A. Hartmann and S. Hoyer, Eds. (Springer-Verlag, New York, 1984).
14. Under ideal circumstances (in the absence of significant concentrations of metabolite within extravascular brain tissue), it can be shown that the normalized integral of the metabolite concentration in the cerebellum is related to the normalized integral of the free ligand concentration in the caudate (C. S. Patlak, personal communication).
15. The slopes of these plots for males ranged from 0.017 to 0.07 min^{-1} (average, 0.053 min^{-1}) and decreased exponentially with age ($m = 0.0279 + 0.177e^{-0.0715x}$; standard error = 4.6×10^{-3}, 9.0×10^{-2}, and 2.4×10^{-2}). The 95 percent confidence intervals of the experimental regression at ages 20, 40, and 65 years were 0.070 ± 0.01, 0.038 ± 0.0049, and 0.030 ± 0.0064, respectively, and the prediction limits of a new slope value at these ages were 0.070 ± 0.019, 0.038 ± 0.016, and 0.030 ± 0.017, respectively. The slopes of these plots for females ranged from 0.0765 to 0.036 min^{-1} (average, 0.05057 min^{-1}) and had a linear fit ($m = 0.040x + 6.39$; standard error = 0.0002). For the females the 95 percent confidence limits on the straight-line regression at ages 20, 40, and 65 years were 0.056 ± 0.0090, 0.048 ± 0.0061, and 0.038 ± 0.014, respectively, and the prediction limits for a new value of slope at these ages were 0.056 ± 0.029, 0.048 ± 0.028, and 0.038 ± 0.031, respectively.
16. J. A. Severson *et al.*, *J. Neurochem.* **39**, 1623 (1982); J. A. Severson and C. E. Finch, *Brain Res.* **210**, 201 (1980); J. A. Joseph *et al.*, *Life Sci.* **29**, 575 (1981); L. J. Thal *et al.*, *Brain Res.* **192**, 185 (1980); A. DeBlair and T. Menrini, *ibid.* **242**, 361 (1982); J. K. Marquis *et al.*, *Biochem. Pharmacol.* **30**, 1876 (1981); M. Meino *et al.*, *Brain Res.* **202**, 488 (1980); C. H. Misra *et al.*, *Life Sci.* **27**, 526 (1980); J. Marcusson, *Clin. Neuropharmacol.* **7** (suppl. 1), 22 (1984).
17. The declines in cerebral blood flow over a comparable range of ages are variable and in the range of 0 to 29 percent. Also, in some cases the data are not directly comparable [N. A. Lassen *et al.*, *J. Clin. Invest.* **9**, 491 (1960); H. Naritomi *et al.*, *Arch. Neurol.* **36**, 410 (1979); P. Scheinberg *et al.*, *AMA Arch. Neurol. Psychiatry* **70**, 77 (1953); W. D. Obrist, *Aging* **7**, 213 (1978); S. S. Kety, *J. Chronic Dis.* **3**, 478 (1956)].
18. Assessment of CT images of the caudate and putamen did not reveal a decrease in size with age, nor was significant atrophy observed. It is possible that a small decrease in size of the caudate or putamen with age partially contributes to the decrease in the measured activity in these regions because of the so-called partial volume effect. Structures similar in size or smaller than the spatial resolution of the PET scanner result in lower measured activity than the true activity. The lack of evidence from CT scans showing a recognizable decrease in caudate or putamen size suggests that the decrease in activity with age is not solely an effect of size change. This decrease is maximum in the 20- to 40-year age group, where atrophy would be unusual.
19. R. Duara *et al.*, *Brain* **106**, 761 (1983); D. E. Kuhal *et al.*, *J. Cereb. Blood Flow Metab.* **2**, 163 (1982); R. A. Hawkins *et al.*, *ibid.* **3**, 250 (1983).
20. O. Bugiani *et al.*, *Eur. J. Neurol.* **17**, 286 (1978); P. L. McGeer *et al.*, *Arch. Neurol.* **34**, 33 (1977).
21. P. L. McGeer and E. F. McGeer, *J. Neurochem.* **26**, 65 (1976); A. Carlsson and B. Winblad, *J. Neural Trans.* **38**, 271 (1976).
22. S. H. Snyder and R. R. Goodman, *J. Neurochem.* **35**, 5 (1980); R. Schwarcz and J. T. Coyle, *Brain Res.* **127**, 235 (1977); L. C. Murrin *et al.*, *Eur. J. Pharmacol.* **60**, 229 (1979); N. Klemm *et al.*, *Brain Res.* **169**, 1 (1979); M. Quik *et al.*, *ibid.* **167**, 335 (1979); J. W. Kebabian and D. B. Calne, *Nature (London)* **277**, 93 (1979).
23. The relation between the A_{ca}/A_{cb} ratio and age in females is best represented by a straight line. In males a second-degree polynomial regression gave a significantly better fit ($P < 0.01$) than a straight line, thus demonstrating a statistically significant difference between males and females in the decline of receptor with age. An exponential function was approximately as good a fit. (The mean square errors of polynomial and exponential fit were 0.114 and 0.123, respectively). Because of the partial overlap of the data for males and females, the biological significance of this statistical difference has yet to be determined.
24. R. Hruska *et al.*, *Pharmacol. Biochem. Behav.* **16**, 285 (1982); T. DiPaolo *et al.*, *Molec. Cell. Endocrin.* **16**, 99 (1979); J. C. Miller, *Psychoneuroendocrinology* **8**, 225 (1983); T. DiPaolo *et al.*, *Neuropsychopharmacol. Biol. Psychiatry* **6**, 377 (1982).
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26. Supported by U.S. Public Health Service grants NS15080 and MH00053. We thank S. Wrightson, M. Flutka, F. Gilbert, M. J. Stumpf, J. K. Rhine, D. Koller, P. Zorich, M. Murrell, M. Bryan, P. D. Wilson, B. Jensen, A. Kimble, G. Pearlson, G. Uhl, P. Worley, R. D. Parker, G. J. Wang, L. Buhle, T. Duelfer, T. K. Natarajan, A. Bice, N. D. LaFrance, J. Alano, G. Wand, R. Ney, H. M. Drew, B. D. Scheinin, K. Stolz, and H. Rothenburg for assistance and S. H. Snyder for general discussions.

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Daniel E. Koshland, Jr., New Editor of *Science*

Bruce N. Ames

In January of 1985, Philip Abelson will hand over the reins of *Science* to a new editor to build on the fine foundation he has created for this distinguished magazine. The AAAS has been fortunate to persuade Daniel Koshland to assume this responsibility.

Dan Koshland became interested in science at the age of 13 when he read *Microbe Hunters* and *Arrowsmith*. He obtained at B.S. in chemistry from the University of California, Berkeley, and a Ph.D., also in chemistry, from the University of Chicago. His graduate work under the direction of Frank Westheimer was leaning toward the biological side of chemistry, and it is to the application of chemistry to biology that he has devoted his efforts. After a postdoctoral fellowship at Harvard he had joint appointments at Brookhaven National Laboratory and Rockefeller University until moving to the University of California, Berkeley, as professor of biochemistry in 1965.

Koshland has a tremendous curiosity about all things scientific, and his career has been noteworthy for the contributions he has made to numerous areas of science. His enthusiasm, high energy level, and low activation energy for mastering new fields are ideal characteristics for editorship of a multidisciplinary journal such as *Science*.

His research has been reported in approximately 300 articles, ranging from theoretical papers involving pure mathematics to a paper on "The walking rate of ants." It is impractical to describe all of his contributions here but a few illustrative examples can be chosen.

Koshland's early work was focused on enzyme mechanisms. His first major contribution was the concept of single and double displacement reactions in biology, a concept that applied the stereochemistry of organic chemistry to the understanding of enzymatic mechanisms. It provided a unifying theory to many reactions that seemed widely disparate and was typical of many of his subsequent contributions. In demonstrating the validity of his theories, he developed a number of experimental tools—methods for modifying carboxyl and tryptophan residues in proteins, the all-or-none assay, oxygen-18 isotopic techniques for interpreting mechanisms of muscular contraction, and the first "chemical mutation" (the conversion of a serine to a cysteine residue at the active site of chymotrypsin by chemical modification)—and a theoretical analysis of the "proximity effect."

His next major contribution was the development of the "induced fit" theory, now included in textbooks of biochemistry. At its first promulgation, however, it was not easily accepted, for it proposed that enzymes were flexible molecules, not the classical keylock or template model of Emil Fischer, which was standard doctrine at the time. Koshland's proposal was that the fit between a protein molecule and its substrate was more like the fit of a hand in a glove than the fit of two pieces of a rigid jigsaw puzzle. Moreover, the change in shape of the protein "induced" by the small molecule was essential to its biological properties. Koshland and others, of

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whom Jacques Monod and Arthur Pardee were particularly important, extended this concept to regulation of biological systems in general. Further contributions from Koshland's laboratory in this area were theoretical papers, one of which proposed the well-known sequential model for cooperative effects now established in many enzymes. "Negative cooperativity," a new phenomenon, was predicted by this sequential model and was demonstrated experimentally in his laboratory 2 years later. To delineate these conformational changes, he introduced the concept of a "reporter" group, a spectrally sensitive chemical group that covalently attached to the protein in a sensitive but not vital region. This group then "reports" changes in the shape and activity of the macromolecule during its function.

Conformational flexibility is now accepted as a key element in the control of all biological systems. In addition to playing a role in enzymatic catalysis, it has been demonstrated in the action of sensory receptors, ion channels, gene repressors, and hormone action.

In the 1970's Koshland turned to more complex problems of control, that is, behavior and memory. He chose the study of bacterial chemotaxis because it was a simple behavioral system that could be analyzed by both genetic and biochemical techniques. Robert Macnab and Koshland solved the puzzle of how such a small organism could detect gradients by demonstrating that the bacteria had a rudimentary memory that allowed them, in effect, to compare the past with the present. In these studies they also showed that bacteria adapt to sensory input as higher species adapt to light, odor, and taste. Koshland has applied recombinant DNA techniques to these behavioral studies and, among other contributions, has used these methods to clone a receptor for bacterial sensing and to dissect its properties by genetic engineering. These studies have provided models for information processing and adaptation to sensory phenomena. At present his laboratory is pursuing these behavioral studies and is concerned with threshold phenomena, since he is convinced they are important in the conversion of short-term to long-term memory.

Koshland has received numerous awards for his work, of which the Pauling award of the American Chemical Society and the Rosenstiel award mentioned his work on memory and behavior; the Edgar Fahs Smith award of the American Chemical Society and the T. Duckett Jones award mentioned his work on protein flexibility; and the Waterford prize of the Scripps Clinic and Research Foundation mentioned his contributions to unifying concepts in biology. He has been elected an honorary member of the Japanese Biochemistry Society and the Royal Swedish Academy of Sciences.

Daniel Koshland (on the right) receiving congratulations of V. N. Woolfolk of the Rosenstiel Foundation as he and Eric Kandel of Columbia University received the Rosenstiel award at Brandeis University in April.

Koshland's colleagues, of whom I am honored to be one, will testify to his being an unusually good citizen in the department and the university. He served very successfully as chairman of our department for many years. He is an unusually popular teacher with our undergraduate students. He was chairman of a committee to reorganize the biology program at Berkeley, and he has been a major figure in the acquisition of two new buildings and the recruiting of excellent young faculty to the campus.

In addition, Koshland has been an unusually good citizen in the scientific community. He has, for example, been president of the American Society of Biological Chemists and of the Council of the National Academy of Sciences. Koshland also served as chairman of the Advisory Committee of the Weizmann Institute. He served as chair of the Academy Forum of the National Academy of Sciences, which dealt with controversial issues of societal concern. The forum sponsored debates on issues ranging from hazards of nuclear reactors to the ethical issues of research on humans. Koshland developed a reputation for fairness in the handling of these emotionally charged issues. His most recent editorial experience has been as chairman of the editorial board of the *Proceedings of the National Academy of Sciences*. Before that he served on the editorial boards of such diverse journals as the *Journal of Biological Chemistry*, *Accounts of Chemical Research*, the *Journal of Molecular Biology*, the *Journal of Molecular Pharmacology*, and *Science*.

Koshland and his wife, Marian (also a member of the National Academy of Sciences and a professor at Berkeley), have five children with whom they maintain close ties.

Koshland was brought up in San Francisco in a large, successful, extended family that includes many well-known civic figures who have left their mark on the city of San Francisco and the University of California (Dan represented the third generation to attend the university). The family is noted for its social responsibility. For example, his father (D.E.K., Sr.), who was chief executive officer of a large manufacturing company, was also very active in promoting civil rights legislation. To understand Dan's ebullience and willingness to take controversial positions one should know that he considers "that he got tenure in the family at age 2" and that he might have a gene in common with his Aunt Carrie, who, when requested to give some of her favorite recipes to her daughter, did, of course, but only in her will.

Dan Koshland's training and experience are ideal for an editor of *Science*. He has a record of fairness in dealing with diverse opinions. He is an avid reader, and he likes to write (including humorous poems at birthday parties of friends and relatives). Most important, he has great enthusiasm for science, and living in general, and regards the *Science* editorship as an exciting new challenge.