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Beta-rich intermediates in denaturation of lysozyme: accelerated molecular dynamics simulations

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Abstract

Amyloid fibrillar aggregates play a critical role in many neurodegenerative disorders. Conversion of globular proteins into fibrils is associated with global conformational rearrangement and involves the transformation of α-helices to β-sheets. In the present work, the accelerated molecular dynamics technique was applied to study the unfolding of hen egg-white lysozyme at elevated temperatures, and the transformation of the native structure to a disordered one was analyzed. The influence of the disulfide bonds on the conformational dynamics and the energy landscape of denaturation process was considered. Our results show that formation of the metastable β-enriched conformers of individual protein molecules may precede the aggregation process. These β-rich intermediates can play a role of bricks making up fibrils. Communicated by Ramaswamy H. Sarma.

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Keywords

accelerated molecular dynamics, lysozyme, protofibrils, secondary structure, unfolding

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