

Phase diagram of alpha-helical and beta-sheet forming peptides

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The intrinsic property of proteins to form structural motifs such as alpha-helices and beta-sheets leads to a complex phase behaviour in which proteins can assemble into various types of aggregates including crystals, liquid-like phases of unfolded or natively folded proteins, and highly ordered filaments such as amyloid fibrils. Although a phase diagram is a prerequisite to understand fundamental aspects of formation of ordered structures of proteins, the experimental determination of such a diagram including the aggregates that are formed in the folded and unfolded conformation is extremely challenging. This is so, because the characterisation of the various protein phases is rather difficult and the conditions under which they form may differ considerably. Also, the complex phase behaviour of proteins has prevented adequate theoretical calculations of their phase diagrams even for simplified protein models. Here we use a coarse-grained protein model that enables us to perform Monte Carlo simulations for determining the phase diagram of natively folded alpha-helical and unfolded beta-sheet forming peptides. The simulations reveal the existence of various metastable peptide phases. The liquid-like phases are metastable with respect to the fibrillar phases, and there is a hierarchy of metastability. Our finding of the existence of metastable protein phases is of fundamental significance for gaining a deeper insight into why proteins form amyloid fibrils that are often associated with protein misfolding diseases.