Sam Karlin
1924—2007

This paper was written by Richard Olshen (Stanford University) and Burton Singer (Princeton University). It is a synthesis of written and oral contributions from seven of Karlin's former PhD students, four close colleagues, all three of his children, his wife, Dorit, and with valuable organizational assistance from Rafe Mazzeo (Chair, Department of Mathematics, Stanford University.)

The contributing former PhD students were:
Krishna Athreya (Iowa State University)
Amir Dembo (Stanford University)
Marcus Feldman (Stanford University)
Thomas Liggett (UCLA)
Charles Micchelli (SUNY, Albany)
Yosef Rinott (Hebrew University, Jerusalem)
Burton Singer (Princeton University)

The contributing close colleagues were:
Kenneth Arrow (Stanford University)
Douglas Brutlag (Stanford University)
Allan Campbell (Stanford University)
Richard Olshen (Stanford University)

Sam Karlin's children:
Kenneth Karlin
Manuel Karlin
Anna Karlin

Sam's wife -- Dorit

Professor Samuel Karlin made fundamental contributions to game theory, analysis, mathematical statistics, total positivity, probability and stochastic processes, mathematical economics, inventory theory, population genetics, bioinformatics and biomolecular sequence analysis. He was the author or coauthor of 10 books and over 450 published papers, and received many awards and honors for his work. He was famous for his work ethic and for guiding Ph.D. students, who numbered more than 70. To describe the collection of his students as astonishing in excellence and breadth is to understate the truth of the matter. It is easy to argue—and Sam Karlin participated in many a good argument—that he was the foremost teacher of advanced students in his fields of study in the 20th Century.

Karlin was born in Yonova, Poland on June 8, 1924, and died at Stanford, California on December 18, 2007. He came to Chicago as a young child and attended the Illinois Institute of Technology, from which he graduated with a B.S. in 1944. He earned his Ph.D. in Mathematics from Princeton University in 1947 under the direction of the celebrated Salomon Bochner. His first academic position was at the California Institute of Technology, where he attained the rank Professor in 1955. In 1956 Professor Karlin moved to Stanford University, where he was Professor of Mathematics and of Statistics. In 1978, he was named the Robert Grimmett Professor of Mathematics. For six years, starting in 1970, Karlin divided his time between Stanford and the Weizmann Institute of Science in Rehovot, Israel, where he rose to be Head of Applied Mathematics and Dean of what is now the Faculty of Mathematics and Computer Science.

Professor Karlin received many honors, including but not limited to elected membership in the American Academy of Arts and Sciences, the National Academy of Sciences, USA, and the American Philosophical Society, a membership in which he was especially proud. He received a National Medal of Science in 1989, the Lester R. Ford Award of the Mathematical Association of America, and the John von Neumann Theory Prize of the Operations Research Society of America. From 1975-81 he was Andrew D. White Professor-at-Large at Cornell University. He gave many invited lectures, including the Josiah Willard Gibbs Lecture of the American Mathematical Society, the Sir Ronald Fisher Lecture of the Royal Society of Great Britain, the Mahalanobis Memorial Lecture of the Indian Statistical Institute, and the first Abraham Wald Memorial Lectures of the Institute of Mathematical Statistics (IMS). He served as IMS President in 1978-79.

Early in Karlin's career he was part of the group at the RAND Corporation that extended von Neumann's analysis of two-person, zero sum games. These efforts were collaborative with H.F. Bohnenblust, primarily of Caltech, and L. Shapley of RAND. They characterized the solutions to game theoretic problems and showed how to compute solutions. Karlin's most original contribution was the analysis of games with continuous, as opposed to discrete, spaces of strategies. The famous minmax theory was known not to hold if payoff functions were discontinuous. Karlin gave precise sufficient conditions regarding payoff functions so as to ensure the existence of minmax equilibria in mixed (that is to say, randomized) strategies. Karlin's work on game theory opened the way for analysis of games of pursuit and evasion, for example, the fighter-bomber duel.

Karlin was fascinated by the development of dynamic inventory theory. As with many areas that were new to him, his insights came quickly, but were nonetheless deep. He adapted the calculus of variations to situations where the relevant variables are subject to non-negativity and upper bound constraints, his specific results being generalized later by L.S. Pontryagin (the maximum principle) and R. Bellman (dynamic programming). Bellman had been a classmate of Karlin at Princeton. Karlin's research in dynamic inventory theory included extensive study of deterministic cases. However, the deepest results were obtained in characterizing both optimal solutions and operating characteristics of given policies in dynamic inventory models with random demands. Karlin was the first to give sufficient conditions for the optimality of so-called (s,S) policies when the distribution of demands satisfies a certain determinental inequality that is satisfied by some Gaussian and double-exponential distributions, and logistic distributions.

In 1953 both Samuel Karlin and the mathematical community were fortunate that he met I.J. (Iso) Schoenberg, who was visiting the Department of Mathematics at UCLA. In Sam's own words, Schoenberg was, "charming, broadly cultured, and elegant in all his mathematical …" Schoenberg's influence was profound, for he had pioneered aspects of the theory of total positivity, which became a subject of passionate interest to Karlin. Indeed, Karlin wrote a book on the topic, *Total Positivity*, *Volume One*, that was published in 1968. While this is not the place for mathematical details, suffice it to begin with a function of two variables, discrete if the function is a matrix and continuous if the function is an integral kernel. Either way, the matrix/kernel operates on functions of a single variable by matrix multiplication, alternatively by integration against the function multiplied by the kernel with respect to some positive measure. Total positivity is defined by positivity of an obvious determinant of the matrix/kernel as a function of any two of its dummy variables. An equivalent characterization of totally positive kernels can be given in terms of a certain variation-diminishing property.

Karlin discovered that totally positive kernels appear often in statistical models, for example in the so-called exponential family of distributions; in approximation theory; in probability, in particular in stochastic processes, for example as transition kernels, and in differential equations. The cited variation diminishing property implies preservation of monotonicity, unimodality, convexity, and other properties of functions that can be expressed by changes of sign. There are further implications in statistics on uniformly most powerful (UMP) tests against one-sided alternatives and unbiased tests against two-sided alternatives.

A particularly beautiful and somewhat surprising example of a totally positive kernel was discovered by Karlin and his student and later Stanford faculty colleague James McGregor. The formula allows calculation of the probability of non-collision, up to any given time, of any adjacent pair of an arbitrary number of particles arranged in some order on a line, and then allowed to undergo independent random motions. The probability of non-coincidence is the determinant of a matrix of transition probabilities. Karlin recognized in this example the germ of a general idea that unified and extended a large literature in combinatorics with applications to voting behavior, counting the number of non-crossing paths in planar random-walk trajectories that move upward and to the right, and other areas.

The variation diminishing property for so-called diffusion processes says that if two processes start at different points, then the one that starts to the left of the other is always stochastically the smaller of the two processes.

Tchebycheff (T-) systems are ordered, discretely indexed sets of functions of a single variable for which an associated kernel of the two variables, one the index and the other the dummy variable of the function, is totally positive. One simple example is the monomial functions: non-negative integer powers of a dummy real variable. T-systems are the subject matter of the well-known book, *Tchebycheff systems: With applications in analysis and statistics,* by Karlin and his former student William Studden that appeared in 1966. T-systems enable study of "moment spaces," spaces for which the coordinates are the respective values, as the index varies, of the integrals of the functions that comprise the system. In consequence, one is able to compute maxima and minima of functionals of probabilities. These extrema tend to be simple mixtures. General theory enables computation of extrema, in particular the cardinality of the support of the mixing distributions.

Karlin's interest in total positivity led him in a natural way to interest in what is termed approximation theory. Both the book on Tchebycheff systems and the book on total positivity addressed aspects of approximation theory. Among the most important sets of functions by which other functions are approximated are splines. These are functions that are polynomials of specified degree between specific points, termed "knots," for which the function and its derivatives up to one less than the cited degree are continuous across knots. Among the most important splines are so-called B-splines, which are non-negative, have bounded support, and sum to one at each point. Karlin proved the total positivity of the B-spline collocation matrix, a result of some practical consequences in the design of curves and surfaces. He used deep topological methods to describe a function that passes through prescribed data and that has the least maximum absolute derivative of specified degree in a prescribed interval. While there had been previous work on the subjects, Karlin's is definitive and is a complete solution to this problem. He clarified the importance of what are termed "perfect splines" that enabled solution of the "Landau-Kolmogorov" problem. Karlin gave a fundamental theorem of algebra for monosplines and established a Gaussian quadrature for B-splines, resolving a conjecture of Schoenberg.

Among Karlin's Princeton classmates who also went on to great distinction was the late Theodore (Ted) Harris of RAND and the Department of Mathematics at the University of Southern California. His *Theory of Branching Processes,* published in 1963, influenced probabilists, and also Karlin and his students. One of them, K. Athreya, went on to coauthor a book on the subject nine years later. These random processes, as Sam Karlin formulated them, are examples of "Markov" processes, whereby for any fixed time, the future and past are independent, given the present. Path-breaking work by Karlin and McGregor about total positivity, transition kernels for branching and related birth and death stochastic processes, and applications such as to the successive counting of ballots was mentioned. The so-called transition semi-groups for birth and death processes are "self-adjoint." This fact, which means a sort of symmetry, enables spectral techniques to be brought to bear upon the study of such processes. An explicit spectral decomposition is possible. Karlin studied the asymptotic behavior of "stationary distributions," distributions for the process that are unchanged under shifts in time, in the most difficult case, the "critical case." To get a feeling for this case, think of a population that evolves in time where the expected (average) number of surviving offspring of each member of the population is exactly one. Among other topics to which he lent insight are those of embedding discrete time branching processes in continuous time Markov branching processes; embedding urn schemes, that is, probabilistic schemes whereby one samples from an urn with particular composition of balls and replaces them with fixed numbers of balls of the color drawn and/or of other colors of other balls in the urn; and branching processes in "random environments."

Karlin published a widely used textbook on stochastic processes, with second and later expanded editions written in collaboration with Howard Taylor. These books contain a remarkable diversity of examples and problems derived from the many scientific fields in which Sam Karlin had contributed directly. Indeed, these textbooks are unique in their ability to demonstrate the applicability of stochastic process models to deep problems in many areas of science.

Karlin began his work on theoretical population genetics in the early 1960s. Early research involved application of probability and mathematical analysis to models of genetic evolution that were developed by Sewall Wright and Ronald Fisher. Karlin and McGregor used their earlier research on branching processes to produce generalizations of the Wright-Fisher process, the standard framework for studying the role of chance effects in evolution. This led to a series of studies of the role of diffusion theory approximations in these stochastic evolutionary models. The first 10 years of Karlin's work on population genetics saw formalization of the theory of evolution under mutational processes and multiple loci, evolution under fluctuating sizes of populations, as well as what might be expected for the frequency distribution of protein variants collected in finite populations subject to mutation. These and related matters are summarized in a book, published in 1969.

Walter Bodmer, the next to last student of Ronald Fisher, came to Stanford in 1961 to work as a postdoctoral student of Nobel Prize winner Joshua Lederberg. He and Karlin were responsible for making Stanford the center of rigorous mathematics in population genetics and evolution during the 1960s and '70s. Karlin's studies of evolution under the joint effects of linkage and selection became the standard for future work on multilocus theory. He brought others doing similar research to Stanford, to expose himself to new biological problems, that invariably led to new mathematical formulations of such problems as the evolution of quantitative traits, or population subdivision, or sex determination and the sex ratio (regarding which he wrote a book with S. Lessard), and the evolution of altruism. His deep knowledge of functional analysis was invaluable to his work on posing and solving central problems in evolutionary population genetics. He emphasized the importance of work on applied problems in biology to his continuing mathematical work on total positivity, approximation theory, combinatorics, and probability. Karlin's influence on the way population genetics was conceptualized cannot be overemphasized.

In recent decades, Karlin's principal areas of concern were molecular biology and bioinformatics[1]. He pioneered the method for estimating the likelihood of molecular subsequences within genes and proteins. This work, published together with Stephen Altschul, formed the essential basis for the most highly used sequence similarity program, BLAST (Basic Local Alignment Search Tool). The program enables comparison of a new molecular sequence with a large database of protein sequences so as to discover strong similarities between the query sequence and a known sequence. The object is to identify the structure, function, and other properties of the query sequence. Karlin and collaborators developed other methods for characterizing biological sequences, including genome signatures and amino acid clusters.

Karlin's comprehensive analysis of the nonrandom distribution of oligonucleotides within genomes demonstrated—more directly and accurately than in any prior literature—that the pattern of dinucleotide relative abundance is nonrandom and much more uniform within genomes than between genomes, thereby giving each species a unique dinucleotide signature. He developed a more effective method to analyze patterns of codon usage than was previously available and classified genes into highly expressed, poorly expressed, and alien based on the correlation s between codon usage and protein expression levels in well studied species such as *E.coli*. He boldly postulated and published supporting evidence that the expression levels in other species could be inferred from a similar breakdown into statistical classes of codon usage patterns.

With Ph.D. student Chris Burge, Karlin developed a statistical model for human genes that enabled them to locate all putative genes in the human genome with high precision. This method, GenScan, has been used to identify locations of genes in the Human Genome Project and, in modified form, in other genomes.

The depth and breadth of Karlin's research is extraordinary. Perhaps even more impressive, however, was his unparalleled role as advisor and teacher of Ph.D. students. Karlin's students have attained senior positions at institutions ranging from Harvard Business School to the Department of Biology at MIT, to the Department of Biological Sciences at Stanford, Departments of Mathematics from UCLA to Stanford to the Technion, Departments of Statistics at Berkeley, the Hebrew University, Purdue University, and Iowa State University, the School of Medicine at Stanford, the Office of Population Research at Princeton, the RAND Corporation, IBM, the National Institutes of Health, and many other important scientific venues. Quite deservedly, these remarkable former students have chaired major departments, have been elected to all manner of honorary academies and have edited major journals, have written important books, and have given many honorary lectures. One former student said that Karlin had, "an uncanny sixth sense about the capabilities, interests, and psychological makeup of each student. He … knew how to pull the maximum [from each], when to intervene with close guidance, [and] when to leave [each student] alone to struggle." This gift is so very rare, and we are fortunate that Samuel Karlin used it to guide his teaching for so many decades.

---

[1] Indeed, over the last 17 years, when asked what his field was, Karlin answered that it was molecular biology.

Karlin is survived by widow Dorit Carmelli of Palo Alto, children Kenneth of Baltimore; Manuel of Portland, Oregon; and Anna of Seattle; stepson Zvi Carmelli of Germany and Israel; and nine grandchildren.