

Daniel E. Koshland, Jr. 1920–2007

The world has lost one of its great scientists and the University of California its most influential educator with the death of Daniel E. Koshland, Jr. on Monday, July 23, 2007. Dan's career spanned 60 years of creative biochemical research, and he was actively planning his next experiments on the Friday before his sudden death. Those of us fortunate enough to have experienced Dan's extraordinary personality will always remember his wisdom, sharp wit, and kindness, especially toward students and young scientists.

My first encounter with Dan was in 1969 as an undergraduate student at the University of California, Berkeley, better known as Cal. I was taking his renowned biochemistry class. He invariably started his lectures with some hilarious joke or witty one liner that quickly engaged us all. However, we soon realized that Dan was both funny and very serious about science. Somehow he managed to teach us more about protein chemistry and the properties of biological macromolecules in ten weeks than we thought possible. Most memorable were his infectious enthusiasm for the subject and his depth of knowledge, which was frequently punctuated by stories of famous biochemist colleagues and their foibles. We learned from him about the flexibility of protein structures and delved deeply into enzyme catalysis, induced fit mechanisms, negative and positive cooperativity, orbital steering, and feedback control. The bold idea of induced fit came to Dan 20 years before hardcore crystallographic data proved him correct. Back then, Dan was struggling with the paradox that enzymes such as hexokinase were lousy ATPases. Yet if hexokinase and other kinases worked

in a rigid "lock & key" fashion, why didn't a water molecule attack ATP as efficiently as a sugar substrate? He reasoned that the correct sugar substrate was needed to sculpt the enzyme and thus induce the right fit, a prescient idea that is still current.

My next contact with Dan was in his office when I interviewed for a coveted position as an undergraduate research fellow. I went in tongue tied and brain frozen, but he adeptly put me at ease with a few gentle words of encouragement sprinkled with his trademark humor. "It's easy to ruin any good scientist's career—just provide them with unlimited resources and money."



Daniel E. Koshland, Jr.
Photograph courtesy of U.C. Berkeley.

The next day I began working in Dan's lab and an entirely new world of biochemistry research unfolded before me, which I absorbed like a sponge. Working with the likes of Alex Levitzki, Dan Storm, and Rick Dahlquist made it painfully clear that it would be a chal-

lenge achieving the level of science and sheer intellectual horsepower that Dan had assembled at Berkeley.

Dan's scientific contributions, especially "induced fit," continue to influence our thinking today about how proteins and protein complexes work, from enzymes and receptors to transcription factors and signaling molecules. As befits Dan's bold and creative science, he received many awards including the National Medal of Science (1990), the Albert Lasker Award for special achievement in medical science (1998), and the Welch Award in Chemistry (2006). His reaction to these awards was that "If you really wanted to be famous you should be mayor of a small town in the Midwest where you would be recognized by at least 10,000 people, which is way more than the number of people worldwide that recognize almost any famous scientist."

Despite Dan's pre-eminence in the field of enzyme catalysis and protein function, what distinguished his scientific philosophy from many was his keen desire, almost addictive affinity, for taking risks and changing fields just when others might begin to feel accomplished and content. Although a significant fraction of his lab in 1970 continued to work on various aspects of enzyme kinetics and protein structure, even a naive undergraduate student could see that Dan was already moving on to other new and exciting areas of research, in this case, bacterial chemotaxis.

The challenge was that Dan first had to learn bacterial genetics, which he did with help from Bruce Ames. Dan brought to the chemotaxis field a fresh series of clever, elegant, and quantitative assays. This biochemical approach subsequently led his

team to gain many insights into the molecular mechanisms driving bacterial chemotaxis. This same thirst for charting new research territory sustained Dan throughout his more than 60 years of research, taking him from organic chemistry and the Manhattan Project to enzyme mechanisms, bacterial chemotaxis, receptors and signaling in neurobiology, and most recently cyanobacteria and potential new ways to generate CO₂-neutral sources of energy.

Not one to shirk responsibility or community service, Dan was elected President of the Board at his children's school in Brookhaven, Long Island, became Chairman of Biochemistry at Berkeley, took on the Editorship of *PNAS*, and in 1985 became Editor-in-Chief of *Science* magazine. Throughout his more than 45 years at Cal, Dan was an ardent supporter of Cal sports teams, especially the football team. He was also an exceptionally generous philanthropist—a long tradition of the extended Koshland family in the San Francisco Bay Area. He donated many major gifts: to the National Academy of Sciences in Washington DC for the Marian Koshland Science Museum dedicated to his first wife; Haverford College; the Weizmann Institute; Ben Gurion University in Israel; and the San Francisco Exploratorium. But, perhaps Dan's most generous gifts were to his favorite cause, UC Berkeley.

Of all the "extracurricular" activities that Dan embraced, the one that stands out in my mind (and I believe in his) was spearheading the radical reorganization of the biological sciences at Cal. Around 1980, Dan and his first wife Marian (Bunny), an accomplished molecular immunologist, realized that the prevailing departmental structure at Berkeley, which had served the institution well from the 1930s to the 1960s, could not continue to be viable, particularly given the funding

constraints of a state university. With characteristic high energy and political savvy, Dan forged ahead with what has become one of the most comprehensive and transformative academic reorganizations in the history of the University of California. Despite initial opposition and foot dragging by faculty and administrators, Dan convened a stellar outside advisory board to overcome internal bickering. Many of us will remember Dan's uncanny ability to diffuse tensions during the many heated discussions at our faculty meetings with sharp humor: "What good is power if you can't abuse it?"

With a combination of thoughtful diplomacy, persuasive logic, and dogged determination, Dan gained strong endorsements for the reorganization from Chancellor Mike Heyman and Provost Rod Park. This required eliminating nearly a dozen departments and coalescing approximately 170 faculty into three major departments: Molecular and Cell Biology, Integrative Biology, and Plant and Microbial Biology. This massive realignment required cutting across multiple colleges and the construction of two new research and teaching buildings plus a total renovation of a third. Dan's operating philosophy was that "It is amazing how much more you can accomplish if you don't care who gets the credit." By 1985 the reorganization was on its way and we could begin to see a remarkable improvement in attracting the best PhD students and recruiting top faculty. Dan's leadership and philanthropy continues today with Phase II of the reorganization, which includes the recently completed QB3-Stanley building for quantitative biology and the new Li Ka Shing Center for Biomedical and Health Sciences.

Dan was one of the most admired scientists of his time, and he was also one of the luckiest. He was born into a remarkable family and after mar-

rying Bunny had five children (Ellen, Phlyp, Jim, Gail, and Doug), each with unusual talents and achievements in a range of fields, from author and sculptor to lawyer and scientist. He also had the great fortune of two wonderful marriages, the first of 50 years to Marian until her death in 1997. At age 80, he reconnected with and married Yvonne, whom he first dated at Cal some 60 years earlier when he was a junior and she a freshman. He announced this happy event to me with "Tij, I have to confess something—I met a younger lady and we are getting married."

Dan expected the best from his children, students, and colleagues, but this message was delivered with humor and wit; he always let you know he cared. Over the 40+ years of our student/mentor relationship, Dan and I held frequent lunch meetings (usually at the greasiest hamburger joint in town) where we discussed everything: local and international politics, his role as Editor-in-Chief of *Science*, campus politics, family, finances, sports, teaching, and of course science and how to do it better. Dan's passing is a huge loss for science, UC Berkeley, his family, and the Bay area—a loss too difficult for me to contemplate. My last conversation with Dan two weeks before his death from a stroke was about his newest adventure with cyanobacteria. I will always remember Dan's pure joy and enthusiasm as he proudly showed me his latest lab acquisition, a shiny new glove box for growing bacteria anaerobically.

Dan was more than a scientific role model—he was my hero, best friend, and trusted advisor, an extraordinary human being with an unwavering moral compass. His humor, humanity, and wit will be sorely missed, and it will be a long time before I stop looking for that beat up old Lexus of his when I drive by his uniquely designated parking space.

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