Determination of factors governing fibrillogenesis of polypeptide chains using lattice models

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Using lattice models we explore the factors that determine the tendencies of polypeptide chains to aggregate by exhaustively sampling the sequence and conformational space. The morphologies of the fibril-like structures and the time scales (τ_{fib}) for their formation depend on a subtle balance between hydrophobic and coulomb interactions. The extent of population of $\mathbf{N}^*$, which is a fibril-prone structure in the spectrum of monomer conformations, is the major determinant of τ_{fib}. This observation is used to determine the aggregation-prone consensus sequences by exhaustively exploring the sequence space. Our results provide a basis for genome wide search of fragments that are aggregation prone.

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