MBL

Catalyst

Biological Discovery in Woods Hole

Founded in 1888 as the Marine Biological Laboratory

Fall 2010
Volume 5, Number 2

IN THIS ISSUE

Where Are They Now

MBL People Shaping Science and Society

Page 2

From the Director

MBL Catalyst

Fall 2010 Volume 5, Number 2

MBL Catalyst is published twice yearly by the Office of Communications at the MBL in Woods Hole, Massachusetts. The Marine Biological Laboratory (MBL) is dedicated to scientific discovery and improving the human condition through research and education in biology, biomedicine, and environmental science. Founded in 1888, the MBL is an independent, nonprofit corporation.

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About the cover: Dreamstime.com *(Earth)*, MBL Archives *(1957 Invertebrate Zoology class)*.

Online extras: For full image descriptions, supplemental materials, and other information related to this issue, visit:

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Dear Friends,

One of the great pleasures of teaching is hearing good news from former students. For those who have taught at the MBL—whether it was in a summer course, or in our resident undergraduate and graduate programs—alumni news is often very rewarding. We hear from former undergraduates who are now enrolled in the best Ph.D. programs in the country. We hear from post-docs who have published exciting research, and who find the dream of establishing their own lab is within reach. We are delighted to hear from senior scientists who are in leadership positions, or are recipients of the highest accolades in science and scholarship, yet who stay in touch with their colleagues or mentors at the MBL.

This is the scientific family that so much defines the MBL: the successive generations of teachers and their students, many of whom eventually come back to the MBL to teach. The same bonds of lineage form among our visiting investigators: they often bring a few lucky students with them to Woods Hole, who then become imbued with the MBL “magic” and find a way to return, sometimes as independent researchers themselves. Some of our alumni may come back and deliver one lecture; others return to lead a course, or become MBL trustees. Some of them haven’t yet returned, but we look forward to the day they will!

This issue of *MBL Catalyst* profiles just a few of the extraordinary scientists who have been, or still are, connected to the MBL. They include exceptionally creative and notable people, such as polymath writer/scientist Jared Diamond (Invertebrate Zoology, ’57) and biologist Mark Roth (Embryology, ’80), both of whom are recipients of MacArthur Foundation “genius” fellowships. Porter Anderson (Microbial Diversity, ’89) co-invented a vaccine that has protected millions of children from scourges such as bacterial meningitis. And while Gregory Henkes only recently (2006) completed the MBL Semester in Environmental Science program, he found himself in headline news stories in 2009, thanks to expertise he gained partly at the MBL.

MBL alumni are the leaders in their fields. Dyann Wirth was a young post-doc looking for her path when she took Biology of Parasitism in 1980. Now she leads a department at Harvard School of Public Health. Molly Miller Jahn (Microbial Diversity ’81) recently served in a leadership post at the U.S. Department of Agriculture, which further expanded her vision of how to apply scientific discoveries for the betterment of our world.

The names of some MBL alumni are known the world over, such as Rachel Carson. In fact, this issue of *MBL Catalyst* could have turned into a book, and we still would not have exhausted the pool of fascinating and influential scientists who have ties to the MBL. We love to hear from them, and we hope you like reading about where they are now.

My deep thanks to Donald Faber, chairman of the Department of Neuroscience at Albert Einstein College of Medicine, who served as guest science editor for this issue of *MBL Catalyst*. Past chairman of the MBL Science Council, and formerly a Grass Fellow (1969) and Neurobiology course co-director (2000-2003) and instructor (1995-2003), Don is well woven into the MBL family.

Gary Borisy

Gary Borisy
Director and Chief Executive Officer

Catalyst

In this Issue

Features

Departments

MBL

Where Are They Now?

A vaccine inventor, an explorer of suspended animation, and a Pulitzer Prize-winning author are some of the members of the MBL family.

They tend to be high flyers, the MBL's alumni, trustees past and present, and Corporation members.

Many of them credit the MBL with playing a pivotal role in their careers, and in shaping the mark they are making in the world.

They are leaders at esteemed institutions, entrepreneurs, governmental advisors, founders of global health initiatives.

They are behind major breakthroughs in cell, developmental and regenerative biology, neuroscience, microbiology, and environmental research.

They are recipients of some of the world's top awards: the Nobel Prize, the Lasker Award, the Tyler Prize for Environmental Achievement, to name a few.

Wise Young
MBL ties: Student, Neurobiology course, 1972; Grass Fellow, 1973; spent winter 1973-74 completing Ph.D. thesis in Loeb Laboratory

Present position: Distinguished researcher on spinal cord injury; chaired professor, Rutgers University; founding director, W.M. Keck Center for Collaborative Neuroscience at Rutgers

Judy St. Leger
MBL ties: Student, Aquavet course, 1990, 1991

Present position: Director of pathology and research, SeaWorld Parks and Entertainment, San Diego

Adam Cohen
MBL ties: Student, Physiology course, 2007

Present position: Assistant professor of Chemistry and Chemical Biology and of Physics, Harvard University; Scientific advisor to Liberian Ministry of Education and the University of Liberia

In this issue of *MBL Catalyst*, we'll hear from several scientists whose work is making a vital contribution to society. They share the MBL as a common touchstone, though their paths are diverse and worldwide.

As you read about their experiences, you may see a common theme in many of their reflections. While they recognize the powerful insights coming from our era's emphasis on how genes work, they keep in mind the "macro" questions about biology, health and the environment, and about life itself.

At the MBL, they were exposed to those big questions—and they never forgot it.

Shimere Williams
MBL ties: Student, Summer Program in Neuroscience, Ethics and Survival (SPINES), 2005

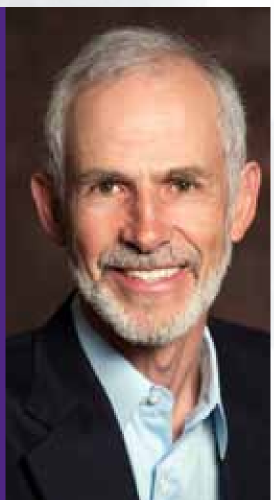
Present position: Professional staff member, U.S. House of Representatives, Committee on Science and Technology

Justin Widener
MBL ties: Ph.D., Brown-MBL Graduate Program in Biological and Environmental Sciences, 2007

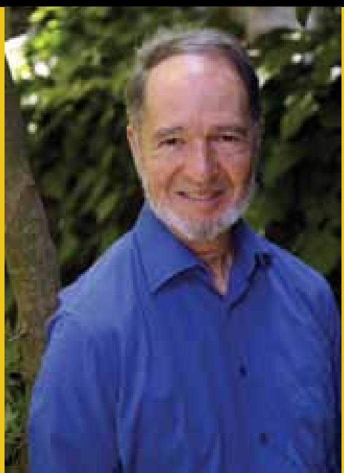
Present position: New project planner at Merial, a global company producing animal drugs and vaccines

Matt Winkler
MBL ties: Student, Embryology course, 1979; Consultant, Physiology course (1981); Faculty, Embryology course (1983, 1987).

Present position: CEO/chief scientific officer at Asuragen, an RNA-based therapeutic and diagnostics company; also founded Ambion, a biotech company sold in 2006 to Applied Biosystems



Diamond in the Rough



JARED DIAMOND
scientist and author

1973
Fellow, American Academy of Arts and Sciences

1979
Member, National Academy of Sciences

1984-present
Contributing editor, *Discover Magazine*

1985
MacArthur "Genius" Fellowship

1988
Member, American Philosophical Society

1992
Britain's Science Book Prize (*The Third Chimpanzee*)

1993-present
Director, World Wildlife Fund

1998
Pulitzer Prize (*Germs, Guns and Steel: The Fate of Human Societies*)

1998
Japan's International Cosmos Prize

1999
National Medal of Science

2001
Tyler Prize for Environmental Achievement

2005
Member, Institute of Medicine

The MBL inspires a future master of science and

Not many scientists get to dine on their own experiments. But for students in the MBL's Invertebrate Zoology course in the 1950s, extracurricular taste tests of marine creatures were part of the fun. Sometimes raw. Or cooked—even boiled into rubbery oblivion.

According to famed author/scientist Jared Diamond, now professor of geography and physiology at the University of California, Los Angeles, the summer-long MBL "Invert" course he took in 1957 was an exciting way to be introduced to the nuts and bolts of biological research.

"It was the best course that I ever took on any subject at any institution," Diamond says. "There were about 100 students, ranging from undergraduates—like myself—to junior faculty members. The instructors were outstanding zoologists headed by John Buck of the National Institutes of Health, along with Howard Schneiderman, then a starting assistant professor at Cornell." (The course "morphed" in the 1970s into the MBL Neural Systems & Behavior course.)

For Diamond, at the time a student at Harvard University, it was an auspicious start for a sterling career. A recipient of the National Medal of Science (1999) and the Tyler Prize for Environmental Achievement (2001), Diamond also won a 1998 Pulitzer Prize for his book *Guns, Germs and Steel: The Fates of Human Societies.* The book offers a clear scenario for how human civilizations arose and why some, such as those in Eurasia, flourished and gained hegemony over others. Diamond has published

"Invertebrate Zoology was pu

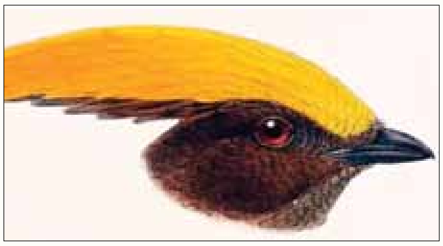
more than a dozen other books, most of them technical, as well as the more popular treatments *Collapse: How Societies Choose to Fail or Succeed* (2005) and *The Third Chimpanzee: The Evolution and Future of the Human Animal* (1992).

Predictably, Diamond's books, research papers, articles, and lectures often stimulate controversy, since he delves boldly into contentious topics such as evolution, racism, environmentalism, war and behavior.

As a scientist, Diamond qualifies for the title of Renaissance man. A Boston native, he graduated from Harvard in 1958, then went on to study physiology and the biophysics of membranes at Cambridge University, earning his Ph.D. in 1961. Diamond's appointment at UCLA School of Medicine in 1968 was originally in physiology, but he soon began a parallel career in ornithology and led 22 field expeditions to New Guinea and nearby tropical islands.

storytelling

One of his victories was finding the exotic, long-lost, golden-fronted bowerbird alive in New Guinea. The bird had not been seen by Western observers in nearly a century, and its existence was known only through preserved skins in a London museum.



Along the way, Diamond also developed a third career—environmental history—and was subsequently named professor of geography at UCLA while retaining his appointment in physiology.

Diamond recalls that one lesson learned at the MBL was to expect the unexpected. "Every animal proved to hold its surprises," he says. "I recall that tunicates have a blood pigment containing the rare element vanadium, and blood high in sulfuric acid. Ribbon worms have a pointed poison stylet [a hard, sharp protrusion] on their tongues, and a spare poison stylet within the brain. And *Crepidula fornicata* [sea snails] are found in piles of up to a dozen individuals, of which the top one became male and all the others female. We reshuffled piles to produce sex changes."

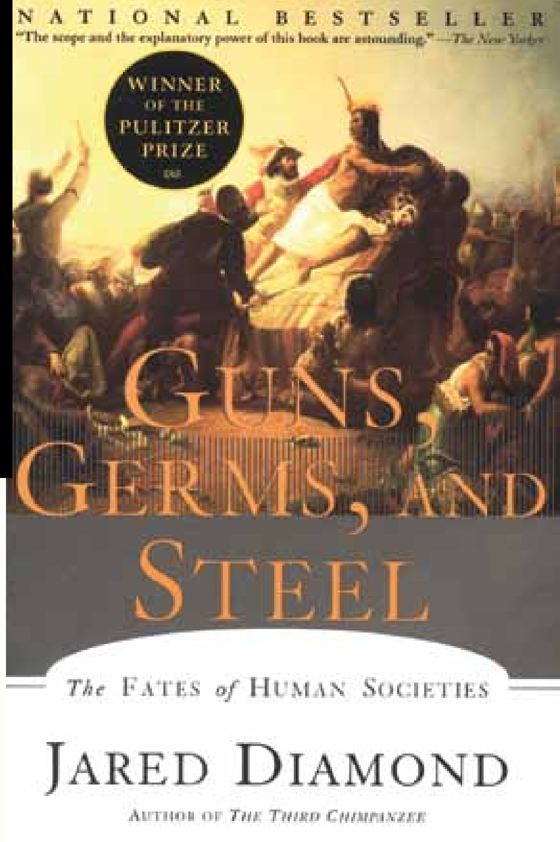
And the tasting episodes generally came at the end of the day. "We began with a lecture about 9 AM, and then went into the field to collect the animal and see where it lived," he recalls. "We brought it back to the lab, observed its behavior, did experiments in physiology, dissected it, and then—just out of curiosity—we

re pleasure and excitement."

concluded by attempting to eat it. Many of them were interesting to eat. In the case of *C. fornicata*, we ate it raw, from one side to the other, but other times we ate it organ by organ, as in the case of the large surf clam. Or uselessly boiled, in the case of sea cucumbers. Its texture merely grew more rubbery, and the tastelessness even more tasteless over the course of 45 minutes of boiling."

Many such things made the MBL course a unique experience, Diamond adds, "which I think no biology student would get today. We obtained an overall sense of each organism—from ocean environment to behavior to molecules—not merely as a name attached to an extracted molecule. We were introduced to more than enough research problems to keep us going for a lifetime."

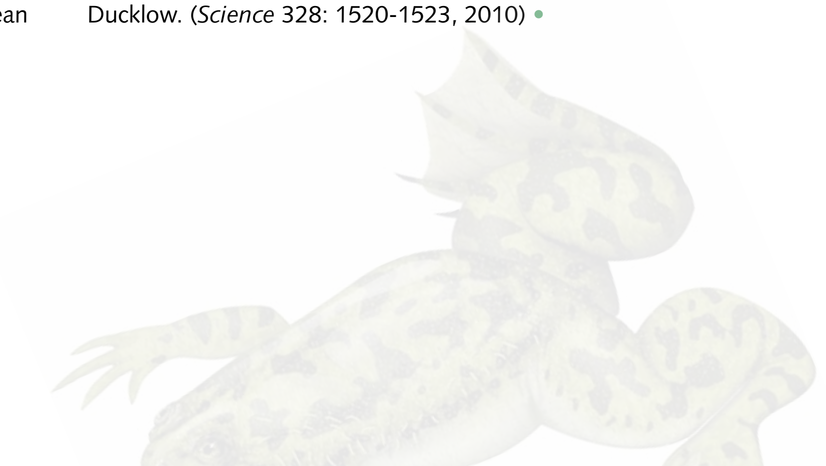
Invertebrate Zoology, Diamond says, "was pure pleasure and excitement." •
—RC



"It was the best course that I ever took on any subject at any institution."

A New Strategy for Polar Ocean Observation

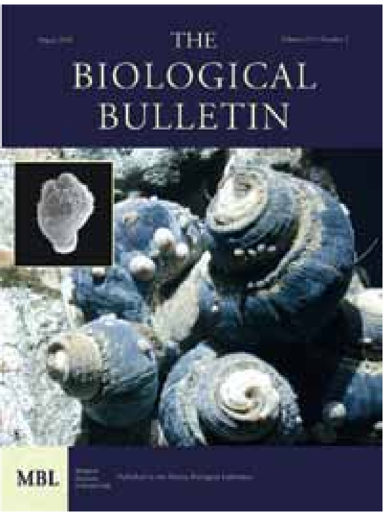
Ecosystems Center director Hugh Ducklow and his colleagues recently outlined a polar ocean observation strategy they say will revolutionize scientists' understanding of marine ecosystem response to climate change. The approach calls for a suite of automated technologies, including robotic networks, satellites, ships, and instruments mounted on animals and ice, to complement traditional data collection. "We know more about Venus than we do about the Earth's oceans," says Ducklow. "We need an ocean observation system analogous to meteorological monitoring for weather forecasting." Ducklow and his colleagues conduct research on the Western Antarctic Peninsula, where high operation costs and harsh conditions restrict the data coverage provided by research ships. "The comprehensive deployment of these observational systems in this location will revolutionize our understanding of how marine ecosystems are responding to climate change everywhere, not just in Antarctica," says Ducklow. (*Science* 328: 1520-1523, 2010) •



Regeneration Research Leaping Forward

The aquatic frog *Xenopus* is a major model in biomedical research. The animal's ability to regenerate some of its tissues and organs, including the lens of its eye, makes it a particularly valuable tool for understanding how regeneration might be made possible in humans. The MBL recently received a five-year, $3.4 million grant from the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the National Center for Research Resources to establish a national *Xenopus* resource. Until now, there has been no central location in the United States for breeding these animals, maintaining genetic stocks, providing stocks to researchers, developing new experimental tools and husbandry techniques, or meeting other needs of the *Xenopus* research community. "This facility will play a key role in our new Eugene Bell Center for Regenerative Biology and Tissue Engineering and will serve as the premier national stock facility for *Xenopus* research," says MBL Director and CEO Gary Borisy. "By studying this important research model, scientists will learn a great deal about the mechanisms of regeneration, knowledge that may one day lead to developing replacement tissues and organs for individuals suffering from medical conditions including diabetes, heart, liver and renal failure, emphysema, retinal disease, and spinal cord injuries." •

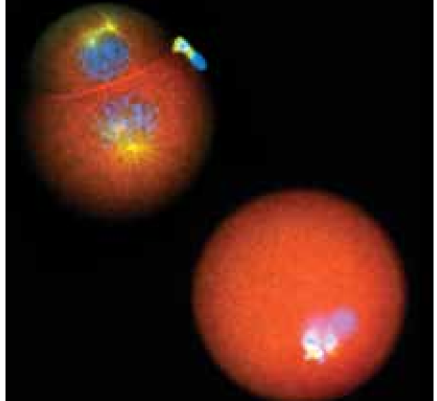
Transition Metal Catalysts Could Be Key to Origin of Life



In *The Biological Bulletin*, an international, peer-reviewed journal published by the MBL, scientists propose a solution to a paradox in origin-of-life theory: How could the basic biochemicals—such as nucleotides—have arisen before the biological catalysts (proteins or ribozymes) existed to carry out their formation? Harold Morowitz of George Mason University and his colleagues propose that a third type of catalyst could have jumpstarted metabolism and life itself, deep in hydrothermal vents. According to the scientists' model, structures involving transition metal elements (iron, copper, nickel, etc.) and ligands (small organic molecules) could have catalyzed the synthesis of basic biochemicals (monomers) that acted as building blocks for more complex molecules. "There has been a big problem in the origin of life (theory) for the last 50 years in that you need large protein molecules to be catalysts to make monomers, but you need monomers to make the catalysts," Morowitz says. However, he suggests, "You can start out with these small metal-ligand catalysts, and they'll build up the monomers that can be used to make the (protein catalysts)." These increasingly complex molecules, they propose, then acted as ligands in increasingly efficient transition metal-ligand complex catalysts. Gradually, the basic molecular ingredients of metabolism accumulated and were able to self-organize into networks of chemical reactions that laid the foundation for life. (*Biol. Bull.* 219: 1-6, 2010) •

A Future With or Without Trees

In some cases, it can be difficult for scientists to see the deforestation for the trees. Not so for Gillian Galford, a recent graduate of the Brown-MBL Graduate Program in Biological and Environmental Sciences (and now a fellow at Columbia University's Earth Institute). In a recent study, Galford and her colleagues considered two scenarios for future land-use change in the Brazilian Amazon state of Mato Grosso, one of the most dynamic places of changing land cover on the planet. In the business-as-usual scenario, deforestation occurs at the same rates associated with the early 21st century, when native forest and grasslands were being rapidly converted for agricultural uses. The other scenario, which better reflects trends of the past few years, takes into account the government's pledge to reduce deforestation by 89 percent by 2020. The result is more than two times lower greenhouse gas emissions estimated through 2050. The study also demonstrates that future emissions estimates must account for historical land use, as the land use influences current and future emissions. Galford says that the strategies used in her study could be used in other tropical regions to predict the results of land-use changes. "With this type of exercise you could analyze a few different scenarios to determine what the consequences for your greenhouse gas emissions would be," she says. (*PNAS* 107: 19649-19654, 2010). •



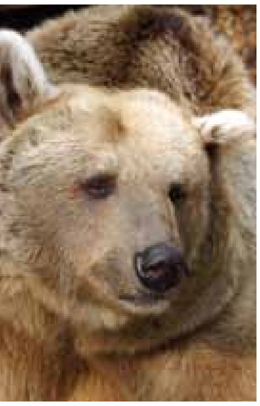
Rediscovery of the Nucleolinus

When searching for long-lost treasure, sometimes all you need are the right tools. Such tools, in the form of an ideal model organism and a new molecular probe, have now been used to rediscover a long-neglected cellular component—the nucleolinus—and confirm its role in cell division. In a recent issue of *Proceedings of the National Academy of Sciences,* MBL scientists Mark and Mary Anne Alliegro, and visiting investigator Jonathan Henry of University of Illinois, Urbana, report that the nucleolinus is required for normal cell division, and is spatially related to the developing spindle axis and pole. "Our paper reintroduces (a cell component) that was discovered, and forgotten, long ago," says Mark Alliegro, who, with his colleagues, developed a probe that binds to specific nucleolinar molecules in surf clam egg cells. Using the label and other means to visualize the nucleolinus during early development, they found that it was associated with structures required for cell division. "We've known for a long time that there are elements in the cytoplasm that need to be assembled for the cell to divide," Mark Alliegro says. "But this tells us that elements in the cytoplasm and in the nucleus have to join together to make the apparatus that separates chromosomes equally into daughter cells." (*PNAS* 107: 13718-13723, 2010) •

Life, Interr

MARK ROTH STAKES OUT THE NETHER WORLD OF SUSPENDED ANIMATION

When biologist Mark Roth was named a MacArthur "Genius" Fellow in 2007—a $500,000, no-strings-attached award for individuals doing original, highly creative work—he took the opportunity to explain his unconventional approach.



Hibernating mammals "turn themselves off," later reanimating with no ill effects.

"The biggest risk I have taken in my career is to let go of the most common means by which science is done, and that is through taking things apart and doing reductionist analysis," he said in an interview with the MacArthur Foundation, which bestows the awards. Instead, Roth is attempting "the reverse approach, to try and be expansionist, and see things as a whole."

Roth, a 1980 MBL Embryology course alumnus and a researcher at the Fred Hutchinson Cancer Research Center in Seattle, has certainly travelled the terrain of reductionist science. Over the course of his varied career, he has studied many facets of cells and their molecules (and he discovered a class of proteins, the SR proteins, along the way).

"In this era of inquiry, we are very dictated by what we can show by genes," Roth says. "There is definitely a campfire, and many people are warming themselves around that magic molecule (DNA)."

Yet Roth, over the past decade, has found the questions that interest him most go beyond the intricacies of a specific life process—such as cell division—in order to address the larger picture.

"I am very interested in what we call *life*," he says. "That leads me immediately to life and death and the bridge between them."

That bridge is a place Roth calls "suspended animation," the interzone in which all observable life processes are stopped—the creature doesn't move, breathe, the heart doesn't beat, even the cells don't divide—and yet it is not dead. Some animals, such as hibernating mammals, regularly turn themselves off in this way, later reanimating with no ill effects, which Roth terms "metabolic flexibility."

"This metabolic flexibility is also present in the human condition, to various extents, if you are willing to consider near-death experiences where people are clinically dead, yet in some instances can be reanimated," he says.

Roth is convinced that "creatures, and even cells, that have leanings toward being immortal tend to have a tremendous amount of metabolic

> "I AM VERY INTERESTED IN WHAT WE CALL *LIFE*. THAT LEADS ME IMMEDIATELY TO LIFE AND DEATH AND THE BRIDGE BETWEEN THEM."

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flexibility. They can sit very quietly, or in suspended animation, for extended periods of time." One example is bacterial spores, which are bacteria in a resting phase that can last as long as 250 million years. Another is human female egg cells. A baby girl is born with a lifetime supply of eggs, but they are "paused"—arrested mid-division. After she matures, however, her eggs can "engage in fertilization, embryogenesis, all these life processes that lead to the next generation. And yet they have this incredible capacity to meditate or suspend or whatever your word is for doing nothing," Roth says.

And that led Roth to wonder if such an agent existed that could bring a larger animal, such as a human, into suspended animation. The medical possibilities were profound. If heart attack or trauma victims, for example, could be put into suspended animation, it could "buy time" for them en route to the hospital, and protect them from the damage they would otherwise suffer due to lack of circulating oxygen.

Roth found that missing agent serendipitously one night at home, while watching a TV program about Mexican caves

Suspended animation is a state in which all observable life processes are stopped—the creature doesn't move, breathe, the heart doesn't beat, even the cells don't divide—and yet it is not dead.

Roth's first published foray into this intriguing field was in 2001, when he figured out how to induce suspended animation in zebrafish embryos through controlled oxygen deprivation to the cells. After 24 hours, he "reawakened" the embryos by exposing them to normal oxygen levels, and they went on to develop normally. Over the next few years, Roth repeated his results in other creatures (yeast, worms, fruit flies, frogs). Strikingly, he found that the oxygen concentration that induces suspended animation is just *below* the level of oxygen deprivation at which the animals die.

"This should freak you out," Roth said in a talk at the TED Conference in California in 2010. "Being exposed to low oxygen does not always kill. Lower the oxygen just a bit more, and you get suspended animation."

Even more startling, Roth discovered with worms that if he reduced oxygen to the level that normally would kill them, and then gave them carbon monoxide, they went into suspended animation. And the cells and tissues suffered no harm due to lack of oxygen.

"That birthed for us the idea that you could use really toxic molecules to regulate the creature's ability to burn oxygen," he says.

filled with the toxic gas hydrogen sulfide. When people entered the caves, they slumped over as if dead. However, if they were brought back into fresh air fairly quickly, they recovered with no damage done.

Roth tried giving mice hydrogen sulfide and "it worked like a shot," he says. The mice de-animated, their oxygen consumption was reduced to "rock bottom," and yet upon re-exposure to air they recovered without harm.

Roth was amazed by these discoveries. In 2005 he founded a company, Ikaria, that is currently in phase II clinical trials to test the hypothesis that hydrogen sulfide improves outcomes in critical care medicine.

"Hydrogen sulfide is naturally produced in the human body, mostly in the brain," he says. "It has probably been regulating our (oxygen burn) since the beginning of time."

Thirty years ago, Roth's experience in the MBL Embryology course awakened his appreciation for the "big questions" in biology. "It was incredible, because the MBL collection boats bring back such a diversity of things. You are looking at sea urchins one class, sea stars the next, and so on. It was a wonderful, eye-opening experience about the diversity of biology," he says. "It gives you a feel for the broader issues surrounding biology, which are sometimes lost when people are forced to streamline on one single (signaling) pathway in some tissue culture cell for 40 years. Which happens." • —DK

Bird Strike!

A graduate of the Semester in Environmental Science program identifies the culprits that brought down a passenger plane

It was one of those calamities that ends up bringing out the best in everyone involved—"a miracle on the Hudson," in the words of New York Governor David Paterson.

On January 15, 2009, three minutes after lifting off from LaGuardia Airport in New York City, the passenger jet US Airways Flight 1549 collided with an oncoming flock of birds. Both engines immediately lost thrust and the pilot, Chesley Sullenberger, radioed that he would try to return to LaGuardia or reach a small airfield in New Jersey.

But three minutes later, with no engine power, Sullenberger had to ditch the airliner into the icy Hudson River, which he accomplished with minimal impact and maximum skill. The crew quickly evacuated the 155 passengers onto the wings of the sinking plane, where they were rescued by a river ferry and sightseeing boats. All the passengers survived, and only five were injured. As video of the dramatic event began to circulate, Sullenberger and his crew were justly celebrated for their heroic professionalism.

The crew ended up in front of the TV cameras, but they weren't the only ones who were called to respond. Gregory Henkes, a graduate of the MBL's Semester in Environmental Science (SES) program in 2006, soon found himself involved in the drama.

Henkes, then a research specialist at the Smithsonian Institution, and eight colleagues, including Peter Marra of the National Zoo, were asked by the Federal Transportation Security Board to sort out the details of the bird-plane collision. Both engines had swallowed up the birds as the plane made its ascent.

As the team noted later in their research report in the journal *Frontiers in Ecology*, bird collisions with aircraft are common and dangerous, and "information on frequency, timing and species involved, as well as the geographic origin of the birds, is critical" for avoiding repeat accidents.

From their analysis, Henkes and the team identified the birds as migratory from the Labrador region of Canada, rather than "resident" New York City geese.

Left: US Airways Flight 1549 is lifted out of the Hudson River.

Right: Greg Henkes collects sediment samples as a 2006 Semester in Environmental Science student.

The team's approach included DNA bar-coding of feather fragments and tissue found in the jet engines, to determine what species had hit the plane. Once they identified them as Canada geese (*Branta canadensis*), they had to find out where the birds came from. For this, they analyzed the bird remains for their stable hydrogen isotope composition, which can be used to characterize precipitation, soils, and vegetation, and which varies with latitude. Birds incorporate this isotope signature into their growing feathers after molt, which occurs near their "home" breeding site. From this analysis, Henkes and the team identified the birds as migratory from the Labrador region of Canada, rather than "resident" New York City geese.

For Henkes, participating in the MBL's SES program was an important stepping stone in a so-far fascinating career. The course, he says, "was everything I thought it would be: challenging, mildy isolated and very fun. What I didn't expect was how much I enjoyed Woods Hole. You are in the epicenter of all things marine science, biological, and oceanographic."

Indeed, he says, "There was little room to escape—but that's part of what makes it great. You do science all the time! My interest in stable isotope ecology and biochemistry grew in the SES program, especially during the independent research part of the semester."

At the MBL, Henkes met scientists whose names he'd only read on research papers, and there they were "in the same room and better yet, I was listening to them lecture." Also, "one of my favorite things was the bi-weekly seminars we went to, which were given by big names outside of the MBL. I recall having dinner after one of these lectures with John Holdren, now President Obama's science advisor. I'm still in awe from that experience."

At the same time, Henkes says, he made valuable connections with fellow students, ties that have endured as they've spread out in pursuit of their own research careers.

Henkes first learned about the SES program through his faculty advisor, William Ambrose at Bates College in Maine, where he was pursuing a B.S. in biology. Based on his own experience in SES and his rapid progress in his chosen field of research, Henkes concludes, "SES is a wildly successful program. They take the 'invested' approach in each one of their students to an extreme, and I think that is validated by their track record for producing many, many passionate science students." Ken Foreman, a scientist in the MBL's Ecosystems Center, directs SES.

"There was little room to escape—but that's part of what makes [Woods Hole] great. You do science all the time!"

Henkes recently left the Smithsonian, where he was laboratory manager for the stable isotope ratio mass spectrometry laboratory at the Museum Conservation Institute, to enroll in a graduate program in geochemistry at the Johns Hopkins University. His interests now focus on paleoceanographic questions, such as ocean water temperatures deep in the Earth's past history.

"There are all sorts of interesting applications in (the study of) paleothermometry of past climates," he says, with evident anticipation. •
—RC

. . . *with*

Dyann Wirth

Chair, Department of Immunology and Infectious Diseases, Harvard School of Public Health
Co-Director, Infectious Diseases Initiative, Broad Institute

Dyann Wirth was a postdoctoral fellow at Harvard University in 1980 when the late Joshua Lederberg, then president of The Rockefeller University, encouraged her to enroll in a new course at the MBL, Biology of Parasitism (BoP). Wirth did so, and by the following summer she had been promoted to the faculty both of BoP and of Harvard School of Public Health. Today, she is the school's Richard P. Strong Professor and Chair, Department of Immunology and Infectious Diseases. She has developed many of the molecular genetic tools used in the investigation of malaria and leishmania, and her group was the first to discover multidrug resistance in these organisms. Wirth received her Ph.D. in cell biology and virology at Massachusetts Institute of Technology. She has served on numerous national and international panels, including a tenure as president of the American Society of Tropical Medicine and Hygiene, and in 2004 she was elected to the Institute of Medicine, National Academy of Sciences. The co-author of 170 scientific publications, Wirth has received numerous honors for her work.

The Evolution of A Cure

Every year, more than one million people die of malaria, and hundreds of millions are infected but survive. The majority of deaths are children under age five in sub-Saharan Africa and other tropical regions where the mosquitoes that carry the malaria parasite, *Plasmodium falciparum*, thrive. Only a few anti-malarial drugs and no vaccine exist, and resistance to the most widely used drug, chloroquine, is now widespread. Dyann Wirth was in the first MBL Biology of Parasitism (BoP) course in 1980, and since that time she has devoted her research to understanding and combating malaria and other tropical diseases. As director of the Harvard Malaria Initiative since 1997, Wirth's work encompasses both basic science and field-based studies, primarily in Senegal. Her team at the Harvard School of Public Health and the Broad Institute has created a map of the most common genetic variants in the *P. falciparum* genome, which has led Wirth to think formally about the malaria parasite in evolutionary terms. She is keenly interested in the mechanisms of drug resistance in the parasite: how they evolve and how scientists might outsmart them.

MBL You have said, "Drug resistance is just a special case of evolutionary biology." What do you mean by that?

DW Evolution is the selective pressures on an organism over time. In the case of an organism that infects humans, such as the malaria parasite or the HIV virus, obviously the human immune system is going to make a big difference to its evolution. And when we take drugs to combat these infections, that's an externally applied force that provides selective pressure by killing the organism. I call it a special case of evolutionary biology because often we know where (in the organism's genome) the drug is targeted, so we know in what genes we expect resistance to occur. For instance in the *Plasmodium* genome, we can see very clearly the evolutionary footprint of the introduction and success of chloroquine in selecting parasites (that survived). So in our fundamental work, we are analyzing the parasites that exist today and asking: What do these survivors look like? These are the parasites that have made it through the human immune system, drug treatment, different mosquito vectors, and so forth.

MBL Your studies of the *Plasmodium* genome show a high degree of genetic variability in the species. What does that imply for strategies to prevent and treat malaria?

DW With *Plasmodium*, we can see that many of the most highly variant genes are on the surface of the parasite and hence are probably interacting with the external environment, which is the human immune system when they are in humans. So that tells us probably the biggest single footprint on the parasite genome is the human immune system.

"We are analyzing the parasites that exist today and asking: What do these survivors look like?"

And, certainly we've learned that the molecules that are currently being used in malaria vaccine trials are among the most variant molecules in the parasite. So our prediction is that if we want to develop a *Plasmodium* vaccine, it will have to take into account this genomic variability. This is a problem with other vaccines, such as for influenza, where every year there has to be a new vaccine because of variation in the underlying population of flu viruses. We suggest that the flu paradigm might be the appropriate way to think about *Plasmodium* vaccine development, rather than looking for that single magic bullet where you pick a molecule as the vaccine target and that molecule protects the worldwide population forever.

MBL In your work with the Harvard Malaria Initiative, there has been a substantial effort to train scientists and public health officials in Senegal and other affected countries in methods for malaria research. What is your rationale for that? Why not just bring the research expertise of Harvard and the Broad Institute to them?

DW Part of it is philosophical. As part of our mission, we feel that building the intellectual infrastructure in disease-endemic countries is a very important pillar of the goal to control and eradicate the diseases. These are primarily diseases of the developing world, and it is very important that there be local expertise.

Scientific colleagues in Ndioukhane, Senegal.

Secondly, and equally importantly, diseases such as malaria are primarily diseases of humans. There is no animal reservoir; there aren't good animal models for research. So to make fundamental discoveries that will be important for prevention, treatment, and cure, it is essential that one study the disease in the natural setting. And that means that you really need, on the ground, not only intellectual infrastructure but also the experimental infrastructure. The most important scientific advances are occurring by analyzing the genomes of infectious organisms, and then testing the hypotheses created by those analyses both in the laboratory and in natural populations. So you really need people in the local area who have expertise in the laboratory and in biological sciences, who will run epidemiological field trials, clinical trials.

But beyond that, you also need local people who are trained to translate basic science into medical and economic applications. We refer to this as "from the genes to the globe." You need the whole value chain. In the end, for this disease to be dealt with at a nationwide and then worldwide level, there will need to be not only medical and humanitarian justifications for doing so, but also economic development applications that will cause governments to embrace the idea of eradication.

MBL What role did the Biology of Parasitism course play in your scientific life?

DW It was very important in the development of my career. It cemented my interest in parasitology, but it also helped me define initially what I would work on from a research standpoint. One of the things BoP has always done is introduce students to the leaders in the field. Over the five years I was associated with the course, first as a student and then as faculty, I met all the major people in the then-emerging field of molecular parasitology. And because I had particular molecular biology skills, it allowed me to establish collaborations with people who were more focused on the biology or biochemistry side of things. So it was a great opportunity for me to establish my initial research program and make those very important connections with people in the field. •

Millicent Bell contributed $6 million to establish the Eugene Bell Center for Regenerative Biology and Tissue Engineering at the MBL.

John W. Rowe and Valerie Rowe contributed $5 million in endowment support for the Eugene Bell Center for Regenerative Biology and Tissue Engineering.

The Eunice Kennedy Shriver National Institute of Child Health and Human Development and the National Center for Research Resources awarded $3.4 million to establish the "National *Xenopus* Resource Center" at the MBL. Robert Grainger of the University of Virginia is the principal investigator.

The National Institutes of Health awarded $1.5 million in support of the purchase of a "Live Cell, High Speed and Resolution Spectral Confocal Microscope." Peter Smith and Rudolf Oldenbourg are the principal investigators.

The National Institutes of Health awarded $1.2 million in support of the MBL's Frontiers in Reproduction course.

Course Director Mario Ascoli of the University of Iowa is the principal investigator.

DARPA awarded $1.1 million for a project titled "Cephalopod Inspired Adaptive Photonic Systems." Roger Hanlon is the principal investigator. •

Accolades

Distinguished Scientist **Shinya Inoué** was honored by the Government of Japan with the Order of the Sacred Treasure, Gold Rays with Neck Ribbon award.

Corporation member, former trustee, and alumnus **Porter Anderson** was elected to the National Academy of Sciences. Other members of the MBL community receiving the honor include: **Douglas Koshland**, faculty, Physiology and Katsuma Dan Fellow; **Susan Golden**, faculty, Microbial Diversity; **Terrence Sejnowski**, alumnus and faculty, Neurobiology and Methods in Computational Neuroscience; and **David Weitz**, faculty, Physiology.

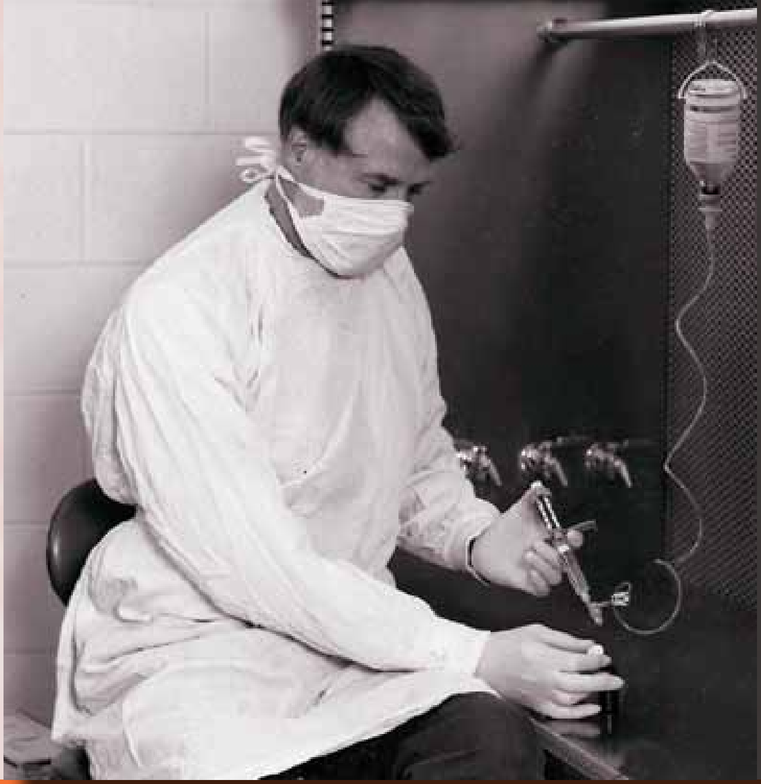
Jerry Melillo was named MBL Distinguished Scientist.

Peter Smith was awarded the Massachusetts General Hospital Martin Research Prize for excellence in basic research for a collaborative study of the acidification of the male reproductive system.

Microbial Diversity course faculty **Thomas Schmidt** received the 2010 American Society for Microbiology Graduate Microbiology Teaching Award for dedication to students and for fostering an intellectually stimulating environment.

Trustee **Gerald Fink** was awarded the 2010 Genetics Prize of The Peter and Patricia Gruber Foundation for his groundbreaking research in yeast genetics.

Bay Paul Center director **Mitchell Sogin** was awarded the Dr. Gordon Moore Environmental Grant from Ion Torrent.



A Life-Saving Test

Before 1990, thousands of children each year were infected by *Haemophilus influenzae* type b (Hib), a virulent bacterium that causes meningitis, pneumonia, and other serious diseases. In the 1970s, microbiologist Porter Anderson (an MBL Corporation member, former trustee, and '89 Microbial Diversity alumnus) and pediatrician David Smith began developing a vaccine for Hib in infants, which was brought to market in 1990. Today, Hib is nearly eradicated in the United States and Hib vaccines, used worldwide, have saved hundreds of thousands of lives. Anderson and Smith were honored by a Lasker Award in 1996.

But the road from basic research to saving lives is typically far from smooth, and the MBL played an important role in helping Anderson to navigate its bumps. Anderson's first attempt at the vaccine used the outermost component (a polysaccharide) of the Hib microbe as the crucial molecule recognized by the recipient's immune system. However, early preparations caused inflammation and fever because when the polysaccharide was isolated from the Hib microbe, it was often contaminated with another molecule, an endotoxin, which was causing the adverse reaction. So Anderson, who was then at Boston Children's Hospital, needed a simple, practical way to identify when endotoxin was present in the vaccine preparation.

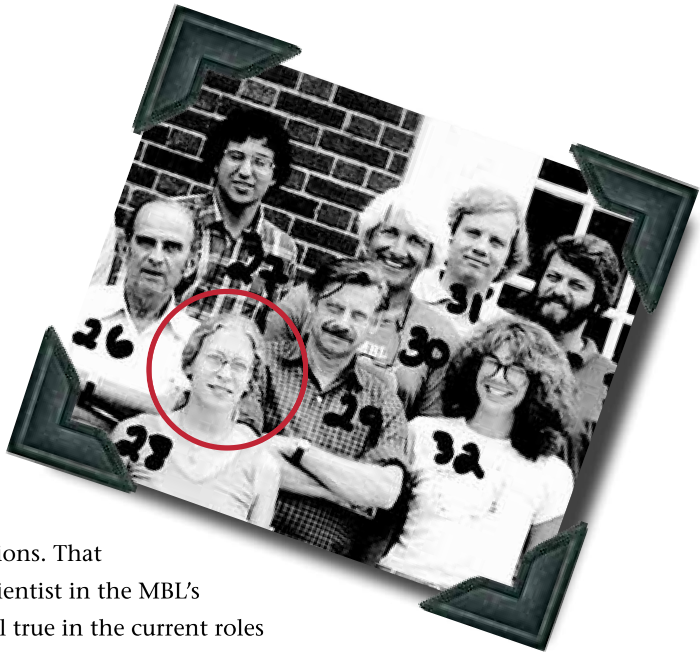
"Fortunately, I was told that some folks at the MBL had discovered proteins in the blood of the horseshoe crab that would clot if exposed to tiny amounts of endotoxin," Anderson said to well-wishers gathered at the MBL last summer to celebrate his election to the National Academy of Sciences. "I found my way to the old Marine Supply Building and asked for some of this reagent. A helpful guy said, 'We have none to offer, but I will sell you some horseshoe crabs, show you how to bleed them, and if you take the blood into yonder brick building (Lillie), maybe somebody will let you use a centrifuge to process the blood into the reagent.' I did this, and drove back to Boston with supply of the so-called Limulus Amebocyte Lysate (LAL). With this assay, it was straightforward to devise a method to remove the endotoxin from the polysaccharide. The latter proved non-toxic, as hoped, and it became the first-generation Hib vaccine." •

Porter Anderson (above) completes a sterile filling of vaccine vials circa 1990. In the 1970s, Anderson relied on the nascent *Limulus* Amebocyte Lysate (LAL) test to ensure purity in his first-generation Hib vaccine. The LAL test sprang from basic research at the MBL in the 1950s and 1960s, and is now used in medical settings worldwide. "I am a poster child for the concept that basic-discovery science can have a practical payoff years later," Anderson says. "It continues to help in my current work toward an inexpensive pneumonia vaccine for infants."

A participant in the 1981 MBL Microbial Diversity course, Molly Miller Jahn is dean of the College of Agricultural and Life Sciences at the University of Wisconsin-Madison. She recently completed a seven-month tenure as acting under secretary for research, education and economics at the U.S. Department of Agriculture. Prior to her appointment at UW-Madison in 2006, Jahn established a highly recognized research career at Cornell University in genetics, genomics, and breeding of crop plants, releasing more than two dozen varieties currently grown commercially on six continents including an All America Selection Gold Medal winner. She founded the Public Seed Initiative in 2001 and later the Organic Seed Partnership to engage hundreds of U.S. farmers in participatory plant breeding and germplasm conservation activities. She has also worked extensively in Africa, Asia and Latin America to link crop breeding objectives to improvement in human nutrition and income, and has held leadership roles in major international agricultural projects. Under Jahn's tenure at UW-Madison, funding for several major facilities and research centers has been secured, including the Wisconsin Energy Institute for sustainable and renewable energy research; the $135 M DOE Great Lakes Bioenergy Research Center; and the Wisconsin Bioenergy Initiative. Jahn received her B.A. with Distinction from Swarthmore College, holds graduate degrees from Cornell and MIT, and was named an American Association for the Advancement of Science Fellow in 2006.

The Whole Landscape

By Molly Miller Jahn



Like many of us who choose science as our life's work, I spend a fair amount of time asking questions. That was true in my earliest days as a scientist in the MBL's Microbial Diversity course. It is still true in the current roles I play, supporting large, complex research and educational institutions toward excellence and impact. In fact, it turns out that the questions we ask, and how we choose to pursue their answers, matter at least as much as the answers themselves.

From the beginning, my research has focused on interactions among organisms and with the environment, with outcomes that matter to human beings. The Microbial Diversity course illuminated the vast expanse of metabolic diversity on this planet. I took those insights to agriculture, the dominant human activity on Earth, and one that has planet-scale implications for biodiversity, air and water quality, and the human condition. For 15 years, within the reductionist paradigm of molecular genetics, I worked to define the mechanisms that govern plant disease resistance and bred vegetable varieties resistant to disease, many of which are grown commercially today. We could measure the reductions in pesticide use and the improvements in yield, nutrition and income.

This work was satisfying, and the results rewarding. And then I looked up. With great gains in agricultural productivity, our nation still has not declared food security a human right. This generation of American children may be the first to face life expectancies shorter than their parents. In the developing world, obesity now rivals food insufficiency as a health threat for the world's poorest. And over those same 15 years, our planet crossed some significant lines. Millions of acres have been deforested. Glaciers are vanishing at an astonishing rate. From my niche in the reductionist paradigm, the incremental advances within my reach, as worthy and important as they may be, were not stacking up as I had expected.

So I shifted gears. For the past five years, I've held two roles that have allowed me to push hard into this uncomfortable space. As dean at a large research university, and recently in an interim leadership post with the U.S. Department of Agriculture, I have begun working across larger communities to deliver the strengths of the scientific community into these larger challenges. In doing so, I live in the collision between the power and clarity of reductionist science and the urgent need to address the largest dynamics on our planet as systems. How should our scientific organizations be structured to deliver excellence in both models? How should scientists be trained and supported to continue the catalytic advances available within reductionist frameworks while gaining meaningful understanding of systems-level dynamics that begin with complexity and uncertainty?

The questions that call me today are hardly the ones I anticipated during my days at MBL. These questions call us as scientists into new communities with new tools and new views, toward threats and opportunities that didn't even have names 20 years ago. My belief that science will provide absolutely essential insights as we set our course for the future has only strengthened. Now it is clear. Our planet is the experiment. •

Rachel Carson in Woods Hole in 1929, when she spent six weeks at the MBL as a beginning investigator in zoology. She returned to the MBL in 1932 to carry out research on teleosts (bony fish), while she was a master's student at the Johns Hopkins University. Photo by Mary Frye.

A Gift to the Sea

Rachel Carson had her first taste of living by the sea when she spent the summer of 1929 at the MBL, and it left a deep impression that would carry through her life and career. Carson went on to blend her talents as a biologist and a writer at the U.S. Bureau of Fisheries, where she became chief editor. Her second book, *The Sea Around Us* (1951) made her famous, spending months on the bestseller lists and winning the National Book Award. Carson returned to Woods Hole in 1951 and 1952 to conduct research for *The Edge of the Sea* (1955), and at that time she became a member of the MBL Corporation. Her final book, *Silent Spring* (1962), carved her place in history, as its account of the devastating impact of chemical pesticides on wildlife and the environment was a wake-up call that led to the establishment of the Environmental Protection Agency in 1970. While Carson's reputation rests on having galvanized a major cultural awakening, her heart, more simply, belonged to the sea. •

MBL Biological Discovery in Woods Hole

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In the Next *MBL Catalyst*

Our Home Planet: Seeking Balance

When the MBL Ecosystems Center was founded in 1975, the idea that human activities were leaving a big footprint on our environment was just entering the public debate. Today, the evidence of our impact is everywhere—in our atmosphere, oceans, ice sheets, coastal zones, our drinking water sources, trees and plants, even the ground beneath our feet. In the next issue of *MBL Catalyst*, MBL scientists will share what is known about human impacts on the environment, what is not known, and what we must do to restore a healthy balance.