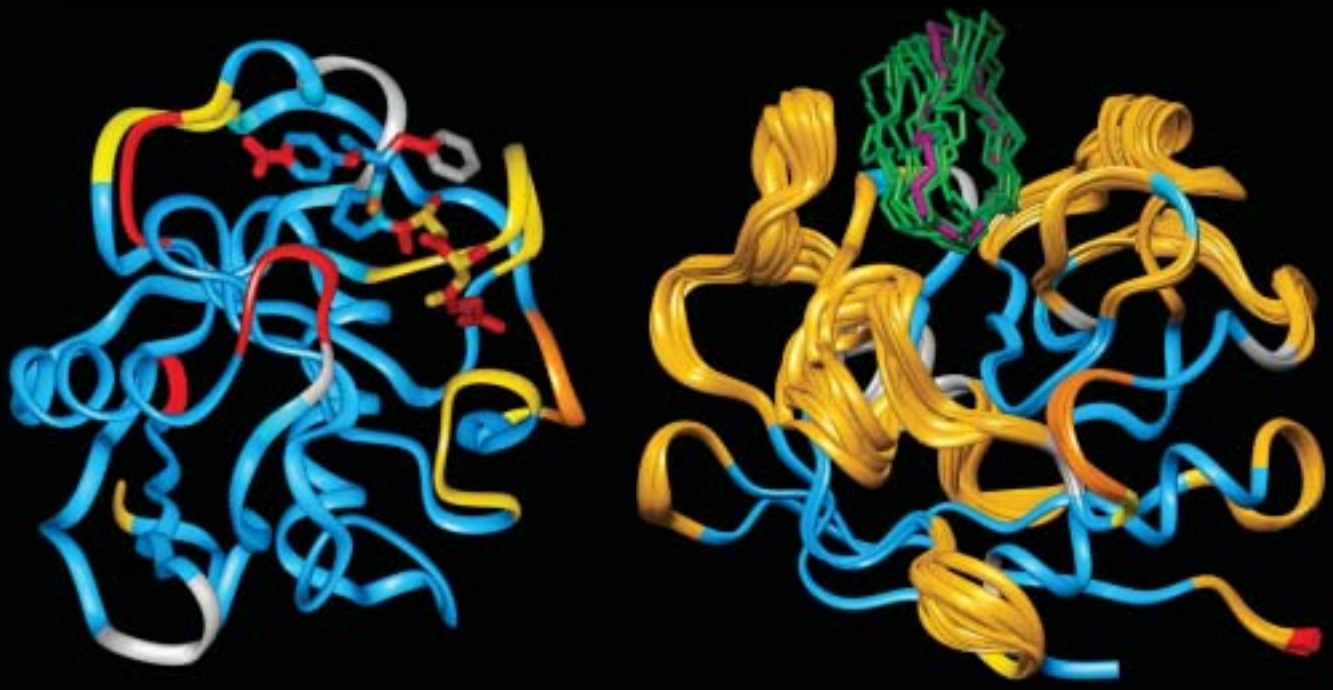
MICHIGAN STATE
UNIVERSITY

BIOCHEMISTRY & *Molecular* BIOLOGY 2003

Life at the Interface...

Development of high speed computational methods for studying interactions between proteins and small molecules (ligands) has led to discovery of drugs that may be effective against lymphatic filariasis, a disease caused by a blood-borne parasite that afflicts more than a hundred million people worldwide — see feature article on page 18, and figures with legends on back cover.



BIOCHEMISTRY & *Molecular* BIOLOGY

2003

MICHIGAN STATE UNIVERSITY

Editor: John E. Wilson

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Contents

Transition in Leadership
of the Department

William L. Smith

After eight years as Chair, Bill Smith resigned the position at the end of December, 2002. Bill has traded green-and-white for the maize-and-blue. In May of 2003, he became Professor and Chair of the Department of Biological Chemistry at the University of Michigan. He also has been named as the Minor J. Coon Collegiate Professor of Biological Chemistry, a Professorship established to honor Dr. Minor J. (Jud) Coon, who previously served as Chair of the Department of Biological Chemistry at UM from 1970-1990. Succeeding Bill as Chair of the Department at MSU is Shelagh Ferguson-Miller **(http://www.bch.msu.edu/faculty/fmiller.htm),** who has served as Associate Chair since 1989 and is well qualified to continue the exceptional record of leadership that is Bill's legacy at MSU.

Bill joined the Department as an Assistant Professor in 1975, and had a distinguished academic career during his 28 years as an MSU faculty member. He is internationally recognized for his work on synthesis and function of prostaglandins. Among the many honors received in recognition of his outstanding research accomplishments are *two* NIH-MERIT awards (1987-1995, and again 1995-2003), the Treadwell Award (1991) and Abraham White Distinguished Scientific Achievement Award (1996), both given by George Washington University, and the Senior Aspirin Award from the Bayer Corporation in 1997. (For those of you who might be wondering about the connection between aspirin and Bill's work on prostaglandins, let us mention that the anti-inflammatory activity of aspirin results from its activity as an inhibitor of prostaglandin synthesis, with prostaglandins being involved in the inflammatory response.) MSU has also recognized Bill's achievements with the Distinguished Faculty Award in 1992, and by his being named University Distinguished Professor in 2001. Bill's many contributions to the Department are greatly appreciated and he surely will be missed by his colleagues and friends (and golfing buddies) at MSU. His move to UM is, however, a homecoming in a sense, since Bill received his PhD in Biochemistry from UM in 1971.

Our new Departmental Chair, Shelagh Ferguson-Miller, will be familiar to many of you because she has been with the Department since her initial appointment as Assistant Professor in 1978. Shelagh has established an international reputation for her work on cytochrome oxidase and ion transport in mitochondria. She has a record of uninterrupted research support from several intramural and extramural sources, including NIH, and she received an NIH-MERIT award in 2000. Shelagh has been actively involved in a number of professional activities, including service on the editorial boards of several journals, on the Gordon Research Conferences' Selection and Scheduling Committee, on review panels for various funding agencies (NSF, NIH, and others), and on the Council for the American Society for Biochemistry and Molecular Biology. Her accomplishments were recognized with the MSU Distinguished Faculty Award in 1996 and by designation as an MSU University Distinguished Professor in 1997. Shelagh has been a major force in leading MSU's involvement in the Michigan Life Sciences Corridor (see related articles in previous issues of this magazine), and she currently serves as Co-Director of the MLSC Center for Structural Biology.

A Message From

Shelagh Ferguson-Miller
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Mission Statement of the Department of Biochemistry and Molecular Biology:

To enhance the research stature of the department, maintain a collegial atmosphere and quality teaching, and promote synergistic interactions with other departments and programs.

Dear Friends and Alumni,

The mission statement has not changed much, but we have lost Bill Smith, who has led us so effectively in that mission for the past 8 years. He will be sorely missed, not only as an excellent Chair, but as one of our most distinguished scientists. The only good news is that his new appointment as Chair of Biological Chemistry at University of Michigan allows him to still keep in touch and maintain his collaborations at MSU. I took over as Chair January 1, 2003, realizing what a tough act Bill is to follow and hoping that I have learned enough in my years as Associate Chair to ease the transition. With Lee Kroos as the new Associate Chair, I think I have a chance of keeping the department moving forward.

BMB will continue to emphasize three broad areas of research: Macromolecular Structure & Modeling, Genes & Signaling, and Plant Biochemistry. In the Modeling area, I am delighted to report that Leslie Kuhn has returned to the department after a year's leave at Aguron/Pfizer in San Diego. Leslie has re-assumed her position as Director of the REF Center for Biological Modeling, which she initiated (see article on this REF Center later in this magazine). Upon her return in January 2003, she led a successful search for two more computational biochemists, Michael Feig from Scripps (hired as a joint appointment with Chemistry) and Bill Wedemeyer from University of Washington (a joint appointment with Physics). Another big plus from this search was the hire of Jennifer Ekstrom, a crystallographer from Philos Inc., Boston, and the wife of Bill Wedemeyer. These three new faculty are a great addition to the department and a wonderful fit for the Program in Quantitative Biology that we are developing as an interdisciplinary dual PhD program between the biological and physical/mathematical science departments (see more on our web site soon).

These new hires will also enhance the Life Science Corridor effort that was initiated in 2000 by the State of Michigan to promote

the Chairperson

research and economic development in the Life Sciences throughout the State, and funded by $50 million dollars a year from the tobacco money settlement. Michigan State University was chosen as the location for the Center for Structural Biology. In spite of the devastated condition of the State's budget, we are approved for the fourth year of funding in a five year commitment to the development of state-of-the-art facilities for macromolecular structure analysis. These facilities include the design and building of a sector at the Synchrotron at Argonne National Labs for the highest resolution x-ray crystallography (see article by Mike Garavito in last year's magazine), as well as the installation of a 900 MHz NMR (on order, and we are about to break ground on a building to house it). The plans are on schedule, including the hiring of a Director for the new Biomolecular NMR Facility, Dr. Aizhuo Liu, an excellent addition to our NMR community.

On the construction front, the major ($15 million) renovation of the ventilation system in the Biochemistry Building is underway. We have made it into Phase One of four phases, with much help from Joyce Robinson and Ron Norris, and Loran Bieber's expert and knowledgeable oversight. Although there is a lot of moving and inconvenience for all (and noise and dust and occasional disasters), our colleagues in the department and in the new Biomedical and Physical Sciences Building have been generous in accommodating the refugees, as each quadrant of the building is torn up–and hopefully put back together again.

We had an excellent turnout of over a hundred faculty and students for our annual Awards Banquet in April. At this event, we recognize the Boezi Award recipient–this year, Dr. Marcia Kieliszewski–as well as the special accomplishments of our faculty and students (see article later in this magazine). The Awards Banquet is subsidized by, and the Boezi Award and student awards made possible by, donations to the department from many of you, and we are most appreciative of that support. While we are on the topics of awards, let me interject here that, subsequent to the Awards Banquet, we learned that Professor John Wang was named as recipient of the College of Osteopathic Medicine's Award for Outstanding Curricular Contributions. This is richly deserved recognition of John's dedicated service to medical education, not just in COM but also in MSU's MD-granting College of Human Medicine.

Dr. Robert Kingston, Professor of Genetics at Harvard Medical School and Massachusetts General Hospital, gave the William Wells Lecture, and Dr. Steven Huber, Professor of Crop Science at North Carolina State University and USDA Plant Physiologist, delivered the Tolbert Lecture this year. The funding for these endowed lectureships has also come from many of you, for which we are very grateful. The department benefits enormously from visits of these distinguished scientists. Although the State of Michigan has been exceptionally supportive of the universities even in these difficult budget times, every year a greater proportion of university costs need to be covered by endowment funding. Your contributions are increasingly important to the quality of education and research we can support.

I note with sadness the passing of Emeritus Professors Jim Fairley and Bill Deal this past year. They were dedicated faculty members and friends to many of us.

I would like to end by thanking you for keeping us informed of happenings in your world. You can complete and return the form printed at the end of this magazine and we will highlight this information in the Alumni News section, a popular feature of this magazine.

Best wishes to all of you for a happy and prosperous 2004.

Best personal regards,

Shelagh Ferguson-Miller

New Faculty

New Assistant Professors

Jennifer L. Ekstrom - BS in Chemistry from the University of Illinois and PhD in Biochemistry from Cornell University. Subsequent to her PhD work, Dr. Ekstrom was a Pfizer Postdoctoral Fellow, a postdoctoral program that combined both academic and industrial experience. She spent 18 months working with Dr. Robert Fletterick at University of California- San Francisco, and 18 months working with Dr. Virginia Rath at the Pfizer research facility in Groton, CT. Just prior to joining the faculty at MSU, Dr. Ekstrom had been working for Phylos, Inc., a biotech company in the Boston area. Dr. Ekstrom's skills as an x-ray crystallographer will bolster structural biology research, a focus within the Department that has been further enhanced through establishment of the Michigan Life Sciences Corridor Center for Structural Biology, headquartered at MSU.

Michael Feig - Dr. Feig received a Vordiplom in Computer Science as well a Diplom (MS) in Physics from the Technical University of Berlin, followed by his PhD work in Chemistry at the University of Houston. Prior to joining the MSU faculty, Dr. Feig was engaged in postdoctoral research with Prof. C.L. Brooks, III, at The Scripps Research Institute in La Jolla, CA. His research interests center around the application of advanced computational methodologies to gain understanding of biologically important processes. His initial focus will be a study of the DNA mismatch repair system.

William J. Wedemeyer - BS in Physics and in Humanities (Music) from Massachusetts Institute of Technology, and MS and PhD degrees in Physics from Cornell University. He did postdoctoral work with Prof. Harold Scheraga at Cornell, and then with Prof. David Baker at the University of Washington before joining the MSU faculty. His research interests are in development of computational methods for protein structure prediction.

New Instructor

Those who remember back to the early days of this department will remember Ruth Allen. Ruth was an Instructor who nurtured the newly established undergraduate program of the fledgling department. After Ruth moved on to other things, the position of Instructor remained unfilled and professorial faculty handled the teaching responsibilities of the department. However, there has been a continued increase in demand for undergraduate biochemistry courses, e.g., just a few years ago, the undergraduate BMB 461 course had an enrollment of approximately 250, but in Fall Semester 2003, over 500 students are enrolled, and BMB 401, which had been offered only once per year, now is offered in both Fall and Spring Semesters with approximately 150 students each term. Such increases in teaching demands led to revival of interest in the Instructor position, and to the hiring of Dr. Jon R. Stoltzfus in Fall, 2003. Dr. Stoltzfus received his BS from Purdue in 1993, followed by a PhD in Genetics from MSU in 1999 and subsequent postdoctoral work with Dr. Mike Grotewiel of MSU's Zoology Department. Initially, Dr. Stoltzfus is working with other faculty members teaching the 400 level undergraduate courses, and in Spring Semester, 2004, he also will be teaching ISB 204 (Applications of Biomedical Sciences), an integrative biological sciences course for non-science majors that has been taught by BMB faculty. The addition of Dr. Stoltzfus to the faculty will be a big help in meeting the increased teaching demands at the undergraduate level and ensuring the continued quality of the undergraduate course offerings in which this Department justly takes pride.

An Overview

Department of Biochemistry and Molecular Biology
Michigan State University

Administration (% Funding): College of Natural Science (Lead Dean; 50%), College of Human Medicine (14%), Michigan Agricultural Experiment Station (23%), College of Osteopathic Medicine (13%)

Faculty: 27 wholly appointed in Biochemistry & Molecular Biology, and 14 jointly appointed in other units
5 University Distinguished Professors
8 MSU Distinguished Faculty Awardees
1 NIH MERIT Awardee

Specialists: 3 (Laboratory, Bioinformatics and Structure Facilities)

Staff: 17 (secretarial, accounting, Biochemistry Instrument Shop, Biochemistry Stores, Animal Room)

Undergraduate Majors: 242

Graduate Students: 61

Postdoctoral Fellows: 46

University Facilities: Macromolecular Structure, Mass Spectrometry, Genomics, Bioinformatics, Computer Graphics, Proteomics, Flow Cytometry, NMR

Centers: REF Center for Biological Modeling
MLSC Center for Structural Biology

Research Emphases: Macromolecular Structure & Modeling
Plant Biochemistry
Genes & Signaling

2002-2003 GrantSupport: 45 grants in all, 24 NIH, 6 NSF, 1 USDA, 2 DOE, 3 Industrial, 9 Other; Approximately $16.1 million in extramural support for 26 faculty wholly supported by BMB.

Teaching: Undergraduates (lectures, labs, independent study)
Graduate students (core Biochemistry and Molecular Biology)
Medical Schools (BMB 514, BMB 526, Problem-based Learning, Systems Biology)

2003 Boezi Award Recipient, Marcia Kieliszewski

Perhaps the most common pattern of progress through formal academic training is completion of an undergraduate degree in a particular major, followed by (for those who choose to do so) prompt entry into a graduate program to which the undergraduate major is more-or-less directly related. But there are always some who take a less direct route. And the recipient of the 2003 Boezi Award is an example. Marcia Kieliszewski received a B.A. in Psychology, with highest honors, from MSU in 1974. The next few years were filled with raising a family and, we suspect, provided little time to think about academics. But in 1985, Marcia found it possible to return to Michigan State, entering the graduate program not in psychology, but in biochemistry–and the field of biochemistry, particularly plant biochemistry, is richer for it.

For her PhD thesis work, Marcia worked with Dr. Derek Lamport who was jointly appointed in the Department of Biochemistry and the MSU-Department of Energy Plant Research Laboratory. This work was focused on the isolation and characterization of extensins from *Zea mays* (corn). Extensins are glycoproteins that constitute major structural proteins in plant cell walls. They are characterized by a high content of hydroxyproline residues, with one or more carbohydrate residues being attached to the protein through the hydroxyl group of the hydroxyproline. Marcia received her PhD in 1989, and was recognized with the Outstanding Graduate Student Award from this Department.

Marcia Kieliszewski

After completion of her degree, Dr. Kieliszewski continued working with Dr. Lamport until 1991, when she moved to the Complex Carbohydrate Research Center at the University of Georgia. It was during the latter time that she began work on defining the "code" which determines the relationship between amino acid sequence and the carbohydrate structures that are added at specific hydroxyproline residues in extensins and other hydroxyproline-rich glycoproteins (HRGPs). In 1995, she joined the faculty in the Department of Chemistry and Biochemistry at Ohio University, where she currently is an Associate Professor.

Her research has been funded by both the U.S. Department of Agriculture and the National Science Foundation, including a prestigious NSF CAREER grant, with additional funding from the State of Ohio and the Ohio Plant Biotechnology Consortium. Dr. Kieliszewski's work has led to development of the Hyp Contiguity Hypothesis, which defines the relationship between amino acid sequence and various post-translational modifications that are found in the HRGPs. This, together with generation of synthetic gene analogs of HRGPs, has provided insight into the relationship between amino acid sequence, post-translational modifications, and functional properties of HRGPs, and also permits generation of novel HRGPs that may be of commercial importance. In addition to her extensive scientific publications, Dr. Kieliszewski holds three patents for production of synthetic HRGPs and plant gums. She has served as a reviewer for several journals and on grant review panels for various US federal agencies, and has also served on the Biological and Biotechnology Science Research Council of the United Kingdom.

John A. Boezi

Remembered & Honored

Professor John A. Boezi joined the newly formed Department of Biochemistry in 1963. Together with colleagues like Fritz Rottman and Allan Morris, John represented the emerging field of "molecular biology" and played a major role in shaping the research and teaching program in the early days of the Department. John's sudden death in 1980 was deeply felt by his students and faculty colleagues alike. In his memory, they established an award to be given annually to a recipient of a B.S., M.S., or Ph.D. degree from this department who had gone on to a distinguished career that reflects the qualities personified by John Boezi.

Past Recipients of the Boezi Award

In the many years that have passed since establishment of this award, the number of degree recipients from this department has continued to grow steadily. Communications being imperfect, the Department recognizes that it may not be aware of some graduates whose accomplishments since leaving MSU would make them worthy candidates for the Boezi Award. We thus solicit your assistance in identifying past graduates of this department, undergraduate or graduate, who would merit consideration. Please send suggestions and pertinent information to Dr. Shelagh Ferguson-Miller, Chairperson, Department of Biochemistry and Molecular Biology or e-mail us at bchalumn@msu.edu.

1983	Donald W. Carlson	Ph.D.	1961
1984	Allen T. Philips	Ph.D.	1964
1985	John A. Gerlt	B.S.	1969
1986	George H. Lorimer	Ph.D.	1972
1987	Lawrence B. Dumas	B.S.	1963
1988	Douglas D. Randall	Ph.D.	1970
1989	Ronald C. Desrosiers	Ph.D.	1975
1990	George M. Stancel	Ph.D.	1970
1991	Raymond J. Dingledine	B.S.	1971
1992	Howard C. Towle	Ph.D.	1974
1993	A. Stephen Dahms	Ph.D.	1969
1994	Sherwood R. Casjens	M.S.	1967
1995	Friedhelm Schroeder	Ph.D.	1973
1996	Philip L. Felgner	Ph.D.	1978
1997	Arlyn Garcia-Perez	Ph.D.	1984
1998	Ann E. Aust	Ph.D.	1975
1999	Peter Steck	Ph.D.	1981
2000	Sally Camper	Ph.D.	1983
2001	Tony Serianni	Ph.D.	1980
2002	John Blenis	Ph.D.	1983

2003 Departmental Awards Banquet

On the evening of April 17, students, faculty, and various friends of the Department gathered for the annual Awards Banquet. Dr. Marcia Kieliszewski was presented with the Boezi Award, but this was also the occasion to recognize the accomplishments of others.

In her role as recently appointed Chairperson of the Department, Shelagh Ferguson-Miller presided over the after-dinner program and had the pleasure of recognizing one of her own graduate students, Bryan Schmidt, as this year's recipient of the Outstanding Graduate Student Award. Shelagh noted Bryan's many contributions to the laboratory, including his role as "in-house computer guru" whose expertise would be sorely missed by other lab members when he moved on. Meghana Kulkarni, a graduate student in the David Arnosti laboratory, was honored with the Outstanding Graduate Student Teaching Award.

The Outstanding Undergraduate Student Award was presented to Woo Jung Moon by Professor Zach Burton, in whose laboratory Woo Jung had done undergraduate research. Dr. Burton noted that Woo Jung also had done undergraduate research with Dr. David Morrissey, Professor of Chemistry in the MSU Cyclotron Laboratory–unusual diversity in undergraduate research experience.

Undergraduate Research Awards were presented to Sze-Ling Ng, who is doing undergraduate research with Dr. Min-Hao Kuo, to Cassandra Campbell, who is working with Dr. Laurie Kaguni, to Greta Monterosso, who is doing research with Dr. Bob Hausinger, and to Erica Scheller, who is working with Dr. Leslie Kuhn. The Undergraduate Research Awards are made possible by contributions to the Department (further information elsewhere in this magazine), and provide financial support so that undergraduates can work in research in lieu of alternative types of employment.

Dr. Ferguson-Miller mentioned the several faculty promotions that had occurred in the past year, with Dr. Dean DellaPenna promoted to Professor, and Drs. David Arnosti, Kathy Gallo, and Gregg Howe all promoted to Associate Professor, with tenure. Chairperson Ferguson-Miller also noted that the outstanding teaching efforts of another faculty member, Dr. John LaPres, had been recognized with the Golden Apple Award from the College of Osteopathic Medicine.

It has been customary to invite a speaker to provide some brief comments as part of the after-dinner program. In years past, this has been someone without current affiliation with the Department but, this year, Dr. Ferguson-Miller surprised attendees by introducing our own Professor Rawle Hollingsworth. Based on his experience bridging academia and the biotechnology industry (see following article), Rawle offered his comments on what he viewed as essential elements for success in science.

Honors 2003

Honors 2003

Newspaper Today, Pharmaceutical Tomorrow

The introduction to a recent publication ("Toward a Carbohydrate-Based Chemistry: Progress in the Development of General-Purpose Chiral Synthons from Carbohydrates," R.I. Hollingsworth and G. Wang, *Chem. Rev.* **100**, 4267-4282, 2000) provides a succinct comparison of the current largely petroleum-based chemical industry and the carbohydrate-based chemical industry envisaged by Professor Rawle Hollingsworth and his colleagues. The chemical industry as it currently exists relies predominantly on small molecules ("synthons"), produced by "cracking" petroleum, as precursors for synthesis of the vast array of chemicals utilized in modern life, from detergents to pharmaceuticals. As noted by Drs. Hollingsworth and Wang, the petroleum-based industry is far from ideal in several ways, including cost and concerns about future availability of petroleum, as well as the intrinsic inefficiency of the cracking process as a source of synthons. In contrast, plant-derived carbohydrates are a renewable resource, abundant in nature, and many carbohydrates are more readily accessible than petroleum and possess desirable chemical features that are not found, or found to only limited extent, in petroleum. In particular, carbohydrates, which characteristically contain chiral centers, may offer substantial advantages in providing chiral synthons that can be obtained only with special difficulty and cost from achiral petroleum. (Those interested in a more extensive discussion of the importance of chirality in synthesis of commercially important fine chemicals, such as pharmaceuticals, might want to have a look at the article entitled "Chiral Business" in the May 5, 2003, issue of *Chemical and Engineering News*.) Furthermore, carbohydrates are readily soluble in water, in contrast to the hydrophobic petroleum-based products, and thus chemical reactions can be performed with environmentally-friendly water as solvent ("green chemistry"), avoiding the requirement for organic solvents which may pose environmental concerns. Thus, Rawle and his associates have focused on developing ways for "cracking" readily available, relatively inexpensive carbohydrates (e.g, recycled newspaper, which consists largely of the glucose polymer, cellulose) to produce synthons as precursors for production of commercially important chemical products.

In 1995, Professor Hollingsworth founded Synthon Corporation, subsequently renamed Synthon Chiragenics, a company focused on development of carbohydrate-based synthons as precursors for the chemical industry. Dr. Hollingsworth serves as Chief

R.I. Hollingsworth

Scientific Officer and member of the Scientific Advisory Board for the company. In January, 2003, the chiral aspects of Synthon Chiragenics' business were sold to the British pharmaceutical company, Avecia, and Dr. Hollingsworth indicated that the remainder of Synthon Chiragenics was (in May, 2003) in the process of merging with another company.

Rawle Hollingsworth **(http://www.bch.msu.edu/faculty/hollings.htm)** received his PhD in Organic Chemistry from the University of the West Indies in 1983. He then came to Michigan State as a postdoctoral associate with Dr. Frank Dazzo in the Department of Microbiology (now Department of Microbiology and Molecular Genetics). During his postdoctoral work, he was the first to determine the complete chemical structure of an acidic heteropolysaccharide that is

Continued on page 12

Newspaper Today, Pharmaceutical Tomorrow

Continued from page 11

produced by *Rhizobium* and serves as a recognition signal in establishment of the symbiotic relationship between this organism and its leguminous plant host. Structure-function relationships in bioactive glycoconjugates have been an enduring interest of Professor Hollingsworth, and this remains one of several research foci in his laboratory. It was during his postdoctoral work that Dr. Hollingsworth came to the attention of Professor Charles Sweeley, then Chairperson of the Department of Biochemistry. Recognizing Rawle's exceptional talents, Dr. Sweeley recruited Rawle into the Department, where he was jointly appointed as an Assistant Professor of Biochemistry and Chemistry in 1988, with promotion to Associate Professor in 1993, and Professor in 1997. Dr. Hollingsworth retains his joint appointment between the Department of Chemistry and the Department of Biochemistry and Molecular Biology, with graduate students from both departments benefitting from the opportunity to work in his laboratory.

While, as noted above, Dr. Hollingsworth has a strong research interest in developing carbohydrate-based industrial chemistry, the research activities in his laboratory are by no means exclusively in this area. A continuing interest has been in the structure and behavior of macromolecular ensembles, especially biomembranes. Since the latter typically include lipids and proteins, as well as carbohydrate components, Dr. Hollingsworth's research also involves work on the structure and chemistry of lipids and proteins. He employs an extensive variety of techniques in his research, ranging from chemical synthesis and various computational methods to sophisticated NMR, IR, and mass spectrometry procedures. His research has resulted in more than 100 publications in the scientific literature and (at last count, and not including non-US patent applications) more than 40 patents.

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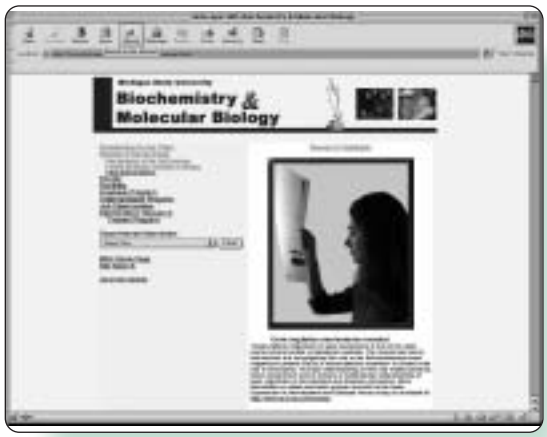
Information about many aspects of the department is available on our web site at **http://www.bch.msu.edu**. Faculty and their research interests? Information about graduate and undergraduate programs? The "Biochem Weekly?" Current and past issues of this departmental magazine? These and more are available with a few clicks of the mouse. If you don't find what you are looking for, contact us at **bchalumn@msu.edu** and we will be happy to provide additional information.



We Remember Jim Fairley

James L. Fairley

Professor Emeritus James L. Fairley passed away on Oct. 23, 2002. Jim first joined the MSU faculty in 1952 as a member of the Department of Chemistry. A few years later, he and other pioneering faculty members staffed the newly formed Department of Biochemistry, and he retained his affiliation with this Department until his retirement. Jim's research interests were primarily focused on enzymes involved in nucleotide and nucleic acid metabolism. He served as major professor for several of the graduate students that were the initial degree recipients from this Department. In addition, he served as Associate Chair of the Department for several years, and contributed in important ways to development of the Department's teaching and research programs. Jim was well known for his love of the outdoors, with hunting, fishing, and golfing being high on his list of leisure activities.

Jim originated from warmer climes, being born in Palo Alto, CA, in 1920. His early years and formal education were also in California, where he received his undergraduate degree from San Jose State University and, after service as a meteorologist in the Army Air Corps during World War II, earned his PhD from Stanford University. It was at Stanford where Jim met his future wife, Dee, who preceded him in death in 2001. Jim and Dee are survived by their children, daughter Laurel, of Fresno, CA, and son Joel, of Ogden, UT.

And We Remember Bill Deal

Bill Deal

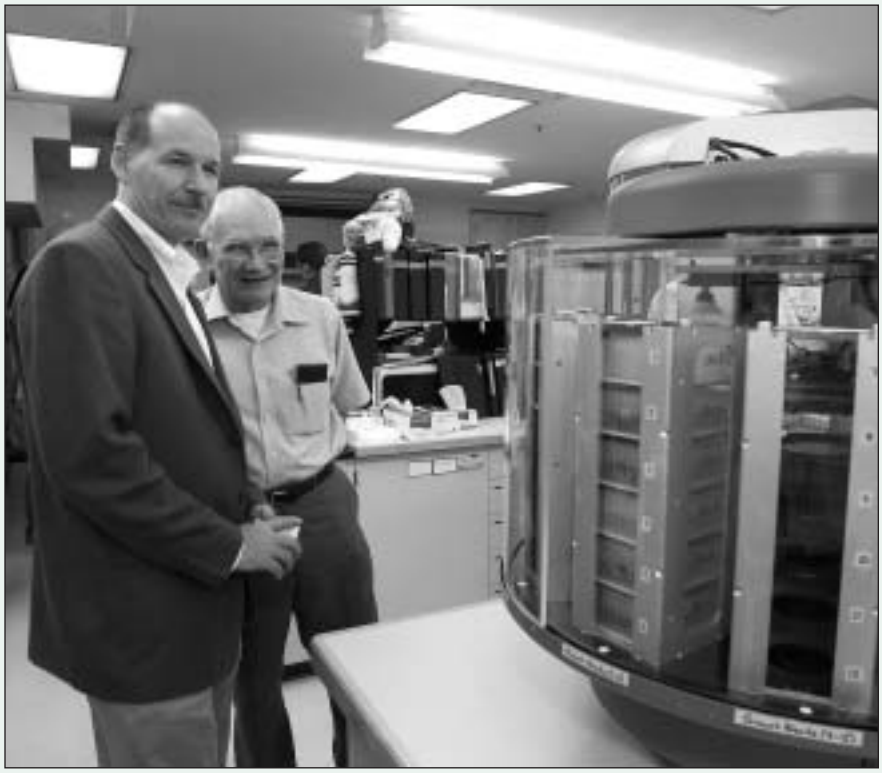
On Sept. 11, 2003, Professor Emeritus William C. Deal, Jr., succumbed after a brief battle with ALS (Lou Gehrig's disease), which had been diagnosed in May, 2003. Bill joined the Department as an Assistant Professor in 1962, and was thus one of the first faculty members recruited to join the newly-formed (in 1961) Department of Biochemistry at MSU. Born in Louisiana in 1936, Bill's early years were spent in his native state, and he received a BS in Chemistry from Louisiana College in 1958 before heading north where he earned his PhD degree in Physical Chemistry from University of Illinois (Champaign-Urbana) in 1961. Bill's particular expertise was in the use of ultracentrifugal and other physical methods for the study of protein structure. His laboratory was home to two Beckman analytical centrifuges which he and his students applied to studies of the molecular properties of various enzymes, a particular interest being enzymes of the glycolytic pathway. He and his students developed several innovative methods for ultracentrifugal analysis. In addition to his contributions to the research activities of the Department, Bill was a highly respected teacher and served the Department as Undergraduate Program Director for several years.

Bill was very active in various capacities at Bethany Baptist Church in Lansing, and was also deeply involved in work aimed at maintaining the environment in his Meridian Township community. Bill is survived by his wife, Barbara, whom he married in 1957, their children, Elizabeth Kay Deal and William C. Deal, III, grandchildren Matthew William and Jacqueline Nicole Deal, and by many other family members, including his parents, Minnie Belle and William C. Deal, Sr., and four brothers and four sisters.

GTSF Celebrates Completion of Its State-of-the-Art Genomics Core Facility

Contributed by David L. DeWitt, Associate Professor of Biochemistry and Molecular Biology and Co-Director of the Genomics Technology Support Facility

On May 16, 2003, the Genomics Technology Support Facility (GTSF) celebrated the completion of its 2500 ft^2 Genomics Core facilities (Room S18, Plant Research Laboratory) with an open house attended by MSU Vice President for Research & Graduate Studies Robert Huggett and several hundred faculty, staff, post-docs and graduate students. The GTSF came into existence through the efforts of a few far-sighted individuals and the fortuitous concurrence of organizational and political events both on campus and in the Michigan legislature. In early 2001, Professor Loran Bieber recognized the need for infrastructure support in genomics and spearheaded an effort to establish a service facility. The first equipment, an ABI 3700 high throughput DNA sequencer and an Affymetrix™ Chip analysis system, was purchased and renovation of Room S18 in the Plant Research Laboratory begun with monies provided by a coalition of stakeholders from the College of Natural Science, the College of Agriculture and Natural Resources, and the Offices of the Provost and the Vice President for Research & Graduate Studies. These efforts coincided with the funding in 2002 of the Michigan Life Science Corridor Core Technologies Alliance, a program directed at providing infrastructural support in the areas of Genomics, Bioinformatics, and Proteomics for biological scientists at



GTSF Co-Director David Dewitt (left) and Professor Loran Bieber (right) view some of the advanced instrumentation available in the GTSF.

Michigan State University, University of Michigan, Wayne State University, and The Van Andel Institute. To consolidate these efforts, the fledgling genomics facility started by Dr. Bieber, Biochemistry's Macromolecular Structure Facility, and the MLSC Core Technology Alliance were combined under the umbrella of a single administrative unit called the Genomics Technology Support Facility, which is administered and supported through MSU's Office of the Vice President for Research and Graduate Studies.

David DeWitt **(dewittd@msu.edu)** and Joe Leykam **(mssf@msu.edu)** serve as Co-Directors. With a staff of sixteen individuals, including 7 PhD scientists, organized into four "Cores," GTSF provides services not just for MSU but also for educational institutions and biotechnology and pharmaceutical companies throughout the world. A full listing of GTSF's services, resources and employees, as well as contact information, is provided on the GTSF web site **(www.genomics.msu.edu)**. Here we simply provide a brief overview of the services offered by each Core.

Shari Holland (right) of the Genomics Core demonstrates how the ABI3100 DNA analyzer is used for fragment analysis to determine genotypes of different organisms or individuals. This type of analysis is commonly used in forensic investigations to confirm or reject the identity of suspects. In the GTSF, however, these analyses are used solely for research purposes, e.g., to examine differences in populations of wild animals or to identify specific strains of bacteria and other microorganisms.

The Genomics Core–
Genomics researchers seek to know the entire DNA sequence of organisms and to understand how regulation of gene expression allows the organism to function and respond to the external world. This can include, for example, how mammalian cells respond to nutrients or to cancerous transformation, or how plants respond to sunlight or pest depredation. The major services provided by the GTSF Genomics Core are sequencing genes and genomes, and measuring global changes of gene expression using high density microarrays and real-time PCR assays. GTSF has the most advanced high throughput sequencer in the world, the ABI 3730XL, which is capable of determining the sequence of over 1.5 million base pairs per day. The GTSF operates one of only two 3730XL instruments in the Midwest. Also available is an ABI 3700, the instrument on which the human genome was sequenced, and two smaller ABI 3100 sequencers used for custom sequencing of individual samples and for genetic haplotype analysis.

Two types of microarray analysis are available. High density (10^6 spots/cm^2) Affymetrix Microarray chips can measure changes in the expression of up to 30,000 genes using a 2 cm^2 square chip. The Genomics Core can also print custom spotted arrays of medium density (10^4 spots/cm^2) that are used to measure gene expression either from preselected genes or from organisms for which Affymetrix chips are not available. Changes in expression of genes identified by microarray analysis can be more accurately measured using quantitative PCR on an ABI Prism 7900 Sequence Detection System, a fully automated instrument capable of making 35,000 individual determinations per day.

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Genomics Core Facility

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The Proteomics Core–
Proteomics is to protein analysis what genomics is to gene analysis, an attempt to map global changes in protein expression. The most widely used technique for such analysis is mass spectrometric identification of proteins. GTSF's Proteomics Core provides high throughput analysis of protein expression patterns and protein interactions. Protein mixtures are first fractionated by gel electrophoresis (1-D and 2-D) or by chromatography using multidimensional protein identification technology (MudPIT). MALDI-MS and LC-MS/MS are then used to collect high throughput mass spectra of peptides whose identities are determined by computer comparison with masses calculated from the GenBank database.

The Proteomics Facility will take delivery of a Thermo-Finnigan Linear Trap Fourier Transform mass spectrometer in the Fall of 2003. The Thermo-Finnigan FTMS "Super Trap" is the first hybrid linear ion trap FTMS mass spectrometer to be commercially available. This promises to have up to 100 times the sensitivity of current instruments, and provides exceptional accuracy, resolution, and duty-cycle. The addition of this instrument should help maintain the MSU Proteomics Facility as one of the best in the nation.

Joe Leykam (left), Co-Director of GTSF and head of the Macromolecular Structure Core, talks about future interactions with Sarah Elsea, Director of the MSU DNA Diagnostic Laboratory.

Sheng Quan (left), who is in charge of protein expression services for the Genomics Core, talks with Brett Phinney (center), head of the Proteomics Core. Doug Whitten (right) is a technician in the Proteomics Core.

Macromolecular Structure Core– The Macromolecular Structure Facility is the oldest and most successful of the research service facilities on campus. Joe Leykam has managed the Macromolecular Structure Facility for the last 16 years and has established an international reputation for his protein sequencing expertise. Joe continues to oversee the operation of this Core, and has lent his considerable talents and expertise to the management of the other three Cores in his role as Co-Director of the GTSF. The Macromolecular Structure Core provides the types of analyses that were the foundations of the genetic revolution: Edman degradation protein sequencing, sophisticated HPLC fractionation of proteins and peptides, and peptide and oligonucleotide synthesis. With the advent of custom oligonucleotide microarrays, demand for oligonucleotides has become even greater.

(From left) Kevin Carr, Matt Larson, Rob Halgren, and Curtis Wilkerson (far right) of the GTSF Bioinformatics Core, describe a database programming project with Richard Miksicek (second from right) of the Department of Physiology.

Bioinformatics Core– Little gets done without a computer anymore, especially in modern biological research. Unfortunately, no one can be an expert in everything, and few people can be a computer scientist and biologist at the same time. In fact, bioinformatics typically requires a group of people, each with complementary skills, and few single laboratories can afford them. Fortunately, the GTSF Bioinformatics Core has high powered computers, as well as top notch web designers, database experts, programmers, and systems administrators who understand biology and biochemistry. Together they can analyze sequence and microarray data, develop a web site to make the data available to the general scientific community, and make sure that data on the web is safe from hackers and backed up regularly. One of the hardest tasks in modern research is organizing large data sets from multiple sources, such as might be generated from microarray and proteomic analysis. The GTSF Bioinformatics Core is at the leading edge in designing and developing new data schemas for databases that allow researchers to ask complicated questions and come up with insightful answers.

Life at the Interface... Modeling and Designing Interactions between Proteins and their Partners

Contributed by Leslie Kuhn, Associate Professor of Biochemistry and Molecular Biology

How does a protein choose its partner? In human cells, there are about 40,000 different possible protein partners, and a vast array of other potential molecular partners (metabolites, lipids, etc.) in the crowded intracellular environment. My research group's goal is to understand the features that result in the incredible specificity of interaction between proteins and the molecules they bind. These protein partners, or "ligands," may be other proteins, DNA, RNA, lipids, sugars, or small organic molecules. Specificity comes, in part, by spatial regulation, through the separation of proteins and ligands into different compartments of the cell. There is also very significant temporal regulation through the control of gene expression and breakdown of RNA and proteins. Our focus is on how the shape, flexibility, and chemistry at protein surfaces yield specificity, or, in some cases, polyspecificity (the ability to bind a set of different molecules). Some proteins, like the major histocompatibility complex, must recognize and bind a broad range of foreign molecules, whereas other proteins, such as protein kinases involved in cell cycle control, must be incredibly selective in their partners.

We use computational approaches to study protein-ligand recognition. I've often heard, "why model or predict structure–just do the experiment!" However, the primary goal of computational modeling is not to predict something that could be determined experimentally, but rather to understand why it is so. For instance, the software, SLIDE, developed in my laboratory by Volker Schnecke, Paul Sanschagrin, Maria Zavodszky, and Rajesh Korde, can screen hundreds of thousands of potential small molecule partners for binding to a protein structure, and will indicate how well each molecule can bind (if at all), and in what orien-

tation. To do this, SLIDE must encode an explicit model for which parts of the protein and potential ligand molecule are involved in the interaction, including their flexibility, solvation, and chemistry. If SLIDE identifies true ligands for a number of proteins from a set of decoy molecules, and accurately predicts their binding modes, then it is correctly modeling the essential features of the protein-ligand interaction. Beyond the utility of using SLIDE as an efficient pre-screen to focus high-throughput, *in vitro* testing on the most promising compounds (as we are doing in collaboration with Basilea Pharmaceutica), identifying the key features of the protein-ligand interaction aids us in designing new proteins with defined ligand interactions, and in designing ligands that are more specific, and therefore less toxic, as lead compounds for drugs.

One of the major projects in the lab, funded by an NIH partnership grant, is aimed at protein structure-based drug discovery to stop lymphatic filariasis. This disease is caused by a blood-borne parasite that afflicts more than a hundred million people worldwide, with serious consequences such as elephantiasis and blindness. However, pharmaceutical companies tend to focus on diseases and countries that will yield significant profits, and therefore there is a major gap in meeting the needs of third-world countries in controlling infectious diseases. Working with Michael Kron (Professor of Medicine, MSU), Morten Grotli (Assistant Professor of Chemistry, Göteborg

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Biographical Sketch– Leslie A. Kuhn

Dr. Kuhn studied Computer Mathematics for her bachelor's degree at the University of Pennsylvania, followed by a PhD in Biophysics at Penn with Dr. John S. Leigh, Jr., developing new methods for predicting protein transmembrane segments and their packing. Her postdoctoral research with Drs. John Tainer and Elizabeth Getzoff at The Scripps Research Institute focused on modeling the atomic structures of proteins and peptides, analyzing the interactions of ligands with proteins, and designing proteins that bind new ligands. Dr. Kuhn currently is an Associate Professor in the Department of Biochemistry & Molecular Biology, with an adjunct appointment in the Department of Physics & Astronomy. She recently spent a year as project scientist and global leader of the Structure-Based Docking, Scoring, and Virtual Screening working group at Pfizer, in La Jolla, CA. Dr. Kuhn is a member of the Editorial Board of the *Journal of Computer-Aided Molecular Design* and participates in NIH review groups in computational and structural biology.

photo by Lynne Brown, Media Graphics, Inc.

Leslie A. Kuhn

In the adjacent article, Dr. Kuhn **(http://www.bch.msu.edu/labs/kuhn)** describes the work of her research group, which develops computational techniques for modeling protein-ligand interactions, designing and testing new ligands, and predicting the influence of hydration and flexibility on molecular recognition. She works in collaboration with physicists, computer scientists, chemists, biochemists, molecular and structural biologists, and physicians to apply these techniques to real-world problems and generate new insights into how proteins bind other molecules with such great specificity. Dr. Kuhn also directs the cross-departmental Center for Biological Modeling at MSU, and in a succeeding article (page 22), she describes this innovative program which fosters collaborative work and training at the interface between computational/mathematical modeling and the life sciences.

Modeling and Designing Interactions

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University, Sweden), Stephen Cusack (Director of EMBL Outstation, Grenoble), and Malcolm Page and Franck Danel (Basilea Pharmaceutica, Zurich), we are using molecular biology, crystallographic structure determination, structure-based ligand screening and design, synthetic chemistry, high-throughput screening, and biological activity assays in a design cycle to develop new inhibitors of tRNA synthetase proteins in the parasite, B*rugia malayi*. By blocking its ability to make new proteins, and targeting features of the B*rugia* protein that are not present in human tRNA synthetases, we aim to develop a new class of highly specific compounds that are effective in both adult and larval stages of the parasite. Through SLIDE screening, we have already identified a new class of inhibitors for the parasite's asparagine tRNA synthetase.

A second major project, funded by an NIH Mathematics in Biology grant, focuses on modeling the flexibility of proteins and ligands during binding. Maria Zavodszky, Brandon Hespenheide, and I have been working with Professor Michael Thorpe (Physics) and his graduate students, AJ Rader and Ming Lei, to predict the flexible regions in proteins based on their networks of covalent and non-covalent interactions (including hydrogen bonds and hydrophobic contacts). We then sample the full range of shapes, or conformations, that the flexible regions can adopt, consistent with the bond network and the absence of overlaps between atoms. The conformational sampling software we have developed, ROCK, allows us to take significant molecular flexibility into account when we predict interactions between proteins and ligands using SLIDE. The ability to accurately model conformational change of both the protein and ligand will help us to design new ligands that are conformationally specific, as well as to model protein-ligand recognition as it truly occurs: as recognition between conformational ensembles of the two molecules.

UNDER CONSTRUCTION

Motion and Commotion

When the Biochemistry Building was constructed in the early 1960s, the air handling system was state-of-the-art. But standards change, and mechanical systems age. Thus it is that a multimillion dollar renovation of the ventilation system in the Biochemistry Building is now underway. It will be done in four phases over a 1½ year period. Each phase will deal with the air handling system in one vertical "quadrant" of the building, i.e., a vertical section encompassing all floors as a single unit. Duct work will be replaced, and air handling capacity upgraded to meet current standards. New hoods will be installed in the laboratories, and lighting fixtures and hanging ceilings replaced. As you might guess, this is not done without considerable disruption of normal activity. All laboratories and offices located within each vertical quadrant must be temporarily relocated while that phase is being done.

In mid-May, the lucky occupants of laboratories and offices

Motion and Commotion

Continued from page 20.

Photographs by Lynne Brown, Media Graphics, Inc.

located in the "Phase 1" quadrant were busy packing up and moving to temporary quarters. Assuming things proceed as scheduled, at about the time this magazine is going to press, those displaced by Phase 1 should be returning to their refurbished quarters and those affected by Phase 2 moving to their temporary quarters. The traditional collegiality at MSU has been an important factor as colleagues not affected (at least not yet–their turn is coming) by the move have made space available to accommodate their displaced comrades.

Biochemistry Stockroom Supervisor and Jack-of-all-Trades Joyce Robinson has handled the logistics of the moves and made arrangements for moving heavy items or instruments requiring special handling. Assisting Joyce is Professor Emeritus Loran Bieber, who returned to duty on a part-time basis, once again answering the call to service as he has done so many times in the past. Also playing a vital role in the process is departmental handyman, Ron Norris. It turns out that the building plans have not been updated since the originals were done back in the 60s. In addition to providing much of the muscle for the actual moving, Ron is providing vital information to guide the renovation process. It seems that Ron is the only one who actually knows the location of most of the things (e.g., additional telephone lines, ethernet cables, new valves and switches) installed in recent years, and he is proving to be an invaluable information source for the construction crews as they dismantle the infrastructure in the course of the renovation.

(Top Left) Joyce Robinson has played a critical role in locating temporary space for those displaced by the renovations and supervising the moves to temporary quarters. Despite the hassles, Joyce has kept her good humor and continues to flash her cheery smile.

(Top Right) A typical view of a laboratory under renovation. The original ceiling and ventilation ductwork has been removed. In addition to new ductwork, new ceilings and light fixtures will be installed as part of the renovation.

(Above) Ron Norris has been a vital part of the renovation process, helping with the moves and serving as a source of information about the location of various facilities that were added in more recent years and thus not noted in original blueprints for the building.

The REF Center for Biological Modeling

Contributed by Leslie Kuhn, Director, REF Center for Biological Modeling, and Associate Professor of Biochemistry and Molecular Biology

At the cellular level, all biological activity occurs at the interfaces between molecules–the association of lipids and proteins to form cell membranes, the movement of molecules along microtubules formed by structural proteins, and the catalysis of chemical reactions on a range of molecules by proteins. Similarly, a number of the major discoveries in science have happened at the interfaces between fields, when ideas from one field suddenly provided the key to another. A famous example is the double-helix model of the DNA structure by zoologist James Watson and physicist Francis Crick, which was guided by biophysicist Rosalind Franklin's powder diffraction experiments that defined the spacing of atoms in DNA. Such interfaces between fields also have taken unexpected directions, such as the development of genetic algorithms, which mimic the mutation, recombination, and replication events of DNA, as a general way of encoding a set of adaptable features to optimize the behavior of a system. Genetic algorithms have been used in such broad contexts as dynamically adjusting car engine parameters to minimize vibrations in the camshaft (through the work of Ford Research in Dearborn), and predicting binding sites in proteins based on the structural and chemical features of their surfaces (the work of Mike Raymer, Bill Punch, Erik Goodman, and Leslie Kuhn at MSU).

The Research Excellence Fund Center for Biological Modeling (CBM), which was founded in July 2000, is based on this paradigm: that the cross-fertilization of ideas and techniques between fields leads to major progress and breakthroughs in research, and reduces the limitations we might otherwise face because no one scientist can become an expert in all the areas of theory and experiment that would be helpful for advancing his or her work. Working with scientists who view a problem totally differently, and speak a different language, is also intellectually expansive in the same way as it is to spend time in Rhodes or Morocco–aside from the intellectual stimulation of experiencing a new culture, you realize that societies (even scientific disciplines) come with their own sets of assumptions and approaches that are just some of the many good choices.

To encourage interchange between scientific disciplines and lower the barriers to interdisciplinary collaboration, the Center for Biological Modeling aims to foster collaborations and graduate and postdoctoral training that develop or apply techniques from the physical, mathematical, statistical, and computational sciences to model important biological processes. Part of this can be achieved through the "Small World" phenomenon, since researchers who are highly interdisciplinary and collaborative essentially act as hubs for other scientists to make new collaborative connections. Research projects in the CBM involve protein folding, biomolecular catalysis, the rational development of drugs, and modeling the spread of disease and the evolution of organisms and molecules.

The key faculty of the CBM represent such a highly interdisciplinary group: Peter Bates (CBM Advisory Committee; Chair, Mathematics), Wolfgang Bauer (Chair, Physics & Astronomy), Christina Chan (Chemical Engineering), Robert Cukier (CBM Associate Director; Chemistry), Phil Duxbury (CBM Advisory Committee; Physics & Astronomy), Shelagh Ferguson-Miller (CBM Advisory Committee; Chair, Biochemistry & Molecular Biology), Wenjiang Fu (Epidemiology), Joseph Gardiner (Statistics & Probability), Thomas Getty (Zoology), Marianne Huebn-

er (CBM Advisory Committee; Statistics & Probability), Leslie Kuhn (CBM Director; Biochemistry & Molecular Biology), Richard Lenski (CBM Advisory Committee; Zoology, Microbiology, and Crop & Soil Sciences), Charles Ofria (CBM Advisory Committee; Computer Science & Engineering), Piotr Piecuch (Chemistry), Sakti Pramanik (Computer Science & Engineering), William Punch (CBM Advisory Committee; Computer Science & Engineering), Michael Thorpe (CBM Advisory Committee; Physics & Astronomy), and Eric Torng (Computer Science & Engineering). The External Advisory Board for CBM includes Christoph Adami (Physics, Caltech), Jayant Banavar (Chair, Physics, Penn State), Ronald Levy (Chemistry, Rutgers), Gerald Maggiora (Computer-Aided Drug Discovery, Pharmacia), and Fengzhu Sun (Molecular Biology & Mathematics, USC), and works with the CBM Advisory Committee to review and develop CBM programs.

The CBM's three focus areas are biomolecular structure and function, evolutionary modeling, and biological networks. These areas link us to some of the most active modeling and experimental efforts on campus and in the Michigan Life Sciences Corridor, in structural and quantitative biology, bioinformatics, and genomics, as well as the proposed NSF Center for Applied Evolutionary Dynamics and Computation. The CBM's activities are open to all faculty, postdoctoral fellows and students, and bring many interdisciplinary scientists to MSU as collaborators and seminar speakers.

CBM has actively supported a number of activities that foster interdisciplinary scientific interactions. Thus, CBM has been involved in coordination of interdepartmental faculty hires (e.g., the recent hiring of Dr. Michael Feig, who is jointly appointed in Chemistry and in Biochemistry and Molecular Biology, and Dr. Bill Wedemeyer, who is jointly appointed in Physics and Astronomy and in Biochemistry and Molecular Biology) to enhance the core of collaborative faculty expertise. In addition, CBM has sponsored the development of several new graduate courses, and is now working to develop a formal *Training Program in Quantitative Biology and Biological Modeling* (PQB^2M). Each graduate student and postdoctoral fellow in PQB^2M will receive training and research experience in two fields, providing superior preparation for an innovative research career and clearly distinguishing this program from more traditional programs in bioinformatics and biophysics at other schools. To encourage new collaborations between biological, physical, and computational scientists, CBM has sponsored a range of workshops and conferences as well as an active seminar program. In Spring 2002, faculty from the Stanford Biomedical Informatics program and CBM faculty from four departments presented a series of video teleconference seminars as simulcasts to Stanford University and MSU. In 2001-2003, CBM also hosted eight faculty visitors (mathematicians, physicists, biophysicists, and chemists) collaborating with two or more MSU faculty.

CBM has addressed the need for more advanced computing hardware, and has devoted part of its budget to develop a 32-processor computing facility. This cluster provides computing resources beyond what most research labs can build on their own and is freely available to MSU researchers in biological modeling. Lack of familiarity with computers and software might deter those interested in using modeling in their research. To address this, CBM computing staff members Roy Day (PhD, Physics) and Stepan Sklenak (PhD, Chemistry) have tutored new users, helped others tailor their software to work more effectively, and taught courses in biocomputing.

Planning for other innovative developments is currently underway. For more information about CBM and its many activities, go to the CBM website, **http://www.cbm.msu.edu**. We encourage you to browse our website and contact us with your questions and ideas! I can be contacted by e-mail to **KuhnL@msu.edu**.

Whatever happened to Woody?

Many of the older readers of this magazine will remember Professor Willis A. Wood, "Woody" to all but the most respectful of his students and colleagues. Woody was one of the first faculty members recruited by R. Gaurth Hansen, founding Chairperson of this Department. Together with Professor Ed Tolbert, Woody was largely responsible for the highly functional design of the Biochemistry Building that was completed in 1964 to house the newly formed department. Professor Wood was internationally known for his work on microbial carbohydrate metabolism, and maintained an active and rather large research group that, among other things, was responsible for isolation and characterization of several of the novel enzymes involved in these metabolic pathways.

Professor Wood and members of his research group (*circa* 1967). From left in front row: Woody, Jean Deupree, Ken (Rabinowitz) Warren, Don Beitz, Bob Niederman, Wyjaya Altekar, Les Barran, Mark Roseman, Jeanette Piperno (now deceased), and Patti (Vignola) Prokopp. From left in back row: Harvey Mohrenweiser, Karl Decker, Don Schneider, Hans Moeller, Dennis Shada, Howard Brockman, and Don Robertson.

Woody's laboratory (the "Wood Institute"), located on the 4th Floor of the new building, was well equipped with state-of-the-art instrumentation for enzymological studies. Perhaps of particular note were the Gilford spectrophotometers with multi-sample changers for simultaneous measurement of up to six enzymatic reaction rates. Cuvettes were moved into the light path on a repetitive programmed basis and changes in absorbance recorded for a determined period before the next cuvette was moved into the observation beam. "Connecting" the recorded segments provided the plot of absorbance vs. time required to calculate the rate. This ingenious device, the product of the fertile brain of Professor Wood and marketed by the Gilford Company, was a tremendous time-saver in an enzymology laboratory where enzyme assays are the staff of life. Woody's laboratory was also the location for sophisticated amino acid analysis instrumentation, capable of analyzing much smaller samples than were typically required for other amino acid analysis methodologies at the time. (The notion of analyzing amino acid content of a protein must seem quaint to younger readers, for whom the standard route to determining amino acid composition has been to clone and sequence the cDNA, then deduce not only the composition but amino acid sequence as well. T'was not so in the old days!) Professor Wood was also the first Biochemistry faculty member to crystallize an enzyme of interest, and his group collaborated with Professor Alex Tulinsky, an x-ray crystallographer on the Chemistry Department faculty (and *the* x-ray crystallographer on campus in those days), in determining the structure.

In addition to his outstanding contributions to the research environment of the department, Woody played an active role in developing the course structure of the fledgling graduate and

undergraduate programs, and it was widely recognized that founding Chairperson Gaurth Hansen valued the wise counsel provided by Woody on many issues that faced the developing department. When Dr. Hansen decided to move to Utah State University in 1968, Professor Wood was selected to succeed him as Chair.

Some years later, Woody himself decided to move west, even further west than Utah, all the way to La Jolla, CA, where he took a position with the Agouron Institute. The latter had been founded in 1978; one of its primary research interests initially was in environmental microbiology, and the microbiological expertise of Professor Wood was a valued addition. In subsequent years, the Agouron Institute evolved, spinning off a commercial operation, Agouron Pharmaceuticals, in 1984. As part of this separation, the Agouron Institute received a major portion of the founding stock of Agouron Pharmaceuticals. The latter was a successful endeavor, including among its products the widely prescribed HIV protease inhibitor, Viracept™. In 1998, Agouron Pharmaceuticals was purchased by Warner Lambert, which subsequently merged with Pfizer. The net result of all this was that the original Agouron Pharmaceuticals stock appreciated greatly in value, leaving the Agouron Institute in excellent financial condition.

As it currently operates, the Agouron Institute does not function as a research institute *per se*, but rather as a funding and science policy resource, using the financial benefits realized from the success of Agouron Pharmaceuticals to make "highly leveraged investments in basic biology and chemistry." The Institute seeks to identify areas considered to have particular promise, one being structural studies on supramolecular assemblies such as the ribosome, and then provides funding for research infrastructure and innovative research in those areas. Another identified area of interest is geobiology. In May, 2000, the Agouron Institute supported a meeting at which experts assessed current status and future needs for the field of geobiology. The resulting "white paper" provides a basis for future funding decisions of the Agouron Institute in this area of study.

Woody and his wife, Kitty, live in Poway, located just north of San Diego. Woody currently serves as Vice President of the Agouron Institute, a position that he says requires about one day per week of his time, leaving ample time for him and Kitty to enjoy the delights of Southern California life.

The annual meeting of the American Society for Biochemistry & Molecular Biology was held in San Diego in April, 2003, and provided an occasion for several of Woody's former students and colleagues to renew old ties. Enjoying a luncheon get-together were Woody's former students, Jean Deupree and Don Beitz, former postdoc Phil Whanger, as well as two other former Spartans from Woody's time, Fred (Clarence Suelter lab) and Marlene (Bill Deal lab) Kayne, and yours truly.

Professor Willis Wood (Woody) and former students and colleagues met for lunch during the ASBMB meeting in San Diego, April, 2003. From left: Jean Deupree, Woody, Phil Whanger, Don Beitz, John Wilson, Marlene Kayne, Fred Kayne.

Always an Outsider

Contributed by Philip L. Felgner BS '72, MS '75, PhD '78

"Lipofection" is the term coined for cationic lipid-mediated DNA transfection that was discovered in my lab at Syntex Research. Syntex was a pharmaceutical company in Palo Alto, California, where I was studying the use liposomes for drug delivery. One day we mixed some cationic liposomes with negatively charged plasmid DNA and found that they formed well behaved little complexes which we called "lipoplexes." An undergraduate summer student working in my lab knew how to do chloramphenicol acetyltransferase (CAT) assays, so we decided to see whether lipoplexes could deliver a plasmid encoding the CAT gene into cultured cells. Low-and-behold, it worked, and we recovered lots of CAT enzyme activity from the transfected cells. In those days, the mid-1980s, investigators were looking for more convenient and effective ways to transfect cultured cells and lipofection fit the bill. Pretty soon we were sending samples of "Lipofectin" all over the world.

This was also a time of great enthusiasm, both in academia and in the biotechnology industry, for the promise of gene therapy. Since Syntex was a pharmaceutical company, we decided to try Lipofectin for *in vivo* gene delivery. But there was a hitch. The NIH Recombinant DNA Advisory Committee had so many regulations in place that it took forever for Syntex to figure out how to get approval for the experiments. Meanwhile, I took a job in San Diego to help start up a new biotechnology company called Vical. Vical was an AIDS antiviral nucleotide company, but we decided to keep a gene therapy project going on the back burner. We synthesized some new cationic lipids and established a collaboration with Jon Wolff, a faculty member at the University of Wisconsin-Madison, to do the animal studies, and finally in January of 1989, we were ready to do the experiment.

Vaccines offer one of the oldest and most effective ways to fight disease, and Naked DNA vaccines represent one of the most significant, fundamental additions to vaccine technology in recent years. It certainly has been exciting to participate in these discoveries.

It was a memorable day in the lab when we looked at the first set of data and saw levels of CAT gene expression in mouse skeletal muscle (we called it "CAT-in-mouse") comparable to the best results we had obtained by transfecting cells in culture. But the next observation was an even bigger surprise. We found that DNA by itself, which was supposed to be the negative control, gave expression levels similar to or greater than the lipid formulations. At first we brushed it off as some kind of artifact, but after a few weeks and several more experiments, as well as several accusations that "somebody switched the tubes," we finally accepted the conclusion that lipofection wasn't necessary for the expression. In fact the formulations with cationic lipid were less effective than those without lipid. "Naked DNA" could be expressed *in vivo* and cationic lipids were inhibitory–exactly the opposite of what was predicted from experiments in cultured cells! Because of these results, Vical completely changed its focus and became the "Naked DNA Company."

Although the reporter gene expression levels at the injection site were comparable to those obtained from cultured cells, the nanogram amounts of expressed protein seemed too small to

PROFILES

Philip L. *Felgner*

Philip Felgner is a native of Frankenmuth, Michigan. He received both his undergraduate and graduate degrees from MSU, and subsequently did postdoctoral work at the University of Virginia. In 1982, he joined Syntex Research as a Staff Scientist, and until recently, when he accepted a faculty position in the Center for Virus Research at the University of California-Irvine, he has worked in the biotechnology industry thoughout his career. And what a career it has been! He has participated in the founding of two biotechnology companies (Vical, and Gene Therapy Systems) and served as their Chief Scientist and in various other administrative capacities. In 1996, Dr. Felgner's outstanding accomplishments were recognized with the John A. Boezi Memorial Award from this Department. In that same year, he was named as Southern California's "Inventor of the Year." He has served on the advisory boards for several professional organizations and biotechnology industries, and on the editorial boards of prominent journals in his field.

An abiding interest since his undergraduate days has been the function and properties of lipids, and their application to processes of biological importance. In the accompanying article, Dr. Felgner gives his personal account of the development of one of the most promising recent developments in vaccine technology, the use of "naked DNA" as immunogen ("DNA vaccines"). It seems ironic that one of the major outcomes of a research career focused on lipids should be development of a technique that, in fact, is inhibited by lipids. But who knows where the road will lead? And the good scientist follows it, unimpeded by whatever preconceptions might have to be abandoned in the process.

effectively address classical gene therapy targets like hemophilia, hypercholesterolemia, or muscular dystrophy. However, around the time of our discovery, immunologists were describing pathways of antigen presentation and immune stimulation that suggested a unique way to take advantage of the Naked DNA effect. They described two different pathways of antigen processing. Proteins that are taken into cells by endocytosis are processed by one pathway, leading to activated helper T cells and ultimately to the stimulation of antibody production. Stimulating antibody production was something that was relatively easy to do with established, old fashioned adjuvant technology, so this was not such a big deal. But proteins that are synthesized within a cell, like those that are made after transfecting DNA into them, are degraded by a separate pathway

and lead to the stimulation of cell mediated immunity. We hypothesized that the ability to deliver functional nucleic acids into cells, leading to intracellular expression of antigen, should specifically stimulate cellular immunity and cytotoxic T-cells. The consequences of enhancing the cytotoxic response to a viral protein might allow the control of chronic or latent viral infections. Thus, in addition to disease prevention, vaccination could be used for the *treatment* of diseases.

So then I went to an HIV conference at the NIH, looking for a collaborator who had a strong eukaryotic expression vector encoding a potent immunogenic antigen, and had all the reagents and expertise to evaluate the immunogenicity in animals. Dr. Nancy Haigwood, then an investigator at Chiron but now a faculty member at the University of Washington, was working on a recombinant HIV gp120 vaccine. Nancy had everything we were looking for, and she took an interest in what we were doing so we began a collaboration. In our 1991 N*ature* article, Gary Rhodes and I summarized the (then, still unpublished) results of the initial experiments with Dr. Haigwood:

"S*ome of these concepts have been tested by using a plasmid containing the gene for the human form of immunodeficiency virus gp*120 *protein and driven by the cytomegalovirus immediate early promoter.* A *single intramuscular injection of this plasmid induces a high titre of* IgG *antibodies.* T*he same injection scheme also induces cellular immunity to the protein.* T*hese preliminary findings suggest that vaccines may be one of the first applications of direct gene delivery techniques.*"[Felgner and Rhodes, 1991]

Vaccines offer one of the oldest and most effective ways to fight disease, and Naked DNA vaccines represent one of the most significant, fundamental additions to vaccine technology in recent years. It certainly has been exciting to participate in these discoveries.

Today I've "retired" to more of an academic lifestyle at the University of California in Irvine. When I worked in biotechnology companies, I used to be able to do research all day long. Now I get to read grants, write grants, and review other people's grants all day long. My university colleagues ask me: "Why did you stop working in biotechnology? So that you could attend faculty meetings!?" I guess there was always a kind of academic twist to the work that I did in the companies I worked with, so in a way I was kind of an outsider. Now at Irvine, I'm a biotechnology-oriented guy in an academic environment, i.e., an outsider again. But I'm finding that the faculty are interested in biotechnology and I'm helping to create a bridge, to encourage linkages between the university and industry. I'm not really looking for a place where the grass is greener, but Irvine does have a beautiful campus, and it makes life interesting to roam around in a different pasture.

Selected references:

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4. Ulmer, J.B. *et al.* (1993) Heterologous protection against influenza by injection of DNA encoding a viral protein. S*cience* **259**, 1745-1749.
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Graduates during the 2002-2003 Academic Year

PhD and MS Degrees

Kirsten Fertuck	PhD
Rodrigo Gutierrez	PhD
Brandon Hespenheide	PhD
Wayne Hicks	PhD
Sören Ottosen	PhD
Bryan Schmidt	PhD
Lyle Simmons	PhD
Jun Yang	MS
Maria Zavodszky	PhD

BS Undergraduate Degrees

Fall, 2002

Bonnie Ellen Ebendick	BMB/BT
Andrew J. Koshorek	BMB/BT
Todd Andrew Lydic	BMB/BT
Brandon A. Pabst	BMB/BT
Alicia M. Weldon	BMB/BT
Justin Aaron Barnes	BMB
Alia Vashti Hecht Hinz	BMB

BS Undergraduate Degrees continued

Spring, 2003

Shanna L. Ashley	BMB/BT
Phillippe Spencer George	BMB/BT
Brian Gregory Gronowski	BMB/BT
Jessica Fernand Miller	BMB/BT
Michael Edward Ruckle	BMB/BT
Brian Daniel Facione	BMB
Zinah Sungae Hong	BMB
Dana L. Meerschaert	BMB
Woo Jung Moon	BMB
Katie Johanna Porter	BMB
Patricia Jeanne Terwillegar	BMB
Matthew Scott Worges	BMB
Joan Erica Frando	LBS/BMB
Jonathan Russell Hall	LBS/BMB
Shawn Matthew Martin	LBS/BMB
Dana Anne Seror	LBS/BMB

Summer, 2003

Elizabeth Susan Askin	BMB/BT
Trevor Thomas Pled Barkham	BMB/BT
Faiza Mohamed Hajiabdi	BMB/BT
Paul Stephen Hastings	BMB
Wayne Edward Jenkins	BMB
Jerry Eugene Koroniotis	BMB
Elias O. Lemoine	LBS/BMB
Laura E. Miller	LBS/BMB
Lizabethann Cynthia Nolff	BMB/BT

2002
2003
Congratulations
Graduates

The Origin and Evolution of Biochemistry and Molecular Biology at Michigan State University

Contributed by Professor Emeritus Clarence H. Suelter

The Department of Biochemistry and Molecular Biology at Michigan State University has roots that go back to 1855, when the University, then known as the Agricultural College of the State of Michigan, was established. (The rather cumbersome name of the institution was shortened to State Agricultural College in 1861, then changed to Michigan Agricultural College in 1909, again lengthened to Michigan State College of Agriculture and Applied Science in 1926, which became Michigan State University of Agriculture and Applied Science in 1955, and simply Michigan State University in 1963.) In 1863, the Agricultural Chemistry Department of Instruction was created. This Department was subsumed into the Department of Chemistry in 1884 and eventually became a Division of Biochemistry within the Chemistry Department. The Michigan Agricultural Experiment Station was established in 1887 as a result of the Federal Hatch Act, which provided annual research funding to Agricultural Colleges. In 1961, the chemists in the Division of Biochemistry and those in the Department of Agricultural Chemistry in the Agricultural Experiment Station formed a new Department of Biochemistry, subsequently renamed the Department of Biochemistry and Molecular Biology in July of 2001.

The Agricultural College adopted its first four year course of study in September, 1858. The faculty, particularly those in chemistry, botany, entomology, and agriculture, also initiated experimental work. By 1888, before any funds were received through the Hatch Act, 42 bulletins and numerous reports had been published.

The first Professor of Chemistry, Lewis Ransom Fisk, was appointed in 1857. Professor Fisk had a rather remarkable career. In 1859, he became the second President of the Agricultural College and served until March of 1863, at which time he resigned and began a second career as a Methodist minister. He served at various Methodist churches in Jackson, Detroit, and Ann Arbor, before returning to academia as President of Albion College in 1877.

In February, 1863 (just one month before Professor Fisk's departure from East Lansing), Robert Clark Kedzie, at the age of 40, was appointed Professor of Agricultural Chemistry. Kedzie was a member of the first medical school class at the University of Michigan, receiving his MD degree in 1851, but chose to follow his interests in chemistry rather than practice medicine. Professor Kedzie was to have a major influence on the development of chemistry and biochemistry at the Agricultural College. After his appointment, the Chemistry Department of Instruction was divided into three Departments: Elementary Chemistry, Analytical Chemistry and Agricultural Chemistry. Agricultural Chemistry dealt with studies on: the formation and composition of soils; the composition of air and its relation to vegetable growth; effects of heat, light and electricity on the growth of plants; the nature and sources of food for plants; chemical changes attending vegetable growth; chemistry of various farm practices such as plowing and draining; methods for chemically improving soils by mineral manures, vegetable manures and animal manures. The chemical composition of various crops and their uses as food, and the chemistry of dairy products and food preparation were also covered.

Built in 1856, College Hall was the first building erected on the new campus. Chemistry, being a central feature in the curriculum of the new College, occupied the entire first floor. College Hall collapsed in 1918. Photo from the Michigan State University Archives and Historical Collections.

This course was offered every year from 1863 until 1923. The 1923 College Catalog shows that the Department of Chemistry also offered other courses with biological content, including Biological Chemistry, Physiological Organic Chemistry, Plant Chemistry, Crop Chemistry, Fertilizer Chemistry, Food Analysis, and Dairy Chemistry.

R.C. Kedzie was a prolific writer of popular and technical articles on chemistry, agriculture, and public health. He authored publications dealing with the toxic pigment made from arsenic trioxide and copper acetate, commonly known as Paris Green and used as a coloring by the wallpaper industry, with the labeling of medicines, with resuscitation of drowning victims, and with the analysis of lamp oils. His work in the fertilizer industry led to the establishment at the College of a laboratory to analyze commercial fertilizers. Kedzie was also responsible for the origin of the sugar beet industry in Michigan and authored the first Bulletin of the Michigan Agricultural Experiment Station reporting work supported by the Hatch Act: Bulletin No. 1, entitled "Early Amber Cane as a Forage Crop."

R. C. Kedzie remained as Head of the Chemistry Department until shortly before his death on November 7, 1902. His son, Frank Kedzie (affectionately known as "Uncle Frank" to his students), was then appointed Head of the Department. He held this position until he was appointed President of the College in 1915. Presidents Fisk and Kedzie were

Continued on page 32

The first Chemistry Building, designed by Professor R.C. Kedzie, was built in 1871; it was enlarged in 1881, and again in 1911, and finally demolished in 1955. Photo from the Michigan State University Archives and Historical Collections.

Origin and Evolution

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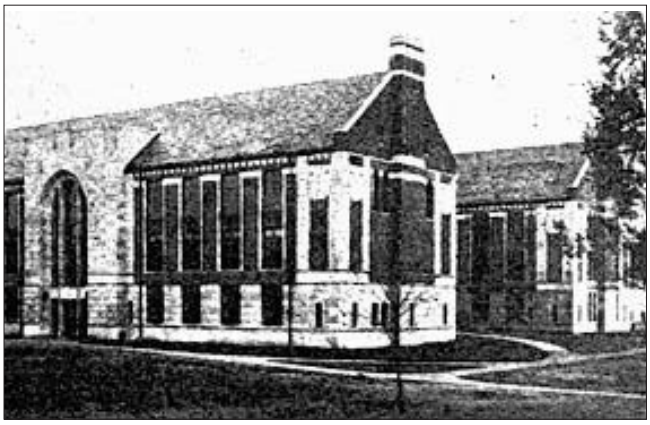
the only two chemists to be appointed as President of the institution. (For interesting biographical information on these and other MSU Presidents, go to **http://www.msu.edu/unit/msuarhc/presdnt.html**.) Frank Kedzie's interests, like his father's, were closely allied with Agricultural Chemistry.

Due to increased enrollment at the College and in chemistry courses, a new chemistry building was built and dedicated on May 12, 1927. This new building, now called the North Kedzie Chemical Laboratory, relieved laboratory congestion and made it possible for graduate students to work without interfering with undergraduate instruction. The first PhD degrees awarded for work in biochemical areas were to Perry A. Webber in 1931, whose thesis was entitled "The Effects of Certain Diets on the Teeth of the Albino Rat with Special Reference to the Development of Dental Caries," and to Alfred Day Hershey (joint degree in Chemistry and Bacteriology) in 1934, whose thesis title was "The Chemical Separation of Some Cellular Constituents of the *Brucella* Group of Micro-organisms." Alfred Day Hershey went on to an exceptional research career, sharing (with Max Delbrück and Salvador Luria) the 1969 Nobel Prize in Medicine, the only "Spartan" to have attained this distinction.



Kedzie Chemical Laboratory, built in 1927. Photo from the Michigan State University Archives and Historical Collections.

On March 31, 1961, the Board of Trustees approved the establishment of a Department of Biochemistry responsible to the College of Agriculture and to the College of Science and Arts, with R. Gaurth Hansen designated as the first Chair of the Department, effective April 1, 1961.

Biochemical roots at the College were also nourished by the Agricultural Experiment Station (AES). AES faculty with chemical backgrounds were called Experiment Station Chemists or Agricultural Chemists. In addition to their own research, they responded to the technical needs of faculty in various departments at the Agricultural College. In 1955, AES Professor Bob Evans worked with Poultry, Professor Harold Sell with Horticulture, Professor Cliff Duncan with Dairy, and Professor Richard Luecke with Animal Husbandry. Professor Erwin Benne provided analytical services to all departments. These faculty had 100 % research appointments; they did not teach nor did they have graduate students.

On November 1, 1957, Roger Gaurth Hansen was appointed Head of the Agricultural Chemistry group in the AES. When Professor Hansen met with President Hannah as part of the hiring process, President Hannah was delighted to learn that Hansen envisioned a diverse department that would support Hannah's goal of establishing a medical school on campus. Moreover, Professor Hansen urged that, in the proposed Biochemistry Department, *all* faculty would have full citizenship in the academic community, participating in teaching and eligible to serve as major professors for graduate students. Hansen saw a Department in which faculty members were equal in terms of

their ability to initiate and participate in research, from planning to the final publication stages.

In 1958, the Department of Agricultural Chemistry moved into the old Dairy Building which had been extensively remodeled. In 1959, the Board of Trustees adopted a resolution to drop the word "research" from the academic titles of AES faculty members in the Department of Agricultural Chemistry; henceforth, these faculty were to have the same status as all other members of the faculty, as envisioned by Professor Hansen. On March 31, 1961, the Board of Trustees approved the establishment of a Department of Biochemistry responsible to the College of Agriculture and to the College of Science and Arts, with R. Gaurth Hansen designated as the first Chair of the Department, effective April 1, 1961. This new Department was to meld the Department of Agricultural Chemistry with the Division of Biochemistry from the Chemistry Department. The administrative structure requiring the Chair to report to two Deans set the pattern–the "shared department"–for subsequent development of other preclinical departments in the medical school. The staff of the newly formed department included, from Chemistry, R.U. Byerrum, J.L. Fairley, C.A. Hoppert, G.L. Kilgour, H.A. Lillevik, and J.C. Speck, and, from Agricultural Chemistry, R.L. Anderson, S.L. Bandemer, E.J. Benne, C.W. Duncan, R.J. Evans, A.S. Fox, R.G. Hansen, R.W. Luecke, R.L. Salsbury, H.M. Sell, N.E. Tolbert, and W.A. Wood. An undergraduate program in Biochemistry was initiated in 1962.

Soil Science building, originally the college dairy, was built in 1913 and demolished in 1987. The Biochemistry group occupied the basement and the second floor. Photo from the Michigan State University Archives and Historical Collections.

The new Biochemistry Department lacked coherence, however, since faculty were spread among four buildings: Agriculture Hall, the Horticulture Building, the old Dairy Building, and Chemistry. They needed a common facility. Professors Hansen, Wood and Tolbert headed the effort to design a new building and, in May, 1961, submitted a proposal to the Facilities Division of the National Institutes of Health for one-half of its estimated cost of $5.2 million; the other half was to be matched by the University. This proposal was approved by NIH but because of decisions by the University's central administration, only half was designated for the new Biochemistry Building, the remainder going for construction of a building for the College of Veterinary Medicine. (E*ditor's note*: Rumor has it that some in central administration didn't believe that Biochemistry really needed such a large building as proposed.) Undaunted, Hansen and his colleagues submitted another proposal to the National Science Foundation in January, 1962, carefully wording it so that any funds received could be used *only* for construction of the Biochemistry Building. When this proposal was approved, a combined total of $5.2 million became available. Construction of the new building began on April 5, 1963, and it was completed by December, 1964. Professor N.E. Tolbert was placed in charge of the building plans. Initially, the University architects and physical plant offi-

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cials wanted the new building placed south of the railroad tracks and west of Baker Wood Lot, i.e., between Farm Lane and the Power Plant. Due to intervention by Dean Tom Cowden of the College of Agriculture, placement at this more isolated location was avoided and the building was constructed on its present site.

R.G. Hansen served as Chair of the Department from 1961 to 1968. Subsequent Chairs were: W.A.Wood (1968-1974), R.A. Barker (1974-1979), C.C. Sweeley (1979-1984), J. Preiss (1985-1989), J.E. Wilson (1989-1994), W.L. Smith (1994-2002), and presently, S. Ferguson-Miller.

Biochemistry Building, completed in 1964. Photo from the Michigan State University Archives and Historical Collections.

Administration of the Department became more complex after the Colleges of Human Medicine and Osteopathic Medicine were established in 1964 and 1969, respectively. Because these Colleges required participation of Biochemistry faculty in their programs, the Department became affiliated with these Colleges as well as retaining its association with the College of Natural Science and the College of Agriculture and Natural Resources. Thus, the Departmental Chairperson was now responsible to four Deans, instead of just two. This situation prevailed until July 1, 1994, when the College of Agriculture and Natural Resources' component of the Biochemistry budget was transferred to the College of Natural Science. Thus, formal affiliation with Agriculture, which had played a major role in forming and nurturing the Department of Biochemistry for almost 150 years, came to an end. Despite this, the Department remains true to its traditions; plant biochemistry and other agriculturally-relevant areas of research continue to be a major focus for some of the faculty, and several faculty retain some percentage appointment in AES. The Department of Biochemistry was renamed the Department of Biochemistry and Molecular Biology on July 1, 2001.

Acknowledgment: *Materials for this article were obtained from the Michigan State University Archives and Historical Collections and from personal communications with* R.G. *Hansen*, W.A. *Wood*, R.W. *Luecke and* R.U. *Byerrum*.

Alumni News

The concluding section in the last issue of this magazine provided some information about several past graduates of this department. Since that time, several other alums have responded to the request to let us know what life has brought to them since they left MSU, and we thank them for that. Their responses are collated below. Look them over and you might see a familiar name, and perhaps the opportunity to renew contact with a friend from your days at MSU. If you don't see your name below (or even if you do), we invite you to use the form attached to this publication to bring us up-to-date on your post-graduation activities and current position. You can use the postage-paid envelope to return the form to us or, if you prefer, send the information by e-mail to bchalum@msu.edu. *We look forward to hearing from you*!

Anderson, Matt - BS '80

Matt is currently a Senior Research Fellow at the Merck Research Laboratories in Rahway, NJ. He can be contacted by e-mail to matt_anderson@merck.com.

Beitz, Donald C. - PhD '67

Don Beitz, as a graduate student, can be seen in the photo of Professor Willis Wood's research group while the present-day Don Beitz is shown in a more recent photo (see article on pages 24-25). Don did a joint degree, receiving a PhD in both Biochemistry and Dairy Nutrition in 1967. Upon completion of his PhD, Don joined the faculty at Iowa State University in Ames, IA, where he has had an outstanding academic career and currently holds the position of Charles F. Curtiss Distinguished Professor of Agriculture. Don says that he and his wife, Judy, have very much enjoyed their life in Ames, where they raised two children and now have five grandchildren to enjoy. Judy has been a social worker at the local hospital, and served as Director of the Social Services Department. Don holds appointments in both the Department of Animal Science as well as the Department of Biochemistry, Biophysics, and Molecular Biology. His research in the area of nutritional biochemistry has brought him numerous honors, including most recently election as a Fellow of both the American Dairy Science Association and the American Society of Animal Science. Don can be contacted by e-mail to dcbeitz@iastate.edu.

DesRosiers, Ronald - PhD '75

Ron earned his PhD with Professor Fritz Rottman, and has subsequently had a distinguished career which was recognized with this department's Boezi Award in 1989. Ron is Director of the New England Primate Research Center (http://www.hms.harvard.edu/nerprc) and Professor of Microbiology and Molecular Genetics at Harvard Medical School (http://micro.med.harvard.edu/faculty/desrosiers.html). His research activities are focused on mechanisms of AIDS pathogenesis and AIDS vaccine development. He has two grown children. Ron's e-mail address is ronald_desrosiers@hms.harvard.edu. He says he welcomes e-mails from old friends as long as it is not to gloat over University of Minnesota's defeating the University of New Hampshire for the national hockey championship. Condolences go to New Hampshire native Ron and other New Hampshirites since they lost not only the hockey game, but also, in early May of 2003, their state landmark, the "Old Man of the Mountain," when the strains became too great and the granite profile of the "old man" came sliding down Profile Mountain (http://www.mutha.com/oldmanmt.html).

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We look forward to hearing from you!

Felgner, Philip L. - BS '72, MS '75, PhD '78

After an exceptional career in the biotechnology industry (see article on pages 26-27), Phil Felgner recently accepted a faculty position in the Center for Virus Research, University of California-Irvine. Phil's wife, Jiin, is a pharmaceutical formulation scientist with Sicor, a pharmaceutical company also located in Irvine. Their oldest son, Jeff, just finished his first year at UC-Riverside, majoring in biosciences. Younger son, Scott, will be starting at the University of Colorado in Fall, 2003, majoring in aerospace engineering. Phil is originally from Frankenmuth, MI, and says that his mother, at age 92, is "still kicking around Frankenmuth." However, Phil seems quite happy with the Southern California lifestyle, including the extended golfing opportunities available in that climate. He can be contacted by e-mail to pfelgner@uci.edu.

Fischer, William - BS '70

After graduation from MSU, William Fischer went on for a PhD in Biochemistry and Biophysics from Oregon State University, awarded in 1974. Subsequently, he was employed as a Senior Chemist at CIBA-Geigy. In 1980, he made the move from lab bench to computer room when he was appointed to a newly created position as Biochemistry Department System Manager. He left CIBA-Geigy in 1986 to become Senior Manager of Laboratory Automation Systems at Glaxo, Inc., which is headquartered in Triangle Park, NC. In 1992, he started his own company, Validex, Inc., that specializes in laboratory automation for regulated industries. He says he enjoys the benefits of a superb client list as well as a great staff that he can depend on to provide exceptional service to those clients. Dr. Fischer notes that running a company requires constant travel "which is not without its rewards." At the time of his e-mail in June, he was about to leave for a three week trip to Russia, his fifth visit since 1988. While in Russia, he planned to meet with faculty in the Biochemistry Department at the University of Moscow, "the original U of M." He had also recently returned from a week in Prague, Czech Republic (see adjacent photo). Dr. Fischer says his children have left home, providing discretionary time for activities of his own choosing, most of it spent in his woodshop or cruising the rivers of Europe. He continues to reside in Durham, NC, and can be contacted by e-mail to wcfischer@mindspring.com.

Dr. William Fischer and his Russian friend of many years, Larisa Lykhenko. They met in Prague recently, and this photo was taken prior to their attending a concert in that beautiful city.

Gehm, Barry D. - PhD '88

Barry Gehm wrote to tell us that in August, 2003, he would be starting a new position as Assistant Professor of Biochemistry in the Science Division at Lyon College, 2300 Highland Road, Batesville, AK 72501. Barry can be contacted by e-mail to barry.gehm@gt.org.

Hicks, Wayne - PhD '02

Wayne is currently a postdoc with Dr. Michael Olivier at the Medical College of Wisconsin in Milwaukee, where he is part of a large collaborative effort between industry and academe for development of new technologies and methodologies for proteomics. Wayne can be contacted by mail to the Medical College of Wisconsin, HMGC/HRC 5th Floor, 8701 Watertown Plank Road, Milwaukee, WI 53226-0509.

Jardieu, Paula - MS '80 (PhD, Microbiology, '82)

After several years working at Genentech in San Francisco, Paula has taken a new position with Prevalere Life Sciences, Inc., 1 Halsey Road, Whitesboro, NY 13492.

Kadrofske, Mark - PhD '99

Mark was a graduate student with Professor John Wang and enrolled in the joint MD-PhD program at MSU. Mark is currently a Fellow in Neurology at Case Western Reserve Univer-

sity in Cleveland, OH. Mark and his wife, Gwynne, have two sons, Elliot (age 5) and Samuel (age 2). He can be contacted by e-mail to mkadrofske@metrohealth.org or by phone (216) 778-5909 (W), (216) 381-3986 (H).

Kornosky, Jennifer - BS '02

Jennifer completed her degree as a Biochemistry major in Lyman Briggs School. She is now employed at Los Alamos National Laboratory, Los Alamos, NM, where she is involved in research on the effects of global warming on desert soil crusts. Jennifer can be contacted by e-mail to kornosky@lanl.gov.

Lichtstein, Danny - BS '70

After completion of his undergraduate degree at MSU, Danny went on for an MD degree and is currently Associate Professor of Medicine and Director of Education for the Department of Medicine at University of Miami School of Medicine. Danny's wife, Shirley, is also an MSU grad (BA, Education, '70).They have two children, a son (BS, Univ. of Michigan, '95) and a daughter (BS, MSU, '99). Danny can be contacted by e-mail to dlichtstein@med.miami.edu.

Danny Lichtstein

Lippitt, Denise (Messing) - BS '90

After graduation from MSU, Denise earned her MD from the University of Michigan Medical School in 1994. She did a residency in Pediatrics at the Children's Memorial Hospital (residency program of Northwestern University) and is now in general pediatric practice in Glenview, IL. Denise said she is currently living in Evanston, IL, married, and "with one gorgeous little girl, Maureen." Denise would welcome hearing from old friends by e-mail to dmlippitt@yahoo.com or phone (847) 729-6445.

Machalek, Alisa Zapp - BS '89

Alisa is a Science Writer at the National Institutes of Health (NIH). After graduating from MSU, Alisa earned an MS in Biochemistry from the University of Wisconsin, Madison, and then a Science Writing Certificate from the University of California, Santa Cruz. A recent profile on Alisa, produced by the NIH Office of Science Education, may be found at http://science.education.nih.gov/LifeWorks.nsf/Interviews/Alisa+Machalek. Alisa worried that, from the pictures found at that web site, "all my friends are going to think that I've put on a lot of weight. In reality, I'm 5.5 months pregnant in those pictures (due date, August 1, 2003)." The new baby will join the young son that Alisa and her husband already have. In addition to spending time with her family, Alisa enjoys swimming, hiking, mountain biking, gardening, cooking, and playing the oboe in chamber music groups. Alisa can be contacted by e-mail to machalea@nigms.nih.gov or snail mail to: Alisa Zapp Machalek, NIH/NIGMS, 45 Center Dr., Room 3AN.32, Bethesda, MD 20892-6200.

Merski, Matt - BS '99

Matt graduated from MSU with degrees in both Biochemistry and Philosophy. He is currently a graduate assistant at Johns Hopkins University in Baltimore, where he is working on a PhD in Biophysics. He can be contacted by e-mail to mtm1@jhunix.hcf.jh.edu.

Peterson, Donna Neal - MS '67

Donna sent us a note saying that she continues her work in the Minnesota Technical Assistance Program at the University of Minnesota, a program that provides assistance to companies dealing with various environmental issues. Donna has also been involved in numerous activities with international students and finds that very rewarding. Her husband, Dick, is Professor of Physics at Bethel College in St. Paul, MN. Donna's home address is 2436 N. Pascal, Roseville, MN 55113, phone is (651) 633-0923, and e-mail is peter080@umn.edu. Donna says that she would welcome hearing from former friends and colleagues.

Pike, Lee M. - MS '71, PhD '74

After completing his PhD with Professor Fritz Rottman, Lee did postdoctoral work at Hahneman Medical College in Philadelphia, and subsequently at the Baylor College of Medicine in Houston. In 1976, he

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joined the Biological Sciences faculty at East Tennessee State University and has remained there since. Lee says that he has had a good career at ETSU, teaching biochemistry and biology, and he also works with students in the biological sciences MS graduate program as well as those in the biochemistry graduate program in the medical school. Lee looks forward to retirement a few years hence, and says that he and his wife will probably move closer to their children and grandchildren, who live in Kokomo, IN, and Cincinnati, OH. However, Lee also says that he is "spoiled with respect to winters, so we will not go too far north." Lee can be contacted by e-mail to pikel@etsu.edu.

Prohaska, Joseph R. - PhD '74

Joe's PhD work with Professor Bill Wells was focused on the effects of dietary copper deficiency, and he has continued to work in this area during his subsequent academic career at the University of Minnesota, Duluth, where he currently is Professor of Biochemistry and Molecular Biology (**http://umn.edu/home/jprohask**). In research supported by both NIH and USDA, Joe is investigating the impact of copper deficiency on development of the central nervous system, elucidating the mechanism by which copper deficiency leads to cardiac hypertrophy, and evaluating the potential for measuring the activity of a copper-dependent enzyme as a way to assess copper status in humans. Joe can be contacted by e-mail to jprohask@d.umn.edu.

Sasavage, Nancy - PhD '81

Nancy works in Washington, DC, for the American Association for Clinical Chemistry (AACC), an organization of clinical laboratory professionals. Nancy is the editor for the AAAC publication, *Clinical Laboratory News*, and also coordinates an annual conference on emerging technology for clinical laboratory testing. After a vacation on Mackinac Island last year, Nancy stopped in East Lansing to visit with her old friend from days in the Fritz Rottman laboratory, Karen Friderici (Karen is now an Associate Professor of Microbiology and Molecular Genetics at MSU). Nancy also enjoyed seeing the new Biomedical and Physical Sciences Building and taking a nostalgic walk through the halls of Biochemistry. She lives with her 10-year old son, Russell, in North Potomac, MD, and may be contacted by e-mail to nsasavage@aacc.org.

Schneider, D. - PhD '69

Don Schneider was a PhD student with Professor Willis Wood. We suspect that he no longer looks quite like he did in the photo of Woody's research group (*circa* 1967) that appears elsewhere in this magazine. Currently, Don is Director of the Division of Molecular and Cellular Mechanisms, in the NIH Center for Scientific Review, Bethesda, MD. Don mentioned that three of the five Division Directors in the Center for Scientific Review are MSU graduates, the others in addition to himself being Suzanne Fisher (Director, Receipt and Referral Division) and Elliott Postow (Director, Biological Basis of Disease Division). Former faculty member, Arnold Revzin, is also involved in the review process at NIH; Arnie administers the Biophysical Chemistry Study Section and also works with Suzanne as a Referral Officer. Quite remarkable that such a cluster of Spartans are involved in shepherding NIH research proposals through the peer review process. Don also reminded us that two other MSU PhDs from his era, George Johnson (PhD with Professor Bill Deal) and Ken Rabinowitz Warren (also did his PhD work with Professor Wood, and also seen in the group photo along with Don) are at NIH. Don can be contacted by e-mail to schneidd@csr.nih.gov.

Spellman, Michael - PhD '83

A former PhD student with Professor Ed Tolbert, Michael sent us a note to give his present home address as 2 Hastings Road, Weston, MA 02493.

Stancel, George M. - PhD '70

Since his departure from MSU many years ago, George Stancel has had a distinguished career as teacher, researcher, and administrator. His accomplishments were recognized with this Department's Boezi Award in 1990. George is currently Dean of the Graduate School of Biomedical Sciences and John P.

McGovern Professor of Biomedical Sciences at the University of Texas Health Science Center in Houston. Despite his administrative responsibilities, George still teaches and maintains an active extramurally-funded research laboratory, and says he's "still enjoying what we do." George and his wife, Mary, have three grown children; their oldest son works in patient relations at the M.D. Anderson Hospital in Houston, another son is about to enter third year of medical school, and a daughter will be finishing her undergraduate work at University of Texas, Austin. George can be contacted by e-mail to George.M.Stancel@uth.tmc.edu.

Washburn, Michael - PhD '98, and Florens, Laurence

After completing his PhD with Professor Bill Wells, Mike did postdoctoral work with Professor John Yates III in the Department of Molecular Biotechnology at the University of Washington. During this time, he developed a multi-dimensional chromatography and tandem mass spectrometry system for assessing the "proteome" (the protein population in a cell or organism). In 2000, Mike moved to a position as Senior Staff Scientist in Proteomics at the Torrey Mesa Research Institute in San Diego, CA. Dr. Yates also moved to the San Diego area, taking a position at the Scripps Institute, and their collaborative work on quantitative proteomics continued. Recently, Mike accepted the position as Director of Proteomics at the Stowers Institute for Medical Research in Kansas City (http://www.stowers-institute.org). In an extensive e-mail to former Chairperson Bill Smith last February, Mike made clear his excitement about his new position. The Stowers Institute is making a very substantial commitment to research in proteomics, and Mike is clearly "in on the ground floor," so it is easy to see why he should be so excited about this opportunity. During his graduate student days at MSU, Mike met and subsequently married Laurence Florens, then a postdoctoral associate with Professor Ferguson-Miller. With the move to the Stowers Institute, Laurence will also have an independent position there. Mike says that they will continue to work closely, even though their positions are independent, and notes that "...each position is ideally tailored to our skills. It is almost too good to be true."

Welch, Shirley L. - BS '73

After MSU, Shirley proceeded to the University of California, Berkeley, from which she received her PhD in Biochemistry in 1977. During her undergrad years, Shirley worked in Clarence Suelter's laboratory, and the acquaintance was renewed when Clarence spent a sabbatical at UC-Berkeley while Shirley was a student there. Shirley did postdoctoral work in biochemistry and biophysics at Oregon State University in 1977-1980, and for the past 23 years, has been a resident of Portland, OR, where she is currently Director of Chemistry for Kaiser Permanente NW Regional Laboratory, and also an Asst. Professor of Pathology at Oregon Health Sciences University. Off duty, Shirley enjoys hiking, climbing and skiing in the Northwest and other mountainous regions of the world. Her address is 3724 NE 24th, Portland, OR 97212, or she can be contacted by e-mail to Shirley.L.Welch@kp.org.

Shirley L. Welch

Thank You!

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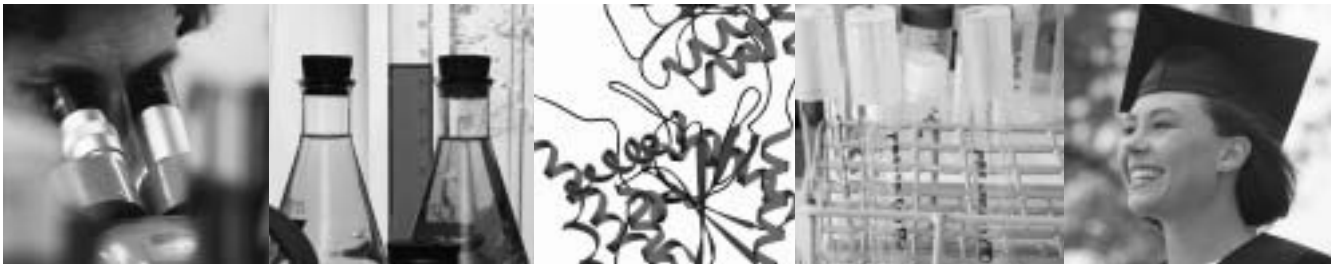

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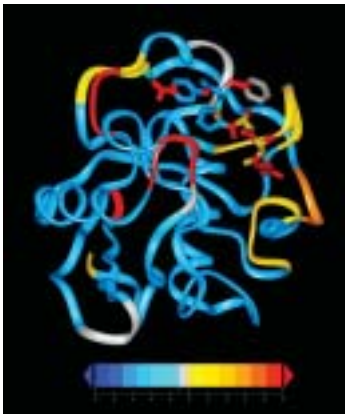
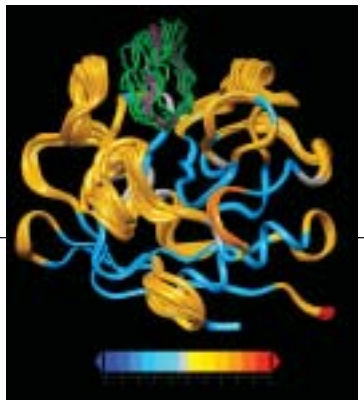


Flexible molecular recognition: The relative flexibility of various structural regions in the protein cyclophilin A is indicated by the color scale at bottom, from rigid regions colored blue to highly flexible regions in red. Bound to cyclophilin A is part of an HIV capsid protein (tubes at top center, also colored by their degree of flexibility). Cyclophilin A catalyzes the isomerization of a backbone bond in HIV capsid and other proteins, and thus must be able to recognize and bind a variety of proteins. Flexibility in both cyclophilin A and its partner proteins is required for this to occur. (M. I. Zavodszky and L. A. Kuhn)

The new Biomedical and Physical Sciences (BPS) Building is in the foreground. The Biochemistry Building, at the right, is connected to BPS by walkways at the basement and fifth floor levels of Biochemistry. Not seen, but at the left in this view, is the Chemistry Building, to which BPS is also connected by walkways.



Flexible molecular recognition: The relative flexibility of various structural regions in the protein cyclophilin A is indicated by the color scale at bottom, from rigid regions colored blue to highly flexible regions in red. Bound to the cyclophilin A is cyclosporin (average shape shown in pink while the entire range of shapes it can assume when binding to cyclophilin A are shown in green). Binding of cyclosporin to cyclophilin A regulates the immune response, and cyclosporin is commonly used as an immunosuppressant to prevent rejection of organ transplants. (M. I. Zavodszky and L. A. Kuhn)

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