PREFACE

Physics and biology of neurodegenerative diseases

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PREFACE

Physics and biology of neurodegenerative diseases

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In 1939, William T Astbury, who was at the time a professor at the University of Leeds, wrote a letter to Dorothy Hodgkins, a crystallographer colleague who would eventually be awarded a Nobel Prize (1964) [1]. Astbury was working on determining the structure of silk and had found that these fibres had a so-called cross-beta arrangement, with the hydrogen bonds holding a beta-sheet structure perpendicular to the fibre axis. This structure was very robust and thus would account well for the properties of the silk fibre. Being very impressed by this structural solution at a time when protein structure was just being discovered, he wrote to Dorothy Hodgkins formulating the hypothesis that all proteins could adopt a cross-beta structure similar to that found for silk as a sort of ultimate solution.

Approximately 70 years later, this prediction was reconsidered and is now generally accepted to be correct: most if not all proteins seem to be able to form fibrils, commonly named amyloids, that adopt the same structural features found in silk. The field of amyloid fibres bloomed in the mid-90s when several researchers—among them Chris Dobson, a professor first at Oxford and then at Cambridge—observed that proteins could aggregate by concomitant formation of fibrillar structures (reviewed in [2]). It was certainly not news that proteins could aggregate with an irreversible mechanism. However, what nearly came as a surprise was the realization that aggregation is often accompanied by a major structural rearrangement, which almost invariably associates with protein misfolding (i.e. loss of the native structure and adoption of a beta-rich structure) and amyloid fibre formation. Even more interesting was the growing evidence that amyloid fibres have very special mechanical properties, being extremely resilient and not easily degraded. At the same time it was noticed that different diseases, generically named amyloidoses, are associated with fibrillar aggregates.

Today, about 15 years after the original reports, it is clear that amyloids are special structures that occur in nature under several different guises, some good, some evil [3]. The number of diseases associated with misfolding and fibrillogenesis has steadily increased. Examples of fairly common pathologies associated with fibre formation include Alzheimer’s disease (currently one of the major threats for human health in our increasingly aging world), Parkinson’s disease and several rare, but not less severe, pathologies. On the other hand, it is also clear that amyloid formation is a convenient mechanism for storing peptides and/or proteins in a compact and resistant way. The number of organisms/tissues in which amyloid deposits are found is thus increasing. It is also not too far-fetched to expect that the mechanical properties of amyloids could be used in biotechnology to design new materials.

Because of the importance of this topic in so many scientific fields, we have dedicated this special issue of Journal of Physics: Condensed Matter to the topic of protein aggregation and disease. In the following pages we have collected two reviews and five articles that explore new and interesting developments in the field.
References