Amyloid peptide Aβ_{40} inhibits aggregation of Aβ_{42}: evidence from molecular dynamics simulations

Man Hoang Viet and Mai Suan Li*
Institute of Physics, Polish Academy of Sciences, Al. Lotnikow 32/46, 02-668 Warsaw, Poland
(Dated: June 8, 2012)

Effects of amyloid beta peptide Aβ_{40} on secondary structures of Aβ_{42} are studied by all-atom simulations using the GROMOS96 43a1 force field with explicit water. It is shown that in the presence of Aβ_{40} the beta content of monomer Aβ_{42} is reduced. Since the fibril-prone conformation $\mathbf{N}^*$ of full-length Aβ peptides has the shape of beta strand-loop-beta strand this result suggests that Aβ_{40} decreases the probability of observing $\mathbf{N}^*$ of Aβ_{42} in monomer state. Based on this and the hypothesis that the higher is the population of $\mathbf{N}^*$ the higher fibril formation rates, one can expect that, in agreement with the recent experiment, Aβ_{40} inhibit fibril formation of Aβ_{42}. It is shown that the presence of Aβ_{40} makes the salt bridge D23-K28 and fragment 18-33 of Aβ_{42} more flexible providing additional support for this experimental fact. Our estimation of the binding free energy by the molecular mechanics-Poisson-Boltzmann surface area method reveals the inhibition mechanism that Aβ_{40} binds to Aβ_{42} modifying its morphology.

* masli@ifpan.edu.pl