

## Tribute to Biman Bagchi



Photo by S. R. Prasad

Professor Biman Bagchi has made pivotal contributions to the area of dynamics of chemical and biological systems in an academic career spanning more than three decades. He has been a great teacher and mentor for a large number of young theoretical physical chemists of India and a creative and insightful collaborator with leading scientists worldwide. We take great pride in guest editing this special issue of *The Journal of Physical Chemistry B* in honor of Prof. Bagchi who is, arguably, the finest theoretical physical chemist India has ever produced. Prof. Bagchi has spent about 30 years at the Indian Institute of Science (IISc), Bangalore, during which he has traversed a wide landscape of physical chemistry. It is impossible to discuss all of his work; it is not even possible to mention each area he has worked in. In the following, we choose only a few selective topics and give short comments on their impact as we understand them. This is how we chose to pay our tribute to this ever-young, dynamic, and completely apolitical scientist who is so dear to all of his students, postdocs, and collaborators and will remain so forever.

Professor Bagchi joined IISc, Bangalore, in 1984. His major research interests during the first ten years at IISc included dynamics of polar solvation, dielectric relaxation, and dynamic solvent effects on activated and barrierless chemical reactions. In the next ten years, starting from the mid-nineties, he primarily worked on conductance and viscosity of electrolyte solutions, dynamics of biological water, solvent relaxation near micellar surfaces, vibrational energy relaxation and dephasing, and dynamics of glassy and supercooled liquids and liquid crystals. In the next ten years, up to the present, he further extended his studies of vibrational dynamics to two-dimensional infrared spectroscopy of aqueous systems and continued to work on glassy and supercooled systems and liquid crystals. During this period, he also entered into new areas of research in chemical biology such as protein–DNA interactions, enzyme catalysis, and theory of autoimmune disorders and human immune response.

Solvation dynamics was a topic of huge contemporary interest in the mid-eighties. New results were coming in from the ultrafast

laser spectroscopic groups of one of us (G.R.F.), Paul Barbara, and others. The solvation dynamics was reported to have times scales faster than dielectric relaxation, which posed a challenge to theorists for proper explanations. Just before joining IISc, Bagchi, in collaboration with G.R.F. and David Oxtoby, had developed a theory of dipolar solvation using a continuum model of the solvent and a frequency dependent dielectric function. The theory predicted a solvation time that was faster than the dielectric relaxation time of the solvent, thus providing an explanation of the experimentally observed fast relaxation of the time dependent solvation energy. The continuum theory was subsequently generalized by Bagchi and co-workers in many different directions such as incorporation of multi-Debye relaxation, non-Debye relaxation, inhomogeneity of the medium around a solute, etc. Still, being based on continuum models, all these extensions lacked the molecularity of the solvent. Besides, these theories considered only the rotational motion of solvent molecules because the dynamics came through the frequency dependence of the long wavelength dielectric function. Microscopic theories based on molecular solvent models also started coming from other groups; however, these microscopic theories also included only the rotational motion of solvent molecules. These rotation-only microscopic theories predicted an average solvation time that was longer than the long-wavelength continuum theory predictions due to contributions from finite wavevector processes. Subsequently, a microscopic theory was developed by the Bagchi group that included translational contributions of solvent molecules in addition to their rotational motion. The theory showed that the polarization at finite wavevectors can relax at a faster rate in the presence of finite translational contributions. This was indeed an important result because, in many dynamical processes, it is the finite wavevector response of the solvent that matters most. Hence, the overall solvation can occur with a time scale faster than that predicted by rotation-only theories but in better agreement with then available experimental results. Subsequently, the theory was further extended to incorporate many subtle dynamical aspects such as inertial effects, viscoelastic effects, self-motion of the solute, and the connections between the so-called microscopic and macroscopic orientational relaxation times, etc., which lead to quantitative agreements of the theoretical predictions with the experimental results for a variety of solute–solvent systems.

The theories of orientational and dielectric relaxation were also used in arriving at microscopic theories of dielectric friction. A self-consistent theory was developed for the dielectric friction and dielectric relaxation where it was shown that the presence of translational contributions can make dielectric relaxation more Debye-like for cases where only rotational contributions give rise to a highly non-Debye form of dielectric relaxation.

The possible roles of solvent dynamics on rates of chemical reactions constituted another topic of huge interest in the eighties and also in years to follow. The celebrated Grote–Hynes

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theory on the effects of frequency dependent friction on activated barrier crossing came in 1980. The Bagchi group showed how the dynamics of ultrafast solvation can affect the rates of outer sphere electron transfer reactions in dipolar liquids. Bagchi and co-workers also developed microscopic theories on the effects of solvent dynamics such as viscosity and diffusion on chemical processes, which proceed without the presence of any significant barrier along the reaction coordinates. Before Bagchi's work, the only existing theoretical description produced unphysical excited state decay profiles, and this work stimulated substantial experimental and related theoretical efforts in a wide variety of areas.

It was known for a long time that the mobility of small ions does not follow the Stokes–Einstein relation. The concept of dielectric friction on ions was brought in by Onsager to explain the discrepancy but still it was not good enough to explain the anomalous diffusion behavior such as the diffusion maximum that ions exhibit in water on increase of size. Further improvements of the dielectric model and early microscopic theories from different groups were not fully successful in explaining the diffusion anomaly. Bagchi and co-workers developed a microscopic theory that self-consistently included the self-motion of a solute ion and the dynamics of surrounding solvent and was able to explain the anomalous increase of diffusion for larger ions in a quantitative manner. A salient feature of their work was to show how the slow diffusion of ions is controlled by ultrafast dynamics of the surrounding solvent. Subsequently, the group extended the work to higher concentrations and developed a mode coupling theory of ion conductance that accurately explained the concentration dependence of ionic mobility up to a fairly high concentration. Moreover, the theory correctly reproduced the celebrated Debye–Huckel–Onsager expression in the limit of low concentration, thus providing a molecular basis of the limiting law. Subsequently, the theory was extended to derive microscopic expressions for frequency dependent conductivity and viscosity, which correctly reduced to the well-known Debye–Falkenhagen and Falkenhagen expressions, respectively, in the limit of low ion concentration. The theory also explained correctly the weaker concentration dependence of ion diffusion than that of conductance which had remained a puzzling experimental fact for quite some time.

Water in contact with biological systems such as proteins, DNA, reverse micelles, and other macromolecules, which is now collectively referred to as biological water, was known to behave in a different manner than normal water. For example, experiments revealed that the dielectric and NMR relaxation of such biological water can be described by two seemingly unconnected and very different time scales: One is in the picosecond regime and the other one is in the regime of nanoseconds with a gap of about 3 orders of magnitude between the two. Bagchi and co-workers developed a simple yet pioneering theory of dielectric relaxation in biological water by describing the dynamics in terms of a dynamic equilibrium between water molecules that are free and those bound to the biomolecule. The dielectric relaxation was then determined by the equilibrium constant between the two species and the rate of interconversion between the bound and free states. The theory could provide a microscopic explanation of the experimentally observed dielectric relaxation in biological water and provided a way to study solvation of biomolecules in water and other dipolar liquids. The idea of a dynamic equilibrium between bound and free states was used in many of the subsequent investigations of the group to explain many outstanding problems of macromolecular solutions such as complex frequency dependence of the dielectric function of

protein solutions and anomalous diffusive behavior of a solute like the cross over from subdiffusive to superdiffusive dynamics near biological surfaces. The dynamic equilibrium between the free and bound states was further quantified in terms of interconversion rates through computer simulations of model proteins in water. An important finding of the simulations was the roles of protein–water and water–water hydrogen bond fluctuations in determining such dynamic equilibrium and their possible correlations with the biological activity of proteins.

Beginning in early nineties, experiments from different groups (one of the pioneers being Prof. K. Bhattacharyya, a long-time friend of Prof. Bagchi since his college days) showed that solvation dynamics in restricted environments such as in a cyclodextrin cavity, at the surface of micelles or inside reverse micelles involves time scales which are 2–3 orders of magnitude slower than that of bulk water. The initial experiments on these systems of so-called organized assemblies used nanosecond pulses. Later experiments involving pico- and femtosecond pulses revealed the presence of a faster component with time scales similar to that of bulk water in addition to the slower component extending to nanoseconds. These systems are very complex containing not only macromolecules, which themselves are in motion, but also moving water in a variety of environments such as in bound and free states. Bagchi and co-workers carried out, for the first time, a set of pioneering dynamical simulations to study solvation dynamics at the surface of micelles. Their simulations did show a time scale in the nanosecond regime for the solvation dynamics at a micellar surface. In addition, their studies revealed many molecular details of the dynamics that were not known before for these systems. For example, their studies showed that the slow part of the solvation dynamics mainly originates from dynamical interactions of the solute ion with polar head groups of the surfactants. Thus, slow movement of the micelle contributes significantly to the observed slow dynamics of solvation. The slow orientational motion of water molecules on the micellar surface also contributes but was found to play more of a secondary role in the overall dynamics.

Studies of vibrational dynamics has constituted another area of active research of the Bagchi group since the late nineties. Initial work in the area involved formulation of a mode coupling theory for vibrational energy relaxation and providing a molecular basis for the similarity between the vibrational energy relaxation and nonpolar solvation dynamics observed in experiments. Subsequent studies dealt with vibrational dephasing in liquid nitrogen and water and also extension of these studies to time dependent infrared spectroscopy of aqueous systems.

The dynamics of supercooled liquids are known to show many fascinating properties such as nonexponential relaxation of stress, density, polarization, and orientational correlations. Bagchi and co-workers showed that in a deeply supercooled liquid, the stress relaxation is locally anisotropic, which can provide the necessary driving force for hopping on the free energy surface. Their work suggested a decoupling of diffusion from viscosity even at the local level, thus providing a deep understanding of the stress relaxation, hopping, and diffusion in deeply supercooled liquids. A subsequent study from the group established a correlation between the breakdown of the well-known Debye model of rotational diffusion and the manner of exploration of the underlying energy landscape. Their study also helped in understanding the correlations of decoupling between rotational and translational motion with the energy landscape. The energy landscape view was further extended to understand antiplasticization and growth of dynamic heterogeneity in supercooled polydisperse liquids.

Thermotropic liquid crystals form another area of major interest of the Bagchi group because of their rich phase behavior and fascinating dynamics on variation of temperature. The two most important phases of thermotropic liquid crystals are the nematic and smectic phases. While the former phase is orientationally ordered but translationally disordered, the latter phase possesses partial translational order in addition to an increased orientational order. Bagchi and co-workers investigated the potential energy landscapes of a family of model liquid crystals to understand the interplay between orientational and translational orders in different phases that liquid crystals typically exhibit upon cooling. It was shown that the depth of the potential energy minimum explored by the system grows through the nematic phase upon cooling. The onset of the growth of the orientational order in the nematic phase induces a translational order leading to smectic-like layers. Subsequent studies from the group looked at orientational dynamics of thermotropic liquid crystals across the isotropic–nematic phase transition and provided molecular explanations for many interesting dynamical properties such as power law behavior at intermediate times. Interestingly, a critical analysis of their dynamical results of thermotropic liquid crystals and supercooled molecular liquids revealed an array of analogous features in these two important types of soft matter systems.

Studies of protein folding constituted another area of active interest of the Bagchi group, beginning with a seminal paper in 1991 written in collaboration with Zwanzig and Szabo in which the authors showed an elegant biased search resolution of Leventhal's paradox—the notion that protein folding via a random search would take enormously long times. Understanding the mechanism or the pathway followed by an unfolded protein to its final folded state, the so-called native state, has remained a challenging task in chemical biology. Bagchi and co-workers looked at the correlations between the energy landscape and topology in the folding of a model protein (chicken villin headpiece or HP-36) by using a minimalistic model that incorporated the effects of water through a hydrophobicity scale and the role of helical propensity of amino acids through a nonlocal harmonic potential. The dynamics of folding was found to involve multistage decay in energy and other relevant quantities such as the radius of gyration, relative contact order, etc. There was a fast initial decay due to hydrophobic collapse, which was then followed by two distinct slow stages. The very slow last stage of folding, which could be identified as the rate-determining step of folding, was found to be accompanied by a significant increase in the contact order parameter but a relatively small decrease in energy. These are important findings which seemed to suggest that the slow late stage of the folding process arises due to long-range contact formation and also that the free energy barrier of the rate-determining step of folding is entropic in origin. The process of unfolding of the same protein from its native to an open state has also been studied by the group, which again confirmed the presence of multistage decay involving multiple intermediates. Subsequent studies on effects of denaturant cosolvents such as dimethyl sulfoxide (DMSO) on the unfolding mechanism revealed that the mixed solvents can profoundly transform the nature of the energy landscape, thereby change the route accessed by the unfolding process.

Interparticle interactions leading to complexation and association of macromolecules are ubiquitous in nature. Examples include DNA–dendrimer and drug–DNA complexation, protein–DNA interaction and protein association, macroion–polyelectrolyte complexation, etc. With an aim to achieve a

molecular-level understanding of the pathway and mechanism of some of these complexation processes, Bagchi and co-workers considered the cases of DNA–dendrimer and DNA–drug complexation through atomistic simulations. These are complex processes because of the involvement of many degrees of freedom of not only the reactants but also of the surrounding water and counterions. The group determined the free energy landscape along the complexation pathway and discovered the existence of a stable bound state between the DNA and the dendrimer that was separated from a metastable state by a free energy barrier. Their study also showed that water molecules along the DNA backbone move away as the DNA bends to embrace the dendrimer, thus revealing the role of water in such binding processes for the first time. Their work also elucidated some of the finer details of macroion–polyelectrolyte complexation at a molecular level. Subsequently, Bagchi and co-workers investigated the binding of a drug (Daunomycin which is an anticancer drug) with DNA and constructed the free energy landscape, which allowed a molecular-level understanding of the thermodynamics, DNA structural changes, and kinetic pathways for the intercalation process. Their work revealed a mechanism in which the drug first binds to the minor groove and then intercalates into the DNA in an activated process, thus providing a molecular picture of the experimental kinetic results.

Understanding the molecular details of enzyme catalysis of biochemical reactions has remained a long-standing challenge in chemistry and biology. It is known that the same biochemical reactions would still occur in water without the enzyme but at a hugely slower rate. The presence of the enzyme alters the reaction pathway so as to provide a more favorable path with a much lower activation energy. Although the role of water in controlling the enzyme catalysis and reaction pathway had often been discussed in the literature, the molecular details of how water molecules assist an enzyme in altering the reaction pathway and its free energetics were still unclear. Bagchi and co-workers investigated the catalytic conversion of adenosine triphosphate (ATP) and adenosine monophosphate (AMP) to adenosine diphosphate (ADP) by the enzyme adenylate kinase (ADK) in the presence of explicit water interactions. The process involved binding of one ATP molecule and an AMP molecule to two different domains of the enzyme followed by a phosphate transfer and subsequent release of two ADP molecules. They calculated a novel two-dimensional free energy surface that revealed the presence of a half-open half-closed intermediate state of the enzyme. Cycling the enzyme through such an intermediate state was found to greatly reduce the conformational free energy barrier of the reaction. The intermediate state of the enzyme was stabilized largely by enhanced attractive interactions of the polar amino acid side chains with surrounding water, thus showing the importance of explicit involvement of water in providing an alternate reaction pathway through enzyme catalysis. Subsequent studies revealed the presence of interesting cross correlations between the two domains of the enzyme that bind the ATP and AMP molecules, thus providing further insights into the key factors that can influence an enzymatic reaction.

Prof. Bagchi continues to move into new areas and generate new insights, which is typified by his recent work on the human immune system.

Prof. Bagchi has contributed immensely to our understanding of the dynamics of complex chemical and biological systems over his long academic career. When Prof. Bagchi returned to India from the USA about 30 years ago, theoretical chemistry in India essentially meant quantum chemistry. Prof. Bagchi

single-handedly changed the scenario by his intellectual leadership and tireless commitment. Over the past three decades, he has guided a large number of Ph.D. students and postdoctoral scholars many of whom are now pursuing independent research in the area of statistical mechanics and molecular simulations. In any major science university or institute in India today, one can easily find a faculty member who is a student of Prof. Bagchi or a student of a student of Prof. Bagchi. For the younger generation, the biggest contribution of Prof. Bagchi is that he has changed the landscape of theoretical chemistry research in India—a nontrivial feat!

Prof. Bagchi has always remained an internationally renowned physical chemist. This Festschrift issue of *The Journal of Physical Chemistry B* is a fitting way to honor his huge contributions in the field of chemical dynamics and impact on the physical chemistry community in general. To our knowledge, this is only the second time a *JPC* Festschrift has been dedicated to an Indian. On behalf of all students, postdoctoral scholars, and collaborators of Prof. Bagchi, we thank the Editor-in-Chief of *The Journal of Physical Chemistry* for bringing out this special issue. Prof. Bagchi turned 60 in 2014. We wish him many more years of creative, productive, and enjoyable life in the deep mist of physical chemistry.

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