MBL

Biological Discovery in Woods Hole

Catalyst

Founded in 1888 as the Marine Biological Laboratory

FALL 2009
VOLUME 4, NUMBER 2

IN THIS ISSUE

Creature Feature

Why Biodiversity Matters

page 2

MBL Catalyst

Fall 2009 Volume 4, Number 2

MBL Catalyst is published twice yearly by the Office of Communications at the MBL in Woods Hole, Massachusetts. The MBL is an international, independent, nonprofit institution dedicated to discovery and to improving the human condition through creative research in the biological, biomedical, and environmental sciences. Founded in 1888 as the Marine Biological Laboratory, the MBL is the oldest private marine laboratory in the Americas.

About the cover: "Developing Megalops" by Chris Rieken, a research assistant in the MBL's Bay Paul Center. This image of a larval crab in the final stage of development, known as megalops, won first place in the 2009 MBL Scientific Photography Contest.

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

www.mbl.edu/catalyst

Send correspondence to:
MBL Communications Office
7 MBL Street, Woods Hole, MA 02543
508-289-7423, comm@mbl.edu

From the Director

Dear Friends,

One of the most memorable moments of the 2008 Nobel Prize ceremonies came during a speech by Roger Tsien, co-recipient of the Chemistry Prize with the MBL's Osamu Shimomura and Martin Chalfie of Columbia University. After thanking the many scientists who made green fluorescent protein (GFP) the powerful tool it is today for seeing the inner workings of live cells, Tsien thanked the bioluminescent jellyfish, *Aequorea*, from which Shimomura originally isolated GFP.

Sadly, Tsien continued, the number of jellyfish in their Pacific Northwest habitat has declined by more than a thousand-fold over the past 10 years, probably due to polluted runoff from the land. Fortunately, Shimomura did his early, crucial work on GFP before the jellyfish population collapsed. "But what other potential scientific breakthroughs may never happen because of man-made pollution and global warming?" asked Tsien, who is from the University of California, San Diego.

It's a question of great importance. The oceans sustain life in numerous ways, not least in what they have to offer in terms of biomedical science and medical therapies. Where would neuroscience be today without the Atlantic squid, an experimental animal that has given us more insight into the nervous system and its pathologies, than any other? Where would developmental biology be without long-valued model animals such as the sea urchin and the surf clam?

This issue of *MBL Catalyst* celebrates the animals—particularly the marine creatures so well studied at the MBL—that have so much to tell us about our own biology, our own health, and the health of our planet. While biomedical science has, for decades, largely focused on classical genetic model animals such as the fruit fly and mouse, there is a renaissance of interest in marine models as their genomes are being decoded. Once again, the MBL is well poised to take the lead in an emerging field, as our initiative in Regenerative Biology and Medicine (p. 4) demonstrates. We just received word of federal stimulus funding to recruit two new scientists to this important initiative, which is centered on the many regenerative organisms, both marine and freshwater, that have long been studied at the MBL.

This issue of *MBL Catalyst* also celebrates two distinguished scientists who are champions of the need to assess and protect marine biodiversity: Jesse Ausubel, vice president of the Sloan Foundation (p. 12) and Jane Lubchenco, the new head of the National Oceanic and Atmospheric Administration (p. 8). Ausubel, along with the MBL, is deeply involved in global efforts to catalogue biodiversity, both on land and sea. And Lubchenco, an MBL course alumna, is a first-rate marine ecologist and passionate leader in a new federal effort to protect and restore our oceans and coasts.

Many thanks to our guest science editor for this issue, Mike Greenberg, editor emeritus of *The Biological Bulletin* and emeritus professor at the University of Florida's Whitney Laboratory for Marine Bioscience. Greenberg's expansive knowledge of marine animal models—and his sense of humor!—contributed much in readying this issue.

Gary Borisy

Gary Borisy
Director and Chief Executive Officer

Catalyst

In this Issue

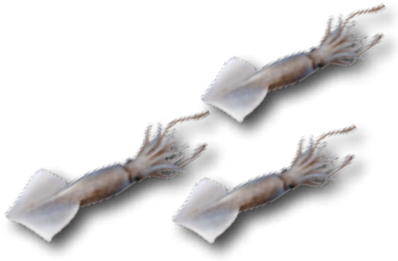
Features

2 **Creature Feature**

The colorful diversity of the animal world has special meaning to scientists—but so does its underlying unity.

4 **It's Back!**

Why can some animals re-grow missing body parts, but humans can't? Armed with powerful new tools, research on regeneration makes a comeback at the MBL.



8 **Steward of the Seas**

Jane Lubchenco fell in love with scientific research as a student at the MBL. Today, she is the first marine ecologist to lead the National Oceanic and Atmospheric Administration.

10 **One Fish, Many Hats**

Some experimental animals are best suited for just one type of biomedical research. Not the versatile zebrafish, which is proving to be a widely popular model system.

Departments

Creature Feature: *Why Biodiversity Matters*

To the scientist, the animal world presents a wonderful paradox. On the one hand, it contains endless and multi-faceted diversity. Each of the millions of species, from microbe to monkey, is uniquely shaped by evolution to prosper in its own planetary niche. This creates a magnificent variety of distinct features, from the signaling skin of cuttlefish to the articulate hands of human beings.

From this diversity in the animal world, the concept of a model organism in science arose: "For a large number of (biological) problems, there will be some animal of choice on which it can be most conveniently studied," wrote MBL investigator August Krogh in 1929. A scientist interested in fertilization, for instance, will make faster progress studying the prolific sea urchin, which releases thousands of eggs each summer, than a slowly reproducing mammal.

Don't call the toadfish (*Opsanus tau*) ugly in front of MBL scientist Stephen Highstein, whose studies of balance and equilibrium in this handsome fish have implications for the human condition.

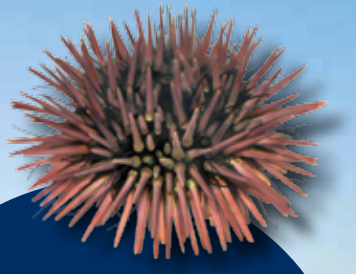
The Atlantic squid (*Loligo pealei*) is well known as a batter-fried appetizer, but it has also long served scientists who explore the intricacies of the nervous system, including how electrical signals are generated and transmitted and how cellular parts are transported in the neural network.

The horseshoe crab (*Limulus polyphemus*) is a "living fossil" that has been on Earth about 200 million years longer than humans. *Limulus* has long been prized by MBL researchers of immunity and also of vision.

Below the boundless diversity in the animal world lies an astonishing degree of commonality at the genetic level.

But here also lies the paradox. How can insight gleaned from simple animals in any way translate to cures for human disease and disorders? The answer lies in the genes. Below the boundless diversity in the animal world lies an astonishing degree of commonality at the genetic level. The genes that control cell division or hormone release—or any aspect of growth, disease, or aging—are essentially the same in the worm and the fish and the mouse and the human.

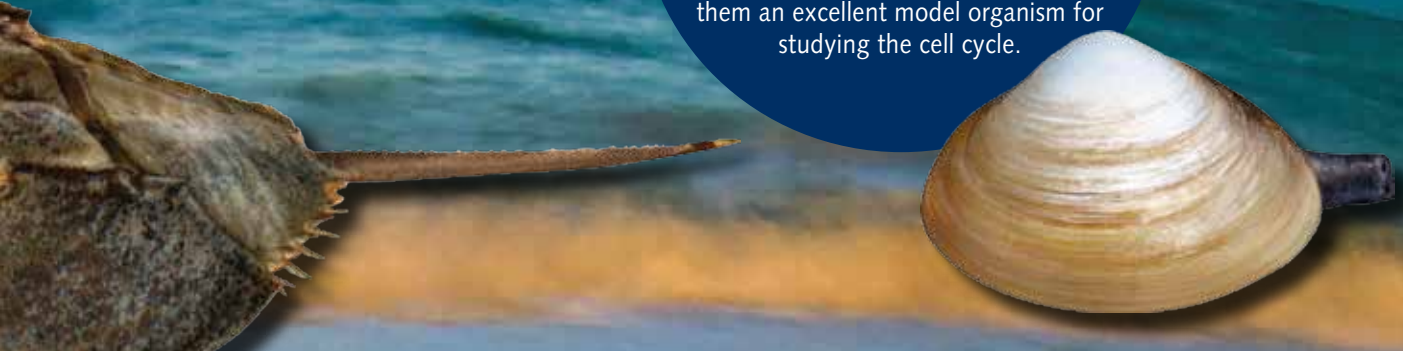
As this issue of *MBL Catalyst* celebrates, scientists at the MBL study animals at all levels of organization—from the single gene in a fish that may explain autism in a child; to the communities of microbes that power our planet; to the entire kingdom in the Encyclopedia of Life. Much of the animal world remains unexplored, yet discovering and preserving biodiversity is key to advances in medicine, as well as the protection of life on Earth. Read on, and see what the animals are telling us.



Historically, the purple-spined sea urchin (*Arbacia punctualata*) has been an important research model in cell and developmental biology. More recently, the purple sea urchin (*Strongylocentrotus purpuratus*, above) has surpassed it in popularity, as researchers delve into the molecular basis of development.

Despite those rabbit-ear protrusions, the sea hare (*Aplysia californica*) is a slug, not a bunny. Due to its extra-large neurons, former MBL researcher Eric Kandel chose it for his research on learning and memory, for which he was awarded the Nobel Prize in 2000.

In many coastal areas, the tasty surf clam (*Spisula solidissima*) has been overharvested. MBL scientist Scott Lindell leads a surf clam restoration project in Truro and Provincetown, Massachusetts, where a "no take zone" has been set up as a refuge for clam brood stocks. Surf clams produce hundreds of eggs that divide in sychrony when fertilized, making them an excellent model organism for studying the cell cycle.



It's Back!

The MBL's initiative in Regenerative Biology and Medicine takes shape

The South African clawed frog (*Xenopus laevis*) can regenerate the lens of its eye, a process that could one day be replicated in humans. The frog is used for a wide range of studies at the MBL, including cell division, embryonic development, and the neural circuitry of vision.

Hercules was a strong man, but was he a scientist? In one Greek myth, Hercules is ordered to slay the hydra, a monstrous swamp serpent with nine heads. To his amazement, Hercules finds that each time he smashes one head, two more sprout in its place. Hercules smartly conquers the beast using fire, but he has also revealed the hydra's astonishing power of regeneration.

It's a power that is widely found in the animal kingdom. Cut the hydra—actually a tiny aquatic animal—in two, and each half regrows into a whole body. If a starfish loses an arm, it shoots out another. And the zebrafish heart, when it sustains damage, doesn't scar the way a human heart does: It regrows healthy new heart muscle.

If so many animals can regenerate lost limbs, nerves, organs, even a whole body, why can't human beings? The question is a big one, but answering it could lead to therapies for some of our most serious medical challenges, from heart disease to spinal cord injury. With this in mind, the MBL's new initiative in Regenerative Biology and Medicine is rapidly taking shape.

If so many animals can regenerate lost limbs, nerves, organs, even a whole body, why can't human beings?

"We all share basically the same complement of genes, whether that be a fish or a frog or a human being," says Jonathan Henry of University of Illinois, an expert on lens regeneration and a faculty member in the MBL Embryology course. "Of course, the genes are regulated differently in these various animals. But if you assume the [same] genes are there, why can't humans exhibit extensive regeneration, while other animals can?"

The MBL, scientists are finding, is an excellent place to probe this question. Many marine organisms are highly regenerative, and they are readily collected and maintained at the MBL, sometimes by the researchers themselves.

"Eel Pond is full of these critters," says Stefano Tiozzo, pulling a collecting cage encrusted with sea squirt colonies out of the Woods Hole pond. Tiozzo, an MBL Research Awardee from the University of California-Santa Barbara, wants to know how this creature—familiar as a pest that clumps onto boat propellers and piers—can so faithfully regenerate its entire body.

"If we pull the animals out of the matrix in which the colony grows, and leave just a few blood cells behind, within 48 hours the blood cells plaster together and attempt to rebuild the organism," Tiozzo says. "The first attempt doesn't work; it looks like a cancer. But soon the cells find a way to reorganize, to remember what is front and back in the organism, what will be the nervous system, what will be muscle. And they rebuild the animal."

Expertise in marine animal husbandry is just one of the strengths supporting the MBL's goal of leadership in regenerative biology. The MBL also has longstanding expertise in cell and developmental biology, both among its researchers and in the faculties of the Physiology and Embryology courses. They enjoy excellent resources at the MBL, including cutting-edge microscopy and imaging equipment. Facilities for advanced genetic analysis are also critical, and are available on site.

All of this will serve to answer the central and exciting questions in regenerative biology today. Where do regenerative cells come from? Were they always there, or did they recruit to the site after injury? Are they stem cells, which are capable of becoming any type of cell? Or are they just heart muscle cells, or nerve fiber cells, that are amazingly able to reorganize as a new body part?

And the ultimate goal is to translate the basic science of animal regeneration to medical therapies. To do this, two research communities must regularly meet and mingle—the regenerative biologists, and the experts in human stem-cell science. Where does this happen? In the MBL's Frontiers in Stem Cells and Regeneration course, which has just received a grant of $557,000 over five years from the National Institutes of Health.

But perhaps one of the biggest advantages of the MBL is the collegiality and "buzz" that surrounds the regenerative biologists. They all share the exciting feeling that they are breaking ground in a promising field. Sharing Tiozzo's lab in Rowe Laboratory is a group of scientists from the University of Massachusetts-Dartmouth, under the direction of Professors Paul Calvert and Alex Fowler. With the support of a Eugene and Millicent Bell Research Award in Tissue Engineering, they are busy testing marine tissues that could serve as models for medical implants, such as replacement cartilage.

And downstairs is the sea lamprey group. "We want to understand the differences between the robust recovery from spinal cord injury we see in lampreys, and what happens in humans," says Jennifer Morgan from University of Texas at Austin. Within 12 weeks of severe spinal cord injury, the sea lamprey has regrown the damaged neural and anatomical connections and is swimming again. Humans, of course, aren't so fortunate.

Each year, more and more regenerative biologists are finding common ground at the MBL. "Regeneration is a very productive field at the MBL," says Tiozzo's collaborator Ulrich Kuern, also from UC-Santa Barbara. "You walk around, and someone says, 'Oh! I have this method! You should try that!' That's just great, you get input from all people. That is the biggest advantage here." • — DK

Right Tools, Right Time

Like the animals themselves, regeneration isn't a brand-new research field, but one that has come charging back.

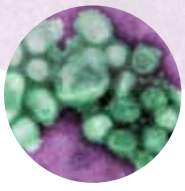
"Regeneration was a brisk business at the MBL from the 1940s to 1970s," says Mike Greenberg, emeritus professor at the University of Florida. "What we are seeing now is a re-emergence of regenerative biology and medicine, with great new tools."

In fact, regeneration was a hot topic at the MBL more than a century ago, when it fascinated pioneering scientists like Thomas Hunt Morgan and Jacques Loeb. But what they lacked are today's powerful molecular tools. Scientists can now turn genes on or off and ask which genes take part in a regenerative process, or even which cells regrow a certain body part. Regeneration is resurging—particularly at the MBL.

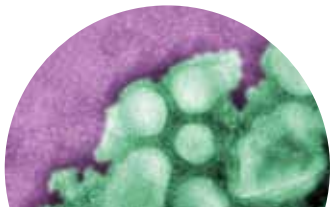
MBL Scientist Spearheads White House Climate Change Report

Ecosystems Center senior scientist Jerry Melillo co-chaired and co-edited a recent report offering the most comprehensive assessment to date on the impacts of climate change on the United States. The report, released by the Obama Administration, emphasizes that the choices we make now will determine the severity of climate change in the future. "We now have strong evidence that the global warming observed over the past 50 years is due primarily to human-induced emissions of heat-trapping gases," says Melillo. Climate-related changes, including increases in air and water temperatures, reduced frost days, increased frequency and intensity of downpours, a rise in sea level, and reduced snow cover, glaciers, and sea ice, have already been observed globally and in the United States. These changes are expected to increase with continued global warming and will impact human health, water supply, agriculture, coastal areas, and many other aspects of society and the natural environment. According to the report, responses to climate change should not only include mitigation measures to reduce greenhouse gas emissions, but also adaptation measures to improve our ability to cope with or avoid harmful impacts, and take advantage of the beneficial ones. "An important message is the need to begin to focus our attention on the issue of adaptation," stresses Melillo. "What might we do for the climate change that is inevitable, beyond slowing down emissions? What are our adaptation options?" (A full report is available at www.globalchange.gov) •

Scientists Link H1N1 Flu Susceptibility to Common Levels of Arsenic Exposure



MBL Chief Academic and Scientific Officer, Joshua Hamilton, and his colleagues have recently reported that the ability to mount an immune response to H1N1 flu infection is significantly compromised by a low level of arsenic exposure that commonly occurs through drinking contaminated well water. In mice that had ingested 100 parts per billion (ppb) arsenic in their drinking water for five weeks, the immune response to H1N1 infection was initially feeble, and when it did take effect, it was too robust and too late. Morbidity over the course of the infection was also significantly higher for the arsenic-exposed animals than the normal animals. "One thing that did strike us, when we heard about the initial H1N1 outbreak, is that Mexico has large areas of very high arsenic in their well water, including the areas where the flu first cropped up. We don't know that the Mexicans who got the flu were drinking high levels of arsenic, but it's an intriguing notion that this may have contributed," Hamilton says. The U.S. Environmental Protection Agency considers 10 ppb arsenic in drinking water "safe," yet concentrations of 100 ppb and higher are commonly found in well water in regions where arsenic is geologically abundant, including upper New England, Florida, and large parts of the Upper Midwest, the Southwest, and the Rocky Mountains, Hamilton says. (*Environmental Health Perspectives* 117: Volume 117, 1108-1115, 2009) •



Back to Basics: Scientists Discover a Fundamental Mechanism for Cell Organization

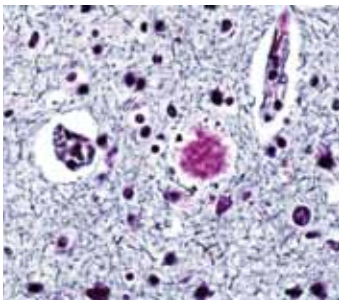
Scientists have discovered that cells use a very simple phase transition—similar to water vapor condensing into dew—to assemble and localize subcellular structures that are involved in formation of the embryo. The discovery, made during the 2008 MBL Physiology course, is reported in the journal *Science* by course teaching assistant Clifford Brangwynne and faculty member Anthony Hyman of the Max Planck Institute for Molecular Cell Biology and Genetics and their colleagues. Working with the worm *C. elegans*, the scientists found that subcellular structures called P granules, which are thought to specify the germ cells that ultimately give rise to sperm or eggs, are liquid droplets that transition between a dissolved or condensed state. In newly fertilized one-cell embryos, the P granules are dissolving throughout the cell, like water droplets at high temperature. But prior to the first cell division, the P granules rapidly condense at one end of the cell, as if the temperature were suddenly lowered there. The progenitor germ cell subsequently forms where the P granules have condensed. "This kind of phase transition could potentially be working for many other subcellular structures similar to P granules," says Brangwynne, who credits the discovery to the "dynamic nature" of the MBL Physiology course. "It is interesting to think about this in the context of evolution and the origin of life," he says. (*Science* 324, 1729-1732, 2009) •

From Phytoplankton to Penguins

New research using detailed satellite data indicates that climate change is affecting not just the penguins at the apex of the Antarctic food chain, but simultaneously the microscopic life at the base of the food web. A team of scientists including MBL Ecosystems Center director Hugh Ducklow reports in the journal *Science* that climate warming has decreased levels of phytoplankton—the base of the Antarctic food chain—as much as 80 percent over the past 30 years off the Western Antarctic Peninsula. These phytoplankton changes, the scientists say, may help explain the observed decline of some penguin populations. "We've known for some time about many climate and food-web changes in this region," says Ducklow, including rapidly decreasing populations of species that depend on sea ice for habitat, such as Adélie penguins and krill. "What we didn't know until now was that phytoplankton are also responding to climate changes," Ducklow says. "That's very important. Now we know that climate changes are impacting the base of the food web and forcing their effects on up through the food chain." (*Science* 323: 1470-1473, 2009) •

Tiny But Toxic

Tiny, toxic protein particles severely disrupt neurotransmission and inhibit delivery of key proteins in Alzheimer's disease, two separate studies by MBL researchers have found. The particles, minute clumps of amyloid beta, have long been known to accumulate and form plaques in the brain of Alzheimer's patients. "These small particles that haven't aggregated into plaques—these are increasingly being seen as the really toxic species of amyloid beta," says MBL investigator Scott Brady of University of Illinois College of Medicine. The particles inhibit neurons from communicating with each other and with other target cells in the body. They also activate an enzyme, CK2, which disrupts "fast axonal transport," a system comprised of motor proteins that move cargo from place to place in the neuron on microtubule tracks. Brady's findings are complemented by another study by MBL investigator Rudolfo Llinás of New York University School of Medicine who found that activation of CK2 blocks neurotransmission at the synapse—the point where the neuron connects to its target. "Disruptions in the fast axonal transport system are probably key elements in the pathogenesis of Alzheimer's and other adult-onset neurodegenerative diseases, such as Parkinson's and ALS," says Brady. "It doesn't mean that is the only thing going on, or that it is the triggering feature of the disease. But we do know that changes in the fast axonal transport system are sufficient to cause the 'dying back' of neurons that is characteristic of these diseases." (*PNAS* 106: 5901-5906, 2009; *PNAS* 106: 5907-5912, 2009) •



Steward of the Seas

MBL alumna Jane Lubchenco takes a holistic approach to ocean policy as NOAA's new head

When the president of the United States nominates you to lead a national agency, it's surely a life-changing event. Just ask marine ecologist Jane Lubchenco, who in March was confirmed as the new head of the National Oceanic and Atmospheric Administration (NOAA).

Lubchenco had barely settled into her new office when the president placed her on his Ocean Policy Task Force, which is on a fast track to define policy to restore and protect our marine ecosystems. A coherent plan to keep the oceans healthy has never been achieved in the United States, where a patchwork of federal, state, and tribal laws and private marine interests abides. Yet Lubchenco is energized by the task force's "willingness to tackle some tough issues and do the right thing."

"We know that there are many changes underway that are resulting in degradation of ocean systems, including climate change, nutrient pollution, transport of invasive species, and overfishing," she says. That is driving the task force members, who are from agencies as far-flung as the Navy and the Department of Health, toward a common purpose. "Our focus is very much on having healthy, productive, resilient ocean systems," she says. "There is a common commitment to be good stewards, to work together as partners. And that is pretty remarkable and exciting to be a part of!"

"Our focus is very much on having healthy, productive, resilient ocean systems," she says. "There is a common commitment to be good stewards, to work together as partners. And that is pretty remarkable and exciting to be a part of!"

While Lubchenco is thrilled to help shape a national solution to marine problems she cares deeply about, she is no less enthusiastic about another defining period in her life, when she first discovered her passion for science. Like many other scientists, it was during a summer she spent at the MBL.

"It was just a life-changing experience for me," says Lubchenco of taking the MBL Invertebrate Zoology course which, in its present form, is called Neural Systems and Behavior. Lubchenco grew up in the Colorado Rockies, and was no stranger to freshwater exploration. But in 1968, when she came to the MBL after her junior year in college, she says, "I discovered a whole new (marine) world that I didn't really know existed. And I found it endlessly fascinating. All those exotic creatures, so many different ways of making a living, so many types of body plans. The opportunity to be with world-class faculty at the MBL, each of whom was a specialist in a different type of marine invertebrate . . . the stimulating Friday Evening Lectures, the amazing culture and ambiance of the MBL and Woods Hole. Everything about it was exciting and energizing."

Vital Statistics

POSITION: Under Secretary of Commerce for Oceans and Atmosphere and Administrator of the National Oceanic and Atmospheric Administration (NOAA), the nation's top science agency for climate, oceans, and atmosphere. Lubchenco is the first woman and the first marine ecologist to lead NOAA, which has a $4 billion budget and 12,800 employees.

DEGREES: B.A. Biology, Colorado College; M.S. Zoology, University of Washington; Ph.D. Ecology, Harvard University.

HONORS: Include a MacArthur ("Genius") Fellowship, nine honorary degrees, membership in the National Academy of Sciences, and former presidency of the American Association for the Advancement of Science and of the Ecological Society of America.

BEST MEMORY OF HER MBL EXPERIENCE: "My exposure to the oceans was love at first sight and my life's work was set in motion."

Lubchenco had her first encounter with independent research at the MBL, learning "how to ask research questions and design experiments," she says. "It was a pivotal experience. It was transformative in helping me decide to pursue graduate research in marine sciences. I couldn't get enough of this stuff that I thought was really cool!"

In graduate school, Lubchenco's interests widened from marine invertebrates to the ecological interactions among them. "More recently, I've studied coastal ecosystems around the world," she says. "How do large marine ecosystems work? How are they changing? How are they influenced by human activities? How can we do a better job of managing them? Over time, my questions have evolved, which is what is fun about science."

As the scope of Lubchenco's research expanded, so did her awareness of human-induced threats to ocean health. Her work eventually intersected with that of MBL senior scientist Jerry Melillo, who has long studied the impacts of human activities on the environment. In 1997, Lubchenco and Melillo were among the co-authors of "Human Domination of Earth's Ecosystems," a paper published in the journal *Science*, and now a "citation classic" in the field of ecology. (Eight of Lubchenco's papers have earned this designation, and she is in the top 1% of highly cited ecologists in the world.)

While keeping both feet in marine sciences research as a faculty member since 1977 at Oregon State University, Lubchenco has engaged more and more in public policy, including service on the Pew Oceans Commission and the Joint Ocean Commission Initiative. She has come up against the difficulties of trying to manage the oceans rationally, when so many agencies and national groups have conflicting interests. Yet she sees something different happening on the new Ocean Policy Task Force, which gave its interim report to the president in September and will roll out its full report early next year.

"Our interim report states that healthy oceans matter, that stewardship is important, that we need to do a better job of managing more holistically," she says. "These are very powerful statements that have never been articulated by the federal family before."

As a scientist, the word "holistic" means a great deal to Lubchenco. For the first time, the nation is taking a scientific, ecosystems-management-based approach to stewarding our oceans, rather than tackling problems sector-by-sector and issue-by-issue. This is vital if the oceans are to provide us with "the full suite of ecosystem services that people want and need, whether it's safe seafood, clean beaches, stable fisheries, abundant wildlife, or vibrant coastal communities," Lubchenco says.

In the end, it's an affirmation of what the ecologist in her knows to be true. "It's more a holistic understanding of how our own health, prosperity, and well-being depend intimately on having healthy oceans and coasts." • — DK

One Fish, Many

Zebrafish swim to the fore of biomedical research

Joan Ruderman and Joseph Buxbaum took the MBL Zebrafish course to introduce this versatile fish into their research labs.

Hats

You can sense the collective exhale in the room when Megumi Hashiguchi succeeds at her delicate task. With a quiet huddle of students gathered around her, Hashiguchi, a teaching assistant in the MBL Zebrafish course, is carefully poking a one-celled zebrafish embryo with a thin microinjection needle. These students aren't kids—they include professors from places like MIT and the University of Barcelona—and they want to master this precise procedure so they can transfer it back to their home labs.

Conversations buzz and the students scatter, finding a seat at a lab bench where they try the microinjection themselves. Inside the needle are tiny molecules that are meant to "knock down," or disrupt, a certain gene in the new embryo. If all goes well, the transparent embryo will integrate the molecules, and the students will observe how disturbing that gene affects normal development. It's helpful that the zebrafish embryo develops quickly: a heartbeat within 24 hours, and two days later the larva hatches and swims. What's even more convenient is that their mutated zebrafish, once mated, will produce a prodigious number of young with the same mutation.

"You can think of a zebrafish as a mini, aquatic mouse, except when you put a few males and females together; the next morning you've got several hundred embryos," says Joan Ruderman, a professor at Harvard Medical School and president of the MBL Corporation, who was a student in the Zebrafish course in 2008.

"All the superstars in the field teach in the Zebrafish course."

Ruderman is one of many senior-level researchers who have taken this course in recent years, as the tropical freshwater fish has earned a vaunted spot as a vertebrate model organism, right up there with the laboratory mouse. The fish's fecundity, as well as the ease with which its DNA can be manipulated, are huge pluses for biomedical researchers.

"If you've got a gene of interest, you can knock it out in the zebrafish within a week, and get some real data back within two months. That same experiment can take two years in a mouse," says Joseph Buxbaum, a professor at Mt. Sinai School of Medicine and a Zebrafish course alumnus.

Buxbaum spent last summer at the MBL studying genes associated with autism and schizophrenia, which are a main focus of his lab at Mt. Sinai. He took advantage of the expertise in the MBL's Zebrafish Facility, where the fish are husbanded for research use.

"We think one of the critical parts of schizophrenia is changes in the cells that provide insulation around neurons," Buxbaum says. "We've identified a gene that we believe affects those insulating cells. So I am testing that hypothesis. That is really hard to do in a petri dish. I could do it in a mouse, but it would be a huge endeavor. The zebrafish is a really good intermediate model for manipulating the gene, and seeing whether the cells are affected."

The zebrafish, in fact, has become a mutation model in the world of vertebrate research. Since the mid-1980s, hundreds of mutations that perturb basic developmental processes have been described in the zebrafish. As a result, the fish is now routinely used for discovering and assessing drugs.

"You can take zebrafish embryos that have some deficit you have engineered, and screen a library of drugs to see what rescues that deficit," says Buxbaum.

The little fish—which is often found in home aquariums—has also "crossed over" into toxicology research. Ruderman, for example, is developing zebrafish embryos to be used as sensors for environmental estrogens. These are a bewilderingly large and diverse group of manmade chemicals—plastics, herbicides, pesticides—that, once they enter the environment and the bodies of living creatures, mimic the effects of estrogen. "The right amount of estrogen is good. Too much estrogen at the wrong time can be bad," says Ruderman, creating problems such as feminizing developing males or triggering hormone-dependent diseases, such as breast cancer.

Ruderman is creating zebrafish embryos that will glow whenever they encounter an estrogenic compound. "You can do two things with this zebrafish sensor," she says. "You can take water samples from real life, say from a sewage outfall pipe, put the embryos in and ask, 'Does something in the water make them glow?'" Or, you could set up screens to test the estrogenic effects of some of the nearly 90,000 chemicals used in the United States in manufacturing, agriculture, and consumer products.

Recently, zebrafish have moved into yet another research niche: regenerative biology. "The zebrafish has tremendous potential for regeneration, including its nervous system, heart, and fins," Ruderman says. MBL Zebrafish course co-director David Raible, for example, is studying how zebrafish regenerate the "hair cells" used for hearing—which may one day lead to treatments for humans with hearing loss.

The fish's popularity in research circles widens every year, thanks in no small part to the MBL course dedicated entirely to its use. "All the superstars in the field teach in the Zebrafish course," says Lenny Dawidowicz, the MBL's recently retired director of education. "People love to come to it because they consider it halfway between a course and a scientific conference." • — DK

MBL Moment

The Big Picture

. . . with

Jesse Ausubel
Vice President, Programs
Alfred P. Sloan Foundation

Jesse Ausubel is vice president at the Alfred P. Sloan Foundation, where he directs programs in basic science and technology. Ausubel also directs the Program for the Human Environment at The Rockefeller University; and is an adjunct faculty member at Woods Hole Oceanographic Institution. Associated from 1977 to 1988 with the National Academy complex in Washington, D.C., he was one of the principal organizers of the first U.N. World Climate Conference in 1979 and has authored and edited more than 150 publications on technology and environment.

"Big science" projects are rare in biology, but Jesse Ausubel has catalyzed two that aim to embrace the biodiversity of life on Earth. The first, the Census of Marine Life (www.coml.org) is a global network of scientists who are exploring the oceans and gathering data on the diversity, distribution, and abundance of all marine life forms. Even the millions of microbial species are being counted, by a team led by the MBL's Mitchell Sogin and Linda Amaral-Zettler. Next fall, the decade-long Census will roll out its results

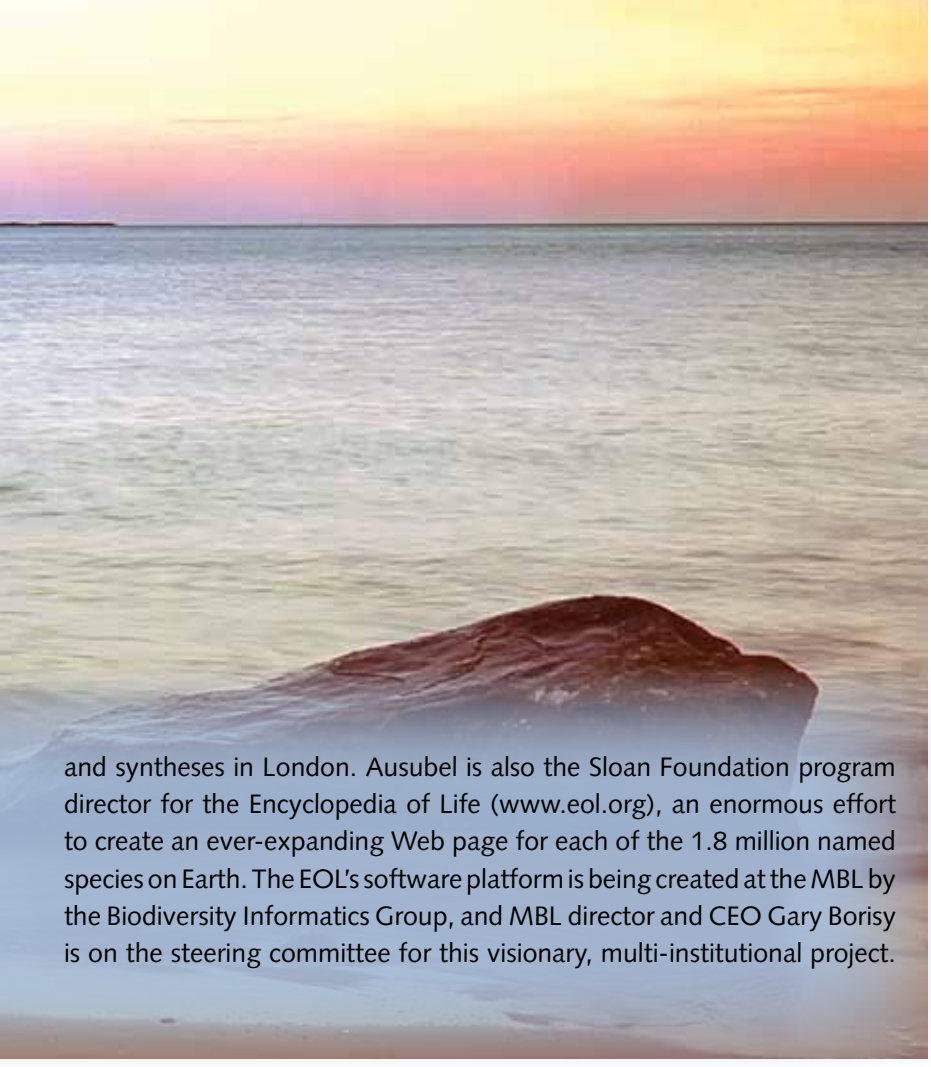
MBL What led you to your interest in "big science" biodiversity projects, such as the Census of Marine Life and the Encyclopedia of Life?

JA As a small child, I loved almanacs, encyclopedias, and atlases; by age 10 I had memorized the New York City subway system. I identify with the 18th century vision of science, of exploration and discovery and documentation. So naturally, I liked the idea of appreciating all life in the sea, or creating an encyclopedia of all species.

MBL Were you driven to launch these projects by environmental concerns?

JA In about 1990, I asked, "How much land could 10 billion people spare for nature?" Conventional wisdom projected that more people on Earth would leave less land for nature, while I was interested in the chance of a great restoration of wild nature. Clearly, sparing the sea equals sparing terrestrial habitat in importance. I was shocked to learn how little we know about what lives in the ocean. In marine biology, the models were better than the data. In seminars at Woods Hole Oceanographic Institution and MBL, researchers would present sophisticated mathematical simulations of ecosystems with very few measurements at the level of species, whether tuna or jellies. In fact, the expert consensus was that about 90 percent of the ocean was unexplored and poorly documented biologically.

In 1996, Fred Grassle, a benthic ecologist formerly at WHOI, and I began talking about this lack of observation of marine biodiversity. Something big needed to be done to generate more information on all life in the oceans, top to bottom, to generate more understanding and eventually more beneficence. From the World Climate Program and other early career experiences, I knew how to organize cooperative international scientific programs. After lots of consultations, many on summer days on Water Street in Woods Hole, the Census officially kicked off in May 2000.



and syntheses in London. Ausubel is also the Sloan Foundation program director for the Encyclopedia of Life (www.eol.org), an enormous effort to create an ever-expanding Web page for each of the 1.8 million named species on Earth. The EOL's software platform is being created at the MBL by the Biodiversity Informatics Group, and MBL director and CEO Gary Borisy is on the steering committee for this visionary, multi-institutional project.

"How do you understand the relatedness of all 200,000 forms of marine life? Or longevity across many taxa? Or the effects of climate change on the diversity of life in ecosystems? For such questions, science needs macroscopes, and happily the MBL and its sister institutions are creating them."

MBL How did the Encyclopedia of Life come about?

JA In late 2005, at a meeting in Frankfurt, the Census scientists raised the issue of how to standardize and provide access to the fast-growing information on the 200,000 or so named marine species. Would each Census team need to create its own software and user interfaces, its own species Web pages? This would be extremely inefficient, and bewildering for users of the information. The Census community emphatically asked me, as a manager of the program, for a convenient, open-access, open-source informatics framework.

A few weeks later, in a happy convergence, the president of the MacArthur Foundation, Jonathan Fanton, contacted me. Jonathan had received a one-page letter from Ed (E.O.) Wilson at Harvard about his concept for an online Encyclopedia of Life. Jonathan invited me to lead a feasibility study on the EOL for MacArthur, which I did in 2006 and 2007. We concluded that advances in software, including some developed in the MBLWHOI Library and in Mitchell Sogin's lab at the MBL, meant the EOL could happen fast and economically. Moreover, the Marine Census illustrated the demand for an EOL, both from researchers and the general public.

In practice, the EOL is a godsend, and not just for the Census. If every expert had to create the software that the EOL's Biodiversity Informatics Group has created, most species would never have pages. The growth of the EOL has been incredible. Within a year of Ed Wilson's letter to MacArthur, the MBL and other cornerstone institutions involved in the project had funding commitments for $45 million. With the leadership of MBL scientist David Patterson, the EOL site went public a year later, and now it contains more than 150,000 species pages with vetted content that have benefited about two million unique visitors. No other project in my career has moved as fast.

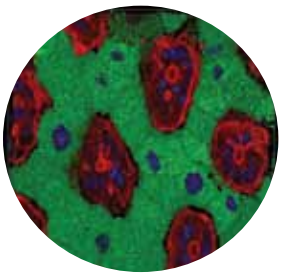
MBL When will the Census converge with the EOL?

JA Many marine species already have good pages, and by the crescendo of the Census in October of 2010, a large fraction of marine species will be vividly present in EOL. The Census is also working with Google Earth and National Geographic to share information through maps and new forms of visualization. The biodiversity community is moving toward a much more integrated vision of services, an "e-Biosphere" in which users will navigate seamlessly from species names to DNA sequences to historical literature to maps and images.

MBL What do you feel is the most important implication of global biodiversity projects such as these?

JA "Macroscopes" are joining microscopes as premiere tools for 21st century biology. For centuries, biology discovered by zooming into smaller and smaller things. Now, projects including the Census and the EOL enable us to discover and appreciate patterns and phenomena that before were too big to see. How do you understand the relatedness of all 200,000 forms of marine life? Or longevity across many taxa? Or the effects of climate change on the diversity of life in ecosystems? For such questions, science needs macroscopes, and happily the MBL and its sister institutions are creating them. •

Gifts & Grants



The National Institutes of Health awarded $2.5 million for "Synaptic Determinants of Vestibular Afferent Dynamics." Senior scientist Stephen Highstein is the principal investigator.

The National Institutes of Health awarded $2 million for "Advanced Optical Methods in Cell Biology." Senior scientist Rudolf Oldenbourg is the principal investigator.

The National Institutes of Health/ National Library of Medicine (NLM) awarded $1.7 million for "Professional Services in Support of NLM's Outreach Efforts to Encourage the Use of Computers and Information Science in Medicine." MBLWHOI Library director Cathy Norton is the principal investigator.

The National Science Foundation awarded $1.3 million for "Collaborative Research: Shifting Seasonality of Arctic River Hydrology Alters Key Biotic Linkages Among Aquatic Systems." Senior scientist Linda Deegan is the principal investigator.

Futaba Koike contributed $500,000 to support the Shinya and Sylvia Inoué Endowment for Cellular Dynamics Imaging.

The Department of Defense awarded $1.2 million for "Proteinaceous Light Diffusers and Dynamic 3-D Skin Texture in Cephalopods." Senior scientist Roger Hanlon is the principal investigator.

The Ellison Medical Foundation awarded $915,000 for "Aging in Bdelloid Rotifers." Adjunct scientist Matthew Meselson is the principal investigator.

Accolades

• MBL director and CEO **Gary Borisy** was elected to the National Academy of Sciences. Other members of the MBL community receiving the honor include: **Lorena Beese** (Duke University), alumna, Ecology; **Jay Dunlap** (Dartmouth College), alumnus, Botany, Physiology; **Caroline Harwood** (University of Washington), former co-director, Microbial Diversity; **Paul Sternberg** (California Institute of Technology), faculty, Embryology; and **Jonathan Weissman** (University of California, San Francisco), faculty, Physiology.

• The following members of the MBL community have been elected to the American Academy of Arts and Sciences: **Stevan Arnold** (Oregon State University), alumnus, Molecular Evolution; **Sean Carroll** (University of Wisconsin), faculty, Embryology; **Scott Edwards** (Harvard University), faculty, Molecular Evolution; **Marianne Bronner-Fraser** (California Institute of Technology), former co-director, Embryology; and **James Truman** (HHMI), faculty, Neurobiology, Neural Systems & Behavior.

• **William Reznikoff**, interim director of education and senior research scientist, Bay Paul Center, was elected to the American Academy of Microbiology.

• Ecosystems Center associate scientist **Christopher Neill** was awarded a Bullard Fellowship by Harvard University for 2009-2010. The Bullard Fellowship supports advanced study and research of individuals looking to make important contributions as scholars or administrators in forestry and forest-related subjects. Neill plans to spend his time in residence at Harvard Forest in Petersham, MA, combining his interests in Amazon science and journalism.

• Four MBL course alumni received Howard Hughes Medical Institute Young Investigator Awards: **Karl Deisseroth** (Stanford University), alumnus, Methods in Computational Neuroscience; **Mark Frye** (University of California, Los Angeles), alumnus, Neural Systems & Behavior; **Anita Sil** (University of California, San Francisco), alumna, Molecular Mycology; and **Ryohei Yasuda** (Duke University Medical Center), alumnus, Neurobiology.

• The Society for Developmental Biology recognized the **MBL Embryology course** with a special award at the Society's 68th Annual Meeting in July, 2009. The award was presented to the MBL for "its outstanding heritage of teaching generations of developmental biologists."

Nancy Eve Cohen

Tagging Along with an Arctic Fish

Top: MBL scientist Linda Deegan holds an Arctic grayling (*Thymallus arcticus*), one of the few species able to survive the winter in deep lakes in northern Alaska.

Bottom: Miniature PIT tags inserted into grayling allow Deegan to track the fish's movement in rivers "wired" with antennae.

As someone who loves to fish, Linda Deegan knows how hard it can be to find them. Deegan, a senior scientist in the Ecosystems Center, has been studying the Arctic grayling for years. "A beautiful fish," she says, "with silvery purple sides, graceful dorsal fin, and sleek river-adapted silhouette," grayling is one of the few fish species that can survive the winter in Arctic Alaska. Yet, since the early 1990s, its population has diminished by two-thirds.

Grayling spend the brief Arctic summer eating insects in the rivers, and before the rivers freeze solid they migrate to deep lakes in northern Alaska. Unlike in most fish, migration is not "pre-programmed" into the entire grayling species: distinct populations will migrate in different directions, upstream or down, to reach their overwintering lake. That makes them a good model for studying the development of fish migration. But Deegan is interested in grayling migration for a second reason. She believes climate change is driving the grayling's disappearance, because the rivers are drying up during their crucial migration period in the fall.

For Deegan, a central question is when the grayling initiate migration, and at what stage of growth. Do the "young-of-the-year," or very small fish, head for the lake at the same time as the adults? Tracking individual fish is critical, due to a growing appreciation that individual variability has important population and ecological consequences. To do this, Deegan uses an ingenious tool.

For years, researchers have used passive induced transponders, or PIT tags, for tracking animals. Deegan uses these tags along with antennae that run across the river bottom and then loop back, encompassing the river's width. Each loop antenna is attached to a solar panel and a data logger. When a tagged grayling swims through the loop, the tag charges—and the fish is identified and counted. This is not so different from the Speedpass programs for counting cars on highways. By placing loop antennae along many miles of inaccessible rivers, Deegan can follow thousands of grayling as they disperse to spawning and feeding habitats for the summer, and then return to the lakes for the long Arctic winter. • — DG

Signals from the Squid

By Scott Brady

Scott T. Brady is professor and head of the department of Anatomy and Cell Biology at the University of Illinois College of Medicine in Chicago. He has been conducting research at the MBL since the early 1980s. During that time, Brady, Robert Allen, and Ray Lasek developed a novel preparation for study of axonal transport based on digital microscopy of isolated axoplasm from squid giant axons. Using these methods, Brady showed that fast axonal transport depended on a new class of molecular motor, named the kinesin family of molecular motors. His subsequent research focused on kinesins in neurons, and made significant contributions to our understanding of the structure, regulation, and molecular biology of kinesins. His current research includes a focus on the role that axonal transport and regulation of molecular motors play in adult-onset neurodegenerative diseases such as Alzheimer's, Parkinson's and Huntington's disease. Brady earned bachelor's degrees in both Physics and Biology from Massachusetts Institute of Technology and a Ph.D. in Cell and Molecular Biology from University of Southern California. He previously held faculty positions at Case Western Reserve University and at University of Texas Southwestern Medical Center.

"Study Nature, Not Books." This famous advice from naturalist Louis Agassiz has informed science at the MBL for over a century, but in recent years it has gained a new meaning.

In looking at the diversity of the natural world, we see that nature has done many experiments for us. If we just ask the right questions, we will find organisms in which solutions are laid out for our consideration. The squid, *Loligo pealei*, is such an animal. For nearly a century, neuroscientists have found it uniquely well suited for asking questions about how the nervous system works.

What is special about the squid to neuroscientists? A squid escapes its predators by sudden contraction of its mantle (the outer body muscle), which produces a seawater jet that allows it to dart quickly to safety. To achieve this rapid muscular contraction, squid must have the right combination of synaptic connections and rapidly conducting nerve fibers. In mammals, nerve impulses are speeded up by a myelin sheath that surrounds the nerve fibers, but invertebrates cannot make myelin. So squid are left with only one option for boosting their nerve conductivity: making a bigger nerve fiber, or "giant axon."

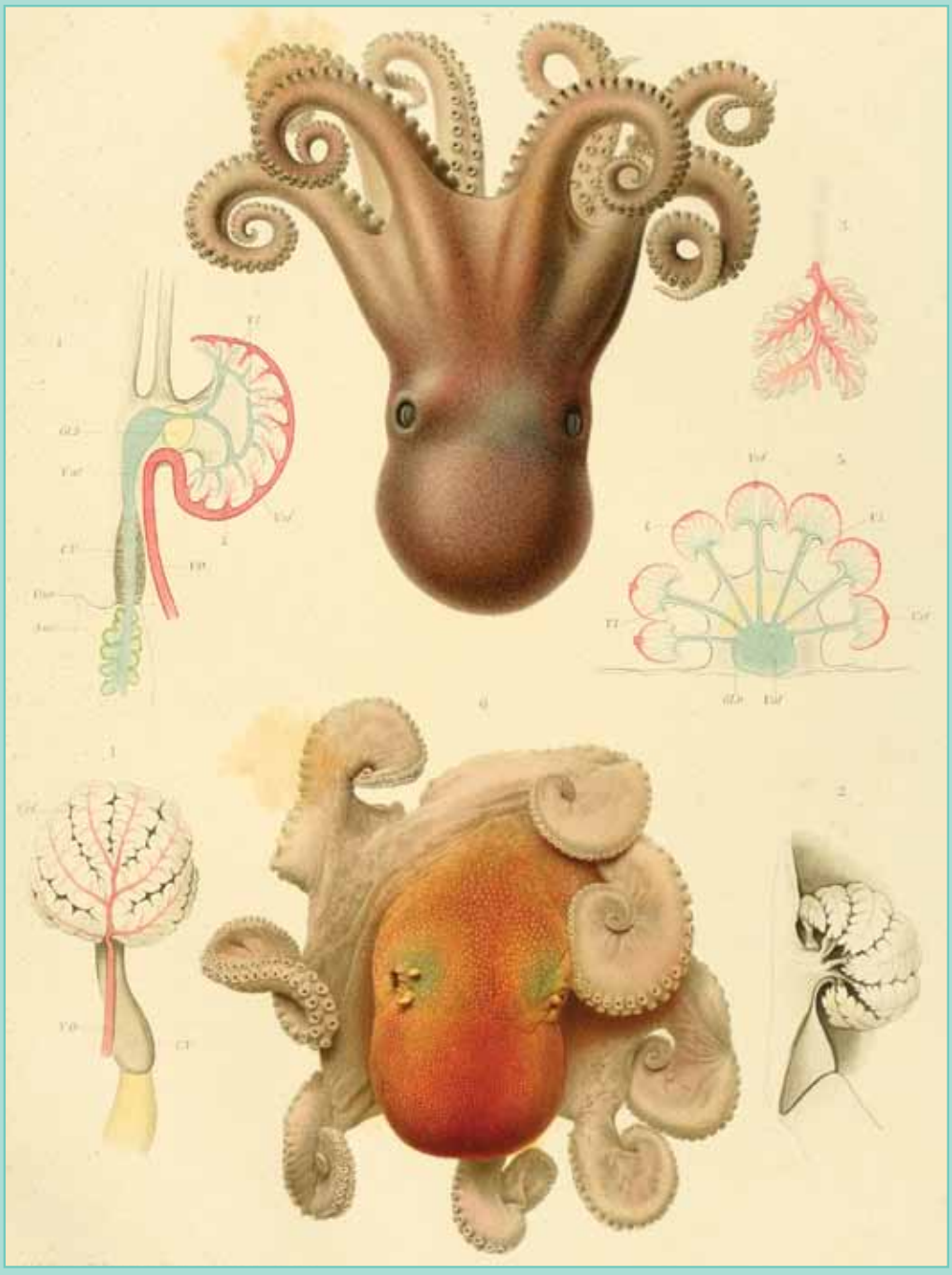
Squid giant axons used at the MBL are readily seen by the naked eye. To trigger a nerve impulse in such a large axon, a giant synapse is needed. Mammalian neurons also have axons and synapses, but their small size limits the ability of scientists to access and manipulate them. The squid neural system enables experiments that are unimaginable in other models.

Remarkably, recent studies using squid are starting to provide answers about some of the most challenging human diseases, such as Alzheimer's and Huntington's. These devastating diseases have bedeviled many of our best scientists for decades, but squid experiments are revealing what goes wrong in the afflicted: why critical neurons and their connections are lost. Answers found in squid are being confirmed in humans.

Still, experiments proposed in squid are often challenged. Why do it in squid and not in a standard model like the mouse? Often the answer is that it can *only* be done using squid. And history tells us that the answers we find in squid often apply to humans as well. For example, research on squid giant axons in the 1930s-1940s at the MBL and elsewhere revealed how nerves generate impulses (action potentials). Later MBL studies led to the discovery of kinesins, a class of motor proteins essential for neuronal function. Research at the MBL continues to take advantage of the squid's unique nervous system to reveal how it works, and what goes wrong in diseases like Alzheimer's. As long as we keep studying what nature has given us, the answers will come. •

Treasures from the MBL's Archives

From the Deep



Prince Albert I of Monaco was an avid oceanographer. He arranged many scientific campaigns on his four yachts, and the biologists aboard made hundreds of drawings of the organisms they encountered. This culminated in *Resultats des Campagnes Scientifiques* (1900), a massive, multi-volume work devoted to marine organisms, such as the rare deep-sea octopi in this colorized print. Now, for the first time, the *Resultats* have been scanned by the MBLWHOI Library and are available online through the Biodiversity Heritage Library (www.biodiversitylibrary.org). The BHL is a consortium of more than 40 libraries in the United States, Europe, and Asia that is digitizing tens of thousands of volumes of biodiversity literature. This trove is a magnificent resource for the Encyclopedia of Life (www.eol.org), which is creating an authoritative Web page for every species on Earth. Prints like this one, of graceful octopi, are vital for taxonomists who are tracking how species names—and even distributions—have changed since Albert I, "Prince of the Sea," sailed the Atlantic over a century ago. • — JD

From Joubin, Louis (1900) "Fascicule XVII: Cephalopodes provenant des campagnes de la Princesse-Alice (1891-1897)," in Resultats des Campagnes Scientifiques Accomplies sur Son Yacht par Albert Ier, Prince Souverain de Monaco. PL III. *The octopi are now known as* Pteroctopus tetracirrhus *(top),* Benthoctopus levis *(bottom), and* Grimpoteuthis umbellata *(side diagrams).*

Catalyst

IN THE NEXT *MBL CATALYST*

Powerful Partnerships

On its own, the MBL is a world leader in biological research and education. Together with its partners, it is a powerful force for social change. In the next issue of *MBL Catalyst*, we profile some of the dynamic people and organizations that ally with the MBL to solve some of the pressing medical and environmental issues facing society today.




MBL
Biological Discovery in Woods Hole

NON-PROFIT ORG.
U.S. POSTAGE PAID
PERMIT NO. 55
PLYMOUTH, MA

MBL
7 MBL Street
Woods Hole, MA 02543 USA

www.mbl.edu