

April 30, 1998

Dr. Joy Pauschke
Division of Engineering Education and Centers
National Science Foundation
4201 Wilson Blvd., Rm 585
Arlington VA 22230
FAX: 703-306-0290
e-mail: jpauschk@nsf.gov

Dear Dr. Pauschke,

This letter documents our intention to submit an ERC proposal in response to NSF-98-68: An Engineering Research Center for Bioengineering Educational Technology.

Background:

For the past several hundred years, the so-called hard sciences and engineering have very effectively utilized the dissection model of investigation and analysis, attempting to analyze, understand, and engineer simple systems. This dissection and penetration approach has served us well. It has provided us with an enormous depth and range of understanding of simple systems with an almost infinity of data and detail.

There has been a growing understanding, however, that the problems and opportunities which we face cannot be addressed solely through our knowledge of simple systems nor even through modern approaches to more complex systems. We must deal with complex, interacting, hierarchical systems. Such structures and organisms generally have properties which cannot be predicted or engineered using a linear or even non-linear additivities. Examples include neural networks, parallel processing, and indeed the complex relationships between living systems and "inorganic" systems in the very stability and dynamic equilibrium of the entire planet. There is a growing appreciation that we can begin to understand and even design and engineer highly complex systems, and that the emergent properties and characteristics which we now think of as "complex" may actually have relatively simple and straight forward bases. We have begun to appreciate that the complexity of our natural world, including the living world, has arisen as a result of four billion years of statistical, combinatorial, simple "experimentation" and that much of the result of that four billion years of evolution has resulted in incredibly "complex" systems based on simple principles.

Vision:

Our thesis, our vision, is that we wish to treat education in a more Renaissance-like and integrated manner and that real understanding of complex systems will come from studies of living systems coupled with our now over two hundred year old history of being able to dissect, analyze, reassemble, and reanalyze the components of systems. Some obvious modern examples include going from neurons to neural networks, from a set of organs and tissues to a living organism, from an enzyme catalyzed single reaction to a metabolic or biochemical network, from an individual family unit to an entire culture and social system. Our faculty and our students must

begin to appreciate and understand the scaling concepts, the overlapping hierarchies, the multiple parallelisms, and the emergent complexities of living organisms—of life itself.

We tentatively call our approach *From Simplicity to Complexity, and from Complexity to Simplicity* (SCCS). What that means, we think, is that we will begin to learn that the "complex" properties, or emerging characteristics, of highly hierarchical and parallel systems will eventually yield to relatively simple rules and laws, although we fully realize that there will be statistical and probabilistic components to those rules.

Research Areas:

1. The Web as an Experimental Tool. The World Wide Web/Internet is being developed extensively for education purposes, and we also propose to enhance education via the use of these resources. However, we feel that the Web can also be effectively used as a model. The Web itself can be used as a metabolic network, a neural network, and can eventually be used to simulate organisms. The three initial projects will involve metabolic networks, neural networks, and multi organ systems, the latter leading to the modeling of a complete, complex organism.
2. Technologies for Enhanced Visualization. A key limitation in the learning and understanding of "complex" phenomena and processes is the ability to view or visualize the many variables, the many components, the many "dimensions" of those highly complex systems. We will develop and apply technologies in this area.
3. Integrated Project-Based Curricula. The key to learning is motivation. We propose to improve and enhance the graduate school project-based model in the undergraduate curriculum.

Participants and Collaborators:

Center Director: J.D. Andrade; Professor of Bioengineering, Materials Science and Engineering, and Pharmaceutics; co-Director of the Center for Integrated Science Education; co-Chair, effective July 1, 1998, Department of Bioengineering.

Center Associate Directors: Ken Horch, Professor of Bioengineering and Physiology and co-Chair, effective July 1, 1998, Department of Bioengineering. R. Rabbitt, Professor of Bioengineering and Director of Graduate Studies

An additional twelve major University of Utah faculty participants will be involved from a variety of Departments.

Collaborating Institutions:

The Department of Biological Engineering, Utah State University (W. Walker, Chair).

Drexel University, School of Biomedical Engineering (B. Onaral, Director). Drexel is submitting an independent letter of intent/preproposal which cross references the University of Utah as a potential collaborating institution. The Drexel and Utah groups will be meeting during the months of May and June to work out the details of the potential collaboration.

Yale University Center for Advanced Instructional Media (C. Jaffe, Academic Director, Professor of Diagnostic Radiology and Medicine). The Yale Center is a leader in the development of innovative approaches to education using the power of modern digital communication networks.

This application is enthusiastically endorsed and supported by Dr. David Pershing, Dean College of Engineering, University of Utah (david.pershing@dean.eng.utah.edu).

Please let me know if you need any further information.

Sincerely,

J.D. Andrade, Ph.D. (joe.andrade@m.cc.utah.edu)
Professor, Bioengineering
co-Chair Designate, Department of Bioengineering

cc: D. Pershing, Dean, College of Engineering
K. Caldwell, Chair, Department of Bioengineering
K. Horch, co-Chair Designate and Associate Director, Department of Bioengineering
R. Rabbitt, Associate Director, Department of Bioengineering
B. Onaral, Director, School of Biomedical Engineering, Drexel University
C. Jaffe, Director, Center for Advanced Instructional Media, Yale University
W. Walker, Chair, Department of Biological Engineering, Utah State University

Document Summary Sheet,
University of Utah, Office of
Sponsored Projects
Version date: June 3, 1998

Comp
7/25/98

98-187

98 JUL 28 AM 11:37

Date &
Time
Received

PID # 9607087

# Copies Req. (Orig + copies)	Mailing Address	Parcel Delivery
Receipt Date: 7/28/98	National Science Foundation (PPLU)	
Postmark Date: <i>CR</i>	NSFA 98-68: Engineering Research Centers	
Electronic Transmission <input checked="" type="checkbox"/>	4201 Wilson Blvd., Rm P60	
	Arlington, VA 22230	
	Attn:	Phone:
		Attn:

Dept.
College Code
Agency Code

If OSP is mailing,
account # to be charged:

Initials of Administrator
reviewing proposal:

Project Information	
Project Title:	Bioengineering Education: Simplicity of Complexity to Simplicity
Sponsor: NSF	*CFDA#: _____
Project Duration: From 01-Apr-99	To: 30-Mar-04

Proj. Liaison/Contact
Name:
J. Andrade
Phone:
581-4379
E-mail (break into 2 lines):
joe.andrade@m.cc.utah.edu

Principal Investigator	Co-Principal Investigator
(1) Name: Joe Andrade	(2) Name: Ken Horch
Campus Address: 2480 MEB	Campus Address: 2480 MEB
Phone: 1-4379	Phone: 1-8526
E-mail: joe.andrade@m.cc.utah.edu	E-mail: k.horch@m.cc.utah.edu
Dept.: Bioengineering	Dept.: Bioengineering
College: Engineering	College: Engineering
Ctr/Inst/Div:	Ctr/Inst/Div:

*Use if across college lines from first PI

Current U of U Account Number: N/A
Current Contract/Grant Number: N/A

Project Details	
<input checked="" type="checkbox"/> New	<input checked="" type="checkbox"/> Grant
<input type="checkbox"/> Renewal/Competing Contin.	<input type="checkbox"/> Contract
	<input type="checkbox"/> Clinical Test
	<input type="checkbox"/> Other Agreement
	<input type="checkbox"/> Subgrant/subcontract

Categories	Source
<input checked="" type="checkbox"/> Research	<input checked="" type="checkbox"/> Federal/flow-thru
<input checked="" type="checkbox"/> Instruction	<input type="checkbox"/> Public/non-Federal
<input checked="" type="checkbox"/> Service	<input type="checkbox"/> Industry
	<input type="checkbox"/> Other Private
	<input type="checkbox"/> Intramural

F&A rate - descrip. of basis (see MTDC): 46.5%

Budget Summary		Years 3-5		
Source of Funds	1st Year	2nd Year	3rd Year	Total Request-5 yrs
Sponsor NSF	\$1,995,825.00	\$1,973,400.00	\$1,995,500.00	\$9,954,225.00
University of Utah (if applicable)				
Other (if applicable)				
TOTAL				

Cost Sharing Summary (if a VP provides matching, attach approval letter)
Sponsor requires matching: (do NOT fill in blanks below) (fill in blanks below)

CATEGORY	1st Year	Total	Approved By:	Existing FAS Acct. or PeopleSoft #
Salary + F.B.				
Other Direct				
F&A Cost				
In-Kind				
TOTAL				

7/26/98

Prime Fed. Acronym:
NSF
(if flow-through)

Request Review Required
30% F&A for All
1/2 calculated
at all
Monthly to be
negotiated
R

Date version: June 3, 1998

Assurances and Certifications

Research Involves:	Date	Approval No.	Reviewed By	Other Information
Human Subjects				Space: <input type="checkbox"/> New <input checked="" type="checkbox"/> Renovation
Animal Use				Number of students: Graduate: 60 Undergraduate: 60
Biosafety				Subcontract required: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Radioisotope				Potential patent or copyright: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Hazardous/Toxic Substance				Proprietary Research: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
EPA Permits				*See Policy & Procedures
Good laboratory practices:				Related to the 2002 Olympic Games? <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Have you been debarred or suspended by the Federal Government in the last 3 years?				
	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No			

INTEREST - To the best of your knowledge, do you or does any member of your immediate

a. Sponsoring the proposed research or substantially related research? Yes No

b. Whose business is substantially related to subject matter of the proposal for sponsored research or substantially related research? Yes No

c. That you are aware is requesting rights to any University technology? Yes No

d. That may compete for provision of goods or services to be paid for with funds provided by the sponsoring entity? Yes No

ARE ANSWERED YES: COMPLETE
THE UNIVERSITY OF UTAH

Approvals/Signatures

Principal Investigator(s)	Date	Department Chair	Date
J. Andrade		J. Andrade	
K. Horch		K. Horch	

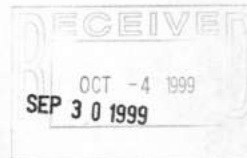
First PI's Approving Department: _____
 (use if Co-PI named on p. 1)

College	College Dean	Date
Engineering	K. Zaldar	7/27/98

OSP Administrator	Date	Director-Sponsored Projects	Date
B. 7-18-98			

Additional Project Information

NATIONAL SCIENCE FOUNDATION
4201 WILSON BOULEVARD
ARLINGTON, VIRGINIA 22230



Dr. J. D. Andrade
Department of Bioengineering Educational
Studies
University of Utah
Salt Lake City, UT 84112

RE: Proposal EEC-9876378

Dear Dr. Andrade:

We regret to inform you that the National Science Foundation is unable to support your proposal to establish a new Engineering Research Center for Bioengineering Educational Technology. We received seven proposals, and based on the recommendation of an initial panel, site-visited two of the proposed centers. As a result of the recommendations of the site visitors and a second panel, we have selected one of these proposed centers for funding.

The seven proposals received in response to this funding initiative were reviewed under the review criteria given in the Program Announcement "An Engineering Research Center for Bioengineering Educational Technology" (NSF 98-68). Each proposal was reviewed prior to the first panel meeting by a subset of these panelists, who then assigned it a rating. When they assembled at NSF, these panelists discussed each proposal and its individual reviews. On the basis of these discussions, the panel arrived at a consensus recommendation for each proposal to either site visit or not site visit the proposed center. After the two site visits recommended by this panel were completed, a second panel was convened to make the final recommendation.

For your information we have enclosed verbatim reviews on your proposal that contributed to this decision. If you have any questions regarding the process or the reviews, please contact Dr. Joy Pauschke, Program Director for the Engineering Research Centers Program, at (703) 306-1380.

Sincerely,

Marshall Lih
Division Director
Engineering Education and Centers Division

Enclosures

Copy to: Lynne Chronister
Authorized Org. Rep.

① NSF-ERC

COVER SHEET FOR PROPOSAL TO THE NATIONAL SCIENCE FOUNDATION

PROGRAM ANNOUNCEMENT/SOLICITATION NO./CLOSING DATE (if not in response to a program announcement/solicitation enter NSF 98-2)		FOR NSF USE ONLY	
NSF 98-68 07/28/98		NSF PROPOSAL NUMBER	
FOR CONSIDERATION BY NSF ORGANIZATION UNIT(S) (indicate the most specific unit known, i.e., program, division, etc.)		9876378	
ENGINEERING RESEARCH CENTERS			
DATE RECEIVED	NUMBER OF COPIES	DIVISION ASSIGNED	FUND CODE
EMPLOYER IDENTIFICATION NUMBER (EIN) OR TAXPAYER IDENTIFICATION NUMBER (TIN)		SHOW PREVIOUS AWARD NO. IF THIS IS <input type="checkbox"/> A RENEWAL OR <input type="checkbox"/> AN ACCOMPLISHMENT-BASED RENEWAL	DUNS# (Data Universal Numbering System)
876000525			009095365
NAME OF ORGANIZATION TO WHICH AWARD SHOULD BE MADE		ADDRESS OF AWARD ORGANIZATION, INCLUDING ZIP CODE	
University of Utah		University of Utah 1471 Federal Way Salt Lake City, UT. 841021807	
AWARDEE ORGANIZATION CODE (IF KNOWN)			
0036756000			
NAME OF PERFORMING ORGANIZATION, IF DIFFERENT FROM ABOVE		ADDRESS OF PERFORMING ORGANIZATION, IF DIFFERENT, INCLUDING ZIP CODE	
PERFORMING ORGANIZATION CODE (IF KNOWN)			
IS AWARDEE ORGANIZATION (Check All That Apply) (See GPG I.D.1 For Definitions) <input type="checkbox"/> FOR-PROFIT ORGANIZATION <input type="checkbox"/> SMALL BUSINESS <input type="checkbox"/> MINORITY BUSINESS <input type="checkbox"/> WOMAN-OWNED BUSINESS			
TITLE OF PROPOSED PROJECT Bioengineering Educ: Simplicity to Complexity to Simplicity			
REQUESTED AMOUNT	PROPOSED DURATION (1-60 MONTHS)	REQUESTED STARTING DATE	
\$ 9,954,225	60 months	04/01/99	
CHECK APPROPRIATE BOX(ES) IF THIS PROPOSAL INCLUDES ANY OF THE ITEMS LISTED BELOW			
<input type="checkbox"/> BEGINNING INVESTIGATOR (GPG 1.A.3)		<input type="checkbox"/> VERTEBRATE ANIMALS (GPG I.D.12) IACUC App. Date <u>01/01/00</u>	
<input type="checkbox"/> DISCLOSURE OF LOBBYING ACTIVITIES (GPG I.D.1)		<input type="checkbox"/> HUMAN SUBJECTS (GPG I.D.12)	
<input type="checkbox"/> PROPRIETARY & PRIVILEGED INFORMATION (GPG I.D.10)		Exemption Subsection _____ or IRB App. Date <u>01/01/00</u>	
<input type="checkbox"/> NATIONAL ENVIRONMENTAL POLICY ACT (GPG I.D.10)		<input type="checkbox"/> INTERNATIONAL COOPERATIVE ACTIVITIES: COUNTRY/COUNTRIES	
<input type="checkbox"/> HISTORIC PLACES (GPG I.D.10)			
<input type="checkbox"/> SMALL GRANT FOR EXPLOR. RESEARCH (SGER) (GPG I.D.12)		<input type="checkbox"/> FACILITATION FOR SCIENTISTS/ENGINEERS WITH DISABILITIES (GPG V.G.)	
<input type="checkbox"/> GROUP PROPOSAL (GPG I.D.12)		<input type="checkbox"/> RESEARCH OPPORTUNITY AWARD (GPG V.H)	
PVPD DEPARTMENT Bioengineering Educational Studies		PVPD POSTAL ADDRESS	
PVPD FAX NUMBER		Salt Lake City, UT 84112 United States	
NAMES (TYPED)	Social Security No. *	High Degree, Yr.	Telephone Number
PVPD NAME J. D Andrade	SSNs are confidential and are not displayed	Ph.D., 1969	801-581-4379
CO-PVPD			
CO-PVPD			
CO-PVPD			
CO-PVPD			
NOTE: THE FULLY SIGNED CERTIFICATION PAGE MUST BE SUBMITTED IMMEDIATELY FOLLOWING THIS COVER SHEET.			
*SUBMISSION OF SOCIAL SECURITY NUMBERS IS VOLUNTARY AND WILL NOT AFFECT THE ORGANIZATION'S ELIGIBILITY FOR AN AWARD. HOWEVER, THEY ARE AN INTEGRAL PART OF THE NSF INFORMATION SYSTEM AND ASSIST IN PROCESSING THE PROPOSAL. SSN SOLICITED UNDER NSF ACT OF 1950, AS AMENDED.			

List of Participants

Academic Participants:

- Andrade, J.D. Professor & Co-Chair, Dept. of Bioengineering, Univ. Utah
 Bermudez, J. Associate Professor, School of Architecture, Univ. Utah
 Blair, D. Associate Professor, Dept. of Biology, Univ. Utah
 *Budinger, T. Professor, Dept. of Radiology, Univ. California—Berkeley
 Caldwell, K. Chair Professor, Dept. of Biotechnology, Uppsala Univ (Sweden)
 *Chauvet, G. Professor & Director, Inst. of Theoretical Biology, Univ. of Angers (France)
 Christensen, D. Professor, Depts. of Bioengineering & Electrical Eng., Univ. Utah
 *D'Argenio, D. Professor & Chairman, Dept. of Biomedical Engineering, Univ. of Southern California
 Frazier, B. Assistant Professor, Dept. of Bioengineering, Univ. of Utah
 Herbst, M. Dept. of Bioengineering, Fachhochschule Hamburg
 Hlady, V. Associate Professor, Dept. of Bioengineering, Univ. Utah
 Horch, K. Professor & Co-Chair, Dept. of Bioengineering, Univ. Utah
 Jaffe, C. Professor, Dept. of Medicine, Yale University
 Johnson, C. Associate Professor, Dept. of Computer Science, Univ. Utah
 Johnson, R. Emeritus Professor, Dept. of Computer Science, Univ. Utah
 Johnson, S. Research Professor, Dept. of Bioengineering, Univ. Utah
 Kern, S. Assistant Professor, Depts. of Anesthesiology & Bioengineering, Univ. Utah
 *Linehan, J. Professor & Chair, Dept. of Biomedical Engineering, Marquette, Univ.
 MacLeod, R. Assistant Research Professor, Dept. of Bioengineering, Univ. Utah
 *Onaral, B. Professor & Director, School of Biomedical Engineering, Drexel Univ.
 Othman, H. Professor, Department of Mathematics, Univ. Utah
 Pantalos, G. Research Professor, Dept. of Bioengineering, Univ. Utah
 Price, R. Professor, Dept. of Physics, Univ. Utah
 Rabbitt, R. Associate Professor, Dept. of Bioengineering, Univ. Utah
 Romer, R. Professor & Chair, Dept. of Mechanical Engineering, Univ. Utah
 Trujillo, E. Professor, Dept. of Chemical Engineering, Univ. Utah
 *Walker, W. Professor, Dept. of Biological Engineering, Utah State Univ.
 Westenskow, D. Professor, Depts. of Anesthesiology & Bioengineering, Univ. Utah
 Wiley, S. Associate Professor, Dept. of Pathology, Univ. Utah
 Wiskin, J. Associate Research Professor, Dept. of Bioengineering, Univ. Utah
- Industrial, Practitioner, and Other Partners:
 Ash, O. Executive Director, ARUP, Inc. (Associated Regional University Pathologists, Inc.) a major clinical and diagnostic testing laboratory.
 *Blake, L. Vice President, Sorenson-Vision, Inc., Logan, Utah—a data compression company whose technology allows full time video over normal telephone lines.
 DiCaprio, V. Senior Vice President & Chief Technical Officer, Becton-Dickinson Co.
 *Jacobson, S. President, Sarcos, Inc., Salt Lake City, a pioneering and leading firm in robotics and advanced biomedical products (www.sarcos.com)
 *Johnson, R. Principle of nDV Ltd., whose unique parallel coordinates software is described in Thrust 3—Visualization.
 McRea, J. Chairman, Dept. of Bioengineering Industrial Advisory Board and President/CEO, Device-Based Therapeutics, Inc., Salt Lake City
 Suggett, A. Director of R & D, Smith and Nephew Ltd., London
 *Van Wagenen, R. Vice President for R & D, Protein Solutions, Inc., Salt Lake City
- * letter in Appendix A

COVER SHEET FOR PROPOSAL TO THE NATIONAL SCIENCE FOUNDATION

PROGRAM ANNOUNCEMENT/SOLICITATION NO./CLOSING DATE (not in response to a program announcement/solicitation enter NSF 98-2)		FOR NSF USE ONLY	
Engineering Research Center (ERC) Announcement NSF 98-68		NSF PROPOSAL NUMBER	
FOR CONSIDERATION BY NSF ORGANIZATIONAL UNIT(S) (Indicate the most specific unit known, i.e., program, division, etc.)			
Engineering Education and Centers			
DATE	NUMBER OF COPIES	DIVISION	FILE LOCATION
EMPLOYER IDENTIFICATION NUMBER (EIN) OR TAXPAYER IDENTIFICATION NUMBER (TIN)	SHOW PREVIOUS AWARD NO. IF THIS IS	IS THIS PROPOSAL BEING SUBMITTED TO ANOTHER FEDERAL AGENCY? YES <input type="checkbox"/> NO <input checked="" type="checkbox"/> IF YES, LIST ACRONYM(S)	
876000525	<input type="checkbox"/> A RENEWAL OR <input type="checkbox"/> AN ACCOMPLISHMENT-BASED RENEWAL		
NAME OF ORGANIZATION TO WHICH AWARD SHOULD BE MADE		ADDRESS OF AWARDEE ORGANIZATION, INCLUDING ZIP CODE	
University of Utah		Office of Sponsored Projects	
AWARDEE ORGANIZATION CODE (IF KNOWN)		1471 Federal Way	
0036756000		Salt Lake City, Utah 84112	
NAME OF PERFORMING ORGANIZATION, IF DIFFERENT FROM ABOVE		ADDRESS OF PERFORMING ORGANIZATION, IF DIFFERENT, INCLUDING ZIP CODE	
PERFORMING ORGANIZATION CODE (IF KNOWN)			
IS AWARDEE ORGANIZATION (Check All That Apply) (See GPG II.D.1 For Definitions) <input type="checkbox"/> FOR-PROFIT ORGANIZATION <input type="checkbox"/> SMALL BUSINESS <input type="checkbox"/> MINORITY BUSINESS <input type="checkbox"/> WOMAN-OWNED BUSINESS			
TITLE OF PROPOSED PROJECT Bioengineering Education: From Simplicity to Complexity to "Simplicity"			
REQUESTED AMOUNT	PROPOSED DURATION (1-60 MONTHS)	REQUESTED STARTING DATE	
\$9954,225	60 months	4/1/99	
CHECK APPROPRIATE BOX(ES) IF THIS PROPOSAL INCLUDES ANY OF THE ITEMS LISTED BELOW			
<input type="checkbox"/> BEGINNING INVESTIGATOR (GPG I.A.3)		<input type="checkbox"/> VERTEBRATE ANIMALS (GPG II.D.12) IACUC App. Date _____	
<input type="checkbox"/> DISCLOSURE OF LOBBYING ACTIVITIES (GPG II.D.1)		<input type="checkbox"/> HUMAN SUBJECTS (GPG II.D.12) Exemption Subsection or IRB App. Date _____	
<input type="checkbox"/> PROPRIETARY & PRIVILEGED INFORMATION (GPG II.D.10)		<input type="checkbox"/> INTERNATIONAL COOPERATIVE ACTIVITIES: COUNTRY/COUNTRIES	
<input type="checkbox"/> NATIONAL ENVIRONMENTAL POLICY ACT (GPG II.D.10)			
<input type="checkbox"/> HISTORIC PLACES (GPG II.D.10)			
<input type="checkbox"/> SMALL GRANT FOR EXPLOR. RESEARCH (SGER) (GPG II.D.12)		<input type="checkbox"/> FACILITATION FOR SCIENTISTS/ENGINEERS WITH DISABILITIES (GPG V.G.)	
<input checked="" type="checkbox"/> GROUP PROPOSAL (GPG II.D.12)		<input type="checkbox"/> RESEARCH OPPORTUNITY AWARD (GPG V.H.)	
PI/PO DEPARTMENT		PI/PO POSTAL ADDRESS	
Bioengineering		University of Utah	
PI/PO FAX NUMBER		50 s Campus center Dr Rm 2480	
801 585-5361		Salt Lake City, Utah 84112-9202	
NAMES (TYPED)	Social Security No.*	High Degree, Yr	Telephone Number
			Electronic Mail Address
PI/PO NAME			
Andrade JD	565-52-0772	PhD 69	801-581-4379
CO-PI/PO			Joe.Andrade@m.cc.utah.edu
Horch, K	041-34-2416	PhD 71	801 585 1981
CO-PI/PO			k.horch@m.cc.utah.edu
Kern, S.	158-56-9840	PhD 95	801-581-6393
CO-PI/PO			skern@card.med.utah.edu
CO-PI/PO			
CO-PI/PO			
NOTE: THE FULLY SIGNED CERTIFICATION PAGE MUST BE SUBMITTED IMMEDIATELY FOLLOWING THIS COVER SHEET			
*SUBMISSION OF SOCIAL SECURITY NUMBERS IS VOLUNTARY AND WILL NOT AFFECT THE ORGANIZATION'S ELIGIBILITY FOR AN AWARD. HOWEVER, THEY ARE AN INTEGRAL PART OF THE NSF INFORMATION SYSTEM AND ASSIST IN PROCESSING THE PROPOSAL. SSN SOLICITED UNDER NSF ACT OF 1950, AS AMENDED.			

Project Summary

The University of Utah proposes an Engineering Research Center in Bioengineering Educational Technology (NSF-98-68) with the title "From Simplicity to Complexity to "Simplicity" (SCS), with J.D. Andrade as principle investigator and Director.

We propose to develop and implement undergraduate and graduate curricula which will empower students, faculty, and practitioners to study, interpret, research, and apply the emerging field of bioengineering from a non-traditional set of perspectives, using a set of new as well as traditional tools. Our approach is based on the growing appreciation and realization that the spatial and temporal organization and interaction of living matter provides it with unique sets of properties and behaviors which cannot be understood using traditional reductionist and even synthesis approaches and tools. Although we must continue to use and apply those traditional tools, which have proven so powerful and effective, we can now add and develop powerful new tools and perspectives. Three research thrusts will develop such key tools.

We specifically propose to research, develop, and implement an integrated biology and engineering-based four year undergraduate curriculum using a set of complex and challenging bio-based projects as the basic structure. Students, faculty, graduate students, and advisors will compose teams with strong interests in a particular project. Graduate students will participate as mentors, advisors, teachers, and "senior" participants in the projects and courses. Industrial and academic bioengineering, biology, biotechnology, engineering, and medical professionals will participate in all aspects of the curriculum, including design and supervision of the projects. Participating institutions and corporations will play major roles.

The projects will be fully integrated over the four years of the curriculum. The projects themselves are considered a "research thrust." The program is designed primarily for those students who learn best by doing—by being involved in, committed to, and empowered by a challenging project. The different project teams will interact, educate, and empower each other. Many of the project topics and problems will be related to two or more projects. We expect considerable project synergism and cross fertilization.

A set of courses and related experiences will help provide knowledge, understanding, and tools directly applicable to the projects. The courses, seminars, and other experiences will connect and relate to the integrating project. Although project needs and interests will require traditional tools and courses, new tools and capabilities will be needed, including a set of bio-derived perspectives. The other three research thrusts will develop tools and resources needed for such complex and inclusive projects. These thrusts are the "Living" Internet, Multi-dimensional Visualization, and Modeling and Simulation.

We propose to utilize the Internet as a participation and involvement vehicle, as a research tool, and as a means for wide and effective dissemination of the curriculum, project progress, and related information. We further propose to use the Internet itself as a model for biological processes. Individual computer nodes and their human operators will represent and function as "self-motivated biological components." Students themselves will play the role of a particular biological reaction, function, or device and will interact with other students and functions through the net. We call this the "Living Internet." Analysis of the outputs of such complex experiments will likely lead to a greater understanding of their complexity.

The four year integrated project will be designed to implement our Simplicity—Complexity—"Simplicity" objective and theme. The bioengineering/pathological problem or need will be presented and dissected (reductionist) to enable "simple" subsystems and components to be modeled, studied, designed, constructed, and analyzed, always keeping the big picture—the complex problem—in mind. These simple components will then be assembled (synthesis) into more complex subsystems/systems, and the system's properties/characteristics will be measured and analyzed. Like living systems, the more complex systems will begin to exhibit complex behavior—new properties/behavior will emerge with the increasing complexity. As this complexity is characterized and analyzed, new and simple (but different!) rules will evolve and emerge—hence "simplicity" from complexity. We will apply many of the new, powerful, and

List of Participants

Academic Participants:

- Andrade, J.D. Professor & Co-Chair, Dept. of Bioengineering, Univ. Utah
 Bermudez, J. Associate Professor, School of Architecture, Univ. Utah
 Blair, D. Associate Professor, Dept. of Biology, Univ. Utah
 *Budinger, T. Professor, Dept. of Radiology, Univ. California—Berkeley
 Caldwell, K. Chair Professor, Dept. of Biotechnology, Uppsala Univ (Sweden)
 *Chauvet, G. Professor & Director, Inst. of Theoretical Biology, Univ. of Angers (France)
 Christensen, D. Professor, Depts. of Bioengineering & Electrical Eng., Univ. Utah
 *D'Argenio, D. Professor & Chairman, Dept. of Biomedical Engineering, Univ. of Southern California
 Frazier, B. Assistant Professor, Dept. of Bioengineering, Univ. of Utah
 Herbst, M. Dept. of Bioengineering, Fachhochschule Hamburg
 Hlady, V. Associate Professor, Dept. of Bioengineering, Univ. of Utah
 Horch, K. Professor & Co-Chair, Dept. of Bioengineering, Univ. Utah
 Jaffe, C. Professor, Dept. of Medicine, Yale University
 Johnson, C. Associate Professor, Dept. of Computer Science, Univ. Utah
 Johnson, R. Emeritus Professor, Dept. of Computer Science, Univ. Utah
 Johnson, S. Research Professor, Dept. of Bioengineering, Univ. Utah
 Kern, S. Assistant Professor, Depts. of Anesthesiology & Bioengineering, Univ. Utah
 *Linehan, J. Professor & Chair, Dept. of Biomedical Engineering, Marquette, Univ.
 MacLeod, R. Assistant Research Professor, Dept. of Bioengineering, Univ. Utah
 *Onaral, B. Professor & Director, School of Biomedical Engineering, Drexel Univ.
 Othmer, H. Professor, Department of Mathematics, Univ. Utah
 Pantalos, G. Research Professor, Dept. of Bioengineering, Univ. Utah
 Price, R. Professor, Dept. of Physics, Univ. Utah
 Rabbitt, R. Associate Professor, Dept. of Bioengineering, Univ. Utah
 Romer, R. Professor & Chair, Dept. of Mechanical Engineering, Univ. Utah
 Trujillo, E. Professor, Dept. of Chemical Engineering, Univ. Utah
 *Walker, W. Professor, Dept. of Biological Engineering, Utah State Univ.
 Westenskow, D. Professor, Depts. of Anesthesiology & Bioengineering, Univ. Utah
 Wiley, S. Associate Professor, Dept. of Pathology, Univ. Utah
 Wiskin, J. Associate Research Professor, Dept. of Bioengineering, Univ. Utah

Industrial Practitioner and Other Partners:

- Ash, O. Executive Director, ARUP, Inc. (Associated Regional University Pathologists, Inc.) a major clinical and diagnostic testing laboratory.
 *Blake, L. Vice President, Sorenson-Vision, Inc., Logan, Utah—a data compression company whose technology allows full time video over normal telephone lines.
 DiCaprio, V. Senior Vice President & Chief Technical Officer, Becton-Dickinson Co.
 *Jacobson, S. President, Sarcos, Inc., Salt Lake City, a pioneering and leading firm in robotics and advanced biomedical products (www.sarcos.com)
 *Johnson, R. Principle of nDV Ltd., whose unique parallel coordinates software is described in Thrust 3—Visualization.
 McRea, J. Chairman, Dept. of Bioengineering Industrial Advisory Board and President/CEO, Device-Based Therapeutics, Inc., Salt Lake City
 Suggett, A. Director of R & D, Smith and Nephew Ltd., London
 *Van Wageningen, R. Vice President for R & D, Protein Solutions, Inc., Salt Lake City

* letter in Appendix A

rapidly evolving tools and concepts represented by the names complexity scaling, networks, hierarchy, parallelism, non-linear, chaos, and emergence.

We propose to evaluate and compare this approach with a more traditional approach, using our new undergraduate curriculum. Our first undergraduate class will begin in the Fall of 1999, utilizing a traditional undergraduate bioengineering curriculum. We will start this project-based experimental curriculum with a 15 to 20 person "freshman" class in Fall 2000. The project-based group will be assessed and compared with the parallel, traditional class for the entire duration of the grant.

We also propose an extensive high school and general public outreach effort, building on our existing outreach activities, emphasizing the involvement and participation of minority populations. Summer workshops will help provide high school students and some of their teachers with the motivation and skills to address bioengineering topics and problems.

We will establish a set of advisory boards. An International Advisory Board (IAB) will focus on project-based undergraduate education and will include individuals with experience in the key research thrusts. The group will meet annually at the University of Utah to provide advice, critique, and assessment. We will also have a rich seminar and visiting faculty program, focused on the research thrusts and project topics. These advisors and visitors will actively participate in the program and in specific project groups. Strong international participation will be a key emphasis. The Academic and Industrial Advisory Council, composed of representatives of the participating institutions and companies, will meet twice a year, one of those meetings joint with the IAB.

The project will be managed by an Executive Committee, responsible for the day to day management and conduct of the project.

The project's experiences, output, and deliverables will be disseminated to the community via an aggressive program of faculty lectures and visits to other institutions, particularly in years 3-8. We will also participate extensively in the meetings of the Biomedical Engineering Society, the American Society for Engineering Education, the Engineering in Medicine and Biology Society, and the American Institute for Medical and Biological Engineering. We will also develop internet and video/multi-media vehicles for effective dissemination and delivery, as well as for assessment purposes.

We propose a five year effort with an anticipated three year renewal (eight years total). The University and the Department are committed to maintaining the program as NSF funding is phased out in years 6-8.

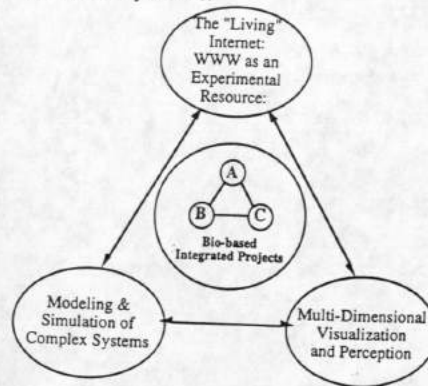


Figure 1. Key components & projects of the ERC in Bioengineering Education Technology: Simplicity <--> Complexity --> "Simplicity. The small group bio-based integrated projects, discussed in Sections D and F, are the key integrating and motivational parts of the program. Dealing with such challenging projects at the undergraduate level requires a set of skills and tools to facilitate learning, analysis, and design. Three key research thrusts of the project will such tools, represented in the three outer ellipses and described in Sections D and F.

University of Utah
NSF ERC BET:
From Simplicity to Complexity—to "Simplicity"
Table of Contents as per NSF 98-68

Cover Sheet	
List of Participants	
Academic	
Industrial, Practitioner, Other	
Project Summary	
Table of Contents	
Results from Prior Support	

Narrative	
A. Vision, goals, and rationale	1
B. Bioengineering education and curricula	3
C. Value added by the ERC	4
D. Strategic plan	4
• Overview	4
• Thrust 1: Bio-based Integrated Projects: the Core of the Curriculum	5
• Thrust 2: The "Living" Internet: the Web as an Experimental Tool	9
• Thrust 3: Multi-dimensional Visualization	9
• Thrust 4: Modeling and Simulation of Complex Systems	10
• Time Line	12
E. Deliverables	11
F. Research Program	14
Thrust 1: Bio-based Integrated Projects	14
Objectives:	14
Project A: Neuromimetic Systems: Vision	17
Project B: Engineering Bioenergetics	19
Project C: Cardiomimetic System	21
"Research" Thrusts—Objectives	23
Thrust 2: The "Living" Internet: the Web as an Experimental Tool	24
Thrust 3: Multi-dimensional Visualization	28
Thrust 4: Modeling and Simulation of Complex Systems	29
Integration and Interactions	
G. Education	32
H. Outreach and Dissemination	33
I. Assessment, Evaluation, and Advisory Boards	35
J. Industrial and Academic Collaboration	37
K. ERC Infrastructure (Joe)	38
• Leadership and Management	
• Personnel	
• Facilities, Space, Equipment	
• Financial Planning & Support	
• Role of ERC within Institution	

References

Appendices

A. Letters of Interest and Support	
B. Budget Estimates and Justifications	
Individuals Years 1-5 (Form 1030)	
Total Years 1-5	
Functional Budget Plan—Year 1—Table	
Support Strategy	
C. Bio Sketches	
D. Facilities and Equipment (Form 1363)	
E. Current and Pending Support (Form 1239)	
F. Justification for Secretarial and Administrative Support	

Results from Prior Support

We have not had extensive support in areas of bioengineering or engineering education.

The College of Engineering has each year, for the past 10 years received a small base budget supplement from the state to enhance undergraduate education. Bioengineering has received funds to develop undergraduate bioengineering minors or tracts in the traditional departments and to develop its own undergraduate program.

Our Whitaker Department Development Award was focused on bio-based engineering and resulted in new faculty, courses, and research activities with a bio-based emphasis. Several key ERC participants have been involved in revising undergraduate education on this campus (Andrade, Christensen, Horch) and elsewhere (Rabitt, Washington University), but we have published little in this area (6, 64, see also Rabitt Biosketch in Appendix C).

The University of Utah's major science education and outreach activity, the Center for Science Education and Outreach (formerly the Center for Integrated Science Education) was founded by and operates through the Department of Bioengineering. The Center's activities, and particularly the *Science Without Walls* telecourse and textbook (31) represent a major deliverable, produced solely with local resources.

Our bioengineering research activities and productivity are best assessed through the biosketches and current support in Appendix C and E.

A. Vision, Goals, and Rationale

Vision

We have a dream. We dream of an integrated, motivated, creative, and practical undergraduate experience which will help students, graduates, faculty, and practitioners evolve the skills and interests to address problems and opportunities in a renaissance-like, "conciliate" (1), holistic manner. We dream of students and colleagues who choose to work on less defined and complex problems and are stimulated by, indeed addicted to, the intellectual and inventive challenges which such problems demand. Part of our dream involves participants who do not accept the often common attitude in the engineering and education community that "renaissance," unitary, conciliate, or holistic approaches equate to superficiality. We believe that the human mind has the capabilities and even the need to develop an integrated, coherent view of complex phenomena with as much detail and depth as may be required. We firmly believe that students at all levels are generally inefficiently and inadequately stimulated and motivated, but that their potential for enhanced learning and development is almost infinite.

We will work with groups of appropriately selected students to help them evolve strong backgrounds in the basic sciences, mathematics, and engineering at the undergraduate level. They will concurrently develop strong backgrounds in complex, integrated, interdisciplinary projects which will challenge, enhance, and expand their mathematics, scientific, and engineering skills. With their engineering design and project development skills, these engineers will be well equipped to tackle complex bioengineering projects.

We will use a Simplicity to Complexity to "Simplicity" (SCS) approach. By this we mean that students will be exposed to topics and projects in a societal context, then rapidly and efficiently apply reductionist principles to break the project down to simple, fundamental primitive components and models which can be individually studied using their appropriate scientific, mathematical, and engineering backgrounds. As background knowledge and expertise are acquired, the simpler building blocks will be connected; the synthesis approach. As those more complex, multi-component systems are studied and characterized, new tools will be used to facilitate their analysis and understanding. As the project evolves in complexity, students will discover and appreciate that complex systems may exhibit non-linear characteristics (2). As the project proceeds, their enhanced analytical and engineering skills will allow them to evolve guidelines and even sets of rules for their now complex system (2, 3). This new "simplicity" will not be an extrapolation or additivity of the original simplicity, which was achieved by reduction to individual components or building blocks, but rather will be a "simplicity" achieved by analyzing the now complex system from a different hierarchical perspective (2). Such experiences will give them the perspective and experience to tackle complex systems and problems in their future endeavors.

We really do want to produce Leonardo da Vinci-like individuals, whose creativity, ideas, and inspiration are matured and modulated by engineering ethics and the need to complete and deliver projects on time, under budget, and with enhanced specifications and performance.

Our dream is to produce such unique individuals and to develop faculty and practitioners who can disseminate these experiences and processes to the broader community.

Our goal is to apply this conciliate, renaissance-like approach to undergraduate and graduate bioengineering education. We believe that this will be one of several steps in the significant restructuring and enhancement of Engineering in general (4-6). The challenges and problems our society and civilization must now confront, in our opinion, require nothing less.

Goals

Our primary goal is to design, develop, and implement a complex project-based bioengineering curriculum. The immediate product or deliverable will be the students prepared via

In designing an undergraduate bioengineering program, it is important to recognize the interdisciplinary nature of the field. Biomedical engineers are faced with a wide variety of tasks covering all fields of engineering, physics, chemistry, mathematics, and the life sciences. The diverse nature of the field sometimes leads to curricula that survey a wide number of topics, forcing the students to memorize a large set of "factoids". The engineering approach, however, requires dexterous deductive reasoning to solve practical problems. It is therefore important to establish within each student a solid foundation upon which he or she can build. Graduates must be able to dissect the problem, recognize salient physical principles governing the situation, and apply the scientific methods to arrive at a solution. In this spirit, we have designed a rigorous undergraduate program that we believe will provide this training and prepare students for the future.

We are committed. The timing and resources are in place. We are eager to begin this experiment.

B. Bioengineering Education and Curricula

In its 1995 Survey of Academic Bioengineering Programs, the American Institute for Medical and Biological Engineering (AIMBE) noted that the most often cited skill acquired by graduates of bioengineering programs was "research/problem solving," followed by "work at the engineering/medicine interface" (9). However, the most cited need in undergraduate programs was for "active involvement with other disciplines, primarily in application areas in the life sciences". Although there was agreement that biomedical engineering is and will continue to be an engineering discipline, current undergraduate programs in the field are viewed as primarily serving to prepare students for graduate school, rather than for careers in biomedical engineering, per se, in spite of the fact that less than 25% of bioengineering graduates end up in academic careers. Clearly the field would benefit from an undergraduate curriculum that better prepares graduates for both academic and nonacademic careers.

A survey of curricula from some of the more prominent undergraduate programs in the country shows that they all tend to follow the traditional academic approach: students start with basic courses in math, physics and chemistry, and only later get into subjects that are directly affiliated with their major interests. The typical rationale for such an approach is that students need the basics before they can understand or appreciate the more specialized, "advanced" topics of a specific engineering discipline.

The shortcoming of this approach, as the Colorado Commission on Higher Education's Physics-2000 Project points out (10), is that there is little context in which the students can place this material with respect to their interests, which interferes with learning. Rather, by "proceeding from familiar technological devices to the abstract underlying concepts", the subject "is made more relevant and the (student) is motivated to explore abstract ideas." In biomedical engineering, this might take the form of simulating or interfacing with one or more anatomical/physiological systems of the body, from which one would quickly come to appreciate the need to have a basic understanding of physics and chemistry, and to have the mathematical tools to apply these principles to a living system.

It is often claimed that such an approach is unworkable because students can't hope to obtain any sort of understanding of something as complex as a physiological system without a background in calculus, differential equations, and matrix algebra. However, it should be kept in mind that these are just artifacts—tools—created by man in an attempt to make analysis of certain classes of natural events more amenable to solution. In principle, with the power of modern day desktop computers, by solving difference equations directly rather than by limiting oneself to those subset of problems for which closed form solutions using calculus are possible, the student can obtain a more intuitive insight into the process being modeled and is free to look at a broader range of more interesting, non linear problems. It is the latter, of course, that makes the study of living processes in general, and bioengineering in particular, such an interesting challenge. Similarly,

once one starts studying living processes, it quickly becomes apparent that knowledge of organic chemistry, thermodynamics, properties of materials and mechanics is essential to understanding what is going on.

This approach also has the advantage of mimicking how science itself has developed. It is not the development of analytical tools that drives scientific exploration. Rather, it is the challenge of understanding complex, existing natural phenomena that leads to the development and application of mathematical and physical tools to scientific endeavors. By presenting students early on with a "real life," relevant, practical problem to be solved over the course of their undergraduate careers, we expect them to be better motivated not only to take the basic course work in math, physics and chemistry, but to actually learn the material well (as distinct from simply getting high grades in the courses) since they will have a better appreciation of how it can help them achieve a goal of real interest to them.

This approach and argument is applicable to engineering education in general (4). The National Academy of Engineering and the National Research Council's report "Engineering Education in Practice in the United States" (5) has argued for very significant changes in undergraduate engineering education, including a project-based emphasis. Although many schools do indeed include project-based education in their undergraduate curricula, there are very few which utilize the four year integrated project approach as we propose here.

C. Value Added by the ERC

Please refer to sections D (Strategic Plan) and E (Deliverables).

D. Strategic Plan

Overview

The key components and projects are presented in Figure 1, already given in the Project Summary.

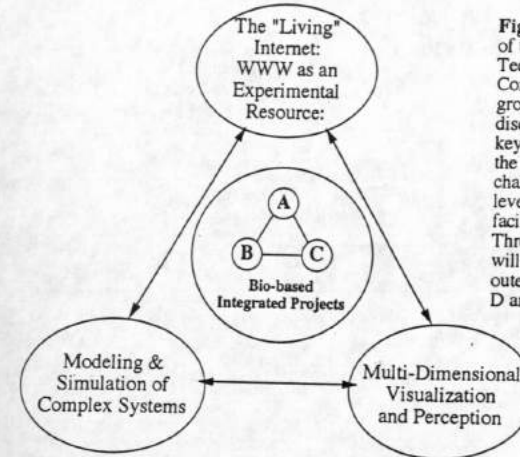


Figure 1. Key components & projects of the ERC in Bioengineering Education Technology: Simplicity <-> Complexity --> "Simplicity. The small group bio-based integrated projects, discussed in Sections D and F, are the key integrating and motivational parts of the program. Dealing with such challenging projects at the undergraduate level requires a set of skills and tools to facilitate learning, analysis, and design. Three key research thrusts of the project will such tools, represented in the three outer ellipses and described in Sections D and F.

Thrust 1: Bio-Based Integrated Projects: The Core of the Curriculum (K. Horch and D. Christensen)

The students we attract will have strong interests in significant societal problems. They will also have strong interests in the physical sciences, the life sciences, and in engineering/technology.

The undergraduate bioengineering program utilizes a set of complex, open-ended, integrating projects and teams. Figure 2 presents the pedagogic rationale for the integrated four year bio-based, complex project as the key component of this new curriculum. Time is represented vertically. Much of the first semester will be devoted to the development of the big picture, a comprehensive integrated view or perspective of the various projects (the base of the cone in Figure 2). The students will then be assembled into their respective teams based in large part on their interests and aptitude. They will then simplify the project, applying the traditional reductionist approach. The shaded area at the base of the cone (Figure 2) represents their accumulating academic and engineering knowledge. As time proceeds that knowledge increases, but project needs will define and demand additional knowledge and tools. Those tools and knowledge will be acquired via traditional courses, as well as by special project short courses, laboratories, and self-study. The information and skills will be applied to the project, whose growing complexity will then demand additional knowledge and tools, and the cycle will continue. At the conclusion of the four years, the student will have a broad and yet deep knowledge in most relevant fields, together with an unusually rich and comprehensive tool and skill set. Perhaps most importantly, the students will have the interest and confidence to deal with complex problems and projects.

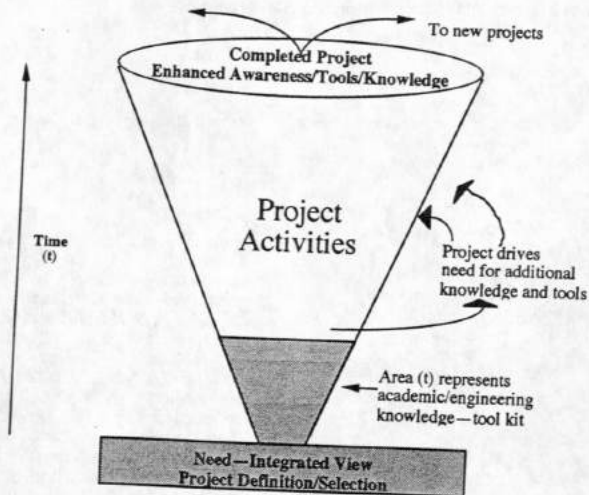


Figure 2. The integrating project as a driver/motivator for education (see text for complete description). Refer also to Figure 3.

Figure 3 shows the approximate credit distribution between traditional courses and project-based activities.

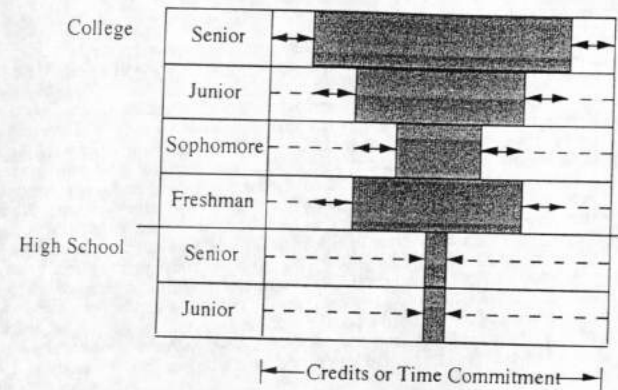


Figure 3. Schematic of the general structure of the curriculum. The central shaded zones represent project activities—research, design, assembly, testing, and analysis. Time and effort in courses and related traditional means of instruction and learning are indicated to the left and right of the central project zone. The arrows simply denote that the courses will connect and relate to the central projects, and vice versa. Many topics included in traditional bioengineering undergraduate curricula are integrated and contained within the project zone, as project activities also involve lecture/simulation/demonstration components. Over half of a student's credits and time over his/her four year programs are in project-based activities.

Complex projects require the learning and appreciation of traditional engineering and scientific knowledge. But they also require new or non-traditional tools, so the students, faculty, and staff can effectively deal with the complexity of these problems. The development of such tools is the objective of the other research thrusts.

The projects developed and conducted to meet this range of interests and motivations must be challenging and relevant but doable. We prefer that they be bio-based, that is have a biological basis to help facilitate the learning of biology. A key challenge is how to select projects which are complex, challenging, relevant and novel and which can provide the connections needed to meet our educational objectives. These projects must also be of interest to our faculty, to visiting faculty from participating institutions, and to our graduate students, as they are all key components of each project team. In subsequent years of the program, we expect projects to be suggested by the students themselves. We will actively solicit project suggestions through the community, possibly from contests or competitions.

We will formulate three such projects per year. From year five on, at steady state, twelve project groups will be working in parallel. Although, there will be considerable synergism and interaction among these projects, they are indeed distinct, consisting of a team of five undergraduate students and of the order of five faculty, graduate students, technical staff, and key advisors (Figure 4). This means about 100 individuals actively involved in the steady state phase of the program.

A preliminary matrix of projects is given in Table 1. Projects A, B, and C listed for Class 1 (2000-2004) could be considered somewhat traditional, albeit exceptionally challenging. One could think of the A Project List as representing sensory and neurophysiology interests and activities. The Project B list represents chemistry and biochemistry, together with tissue

engineering and biohybrid devices. The Project C list tends to reflect a biomechanics emphasis. Our faculty has interests and activity in all twelve of these topics. We will briefly describe our approaches to Projects A, B, and C in Section F.

Each project team will develop multiple approaches to each of their long range goals. For example, the project on vision could involve a very strong bio-based and even tissue engineered component, as well as a more traditional photonic device, electro-optical instrumentation approach. The same could be said for the biomimetic liver: one can consider a substitute approach (transplantation), a purely chemical or biochemical engineering approach, and a tissue engineering or biohybrid approach. Although the faculty on the project teams will have their own ideas, each student team will evolve and develop its own relevant approaches to the challenge.

We will begin the project-based class in Fall of 2000 (see time line in section D). We are assuming NSF funding begins in April 1999. That gives us one year to recruit and hire appropriate staff, visiting faculty, and others, and to work closely with our team of advisors and participating institutions to fully formulate and organize the program. It also gives us a year to remodel and equip the needed project-based laboratory space.

Our mission is to provide an environment which will enable the students to address complex problems from both biological and engineering perspectives, and to enjoy and almost literally level in the complexity itself.

Table 1. Bio-Based Integrated Projects for SCS ERC Program (tentative).

Class/Dates	Projects (Tentative)		
	A	B	C
Class 1 (2000-2004)	Neuromimetic Systems: Vision	Engineering Bioenergetics	Cardiomimetic System
Class 2 (2001-2005)	Biomimetic Hearing	Biomimetic Liver	Biomimetic Knees
Class 3 (2002-2006)	Bioelectric Fields	Bio-batteries	Biomimetic Hip
Class 4 (2003-2007)	Biomimetic Touch	Bio-photon Devices	Biomimetic Lungs

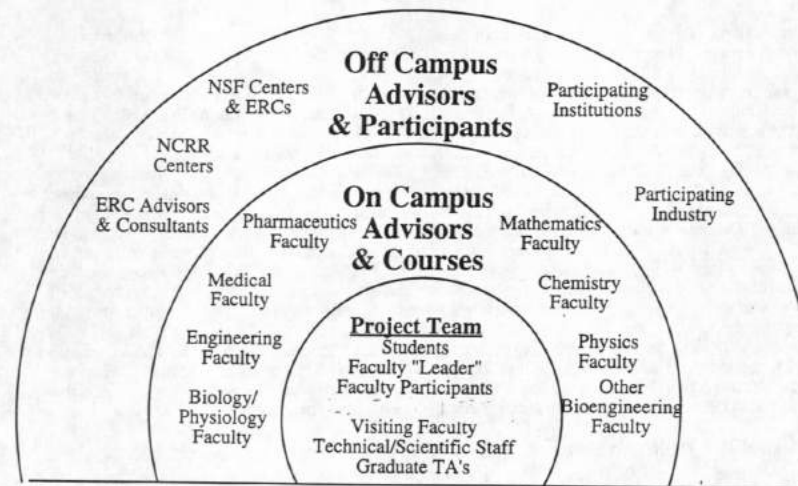


Figure 4. Typical project teams and resources. The central circle represents the Project Team, which includes the 5 to 8 undergraduate students and their faculty advisor. One or two additional bioengineering faculty and one to three faculty from other relevant departments will also be part of the team (they will be partially compensated from grant funds). Visiting faculty will also be team participants. Other paid team members and resources include technical staff and 1-3 graduate TAs.

Thrust 2: The "Living" Internet—The Web as an Experimental Tool (R. Rabbitt and K. Horch)

Large scale communication networks may be among the most complex man-made systems in the world. The multi-layered systems designed to control and manage information flow span multiple abstraction levels from physical signals and switching to service and business management software. Interestingly, the traffic and signaling in packet networks such as the internet show emergent, collective phenomena, including fractal network traffic patterns, that are not seen in single network elements. We see here very strong parallels to biological systems where interacting components, each of which operates on the basis of its own set of rules, give rise to emergent behavior and ultimately to behavior of the organism itself (2). Parallelism and redundancy are key components necessary for emergent behavior and for the ability to invoke self repair in the event of injury.

We will use the internet to study, learn and teach about biological systems. Our use of the internet will include powerful tools for information exchange.

We further propose to use the computer network itself as a physical model for biological signaling and communication, and to use individual computer nodes and their human operators as self-motivated biological components.

Student-faculty teams will work together using interactive software to study the behavior of biological systems via the collective basis of molecular, cellular, tissue, organ, systemic and organism level phenomena. These levels are not independent, but rather define a hierarchy of interactions that can usually only be understood by invoking higher and higher degrees of

abstraction. Intracellular molecular cascades, for example, can be viewed on an individual component level and simulated as kinetic reactions taking place on individual computer nodes with time delayed signaling to related events taking place on other nodes. The inter-node communication implemented in this way is interesting in its ability to reproduce stochastic behavior on a local scale (molecular level diffusion and signaling), blurring on an intermediate scale (Fickian diffusion), and cumulative or distance related delays on a large scale. Beyond the molecular level, internet node-based activities can represent the macroscopic behavior of cells.

The internet is being applied to education at all levels. It has already revolutionized the exchange of data and information and the enhancements of collaborations and interactions in the research community. It has also been enthusiastically adopted by the elementary, junior high, and high school community, including national and even international projects (20, 21), such as the globe weather data gathering project sponsored by the National Oceanic and Atmospheric Administration, NSF, and NASA (www.globe.gov). The World Wide Web has also been applied as a distributed computing resource, allowing interested parties to participate in computational projects which otherwise would require relatively inaccessible super computer capabilities.

We will utilize the web for similar activities and projects, as well as for information dissemination and information acquisition. We will develop a practical and comprehensive web site for the project, for our own acquisition of information and advice as well as for dissemination of project deliverables and for the recruitment of students and participants.

Thrust 3: Multi-dimensional Visualization (S. Kern and K. Horch)

One of the difficulties in dealing with large, complex, non-linear interacting systems is obtaining a clear understanding of how such a system responds to different inputs and evolves over time, particularly in response to changes in its operating characteristics. Ideally one would like a method of visualizing the system that would work equally well on both a large (macroscopic) and small (microscopic) scale. The nature of the systems to be developed in the proposed projects are such that a mathematical description of the system, or even of significant subsets of it, would be sufficiently complex to preclude such an intuitive or conceptual understanding on the part of the students (or faculty).

Graphical representation and visualization of the system inputs, the states of its nodes (interacting components), and its outputs would seem to be the answer. However, each such parameter would represent a single dimension of such a representation, so a method of visualizing large multi-dimensional (such as hundreds) structures is needed (22). To do so, we propose to use a variation of a technique developed by a local company (nDV, LLC) founded by Robert Johnson, former chairman of the Department of Computer Science (see letter in Appendix A).

nDV has developed several new intellectual structures which provide n-dimensional graphical viewing to aid in understanding of structure and relationships in arbitrarily many dimensions. The techniques are visually intuitive and mathematically tractable.

nDV's version of Parallel Coordinate representation generates multi-dimensional display space images that look like overviews of mountainous terrain. As the system changes (for instance, in response to a new input), the terrain changes, and the evolution and propagation of this change is easily visualized at whatever scale the user desires.

We will also work with Dr. Dwayne Westenskow, Professor of Bioengineering and Anesthesiology, who is principal investigator on a project with Dr. Julio Bermudez from the School of Architecture. They are applying basic principles of 2D and 3D design (e.g., scale, shape, color, unity, etc.) and sound to produce "an interactive multi-sensory information system" that will allow us to more readily see and follow critical events in the functioning of the systems they have developed. The Bermudez/Westenskow approaches can (and will) be combined with nDV's parallel coordinates technology to further develop and enhance multi-parameter and hierarchical visualization.

Our institution has always been involved in computer graphics, scientific visualization, and computer art, beginning with the pioneering work of David Evans and Ivan Sutherland in the early

1960s. The Department of Computer Science is generally well recognized as a leader in computer graphics and in its application to scientific and engineering problems. We participate in a major NSF science and technology center titled the Graphics and Visualization Center, directed by R.F. Riesenfeld and E. Cohen (www.cs.utah.edu/projects). That Center includes a Scientific Computing and Imaging Group. Drs. Chris R. Johnson and Robert S. MacLeod are Bioengineering faculty involved in the Center, specifically in modeling and visualizing cardiac bioelectric potentials (29, 30, 34, 35). In addition, the new Center for the Simulation of Accidental Fires and Explosions (C-SAFE), funded primarily by the Department of Energy and directed by David Pershing, Dean of the College of Engineering, has major activities related to scientific visualization and multi-parameter, multi-dimensional data presentation (www.csafe.utah.edu).

We are well aware of the potential of the graphic arts, music, and even the performing arts in the analysis and presentation of scientific and engineering data and problems. Indeed, the Bermudez/Westenskow collaboration falls into this category. We have even integrated science, technology, and art into a unique liberal education science course for non-science majors (31). Through collaboration with our colleagues in the Graphics and Visualization Center and in C-SAFE, we are well aware of the rapid progress being made in enhancing scientific and engineering visualization of complex systems (32).

Thrust 4: Modeling and Simulation of Complex Systems (J. Wiskin and R. MacLeod)

"Formulation of such a mathematical model forces the modeler to identify explicitly the key components, the key reactions, the key interactions, and also to describe their quantitative interconnections. This exercise in systematic organization of assumptions and key features of the metabolic subsystem of interest can be a critically important contribution of the modeling effort to the intuition and insight of the researcher, almost independent of the consequences of the modeling calculations. The modeling exercise enforces a high level of intellectual rigor, careful study of prior work on the system, and systematic thought about its most important features."

J.E. Bailey (38)

Modeling and Simulation are well known to bioengineering (16, 33). Indeed, bioengineers have made many advances and contributions in these areas. The various NIH-NCRR Simulation Resources (33) and other groups and labs have made very significant and important contributions, some of which are now being called mathematical biology (11-19). There is a growing interest in applying some of these methods and techniques in general undergraduate biology as well as in molecular and cellular biology (17, 18). We are fortunate that such programs and interests have evolved in our own Mathematics and Biology departments in recent years, including collaborative activities. This growing theoretical biology emphasis at our institution, coupled with Bioengineering's interest in the application of engineering modeling and simulation in our undergraduate and graduate curricula, makes this Thrust area timely and important.

The Departments of Computer Science, Chemical Engineering, Mathematics, and others are involved in major modeling and simulation activities. C-SAFE, described briefly in the previous section, is primarily a modeling and simulation activity. We will certainly collaborate closely with C-SAFE and apply their tools, interests, and expertise to bioengineering problems and opportunities. C-SAFE makes extensive use of the University's Center for High Performance Computing, as do Drs. Johnson and MacLeod for their studies on the modeling and visualization of bioelectric potentials for electrocardiology applications. In addition, the Graphics and Visualization Center, referred to briefly in the previous section, has as a major activity Computational Medicine, again represented primarily by the work of C.R. Johnson and R.S. MacLeod (29, 30, 34, 35).

The Departments of Pharmaceutics and other components in the College of Pharmacy are developing programs and interests in pharmacokinetics and pharmacodynamics. We also have a

significant medical informatics activity in both the Computer Science and Medical Informatics Departments applied to molecular biology and human genome problems.

There has been a recent explosion of books dedicated to theoretical biology and its relationship to mathematics (11-15). It behooves the bioengineering community to continue to take advantage of, and to continue to contribute to, these abundant resources, and to use them to develop a balanced curriculum.

The students will be exposed to a succinct and accurate summary of the various analytic tools available, including both modern and more traditional mathematics. He/she will then be able to assess which techniques would be most appropriate to his/her project and interests. These will then be explored and developed in more detail.

Emergent order in complex systems is one unifying theme. Our approach to this paradigm is reflected in our motto and subtitle: Simplicity <--> Complexity ---> "Simplicity". This phrase is relevant not only to the actual operation of complex systems, but also to our appreciation and understanding of these systems.

The ECG is a good example, in which medical practice has been based on an almost empirical linking of disease state and signal features. A more appropriate and in the end much more powerful approach is to apply reductionist methods to deconstruct the ECG into component features (cardiac cells, coupled systems, volume conductors) and study the relevant behavior and features. The subsequent synthesis can then allow us not only to understand the features of the system we once observed empirically, but to see new things in those feature sets, and thereby improve both fundamental understanding and medical practice. Again from the ECG example, this has to some extent occurred in that we now can interpret, at least partially, the ECG in terms of fundamental sources and thus interpret more subtle features and pathologies. Examples of that include at least some ability to localize sites of myocardial infarction or initiating events in some cardiac rhythm disturbances. So the ability of the SCS approach is to both improve our understanding of high level data we already collect and use, as well as make these data effectively richer in content and value.

The purpose of simplified models is not to attempt to explain everything, but rather to isolate or 'abstract' those particular elements of the process being modeled that are relevant to the understanding of a particular behavior exhibited by the system (2, 17, 18).

Nonlinear systems are prevalent in biology and thus in bioengineering. Such systems exhibit hysteresis, catastrophes, bifurcations, chaos, resonance, fractal dimension, entrainment, self-sustained oscillations, and quasi-periodicity. All are important in understanding, controlling, modifying, and engineering biologically based systems.

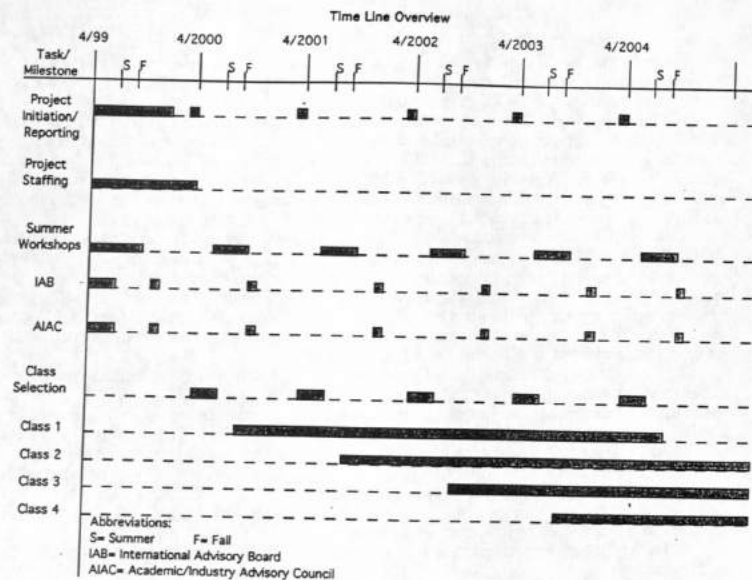
An overview Time Line for the ERC's first five years is given on the next page. We will rapidly implement the Executive Committee and the Bioengineering Summer in Utah Advisory Committee to begin organizing the high school summer program. The technical and administrative staff will be hired and on site shortly after funding is available. As soon as we know there is a high probability of receiving the award, we will initiate a search for those individuals, so that commitments can be made shortly after startup.

The Time Line shows the schedule for class selection and the class start/finish dates for the first five years of the ERC.

We will also meet via phone and E-mail with both the IAB and the AIAC to obtain their collective inputs early in the project. Their first joint meeting will be in Fall, 1999, to review the first summer program and to review our plans for the projects, courses, and research projects.

E. Deliverables

Our initial deliverable will be a set of projects for the first class of students, as well as a set of smaller projects to be used in the high school summer workshops. The four year integrated curriculum projects will be developed during the first 14-15 months of the grant and will be applied with the first class in the Fall of 2000. Other deliverables will include: a means of organizing, staffing, and conducting such a complex integrated project and means to efficiently provide needed resources and analytical tools. The deliverables will also include a set of special courses designed



to optimally interact with and support the integrated projects. One course is Measurement and Medicine, an introduction to quantitative biology, physiology, medicine, and pathology, and will provide the students with a comprehensive perspective of living systems, the basic principles and concepts of biology, and the challenge of parameterizing and quantitating biology, pathology, and medicine. The first semester of this course will focus largely on normalcy, i.e. normal biology and physiology, whereas the second semester will focus on abnormality, i.e. pathology and medicine. This course has been in the conceptual design stage for the last year as a joint project of Professors Andrade, Horch, and Kern. Its development will be a major effort of the first year of the project.

Professors Rabbitt and Christensen are developing a new freshman bioengineering course for our new (1999) undergraduate curriculum. Their freshman sequence in undergraduate bioengineering applies fundamental laws of physics and chemistry to the analysis of biological systems and to the design of biomedical devices. Diffusion and molecular transport, electrochemical gradients, heat and mass transport, and related topics are used to explain some of the basic principles of cellular, organ, and systemic physiology. The same tools are also applied to the design of biomedical devices such as the artificial kidney and neuroprosthetic devices. The course consists of three lectures and one laboratory session each week. Lectures are unified around the theme of flux laws and conservation laws with motivation and applications derived from biology and biomedical engineering. Freshman calculus will be taken concurrently. This course will also be taken by the students in this project-based program.

Other specialized courses and short courses will evolve and develop during the conduct of the projects themselves (see Section F). These will also be "deliverables" and will be available on the web site for access by the larger community.

The web site itself is also a "deliverable" in that information on the design, organization, utilization, and general evolution of the web site will be available for those interested in developing and constructing other such sites. We will work closely with the Center for Advanced Instructional Media at Yale University (Carl Jaffe, Director) in the design and development of such a site as well as its use for the assessment of our projects, courses, and general project activities by the larger community (see Section I, Assessment and letter in Appendix A).

We will develop a set of tools in a range of areas, utilizing existing experience, technology, and analytical tools as much as possible. This will include a methodology for the analysis, reduction, and simplification of complex biological and bio-based systems, what we might call reductionist tools. Much of this is already in place in the literature on theoretical biology and on modeling and system simplification (11). These tools will evolve from our project experiences, as the first year of each project will be devoted to simplifying it into a set of basic components which can be modeled, simulated, constructed, tested, and evaluated.

We will also develop a set of synthesis tools, again using the existing literature and experience, but deriving from our particular experience in the projects. These will begin to evolve in the second year of the class projects, as the teams take the components of their complex system and begin to assemble them into subsystems, the synthesis approach. The means by which these subsystems are mentally assembled and modeled, the construction of operating subsystems, and their analysis and assessment will all be part of the synthesis tool kit. We will develop means to view the assembled subsystem and overall complex system in a hierarchical manner, i.e. from different perspectives, with the eventual goal of obtaining the new "simplicity" derived from the hierarchical analysis of this now complex system.

Each of the major research thrusts in the program will also develop a tool kit specific to that thrust area:

The "Living" Internet as an Experimental Tool
Multi-dimensional Visualization
Modeling and Simulation

We will of course integrate the kits. Two biology-based "tools" are of particular interest. There are two key biological concepts which are largely unknown to practically all engineers and indeed to practically all non-biologists. One is Darwinian evolution, which one might simplistically view as survival weighted combinatorial science and engineering. The second such area is embryology and development—the means by which incredibly complex organisms can result from essentially a long string of linear information (53). These two basic biological concepts have rarely been treated as such in bioengineering education. Appropriate understanding of such basic concepts are likely to dramatically change how we approach many bioengineering problems and opportunities.

The Department's goal is to produce a unique undergraduate bioengineering experience which also challenges and enhances the graduate program. We want to produce student, faculty, and other participants who are comfortable with complex bioengineering-based problems, but in addition have the communication and leadership skills, and the community and societal interests, to select important and relevant problems and to help garner the resources to permit such problems to be successfully addressed. Although we do not anticipate a very large undergraduate or even graduate program, we do anticipate that those people products from our programs will effectively disseminate the philosophy, activities, approach, and tools.

This project is entirely consistent with the Department's long range goals. J. Andrade, the PI, is Co-Chair of the Department. K. Horch, who leads two of the key thrust areas, is also Co-Chair of the Department of Bioengineering. The development and implementation of our new undergraduate program was encouraged, even pushed, by our then Dean of Engineering, David Pershing, now the Executive Vice President of the University of Utah. Our new President, Bernie Machen, is deeply committed to the enhancement of interdisciplinary education and research. He is also deeply committed to significant enhancement and improvement of undergraduate education at

the University of Utah. Our Vice President for Research, Dr. Richard Koehn, is himself a bioengineer, having directed a major biotechnology center at the State University of New York prior to his appointment as VP for Research six years ago. There is strong commitment at all levels for this program.

The bioengineering community has grown and developed dramatically in recent years. There are many more departments and programs, in large part fueled by the Whitaker Foundation's Special Opportunity and Departmental Development Awards. There has also been a considerable development and expansion in what is called Biomathematics and Quantitative Biology. Indeed, we feel that Gilbert Chauvet's three volume treatise, *Theoretical Systems in Biology* (11), together with the other works previously cited (12-19), will launch new directions and approaches in both biology and medicine. This may be helped the Whitaker Foundation's Teaching Materials Program, which is striving to induce the community to provide an integrated, quantitative, engineering approach to basic biology to aid the education of the next generation of bioengineers.

We feel that the bioengineering community, the biology and mathematics communities, and even the medicine and clinical communities are ready for, indeed anxious for, the programs, courses, projects, and tools which we propose to develop and evolve. Although effort is required to disseminate the materials and to inform and involve the community at large, we feel this will be the easiest part of the project, as the community is eagerly receptive to such activities and developments (36, 37).

F. Research Program

Thrust 1: Bio-Based Integrated Projects

"It is not the answer that enlightens but the question."
Eugene Ionesco (65)

"Students respond enthusiastically to their first taste of science or engineering in a research or design project. Their book learning suddenly comes to life, and they discover talents they never realized they had. Scientists known only as remote instructors often become mentors, colleagues, or even friends." (58)

Integrated bio-based projects are the key to our approach to bioengineering education and to the application and development of technologies for the enhancement of bioengineering education. The projects have been discussed in earlier sections. Table 2 summarizes key criteria for the selection and development of the projects.

Table 2. Project Characteristics and Needs (see also Figures 2-4)

Complexity:	Must be sufficiently complex to require hierarchical and complexity analyses and to exhibit non-linear, emergent properties.
Reductionable:	Must be reducible to a set of subsystems and a larger set of primitives or components, many of which can be easily analyzed, constructed, and tested.
Synthesizable:	Primitives or components can be combined and assembled into systems which begin to exhibit complexity.
Bio-based:	Must involve sufficient biological knowledge and concepts to serve as a means of learning biology and doing "bio-based" engineering.
Practical:	Must be applicable to one or more areas of medicine, industry, or to other societal needs or problems.
Relevant:	Must be of interest to project team and thus serve as a pedagogical tool for motivation and involvement.
Intellectual Resources:	In house, on campus, and more extended intellectual resources (Figure 3) must be available.
Material Resources:	Must not require overly expensive tools, materials, equipment, or specialized, expensive services.
Safety:	Must not involve any unreasonable or inappropriate risk or hazard to those involved.

Although the make up of a typical project team was illustrated briefly in Figure 3, Table 3 provides more complete information.

Although our institution and College has considerable undergraduate project experience, most of it is for limited or short term projects. An Engineering Clinic, directed by Electrical Engineering Professor M. Iskander and sponsored by industry, utilizes a set of short team-based projects and is effective. There is a senior design project requirement in the Department of Mechanical Engineering. The Department of Materials Science has a senior thesis project, essentially a capstone 12-18 month project. The only group on campus affiliated with engineering that has such extensive long range projects is the Center for Engineering Design (CED), originally the Center for Biomedical Design, founded and directed by Dr. Stephen Jacobsen in Mechanical Engineering and Bioengineering. But CED's objectives are somewhat different. The students are involved in projects for various research and development sponsors, and, although in many cases students were involved for multiple year periods, they were generally hired to provide services on a sponsored project. Although these projects did often tie to course work and involved laboratory/project based credits, they again served a different overall need. Dr. Jacobson is our most experienced faculty member when it comes to engineering projects related to those we are proposing to develop and implement. He has agreed to serve on our advisory board and will play an important role during the first several years of the program in helping to assess and evaluate our project development and implementation activities (Appendix A).

Table 3. A Typical Project Team

Students (5-8)	Selected from the project-based entering class after about 3 months of exposure to all projects. Team assignment based on interest, motivation, background, and project balance. Each team will select a team chairperson, organize into subteams and tasks, and work with faculty to select and involve other team members.
Faculty Advisors (3-4)	A faculty resource team will initially design and develop the project prior to presentation to the class and prior to the selection and formulation of the student team. Faculty will have expertise and interests in the project topic and will generally commit to the project for the entire 4 years. One faculty member will serve as key or principle advisor to the team. This position may rotate among the faculty team each year. The principle faculty advisor will likely spend ~ 10 hours/week/team. Other faculty will each spend 5-10 hours per week per team. They will be compensated for this work.
Visiting Faculty (0-1)	Visiting faculty are budgeted and will give lectures, short courses, and be directly involved with the teams. Visiting periods range from 1 day to one semester. There should be 2-7 visiting faculty per year, depending on resources. These faculty will also be available via the Internet and by telephone.
Graduate TAs (1-2)	Graduate TAs will be second or subsequent year graduate students working in an allied area. They will spend up to 10 hours/week/team and be compensated for their services. They will be evaluated by the undergraduate team members and retained or released based on their usefulness to the project.
Technical Staff (1-2)	Technical staff will be hired by the ERC specifically to assist with the projects. We expect 1-2 design/prototype engineers, 1-2 biologists, and 1-2 physicists-chemists, and 1 mathematician. These will be "allocated" to the 3-12 projects based on need and time available. These will be MS/ME level individuals, generally with substantial industrial and/or lab expertise. One staff person with both administrative and technical skills and interests will manage and "run" the special projects laboratory and stock room.
Others (0-1)	Retired and other individuals with appropriate experience will be recruited as volunteers. Visitors from industry will also be involved.
Total (~ 10-15)	

Dr. Robert Romer, Chairman of the Department of Mechanical Engineering (ME) and Coordinator of ME's senior design activities will also serve as a key project advisor, as will a number of our industrial representatives and participating institution representatives, particularly Dr. B. Onaral, Chairman of the Bioengineering Program at Drexel University, because of Drexel's strong commitment to project-based undergraduate education in their College of Engineering (Appendix A).

Project A: Neuromimetic Systems: Vision (R. Rabbitt, Faculty Advisor)

"Although human genius through various inventions makes instruments corresponding to the same ends, it will never discover an invention more beautiful nor more ready nor more economical than nature because in her inventions nothing is lacking and nothing is superfluous."

Leonardo da Vinci

INTRODUCTION

Across the animal kingdom one can identify common design principles that appear to be fundamental and perhaps salient to the success of all life on earth. On a low level nature routinely employs elemental redundancy, self organization and self assembly. And on a higher level sensory fusion, hierarchical control, and adaptive plasticity are common if not universal themes. The potential for application of these basic principles to solve engineering problems is immense. It is this promise that underlies recent trends towards biobased and biomimetic systems.

One of many elegant biological designs is the human visual system. The foveal region of the human retina spans only 4% of the retinal surface area yet it contains a majority of the sensory cells (about 7×10^6 cones and 100×10^6 rods). Since resolution of the peripheral region of the retina is greatly reduced relative to the fovea, we articulate our eyes within their orbits to focus visual targets on the high-resolution foveal region. This multi-resolution design strategy greatly increases the acuity of selected regions of the visual scene without the massive increase in information content that would come with spatially homogeneous sensors, such as standard rectangular CCD arrays. Machine vision would benefit from application of this biological approach. To engineer such an apparatus it is necessary to have in place systems to accurately control the motion of the articulated visual sensors -- one that can accommodate head motion, target motion, unexpected changes in the environment, and/or system degradation. The human ocular control system achieves exactly this. This system exhibits motor learning, draws from a multiplicity of sensors (vestibular, ocular, somatosensory), activates a multiplicity of actuators (extraocular muscles, neck muscles, autonomic system), employs a hierarchical control strategy (peripheral, brain stem, cerebellum, cortex), and invokes multiple feedback loops between each of these subsystems (central and efferent).

OBJECTIVE

Our primary objective is learn how the visual system achieves its remarkable multi-resolution acuity and to express these same design strategies in a biomimetic machine vision system. To accomplish this goal we must study the biological system and develop a quantitative understanding of the biological sensors, actuators and control systems involved. The engineering challenge is to identify/design devices to mimic the salient function of each biological component and to implement a control system capable of accommodating system degradation and/or changes in the environment in a manner which mimics biology. Your goal as a student is to develop the skills necessary to meet this challenge and, ultimately, to construct a functional biomimetic vision system. This challenge has been framed as a series of laboratory projects outlined below.

LABORATORY PROJECTS

Freshman Year

Psychophysics of vision.

Perception of intensity, color and spatial resolution.

Compare visual performance to CCDs and vacuum tubes.

Optical illusions.

Optics.

Geometrical optics. Huygens' principle and refraction. Fermat's principle.

Camera optics. Role of the aperture and shutter.

Optics of the eye. Cornea, lens and pupil.

Glasses and contact lenses. Cornea transplants, lens implants.
Microscope optics. Polarization. Differential interference contrast microscopy.
Computer analysis of optical systems.

Anatomy of the eye.

Dissection. Microsurgical techniques.

Ocular kinematics and ocular muscles.

Histological techniques.

Microscopic study of retina, optic nerve, ocular muscle, cornea and lens.

Comparison of the eye to video camera design

Electronic retina

CCDs. Intensified. Integrating.

The VLSI retina.

Spatial sampling and the Nyquist frequency.

Computer-aided design of a multi-resolution biomimetic eye.

Fabrication and testing of a biomimetic eye.

Sophomore Year

Photochemistry of vision.

Ultrastructure of rods and cones.

The chromophore and the visual cycle.

Rhodopsin breakdown to retinal and opsin.

G-protein disfacilitation of Na^+ channels and neuronal generator potentials.

Chromophore wet lab.

The ocular plant

Statics and dynamics of eye movements.

Muscle mechanics.

Actin-myosin motors.

Measurement of force-velocity relationship in skeletal muscle.

Actuators.

Hydraulic and pneumatic systems.

Compare dynamics to muscle.

Electric motors. DC, servo, stepper motors.

Open-loop control of actuators.

Biomimetic ocular plant

Computer aided design of articulated ocular plant (eyeball)

Modeling and simulation.

Iterate design.

Fabrication.

Open-loop testing.

Junior Year

Sensors

Muscle spindles. Physiology, resolution and coding.

LVDTs, digital encoders, and other position sensors.

Vestibular system. Physiology, resolution, coding, and models.

Gravito-inertial sensors. Accelerometers, tilt sensors and velocity sensors.

Build a biomimetic angular velocity sensor.

Feedback control.

Physiology of the vestibulo-ocular control system - slow phase and saccadic systems.

System modeling. Incorporation of controller in the system model.

Design a biomimetic ocular feedback control system.

Build a system to control angular position of a biomimetic ocular plant.

Optical flow

Visual feedback and the accessory optic system.

Optical flow computations and the retina.
Computational optical flow algorithms.
Hard-wired optical flow sensors.
Construct an optical flow sensor.

Neuronal computations

Visual processing of form, color and motion.
Neurons and the computational brain.
Central pattern generators and small networks.
Program a large-scale associative neural network for pattern recognition.

Senior Year

Neuromimetic control

Feedback control and neural reflex systems.
Redundant pathways.
Sensory fusion.
Motor learning in neural systems.
Experiments to modify vestibular-ocular interactions with magnifying/minifying goggles.

Senior project

Build a biomimetic vision system with the following features:

- multi-resolution "foveal" optical sensor,
- articulation system to allow for target tracking, movement compensation and saccades,
- optical flow and gravito-inertial sensors for feedback control,
- neuromimetic feedback control to maintain targets on the foveal sensor and
- video display of captured images.

SUMMARY

Robotic implementation of an articulated biomimetic vision system has never been attempted before. Your work will have important applications in areas such as machine vision, biorobotics and tele-robotic man-machine interactions. Present machine vision technologies do not stabilize images in the presence of sensor motion, are poor at target tracking, do not have multi-resolution acuity and fall short of providing the appropriate man-machine interface for haptic or tele-robotic applications. Your biomimetic vision system will speak directly to these engineering challenges.

Project B: Engineering Bioenergetics (J. Andrade, Faculty Advisor)

"If you want a quantitative answer, you must ask a quantitative question."

H. Kacser (49)

INTRODUCTION

Our chemical and biochemical genealogy go back nearly four billion years to the most primitive life forms. These ancient anaerobic reactions likely constitute the oldest part of our personal biochemistry. Much, much later, after the evolution of photosynthesis dramatically changed the environment, an aerobic bioenergetics evolved, leading to highly efficient means to fuel and power life. We are among the beneficiaries of that four billion year old combinatorial, chemical genealogy. Our personal biochemistries, albeit complex, are very similar, but not identical. We are biochemical individuals (52), just as we are unique in features and character.

We wish to understand our personal biochemical individualities. We must be able to measure it. We often need to modify it, due to abnormalities or perturbations which are undesirable (diabetes, phenylketonuria, liver disease, etc.). We may wish to engineer the biochemistry of an organism to enhance a particular biotechnological process. We may need to grow specific tissues under non- "natural" conditions (tissue engineering). We may want to

enhance our own physical performance (diet, nutrition, and conditioning). We may wish to perturb—to slow down—certain aspects of aging, related to changes in metabolism and thus to the need to optimize diet and nutrition.

We may also want to become inspired and stimulated by nature's bioenergetic processes, in order to synthesize chemicals and fuels from the air itself—from CO₂ (the dark side of photosynthesis), using only solar photons as energy (the light side). We want to engineer efficient energy storage and energy transformation devices (bio-batteries? fuel cells? "artificial" chloroplasts?).

Metabolism is a very complex interacting chemical network—a complex system. Much of metabolism and enzyme biochemistry is resolved and mapped, what Koshland calls "The Era of Pathway Identification" (49). By the early 1980s extensive work led to "the Era of Pathway Regulation." Koshland says we are now entering "The Era of Pathway Quantification." We now have tools such as metabolic control analysis (42-48). The complex biochemical network charts found in biochemistry textbooks are being modeled and analyzed. Their complexity, typical of complex systems, is yielding to a fuller understanding—to a new "simplicity".

OBJECTIVE

Our immediate (four year!) practical objective is to design and develop an artificial liver (50, 51). But a deeper objective is to be able to design, apply, and "build" biochemical processes and systems ranging from "simple" biosensors to "complex" livers. The simplicity and complexity of biochemistry are critical keys to the understanding of life itself.

LABORATORY PROJECTS (tentative)

Freshman Year

Laws of conservation and thermodynamics—Physics rules!
mass and energy balances
Chemical reaction principles—Chemistry builds!
equilibrium, activation energy, catalysts
Multiple and driven reactions—"Beating" entropy!
Evolving prokaryotes— "Simple" cell bioenergetics
Evolving eukaryotes— "Complex" cell bioenergetics
dinoflagellates, photosynthesis, respiration
Anatomy of bioenergetics
mitochondria, chloroplasts

Sophomore Year

Biomacromolecules—Good-bye to chemical "simplicity"!
Enzyme and reaction engineering
Modeling coupled reactions
Heterogeneity of biochemistry—Welcome to surface and interfacial chemistry!
More anatomy of bioenergetics
Biosensor design and development
Drug and nutrient delivery devices
Beyond dinoflagellates

Junior Year

Coupling of biochemical modules
Channeling
Bioelectronics—electron and proton fluxes
pH, potentials, and ion fluxes
Multiple enzyme reactions and cascades
Amino acid synthesis
Control and regulation

Liver cells, tissue, and structure
Extremophilia

Senior Year

Multichannel biosensors
Feedback controlled release and delivery
Protein design and engineering
Mammalian bioenergetics and obesity
Aging, nutrition, and sensors
Coupled bio-synthetic systems—biochemical engineering
Bio-batteries
Artificial liver

SUMMARY

It's been a long, busy, productive, motivating, and educational four years. We now have an understanding of and experience with the chemical bases of living systems. We know how to perturb, control, regulate, and engineer biochemistry. We have ideas for biochemistry-based devices and processes which are probably unique and highly creative. We are now project-based, hands on, chemically confident bioengineers. On to other problems and challenges!

Project C: Cardiomimetic System (very tentative) (G. Pantalos and S. Kern,
Faculty Advisor)

INTRODUCTION

Another elegant biologic design is the cardiovascular system. In its simplest representation, the heart is a pump responsible for fluid delivery within the body. However, unlike most pumps, it modulates its output based on upstream and downstream loading conditions, the presence of chemical agents within the fluid stream that alter the loading conditions and the pump function itself, and by direct signals created from neural pathways. These mechanical, chemical, and electrical inputs all serve to regulate power from the pump in unique ways. To mimic this system requires the ability to dynamically respond to multiple sensory inputs to adapt the rate, stroke volume, and force generated by the pump to meet the metabolic demands of the organism. Like the visual system, this system draws from a multiplicity of sensors, activates many actuators, employs hierarchical control and uses multiple feedback loops, some of short and some of long time constants, to achieve its means.

OBJECTIVE

The primary design objective of this project is to understand how the cardiovascular system achieves its dynamic range of function and how that range can be mimicked by an engineered system. The engineering challenge is to design a biomimetic system of cardiovascular function and compare and contrast your system with those developed as ventricular assist devices, artificial hearts, and coronary bypass machines.

Freshman Year

Functional Cardiovascular Control
blood flow through the cardiovascular system
segmentation of the heart
role of valves and flow control
bipump balance
fluid balance within the system, within regions

Structure and function of pumps
how does form serve function?
geometric relationships
law of laplace / pressure/force relationships
power laws related to function, size versus efficiency
cardiac work - pressure/volume loops
scaling and comparative anatomy: elephant heart vs hummingbird

Pressure flow relationships
bernoulli conditions
branching networks
resistance in tubes
fractal structures

Anatomical dissection
relative chamber thickness
mechanical properties of different regions
functional operating differences between valves

Mechanical circulation devices
comparison to assist devices/bypass machines
functional similarities and differences
in situ use of devices, how the plumbing is connected
building a mechanical analog

Sophomore Year

Physicochemistry of cardiac muscle contraction
measurement of force/velocity generation
cardiac action potential
sodium - potassium - calcium roles
muscle mechanics

Blood Rheology
properties of blood as a tissue
fluid mechanical properties
oxygen dissociation properties
protein binding, osmotic control, diffusional aspects

Actuators
hydraulic and pneumatic systems
comparative dynamics to muscle
motors - electric, dc, stepper motors
open loop control concepts

Vascular dynamics
resistance and compliance relationships, impedance matching
changes with age, pathology, development
pharmacologic changes. endogenous and exogenous
quantifying hemodynamics, measuring pressure and flow
pulsatile versus continuous flow

Cardiomimetic system
modeling and simulation
iterative design changes to using mechanical analog

computer aided design of pump
fabrication and initial functional testing

Junior Year

Ventricular energetics

conduction/convection/radiation principles
energy balance within the heart
thermoregulation in the body
functional thermodynamics

Cardiopulmonary interactions

diffusion principles
membrane physiology
elastic coupling between chest, lung, and heart
pressure/flow relationships in oxygenation and ventilation.
cardiac interactions

Sensors

pressure sensing and impact of cardiovascular muscle
flow sensing and impact on oxygen content
measurement of low concentration substrates
integrating a biomimetic control system

Feedback control

physiology of cardiovascular control
systolic versus diastolic function
endogenous substance impact on the cardiovascular system
designing control rules for multiple feedback sensors

Senior Year

Cardiomimetic control

understand the physiologic interrelationships between biomechanical, biochemical, and bioelectrical phenomenon that alter cardiovascular function in terms of pressure and flow.

Integrative project

build a cardiomimetic fluid delivery system that responds to changes in preload, afterload, oxygen and carbon dioxide concentrations and concentrations of specific endogenous analytes such as sympathetic amines.

SUMMARY

Development of a fully operative cardiomimetic system that responds to pressure, flow, and biochemical alterations in the fluid being delivered (blood) represents an extremely challenging project with implications in many areas outside of bioengineering. This concept AND comparison to artificial heart systems and temporary bypass devices will highlight the functionality of the cardiovascular system as a dynamic pump.

Thrusts 2-4: Common Aspects

The "research" in this application is defined differently from that in a normal NSF grant. This ERC application is focused on education. Our "research" here is to develop tools, methods, resources, and programs to enhance bioengineering education at both the undergraduate and graduate levels.

Thrusts 2-4 have common objectives and goals: to develop, apply, and continue to improve and enhance a set of "tools" which will aid students in the study and understanding of

complex subjects and systems—efficiently and effectively. We do not wish to reinvent "wheels" which already exist. Thus we will thoroughly and completely determine and assess the tools which already exist, many of which are developed and used by scientists and engineers in their research and for graduate education. We will test and evaluate these tools using the data sets, systems, and subjects appropriate to our complex, integrated, bio-based projects. The useful tools will be modified, improved, and enhanced as required.

Thrusts 2-4 are budgeted most heavily in Years 1 and 2, with the goal that by Year 3 the tools will be largely developed and will be applied by the students, faculty, and staff in the respective projects. Funding in Years 3-5 is to test and improve the tools. Our participating institutions will also be involved in tool development, testing, and evaluation, as will the industrial participants.

Key faculty involvement in the four research thrusts are summarized in Table 4.

Thrust 2: The Living Internet: The Web as an Experimental/Analytical Resource

We said in Section D that

"Student-faculty teams will work together using interactive software to study the behavior of biological systems via the collective basis of molecular, cellular, tissue, organ, systemic, and organism level phenomena."

This is easy to say and very hard to do. The exponential expansion of information technology both creates and demands an expansion of our knowledge of the nature of information. Information networks may be among the most complex and fastest growing man-made systems in human history. Interestingly, information networks and their use patterns are similar to biological systems. At a low level, traffic and signaling in packet networks such as the internet show emergent, collective phenomena, including fractal network traffic patterns, not seen in single network elements. Likewise, overall network behavior does not originate centrally nor is it centrally coordinated. It cannot be explained by technical details of infrastructure, hardware or software alone. Instead, these structures parallel biological phenomena, in that interacting self-autonomous components give rise to emergent behavior, spontaneous self-organization, and self-repair. Informational relationships become as important as physical and material ones in the network.

Tools traditionally used to study biological systems could be used to understand the behavior of informational structures, through all levels, from the single node hardware, the interfaces to the network, the network itself, and, ultimately, the different 'agents' using this system. Likewise, treating informational structures as expressions of biological phenomena could enhance the understanding and knowledge of biological systems.

In the context of this proposal, the internet will serve two purposes. First, it will provide the informational infrastructure serving the intra- and inter-project communication needs. Projects pursued by the student-faculty teams, while designed to be stand-alone, do revolve around a common theme of simulating biological systems. Ultimately, these different systems will be interconnected into a whole biological organism. This will necessitate communication between the project teams to exchange information about system-to-system interfaces, contexts of simulated biological behavior, data and signals generated from each individual system.

Initially, project members will communicate with each other and with members of other projects. As the projects mature, software and hardware interfaces will be developed, through which the modeled and simulated organ systems communicate. Additionally, the internet will be used in the lectures, outreach efforts, and administrative coordination aspects of the grant. Collaborations with other institutions on other campuses will be added to and become part of the informational structures growing around this grant.

Table 4. Key faculty involved in the four research thrusts.

Key Faculty	Thrust 1 Projects	Thrust 2 Living Internet	Thrust 3 Visualization	Thrust 4 Simulation
Andrade, J. biomaterials, biosensors, biochemistry	X		X	
Christensen, E. electrical eng. optics biosensors	X			
Frazier, B. instrumentation electrical eng.	X			
Hlady, V. physical chem. biomaterials	X	X		X
Horch, K. instrumentation neurophysiology	X	X	X	
Johnson, R. computer science mathematics			X	
Kern, S. anesthesiology instrumentation	X	X	X	X
MacLeod, R. computer science mathematics			X	X
Pantalos, G. biomechanics physiology	X			
Rabbitt, R. biomechanics sensory physiology	X	X		X
Trujillo, E. biochemical eng	X			
Westenskow, D. instrumentation anesthesiology			X	X
Wiskin, J. mathematics				X

Second, this growing informational network, which uses the internet as its infrastructure, will serve as a 'petri-dish' in which the biological phenomenology of communication networks can be studied. The informational structure surrounding this grant is expected to be very plastic and will go through different phases, paralleling that of the grant itself. As project structures change, the informational structure will go through periods of renewed growth and degeneration. Close

monitoring and analysis of the informational structure will accompany each of these different phases.

The specific aims of these efforts are:

1. Develop tools which allow data acquisition on network traffic, informational relationships, and network morphogenesis.
Very early in the grant, simple software tools will be assessed and developed, which will allow automatic monitoring of internet network traffic associated with this grant. Initially this traffic will be mostly limited to intra-campus communication, making the monitoring task relatively easy. Monitoring will include the amount and type of information, but also timing issues. For example, we will analyze how fast information travels between senders and recipients, when information is received by the participant-- and when the information is actually acted upon. This will help to characterize the temporal aspects of a local network.
2. Develop tools which allow selective constraining of the informational infrastructure
Additional tools will be developed allowing artificial restriction of information flow, for example, by temporarily slowing down (or dramatically speeding up) traffic within limited areas of the informational structure. Biological systems often react to such restrictions with compensatory actions. We will learn how the informational structure react to these interventions.
3. Identify biological phenomena which parallel the development, growth, and plasticity of informational structures.
An attempt will be made to draw parallels between the informational structures developing within this grant and the development of growing and evolving biological structures, such as the neural system, the immune system, or metabolic relationships.
4. Using the tools developed in aims 1 and 2, gather data to support, quantify, and further establish the parallels of informational networks and biological phenomena.
Biologically based models will be developed to attempt to describe the behavior of the informational structures. The models will be tested for scalability and ability to predict future behavior and structure, as the informational structures evolve and grow.
It may be possible to develop techniques to estimate internal network parameters (such as the ones obtained by the tools mentioned above) by observing easily accessible, less intrusive network parameters. Likewise, since low level internal parameters are much more accessible in this informational structure than they usually are in biological systems, it may be possible to increase our understanding of relationships between external biological phenomena and their low level, internal counterparts.
5. Use the internet network infrastructure to simulate biological informational structures.
In the later stages of this grant, the individual projects will have matured to a point where they can be connected with each other. The infrastructure provided by the internet can then be used to establish informational links between the different projects. In this way, the internet is used to simulate aspects of the nervous system, the endocrine system, and metabolic pathways. Knowledge and understanding of the general behavior of this infrastructure will help in this effort. The software tools, protocol specifications, and interfaces developed to interconnect the different projects can form the initial tool set of the next exciting phase of interconnected distributed biological simulation research.

A straight forward model is a subset of metabolism, wherein a network of interacting enzyme reactions can be modulated or modified one reaction at a time by an internet "player," noting the effect of that unique perturbation on the behavior and outputs of the reaction network. This relates closely to the Engineering Metabolism project. There already exists a set of websites

with the appropriate networks, data, and sets of simulation and modeling tools with which to conduct the analysis. We simply need to implement this on a local intranet with the appropriate software. Since every active perturbation produces a simulation, the software must carefully record and analyze all such interactions. Eventually the result of these many individual perturbations and simulations will be further analyzed by the visualization tools so we can "see" the behavior and response of a complex biochemical network. We will also apply the novel modeling and simulation tools to provide higher level analyses of the "living" network.

Such activities must involve faculty from a wide range of disciplines, working closely with each other. For example (refer to Table 4 and larger list of participants):

Andrade, Trujillo, and Hlady (biochemistry)
Johnson and MacLeod (computer science)
Wisikin and Othmer (mathematics)
Westenskow and Horch (both involved in neural networks)

As these activities develop, the appropriate colleagues from across campus, as well as from participating institutions, will be motivated and induced (seduced?) to become involved. We are a highly interdisciplinary place. A few shared graduate students and/or post docs can facilitate much interdisciplinary activity.

Using higher levels of abstraction, we expect to quantify relevant whole-cell behaviors, including activation, voltage, motility, and exocytosis. On the next level individual cells will interact to exhibit collective behaviors, giving rise to tissues and organs. Internet experiments designed to model organs will use even higher levels of abstraction to describe the time dependent state of the organ including variables as temperature, pH, and stress. Health and behavior of the organ of course depends upon the underlying state of cells and their molecular cascades, levels which will interact with the organ via network carried signals. The endocrine and nervous systems will be modeled in this way and implemented to interact with organs such as the heart, kidney and the brain. This ties directly to the "Project-based curriculum" in that individual student-faculty teams will be responsible for implementation of specific aspects of the total system. The effort will be facilitated by the expertise of our industrial partners and by the diverse skills of our faculty.

Not all of the internet-based simulations will be strictly mathematical. In some cases, students themselves will play the role of a particular biological reaction or function and will interact with other students and functions through the keyboard and mouse. One can imagine very challenging "games" whose goals and outcomes are the understanding of complex systems and their emergent properties. Each student will have a limited view of the environment and will react on the basis of a relevant physiological question. The independent action of each student will combine to give rise to modifiable collective behavior. Different students can operate at different hierarchical levels for the purpose of integrating various subsystems. In some cases, graphical representation of higher level variables will be displayed to allow the students to observe the overall progression of the experiment. The time course of relevant variables will be monitored and saved for future classroom discussion and case study.

We learn from both success and failure. The students involved in these experiments will be encouraged to do both—in some cases by attempting to prevent a pathology through regulation of their biological role, and in other cases by attempting to generate a pathology through roguish behavior within their confined domain of influence.

The influence of redundancy, parallelism and competition will be investigated. Ultimately, models of simple organisms will evolve to include sensory systems and motor outputs which, may allow us to even address animal behavior. Constructed in this way, we will be able to view and manipulate the simulated living machine at various levels of abstraction. Without a doubt, such models will exhibit complex emergent behaviors and hence will provide a vehicle through which to study and understand some of the most complicated and elusive aspects of nature.

Thrust 3: Multi-dimensional Visualization

"Strange! I don't understand how it is that we can write mathematical expressions and calculate what the thing is going to do without being able to picture it."

R. Feynmann (66)

A simple but highly useful approach to multi-dimensional "visualization" is the use of spider or star plots utilizing radial, polar, or even spherical 3-D coordinate systems to present multi-dimensional data (23-26). We have used this in a preliminary way to simplify and to visualize the complexity of protein interfacial reactions (23). We are now using it as a means to present multi-parameter clinical chemistry data so that the visual pattern generated by the locus of points on the spider plot is designed to reflect particular disease states and metabolic conditions (24-25). Although such plots are incorporated in some plotting and graphical analysis packages and software, and widely used in certain specific fields such as sensory assessment (26), they have not been widely applied in most other areas of science. There has been limited use in clinical medicine, demonstrating that such approaches have enormous potential (24). There are many other very effective means of plotting and presenting data, including n-dimensional data (27-28), but which are not really widely applied.

The n-dimensional parallel coordinate approach from the local firm, nDV, was briefly described earlier. nDV-Explorer is a set of new intellectual structures for analysis of relationships of multidimensional data using Parallel Coordinates. Parallel Coordinates are used to allow representation of arbitrarily many dimensions (parameters) or coordinates, allowing one to "see" in many dimensions using a proper display space model.

Of particular interest to our application is their display space model, viewed using 3D virtual reality techniques, and capable of showing multiple instances (experiments) superimposed or in adjacency. They also have a directrix technique for mapping geometries back and forth between orthogonal and parallel coordinates. This provides the basis for curve fitting, modeling the data in each coordinate for extrapolation or interpolation, coordinate transformations, and understanding the relationships between the many coordinates. They also note a new "dimension" to functional analysis, in that the data models show that there are finite-difference slopes that are important in the data spaces, but that are not defined in classical functional analysis.

This is a good case of building on an existing technology which will likely be commercially available in the next several years. By becoming involved with nDV at this early stage, we can provide data sets, challenges, and other motivation to help them produce a product highly useful for bioengineering education.

Visualization is also a popular and productive activity in the radiology and medical imaging community. We will involve our local bioengineer/medical imagers and our other collaborators in discussions to quickly and efficiently learn what is available in their communities. The whole issue of perception of these visualization tools is critical—a subject also of interest to medical imaging (54).

We have just learned that C. Johnson and R. MacLeod will likely soon receive an NIH grant from the National Center for Research Resources for a center for Bioelectric Field Modeling, Simulation, and Visualization. This will be discussed in the next section. The relevant part from their proposal for this section is:

"Another category of computer applications is scientific visualization. Visualization is an essential component of virtually every bioelectric field problem and provides a means for viewing geometric models, experimental results, simulation results, and clinical observations. For example, to visualize a three-dimensional head model along with the MRI scans from the patient and the results from a source localization simulation would require the integration of many different types of visualization techniques—visualization of the geometrical mesh, visualization of the MRI data using volume rendering, visualization of the shading—integrated into a single frame."

Although their work is focused on research and graduate education applications, we will work closely together to simplify and transfer those tools and methods which are appropriate to our visualization needs.

We are interested in very simple ways to illustrate and help understand complex phenomena, hence our interest in working with artists (noted in Section 4), cartoonists, etc. In the words of Martin Kemp and Richard Feynman (66):

"Feynman diagrams look superficially like the simple graphics that physicists have uses for centuries. But they are devices of exceptional power. Within their space-time coordinates, Feynman was able to sidestep the long winded algebraic formulas that treated electrons and positrons separately. All the equations came together in one picture in a way that preceded and even directed calculation.

The diagrams mirror his conviction that "there is...a rhythm and a pattern between the phenomena of nature which is not apparent to the eye, but only to the eye of analysis".

Such a potent grammar of diagrams and matching equations provides a marvelous tool."

Thrust 4: Modeling and Simulation of Complex Systems

"Much has still to be done towards the elaboration of an integrative physiology, i.e. a formalised general physiology. This would call for the development of novel mathematical methods, the interpretation of experimental results, and the construction of appropriate models inspiring further experimentation. Instrumental and technological advances are today producing vast amounts of highly refined data which are far too scattered to be readily encompassed. A formalised integrative physiology may be expected to rationalise this extraordinary diversity of information within a sound theoretical framework, thus contributing to a deeper insight into the wonders of the living organism."

G. Chauvet (11), Vol. 3, pg. 626.

A key aspect to the project based curriculum is the ability to simulate and model physiologic systems and subsystem components. To do this, we will assemble and develop a toolbox of simulation algorithms, subroutines, and methods to support the individual projects. A significant core set of tools will be available and used for all the projects in the curriculum. Also, tools specific to each project will be developed or assembled from existing sources to augment the simulation aspect of each project. Students will complement a traditional curriculum in mathematical foundations, including calculus, linear algebra, and matrix and vector calculus, with these applied tools for solving aspects of biologic problems.

An emphasis of these tools will be towards solving non-linear problems due to their ubiquity and importance in biologic systems. Though non-linear systems are typically approached using numerical methods, we will use exact and "almost" exact solutions based on ordinary and partial differential equations. Usually the first inclination is to linearize these problems to solve them. Instead we will focus on simplifying models to analytic and semi-analytic solutions. These simple models can then be evolved to more complex models by increasing dimension or parameter space. Finally, simple models and control strategies are abstracted from the complex models. In this manner, the toolbox and teaching methods will support the Simplicity → Complexity → Simplicity theme of this proposal.

During the first two years of this project, significant effort will be devoted to assembling and developing the algorithm toolbox. Following this initial effort, the focus will shift towards implementation of these modeling and simulation tools, adaptation of tools for specific projects, and assessment of their utility for iterative modification as the project based curriculum is continually refined. We will address the following specific aims:

1. Assemble and develop a toolbox of algorithms for modeling and simulation of physiologic systems as examples of classical engineering concepts.

We will begin by searching the Internet for a broad spectrum of codes and subroutines which are available for public domain use. A large list of bookmarked sites with valuable subroutines and algorithms will be compiled after these routines have been evaluated and used by project staff. Methods and routines which are not readily available will be further investigated through published sources of software code. Finally, the project staff will write subroutines for use by the student for those critical tools that are not available in a form which suits the project based curriculum.

The focus in creating this toolbox is to make available to the student algorithms which can be conceptually explained in brief terms and readily applied once the conditions of the algorithm's applications are understood. A goal of the toolbox is to provide as many different methods for solving similar problem types so that the students can compare the advantages and shortcomings of different approaches based on the results each produces to a common problem. It is our belief that many techniques can be fruitfully applied even if the detailed theory of the method is not known. There are a large number of techniques that are not covered in elementary courses because to address them "properly" requires more knowledge than is generally available to beginning engineering students. However, it is possible to communicate the fundamental ideas of many techniques and see them applied to biologically relevant systems in order to supplement their comprehension. The important aspects of theorem proof can then be left to more formal math classes.

2. Create introductory and follow up classes to present the mathematical toolbox concepts developed in Task 1.

There are rarely closed form solutions to linear or nonlinear models that arise naturally in biology. However, there are many techniques available in mathematics and physics literature which give closed form or almost closed form solutions to ordinary and partial differential equations. This course would be an introduction and overview to the full spectrum of mathematical techniques; exact, approximate, and numerical; available for engineering problems. These techniques would be highlighted through the toolbox functions created in task 1.

The introductory class would cover two semesters and would have two course teachers who would be responsible for curriculum implementation, administration of the class effort, and roughly half of the teaching (initially MacLeod and Wiskin). The remaining portion of the class would be taught by the individual instructors responsible for each project in the project based curriculum. The class would begin in the 2nd semester of the freshman year for bioengineering students and end after the 1st semester of their second year.

The course will unify and enumerate many techniques that are useful in applications. The underlying theory will be minimally considered not because of its lack of importance, but to allow students to be exposed to a broad range of mathematical and simulation techniques. The course will cover topics such as:

- Nonlinear systems of equations
- Methods for solving dynamic models including topological, analytic and numeric.
- Newtownian-Lagrangian dynamics
- Linear dynamic systems including phase plane analysis
- Chaos in forced oscillation systems
- Introduction to fractal analysis and strange attractors
- Stability analysis
- Nonlinear Programming functions
- Perturbations, Scaling

Statistics and Probability

The course approach will be similar in style to one already in place in the Mathematical Biology program at the University of Utah, where simulation and modeling are used as tools in the context of a specific biological problem (60). The goal is not to provide students with a set of tools that they apply like following a recipe, but instead to instill context based understanding of principles so that these tools can be applied to a variety of situations and problems.

3. Evaluate and assess the progress of conceptual comprehension of students in the project based curriculum with students in a normal didactic curriculum which will precede this novel approach. Adapt both curriculums to capture the aspects which work best from both to evolve a hybrid approach for teaching mathematical concepts to bioengineering undergraduates.

To do this, we will use formative evaluation techniques which are designed to provide implementation and process feedback for program adaptation. At the end of each program year for the first three years of the project, a formative evaluation will be conducted to address whether the program is being phased in appropriately, whether presentation and comprehension of the mathematical toolbox concepts are succeeding in providing the students with skills to follow the project goal of Simplicity → Complexity → Simplicity. We will address issues such as are adequate tools available for students to use, are there issues regarding access to tools (hardware or software limitations) that are preventing full dissemination of these concepts, is the methodology of project context based presentation of the material adequate to promote comprehension, are the students succeeding in migrating skills among problems.

During the fifth year of the program, a summative evaluation will be performed for students in the project based curriculum and for students in the traditional curriculum. This evaluation will attempt to determine the aspects of each program which appear to be most successful in order to combine them in a hybrid fashion for the next three years of the program. Following these recommendations, the formative evaluation will be modified as needed and reapplied during years six through eight to again address implementation issues pertinent to the project. A summative evaluation, specific to the modeling and simulation component of the total project will be completed at the end of the funding period.

Our French collaborator, G. Chauvet (11), is now developing a virtual laboratory for physiologic "experiments" which incorporates theory from his three volume treatise (11), modeling and simulation, and multi-media visualization (55). He has already developed modules for ion transport, membrane-excitability, step-gated and voltage-gated channels, and synaptic transmission. His efforts, and those of others (56), focusing on individual biophysical or biochemical components of cells and tissues, constitute an enormous resource. The challenge is to expand such efforts to address the needs of hierarchical complex systems. Chauvet is, of course, aware of, versed in, and very interested in expanding his activities, in collaboration with ours, to consider complex properties. He has agreed to serve on our International Advisory Board and to serve as a visiting professor on a regular basis (he serves as a Research Professor in the Department of Biomedical Engineering at the University of Southern California, where he visits and works regularly).

The new NIH-NCRR Center (noted in the previous section) will conduct research and development in advanced modeling, simulation, and visualization methods for solving bioelectric field problems. Johnson, MacLeod, and co-workers will create and disseminate a computational workbench to drive the development of a bioelectric problem solving environment. It should be easy to move around within such a software environment. The programs should be robust enough to support expert-users and novices alike. With their system, researchers of bioelectric fields will

be empowered to analyze their data, their methods, and the full range of their problem space in ways they had never before considered.

The users will be free to apply their expertise where it makes the most sense—to steer an integrated computational system, to visually explore their data, to experiment with model parameters. When the tools integrate seamlessly, they fade into the background—the user is freed to concentrate on the problem at hand, rather than on the software tools. Such a seamless computational workbench is the ultimate goal. The use of computers in the study of biology and medicine is now ubiquitous. While the range of computational tools and the ways computers are being used in bioelectricity applications is as broad as the field itself, many fall into categories that circumscribe the cope of the proposed Center—modeling, simulation, visualization, and the development of specialized software for these tasks.

Although their tools are designed for bioelectricity studies, they clearly have a very wide applicability. We will work together to adapt and adopt their "computational workbench" to our needs for tools for complex projects in an undergraduate environment.

There is a growing interest in what *The Economist* recently dubbed "virtual biology" (67). Computer modeling of whole organs, particularly the heart, is well advanced. Bassingthwaite's Physiome Project and the Cardiome Consortium are specific initiatives which are launching this new field. Even the FDA has agreed that such models may be relevant and useful (67). The challenge is to transform and translate the output of such activities into a form suitable for undergraduate bioengineering education. That is one of the goals of this research thrust.

G Education

This has already been covered in Sections A-D and Thrust 1 of Section F. As noted earlier, we expect most of our graduate students to be directly involved in the project teams. We frankly expect the graduate students to be challenged and empowered by the undergraduates and by their projects. We expect that the graduate program will be greatly enhanced as the interests, activities, and output of the undergraduate program trickle upward.

It is clear that the project teams will emphasize and facilitate teamwork, project management, communication, and indeed the wide range of skills and experience which we desire in our graduating engineers (4, 5). As the project proceeds, it is likely that our colleagues in Physics (R. Price), Mathematics (H. Othmer), and Biology (D. Blair) and their colleagues will begin to involve their undergraduates and graduates in our complex projects. R. Price, Professor of Physics and an advocate of project-based education, is developing a project-based undergraduate program which will enroll a group of physics majors. We will, of course, work closely with him. Perhaps a physics undergraduate will be a member of each of our project teams.

Our advisors, visiting faculty from participating institutions, industrial participants, and Internet participants (see Figure 4) will represent all relevant disciplines.

There are a number of practical issues which must be addressed. Our program is designed for 15 students per class—60 at steady state. We feel that teams of five students are the optimum size. In order to allow for attrition, due to a wide range of student personal issues and needs, we will admit 20 students and organize teams of 6 to 8. We expect several students will choose the more traditional curriculum, change majors, go to work, etc. We expect to have three teams of 5 to 6 students by the end of the first year. If the attrition rate is less, all students will be accommodated in the three project teams.

We will strive for diversity in culture and in technical interests in the teams, including representation of out of state students (see Section H).

We will work closely with our industrial participants (next section) to provide project-related internships. Having industrial participants as volunteer members of the teams will facilitate such opportunities.

The issue of intellectual property for undergraduate projects and inventions is now being addressed at the University of Utah. The Department of Bioengineering is now drafting a policy statement on intellectual property as it relates to undergraduates, visitors, and summer participants.

This ERC will certainly "...prepare a diverse group of students for teaching and practice in bioengineering by encouraging teamwork, providing cross-disciplinary experience in research and education, and expose...them to industrial/practitioner views" (57).

H. Outreach and Dissemination

Linking High School Students and Teachers to the New Integrated Project-based Curriculum

INTRODUCTION

Major shifts in the education of undergraduate students in the bioengineering and biomedical fields are forcing us to look at how we prepare high school students who are motivated by the subjects and prospects in these fields. National reforms in science education at the high school level have focused on interactive learning and have begun to shift away from didactic teaching (31, 59).

Our new integrated project-based curriculum expects that students come prepared for a new type of learning experience; one that engages them in practical application of basic scientific knowledge and one that requires team-building skills. Exposing high school science teachers to the new curriculum has the potential to refresh their teaching methods, spark new ideas into their classroom lessons, and allow them the opportunity to interact with research scientists and engineers. We propose a "mini experience" for high school students and teachers to introduce them for the new project-based, team-oriented curriculum..

PROGRAM DESIGN

Each summer twenty high school juniors and five high school teachers will be selected for a four-week academic program on the University of Utah campus. We will work closely with high school teachers, counselors, and "resource" faculty to make junior students aware of the new program. Our high school colleagues will identify and nominate students for special summer workshops, which will serve to evaluate and identify those students who could benefit most from—and contribute to—the program. The course work and activities will be lead by faculty members from the project areas, together with bioengineering project staff, and graduate students, and the Center for Science Education and Outreach (CSEO). An advisory committee composed of representatives from the ERC faculty, the Center for Science Education and Outreach, and local school teachers and administrators will assist in the selection process, selection of curricular content appropriate to grade level, and in project evaluation.

The Summer Bioengineering Advisory Committee will include Dr. Brett Moulding, Science Curriculum Coordinator, State Department of Education. We have worked closely with Brett over the last five years on a range of science/technology outreach and education activities. Brett will help identify high school teacher participants and review and assess all aspects of the program. The current president of the Utah Science Teachers' Association (chapter of the National Science Teachers Association) will also serve on the Advisory Committee.

The Center for Science Education and Outreach is administered through the Department of Bioengineering and co-directed by Dr. Joe Andrade, PI for this ERC request. Dr. Andrade's interest in science education for the K-12 student and teacher populations was formalized with the Center's initiation in 1992. Since that time the Center has become established as the University of Utah's outreach arm to the community with regard to science and engineering education. The Center's staff has collectively over 20 years experience in providing academically linked educational programs for students and teachers and will be responsible for administering the summer program; recruitment of participants, setting up the selection process, arranging industry visits, making necessary logistical arrangements, and preparing evaluation reports.

Recruitment efforts will be directed toward the Utah MESA (Math, Engineering, and Science Association) chapter, Utah Science Teachers Association, Utah Science Olympiad, and

various science clubs at the local high schools. These meetings will provide a forum for the Center's staff to periodically present an outline of the field of bioengineering, career opportunities in the field, and opportunities under the auspices of the summer program. Recruitment efforts will not be limited to the University of Utah region. Area-wide efforts will focus on under-represented groups, and will be coordinated with other diversity programs at the University of Utah and the College of Engineering, i.e. Program for Diversity in Engineering, Center for Ethnic Student Affairs.

We will work closely with our participating institutions and companies, and with the National Science Teachers Association (NSTA) to make the national community aware of the program. We will seek other funds for the additional expenses associated with the housing and supervision of out of area participants.

Criteria for selection will be based on motivation, interests, ability to work well in a team setting, and potential to do well in a project-oriented format. We will ask high school teachers, counselors, and resource staff to nominate students for the program.. Consideration will be given to underrepresented students which includes African-Americans, Asian-Americans, American Indians, Hispanics, and Pacific Islanders/Alaska Native. Students who are low income and first generation college-bound students will be given particular consideration.

Students selected will be awarded a \$1,000 scholarship upon successful completion of the program. This will help encourage low income students who are required to work in the summer to consider applying for this unique experience. High school teachers in the summer programs will function partially as students and partly as staff, depending on their background. They will be compensated for their service (\$2,000/teacher).

Curricular content will be largely derived from projects areas described earlier. High school students and teachers will work in teams with lead faculty members, undergraduate students, graduate students, and staff. The selected projects and related topics will be components of the larger undergraduate projects, but will be scaled and presented in a manner appropriate to a high school junior background.

The program is designed to include not only an introduction to project based learning, but, more importantly, to the skills required to approach a solution through the proper use of scientific and engineering methodology—including structured observation, hypothesis formation, experimental design, prototype design, data collection and collation, data analysis and interpretation, scientific writing, and oral presentation. Projects and activities will need multi- and inter-disciplinary approaches, thus encouraging the students and their teachers to appreciate an integrated, synergistic approach to the sciences and technology (31, 59). Student-teacher teams will be introduced to the interactive software that will be used in the undergraduate program to study the behavior of biological systems.

Over the four weeks, participants will visit with other faculty, tour their labs, and be introduced to their research specialties. Participants will also visit local biomedical engineering companies to learn how bioengineering research transfers to business and industry.

The high school students and teachers will present their projects to other faculty, graduate and undergraduate students, and other high school teachers. The participants will be asked to further present their experiences at regional conferences and events to local audiences.

Summer program alumni will be regularly contacted and "reinforced," including receiving invitations to open houses and other activities sponsored by this ERC and by CSEO.

The summer program will begin Summer, 1999, assuming the grant is funded effective about April 1, 1999. By this time an advisory team will be established, the appropriate staff and visiting faculty will be hired, and the other participating institutions will have an opportunity to review and offer input into the program design.

We expect that many "alumni" from the summer program will apply for admission to our project-based undergraduate program. Alumni from the first program (Summer, 1999) will return to their schools as seniors, hopefully participating in high school science "fairs" or design competitions during their senior year. If they are indeed admitted to our program, we will provide summer opportunities for them during the summer prior to their University enrollment. Some of them might be involved as peer aids in the on-going summer programs.

An internal evaluation will be conducted by the staff and consultants of the Center for Science Education and Outreach. Individual interviews will be part of the evaluation process (see also Section I).

Grant funds will be used to support student scholarships, provide honoraria for the teachers involved, provide salaries for the summer instructors, and provide support for staff members from the Center for Science Education and Outreach.

The program will be organized, managed, and implemented by the CSEO and College of Engineering Dean's office staff, working closely with the ERC Executive Committee. Mary McDonald, Manager of CSEO, has considerable experience in summer programs, teacher inservices, science museums, and related activities directly relevant to this program.

The General and Wider Public

Measurement and Medicine is a liberal education, general science and technology course, now in the advanced planning stages, to be offered in both on campus and distance education formats. We already have experience with such projects through the *Science Without Walls: Science in Your World* course and program (31—available on www.utah.edu/cise, click on Science Without Walls).

We do not have the resources in this ERC grant to fully develop *Measurement and Medicine*. We do propose, however, to use grant funds in Years 1-5 to complete the design and planning of *Measurement and Medicine*, and to solicit the funds required to fully develop and implement the course (~\$500,000). Such a course, offered regularly via public educational television distance learning channels (local Channel 9 in Utah) will help inform and educate the public as to bioengineering in particular and engineering in general. Tentative programs and topics are (each a one hour telecast/video):

Course 1: Measurement in Physiology - Are You Normal?

- | | | |
|--------------------------------------|-----------------------------------|-------------------------------------|
| Prog 1: You are Abnormal! | Prog 6: You Can't Even Break Even | Prog 11: Newton Rules Biology & You |
| Prog 2: You are Imperfect? | Prog 7: Hot Stuff - Warm Blood | Prog 12: Where Did the Energy Go? |
| Prog 3: Lies and Electrons | Prog 8: The Body Electric | Prog 13: Senses and Sensibility |
| Prog 4: More Power to You | Prog 9: The Body Magnetic? | Prog 14: The Photon World |
| Prog 5: Hiking, Diving, and Running. | Prog 10: Gravity Wins! | Prog 15: Summary |

Course 2: Measurement, Pathology, and Medicine - How Abnormal Are You?

- | | | |
|----------------------------------------|-----------------------------------------|-------------------------------------|
| Prog 16: You're Even more Abnormal! | Prog 21: Cystic Fibrosis and Oxygen | Prog 26: Neurodegenerative Diseases |
| Prog 17: Multiplying and Killing Cells | Prog 22: Hypertension and Heart Disease | Prog 27: Nerves and Brains |
| Prog 18: It's Your Parents' Fault! | Prog 23: Hopeless Organs | Prog 28: New Eyes and Ears |
| Prog 19: Problem Babies | Prog 24: Artificial Organs | Prog 29: Bio-Hybrid Devices |
| Prog 20: Diabetes and Metabolism | Prog 25: Old Bones - and Joints | Prog 30: Summary |

Dissemination

We will work closely with our participating institutions, advisors, the BMES, IEEE-EMBS, ASEE, AIMBE, Whitaker Foundation, and other groups to inform the wider community and to encourage their participation and involvement.

I. Assessment, Evaluation, and Advisory Boards

Assessment and Evaluation

We will work with Carl Jaffe, M.D. (letter in Appendix A) and the Center for Advanced Instructional Media to structure an assessment program for this project. The Yale Center has been responsible for computer based self-test assessment programs which can be accessed via the world wide web. We will determine a set of criteria for comprehensive knowledge and design/problem solving skills which we anticipate the students will acquire during their projects and courses. Irrespective of the specific projects, there will be fundamental tools which will be presented to the

students through the curriculum in each year. We will assess the student's ability to understand these principles via computerized evaluation. The evaluations will present the student with a situation that is different from their project based curriculum experience yet utilizes the same skills. The evaluations will enable us to gauge the students' ability to apply these concepts to other areas. Students will complete these evaluations at regular intervals but will only address the concepts which they understand at the time of evaluation. As they progress through the curriculum, they will participate in more extensive evaluations as their education expands.

We will use this information to compare how well these core principles are understood between project groups. This will provide comparative input between different projects to determine whether one project's method of presenting a concept may be more lucid than another project's. Since different projects will cover these concepts in different sequential order, this method of evaluation will allow comprehension to be measured at different times rather than at specified points in the curriculum. The dynamic basis of this evaluation allows for adaptation to be made in the curriculum for situations where a core principle is not well understood from a particular project or for a particular project group. This data will be stored in an interactive database that can be queried.

Yale's Center for Advanced Instructional Media (C/AIM), founded in 1987, develops innovative educational and communications programs using interactive multimedia by employing the newly emerging computing and digital network technology. C/AIM is a recognized leader in information design, medical illustration, and interface design for electronic publications and networked information systems.

C/AIM has a variety of on-going research and education projects involving multimedia software design and networked delivery of multimedia educational resources including course for first-year medical students, biomedical engineering curriculum support programs, Web-based student testing and professional post-graduate self-assessment, graphic design for the user interface, and interactive three-dimensional graphics in medical visualization. We have worked closely with Carl Jaffe on other projects and look forward to learning a great deal from him and C/AIM on these topics.

We will also work closely with our Advisory Boards (next section) to develop appropriate assessment tools, with particular attention to the needs and input of our advisors from industry.

Advisory Boards

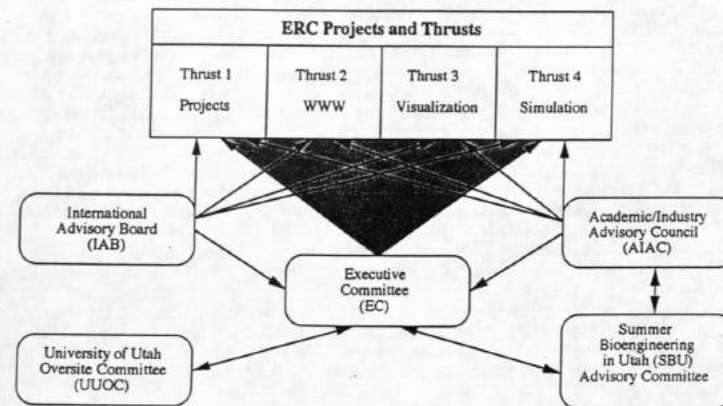


Figure 5. The several advisory boards to be organized and utilized in this ERC.

The International Advisory Board (IAB) has not yet been assembled. We have talked with some prospective members. Some of the people we expect to involve are represented in the References (4, 11, 13, 19, 32, 33, 38, 41, 42, 46, 47, 48, 53-56, 63). There are also several others we are considering. Gilbert Chauvet will be a key member and participant. We frankly expect to ask one or more of the PI's of other ERC NSF 98-68 applicants to participate, as all of these programs certainly have ideas and experience relevant to our efforts and goals. The IAB will meet annually at the University of Utah, beginning approximately in September, 1999, to provide input, critique, advice, and assessment. We are planning for about 12 members. Their expenses and honoraria are budgeted (token honoraria of \$400/day, well within NSF/NIH guidelines).

The Academic/Industry Advisory Council (AIAC) is discussed in the next section.

The University of Utah Oversight Committee (UUOC) is described in Section K on Infrastructure.

The Summer Bioengineering in Utah (SBU) Advisory Committee (the high school summer program noted in Section H) will include the ERC Director (in Section K), Mary McDonald (Manager of the Center for Science Education and Outreach), Brett Moulding (State Office of Education), and the current President of the Utah Science Teachers' Association (USTA). That group will meet quarterly to plan and assess the summer programs. Their first meeting will occur in April, 1999 to rapidly plan the first program, Summer, 1999.

Only the International Advisory Board and the academic participants of the AIAB will receive honoraria.

J Industrial and Academic Collaboration

Industrial and academic collaborators were listed in the List of Participants at the very front of the application.

Participating Institutions

Initial participating institutions include the University of Southern California (Los Angeles), Drexel University (Philadelphia), University of California-Berkeley, Utah State University (Logan), Marquette University of Angers (France), Uppsala University (Sweden), and Fachhochschule Hamburg Department of Engineering (Germany). Each participating institution is represented on the Academic/Industry Advisory Council, which will provide input and guidance related to academic issues and opportunities in the ERC. These participating institutions will also be directly involved in the ERC's visiting faculty program wherein their faculty members will be in residence at the University of Utah for periods ranging from days to months, depending on schedules, needs and resources available. In addition, participating faculty in the participating institutions will be available via the Web and by telephone to serve as advisors and consultants on the student projects and on other components of the ERC (Figure 3). Depending on the specific institution and its resources and needs, we anticipate an exchange and trade of curricular materials and even courses via the world wide web. It is likely that there will be some student exchange as well.

The basic idea is to make the resources and new tools of the ERC available initially to participating institutions. We expect the number of participating institutions to grow significantly during the first several years of the ERC. Indeed, we plan to invite all institutions who submitted proposals to this ERC competition to participate.

These participating institutions will then serve as a very effective test mechanism for ERC developed curricula and tools as well as a dissemination mechanism for those deliverables produced via the ERC.

We will also work with the Council of Academic Programs of the American Institute for Medical and Biological Engineering (AIMBE) and the Biomedical Engineering Society (BMES). The participating institutions will assist the University of Utah and the ERC staff in testing and disseminating all products and activities of the program.

Participating Industries

Our Department has substantial industry interaction and involvement. The Department's Industrial advisory Board is active and involved, including developing and presenting several industrially relevant courses and seminar series. Our Center for Biopolymers at Interfaces, V. Hlady, Director, has 20 member companies. Most of our faculty consult, and many are involved with start up companies.

Given the short time line from announcement to deadline for NSF 98-68, we have not yet approached many firms as potential participants. We are confident, however, that there will be considerable industrial interest and involvement in our activities. First the integrating projects themselves are of interest to specific companies. There are several companies directly interested in the WWW as an interactive, collaborative tool. Several software firms are specifically interested in Thrusts 2-4, and many firms are interested in the future graduates of this program.

Our confirmed industrial participant list at this time is small, not because of lack of interest but simply due to lack of time.

Those we have approached and involved to date are:

- Ash, O. Executive Director, ARUP, Inc. (Associated Regional University Pathologists, Inc.) a major clinical and diagnostic testing laboratory.
- *Blake, L. Vice President, Sorenson-Vision, Inc., Logan, Utah—a data compression company whose technology allows full time video over normal telephone lines.
- DiCaprio, V. Senior Vice President & Chief Technical Officer, Becton-Dickinson Co.
- *Jacobson, S. President, Sarcos, Inc., Salt Lake City, a pioneering and leading firm in robotics and advanced biomedical products (www.sarcos.com)
- *Johnson, R. Principle of nDV Ltd., whose unique parallel coordinates software is described in Thrust 3—Visualization.
- McRea, J. Chairman, Dept. of Bioengineering Industrial Advisory Board and President/CEO, Device-Based Therapeutics, Inc., Salt Lake City
- Suggatt, A. Director of R & D, Smith and Nephew Ltd., London
- *Van Wagenen, R. Vice President for R & D, Protein Solutions, Inc., Salt Lake City

* letter in Appendix A

K. ERC Infrastructure

Leadership and Management

ERC management and administration will be located in the Dept. of Bioengineering. Center Director Andrade will devote at least 25% time to the project. The ERC Executive Committee, chaired by J. Andrade, Director and co-chair of the Department, will include

- K. Horch, co-Chair and co-leader of Thrusts 1, 2, and 3;
- R. Rabbitt, Director of Graduate Studies and co-leader Thrust 2;
- S. Kern, co-leader Thrust 3;
- J. Wiskin, co-leader Thrust 4;
- R. MacLeod, co-PI of new NIH NCRR and co-leader Thrust 4;
- D. Christensen, Director of Undergraduate Studies and co-leader Thrust 1.

Andrade, Horch, and Kern, the three co-PIs, will be responsible for day to day implementation and management.

The Executive Committee will meet at least monthly, as will each of the research thrust groups. At each monthly meeting each of the thrust groups will present progress reports and plans for the next month. An annual presentation will be made to the joint meeting of the International Advisory Board and the Academic/Industry Advisory Council.

The general vision and development of this proposal is largely due to the members of the Executive Committee. They will all continue to be actively involved throughout the project. Their individual time commitments to the ERC will be about 25%, largely charged to the ERC budget in Years 1 to 5.

Figure 5 presented the overall organization. The Center will report directly to the Dean of Engineering, with direct input and involvement of the Associate Deans for Academic Affairs and Research.

Personnel

Bio sketches for the key participants are given in App. C. As noted in the Thrust 1 discussion (Section F), we will hire staff scientists and engineers to aid the students with their projects. These same individuals will also work, as appropriate, in Thrusts 2 to 4 and with the summer program. All searches and hires will give full consideration to minority participation. A full time administrative assistant is also budgeted to help coordinate, plan, implement, and otherwise facilitate the conduct of the program. There are summer students, advisory boards, undergraduates, graduate students, faculty, staff, and visitors who all require administrative support.

Facilities, Space, Equipment

Thrust 1, Projects, will be largely conducted in several new undergraduate project laboratories, remodeled for this ERC. This 1500 sq. ft. complex is nearly adjacent to the Dept. of Bioengineering offices and to the offices of Horch, Andrade, and Rabbitt. Project technical staff will have desks in the undergraduate laboratory, enhancing their access to students. All participants will have access to these facilities on a 24 hour basis.

The activities of Thrusts 2 to 4 will be conducted partly in research space assigned to the faculty participants as well as in the undergraduate project laboratories.

The summer high school program will use the same undergraduate laboratories. Administrative space and services for the summer program will be provided by the Center for Science Education and Outreach, located in the same building.

No major equipment is requested. All needed equipment is less than \$5,000, thus no separate equipment category is budgeted. The College of Engineering will provide funds for small equipment items and supplies for the undergraduate laboratories from two University sources: the Base Engineering Equipment Fund (BEEF) and the Research Equipment Support Fund (RESF), the latter primarily for needs in Thrusts 2 to 4.

The ERC will have access to all laboratories, equipment, and related resources in the Dept. of Bioengineering for teaching, project, and research purposes. Individual faculty laboratories and equipment are also generally available. We are a highly cooperative and interactive group.

Financial Planning and Support

Management and allocation of support will be the responsibility of the Executive Committee, which will consist of seven members, including the PI/Director. The budget is already allocated for the different functions and activities (App. B 5 Year Summary Budget and Year 1 Budget -- both by areas of activity), thus each Thrust and area knows what it has available. Nevertheless, it is difficult to prepare Year 3 to 5 budgets from today's information, so some budget redistribution may be necessary.

We will form a University Oversight Committee (UOC) to review the program twice a year and provide critique and advice. In the unlikely event of a strong disagreement within the Executive Committee, the UOC will serve as an arbitrator. Members of the UOC will be:

- R. Koehn, VP for Research, chairperson;
- J. Lighty, Interim Dean, College of Engineering;
- J. Francis, Dean, Undergraduate College;
- J. McRea, Chair of Dept. of Bioengineering Industrial Advisory Board;

Student, Chair of Undergraduate Student Advisory Committee (SAC),
Dept. of Bioengineering.

We have frankly not attempted to secure firm resource commitments from industry or from the State at this time. The State and the University have provided significant new support for the Dept. of Bioengineering, allowing the tenure tract faculty (FTE slots) to grow by over 60% in the last three years. It is indeed this growth that permits us to now initiate an undergraduate program. Although we expect increasing support and growth, it is not reasonable, particularly given the short time available to respond to NSF 98-68, to secure a significant match. We will request (and expect to receive) such support in Years 3 and thereafter.

We have leaned heavily on our Industrial Advisory Board for graduate fellowships and projects. They are very supportive of our undergraduate initiatives. As they become more aware of and participate in this unique program, they will provide significant support.

A key question is support of project growth in Years 3 to 5, support for the NSF phase out in Years 6 to 8, and continuance of the program after Year 8. There are four sources: the State and University, philanthropists and foundations, industry, and the Dept. of Bioengineering.

The State/University:

As noted earlier, the University of Utah Administration is very supportive. They will work with us to generate the State appropriations to permit the growth and continued operation of the program. Utah's Legislature and Governor are proud of the State's evolving biotech/health care industries and reputation. They are well aware of the need for, and the costs of, education in engineering and related fields. Our Legislature has many rural representatives who appreciate hands on, project-based, practical education and who are uncomfortable with traditional lecture-based education. We think they will understand, appreciate, and support this program.

J. Andrade served as Dean of Engineering from 1983-87 and, with the encouragement and clout of the College's then new Industrial Advisory Board (IAB), launched the first Engineering Initiative in Utah, which provided increased base budget support for undergraduate programs. That initiative has gone forward each year to the present. The Engineering Initiative funds have allowed the significant growth of Bioengineering and its new undergraduate program.

We will work closely with the Department and College IABs and with the Administration to launch a Bioengineering Initiative with the goal of providing base budget support for this program for Years 3 to 8 and beyond. We will work closely with key legislators and the Governor's Office staff, involving them in our outreach and dissemination activities, including the summer program. Although we cannot promise success, it is a high probability.

Philanthropists and Foundations:

There is a lot of wealth in Utah -- much of it relatively new and derived from technically-based businesses. For example, the Huntsman family (Huntsman Chemical Corp.) recently provided \$100 million for the Huntsman Cancer Institute, with more to come. Utah has several billionaires and about ten deci-billionaires. We are just beginning to involve them in our activities. This ERC will appeal to such self-made individuals, who tend to resonate with a project-based, hands on approach -- and tend to not appreciate more traditional approaches to education. We are confident that some of their philanthropic activities will be in Bioengineering.

Industry:

Our local IAB has generally been more interested in undergraduates than PhDs. They are very supportive of our new undergraduate program. Many of the local firms are owned by large biomedical companies (Becton Dickinson, Baxter, Bard, etc.). We expect these national firms to compete for exposure to our project-based students. We expect that most of the students in this program will be receiving industry-derived undergraduate fellowships. Industry alone cannot fully support this program after Year 8, but it will provide significant assistance.

Department of Bioengineering:

As the project-based curriculum expands and develops, we expect that most of our undergraduate students will want to participate. Our traditional undergraduate program is designed for 35 students--this ERC is for 15 to 20. We may well choose to restructure our entire undergraduate program in Year 8 and beyond to reflect the best of both approaches, perhaps settling on a total class of 25 to 35. If this happens existing Department resources could provide much of the ongoing support. There are also economies of scale with more projects and a larger class.

Summary:

We are confident that, using the four sources noted above, we can fully support ERC activities beyond Year 8. We are committed. The key to dealing with complex socio-political systems is not unlike dealing with complex biological systems -- in E. O. Wilson's words again: "Knowledge, Obsession, Daring."

Role of ERC Within Institution

This has already been discussed. We are a collaborative place. Our academic retention, promotion, and tenure (RPT) criteria are rigorous and require strong, peer-reviewed evidence of independence, originality, significance, and quality. But that does not mean that we discourage collaboration or multi- and inter-disciplinary activity. Just the opposite. The entire Administration, from Department co-chairs to the President, encourage and support collaborative interests and activities.

Management issues were discussed in the beginning of this Section.

References

1. Wilson, E.O. *Consilience*, 1998. (Although this book has been criticized by reviewers for being far too sweeping and gradiose, there are many parts of the book and many ideas which are highly relevant to this proposal.)
2. Pattee, H.H. Ed., *Hierarchy Theory: The Challenge of Complex Systems*, Braziller, 1973; see also Pattee, H.H., "Physical Theories of Biological Coordination," *Quart. Rev. Biophys.* 4 (1971) 255-276.
3. Nichols, G., and Prigogine, I. *Exploring Complexity*, Freeman and Co., 1989; see also Prigogine, I., *The End of Certainty*, Free Press, 1997.
4. Bordogna, J. "Making Connections: The Role of Engineers and Engineering Education," *The Bridge* 27 (1997) 11-16; Bordogna, J., Fromm, E., and Ernst, E.W., "An Integrative and Holistic Engineering Education," *J. Sci. Ed. Tech* 4 (1995) 191-198.
5. *Engineering Education and Practice in the United States*. National Academy Press, 1985, Executive Summary, pp. 11-23
6. Andrade, J.D. "Bioengineering: A Model for Engineering Education," *BMES Bulletin* 15/1 (1991) pp. 3-6.
7. Gardner, H. *Frames of Mind: The Theory of Multiple Intelligences*, Basic Books, 1983; and *The Unschooled Mind: How Children Think and how Schools Should Teach*, Basic Books, 1991.
8. www.sarcos.com (see also letter in Appendix A)
9. Should be available via www.aimbe.org.
10. There is a reference to this in the American Physical Society newsletter (www.aps.org). See also www.colorado.edu.
11. Chauvet, G.A. *Theoretical Systems in Biology*, Vol. 1-3, Elsevier, 1996.
12. Murray, J.D. *Mathematical Biology*, 2nd ed., Springer, 1993.
13. Yeagers, E.K. et al., *Intro. to the Mathematics of Biology*, Birkhauser, 1996.
14. Lumsden, C.J., et al., *Physical Theory in Biology*, World Scientific, 1997.
15. Stewart, I. *Life's Other Secret: The New Math of the Living World*, Wiley, 1998.
16. Bronzino, J.D., ed., *Biomedical Engineering Handbook*, CRC Press/IEEE Press, 1995, Section XV: "Physiologic Modeling, Simulation, and Control," Chizeck, H.J., section editor.
17. Brown, D. and Rothery, P. *Models in Biology*, Wiley, 1993.
18. Segel, L.A., ed., *Math. Models in Molecular and Cellular Biology*, Cambridge U. Press, 1980.
19. Paton, R., ed., *Computing with Biological Metaphors*, Chapman and Hal, 1994.
20. Basnall, P., "The Internet," *Physics Education* 33 (1998) 143-148.
21. Nussbaum, D. "Global Weather Project Unites Students on Web," N.Y. Times, June 4, 1998, D-5, also the SET1@homeproject for distributed data processing--see *The Economist*, April 1998, p. 78.
22. Johnson, R. "Discerning Relationships in Multidimensional Spaces," nDV, internal report, July 1998.
23. Andrade, J., et al., "Proteins at Interfaces," *Clinical Materials* 11 (1992) 67-84.
24. Cerra, F.B., "Hypermetabolism..." *Surgery* 101 (1987) 1-10.
25. Vogt, W., et al., *Cluster Analysis in Clinical Chemistry*, Wiley, 1987; see also Vogt, W., et al., *Trends Anal. Chem* 3 (1984) 166-171.
26. McEinan, J., "Harmonizing Sensory Evaluation," *Food Tech.* 52(4) (1998) 52-56.
27. Wainer, H., *Visual Revelations*, Copernicus, 1997.
28. Tufte, E.R.T., *Envisioning Information*, 1990; *Visual Explanations*, 1997; *Visual Display of Quantitative Information*, 1983, Graphics Press, Cheshire, CN.
29. MacLeod, R.S., Johnson, C.R., and Matheson, M.A., "Visualization Tools for Computational Electrocardiology," *Visualization in Biomedical Computing*, 433-444, 1992.
30. MacLeod, R.S., and Johnson, C.R., "Map3d: Interactive Scientific Visualization for Bioengineering Data." In *IEEE Engineering in Medicine and Biology Society 15th Annual International Conference*, IEEE Press, 1993.
31. Andrade, J.D. *Science Without Walls: Science in Your World*, Simon and Schuster Custom Publishing, 1998; see also *The Scientist*, April 27, 1998, pg. 9 and www.utah.edu/cise.
32. Pickover, C.A., ed., *Visions of the Future: Art, Technology, and Computing in the 21st Century*, St. Martin's Press, 1991 and his other books on scientific visualization.
33. Marmarelis, V.Z., Bassingthwaite, J.B., D'Argenio, D.Z., and Foster, D.M., "Overview of NIH-funded Biomedical Modeling and Simulation Resources," Patterson, B.W., ed., *Modeling and Control*, Pergamon Press, 1994, 15-16.
34. Johnson, C.R., "Computational and Numerical Methods for bioelectric field Problems." *Crit. Revs. in BioMed. Eng.*, 1997 (to appear).
35. Johnson, C.R., "Numerical Methods for bioelectric Field Problems." In *Biomedical Engineering Handbook*, Bronzino, J.D., Ed., CRC Press, pp. 161-188, 1995.
36. Wastney, M.E., et al., "Using Models to Explore Whole-Body Metabolism..." *Metabolism* 46 (1997) 330-332.
37. Healy, P.M., and Jacobsen, E.J., *Common Medical Diagnoses: An Algorithmic Approach*, 2nd ed., Saunders, 1994.
38. Bailey, J.E., "Metabolic Engineering," *Adv. Molec. Cell Biol.* 15A (1996) 289-296.
39. Zhu, Y.-H., Linko, S., and Linko, P., "Neural Networks in Enzymology," *Adv. Molec. Cell Biol.* 15A (1996) 47-57.
40. Paton, R.C., "Computational Models at the Cellular Level," *Biosystems*, 29 (1992) 64-75.
41. Holland, J.H., *Emergence: from Chaos to Order*, Helix Books, 1998; see also his *Hidden Order: How Adaptation Builds Complexity*.
42. Fell, D., *Understanding the Control of Metabolism*, Portland Press, 1997.
43. Agius, L. and Sherratt, H.S.A., *Channeling in Intermediary Metabolism*, Portland Press, 1997.
44. Kacser, H. "Beyond Metabolic Control Analysis," *Biochem. Soc. Trans.* 23 (1995) 387-391.; see also "The Control of Flux," reprinted in *Biochem. Soc. Trans.* 23 (1995) 341-366.
45. Quant, P.A., "Top-Down Control Analysis," *Trends Biol. Sci.* 18 (1993) 26-30.

46. Stephanopoulos, G. and Wimpson, T.W., "Flux Amplification...", *Chem. Eng. Sci.* **52** (1997) 2607-2627.
47. Palsson, B.O., et al., "Reducing Complexity in Metabolic Networks," *Fed. Proc.* **46** (1987) 2485-2489.
48. Westerhoff, H.V., and Welch, G.R., "Enzyme Organization and the Direction of Metabolic Flow," *Curr. Topics Cell Regulation* **33** (1992) 361-290.
49. Koshland, D.E. Jr., "Era of Pathway Quantification," *Science* **280** (1998) 852-853.
50. Michalopoulos, G.K. and DeFrances, M.C., "Liver Regeneration," *Science* **276** (1997) 60-66.
51. Sussman, N.L. and Kelly, J.H., "Artificial Liver," *Sci. and Medicine*. May/June 1995, pp. 68-77.
52. Williams, R.J., *Biochemical Individuality*, U. Texas Press, 1976.
53. Slocum, D.L., "The Future of Bioengineering," *Science* **281** (1998) 175-176.
54. Hendee, W.R. and Wells, P.N.T., eds., *The Perception of Visual Information*, Springer-Verlag, 2nd edition, 1998.
55. Chauvet, G., "A Physiological Multimedia Laboratory System for Virtual Experiments," PhysiLAB Education ©, 1998.
56. Weiss, t.F., *Cellular Biophysics*, Volumes 1 and 2, MIT Press, 1996 and Software Under Development.
57. NSF 98-68: An ERC for Bioengineering Education Technology.
58. "Interfaces," an NSF Publication, Division of Materials Research, MRSEC Educational Activities.
59. Rutherford, F.J. and Algren, A., *Science for All Americans*, Oxford Univ. Press, 1990
60. Adler, F.R., *Modeling the Dynamics of Life: Calculus and Probability for Life Scientists*. Pacific Grove: Brooks/Cole Publishing, 1998.
61. National Science Foundation, *User-Friendly Handbook for Mixed Method Evaluations*, 1997.
62. Andrade, J., et al., "Measurement and Medicine: Normal and Abnormal You!" a proposal (unfunded) submitted to the Department of Commerce TIIAP, March 1997. Copies available upon request. See also www.utah.edu/cise. Click on "Measurement and Medicine" for a list of programs, topics, and final description.
63. Bugliarello, G., "Merging the Artifact and its Maker," *Mech. Eng.* (Sept., 1989) pg. 46-48.
64. Norman, R.A., et al., "Bioengineering Education" A Survey of Industrial Images, Needs, and Usage," *BMES Bulletin* **15/4** (1991) 57-60.
65. Quoted by N. Lane, *Assoc. Sci. Tech. Centers Newsletter* **5/6** (1997) pg. 2.
66. Kemp, M., "Feynman's Figurations," *Nature* **394** (1998) 231.
67. _____, "Model Behavior," *The Economist*, July 18, 1998, pg. 69-70.

Appendices

- A. Letters of Interest and Involvement
- B. Budget Estimates and Financial Plan (refer also to Section K)
- C. Biographical Sketches
- D. Facilities and Equipment (refer also to section K)
- E. Current and Pending Support
- F. Justification for Secretarial and Administrative Support (refer also to Budget Justification, Appendix B)

Sorenson[™] Vision, Inc.

July 22, 1998

J.D. Andrade, Ph.D.
Professor
University of Utah
Department of Bioengineering
50 S Central Campus Dr., Rm. 2480
Salt Lake City, UT 84112-9202
801-581-4379
801-585-5361 (fax)
joe.andrade@mc.utah.edu

Dear Joe,

Thank you for the opportunity to become involved as a corporate participant in your exciting Engineering Research Center on Engineering Education Technology: Simplicity-Complexity-Simplicity.

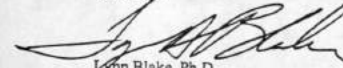
Sorenson Vision's unique data/video compression technology is directly applicable to many of your goals and objectives. You're proposed use of the World Wide Web, as a living experimental resource is absolutely fascinating. I am aware of a number of projects along that line at the junior high/high school level dealing with local environmental observations and data input which have been very powerful, have involved literally thousands of schools and tens of thousands of students throughout the world, but your application to use the Internet as a true experimental tool in its own right with various individuals, groups, or even schools and institutions participating as dynamic nodes or components of that biological or engineering network is very exciting. I am sure that this approach will greatly contribute to your objective of involving and deducing "simple" rules for the emergent behavior of complex systems. What better place to develop such a unique tool and approach than in biomedical engineering and quantitative physiology.

As you know, our technology allows full frame, full color dynamic video to be sent over normal telephone lines as well as over the Internet. This means that any of your participants and collaborators anywhere in the world who have access to normal telephone communications can be full participants in your unique projects. Although most of your academic and industrial participants will have access to high speed, high bandwidth Internet links, the Sorenson Vision technology allows them to participate from home and allows the participation of those in perhaps more rural environments and second and/or third world situations.

I know that your program has a very strong international focus and that part of its goal is to help develop transcultural experiences and appreciations. The Sorenson Vision technology will be of great assistance in this regard.

I will be pleased to serve on your Industrial Advisory Council and look forward to working with you and to participating in this unique and timely project.

Sincerely,



Lynn Blake, Ph.D.
Chief Operating Officer

Administration
2511 South West Temple
Salt Lake City, Utah 84115
(801) 461-9700 • Fax (801) 461-9722

Sales & Marketing
2060 Walsh Avenue, Suite 194
Santa Clara, CA 95050
(408) 970-0696 • Fax (408) 970-0906

Operations/R&D
1011 West 400 North
Logan, UT 84321
(801) 792-1100 • Fax (801) 792-1101



CENTER FOR ADVANCED INSTRUCTIONAL MEDIA
Yale University School of Medicine
47 College Street, Suite 224
New Haven, CT 06510

June 30, 1998

Joseph D. Andrade, Ph.D.
University of Utah
Department of Bioengineering
50 S. Central Campus Dr., Room 2480
Salt Lake City, UT 84112-9202

Dear Dr. ^{Joe} Andrade:

I am particularly pleased to be able to offer my support and future collaboration with your proposed Engineering Research Center on Biomedical Engineering Education. Clearly, the approach you have taken will offer a fresh look at an integrated approach to this curriculum. There is no question that the educational need for improved approaches and tools to teach biomedical engineering is acute.

As academic director of Yale's Center for Advanced Instructional Media, I have had a great deal of experience over the last decade in assisting our faculty and others to improve the process of the electronic curricular material. I believe I can be equally useful in collaborating with your project and am genuinely enthusiastic about the prospect. We have been investing considerable resources and time in developing electronic course support for our biomedical engineering undergraduate major, and I believe there will be many common areas which will benefit from interactions and the advice and support that I can give.

Knowing your long term commitment and past investments in these areas of educational development, I am confident that a successful long term project integrating multiple collaborators will not only be possible but effective under your leadership.

Sincerely,

C. Carl Jaffe, M.D., F.A.C.C.
Professor of Medicine
Academic Director, Center for Advanced Instructional Media

ccj/med

203.737.5026, phone
203.737.5034, fax
URL: http://info.med.yale.edu/caim/C_HOME.HTML

nDV LLC
1338 Kensington
Salt Lake City, UT 84105

J.D. Andrade, PhD
Professor
University of Utah
Dept of Bioengineering
50 s. Central Campus Drive, Rm 2480
Salt Lake City, UT 84112-9202

Dear Dr. Andrade,

Thank you for the opportunity to present nDV's parallel coordinate methods for handling and visualization of complex, multidimensional data sets. The name of our company, nDV, stands for n dimensional visualization; I believe we are unique in the world with our ability to see and understand the (visual) geometry of parallel coordinate spaces. I am pleased that this has evolved into a major thrust and research area in your proposed ERC. We are delighted to have our techniques and our team plan to play a key role in your project.

We are eager to apply our approaches to a range of biological and medical needs. Although much of our experience to date has been in applying these approaches to complex economic problems and systems, our major interest and objectives are in biological and medical systems. As you may recall, my son Royce has a PhD. in Bioengineering from your program.

A reason for our interest in biological systems at Utah originates in the contact we have had with the human genome project here at the University and the Hughes center. In 1987 Ray Gesteland reviewed his program and plans with us in the Computer Science Dept, and my principle interest and concern at the time was how to search (and match) those large DNA sequences using classical computer techniques. My interest in biology and medical systems has continued, and we now think we have a new and uniquely powerful way for people to see (and tour) multidimensional structures.

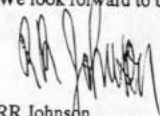
The technique we use for this sort of thing we call SB (Single-point Broken-line Parallel) Coordinates because it allows us to generate a single point (for multidimensional data spaces) superimposed on classical 3D orthogonal coordinate geometric spaces. This technique promises to be especially useful for discerning relationships in data defined multicoordinate (or multiparameter) spaces in conjunction with classical 3D geometries of other related structures.

Conventional Parallel Coordinate techniques generate n (visualizable) points in n parallel coordinates from the (conceptual)(not see-able) single point in n coordinate orthogonal space. These techniques when supplemented with our unique understanding of the visual geometry of Parallel Coordinate Spaces allow people to understand, and generalize on (curve fit) what has previously been "seen" to be only noisy, confusing, or apparently random behavior. This appears to be particularly important when interesting data structures do not line up with the (parallel) coordinates; rotating the data space allows generation of "new" coordinates that parallel the data structures of interest. With these new coordinates that align to the data structures of interest, we believe we will be able to curve fit and analyse data that has never previously been understood.

Our multidimensional visualization work originated in my personal research aimed at understanding million dimensional spaces; we used the Digistar projector at the Hansen Planetarium for this work. nDV's visualization techniques can be readily projected on any large dome driven by an E&S Digistar Projector. This huge display literally envelopes the viewer in his data space. This capability appears to be of interest to people in the military for Command and Control Situation Management, and I expect it to be of interest to people working in very large data spaces involving many dimensions or parameters.

nDV is a small company, so we cannot promise nor commit significant monetary resources to your Center yet. We can commit and make available our scientists and engineers, our facilities, and our rapidly evolving technologies for multi-parameter visualization.

We look forward to being a key participant.



RR Johnson
Principal

Protein Solutions, Inc.

391 G Chipeta Way Suite 320 Salt Lake City, UT 84108 Phone/FAX 801-583-9301/801-583-4463

July 22, 1998

Dr. J.D. Andrade
Department of Bioengineering
College of Engineering
University of Utah
Salt Lake City, Utah 84112

Dear Joe,

Thank you for the opportunity to discuss and review your NSF Engineering Research Center application on Bioengineering Education Technology.

Protein Solutions, Inc. (PSI) is very interested in being an industrial participant in this unique and important project. Like many biotechnology companies we are looking for the kind of bioengineers you are proposing to produce in your program. While traditional skills, motivation, commitment and persistence are always essential characteristics of a good employee the creativity and ability to deal with a complex non-traditional project involving biology, physiology and biochemistry is highly desirable in a multi-disciplinary, biotechnology company such as ours.

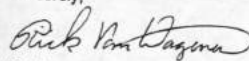
As you well know, our particular interest and focus is biosensor development, specifically the monitoring and eventual management of metabolic diseases. We are, therefore, particularly interested in your undergraduate project dealing with a biomimetic liver. Although we are certainly not interested in producing an artificial liver, the biochemical, metabolic and bioengineering knowledge which the students working on that project will develop and generate would make them extremely valuable to PSI.

I am also intrigued by your use of the World Wide Web as a research tool. Our present interests in this area are to use the web as a means of interacting with both patients suffering from chronic metabolic diseases and health care providers. Your idea of using the web as an experimental tool with patients or students serving as nodes or components is quite fascinating. One could envision a network of phenylketonuria patients, for example, learning about and experimenting with the management of their disease using a small network model representing all the known components and influences on phenylalanine metabolism.

At this time we are still a small company, so we cannot promise nor commit major monetary resources. We can, however, commit to make available to your students our scientists and engineers, our facilities and our rapidly evolving and developing quantitative dipstick assays for key components of metabolism. Given our corporate focus on metabolism and metabolic networks, we will certainly wish to utilize the tools and models you develop related to metabolic network modeling, simulation, and visualization.

Let me assure you that your project and the results and students that it produces means a great deal to us. We look forward to being a key participant and wish you the best of luck in obtaining support for this innovative program.

Sincerely,



Rick Van Wagenen, Ph.D.
Vice President for Research & Development

X-Sender: jlinehan@mcw.edu
Date: Thu, 23 Jul 1998 14:17:12 -0500
To: joe.andrade@m.cc.utah.edu
From: Jack Linehan <jlinehanj@vmsb.csd.mu.edu>
Subject: NSF/ERC proposal
Cc: *Kristina Ropella, Ph.D.* <k.ropella@vmsb.csd.mu.edu>,
clough@marque.mcs.mu.edu (Anne Clough)
Mime-Version: 1.0
Status: U

Hi,
Hope it's not too late to respond to your kind invitation to join your initiative as a participating institution. We'd be very pleased to be included. In particular, Kris Ropella (biomedical engineering) and Anne Clough (biomathematics) are enthusiastic about your concept and would specifically like to be considered as contact faculty at Marquette. Anne will be in San Diego with us and would be pleased to meet you there. She is giving an exciting poster related to her work as a "young investigator". Kris Ropella will be there next year.
Cheers..... jack

John H. Linehan, Ph.D.
Bagozzi Professor and Chair
Biomedical Engineering Department
Marquette University
P.O. Box 1881
Milwaukee, WI 53201-1881
Office #'s (414) 288-3375 (MU)
(414) 288-7522 (voice mail)
(414) 384-2000 (VA)
ext. 1440
Fax #'s (414) 288-7938 (MU)
(414) 384-0115 (VA)
<http://www.eng.mu.edu/~bien/index.html>

Printed for joe.andrade@m.cc.utah.edu (Joseph Andrade)



July 22, 1998

Prof. J.D. Andrade, Ph.D.
Department of Bioengineering
The University of Utah
2480 Merrill Engineering Building
Salt Lake City, Utah 84112

School of Engineering
Biomedical Engineering
David Z. D'Argenio
Professor and Chairman

Dear Prof. Andrade:

On behalf of the faculty in the Department of Biomedical Engineering at the University of Southern California, I enthusiastically accept the invitation to serve as a Participating Institution in your proposed Bioengineering Education Technology Center.

As you know, the Department of Biomedical Engineering at USC has been actively involved in modeling and simulation of biomedical systems for many years. Since 1985 these activities have been carried out in the Department under the auspices of the Biomedical Simulations Resource (BMSR) Center, which is supported by the National Center for Research Resources at the NIH. The BMSR focuses on the development of advanced modeling and simulation methodologies for studying a variety of biomedical phenomena including mechanisms of memory and learning, sleep disorders and mechanisms of action of therapeutic drugs. The methodologies developed have been applied broadly by ourselves and other investigators working in neural science, sensory systems, cardiorespiratory physiology and therapeutic drug development. Four of the Department's eight primary faculty (Profs. Berger, D'Argenio, Khoo and Marmarelis) serve as principal scientists of the BMSR, which also includes other collaborators including Dr. Gilbert Chauvet. Dr. Chauvet, who as you know is internationally known for his texts which implement a rigorous and extensive systems framework for studying biomedical processes, also teaches in our graduate course on neural engineering.

Taken together, the robust research and established academic programs of the Department of Biomedical Engineering at USC, along with our undergraduate and graduate student body and aforementioned faculty, could serve as a valuable member of your group of Participating Institutions. We look forward to working with you in the establishment of an Engineering Research Center in Bioengineering Educational Technology.

University of
Southern California
Olin Hall of
Engineering 500
Los Angeles,
California 90089-1481
Tel: 213 740 0838
Fax: 213 740 0343
e-mail:
dargenio@bmsr.usc.edu

Sincerely,

David Z. D'Argenio, Ph.D.



Center for Functional Imaging
June 22, 1998

Joseph D. Andrade, Ph.D.
University of Utah
Department of Bioengineering
50 S Central Campus Drive, Room 2480
Salt Lake City, UT 84112-9202

Dear Joe,

Thank you for the information on your proposed ERC on Biomedical Engineering Education. The UCB/UCSF team have already begun a proposal with Stanford with Professor James Casey as the PI. I proposed that we interact with your program and, whereas we believe your personal as well as institutional strengths would handsomely compliment our approaches, the team here decided to submit the UCB/UCSF/Stanford ERC.

In any event, a number of our faculty will be interested in your proposed visiting professor program as well as serving as off campus advisors for the projects and other activities.

Sincerely,

Thomas F. Budinger, M.D., Ph.D.
Henry Miller Professor of Medical Research, UCB
Professor of Radiology, UCSF
Head, Center for Functional Imaging, LBNL

TFB:hj



School of Biomedical Engineering,
Science and Health Systems
32nd and Chestnut Streets
Philadelphia, Pennsylvania 19104
TEL 215 895-2215
FAX 215 895-4983

July 22, 1998

Joseph D. Andrade, Ph.D.
Department of Bioengineering
2480 Merrill Engineering Building
The University of Utah
Salt Lake City, Utah 84112
Tel# 801-581 8528

Dear Dr. Andrade,

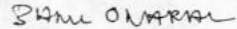
On behalf of our faculty, I am delighted to accept your invitation for Drexel University to take part in the Engineering Research Center proposal titled "From Simplicity to Complexity to 'Simplicity'" which you plan to submit to the National Science Foundation. I will also be pleased to serve on the Academic Advisory Council as the representative from Drexel. As a participating institution, we will be prepared to exchange curricular materials, faculty and students as well as share with you and your colleagues our many years of experiences with an integrated engineering curriculum and the project-based approach to education. As we have discussed, a recent development at Drexel which may have impact on your project is the 'Engineering Collaboratory 2001' initiative. This effort is an extension of our already successfully tested and implemented Web-based Engineering Design Laboratories which serve our entire class of engineering freshmen and a portion of our sophomores. We are currently working with a consortium of Universities willing to participate in the national deployment of the collaborative experiential learning opportunities in engineering education.

At the research thrust level, we are particularly excited about the opportunity to actively contribute to the Modeling and Simulation of Complex Systems Research Thrust of your Center. As we have discussed in our earlier meetings, the 'complex systems' and 'evolutionary systems' curricula have been part of the graduate education experience at Drexel since early '90s; we have offered, advised and supervised courses and research/design projects. These emerging concepts, theories and tools have also been embedded in our undergraduate Biomedical Engineering curriculum which will begin with the Fall'98 inaugural class. We look forward to exchanging with you our course and project material and to enriching our offerings with your contributions.

Let me take this opportunity to review with you once again our counterpart plans to establish the Center for Educational Research and Development in Biomedical Engineering and reiterate my invitation to you to serve on our External Advisory Board. As in your case, we view our Center as an 'imperative' for Drexel, an initiative which is an evolutionary consequence of our traditional investment in targetted engineering research, our deep commitment to experiential learning and our decade-long efforts to reengineer engineering education.

As we have agreed, the synergy between our two centers is enticing. By linking our two operations and leveraging our complementary resources, I am confident that we are jointly poised to affect biomedical engineering education in a unique and compelling way.

With warm regards,



Banu Onaral, Ph. D.
H. H. Sun Professor and Director



27 July 1998

J.D. Andrade, Ph.D.
Professor
University of Utah
Department of Bioengineering
50 S Central Campus Dr., Rm 2480
Salt Lake City, UT 84112-9202
801/581-4379
801/585-5361 (fax)
joe.andrade@m.cc.utah.edu

Dear Joe,

I enjoyed our discussions the other day at Sarcos on your integrated four year, project-based program for undergraduate bioengineering education. As you know, I have been a proponent of project-based education for over thirty years, indeed, it is one of the objectives of the Center for Engineering Design (CED) which I established at the University of Utah over twenty years ago.

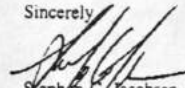
I am a firm believer that engineering education should be turned upside down. Rather than present three to four years of didactic classroom, cook book laboratory course work and experience, followed by a relatively small short duration senior design project, students should become involved with a project at the earliest possible time, possibly even in high school or junior high. If they have an interest, preferably a passion, in a project or subject they should be given the opportunity to work on that almost immediately. We both know and appreciate that motivation and interest is the key to learning. Leonardo perhaps said it best: "Study without a liking for it spoils the mind and retains nothing." The truly motivated student/engineer will learn what he/she needs to learn in order to pursue and complete the project.

Key aspects of a successful engineer include creativity, commitment, perseverance, and intelligence. The most important attribute, however, is interest and passion in the subject. These are the engineers we like to hire at Sarcos and our affiliated companies. These are the engineers that we try to produce via the CED and its projects and activities at the University of Utah. What you are proposing to do is right on and long overdue.

We will be happy to assist in any way we can.

Thanks for the opportunity to participate.

Sincerely,



Stephen Jacobsen, Ph.D.
Director, Center for Engineering Design

Center for Engineering Design
College of Engineering
3176 Merrill Engineering Building
Salt Lake City, Utah 84112
(801) 581-6699 / FAX (801) 581-5304

July 6, 1998

Dr. J. D. Andrade
Professor
Department of Bioengineering
2480 Merrill Engineering Building
University of Utah
Salt Lake City, Utah 84112

Dear Dr. Andrade:

The Department of Biological and Irrigation Engineering at Utah State University would be most interested in collaborating in the proposed "Engineering Research Center on Biomedical Engineering Technology". We understand we would be a "participating institution" in the ERC application.

I would have three specific areas of interest. First, I would like to involve one or more of our biological engineering courses. Those courses that may be considered would include: (1) BIE 1880 "Biological Processes"; (2) BIE 2330 "Engineering Properties of Biological Materials"; (3) BIE 3000 "Biosensors and Instrumentation"; (4) BIE 3200 "Bioengineering Unit Operations"; (5) BIE 5160 "Methods of Cell Culture"; (6) BIE 5240 "Protein Purification"; (7) BIE 5260 "Methods of Molecular Cloning"; (8) BIE 581 "Biochemical Engineering"; and (9) BIE 5850 "Biomaterials Engineering". I can send more detailed descriptions should you need them.

The second area of USU interest would be in student exchange. In addition to the use of our courses by your students, we would be particularly interested in your biomedical courses as technical electives for our students. This is an area of our program that is deficient.

And finally, we would enjoy the opportunity to exchange faculty. We would only have one or two of ours that would be directly involved as the rest are irrigation engineers. Thus, such exchanges would substantially enhance our program.

I'll be in Ecuador until the week of July 13th but should be at USU for most of the rest of the summer. I'll look forward to your visit and an opportunity or renew our discussion of biological engineering.

Best Regards,



Wynn R. Walker
Professor and Head

Gilbert A. Chauvet, M.D., Ph.D.

Professor of Theoretical Biology

Sciences Faculty Poitiers University
Sciences Faculty Poitiers University
Sciences Faculty Nantes University
Sciences Faculty Nantes University
School of Medicine Angers University

B.S. 1964 Pure Mathematics
M.S. 1965 Applied Mathematics
Ph.D. 1968 Solid Physics
Ph.D. 1973 Molecular Physics
M.D. 1976 Medicine

PROFESSIONALEXPERIENCE

1969-72 Assistant Researcher in Molecular Structures, Angers University
1972-76 Associate Professor of Biophysics, Macromolecular Physics & Modeling, Angers
1976-80 Professor, Biomathematics, Modeling & Medical Computing Systems, Angers
1980- Professor, Theoretical Biology, Modeling & Medical Computing Systems, Angers
1984- Director of the Medical Computing Department, Regional Hospital Center, Angers
1986-87 Chairman-Founder, French Society for Theoretical Biology
1988- Director-founder, Institute of Theoretical Biology, University of Angers
1994- Research Professor, Dept of Biomedical Engineering, USC, Los Angeles

PUBLICATIONS RELATED TO THE PROPOSED RESEARCH

- Chauvet G., Taravel B., Lorenzelli V., A preliminary method of frequency assignment to molecular vibrations, *Journal of Molecular Structure*, 20, 189-196 (1974).
Chauvet G., On the resolution of the secular equation in the vibrational analysis of biological macromolecules, *Annales de Physique Biologique et medicale*, 9, 3, 157-172 (1975)
Chauvet G., Taravel B., Lorenzelli V., Delorme P., Vibrational study of Cu-environment in malachite, *Materials Chemistry*, 1, 255-266 (1976).
Lorenzelli V., Chauvet G., Taravel B., Spectroscopic investigations of metal ions in complexes and biological systems using a preliminary method of vibrational assignment, *Journal of molecular structure*, 45, 217-238 (1978).
Six P., Chauvet G., Taravel B., Lorenzelli V., On the vibrational assignment of N2O4, *Physica*, 95C, 244-250 (1978).
Six P., Chauvet G., Comparison of resolution algorithms for the secular equation in the vibrational analysis of biological molecules, *International Journal of Biomedical Computing*, 10, 97-112 (1979).
Thomas Y., Six P., Chauvet G., Taravel B., Lorenzelli V., Structural study of simple and complex oxalates in lanthanides by IR Spectroscopy, *Physica*, 98, 131-139 (1979).
Six P., Chauvet G., Mathematical Analysis of the Bronchial Elasticity, *Mathematical Biosciences*, 45, 209-226 (1979)
Six P., Chauvet G., Estimation of visco-elastic parameters of the bronchial system from dynamical trachéobronchography measurements, *Int Journal of Biomedical Computing*, 12, 349-357 (1981).
Chauvet G., Girou D., On the conservation of physiological function in a population of interactive and self-replicative units, *Lecture Notes in Biomathematics*, Springer-Verlag, Berlin, 48 (1982).
Chauvet G., The use of contact reflectometry in the investigations of dental surfaces, *Material Chemistry and Physics*, 13, 503,516 (1985)
Chauvet G., Habituation rules for a theory of the cerebellar cortex, *Biological Cybernetics*, 55,1-9 (1986)
Chauvet G., Jacquez J.A., *Proceedings: physiological regulations*, theoretical biology series Masson publisher, 250 pp. (1986).

STEVEN EDWARD KERN

April 1998

Birth Date: 24 July 1961
Birth Place: Plainfield, New Jersey
U.S. Citizen Soc Sec # 158-56-9840

Department of Anesthesiology
University of Utah School of Medicine
50 North Medical Drive
Salt Lake City, Utah 84132
(801) 581-6393 (801) 581-4367 fax
skern@carf.med.utah.edu email

Education

B.S. Mechanical Engineering: 1983, Cornell University, Ithaca, New York.
M.S. Bioengineering: 1986, Pennsylvania State University, State College,
Pennsylvania.
Ph.D. Bioengineering: 1995, University of Utah, Salt Lake City, Utah. (June 1995)

Professional Experience

Department of Anesthesiology, University of Utah School of Medicine, Salt Lake City , Utah
Research Assistant Professor, 1996 - Present.

Department of Bioengineering, University of Utah, Salt Lake City, Utah
Adjunct Assistant Professor, 1996-Present.

SensorMedics Critical Care Corp., Los Altos, CA
Product Development / New Business Manager, 1995 - 1996.

Department of Anesthesiology, University of Utah, Salt Lake City, Utah
Graduate Research Assistant, Anesthesia Bioengineering Lab 1990-1995.

C.R. Bard, Inc., Bard MedSystems Division, North Reading, MA
Development Engineering Manager, 1988-1990
Product Development Engineer, 1985-1988

Academic Awards

1. Research Award, Society for Intravenous Anesthesia, 1994.
2. Meritorious Award, Cost-Effectiveness in Anesthesia Awards Program, 1993, Zeneca Pharmaceuticals and Anesthesiology News.
3. Becton-Dickinson Graduate Fellowship Award, 1990, Dept of Bioengineering, University of Utah.

Research Awards

1. Co-Investigator: Development of a Closed Loop System for a Neuromuscular Blocking Agents given in Intensive Care. 1/93-1/95, NIH Phase II SBIR Grant #NS29311-04. \$498,675. J.A. Orr, Ph.D. - PI.
2. Co-Investigator: A fluid flow model for optimizing high frequency ventilation of the lung. 3/97-2/98. University of Utah Incentive Seed Grant. \$35,000. M.A. Lewis, Ph.D. - PI.

Research Awards (continued)

3. Co-Investigator: Impact of hypovolemic shock on the pharmacokinetics and pharmacodynamics of remifentanyl in pigs. 6/97-5/98, Glaxo-Wellcome. T.D. Egan, M.D. - PI.
4. Co-Principal Investigator: Personal Sensors for the diagnosis and management of metabolic disorders. 7/97-6/00 Whitaker Foundation Cost-Reducing Health Care Technologies Grant. \$769,327 J.D. Andrade, Ph.D. - PI.
5. Co-Investigator : Quantitative pharmacodynamic analysis of hypnotic and opioid interactions in volunteers. 1/98-12/98 Foundation for Anesthesia Education and Research Clinical Research Starter Grant. \$25,000 T.D. Egan, M.D. - PI.
6. Co-Investigator: Ultiva (Remifentanyl HCl): Safety evaluation of bolus doses in volunteers. Glaxo Wellcome 9/97-8/98 T.D. Egan, M.D. - PI.
7. Co-Investigator: The comparison of the clinical durations resulting from the interaction between Zemuron (rocuronium bromide) and Pancuronium Bromide in Adult general surgical subjects. Organon Inc. 12/97-12/98. J.O. Johnson, M.D., Ph.D. -PI.
8. Principal Investigator: Initial analysis of a method to use magnetic fields to induce a collision block in an explanted nerve. 4/98-3/99 TH Stanley, M.D.- Co-PI.

Publications

1. Pourdeyhimi B, Kern S: Ease of suturing surgical fabrics: a quantitative evaluation. *Am J Surgery* 1985; 149: 387-9.
2. Shafer SL, Kern SE, Stanski DR: *The Scientific Basis of Infusion Techniques in Anesthesia*. Published by Bard MedSystems Division, CR Bard, Inc. 1990.
3. Kern SE, Westenskow DR, Orr JA, Johnson JO: An effectiveness study of a new piezoelectric sensor for train-of-four measurement. *Anesth Analg* 1994; 78:978-82.
4. Kern SE, Johnson JO, Westenskow DR, Orr JO: A comparison of dynamic and isometric force sensors for train-of-four measurement using submaximal stimulation current. *J Clin Monit* 1995; 11:18-22.
5. Kern SE, Westenskow DR: Pharmacokinetic-based mini bolus delivery as an alternative to continuous infusion for drugs that exhibit a biophase lag. *J Pharmacokinet Biopharm*, in press.
6. Kern SE, Westenskow DR: Fuzzy logic for model adaptation of a pharmacokinetic-based closed loop delivery system for pancuronium. *Artificial Intelligence in Medicine*, 1997; 11:9-31.
7. Kern SE, Johnson JO, Orr JA, Westenskow DR: Clinical analysis of the flexor hallucis brevis as an alternative site for monitoring neuromuscular block from mivacurium. *J Clin Anesth*, 1997; 9:383-387.
8. Lu JK, Manullang TR, Staples MH, Kern SE, Bailey PL: Maternal respiratory arrests, severe hypotension, and fetal distress after administration of intrathecal sufentanyl and bupivacaine after intravenous fentanyl. *Anesthesiology* 1997; 87:170-172.
9. Johnson JO, Kern SE: Bispectral electroencephalographic analysis for patient monitoring during anesthesia. *Advance in Anesthesiology*, in press.