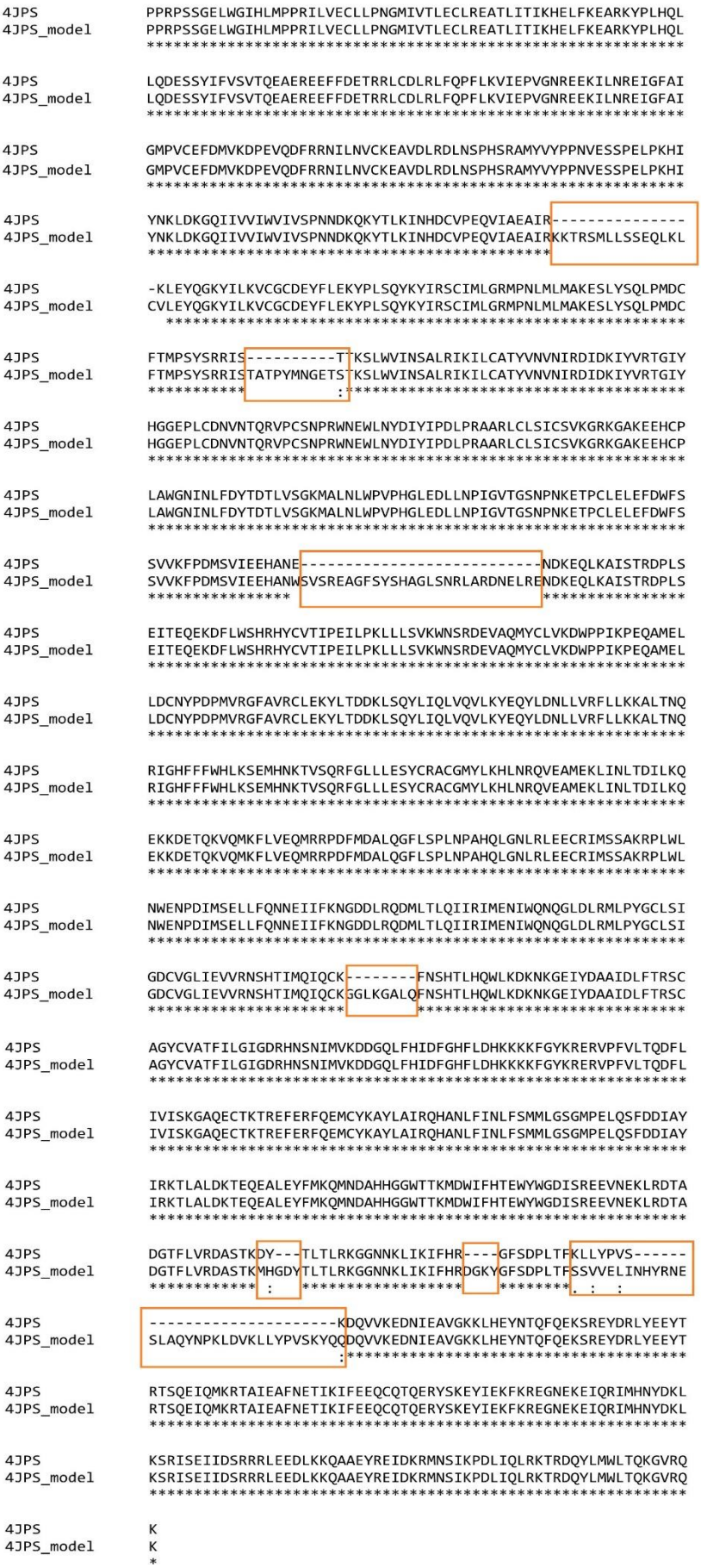
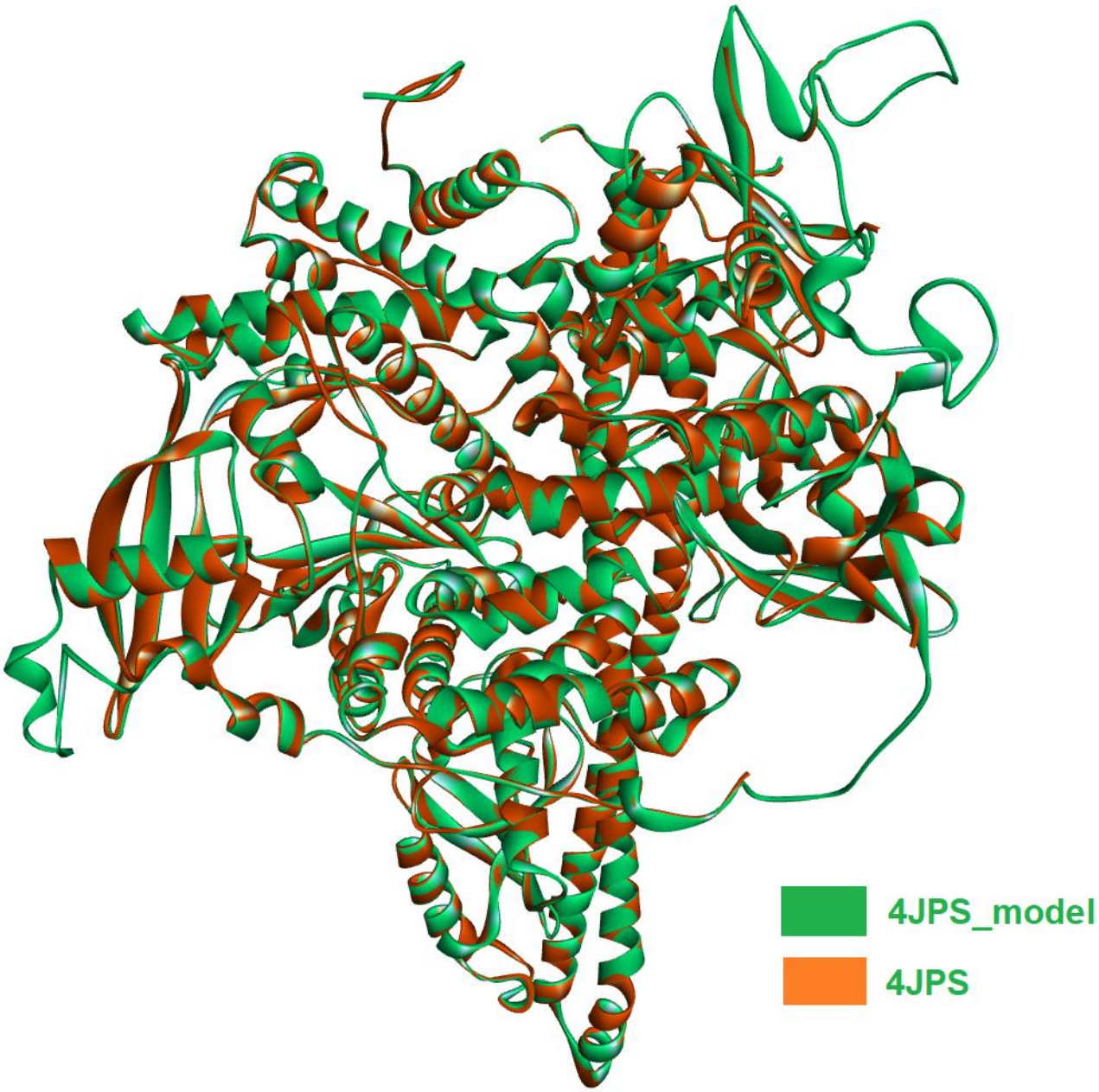
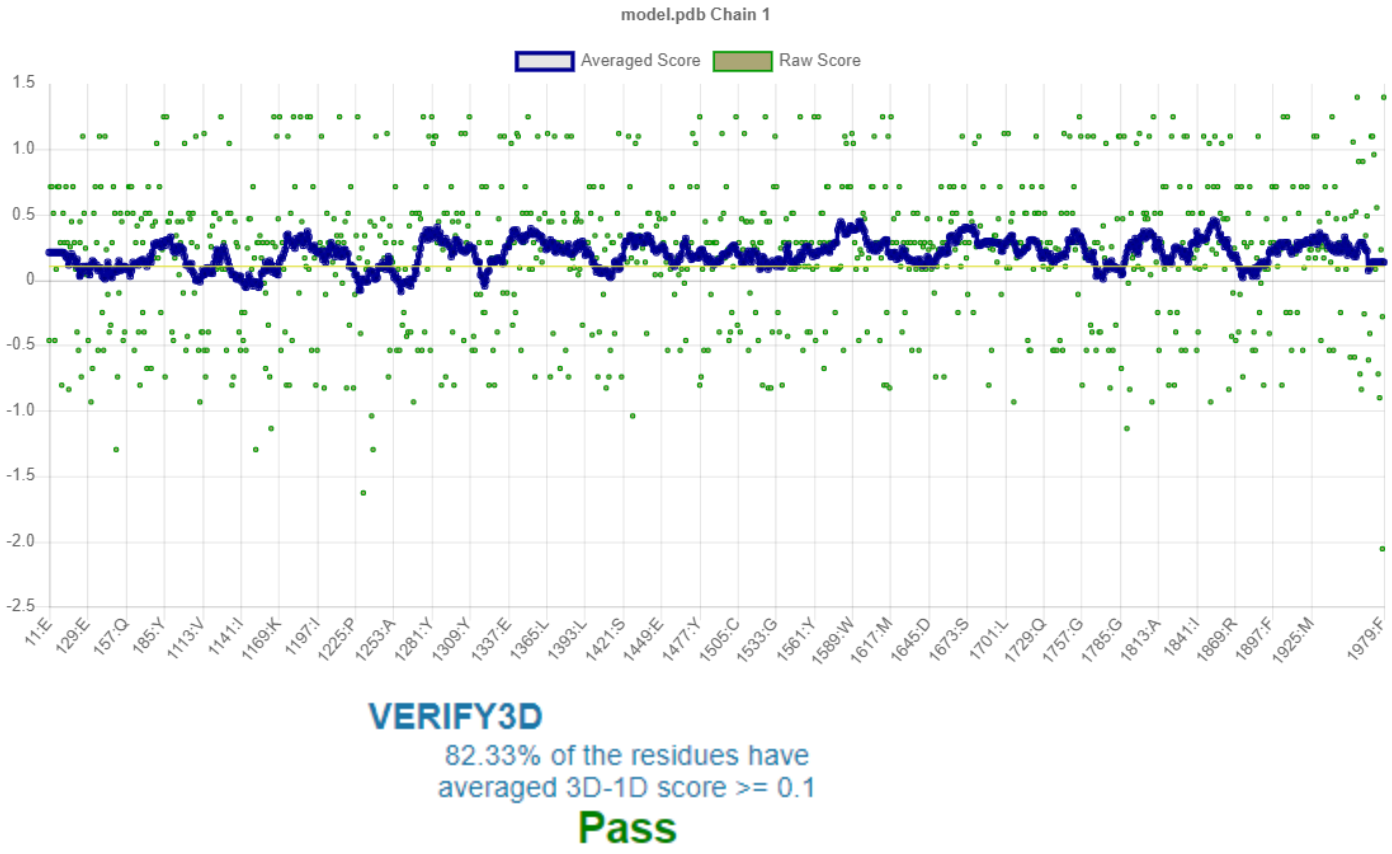


Supplementary Figure 1a: CLUSTAL 2.1 Multiple Sequence Alignments of PDB ID: 4JPS (PIK3CA) with its model structure from the SwissModel.



Supplementary Figure 1b: Alignment (overlay) of 4JPS (orange) obtained from the RCSB PDB with model (green) obtained from the SwissModel.



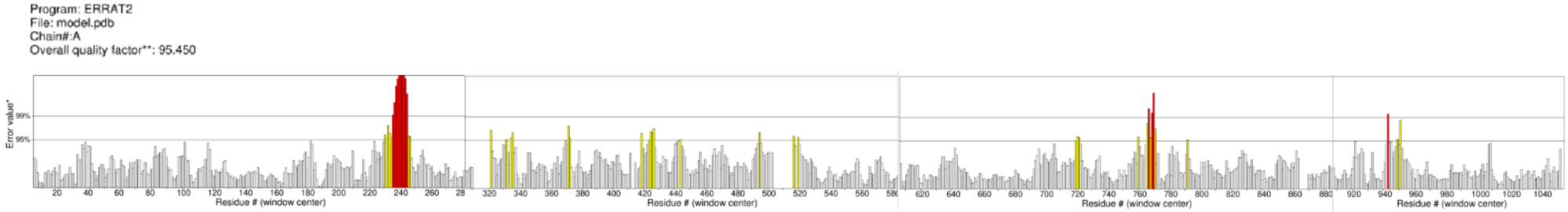
VERIFY3D

82.33% of the residues have
averaged 3D-1D score >= 0.1

Pass

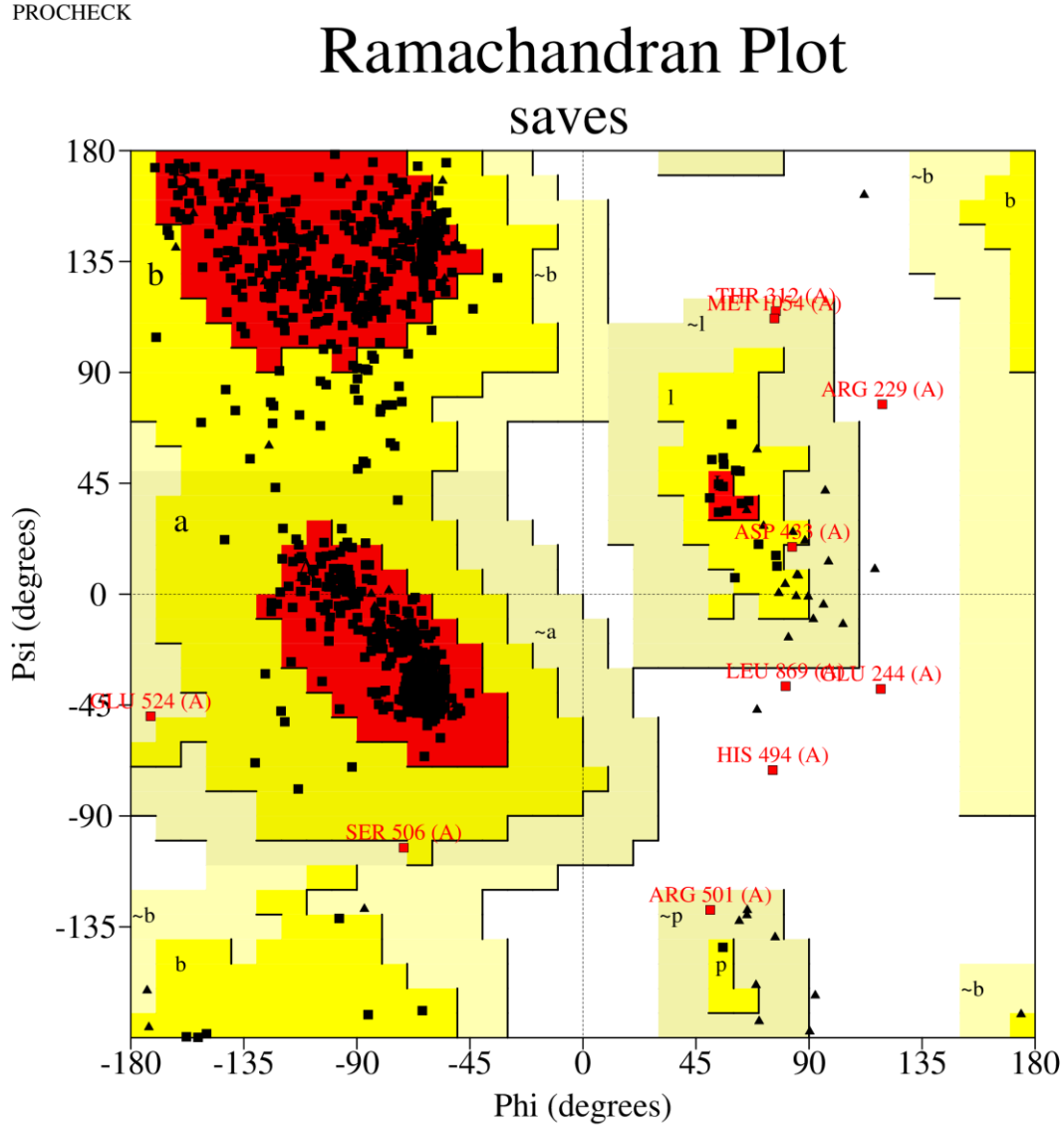
At least 80% of the amino acids have scored >= 0.1 in the 3D/1D profile.

Supplementary Figure 1c: Validation of 4JPS_model using Verify3D.



Supplementary Figure 1d: Validation of 4JPS_model using ERRAT2 showing 95.45% of quality factor.

PROCHECK

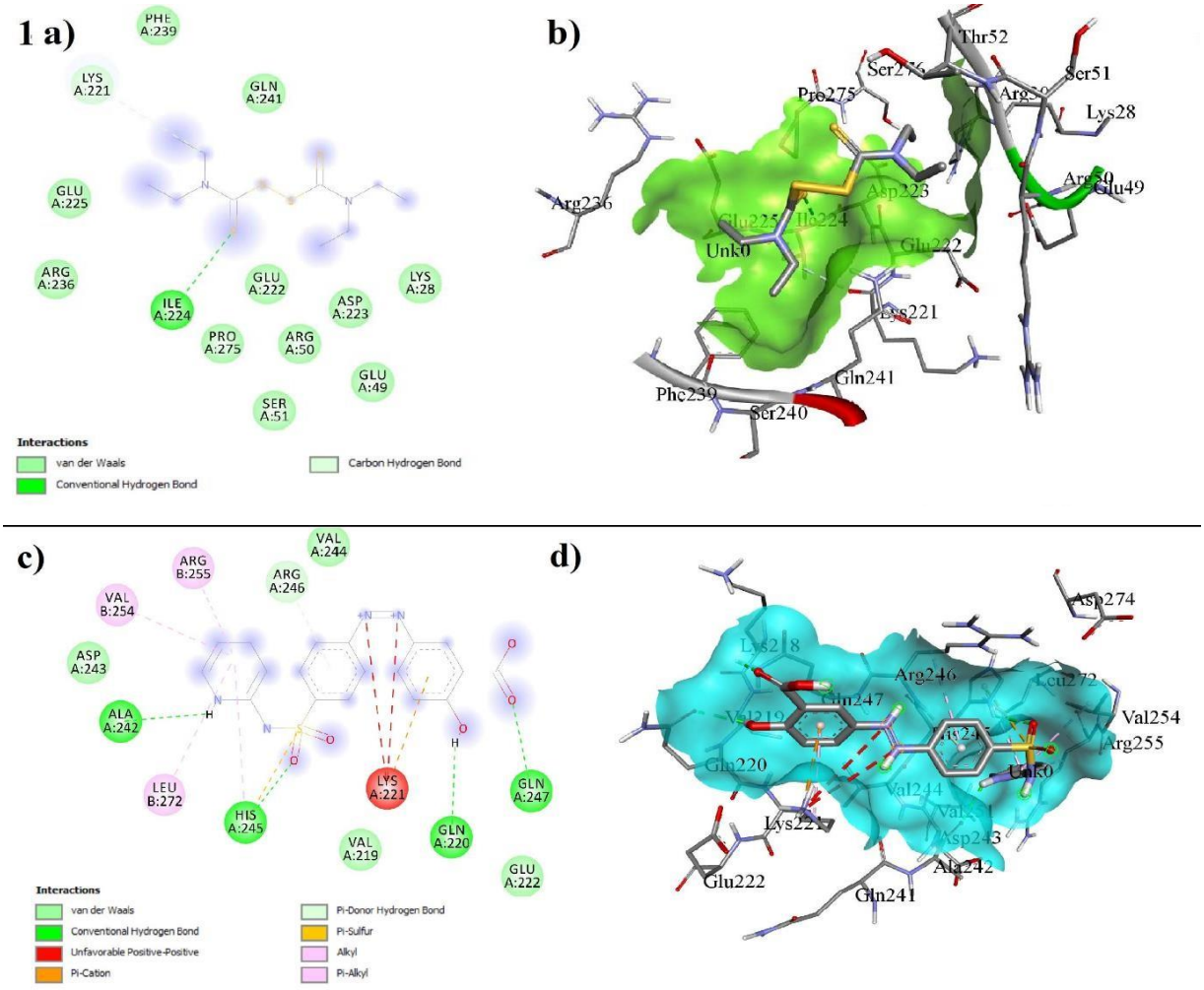


Plot statistics

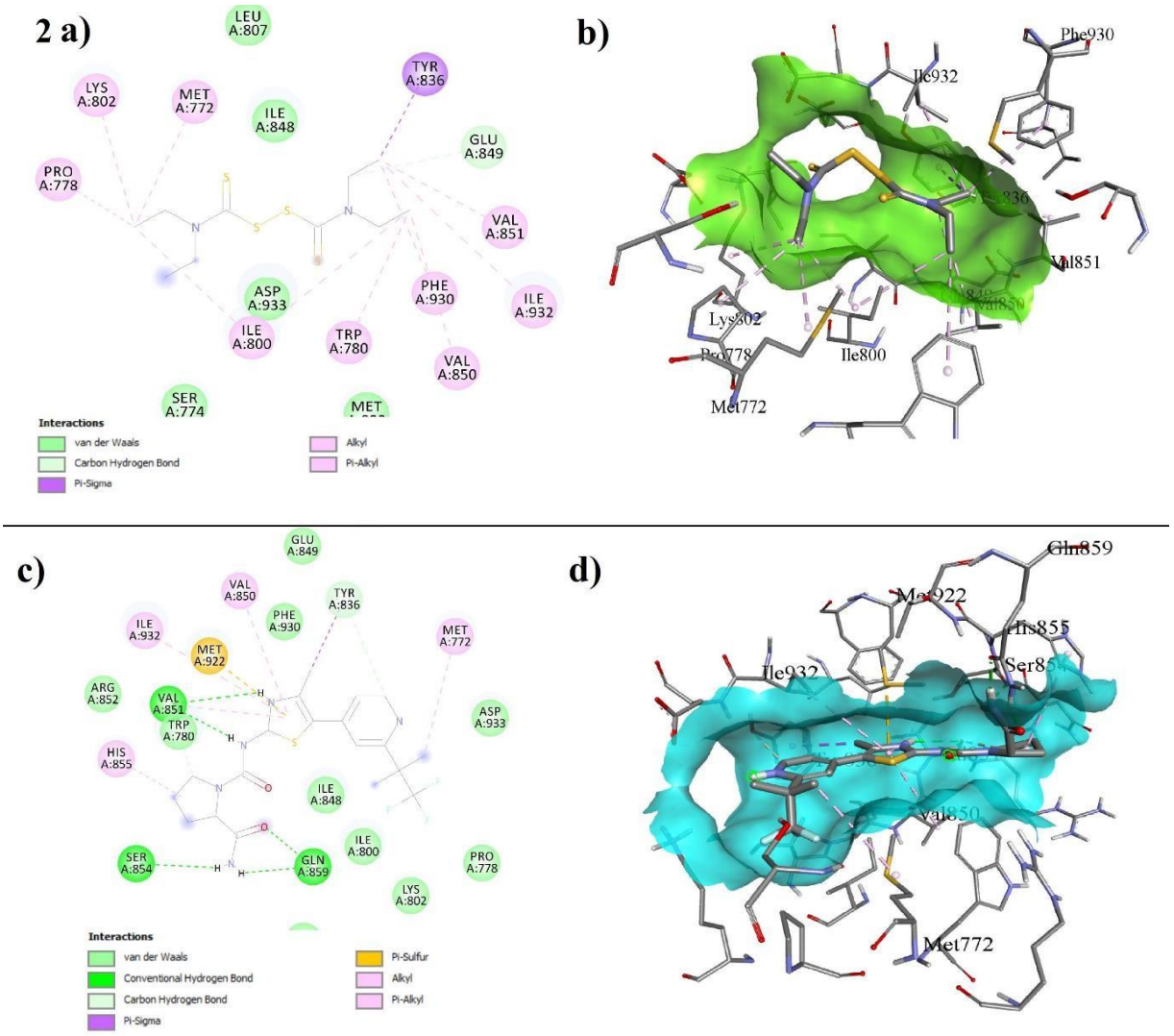
Residues in most favoured regions [A,B,L]	873	91.0%
Residues in additional allowed regions [a,b,l,p]	76	7.9%
Residues in generously allowed regions [~a,~b,~l,~p]	6	0.6%
Residues in disallowed regions	4	0.4%
	----	------
Number of non-glycine and non-proline residues	959	100.0%
Number of end-residues (excl. Gly and Pro)	3	
Number of glycine residues (shown as triangles)	49	
Number of proline residues	51	

Total number of residues	1062	

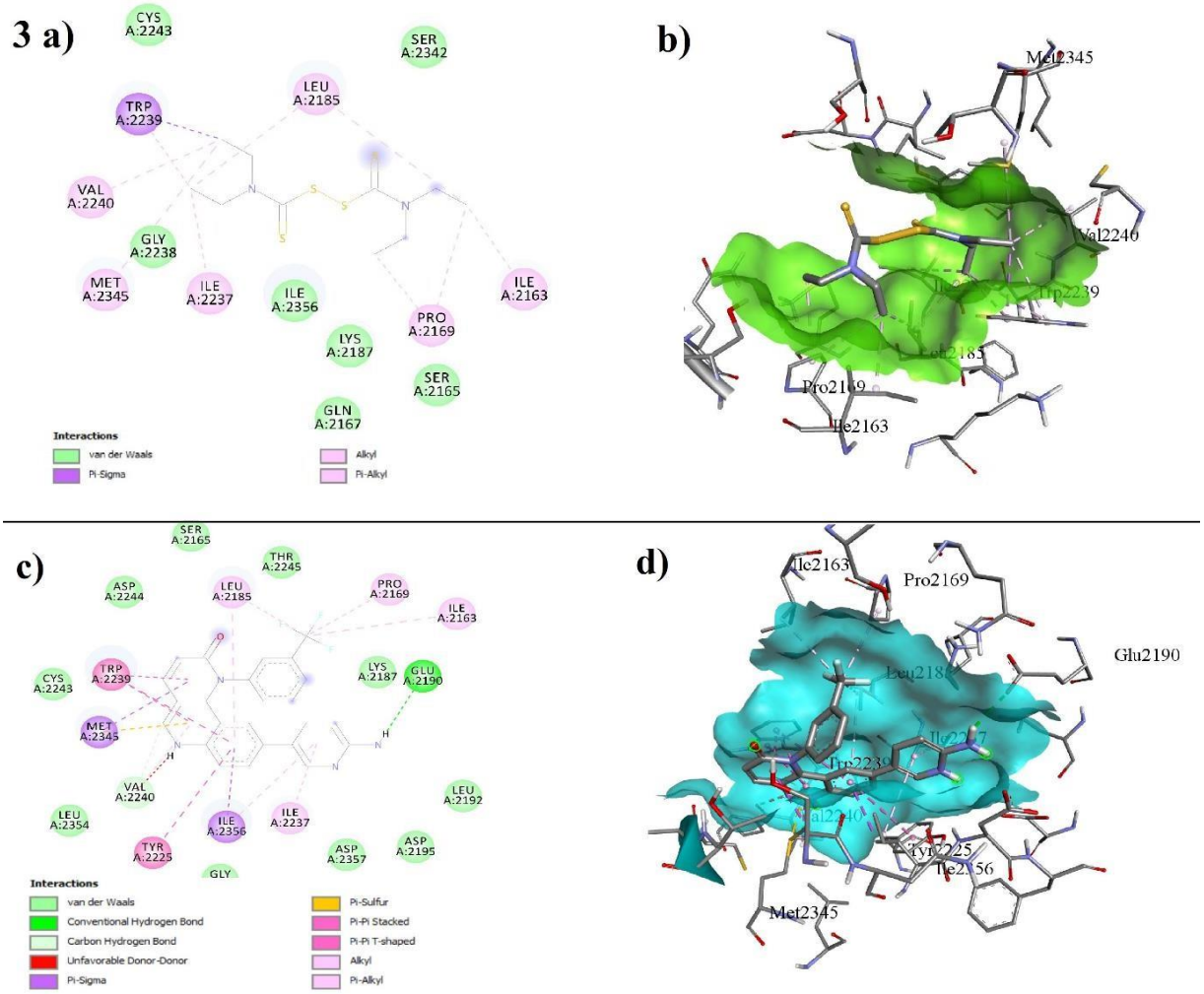
Supplementary Figure 1d: Validation of 4JPS_model using Ramachandran Plot showing about 98.9% residues in most favoured and additionally allowed region.



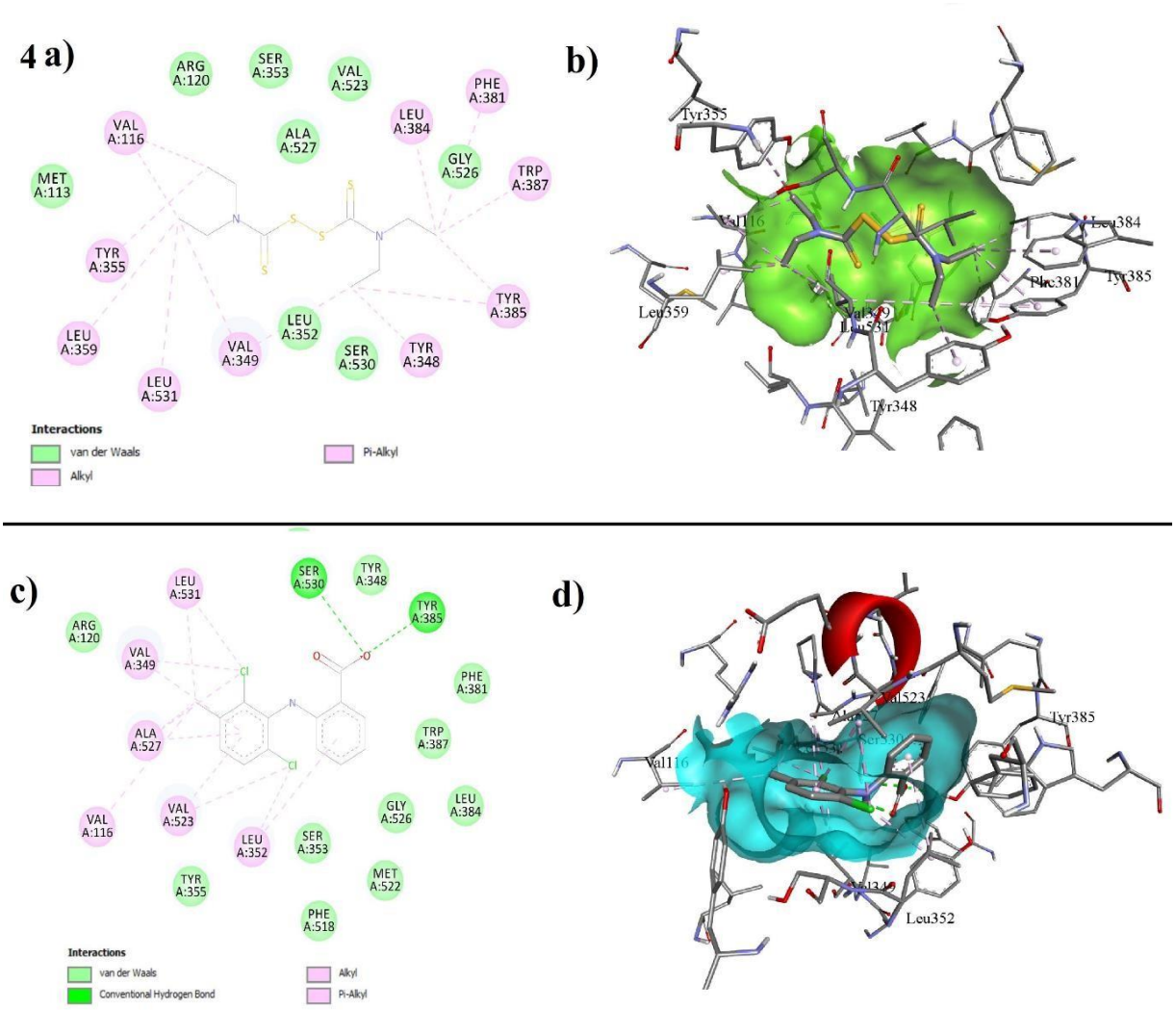
Supplementary Figure S2: 2D and 3D representation of Intermolecular interaction of DSF (a and b) and sulfasalazine (c and d) with NFKB. DSF formed one H-Bond with Ile224 and one hydrophobic bond with Lys221, whereas, sulfasalazine formed four H-Bond with Ala243, His245, Gln220, Gln247 and 6 hydrophobic bonds with Val254, Arg255, Leu272, His245 (2), Lys221.



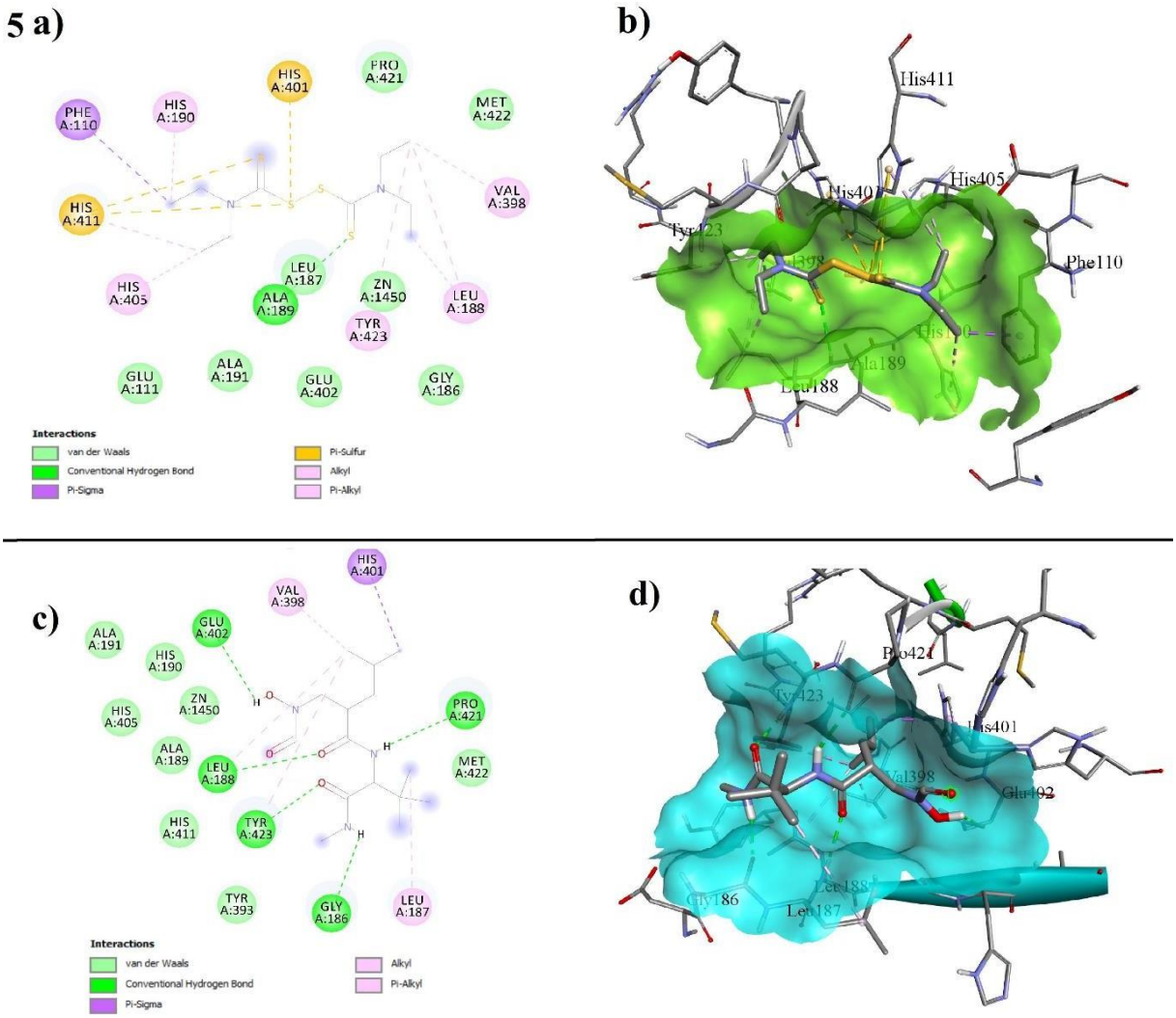
Supplementary Figure S3: 2D and 3D representation of Intermolecular interaction of DSF (a and b) and Alpelisib (c and d) with PIK3CA. DSF formed 11 hydrophobic bonds with Pro778, Lys802, Met772, Ile800, Trp780, Phe930, Val850, Ile932, Val851, Glu849, Tyr836, whereas, Alpelisib formed five H-Bond with Val851 (2), Ser854, Gln859 (2) and 11 hydrophobic bonds with His855, Val851 (4), Ile932, Met922, Val850, Tyr836 (2), Met772.



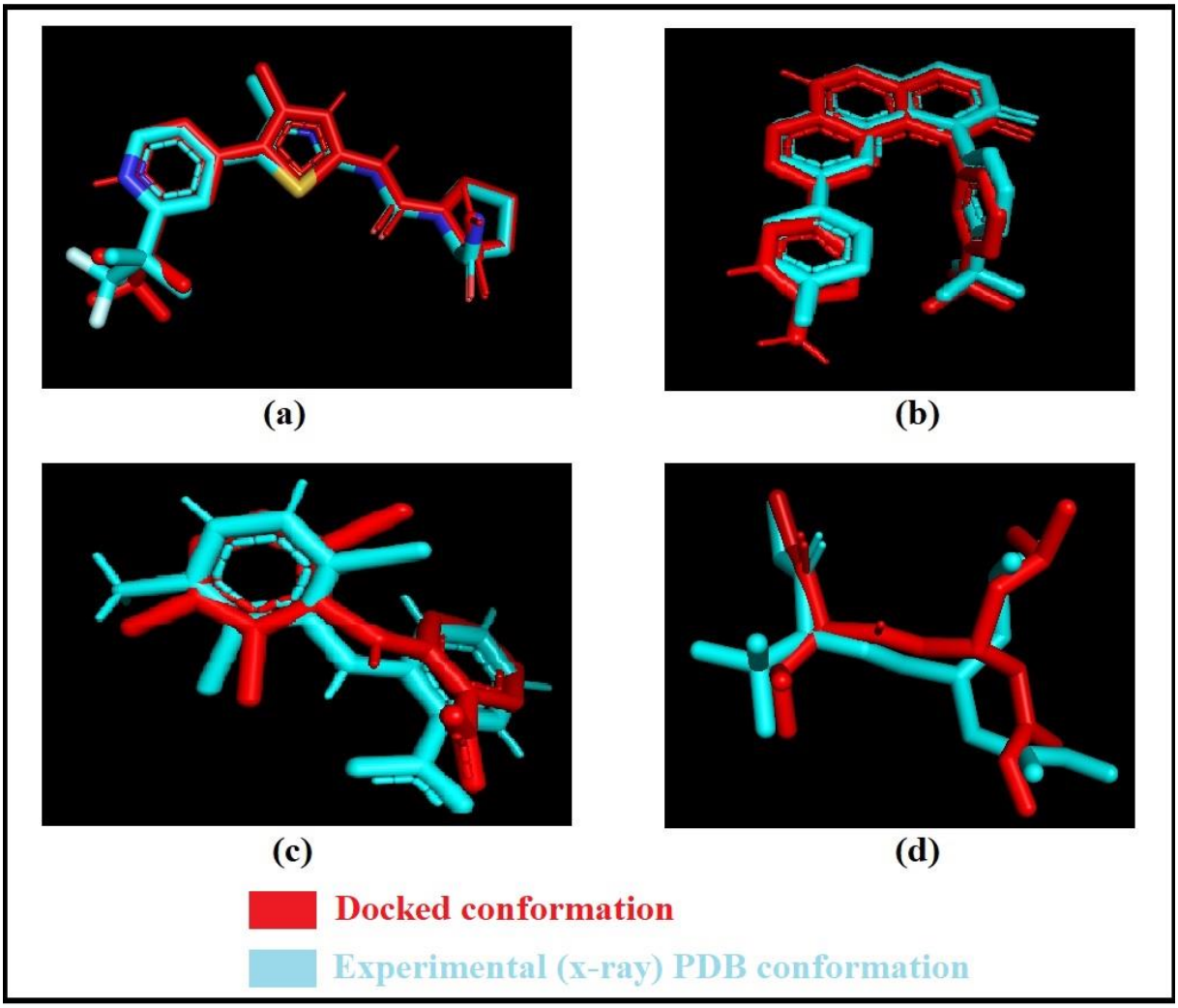
Supplementary Figure S4: 2D and 3D representation of Intermolecular interaction of DSF (a and b) and Torin- 2 (c and d) with MTOR. DSF formed 10 hydrophobic bonds with Leu2185 (2), Trp2239 (2), Val2240, Met2345, Ile2237, Pro2169 (2), Ile2163, whereas, Torin-2 formed one H-Bond with Glu2190 and 14 hydrophobic bonds with Ile2237, Ile2356 (2), Tyr2225, Val2240 (2), Met2345 (2), Trp2239 (2), Leu2185 (2), Pro2169, Ile2163.



Supplementary Figure S5: 2D and 3D representation of Intermolecular interaction of DSF (a and b) and Meclofenamic acid (c and d) with PTGS2. DSF formed 13 hydrophobic bonds with Val116 (2), Tyr355, Leu359, Leu531, Val349 (2), Tyr348, Tyr385 (2), Trp387, Phe381, Leu384, whereas, meclofenamic acid formed 2 H-Bond with Ser530, Tyr385 and 11 hydrophobic bonds with Leu531 (2), Val341 (2), Ala527 (2), Val116, Val523 (2), Leu352 (2).



Supplementary Figure S6: 2D and 3D representation of Intermolecular interaction of DSF (a and b) and NFH (c and d) with MMP9. DSF formed 1 H-bond with Ala189 and 11 hydrophobic bonds with His411 (3), His405, Tyr423, Leu188 (2), Val398, His401, His190, Phe110, whereas, NFH formed 5 H-Bond with Glu402, Leu188, Tyr423, Gly186, Pro421 and 5 hydrophobic bonds with Leu188, Tyr423, Leu187, Val398, His401.



Supplementary Figure S7: Overlay of docked conformations (red) and experimental (X-ray) PDB conformations (cyan) for (a) Alpelisib (PIK3R1/PIK3CA), (b) Torin-2 (mTOR), (c) Meclofenamic acid (PTGS2), and (d) NFH (MMP9). The RMSD values between the conformations were found to be 0.498, 0.657, 0.625, and 1.336 Å, respectively, showing the accuracy of the docking protocol in predicting binding poses with close alignment to experimental structures.

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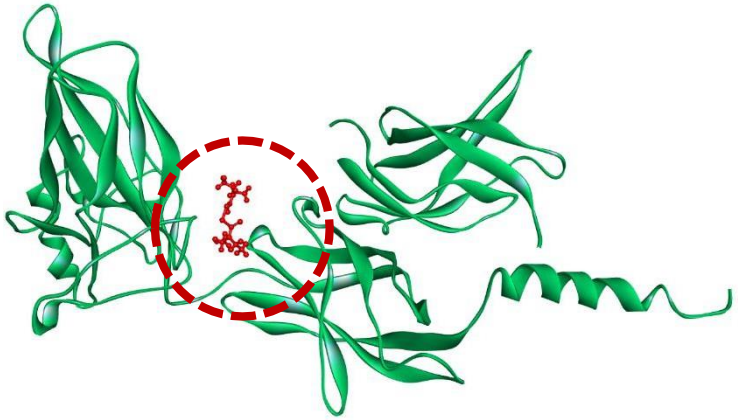
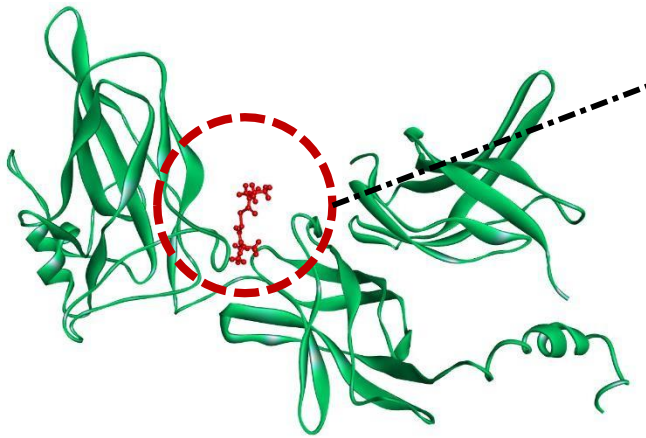
Supplementary Figure S8: NFKB - DSF

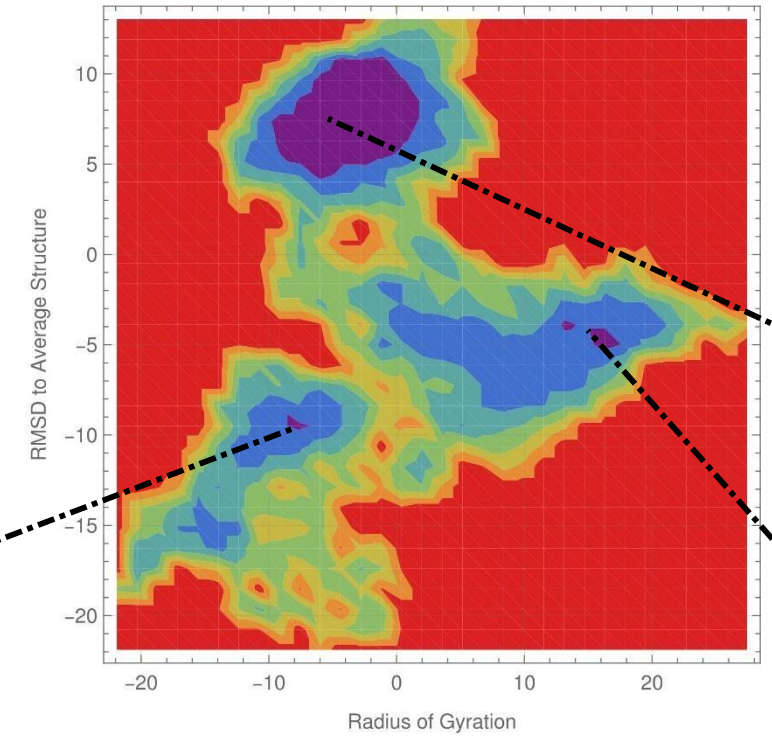


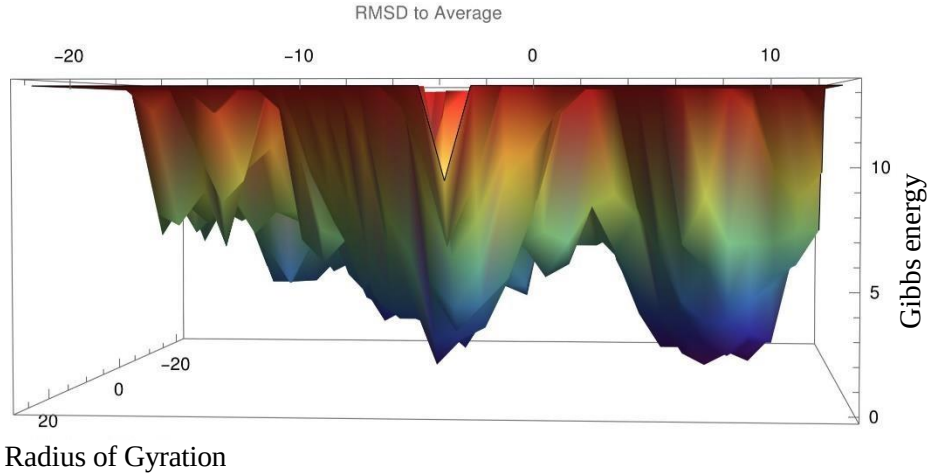
0ps

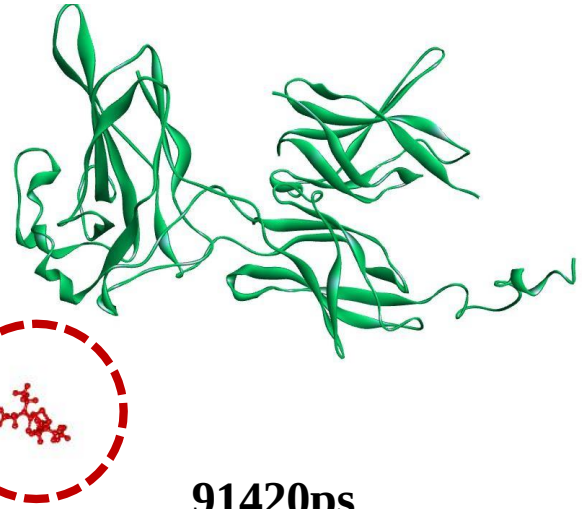


10020ps

DSF is within the active site

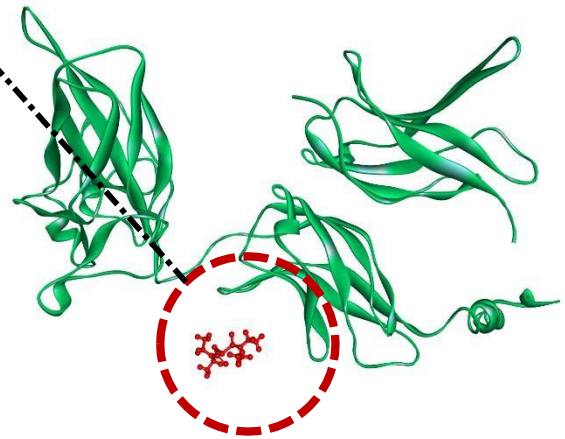






91420ps

DSF is out of active site

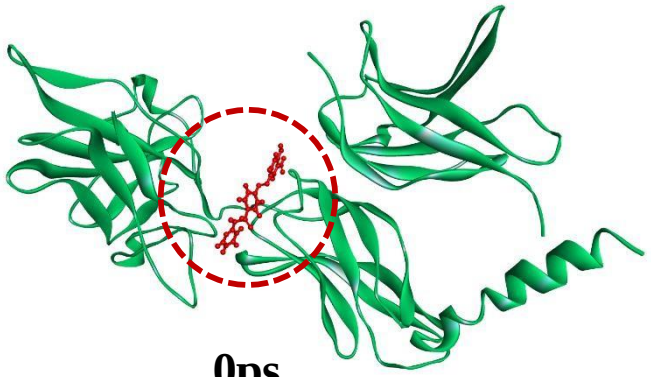


<u>27420ps</u>

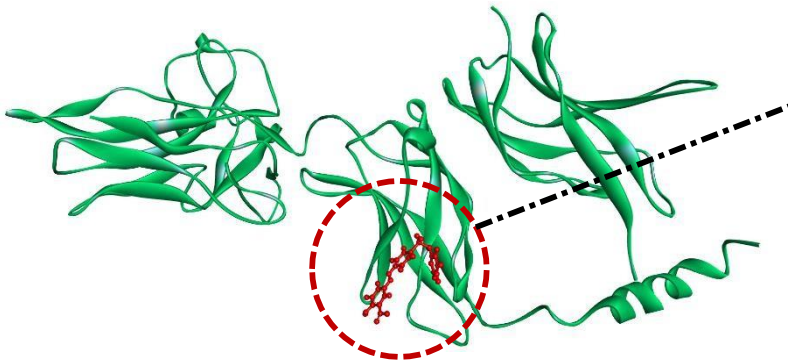
At this point

DSF is moving out of active site

Supplementary Figure S9: NFKB - Sulfasalazine

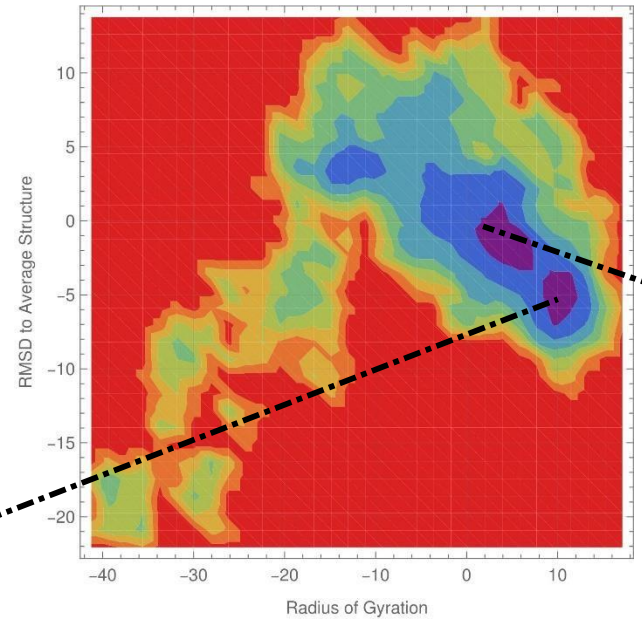


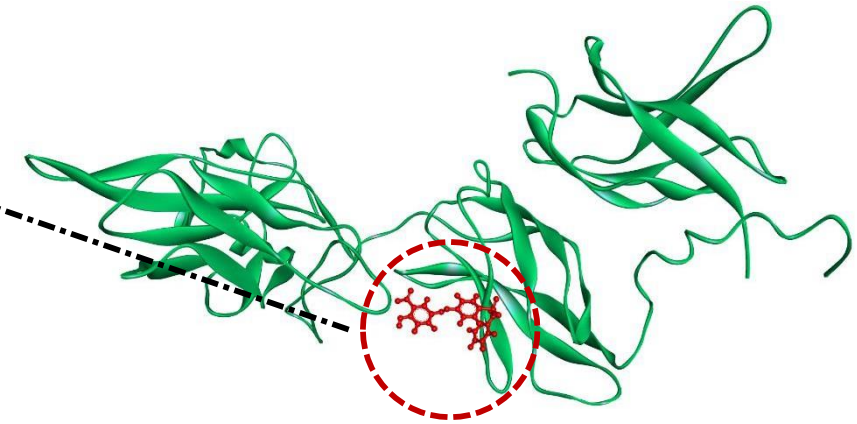
0ps



33400ps

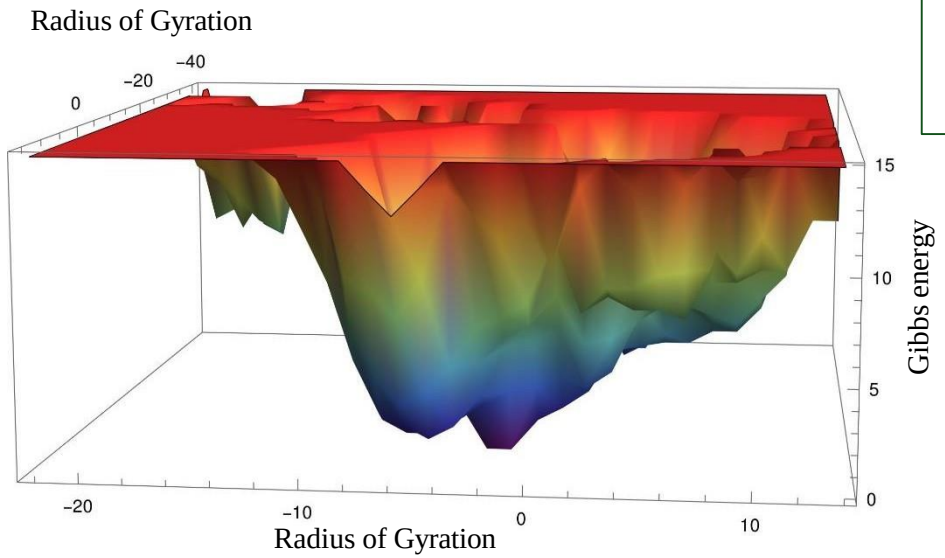
Sulfasalazine is within the active site





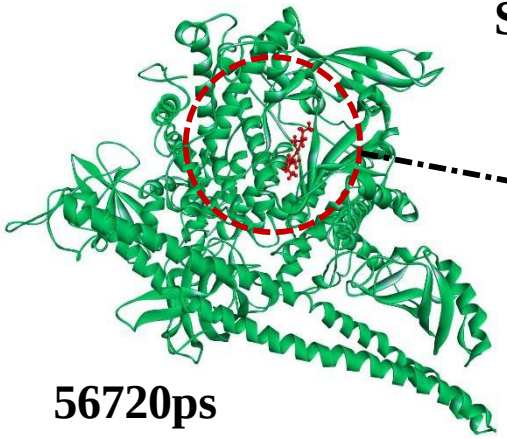
75320ps

Sulfasalazine is within the active site and well stabilized

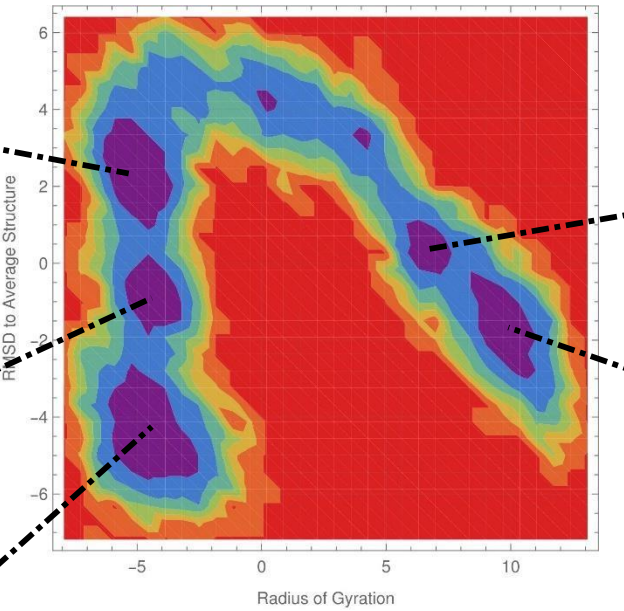


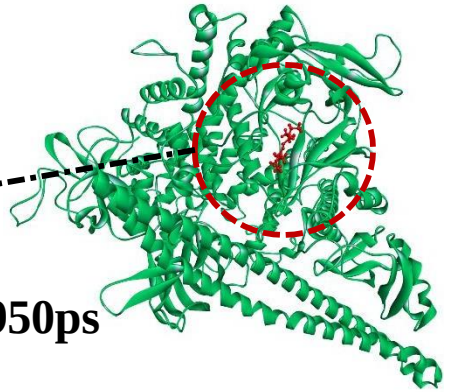
Supplementary Figure S10: PIK3R1/PIK3CA - DSF

PIK3 and DSF system stabilized after 50ns

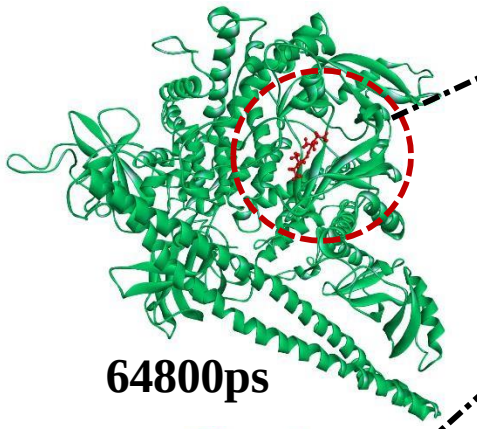


56720ps



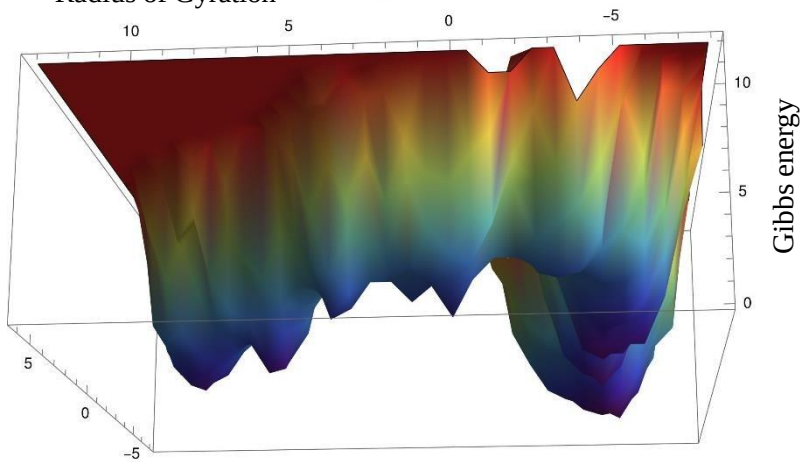


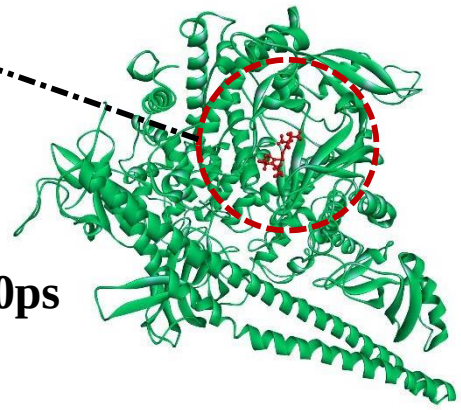
19950ps



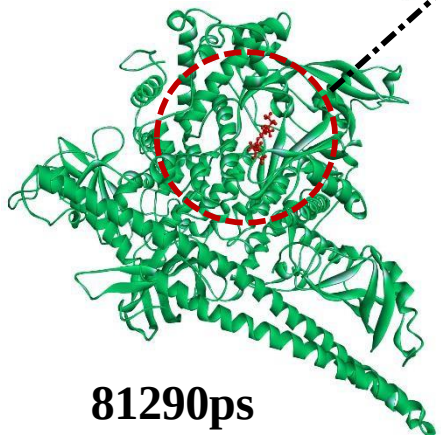
64800ps

Radius of Gyration



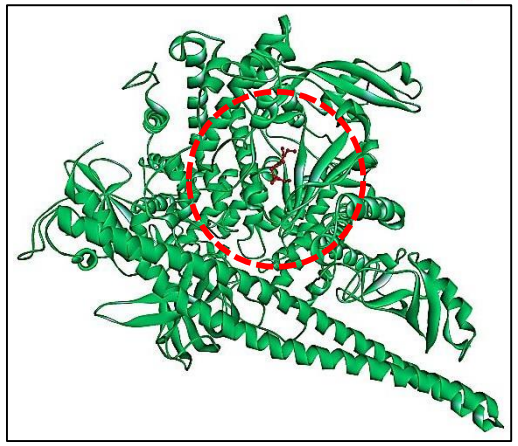


9820ps

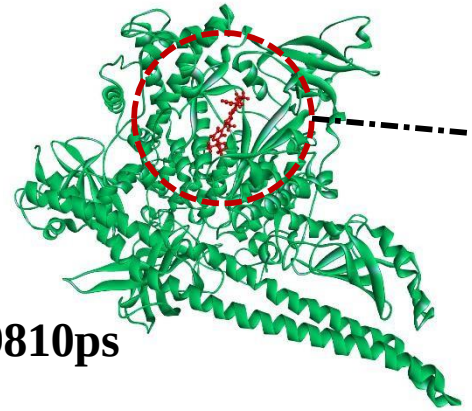


81290ps

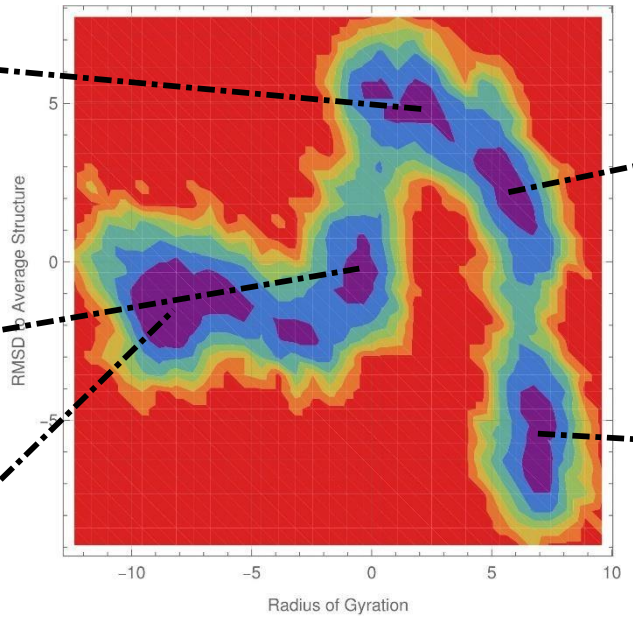
0ps

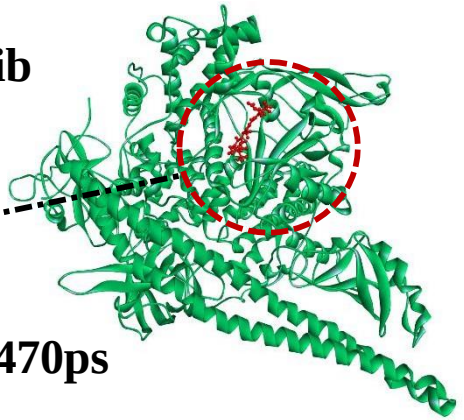


Supplementary Figure S11: PIK3R1/PIK3CA - Alpelisib

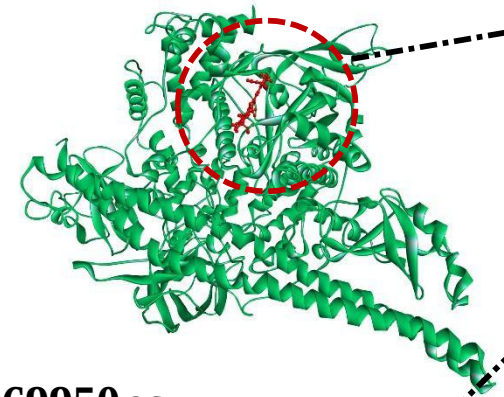


49810ps





40470ps



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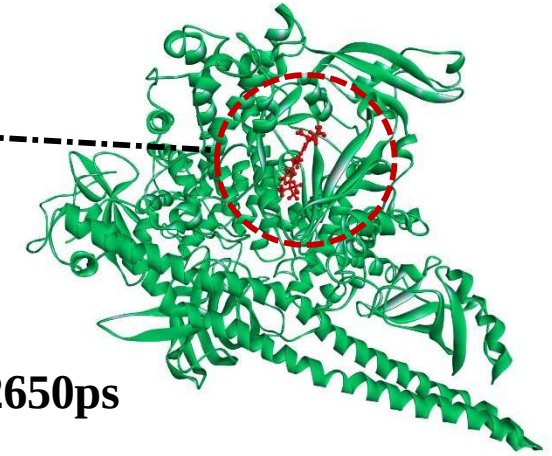

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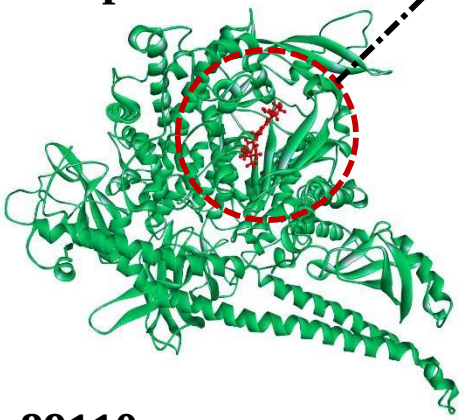

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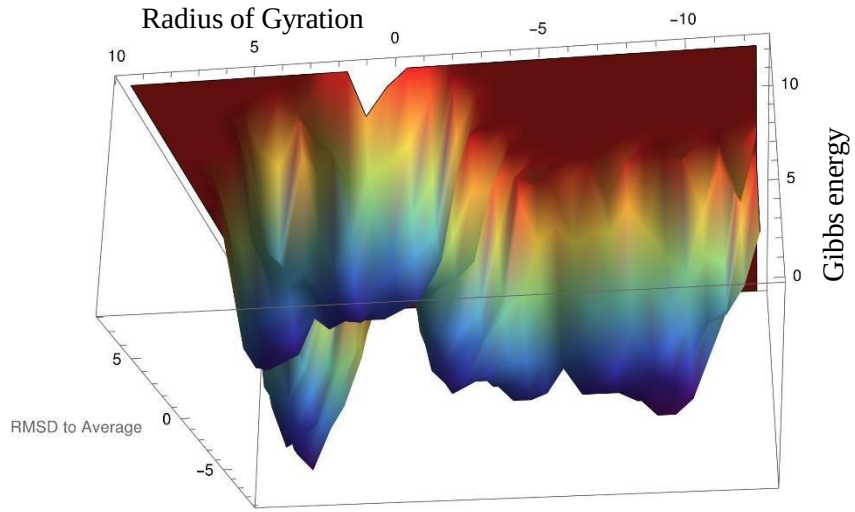

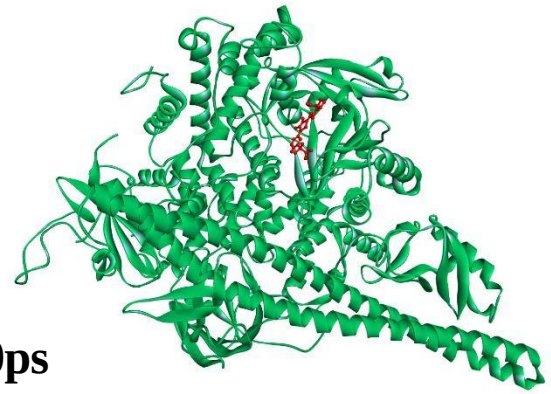

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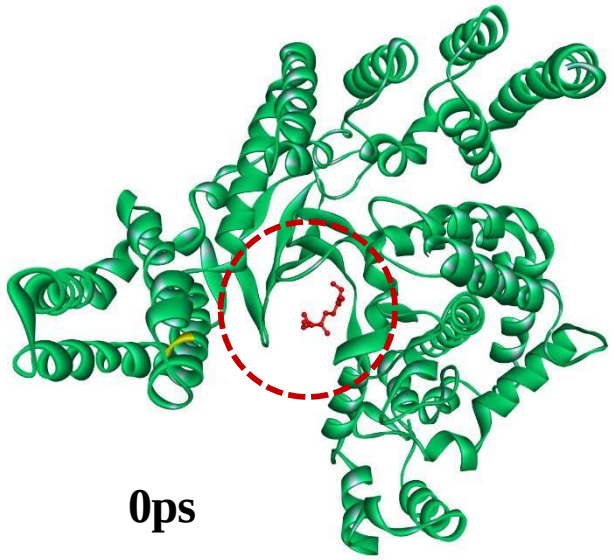
Supplementary Figure S12: MTOR - DSF



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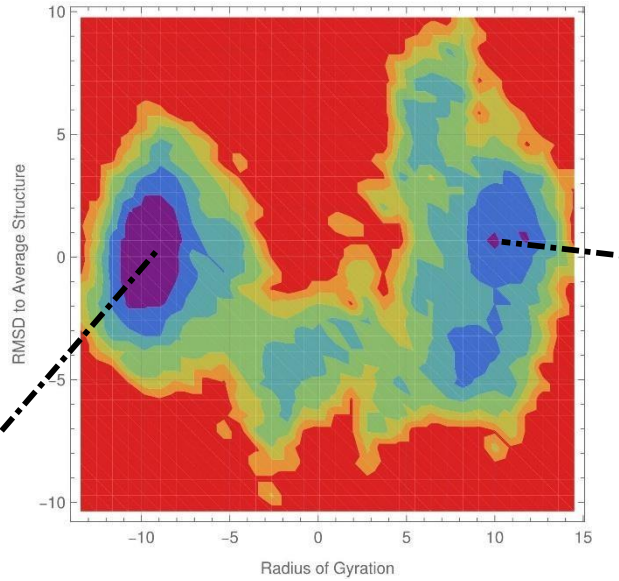

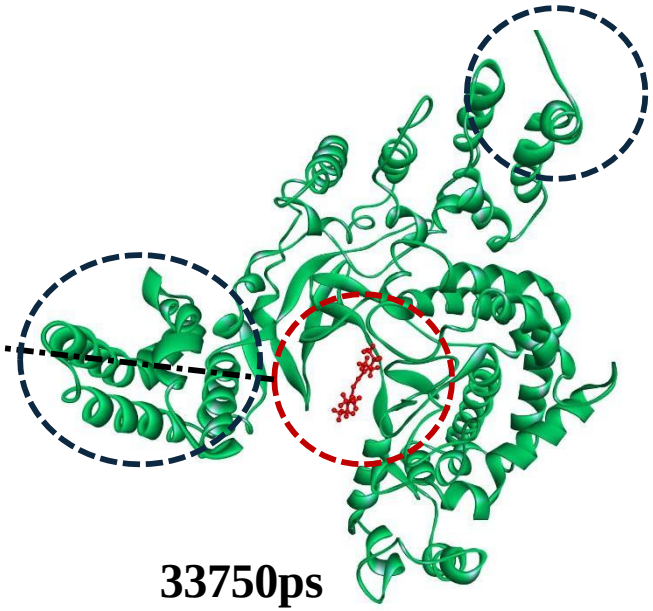

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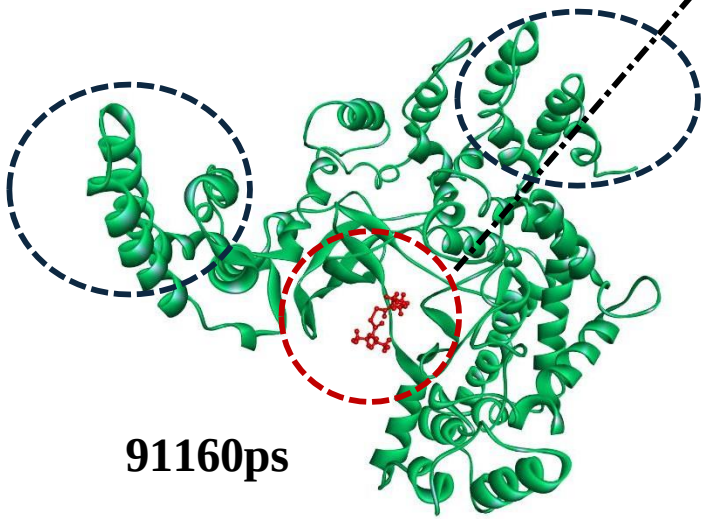
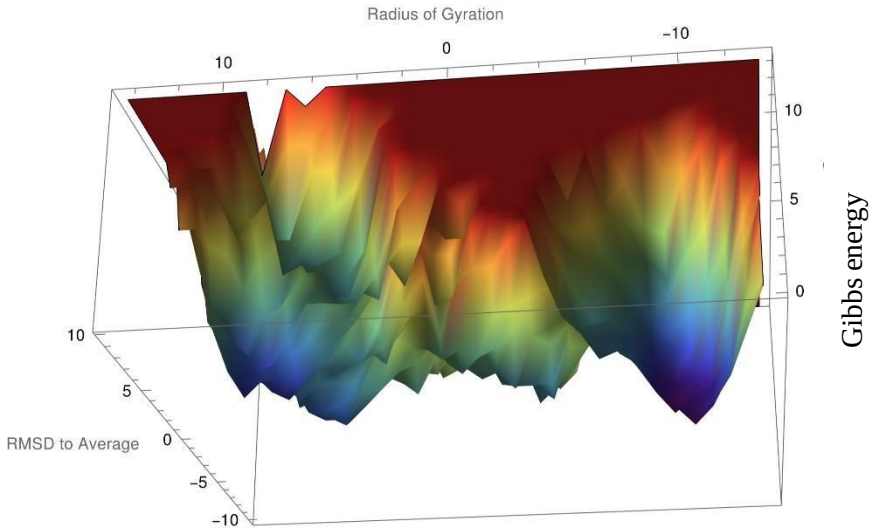
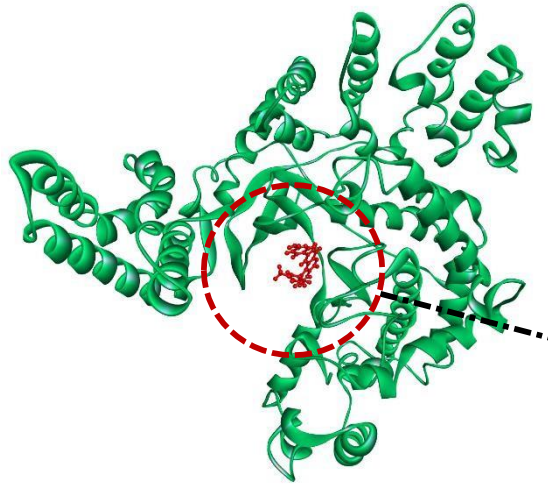


91160ps



Supplementary Figure S13: MTOR - Torin-2



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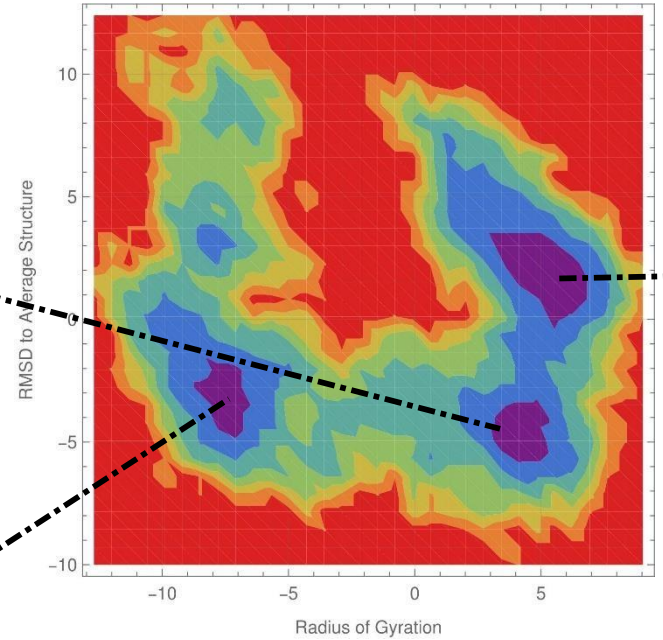
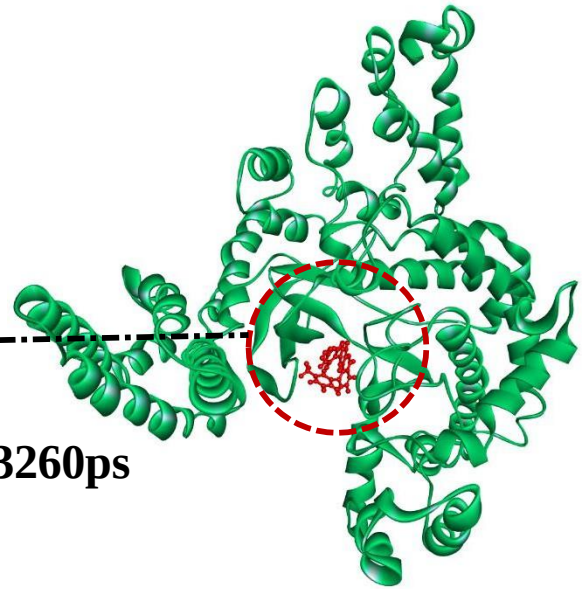
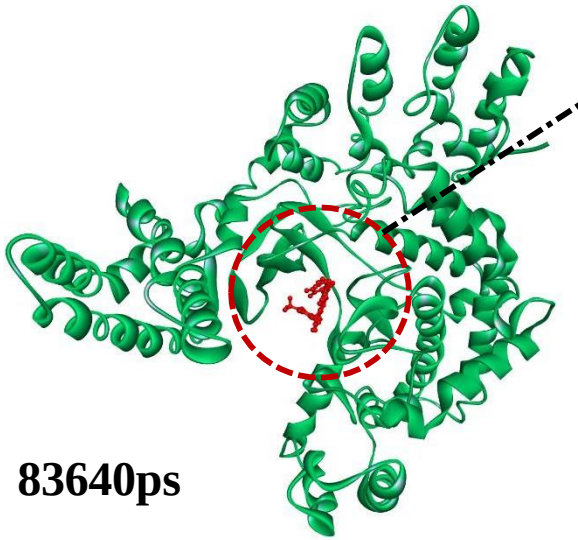




23260ps



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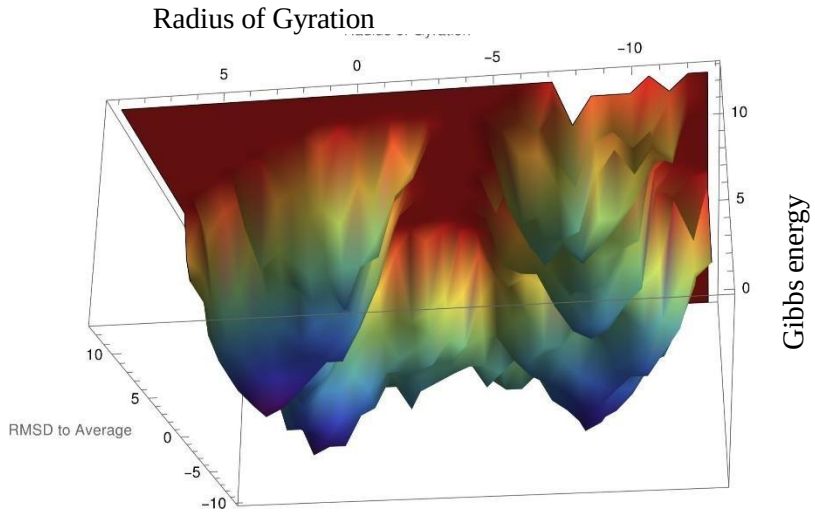

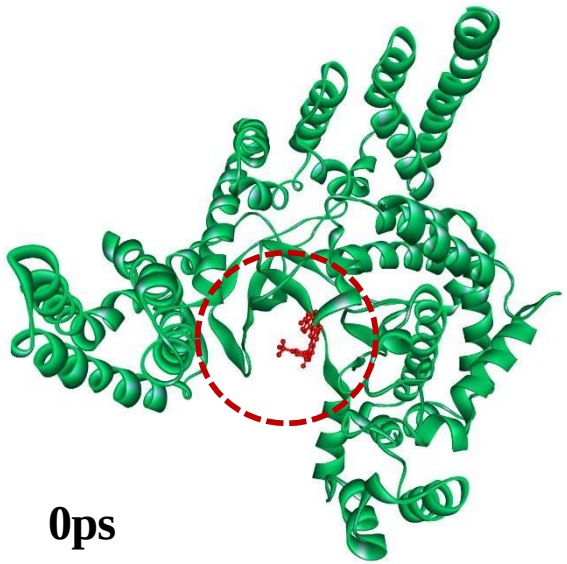

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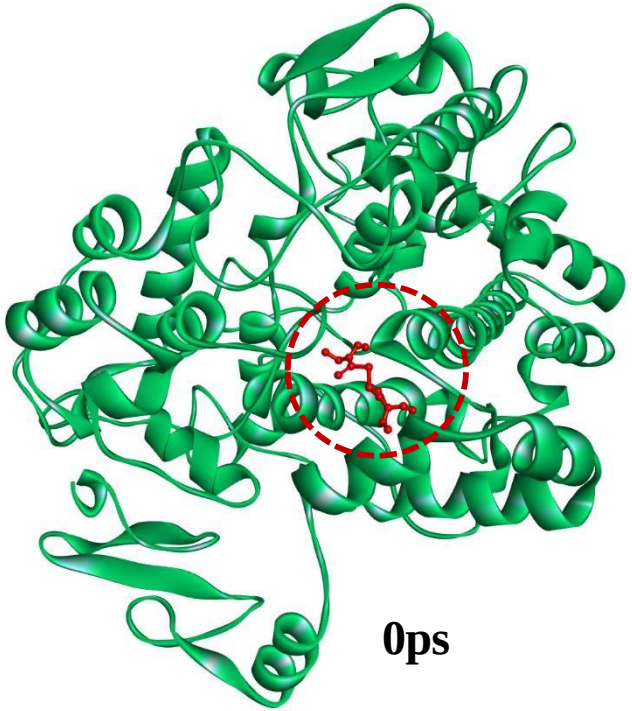
Supplementary Figure S14: PTGS2 - DSF



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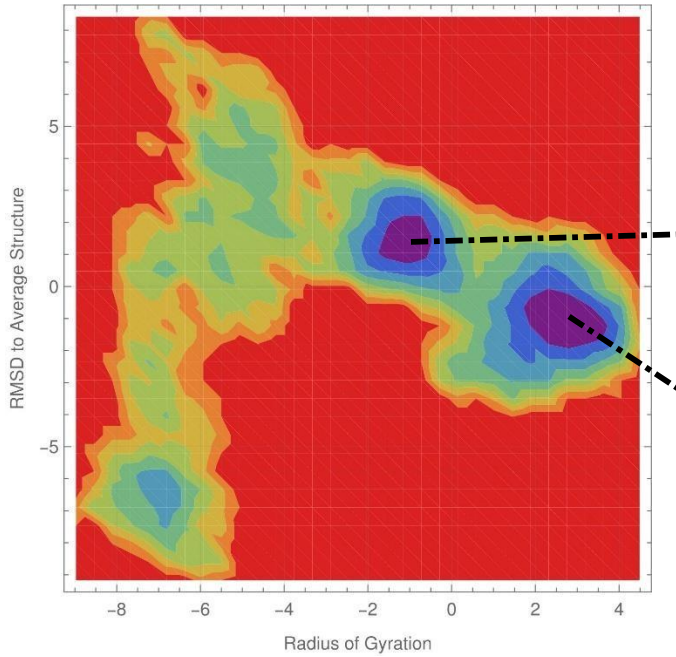

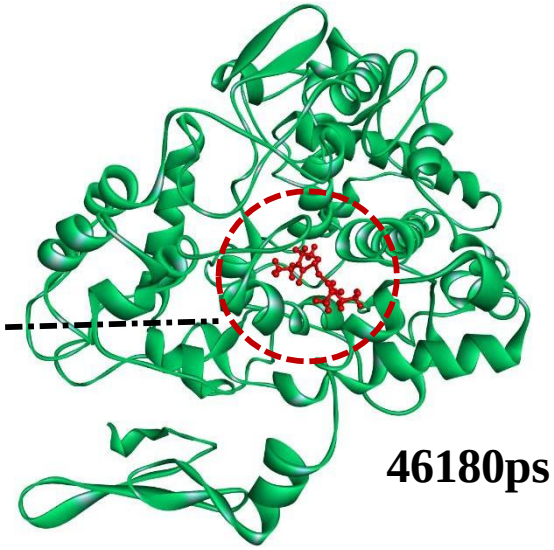

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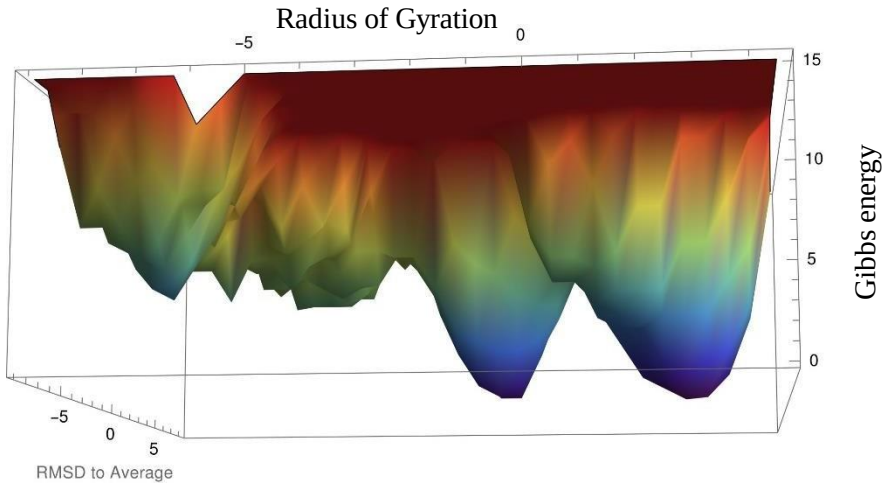

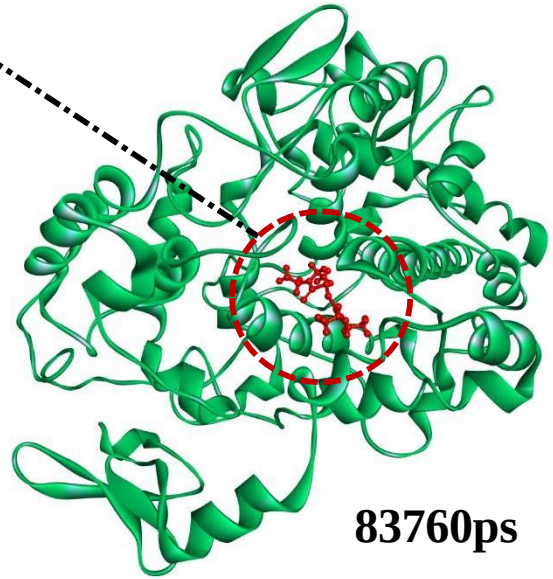

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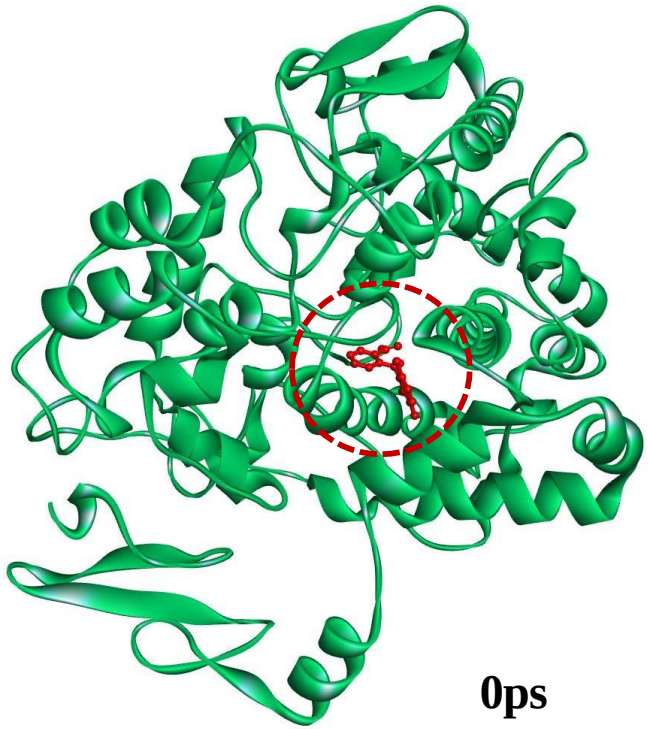
Supplementary Figure S15: PTGS2 – Meclofenamic acid



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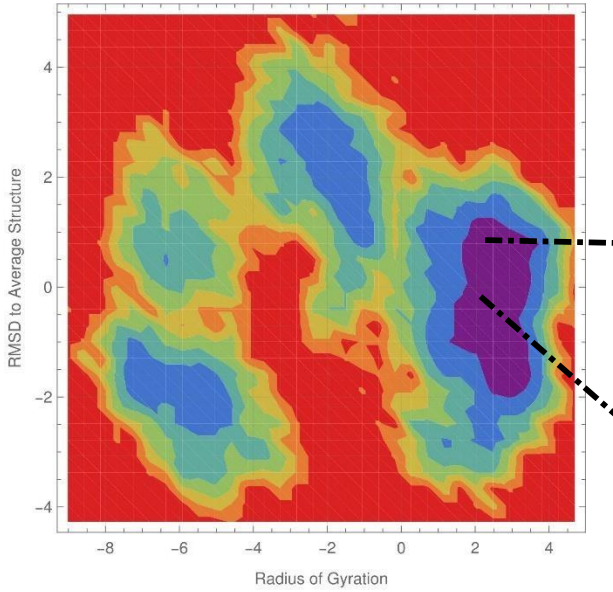

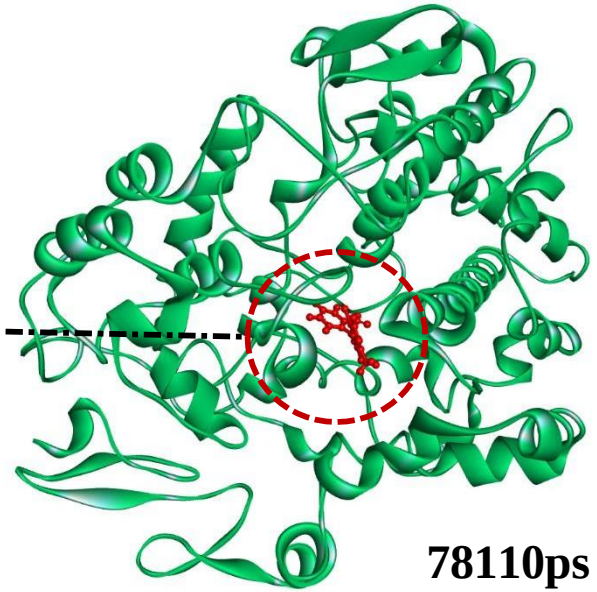

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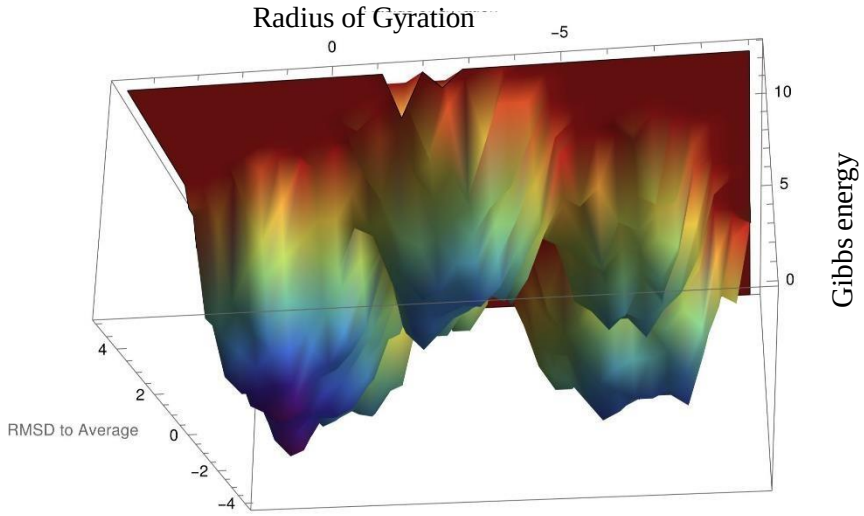

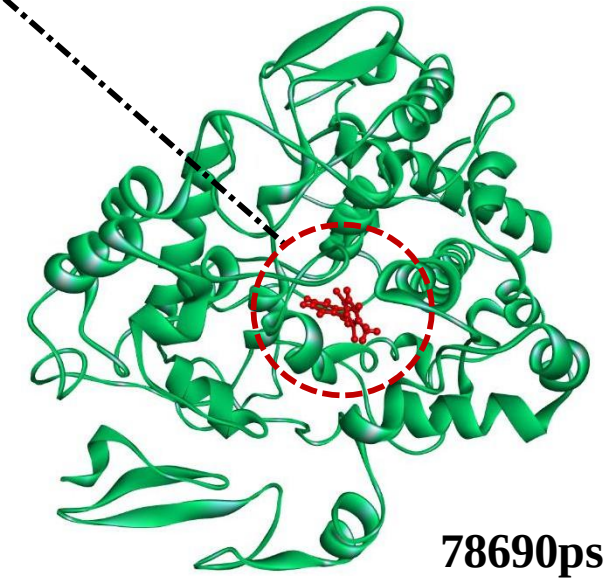

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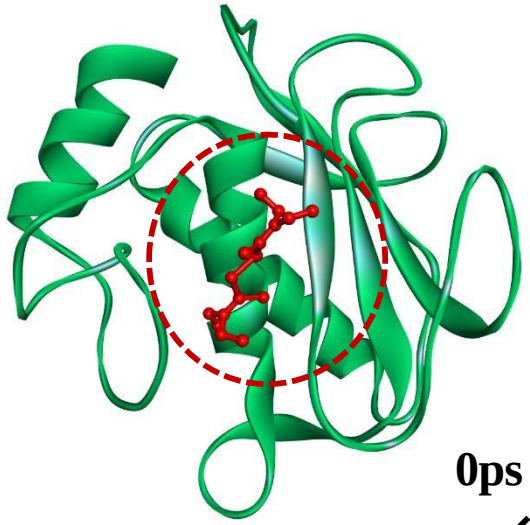
Supplementary Figure S16: MMP9 – DSF



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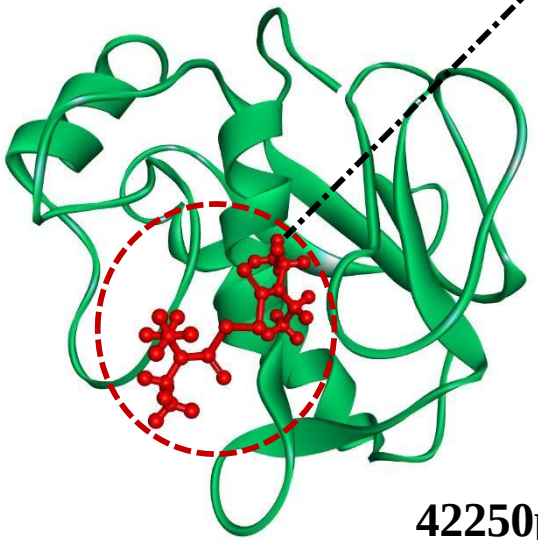

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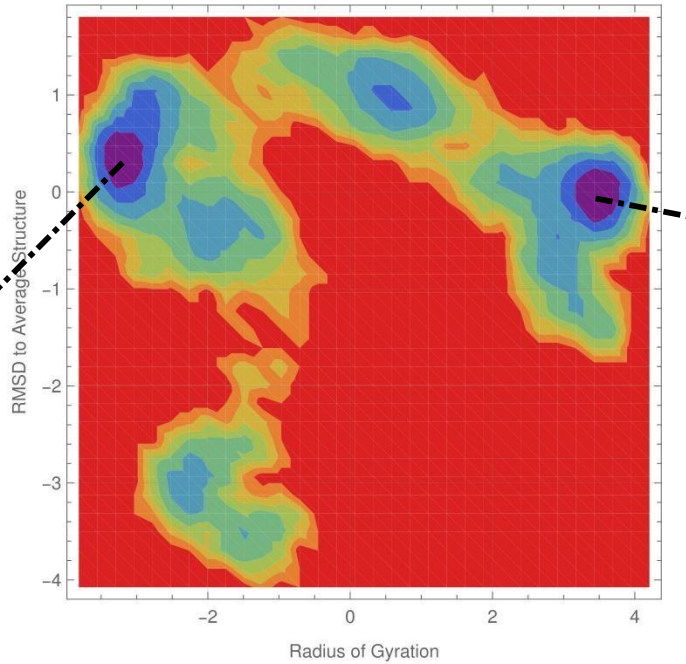
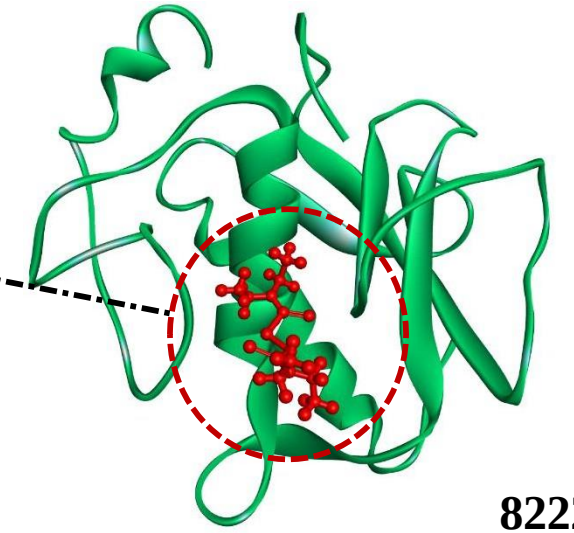
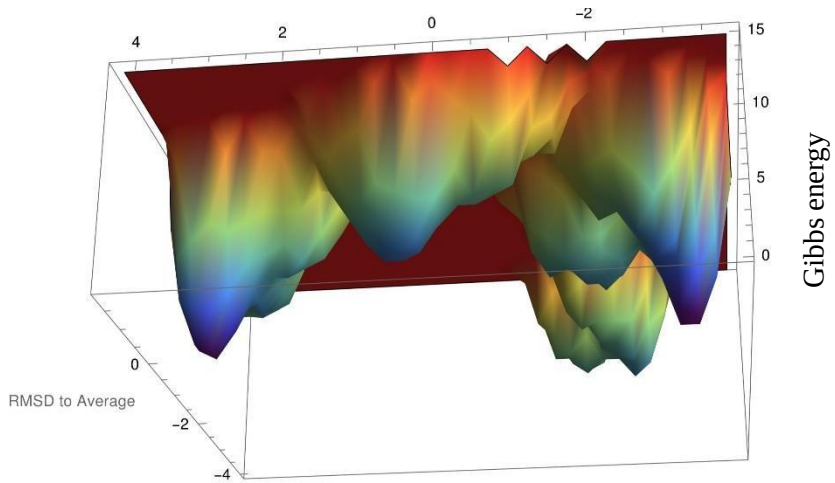


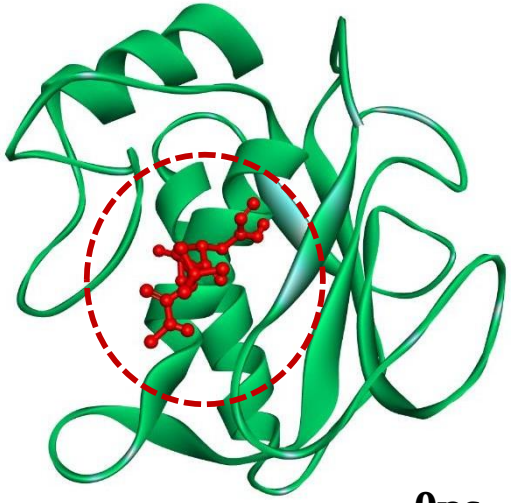


82220ps

Radius of Gyration



Supplementary Figure S17: MMP9 – NFH



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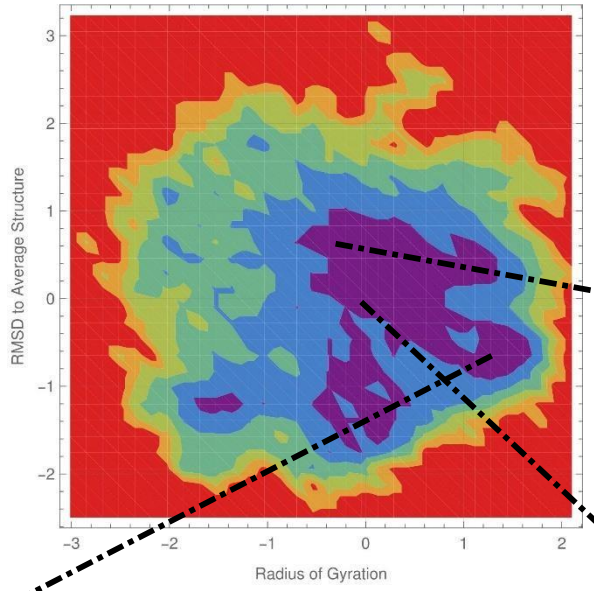

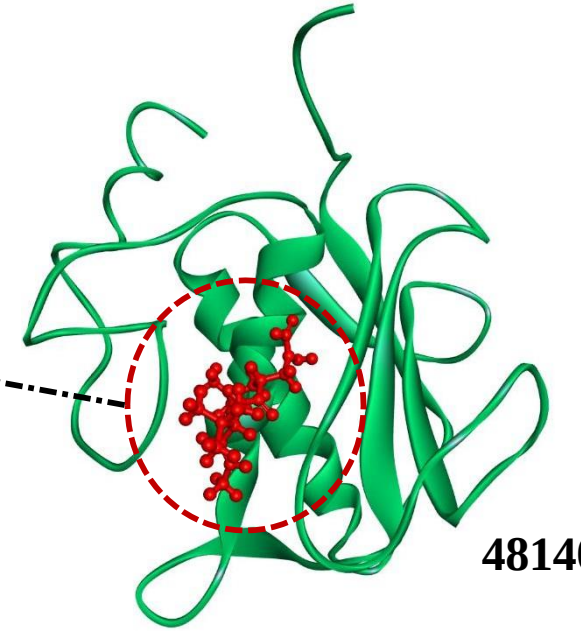

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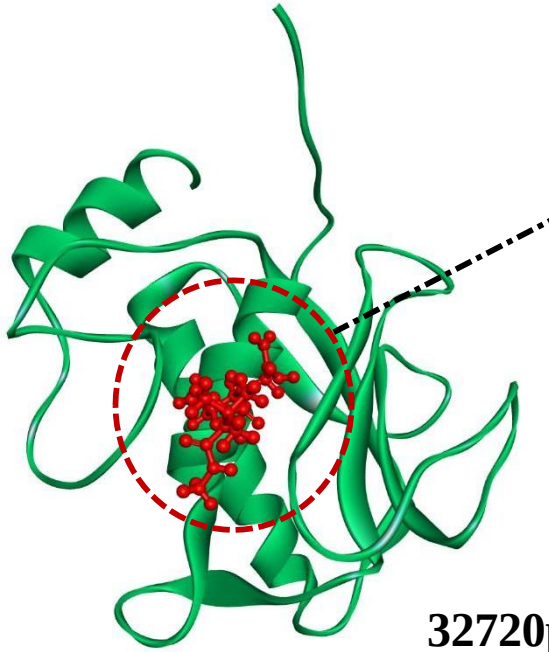

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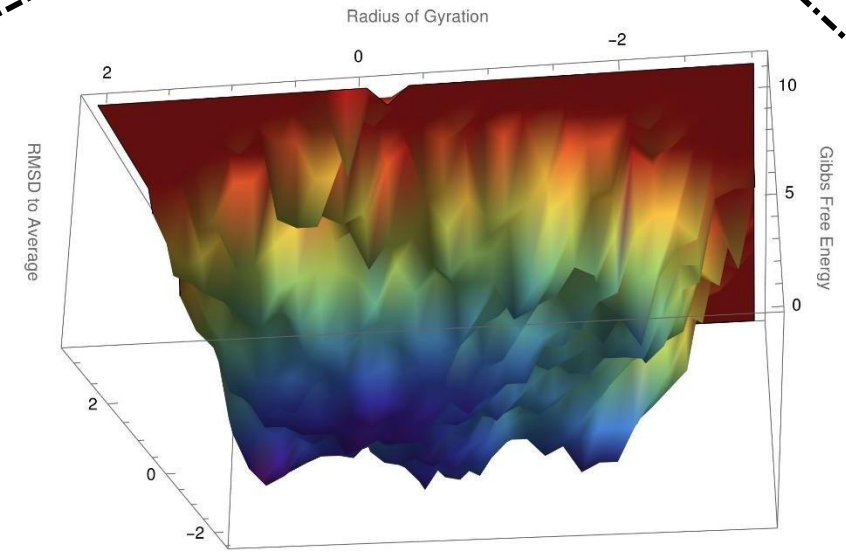

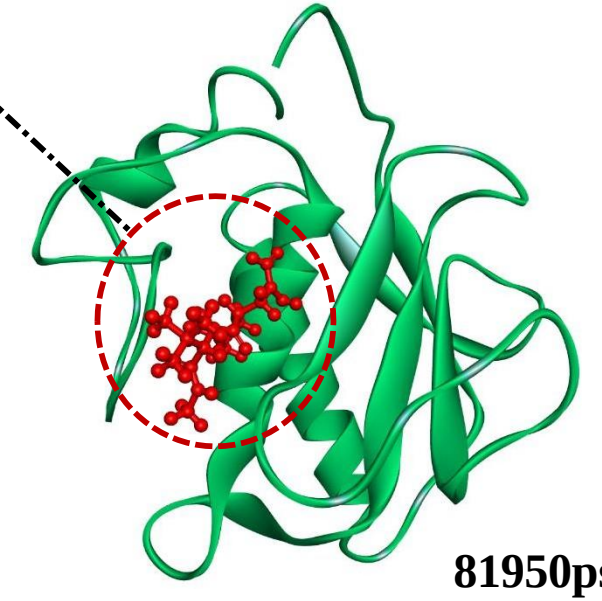

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