

Article

# Molecular Dynamics Simulations of a Cytochrome P450 from *Tepidiphilus thermophilus* (P450-TT) Reveal How Its Substrate-Binding Channel Opens

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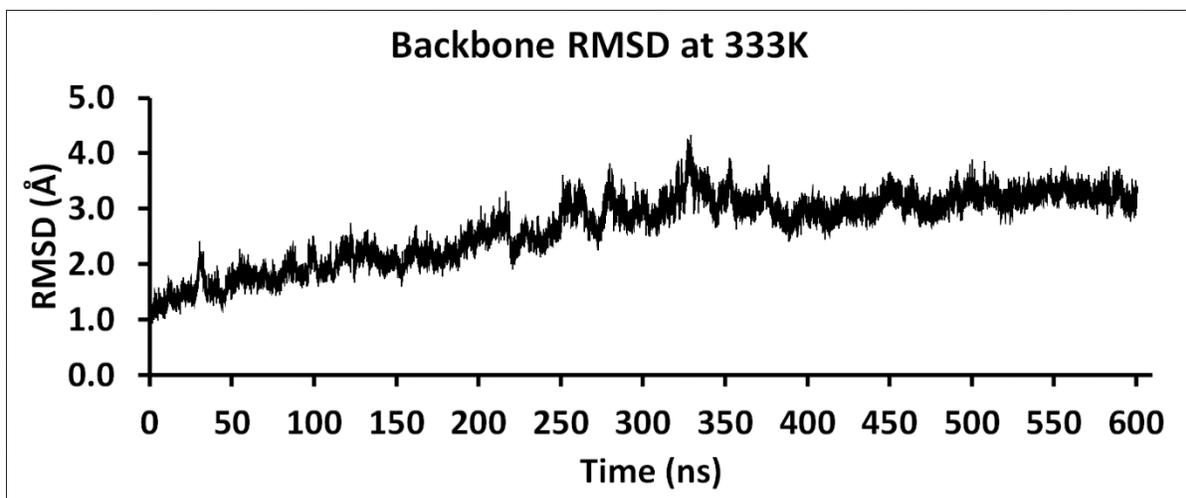
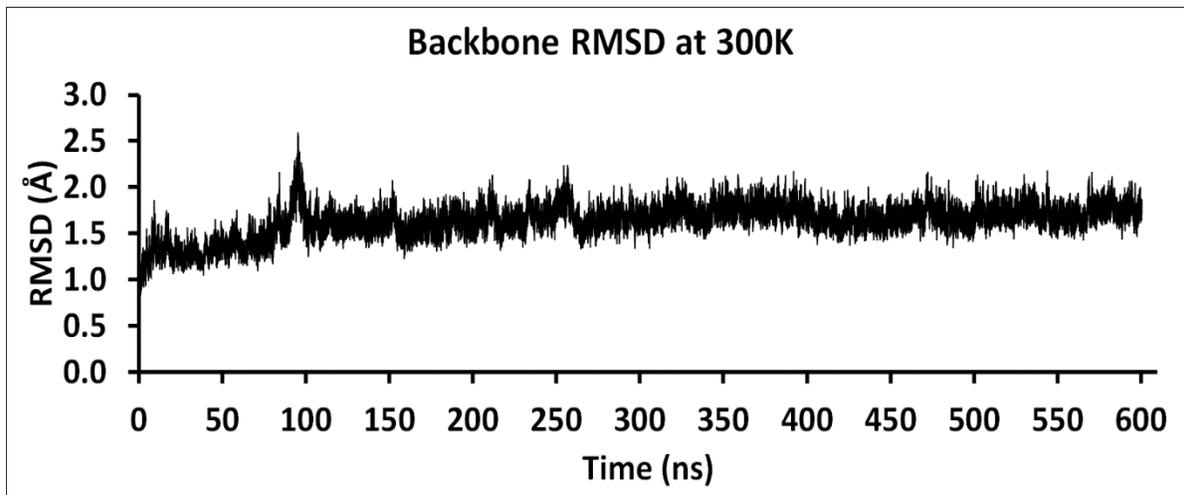
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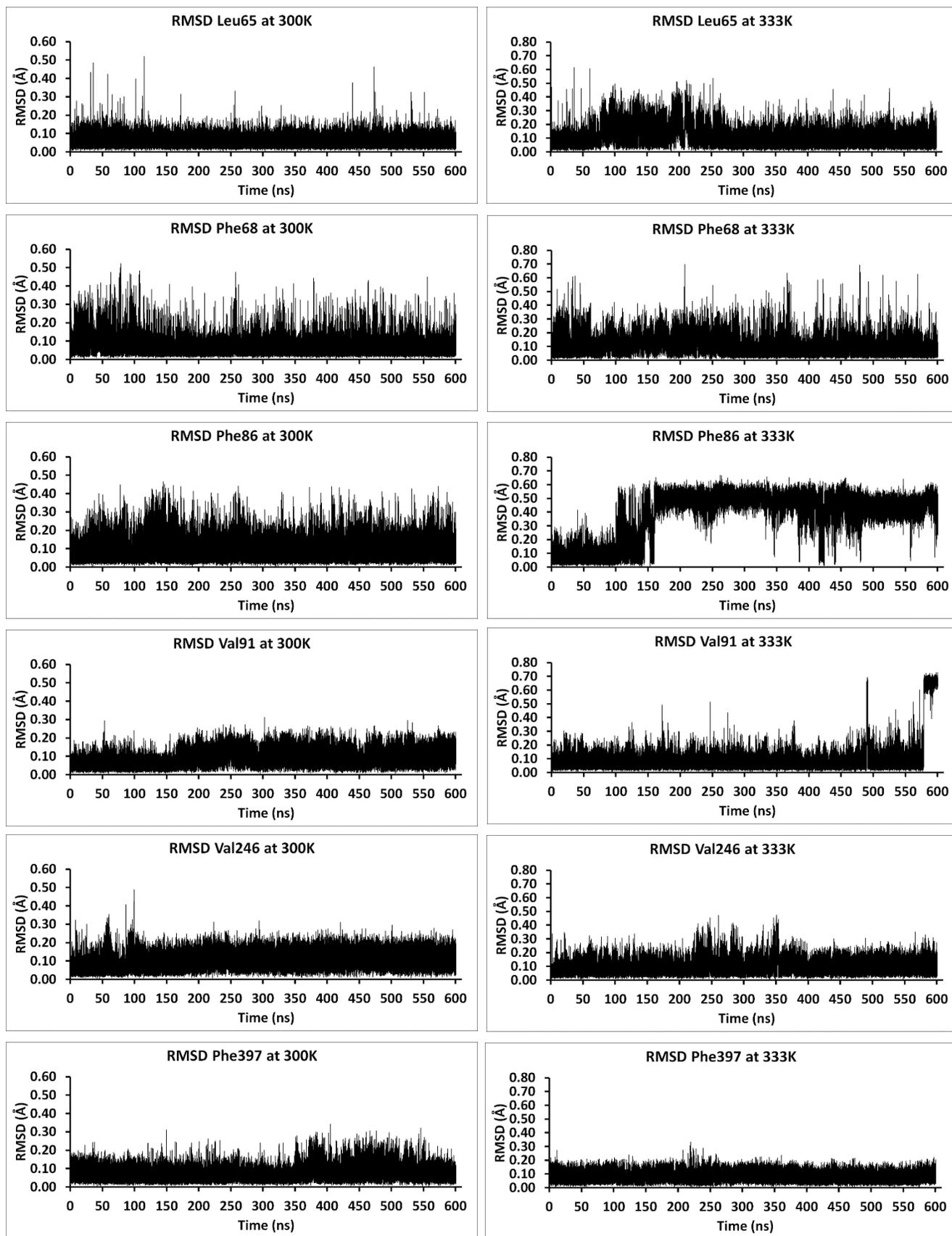
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## Supporting Information

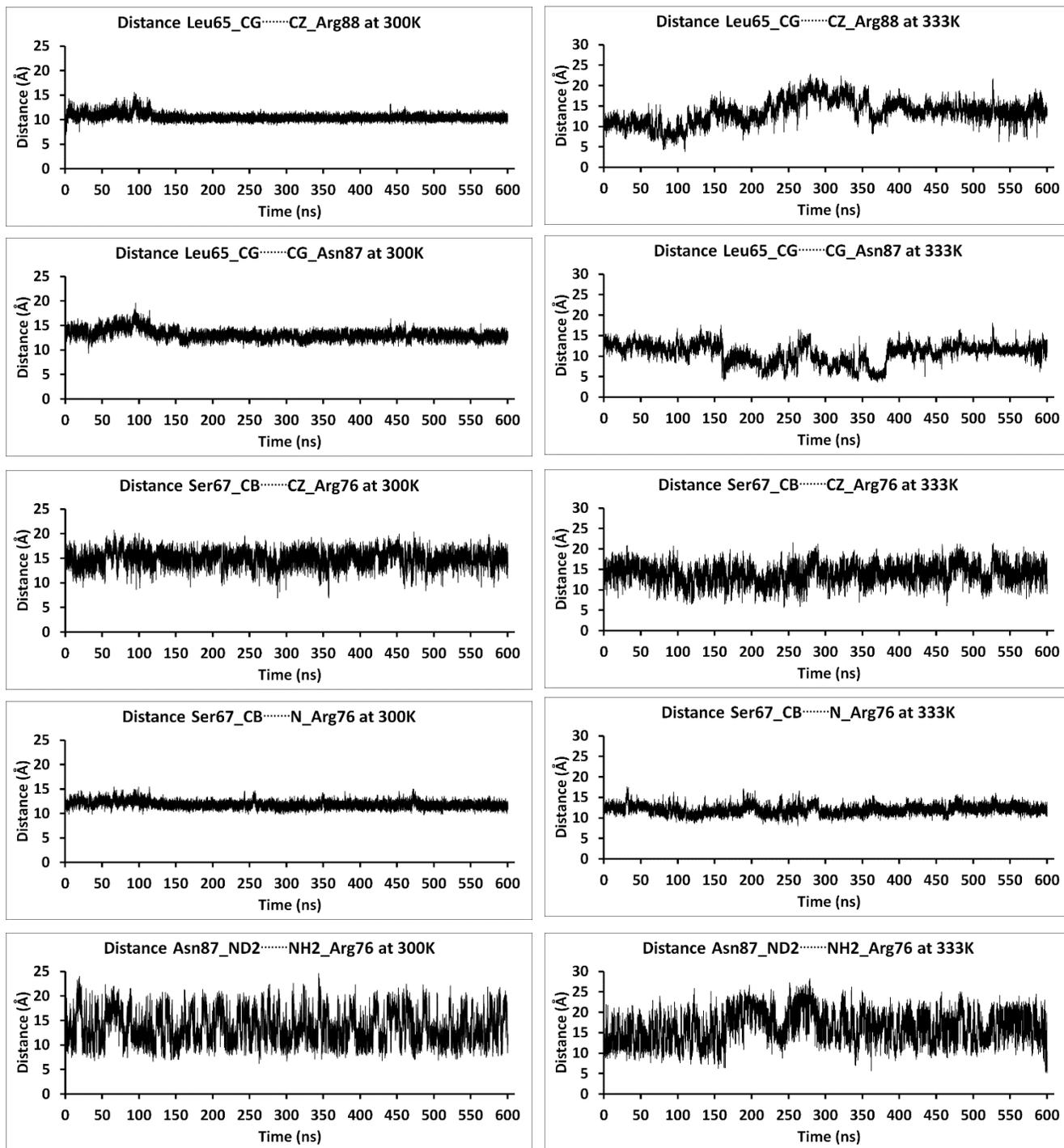
Total pages: 19  
(Figures S1-S18)



FigureS1: Backbone RMSD at 600 ns MD simulations of p450-TT enzyme as observed at 300K and 333K.



FigureS2: RMSD of Leu65, Phe68, Phe86, Val91, Val246, and Phe397 residues at 600.5 ns MD simulations of p450-TT enzyme as observed at 300K and 333K



FigureS3: Measured distances of Leu65-Arg88, Leu65-Asn87, Ser67-Arg76, and Asn87-Arg76 at 600.5 ns MD simulations of p450-TT enzyme as observed at 300K and 333K.

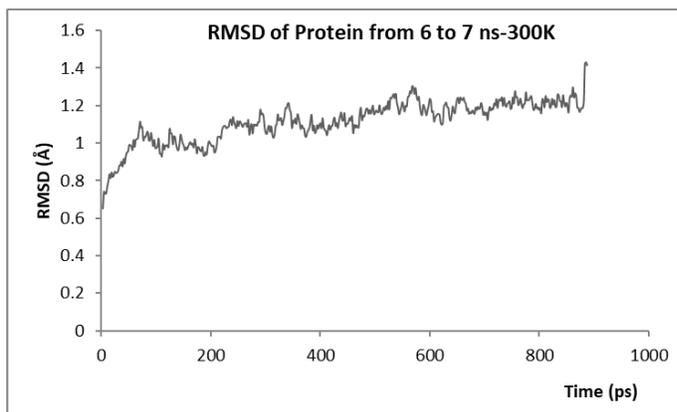
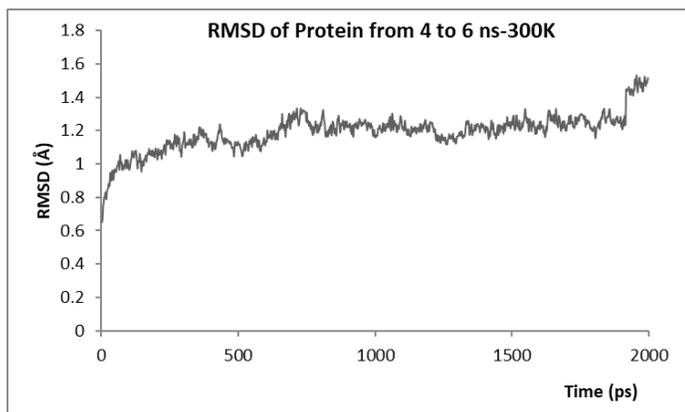
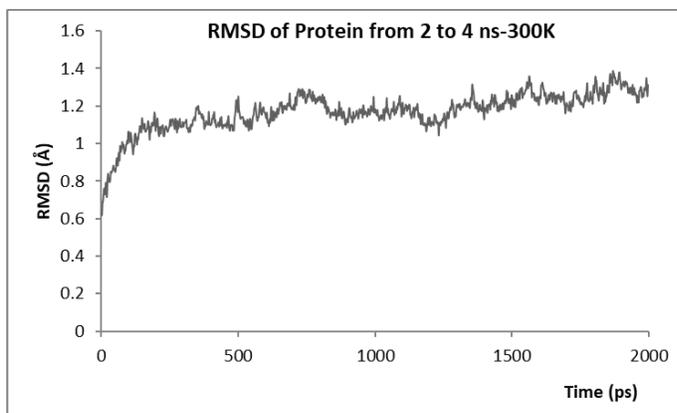
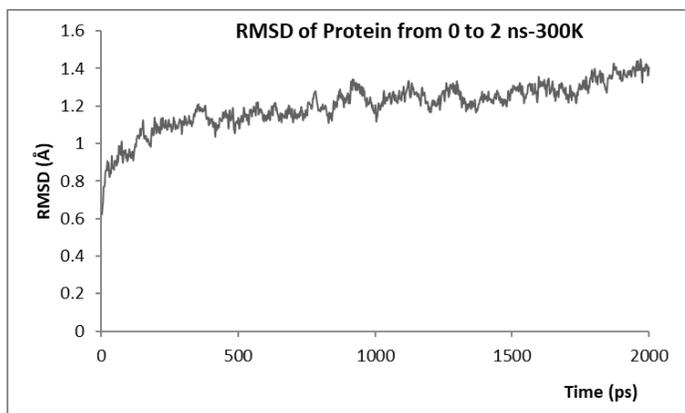


Figure S4: Root mean square deviation of protein from 0 to 2, 2 to 4, 4 to 6, and 6 to 7 ns MD simulations of P450-TT enzyme as observed at 300 K.

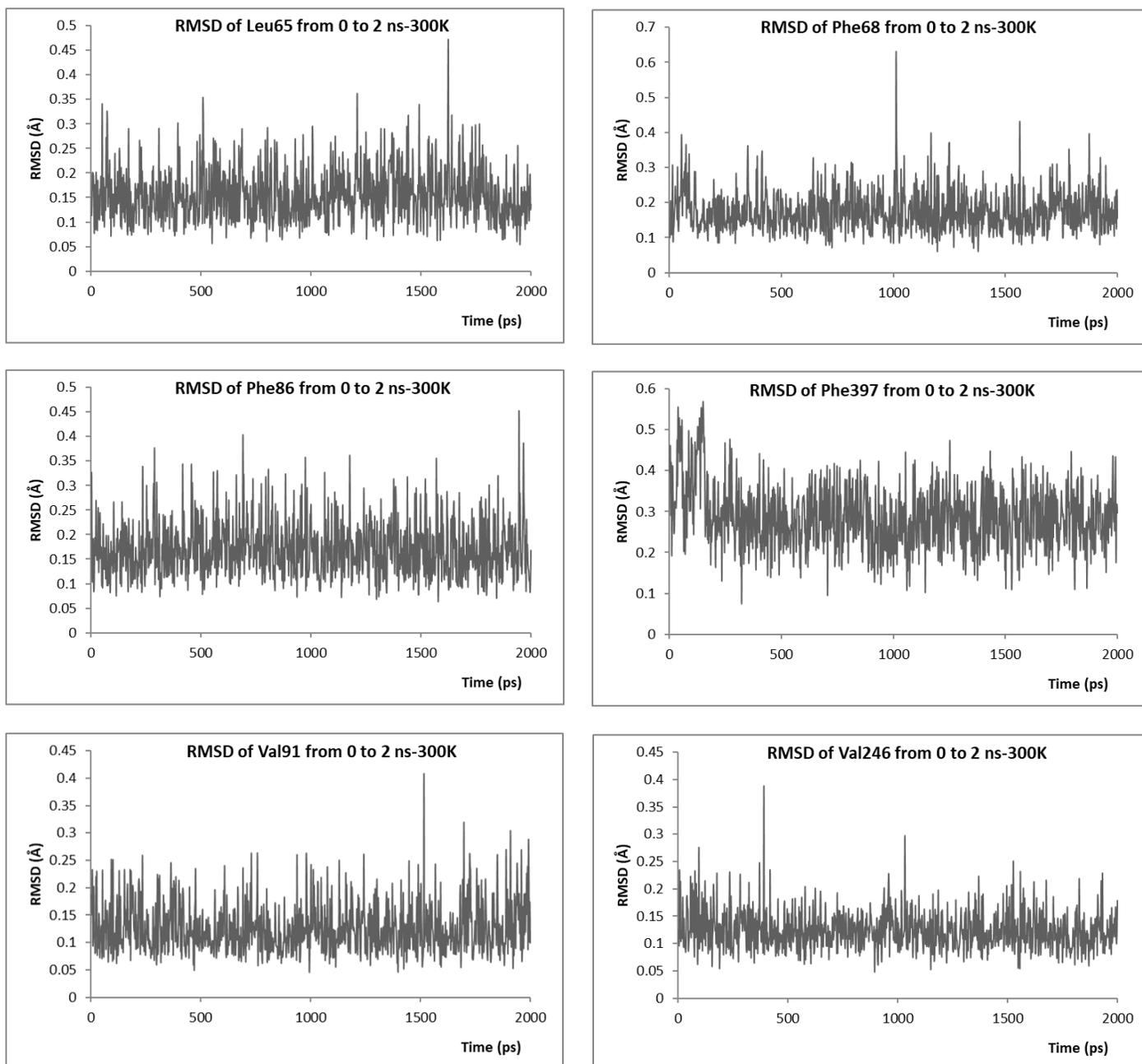


Figure S5: Root mean square deviation of Leu65, Phe68, Phe86, Phe397, Val91 and Val246 from 0 to 2 ns MD simulations of P450-TT enzyme as observed at 300 K.

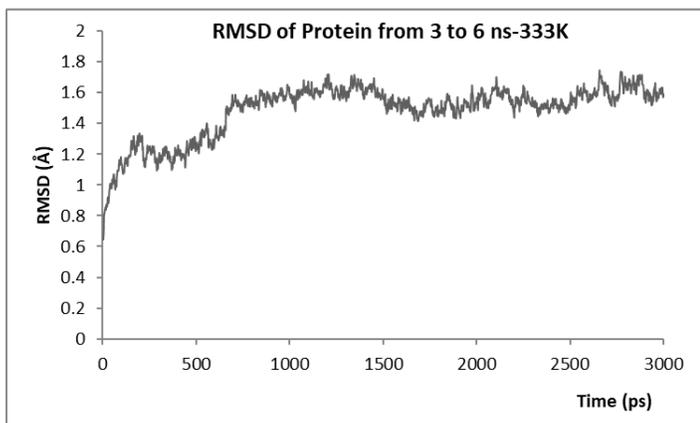
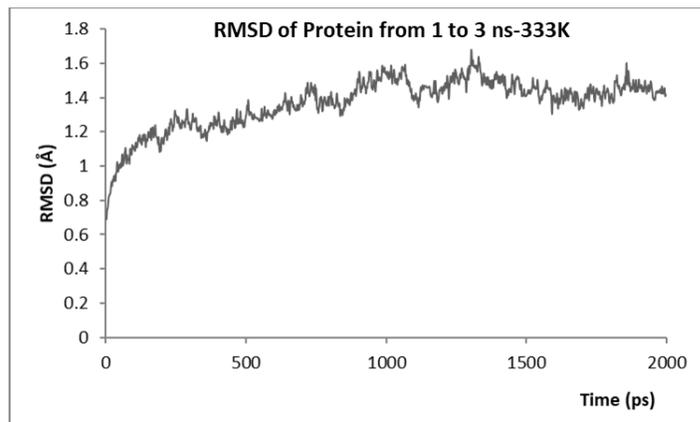
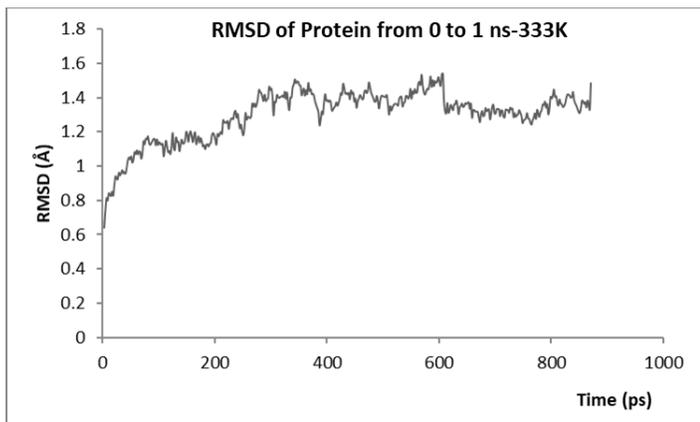


Figure S6: Root mean square deviation of protein from 0 to 1, 1 to 3, and 3 to 6 ns MD simulations of P450-TT enzyme as observed at 333 K.

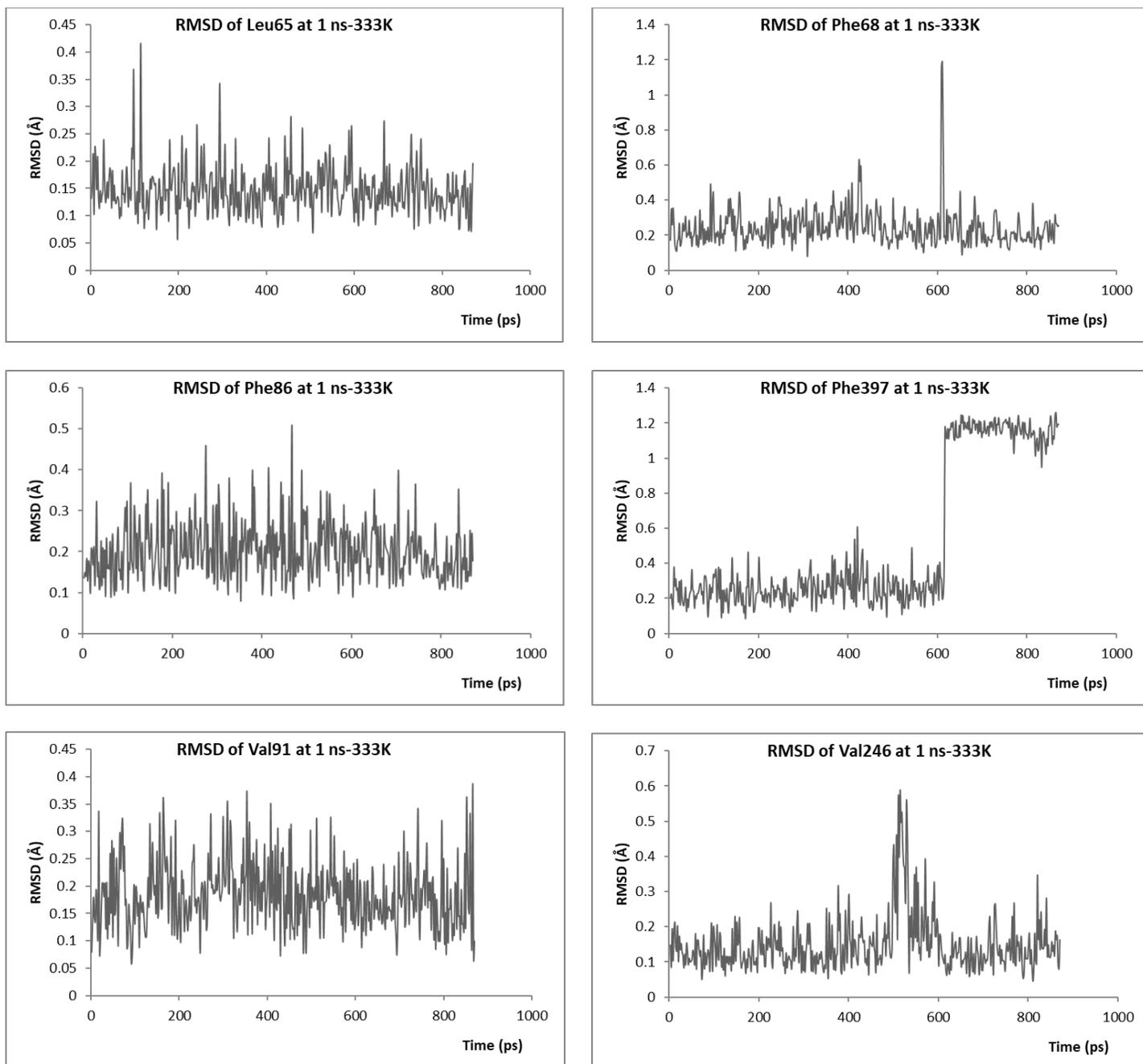


Figure S7: Root mean square deviation of Leu65, Phe68, Phe86, Phe397, Val91 and Val246 at 1 ns MD simulations of P450-TT enzyme as observed at 333 K.

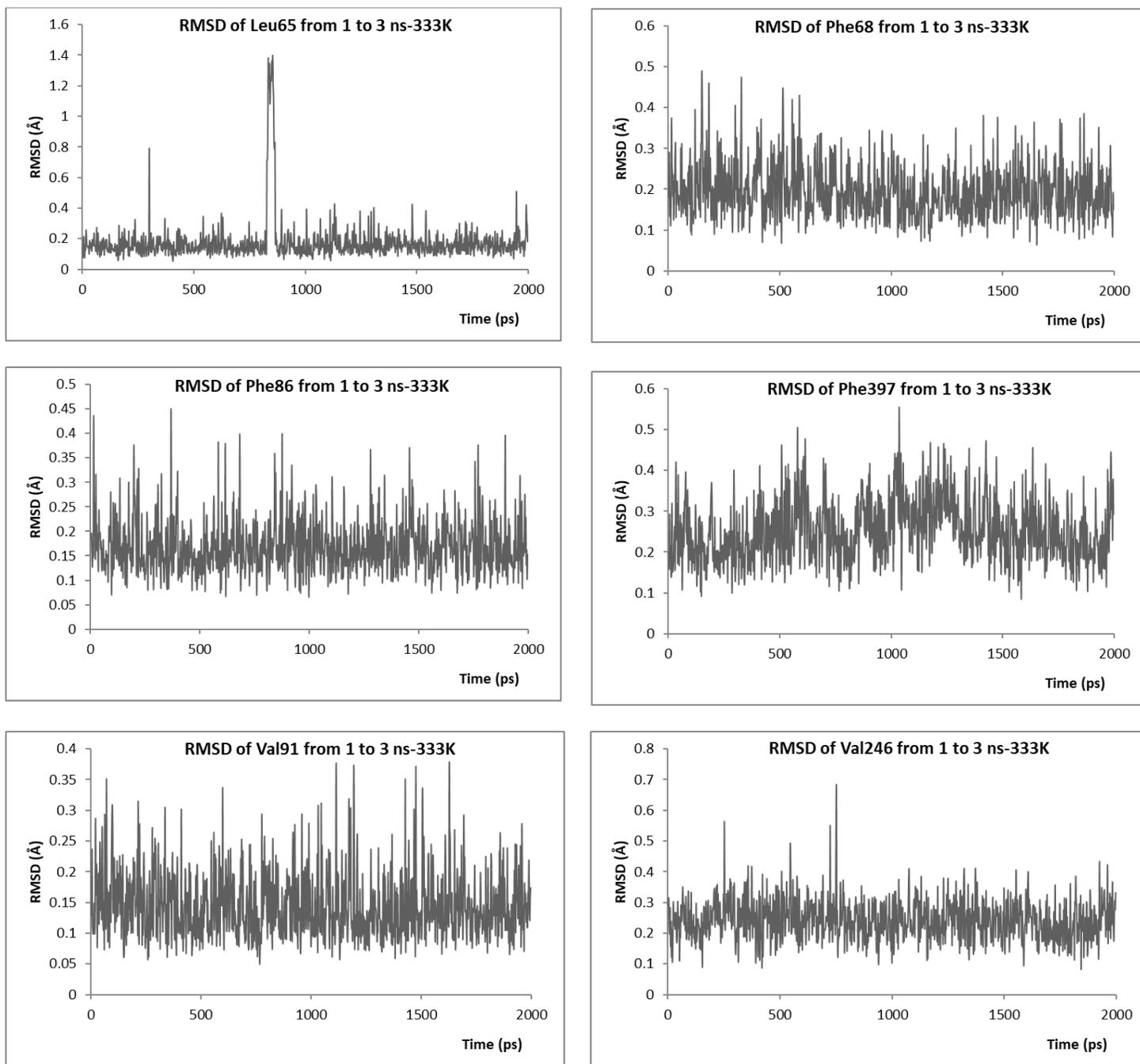


Figure S8: Root mean square deviation of Leu65, Phe68, Phe86, Phe397, Val91 and Val246 from 1 to 3 ns MD simulations of P450-TT enzyme as observed at 333 K.

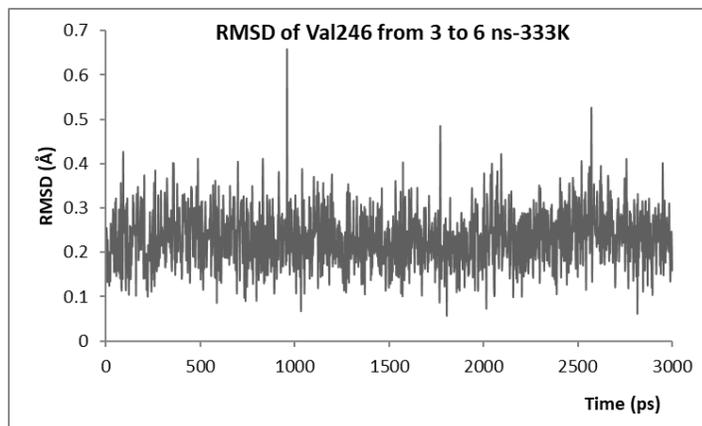
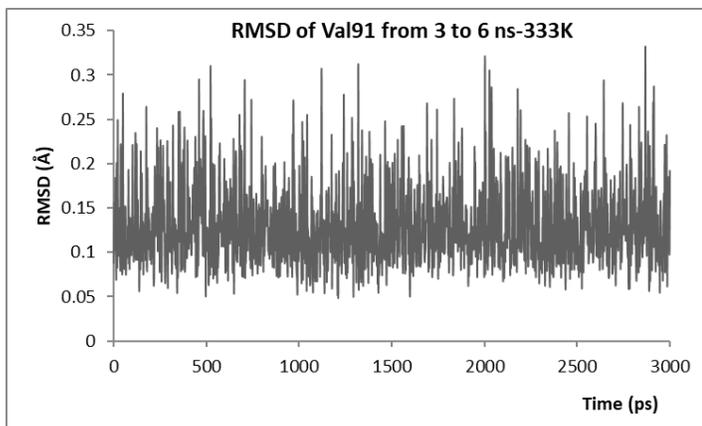
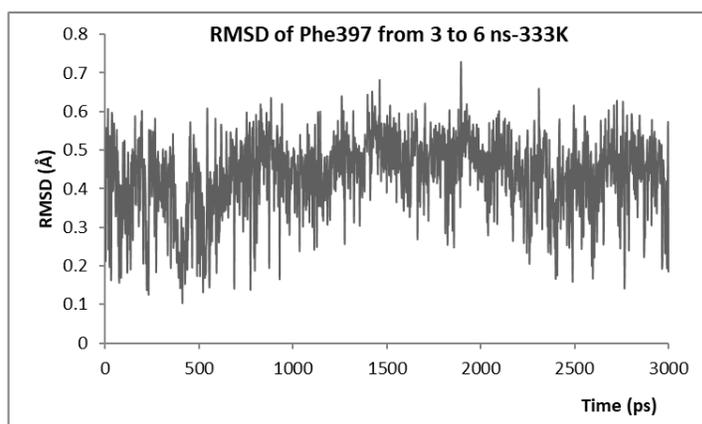
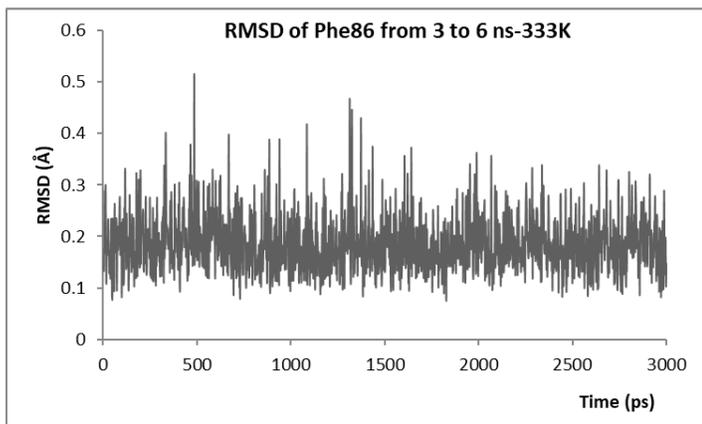
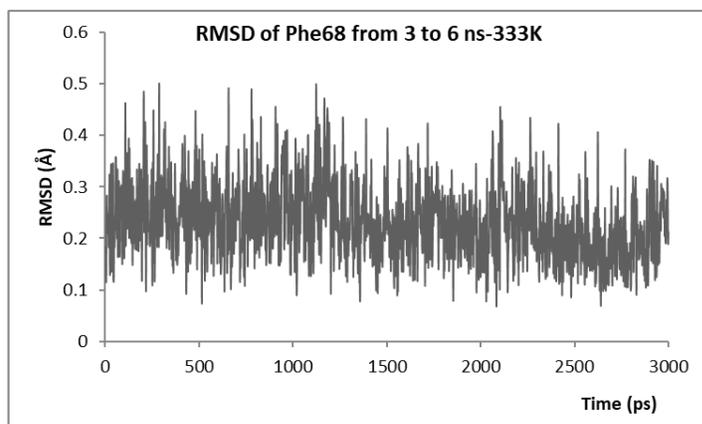
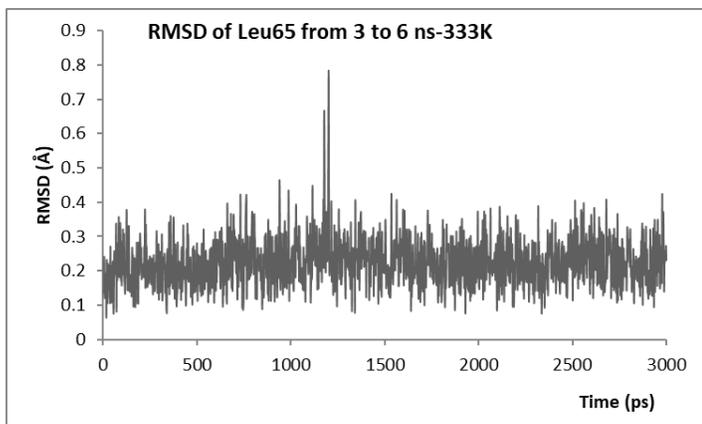


Figure S9: Root mean square deviation of Leu65, Phe68, Phe86, Phe397, Val91 and Val246 from 3 to 6 ns MD simulations of P450-TT enzyme as observed at 333 K.

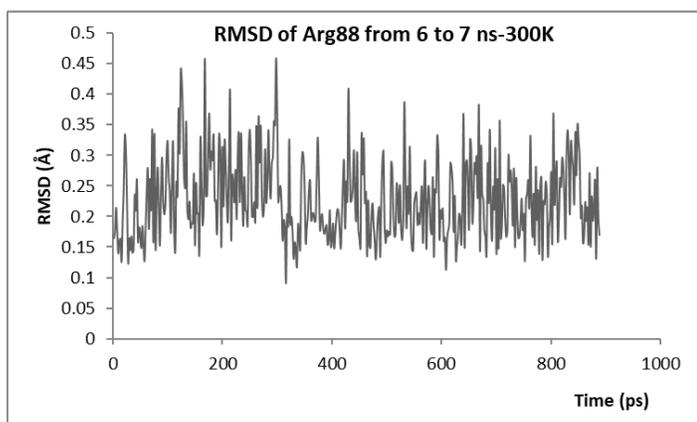
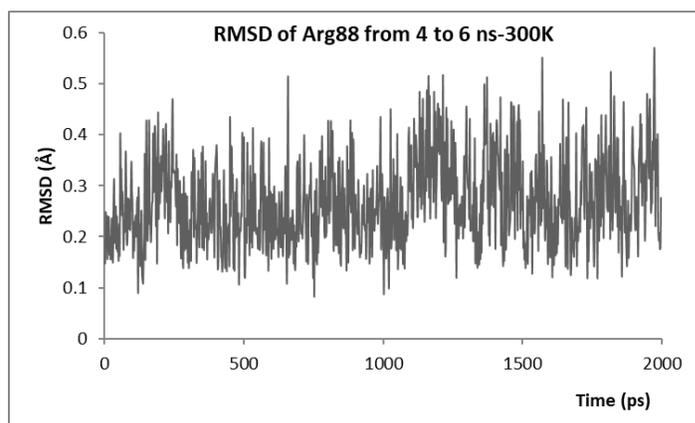
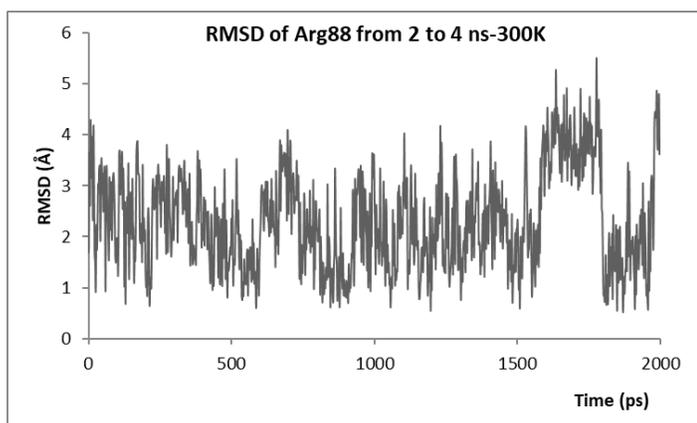


Figure S10: Root mean square deviation of Arg88 from 2 to 4, 4 to 6, and 6 to 7 ns MD simulations of P450-TT enzyme as observed at 300 K.

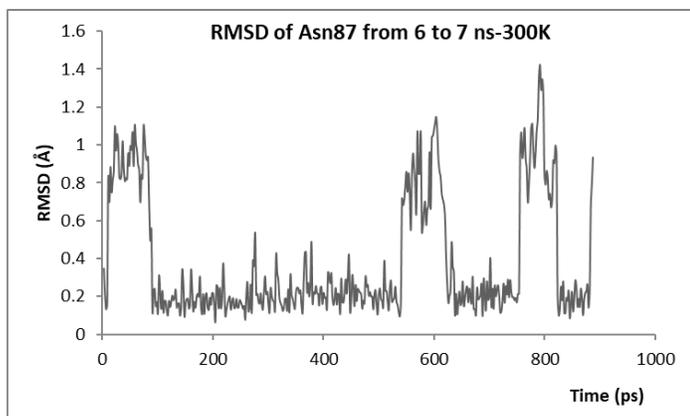
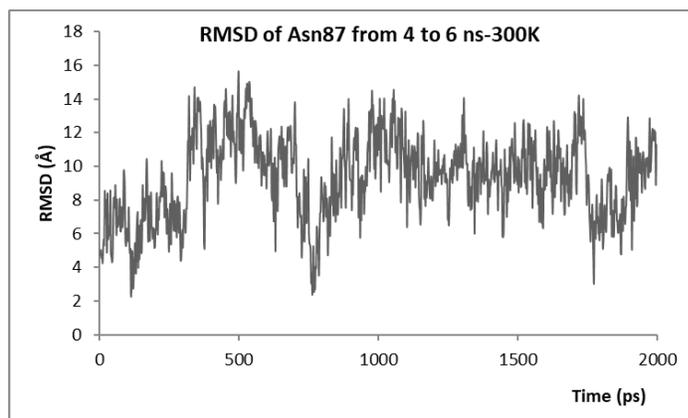
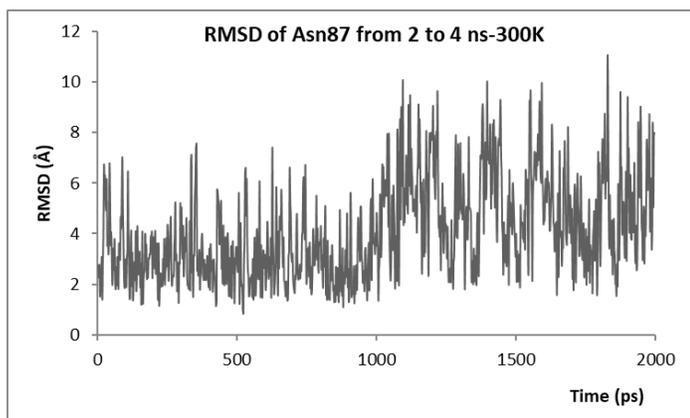


Figure S11: Root mean square deviation of Asn87 from 2 to 4, 4 to 6, 6 to 7 ns MD simulations of P450-TT enzyme as observed at 300 K.

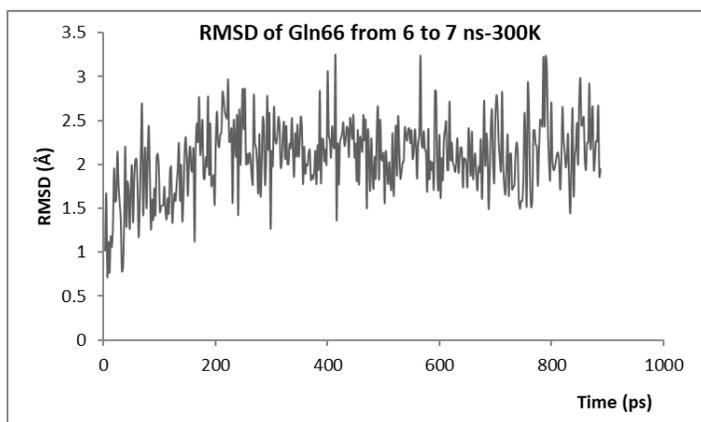
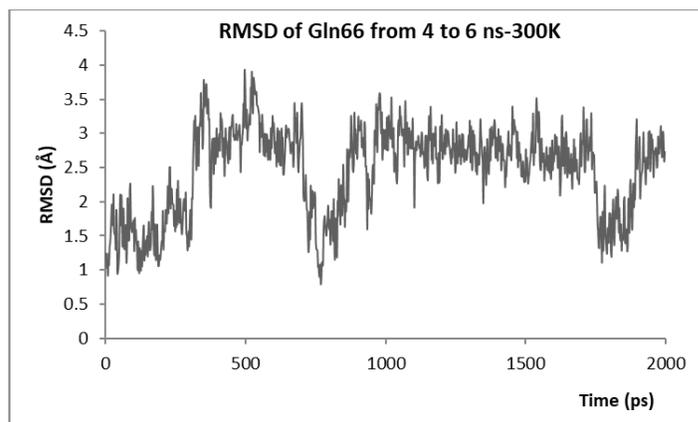
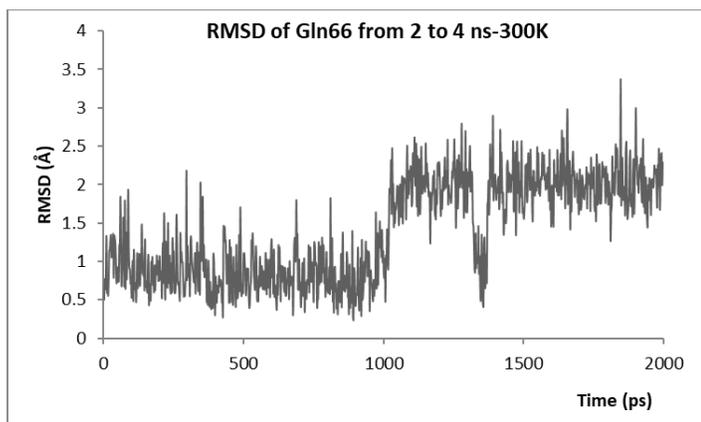


Figure S12: Root mean square deviation of Gln66 from 2 to 4, 4 to 6, and 6 to 7 ns MD simulations of P450-TT enzyme as observed at 300 K.

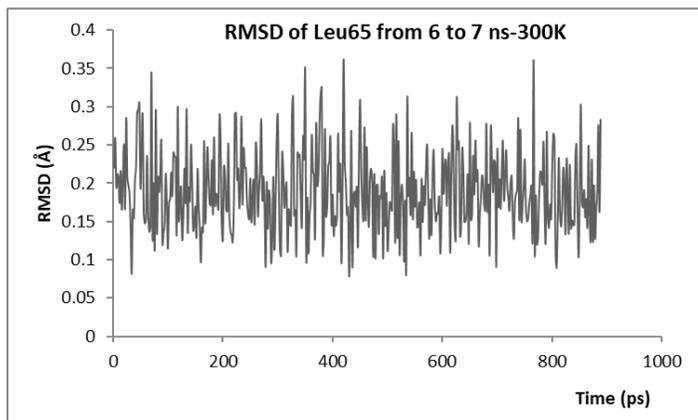
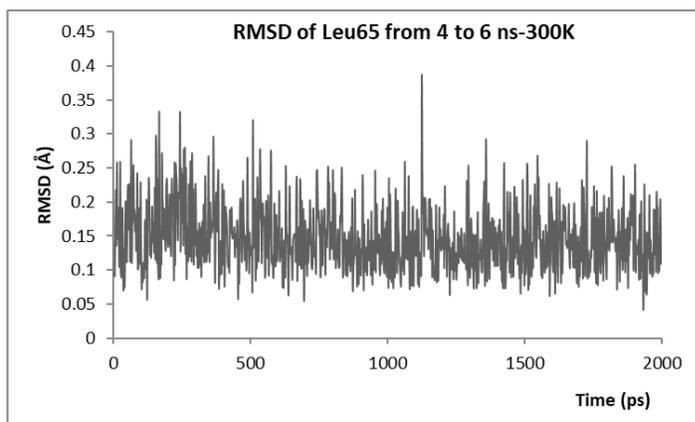
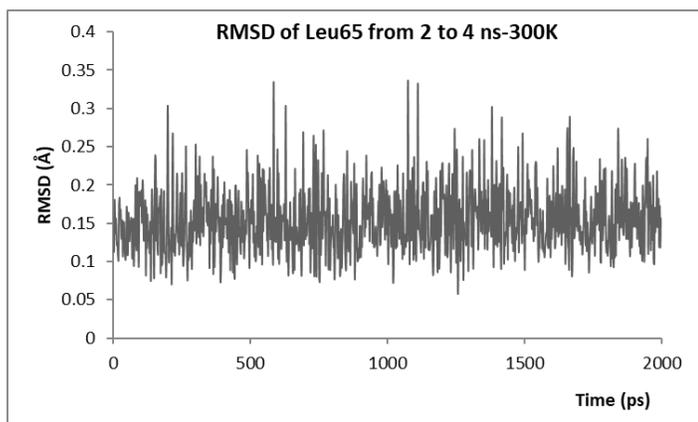


Figure S13: Root mean square deviation of Leu65 from 2 to 4, 4 to 6, and 6 to 7 ns MD simulations of P450-TT enzyme as observed at 300 K.

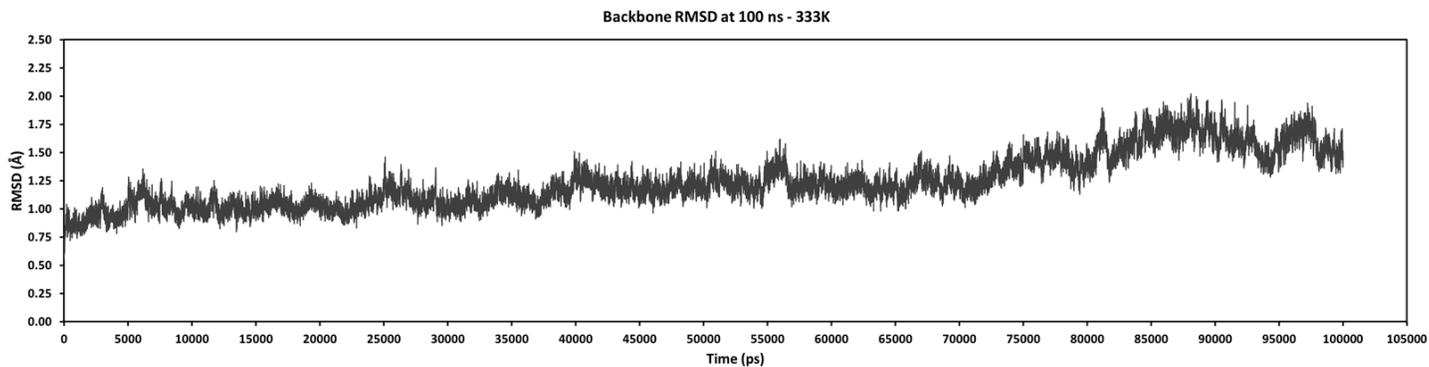
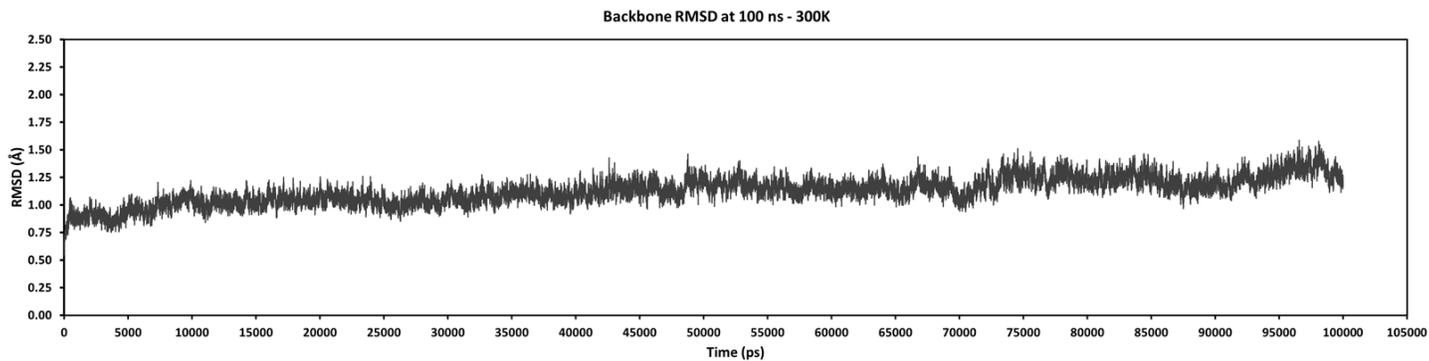


Figure S14: Backbone RMSD at 100 ns MD simulations of P450-TT enzyme as observed at 300 K and 333 K.

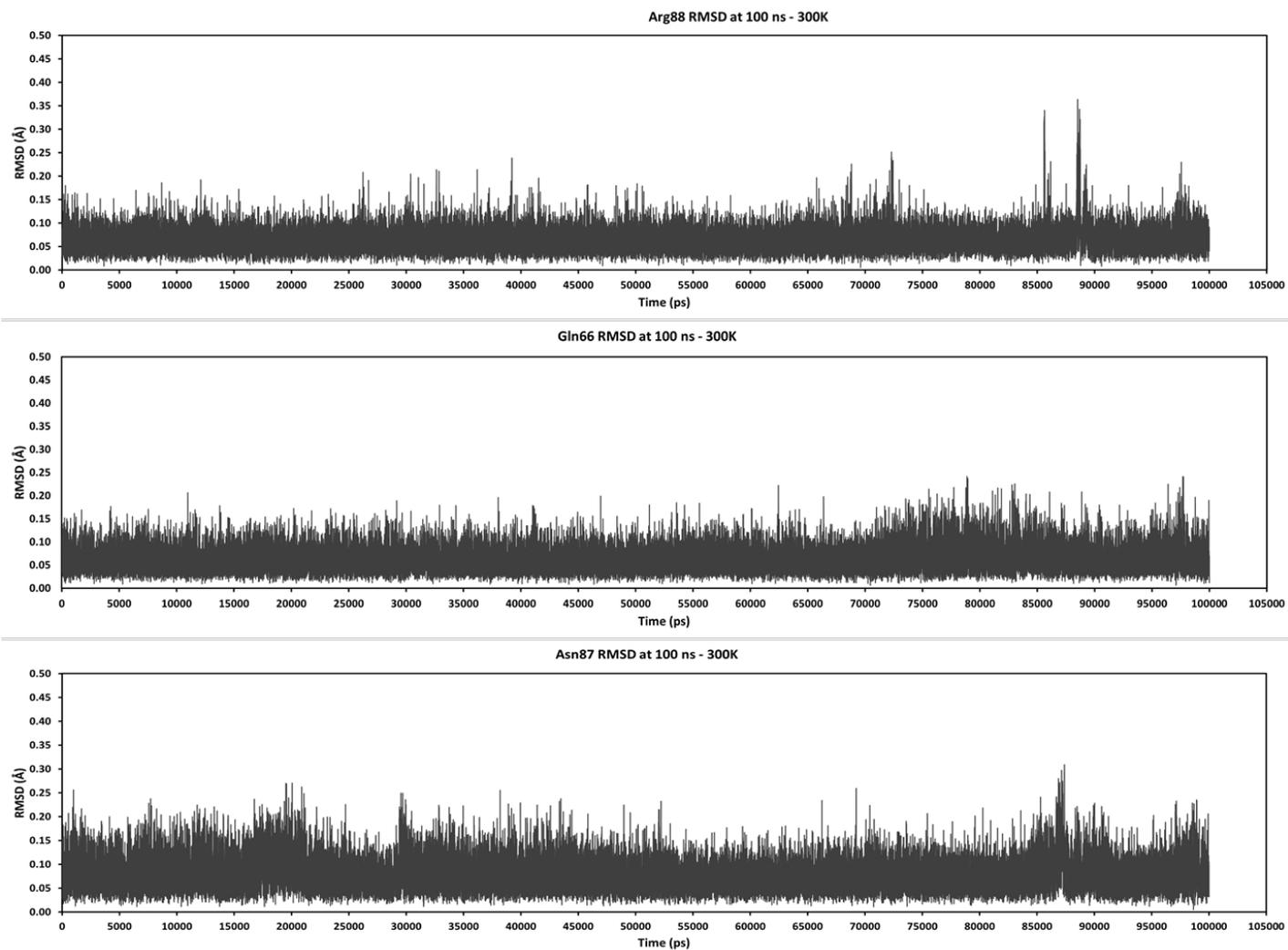


Figure S15: Root mean square deviation of Arg88, Gln66 and Asn87 at 100 ns MD simulations of P450-TT enzyme as observed at 300 K.

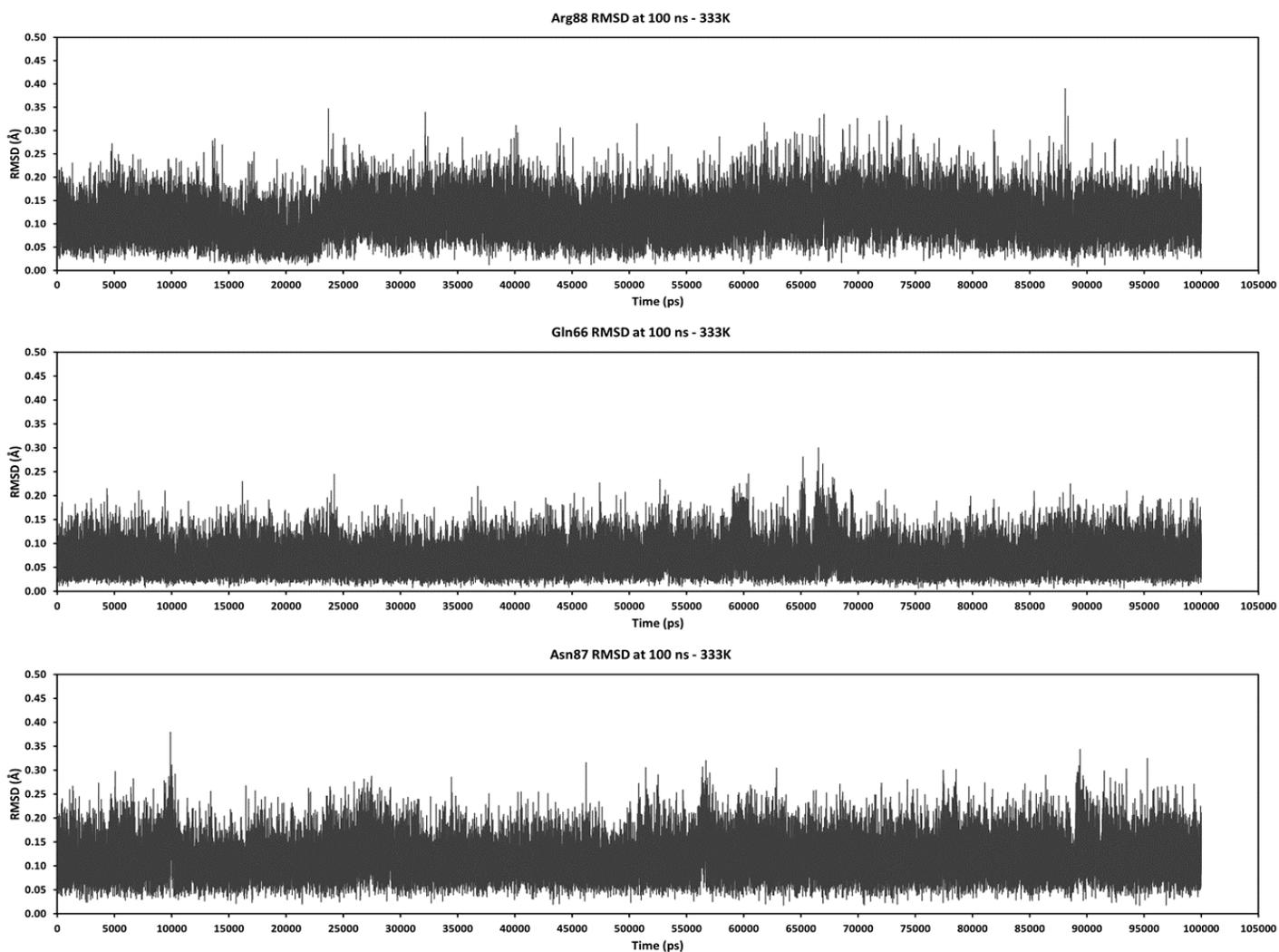


Figure S16: Root mean square deviation of Arg88, Gln66 and Asn87 at 100 ns MD simulations of P450-TT enzyme as observed at 333 K.

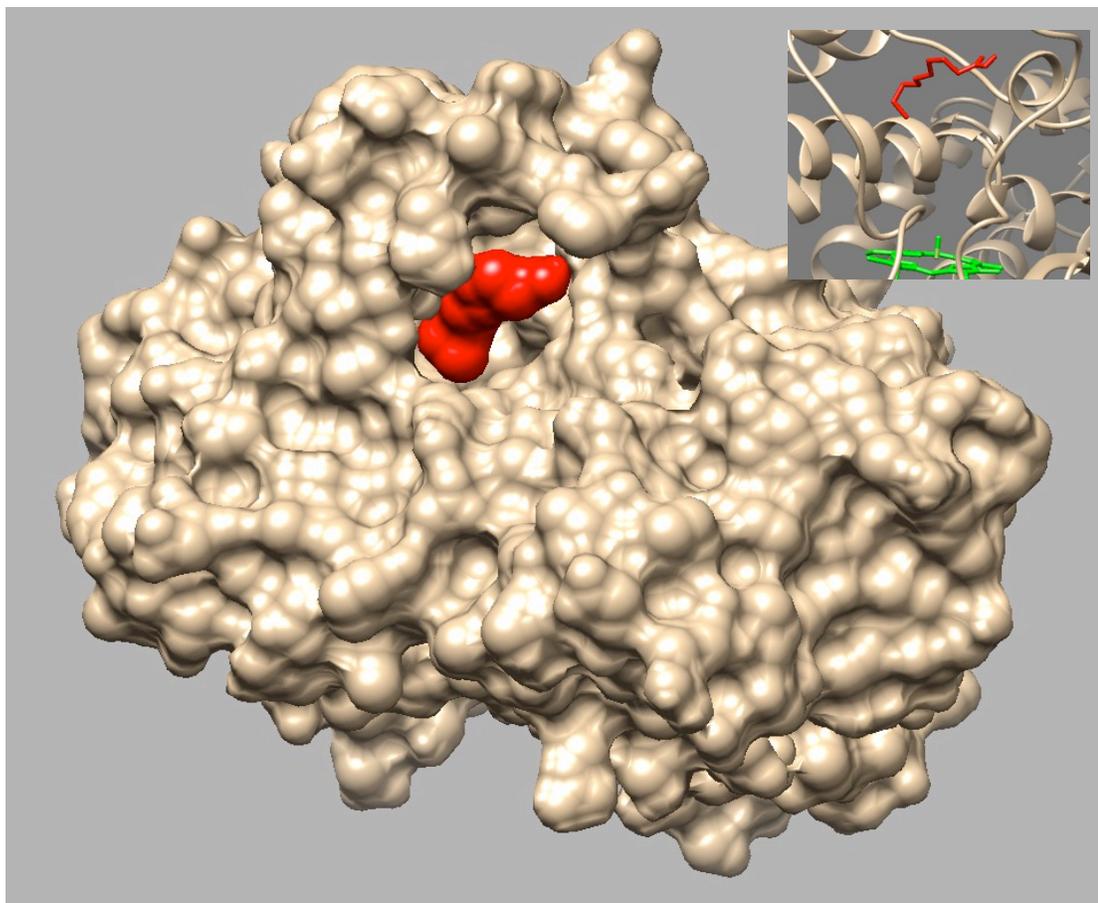


Figure S17. Illustration of the putative substrate decanoic acid docked within the substrate-binding channel of P450-TT conformation obtained at 100 ns of the 300 K MD Simulation. Inset: docking orientation 1 with binding affinity  $-3.5 \text{ kcal mol}^{-1}$ .

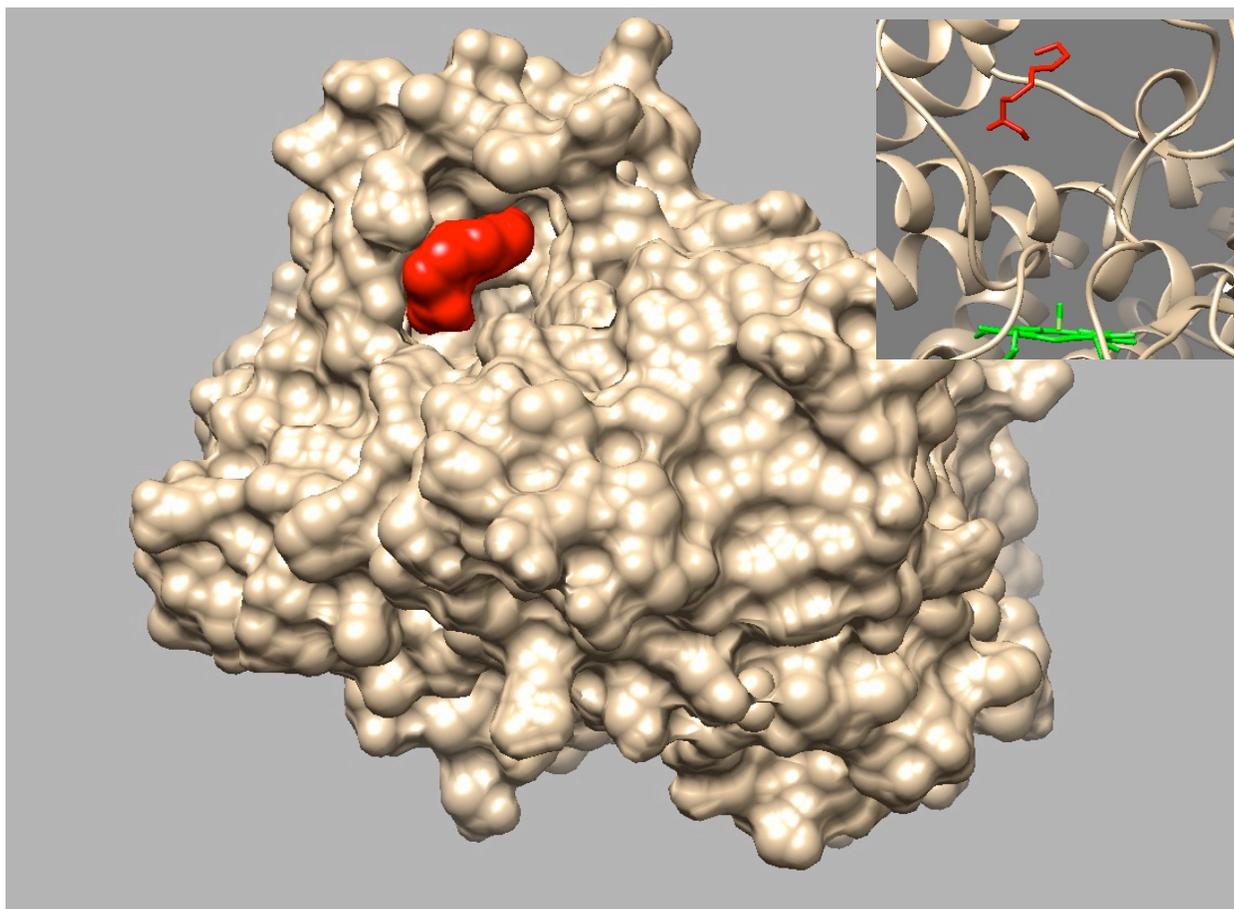


Figure S18. Illustration of the putative substrate decanoic acid docked within the substrate-binding channel of P450-TT conformation obtained at 100 ns of the 300 K MD Simulation. Inset: docking orientation 2 with binding affinity  $-3.3\text{kcal mol}^{-1}$ .