The Mechanisms of Conversion of Proteins into Amyloid Fibrils

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In addition to folding to unique and well-defined three-dimensional structures that are relatively easy to crystallise and analyse with X-ray crystallography, proteins also have a tendency to misfold and self-assemble into stable fibrillar aggregates. These structures, known as amyloid fibrils, are responsible for over 20 human diseases including Alzheimer and Parkinson's diseases and various systemic amyloidoses.

Amyloid formation is not limited, however, to the few macromolecules associated with diseases but is a generic property of natural and synthetic proteins. An understanding of the process of amyloid formation is therefore essential not just for elucidating the pathogenesis of amyloid diseases, but also for the rational design of proteins with the ability to escape aggregation. Given the wide range of morphologies and structures that can be achieved by converting different proteins into amyloid fibrils, the rational and controlled formation of these structures can give rise to a number of materials with useful but yet unexplored properties.

I will describe the mechanism of amyloid formation of proteins, with particular emphasis on the structural and amino acid sequence determinants of this process. Experimental evidence suggests that amyloid formation follows rules that are rather general and applicable to various systems.

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