

Center for Biofilm Engineering

*a National Science Foundation
Engineering Research Center
at Montana State University–Bozeman*

2003 Annual Report

Text Only

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Mission

The mission of the National Science Foundation Center for Biofilm Engineering is to advance the basic knowledge, technology and education required to understand, control and exploit biofilm processes.

Goals

The CBE has identified goals in three areas of activity:

Research:

The CBE's goal is to do leading edge fundamental and applied research to elucidate the nature and behavior of microbial biofilms.

Education:

Key to the CBE's success is the goal to sustain an interdisciplinary undergraduate and graduate education program, involving team research on industrially relevant projects.

Technology Transfer:

The CBE's goal is to make its research relevant to real systems through regular, intentional interaction with, and input from, industrial partners.

Director's Message

Dr. J.W. Costerton

During the past year, the CBE has solidified its position as the world's premier center for study in the burgeoning fields of biofilm microbiology and biofilm engineering. This reinforced position constitutes the fruition of a three-part strategy that is deeply embedded in the leadership of the Center (the Executive Committee and the Director).

First, the CBE has built a dynamic team of talented researchers from a wide range of disciplines. A constant stream of motivated students and post-doctoral researchers contributes to, and benefits from, the CBE research/education program. The tenured professors are solidly successful, the research staff are "seething" with activity, the students grow from strength to strength, and the team has never been stronger!

Second, the CBE team is balanced in its research programs, in its personnel, and in its approach to the study of biofilms. As we prepare for the ASM Conference on Biofilms 2003 (Nov. 1–6, in Victoria, B.C.), it becomes very obvious that many of the biofilm groups that have sprung up in the last three years have been restricting their attention to the details of the genetic mechanisms of major discoveries made (at least in part) in the CBE. In contrast, the CBE team includes people from at least nine different departments—with an even larger range of conventional academic disciplines—and the balance of perspectives provided by these interdisciplinary teams keeps CBE research properly focused on critical issues that can limit the field or move the field forward.

Third, the CBE is faithful to its original charter as an Engineering Research Center (ERC), in that it links education and technology transfer firmly to its innovative research in biofilms. The 76 graduate and undergraduate students who participated in the CBE education program during the past year were remarkably productive, as the following pages will demonstrate. In addition, a large grant from the Murdock Charitable Trust has enabled us to add the latest in confocal microscope technology to our facilities, and we are proud of the fact that our students have access to training on all of this equipment.

In the past year the CBE has assumed an even more proactive stance in matters of outreach and

technology transfer. While many articles have been written about the CBE (*Science*, *Nature Biotechnology*), we are also well represented by CBE-authored articles in high-profile publications (*Scientific American*, *JAMA*, *Lancet*). This concerted outreach effort is positioning the CBE as a primary source for biofilm information and education beyond the MSU–Bozeman campus. Discoveries made in other laboratories are now routinely brought to the Center for confirmation by our research teams and for presentation to our sponsoring companies. Industrial membership (23 companies, currently) remains stable and strong, and the volume of industry-sponsored research (\$1.4 million) is higher than at any time during direct support from the ERC program.

As direct financial support from the NSF's ERC program neared termination in April, 2001, the CBE's leadership reconfirmed its commitment to the interdisciplinary team approach established by the ERC grant. The CBE has held fast to its original goals: to make industrially relevant advances in biofilm research and to re-shape university science and engineering education. By any objective set of criteria, these goals have been achieved, and the Center can look back on a remarkably successful year.

Full text of the Director's Message is available in Appendix 2: Supplemental Information, as well as on the CBE's web site.

Research

Research activity continued very strong over the past year, with \$3.6 million of new grant activity projected to be awarded to CBE researchers by the end of the fiscal year.

Significant new projects include:

- a federal earmark through the Department of Defense to investigate aspects of drinking water microbiology related to bioterrorism,
- a grant from the NIH to develop computer models of biofilm resistance to antibiotics,
- a large equipment award from the Murdock Charitable Trust,
- an NIH SBIR subcontract from Sequoia Scientific to develop natural products for biofilm control,
- continuations of projects related to middle ear infections funded through NIH via subcontracts from the Allegheny-Singer Research Institute,
- an award from the state of Montana that will develop biobarrier technology for preventing acid mine drainage, and
- a subcontract from Portland State University to develop a mobile field microscope unit for the direct observation of biofilm formation in nature.

Sixteen different companies, along with seven private institutions, sponsored research or sales and service projects at the CBE in the past year. These statistics illustrate that the CBE is drawing support from diverse sources.

Research Publications Impact

One way to assess research output is through publications. Fifty-five research articles were published by CBE authors during the 2002 calendar year—an all time high. These articles appeared in 37 different journals or books, showing that this research reaches a broad audience. Another interesting way to evaluate the impact of CBE publications is by using the Institute for Scientific Information (ISI) database to find out which authors in the biofilm field have been particularly prolific or influential. Of the top twenty individuals who have the most papers indexing to the keyword biofilm (or

biofilms), six are CBE researchers (Table 1). Of the top twenty individuals whose papers indexed to the keyword “biofilm” have been most cited in the scientific literature, seven are CBE researchers, or were until recently (Table 2). No other single institution has more than two researchers in either of these categories.

Murdock Award Expands Research Facilities

A very exciting development on the research front this year was the award of \$629,500 from the Murdock Charitable Trust for the purchase of a new confocal scanning laser microscope and a flow cytometer. The pairing of these instruments will give the Center a special capability: the ability to quantify the colors in an image by harvesting the biofilm and running the cells through a flow cytometer. The new microscope also has a two-photon unit attached that will provide greater depth of light penetration. This will allow CBE researchers to image thicker biofilms than we have been able to in the past.

Grants and Awards

NIH Award: Modeling Antibiotic Susceptibility of Bacteria in Biofilms

Dr. Phil Stewart, Chemical Engineering Professor and the CBE’s Deputy Director, has been awarded a four-year grant from the NIH to develop mathematical and computer models of biofilm formation that can be used to investigate antibiotic resistance mechanisms in biofilms. Collaborating faculty include Drs. Paul Stoodley, Jack Dockery, Isaac Klapper and Marty Hamilton. An experimental portion of the project is designed to integrate with the large ongoing project sponsored by the W.M. Keck Foundation.

Grants to Study S. aureus

Dr. Mark Shirtliff received an NIH Materials Grant for reagents and microarrays to study *Staphylococcus aureus* biofilms. He also received awards from the Culpepper Foundation, Rockefeller Brothers Fund, and the Montana Network for Biomedical Research Opportunities to assist in the study of *S. aureus*.

NIH Small Business Technology Transfer Grant

Dr. Luanne Hall-Stoodley received a National Institute of Allergy and Infectious Diseases (NIAID) grant titled “Tubercle bacilli binding to host cells: Vaccine design” in collaboration with LigoCyte Pharmaceuticals in Bozeman, Montana.

Engineered Biofilms to Detect Bioterrorism Agents

The CBE received federal funding, via the Department of Defense (DOD), for a new initiative in the use of engineered biofilms in the detection of bioterrorism agents. The CBE's partner in this cooperative project is MSE Technologies, Inc., of Butte, Montana.

Sequoia Grant Award

Sequoia received a Phase II SBIR grant for \$1 million, of which the CBE will receive a subcontract to screen various plants for anti-biofilm activity. Dr. Mark Pasmore and Jennifer Sestrich will participate in this project.

Monitoring Biofilms in Remote Environments

Drs. Paul Stoodley and Peter Suci were subcontracted to work on a project funded by a W.M. Keck Foundation grant via Portland State University to develop a mobile biofilm field unit for observing biofilms microscopically in remote environments.

Biofilms in Advanced Prostatitis Research

Dr. Richard Veeh is collaborating with Drs. Rod Donlan and Lisa Hodges of the Centers for Disease Control (CDC) on a prostatitis project recently funded by the National Center for Infectious Disease. Ultimately, the technique developed in this collaborative work will be used to assess microbial colonization in clinical prostate tissue biopsies.

Research Highlight:

Biofilm Mechanics at the CBE

Researchers are just beginning to think about biofilms as multicellular organisms. One of the ways that microbial cells interact in a biofilm is mechanically. Aggregates of cells experience forces from fluid flow and transmit these forces, via the extracellular matrix, to other cells. Mechanical forces deriving from fluid shear can cause biofilm structures to deform and move. The importance of mechanical interactions is intuitively obvious, but it has only been in the last few years that researchers have begun to address these phenomena in earnest. The largest effort of this kind is here at the CBE under the direction of Dr. Paul Stoodley. He has built an interdisciplinary group of mechanical, civil, and chemical engineers, as well as mathematicians and microbiologists to look at biofilms as complex interactive materials.

One of the insights now emerging from this team is that the mixture of cells and extracellular polymeric substances in a biofilm behaves as viscoelastic fluid. This means that over long time scales (hours or days) the biofilm will respond to fluid shear forces by flowing. Over short time scales (seconds or minutes), biofilms respond to forces as if they were elastic; they deform, but return to their original shape once the stress is relieved. Viscoelasticity has been observed for every biofilm the Stoodley group has examined. It is intriguing that biofilms are fluid and can "morph" into a wide variety of forms in response to fluctuating nutrient and mechanical stresses in the local environment. It invites the question: how much of this is an incidental property of the biofilm and how much is it an adaptive survival trait?

Biofilm Mechanics Research Team

Dr. Paul Stoodley, Research Team Leader
Civil Eng. & Microbiology
Suzanne Wilson, Research Associate
Boloroo (Laura) Purevdorj, PhD, Microbiology
Todd Shaw, PhD, Mathematics
Brett Towler, PhD, Civil Engineering
Patrick Norris, MS, Mechanical Engineering
Zachary Bell, BS, Microbiology
Cory Rupp, BS, Mechanical Engineering
Margo Schurman, BS, Statistics
Scott Warnick, BS, Electrical Engineering
Matt Winston, BS, Mechanical Engineering

Collaborating Faculty

Dr. Al Cunningham, Civil Engineering
Dr. Marty Hamilton, Statistics
Dr. Isaac Klapper, Mathematics
Dr. Joseph Seymour, Chemical Engineering
Dr. Phil Stewart, Chemical Engineering
Dr. Aleksandra Vinogradov, Mechanical & Industrial Eng.

CBE Publications Highlights

Two CBE papers were featured as ASM News Highlights in this reporting period. These journal highlights consist of summaries of the six best ASM journal articles for the month. Authors of the papers were (September 2002 issue): B. Purevdorj, J.W. Costerton and P. Stoodley; and (February 2003 issue): M.C. Walters, F. Roe, A. Bugnicourt, M.J. Franklin and P.S. Stewart.

A complete list of publications is available in Appendix 2: Supplemental Information, or on the CBE's web site at:

<http://www.erc.montana.edu/Res-Lib99-SW/pubs/>

More about CBE research:

CBE Annual Report
Appendix 1: Research Project Summaries
(restricted to CBE Industrial Associates)
or on the CBE's web
site at:

<http://www.erc.montana.edu/CBEssentials-SW/research/>

Education

The Center for Biofilm Engineering continues to take pride in its innovative education program, established during the formative years of its funding as an NSF Engineering Research Center. The foundations of the CBE's education experience include a multi-disciplinary approach to research projects, state-of-the-art facilities in contiguous laboratories, interaction with industry, and the CBE's long-standing reputation as a pioneering leader in biofilm research. The CBE education program trains students to bridge the gaps between academic disciplines, as well as between fundamental knowledge and applied technology. During the academic year 2002–2003, the CBE provided research experiences for 24 graduate and 52 undergraduate students (including Summer 2002 REU program participants). The CBE continues to attract outstanding students to participate in its programs.

Goals of the CBE Education Program

The primary goal of the CBE's education program is to train graduate and undergraduate students in concepts and methods that make them attractive candidates for positions in academia, industry, government agencies, and consulting. The CBE aims to provide students with a high quality research education experience in a specific discipline while giving them opportunities to work as members on multidisciplinary teams. During this past year, research projects were sponsored by federal agencies (NSF, NIH), the State of Montana, the W. M. Keck Foundation, and industry.

Interaction with Industry

Students within the CBE value the interaction provided by our industrial partners and the companies directly supporting research. Because of contact with the Center's industrial partners, students are acquainted with industry needs and perspectives. Students present their research results verbally or in poster format at meetings held twice yearly with CBE Industrial Associates. Additionally, some students are invited to present their research results to a sponsoring company. CBE students also have the opportunity to meet individually with representatives from member companies and with non-member representatives who visit the Center each year.

Integrating Communication

Another key component of the CBE's education program is communication skills development. Students learn to express themselves in seminars, written work, and formal presentations to a wide variety of audiences. Over the years CBE undergraduates have co-authored twenty-two peer-reviewed articles, including eight during this reporting period. This kind of experience provides them with the knowledge and confidence necessary for a successful professional career.

Graduate Program

Each graduate student pursues a degree in a specific discipline offered through an academic department at MSU–Bozeman, but conducts research at the CBE and participates in CBE activities and programs. Enrollment typically includes students from the life sciences, physical sciences, and engineering.

During this past year, there were ten MS and fourteen PhD students at the CBE. Seventeen were male and seven were female. The majority of students (17) were enrolled in engineering disciplines, with the remainder in microbiology (5) land resources and environmental sciences (1), and mathematics (1).

Graduates Through the Years

121 Masters and Doctoral students have earned their degrees in the CBE's graduate program since the Center was founded in 1990.

2003 W.G. Characklis Award Winners

The annual W.G. Characklis Award, created in honor of the Center's founder, is presented to a CBE doctoral student in recognition of his or her exemplification of the Center's core values and excellence in research. This year's awardees were Thomas Borch, Environmental Sciences; and Stephen Hunt, Chemical Engineering.

Thomas Borch's research projects address the fate and bioavailability of explosives in model soil systems. He has had four articles published in peer-reviewed journals and has been invited to present his work at several national and international conferences. Thomas has also assisted in teaching classes and in the development of a new graduate level course, mentored undergraduate research students, and helped coordinate the weekly CBE seminar series. Stephen Hunt's dissertation project is probably one of the most interdisciplinary of all projects ever conducted at the CBE. He has built a computer model to simulate biofilm dynamics in 3-D, and he is applying that model to study important questions about biofilms. His model is an important research tool that will benefit the CBE for years. In addition to his research responsibilities, he is a resident computer technology expert; his assistance is often requested—and never denied.

Coursework in Biofilms

In addition to courses required for the student's home department and degree program, the CBE suggests a suite of courses for graduate students:

ENVE 566 Fundamentals of Biofilm Engineering I
(recommended for all CBE students)
ENVE 534 Environmental Engineering
Investigations
ENVE 565 Chemical Sensors for Environmental
Biotechnology
Microbiology Elective
(suggested for CBE engineering students)
Thursday Seminar Series

Information about these courses can be found in the 2003 Appendix 2: Supplemental Information.

Graduate Student Highlight

Stephen M. Hunt
Ph.D. Candidate, Chemical Engineering

“During my Master's work in Chemical Engineering, I became interested in the statistical evaluation of computer models by comparison to experimental data. I explored the possibilities of PhD work and was directed to a statistical modeling project of interest to scientists in the Center for Biofilm Engineering (CBE). The model would synthesize the biological, chemical, and physical processes known to determine the life-cycle of a bacterial biofilm and be a tool for exploring the implications of the scientific conjectures. Fortunately, I decided to take on the task of building the computer model as my PhD dissertation research project. In doing so, I ventured into one of most interdisciplinary projects at the CBE. My project has required that I become proficient in the fields of computer science, mathematics, microbiology, and statistics. As a computer modeler, I feel that my breadth will be a great asset in either an academic or industrial career.”

Stephen Hunt's Awards and Activities

- W.G. Characklis Award
- Keck Fellow
- Instructor for ChE220 Computations and ChE525 Numerical Analysis
- Youth program director and active board member of the Five Rivers District of the American Red Cross

Undergraduate Research Program

The CBE offers excellent research opportunities for undergraduate students who are interested in interdisciplinary research, exposure to industry, a unique educational experience, and a competitive advantage in their career choices following graduation. Students may work on projects individually or on teams with other CBE research staff and students; for one semester or for several years; and for course credit or stipend. Upon completion of their undergraduate degree, many of these students are recruited by the CBE's industrial partners. For those pursuing graduate degrees, their CBE research experience is often cited as a key component in being recruited and selected by the program and institution of their choice. Figure 2, below, provides an overview of the 2002–2003 undergraduate student participation.

Undergraduate Student Recruitment and Funding Opportunities

The CBE is assertive in recruiting a high-caliber and diverse undergraduate student contingent.

Undergraduates are recruited for CBE program participation from MSU as well as from other domestic and foreign colleges and universities.

Women have historically been well represented in the education program. In recent years the CBE has put particular effort into working with MSU's Native American Studies program to attract Native American students to science and engineering research. Undergraduate funding comes from a number of programs:

Biofilm Systems Training Laboratory (BSTL)

Internship Program and Industrial Sponsorship

Undergraduate Scholars Program

Computer Science, Engineering, and Mathematics Scholarship (CSEMS)

Montana Apprenticeship Program (MAP)

through MSU's Native American Studies

NIH BRIN Program

Summer program through MSU's Native American Studies

NSF Research Experience for Undergraduates (REU): Summer program

Information about these programs and funding opportunities can be found in the 2003 Appendix 2: Supplemental Information, or on the CBE web site at: <http://www.erc.montana.edu/CBEssentials-SW/education/ed-basics-03-ug.htm>

Undergraduate Student Highlight

Jeremy Mitchell, CBE Undergraduate Researcher, Chemical Engineering

“Working in the CBE has been one of the best opportunities I have had while being an undergraduate at Montana State in Chemical Engineering. I have worked under the mentorship of both Dr. Jeff Leid and Dr. Mark Shirliff on a variety of projects. Under Dr. Leid, I was able to research human leukocyte interactions with *Staphylococcus epidermidis* biofilms and to test Ted Turner's local herd of buffalo for Johnes disease. With the supervision of Dr. Shirliff I am looking into the changes in gene expression and protein production in *S. aureus* biofilms using microarrays and two-dimensional gel electrophoresis. By finding genes and their products that are responsible for the biofilm mode of growth, we hope to identify effective vaccine candidates, novel targets for antimicrobial agents, and new diagnostic strategies. Dr. Shirliff, Dr. Leid and the other members of the CBE have helped me to understand the importance of research and have significantly aided my educational experience through hands-on learning. After graduation, I am planning to attend medical school in Missouri and eventually return to Montana to be a primary care physician.”

Jeremy Mitchell's Awards and Activities

- Undergraduate Scholars Program research grant, 2001 & 2002
- Gary Norby Foundation Scholarship, 1998 & 1999
- Campus Crusade for Christ President, 2001-2002
- Student Health Advisory Committee Chair, 2002-2003

2002–03 Undergraduate Scholarship Program Awards

Seven students were awarded undergraduate scholarships for the 2002–03 academic year to work on CBE biofilm research projects:

Suriani Abdul Rani, Chemical Engineering
Mentor: Phil Stewart
“Diffusion of stains in *Staph epi* biofilms”

Wesley Bauman, Civil Engineering
Mentor: Anne Camper
“Effectiveness of chloramines used as the recharge biocide on rechargeable biocidal surfaces”

Sarah Golden, Biological Sciences
Mentor: Haluk Beyenal
“Microbial fuel cells”

Amber Harrer, Chemical Engineering
Mentor: Phil Stewart
“Spatial patterns of killing in *Pseudomonas aeruginosa* biofilms”

Jeremy Mitchell, Chemical Engineering
Mentor: Mark Shirliff
“Leukocyte response to biofilms”

Deanne Stookey, Biological Sciences
Mentor: Haluk Beyenal
“Reproducible *Pseudomonas aeruginosa* biofilms”

Erin Werner, Chemical Engineering
Mentor: Phil Stewart
“Spatial patterns of growth in *Pseudomonas aeruginosa* biofilms”

A Sampling of CBE Undergraduate Projects

These research projects were being conducted by undergraduate students from a variety of disciplines in the spring of 2003:

Ivy Able, Chemical Engineering
“Developing a method to test efficacy of chemical hot tub disinfectants”

Judy Hepner, Civil Engineering
“Biobarriers to reduce acid rock drainage from mine tailings”

Shamus McCarthy, Computer Engineering
“Developing and maintaining a biofilm database”

Cory Rupp, Mechanical Engineering/Physics
“Biofilm viscoelasticity”

Woodrow Star III, Microbiology
“Mycobacterial biofilms: Preliminary assessment of attachment mechanisms”

Alison Ziegler, Biomedical Sciences
“Anti-biofilm efficacy of antibiotic bone cement”

REU Program: A Summer Dip into Biofilms

Each summer the NSF-sponsored Research Experience for Undergraduates Program brings several motivated students from across the U.S. to study biofilms at the CBE for 10 weeks. High-achieving students interested in pursuing a graduate degree or a career in industry are selected to participate in research projects defined by CBE industrial partners or principal investigators. In addition to learning new laboratory skills, all REU students participate in communications and ethics education components. REU students have authored peer-reviewed publications and presented their project results to industrial sponsors or at the CBE’s Technical Advisory Conferences.

Undergraduate Biofilm Movies

CBE undergraduates Cory Rupp and Ryan Cargo each had a biofilm movie accepted to the ASM MicrobeLibrary (<http://www.microbelibrary.org>). Cory’s movie is titled: “Staphylococcus aureus Biofilm Rolling Along the Lumen of a Glass Tube.” Ryan’s movie is: “Viscoelasticity of Staphylococcus aureus Biofilm II.” The Principle Investigator for both students’ projects is Dr. Paul Stoodley.

Undergraduate Authors

CBE undergraduates were listed as authors on eight peer-reviewed publications from June, 2002–May 2003.

Technology Transfer

Our Industrial Associates program continues to be the single largest source of research funding for the CBE. Membership in the program remained stable during 2002–2003, with 23 subscribing companies and governmental agencies. A listing of current members is shown on page 15. Continuing a trend from the past two years, the healthcare and biomedical arena remains the largest segment of the CBE's industrial support base. Household products, specialty chemicals, and water treatment industries remain strong supporters of the CBE as well. In addition to funding general CBE research, many Industrial Associate companies sponsor directed research and/or testing projects. These projects may be funded either by a single Industrial Associate company or by a consortium of members. In 2002–03, the CBE received \$1.4 million in research support from a total of 23 sponsoring companies.

Technical Advisory Conferences

The major mechanisms for interaction between CBE researchers and representatives from sponsor companies are the semi-annual Technical Advisory Conferences (see following section for details). In addition to these meetings, CBE staff routinely interact with member companies through common membership on regulatory advisory boards, such as the ASTM Subcommittee for Antimicrobial Agents and the USEPA Task Group on Disinfectant Testing. Other venues for interaction include visits by CBE faculty and staff to member companies, joint authorship on research publications, and CBE workshops (see following section).

In addition to being the primary showcase for new CBE research, the Technical Advisory Conferences (TAC) are also intended to function as a clearinghouse for biofilm-related information for industry and as a vehicle to maximize interaction between industrial representatives and CBE faculty, staff, and students.

Technical Advisory Conferences for the past year were held in Bozeman on July 23–25, 2002 and February 6–7, 2003. The Summer 2002 meeting featured more than 20 research presentations over three days, including invited presentations by outstanding non-CBE researchers: Matt Parsek, Northwestern University; Naomi Balaban, UC Davis; Craig Criddle, Stanford University; Rod Donlan, Centers for Disease Control. The Winter

2003 meeting included invited presentations by visitors from Mayo Clinic and the Center for Industrial and Medical Ultrasound (University of Washington).

Presentations at the Technical Advisory Conferences reflect the broad interests of our member companies, with sessions on biofilm control, biofilm methods, regulatory issues, cell signaling, environmental biofilms, biofilm structure and function, water distribution system biofilms, mechanical disruption of biofilms, and medical biofilms.

To keep our industrial members current on the latest techniques in laboratory biofilm study, a hands-on workshop is presented for Industrial Associates the day preceding each TAC. These workshops provide instruction on both basic and advanced techniques for biofilm study, including microscopy, proteomics, molecular techniques, cryosectioning, and respirometry. The basic and advanced workshops were attended by over 20 industry representatives during the year.

Both Technical Advisory Conferences were attended by approximately 50 Industrial Associate representatives, as well as invited guests from prospective member companies. The meetings are highly interactive, with significant time set aside for questions and discussion.

New CBE Industrial Associates

Smith and Nephew, Inc. is a technology medical device business in orthopaedics, endoscopy and wound management.

Edstrom Industries, Inc. designs automated watering systems for small animals, including sophisticated systems for animal research facilities.

CBE Industrial Associates

Aramco Services Company
Arch Chemicals
Church & Dwight Co., Inc.
Colgate-Palmolive
DePuy, Inc.
Dow Chemical Company
DuPont
Eastman Kodak Company
Edstrom Industries, Inc.
Gambro Corporate Research
Genencor International, Inc.
Genome Therapeutics Corp.
Idaho National Engineering
& Environmental Laboratory
Kurita Water Industries Ltd.
Microbia, Inc.
Philips Oral Healthcare, Inc.
Reckitt Benckiser Inc.
S.C. Johnson & Son
Smith & Nephew, Inc.
Tyco Healthcare
Union Carbide Corporation
U.S. Bureau of Reclamation
W.L. Gore & Associates

Technology Transfer Highlights

Biofilm Methods Workshops

The CBE hosted two Biofilm Methods Workshops in 2002–2003. These 2-day workshops are intended for researchers from academia, governmental bodies, and non-Industrial Associate companies. The content of the workshops is similar to that presented at the Technical Advisory Conferences (which are reserved for CBE member companies). Each workshop was attended by six to eight professionals from diverse backgrounds, including medical diagnostics, food preparation, academic biofilm study, and small business.

Biofilm Reactors

The CBE continued its close interaction with BioSurface Technologies, Inc., a Bozeman, MT, company that manufactures and sells biofilm reactors used at the CBE. The CBE has received grant funding from the State of Montana to assist the design and commercialization of new reactor designs.

Standard Methods Committee Involvement

As a member of the ASTM Pesticides and Antimicrobial Agents subcommittee, Darla Goeres, CBE Research Engineer, has been instrumental in the adoption of a standard method for the growth and enumeration of biofilm (ASTM E2196.02). Marty Hamilton, CBE Statistics Professor Emeritus, is a member of the AOAC Task Group on Disinfectant Testing. Through a contract with the CBE, he provides statistical support to the Antimicrobials Division of the EPA, a position which provides a forum to help regulatory agency personnel understand the challenges of biofilm quantification and eradication. Paul Sturman, CBE Industrial Coordinator, is a member of the Organization for Sepsis and Aseptic Procedures (OSAP) committee to develop standards for testing dental unit water line biocides.

CDC Biofilm Reactor

The CBE Standardized Biofilm Methods Research Team received \$142,100 over two years from the Montana Board of Research and Commercialization Technology to develop the CDC Biofilm Reactor into a commercial product. The Montana company BioSurface Technologies, Inc. (BST), at <http://www.biofilms.biz>, which now manufactures and sells the reactor, was a collaborator on the project. Mr. Ricardo Murga and Dr. Rodney Donlan of the Centers for Disease Control and Prevention (CDC) created the prototype reactor, and BST licensed that original design from the CDC. CBE researchers collaborated with BST to produce a marketable model that is practical to manufacture. The CBE crafted and validated the standard operating procedure for the reactor. The CDC Biofilm Reactor is useful for growing a repeatable laboratory biofilm in the presence of a continuous flow of nutrients and defined mixing. The market base for the reactor includes industrial, governmental, and academic laboratories interested in conducting biofilm research. The CDC Biofilm Reactor is used in the basic biofilm workshop that the CBE offers three times per year. In September 2003 the CBE will nominate the standard operating procedure associated with this reactor to AOAC International. If accepted, it will become the first official AOAC method specifically pertaining to biofilm research.

In the period from June 1, 2002–May 31, 2003, CBE faculty made 18 visits to industry sites to present biofilm information, tour industry facilities and discuss collaborations. Industry and government representatives made 24 visits to the CBE, besides the Summer and Winter Technical Advisory Conferences. Specific information is available in the 2003 Appendix 2: Supplemental Information.

Outreach

While undergraduate and graduate programs are the CBE's primary educational focus, CBE faculty, staff and students disseminate biofilm information to people outside the Center in a number of ways: through on-site and off-site workshops, presentations, continuing education courses, media contacts and the CBE's extensive web site.

The Center for Biofilm Engineering and its Industrial Associates are founding partners of The Biofilm Institute (<http://www.biofilm.org>), a non-profit, public-benefit corporation dedicated to providing information and education about microbial biofilms. The Institute's publication Biofilms Online (<http://www.biofilmsonline.com>) reaches a subscribed readership of 579—an increase of 386 in the past year.

Instruction Through Workshops

CBE faculty and staff participated in at least 14 workshops in the 2002–03 reporting period. Seven workshops were hosted at the CBE's laboratory facilities; three of these were developed exclusively for Industrial Associates.

Workshops on Image Analysis and Microsensors
Two workshops were offered by the CBE Structure-Function group in the summer of 2002. A Biofilm Image Analysis workshop included lectures and laboratory training in the acquisition of biofilm images and instruction in the use of biofilm image analysis software developed by the research group. A Microsensors workshop in August covered the electrochemical principles of measurements, manufacture of microsensors and demonstrations of their use in the study of microbial biofilms.

International Workshops

CBE personnel organized and delivered workshops to biofilm researchers at the Danish Technical University (Denmark) in April 2002, and the

University of New South Wales (Australia) in October 2002. These workshops featured laboratory and lecture components and will facilitate collaborative research with these institutions.

Specific information about CBE workshops can be found in the 2003 Appendix 2: Supplemental Information. Upcoming workshops are advertised on the CBE web site.

Presentations

CBE faculty and staff researchers were invited to present biofilm research in 25 states and the District of Columbia (map at right) and 12 countries during the reporting year, including:

Australia
Belgium
Chile
Denmark
England
Germany
Ireland
Italy
Japan
Sweden
Tanzania
Granada, West Indies

Outreach to Professional Science Writers

Bill Costerton was invited to present "Taming Microbial Biofilms," at the Council for Advancement of Science Writing, Inc. (CASW) Fortieth Annual Briefing: New Horizons in Science, St. Louis, Missouri, October 26–28, 2002. This gathering was held to provide science writers with the background, perspective and context they need to better understand and interpret new developments in the frontier areas of science and technology. It was also geared to meet their immediate need for "spot" news targeted to the general public.

CBE Outreach Through the Web

The CBE's web site was listed as a "Great FrontPage-Based Educational Web Site" in an online bulletin published by Microsoft.

Web Resources Reach the World

The CBE's Resource Library has been accessed nearly 7,000 times per month in this reporting period (more than 230 times a day). The Resource Library

is home to CBE publications, biofilm movies, the image library, interdisciplinary glossary, newsletter archives, directories of CBE personnel, TAC proceedings and theses. Details of the CBE web statistics can be found in the 2003 Appendix 2: Supplemental Information.

The CBE's Image Library has proved to be a useful educational resource for people around the world who wish to present biofilm concepts. Requestors include:

- Graduate students, in connection with thesis preparation;
- Professors/instructors in colleges and universities, for classroom lectures;
- CBE industrial associates, for internal company education or trade journals;
- Dental professionals and medical doctors, for educational presentations or trade journals;
- Science writers, for magazine articles;
- Academic writers, for use in textbooks.

While many requests come from the U.S., in the past year the CBE also received permission requests from Australia, New Zealand, Finland, the UK, Denmark, Germany, France, Sweden and Canada.

The CBE Image Library is accessible at:
http://www.erc.montana.edu/Res-Lib99-SW/Image_Library/

Bioglyphs Glowed in New York City

The second art-science Bioglyphs installation was shown at Manhattan College in Riverside, NY, December 5–7, 2002. CBE doctoral graduate Robert Sharp, now Assoc. Prof. of Environmental Engineering at the college, opened up his labs to this collaboration, involving 12 of his graduate and undergraduate students, and four Bozeman participants (including two from the CBE). The Bioglyphs projects have subsequently been covered in *Analytical Chemistry*, *Photonics Spectra* and the *NSF Engineering News* (online). For more information see the Bioglyphs web site:
<http://www.erc.montana.edu/Bioglyphs/>.

Media Highlight

A documentary film team from Oregon Public Broadcasting visited the CBE in September, 2002, to interview several CBE researchers for an upcoming science documentary on microorganisms.

For more media highlights, refer to the 2003 Appendix 2: Supplemental Information.

People

Costerton's Work Recognized in Two Awards

The Surfaces in Biomaterials Foundation presented Dr. William (Bill) Costerton with the 2002 Excellence in Surface Science Award in honor of his achievements in the field of biofilm study, and in recognition of his illustrious career in academia. Dr. Costerton received the award and was keynote speaker at the BioInterface 2002 Conference sponsored by the foundation and held in Scottsdale, Arizona, in September.

Dr. Costerton also received the 2003 Charles and Nora L. Wiley Faculty Award for Meritorious Research at MSU–Bozeman, sponsored by the MSU Foundation. He was recognized for his revolutionary ideas about bacteria, for his pioneering work in the study of microbial biofilms, and for promoting the concept of biofilms more than any other individual in the world. He is also the most prolific and influential author in the biofilm field based on searches of the ISI Web of Science databases. Dr. Costerton has organized numerous conferences, and has mentored scores of graduate students, postdoctoral researchers and collaborating scientists.

American Statistical Association Fellow

CBE's statistician and Professor Emeritus of Statistics, Dr. Marty Hamilton, was elected as a Fellow of the American Statistical Association (ASA). The ASA elects members as Fellows in recognition of outstanding professional contribution to, and leadership in, the field of statistical science. The designation of Fellow has been a superlative honor in the society for 87 years. In order to be honored with the title of Fellow, members must have an established reputation and have made an outstanding contribution in some aspect of statistical work. Dr. Hamilton is the Standardized Biofilm Methods Team Leader, and represents the CBE in the Association of Official Analytical Chemists International (AOAC). He promotes statistical principles in regulatory evaluations of antimicrobial agents, provides creative solutions to statistical problems in microbiology and toxicology, and effectively disseminates new ideas from academia to industry and government.

College of Engineering Awardees

Drs. Phil Stewart and Paul Stoodley received College of Engineering “Outstanding Researcher” awards in May, 2003, in the departments of Chemical Engineering and Center for Biofilm Engineering, respectively.

CBE Award

Dr. Mark Shirtliff received the inaugural “CBE Outstanding Researcher” award in July 2002. Dr. Shirtliff studies *Staphylococcus aureus* in search of novel vaccines and more effective antimicrobial strategies.

A list of CBE faculty and their specialty areas of study can found in Appendix 2: Supplemental Information, or on the CBE web site, under “People.”

Visitors

Visitors to the CBE in 2002–2003 came from as near as Bozeman and as far as Seoul, Korea, to learn about the Center and biofilm research. The range of CBE visitors includes international scientists who come for extended stays and workshop attendees who study in CBE laboratories for a day, as well as touring classes of grade school and high school students, and visiting government and industry representatives.

Introducing Kids to World-Class Research

Not all student visitors to the CBE are filling out college application forms—yet. In February, 2003, fifty middle school students from Helena, Montana, were brought to visit the CBE and MSU’s Department of Microbiology by Jane McDonald, Director of the Peak Enrichment Program. CBE students, staff and faculty who provided tours and instruction included: Ivy Able, Robin Gerlach, Laura Jennings, Linda Loetterle, Joe Menicucci, John Neuman, Mark Pasmore, Laura Purevdorj, Allison Rhoads, and Phil Stewart.

Special Visitors from Washington, D.C.

Austin Yamada, Assistant Deputy of the Department of Defense, visited the CBE in connection with his tour of the MSU campus September 24–25, 2002. Mr. Yamada met with Dr. Paul Stoodley and Garth James of MSE Technologies, Inc., Butte, Montana,

to discuss the CBE’s proposal for using biofilm to identify water-borne agents introduced into distribution systems by bioterrorists.

Dr. John “Jack” Marburger, Science Adviser to the President and Director of the Office of Science and Technology Policy, visited the CBE October 18, 2002. As he toured the center with Dr. Phil Stewart, CBE researchers did their best to “inoculate” him with their enthusiasm for biofilm studies.

Visiting Researcher Highlight

Dr. Christoph Fux, a visiting scientist from Switzerland, will be working at the CBE until July, 2004. Dr. Fux is an M.D. specializing in Internal Medicine and Infectious Disease from the University Hospital in Berne, Switzerland. Christoph is particularly interested in medical biofilms. He said, “The daily sorrow with catheter-related infections brought me in contact with the biofilm concept.” Dr. Fux’s project at the CBE, supported by the Swiss National Science Foundation, will concentrate on the development of an *in vitro* biofilm model for the study of pneumococcal nasopharyngeal colonization. Colonization mechanisms are poorly understood but clinically relevant, since pneumococci frequently colonize the upper respiratory tract, are the most common cause of respiratory tract infections, and comprise a significant cause of bacteremia and sepsis.