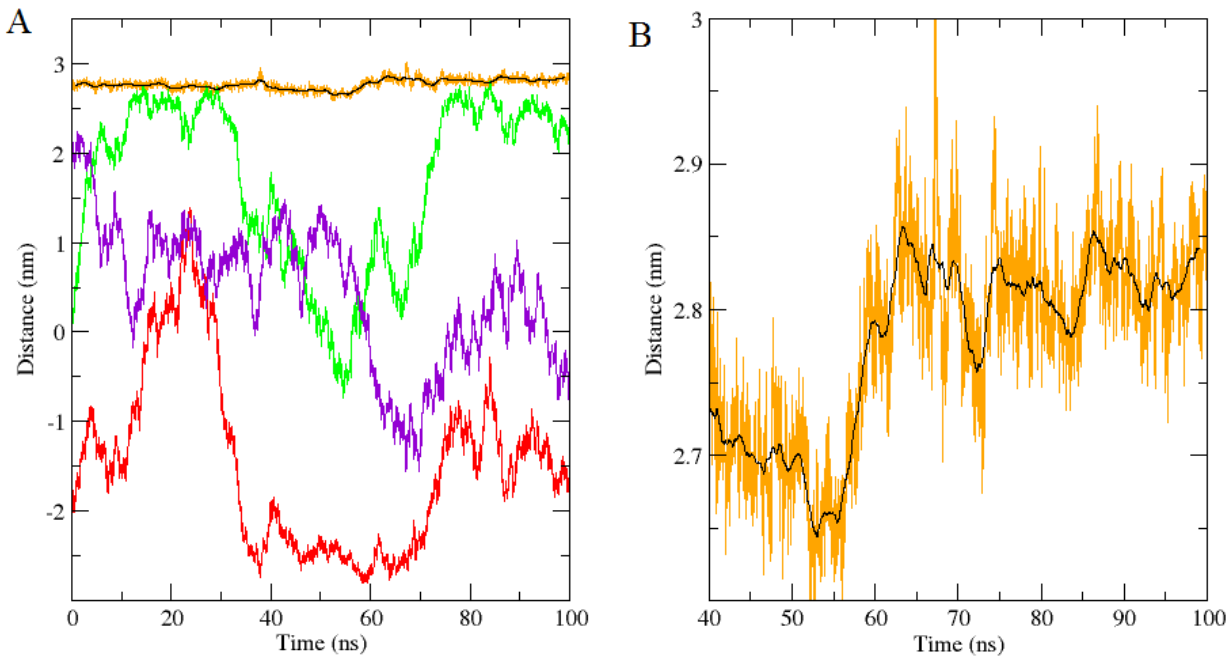

Figure S11: The running average distance between centres of mass plots of α-domain and α/β-domain (panel A) and angle between two planes of α-domain part A and α/β-domain part A (panel B) of unliganded monomer (black), unliganded dimer (red), monomer complexed with neutral 5-FU (green) and monomer complexed with protonated 5-FU (blue). Each running average single point was generated by averaging 100 frames.

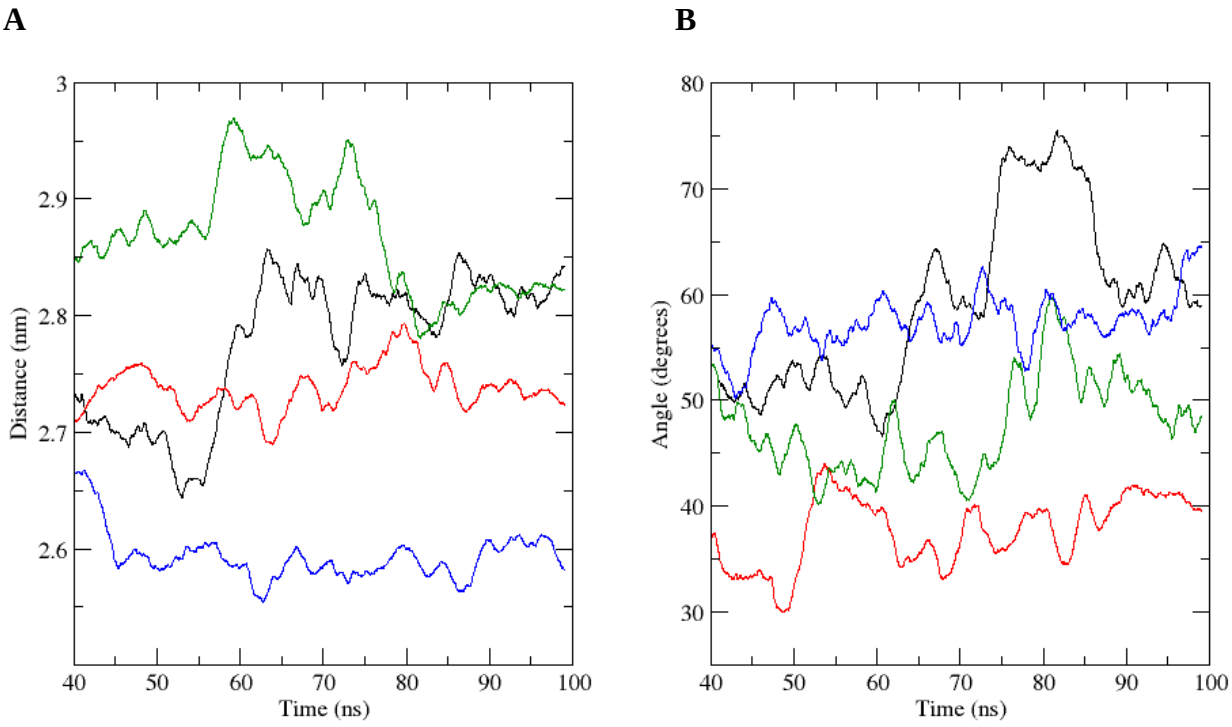

Figure S12: The running average distance between centres of mass plots of α-domain and α/β-domain (A) and angle between two planes of α-domain part A and α/β-domain part A (panel B) of unliganded monomer (black), unliganded dimer (red), monomer complexed with neutral 5-FU (green) and monomer complexed with protonated 5-FU (blue). Each running average single point was generated by averaging 100 frames.

A **B**

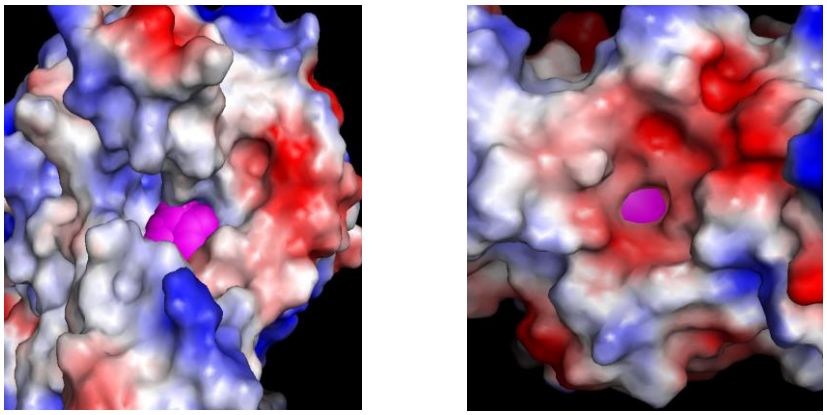

Figure S13: The Uracil fragment (magenta) in the binding site of (A) DPD and (B) in the hTP. The positive electrostatic surface (blue) and the negative (red).

A **B**

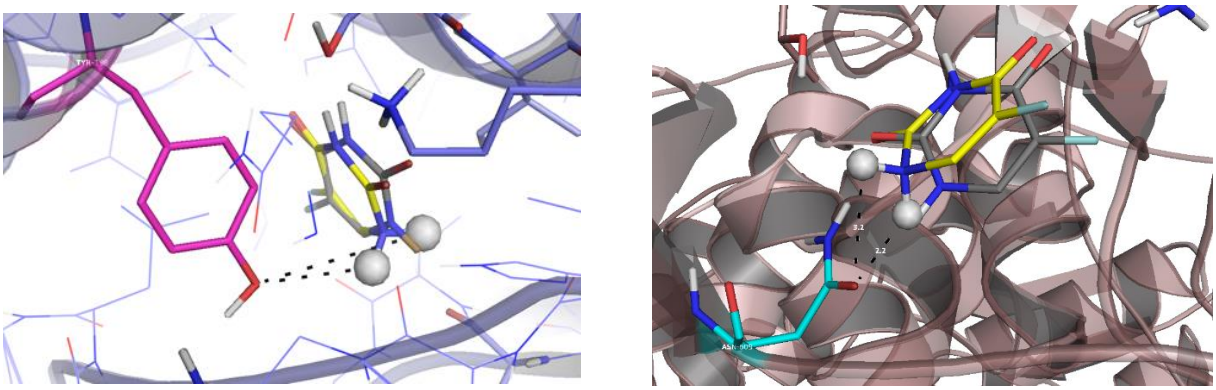

Figure S14: Superposition shows the slight displacement of the protonated 5-FU (yellow stick) compared to the position of the neutral (unprotonated) ligand (gray stick), (A) in the hTP, Tyr 199 (magenta); (B) in the DPD, Asn 609 (cyan), hydrogen bond (dashed line).