

Replica Exchange MD Investigation of the Conformational Space of Prion Proteins

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Prion proteins are found on the surface of nerve cells. Their function is not fully understood yet, but they are related to the etiology of certain rare diseases, like CJD, GSS, Kuru, FFI etc [1]. Prions exist in a native (PrP) and in a highly infective pathological form (PrPSc scrapie form). PrPSc proteins can transform native prions into scrapie forms, aggregate and thus lead to cellular death. Experimental insights on the scrapie form suggest a higher fibrillar beta-structure content, in contrast to the mostly globular alpha-helical native form [2]. However, the 3D structure of PrPSc is still unknown. The present study aims at identification of scrapie form candidates, investigating the prion conformational space by means of replica exchange molecular dynamics. Thus, a conformation of a chicken prion protein is constructed with beta-structure content in agreement with the experimental data.

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