

# Woods Hole Oceanographic Institution

## Tiny Sentinels Could Keep World Water Supplies Safe

Just as coal miners once carried canaries to alert them to toxic gases, Woods Hole Oceanographic Institution biologist Scott Gallagher, Ph.D., envisions living sentinels watching over the world's water supplies.

But rather than the warbling of canaries, Gallagher and colleagues at Petrel Biosensors Inc., based near the Woods Hole institution on Massachusetts' Cape Cod, are targeting the swimming talents of protozoa in the genus *Tetrahymena*, each organism smaller than the width of a human hair.

Petrel's prototype monitoring system, the Swimming Behavior Spectrometer (SBS), is designed to provide virtually instant warning for a broad range of toxins that might be introduced to water supplies as diverse as municipal reservoirs, industrial water caches and military water sources in the field.

"Current testing techniques are somewhat cumbersome," says Bob Curtis, Pharm.D., Petrel's interim chief executive officer (CEO). "Generally, they require manual sampling, laboratory analysis, testing for specific agents and waits as long as 72 hours for results.

"By introducing protozoa into water samples in small test chambers, and comparing them to control samples, SBS continuously monitors for toxic agents or contaminants," he says. "It's sensitive to a full spectrum of chemical and biological contaminants — pesticides, industrial chemicals and biological warfare agents."

### The Beginning: Ocean Research

Gallagher, an associate scientist at Woods Hole Oceanographic Institution (WHOI), was concerned with understanding how global climate change might affect microscopic plankton in the ocean when he began to look for ways to characterize their behaviors.

Specifically, amidst the plankton's soup of bacteria, larvae and other microscopic organisms, he was focused on protozoa, a myriad of one-celled creatures that swim using tail-like flagella or short, hair-like cilia. There are tens of thousands of protozoa species, typically ranging in size from 20 to 60 microns. Collecting water samples,

Gallagher developed a technique for visualizing their swimming patterns with a digital camera and created a system for defining their swimming behaviors under differing conditions — temperatures, nutrients in the water, pH levels and other factors.

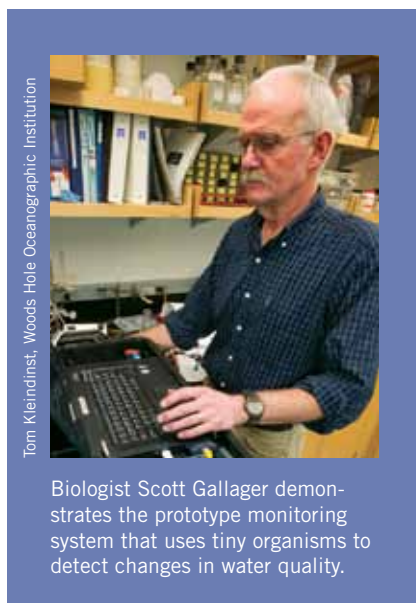
"Sometime after the 9/11 attacks," he notes, "a friend told me the Defense Department was looking for ways to monitor water supplies. We submitted a proposal in 2002 — and never heard back. I literally forgot about it."

But he did hear the next year. With a Defense Department grant, Gallagher developed a model for predicting how different protozoa react to varying water conditions. After narrowing it down to 15 species of protozoa that worked well, he selected a handful of species that were ideal for specific uses — two or three for fresh water, a few for brackish water.

### Swimming Behaviors Key

It's protozoa's cilia that make Gallagher's system of assessing water quality possible. An individual protozoan can have hundreds of thousands of cilia covering its body.

"Protozoas achieve propulsion by beating their cilia like paddles in water," he says. "The shorter the cilia, the faster they can beat. Some normally swim with a rotational torque — sort of a corkscrew motion. Except that when water conditions change, behavior changes.



Tom Kleindinst, Woods Hole Oceanographic Institution

Biologist Scott Gallagher demonstrates the prototype monitoring system that uses tiny organisms to detect changes in water quality.

“The key is calcium. It’s always present in an ionized form, and its presence fundamentally controls how the cilia work. Toxins like heavy metals inhibit calcium transport and affect cilia motion. Sometimes the cells just stop, sometimes they begin spinning around.

“It depends on whatever is inhibiting the cell, whether it’s changing uniformly or just in a part,” Gallagher explains. “If the front cilia move into a toxin and slow down while the back cilia don’t, the cell is likely to start tumbling.”

Biological products like anthrax produce toxins that don’t affect the cilia but do inhibit the protozoa’s metabolism at the cellular level. Because so many variables are possible, it’s important that any monitoring system also be able to assess control samples — water with known characteristics — for comparison.

### Enter Petrel Biosensors

Gallagher and a team of engineers constructed the first sampling prototype on a workbench in his laboratory — a device measuring 2 feet by 3 feet. A nonprofit virtual incubator affiliated with WHOI, the Regional Technology Development Corp. (RTDC) stepped in to assist Gallagher and his team in forming a new company to commercialize their invention.

With that assistance, Petrel Biosensors — named for a sea bird that flies in circles as a sentinel to an approaching storm — was incorporated in 2009 as RTDC’s first endeavor. Under the arrangement, Petrel was granted an option for an exclusive worldwide license for the intellectual property

surrounding SBS technology.

Curtis, the development group’s CEO, also presently functions as Petrel’s interim CEO. The company started in 2010 with two employees — Chief Technical Officer Kevin McManus and Vice President of Engineering Lamar Bullock, Ph.D. Gallagher, who remains a full-time member of the WHOI staff, serves as chief scientific officer.

### A Strong Outlook

Curtis notes that the company is in discussions with several large corporations about partnership arrangements and that it hopes to achieve significant funding by the end of 2010.

As chief technical officer, McManus says his role “is to take this very elegant technology, make it into a commercial product that can be put in the back of a pickup truck and taken to a water supply, where it can provide continuous sampling and transmit the results to those in charge.

At present, an emphasis is on updating the software, optics and other aspects of the technology first developed in 2004-2005. Future efforts will focus on miniaturization, with the goal of developing units that can be hand-carried — perhaps the size of a laptop computer.

“Municipal water supplies aren’t generally space-limited,” McManus notes, “but it probably won’t be sufficient to just place one at a reservoir and ignore the upstream source waters and downstream flow channels. This is where smaller units will be

valuable. And portability will be important for industrial operations and military units in the field.

“Ideally, a water system would have a distributed network of these sensor systems to provide ongoing real-time local, regional and, ultimately, global assessments of water supply quality.”

SBS’s current prototype, Version 1.4, is designed to provide continuous monitoring, simultaneously filling its dual test-sample and control-sample flow chambers at regular intervals, introducing the testing protozoa from a culture, assessing them, emptying the chambers and preparing them for the next sample. Each sample involves about a milliliter (or one-fifth of a teaspoon) of water containing several hundred protozoa. It can be programmed to test as often as the user wants, from every 10 seconds to once a day, or any time period in between.

“The longer the sampling time, the more sensitive the results,” Curtis notes. “It seems to work well with 30 seconds. That means a user can be alerted almost instantly if a problem exists. You may not know what the exact toxin is, but you’ll know you’ve got a problem and be able to take action.”

He adds: “This system has gone through extensive validation trials by outside testers, with very strong results. It offers real-time, broad-spectrum capabilities not available in the market now. I envision commercial opportunities domestically and internationally — the quality of water is a worldwide issue.”

— Ralph N. Fuller

## Other Promising Technologies

### Promising Mayo Clinic Technology Joins the Fight Against Breast Cancer

Most of us know someone who has been affected by breast cancer.

In fact, the American Cancer Society estimates that roughly 1 in 8 woman will have invasive breast cancer at some point in her life, and that approximately 1 in 35 women will die from breast cancer. However, the number of deaths resulting from breast cancer is on the decline, and many people believe this decline is due to earlier detection and better treatment.

A team of researchers at the Mayo Clinic, including Deborah Rhodes, M.D., Michael O'Connor, Ph.D., and Carrie Hruska, Ph.D., has spent the last seven years developing and evaluating ways to improve the detection and monitoring of breast cancer. This research, supported by Mayo Clinic, Gamma Medica Ideas Inc. and the National Institutes of Health, has resulted in technologies exclusively licensed to Gamma Medica Ideas for use in their molecular imaging systems. This set of intricate algorithms and hardware embedded into the imaging device allows for efficient detection of breast cancer and a drastic reduction in the radiation dosage administered to women during screening procedures.

At times, current mammography technology is unable to detect breast cancer, especially in women with dense breast tissue. The molecular breast imaging algorithms and device hardware technol-

ogy from Mayo Clinic, coupled with the detector technology at Gamma Medica Ideas, creates a method of diagnosis and monitoring that can overcome the detection problem involved with dense breast tissue. Molecular breast imaging is also less expensive than alternative techniques like contrast enhanced breast MR.

This technology has the potential to improve the quality of life of large numbers of women, provides a less expensive alternative method for detecting breast cancer and offers a more robust detection system. Most importantly, earlier detection and lower doses of radiation make it very appealing to patients and practitioners.

### National University of Singapore and Others Develop 3D Bone Implants to Improve Skull Repair

"Brain injury occurs more frequently than breast cancer, AIDS, multiple sclerosis and spinal cord injury," remarks Allan I. Bergman, president and chief executive officer of the Brain Injury Association in a recent article (<http://www.medscape.com/viewarticle/412192>).

Standard treatment to prevent brain injury caused by pressure on the brain following stroke or trauma involves drilling burr holes into the skull to relieve pressure. Typically the holes are closed with a titanium plate or bone grafts. These approaches each have drawbacks. The use of a titanium in either mesh or plate form can be expensive, and bone grafts are difficult to perform, painful and prone to

infection. Each of these techniques can lead to deformity of the skull curvature.

A team of doctors and engineers from the National University of Singapore (NUS) and the National University Hospital, collaborating with Temasek Polytechnic, saw the need for something better. Inventors Swee Hin Teoh, Dietmar Hutmacher, Kim Cheng Tan, Kock Fye Tam and Iwan Ziein developed a biocompatible polycaprolactone polymer-based implant for the burr holes that provides a base for the bone of the skull to regenerate after repair at half the cost of a titanium mesh or plate. The invention is currently licensed to Osteopore International Pte Ltd., a NUS spinoff.

The technology works by rapid prototyping and design of a 3D patient-specific burr plug. It uses fused deposition modeling and enables the fabrication of the exact shape needed for the patient without a mold. This approach is not only economical but minimizes infection. This invention has received support from various organizations, including the Ministry of Education, the National Medical Research Council and the Tote Board.

One of the first patients treated was a 23-year-old man who suffered an injury on the job. The engineering team fashioned a precise scaffold infusing some of his living bone cells into the scaffold to "seed" the growth process. The bone plug has achieved wonderful results, and two years later the scaffold has fused with the surrounding tissue, with no trace of the