

Supporting Information:

The α -Synuclein Monomer May Have Different Misfolding Mechanisms in the Induction of α -Synuclein Fibrils with Different Polymorphs

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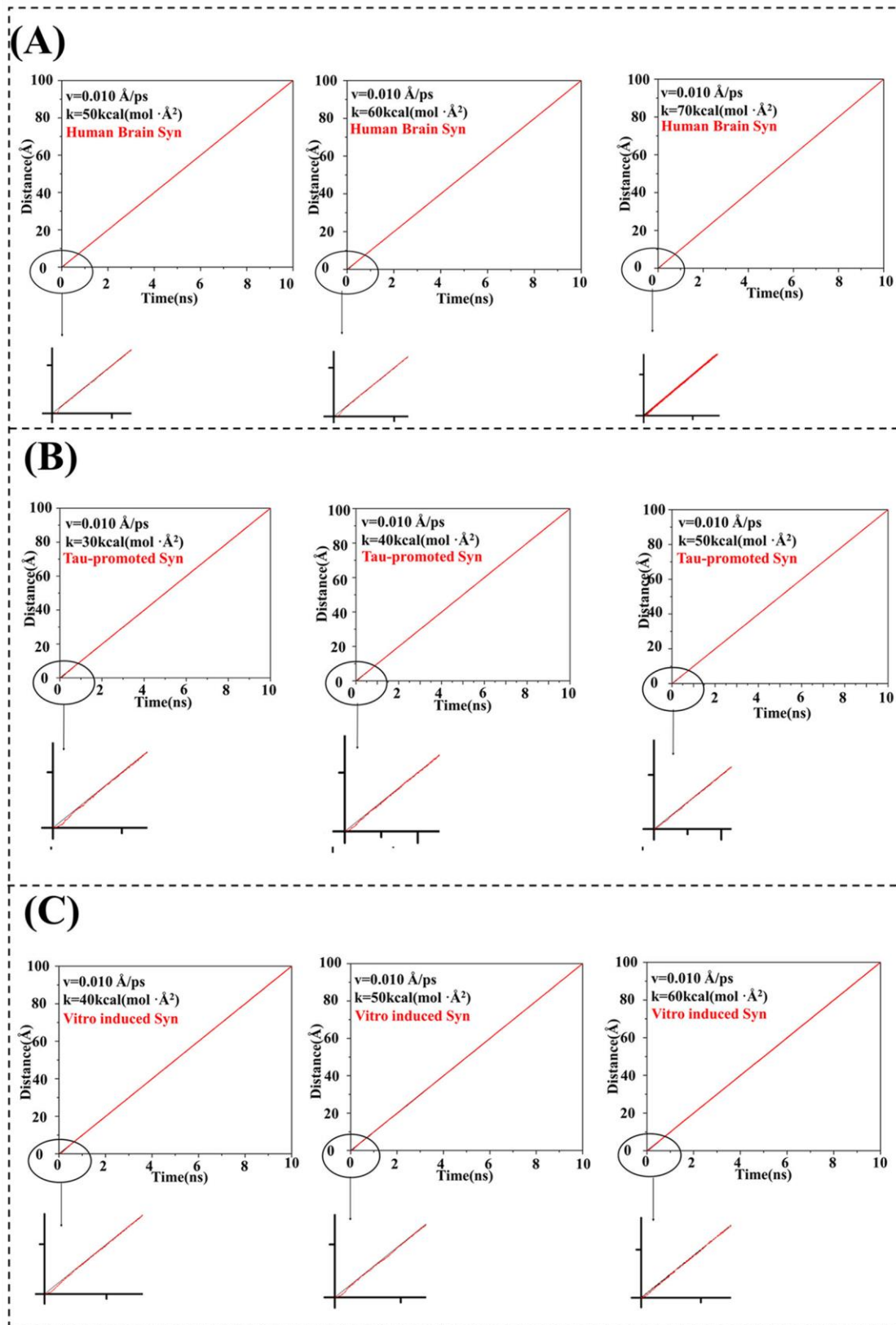


Figure S1. Parameter correction for SMD. (A) Diseased human brain model. (B) In vitro cofactor-tau induction model. (C) In vitro cofactor-free induction model.

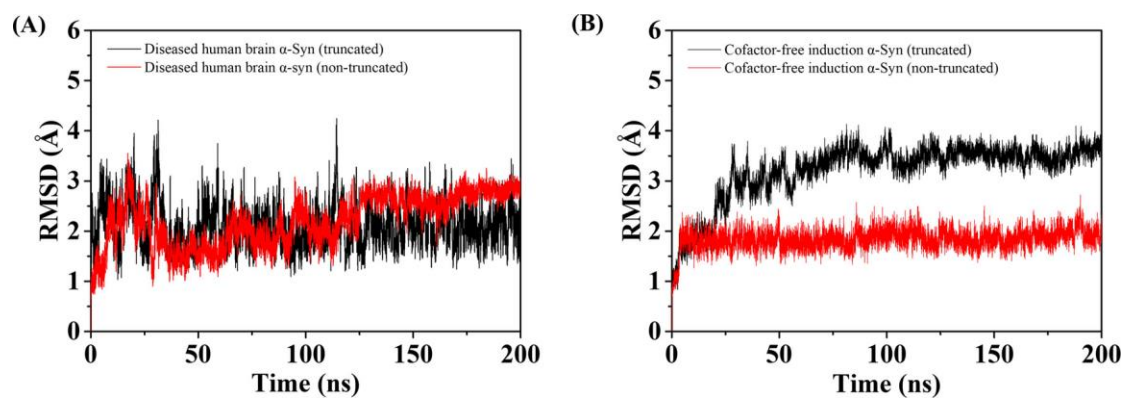


Figure S2. Convergence verification. (A) The backbone RMSDs of diseased human brain α -Syn fibrils as a function of time in truncated structure (black) and non-truncated structure (red). (B) The backbone RMSDs of cofactor-free induction α -Syn fibrils as a function of time in truncated structure (black) and non-truncated structure (red).

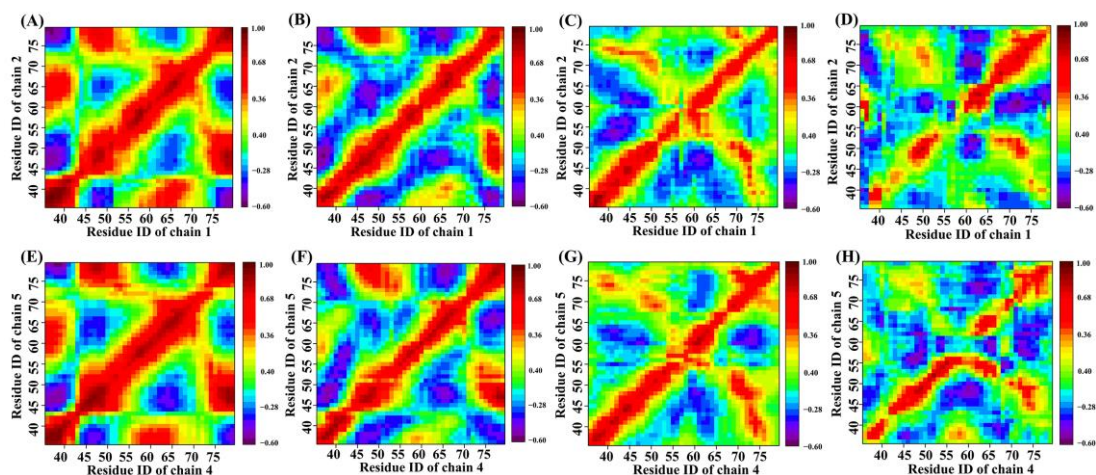
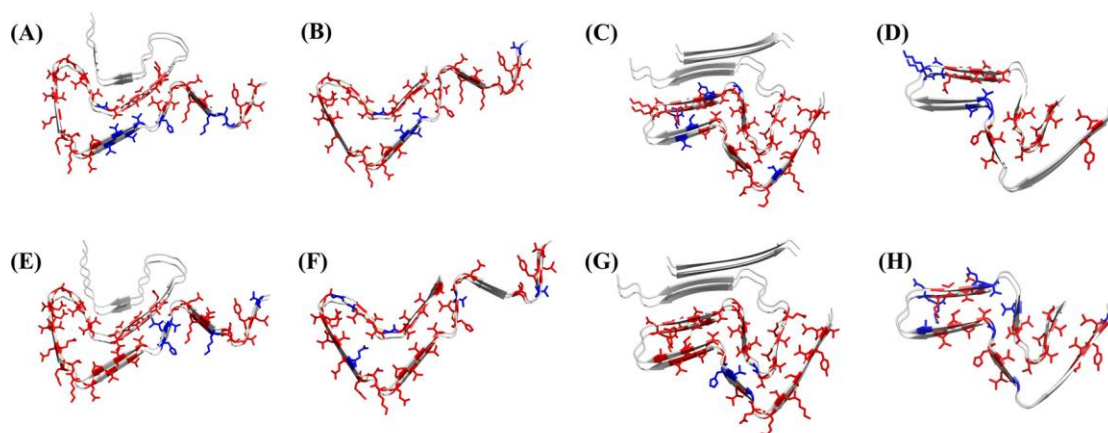


Figure S3. DCCM analysis from converged trajectories of the CMD simulation. (A,B) Chain-1/2 of non-truncated and truncated structures in human brain systems. (C,D) Chain-1/2 of non-truncated and truncated structures in cofactor-free system. (E,F) Chain-4/5 of non-truncated and truncated structures in human brain system. (G,H) Chain-4/5 of non-truncated and truncated structures in cofactor-free system. Red represents a strong interaction between residues, and blue depicts a weak interaction between residues.



■ hydrogen bond occupancies of >90%
 ■ hydrogen bond occupancies of >80%

Figure S4. Backbone hydrogen bonds analysis from CMD simulation. (A,B) Chain-1/2 of non-truncated and truncated structures in human brain system. (C,D) Chain-1/2 of non-truncated and truncated structures in cofactor-free system. (E,F) Chain-4/5 of non-truncated and truncated structures in human brain system. (G,H) Chain-4/5 of non-truncated and truncated structures in the cofactor-free system. Red and blue represent the hydrogen bond occupancies of >90 and >80%, respectively.

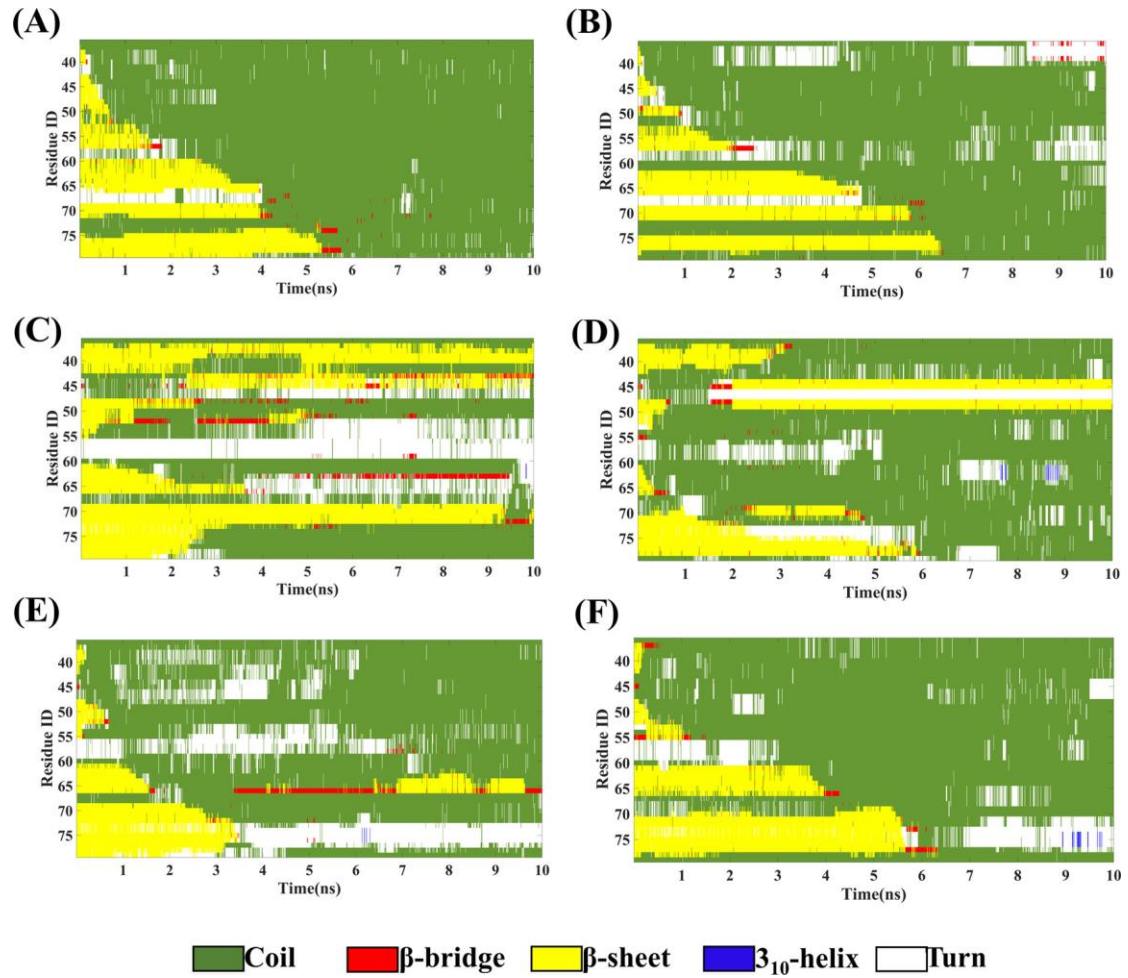


Figure S5. Changes in the secondary structure as a function of time. (A,B) Chain-1 of non-truncated structure and truncated in human brain system. (C,D) Chain-1 of non-truncated structure and truncated structures in cofactor-free system in path1. (E,F) Chain-1 of non-truncated structure and truncated structures in cofactor-free system in path2.

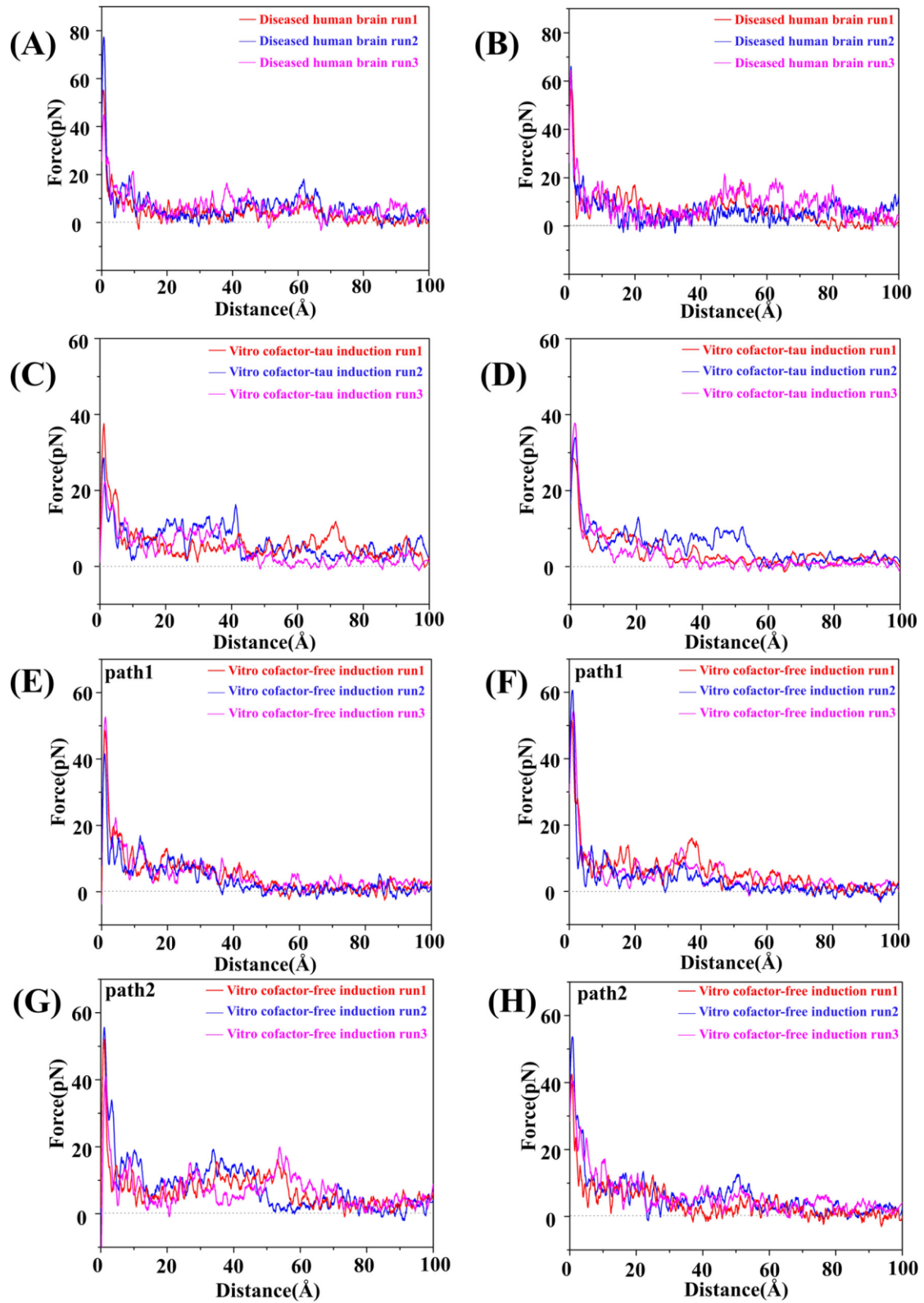


Figure S6. The changes of force over the reaction coordinate. (A,B) Chain-1 and Chain-5 of α -Syn fibrils in diseased human brains. (C,D) Chain-1 and Chain-4 of α -Syn fibrils in the cofactor-tau induction. (E,F) Chain-1 and Chain-5 of α -Syn fibrils in the cofactor-free induction in the path1. (G,H) Chain-1 and Chain-5 of α -Syn fibrils in the cofactor-free induction in the path2.

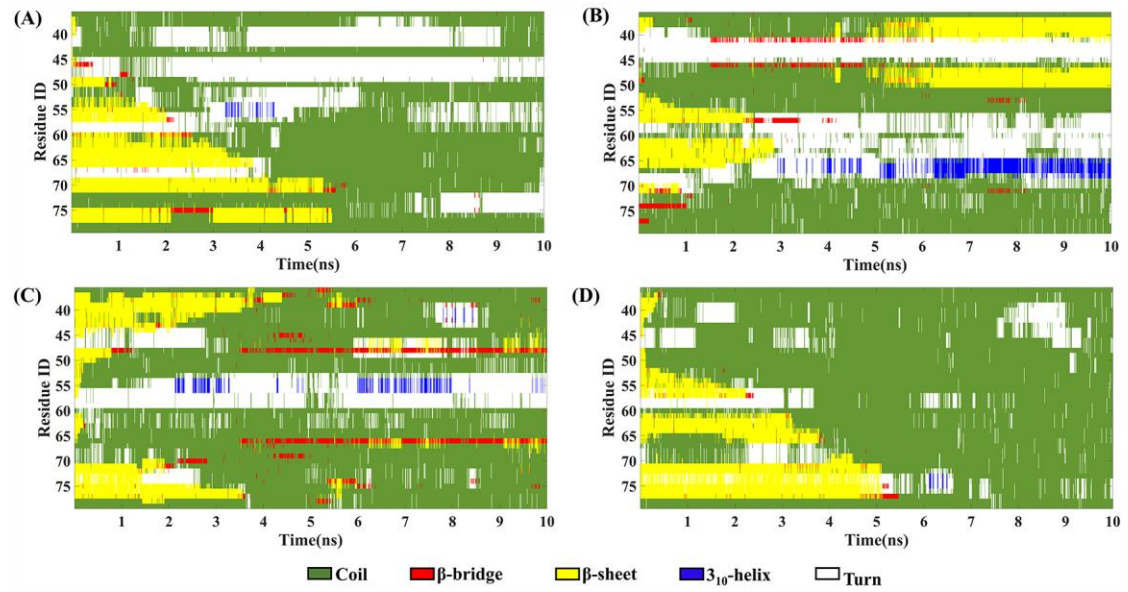


Figure S7. Changes in the secondary structure as a function of time. (A) Chain-5 of α -Syn fibrils in diseased human brain systems. (B) Chain-4 of α -Syn fibrils in the cofactor-tau induction. (C) Chain-5 of α -Syn fibrils in the cofactor-free induction in the path1. (D) Chain-5 of α -Syn fibrils in the cofactor-free induction in the path2.

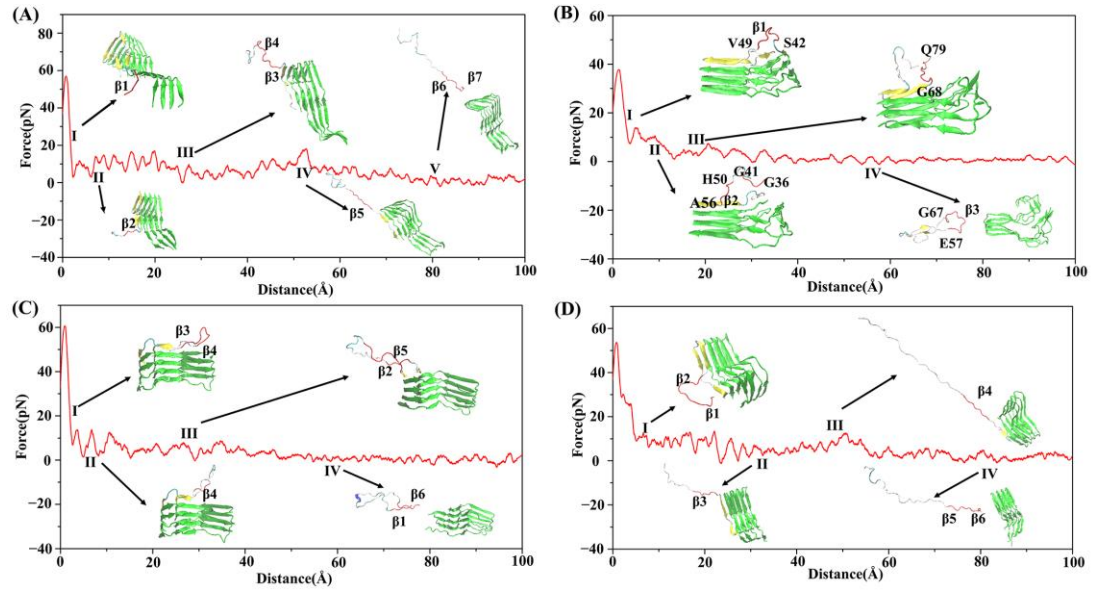


Figure S8. Changes of the force over the reaction coordinate. (A) Chain-5 of α -Syn fibrils in diseased human brain systems. (B) Chain-4 of α -Syn fibrils in the cofactor-tau induction. (C) Chain-5 of α -Syn fibrils in the cofactor-free induction in the path1. (D) Chain-5 of α -Syn fibrils in the cofactor-free induction in the path2. I–IV represents the five stages of dissociation. The arrow points to the representative conformation of each stage.

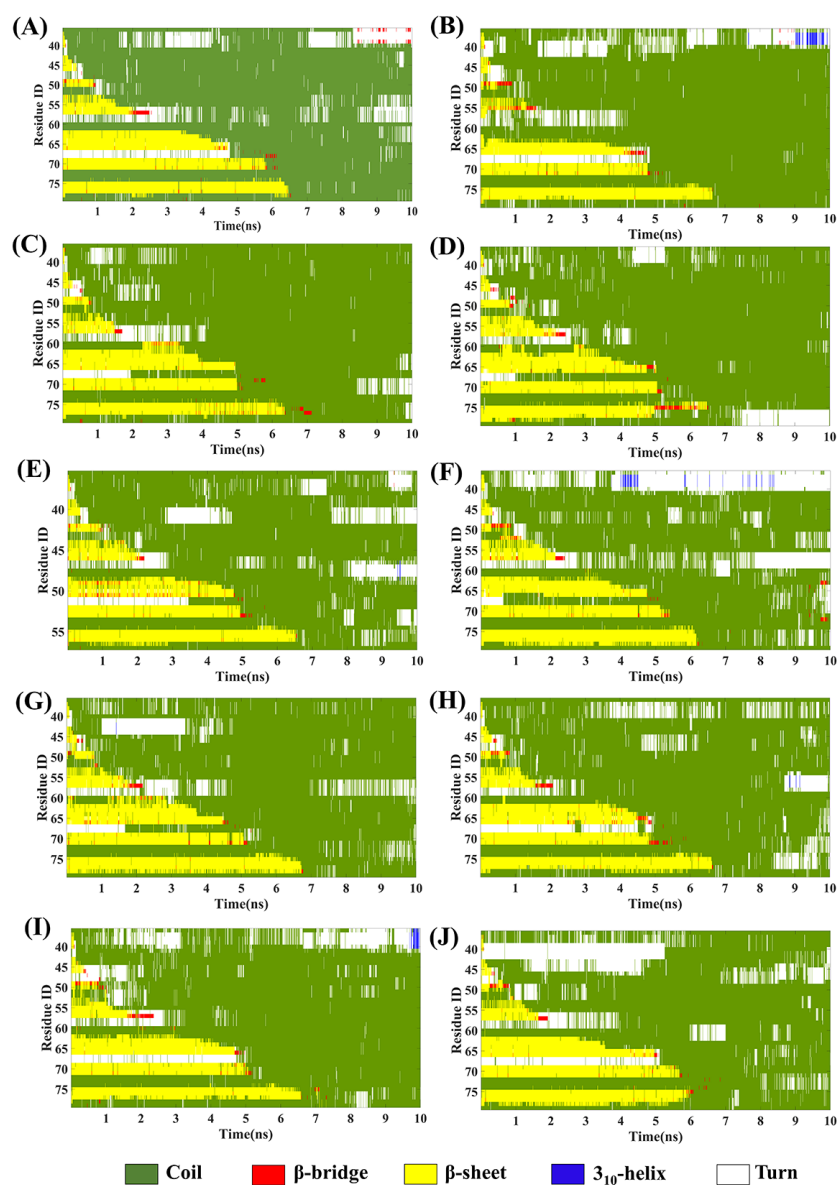


Figure S9. Changes in the secondary structure as a function of time. (A–J) represent run1–run10 on Chain 1 of α -Syn fibrils in diseased human brains.

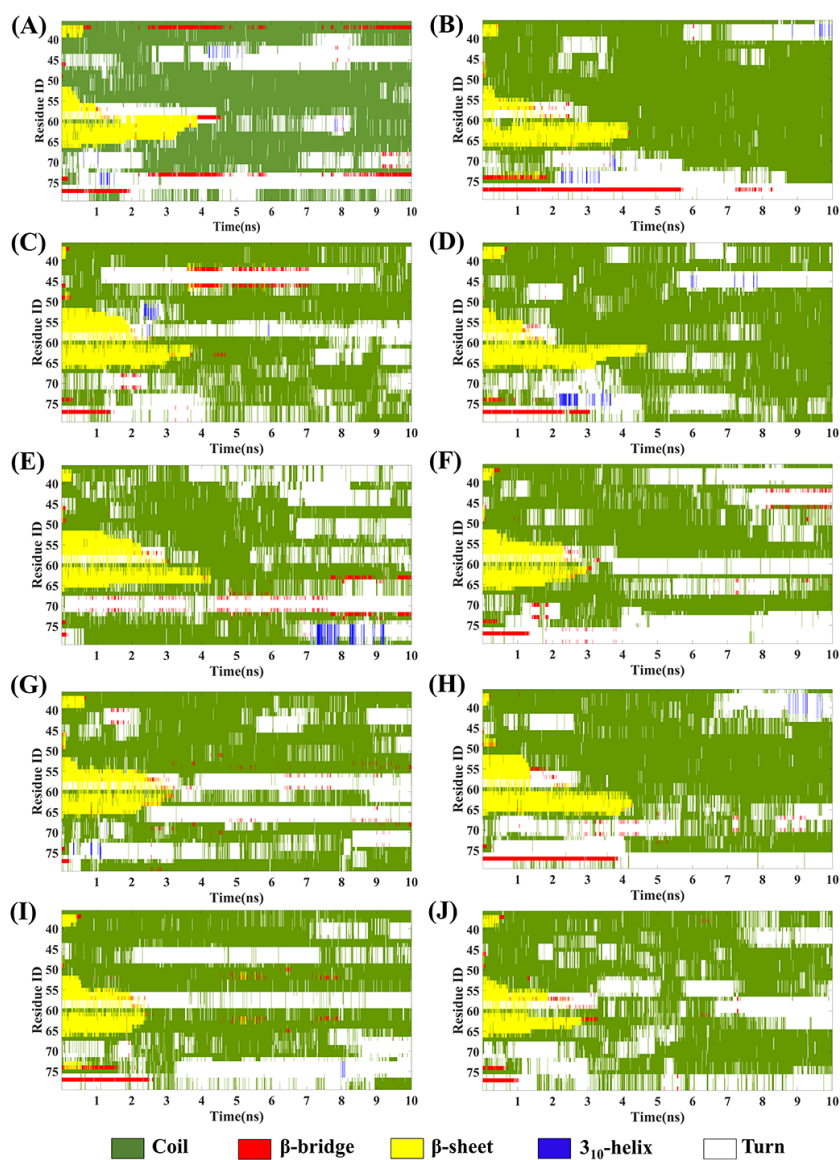


Figure S10. Changes in the secondary structure as a function of time. (A–J) represent run1-run10 on Chain 1 of α -Syn fibrils in the cofactor-tau induction model.

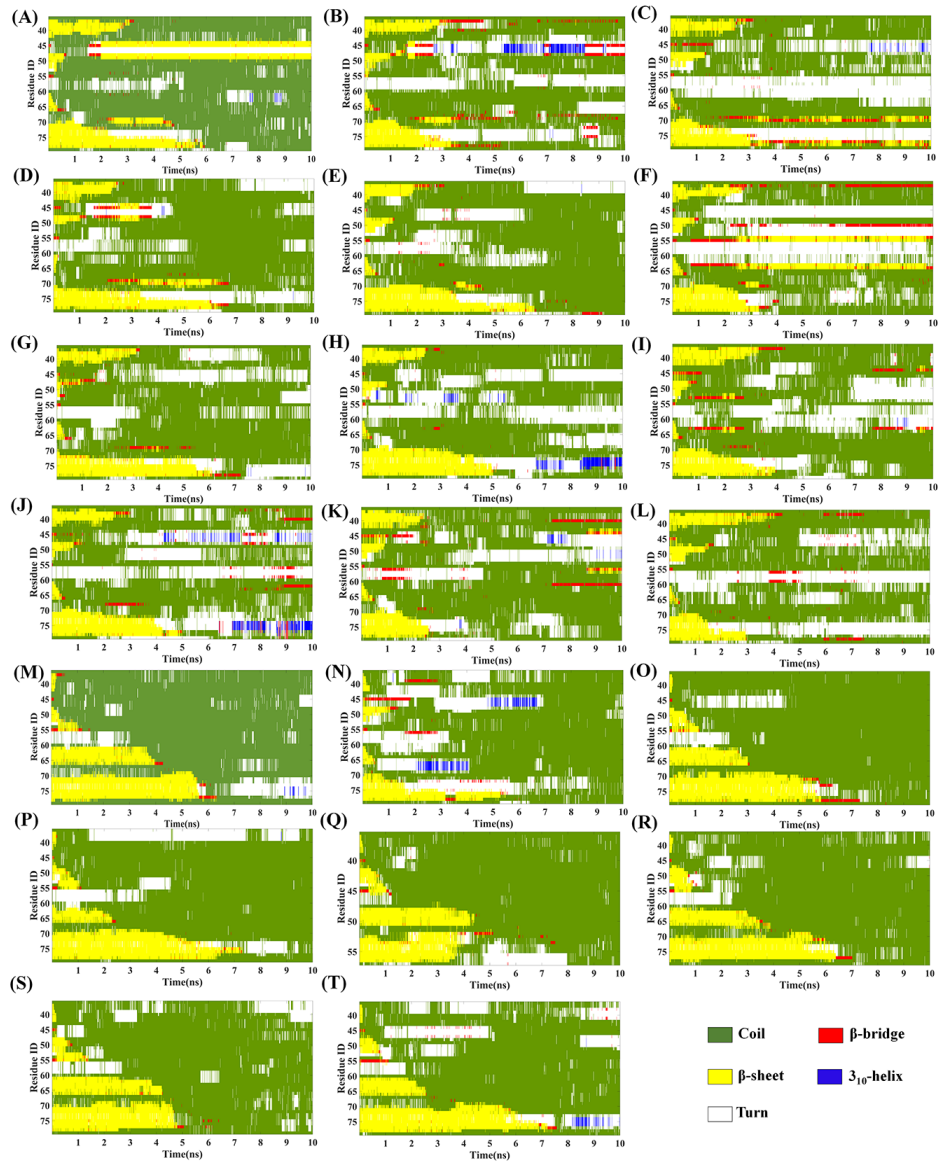


Figure S11. Changes in the secondary structure as a function of time. (A–L) represent run1-run12 on Chain 1 of α -Syn fibrils in the cofactor-free induction in the path 1. (M–T) represent run1-run8 on Chain 1 of α -Syn fibrils in the cofactor-free induction in the path 2.

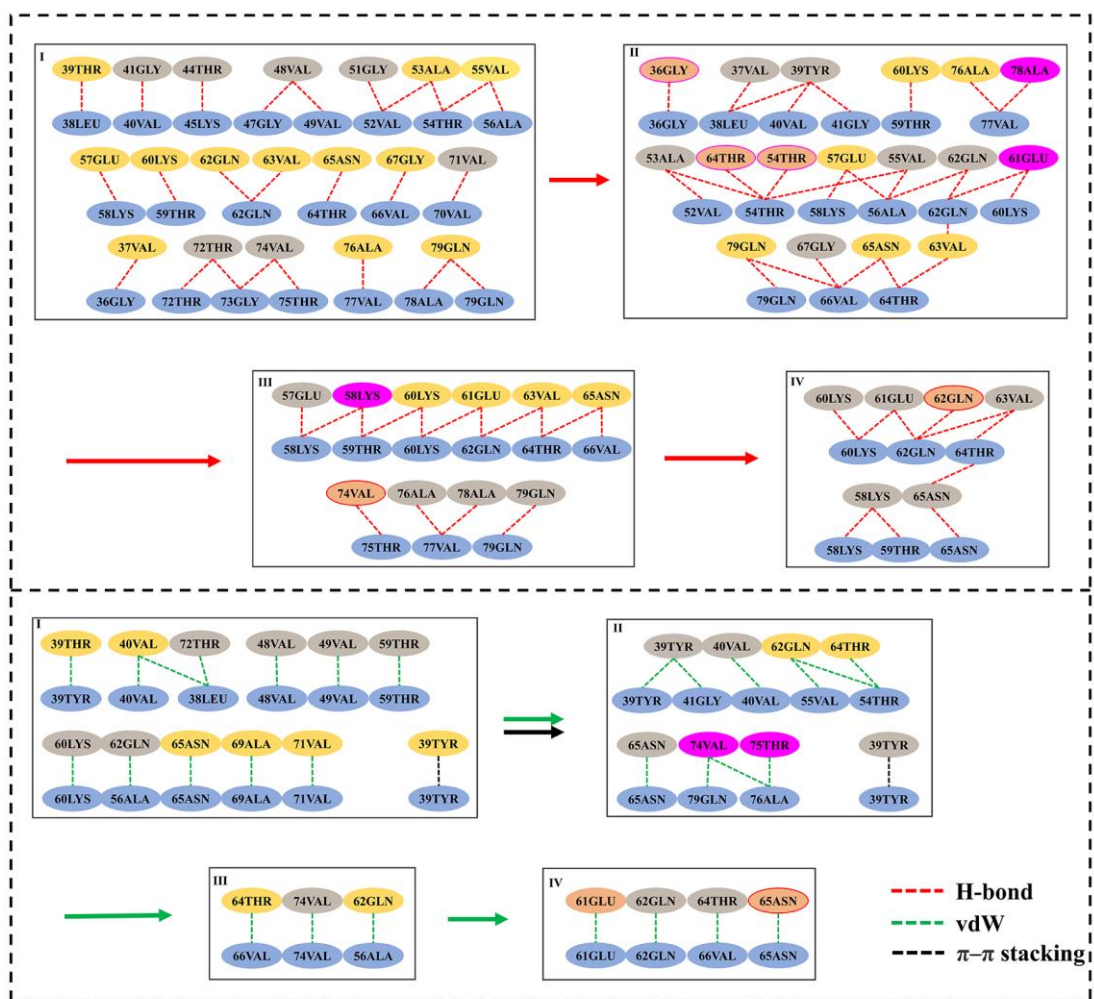


Figure S12. The residue interaction network analysis for cofactor-tau system.

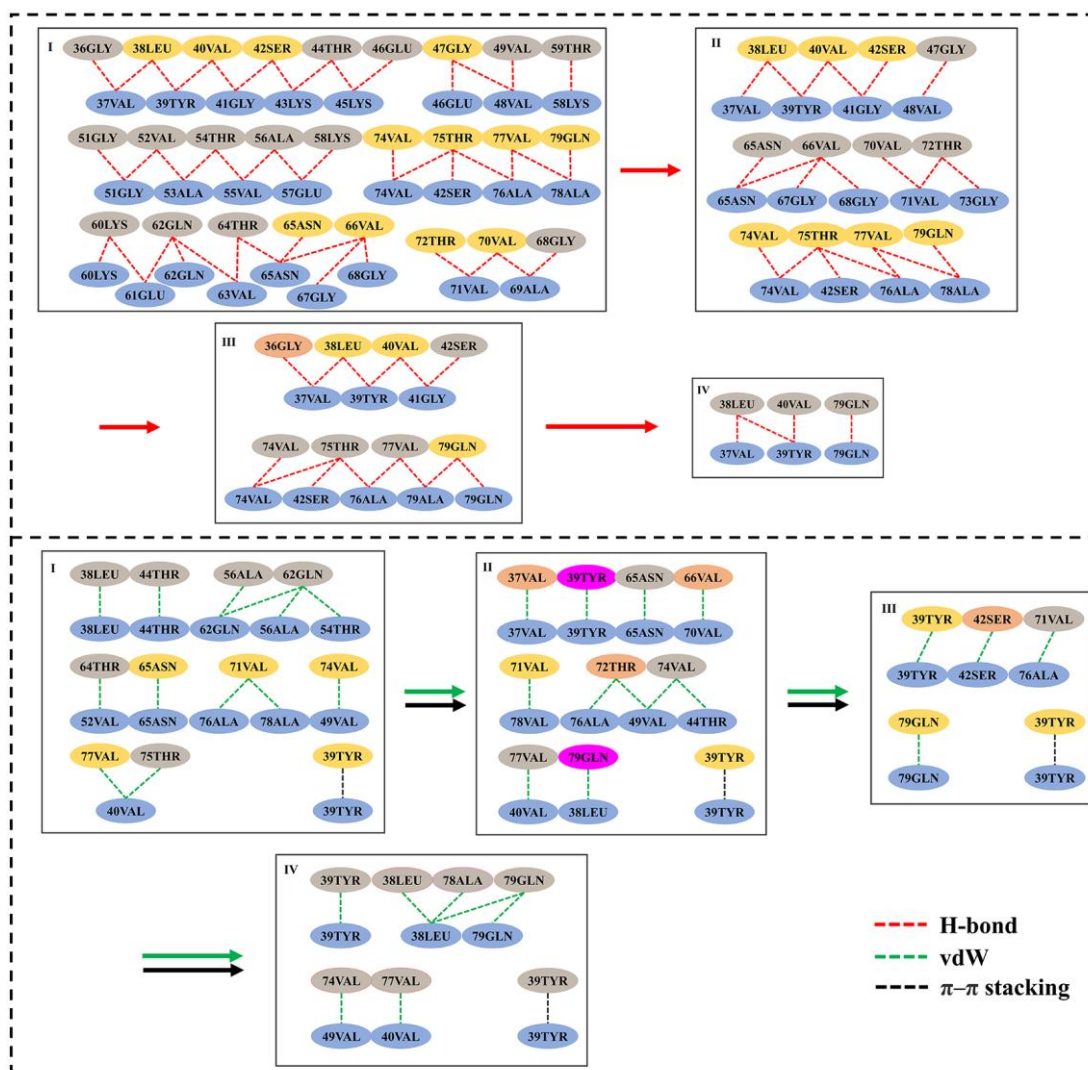


Figure S13. The residue interaction network analysis for cofactor-free system in path1.

