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EDITORIAL

Scientists, Teachers and Writers: Remembering a Remarkable Trio

California has a vibrant set of public and private universities, which act as a magnet for scientists from across the world. Science took root on the Berkeley campus of the University of California less than a century ago. Stanford and the California Institute of Technology (Caltech) are younger, but their rise to the pre-eminent position they occupy today has been spectacularly rapid. Two of the major scientific and technological revolutions of our times, now widely termed as information technology and biotechnology, erupted from the uniquely Californian ambience. The 'Silicon Valley' model is one that governments everywhere would like to emulate; a seamless fusion of academia and industry in an environment where academic idealism and corporate pragmatism coexist. California's institutions have been major drivers in the tumultuous progress that science has made over the past fifty years. They have provided an environment which has fostered creativity and scholarship, which must make institutions elsewhere, envious. California also boasts of the greatest concentration of alumni from the best of Indian institutions. Last summer, the North American gatherings of IIT and IISc alumni, were both held in Silicon Valley. I thought of California, while reflecting on three extraordinary scientists who died in the last few months; Joshua Lederberg (1925–2008), Arthur Kornberg (1918–2007) and Daniel Koshland (1920–2007). All three were major influences on their disciplines. Lederberg and Kornberg moved to Stanford in the late 1950s to chair the newly formed departments of genetics and biochemistry, while Koshland joined the Berkeley faculty in the 1960s. In the years that followed all three men would leave an indelible imprint as scientists, teachers and writers.

Lederberg was precocious, receiving a Ph D at Yale when he was only 22. He began his research career at an exciting time; Oswald Avery had just discovered that DNA was 'the genetic material', at the Rockefeller Institute of Medical Research (later to become a university), not too far from Columbia University, where the young Lederberg was a pre-medical student. Years later, he wrote: 'When biologists of that era used terms like protein, nucleic acid or nucleoprotein it can hardly be assumed that the words had today's crisp connotations of defined chemical structure. Sleepwalking, we were all groping to discover just what was important about the chemical basis of biological specificity. It was clear to the circle I frequented at Columbia that Avery's work was the most exciting key to that insight' (*The Rockefeller University Research Profiles*, Spring 1990). Encouraged by a far seeing mentor, Francis Ryan, Lederberg moved to Edward Tatum's laboratory at Yale, to do the initial experiments establishing transfer of genetic information in bacteria, that would eventually pave the path to his Nobel Prize in 1958. Lederberg reached the pinnacle of scientific success at the young age of 33, the greater part of his famous work being done at the University of Wisconsin, where he began his teaching career. Lederberg's ability to chart new courses and articulate new directions is illustrated by the words and phrases attributed to him in the Oxford dictionary; plasmid, transduction, prototroph and exobiology. It is at Stanford that Lederberg began to influence research and policy in disciplines far removed from microbial genetics. Lederberg saw very early the enormous potential of computers, in problem solving in chemistry and biology. The attempt at Stanford, with the computer scientist Edward Feigenbaum and the chemist Carl Djerassi to teach computers to handle chemical structures and interpret mass spectra, anticipated much of the later developments in the area of artificial intelligence. My own introduction to Lederberg's writings came through the many essays that he penned for the column in Eugene Garfield's *Current Contents* in the 1970s and 1980s. Lederberg's support and encouragement led Garfield to work on the *Genetics Citation Index*, the first attempt to begin the practical realization of the concept of citation indexes for science (Garfield, E., *Science*, 1955, **122**, 108). Lederberg was unwavering in his support for endeavours that allowed scientists to wade through the rapidly exploding scientific literature of recent years. His association with the *Annual Reviews Series* and the Institute of Scientific Information was evidence of a deep interest in organizing scientific information. The prefatory, often biographical, chapters in *Annual Reviews* provide a, albeit brief, glimpse into the lives of scientists, who are recognized by their peers as 'high achievers'. In in-

troducing a compendium of these chapters, *The Excitement and Fascination of Science* (Annual Reviews Inc., 1990), Lederberg reflects: 'Enmeshed in society, scientists may also find themselves with extra-scientific responsibilities and roles, though each of these is grounded in the fundamental one of discovering and telling the truth. . . .

. . . Our chapters abound in examples of the researcher doubling as teacher and publicist; organizer and manager; inventor, agent of technology transfer, and developer of useful applications; adviser to government or industry; prophet; and paragon. Caveat: perhaps those who write are a socially and self-selected sample; others may insist on staying at the bench to the exclusion of all else'.

Arthur Kornberg was an inspirational figure in biochemistry (and what later became popularly known as molecular biology). His discovery of the enzyme DNA polymerase led to the first test tube synthesis of DNA in the 1950s, resulting in the award of the Nobel Prize in 1959. Kornberg's enzymatic synthesis was to be followed by Har Gobind Khorana's *tour de force*; the painstaking chemical synthesis of oligonucleotides, which acted as templates for the Kornberg enzyme, paving the way for the studies that led to the deciphering of the genetic code. Khorana's Nobel lecture (1968) acknowledges the Kornberg influence: 'Some months later I visited Kornberg's laboratory (this was one of the many pilgrimages that I have made to this great laboratory) and started a few experiments with DNA polymerase and here, again, very short synthetic oligonucleotides containing alternating A and T units induced the enzyme to bring about extensive synthesis of the previously characterized high molecular weight dAT polymer'. Kornberg's influence on biochemistry was wide ranging. His autobiography was aptly titled: *For the love of enzymes: The Odyssey of a biochemist* (Harvard University Press, 1989). His prefatory statement that 'in my theater the nucleic acids write the script but the enzymes do the acting' is one that will strike a chord amongst a disappearing generation of biochemists. Kornberg was eloquent when he viewed the broad interdisciplinary interface of chemistry and biology. In a 1987 lecture, Kornberg borrowed C. P. Snow's famous phrase, 'The Two Cultures' to describe the rift between chemistry and biology (*Biochemistry*, 1987, **26**, 6888). In a lecture, whose message is valid even today, Kornberg noted with regret: 'Despite its enormous success. . .biochemistry has nevertheless failed to fill the gulf between chemistry and biology. . . . biochemistry itself is being pulled apart by the separate drifts of the two cultures from which it was assembled'. In his wonderfully worded essay he lamented: 'As long as this inattention to enzyme chemistry and basic biochemistry persists, the fundamental issues of cell growth and development will not be resolved and their application to degenerative diseases and aging will be delayed. . . . Molecular biology appears to have broken into the bank of cellular chemistry but for lack of chemical tools and training, it is still fumbling to unlock the major vaults.'

Daniel Koshland introduced the idea of 'induced fit' in explaining the specificity of molecular interactions involving proteins; an idea that replaced Emil Fischer's 'lock and key' theory of enzyme reactions. He anticipated the ideas of plasticity and dynamic mobility of biomolecular structures, which are so commonly accepted today. Koshland's influence as editor of *Science* for a decade (1985–95) marked a period of unprecedented transformation in one of the most influential journals in science. Koshland's humour and love for science are readily evident in his writings. His editorials which appeared as conversations with the pompous and egotistic Dr Noitall (undoubtedly a man who knew it all) were a delight to read. His 'farewell' editorial in *Science* (1995, **268**, 479) is a tribute to a man who knew how to laugh at himself, an endearing quality that is all too rare. Koshland's writings reveal a man who enjoyed science, teaching and communicating. He begins his biographical essay in *Annual Review of Biochemistry* (1996, **65**, 1–13): 'When writing a prefatory chapter for Annual Reviews a scientist is confronted with the question of what in his or her life might be interesting to others. In my case I was appalled at the absence of material that generates good novels: no broken homes, no misunderstood childhood, no criminal youth gangs, no disastrous liaisons. A landscape of boredom from sea to shining sea. If there is one overlying theme it is that I got paid for doing what I enjoyed all my life'. Koshland's enthusiasm is apparent when he writes: 'The pleasures of doing research and teaching made it difficult to pretend I was working instead of merely having a good time. Scientists are basically puzzle solvers and they get hired to solve puzzles. So someone else is providing the capital for them to satisfy a lifelong desire.'

At times, Lederberg and Kornberg were magisterial in their writings. Koshland's self deprecatory style was captivating. Why have I chosen to reflect on men whom I have never met? It is because over the years I have spent many hours reading what they wrote, and I never failed to come away inspired, challenged and enthused about science. In remembering them, I am, in small measure, paying a tribute to a generation of scientists who are slowly fading, whose passion and commitment act as a beacon for the generations that follow.

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