Kolff (18)

THE UNIVERSITY OF UTAH

Memorandum

To: Joseph Andrade

From: David W. Pershing

Subject: Chairmanship of Bioengineering

Date: June 7, 1988

I am extremely pleased to notify you that the university administration has now approved my recommendation to appoint you as Chairman of Bioengineering effective August 1, 1988. I believe that Professor Christensen has effectively lead and strengthened the department during the past three years and I am confident that you will continue this trend. I believe the Department of Bioengineering is an important aspect of our College and I plan to support its development where possible.

Thank you for your willingness to accept this administrative position. I am looking forward to working with you as a member of the College Executive Committee.

cc: Faculty of Bioengineering
Joe Taylor - Vice-President for Academic Affairs

To Dr Andrade
Please let me know anytime
I can do something for you
Under your guidance B.E should
Prosper.
D.P.

College of Engineering
Office of the Dean

2202 Merrill Engineering Building
Salt Lake City, Utah 84112
Telephone (801) 581-6911

BIOENGINEERING

SPOTLIGHT

Update from University of Utah Autumn 1988

From the Chair

This publication marks the rebirth of the *Utah Bioengineering Newsletter*, which was originally published during the period from 1973 to 1985. The University and the state of Utah are internationally recognized as having one of the largest concentrations of bioengineering activities in the nation. There has not been a convenient forum for communication among the individuals and organizations active in those areas. Although many of these bioengineering activities are internationally known some are not very well known locally. The University of Utah's Bioengineering Department serves as a coordinating center for many of the University's bioengineering-related activities. The Department of Medical Informatics in the College of Medicine, and other campus departments, institutes, and centers, also have strong bioengineering activities.

Bioengineering *Spotlight* provides a forum for the transfer of information between those bioengineering activities on campus and the local community. It is designed for distribution to state and local officials, to the bioengineering/biotechnology and medical products industries in the state, to higher education leaders and officials, to local media interested in the reporting and transfer of technical information, and to alumni outside of the state who are directly interested in economic development and bioengineering education, research, and technology transfer.

All of us affiliated with the newsletter hope it will be a useful means of transferring information and that it will promote a mutually beneficial working relationship between our Bioengineering Department, bioengineering research groups and local industry.

Joseph D. Andrade, Ph.D.,
Chairman,
Department of Bioengineering

Below: New Engineering Mines Classroom Building adjacent to Merrill Engineering Building.

Awards and Honors

The following students received fellowships and awards this year:

Philip D. Baker	Curtis C. Johnson Memorial Award
Gail L. Blomstrom	James LeVoy Sorenson Foundation Scholarship
Eleanor V. Goodall	College of Engineering Scholarship
John D. Marks	Graduate Research Fellowship University of Utah
Harold P. Swerdlow	Graduate Research Fellowship, University of Utah, and National Science Foundation Fellowship

Research Update

The Artificial Eye Project

Faculty of the Bioengineering Department have revived a program which had its origins at the University of Utah some twenty years ago. The long-range goal is to provide a limited sense of vision to the blind. If the directors of this program, Drs. Richard Normann and Kenneth Horch, are successful in their efforts, blind patients will enjoy a fair degree of visually guided mobility without the use of guide dogs, canes, or other aids.

Kenneth Horch, Andrew Schoenberg

Richard Normann

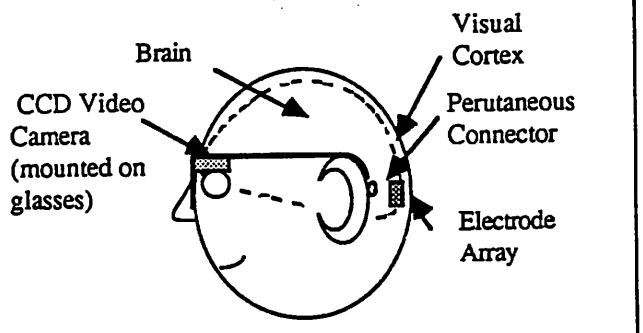
In order to explain how we will achieve this goal, one needs to understand how the visual system normally functions. First, light entering the eye forms an image of visual space on the retina The photoreceptors of the retina change the light patterns of this image into patterns of electrical signals and transmit them to the visual cortex on the rear surface of the brain. Thus, a visual scene in front of an observer becomes a two-dimensional pattern of electrical activity spread over the visual cortex.

Retinal damage is the source of the sensory deficit in most blind individuals. Since the higher visual centers in the brain of most blind individuals are still functional, external electrical currents passed into the visual cortex will produce sensations of spots of light called "phosphenes". If a large number of electrodes are placed in the visual cortex, and if these electrodes are stimulated appropriately with signals originating from a miniaturized video camera, the subject should perceive an array of phosphenes which could be used to produce a limited "visual image" of the world in front of the camera. This is the physiological basis for the artificial vision system which Normann and Horch propose to build (Figure 1). It will consist of an array of electrodes implanted on the visual cortex, a miniaturized television camera (perhaps attached to a pair of spectacles) to encode visual information in front of the blind individual, and processing electronics to transform these video signals into electrical stimuli to be delivered to the visual cortex. The system would use a small percutaneous connector located behind the ear for access to the cortical electrodes.

Previous attempts to provide artificial vision using electrical stimulation of the visual cortex through implanted electrodes have produced mixed results. While these studies confirmed that such stimulation could evoke arrays of visual phosphenes, they did not lead to a functional artificial vision systems.

A key difference between these previous efforts and the present Artificial Vision Program is the use of electrode arrays which will penetrate into the visual cortex. It is expected that a useful artificial vision system based upon electrical stimulation of the visu-

Figure 1 - Schematic diagram of the propsed visual prosthesis system. The main elements of the system are the cortical implant (the electrode array), the percutaneous connector, a video camera and signal processing electronics (not shown).



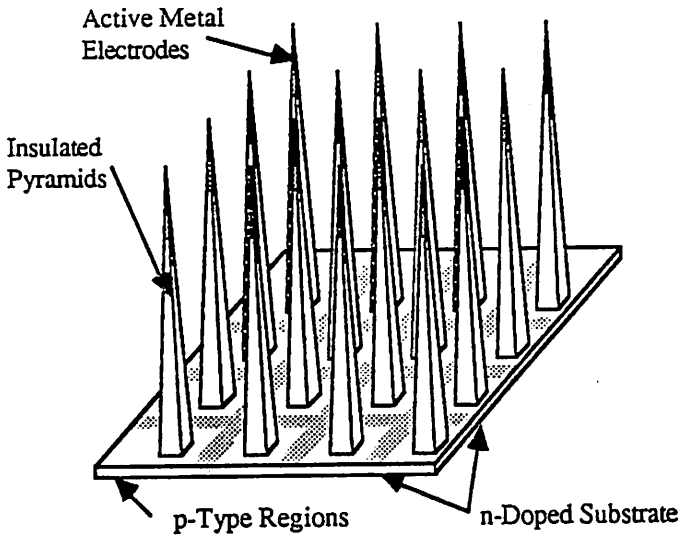


Figure 2 - Diagram of the silicon-based cortical implant system. Note that, for purposes of clarity, the drawing shows only sixteen of the thousand electrodes, and is not to scale.

al cortex will require relatively large numbers of electrodes. While the large-scale integrated circuit technology required to produce three dimensional electrode arrays does not exist today, graduate students in the Artificial Vision Program have begun to explore an approach which will lead to such devices. They are currently developing techniques to produce an integrated, three-dimensional microsystem. The microsystem will consist of 1000 electrodes on a 1 square centimeter "chunk" of silicon. Each electrode will be two millimeters long, tapering from about 100 micrometers at its base to about about one micrometer at the tip. The system's multiplexing circuitry will allow access to each and every electrode in the array through just six wires. Figure 2 shows a diagram of this proposed silicon based microelectrode array, while Figure 3 shows one of the prototype devices already produced.

The development of these microelectrode arrays is progressing well, but more experimentation is necessary before the system is ready for implantation in human volunteers. Normann and Horch have planned experiments on animal models, human psychophysical experiments, biocompatibility studies, development of surgical techniques and tools, and very limited acute experiments in volunteer patients undergoing cortical surgical procedures. As this work proceeds, members of the Artificial Vision Program and the Electrical Engineering and Computer Science Departments will begin to develop a silicon retina which will be used to encode visual signals in a manner similar to the way they are encoded by our own retinas. They will also be developing electronics to interface between the silicon retina and the cortical electrode array.

The ultimate goal of providing a limited visual sense to the blind is at least ten years away, but the University's Artificial Vision Program boasts a unique team of researchers and dedicated graduate students with the combination of engineering and neurophysiological skills which may make this dream a reality.

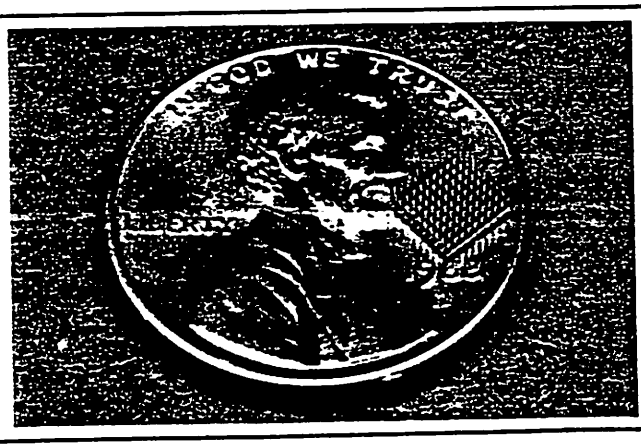


Figure 3 - A photograph of a hundred electrode array, mounted on a penny to illustrate scale.

New Faculty

Welcome to the University of Utah!

Professor Jindrich Kopecek

Professor of Bioengineering
Professor of Pharmaceutics

The Departments of Bioengineering and Pharmaceutics are pleased to announce the joint appointment of Dr. Jindrich Kopecek as Professor of Bioengineering and Pharmaceutics effective January 1, 1989.

This appointment will augment and expand the growing interaction and collaboration between the Departments of Bioengineering and Pharmaceutics.

Jindrich Kopeck attended the Institute of Macromolecular Chemistry, Czechoslovak Academy of Sciences in Prague and received a Ph.D. degree in 1965 in polymer chemistry. He joined the staff of the National Research Council of Canada, Division of Applied Chemistry, as a Postdoctoral Fellow in 1967. Today, his main scientific interests are: biocompatibility of polymers, biodegredability of polymers,and drug delivery systems.

Dr. Kopecek was a pioneer in the development of polymeric drug carrier systems. Polymeric anticancer drugs developed in his laboratory in Prague have been approved for clinical trials in the United Kingdom.

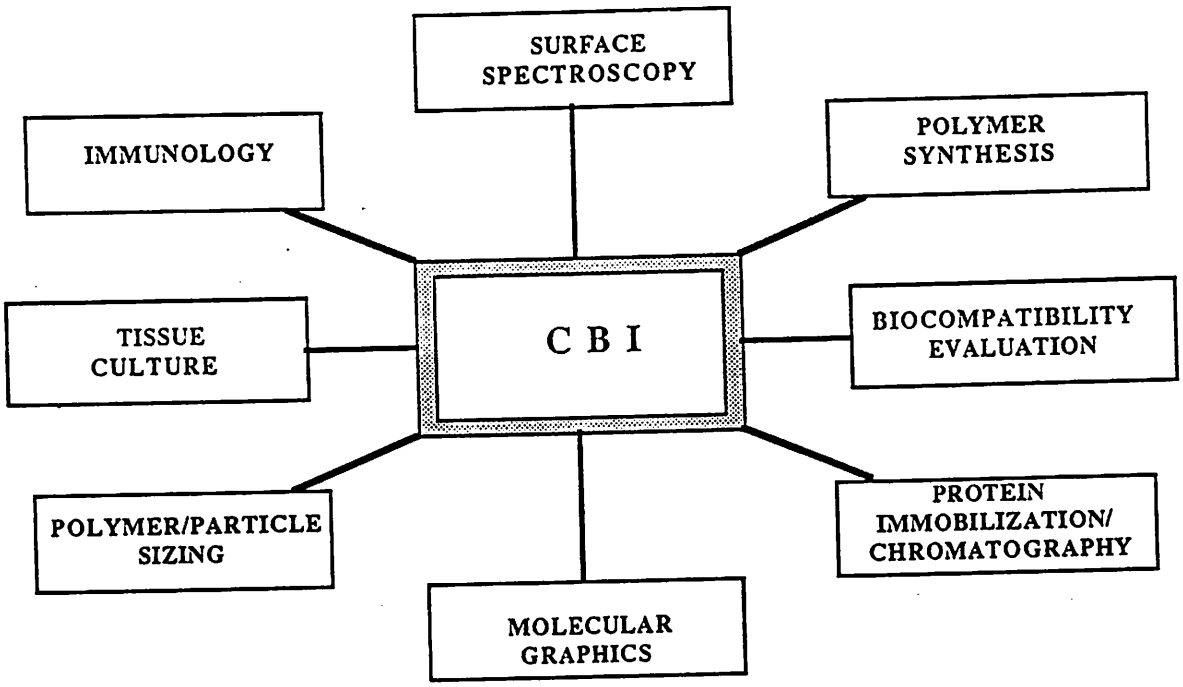
Dr. Kopecek serves on the editorial boards of seven scientific journals; and has been an invited speaker at numerous international meetings. He is the author or coauthor of 140 original scientific papers, 23 reviews or chapters in edited books. Over 30 patents have been issued in his name.

At the University of Utah Dr. Kopecek will teach graduate courses in Bioengineering and Pharmaceutics. As Visiting Professor in 1986/87 he taught a Biocompatibility course for Bioengineering which was highly received by the students.

His research activities are well underway. With a core of graduate students and the funding from federal agencies and industry he is well prepared to contribute to the University. In the short time he has been associated with the University of Utah he has one patent pending and three patent disclosures. He is a member of the Center for Biopolymers at Interfaces, and Co-Director of the Center for Controlled Chemical Delivery (CCCD).

Welcome, Dr. Kopecek! We look forward to working with you.

Centers of Excellence



Bioengineering is the home department of the Center for Biopolymers at Interfaces (CBI), an industry-University cooperative which was formed three years ago. The main goal of this center is to bring together researchers from various colleges and departments across campus for the purpose of shedding light on questions relating to material biocompatibility such as: What proteins adsorb preferentially to a given surface? How does the surface influence the structure of the adsorbate? If the material is used as an implant, such as a vascular graft, do surface-induced conformational changes in adsorbed plasma proteins trigger a rejection mechanisms in the host?

These and numerous related questions have been addressed by the CBI staff of nineteen University of Utah faculty members and their students. The current industrial membership includes twelve corporations.Since its beginning, the Center has received annual support from the State's Centers of Excellence Program and corporations.

CBI Members

Allegan Optical
Bausch and Lomb
Baxter Health Care
Becton-Dickinson
Biosym
Ciba-Geigy
DuPont
Eastman Kodak
Eli Lilly
Johnson and Johnson
Silicon Graphics
Sola Opthalmic

The Plan for Bioengineering: 1989-1994 and Beyond

The Department has recently submitted a five year plan to The University of Utah Administration. This plan proposes a controlled growth in the Department over the next five years, to permit the Department to add one part-time faculty member each year, probably jointly with another department.

Bioengineering and allied fields are a key component of the State's economic development efforts and a major factor in the University of Utah's national and international reputation. We hope the State and the University Administration will recognize these accomplishments and their future potential by making a growth commitment to the Department. You can help in one or more of three ways:

1. Be positive! Make your colleagues aware of the outstanding bioengineering program at the University of Utah particularily if you are with a Utah company or are a University official, legislator, or regent with an interest in and responsibility for higher education in Utah.

2. If you are involved in bioengineering or the biomedical industry nationally, refer to the University of Utah bioengineering program in your conversations with colleagues and coworkers.

3. A major goal in *The Plan for Bioengineering: 1989-1994 and Beyond* is to generate fellowship support for first year students, enabling us to compete with other universities for outstanding graduate students. As we are a graduate-only program, the Department receives very little support from the state of Utah. Most support comes from federal research grants and contracts, and that support is highly restricted and cannot be used for many of our unmet and unfunded needs.

If you are an alumnus of The University of Utah, you have recently received an appeal from The University requesting you to consider the University and College of Engineering in your giving plans for the 1988 tax year. We hope that you will respond generously to this appeal. You may indicate that your gift be directed to a particular program or need on campus. Consider a gift to the Department of Bioengineering or the College of Engineering.

Personal donations are always welcome. Many companies match employee personal contributions to colleges and universities; thus, your one dollar donation could bring two or three to the University.

Your Contribution is Vital

- Send to: University of Utah
  Development Office
  304 Park Building
  Salt Lake City, UT
  84112
- Indicate: Bioengineering,
  College of
  Engineering
- Match: Many companies
  match employee
  contributions

Seminars and Visitors

The Bioengineering seminar program is available to the general public and to the University community. Call the Department of Bioengineering, (801) 581-8528, for seminar information or to have your name added to the seminar mailing list.

1988			
9/6	Herbert Jennissen, Ph.D.	Adsorption of Phosphorylase	Munich, West Germany
10/3	[illegible] Ph.D.	Photoresponsive Polymers Light-Induced Conformational Change	Osaka University, Osaka, Japan
10/3	Chen-De Hu, Ph.D.	Carbon Films	Cardio Pulmonics, Salt Lake City, Utah
10/10	Roy Bloebaum, Ph.D	Backscattering Imaging, Articular Cartilage Fiber Structure	Bone and Joint Research Lab, VA Medical Center, Salt Lake City
10/17	George Pantalos, Ph.D	Process of Getting an Experimental Cardio-vascular Device to Clinical Trial	University of Utah
10/21	D. J. Chattoraj, Ph.D.	Interaction of Proteins and Protein Mixture with Interfaces	Jadavpur University, Calcutta, India
10/24	David Hoeppner, Ph.D.	Research Issues Related to Integrity, Reliability and Quality Based Design of Artificial Hearts (Components and Materials)	University of Utah
10/31	Jarmila Janatova, Ph.D.	Biocompatibility of Bio-medical Polymers: Activation of the Complement System	University of Utah
10/14	Raymond Gesteland, Ph.D.	The Human Genome Project	University of Utah
11/18	Hong Quan Xie, Ph.D.	Polyethylene Oxide-based Block Polymers	Huazhong University P. R. China
11/18	Henry Schreiber, Ph.D.	Confirmational Rearrangement of Macromolecules at Surfaces: Cause and Effect	Ecole Polytechnique, Montreal, Canada
11/21	[illegible]	Ergonomics and Biomechanics in the Workplace	University of Utah
12/5	[illegible]	Application of Biochemical Processes for Energy and Environment	University of Utah
12/5	[illegible]	The Complement System: A Tutorial	Hopital Broussais, Paris, France
12/6	[illegible]	Surface-Induced Complement Activation	

Bulletin Board

Happy

New

Year!

Brochures

The Department of Bioengineering has just completed the design and printing of a new graduate brochure with the latest information on faculty, research programs and facilities, and general entrance requirements. If you wish to obtain a copy please write to:

Mary Reuter
Department of Bioengineering
2480 Merrill Engineering Building
Salt Lake City, UT 84112

Bioengineering *Spotlight* is published biannually by the Department of Bioengineering, University of Utah, 2480 Merrill Engineering Building, Salt Lake City, UT 84112. Please contact Mary Reuter, newsletter editor, to be placed on the mailing list.

Department of Bioengineering
University of Utah
Salt Lake City, Utah 84112

BIOENGINEERING

SPOTLIGHT

Update from University of Utah Autumn 1989

From the Chair

Our first newsletter was published approximately one year ago. This second issue provides information on many activities during the past year.

Our Industrial Advisory Board has helped catalyze the formation of the State Advisory Committee on Biomedical Economic Development, in which the Department is playing a major role.

One of our new areas of emphasis is bioengineering for decreasing the cost of health care. Health care costs are a topic of national importance, and all components of the health care community are going to have to make major efforts in decreasing health care costs.

We are working with the University Administration and the State Legislature to increase the Department's financial support to allow increased interaction with clinical medicine departments.

Your support is greatly needed. You don't have to be an alumnus to make a donation to the Department of Bioengineering; we will accept them from all credible sources!

If your travels bring you to Salt Lake City, stop by to get reacquainted with the Department, its faculty, students and programs. We wish you a pleasant holiday season.

Joe Andrade
Professor and Chair

Becton Dickinson Grants Funding for Six Fellowships

The Department of Bioengineering is pleased to announce a contribution from The Becton Dickinson Foundation for support of six Becton Dickinson Distinguished Graduate Fellowships in Biomedical Engineering. These fellowships will be awarded by the Department of Bioengineering Graduate Admission Committee, with approval of the Department Chairman, to the two best applicants to the Bioengineering Graduate Program for the next three years.

Awards and Honors

The following students received fellowships or awards this year:

Kent N. Bachus	Phi Kappa Phi
Elizabeth A. Cooper	Patricia Roberts Harris Fellowship
Laurie A. Gower	Curtis C. Johnson Memorial Award
Kelly E. Jones	National Science Foundation Fellowship
Cynthia Bruckner-Lea	Phi Kappa Phi
Robert R. Tong	College of Engineering Scholarship
Amy L. Simpson	American Association of University Women Selected Professions Fellowship
Harold P. Swerdlow	Graduate Research Fellowship, University of Utah, and National Science Foundation Fellowship

12 area industry leaders make Industrial Advisory Board a reality

The University of Utah Department of Bioengineering's Industrial Advisory Board was officially organized Friday, Feb. 24, 1989 at a meeting coinciding with National Engineering Week activities.

Initially a 12 member board was established by Dr. Joseph D. Andrade, professor and department chairman. The board consists of corporate leaders of major biomedical/biotechnological companies in Utah, officials with the States' Department of Economic and Development Office and University officials.

The board's primary goals include advising the department on the long-term needs of the industry, providing a means for developing an infrastructure between industry leaders, state officials, department and University faculty and students; and assisting in fund-raising, primarily through fellowships for first-year graduate students.

Vince De Caprio, cochairman, BE Industrial Advisory Board

Board members are Michael Brown of Davol Catheter Technology; Vince De Caprio of Becton Dickinson, Critical Care Monitoring; Gary Crocker of Research Industries Corp.; Peter Meldrum of NPI, Inc.; Jerry Nelson of Nelson Laboratories; George Sims of Albion Instruments; Earl VanWagoner of Hoggan Health Industries, Inc.; Larry Rigby of CardioPulmonics, Inc.; Wm. Dean Wallace of Utah Medical Properties, Inc.; Lynn Blake, director of the State Business and Economic Development; Marvin VanDam director for Business Expansion and Retention for the state; Peter Gerity, assistant dean of the College of Engineering; and Thomas Major of the University's Office Technology Transfer.

Survey in the Mail: January

A SURVEY developed by the Board will be mailed to alumni and industrial managers to determine the needs for bioengineering education in the 1990's. This information will be used to plan future course work and department direction.

$5,500 in Gifts Allow Bioengineering Flexibility

- Mr. and Mrs J. Robert Bonnemort, $1,500, student programs in Bioengineering.
- The Castle Foundation, $2000, Chinese Scholars.
- The Marriner Eccles Foundation, $2000, newsletter.

Curriculum Notes

Graduate students instrumental in development of dissection course

For six weeks during Autumn Quarter of 1989 eleven graduate students in the Bioengineering Department and four graduate students in the Mechanical Engineering Department saw the "insiders view" of bioengineering. They were all part of an experimental course entitled *"Functional Anatomy for Engineers"*. The purpose of this course was to familiarize bioengineers and mechanical engineers with the structure and function of the human muscoloskeletal system through a series of lectures followed by extended laboratory dissection periods.

"Functional Anatomy for Engineers" was presented during the first six weeks of Autumn Quarter 1989. Each week included a 1 1/2 hour lecture by a recognized expert and 3-hour lab dealing with a specific articulation or musculoskeletal structure: abdominal wall, hip, shoulder, hand/wrist/elbow, back/low back, and knee. The laboratory portion of the course was held in the Physical Therapy Laboratory under the direction of Dr. Carolee Moncur. Each group of four or five students were assigned a cadaver which they dissected over the six weeks of the course.

Students completed initial evaluation forms indicating their expectations and also noted their feelings and opinions at course completion. The course content and format were given high marks by the students. The general consensus was that the dissections were a unique educational experience and of direct relevance to their graduate education.

"I think that this was one of the most interesting and valuable classes I've taken. The dissections gave me a much clearer understanding of joint anatomy than I could have gained otherwise".

Melissa Chang

Melissa Chang, graduate student in Bioengineering, and **Dan Baker**, graduate student in Mechanical Engineering were instrumental in the course development and presentation.

Dr. Carolee Moncur lectured on the torso and hip and, with the help of TA's from the Physical Therapy Lab, directed the actual dissection. Lectures were presented by Dr. John Wood (shoulder), Dr. Lee Chick (hand/wrist/elbow), Dr. Alan College (back/low back, and Dr. Paul France (knee). Dr. Don Bloswick was the course facilitator.

Leading expert from the Netherlands gives special topics course

The Department of Bioengineering and the Center of Biopolymers at Interfaces were pleased to host Dr. Willem Norde, Professor of Physical and Colloid Chemistry from Wageningen University in the Netherlands.

Dr. Norde taught a six-week short course: *Proteins and Interfaces.* The class studied: 1) structure and stability of protein molecules dissolved in water; 2) physical characterization of interfaces and; 3) adsorption of proteins from aqueous solution on (solid) surfaces.

Yes, a change in core

Starting Autumn Quarter 1989, students in Bioengineering were required to take the new course, *Integrated Laboratory Experiments in Bioengineering*, for one credit per quarter. This sequence of three laboratory courses under the direction of Dr. Ken Horch provides "hands-on" experience in many of the topics covered in the bioengineering core curriculum. The labs are closely coordinated with the core courses each quarter, and are structured to build on and integrate material from all the core courses as the year progresses.

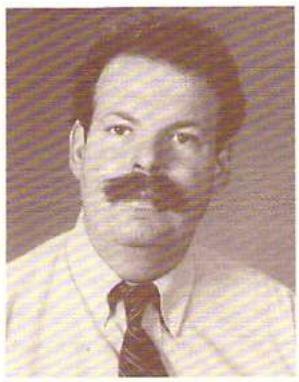
All core subjects are now six credit hours each. The biggest change was the reduction of credit hours required in physiology from twelve to six.

Focus Molecular Bioengineering

Advances in molecular biology in the last decade have spawned several new areas of research that could best be termed molecular bioengineering. These include protein engineering, peptide and protein pharmaceuticals, biosensors and biochips. Furthermore, more traditional disciplines such as biomaterials, chromatographic separations and immunodiagnostics have also profited from both the fruits and labor of the biotechnology revolution.

In this issue, we would like to focus on the research activities of one of the Center's founding faculty members, James N. Herron, who holds joint appointments in the Departments of Pharmaceutics and Bioengineering. Herron received a Ph.D. degree in Microbiology from the University of Illinois, where he studied immunochemistry and biophysical chemistry. He received further training in X-ray crystallography and molecular graphics during a postdoctoral fellowship with Prof. Allen Edmundson in the Dept. of Biology, at the University of Utah. He joined the faculty in Bioengineering in 1984, and in Pharmaceutics in 1988.

Herron describes himself as a protein biophysicist, although his first love is the structure and function of immunoglobulins (commonly known as antibodies). He has active research programs in several areas including biosensors, molecular immunology and computer-aided design of biomaterials. All of these projects contain the common element of molecular conformation. Herron's research program is designed to address the following issues: 1) what are the effects of environmental variables on the conformation of the macromolecule?; 2) how do environmental variables influence biological function?; and 3) can environmental variables or macromolecular structure be exploited in such a way as to optimize or enhance biological function? Herron's approach is to use experimental techniques such as fluorescence spectroscopy and calorimetry to study the function of proteins in solution and to correlate these data with the 3-dimensional structures obtained either by X-ray crystallography or molecular mechanics simulations. Synopses of Herron's research programs are presented below:



James N. Herron, Ph.D.

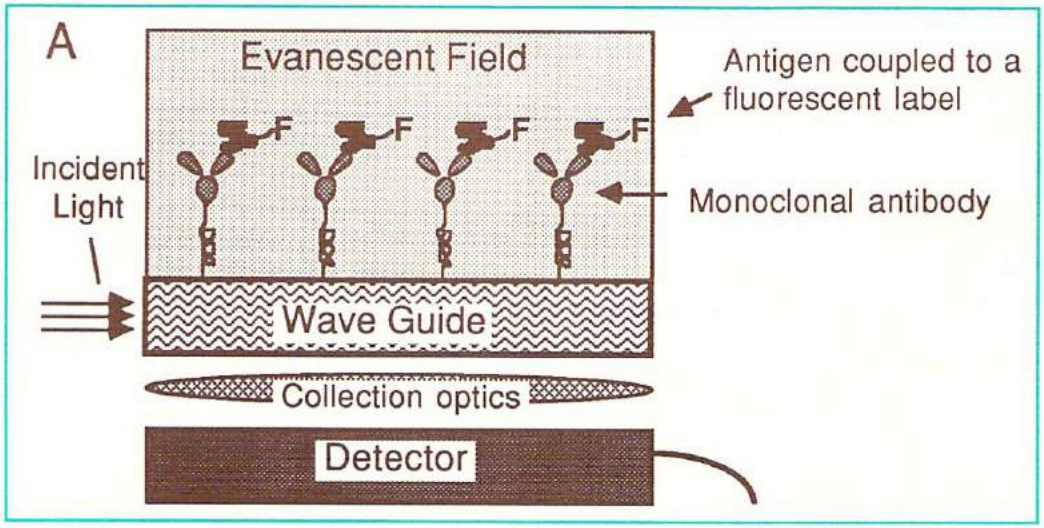


Figure 1 - Optical Immunosensor before the addition of sample. In the resting state, labelled antiben is bound to immobilized antibodies and produces a fluorescent signal, which is detected by a charge-coupled device.

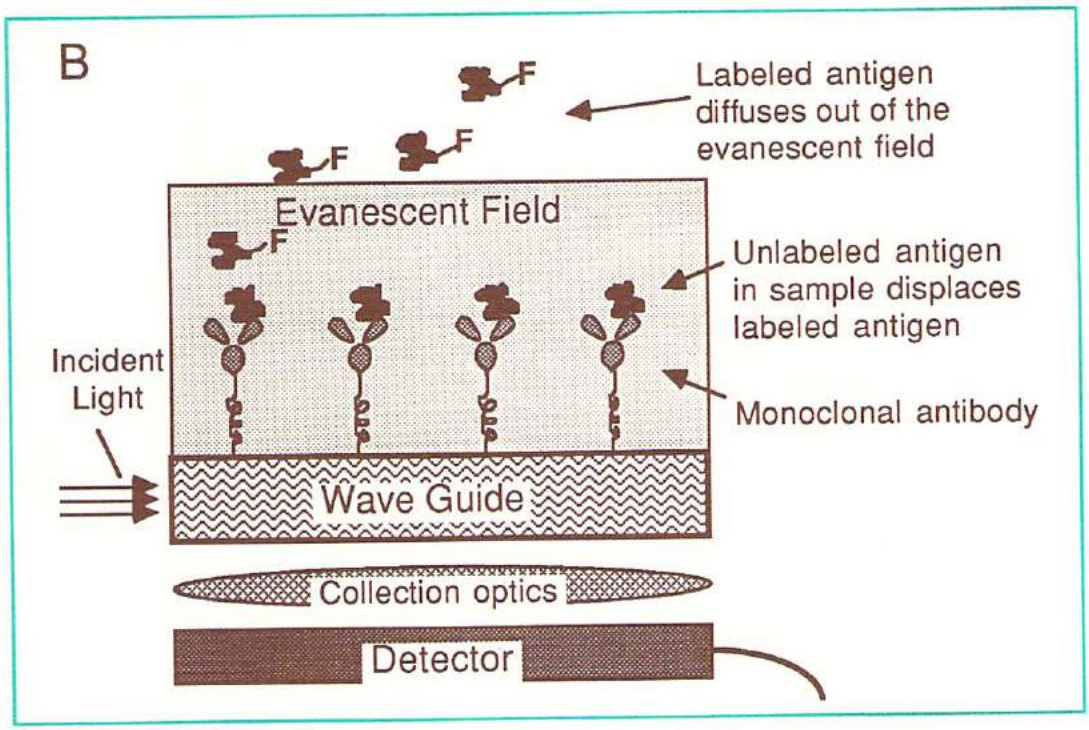


Figure 2 - Upon the addition of sample, the labelled antigen is displaced by unlabelled antigen, which results in a decrease in the fluorescence intensity.

Biosensors

A biosensor is a device that can continuously monitor the concentration of a biological molecule in a remote environment, in the same way that a pH meter responds to changes in hydrogen ion concentration. The potential market for biosensors is huge, encompassing both the biomedical field, and other markets such as environmental testing, food processing, waste disposal, and the military. Most experimental approaches to biosensors are based on using a protein as a recognition element. Typically, immunoglobulins are used in this capacity, but other ligand-binding proteins such as lectins and receptors are also being used. The immunoglobulin is an attractive choice because antibodies of high specificity and selectivity can be elicited to almost any biomolecule. Furthermore, the advent of monoclonal antibodies has enabled the researcher to select the right antibody for the job.

An immunosensors program is active which uses immunoglobulins as recognition elements, and uses an optical means for detection of binding events. Optical detection is based on an interfacial fluorescence technique called total internal reflection fluorescence (TIRF), where only those molecules which are within a few hundred nanometers of the interface are excited. This technique works well with both fiber optics and planar wave guides, and both of these optical geometries are currently being investigated. The program has developed into a collaborative effort between six faculty members (Andrade, Christensen, Herron, Hlady, Kopecek and Lin) and enjoys support from both public and industrial sources.

Herron is involved with the immunochemical portion of the biosensor program. His antibodies which bind fluorescein are ideal model systems for optical detection because fluorescein is strongly-fluorescent. One of the biggest problems with biosensors to date has been the reversibility issue. The prime requisite for a biosensor is that it have high sensitivity, which requires antibodies of high affinity. Unfortunately, this requirement is incompatible with another requisite of

biosensors — reversibility. A biosensor needs to be able to respond to changing concentrations of analyte, but the dissociation rate of the antigen-antibody complex is inversely-proportional to its affinity. So a sensitive biosensor is very slow to respond to changes in its environment.

A possible solution to this problem is to modulate the affinity of the antibody. If the affinity could be lowered reversibly, then bound antigen could periodically be expelled. Herron's biophysical studies of the anti-fluorescein antibodies suggested several possibilities for reversible mediation of antibody affinity: 1) organic solvents; 2) temperature; 3) pressure; and 4) optically-induced changes in antibody conformation. All of these possibilities have been investigated, and temperature perturbation and optically-induced changes in antibody conformation are the most promising. Technology for increasing the temperature of the sensor surface has already been developed, and Herron's graduate student, Justine Turcotte, is currently working on the optical-induction project.

Molecular Immunology

The antigen-antibody interaction is a paradox. While a particular antibody is very selective for its antigen, antibodies with specificities for almost any biomolecule can be generated. The key to this puzzle is the unique three-dimensional structure of the immunoglobulin molecule, which consists of several homologous domains of highly conserved amino acid sequence, and six short regions (ca. 10 amino acids) of highly variable amino acid composition called complementarity-determining regions (CDR), which form the antigen binding site. Although, the CDR's comprise only ten percent of the amino acid sequence, they are responsible for both the antibody's selectivity and its ability to bind to an almost unlimited variety of antigens. Another paradox is the very nature of high affinity binding. The hydrophobic effect is the major thermodynamic driving force of antigen binding, but the selectivity of the active site probably resides in very specific interactions between active site residues and the antigen.

Herron's research program is designed to address these issues by correlating physico-chemical data obtained for antigen binding in solution with three-dimensional structures of antigen-antibody complexes. His laboratory is currently working with three different monoclonal antibodies which bind haptens in both crystal and solution. This work has helped resolve a rather controversial issue in molecular immunology. It has not been clear whether antibodies are preformed into a static conformation which is exactly complementary to the conformation ofthe antigen ("lock and key" hypothesis), or whether the antibody has a flexible structure which can accommodate the conformation of the antigen ("induced-fit" hypothesis). Herron's studies with anti-DNA antibodies have shown that the binding of antigen produced signifi-

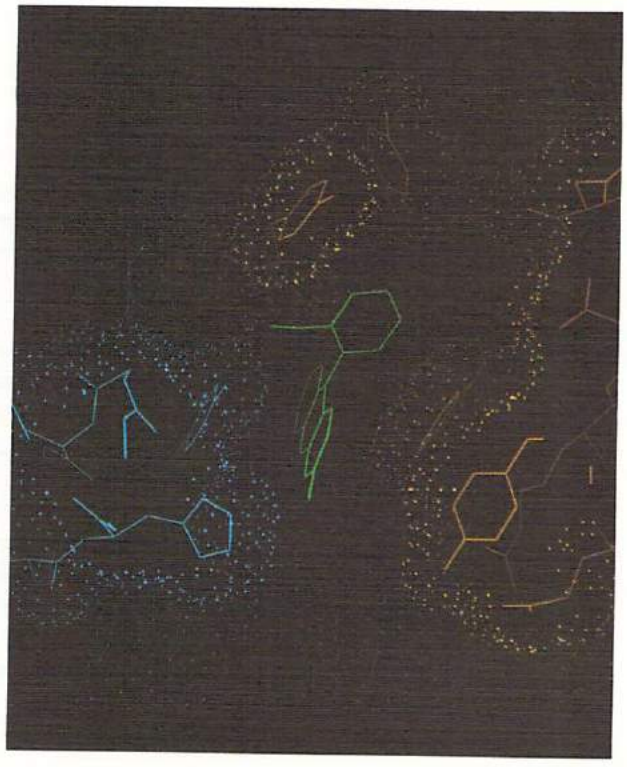


Figure 3 - Three-dimensional structure of an antigen (green) bound to the antigen-combining site of an IgG_{2a} antibody. Light chain residues are shown in blue, and heavy chain residues are shown in orange.

cant changes in the conformation of the antibody's active site, which indicated that the induced-fit hypothesis was probably the operative mechanism.

Using Molecular Mechanics to Simulate Proteins and Polymers

Recent advances in computer technology have led to the development of computer programs which can simulate and display molecular structure and dynamics. These programs come in two generic varieties — molecular graphics and molecular mechanics programs. Molecular graphics programs are used to display and manipulate molecules on a high resolution computer graphics system, while molecular mechanics programs are used to simulate molecular structure. Molecular graphics has long been used by X-ray crystallographers to help determine the three-dimensional structure of molecules, but the advent of molecular mechanics has enabled researchers to design new molecules and predict their physical properties, without the aid of X-ray diffraction data. This process works best with small molecules (< 1000 daltons), and has become an important tool for designing new drugs.

Presently, Herron's research group is pursuing several different projects which use molecular graphics and molecular mechanics. One of these is the X-ray diffraction studies described above. In anothert project, molecular graphics and molecular mechanics simulations are being used to help predict the structure and physicochemical properties of biomaterials. As with drug design, the development of new materials is often a "hit or miss" process, and could greatly benefit from computer-aided screening techniques.

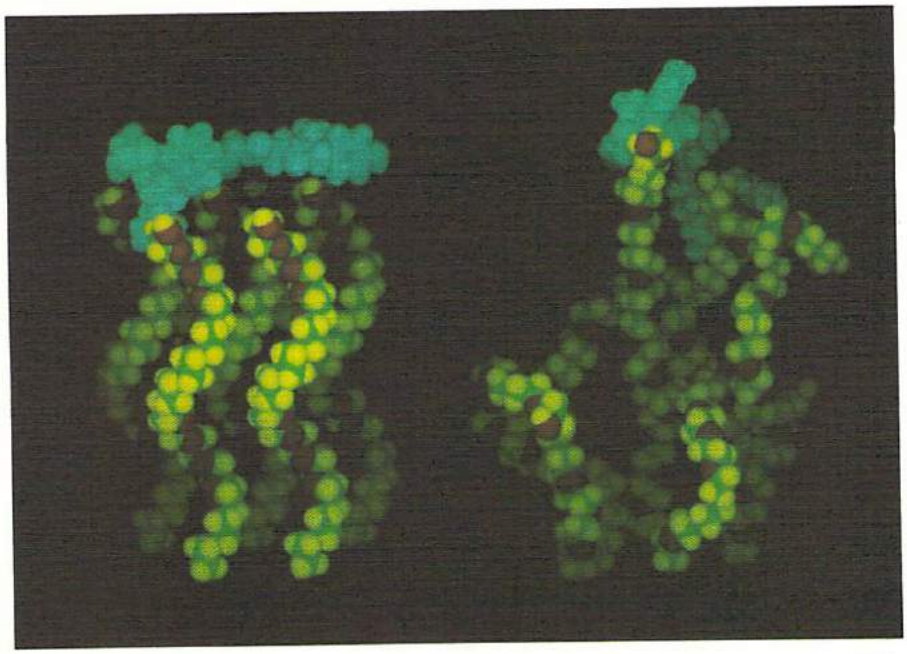


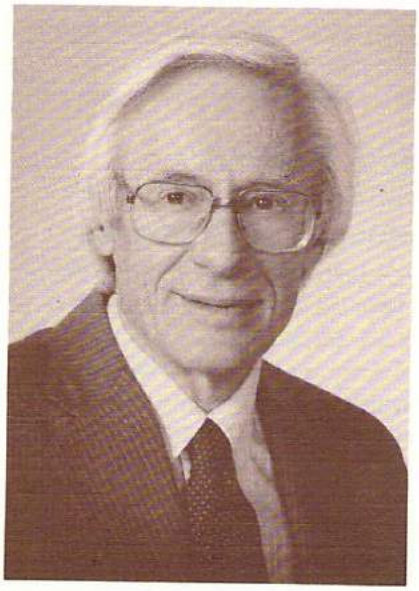
Figure 4 - Molecular mechanics simulation of a peptide (blue) with a grafted PEO surface (yellow). Left: Initial conformation of a molecular ensemble. Right: Conformation after 10 picoseconds of molecular dynamics.

Herron's graduate student, Kap Lim, is using molecular mechanics to study the structure, chain dynamics, and interfacial behavior of polymers such as polyethylene (PE) and polyethylene oxide (PEO). There is a lot of interest in PEO in the biomaterials community because of its protein resistant nature and biocompatibility. The current hypothesis is that these properties are due in part to PEO's high degree of segmental flexibility. Initially, Kap performed a number of molecular simulations with PE and PEO which addressed issues such as the hydrophobic effect, segmental flexibility, and solvent effects. More recently, he has been examining the interactions of peptides at hydrophobic interfaces. Specifically, he is studying the effects of both amino acid sequence and the properties of the interface on the tendency of an oligopeptide to form a-helices. Herron considers this as a first step on the way to simulating the behavior of small proteins at interfaces, and hopes to use the University's new supercomputer (IBM-3090) to help accomplish this goal.

Faculty Notes

Best Wishes!

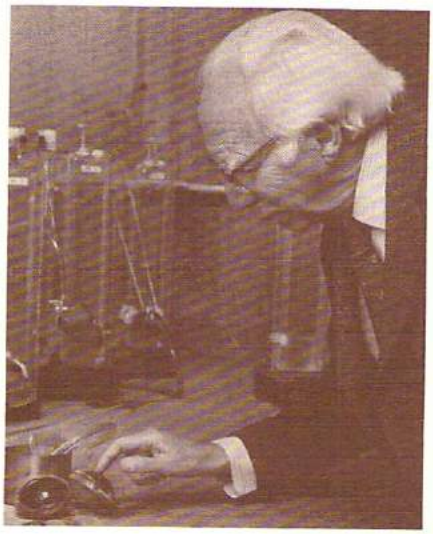
Professor Emeritus Donald J. Lyman



The University of Utah has awarded the honor of Professor Emeritus to Dr. Donald J. Lyman for his dedication to the University for 20 years. October 1, 1989 was the official day Dr. Lyman started to enjoy his decision for early retirement with the plans of more time for travel, writing, and the continuation of his research.

Dr. Lyman is directing three graduate students and is writing a book on polymers in vascular surgery.

Willem J. Kolff
Elected to Prestigious National Academy of Engineering



Willem J. Kolff, Research Professor of Bioengineering and distinguished Professor of Surgery, was recently elected to membership in the National Academy of Engineering.

The National Academy of Engineering is the most prestigious engineering organization in the United States. It was established in 1964 under the auspices of the National Academy of Sciences.

Dr. Kolff was cited for unique and innovative organ research and for leadership in bringing advanced engineering concepts to artificial organ design, construction, and implantation.

Two other Utahns were also elected to the National Academy of Engineering membership at the same time. Since only 97 new members were elected at this time, representing only 22 states, it is clear that Utah's accomplishments and reputation in engineering are beginning to be widely recognized at the national level.

The Department is most proud of the additional honor for Willem Kolff.

Center of Biopolymers at Interfaces doubles in size in one year

The Center is now in its fourth year of operation. Its industrial membership has grown from 12 to 21 corporations in one year, with an increase in Utah corporations from zero to five. Dues from industrial members, and funds from the State of Utah, has permitted support of faculty-inititated research projects which engage about fifteen graduate students and post doctoral fellows. These projects examine various aspects of protein-surface interaction, and the resulting changes in the conformation of the macromolecule. These problems are relevant to many biotechnological products and processes such as the development of immunodiagnostics and blood compatible devices.

To aid in the analytical tasks presented by the CBI projects, the Center supports a number of speciality laboratories, including a two-dimensional electrophoresis facility for protein identification and analysis, an X-ray photoelectron spectroscopy facilty, a particle characterization laboratory and a molecular graphics installation.

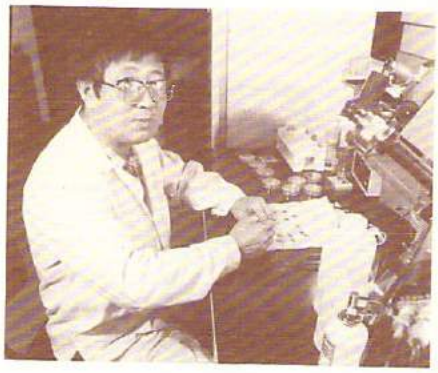
The Center's educational programs include a quarterly newsletter for members, a seminar series, a visiting scholar program, and semi-annual meetings with the corporate members. The first of a planned series of one-day workshops was held in conjunction with the meeting in October. CardioPulmonics Inc. sponsored the first workshop, entitled *"Reactive Gas Plasmas for Biomaterials and Medical Device Applications"*.

Above: Giggi Nyquist in 2-D Electrophoresis CBI Lab looking at tear fluid separation.

CBI Industrial Members:

AKZO
Allergan Optical/Smith, Kline, and Beckman
Applied Immune Sciences, Inc.
Bausch and Lomb
Baxter Healthcare Corp.
Becton Dickinson and Co.
Bio-Metric Systems, Inc.
Biosym Technologies, Inc.
CardioPulmonics
Ciba-Geigy Corp.
Eastman Kodak Co.
Eli Lilly and Company
HyClone Laboratoires
Johnson and Johnson
Idimetsu
Pharmacia
Protein Solutions, Inc.
Silicon Graphics, Inc.
Sola Ophthalmic/Barnes-Hind
Technical Research Associates, Inc.
3M

Research Efforts in Salt Lake City via Beijing, China



Above: Jinyu Wang

Jinyu Wang, Visiting Associate Professor of Bioengineering, has been working on the surface properties of silicon and carbon surfaces. He has set up an ellipsometry facility for the measurement of thin films and adsorbed proteins. Prof. Wang is with the Department of Applied Physics in Tsinghua University, Beijing, China

Left: Yushu Gao
Right: Xingfa Wang

Yushu Gao, Associate Professor of Polymer Physics, from the Institute of Chemistry, Academy of Science in Beijing, China resently joined Dr. Karin Caldwell in the Center of Biopolymers at Interfaces. Dr. Caldwell first met Gao in 1982. They have collaborated and published many research articles. Prof. Gao attended the first international Field Flow Fractionalization Meeting in June. He is working on developing fractionalization methods for DNA and, lately, for tear proteins.

Xingfa Wang, Professor of Mechanics, Beijing Institute of Technology recently joined the Department as Visiting Professor of Bioengineering. Professor Wang is working in the Center of Biopolymers at Interfaces in the lubrication and friction of hydrophilic surfaces, especially as applied to contact lenses. Prof. Wang has also worked in Germany and Japan.

Your Gift is Vital

- Send to: University of Utah
  Development Office
  304 Park Building
  Salt Lake City, UT
  84112
- Indicate: Bioengineering,
  College of
  Engineering
- Match: Many companies
  match employee
  contributions

Seminars and Visitors

The Bioengineering seminars are open to all. For seminar information or to have your name added to the seminar mailing list, call the Department of Bioengineering, (801)581-8528.

1989 Visiting Scientists

1/27	**Paul Bohn**, Ph.D.	Optical Waveguide Techniques for Structural and Chemical Analysis in Thin Thin Film Interfacial Systems	University of Illinois
2/15	**Paul Hansma**, Ph.D.	Scanning Tunneling Microscopy and Atomic Force Microscopy: Application to Biology and Technology	University of California Santa Barbara
3/2	**T. Matsuda**, Ph.D.	Surface Modification by Photoreactive Chemistry	Cardiovascular Research Osaka, Japan
3/13	**Gerald Loeb**, M.D., Ph.D.	Functional Neuromuscular Stimulation. Physiology vs Technology	Queen's University, Kingston, Ontario, Canadaa
5/25	**Dan W. Urry**, Ph.D.	The Hydrophobic Effect	University of Alabama, School of Medicine
7/6	**Karel Ullbrich**, Ph.D.	Susceptibility of Proteins Adsorbed at the Solid-Liquid Interface to Enzymatically Catalyzed Hydrolysis	Institute of Macromolecular Chemistry Prague, Czechoslovakia
7/17	**J. J. Pireaux**, Ph.D.	Polymer Band Structure via XPS Valence Band Spectra	Universitaires Notre-Dame de la Pais, Namur, Belgium
7/25	**Dusan Bratko**, Ph.D.	Water at Interfaces: A Monte Carlo Approach	University of Ljubljana Yugoslavia
7/25	**Alenka Luzar**, Ph.D.	Proteins in Inverse Micelles	University of Ljubljana Yugoslavia
10/20	**Paul Santerre**, M.Sc.E.	Protein Adsorption and Surface Character of Sulfonated Polyurethane Ionomers	University of Ottawa Heart Institute, Ottawa, Ontario, Canada
10/23	**W. R. Seitz**, Ph.D.	Optical Sensors	University of New Hampshire
11/6	**Albrecht Weisenhorn**	Atomic Force Microscopy	Department of Physics Univ. of Calif., Santa Barbara

Bulletin Board

Current Research Areas

Bioinstrumentation and Biosensors

Biomaterials and Medical Implants

Biomechanics

Effects of Electromagnetic Radiation

Medical Imaging

Neuroprosthetics

Total Artificial Heart

Career Opportunities

Looking for a job? Relocating?

The Bioengineering Department receives many requests from employers and search firms looking for Bioengineering graduates. Contact the Department for information.

BIOENGINEERING

SPOTLIGHT

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 Please contact Mary Reuter, newsletter editor, to be placed on the mailing list. Suggestions and information are always welcome.

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Department of Bioengineering
University of Utah
2480 Merrill Engineering Building
Salt Lake City, Utah 84112

BIOENGINEERING

SPOTLIGHT

Update from University of Utah Autumn 1990

From the Chair

This is the third in our series of annual newsletters on the Department of Bioengineering.

I am pleased to report that the 1990 Legislature continued its funding of the Engineering Initiative, to enhance engineering education and growth at the University of Utah. The Department of Bioengineering has benefited from that initiative. The funds provided enabled us to establish a part-time technical staff position. Modest funds were also provided to aid our strong interaction with teaching faculty in the Departments of Anesthesiology and Radiology, thereby strengthening and enhancing clinically relevant components of our curriculum. We are working with the University Administration and with the Department's Industrial Advisory Board to encourage the Legislature to provide ongoing funding of the Engineering Initiative. The continued growth of the Department will ensure the availability of the technology and people required by Utah's expanding biomedical industries.

The Governor's Advisory Panel on Biomedical Industry Economic Development recently issued its report and presented it to Governor Bangerter on November 26, 1990. Copies of the report are available from the Governor's Office (801-538-1000).

The Department's Advisory Board was well represented on the State Task Force and played a major role in the development of the report. It is clear that the biomedical industries in Utah are healthy, growing rapidly, and becoming a large and significant part of the State's economic vitality.

Department faculty have been involved in a number of special courses, in collaboration with other departments. I was pleased to teach a course with the Department of Communications, Spring 1990, titled "Critical Science Communication." We looked at the interaction between scientists, institutional public relations officials, and the press. This course was prompted by the University's cold fusion announcement in May of 1989. The

- continued on page 15

Awards and Honors

The following students received fellowships or awards this year:

Steven E. Kern	BECTON-DICKINSON FELLOWSHIP
Kristen M. Strong	BECTON-DICKINSON FELLOWSHIP
Anne M. Smith	CLYDE CHRISTENSEN SCHOLARSHIP
A. Scott Lea	GRADUATE RESEARCH FELLOWSHIP (University of Utah)
Kelly E. Jones	NATIONAL SCIENCE FOUNDATION FELLOWSHIP
Elizabeth A. Cooper	PATRICIA ROBERTS HARRIS FELLOWSHIP

Research

New Atomic Force Microscope

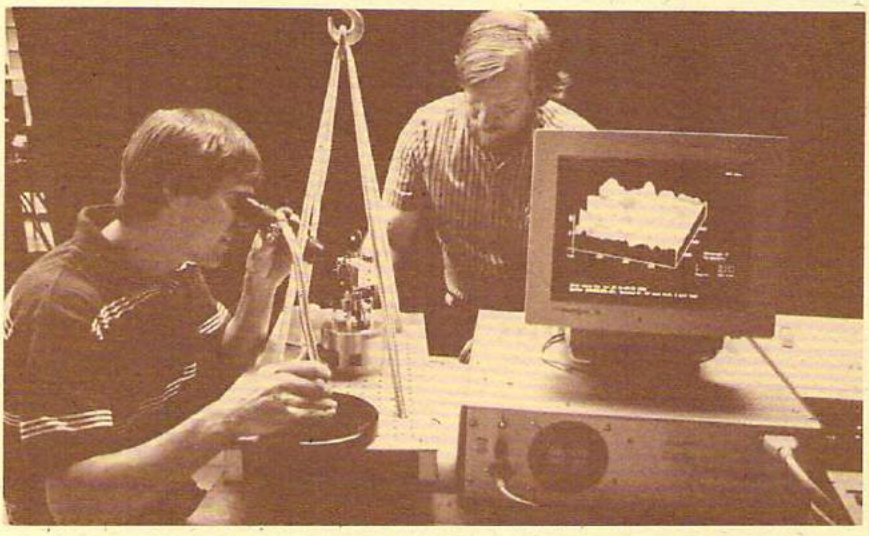
A unique microscope that allows scientists to study individual atoms and molecules has been installed at the University of Utah Department of Bioengineering for use in a wide range of medically related research projects.

The atomic force microscope was built by Digital Instruments Corporation of Santa Barbara, California, and acquired via a new National Institutes of Health research grant awarded to Drs. Joseph D. Andrade and Vladimir Hlady. A similar microscope is under construction by a group of University of Utah chemists headed by assistant professor Thomas P. Beebe, Jr.

"Atomic force microscopy is an entirely new method of providing images of submicroscopic features on the surfaces of materials."

Joe Andrade

The instrument was invented by Gerd Binnig of IBM/Zurich, Calvin Quate, a physicist at Stanford University, and Christoph Gerber of IBM/San Jose. Binnig and Heinrich Rohrer, an IBM colleague in Zurich, won half the 1986 Nobel Prize for Physics for developing another novel atomic imaging technique, the scanning tunneling microscope (STM).



Bioengineering graduate student A. Scott Lea is mounting and adjusting a sample in the Atomic Force Microscope. Staff engineer Andras Pungor is providing helpful advice. A sample AFM image is on the screen.

Binnig, Quate, and Gerber say AFM combines the principles of a scanning tunneling microscope and a stylus profilometer. The instrument makes it possible to see the interactions of proteins and other molecules with solid surfaces.

Quate received his undergraduate degree in electrical engineering at the University of Utah in 1944. The atomic force microscope's current design was developed in the laboratory of Dr. Paul Hansma, a physicist at the University of California at Santa Barbara. The Department's first successful AFM work was done in Hansma's laboratory 18 months ago. The Hansma-Utah collaboration resulted in the first direct observation with an atomic-force microscope of antibody interactions with surfaces in biochemical solutions. Hansma's group has concentrated on imaging complex organic molecules.

Based on this preliminary work with Hansma at Santa Barbara, the team received a National Institutes of Health grant to apply this unique form of microscopy to the behavior of proteins and to a number of other biologically related processes.

Because they now have the capability to study individual atoms and rearrange them individually, scientists hope to construct a new generation of so-called "designer materials" that would lead to

a wide range of new products. This process of nanoengineering involves manipulating materials on a molecule-by-molecule basis. The end result could be an entirely new process for manufacturing products.

Researchers at the Center for Biopolymers at Interfaces are also using the new microscope. The Center already has a scanning tunneling microscope, which makes atomic resolution images of the surface structure of semiconductors and metals. These scanning microscopes are also important in the new field of composites because scientists can examine these materials at the atomic level for signs of defects.

Andrade says AFM is a major development in "being able to study the behavior of molecules. This microscope, for instance, offers the potential of directly observing individual protein molecules."

The microscope is being used in the Department's programs in bioinstrumentation, biosensors, and biomaterials. Students Scott Lea and Eric Stroup and staff engineer Andras Pungor are working with Drs. Hlady, Andrade, and Jinn-Nan Lin on the manipulation and ordering of proteins on surfaces.

Lea is studying the behavior of antibodies, the immunoglobulin proteins responsible for immunologic defense processes, and their behavior at interfaces. He is working closely with Dr. James A. Herron, Assistant Professor of Pharmaceutics and Research Assistant Professor of Bioengineering. Herron is a recognized expert on antibody structures and properties (see last issue of this newsletter).

The group also expects to use the small instrument to directly observe the surface structure of biomedical polyurethanes, which are widely used in artificial hearts, heart-assist devices, and other medical products. Studying proteins at surfaces is important in the development of materials and devices used to measure chemical concentrations for medical diagnoses.

AFM probes the atomic atmosphere of a sample surface by measuring the intermolecular forces present. The instrument charts the distance to the surface in terms of how strongly the atoms on the surface and on the probe repel or attract each other.

To obtain an atomic-scale image, a material specimen is mounted onto a piezoelectric crystal and is rastered

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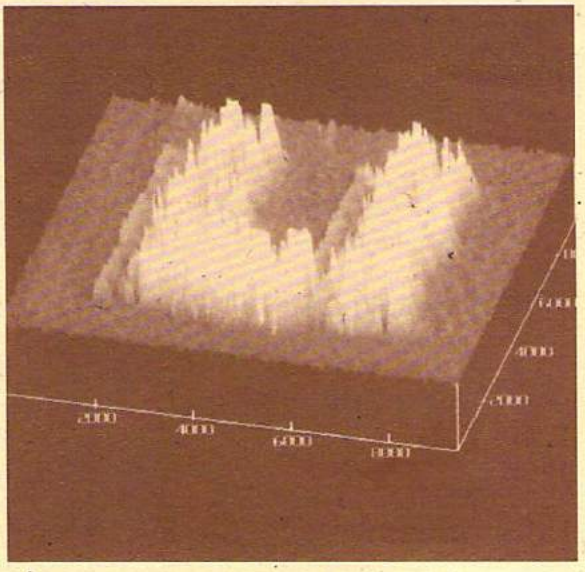


An Atomic Force image of the protein fibrinogen deposited on a mica surface. The uniform distribution has been altered by the scanning process resulting in vertical "lines" of fibrinogen molecules. The "U" area was scanned and then the vertical dimension was amplified. The horizontal dimensions are roughly 10,000 x 10,000 nM. The photo is more for public relations purposes. The instrument was programmed so that the scanning area represents a block "U," representing, of course, the University of Utah.. It is expected that studies with the atomic force microscope will improve understanding of biocompatibility and protein deposition processes and may lead to the fabrication and processing of proteins on surfaces for the production of biomolecular devices. Photo by A.S. Lea and A. Pungor, University of Utah.

Industrial Advisory Board

Among the members of the Department's Industrial Advisory Board are corporate leaders of major biomedical/biotechnological companies in Utah. Each of these companies is making its own unique contribution to Utah's economic development. The Department of Bioengineering is truly appreciative to these industry representatives, as well as other Board members, who continue to be actively involved in advising and assisting the Department with its educational and research programs.

Deseret Medical Division of Becton Dickinson Corporation was originally founded as Deseret Pharmaceutical by J. L. Sorenson and D. Ballard. In 1981 the company was acquired by Warner-Lambert, then in 1986 by Becton Dickinson and Company, with headquarters in Franklin Lakes, New Jersey, and a total workforce of 17,000.

With its major product areas being IV catheters and accessories and disposables for surgical and critical care settings, Becton Dickinson Deseret Medical Division employs 1,300 at its Sandy, Utah, operation. Future plans and objectives include worldwide growth in vascular access systems, introduction of new critical care monitoring systems, and advanced biomaterials research and applications. To fill their manpower needs in Utah, the company is looking for biomedical and manufacturing engineers, as well as individuals with marketing and management skills.

Dr. Vincent DeCaprio, President of BD's Deseret Medical Division, serves as Co-chair of the Department's Industrial Advisory Board and was recently appointed as Adjunct Associate Professor of Bioengineering.

CardioPulmonics, Inc., which was founded in August 1986 by J.D. Mortensen, M.D., and Larry D. Rigby, acquired its initial funding through Phase I & II SBIR grants and later through venture capital. Major product areas include gas transfer membrane technology, thrombo-resistant coatings, and intravascular oxygenators. The company's objective is to enter the ICU markets to support respiratory failure with a variety of device systems, intravascular or extracorporeal. CardioPulmonics, Inc., has a work force of 36, including manufacturing sales/marketing, development, engineering, and biomaterials.

Hoggan Health Industries began operation in Murray, Utah, as the Dean Hoggan Machine Shop. In 1976, the family business was incorporated as Hoggan Machine and Health Equipment and entered the fast-growing fitness industry. In 1985 the company changed names to reflect its broader mix of health-related products and, a year later, released its first medical product, the FETS (Force Evaluation and Testing System). Hoggan Health Industries and the University of Utah were awarded a grant in 1986 from the Shriner's Children's Hospital to build a device for measuring spinal motion.

With approximately 80 employees at its Draper, Utah, facility, Hoggan Health Industries manufactures commercial fitness equipment for both strength training and cardiovascular conditioning (stationary exercise bike, upper body exerciser, stairclimber), as well as muscle-testing systems and custom medical equipment.

Future plans include expanding Hoggan Health's presence within the fitness industry by introducing new products to meet the demands of health-conscious consumers. Within the medical realm, the company is working to expand its offering of medical testing equipment and to develop new medical tools designed to aid health practitioners.

Merit Medical Systems, Inc., was incorporated July 28, 1987, to develop, manufacture, and market disposable proprietary medical products used primarily in interventional and diagnostic procedures (angiography and angioplasty) in cardiology and radiology. Among the company's new products are disposable control syringes with different volume capacities and plunger configurations and a device with an electronic monitor that measures the frequency, duration, and pressures of balloon catheters during angioplasty.

Merit Medical's current efforts include 1) developing a contrast delivery product that leaves little or no contrast media in the IV bottle during angiography procedures, provides adequate flow,

and will not pull out of the IV bottle under pressure; 2) tooling a new Merit-designed manifold that will offer both ease of use, easily identified flow direction, and leak-free operation under the extreme pressures of mechanical injection of contrast media; and 3) marketing an FDA-approved line of high-pressure tubing to be used during angiographic and radiological procedures.

The manpower needs of Merit Medical, which currently has a work force of 70, include engineers, technicians, software engineers, assembly workers, marketing specialists, and clerical workers.

Native Plants, Incorporated (NPI), founded by three University of Utah and BYU professors and one graduate student, was incorporated in 1973 to apply the latest advancements in biotechnology and biology to the development of superior new plants and plant products. Since receiving its first venture capital financing in 1977, the company has become recognized as one of the top three plant biotechnology companies in the world.

With its 104 employees in Utah and subsidiaries in Singapore and Tokyo, NPI develops, manufactures, and markets specialty chemicals and pesticides for the US and world markets, including a biological insecticide and a plant growth regulator used in seedless crops. In addition, the company markets genetic maps for corn, tomato, onion, and *Brassica* (broccoli, cauliflower) to major seed companies throughout the world.

New efforts at NPI include research on several new insecticides that are biologically degradable and will not contaminate the soil or ground water, are completely harmless to man, livestock, birds, and wildlife, and yet are effective against major insect pests. The company is also researching DNA probes and gene mapping to improve plants and to identify new high value compounds from natural plant sources.

Because of its current growth mode status, NPI will be increasing its staff in the areas of molecular biology, chemical engineering, organic chemistry, and formulation chemistry.

Nelson Laboratories Inc., which now employs 28 people, was founded in 1985 by Lynda S. and Jerry R. Nelson with no venture capital and no partners. Having outgrown its original University Research Park location, the company is currently located in Holladay, Utah.

Nelson Laboratories provides contract laboratory services for medical device, drug, and biotechnology firms. Services include preclinical safety and efficacy tests (tripartite biocompatibility), sterilization validation and sterility testing, pyrogenicity, bioburden, chemical product characterization tests, and a wide range of efficacy and comparative performance studies. This rapidly growing company, currently in the design phase of a new laboratory facility, is increasing the range of available laboratory services. The company has added GMP and GLP consulting services and will be adding physical test facilities in the near future.

Nelson hires 4-6 senior technical staff personnel each year, with the heaviest needs being for experienced microbiologists.

Ohmeda, SLC, formerly known as Albion Instruments, has a current work force of 41. This company was originally founded in 1981 by nine University of Utah faculty and was known as Biomaterials International. In 1988 the name was changed to Albion Instruments to reflect emphasis on clinical and critical care monitoring. The company was acquired by British Oxygen Health Care in 1990, at which time the name was changed to Ohmeda, SLC.

Ohmeda's major product areas include anesthesia gas monitors, anesthesia gas delivery machines, and critical care monitors. The Salt Lake City facility develops and manufactures anesthesia gas monitors based on Raman spectroscopy technology..

Future plans and objectives include expansion to support Ohmeda's extensive monitoring product lines, development of Raman gas analysis benches for gas delivery machines, and on-site manufacture of RASCAL II anesthesia gas monitors and Raman

gas analysis electro-optics benches. Manpower needs in Utah include engineers and technicians in electro optics, mechanical, and electrical areas.

Research Medical, Inc., a wholly owned subsidiary of Research Industries Corporation in Salt Lake City, is involved in the development, manufacture, and marketing of over 50 FDA-approved drainage and suction devices for open-heart surgery; specialized cardioplegia (heart cooling) and cardiac-assist devices; RIMSO-50, an FDA-approved proprietary pharmaceutical for the treatment of a bladder disease known as interstitial cystitis; and eye wash and burn cleansing solutions manufactured for other firms under private label.

Additionally, Research Medical, with its 75 employees, has several major development projects underway: 1) heparin removal filter, which utilizes a proprietary chemical that selectively binds heparin molecules without depleting blood proteins; 2) small diameter artificial vascular graft, measuring less than 7 mm in diameter and developed from a proprietary polyurethane plastic; and 3) topical drug delivery system, which delivers antiviral drugs by means of a skin penetrating agent. Current manpower needs include some middle management and some production/assembly staff.

Utah Medical Products, Inc., a medical biophysics and computing company, was formed by individuals from Sorenson Research which merged with Medicor, Inc. (Dean Wallace/Chris Cutler), a University of Utah spin-off company. With a work force of 270, this rapidly growing company develops, produces, and markets disposable plastic components, pressure transducers, and catheter-tipped sensors.

Utah Medical Products, which was recently named by *Forbes* magazine as one of the top "200 Best Small Companies in America" for 1990, plans rapid growth to become a premier medical company in the State of Utah in high tech innovative, disposable products in niche medical markets. To reach this goal will require additional and better-trained plastic engineers, as well as tool and die people.

Becton-Dickinson Distinguished Bioengineering Fellowship recipients (the young folks in the center) Steven Kern and Kristen Strong. Dr. Vince DeCaprio, President of Becton-Dickinson Deseret Medical Division, is on the left; Dr. Joe Andrade is on the right. The location is the patio-like area between the Merrill Engineering and the Engineering Classroom Buildings.

BIOENGINEERING SURVEY RESULTS

In January 1990, a questionnaire developed by the Industrial Advisory Board was mailed to over 1,200 members of the biomedical engineering industrial community throughout the nation. The purpose of this survey was to determine the needs for bioengineering education in the 1990s and to use the information received in planning the Department's curriculum.

Although the response rate was only 7.2%, the results reflect a nationwide sampling without significant bias. Only 8 of the respondees were University of Utah graduates, and only 8 came from the Mountain time zone, which includes Utah.

A few of the findings from the survey are noteworthy:

- Bioengineering is perceived to be a maturing discipline for which a definite need exists in industry.
- Bioengineering training is particularly effective when it is delivered on top of a solid foundation in a traditional engineering discipline.
- Bioengineers are expected to have a good knowledge of physiology.
- Entry-level salaries of B.S., M.S., and Ph.D. bioengineers are competitive with those in traditional engineering disciplines.
- Utah is perceived as one of the very best bioengineering programs in the nation.

Members of the Industrial Advisory Board's Subcommittee on Education are now in the process of drafting papers which describe in detail the results of the questionnaire. These papers will be submitted for publication in appropriate professional journals.

Copies of the itemized survey results can be obtained from the Department of Bioengineering upon request (801-581-8528).

UNIVERSITY PRESIDENT SEARCH

The Utah State Board of Regents has initiated a search for a new President of the University. President Chase N. Peterson resigned early this summer, effective July 1, 1991. Regents hope to have a new president in place before the beginning of the Fall Term, 1991. Nominations for president may be sent to: Dr. Wm. Rolfe Kerr, Commissioner of Higher Education, State Board of Regents, 355 W. North Temple, 3 Triad Center, Suite 550, Salt Lake City, UT 84180-1205.

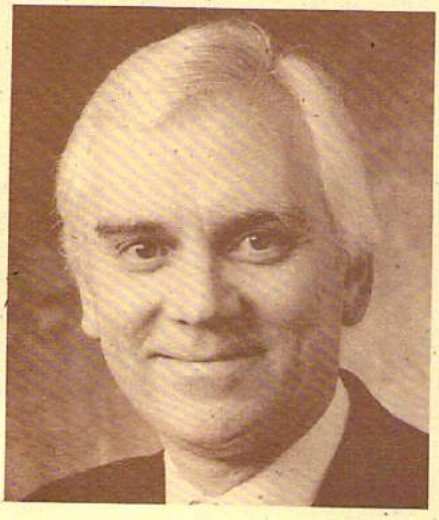
Faculty Notes

Dr. Karin D. Caldwell, Director of the Center for Biopolymers at Interfaces (CBI), has been appointed Associate Professor of Bioengineering, effective July 1, 1990.

Dr. Caldwell received her B.S. (1964) and Ph.D. (1968) degrees from the University of Uppsala, Sweden. After several years of postdoctoral research work with Dr. J. C. Giddings, Department of Chemistry, University of Utah, she was appointed Research Assistant Professor of Chemistry in 1979 and Research Associate Professor of Chemistry in 1982. She joined the Department of Bioengineering in 1985 as Research Associate Professor and Director of CBI.

Dr. Caldwell's main research interests include separation methodology and techniques for characterization of macromolecules and particles of biological origin, as well as surface characterization of polymeric materials. She currently serves on the Editorial Board of Separation Science and Technology, has authored or co-authored over 70 original scientific publications, and has been an invited speaker at numerous international meetings. Her scientific affiliations include American Society of Biological Chemists, American Chemical Society, American Association for the Advancement of Science, The Protein Society, The Fine Particle Society, and The Society for Biomaterials.

Dr. Caldwell co-teaches (with Dr. Jiri Janata) the Chemistry for Bioengineers course and is currently developing a laboratory course on experimental analysis of biomacromolecules, which will become a regular departmental course offering. She also supervises several graduate students in their Master's and Ph.D. programs. Recently elected to represent the Department on the College Council, Dr. Caldwell played a key role in the development of the Utah Biomedical Industry Development Task Force.



Dr. Stephen C. Jacobsen, Professor of Mechanical Engineering, Research Professor of Bioengineering, and Director of the Center for Engineering Design, was recently inducted into two of the most prestigious organizations of scientists and engineers in the United States. Dr. Jacobsen was given double honors from the National Academy of Engineering (NAE) and the Institute of Medicine of the National Academy of Sciences (NAS) for "his distinguished and continued achievements in original research."

The NAE award commends Dr. Jacobsen's work in the construction of artificial kidneys and the Utah Artificial Arm, as well as his work in robotics and micromotors. His induction into the NAS Institute of Medicine was for his contribution to health and medicine, and he is one of only seven engineers to be so inducted.

Dr. Jacobsen's previous awards include the American Society of Mechanical Engineers' 1987 Leonardo de Vinci Award for designing the Utah/MIT Dextrous Hand and the Lawrence Poole

Prize in Rehabilitation from the Faculty of Medicine at the University of Edinburgh. In 1985 he received both the University of Utah Distinguished Research Award and the U.S. Secretary of Health and Human Services Volunteer Service Award. Dr. Jacobsen has also served as visiting scientist at the Department of Mechanical Engineering and the Artificial Intelligence Laboratory at the Massachusetts Institute of Technology (MIT).

Dr. Willem J. Kolff, internationally recognized inventor, physician, Distinguished Professor of Surgery and Internal Medicine, and Research Professor of Bioengineering at the University of Utah, was recently named one of the "100 Most Important Americans of the 20th Century" by Life Magazine. The author of hundreds of scientific papers and the recipient of many prestigious honors and awards, Dr. Kolff joins the ranks of people such as Jonas Salk, the Wright Brothers, and Henry Ford. He is one of only 21 living Americans and the only Utahn to be listed.

Dr. Kolff began his biomedical engineering work in the 1940's in The Netherlands when he created the first clinically useful artificial kidney to save the life of one of his patients. He crafted a small electric motor, 65 feet of cellophane tubing, a wooden drum, and an enamel tub filled with salt water into the first hemodialysis machine.

Today, hundreds of patients benefit from updated versions of the device at the University's Kolff Dialysis Center, and a quarter of a million people worldwide are on some form of dialysis.

Dr. Kolff, who joined the University of Utah faculty in 1967, is also well-known for his work on the artificial heart, which led to the first human recipient of a permanent artificial heart in 1981--Dr. Barney Clark who lived

112 days. Along with other researchers, Dr. Kolff designed the intra-aortic balloon pump, now the most-used cardiac-assist device. He also pioneered work on the pump oxygenator, the so-called heart-lung machine.

Dr. Kolff is in the process of moving his office to the Department of Bioengineering where he will interact with students and faculty and continue his writings and studies in bioengineering and artificial organs.

Intermountain Biomedical Association

The Intermountain Biomedical Association (IBA) is an organization which has been formed to bring together industry professionals in an educational, networking environment. **The purpose of the IBA Committee** is to organize and support programs which will promote the exchange of information vital to enhance the growth and success of research, development, and manufacturing companies in the Intermountain area. Consistent with the mission, quarterly "Breakfast Meetings" are held.

Topics in 1990 ranged from an update of the Governor's Biomedical Industry Development Task Force, including a profile of biomedical companies, to such issues as:

- MRP II implementation processes
- medical device development cycles
- GMP/FDA and quality assurance
- oil embargo
- future for medical plastics users.

Highlights for 1991 will include areas of manufacturing, as well as marketing expertise and management concepts.

The Intermountain Biomedical Association can fulfill its mission by meeting the needs of the industry it serves. We invite your active participation, comments, and suggestions to help us shape future programs to meet YOUR needs. The organizing committee consists of Sherrie Adams; Ping Fong, Bunnell, Inc.; Russ Garrison, Zinetics Medical; and Rick Gaykowski, Cardiopulmonics, Inc.

For more information -
contact Sherrie Adams, (801) 278-7024.

Curriculum

Health Maintenance in Remote Environments

In late spring 1990, the Department organized a seminar series titled, "Health Maintenance in Remote Environments." This series was stimulated by a conference held on campus earlier in the year dealing with the medical aspects of exploration of the inner solar system, i.e., the proposed mission to Mars.

The seminar series was held in conjunction with a two-week workshop organized by the Department's Dwayne Westenskow as part of the activities of the Rocky Mountain Space Grant Consortium. The University of Utah is a member of the consortium and is one of the National Space Grant Universities.

Speakers for the seminar series included:

- **Dr. Bruce Houtchens**, Department of Surgery, University of Texas Health Sciences Center
  "100 Million Miles from the Hospital: Exploration of the Inner Solar System"

- **Dr. Terry Clemmer**, Director of Critical Care, LDS Hospital
  "Telemedicine in the Armenian Earthquake Area: Phase II"

- **Dr. Joseph C. Sharp**, Space Research Director, NASA Ames Space Center
  "Life Support in Space"

- **Dr. Bruce McKinley**, Krug International, Houston, Texas
  "Astronauts as Patients"

- **Dr. M. A. Reynolds**, Project Manager, Crew Health Care, McDonnell-Douglas Corporation
  "The Health Maintenance Facility for Space Station Freedom"

Bioengineering Approaches to Decreasing the Cost of Health Care

The rapidly increasing cost of health care in the United States is now a subject of considerable interest and concern for all segments of society. Historically, the academic bioengineering community has not been particularly concerned with the cost implications of the technologies and instruments which it develops. The medical community, which applies the results of bioengineering research and development, has also been generally unaware and unconcerned with cost considerations until relatively recently. The situation, of course, has changed dramatically in recent years. We feel strongly that at least a portion of academic bioengineering education, research, and development be directed to the health care cost issue.

The graduates of academic bioengineering programs nationally go on to work in the health care products industry, in government regulatory bodies, and in academia. Students in bioengineering programs should be induced to consider the

cost-benefit implications of their graduate research work and should have some general familiarity with the concepts and techniques of technology assessment and cost benefit analysis.

We are now teaching a course titled "Bioengineering and the Costs of Health Care," taken by a range of graduate students at the University of Utah and especially Bioengineering students. It is our expectation that this course will become a permanent part of the curriculum and that the principles and concepts of the course can be expected to be integrated into other courses and, hopefully, into every graduate student dissertation.

We are taking a global look at primary medical care activities in order to evolve new and novel approaches which could have a significant impact on decreasing health care costs.

Course speakers and topics include:

- **Dr. William Gay**, Vice President for Health Sciences, University of Utah
  "How Is Medicine Organized and Practiced?"
- **Dr. Brent James**, IHC, Inc.
  "Technology, Quality, and Costs of Health Care"
- **George Belsey**, Director, University Hospital
  "Health Care Costs and Their Payments"
- **Dr. Ben Eiseman**, University of Colorado Medical Center
  "Cost Effective Surgery"
- **Dr. John Matsen**, Chairman, Department of Pathology, University of of Utah
  "Clinical Laboratories and the Practice of Defensive Medicine"
- **Dr. Seymour Perry**, Institute for Health Policy Analysis, Georgetown University
  "Diffusion and Acceptance of Medical Technologies"
- **Dr. M. David Low**, President, University of Texas Health Care Center, Houston
  "The U. S., Canadian, and Other Health Care Systems"
- **Vincent Bucci**, Vice President, Regulatory & Clinical Affairs, Infusaid, Inc.
  "Health Outcomes Research and Medical Technologies
- **Dr. George Bugliarello**, President, Polytechnic University, Brooklyn
  "The Future of Biomedical Engineering"

Other Activities

Governor's Blueprint for Economic Development

Report of the Utah Biomedical Industry Development Task Force

Governor Norman Bangerter and the Utah Department of Community and Economic Development are following plans and working toward objectives contained in the Governor's Blueprint for Utah's Economic Development, which was first published in the Fall of 1989. A key element of the Governor's Blueprint is to focus on those industries that have the greatest potential for positive development within Utah.

The Utah Biomedical Industry Development Task Force was organized approximately a year ago; it has completed its work, and its report and recommendations have now been issued.

The Task Force is comprised of the chief executive officers of twelve representative Utah biomedical companies. In addition, there are representatives of the University of Utah, Utah State University, and state government. It is co-chaired by Representative Lloyd Frandsen of the Utah State House of Representatives and Marvin VanDam of the Utah Department of Community and Economic Development. Key participants have been Drs. Joe Andrade, Karin Caldwell, and Peter Gerity of the University of Utah Department of Bioengineering, as well as Dr. Vince DeCaprio, President of the Becton Dickinson facility in Sandy, Utah, and co-chair of the Department of Bioengineering's Industrial Advisory Board.

The mission of the Biomedical Task Force is to promote the growth and success of Utah's biomedical industry, such that Utah becomes one of the top biomedical research, development, and manufacturing locations of choice internationally.

The Task Force has studied the strengths and opportunities, as well as the weaknesses and obstacles, of the current Utah biomedical industry. The report also includes a complete listing of Utah's biomedical companies.

The Task Force focused on specific industry strengths/opportunities and weaknesses/obstacles that deserve further analysis and investigation. The result is a set of seventeen recommendations that have been made to Governor Bangerter. These recommendations cover such topics as the biomedical technologies deserving heightened research emphasis, business growth capital, endowed university chairs, several specific recommendations concerning enhanced higher education support, technology transfer, university faculty entrepreneurial fellowships, university research libraries, and the proposed activities of a Utah Biomedical Association. The Industry Analysis, report, and recommendations are now public information and are available from the Utah Department of Community and Economic Development (phone 538-8775).

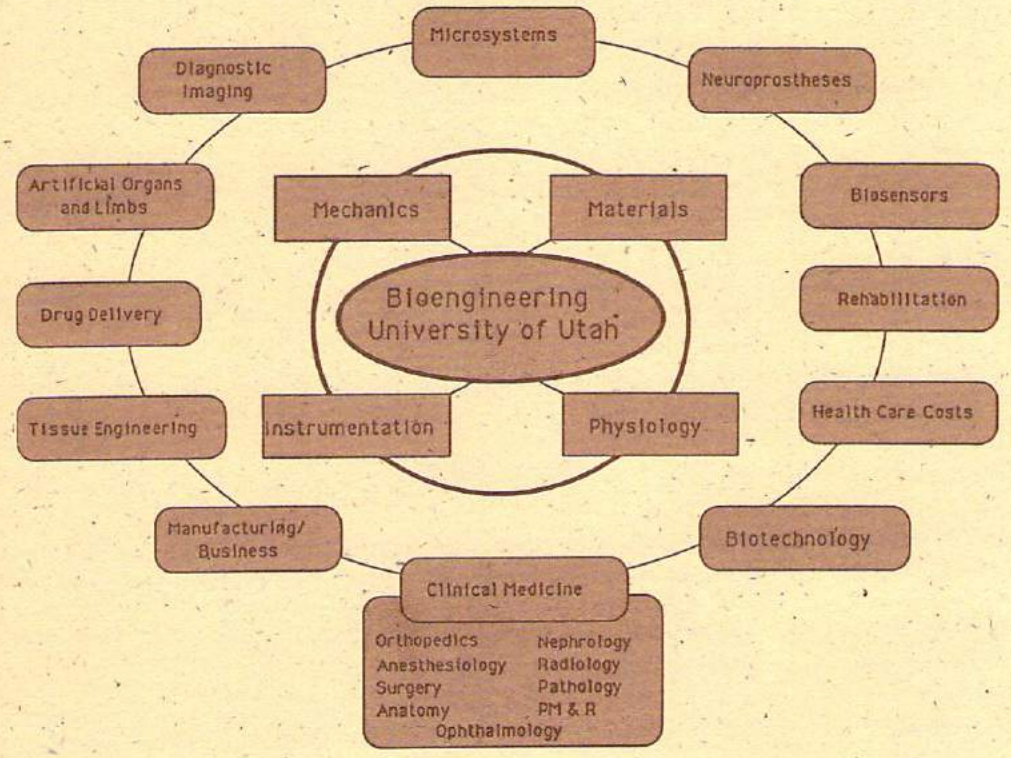
A committee of the Task Force is now studying the possible need for legislation to provide a supportive regulatory environment for biotechnology research and development in Utah. The purpose of such legislation would be to ensure public safeguards, while at the same time providing a supportive and defined regulatory environment for biotechnology research and development in Utah. The committee is expected to issue its report and recommendations early this winter.

Faculty Retreat

The Department held its 2nd annual faculty retreat on June 21, 1990, at Silverfork Lodge in Big Cottonwood Canyon. A major discussion ensued around the Department's areas of expertise and acknowledged strengths. There was also considerable discussion about new areas and new opportunities in the field of bioengineering.

It was felt that in order to maintain the Department's leadership as a dynamic and leading bioengineering department nationally and internationally, the program should maintain its existing strengths and, in addition, should develop one or two new areas of activity and emphasis. It was also agreed that the Department should continue its efforts to strengthen its interactions with the various clinical departments and specialties in the College of Medicine and University Hospital.

These discussions are summarized in the figure below, which attempts to represent the Department's four curricular core areas (the squares) and its present and evolving areas of strength and emphasis (the surrounding circles). This information will be expanded into a revised strategic plan for the Department, which will be made part of a College of Engineering strategic plan now being formulated by the Dean of the College.



Seminars and Visitors, 1990

The Bioengineering seminars are open to all. For seminar information or to have your name added to the seminar mailing list, call the Department of Bioengineering, (801)581-8528.

1/31 Dr. Ted DeYoe,, Medical College of Wisconsin: *"Electrical Activation of Visual Cortex in Alert Monkeys"*

5/24 Dr. Robert Andres, U of Massachusetts at Amherst: *"Probing Neuromuscular Mechanisms: Trade-offs Between Gait Analysis and Posturography"*

7/23 Dr. Christian Salesse, U of Quebec at Trois-Rivieres: *"Ellipsometric Studies of Phospholipid and Protein Monolayers at the Air-Water Interface"*

9/21 Professor Masuo Aizawa, Tokyo Institute of Technology: *"Molecular Design and Fabrication of Electrochemical and Optical Biosensors"*

10/18 Dr. Willem Norde, Landbouwuniversiteit Wageningen, The Netherlands: *"Protein Adsorption in Model Systems"*

10/19 Dr. Harrie Kreuwel, AKZO Research Labs, Arnhem, The Netherlands: *"Optical Principles of Reflectometry"*

Dr. Mirjam Oldenzeel, AKZO Research Labs, Arnhem, The Netherlands: *"Reflectometric Protein Interaction Studies"*

Jan-Christer Janson, Pharmacia LKB Biotechnology, Uppsala, Sweden: *"On the Optimization of Protein Chromatography"*

10/24 Professor H. L. Schmidt, Technical University, Muchen, Germany: *"Causes and Applications of Stable Isotopes in Nature"*

10/30 Dr. Paul Beatty, U of Manchester, England: *"Breath-by-Breath Measurement of Gas Exchange During General Anesthesia"*

11/2 Professor Lev Blumenfeld, Academy of Sciences, Moscow: *"Proteins as Molecular Machines"*

11/5 Hiroaki Kawakubo, Mitsubishi Central Research Lab, Hyogo, Japan: *"Molecular Orientation and Photoelectric Properties of Molecular Heterojunctions Using Flavin-Cytochrome C Multilayers"*

11/19 Dr. Ernst Fischer, Immunochemistry Laboratories, ANAWA, Inc., Zurich, Switzerland: *"Experiences in the Monitoring of Antibodies to Interferon Alpha"*

11/20 Dr. Dan W. Urry, U of Alabama at Birmingham: *"Elastomeric Polypeptides"*

(From the Chair cont'd.)

cold fusion issue was a major item of discussion during the course.

This term, Fall 1990, we are teaching a course with the Department of Political Science titled, "Bioengineering and the Costs of Health Care." Further details are included in a story in this issue.

The Department's efforts to recruit outstanding graduate students have been very successful. We had 27 new students arrive on our doorstep in late September, making it the largest class in the history of the Department. They represent a distillation of some 150 applications during the year. We now have over 70 graduate students in the program, making our small department one of the largest graduate enrollments in the University.

If any of our out-of-state readers are interested in relocating to Utah, our faculty and members of the Industrial Advisory Board can advise regarding possible sources of employment. Please do not hesitate to contact us. The College of Engineering also provides the Utah Engineering Network, a data base to facilitate the relocation of Engineering alumni back to Utah. If interested, contact Dr. Peter Gerity, at (801) 581-8346.

We are in urgent need of funds to help with the publication costs of this newsletter, costs involved in the recruitment of graduate students, and with other needs and expenses of a dynamic department. As most of you know, our State budget covers only a small portion of our total costs. Thus, we have to look to our alumni and friends for help. Your support is greatly needed. You don't have to be an alumnus to make a donation to the Department of Bioengineering; we accept them from all credible sources!

Please send your check, made out to the University of Utah, as soon as possible. Send it to my attention at 2480 MEB, University of Utah, Salt Lake City, UT 84112....Remember, many employers have matching gift programs. If yours is one, be sure to inform your employer of your gift. Your support really is important. Please write and send that check right away!

I hope that 1990 has been a pleasant and productive year for you. The faculty, staff, and students join with me in wishing you a happy holiday season and a happy, healthy and productive new year.

Joe Andrade
Professor and Chair

(Research cont'd)

beneath a sharp tip on a cantilever. The sharp, microscopic stylus moves across the surface, and the forces between the material's surface and the tip deflect the cantilever. The tip traces the shape of the surface, much as a phonograph needle traces the surface of a record, but at much smaller tracking forces. The measurements are later assembled into a computerized picture of the surface, similar to the measurements made with a scanning tunneling microscope. Biological processes are monitored as they occur.

The microscope is primarily used with the sample in aqueous solutions; thus, the protein-surface interactions can be directly observed in a relevant environment and in real time. The group has produced video tapes of protein adsorption processes in which the adsorption of small clusters of immunoglobulin molecules are directly observed.

Call (801) 581-8528 for more information: Bioengineering's friendly, personable and efficient office staff (Linda Twitchell, Carol Felis, Jamie Healey, Mindy Meservy) will answer your inquiries or direct you to someone who can.

Your Contribution is Vital

- Send to:
  University of Utah
  Development Office
  304 Park Building
  Salt Lake City, UT 84112

- Indicate: Bioengineering,
  College of Engineering

- Match: Many companies match employee contributions

The Bioengineering Spotlight is published annually by the Department of Bioengineering, University of Utah, 2480 Merrill Engineering Building, Salt Lake City, UT 84112. Please contact the Department to be placed on the mailing list. Suggestions and information are always welcome.

THE UNIVERSITY OF UTAH

To: All Bioengineering Faculty

From: J.D. Andrade

Date: April 1, 1996

Subject: A Personal Bioengineering Update.

I have been informed that a number of faculty have some concerns regarding the Scientific Presentations course and also possibly regarding my commitment to Bioengineering.

I hope that this update note will help compensate for my inability to interact and communicate with each of you individually during this past year.

1) Scientific Presentations:

This two quarter, required core course for one credit hour has been taught by Ken Horch and I for the past three plus years. Ken normally takes the course in winter term and I take it in spring term. For the past two years the spring course has been titled "Controversial Topics in Bioengineering." This year there was some discussion during the winter quarter course of a possible different direction or flavor for the spring quarter course. In meeting with the students, there was considerable interest in configuring a course around mock oral examinations in the four general areas of bioengineering. Much of the stimulus for this interest is, of course, tied to the upcoming oral qualifying examinations. After some thought and discussion, I agreed with the students, as did Ken Horch, that this might be an interesting experiment for this spring term.

You have each received an e-mail memo describing the basic conduct of the course; the matrix of student assignments is posted, and available on request. I have asked the student groups responsible for generating the oral exam questions in the various areas to run them by a faculty member with responsibility or expertise in one of the four key areas, and to have that professor review and initial or sign off that these questions are, indeed, appropriate to that topic. This does not in any way suggest that these questions will be, or will not be, on the oral examination. This is a screening process to help guarantee against completely inappropriate or irrelevant questions.

Ken and I urge all faculty to try to attend these sessions and to indeed help participate in these mock oral exams. It is likely that, as a result of this exercise, our students will be better prepared for the qualifying oral exams in June. I would appreciate any further suggestions or input you might have.

2) My Lack of Attention at Faculty Meeting:

If my proofreading, or other minimum mentality requirement activities, during faculty meetings annoy any of you, then I apologize. I'm afraid I have been doing that for over 25 years, and it would be difficult to change now. I will try to minimize it. It does not, in any way, imply that I am disinterested, grossly inattentive, or intentionally disrespectful. It's just that we all know we can get the majority of what is said in most meetings without 100% concentrated attention.

Cont/...

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I do apologize for not having had the time to thoroughly review faculty candidates files in time for the meeting. Since my review had been so cursory, I elected not to provide any input, rather than to provide ill informed input.

3) Extra Department Activities:

For the record, and so that everyone knows what's going on, my appointment is 0.52 FTE in Bioengineering and 0.34 FTE in Materials Science and Engineering. I do not take any summer salary. I consider myself to be 66 % time with the University on a 12 month basis. This, therefore, allows me considerable time for consulting activities, for working with a spin-off company, Protein Solutions, Inc., in which I serve as CEO (located in the Research Park). I work on the Utah Science Center Project which, contrary to what you may have read recently in the papers, is indeed alive and well. In addition, I have taken on a number of responsibilities outside of the departments and indeed outside of the College of Engineering, in terms of Liberal Education and public education activities.

The major such activity is a Lib Ed science telecourse titled "Science Without Walls: Science in Your World." This has been an incredibly challenging, time consuming, and intensive activity which has literally consumed me for the past 12 months or so, which is one of the reasons why I appear to be so uninvolved. Although some might argue that this does not directly benefit either of my two departments, I of course argue the opposite, because I expect this course will generate considerable undergraduate student credit hours for the two departments, as well as for the College. Admittedly, it is an enormous investment in time and effort, but I am confident that it will pay back that investment, not just in student credit hours, but in terms of genuine public education and public service. I've taken the liberty of putting a brief description of that project in each of your mailboxes.

Once the production phase of this telecourse project is over, hopefully by mid to late summer, then my time and schedule should be more reasonable. I hope we will find time to mutually interact and get to know each other.

4) Bio-Based Engineering.

This course is now being offered. You have seen the posting of the topics. I will contact some of you to request help with topic areas in which you might be interested or expert. Your suggestions and input would be appreciated. This course is an experiment. I have selected topics in which, with one exception, I have little expertise or credentials. That was on purpose because I feel there is no point in rehashing topics which are already covered in other courses. In any event, I would certainly appreciate your input and help.

I trust that this update might help clarify, and justify some of my actions, and perhaps temper some perceptions.

Thanks for your attention and interest.

cc: G. Stringfellow, MSE
D. Pershing, Engineering

univ/1apr96