

2004 Annual Report

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

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CBE 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 Farewell Message

Dr. J.W. (Bill) Costerton

As I prepare to resign as director of the Center for Biofilm Engineering (CBE), my thoughts turn to "legacy" issues and the future of the wonderful Center we have all worked so hard to build. Research centers live or die on the basis of intellectual leadership. So the questions of this particular moment are: 1) is the biofilm theory of bacterial growth correct? 2) is the notion of predominant growth in biofilms important in natural and engineered systems? and 3) does the CBE lead the world in the generation of biofilm concepts?

The biofilm theory states that bacteria grow predominantly in biofilms in all conditions that favor bacterial growth. Like all theories that turn out to be true, the biofilm theory has become an axiom, and almost everyone connected with biofilm processes or biofilm problems insinuates that "we always knew that." But we really *didn't*, and the CBE carried the ball from the beginning. The biofilm theory looks at individual bacterial cells as members of multicellular—often multispecies—communities and accounts for their remarkable success as a matter of the function of metabolically integrated biofilms adherent to surfaces.

Recent CBE discoveries that biofilm bacteria adopt a series of phenotypes that differ radically from those of planktonic cells, and that cells within biofilms communicate with each other by means of chemical signals, have rationalized this concept of efficient biofilm communities. This concept moves bacteria from the category of simple life forms whose environmental success depends on the properties of single floating cells to a new position in which they self assemble to form multi-genome communities in response to even the most fleeting nutrient opportunities. One CBE researcher observed, very correctly, that it is almost as though we had spent 150 years studying plant seeds and then suddenly discovered that these seeds are just the dissemination mechanisms of bushes and trees that we had seen but ignored, because the seeds were easier to study. So the biofilm theory is correct, and microbiology will never be the same again.

The real driving factor for the burgeoning interest in biofilms, however, is not merely academic. It is the recognition that biofilms have far-reaching impacts. Direct observations have established that these sessile communities predominate in all natural and engineered ecosystems, and in 65–80% of microbial

infections treated by dental and medical professionals in the developed world.

Understanding the biofilm mode of growth explains long-standing mysteries, ranging from the lack of response of biofilms to biocides and antibiotics, to the exact mechanism(s) by which biofilm bacteria create corrosion cells that can “drill” holes in 5/8-inch steel pipes in a matter of months. Recent biofilm research has provided a logical basis for dozens of solutions of long-standing biofilm problems and for dozens of new technologies in which biofilms can be used to our advantage. Examples include using DC electric fields and ultrasonic energy to obviate the natural resistance of biofilms to antibacterial agents, and rendering biofilms susceptible to antibiotics by blocking the genes controlling biofilm formation with analogues of the signals to which they normally respond. In an example of the positive use of biofilms, we have shown that starved ultramicrobacteria (UMB) can be used to place biofilm barriers underground and that these “biobarriers” can be used to enhance secondary oil recovery and to isolate pollutants in subsurface environments.

The importance of biofilms is confirmed by the scores of companies that have joined our industrial program and/or sponsored research in the CBE, and by recent announcements of biofilm requests for applications by defense organizations (DARPA) and by institutes (NIDCR) within the National Institutes of Health. As a notably successful NSF Engineering Research Center, our emphasis on the development of practical technologies has stood us in good stead as we have moved ahead since “graduation” from the ERC program in 2001.

As director of the CBE for over ten years, my recurring nightmare has been to discover, on some rainy Monday morning, that a really pivotal biofilm discovery has been published in *Science* or *Nature* without the CBE having played a role in it. I am delighted and proud that this has never happened. The Center played the lead role in the discoveries of the structural and functional heterogeneity of biofilms, in the discovery of the distinct biofilm phenotype, and in the discovery that biofilm formation is controlled by a wide variety of chemical signals.

The CBE has a galaxy of established stars of the biofilm world, which attracts dozens of “shooting star” students and post-docs that light up our skies and move on (as they must and should)—and there are always four to six visitors who contribute research

ideas and spread the “gospel” when they return home. The CBE is the leading biofilm research entity in the world, maintaining warm relationships with dozens of other centers with related interests, so it will be a vital and healthy center that passes into the care of the next director.

Now about my own plans: I will continue to be involved part-time at the CBE for the foreseeable future while I begin developing a biofilm center in the Dental and Medical Schools of the University of Southern California. I have also promised Vivian that I will be home with her at least half of the time! So I am just going to have to get up earlier in the mornings, network more effectively, and work harder!

Here’s the best of good luck to the Center for Biofilm Engineering and all who sail in her!!

RESEARCH

DIVERSE research activity continued over the past year, with \$2.2 million of new grant activity projected to be awarded to CBE researchers by the end of the fiscal year. This figure appears artificially smaller than last year’s new grant total because it does not include the next installment of a large federal earmark (\$2.0 million) that will go on the books in July 2004. Notable new awards this year are two subcontracts on NIH grants via Garth Ehrlich at the Allegheny-Singer Research Institute (see below for more), a DOE award to exploit biofilms for the long-term management of mixed chemical and radioactive wastes, an NSF award to develop sustainable materials for drinking water distribution systems, a grant from the State of Montana to develop the drip-flow reactor system as a commercially marketed product, an NSF grant to support CBE workshop activities, an award from the W. M. Keck foundation via Portland State University to develop a mobile field microscope unit for the direct observation of biofilm formation in nature, and numerous sponsored projects from private organizations. Eighteen different companies, along with five private institutes, sponsored research or sales and services projects at the CBE in the past year. This slate of new activity gives evidence of the support that the CBE is receiving from diverse federal, state, and private agencies or companies.

The ten named research areas supported by the CBE are summarized in the table below, which provides a

complete listing of areas in which the CBE has significant, sustained research activity.

A complete list of all current CBE research projects is available in the 2004 Appendix.

CBE RESEARCH:

a complete listing of areas in which the CBE has significant, sustained research activity.

Biofilm Control/Antimicrobials

Biofilm resistance mechanisms, effective use of antimicrobials, alternative control strategies

Biom mineralization

Microbially influenced corrosion, deposition and electrochemistry of minerals at interfaces

Bioremediation

Degradation, removal or containment of contaminants in soil and groundwater

Bioterrorism

Persistence and detection of pathogens in drinking water distribution systems

Cell-Cell Communication

Role of signal molecules in biofilm behavior, and disruption of biofilm formation by signal analogues

Industrial and Drinking Water Treatment

Role of biofilms in water quality, corrosion and use of biological pretreatment to improve water quality

Medical Biofilms

Role of biofilms in disease

Souring

Control of bacterial hydrogen sulfide generation in petroleum production

Standardized Biofilm Methods

Development and dissemination of standardized methods for biofilm testing

Structure-Function

Relationship between biofilm structure, transport processes, biofilm rheology, and biological activity

CBE Collaborator Dr. Garth Ehrlich

A productive collaboration has developed between CBE researchers and a group of scientists and physicians at the Allegheny-Singer Research Institute under the leadership of Dr. Garth Ehrlich. Dr. Ehrlich is a geneticist who serves as the executive director of the Center for Genomic Sciences; Dr. Chris Post is an ENT physician who specializes in infections of the upper respiratory tract. Several years ago, they

chanced upon the biofilm concept, quickly made the connection to middle ear infections, struck up a friendship with Bill Costerton, and have been championing the role of biofilms in chronic infections ever since. Their roots and extensive network in medicine have allowed them to be particularly effective in this role. The collaboration between Dr. Ehrlich's group and the CBE pairs medical and molecular genetic expertise in Pittsburgh with engineering and biofilm microbiology expertise in Bozeman. Connections between the two groups were enhanced last year when two CBE researchers, Paul Stoodley and Luanne Hall-Stoodley, made the move to Pittsburgh to join Ehrlich's team. Two new NIH-funded projects of Dr. Ehrlich's will bring a total of \$1.1 million to the CBE over the next 5 years. These projects examine aspects of biofilm formation by *Pseudomonas aeruginosa* and *Haemophilus influenzae*, two pathogens encountered in ear infections.

New Equipment and Imaging Capabilities Spur Research Advances

An award from the Murdock Charitable Trust for the purchase of a new confocal scanning laser microscope and a flow cytometer has come to full fruition. Both instruments have been installed and are expanding the capabilities of CBE researchers.

In addition to the large pieces of equipment, the Murdock award has spurred many smaller improvements. In particular, a new Microscope Resource Room, now houses three high memory computers, DVD and CD burners and readers, and a color printer. The computers are dedicated image processing machines, each with a copy of Universal Imaging's MetaMorph Image Analysis software, PhotoShop, and other qualitative and quantitative programs. One of those computers also has a copy of Bitplane's Imaris image processing software. This resource room has already had a tremendous impact on our imaging capability and understanding. The room is nearly always full with students and staff researchers, examining and manipulating their microscope images and sharing techniques.

Our flow cytometer, confocal microscopes and light microscopy equipment are excellent research tools; CBE researchers are now also able to process and examine that data with equally excellent tools.

Over 30 refereed papers authored by CBE researchers were published in the 2003–2004 reporting period. A complete list of these publications is available in the 2004 Appendix.

FACULTY HIGHLIGHT

New Faculty Bring NMR Microscopy to the CBE

Drs. Joe Seymour and Sarah Codd, recent additions to the faculty in Chemical and Biological Engineering, have established active collaborations at the CBE and have been named as CBE research faculty. Their expertise is in magnetic resonance imaging (MRI), a technique familiar through its widespread application in medicine. When performed at high resolution, the technique is also known as nuclear magnetic resonance (NMR) microscopy. This approach can image a biofilm, but it can also image the fluid flow pattern and diffusive properties of the system in and around the biofilm. Unlike other microscopy methods, NMR can image these parameters in opaque media. Congratulations, Joe and Sarah, and welcome to the CBE!

Sarah Codd recently received an NSF Advance Fellowship of \$387,000 for her work as co-director of MSU's Magnetic Resonance Microscopy Laboratory. The Advance program is designed to increase participation of women in science and engineering by assisting them in developing competitive and sustainable research programs.

Joe Seymour received NSF's Career award. Seymour's \$400,000 award will support his work in magnetic resonance microscopy. The Faculty Early Career Development program recognizes junior faculty who are likely to become academic leaders. The Career award also provides for integration of research into the graduate and undergraduate curricula.

Photo caption: Masters candidate Erica Gjersing's NMR image showing velocity maps of water flowing through a biofilm was featured on the cover of the April 2004 Journal of Magnetic Resonance. "Magnetic resonance microscopy of biofilm structure and impact on transport in a capillary bioreactor," Joseph D. Seymour, Sarah L. Codd, Erica L. Gjersing, and Philip S. Stewart, *Journal of Magnetic Resonance*, Vol. 167, Number 2, April 2004, pp. 322–327.

RESEARCH HIGHLIGHT

CBE Researchers Contribute to Paper in Nature

CBE researchers Betsey Pitts and Phil Stewart were coauthors on a paper concerning bacterial resistance to antibiotics published in the November 20, 2003 issue of the prestigious journal *Nature*. Working with colleagues at Dartmouth and MIT, they have helped identify one answer to the mystery of why bacteria in biofilms are so hard to kill with antibiotics: genetics. For years scientists intuitively thought that the bacterial clusters created a physical barrier that prohibited the antibiotics from getting through. But in a project led by researchers George O'Toole and Thien-Fah Mah at Dartmouth Medical School, the scientists showed that antibiotics do penetrate the biofilm, but don't kill the bacteria. The scientists worked with *Pseudomonas aeruginosa*, a biofilm-forming bacterium that's one of the biggest troublemakers in cystic fibrosis lung infections, burn wound infections and infections associated with the use of catheters. It and other biofilm bacteria can become from 10 to 1,000 times more resistant to antibiotics than non-biofilm bacteria. The scientists traced this resistance to one gene—called *ndvB*—that switches on in a biofilm and protects the bacteria from dying. It's likely that *ndvB* isn't the only gene involved, according to Stewart, but its discovery tells scientists that additional genetic studies of biofilm bacteria may yield even more surprises. "This is the first time anyone has used an unbiased genetic approach to understand why biofilms are resistant to antibiotics," said lead author Mah, a postdoctoral fellow at Dartmouth Medical School. Now scientists can envision drugs that potentially interfere with the expression of specific genes in bacteria, or with the proteins those genes make, as a way of treating biofilm infections.

Picture caption: Model for protection of *Pseudomonas aeruginosa* biofilm cells from antibiotic killing by expression of the *ndvB* gene. Growing, free-floating cells (left) express *ndvB* at reduced levels compared to biofilm-grown cells and are susceptible to antibiotics. As newly attached cells form a biofilm (middle), they induce the *ndvB* gene and make the NdvB glucosyl-transferase (yellow). This enzyme leads to the production of cyclic glucose polymers (yellow circles) localized in the periplasm of the cell. An antibiotic (orange star) can permeate the biofilm, reaching every cell (right). However, the antibiotic interacts with the periplasmic glucans, slowing its

entry into the cytoplasm and reducing the susceptibility of the biofilm cells.

EDUCATION

SINCE the beginning, the Center's education program has been an important part of the CBE's success. Innovative coursework, meaningful research experiences for graduate and undergraduate students, interactions with industry, and a focus on communication skills are the program's hallmarks. Our students learn how to conduct research on multidisciplinary teams in well-equipped, contiguous laboratories. The CBE's reputation as an international leader in biofilm research remains strong, giving our students a competitive advantage in securing industry and academic jobs upon graduation.

For the academic year 2003–2004, including the summer REU program, the CBE provided research experiences for 35 undergraduates. Of the MSU undergraduates, over half were in the laboratories for all three sessions (summer, fall and spring); the remainder participated in both the fall and spring semesters, demonstrating that our students value their long-term participation in the program. During the same period, we had 29 graduate students, two of whom were prior undergraduate research students.

Student Research Opportunities

Graduate and undergraduate students work together on projects sponsored by the State of Montana (Research and Commercialization Board), Montana State University–Bozeman (Undergraduate Scholars Program), federal agencies (NSF, NIH, DOD), the W.M. Keck Foundation, and industry. Students are mentored by faculty, research staff, and visiting scientists and engineers. On industrially sponsored projects students also have the opportunity to interact with a company partner responsible for the research plan. Projects range from short-term applied work—typically undertaken by undergraduate students—to traditional fundamental research conducted by graduate students.

Interaction with Industry

The involvement of industry with the educational program at the CBE is a long-standing and valuable component of the students' experiences. Participating industries include the CBE's Industrial Associates, Montana companies belonging to the Montana

Biofilm Consortium, and additional companies that sponsor research. All students have the opportunity to present their research in oral presentations and posters at the semi-annual industrial conferences at MSU, to meet with industry representatives attending workshops, and to attend seminars presented by industrial visitors. The strong presence of industry at the CBE provides students with exposure to the viewpoints and needs of the corporate world.

GRADUATE PROGRAM

GRADUATE students pursue a degree under the auspices of an individual department and program at MSU–Bozeman and must fulfill the degree requirements of that department. Enrollment includes students from three colleges: Letters and Sciences, Agriculture, and Engineering. Students typically have their desk space at the CBE and conduct their research in a CBE laboratory. As part of the CBE, they participate in coursework on biofilms, the semi-annual industrial conferences, and social activities.

This year 29 students were enrolled in the graduate program; 16 were doctoral candidates and 13 were masters candidates.

For more information about the CBE's graduate program, go to: www.erc.montana.edu/CBEssentials-SW/education/

Graduates Through the Years

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

GRADUATE STUDENT HIGHLIGHT

Laura Purevdorj-Gage

Ph.D. Candidate, Microbiology

“My interest in biofilm research started when I became an intern in the CBE's Biofilm Systems Training Laboratory. I was given an opportunity to work not only on a specific project, but also on research assignments from industrial associates, which allowed direct interaction with industry representatives. This helped me to appreciate research options and possibilities in both academics and industry. Highly trained faculty and staff with a multidisciplinary approach to biofilm science motivated me to pursue my PhD at the CBE.

My research in Dr. Paul Stoodley's lab focuses on the structure and behavior of *Pseudomonas aeruginosa* biofilms and how they may be affected by cell-to-cell signaling and hydrodynamics. During my PhD program, my mentors encouraged research collaboration with other universities to widen the scope of my work. The William Keck Foundation, which funds my research, promotes teamwork with fellow PhD students from different academic backgrounds. These interactions with a diverse group of researchers have been indispensable and have proven to be necessary for my biofilm research."

2004 W.G. Characklis Award Winner

Laura Purevdorj-Gage was awarded this year's W.G. Characklis Award, created in honor of the Center's founder, which is given each year to a CBE PhD student in recognition of their exemplification of the Center's core values of teamwork and excellence in research.

UNDERGRADUATE PROGRAM

UNDERGRADUATE students get involved in CBE research/education through a variety of programs. They may be hired directly on grants, be funded by the MSU Undergraduate Scholars Program (USP), or by other university-sponsored undergraduate research opportunities. Students can participate directly on fundamental research project teams or as members of the Biofilm Systems Training Laboratory (BSTL) or the Biofilm Behavior Laboratory (BBL), where much of the industry-sponsored research takes place. Whether they participate for university credit or stipend, most of our students remain engaged in CBE research for more than one year. Upon completion of their degree, many of these students are recruited by the CBE's industrial partners. For those pursuing graduate degrees, their research experience is often cited as a key component in being selected by their program of choice.

Undergraduate Student Recruitment and Funding Opportunities

Among the high-caliber students recruited by the CBE are undergraduates from diverse backgrounds selected from MSU-Bozeman for school-term projects and other universities for summer programs. Women have always been well-represented in our undergraduate programs, and an increasing emphasis has been placed on engaging Native American students. **Information about these programs and funding opportunities can be found on the CBE website at:**

<http://www.erc.montana.edu/CBEssentials-SW/education/ed-basics-03-ug.htm>

Provost's Award for Undergraduate Research/Creativity Mentoring

Dr. Philip Stewart, the CBE's deputy director, was awarded the inaugural Provost's Award for Undergraduate Research/Creativity Mentoring in May 2004. Since coming to MSU in 1991, Stewart has mentored 25 undergraduate students in substantial biofilm research projects at the CBE. Stewart has eagerly drawn undergraduates into the Center's world-class studies as early as their sophomore years. By getting them started early, Stewart helps them develop their skills over time. Students say they have loved working with Stewart. These students have produced published works, with some listed as the lead authors. Two undergraduates have been recognized with national awards—a Goldwater Scholarship and a Whitaker Graduate Research Fellowship. Eight are pursuing their research in graduate school.

UNDERGRADUATE STUDENT HIGHLIGHT

Cory Rupp

CBE Undergraduate Researcher,
Mechanical Engineering

Cory Rupp is among approximately 1,000 students nationwide who received a National Science Foundation Graduate Fellowship, worth \$121,500 over three years. The fellowship covers \$10,500 a year in tuition and includes a \$30,000 annual stipend, which will allow the Billings native to pursue both a Master's and PhD in mechanical engineering at the University of Colorado at Boulder.

"As a mechanical engineering student, I originally thought I would feel out of place working at the CBE because of the vast differences between the fields of mechanical engineering and microbiology. To my surprise and satisfaction, however, I found that interdisciplinary research is what the Center is all about. This aspect of my research has been one of the most important aspects of my studies at MSU. I have realized that research in the future has no choice but to be interdisciplinary, and my experience at the CBE has given me a huge advantage for my future in this respect. My research in biofilm viscoelasticity has forced me to engage in engineering topics that would normally be years ahead of my current studies. It has also required me to study microbiology, from which I

have been able to draw many ideas for other problems. Overall, the work I have done at the CBE has provided me with invaluable experience that I will continue to use throughout my life.”

Undergrads Get Hands-On Experience in BSTL Program

The Biofilm Systems Training Laboratory (BSTL) is one of the places at the CBE where undergraduate students can get meaningful experience in a research laboratory. Since the BSTL was established in 1997, we have continuously employed four to six undergraduate students majoring in all fields of engineering and the life sciences. Students conduct research in the area of standardized biofilm methods development or on industrially relevant projects. Before starting their individual research, students receive three to four weeks of intensive training. Students are also encouraged to develop their team problem-solving skills and project management strategies. BSTL students are required to make one formal oral research presentation and one literature review every semester during the BSTL’s bi-weekly meetings. Students who have graduated from the BSTL intern program have gone on to enter graduate school, medical school, dental school and the industrial work force.

REU Program: Summer Fun and Relevant Research

For fourteen years the CBE has received funding from the National Science Foundation through the Research Experience for Undergraduates Program. Last year six students were recruited from academic institutions throughout the country, and two were selected from MSU to act as program liaisons for the 10-week program. Research projects were provided by CBE staff and our Industrial Associates. In addition to research, REU participants engage in communications and ethics sessions. Each student prepares and gives three presentations and submits a written final report. If a project is sponsored by industry, the student is in contact with the sponsor throughout the summer. In addition, there may be an opportunity for the student to present research results at the company.

Picture caption: Megan Falsetta, a junior in biology at Alfred University, Alfred, NY, presented results from her REU project “Microarray analysis of *Staphylococcus aureus* biofilms” at the international ASM Biofilms 2003 Conference in Victoria, B.C., Canada in November. Megan’s CBE mentor was Dr. Mark Shirliff.

A Sampling of Undergraduate Projects

Listed below are some of the undergraduate research projects within the CBE in the 2003–2004 reporting period. Students selected to participate in the Undergraduate Scholars Program are indicated by (USP).

Brandon Brooks, Chemical and Biological Engineering

Mentor: Darla Goeres

Testing desouring technology in a porous media column

Krista Cooperstein, Microbiology (USP)

Mentor: Dr. Paul Stoodley

Proteomic study of detached biofilm

Conrad Donovan, Electrical Engineering (USP)

Mentor: Dr. Haluk Beyenal

Microbial fuel cells

Sara Golden, Biological Sciences (USP)

Mentor: Dr. Haluk Beyenal

Microbial fuel cells

Elizabeth Hillblom, Biotechnology

Mentor: Dr. Mark Pasmore

Modeling dental biofilms

Lindsey Hopper, Biomedical Sciences

Mentor: Dr. Robin Gerlach

*Metal reduction by *Cellulomonas* spp.*

Shamus McCarthy, Computer Engineering

Mentor: Dr. Martin Hamilton

Developing and maintaining a biofilm database

Jeffrey Meuli, Electrical Engineering

Mentor: Dr. David Dickensheets

Microconfocal probe engineering

Travis Nelson, Chemistry (USP)

Mentor: Dr. Robin Gerlach

Biofilm and zero-valent iron mediated transformation of explosives

Ellen Swogger, Chemical & Biological Engineering (USP)

Mentor: Dr. Mark Pasmore

Bacterial biofilms in sinusitis

Alison Ziegler, Biomedical Sciences (USP)

Mentor: Dr. Mark Pasmore

Anti-biofilm efficacy of antibiotic bone cement

TECHNOLOGY TRANSFER

CBE technology transfer encompasses our interactions with industry, regulatory agencies and other technology consumers. As biofilm awareness has expanded into new areas of interest, so have our efforts to keep our support base on the leading edge of biofilm science and engineering. The Industrial Associates program remains the primary vehicle for technology transfer at the CBE as well as a major source of operating funds for research. In 2003–2004, the CBE had 24 subscribing Industrial Associate companies (see list on page 16), whose annual dues contributed over \$350,000 to CBE research operations. In addition, the CBE conducted sponsored research totaling more than \$200,000 funded by both Industrial Associate and non-member companies, and received industrial gifts totaling \$250,000.

Major industry sectors represented in the Industrial Associates group include manufacturers of household products, personal care products, medical devices, specialty biocides, and oral care products. A strong growth area for CBE membership has been companies that seek to utilize novel compounds in discovery of effective drugs to combat biofilm bacteria. New members also include the Electric Power Research Institute, whose mission is to combat microbial growth in power plants.

To expand technology transfer efforts to reach small businesses, the CBE began the Small Business Industrial Associate (SBIA) program in early 2004. The SBIA program provides a mechanism for small businesses (by the federal definition) that sponsor CBE research to participate in the Industrial Associates program at a rate discounted commensurately with the research sponsorship. The program has already enlisted two memberships. Montana small businesses continue to take advantage of CBE benefits through participation in the Montana Biofilm Research Consortium (MBRC), a program now in its seventh year that helps Montana small businesses adopt technological advances and increase competitiveness.

Technical Advisory Conferences

The CBE is committed to helping our associate companies stay at the forefront of biofilm-related advances in the scientific disciplines that impact their businesses. We see our role as the biofilm information clearinghouse for industry, and we structure our semi-annual Technical Advisory Conferences (TAC) to

accomplish this goal. At these conferences company representatives interact with CBE researchers, outstanding scientists from other institutions, and members of the regulatory communities which promulgate product-development rules. In the past year, invited presentations at TAC have included noted academic researchers Dr. Barbara Iglewski (Professor of Microbiology at the University of Rochester and former president of the American Society for Microbiology), Dr. Christoph Fux (University of Bern), Dr. Michael Givskov (Danish Technical University), and regulatory authorities Robert Brennis (USEPA) and Janine Morris (USFDA), who, in addition to making presentations, hosted focus sessions to help CBE members better understand the regulatory decision-making process. ***A complete list of industry and government visitors to the CBE during this reporting period is shown in the 2004 Appendix.***

Workshops

Basic and advanced biofilm methods workshops were held in conjunction with each Technical Advisory Conference. These one-day workshops provide a mechanism for Industrial Associate members to stay current with the latest laboratory techniques for biofilm study. Two non-associate workshops were also delivered on October 20–21, 2003 and February 26–27, 2004. These workshops are offered to the public on a semi-annual basis each year.

Visits to Industry

Technology transfer to industry is sometimes most effective within a company's place of business. So CBE researchers make numerous visits each year to our member companies and to prospective members. The focus of these visits can be general biofilm education, or more specific discussions related to product development or problem solving. We offer feedback on R&D direction, marketing ideas, or strategic decisions. ***CBE visits to industry are summarized in the 2004 Appendix.***

New CBE Industrial Associates

Electric Power Research Institute (EPRI) is a research group that represents power plant operators. Their main concerns with biofilms are in power plant (particularly nuclear) cooling systems, biofouling and biocorrosion.

Cumbre, Inc is a drug discovery company based in Austin, TX.

Diversa, based in San Diego, develops commercial enzymes for pharmaceutical, agricultural, and chemical markets.

Both Diversa and Cumbre have joined the CBE under our new program to encourage small businesses to both sponsor research at the CBE and join as industrial members.

CBE Industrial Associates

Aramco Services Company
Church & Dwight Co., Inc.
Colgate-Palmolive
C.R. Bard, Inc.
Cumbre, Inc.
DePuy, Inc.
Diversa
Dow Chemical Company
DuPont
Eastman Kodak Company
Edstrom Industries, Inc.
Electric Power Research Institute (EPRI)
Gambro Corporate Research
Genencor International, Inc.
Genome Therapeutics Corp.
Idaho National Engineering & Environmental Laboratory (INEEL)
Microbia, Inc.
Philips Oral Healthcare, Inc.
S.C. Johnson & Son
Smith & Nephew, Inc.
Tyco Healthcare
Union Carbide Corporation
U.S. Bureau of Reclamation
W.L. Gore & Associates

During the 2003–2004 reporting period, the CBE worked with over 20 additional non-member companies, institutes, foundations and government agencies on biofilm projects. Government agencies included: the Army Research Office, Environmental Protection Agency, National Institutes of Health, National Science Foundation, Office of Naval Research, and U.S. Departments of Agriculture, Defense, and Energy.

TECHNOLOGY TRANSFER HIGHLIGHT

Kodak Selects CBE for Patent Donation

In February 2004 Eastman Kodak and MSU jointly announced the donation of a suite of eight patents from Kodak to the Center for Biofilm Engineering. With the patents, Kodak donated \$200,000 to the CBE

to be used for further research and commercialization of the technologies covered in the patents. The CBE was picked from many applicants as the academic research institution most likely to help these patents realize their full value in the commercial marketplace. The patents cover the immobilization of organic biocides onto surfaces, and have a high potential for success in applications in the areas of drinking water and medical devices. Drs. Anne Camper and Phil Stewart will head up the research in these areas, respectively, and Paul Sturman will lead commercialization efforts. As the technologies are developed through further research, the CBE anticipates working toward commercialization either through licensing the technology to existing contacts within these industries, or through the development of a start-up company.

OUTREACH

CBE Presenters Reach the World

CBE faculty and staff made over 60 biofilm presentations in 15 U.S. states and 12 countries, including: Canada, Chile, England, Germany, Ireland, Italy, Japan, Mexico, the Netherlands, South Africa, Sweden and Wales during the 2003–2004 reporting period. Over 30 CBE students, staff and faculty attended the ASM Biofilms 2003 Conference in November as invited speakers, research poster presenters and workshop leaders. ***A complete list of presentations can be found in the 2004 Appendix.***

Media Highlight: Sprechen Sie “Biofilm?”

The German popular science magazine *PM Magazin* (monthly circulation: 450,000) published an article about biofilm by Marianne Oertl in its May 2004 issue: *Bakterien reden miteinander. Aber worüber?* (Translated title: “Bacteria talk with one another. But about what?”) that features graphics supplied by the Center for Biofilm Engineering. The *PM Magazin* website introduction to the article also contained a link to the CBE’s “Multicellular Strategies” interactive web module that introduces viewers to biofilm concepts and CBE research. ***For more media highlights, refer to the 2004 Appendix.***

The CBE Web is a Hit

The CBE and its website received a rave review in the “Useful Internet Sites” section of the November/December 2003 issue of *SIM News* (Vol. 53, No. 6, p 266). Todd Sandrin, University of Wisconsin, wrote: “Even a cursory perusal of this website quickly

reveals that CBE researchers have made extraordinary progress in elucidating important, once enigmatic facets of biofilms.” CBE webmaster Diane Williams and communications specialist Peg Dirckx collaborate with CBE researchers to produce and maintain the site. Full text of the review is available at: http://www.erc.montana.edu/Res-Lib99-SW/newsarchives/HTML/2004/SIM_News_Review.htm

The CBE’s web Resource Library—which contains vast amounts of information, from publications to biofilm movies—continues to be the most frequently accessed section of the CBE website. CBE images are requested for use by people “at home” and abroad: university and medical school faculty and students, health professionals, industry and government representatives, and the print media. The electronic CBE News Update publication subscribership grew by 32% in the past year.

The Biofilm Institute (www.biofilm.org) founded by the CBE and its Industrial Associates is a non-profit, public-benefit corporation dedicated to providing information and education about microbial biofilms. Subscribership to the Institute’s publication, *Biofilms Online* (www.biofilmsonline.com), rose by 45% in the past year.

Bioglyphs Recognized in Competition

MSU–Bozeman’s Bioglyphs art and science collaboration was selected as one of ten semifinalists in the multimedia category of the inaugural “Science and Engineering Visualization Challenge,” an international competition sponsored by the journal *Science* and the National Science Foundation. The MSU entry, “Bioglyphs: Art/Science Collaborations with Living Bioluminescent Bacteria,” included a slide show, photographs and the Bioglyphs web site: www.erc.montana.edu/BIOGLYPHS. Bioglyphs project directors are Betsey Pitts and Peg Dirckx from MSU’s Center for Biofilm Engineering; and Sara Mast, from the MSU School of Art.

WORKSHOPS

From Chilly to Chile: PASI International Workshops

Bill Costerton’s vision of establishing a world-wide network among sister universities specializing in biofilms for purposes of education and fostering industrial relations moved one step closer to realization in this past year. The first of two biofilm workshops funded through the NSF/DOE-sponsored

Pan-American Advanced Studies Institutes (PASI) Program was held in January 2004 in Concepción, Chile. The second will be held in July 2004 at MSU–Bozeman. The primary goal of these workshops is to broaden student researchers’ knowledge base through lectures and hands-on application of techniques critical to the study of biofilms. In addition, workshops focus on the interdisciplinary nature of biofilm studies—highlighting the fields of biochemistry, microbiology, and engineering. The workshops are open to post-graduate and advanced graduate students. Two other key aspects of the workshops are to foster interactions among students from diverse educational and cultural backgrounds, and to expose students to industrial perspectives and academic/industrial collaborations to solve science and engineering problems.

Biofilm Structure and Function Workshops

At right, participants in the workshop “Microsensors: Manufacture and Applications” sponsored by the CBE’s Biofilm Structure and Function research group, headed up by Dr. Zbigniew Lewandowski and Dr. Haluk Beyenal. Members of this group have extensive experience in constructing microsensors, probing biofilms, and in computing numerical parameters characterizing biofilm activity. This workshop and another titled “Biofilm Structure Quantification and Image Analysis” will be offered again in the summer of 2004.

PEOPLE

MSU College of Engineering Awardees

Dr. Zbigniew Lewandowski was the *Outstanding Researcher for Civil Engineering*, **Dr. Robin Gerlach** received the *Outstanding Researcher for the CBE*, **Dr. Joe Seymour** was the *Outstanding Researcher for Chemical and Biological Engineering*, and **Dr. James Duffy** received the *Outstanding Instructor award for Chemical and Biological Engineering*. Our friend, and CBE doctoral graduate, **Ernest Visser** received an *Outstanding Professional Employee* award from the College. Congratulations to these talented colleagues.

Dr. Rockford (Rocky) Ross, right, a recent addition to CBE’s interdisciplinary collaborating faculty, was selected to receive the 2004 ACM SIGACT Distinguished Service Prize. This award, presented by Hal Gabow, SIGACT Chair, was given to Rocky in recognition of his long-standing service to the

theoretical computer science community. The award included a \$1000 honorarium.

Center for Biofilm Engineering Awardee

Betsey Pitts received the 2003 CBE Outstanding Researcher award during the summer Technical Advisory Conference. As the CBE's microscopist, Betsey has helped Center researchers make tremendous strides in imaging biofilms. As a lead researcher in the Biofilm Control lab, she co-authored a paper in *Nature* with Dr. Phil Stewart and collaborating investigators at Dartmouth and MIT (see Research Highlight, page 8).

Dr. Anne Camper was a co-author of a paper selected as the 2003 American Water Works Association Distribution and Plant Operations Division best paper in the *Journal of the American Water Works Association*.

Center Director **Dr. Bill Costerton** was named 2002–2005 Honorary Professor in the Advanced Wastewater Management Centre, The University of Queensland.

Bill also was the lead organizer for the American Society for Microbiology Conference on Biofilms 2003, held in Victoria, BC, Canada. At the conference he was honored with a reception provided by ASM and the CBE, and received a Career Acknowledgment Award from the Center for Biofilm Engineering.

VISITORS

CBE visitors include international scientists who come for extended stays, workshop attendees who study in CBE laboratories for one to two days, touring classes of grade school and high school students, and visiting government and industry representatives.

CBE Visiting Scientists in 2003–2004

Erik Alpkvist, Malmö University, Malmö, Sweden

Charles Bark, Albert Einstein College of Medicine, Bronx, New York, USA

Erin Field, Long Island University–Southampton College, Southampton, New York, USA

Iolanda Francolini, University of Rome “La Sapienza,” Italy

Dr. Christoph Fux, M.D., University Hospital, Bern, Switzerland

Albert Jacobs, Lyon University, Lyon, France

Gregory Jubelin, Université Claude Bernard, Lyon, France

Birthe Kjellerup, Aalborg University, Aalborg, Denmark

Volker Maczek, University of Duisburg, Duisburg, Germany

Enrico Marsili, University of Rome “La Sapienza,” Rome, Italy

Cathryn O’Sullivan, University of Queensland, Brisbane, Australia

Shu Yeong (Johnny) Queck, University of New South Wales, Sydney, Australia

Wolfgang Uhl, University of Duisburg-Essen, Essen, Germany

Bastian Wittstock, University of Stuttgart, Stuttgart, Germany

... Visitors from Around the Corner

While the CBE hosts visitors from all over the world, we also encourage local groups to find out about our biofilm research. Bozeman Deaconess Hospital administrators, at left, toured the Center with Biofilm Behavior Lab leader Garth James in the spring of 2004 and learned more about the medical implications of biofilm during a session with Director Bill Costerton. Numerous school groups from Bozeman and other Montana towns visit the CBE every year.

Center for Biofilm Engineering Faculty, 2003–2004

Name and Specialty

Haluk Beyenal, Res. Asst. Prof., Chem. & Biol. Eng.

Biochemical engineering

Phil Butterfield, Asst. Res. Prof., Civil Eng.

Biofilms in engineered systems

Anne Camper, Assoc. Prof., Civil Eng.

Biofilms in environmental systems

Sarah Codd, Res. Asst. Prof., Chem. & Biol. Eng.

Magnetic resonance imaging

Bill Costerton, CBE Director

Biofilms in microbial pathogenicity

Al Cunningham, Prof., Civil Eng.

Subsurface biotechnology and bioremediation

David Dickensheets, Asst. Prof., Electrical Eng.

Fiber optics

Jack Dockery, Prof., Mathematical Sci.

Mathematical models of biofilms

James Duffy, Asst. Prof., Chem. & Biol. Eng.

Engineered anti-biofilm materials

Michael Franklin, Asst. Prof., Microbiology

Molecular genetics, gene expression, alginate biosynthesis

Gill Geesey, Prof., Microbiology

Molecular and cellular interactions at interfaces

Luanne Hall-Stoodley, Asst. Res. Prof., Vet. Mol. Bio.

Mycobacteria

Marty Hamilton, Prof. Emeritus, Statistics

Applied biostatistical thinking

Warren Jones, Assoc. Prof., Civil Eng.

Water distribution systems

Isaac Klapper, Assoc. Prof., Mathematical Sci.

Mathematical modeling

Martin Lawrence, Asst. Prof., Chem. & Biochem.

Biochemistry

Zbigniew Lewandowski, Prof., Civil Eng.

Microsensor design and application; chemical gradients / biofilm structure relationships; hydrodynamics and kinetics in biofilms

Timothy McDermott, Assoc. Prof., Land Res. & Environ. Sci.

Biofilms in extreme environments

Bruce McLeod, Dean of Grad. Studies

Bioelectric effect

Mark Pasmore, Asst. Res. Prof., Chem. & Biol. Eng.

Medical biofilms

Rocky Ross, Prof., Computer Science

Web-based, active learning education; design and analysis of algorithms for practical problems; information technology

Joseph Seymour, Asst. Prof., Chem. & Biol. Eng.

Magnetic resonance imaging

Otto Stein, Assoc. Professor, Civil Eng.

Engineered waste remediation

Phil Stewart, Prof., Chem. & Biol. Eng., CBE Deputy Director

Biofilm control strategies

Paul Stoodley, Asst. Res. Prof., Microbiology

Biofilm mechanics, cell-cell communication

Paul Sturman, Research Engineer & Ind. Coordinator

Biofilm detection and quantitation

Peter Suci, Asst. Res. Prof., Microbiology

Biofilm mechanics

Rick Veeh, Affiliate Prof., Land Res. & Eng. Sci. / Civil Eng.

Bacterial identification using oligonucleotide probes

Aleksandra Vinogradov, Prof., Mech. Eng.

Biofilm mechanics