

DEPARTMENT OF CHEMISTRY

THE UNIVERSITY OF KANSAS LAWRENCE, KS 66045

July 1, 1988 - June 30, 1989

FROM THE CHAIRMAN

A year has past since I assumed the chair of the Chemistry Department. It has been more of a task than I had imagined, attesting to the excellent organization and administrative skills of my predecessor, Marlin Harmony. During my brief tenure as the chair, I have truly come to appreciate Marlin's talents for administration.

On the whole, this year has been a good one for us. In August, we welcomed Daryle Busch and his wife, Geri, to the Department along with several of Daryle's students. Another plus was the first-year graduate student class which was one of the strongest groups we have seen in years. Several fellowship recipients were among the group of seventeen new students who arrived in the Fall; the end of the Spring semester found them academically strong and eager to get on with their research.

Several members of the faculty have received awards this year for distinguished research and outstanding teaching. Major awards were presented at national meetings to Buzz Adams, Ted Kuwana and Shih-I Chu. Several younger faculty were recognized with "beginning investigator" grants or awards to support and encourage their research programs. Several others who have received recognition are also listed in the NEWS OF FACULTY section.

Our undergraduate Class of 1989 was outstanding with twenty eight students completing their B. A. and B. S. degree requirements this Spring. Most are returning to school in the Fall attending various graduate schools and medical schools around the country. It is noteworthy that eleven of the twenty eight were recognized for their scholastic achievements at the commencement ceremonies on May 21st. Seven were among the 52 University graduates who earned Highest Distinction, and four were among the 110 who earned Distinction. One of these, Steven St. Peter, was a finalist in the nationwide competition for a Rhodes Scholarship.

The second year of the State's Margin of Excellence support for Regents Institutions helped augment faculty salaries, making them more competitive with our peer institutions. The University again fared well. Unfortunately, the Margin funding did not address the critical need for new instrumentation, for maintenance and replacement of our older equipment and for increased expenses of the Department's general operation. We continue to seek additional support from federal agencies and foundations in order to provide state-of-the-art facilities for our faculty and students. I must emphasize that your support through endowment gifts has greatly assisted us in the past and is just as vitally important today.

The Department has begun the development of a ten-year plan with an in-depth self-study which should be completed at the end of the fall semester. This will serve as the master plan for our future direction and growth. Important considerations addressed by this study include faculty additions,

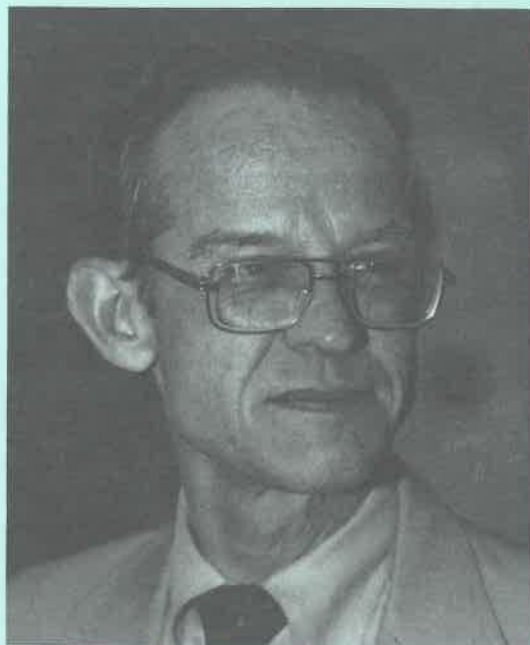
concerns about our graduate and undergraduate programs, recruiting of graduate students, industrial, federal and state support for research, and Departmental peer review, all of which are vital components of the comprehensive Departmental program. A principal component of our plan is the search for new faculty. As noted in previous newsletters several of the faculty have recently achieved emeritus status and their contributions to the department's activities must be taken up by the newer additions. We intend to bring in new faculty in order to continue the special blend of educational and scholarly activity upon which this Department has built such a remarkable tradition and reputation.

I invite you to browse through this year's Newsletter, both to look for familiar names and faces from your years on Mt. Oread and to learn of some of the changes that have occurred since you left. You will also find that we have added a new section to our Newsletter, an account of the research being conducted by our faculty. This year's article, entitled "Chemical and Biological Origins of Enzyme Catalytic Power," was written by Richard L. Schowen, Summerfield Professor of Chemistry and Biochemistry.

In closing, let me encourage you to keep in touch with us. If you have news items which you would like us to include next year, please take a few minutes to write them down and forward them to me. We would really appreciate hearing from you.

Richard S. Givens

HARMONY RECEPTION



Marlin D. Harmony

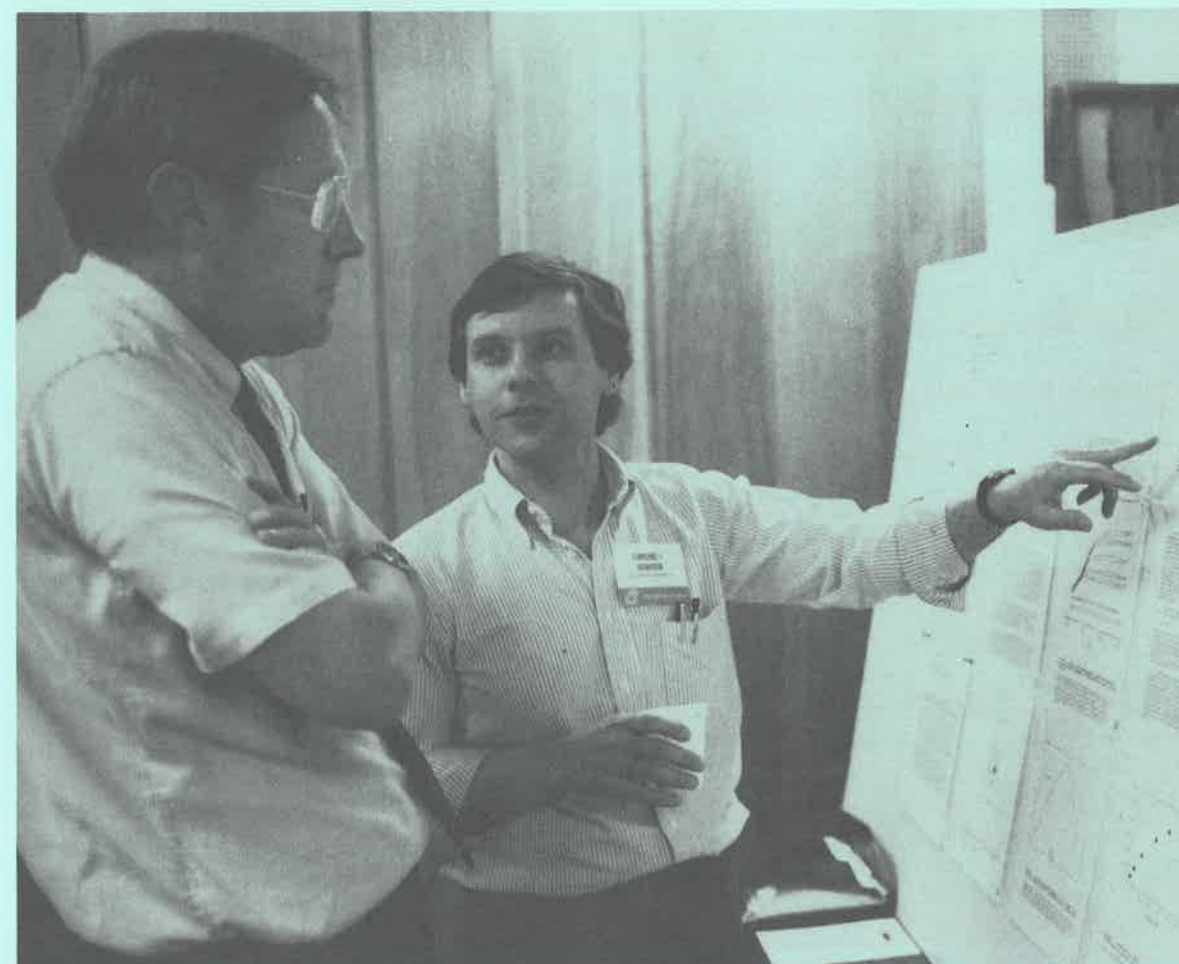
Some 250 guests attended a Department-sponsored reception for Professor and Mrs. Marlin Harmony in honor of Marlin's retirement as chairman of the Department. The event was held from 4:00 to 6:00 p.m. on October 4, in the Adams Alumni Center. At the close of a short program, Marlin's colleagues presented him with gifts of a compact disk player and a collection of disks as tokens of their appreciation for his contributions to the Chemistry Department and the University. The festivities ended with Kristin Mertes at the piano, leading the guests in singing "Marlin's Song", the lyrics of which she had written and set to the tune of "Hello, Dolly".

BIOANALYTICAL WORKSHOP

The second International Bioanalytical Workshop sponsored by the Center for Bioanalytical Research (CBAR) at the University of Kansas was held from May 21-24, 1989. The meeting, which was organized by Professor George Wilson was attended by over one-hundred scientists from universities and private corporations around the world.

The four day workshop featured twenty lectures by invited speakers and thirty-four poster presentations of current research in the rapidly expanding area of bioanalysis and focusing primarily on ultrasensitive analysis of biologically important molecules. Among the topics covered were microdialysis sampling techniques, solvent extraction by segmented flow, new reagents for on-line and off-line derivitization of nucleophilic analytes, computer-aided multichannel detection, transmembrane signaling, catalytic antibodies, receptor-based biosensors, subcutaneous glucose sensors, electroreleasing membranes, and laser detection for CZE.

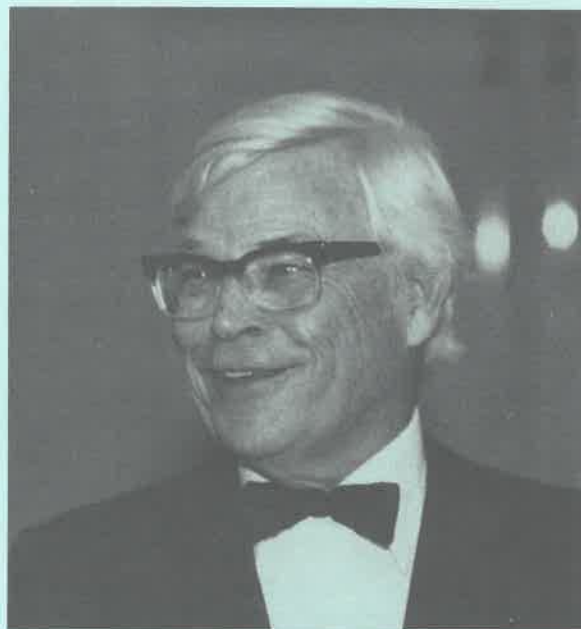
The workshop was supported in part by Eastman Kodak, Marion Laboratories, Yellow Springs Instruments, Inc., and Eli Lilly and Company, with the latter sponsoring a mini-symposium on immunology and bioaffinity.



George S. Wilson, KU, and Edmond F. Bowden, North Carolina State

34th ANNUAL AWARDS BANQUET

The annual Departmental Honors luncheon was held in the Big 8/Jayhawk Room of the Kansas Union on May 6, 1989, with Alfred J. Lata once again serving as toastmaster. Following the presentation of the awards listed below, William J. Argersinger, Professor Emeritus of Chemistry and Dean Emeritus of the Graduate School at the University of Kansas, spoke to the audience, recounting the contributions American chemists have made over the past two hundred years to our knowledge, our health, and our comfort, and pointing out the intellectual, the scientific, and the societal challenges that still remain.



William J. Argersinger

General Chemistry: Two-semester course (A \$40 book certificate)

Robert C. Alvers Scott L. Page
Robert W. Thompson Kirsten A. Unger

Organic Chemistry: One-semester course (A \$40 book certificate)

Catherine S. Spencer

Organic Chemistry: Two-semester course (A copy of the Merck Index)

Jason M. Coleman Kevin E. Hughes Kenon S. Qamar

Analytical Chemistry: (A \$45 book certificate)

Thomas W. Burgoyne Kathryn L. Newell

Physical Chemistry: (A \$50 book certificate)

Sarah E. Baptist Robert A. Wood, Jr.

The Owen W. Maloney Scholarship: To outstanding first-year students in Chemistry (\$900 scholarship and brass jayhawk)

Wei Wu Rhonda K. Yantiss

The Clark A. Bricker Award: To an outstanding second-year chemistry major (\$500 and plaque)

Jason M. Coleman

The Jacob Kleinberg Award: For outstanding research by a junior (\$500 and pen set)

DeAnna L. Puckett

Special Award for Outstanding Achievement in Chemistry to Graduating Seniors Pursuing a Career in Medicine: (Certificate)

Gregory A. Cronin Michael L. Kasper Subramanian Paranjothi
Steven L. St. Peter A.J. Shah Robert A. Wood, Jr.

American Institute of Chemists Award: (A certificate and subscription to AIC Journal and membership)

Sarah E. Baptist

Alpha Chi Sigma Award: To outstanding graduating seniors in chemistry and chemical engineering (Inscription of name on plaque)

David P. Heitmeyer John D. Stuber

The H.P. Cady Award: To an outstanding first-year graduate student (\$200 and plaque)

Michael A. Letavic

Outstanding First-Year Teaching Assistant (\$200 and brass jayhawk)

Michael A. Letavic

The Ray Q. Brewster Award: To an outstanding graduate teaching assistant (\$300 and jayhawk plaque)

Mark A. Williamson

Phillips/McCollum Summer Research Fellowships: To outstanding advanced graduate students (\$1800 summer fellowship)

Phillip S. Athey Steven D. Dietz Sarah A. Mounter

Higuchi Doctoral Progress Award (\$750 and plaque)

Steven A. Soper

Graduate School Awardees

Michael A. Letavic (Graduate School Summer Fellowship)
Rita Palsmeier (Graduate School Summer Fellowship)
Steven A. Soper (Graduate School Summer Fellowship)
Beth Thomas-Miller (Graduate School Dissertation Fellowship)

NEWS OF FACULTY



Ralph N. Adams

Ralph (Buzz) Adams was honored by his former students and other colleagues by the establishment of a \$500,000 endowment fund. The fund drive was co-chaired by Ted Kuwana of the KU faculty along with Dr. Don Leedy (Proctor and Gamble, Cincinnati) and Dr. Gus Manning (Assay Technology Inc., Palo Alto). Major contributions from the Stark Charitable Trust (Sarasota, FL) and from former KU Professor J.K. Lee and his wife Ingrid, pushed the fund over its goal. The fund's income will be used to support Adams' research until his retirement, at which time it will be used to attract a prominent scientist to KU to continue work in areas related to those of Adams. The formal celebration and announcement of the honor was held on May 5, 1989. Buzz presented a seminar entitled "Thirty-Five Years of

Organic Electrochemistry" in which he mentioned nearly every one of his former undergraduate, graduate and post-doctoral students, and Kuwana, Leedy and Manning each reminisced briefly. A gala reception at the Watkins Room in the Kansas Union capped off the celebration.

Shih-I Chu became the third Chemistry Department faculty member to be selected by the University to receive one of the Higuchi/Endowment Association awards upon his selection last Fall as the Olin Petefish awardee in Basic Sciences. The honor was announced by the Chancellor at the opening convocation on Aug. 29, 1988. The award includes a \$10,000 unrestricted research stipend. Previous Chemistry awardees include Dick Schowen and Ralph Adams.

Tom Engler was one of three national recipients of a Lilly Grant which provides \$15,000 in unrestricted research support over a two year period.

Grover Everett returns in July from a half-year sabbatical leave in Australia. He split his time between two locations, the University of Western Australia in Perth, and the James Cook University in Townsville (Queensland). As always, Grover and Carolyn will surely have an extensive photographic record of their travels.

Richard Givens received a Mortarboard Distinguished Teaching Award.

Carey Johnson received a major five-year award from the National Institutes of Health. The FIRST Award (First Independent Research Support and Transition Award) supports newly independent biomedical investigators. It will provide \$350,000 to support Carey's laser spectroscopic studies of bacteriorhodopsin, a protein similar to rhodopsin in the human eye.

Emeritus Professor Jake Kleinberg reached the coveted 50-year membership

status in the American Chemical Society this year. And to show that he has not slowed down, the 3rd Editions of his two textbooks, "Chemistry" and "Chemistry with Inorganic Qualitative Analysis" were both published by Harcourt Brace Jovanovich. The latter book will be used in our general chemistry classes this year.

Ildiko Kovach has accepted a position as Associate Professor of Chemistry at The Catholic University of America, Washington, D.C. where she will teach courses entitled "Mechanistic Chemistry" and "Survey of Organic Reactions" to first-year graduate students. For the present, Ildiko will continue her research program here at KU, where she is an Associate Scientist.

Ted Kuwana, Regents Distinguished Professor of Pharmaceutical Chemistry and Chemistry, received the sixth Charles N. Reilley Award from the Society for Electroanalytical Chemistry. The award was presented at the annual Pittsburgh Conference and Exposition on Analytical Chemistry in Atlanta, GA, on March 8th. Following the presentation, Ted presented a lecture entitled "Bioelectrochemistry: Reminiscing a Bit and Looking to the Future." Kuwana is the second awardee from KU. His mentor, Buzz Adams, was the 1985 recipient. The award is sponsored, in part, by Bioanalytical Systems, Inc. founded and headed by Pete Kissinger, a former postdoctoral student with Adams.



Ted Kuwana

Kuwana also spent three days at Wichita State University as Watkins Visiting Professor. He presented a public lecture "Taking University Research to the Marketplace: Can Kansas Compete?" in addition to two research seminars in the Chemistry Department.

Kristin Mertes was one of two people honored by selection this year to the KU Women's Hall of Fame. The award was presented and announced publicly on April 18, 1989, at the annual Women's Recognition program. Kristin has also been awarded an NSF Career Advancement Award which will permit her to spend a semester at California Institute of Technology sometime during the 1990 calendar year. She plans to work in protein crystallography and may couple the stay with sabbatical leave also.

Having been promoted to the rank of Senior Scientist, Ken Ratzlaff, Director of the Instrumentation Design Laboratory, had the additional pleasure of spending the Fall semester of 1988 on sabbatical leave at the University of Arizona. Ken reports the time was well-spent studying new optical detection methods.

Capping off his always busy calendar, Richard Schowen, was honored by his former students at an informal 25-year reunion held at the Midwest ACS meeting in Iowa City and organized by Dan Quinn and K.S. Venkatasubban. Following this, he traveled to the German Democratic Republic in December where he received an honorary degree (*Dr. rer. nat. honoris causa*) from Martin Luther University in Halle-Wittenberg. He presented an award lecture titled "Biomedical Science and World Peace" in German.

DEGREES CONFERRED

The University of Kansas held its 117th Annual Commencement on May 21, 1989, and thirty degrees in Chemistry were awarded. Twelve of these were B.A. degrees, ten were B.S. degrees, five were M.S. degrees, and three were Ph.D. degrees.

Seven of our undergraduates graduated with "Highest Distinction": Sarah Evelyn Baptist, David P. Heitmeyer, Jack Q. Jaeger, Subramanian Paranjothi, George G. Robinson II, Steven L. St. Peter, and Robert A. Wood, Jr. Another four majors graduated with "Distinction": Gregory A. Cronin, Keith Lawrence Goldberg, Devin M. Sherubel, and Amy Diane Seeber. Sarah Baptist and David Heitmeyer also received Departmental Honors.

M.S. degrees were granted to Clinton Dave Bryan, Jon N. Cammack, Philip James Franklin, Chan-Ho Park, and James Edward Ray.

Those granted Ph.D. degrees, along with their previous degrees, research areas, dissertation titles and present position, if known, are the following:

Elizabeth Gayle Bibbs (B.S., 1984, Stephen F. Austin State University, Nacogdoches, Texas), analytical; Distributions of Amino Acids in the Intracellular and Extracellular Fluids of the Rat Brain; Scripps Institute, San Diego, California.

Jeffrey Alan Bibbs (B.S., 1984, Stephen F. Austin State University, Nacogdoches, Texas), organic; A Transition State Characterization of the Acid-Base Catalytic Features of Serine Protease Action; Scripps Institute, San Diego, California.

Kwangshi Wang (B.S., National Chung Kung University, Tainan, Taiwan, R.O.C.), physical: Nonperturbative Treatments of the Interaction of Light and Matter. Kwangshi was awarded the 1989 Dorothy Haglund Prize by the Graduate School. This prize, which recognizes the person submitting the outstanding doctoral dissertation in the University, was made possible by Professor and Mrs. William J. Argersinger and others through the cooperation of the KU Endowment Association and has been awarded each year since 1979.

GRANTS TO THE DEPARTMENT

Again this year, we have experienced an increase in support from federal agencies for our research programs. The National Science Foundation, National Institutes of Health, Department of Defense, Department of Energy, the National Institute of Standards and Technology (formerly NBS) and Department of Agriculture have provided more than \$1.61 million to the individual and multi-investigator interdisciplinary research programs of our faculty. In addition, foundation and corporate support totaling nearly \$0.5 million has been obtained from the Petroleum Research Fund (ACS), Research Corporation, the Wesley Foundation, G. D. Searle, Eli Lilly, Linde Air Products Company, and 3M. The Center for BioAnalytical Research, comprised of faculty and students in Chemistry and Pharmaceutical Chemistry, also received over \$300,000 for support of projects in Chemistry from the State's Kansas Technology Exchange Commission and from Oread Laboratories. Complementing

this support, the College provided \$300,000 in computational services to our research programs.

Gifts from alumni and friends and unrestricted grants from corporate sponsors have provided over \$27,000, while income from our Endowment accounts has added another \$75,000 for research and scholarly activities of the Chemistry Department. Several of our young faculty have received unrestricted (often unsolicited) grants from corporate sponsors (See NEWS OF FACULTY earlier in the Newsletter) in recognition of the quality and significance of their emerging programs.

As alumni and friends of the Department, you have been generous with personal support and influential in generating corporate and foundation contributions. Your gifts are an important reason that the Department has been able to maintain its high quality during the past decade, and they will enable it to continue its ascent among the outstanding departments into the 1990's and beyond. These monies are given as scholarships which bring bright, young graduate and undergraduate students into our programs, are used for the purchase of new instrumentation which give our younger faculty especially an early boost in their research, and permit us to attract quality lecturers and researchers to the Department for seminars and consultation. Some of these people have later returned to join us a faculty colleagues. Little of this is possible without your annual Endowment gifts and support.

DEATHS

Mathias Mertes, University of Kansas Professor of Medicinal Chemistry and husband of Chemistry Professor Kristin Mertes, died at their home on April 6, 1989, of an apparent heart attack. He was 56.

Matt and Kristin worked together on joint research to synthesize molecules that mimic biological processes. In recent years the couple had collaborated with Nobel Prize-winning French scientist Jean-Marie Lehn. Kristin will carry on the research programs in both departments through a joint appointment arranged with Medicinal Chemistry.

Matt was born April 22, 1932, in Chicago. He received a bachelor's degree from the University of Illinois in 1954, a master's from the University of Texas in 1956, and a doctorate from the University of Minnesota in 1960.

He joined the Medicinal Chemistry Department as an Assistant Professor in 1960 and was promoted to Associate Professor in 1964 and to Professor in 1968. He served as Chairman of the Medicinal Chemistry Department in 1974. He was also the former Chairman of the American Chemical Society Division of Medicinal Chemistry.

Matt was cited twice for teaching excellence by the Rho Chi pharmacy society. He won an Exxon teaching award in 1986, and had been a finalist for the HOPE Award given annually by the senior class at KU.

Chemical and Biological Origins of Enzyme Catalytic Power

by R.L. Schowen

Enzyme Action as a Chemical Problem

Enzymes, the protein macromolecules responsible for essentially all chemical conversions in living systems, are molecules that instantly claim the attention of any chemist interested in dynamics. They are catalysts that produce huge rate accelerations - no acceleration factor less than 10^5 is respectable and values above 10^{15} are known - and they do so under eminently agreeable conditions: temperatures around 35-40 C, aqueous solvent, neutral pH. Furthermore, each enzyme catalyzes a single reaction or at the most a small number of reactions, often choosing a single stereochemical result from among several. These two characteristics, very high catalytic power and very high specificity are the essential features of all enzymes.

From another viewpoint, however, these impressive properties of enzymes should perhaps not be considered so surprising: enzymes are extremely large molecules (MW at least several thousand, commonly several hundred thousand and often several million), and thus have plenty of molecular structure to work with, and they have been iteratively designed, redesigned and fine-tuned over three or four billion years of molecular evolution. Our research group has been engaged for about the last two decades in an effort to understand, from the chemical perspective, what kinds of interactions and strategies enzymes employ in the generation of catalytic power and how these choices were made instead of other possibilities by the mechanism of biological evolution. We have made some progress on the first aim and less on the second.

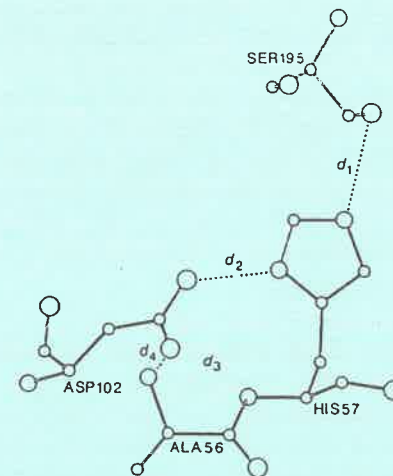
What Have We Learned and Who Learned It?

I would like to devote the remainder of this article to brief summaries of some of the findings that our group has reached. This involves me in the problem of which undergraduate, graduate and postdoctoral coworkers to name, and which findings to emphasize. I will solve the problem by giving the names of NO coworkers in describing our results, and by admitting at this point that I have chosen particular cases for description not because they are more important than those omitted, but because they are easier to treat in an article of this kind. I WILL name our collaborators because they are not as used to my rudeness as are my students and postdocs, and because I want to give the reader an indication of how broadly collaboration in this area is possible.

The omission of the names of my coworkers, however convenient it may be for purposes of fairness among them, cannot be taken as any indication of their less than critical importance to the work. Any other KU faculty member can testify as well as I can to the privilege it is to work with the students who join our programs at every level. In my own case, essentially every problem I have presented to a coworker has been greatly improved by the cleverness, diligence and productivity of these excellent young scientists.

Charge-Relay Catalysis in Serine Proteases

One of the earliest problems that our group attempted to solve in mechanistic biochemistry was that of charge-relay catalysis. The crystallographer David Blow and his colleagues, in their studies of the structure of the enzyme chymotrypsin, noted that there existed in the active site of the enzyme a chain of hydrogen bonds (see illustration).



Charge-relay system: Tsukada & Blow, J. Mol. Biol. 1985, 184, 703.

relay - it could instead hold the structure intact or orient the enzyme functional groups for catalysis, for example. To answer this question, our group developed the proton-inventory method, which can measure the number of protonic centers that contribute to a solvent isotope effect (rate difference in heavy water [DOD] compared to light water [HOH]). For example, two sites would contribute to the isotope effect produced by proton-bridging at the two hydrogen bonds of the charge-relay system.

In the proton inventory, one measures the rates as a function of the atom fraction of deuterium in mixtures of HOH and DOD. Our group introduced this quite old concept to enzymology, starting in the early 1970's, with the goal of "counting" the sites contributing to a solvent isotope effect. In this simple form of the theory, a plot of the rate constant vs. atom fraction of deuterium will be linear for one site, quadratic for two sites, etc.

We find that with "deficient" or "truncated," unnatural substrates (e.g., small esters) serine proteases give linear proton inventories and thus one site contributes to the isotope effect. This means that charge-relay catalysis does not occur with these substrates. However, when any serine protease is presented with a reasonably long-chain substrate (at least three or four residues), which begins to simulate a natural polypeptide substrate, the rate increases by a factor of 10-100 and the proton inventory becomes quadratic (two sites). This suggests that the natural substrate structure is capable of activating the enzyme to become a charge-relay catalyst. Since the enzyme and the substrate have co-evolved in the course of biological history, the catalytic mechanism has emerged as a property not of the enzyme alone but of the enzyme-substrate system.

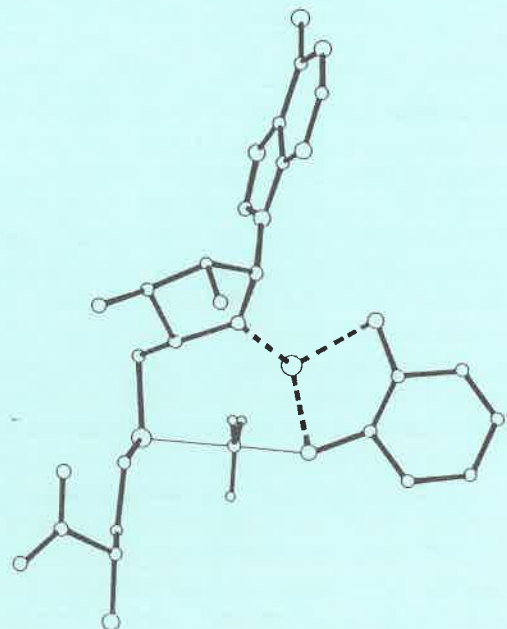
This interpretation has recently been confirmed in collaborative work with Charles Craik at the University of California-San Francisco and Ross Stein at Merck, Sharp & Dohme. Charles Craik used the techniques of recombinant-DNA technology to manufacture a mutant form of the serine protease trypsin. The mutant has the non-basic residue asparagine in place of the normal aspartate of the charge-relay chain. We find the mutant can no longer distinguish "truncated" from "natural" substrates: they react at the same rates and both give linear proton inventories. The substrate-activated catalysis which generates a two-site isotope effect and the attendant rate increase thus arises from the aspartate-histidine-serine charge-relay system.

Similar results are being obtained with more complex serine proteases, such as dipeptidylpeptidase-IV. We are continuing studies of this enzyme with the group of Alfred Barth of the University of Halle in the German Democratic Republic.

Compression in the Catalysis of Nucleophilic Displacement

Transmethylases are enzymes that catalyze S_N2 reactions at methyl centers, a reaction that chemists find difficult to accelerate under mild conditions. We have studied catechol-O-methyltransferase, a transmethylase that employs S-adenosylmethionine (illustration) as the methyl donor. One of the most successful of known enzymes, it produces a catalytic acceleration of over 16 powers of ten. This and similar enzymes are important in brain function, reproduction and the destruction of toxins. Ronald Borchardt of the KU Pharmaceutical Chemistry Department is the world's leading expert on transmethylases. Our group has collaborated with his group and with James Coward, now at the University of Michigan, in studies of transmethylation.

The effects of C-13-for-C-12 substitution and deuterium-for-protium substitution in the transferring methyl group were measured for enzymic and non-enzymic reactions. Theoretical predictions were then made of how these isotope effects would vary with transition-state bond distances, and the predictions were compared with the measured effects. From the results, we concluded that the enzyme is producing its large catalytic acceleration by compressing the methyl donor tightly against the methyl acceptor. This gives the transition state a unique, "tight" structure (see the illustration) very different from the structure of the preceding reactant-pair and the succeeding product-pair. The unique structure of the transition state is strongly complementary to the evolved enzyme structure and the two interact with a large release of free energy, and thus a large catalytic acceleration is generated.



Since the publication of this suggestion, Ian Williams at the University of Bristol in England has tested the concept theoretically. He confirms that this kind of compression does indeed generate catalytic acceleration and that, without such compression, there is no catalysis by his quantum-chemical model enzyme.

Cofactor-Requiring Enzymes

The enzymes described above perform their catalytic tasks by means of interactions solely between the amino-acid structures of the enzyme and the structures of their substrates. The opportunities this offers are too restricted to accomplish all that nature needs to do, and so molecular evolution has invented cofactors, which are small molecules with some catalytic potential of their own; they are bound to enzymes and together the cofactor and enzyme carry out the catalytic task. Two examples studied in our group are the B-vitamins pyridoxal phosphate and thiamin pyrophosphate.

The pyridoxal-dependent enzyme GABA transaminase, which destroys the neurotransmitter γ -aminobutyric acid (GABA), was studied in collaboration with colleagues in the KU Center for Biomedical Research, including Elias Michaelis and Matthias Mertes. Matt Mertes's unexpected death earlier this year was a great personal and scientific tragedy for all of his colleagues here and elsewhere.

The thiamin-dependent enzyme pyruvate decarboxylase generates acetaldehyde, which is then converted to ethanol in fermentation by yeast. Here our studies have been joint with the group of Alfred Schellenberger of the University of Halle, German Democratic Republic, who has been visiting KU this summer.

Isotopic studies with both of these cofactor-requiring enzymes show that the various steps in the reaction mechanism, binding of substrates, chemical interconversions such as prototropic shifts in GABA transaminase or decarboxylation in pyruvate decarboxylase, and then release of products, proceed at very similar rates so that no single step is fully rate-limiting. This is shown for example by comparing isotope exchange rates with overall reaction rates (they are similar) or kinetic isotope effects on overall rate with those on individual steps (the former are smaller, showing that other steps than the isotope-sensitive step also partly limit the rate).

In our view, this situation (different from that of non-enzymic reactions, where a single step commonly limits the rate) is just what is expected for an evolutionarily filtered enzyme. Molecular evolution will have continually selected for those mutant enzymes with the lowest transition-state energies and the highest reactant-state energies (leading to low barriers and high rate). The eventual result should be that all reactant-state energies are similar to each other and that all transition-state energies are similar to each other - thus all steps proceed at about the same rate. The same expectation was arrived at earlier, from a different viewpoint, by Jeremy Knowles of Harvard University and John Albery of Imperial College.

NEWS OF COLLEAGUES, FRIENDS, AND ALUMNI

Anton F. Ahrens (M.S. 1986), who is teaching chemistry at Topeka High School, Topeka, Kansas, and three of his students were selected to participate in government-sponsored science programs this summer. Anton is at Oak Ridge National Laboratory working on a global warming project supported by the Department of Energy.

Keith B. Allen (B.A. 1982) received his M.D. from the University of Kansas School of Medicine in 1986 and is now a third year general surgery resident at Emory University, Atlanta, Georgia.

Francisco Alvarez (Ph.D. 1985), who joined the Pharmaceutical Products Division of Abbott Laboratories as a research scientist in August, 1987, received that company's "Rookie of the Year Award" which recognizes the new employee who has made the biggest impact on the organization in terms of the quality and quantity of his or her scientific and technical contributions.

Elverson E. Baker (A.B. 1937), who retired from the U.S. Army with the rank of Colonel in 1964, served as Deputy Director of the NASA Scientific and Technical Information Facility in Baltimore until 1980. Since his retirement from Informatics General Corporation in 1984, he has been active in civic activities in Rockville, Maryland.

Roger N. Bardsley (B.S. 1978) is working at the Midwest Research Institute in Kansas City, Missouri.

W.H. (Bill) Breckenridge (B.S. 1963), Professor of Chemistry at the University of Utah, and his colleague, Dr. Benoit Soep of the University of Paris, have been awarded a joint U.S.-France Binational Research Grant. This grant, sponsored by the National Science Foundation (U.S.) and the Centre Nationale de Recherche Scientifique (France), will permit the pair to continue their successful collaboration involving laser spectroscopy and dynamic studies of weakly bound complexes in supersonic jets. Bill laments that this project will force(!) him to spend a month in Paris each year, but adds that he is actually beginning to speak some French.

George H. Cady (A.B. 1927, A.M. 1928), Professor Emeritus at the University of Washington, received the first Prix Henri Moissan for research in fluorine chemistry in a ceremony at the 12th International Symposium on Fluorine Chemistry, held at the University of California, Santa Cruz, in August, 1988.

John E. Carpenter (B.S. 1982) received his Ph.D. in Chemistry from the University of Wisconsin. His thesis, entitled "Extension of Lewis Structure Concepts to Open-Shell and Excited-State Molecular Species", was carried out under the supervision of Professor Weinhold.

Jong-In Choe (Ph.D. 1981), Associate Professor of Chemistry at Chung-Ang University in Korea recently spent six months here at KU as a UNESCO Scholar working with Professor Marlin Harmony.

Dean K. Ellison (Ph.D. 1985) was promoted in January to the position of Research Fellow in the Analytical Research Department of Merck.

Greg Gerhardt (Ph.D. 1983) is now an assistant professor of psychiatry and pharmacology at the University of Colorado Health Science Center, Denver. He recently received a 5-year Research Career Development Award from the National Institute on Aging.

Jay Gingrich (B.S. 1983) is in his third year of graduate study at Duke University. Jay reports that his research project is going very well, and that he should finish up in another year with a combined M.D.-Ph.D. (Biochem).

Mike Gresser (B.A. 1967) has recently moved to Merck Frosst in Canada.

M. Dale Hawley (Ph.D. 1965) was appointed Head of the Chemistry Department at Kansas State University last year.

Dale D. Hirsch (B.A. 1984) and his wife **Anne M. (Tholen) Hirsch** (B.S. 1985) have both received their M.D. degrees this year and have just begun their residencies in Internal Medicine at the Oregon Health Sciences University in Portland, Oregon.

Stephen P. Jacober (M.S. 1989) has accepted a position as a computational chemist at Boehringer Ingelheim, Richmond, Connecticut.

Jon K. Jones (B.A. 1978) who received his M.D. from Kansas University School of Medicine in 1983, finished his residency in Internal Medicine in 1987 and is now in private practice in Wichita, Kansas. His wife, Pat, is working toward a degree in social work at Wichita State University. The couple have three children, ages 6, 4, and 2-1/2.

Jack G. Kay (Ph.D. 1960) Professor of Chemistry at Drexel University, Philadelphia, Pennsylvania, was recently elected as a Fellow of the American Association for the Advancement of Science.

The September 22, 1988, issue of the Journal of Physical Chemistry was organized as a memorial to **Edward K.C. Lee** (Ph.D. 1964), who died on September 19, 1986.

Hudson Luce (B.S. 1981) has recently started a postdoctoral appointment at the University of Cincinnati under Professor Rakesh Govind. Hudson will be working on ab initio calculations applied to reactions for organic synthesis.

Hideomi Koinuma, a former postdoctoral fellow with Professor Richard Schowen, became Professor at the Tokyo Institute of Technology.

Carla B. Dittman McBain (M.S. 1984), who received her Ph.D. in Polymer Science from the University of Akron in 1987, is employed as a Chemist I by the ICI Division of the Glidden Company. In February of 1988, she and husband **Doug McBain** (Ph.D. 1984) became the happy parents of a son, Arthur Scott McBain.

Bogdan Marciniak, former postdoctoral fellow with Professor Richard Schowen, has become Rector of the University of Poznan in Poland.

Charles Martin (Ph.D. 1973) was promoted to Associate Scientist in the Dow Chemical Company, Lake Jackson, Texas.

Julio Mata (Ph.D. 1975) Professor of Chemistry at the University of Costa Rica, returned to KU as a Fulbright Fellow to work with Professor Richard Schowen. He is continuing a joint research project on protein glycation with Schowen and Professor **Hermina Gil** (M.S. 1987; Ph.D. Biochemistry 1988) of the University of the Andes in Venezuela.

Sally A. Meyer (Ph.D. 1987) has returned to her teaching position at Colorado College after she and husband **Mark Morgenstern** (M.S. 1986) had participated in the Postgraduate Research Program at Oak Ridge National Laboratory during the Summer of 1988. Sally has just recently been awarded a grant from the Research Corporation to Support her theoretical work at Colorado College.

Kristin Hansen Milbey (Ph.D. 1980) has moved from Monsanto to one of its spin-off ventures, Kinetek Systems, St. Louis, Missouri. Employed as a Senior Scientist, she is developing products for cell culture and protein purification based on hollow fiber membrane technology.

David E. Moody (B.A. 1972), Research Assistant Professor in the Department of Pharmacology and Toxicology at the University of Utah, received an appointment as Associate Director of the Center for Human Toxicology there in August, 1986. He recently was awarded a five-year grant from NIDA to pursue studies on "Polymorphism in the Metabolism of Drugs of Abuse".

Thomas J. Munyon (B.S. 1980) is Public Affairs Officer for the Naval Air Reserve in Jacksonville, Florida.

W. Frederick Oettle (Ph.D. 1971) will be beginning a career as an independent education/management consultant this Fall.

Richard Roberts (B.S. 1987) is currently completing his second year of graduate study, working toward his Ph.D. in Chemistry at Yale University under the supervision of Professor Donald M. Crothers.

Harry E. Robson (Ph.D. 1958) retired three years ago from Esso Research Laboratories in Baton Rouge, Louisiana and has been teaching at Louisiana State University since leaving Esso. He and his wife, Roberta, have been studying German in preparation for Harry's three-month visiting professorship at ETH in Zurich this summer.

Fred G. Rojas (B.A. 1980) received his M.S. degree from the University of Missouri at Kansas City in 1986 and is currently Q. A. Group Leader for Abbott Laboratories.

Rod Schoonover (B.S. 1986) received his M.S. degree in Chemistry from the University of Michigan in June, 1988, and is working toward his Ph.D. degree there, carrying out theoretical research on fractal kinetics.

Paul C. Shellito (B.A. 1973), who received his M.D. degree from Harvard Medical School in 1977, is currently Assistant Professor of Surgery at Harvard Medical School.

Lester L. Shipman (Ph.D. 1972) is a senior consultant in Artificial Intelligence for the Information Systems Department of DuPont. Les helped start the Artificial Intelligence effort at DuPont in 1985, and he reports that many expert systems have been built using the toolkit that he developed.

Steven St. Peter (B.A. 1989) was a finalist for the Rhodes Scholarship Competition. Steve, a native of Wichita, was one of two Kansas representatives in the six-state Midwest competition, from which four Rhodes Scholars were chosen.

William H. Taylor (Ph.D. 1986) is completing a year of postdoctoral work at Monash University in Australia.

Carl M. Unruh (M.S. 1954) returned to KU for a visit last Fall. He retired in June, 1986, after 34 years at Pacific Northwest Laboratories in Richland, Washington. There he was Senior Staff Scientist in the Radiological Sciences Department. As Department Manager he was responsible for 135 people and had a budget of some \$7 million. He has served as national President of the Health Physics Society. He and his wife Doris plan to move to the Olympic peninsula in the spring.

Richard M. Wallace (Ph.D. 1953) recently retired after a long career with DuPont at the Savannah River Nuclear Plant. He and wife June continue to live in Aiken, South Carolina.

George E. Walrafen (B.S. 1951), Graduate Professor of Physical Chemistry at Howard University, Washington, D.C., was the recipient of the 1988 Outstanding Research Award sponsored by the Academic Affairs Division of Howard University. This award was presented to George by Dr. James E. Cheek, President of Howard University, at a luncheon on November 29, 1988.

Wayne C. Wolsey (Ph.D. 1962), Professor and Chair of the Chemistry Department at Macalester College, was on sabbatical leave at Oak Ridge National Laboratory for the 1987-88 academic year, and has since resumed the chairmanship at Macalaster. He reports that the Fifth Edition of Chemical Principles in the Laboratory, co-authored by W.L. Masterton and E.J. Slowinski, will come out this current year.

Vaneica Young (B.A. 1969) received tenure and promotion to Associate Professor of Analytical Chemistry at the University of Florida, Gainesville, Florida.

LECTURE SERIES AND OUTSIDE SPEAKERS

Aavo Aaviksaar, Estonian Academy of Sciences, USSR, "Structure and Medium Effects in Acetylcholinesterase Mechanisms."

Elke Anklam, Hahn-Meitner Institute, West Berlin, "Cyclic Sulfur Radicals as Intermediates in Reactions of Selected Natural Sulfur Compounds."

Daniel Armstrong, University of Missouri-Rolla, "Cyclodextrins in Separations."

William J. Bailey, University of Maryland, "Biodegradable Polymers."

Jacqueline Barton, Columbia University, "Targeting DNA Sites with Metal Complexes."

W.H. Breckenridge, University of Utah, "Laser Excitation of van der Waals Complexes of Metal Atoms: Half-Collision Studies of Energy-Transfer and Chemical Reaction."

David Burgard, Proctor and Gamble Co., "Chemometrics and Analytical Data."

Shengamin Cai, Peking University, "Weak Photo Response of Iron Oxide Electrode and Iron Passive Films."

Michael Chetcuti, University of Notre Dame, "Organometallic Chemistry on Ni-Mo and Ni-W Bonds."

Jong-In Choe, Chung-Ang University, Korea, "High-Resolution Fourier Transform Spectra of HCN(IR), and Carbon Monoxide (Visible)."

Ralph E. Christoffersen, Upjohn Co., "DNA Probes and Molecular Quantum Mechanics."

Rob Coleman, Yale University, "Adventures in Natural Product Chemistry: Studies on CC-1065, FK-506 and Esperamicin."

John W. Connolly, University of Missouri-Kansas City, "Reactions and Rearrangements of $H(SiR_3)Se(CO)_4$."

Catherine Costello, Massachusetts Institute of Technology, "The New Dimensions of Mass Spectrometry."

Tony Czarnik, Ohio State, "Some Recent Studies on Bioorganic Chemistry Brought to Light."

Matyas Czugler, Hungarian Academy of Science Research Institute for Chemistry, "Symmetric Crystalline Molecular Associates."

Victor Day, University of Nebraska, "Is X-Ray Crystallography Really a Structural Panacea? Polyoxo Anions as a Case Study."

Peter B. Dervan, California Institute of Technology, "Sequence-Specific Recognition of DNA."

Dana Dlott, University of Illinois, "Ultrafast Laser Spectroscopy of Chemical Solids."

William Fateley, Kansas State University, "Hadamard Transform Spectrometry."

Warren Ford, Oklahoma State University, "Catalysts Supported on Colloidal Particles."

Kenneth R. Fountain, Northeast Missouri State University, "The Alpha

Effect Through Undergraduate Eyes."

Ekkehard Fluck, University of Heidelberg, "From Diphosphacyclobutadienes to Di- and Triphosphabenzenes."

George Flynn, Columbia University, "Ultrahigh Resolution Spectroscopic Probes of Collision Dynamics."

John Gladysz, University of Utah, "Generation and Binding of a Chiral Transition Metal Lewis Acid."

David G. Gorenstein, Purdue University, "Synthesis, Structure, and Mechanism of Hydrolysis of Cyclic Phosphonate Esters."

Michael Hermata, University of Missouri, "Lewis Acids in Organic Synthesis."

Gary M. Heiftje, Indiana University, "New Approaches to the Laser-Based Measurement of Rapid Events."

Dewey Holten, Washington University, "Primary Photochemical Processes in Wild-Type and Mutant Photosynthetic Reaction Centers."

Laurence Hurley, University of Texas-Austin, "Molecular Mechanisms of Small-Molecule DNA Interactions."

Eugene Inman, Eli Lilly & Co., "Analytical Challenges in Biotechnology: The Role of Fluorescence Spectroscopy."

Alajos Kalman, Hungarian Academy of Science, "Structure-Activity Relationships of the Histamine H_2 -Receptor Antagonist Cimetidines and Famotidines."

Jerome Karle, Naval Research Laboratory, "The Phase Problem in Crystallography: A Nobel Lecture."

S. H. Lin, Arizona State University, "Recent Developments in Radiationless Transitions."

Stephen J. Lippard, Massachusetts Institute of Technology, "Polyiron Oxo Compounds in Chemistry and Biology."

Gerald M. Maggiora, Upjohn Co., "Applications of Computational Chemistry to Problems in Protein and Nucleic-Acid Structure and Function."

Bogdan Matuszewski, Merck, Sharp & Dohme, "Photochemistry, Stereochemistry, Electrochemistry: What Do They Have in Common with Assay Development in Biological Fluid?"

Chris Murray, University of Arkansas, "Mechanisms of Hydrogen Tunneling."

Kenneth M. Nicholas, University of Oklahoma, "Chemistry and Synthetic Utility of Electrophilic Cobalt π -Complexes."

Randy Nielsen, Eli Lilly & Co., "Capillary Electrophoresis of

Biosynthetic Human Proteins."

Marc D. Porter, Iowa State University, "Monomolecular Assemblies - Structure and Reactivity at Liquid-Solid Interface."

Carol Post, Purdue University, "Enzyme-Substrate Interactions Examined by NMR and Molecular Dynamics."

Lev N. Sidorov, Moscow State University, "Ion-Molecule Equilibria, Electron Affinities and Negative Ion Mass Spectrometry."

Steve Scheiner, Southern Illinois University-Carbondale, "Principles of Proton-Transfer Reactions."

James O. Schenk, Washington State University, "Interactions Between Catecholamines and Neuropeptides."

Neil Schore, University of California-Davis, "Synthesis of Polycyclics Using Pauson-Kahnl Cycloaddition Chemistry."

Jonathan Sessler, University of Texas-Austin, "'Texaphrin': A New Pentadentate Porphyrin-like Ligand System."

K. Barry Sharpless, Massachusetts Institute of Technology, "Catalytic Asymmetric Oxidation and the Synthesis of Biologically Active Substances."

K. Barry Sharpless, Massachusetts Institute of Technology, "The Importance of Ligand-Accelerated Catalysis."

K. Barry Sharpless, Massachusetts Institute of Technology, "Selective Abiological Catalysis."

Jerzy Strojek, Silesian Technical University, "Photo- and Electrochemical Oxidation of Magnesium Meso-Tetraaniline Porphyrin."

Doug Tabor, University of Delaware, "Enantiospecific Synthesis of Natural Products."

Richard Taylor, University of Oklahoma, "Metal Complexation of Antibiotic Ionophores."

Michael Tempesta, University of Missouri, "New Mycotoxins from Fusarium."

Robert Ternansky, Eli Lilly & Co., "Synthesis of Novel Pyrazolidinone Antimicrobial Agents."

C. S. Wilcox, University of Pittsburgh, "The Design and Synthesis of Architecturally Interesting Molecules: New Approaches to Synthetic Receptors and Functional Group Arrays."

Jeff Wiseman, Glaxo Pharmaceuticals, "The Lipxygenase Reaction."

Claude Woods, University of Wisconsin, "Microwave Spectroscopy of Molecular Ions."

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