

Supplementary Figures

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sp|Q6IQ55|  -MSGGGEQLDILSVGILVKERWKVLRKIGGGGFGEIYDALDMLTRENVALKVESAQQPKQ  59
6U0K        GMSGGGEQLDILSVGILVKERWKVLRKIGGGGFGEIYDALDMLTRENVALKVESAQQPKQ  60
          *****

sp|Q6IQ55|  VLKMEVAVLKKLQGKDHVCRFIGCGRNDRFNYVVMQLQGRNLADLRRSQSRGFTIISTLL  119
6U0K        VLKMEVAVLKKLQGKDHVCRFIGCGRNDRFNYVVMQLQGRNLADLRRSQSRGFTIISTLL  120
          *****

sp|Q6IQ55|  RLGRQILESIESIHSVGF LHRDIKPSNFAMGRFPSTCRKCYMLDFGLARQFTNSCGDVRP  179
6U0K        RLGRQILESIESIHSVGF LHRDIKPSNFAMGRFPSTCRKCYMLDFGLARQFTNSCGDVRP  180
          *****

sp|Q6IQ55|  PRAVAGFRGTVRYASINAHNRNEMGRHDDLWSLFYMLVEFVVGQLPWRKIKDKEQVGSIK  239
6U0K        PRAVAGFRGTVRYASINAHNRNEMGRHDDLWSLFYMLVEFVVGQLPWRKIKDKEQVGSIK  240
          *****

sp|Q6IQ55|  ERYDHRMLMLKHLPPPEFSIFLDHISSLDYFTKPDYQLLTSVFDNSIKTFGVIESDPFDWEK  299
6U0K        ERYDHRMLMLKHLPPPEFSIFLDHISSLDYFTKPDYQLLTSVFDNSIKTFGVIESDPFDWEK  300
          *****
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Fig SF1: Multiple Sequence Alignment of TTBK2 protein with the selected Template by ClustalOmega

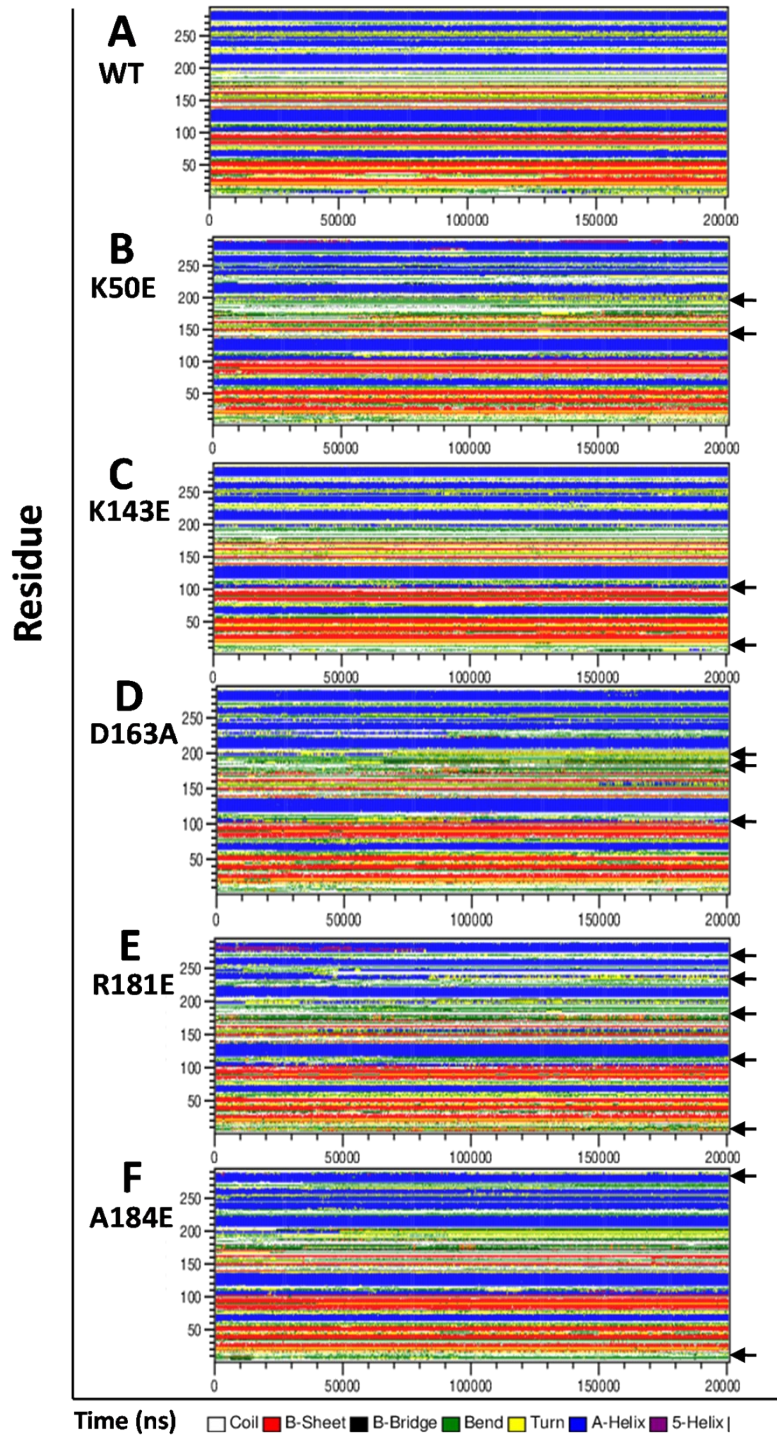


Fig SF2: Secondary structural changes calculated for both WT and mutants (A) WT of TTBK2 (B) K50E (C) D163A (D) R181E (E) A184E and (F) K143E.

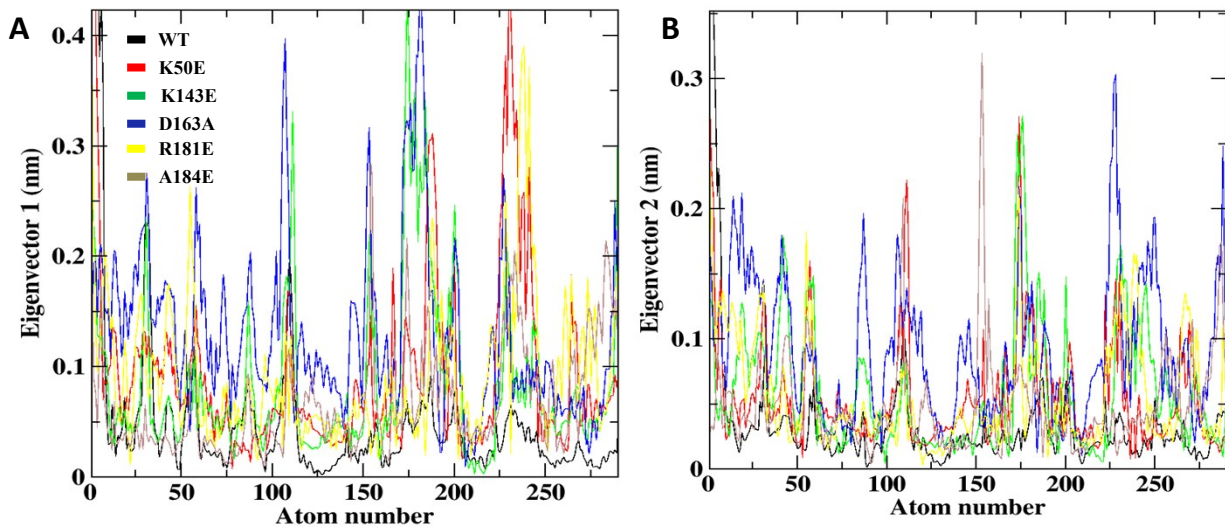


Fig SF3: 2D projection plot: The graph plotted between eigen vector 1 vs eigen vector 2 for the conformational space of $C\alpha$ (alpha atom) (A& B). Comparison of eigen values (nm^2) plotted against the corresponding eigenvector index

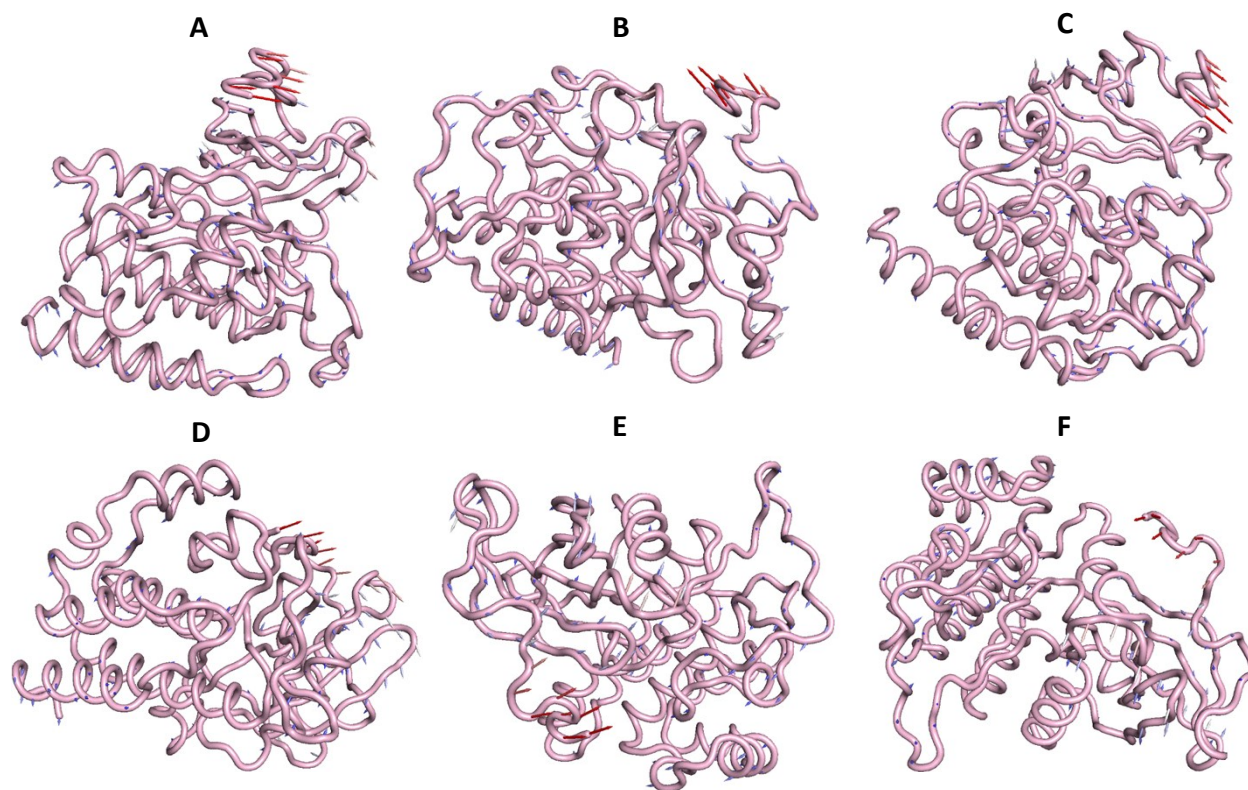


Fig SF4: Elucidation of Porcupine plots depicting the movements and magnitude of $C\alpha$ -atoms obtained through PCA analysis in 200ns MD simulation run time (A) WT-TTBK2 (B) K50E (C) K143E (D) D163A (E) R181E (F) A184E. The direction of the arrow indicates the motion of protein and length of the arrow indicates the magnitude of the motion.

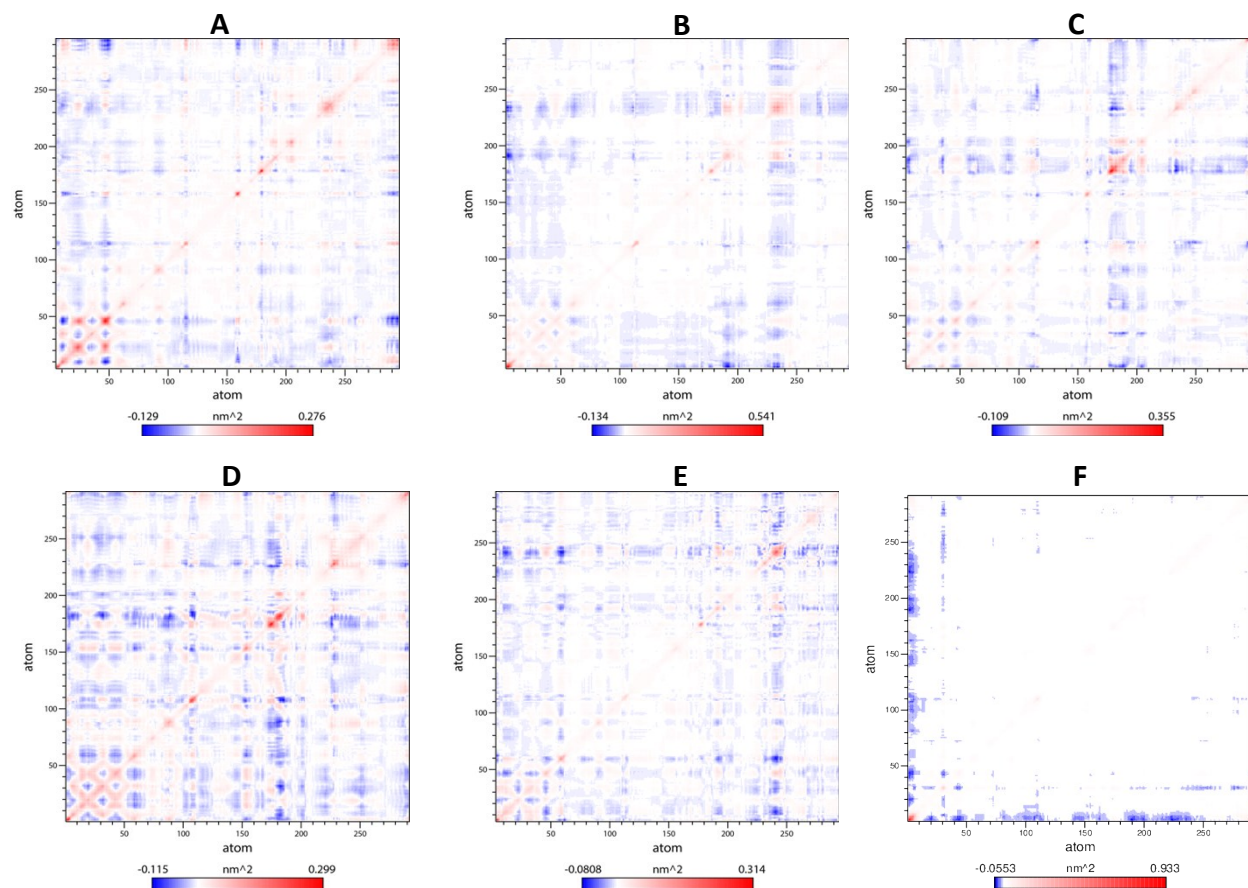


Fig SF5: Diagonalized covariance matrix showing residual cross selection WT and mutants. A) WT-TTBK2 (B) K50E (C) K143E (D) D163A (E) R181E (F) A184E.

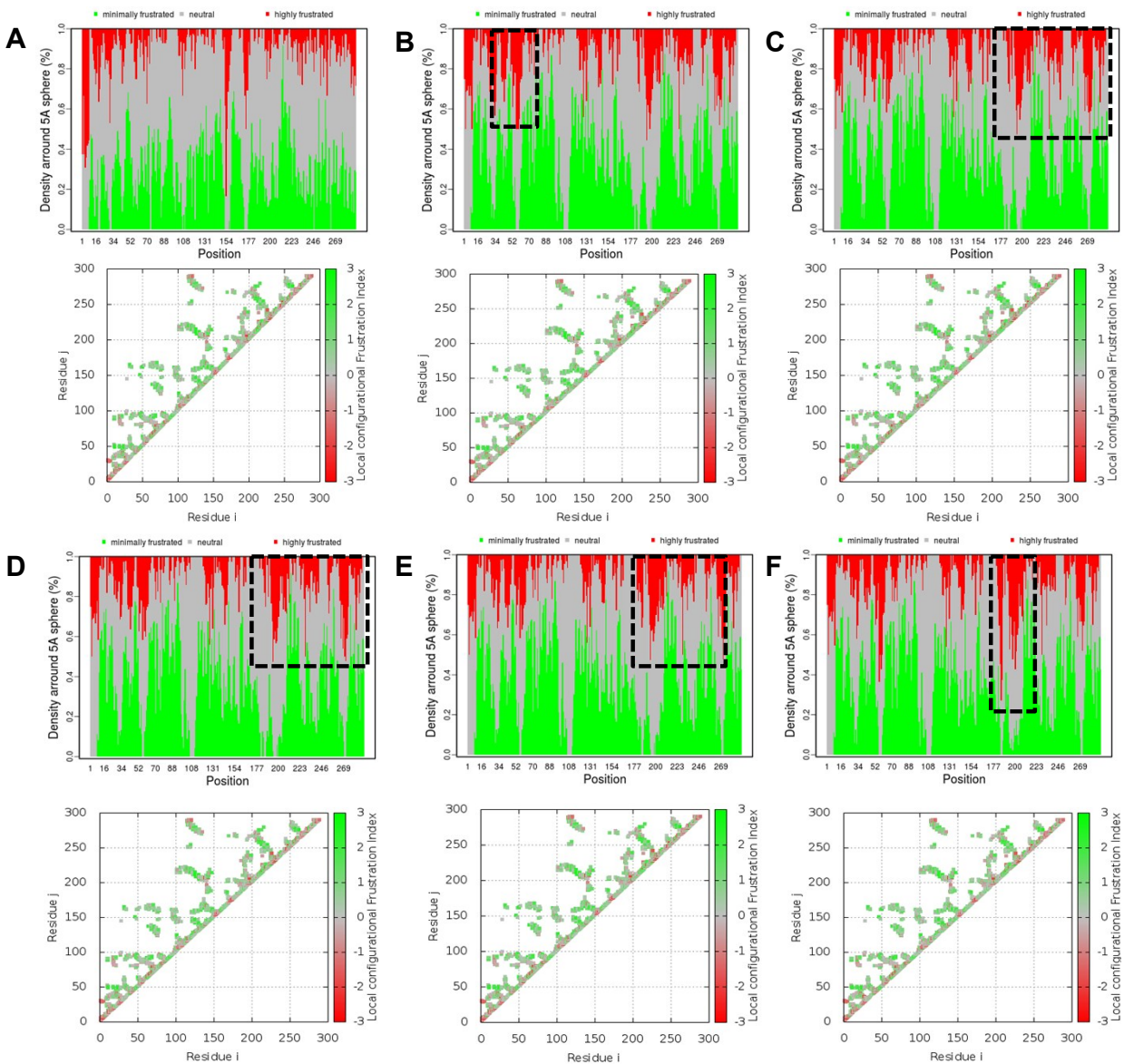


Fig SF6: Depiction of residue frustration of amino acids in WT and mutants. A) WT-TTBK2 (B) K50E (C) K143E (D) D163A (E) R181E (F) A184E.

Supplementary Tables

Table ST1: I-TASSER output on generated top 10 models of TTBK2

Model	RMSD	Identity	Coverage	TM-Score	C-score
Model-1	2.47	0.103	0.936	0.907	0.12
Model-2	9.81	0.040	0.599	0.380	0.12
Model-3	9.60	0.038	0.536	0.347	0.12
Model-4	9.51	0.042	0.515	0.334	0.12
Model-5	9.08	0.039	0.493	0.333	0.12
Model-6	9.89	0.044	0.494	0.310	0.12
Model-7	10.04	0.034	0.494	0.310	0.11
Model-8	9.78	0.044	0.489	0.309	0.11
Model-9	7.14	0.044	0.397	0.309	0.11
Model-10	9.67	0.025	0.471	0.304	0.11

Table ST2: The average values of RMSD, Rg, SASA of WT and mutations of TTBK2 protein observed during MD simulation.

Protein	RMSD	Rg	SASA
WT	0.36nm	2.02nm	165.38nm ²
K50E	0.58nm	1.95nm	161.52nm ²
K143E	0.48nm	1.92nm	162.21nm ²
D163A	0.46nm	1.88nm	164.37nm ²
R181E	0.40nm	1.91nm	165.08nm ²
A184E	0.42nm	1.89nm	162.92nm ²

**values measured from figure 3.*

Table ST3: The average values of H-bonds of WT and mutations of TTBK2 protein.

Protein	H-bonds
WT	227.25
K50E	221.75
K143E	221.81
D163A	215.47
R181E	213.28
A184E	221.60