

Control of protein folding and misfolding in ionic liquid media, and a conjecture on early earth biology

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The folding of proteins is usually studied in dilute aqueous solutions of controlled pH, but it has recently been demonstrated that reversible unfolding can occur in other, very different and in many ways surprising, media. Particular stability against hydrolysis and aggregation instabilities seems to be conferred on the unfolded protein when the process occurs in hydrated (10-20 wt % water) protic ionic liquid solutions (pILs) in which the concentration of ions is enormous and the water activity is only a small fraction of its normal value [1-3]. In these pIL media - which are formed by proton transfer from Brønsted acid to Brønsted base - there is an equivalent of the important pH variable that determines protein stability in aqueous media. It is also a “proton activity” PA, but is now controlled by the acid and base components of the pIL. We will show how it can be understood, and also monitored, by use of ¹H magnetic resonance spectroscopy [2].

In this talk we (i) propose a simple metric, the “refoldability” or “refolding index” RFI, for assessing the stability of biomolecules, such as ribonuclease A and lysozyme, in different solvent media, based on calorimetry [3,4] (ii) use the RFI to demarcate high RFI zones for these proteins in hydrated pIL media of varying PA (“effective pH”) and then (iii) show how exercise of the PA variable can lead to formation of amyloid fibrils and also their redissolution [5].

Finally we show that the high RFIs we demonstrated for native proteins in pILs can be obtained in pIL media that are 90 % inorganic in character (ammonium salts). Natural repositories of such ambient temperature non-hydrolyzing liquid media could be formed by isolation and evaporation of waters that contained ammonium salts formed by primitive chemical processes. Apparently they would be hospitable to biomolecules, and actually encouraging of biopolymer assembly from the Miller-Urey type aminoacids that can also be formed by natural processes. Such primitive biosynthetic media offer a possible resolution of the problem that the hydrolyzing character of ordinary ocean waters presents to conventional “primordial soup” models of biogenesis [6]. An origin of life in such media would provide a natural explanation of our otherwise puzzling observations.

References

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