

Abstract Submitted
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Atomistic Investigation of Cu-Induced Misfolding in the Onset of Parkinson's Disease FRANCIS ROSE, MIROSLAV HODAK, JERRY BERNHOLC, NCSU — A nucleation mechanism for the misfolding of α -synuclein, the protein implicated in Parkinson's Disease (PD), is investigated using computer simulations. Through a combination of ab initio and classical simulation techniques, the conformational evolution of copper-ion-initiated misfolding of α -synuclein is determined. Based on these investigations and available experimental evidence, an atomistic model detailing the nucleation-initiated pathogenesis of PD is proposed. Once misfolded, the proteins can assemble into fibrils, the primary structural components of the deleterious PD plaques. Our model identifies a process of structural modifications to an initially unfolded α -synuclein that results in a partially folded intermediate with a well defined nucleation site as a precursor to the fully misfolded protein. The identified pathway can enable studies of reversal mechanisms and inhibitory agents, potentially leading to the development of effective therapies.

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