INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

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Thesis Title: Perturbation of Amyloidogenic Conditions of Hen Lysozyme, Inhibition thereof by Naturally Occurring Osmolytes and Numeric Code of Amino Acids

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SHORT ABSTRACT

This thesis starts by recognizing seminal discovery of lysozyme amyloid made by point mutations in human Lysozyme. Subsequently several *in vitro* conditions were developed to make lysozyme (both Hen and Human) amyloid but one condition (acidic pH/elevated temperatures) has swamped all others viz., alkaline pH at 25°C, concentrated solution of ethanol at 25°C, moderate concentration of Guandinium Hydrochloride at elevated temperature. All conditions deserve attention if we have to reach to the core of mechanistic insight. In this endeavour it was felt that systematically perturbing biophysical parameters will be useful. Another crucial aspect of this thesis was the chosen methodology using simple instruments but each peeking into crucial events of this multistep process that too into form of 'kinetics' [a pillar of Physical Chemistry but something which seems to have been overlooked by workers of Protein Aggregation]. Eventually a Kinetics matrix was proposed to quick analysis of vast amount results. The same was carried out and forms first part of this thesis, bringing out the rather critical onset and very fast growth thereafter under the alkaline condition. Surprises came out of ethanol and Guandinium Hydrochloride work because they were nearly abandoned. Second part of thesis dwells around osmolytes which derive their name from their role to help cells counter osmotic pressure but which have been shown to be useful for helping proteins retain their structure and function in extreme conditions. It is felt that our understanding of the roles which osmolytes play to help proteins not only in extreme conditions but our normal cellular physiology is highly underestimated and understudied. Apart from relevance to osmolytes, this has close connection with Hofmeister series for which there is no satisfactory theory yet. Osmolytes have been sparingly used in amyloid research, that too on different proteins making cross-comparison difficult. It was reasoned that studying many different osmolytes for a single well studied protein like Lysozyme will help us test theories like 'osmophoic effect' and 'preferential hydration'; compare their efficacy and offer mechanistic insights both for protein amyloidogenesis and mode of osmolyte action. This was carried out using wide variety of naturally occurring osmolytes. Not surprisingly all these osmolytes behaved in different ways at different steps which was in stark contrast to the 'osmophoic' effect' and 'preferential hydration'. These osmolytes were also attempted at acidic pH but could not be studied further due to problems of gelation and precipitation (except Trehalose and Taurine). Results with Trehalose were similar both at acidic as well as alkaline pH. All osmolytes led to inhibition of amyloidogenesis. Finally, an experiment was done where several osmolytes were used together. It emerged that their effect was more than additive pointing to a possibility of a Tonic for susceptible people consisting of minute amounts of hundreds of naturally occurring osmolytes. In third part of the thesis, a new numeric amino acid coding scheme is proposed for visual bioinformatics analysis. In it amino acids are represented as numbers (ranging from **0** to **9** and their underlined counterparts **0** to **9**. With it bioinformatics analysis can be done without computers. Since brain is by far the best computer in doing abstract thinking so it is expected that we can find patterns which a computer can't. Another advantage of numeric code is that it helps with facile memorization and recall of primary and secondary structure of a small protein.