Studying protein function and disease by high-resolution solid-state NMR

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Molecular interactions and complexation events not only play a critical role in protein folding and aggregation but they are also intimately linked to protein function in cellular membranes. In our contribution, we show the utility of solid-state NMR (ssNMR) to study both phenomena at atomic level.

Firstly, we show how ssNMR can be used to probe structure and dynamics of paired helical filaments from the core domain of Tau protein[1] and discuss recent work on α-synuclein fibrils obtained from WT[2] and disease-related mutants[3].

In membranes, interactions between membrane proteins and lipids can be essential to a large variety of cellular processes, and protein functionality is often strongly linked to the surrounding bilayer environment. In the second part of our contribution, we will report on recent progress to study structure and function in lipid bilayers by ssNMR. In particular, we compare the effect of molecular activation and inhibition in a membrane-embedded potassium channel[4-7] and we examine the structural implications of modulating protein function by changes in lipid type, ion concentration or pH.

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