Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supplementary Information

Co-aggregation of α-synuclein with Amyloid-β Stabilizes β-sheet-rich Oligomers and Enhances the Formation of β-barrels

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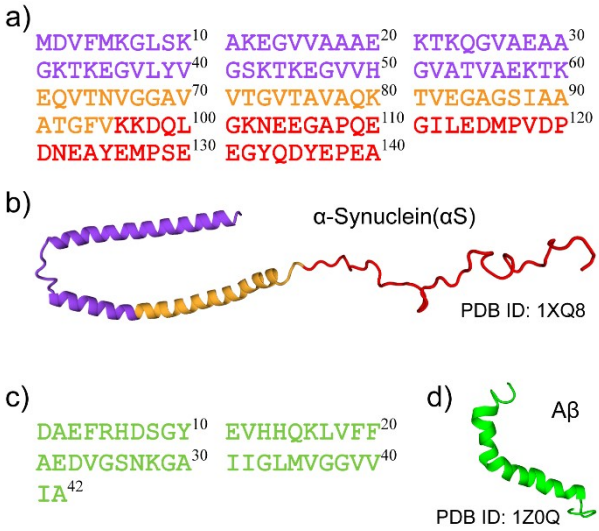

Fig. S1. Amino acid sequence and initial structure of αS and Aβ. The primary sequence and initial structure of full-length αS **a&c)** and Aβ **b&d)** used in our DMD simulation. The N-terminus, NAC region, and C-terminus of αS are colored purple, orange, and red, respectively. The Aβ peptide is colored green.

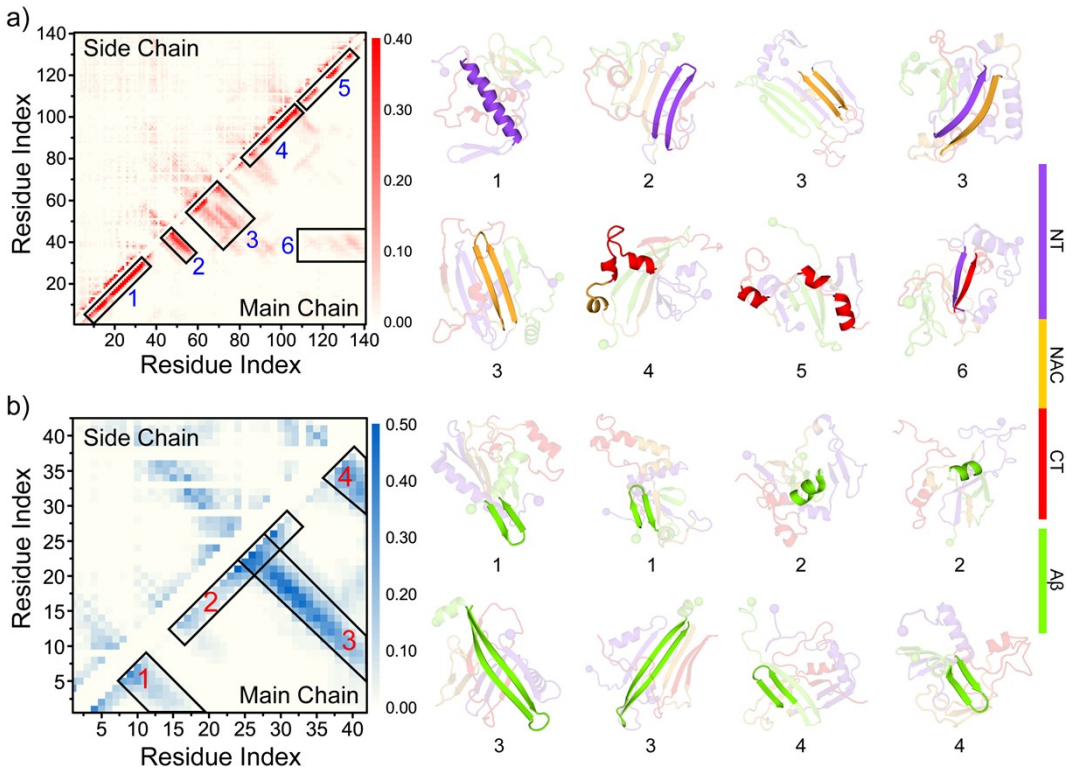

Fig. S2. Intra-peptide contact frequency analysis of αS and Aβ in their hetero-dimer. The intra-peptide residue-pairwise contact frequencies formed by atoms from main-chain (lower diagonal) and side-chain (upper diagonal) atoms of αS **a)** and Aβ **b)** in the hetero-dimer from the last 100 ns of 30 independent 500 ns hetero-dimerization DMD simulations of one αS monomer mixed with one Aβ. The representative structured motifs with high contact frequency patterns, heightened by boxes in the contact frequency map, are also presented on the right.

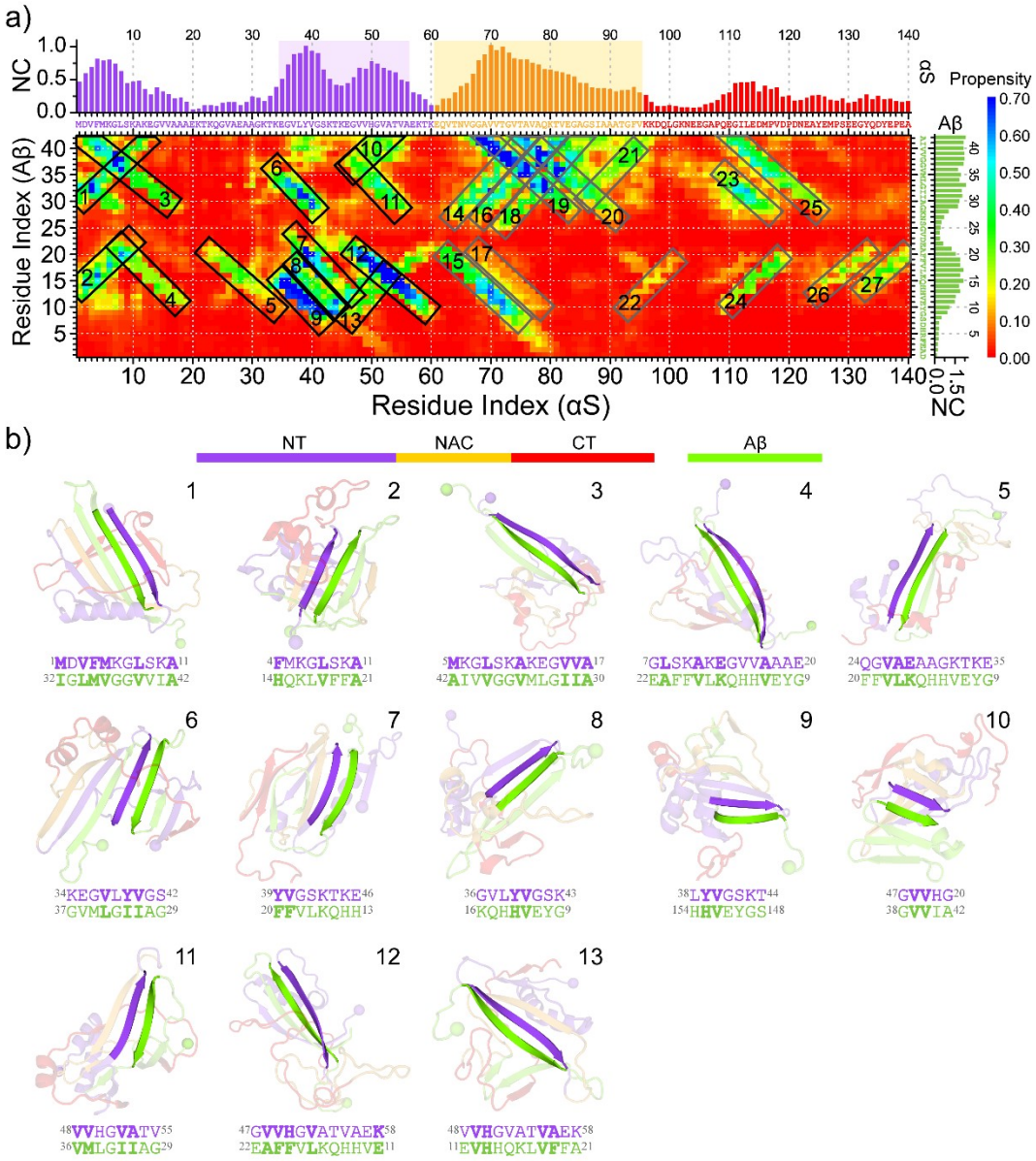

Fig. S3. Conformational interaction between the N-terminus of αS and Aβ in the hetero-dimer. a) The inter-peptide residue-pairwise contact formed among main-chain atoms of αS and Aβ during the last 100 ns of 30 independent 500 ns simulations. **b)** Representative contact pattern structures of the Aβ monomer (green) and N-terminal region of αS (purple) labeled as 1-13 heightened by boxes in the contact frequency map are also presented.

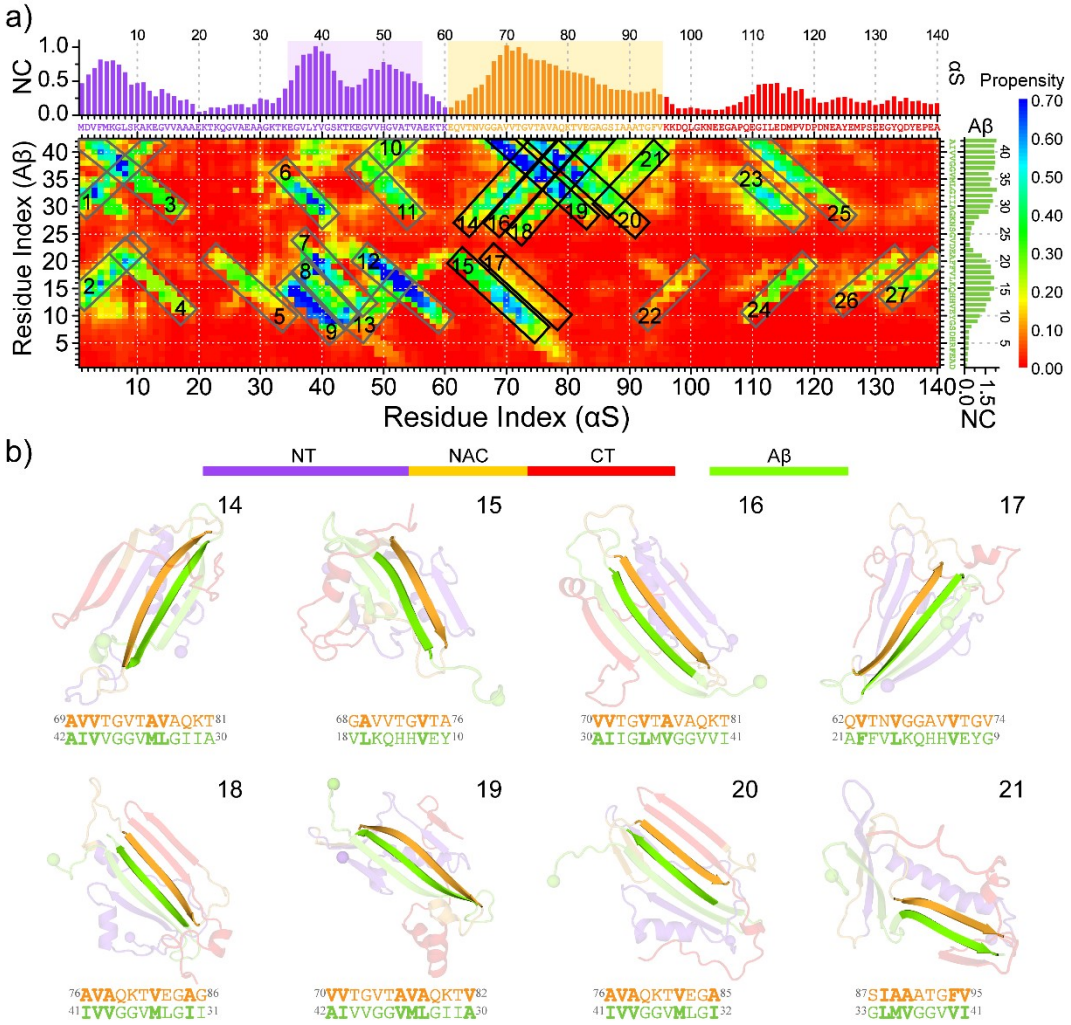

Fig. S4. Conformational interaction between the NAC region of αS and Aβ in the hetero-dimer. a) The inter-peptide residue-pairwise contact formed among main-chain atoms of αS and Aβ during the last 100 ns of 30 independent 500 ns simulations. **b)** Representative contact pattern structures of the Aβ monomer (green) and NAC region of αS (orange) labeled as 14-21 heightened by boxes in the contact frequency map are also presented.

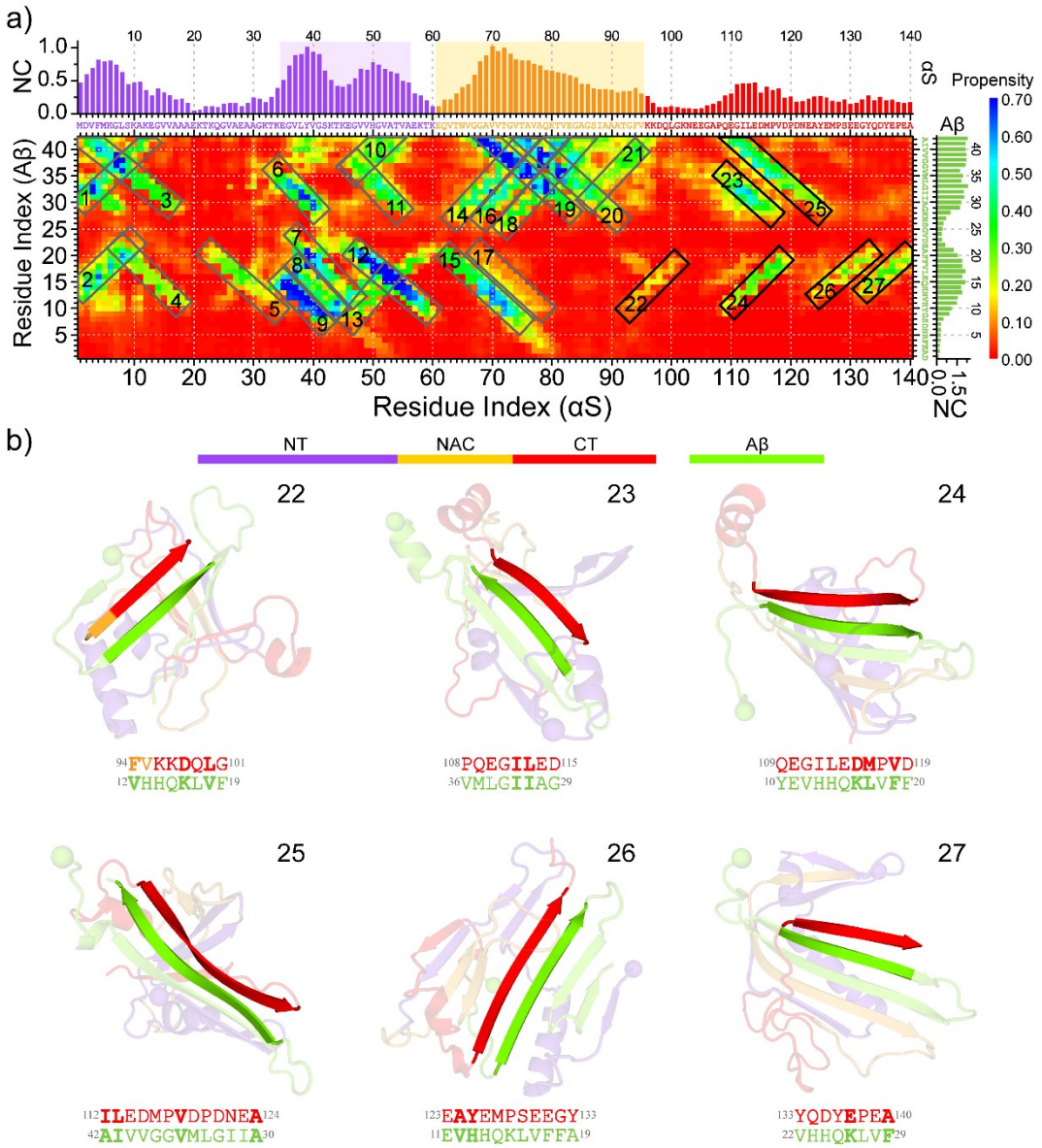

Fig. S5. Conformational interaction between the C-terminus of αS and Aβ in the hetero-dimer. a) The inter-peptide residue-pairwise contact formed among main-chain atoms of αS and Aβ during the last 100 ns of 30 independent 500 ns simulations. **b)** Representative contact pattern structures of the Aβ monomer (green) and C-terminus of αS (red) labeled as 22-27 heightened by boxes in the contact frequency map are also presented.

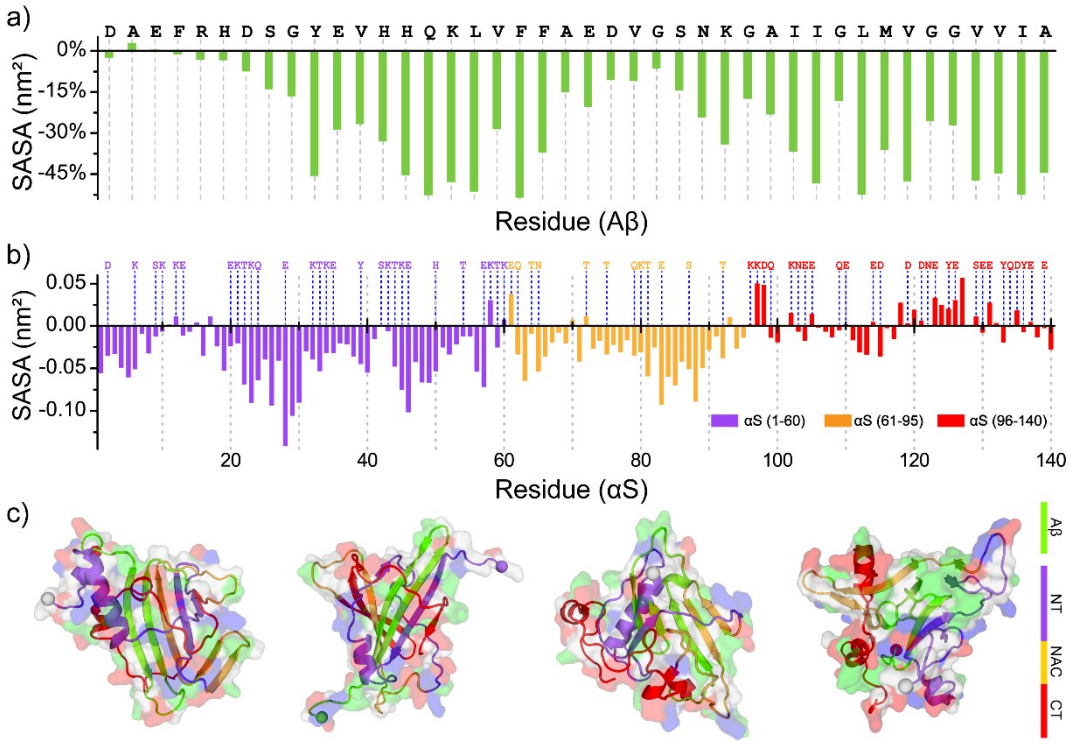

Fig. S6. Exposed surface area analysis for each residue from Aβ and αS hetero-dimer. a&b) Average difference ratios of the accessible surface area per residue from Aβ and αS and in the hetero-dimer compared with their isolated monomer. **c)** The four representative structures are shown in the cartoon and surface by residue type (hydrophobic, polar, negatively charged, and positively charged residues are colored white, green, red, and blue, respectively). Only the conformations of the isolated monomer of Aβ, αS, and hetero-dimer of Aβ and αS in the last 100 ns are used for the above analysis. For each molecular system (including one Aβ, one αS, and one Aβ mixed with one αS), we performed 30 independent 500 ns DMD trajectories.

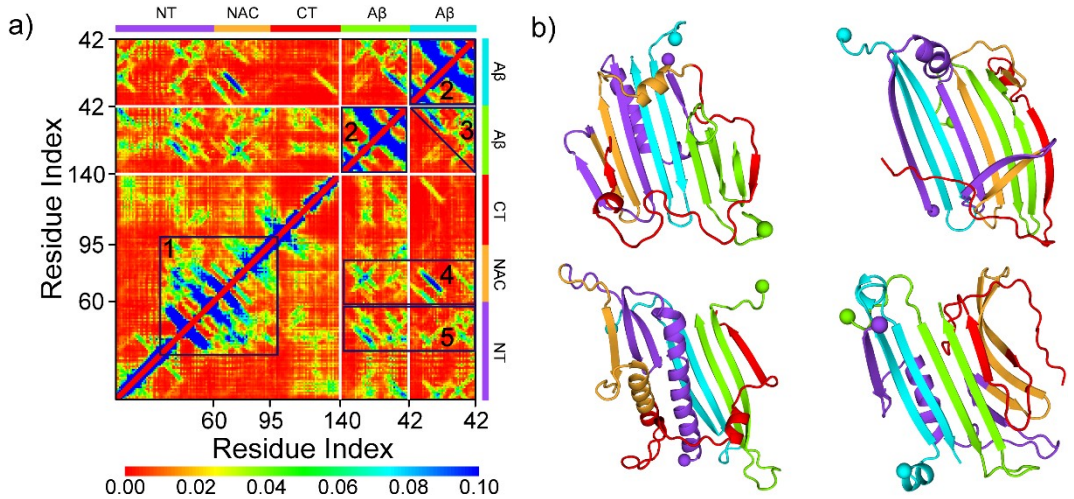

Fig. S7. Residues-pairwise contact analysis in the hetero-trimer formed by two Aβ and one αS. a) The frequency of residue-residue contact formed by heavy atoms of each residue from αS and Aβ in their hetero-trimer. Four representative snapshots featured with typical β-sheet patterns labeled 1-5 in **a)** are also shown in **b)**. Only the last 100 ns data from 30 independent DMD trajectories are used for the above analysis.

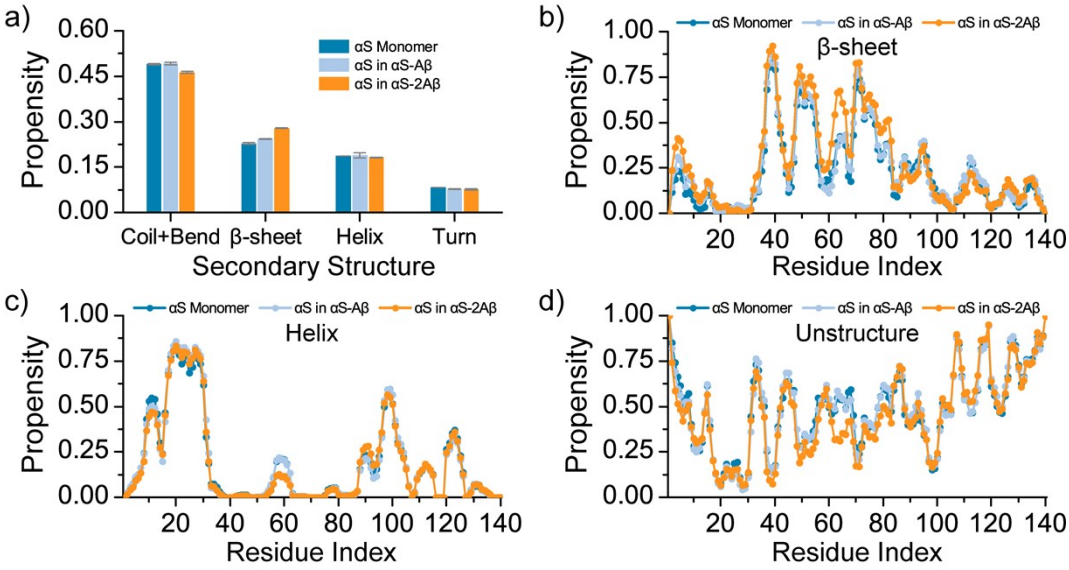

Fig. S8. Secondary structural analysis of αS monomer in the absence and presence of Aβ peptide. The average secondary structure propensity of αS monomer in the absence and presence of Aβ peptides a). The average tendency of each residue from αS monomer adopts β-sheet b), helix c), and unstructured d) formations in the absence and presence of Aβ peptides.