

Personal reflections

Dr. Bimal Kumar Bachhawat was born in August 1925. He got his B.Sc. Hons in Chemistry in 1946 from St. Xaviers College, Calcutta, and M.Sc. from the Department of Applied Chemistry, University of Calcutta, in 1948. He went abroad in 1949 for higher studies and obtained his Ph.D. from the University of Illinois in 1953 with biochemistry as the major. He began his post-doctoral career in USA first at Philadelphia and then as Assistant Professor at the University of Michigan at Ann Arbor.

Dr. Bachhawat returned to India in 1957 as Associate Professor of Neurochemistry, Christian Medical College, Vellore, where he founded one of the most active centres of biochemistry in India. His pioneering work on mucopolysaccharides in brain brought him world recognition and the coveted Shantiswarup Bhatnagar Award in 1962. This was followed by other awards such as the Amrut Mody Research Award in 1974 and the Institute of Science Golden Jubilee Gold Medal in 1976. He was elected a Fellow of the Indian National Science Academy in 1973, and the Indian Academy of Sciences, in 1974.

In 1976 Dr. Bachhawat was invited to take over as the Director, Indian Institute of Chemical Biology (then known as the Indian Institute of Experimental Medicine) and he held the position with distinction and honour upto 31st August 1985. After his retirement from the CSIR he was invited to join the Delhi University as Professor and Head of the Department of Biochemistry.

Among other awards and distinctions, Dr. Bachhawat was honoured with the R. N. Chopra Lectureship of the Indian National Science Academy, National Lectureship (1976) and J. C. Bose award of UGC (1980). Recently he received the prestigious Rameshwardas Birla Smarak Kosh Award for outstanding research in medical field in India.

Dr. Bachhawat's contribution to biochemistry and medicine has been characterized by a rare degree of width and versatility. His early work on the enzymes involved in branched chain amino acids led to the understanding of the linkage between metabolism of amino acids and steroidogenesis.

At Vellore he built an outstanding school of research to study the role of mucopolysaccharides in health and disease. His pioneering work on the deficiency of lysosomal arylsulphatase A in mental disorder and metachromatic leucodystrophy causing infantile mortality has been widely acclaimed.

Dr. Bachhawat also pioneered the work on liposomes, artificial membranes, which can be targeted to specific tissues with the help of specific markers. The liposome therapy, in which drugs, antibodies, enzymes and gene fragments could be delivered specifically to certain sites hold great promise in chemotherapy, immunotherapy as well as in some genetic disorders.

Dr. Bachhawat holds a unique distinction in blending brilliant science with superb leadership. He has had 30 Ph.Ds to his credit and about 175 research publications covering a wide spectrum of biosciences.

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II

Among the few who claim to have the longest association with Prof. Bimal Kumar Bachhawat, I have been assigned the onerous task of writing a foreword to this volume of the Journal of Biosciences commemorating his sixtieth birthday. It would have been easier to present a chronological synopsis of his main achievements starting from his student days through his emergence as a leader in several areas upto his current role of a guiding light to diverse areas of biosciences. However, such an account would not be adequate to describe this unique personality.

I am, therefore, trying to present some of my personal impressions.

I met Bimal for the first time in 1950, when Prof. Carl Vestling brought him to my room at the University of Illinois at Urbana. Carl had told me earlier that he was expecting one B. K. Bachhawat from the Department of Applied Chemistry, University of Calcutta—the same Department that I came from. He also felt that after having about 4 year's seniority, I should be the proper guide to lead him through the complexity of the rehabilitation process in the campus. My first impression of Bimal was that he was a shy, polite, soft-spoken young man. But within a week, it was obvious that Bimal did not need any looking after and within a month he had just as many friends as I could make in the campus after 4 years.

Bimal started his research career with a bang! When Carl Vestling and Dave Gibson crystallized lactic dehydrogenase, the fourth enzyme to be crystallized from liver, Bimal was initiated into the witchcraft of enzyme purification by Carl, who had rare intuition about what methods to avoid. Bimal started soon on his main Ph.D. problem—the purification of liver malic dehydrogenase (MDH).

In 1950, the purification of an enzyme was an art rather than a science. The cellulose ion-exchangers, the molecular sieves and affinity chromatography techniques, which would make the task a trivial one, were 10–20 years ahead in the future. The "hocus pocus" that Bimal employed in the purification of MDH appeared to be childishly simple: (a) remove the junk proteins with ammonium sulphate and (b) precipitate the enzyme in a highly purified state with good yield with zinc and alcohol under highly controlled conditions. The fact that he got his Ph.D. in 1953, almost in a record time of two and a half years, shows that he did not have to move around in blind alleys—his "hunches" worked most of the time.

I have to relate an incident during his student days, an incident ingrained in my memory. Bimal and 5 of his colleagues were trying to move a 200 kg centrifuge into the cold room. The entrance was barely adequate and there was the wall of the deep freeze in front. It was taking a long time with awkward maneuvering and suddenly the centrifuge slipped from the hands of the person in front. But Bimal would not let go. The instrument slid on his patella. When Bimal was extricated, his leg started swelling. I would never forget the expression on his face. He was obviously in acute pain but he had also a triumphant smile. I had a new respect for him. He apparently valued the equipment more than his leg!

When he got his Ph.D., Bimal had already a growing reputation as a budding enzymologist. Minor Coon an alumnus of the Department of Biochemistry University of Illinois, sought him out to work on metabolism of branched chain amino acids. In 1953 it was an exciting field—as the key intermediate to cholesterol and isoprenoid biogenesis was a puzzle. Bimal joined Minor Coon's team first as a post-doctoral associate at Philadelphia and then at the University of Michigan, Ana Arbor, as an Assistant Professor.

The achievements of Bachhawat during the short span of four and a half years is now ancient history. He purified quite a formidable number of enzymes in leucine and valine metabolism each purification bearing the hallmark of his "hocus pocus". During this period the most unusual achievement was the crystallization of what he calls "a functionless" enzyme. Years later a regulatory function has been assigned to his carbondioxide-A TPase. Similarly about 10 years later at Vellore he had again surprised the world by his purification of a "Substrate"—less enzyme Aryl sulphatase 'B'.

The chance discovery of "mevalonic acid" by Pete Tavormina (a mutual friend) at the E. Merck laboratory rather took away the carpet from the seekers of the key intermediate in isoprene biogenesis. It was time for Bimal to make a change.

When he returned to India in late 1957, Bimal already had a reputation as an upcoming biochemist and at the National Chemical Laboratory, we were hoping that he would join us. Jaganathan was frantically moving papers to create a suitable position for him. There were several other lucrative feelers. But Bimal surprised all of us by accepting a poorly paid position of an Associate Professor in the Department of Neurochemistry at the Christian Medical College, Vellore. At first his choice of Vellore puzzled us but now we know that the challenge of the problem of working in a difficult area—the biochemistry of myelination—the intricacy of the process of biogenesis of glycolipids attracted him more.

To realize the extent of his "audacity", one had to go back to the state of the art in 1957 in processing enzymes and membrane components. All selfrespecting biochemists used to avoid the field which required cumbersome, repetitive and often non-rewarding search for enzymes in intractable emulsions, gums and goos. But most biochemists in the world are now familiar with Bimal's work on mucopolysaccharide biogenesis and metabolism of gangliosides and cerebroside in some genetic disorders. Apart from his own impressive contributions, Bimal was able to establish one of the finest centres of biochemistry at Vellore, a Mecca for all biochemists.

However, Bimal had always a streak of scientific "wanderlust" in him. Instead of settling down on his laurels and achievements in the third phase of his life, suddenly he switched fields again. I distinctly remember my visit to Vellore in 1974 after about 3 years when everybody in his laboratory was talking about lectins and liposomes. Bimal told me that this switch was necessitated as he found that he had no funds and instead of complaining he was maintaining his laboratory by selling lectins. In 1975 it was an exciting game for him to introduce through liposomes with appropriate carbohydrate markers, all kinds of bizarre things into liver cells—things which should not be there.

In 1976 his acceptance of the Directorship of a CSIR organization "Indian Institute of Experimental Medicine" later to emerge in the scientific map of the world as the Indian Institute of Chemical Biology, was a pleasant surprise to his friends. All of them are used to Bimal's tenacity to do his highest thinking while having a meagre hand to mouth existence at Vellore. His initial salary of Rs. 500.00 was to continue for several years and then he had a larger existence as a Professor at Vellore for only Rs. 1,000.00 p.m.

His remarkable success as a builder and administrator was really amazing. The formidable task of revitalizing and rejuvenating required not only true scientific leadership but an unbelievable patience in sorting out non-scientific matters. The collection of some of the best young talents from India and abroad and to harness their motivation and energy to work for some common national problems against

the restrictive rules are great achievements no doubt. But Bimal's real triumph was the make the "dead wood" blossom into new buds.

To understand how Bimal achieved this miracle, let me describe a typical scene at the IICB when Bimal was Director. Bimal would be absorbed in a serious discussion with the administrative staff about construction of the animal house, installation of the purified water system and getting a date-line for the library air-conditioning when some irate senior scientist would suddenly barge in to complain about the non-availability of ordinary distilled water. He would be followed by a group of young students who want to have serious scientific discussion about their problems. By this time all the seats in the room have been taken and Sri Rabindra Singh, Bimal's personal attendant has seen to it that everybody present has at least half-a-cup of tea. Suddenly a group of 15 disgruntled professional trade unionists burst into his office demanding the same wages and social status as the scientists. What does one do under such a situation? Bimal fills his pipe with a wad of tobacco, lights it, takes a couple of puff for inspiration and then forgets about it. He talks to everybody, cuts some joke with each one. Only a few problems have been solved but each goes out smiling.

Bimal told me once that his secret of administration is to have no formal administration.

It is really unfortunate that Bimal had to retire when the achievements of the IICB was making their mark. The CSIR or any other organization in the country cannot officially recognize exceptional individuals. Even today the rules are more important than individuals. So his retirement was inevitable.

But from a broader point of view, there is a silver lining. Bimal's current occupation as a Professor in Delhi University is less likely to increase his hypertension than that of the Director of a CSIR laboratory. Now Bimal's friends and admirers are looking for the beginning of the Sixth Phase of his life—creation of more new science and new tradition.

My life has been enriched by having Bimal as a friend and philosopher-and-even though I am older I am not ashamed to gracefully acknowledge his guidance not only in science but also in other problems. Bimal is a remarkable person whose love for science transcends into a love for fellow human being. Although not religious, he typifies the highest principles of Jainism—love, compassion and supreme detachment.

It will be meaningless to wish merely a long life for him. It will be more appropriate to wish him to remain as the shining light to guide all adventurers into the realm of biosciences for many more years to come.

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III

Pleasure and privilege

The title of the statement to follow was selected after some thought about the career to date of our Honoree. Please note the underline which clearly denotes that Bimal is

operating under Bull power in his new assignment as Head of the Department of Biochemistry at the University of Delhi. I refer to him as Bimal without his permission as you see.

It is a privilege for me to be invited to participate in this well deserved celebration. It is also a real personal pleasure for me to comment on the distinguished career of a graduate of the University of Illinois at Urbana, Illinois (Ph.D., 1953). It was both a privilege and a pleasure for me when Bimal elected to do his Ph.D. thesis studies in my laboratory. I have followed his career in a very general way and have been aware of his major impact not only on the scientific aspects of his productive research programs but also on his personal interactions at all levels (students, faculty, government, national and international meetings and the like). Bimal is a true example of the universality of good science and of the continuing challenges to our understanding. This latter point is relevant in spite of the remarkable and explosive leaps forward in biological science during the past 25 years or so.

Let me ask two questions: What exactly can a young graduate student in a major field of study hope for and expect as he pursues his course work and Ph.D. thesis preparation? At the same time what exactly can a graduate student's mentor hope for and expect? The eyes of both are on the specifics of formal and informal education and on the vastness of established knowledge and of the partially explored and unexplored vistas ahead. Graduate study is an exciting time, but it is really only a preparation for future experiments and analysis. It has been a continuing privilege and pleasure for me to observe how a good, active and industrious graduate student can move logically and steadily into his important career. Bimal's example is a strong one indeed.

This account is being written on the shores of Lake Michigan, about 2100 miles from my library. I am armed with Bimal's Curriculum Vitae and with a copy of the abstract of his Ph.D. thesis, entitled 'The Purification of Malic Dehydrogenase from Rat Liver'. I must state that the University of Illinois Library, one of the great libraries in the USA, has lost the original first typed copy of his thesis (no Xeroxing in 1953) and is now making a strong effort to locate it. My personal copy is safely in my study and is not easily available to me because of time constraints related to the publication deadline. What I would like to do is to point out the state of enzyme isolation, purification and characterization then (1953) and now (1986) as shown by Bimal's thesis.

Bimal's first major paper was as a co-author with Dr. David M. Gibson (M.D., Harvard, and postdoctoral fellow in our laboratory), E. O. Davisson (graduate student), Dr. B. R. Ray (Professor of Physical Chemistry) and myself. [Rat Liver Lactic Dehydrogenase. I. Isolation and Chemical Properties of the Crystalline Enzyme, *J. Biol. Chem.*, **203**, 397–409 (1953)]. Suffice it to say two things: Our lactate dehydrogenase (LDH) was the fourth crystalline enzyme from mammalian liver (after catalase, alcohol dehydrogenase, and glutamic dehydrogenase). This result came after more than two years of intensive effort to fractionate liver homogenates. We were at the stage of fractional salting out, low temperature ethanol precipitation at controlled ionic strength and a variety of hopeful efforts to gain in enzymatic specific activity without losing too much of it. Bimal jumped in and helped in what turned out to be a successful effort.

As a thesis project I proposed to Bimal that he devote himself to the liver supernatant phase following 50% saturation with ammonium sulphate. This step

precipitated all the LDH and apparently left behind in solution the malic dehydrogenase [now malate dehydrogenase (MDH)]. At that time we were not aware of the existence of both mitochondrial and cytosolic MDH's (to be announced considerably later by H. A. Lardy and co-workers). I recall that Bimal and I agreed that several week-ends of work would likely lead us to gram quantities of pure MDH to be characterized and studied in terms of kinetic mechanism. As events developed it was clear that we were overly optimistic, and Bimal undertook a careful study of protein separation techniques which led to a highly purified—but not very stable—MDH preparation. He introduced some new approaches, including low ionic strength-ethanol extraction of liver homogenates and zinc precipitation techniques (after E. J. Cohn and co-workers, with the use of ^{65}Zn as a tracer). Bimal also developed a new assay for glutamate-oxalacetate transaminase (now aspartate aminotransferase) by coupling it with the MDH-catalyzed reduction of oxalacetate by NADH. This useful procedure has been widely used since that time. We sent it off to a major journal for publication as a communication but were told that we should use the method further in connection with proposed studies of transaminase. As a result other investigators published the procedure before we were ready. To summarize: Bimal produced a thoughtful thesis with a lot of careful experimentation.

In this connection it can be mentioned that only very recently was cytosolic MDH from liver crystallized and subjected to X-ray structural studies. Mitochondrial MDH turned out to be exceedingly difficult to crystallize in our hands, and we were unable to establish thoroughly the function of tightly bound lipid (s) before we closed our laboratory in 1981. So Bimal's and my "several week-ends" grew into a career-long effort. The extent of progress in protein isolation can be illustrated by our recent use in a class experiment (undergraduate biochemistry majors) of a pseudo-affinity chromatographic column technique (Blue Affi-Gel, Biorad) which allows the recovery of highly purified LDH from chicken breast muscle in about 2 h.

Following Illinois Bimal spent two postdoctoral years at Pennsylvania and then two more, at Michigan before returning to India. Let me say that his career in India can be looked at most definitively by scanning through the titles of his more than 151 papers, most of which are "full papers" and not abstracts of presentations at scientific meetings. He has clearly met the challenge of keeping up with and developing new approaches with sound and innovative enzymology as a recurring theme. While probing neurochemical matters he has studied glycoproteins and other conjugates and has turned to the application of new knowledge to medical and diagnostic problems. He has focused on the study of the role of glycoproteins as cell surface receptor sites and joined the large number of investigators of cell receptors.

Most of all Bimal has been true to his science, to his family, his colleagues and his country, and to himself. The publication of tributes to him brings pleasure to all of us for the privilege of working with him and honoring him at this most active stage of his career in Biochemistry.

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