Characterization of pressure-stabilized functional important protein states by high resolution NMR spectroscopy

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Abstract

The application of high hydrostatic pressure is of keen interest in un/refolding and misfolding processes of proteins. Multidimensional high resolution NMR spectroscopy is the only generally applicable method/technique to monitor pressure-induced structural changes at the atomic level in solution.

Up to now the application of most of the multidimensional NMR experiments is impossible due to the restricted volume of the high pressure glass cells which causes a poor signal-to-noise ratio. There are currently a number of approaches to overcome the filling factor problem, e.g. high strength single crystal sapphire cells, and ceramic cells.

To understand the effect of pressure on proteins, the pressure dependence of ^{1}H chemical shifts in random coil model tetrapeptides is necessary and was recently investigated. The results allow distinguishing structural changes from the pressure dependence of the chemical shifts. In addition, many buffer systems change their characteristica under the influence of pressure.

A number of proteins have been investigated by high-pressure NMR spectroscopy and display global differences in their sensitivity to pressure. The implementation of high pressure into NMR spectroscopy allows to shift the conformational equilibrium in these proteins and stabilize intermediate states important for function. Association/dissociation phenomena of proteins have been investigated as well.

Since high pressure was shown to populate intermediate amyloidogenic states of proteins the investigation of pressure on proteins involved in protein conformational disorders like Alzheimer's Disease (AD) and Transmissible Spongiform Encephalopathies (TSE) in combination with high resolution NMR spectroscopy is currently the only method to monitor and thus understand such transitions at the atomic detail.

Here we review the recent advances made in the methodology of high pressure NMR spectroscopy as well as novel results on protein aggregation and the stabilization of functional important intermediates.