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Supplemental Information

Fatty Acids Compete with Aβ in Binding to Serum Albumin by Quenching Its Conformational Flexibility

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Table S1. Summary of simulation lengths.

System	No. of runs	Time (ns)	Total Time (ns)
Aβ40	1	1000	1000
Aβ42	1	1000	1000
HSA	2	200	400
FA·HSA	2	200	400
Aβ40-HSA	12*2	200[a]	2400
Aβ40-FA·HSA	12*2	200[b]	2400
Aβ42-HSA	12*2	200	2400

[a]Four of these 24 simulations were extended beyond 200 ns, to 300, 400, 400, and 500 ns, respectively.
[b]Two of these 24 simulations were extended beyond 200 ns, to 400 ns.

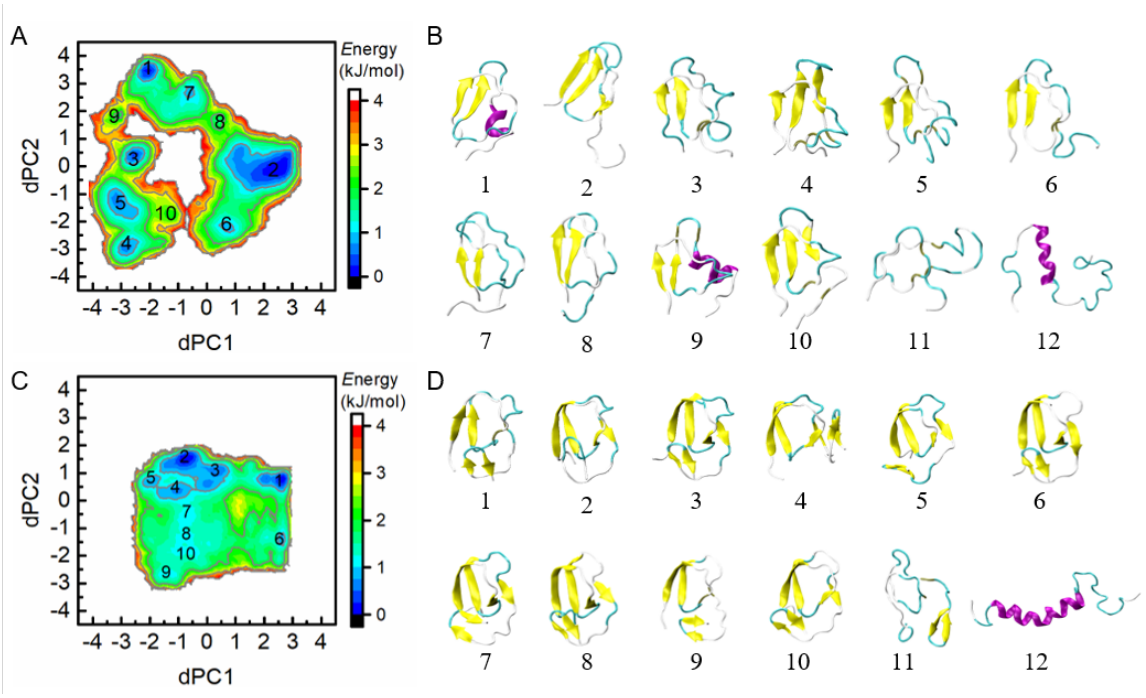

Fig. S1. Coverage of conformational space in backbone dihedral angles by molecular dynamics simulations of isolated Aβ peptides and representative conformations. (*A*) and (*C*) Distributions of the first two dihedral principal components, transformed to free energy surfaces, for Aβ40 and Aβ42, respectively. In each case, 10 local energy minima are numbered. (*B*) and (*D*) Ten conformations at the just-mentioned minima, complemented by a random coil conformation and the starting NMR structure, used as starting structures for simulating binding to human serum albumin. β-strands, bends/turns, helices, and coils are in yellow, cyan, magenta, and gray, respectively.

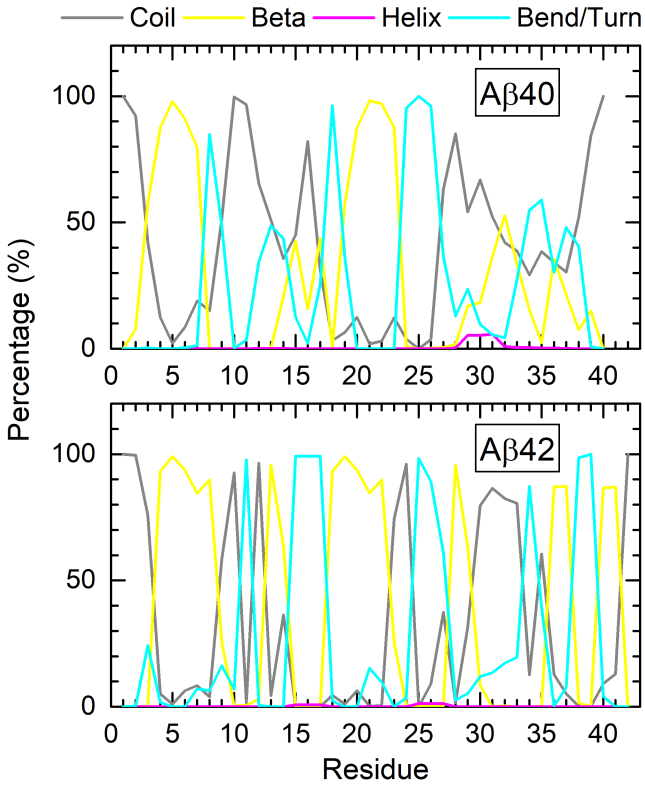

Fig. S2. Secondary structure distributions in molecular dynamics simulations of isolated Aβ40 and Aβ42. The highest propensities are for random coil (42% in Aβ40 and 36% in Aβ42). Short β-strands are transiently formed in both peptides, including residues 2-7, 14-16, 20-23, 29-34 and 36-39 in Aβ40 and residues 4-9, 12-14, 17-22, 28-30, 36-37 and 39-41 in Aβ42, typically interrupted by bends or turns (29% in both peptides). Aβ42 has a slightly higher β-strand propensity than Aβ40 (33% vs. 27%). In both peptides, helices are negligible (< 2%).

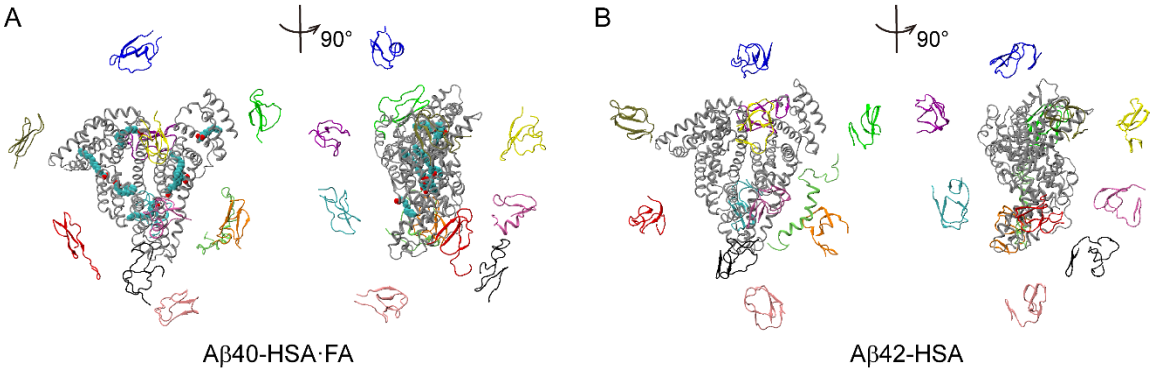

Fig. S3. Starting structures for molecular dynamics simulations of two complex systems. (*A*) Aβ40-FA·HSA. (*B*) Aβ42-HSA. The displaying format is similar to that in Fig. 1.

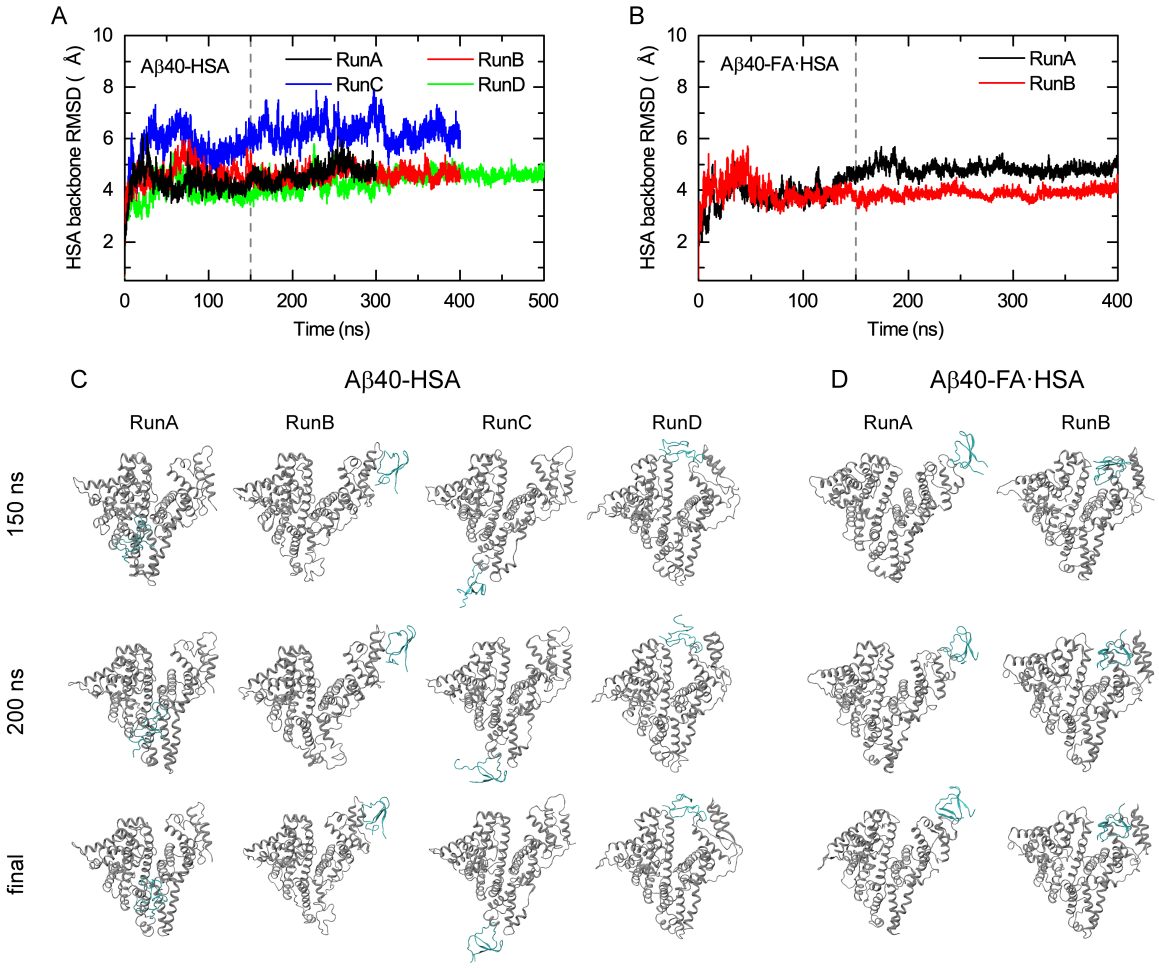

Fig. S4. Results of six simulations extended beyond 200 ns. Four of these were for Aβ40-HAS, extended to 300 ns, 400 ns, 400 ns, and 500 ns (labeled as RunA, RunB, RunC, and RunD); two were for Aβ40-FA·HAS, each extended to 400 ns (labeled as RunA and RunB). (*A*) and (*B*) Time evolution of HSA backbone RMSDs relative to the starting structure. (*C*) and (*D*) Snapshots at 150 ns, 200 ns, and the end of simulation (final).