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OFFICE OF TECHNOLOGY LICENSING
STANFORD UNIVERSITY

Special Edition: MBARI

The Collaboration between OTL and The Monterey Bay Aquarium Research Institute (MBARI)

From the sandy beach below, the glowingly white windows of the Monterey Bay Aquarium Research Institute (MBARI) stand out brightly against the low, early morning clouds. Here at MBARI headquarters in Moss Landing, California, scientists and engineers have already begun their day's research in labs, offices and the video display room. In the harbor beyond MBARI headquarters, MBARI's marine operations crews are loading the ships with boxes of supplies and checking sampling devices on the two remotely operated vehicles (ROVs), preparing for the day's work at sea.

After the long day of research in the deep sea, MBARI's research vessels can be seen cutting through the waves as they return to the harbor. At the dock, the crews unload the vessels: cranes lift the heavy equipment ashore, the researchers carry samples and data-filled computers to labs on shore, and the operations crew checks equipment on the ROVs, parts of which MBARI engineers designed themselves.

In one lab, biologists study a new sea worm they discovered. In another, geologists analyze pieces of rock taken from an underwater fissure. A third research group investigates microbes in mud taken from the seafloor. To analyze the various samples, the researchers use a broad array of high-tech equipment. Some of the instruments were custom-made by MBARI and have promise for commercial applications; likewise, some of the deep-sea samples discovered by MBARI may promote industrial processes or improve human health.

Floating slowly through the ocean water, a gelatinous Corolla is frozen in time by an MBARI camera.

MBARI and Stanford Announce Collaboration

To bring MBARI's inventions to the rest of the world, MBARI and Stanford entered into a technology transfer collaboration (stanford.edu/dept/news/report/news/february7/mbari-27.html). Stanford's Office of Technology Licensing (OTL) will facilitate transfer of the commercially promising discoveries and technologies made by the two institutions.

This collaboration offers unique benefits to MBARI and Stanford. It builds on the institutions' similar goals and missions, and it expands upon MBARI and Stanford's ongoing relationship. By combining both institutions' technologies, the col-

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STANFORD TECHNOLOGY *BRAINSTORM*

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Stanford Technology BRAINSTORM **is published quarterly to provide information about OTL and general information of interest to the licensing community, both within and outside Stanford.**

OTL's services are available to any Stanford faculty, students, or staff who invent technologies which may benefit the public or be of commercial value.

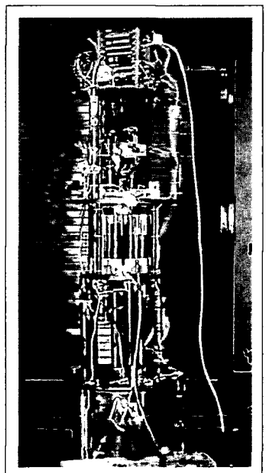
To learn about a specific technology or to disclose one of your own, contact us by any of the above means.

Oceanic ESP:

The Environmental Sample Processor's potential for detecting aquatic health concerns

The ESP is designed to autonomously collect water samples and concentrate microorganisms contained within those samples onto filter disks. The ESP automates application of preservatives as well as molecular probes to the collected samples to enable identification and quantification of particular microbes. A radio modem transmits results in real-time to a remote location for processing and interpretation. This capability provides an entirely new means of detecting microorganisms in the environment, enabling water quality assessments in the absence of ship-based sample collection and time-consuming laboratory analysis.

The ESP is the result of four years of teamwork between MBARI scientists and engineers, under the leadership of Chris Scholin and Gene Massion. Although the current instrument is targeted at harmful algal bloom (HAB) research and issues related to the health of humans and marine wildlife, it is capable of emulating a wide variety of water quality measurements.



ESP with outer housing removed

The teamwork was instrumental in harnessing a new technology to address a fundamental problem in marine research that also has important implications for human health.

For more extensive sampling and analysis, the ESP is typically deployed with another instrument package that includes sensors that monitor aquatic conductivity, temperature, pressure, fluorescence, optical back scattering, and other factors.

For more information view: availtech.stanford.edu/Scripts/otl.cgi/docket?docket=01-M01. To discuss licensing of ESP or any other MBARI technology, contact Luis Mejia at 650-723-0651.

A Selection of Licenses Granted by OTL in the Last Quarter

Docket(s)	Title(s)	Uses	Licensee(s)	License Type
S55-600	"Collaborative Online Curriculum"	Distance education	Densho	Non-exclusive
S98-049 & others	"Synthesis of Single-Walled Nanotubes"	Nanotechnology	Molecular Nanosystems	Field exclusive
S99-216	"Micromachined Two Dimensional Array Droplet Ejectors"	Cleaning for photolithography	Microbar	Field exclusive
S00-033	"Peptide Inhibitors of Picornavirus Polymerase Interactions"	Drug targets for RNA viruses	Eli Lilly	Option
S00-045 & S00-127	"Multiplex Genotyping"	SNP detection	ParAllele	Exclusive
S00-166	"Anti-SUV39H1 Monoclonal Antibody"	Research use	Pharmingen	Non-exclusive to biological material

MBARI... **Continued from page 1**

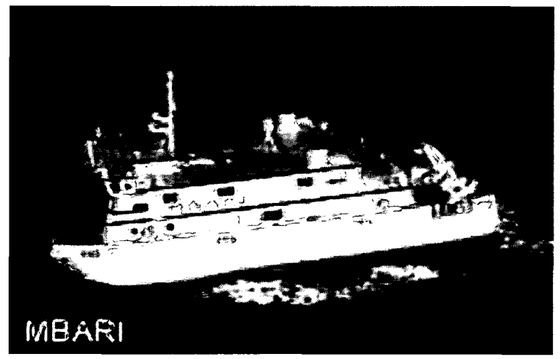
laboration creates a critical mass of complementary technologies in marine and environmental areas.

MBARI Focuses on Research and Innovation
Collaborating with OTL enables MBARI to focus on its strengths of advancing oceanic studies and applying technology to overcome challenges in the field, competencies in which MBARI has been quite successful.

In each of its research areas, including marine ecology, biogeochemistry and microbial oceanography, MBARI strives to overcome technical challenges through innovation (www.mbari.org/rd/research.htm). For instance, to enable extensive, autonomous water sampling, a team of MBARI scientists and engineers created the Environmental Sample Processor (ESP) described in "Oceanic ESP."

In the course of their research, scientists at MBARI have discovered oceanic organisms and developed methods and materials that have commercial value. For instance, MBARI scientists discovered a bacterial rhodopsin (a protein that converts light into energy). The researchers inserted the rhodopsin gene into the common bacteria E. coli. This has for the first time made bacteria a source of energy, as described in the "Technology Spotlight".

Collaboration Centralizes MBARI, Stanford Technologies
For Stanford and MBARI, combining their technologies into a portfolio of inventions creates a nexus to attract commercial interest in environmental and marine technologies. This joint technology portfolio is summarized in "The Growing Patent Portfolio." As Stanford and MBARI continue creating technologies in these areas, more companies will take notice. Stanford will continue to develop a growing network of companies that develop these technologies.



MBARI's large research vessel, *Western Flyer* at sea.

OTL Associate Luis Mejia licenses the technologies that are part of the MBARI / Stanford collaboration. He has a larger vision for what the collaboration can become. Mejia hopes the collaboration will lay the groundwork for OTL to handle marine and environmental inventions created by other oceanographic research institutions. This would extend their work beyond the laboratory, benefiting the public through application of more technologies, benefiting the institutions that receive royalties from the technologies, helping preserve marine environments, and building an even stronger group of complementary inventions.

MBARI and Stanford Share Complementary Missions
MBARI and Stanford are similar in their focuses on research as well as their perspectives on technology transfer. Stanford's primary mission hinges on excellence in research and education. Within this environment, OTL's mission is to promote the transfer of Stanford technology for society's use and benefit while generating unrestricted income to support research and education at the University. Stanford researchers do curiosity-driven research. When in the course of research commercially relevant technologies are invented, OTL steps up to transfer these technologies to the commercial sector for the public benefit.

Likewise, MBARI pursues excellence in oceanographic research and development of technologies to advance ocean sciences. Sometimes MBARI scientists and engineers create technology that has broader commercial applications. The institute is committed to delivering these technologies to the marine science communities worldwide and, where applicable, to other sectors that would benefit from the technology.

Collaboration Expands Stanford, MBARI Relationship
OTL and MBARI's relationship expands the wealth of ongoing connections between MBARI and Stanford. The late David Packard, a Stanford graduate, major Stanford donor, and MBARI's founder, is the most obvious link between the institutions. Other connections between the institutions include:

- Dr. Marcia McNutt is President of MBARI and Professor of Marine Geophysics in the Department of Geophysics at Stanford.

- Dr. Steven Rock is an Associate Professor of Aeronautics and Astronautics at Stanford and adjunct researcher at MBARI.

- Dr. Franklin "Lynn" Orr is Dean of the School of Earth Sciences at Stanford and a member of the MBARI Board of Directors.

- Dr. Judith Connor is Director of Information & Technology Dissemination at MBARI and a lecturer at Stanford's Hopkins Marine Station in nearby Pacific Grove. Hopkins is a marine biology research and educational facility that operates as a branch of Stanford's Department of Biological Sciences.

The collaboration between MBARI and Stanford builds on MBARI and Stanford's ongoing inter-relations and offers unique benefits to both Institutions. As the portfolio of complementary technologies grows, both Stanford and MBARI look forward to the successes that lie ahead.

The History of MBARI and the Collaboration

More on MBARI's Mission, History

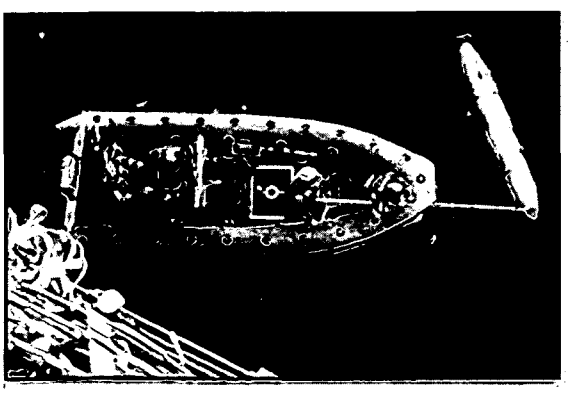
In 1939, Stanford graduate and computer pioneer David Packard joined fellow classmate William Hewlett to create Hewlett Packard, Inc. (HP). In subsequent years HP revolutionized the computer industry through application of innovative technology.

In 1983, Packard founded the Monterey Bay Aquarium to inspire conservation of the ocean through education of the public. Packard founded MBARI in 1987 as a sister institution to the Monterey Bay Aquarium. Packard's vision for MBARI was to revolutionize ocean sciences through application of innovative technology just as HP has done in the computer industry. Packard's mission statement for MBARI and MBARI's goals for achieving its mission are described in "MBARI's Mission and Goals." Fourteen years later, MBARI is fulfilling Packard's vision. MBARI's focus on teams of scientists and engineers has led to the creation of many discoveries and several innovative technologies.

How the Relationship Began

MBARI's initial efforts in technology transfer relied on Stanford OTL staff as advisors. With OTL's help, Dr. Judith Connor, MBARI Director of Information & Technology Dissemination, licensed a novel autonomous underwater vehicle (AUV) tailcone design and its control software to Bluefin Robotics Inc. (a startup from Massachusetts Institute of Technology). Bluefin has been commissioned to build AUVs that incorporate the MBARI tailcone for Scripps Institute of Oceanography, the Navy, and Woods Hole Oceanographic Institute.

Through this experience, MBARI recognized the value of OTL's expertise and assistance with technology transfer, and the relationship between the institutions expanded into a collaboration. OTL Associate Luis Mejia was a natural person to work with MBARI because of his interest in marine research and involvement with groups working to preserve the ocean environment. Mejia had also previously worked with the Monterey Bay Aquarium, so he was acquainted with issues related to marine research in the Monterey Bay Area.



Engineers deploy the ALTEX autonomous underwater vehicle from a support boat.

The Growing Technology Portfolio

Ongoing research at Stanford, MBARI, and Stanford's Hopkins Marine Center is creating many technologies in the environmental and marine sciences. The current portfolio includes:

a) Parthenogenic Activation of Oocytes by Nitric Oxide (Hopkins)
   — Stanford Docket S98-224; available for licensing.
b) Nuclear Transfer Array for High-Throughput Cloning (Hopkins)
c) Tuna Tag for Tracking Fish (Hopkins)
   — Instrument made at MBARI.
d) In Situ Remediation of Hydrophobic Organic Compounds (Stanford) - For aquatic remediation in places such as Elkhorn Slough (an EPA Superfund site).
   — Stanford Docket S00-173; available for licensing.
e) Environmental Sample Processor (MBARI) - Stanford Docket S01-M01; available for licensing; see article on Page Two.
f) Light-Driven Energy Generation in E. coli Using a Novel Marine Gamma-Proteobacterial Proton Pump (MBARI)
   — Stanford Docket S00-M01; available for licensing; see article on Page Four.
g) Microelectrochemical NOx sensor based on tungsten oxide (Stanford)
h) Iridium-Based Mercury Microclectrode Array: Sensor for Heavy Metals in Aqueous Solutions (Stanford)

MBARI's Mission and Goals

"The mission of MBARI is to achieve and maintain a position as a world center for advanced research and education in ocean science and technology, and to do so through the development of better instruments, systems, and methods for scientific research in the deep waters of the ocean. MBARI emphasizes the peer relationship between engineers and scientists as a basic principle of its operation. All of the activities of MBARI must be characterized by excellence, innovation, and vision."

(also at www.mbari.org/about/)

David Packard
MBARI Founder

Science and technology goals:

To carry out its mission, the institute has defined six main goals:

1) Identify important areas of marine science where research progress is limited by lack of appropriate technology.
2) Develop sophisticated systems for investigating aspects of the marine environment and its inhabitants where high scientific potential exists.
3) Meet the highest possible performance standards for the operation of its equipment and technological systems.
4) Conduct high-quality, innovative research that maximizes effective management and use of all MBARI assets.
5) Develop, in collaboration with the Monterey Bay Aquarium, creative programs that maximize educational value of MBARI's research results.
6) Transfer research results, technology, and operational techniques to the marine science community worldwide.

Technology Spotlight:

Bacteria Finally See the Light: Harnessing bacterial rhodopsin to produce energy

By Daniel Weinstein

Until now, scientists believed that oceanic bacteria that did not contain chlorophyll could not produce their own energy from light. It was thought that marine bacteria fed on decaying organic matter or on nutrients spewed from deep sea vents. But recently researchers at Monterey Bay Aquarium Research Institute (MBARI) made the startling discovery that some bacteria may convert sunlight into cellular energy – without using chlorophyll, like most plants and algae. Led by Dr. Edward DeLong, MBARI's Science Department Chair, MBARI researchers discovered picoplankton (oceanic bacteria) containing the light absorbing pigment proteorhodopsin. This groundbreaking discovery marks the first time rhodopsins have been found in bacteria; said DeLong, "Rhodopsins had never been found in bacteria, so that was a big surprise."

The presence of these bacterial rhodopsins opens the door for generating energy in an entirely new way. DeLong and his team have been able to retrieve and amplify proteorhodopsin genes, and express them in *E. coli* to produce a Light-Driven Energy Generator. This technology was published in the September 15, 2000 issue of *Science Magazine* and is available for licensing from OTL.

The Details...

Proteorhodopsin is a type of rhodopsin, a protein that when bound to retinal (vitamin A aldehyde) forms a light absorbing pigment. Before DeLong's discovery there were only thought to be two different types of rhodopsins: visual rhodopsins, found in eyes throughout the animal kingdom, and archaeal rhodopsins found in extremely halophilic archaea (salt-loving microorganisms). Archaeal rhodopsins, and the newly discovered rhodopsins found in picoplankton, have the ability to generate energy by functioning as a light driven proton pump. In response to light, the pump pushes protons out of the cell, creating an electrochemical potential across the membrane. Energy is then generated when protons flow back into the cell. The potential applications of mass-producing such an energy generating proton pump and manipulating it in the laboratory are great, but it has been nearly impossible, until now.

The challenge has been to functionally express rhodopsin genes in common bacteria such as *E. coli* in order to study the pumps in a well-characterized species and to facilitate large-scale energy production. This could not be accomplished easily before, because the genetic origins of archaea are so different from *E. coli*'s. MBARI's discovery has enabled the important accomplishment of retrieving and amplifying rhodopsin genes and expressing them in *E. coli* to create readily manipulable light driven proton pumps.

Unique Uses...

This invention represents the first functional demonstration of generating biochemical energy in *E. coli* via a light driven process. The broad and exciting potential uses of this bacterial energy generator include:

- Enhanced Recombinant Protein Production: This invention may increase the recombinant protein production, including enhancement of yield and increased efficiency.
- Microbial Fuel Cells: The biochemical energy formed by the pump can be converted to electrical energy in light driven fuel cells.
- Modulation of Gene Expression: The light induced membrane potential can be converted into cellular signals, which can be applied to control gene expression.
- Nanotechnology: This invention may provide the energy for light-actuated molecular switches.
- Computing: This invention may be used for pattern recognition or as an optical film for light mediated computer applications.

This Light-Driven Energy Generator has applications in both Life Sciences and Physical Sciences. More information about this technology is online at www.mbari.org/news/media_coverage/delong_science0900.html. To learn more about licensing view availtech.stanford.edu/Scripts/otl.cgi/docket?docket=00-M01. To discuss licensing this or any other MBARI technology call Luis Mejia at (650) 723-0651. ▲

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