

Recollections

How I Became a Biochemist: What Biochemistry has Done for Me?

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I was born in Bangkok, but went to school in London at the age of six, since my parents went to England at the time. When I was 10 years old (1957), I went to Cheam School, a preparatory school near Newbury in the same term as Prince Charles, and as the only schoolboy with camera, have a rare photo of the Prince pretending to catch a tennis ball. Then, I spent nearly 5 years (1960–1965) at Rugby School, where I studied science, because my father thought that this was the subject of the future. This early background enabled me to acquire the English language like a native. I also enjoyed sports, which was essential to survive at a public school at that time and a contemporary whom I met 40 years later at a House reunion, recalled that I was “fearless” in tackling boys twice my size on the

rugby pitch. Then, as a rather spoiled child at home, my spell in an English Public School helped me to integrate with the community and develop a sense of team spirit, as well as to acquire leadership skills as a prefect. My native English and sense of social responsibility developed during these early years may have predisposed me to later involvement in many international scientific organizations. Science teaching was very good at Rugby School then, so many boys took science and performed well. With good grades at GCE “A” and “S” levels in Chemistry, Physics, and Mathematics, I was asked to take the Scholarship Examination to Trinity College, Cambridge. However, I wrote back that I preferred to take the Common Entrance Examination instead, since there were so many excellent science students from Rugby School competing in the Scholarship Examination. Whereupon, Trinity College, Cambridge accepted me directly, so I must be one of the few students accepted into Cambridge University without taking any entrance examination or being interviewed.

Cambridge was an eye-opener, especially for someone brought up in the confines of a Public School environment. I remember vividly philosophical discussions with strangers at parties on the meaning of life and the equality of man, attending concerts, plays and debates, and strolling by the river with my girlfriend while “in love.” The Natural Sciences Tripos (1965–1968) at Cambridge was a very concentrated program, so I took Chemistry, Cell Biology, and Physiology in first year Part IA, Advanced Chemistry and Biochemistry in second year Part IB, and just one subject Biochemistry in the last year Part II Honours program. To say that I became a biochemist because I was not good at other subjects is probably an over-simplification. Certainly, I dropped Physics and Mathematics from the start because I was rather mediocre at these subjects. But the Cell Biology course was probably the turning point. Hardly ever having taken biology at school, I was amazed by the chemistry and molecular biology of living systems, remember, this was just after two Nobel Prizes were awarded in the same year (1962) for discoveries by Watson and Crick on DNA structure and by Perutz and Kendrew on hemoglobin and myoglobin structure. The course itself was really enjoyable, a multidisciplinary effort involving various departments, involving both lectures and laboratory, which really captured the imagination of

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someone trained in physical sciences like myself. Then, in the following year, I felt more comfortable with Biochemistry than Advanced Chemistry, although a good grounding of chemical principles has been important for my career in biochemistry. Part II Biochemistry in the last year was very hard work and very stimulating, and I probably had a more update overall knowledge of biochemistry then than at any time since. Particular mention should be made of my supervisor, Brian Hartley, for his infectious enthusiasm about biochemistry, and of Richard Perham, whose lectures sparked my interest in protein science, which was to become the cornerstone of my research throughout my career.

As a result, I decided to study for a Ph.D. and went to work with Cesar Milstein at the MRC Laboratory of Molecular Biology on the structure of mouse immunoglobulins in 1968, not really because of a deep interest in the genetic basis of immunoglobulin diversity, but more because I wanted to be a protein chemist. Working in the Protein and Nucleic Acid Section, headed by Fred Sanger, one of the few people ever to win two Nobel Prizes (1958 and 1980), helped me to develop good deal of expertise in protein chemistry. My Ph.D. thesis involved determining the amino acid sequence of a mouse IgG1 myeloma protein, which in those days required grams of protein. Cesar, of course, went on to develop hybridoma technology, which won him the Nobel Prize in 1984, so I like to tell my students that I am a “pre-monoclonal scientist,” which amuses them, because they cannot imagine research without monoclonal antibodies. Working at the MRC was a wonderful experience, not only being in the company of some of the best researchers in the world and having excellent equipment, but also because of what I describe to Thai scientists as “tacit networking,” where the system encourages researchers of all ages and fields to meet informally and share ideas, for example by eating in the canteen three times a day or going to other laboratories to use shared equipment. I was Milstein’s third student, so he had time to think deeply about experiments, and sometimes I had the feeling that I could even hear his brain working. Often he seemed more interested in experiments that did not work than experiments that did work, presumably because an unsuccessful experiment might suggest that the concepts upon which they were based were wrong, and that a new paradigm was needed.

After my Ph.D. in 1972, I joined the Department of Biochemistry, Faculty of Science, Mahidol University in Bangkok. Research in Thailand had really only started to expand the early 1960’s, because of support from the Rockefeller Foundation to develop postgraduate and preclinical schools at the faculty. At that time, department courses were taught in English, which was fortunate, because although fluent in speaking, my writing and reading skills in the Thai language were still rudimentary, having been abroad so long. International degree programs in biochemistry started at Mahidol University in 1964 for M.Sc. programs and 1968 for Ph.D. programs, while a Thai language B.Sc. program started at Chulalongkorn University in 1969 (1). I wanted to continue with protein research in Thailand, but the

field of immunoglobulins was too competitive. Fortunately, several young Ph.D.s joined our department at a similar time after overseas training, and some of us formed a Reproductive Biology Group coordinated by Montri Chulavatnatol, focusing on the male reproductive system. Although none of us had prior experience in the field, the project gave us several advantages that allowed us to compete internationally: (a) population growth was still a problem in Thailand, allowing us to obtain overseas funding; (b) there were still no effective methods for male contraception (except for the condom and vasectomy), because of lack of knowledge of the biochemistry of male reproduction; (c) samples such as sperm from donors or autopsy specimens of testis were more readily available locally; (d) coming together to form a group gave us critical mass for research and allowed us to pool our complementary expertise. In retrospect, the Reproductive Biology Group was probably the first protein research group in Thailand, since our main focus was to compare proteins and enzymes from male germ cells with those of somatic cells to find differences that could be used for the rational design of antifertility drugs. Equipment was rather limited, comprising mainly column chromatography, polyacrylamide gel electrophoresis, and high voltage paper electrophoresis for peptide separation, but Milstein helped me with amino acid analyses free of charge. The Reproductive Biology Group continued for 10–12 years, but people formed smaller groups, for example Nongnuj Tanphaichitr and I formed a cross-disciplinary collaboration with an electron microscopist, Prasert Sobhon from the Anatomy Department.

Later, through a Thai-UK collaboration program, funded by the National Research Council of Thailand and the Royal Society, UK, I collaborated with Chris Bucke of the University of Westminster on glycosidase enzymes. I have continued this area of research up to the present day, and later focused on structure-function relationships in Thai plant β -glucosidases, since different enzymes have different natural substrates, and can catalyze reverse hydrolysis and glucose transfer reactions to different extents. Then in 2002, together with four young researchers, our group successfully bid to become a Center for Excellence in Protein Structure and Function at the Faculty of Science, Mahidol University, and we received funding from the faculty to purchase an X-ray diffractometer for protein crystallography and a stopped-flow spectrophotometer for presteady state enzyme kinetics, both firsts for Thailand. Thirty years is rather long to wait for sophisticated equipment, but in the meantime, one must try to be productive with whatever modest equipment is available. I also have an adjunct position as Head of the Laboratory of Biochemistry at the Chulabhorn Research Institute, where we work on protein changes in disease, including genetic diseases and cancer proteomics, and our laboratory there was also the first Thai laboratory to publish in proteomics. In recent years, as a Senior Scholar of the Thailand Research Fund, I placed much emphasis on mentoring of young Ph.D.s, and also arranged Annual Symposia on Protein Research. This led to the founding of the Protein Society of Thailand in 2006.

Another major interest has been involvement with academic societies at international and national level. As outlined in a previous article, the award of an IUB (International Union of Biochemistry) travel fellowship in 1976 (2) was not only important in exposing me to the international biochemistry scene, but gave me the opportunity to attend an Executive Committee of Federation of Asian and Oceanian Biochemists (FAOB) (3, 4), and assist Takashi Murachi with the minutes of the meeting. This made me feel committed to the idea of international collaboration, so when Serene Vimokesant, my former Department Chairman and then Treasurer of FAOB asked me to succeed her, I gladly accepted, and became FAOB Treasurer (1980–1986). I began as Treasurer at the early age of 33, and learnt much about international cooperation from Osamu Hayaishi, the FAOB President at the time. A highlight of these early days was that the Biochemical Section of the Science Society of Thailand first organized an international scientific meeting in 1983, opening up Thai biochemistry to the outside world.

I later became President of FAOB (1990–1992) myself, and this has been one of the most enjoyable memories of my career. Not only did this involve interacting with biochemists from all over the world, but there were many challenging problems to overcome, such as formal registration as a tax-exempt scientific organization in Australia, raising funds through endowments and special company memberships, not to mention a fair share of political problems. In addition, to promote communication with member societies, I wrote a monthly newsletter for 3 years, and dreamt up slogans such as “Lets Help FAOB to Help Us” to promote closer interaction among member societies. Involvement with IUBMB came later, including representing the Thai society as delegate, becoming a Member of the Symposia and Workshops Committee, and also participation in Biochemical Education activities with Frank Vella and Ed Wood. I later became involved in recently established international organizations, and am currently Governing Council Member, Asian Pacific International Molecular Biology Network (A-IMBN) and Council Member, Asian Oceanic Human Proteome Organization (AOHUPO).

I have also played various roles in the Science Society of Thailand under the Patronage of His Majesty The King (5), as Chairman of the Biochemical Section (1986–1987), Editor of the society's research journal (1985–1987, 2001–2008), and now President of the Society (since 2008). I am not sure about other countries, but biochemists in Thailand seem to be highly public spirited, since they have played major roles in the Science Society of Thailand. First, the Biochemistry and Molecular Biology Section represents all the biochemists in Thailand so successfully that there has been no need to establish a separate Biochemistry and Molecular Biology Society, unlike in other fields like Chemistry. Then, over the Science Society of Thailand's 60-year history, three biochemists have served as President spanning a total period of 17 years, with Kamchad Mongkolkul, President for five terms, playing a crucial role in

initiating many activities of the society in promoting public awareness of science, teacher's training, and science activities for schools, as well as encouraging research. In addition, in the 33 years of the publication of the society's international research journal, *ScienceAsia (Journal of the Science Society of Thailand)* (6), three of the six editors have been biochemists, and two biochemists, Yongyuth Yuthavong, the founding editor, and myself have each served 10 years as editor, while the new editor is also a biochemist.

Try as one may, most senior scientists cannot entirely escape from administrative duties, and at various times, I became Chairman of the Biochemistry Department (1980–1984), Associate Dean of the Faculty of Science (1996–1997), Vice-President for International Relations (1997–1999), and Dean of the Faculty of Graduate Studies (2005–2007). The secret in enjoying such jobs for me has been to focus on promoting academic advancement and to continue with research despite time constraints. I have also won my share of prizes, such as the Outstanding Scientist of Thailand Award, but prizes should not be the goal in life, but rather we should do what we are good at and enjoy what we do.

In summarizing my career as a biochemist, I think it's not so important how one becomes a biochemist, but how one feels after a life-time as a biochemist. Personally, I would not have traded my profession as an academic and a biochemist for any other profession, because as an academic, I have been free to do many kinds of jobs, including research, administration, and promoting scientific advancement through various organizations. Research poses constant challenges in solving problems, and makes one appreciate the beauty of science, such as through the intricate architecture of protein molecules, which allow them to function so specifically and effectively. Teaching and mentoring keeps one young, because one is always dealing with young people and can help in their development. Most of all, working with international academic organizations has shown me that science unites people of different countries, languages, religious beliefs, ethnic origins, economic status, and political ideals, so we can all work together to make a better future for this world.

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