Supporting Information

Convergence of REMD sampling

The convergence of REMD sampling for the mutant (MT) hexamer was checked using the number N_s of unique states (E_{eff},C) sampled at least once in the course of simulations. Each state (E_{eff},C) is defined by the effective energy of the hexamer, E_{eff}, which includes the potential and solvation energies, and by the number of side chain contacts between incoming peptide and the fibril, C. Fig. S1 shows N_s as a function of the cumulative equilibrium simulation time τ_{sim}. At $\tau_{sim} > 5$ μs N_s starts to level off suggesting the onset of approximate convergence of REMD simulations. Further test of the quality of REMD sampling is provided by the comparison of $N_s(\tau_{sim})$ computed for each of the two incoming peptides. Because N_s for both peptides in Fig. S1 are in very close agreement, the REMD sampling is approximately converging. Similar results were obtained, if the convergence of REMD is tested using the states (E_{eff},C_h), where C_h is the number of peptide-fibril hydrophobic side chain contacts.

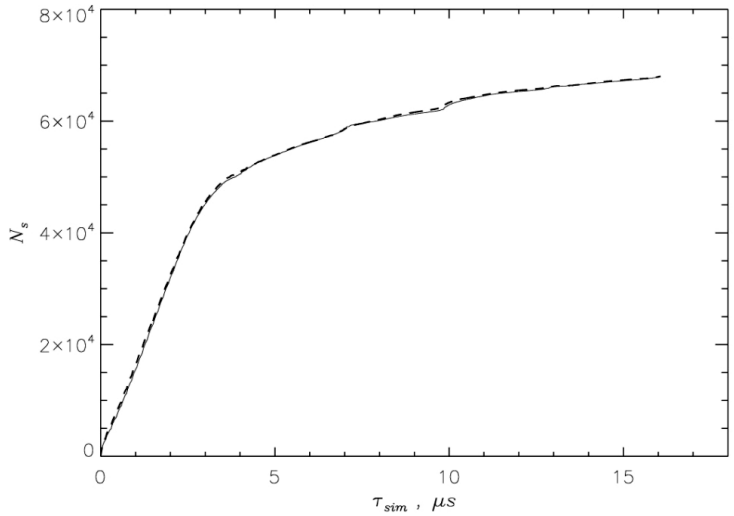

Fig. S1 The number N_s of the new states (E_{eff},C) not previously sampled in REMD as a function of the cumulative equilibrium simulation time τ_{sim}. Continuous and dashed lines represent N_s for each of the two incoming peptides. The data are for the MT $A\beta_{10\text{-}40}$ hexamer.

Additional check of REMD convergence was performed by dividing the simulation data into two equal subsets and analyzing them separately. The thermodynamic quantities probing binding of incoming peptides to the fibril obtained from the two subsets differed by no more than 7%. The errors for the dimer system do not exceed 9%.

Deletion of interpeptide hydrogen bonds in Aβ dimer

We probed the impact of switching off interpeptide backbone hydrogen bonds (HBs) in Aβ dimer by considering its free energy landscape. Fig. S2 shows the peptide free energy as a function of the fraction of β-structure.

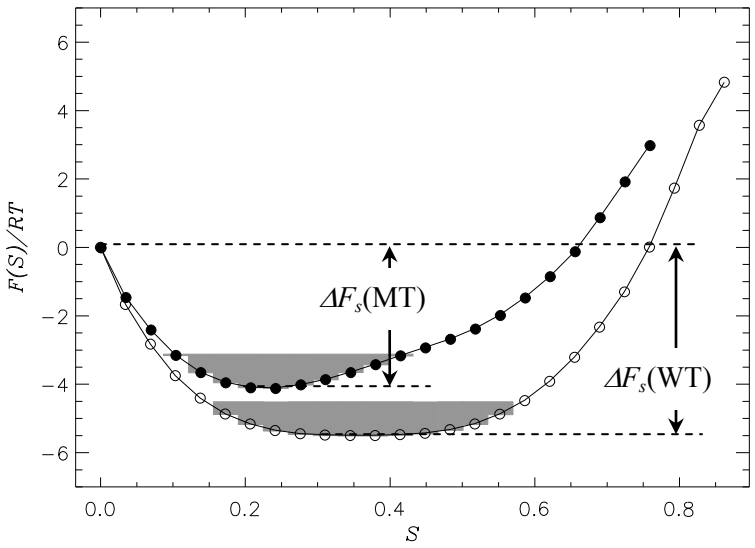

Fig. S2 Free energy of Aβ$_{10-40}$ peptide in the dimer, *F(S)*, as a function of the fraction of residues in β-strand conformation *S*: the MT (filled circles), the WT (open circles). The free energy of the state with large fraction of β-structure is $\Delta F_S = F_S - F(S=0)$. F_S is obtained by integrating over the shaded states, for which $F(S) \leq F_{min} + 1.0RT$, where F_{min} is the minimum in *F(S)*. The free energies *F(S)* are computed at 360K. Deletion of HBs destabilizes β-structure in the dimer.

The contribution of interpeptide HBs is further analyzed by considering the distribution of interpeptide side chain contacts formed by individual residues in Aβ$_{10-40}$ dimer (Fig. S3).

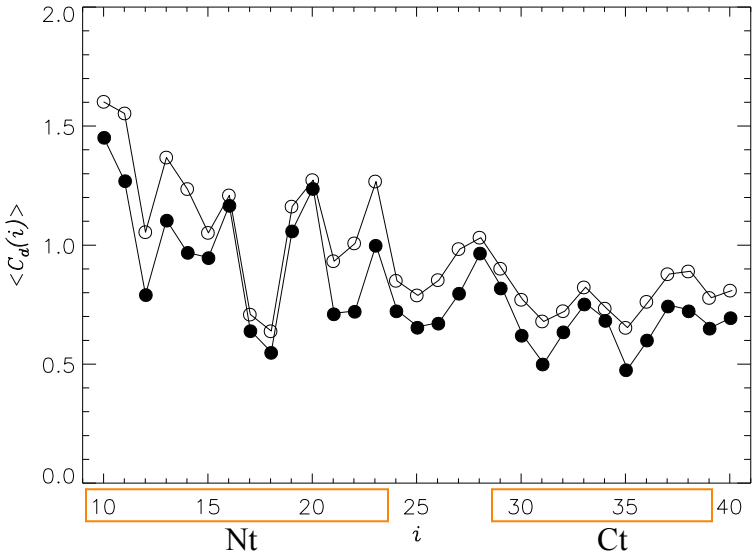

Fig. S3 Number of interpeptide side chain contacts $<C_d(i)>$ formed by individual residues *i* in Aβ$_{10-40}$ dimer: the MT (filled circles), the WT (open circles). The plot suggests that the deletion of HBs has minor impact on the interpeptide interactions in the dimer. The Nt and Ct sequence regions are boxed. The distribution $<C_d(i)>$ is computed at 360K.

Probabilities of binding to distinct fibril edges

To investigate the impact of deletion of peptide-fibril HBs on Aβ fibril growth, we computed the probabilities of MT peptide binding to the concave (CV) and convex (CX) fibril edges (Fig. S4 and also Fig. 1b in the paper).

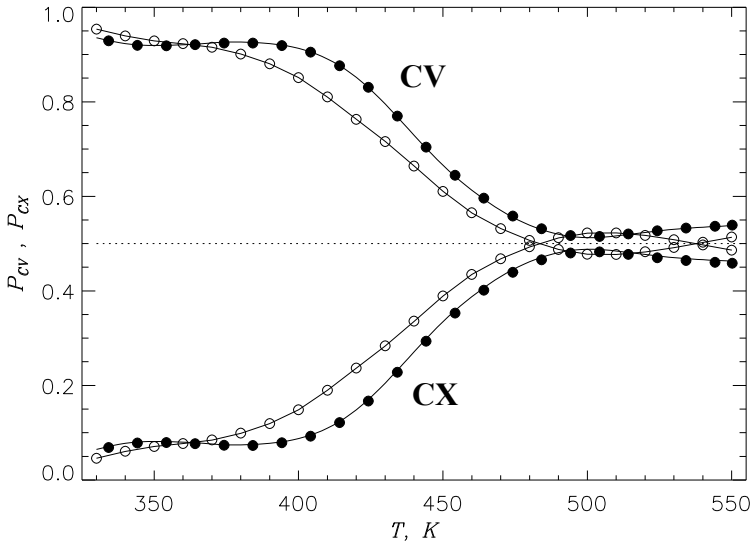

Fig. S4 The probabilities of binding to the CV and CX edges as a function of temperature, $P_{CV}(T)$ and $P_{CX}(T)$: the MT (filled circles), the WT (open circles). Because the MT and WT peptides demonstrate similar preferences to bind to the CV edge, we conclude that the deletion of peptide-fibril HBs does not alter the affinities of the fibril edges with respect to incoming peptides.