Section A:

Results of Abeta protofibril and various peptides for docking and two sets of 100ns simulations

Table S1: Interaction Abeta protofibril and various peptides

System	Hydrogen Bond	Hydrophobic Interactions
APO	113PHE:1HIS 111VAL:1HIS 115GLU:2LYS 123ALA:8GLU 124ILE: 8GLU	112PHE:3GLN 114ALA:2LYS 124ILE:7PHE 125ILE:6PHE 127LEU:4LEU 128MET:5PRO
HFD	111VAL:1HIS 113PHE:1HIS 114ALA:2LYS 115GLU:2LYS 123ALA:8GLU 124ILE:8GLU	112PHE:3GLN 127LEU:4LEU 128MET:5PRO
HYD	88GLU:2GLY 115GLU:4PHE	113PHE:4PHE
RGT	6ALA:1PRO 6ALA:3LYS 7GLU:3LYS 8ASP:5VAL 11SER:7ALA 13LYS:6TYR	8ASP:4LEU 13LYS:6TYR 17ILE:4LEU 19LEU:4LEU
PGK	107ILE:1LYS 132VAL:4VAL 134ILE:2LYS 135ALA:1LYS	101MET:5PHE 110LEU:1LYS 128MET:5PHE 132VAL:3LEU 133VAL:1LYS 133VAL:3LEU
KKL	88GLU:2LEU	88GLU:4PHE 90VAL:4PHE 115GLU:2LEU
KLV	25VAL:3PHE 27ALA:1LEU	24VAL:4PHE 25VAL:3PHE 26ILE:2PRO 27ALA:3PHE
LPN	115GLU:1LEU	115GLU:3PHE 117VAL:3PHE

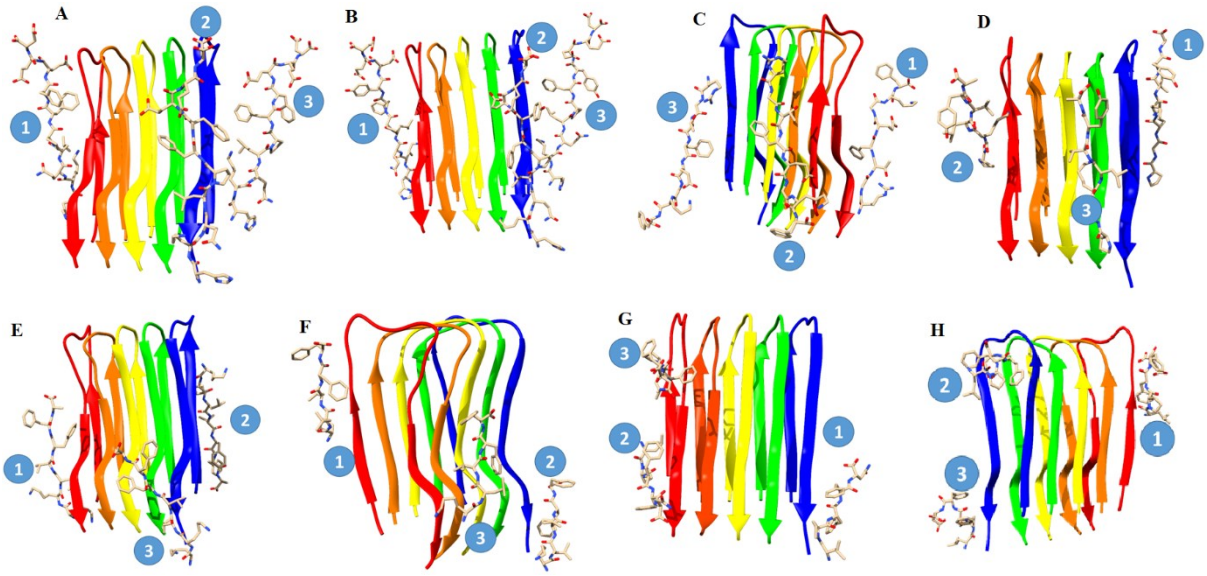

Figure S1: Docking representation of Abeta oligomer with top three pose of different peptides. Abeta protofibril. Each Abeta protofibril consist of five chains represented as blue:chain A, green : chain B, yellow: chain C, orange: chain D and red: chain E

Table S2: Docking results top three pose of different peptides

Peptide	**Dock Score (Kcal/mol) (Top)**	**Dock Score (Kcal/mol) (Second Top)**	**Dock Score (Kcal/mol) (Second Three)**
HKQLPFFEED	-26.59	-23.67	-21.76
HKQLPFYEED	-29.54	-25.92	-23.65
RGTFEGKF	-28.65	-24.13	-22.82
PGKLVYA	-35.04	-33.46	-30.11
KKLVFFA	-33.65	-32.2	-29.96
KLVFF	-32.98	-29.33	-26.43
LPFFN	-27.00	-24.18	-20.11
LPFFD	-31.18	-28.72	-25.04

Table S2 : MM-GBSA free energy of Binding for all the systems (Kcal/mol)

	HFD	**HYD**	**RGT**	**PGK**	**KKL**	**KLV**	**LPN**	**LPD**
VDWAALS	-30.6146	-32.4373	-21.4062	-32.2494	-49.9896	-30.2382	-20.4401	-17.0966
EEL	82.3187	370.5963	-460.896	-316.721	-460.708	-231.524	-35.522	86.36
EGB	-63.5312	-336.544	467.6686	327.3005	480.6365	250.0301	48.4188	-74.9621
ESURF	-4.7872	-5.02	-3.9068	-4.7674	-7.2566	-4.2561	-2.8698	-2.3053
DELTAG gas	51.7041	338.159	-482.302	-348.97	-510.697	-261.763	-55.9621	69.2634
DELTA G solv	-68.3184	-341.564	463.7617	322.5331	473.3799	245.774	45.549	-77.2674
DELTA total	-16.6144	-3.4054	-18.54	-26.4369	-37.3175	-15.9885	-10.4131	-8.004

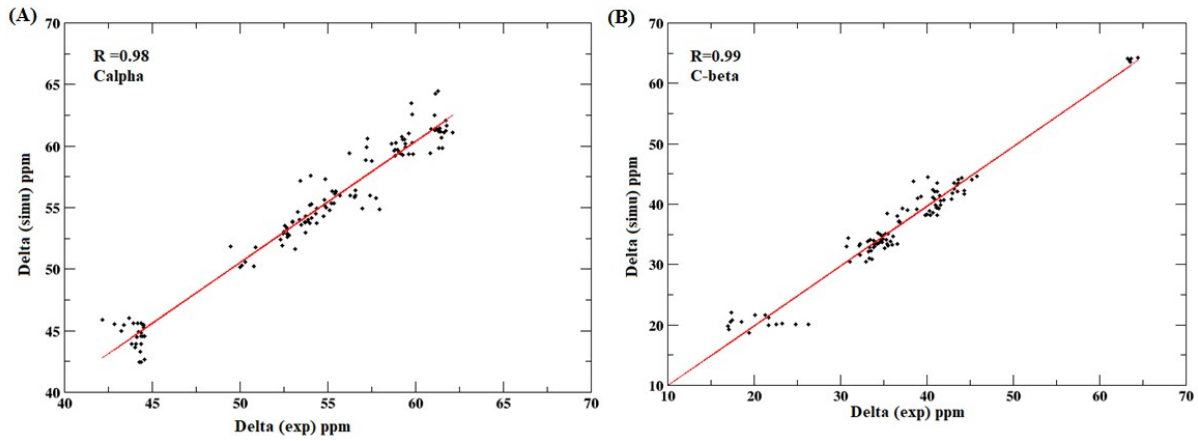

Figure S2 : Comparison of shift from experimental structure with respect to simulated structure

A) Calpha shifts
B) CBeta shifts

Section B

Results of additional set of simulations for the APO and two of 7-mer peptide systems viz. PGK and KKL

Inorder to support the findings obtained through the 100 ns molecular dynamics simulation of the representative Abeta protofibril in the APO and the peptide bound complexes, an additional set of simulations was performed. The additional set of simulations was carried out for best two peptide systems viz. PGK and KKL and APO systems upto 200ns. The Cα and Cβ chemical shifts were computed using SHIFTX2 packages and compared. The correlation coefficient for Cα atoms was 0.97 and for the Cβ atoms were 0.98 (Supplementary figure S3). The high correlation between the theoretical and experimental NMR chemical shift values indicates that MD simulations are able to reproduce the structural ensemble of Aβ42 reasonably. The secondary structure analysis showed that % beta structure decreased while % coil structure increased (Supplementary Table S3). The Hydrogen Bond analysis showed the decrease in average number of hydrogen bond for entire protein as well inter-chain hydrogen for peptide bound system as compared to APO system (Supplementary Figure S4B). The inter-chain salt bridges interactions (Supplementary Figure S4 C and S4 D) and hydrophobic interactions (Supplementary Figure S4 E and S4 F) also showed destabilization in peptide bound system. It was observed that these additional set of simulations shows similar trend as that of results of two sets of 100ns simulations reported. Further the average delta energy of binding for all the PGK and KKL systems were calculated. It was observed that the KKL system had average deltaG binding energy and it was -38.63 Kcal/mol and for PGK system it was around -28.82 Kcal/mol.

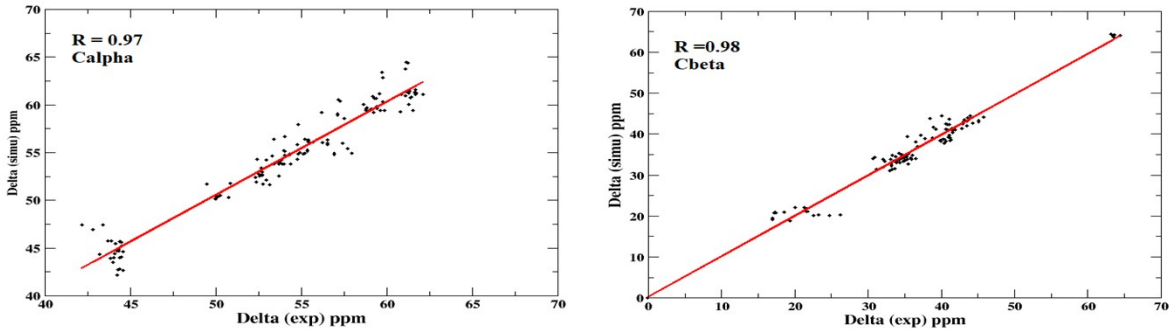

Figure S3: Comparison of shift from experimental structure with respect to simulated structure Calpha shifts and Cbeta shifts

Table S3: Percentage secondary structure content

System	B-structure (B-sheet/B-bridge)	Coil	Turn/Bend	Alpha
APO	60	27	10	0

PGK	44	34	12	1
KKL	48	33	14	0

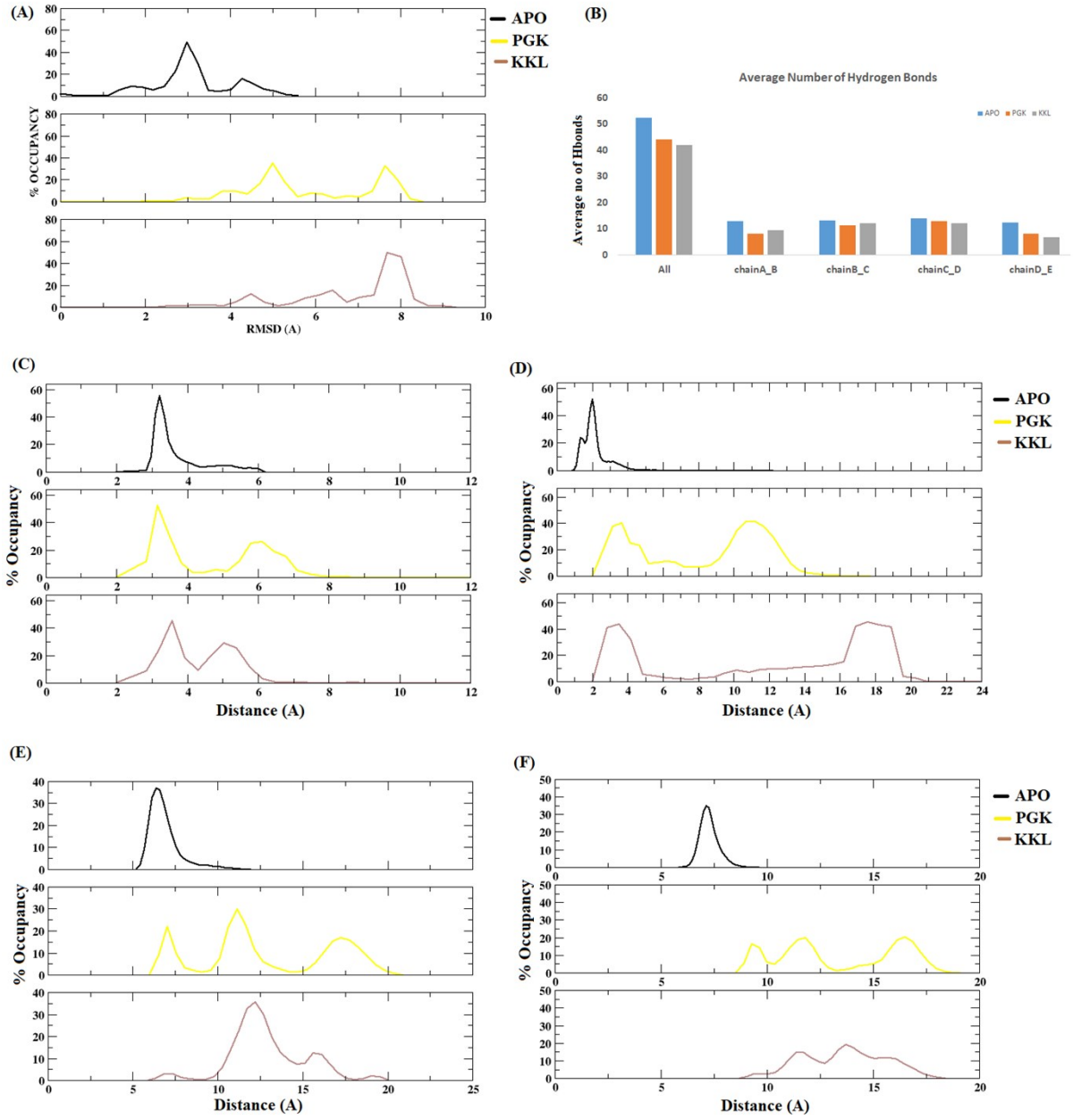

Figure S4: Results of 200ns simulation for APO, PGK and KKL system

- **A)** Root Mean Square Deviation (RMSD) distribution
- **B)** Average Number of Hydrogen Bond for all the systems for the entire system and between neighbouring chains
- **C)** Distance distributions between ASP23 (chain A) and LYS28 (chain B) residues
- **D)** Distance distributions between ASP23 (chain D) and LYS28 (chain E) residues
- **E)** Distance distributions between ALA21 (chain A) and VAL36 (chain B) residues
- **F)** Distance distributions between ALA21 (chain A) and VAL36 (chain B) residues