Understanding the Folding and MisFolding Mechanisms of the Human Prion Protein

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This study seeks to investigate the folding and misfolding mechanisms of the Human Prion Protein. Properly folded prion proteins (PrP^{C}) are found in many healthy, non-disease ridden individuals. When prions misfold, they become resistant to protease degradation, accumulate into aggregates and become the infectious agent known as scrapie, PrP^{SC}, causing other healthy prion proteins to misfold. The mechanism of PrP^{C} folding, the key event in prion diseases including kuru and Creuz-feldt-Jacob disease, is still not understood. The structure of PrP^{C} is well known and well defined. However, despite the clear involvement of an infectious agent, PrP^{SC}, in prion pathogenesis, the composition and structure of PrP^{SC} is not yet well-known. The goal of this research is to determine how prion proteins fold. Computational molecular dynamics (MD) is performed on apo Prion Protein structures using AMBER to (1) investigate the flexibility of Prion Protein folding from extended structures in implicit and explicit solvents and (2) understand the effects of A117V and H111S mutations on the human prion protein.