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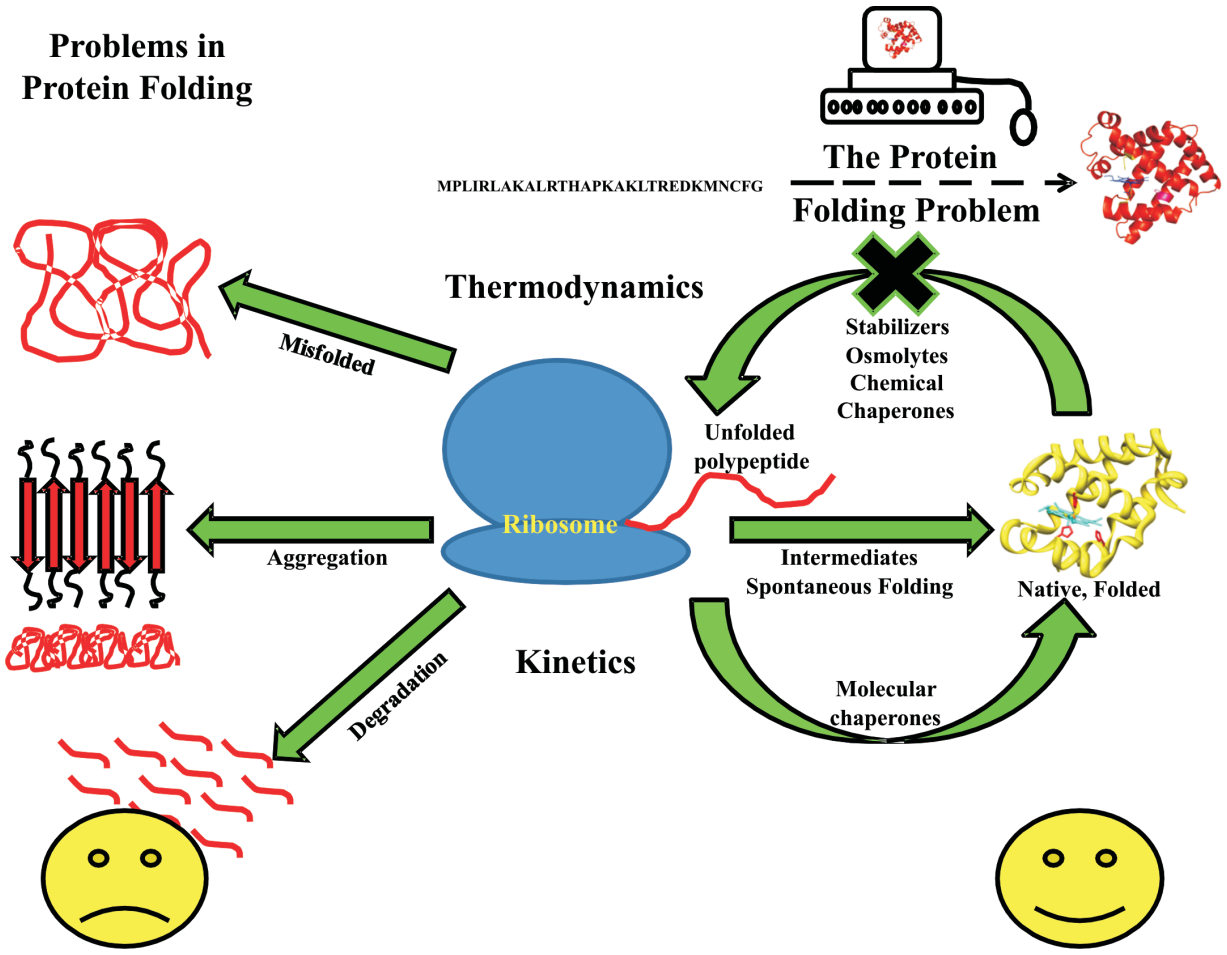

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PROF. J. C. AHLUWALIA - ACHIEVEMENTS OF A LIFE TIME : FROM THERMODYNAMICS OF MODEL COMPOUNDS TO PROTEINS

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Prof. J. C. Ahluwalia

To summarize the many achievements and contributions of Prof. Jagdish Chander Ahluwalia covering a span of several decades is a daunting task. Prof. J. C. Ahluwalia was born on 6-7-1935 and completed high school from Hoshiarpur, Panjab and Bachelor's and Master's degree in Chemistry from Panjab University. He was awarded Ph.D. degree in Chemistry in the area of thermodynamics of solutions from Purdue University, USA under the guidance of Prof. James W. Cobble in 1963. This was followed by postdoctoral work with Prof. Loren G. Hepler at Carnegie Institute of Technology, Carnegie Mellon University, Pittsburgh, USA. The period spent in the US not only changed the life and direction of Prof. Ahluwalia but many of his students that he mentored back in India. Prof. Ahluwalia returned to India in 1964 joining as Lecturer in the Chemistry Department at IIT Kanpur, a place buzzing with activities and enthusiasm to pursue first rate research in Chemistry during the time. Within a year's time along with doctoral students he embarked on setting-up a solution thermodynamics laboratory at IIT Kanpur, building up the first high-precision Calorimetry set-up in the country based on the expertise gained at Purdue and at Carnegie Mellon. Over the years he mentored his students so profoundly that several of them applied the tools of Calorimetry in their own research later and established active groups in the country.

***Early days at IIT Kanpur*:** Early research work of Prof. Ahluwalia focused on water structure and the phenomena of hydrophobic hydration and his first paper from India was published in 1968 in J. Phys. Chem. (Subramanian and Ahluwalia, 1968). His work had an imprint of fascination towards understanding the intricacies of the structure of water and how different solutes and solvents affect it, a hot topic during late fifties and sixties that continues to be an intriguing topic of research in the current days even though techniques to monitor structure and interactions in solution have advanced manifold both in terms of understanding equilibrium and dynamic properties. His group worked extensively on the effect of tetraalkyl ammonium salts on water structure (Sarma *et al.*, 1969; Sarma and Ahluwalia, 1973) which further enhanced our understanding of the hydrophobic effect, a phenomenon that was becoming increasingly applicable to our understanding of protein structure and stability by the pioneering work and concepts generated by Walter Kauzmann and Charles Tanford.

One of the strong contributions from his lab in the early years was on the effect of Urea and Guanidine hydrochloride on water structure

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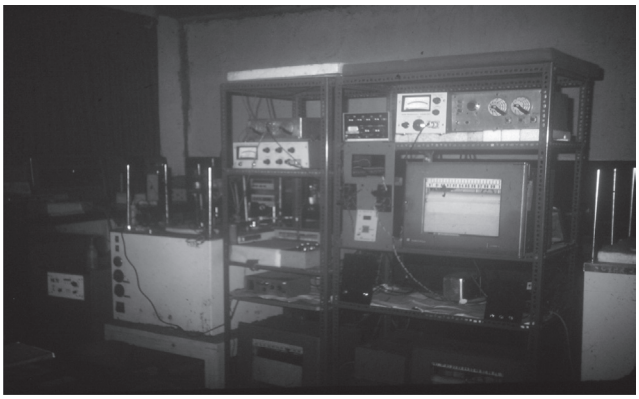
(Subramanian *et al.*, 1971). The thermodynamic studies of transfer of tetraalkyl ammonium salts to aqueous urea (Sarma and Ahluwalia,1972), guanidinium hydrochloride (Chawla *et al.*, 1973) were carried out to understand the effect of these additives on protein stability and denaturation. Prof. Ahluwalia's group also explored a series of carboxylic acid salts (Chawla and Ahluwalia, 1975). The concepts and hypotheses that emerged from this work are being tested and strengthened both by computer simulation studies as well as ultrafast spectroscopic techniques even today.

***Move to IIT Delhi*:** After a stint of little over 10 years Prof. Ahluwalia moved to IIT Delhi in 1975 as Professor and later Head of the Department of Chemistry and served until 2001 in various capacities including Dean of Postgraduate studies and research. He was also bestowed with the fellowship of INSA and was already a fellow of Academy of Sciences, Bangalore and bagged several prestigious awards including S. R. Palit Memorial award, Yeddanapali Memorial award, Lifetime achievement award of the Indian Thermodynamics Society and Silver Medal by the Chemical Research Society of India, etc. to name a few. He along with Prof. D. V. S. Jain of Panjab University founded The Indian Thermodynamics Society in 2001 that has become an active society in the area in the country.

The period in IIT Delhi saw remarkable changes in the development of the thermodynamics research lab, wherein he along with students had to rebuild the heat of solution calorimeter used at IIT Kanpur. With funding becoming increasingly available from DST and other sources, state-of-the art equipment for Thermodynamics research became available enabling the lab not only to keep at par with the best in the world but to excel in many areas as well.

A number of compounds that both affected the structure of water by either perturbing it by decreasing the hydrogen-bonded network and those which promoted the network were explored. The studies supported the mixture model of liquid water against the continuum model. Among a series of such compounds used were a number of surfactants (Choudhury and Ahluwalia, 1982), sugars (Jasra and Ahluwalia, 1984) and polyhydric alcohols that were explored for their effect on water through enthalpy, heat capacity and partial molar volume studies. It was hypothesized that the hydrogen bond promoting properties of sugars and polyols could be related to their efficacy as protein stabilizers. Studies were carried out to measure the enthalpies and heat capacities of transfer of various amino acids (Prasad and Ahluwalia, 1980) from water to aqueous urea solution and from water to aqueous salt and sugar solutions (Bhat and Ahluwalia, 1985, Bhat *et al.*, 1988). Several decades later the projections from such model compound studies proved to be correct and many such compounds were also observed to be selected by nature under various stress conditions like high temperatures, dehydration, high salt, etc. in order to sustain the complex molecular machinery of proteins, nucleic acids and membranes. The principles and ideas generated in his lab have been exploited in the creation of biotech companies dealing with the preservation of biomolecules and stabilization of proteins and nucleic acids. In order to understand the effect of surfactants on water structure, their heat of solution and micellization values and heat capacities were measured to throw light on both hydrophobic effect and ion-solvent interactions (Jha and Ahluwalia, 1991, 1993). Some students in his lab exploited the availability of digital density meter to determine the excess molar volumes of mixtures of a number of aqueous and nonaqueous systems as well.



Home-built Heat of Solution Calorimeter, IIT Delhi, 1981

The shift from pure physical chemistry of solutions to biophysical chemistry and then to the work on proteins was gradual. Some of his

students worked on the interaction of amino acids and peptides with water and aqueous solutions of salts, sugars, polyols and alcohols etc. These studies paved the way for correlating model compound data with that of proteins and the role of side chains of amino acids and that of the peptide backbone to the stability of proteins in various solvent conditions. Work was also carried out on nucleic acid bases, nucleosides and nucleotides to determine the thermodynamics of interaction with water and several solvent conditions affecting nucleic acid structure and function (Kishore and Ahluwalia, 1990; Kishore *et al.*, 1989).

The lab acquired a number of modern instruments like Isothermal Titration Calorimeter, digital density meter, flow microcalorimeter in 1979 which allowed the work to be extended to measure heat of micellization of surfactants, partial molar volumes and direct heat capacity measurements. Later on the lab procured Differential scanning calorimeters (DSC), one that could measure the thermal denaturation of biomolecules and the other that could determine heat capacities of solutions at high temperatures and pressures. The availability of DSC lead to the use of proteins for the first time and a number of proteins were explored for their stability under various solvent conditions many of which were explored as model compounds previously. This was a logical extension of the model compound data whose mechanism of action on water was explored in the early days. Several of such compounds (methylamines, amino acids) have now been known as osmolytes that are naturally occurring in biological systems ranging from bacteria to insects to plants and produced under various stress conditions. Based on the experimental results it was proposed that the structure destabilizing effect of denaturants can be countered by structure-stabilizing effect of osmolytes (Gopal and Ahluwalia, 1993). The centrality of water and modulation of its structural properties by these osmolytes proposed by his lab several decades ago in terms of preferential hydration effect of proteins is an established fact now. Thermodynamic studies of enzyme-substrate (Gopal and Ahluwalia, 1995) and protein-surfactant interactions were also carried out. It was shown that sodium dodecyl sulfate may act as a stabilizer at low concentration (Deep and Ahluwalia, 2001).

His Legacy. Prof. Ahluwalia has been an excellent supervisor, advisor and a mentor who gave absolute freedom to students to explore on their own and provided all the support needed to achieve the desired goals. He always aimed high and insisted on maintaining meticulousness and rigour in research. Prof. Ahluwalia was also a great teacher and inspired generations of students who thoroughly enjoyed his lectures on chemical thermodynamics and kinetics. Many of his students, including the authors, are established researchers in India currently. His contributions to the initiation of chemical thermodynamics research in India and its application to biomolecules and proteins would indeed have a lasting impact.

References

Bhat, R., and Ahluwalia, J. C. (1985). Partial Molar Heat-Capacities and Volumes of Transfer of Some Amino-Acids and Peptides from Water to Aqueous Sodium-Chloride Solutions at 298.15-K. J Phys Chem *89*, 1099-1105.

Bhat, R., Kishore, N., and Ahluwalia, J.C. (1988). Thermodynamic Studies of Transfer of Some Amino-Acids and Peptides from Water to Aqueous Glucose and Sucrose Solutions at 298.15-K. J Chem Soc Faraday Trans 1 *84*, 2651-2665.

Chawla, B., Sunder, S., and Ahluwalia, J.C. (1973). Thermodynamics and Effect of Guanidine Hydrochloride and Potassium-Chloride on Hydrophobic Hydration of Tetra-N-Butylammonium Bromide and Tetra-N-Pentylammonium Bromide in Water. J Phys Chem *77*, 2335-2338.

Chawla, B., and Ahluwalia, J.C. (1975). Enthalpies and Heat-Capacities of Dissolution of Some Sodium Carboxylates in Water and Hydrophobic Hydration. J Solution Chem *4*, 383-389.

Choudhury, N.R., and Ahluwalia, J.C. (1981). Enthalpies and Heat-Capacities of Transfer of Sodium Decanoate, Sodium Dodecanoate and Sodium Dodecyl-Sulfate from Water to Aqueous Urea Solutions. J Chem Soc Faraday Trans 1 *77*, 3119-3127.

Choudhury, N.R., and Ahluwalia, J.C. (1982). Temperature-Dependence of Heat-Capacities of Sodium Decanoate, Sodium Dodecanoate, and Sodium Dodecyl-Sulfate, in Water. J Chem Thermodyn *14*, 281-289.

Deep, S., and Ahluwalia, J.C. (2001). Interaction of bovine serum albumin with anionic surfactants. Phys Chem Chem Phys *3*, 4583-4591.

Gopal, S., and Ahluwalia, J.C. (1993). Effect of Osmoregulatory Solutes on the Stability of Proteins. J Chem Soc Faraday Trans *89*, 2769-2774.

Gopal, S., and Ahluwalia, J.C. (1995). Differential Scanning Calorimetric Studies on Binding of N-Acetyl-D-Glucosamine to Lysozyme. Biophys Chem *54*, 119-125.

Jasra, R.V., and Ahluwalia, J.C. (1984). Enthalpies and Heat-Capacities of Dissolution, Apparent Molar Heat-Capacities, and Apparent Molar Volumes of Some Mono-Saccharides, Di-Saccharides, Tri-Saccharides, and Tetra-Saccharides in Water. J Chem Thermodyn *16*, 583-590.

Jha, R., and Ahluwalia, J.C. (1991). Thermodynamics of Micellization of Triton-X-100 in Aqueous Ethylene-Glycol Solutions. J Phys Chem *95*, 7782-7784.

Jha, R., and Ahluwalia, J.C. (1993). Thermodynamics of Micellization of Some Decyl Poly(Oxyethylene Glycol) Ethers in Aqueous Urea Solutions. J Chem Soc Faraday T *89*, 3465-3469.

Kishore, N., Bhat, R., and Ahluwalia, J.C. (1989). Thermodynamics of Some Nucleic-Acid Bases and Nucleosides in Water, and Their Transfer to Aqueous Glucose and Sucrose Solutions at 298.15-K. Biophys Chem *33*, 227-236.

Kishore, N., and Ahluwalia, J.C. (1990) Partial Molar Heat-Capacities and Volumes of Some Nucleic-Acid Bases, Nucleosides and Nucleotides in Aqueous Urea Solutions at 298.15 K. J Chem Soc Faraday Trans *86*, 905-910.

Prasad, K.P., and Ahluwalia, J.C. (1980). Heat-Capacities of Transfer of Some Amino-Acids and Peptides from Water to Aqueous Urea Solution. Biopolymers *19*, 273-284.

Sarma, T.S., Mohanty, R.K., and Ahluwalia.J.C. (1969). Heat Capacity Changes and Standard Partial Molal Heat Capacities of Aqueous Solutions of Some Tetra-Alkyl Ammonium Halides at 30 Degrees C and Effect on Water Structure. Trans Faraday Soc *65*, 2333-2338.

Sarma, T.S., and Ahluwalia.J.C. (1972). Thermodynamics of Transfer of Tetrabutylammonium Bromide from Water to Aqueous Urea Solutions and Effects on Water Structure. J. Phys. Chem. *76*, 1366-1369.

Sarma, T.S., and Ahluwalia.J.C. (1973). Experimental Studies on the Aqueous Solutions of Some Hydrophobic Solutes. Chem Soc Rev. *2*, 203-232.

Subramanian.S, and Ahluwalia.J.C. (1968). Standard Partial Molal Heat Capacities of Sodium Tetraphenylboron in Aqueous Solution from 0 to 90 Degrees . Effect of Water Structure and Hydrophobic Hydration. J Phys Chem *72*, 2525-2531.

Subramanian.S, Sarma, T.S., Balasubramanian.D, and Ahluwalia.J.C. (1971). Effects of Urea-Guanidinium Class of Protein Denaturants on Water Structure - Heats of Solution and Proton Chemical Shift Studies. J Phys Chem., *75*, 815-820.