MBL
Catalyst
Biological Discovery in Woods Hole

Founded in 1888 as the Marine Biological Laboratory

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IN THIS ISSUE

The Path to Discovery

MBL Catalyst

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

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Inside cover: Huntington F. Willard (Tom Kleindinst); Biology of Parasitism course student (Daniel Cojanu) *P. 1:* Biology of Parasitism course student (Daniel Cojanu); sperm and egg (Dreamstime.com); superpositions of the beat of the flagellum from an *Arbacia* sperm (Luis Alvarez and René Pascal); illustration of neuron surrounded by glial cells (Dreamstime.com). *Pp. 2–3:* Biology of Parasitism course student (Daniel Cojanu). *Pp. 4–5:* sperm and egg (Dreamstime.com); sea urchins (Luis Alvarez and René Pascal); Frank R. Lillie (MBL Archives). *Pp 6-7:* Humpback whales (NOAA); squid (Elaine Bearer); sewage pipe (istock.photo); cameras and sensors on tower continuously collect environmental data, including on photosynthetically active radiation (Jim Tang); communities formed by four different kinds of bacteria in the human mouth (Jessica Mark Welch and Carissa McKinney). *Pp. 8-9:* Toolik Lake field site (MBL Ecosystems Center); Arctic tundra (Seeta Sistla). *Pp. 10-11:* neural cells illustration (Dreamstime.com); human brain illustration (Dreamstime.com); Brains, Minds, and Machines course students (courtesy of Tomaso Poggio). *Pp. 12-13:* Ian Foster (UChicago Computation Institute); MIRA simulation of universe expansion (Hal Finkel *et al.,* Argonne National Laboratory); blood vessels computer model (J. Insley and M.E .Papka, UChicago/Argonne). *P. 14:* Semester in Environmental Science students (Tom Kleindinst). *P. 15:* Dianne Newman (Caltech); microbe illustration (Ernst Haeckel). *P. 16:* William Reznikoff (Beth Liles). *P. 17:* Cornelia Clapp (MBL Archives); illustration from Cornelia Clapp's doctoral dissertation at the University of Chicago (1896), "The Lateral Line System of *Batrachus tau.*"

Back cover: Eel Pond, Woods Hole, winter 2015 (Roger Hanlon).

ABOUT THE COVER: Undergraduate Clara Kao of the University of Chicago collects the *Artemia* species of brine shrimp, essential food for zebrafish, in the MBL's Zebrafish Facility. Kao is spending the summer at MBL as a Metcalf student in the laboratory of Jonathan Gitlin, Director of the Bell Center for Regenerative Biology and Tissue Engineering and Director of Research Administration and Programs. (Daniel Cojanu).

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

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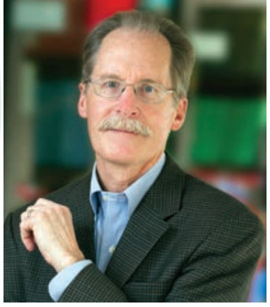


From the Director

Dear MBL Friends and Colleagues,

When I arrived in Woods Hole in early January, there were more than a few who questioned the wisdom of leaving the lush foliage and warm temperatures of North Carolina in the middle of winter. Just wait until spring, they said; that's the time of year when the "real" MBL shows itself.

This is true, of course; it's only when the courses start, the students show up, the Whitman Center investigators move in, the Village storefronts open, and all the moorings on the now-thawed Eel Pond are occupied that one can see the MBL at its most spirited and colorful best. Much like a burst of spring flowers and buds—seemingly invisible one day and yet exploding with brightness and fragrance the next.

But personal and scientific awakenings tend to happen more gradually than that—barely evident in the moment, but fueled silently, one observation at a time, one connection following another, discovery by discovery. While they unfold more slowly, these moments of awakening—whether in the lab, in the field, or in the classroom—depend on a type of dynamic intellectual intimacy that occurs regularly only at a place like MBL.

It is this style of openness, informality, and integrated learning and research that empowers transformation from learning about science (the etymological root of which, after all, is "to know") to a passionate pursuit of what we do *not* know. This awakening combines a confidence to embrace one's ignorance in the moment with the freedom to truly explore intellectually—to discover. True awakening is being open to the unforeseen and unpredictable discoveries that come only from a willingness to wander away from the well-traveled intellectual path in search of explanations for the unexplained; in search of broader implications for what may, at first, seem like an incidental or even counter-intuitive observation; or in search of new tools and approaches needed to peer into the black box of uncertainty that surrounds so much of the biological world. It is these conceptual and technical leaps that not only open doors, but point to the existence of doors where there previously were none.

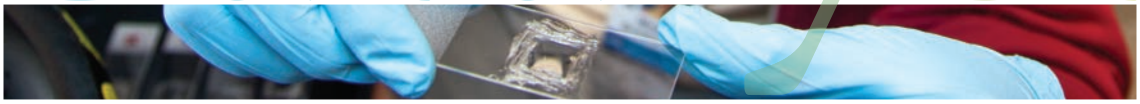
What marks such discoveries is the imagination and intellectual courage that it takes to think the unthinkable. One must be open to the possibility that there are doors we haven't even yet seen and be open to the data that first hint at their existence.

I am so pleased to be a part of this community, which ties together the many strands of my life as a biologist: open-ended discovery, fascination with the unknown, the sheer joy of learning something new, seamless and self-reinforcing integration of research and education, and reflection on what it all means for us as individuals, as a society, and as a species.

Here, with MBL now in full blossom, we are all discoverers, we are all mentors, and we are all students. That is, after all, the MBL way.

Huntington F. Willard, *President and Director*

Catalyst



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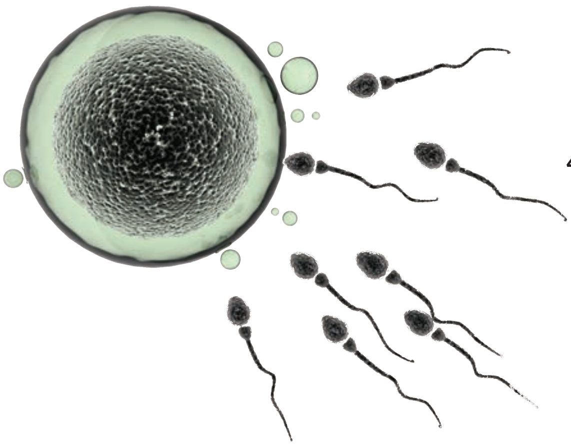
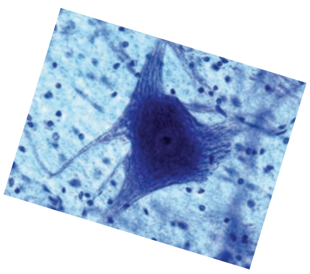




Departments

The Path to Disc

If you spend a good measure of time at the MBL, you'll start to sense that something very special is happening at this seaside lab. Yes, you'll see students and faculty from numerous states and countries, just as you would on many college or university campuses. Yes, they are exceptionally bright and hardworking, sometimes grabbing only a few hours of sleep before rising for breakfast and tumbling into the labs or the lecture hall to start again.

But what you'll also notice is how completely engaged and even merry the faculty and students are. They can't wait to get back to "the chase." After a lecture, they'll spend hours and hours in the lab, exploring scientific questions to which nobody knows the answer—and in some cases don't even know precisely how to frame the question. They are on the thrilling and bumpy and often completely unpredictable road to scientific discovery.

"It's that transformative moment when you are first dipping your toes in the water of research, when the light bulb goes on, and you say, 'Wow! I love this. This is how I want to spend my life,'" says MBL President and Director Huntington Willard. "That's when you switch from learning about science and being interested in what is known, to becoming excited by what we actually *don't* know."

overy

That moment of awakening, for generations of scientists, happened at the MBL—and they will never forget it. "That is the magic of the MBL courses," Willard says. "That's our special sauce: how we teach and 'awaken' students."

Some of the MBL's renowned research-based courses have been offered since the 1880s, while others are new, such as "Brains, Minds and Machines" (see pp. 10-11) and University of Chicago-MBL courses rolling out this year (see p. 6).

The MBL's Discovery Courses form just one strand of the institution's interwoven "triple helix," together with several dozen MBL-based research programs and the hundreds of investigators from other institutions who come here to conduct research in the Whitman Center. Tying together the MBL triple helix is a passion to understand the complexity of life, from microbes to marine organisms to the ecosystems in which they live. What millions of bacteria live in that seawater sample? How does the squid react to a predator with such lightening-fast speed? How are organisms—including humans—adapting to a changing environment? What can knowledge of evolutionary adaptations tell us about conditions today?

The MBL is a convener of scientific explorers from hundreds of institutions who are pursuing a fundamental understanding of life, its origins, and its sustainability.

In this issue of *MBL Catalyst*, you'll meet several of the lab's leaders, investigators, students, and collaborators. It's a community brimming with energy and eager to engage you—to awaken you —as co-discoverer. •

The MBL Welcomes a New Director

On January 1, Huntington F. Willard became the 15th Director and President of the Marine Biological Laboratory. He also holds an appointment as Professor of Human Genetics at the University of Chicago, the MBL's affiliated partner.

Prior to coming to MBL, Willard was on the faculty at Duke University, where he was founding director (2003-2014) of the Duke Institute for Genome Sciences & Policy, a highly interdisciplinary, university-wide unit that spanned the life sciences, engineering, medicine, law, social sciences, and humanities. Prior to that, he held faculty positions at the University of Toronto, Stanford University, and Case Western Reserve University.

A graduate of Harvard College, Willard received his Ph.D. from Yale University in genetics and carried out postdoctoral training at Johns Hopkins Medical Center.

Research: Willard has explored many facets of genetics and genome biology, with a particular interest in the structure and function of chromosomes, the epigenetic regulation of gene silencing, and the evolution and organization of complex genomes. He is a member of the National Academy of Sciences and the American Academy of Arts and Sciences and has won many awards for genetics scholarship, including the William Allan Award from the American Society of Human Genetics. He is the author of over 300 scientific papers and two books.

Scientific Awakening: While attending an undergraduate lecture in the 1970s, Willard first heard about the developmental process by which one of the two X chromosomes in the female mammal is inactivated. "I wrote in my notes, 'How the heck does that work?' It just captured my attention and fascination," he says. "That was my intellectual awakening, but then you also have to have a practical awakening, when you get an opportunity to go into a lab and do something with your own hands. The first time I looked into a microscope, I was hooked. It gave me a way to see chromosomes for real, showing a pattern of behavior that nobody could understand at that time, and to focus on asking, 'How does that work?' I spent 40 years on that question! You just fall in love with the notion that one question begets another and then another."

On Education: A recipient of several teaching awards, most recently the Award for Excellence in Human Genetics Education from the American Society of Human Genetics, Willard is passionate about integrating research and education. "When is the best time to offer a student that 'awakening' moment that every scientist has?" he asks. "Undergraduate? Earlier? We need to find special ways to reach out to people, including disadvantaged students, who haven't had the exposure to the kinds of teaching we do at the MBL—the teaching we can do better than anywhere else." • — DK

When Sperm Meets Egg

It's hard to imagine it attracting a mate, much less how the two might interact. Fortunately, sea urchins are broadcast spawners: they release their abundant eggs and sperm directly into the ocean. The sperm then deploy finely tuned signaling and navigation strategies to seek and find the eggs, and fertilize them.

How sperm do this so well has been explored by MBL Whitman Center Investigator U. Benjamin Kaupp, scientific director of Max Planck Society´s CAESAR Research Center. Every summer for the past 15 years, Kaupp has journeyed (along with nine heavy aluminum crates of equipment) from Bonn, Germany, to the MBL to study sea urchin fertilization. Due to the ease of recreating their spawning environment in saltwater tanks, sea urchins have been a go-to model system for studying fertilization at the MBL for more than a century.

The sperm computes its path

The MBL's second director, Frank R. Lillie of the University of Chicago, discovered in the 1910s that sperm are guided to the egg by a gradient of chemical attractants in a process called chemotaxis (see sidebar). The egg releases a chemoattractant, usually a small protein or peptide. As the chemoattractant diffuses away from the egg, a concentration gradient forms. Sperm can detect this chemoattractant and change their swimming direction toward areas of higher concentration.

Kaupp has taken up Lillie's mantle and made several surprising discoveries. For instance, Kaupp and his team found that sperm are extremely sensitive—they can detect and respond to a single molecule of chemoattractant in the water. This is some feat, considering that a single drop of water contains billions of H_2O molecules. From there, Kaupp's team identified all the ion channels and genes involved in the signaling pathway that starts with a receptor in the sperm cell detecting a molecule of chemoattractant.

Next, Kaupp tackled the computational abilities of sperm. He compares a sperm cell to the captain of a ship, who is responsible for steering the ship in the right direction. "Sperm must do the same thing," Kaupp says. "They use information in the chemical gradient to make calculations about the direction in which they're swimming."

As sperm navigate the gradient, they perform a number of sophisticated computations. "They can count molecules over a certain time, integrate all these together, and then respond by changing their swimming path," Kaupp says. These computations are accomplished through chemical reactions, many of which involve calcium. When a molecule of chemoattractant binds to a receptor on the sperm's flagellum (or tail, which acts as a rudder), it triggers a cascade of signaling events that eventually leads to calcium ions flooding into the sperm cell. This calcium signal controls the beat of the flagellum, allowing sperm to swim straight or make turns.

sperm for 12 years before looking at mammalian sperm; it was only then that he felt the techniques they developed and perfected with urchins were ready to transfer to the more complex sperm of mammals.

"You can discover important mechanisms in sea urchin sperm that are also relevant to humans and other mammals," says Kaupp. For example, last year, Kaupp found that sea urchin sperm use the same ion channel for calcium signaling as human sperm.

Kaupp sees the implications of his studies for diagnosing and treating human male infertility. "There are many reasons why fertilization might fail. There can be defects in swimming, in recognizing the chemoattractant, in recognizing the surface of the egg, or in penetrating the protective layer over the

There is much to learn from sea urchin sperm that can be applied to human fertility issues.

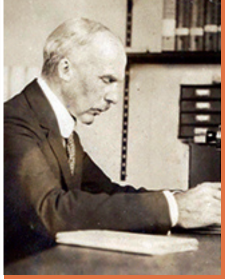
Kaupp discovered that it's not the absolute amount of calcium that matters, but the change in calcium concentration over time. Sperm temporally sample chemoattractant molecules that bind to receptors on their flagella and integrate these events to produce a summed swim response.

Insights on human fertility

Although the similarities may be hard to appreciate at first, there is much to learn from sea urchin sperm that can be applied to human fertility issues. Kaupp and his team studied sea urchin

top of the egg," he says. "If we know how sperm function, then we can look specifically for mutations in our genes that cause infertility."

Kaupp keeps coming back to the MBL not only because it supplies him with fresh sea urchins, but because it's a haven where he can dedicate himself to research. "During the rest of the year I have a lot of other responsibilities, so I cannot spend much time in the laboratory," he says. "But in Woods Hole I can do the research with my students, which I terrifically enjoy—and it keeps me on top of the science." • —MB



Lillie's Hunch

The study of sperm chemotaxis began with Frank R. Lillie, an eminent embryologist of the early 20th century. Lillie was the MBL's second director (1907-1925) and chairman of the University of Chicago's Zoology Department.

Lillie reported chemotaxis in animal sperm for the first time in 1912. Toward the end of his report, he mentioned that the egg likely contains a chemotactically active agent, some substance to which the sperm are attracted. Lillie performed his experiments on the sea urchin *Arbacia punctulata*, an organism that has since become the most valued model of sperm chemotaxis research.

About 70 years after Lillie's report, the chemoattractant from *Arbacia* eggs was identified and named "resact." The chemotactic response of *Arbacia* sperm to resact was firmly established by Gary Ward and Victor Vacquier, then at Scripps Institution of Oceanography, showing that Lillie's ideas about egg chemoattractants were both correct and ahead of their time. • — DK

New UChicago-MBL Educational Programs in Woods Hole

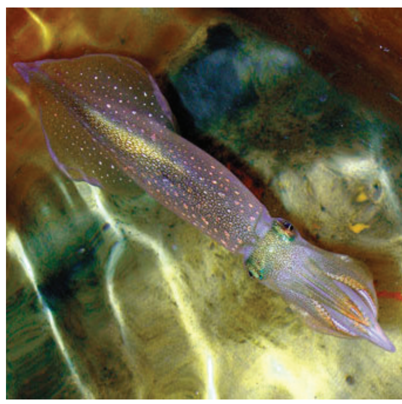
A new undergraduate program cultivated from the MBL-University of Chicago partnership will be held September to December in Woods Hole. "The Whale: Biology, Culture, and Evolution on Nantucket Sound" is a four-course offering for non-science majors interested in the maritime culture and entwined histories of whales and America. Students will be exposed to New England maritime history and culture, and receive a comprehensive overview of biology that includes evolution, environmental science, biodiversity, physiology, and cell and developmental biology. The lead instructors from the University of Chicago are Karl Matlin, Professor of Surgery and a faculty member in the annual MBL History of Biology seminar; Michael Rossi, Assistant Professor of the History of Medicine; and Robert Richards, Distinguished Professor in History of Science and Medicine.

Other new educational initiatives include a "Quantitative Biology Boot Camp" for all incoming graduate students in UChicago's Biological Sciences Division, to be held in September at the MBL. The course is co-directed by UChicago faculty Stefano Allesina, Professor of Ecology and Evolution, and Stephanie Palmer, Assistant Professor of Organismal Biology and Anatomy and a MBL Whitman Center investigator. The Boot Camp will provide students with a working knowledge of computational and statistical approaches through their application to analysis of real-world data sets.

In late August, 12 high school students from the University of Chicago Lab Schools will come to the MBL to spend an intense week engaged in biology experiences that enhance the current high-school curriculum. Plans include a trip on the MBL's *R/V Gemma* to collect samples and gather data on the local marine intertidal ecosystem, visits to salt marshes to study restoration ecology, and image analysis using cutting-edge microscopes available exclusively at MBL. •

Squid Enrich Their DNA Blueprint Through Prolific RNA Editing

One of the surprising discoveries to emerge from comparative genomics is that drastically different organisms—humans, sea urchins, worms, flies—are endowed with a more or less common set of genes. Given a similar DNA blueprint, then, how do species develop such vast differences in shape, size, and complexity? One insight into this question has turned out to be quite surprising. Contrary to the "central dogma" of molecular biology, genetic information does not always pass faithfully from genomic DNA to messenger RNA to the synthesis of proteins. Rather, the information can be significantly altered along the way by a variety of means, including by precision "editing" at the RNA stage to change the code and fine-tune the type of proteins that will be produced. RNA editing was thought to be used sparingly, based on a limited number of prior studies. But recently, Joshua Rosenthal, a Professor of Neurobiology at the Universidad de Puerto Rico and a MBL Whitman Center investigator, led a team that discovered the most prolific usage yet of RNA editing in the common squid, *Doryteuthis pealeii*. The team found that 60 percent of the RNA transcripts in the squid brain had been edited, which is orders of magnitude more "recoding" of the genetic instructions than has been seen in any other species to date, says Rosenthal. The 57,000 recoding sites they found in the squid brain created tremendous protein diversity, suggesting an important role for RNA editing in squid brain physiology. It may, for example, enable squid to fine-tune its response to environmental variables, such as changes in temperature. (*eLife* 10.7554/eLife.05198, 2015) •

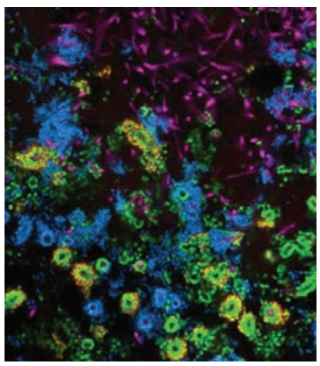


Sewage Provides Insight Into Human Microbiome

Studies of the human microbiome, the collection of trillions of microbes living on the human body, have gained traction in the past decade, and there is great interest in identifying what constitutes a "healthy microbiome." But financial considerations and privacy concerns limit the number of individuals whose microbiomes

can be screened. Recently, a team from the University of Wisconsin-Milwaukee and MBL demonstrated that sewage samples can be used to monitor the general health of large populations of people without compromising the privacy of individuals. The team compared the gut bacteria profiles of 137 healthy adults, provided by The Human Microbiome Project, to the bacterial community profiles of more than 200 sewage influent samples collected from 71 U.S. cities. To differentiate between closely related taxa of bacteria in the samples, the team used a novel computational technique called oligotyping that was developed by A. Murat Eren and colleagues at the MBL. The team found that geographically distributed bacterial populations share a small, core set of bacteria that is common among most American adults. To understand to what extent the composition of these human-associated bacterial populations in sewage samples could provide insights into public health questions, the team used a basic health indicator as a proxy: percent of obese individuals in a city. They found the bacterial community structure to be a very good predictor of a city's estimated level of obesity, with over 80 percent accuracy. (*mBio* 6:e02574-14) •

A Good Reason to Go Out and Play? Scientists Study Immunity and Exposure to Limited Microbiota



Babies are born almost sterile, becoming host to their first set of microbes as they travel through the birth canal. After birth, almost every interaction with the world affects a person's microbiome: from the food and water consumed to the dirt picked up from running around outdoors. Exposure to and growth of a diverse set of bacteria has been linked with healthy development and immune system function, while microbiomes that lack diversity or contain too many detrimental bacteria are associated with asthma, allergies, diabetes, obesity, and inflammatory bowel disease. In a recent perspective piece, University of Chicago and MBL scientist Jack Gilbert of Argonne National Laboratory and colleagues explore how humans, who evolved outdoors, are affected by the 21st-century habit of spending most of their lives indoors, where the growth and diversity of microbiota are restricted. With so much to learn about how microbiomes affect the immune system, the authors argue, it is time to start studying how the built environment can be manipulated to keep us healthier, exposing us to more diverse ecosystems of bacteria. One of their first steps has been to recruit citizen scientists: individuals and families all over the United States that are interested in contributing to the study. The authors send them kits for collecting microbiota samples and will use their samples to study the huge range of unique bacterial ecosystems in homes and how they are linked to humans' health. (*Trends in Immunology* 36:121-123, 2015) •

Measuring Photosynthesis Over Large Areas

A team of MBL and Brown University scientists has devised a novel system to accurately measure photosynthesis, and thus the health of ecosystems, over large areas.

"This work has profound applications, as we can easily install this system into a drone, airplane, or satellite to detect plant photosynthesis on a large scale to assess ecosystem health," says lead author Xi Yang, a postdoctoral associate at Brown University and recent graduate of the Brown-MBL Graduate Program. "We may also apply this to agriculture for predicting crop yield, drought condition, or insect outbreak."

"Measuring photosynthesis on the canopy scale has been challenging, despite established knowledge on how to measure and model photosynthesis on the leaf scale," says Jim Tang, associate scientist in the MBL Ecosystems Center. The team tackled the challenge by mounting cameras and spectral sensors over a forest canopy in central Massachusetts.

Their system measures chlorophyll fluorescence, a byproduct of photosynthesis. Less than one percent of solar energy captured by chlorophyll is emitted as fluorescence, and recording the specific signal from that fluorescence has been extremely difficult. The group discovered a few wavelengths of light where it is now possible to measure the specific fluorescence signal from photosynthesis. Their system can record radiation at high resolution with a frequency of five minutes, thus automating detection of photosynthesis from the canopy. (*Geophys. Res. Lett.* 10:1002, 2015) •

UNFROZEN

In the fast-warming Arctic, MBL ecologists take the long view

When MBL Distinguished Scientist John Hobbie pitched his tent on the shore of cold, deep Toolik Lake in northern Alaska in 1975, the terms "climate change" and "climate resilience" had not yet entered the popular lexicon. Then a virtually untouched Arctic landscape with no trees, permanently frozen soil (permafrost), and deep snow cover much of the year, Toolik Lake was not the most hospitable place to set up a research camp.

But Hobbie did, and with a small band of hardy scientists he began collecting baseline data on the ecology and wildlife of the remote Toolik region. Before long, he was joined by Gaius Shaver and Bruce Peterson; all three scientists were fresh recruits to the new MBL Ecosystems Center. Every year during the short Arctic summer, when the sun doesn't set and the snow melts briefly, they went to Toolik to document both its natural state and nearly imperceptible changes to the ecological processes of its tundra, lakes, and streams.

Today, it's a different story at Toolik Lake. MBL ecologists still go there every summer, now in the company of a sizeable international contingent of scientists (see sidebar). But the ecosystem processes they observe aren't all slow to change. The Arctic is warming faster than any place on Earth, with air temperatures rising twice as quickly as at lower latitudes. The thin layer of soil that thaws each summer is getting deeper, releasing nitrogen previously frozen in permafrost and fertilizing the land. Shrubs and plants are growing taller. "Satellites tell us there has been clearly a greening of the Arctic," Shaver says. And their ongoing Toolik Lake measurements are now part of an extremely important, 40-year dataset on the emergence of climate change and its impacts in the Arctic.

"We're seeing new ecosystems and new disturbance regimes emerge in the Arctic," says Christopher Neill, director of the MBL Ecosystems Center. "Ice melting at the edge of the Arctic Ocean is creating new coastal ecosystems. Permafrost in the tundra is thawing." Wildfires, once exceedingly rare on the cold, moist tundra, have become more frequent as warmer air incites more lightening storms. Eight years ago, the largest wildfire ever to hit the Alaskan tundra burned a 40-by-10-mile swath near Toolik Lake. Led by Shaver, scientists monitored the Toolik burn site and were surprised to discover strong signs of resilience, as much of the vegetation recovered in just a few years.

The landscape respires

Of key concern is the vast reservoir of carbon that is locked inside frozen Arctic soil as ancient organic matter—the remains of plants and animals. When permafrost thaws and soil microbes become active, some of that stored carbon is released as carbon dioxide, the greenhouse gas largely responsible for climate warming. As the Arctic warming trend continues, and the upper layer of permafrost thaws, more carbon dioxide will be released to the atmosphere. But how quickly?

That's a puzzle that Ed Rastetter, a senior scientist at the MBL Ecosystems Center, and colleagues are trying to solve. The picture is complicated by the greening of the Arctic. More plant and shrub growth means more photosynthesis is occurring, a process that removes carbon dioxide from the atmosphere.

"Carbon dioxide release from permafrost and increased photo-synthesis are clearly opposing forces in the Arctic," says Rastetter. "We still don't know which one will win in the long run."

To address this balance between climate change and resilience, Rastetter is developing a model of ecosystem respiration throughout the Arctic with collaborators from the MBL, the University of Chicago, Argonne National Laboratory, Woods Hole Research Center, and other institutions.

Ecosystem respiration is a measure of the gross carbon dioxide produced by all of an ecosystem's organisms, including its animals, plants, and microbes. Respiration and photosynthesis are the two dominant components of an ecosystem's carbon budget.

"We have a pretty good handle on how to represent photosynthesis in our [ecosystem] models. The part we are less confident in is the ecosystem respiration," Rastetter says. "At least half of the respiration is going to be in soil, mostly from microbial activity."

Their research begins on the ground, literally, with scientists digging up Arctic soil in order to analyze its carbon stocks. Julie Jastrow, senior terrestrial ecologist in Argonne's Biosciences Division, is overseeing that part of the collaboration. Rastetter is building off an existing ecosystem carbon-exchange model he developed with Shaver to create a new, more precise model of soil respiration.

The big picture

Field scientists are working hand-in-hand with modelers to understand and predict the changes taking place throughout the Arctic. Another modeler is Robert Jacob, a computational climate scientist at Argonne National Laboratory and a fellow in the University of Chicago/Argonne Computation Institute, who developed one of the first global climate models to use parallel computing.

"The Arctic is a leading indicator of what's happening in the global climate," Jacob notes. "It's a very sensitive part of the climate system."

Jacob is currently part of a team developing a global climate model, called ACME, that will run on the latest Department of Energy supercomputer at Argonne. This model could assist in Arctic research by providing the high resolution needed to simulate ocean heat transport coming into the Arctic Ocean from the Atlantic Ocean, as well as atmospheric, sea ice, and land surface processes in the Arctic region.

"As Arctic sea ice starts to thin and shrink, as we've seen happening, the region is becoming a lot more vulnerable to storms and its climate is changing," says Jacob. "We want to better understand how circulation of the atmosphere and ocean are impacting Arctic sea ice and the land surface. The climate system is one connected system, so it's important to get all pieces working together." •
—SKM

Right Place, Right Time

When John Hobbie began research at Toolik Lake four decades ago, the goal was straightforward: to document the region's organisms and ecological processes. As the reality of a warming climate began to emerge, scientists at Toolik also began large-scale experimental manipulations, such as artificial heating of tundra plots, to see how the ecosystem responded and predict what the Arctic may look like in the next century. In 1987, research at Toolik became the Arctic Long-Term Ecological Research (LTER) project, a part of the National Science Foundation's LTER program, which now includes 25 sites across the United States. The Arctic LTER has been directed by MBL scientists since its inception. Today, Toolik Field Station is an international center for Arctic ecosystems fieldwork operated by the University of Alaska.• —DK

BUILDING INTELLIGENCE

One of the great mysteries of nature is the human mind.

Understanding how the brain produces intelligent behavior—and how that might be replicated by machines—are among the most complex problems facing science and technology. Even on a solely personal level, consider: What's more interesting to you than *you* and how you work? Nothing, except perhaps the prospect of a "robot-you" to help you live and work better.

These provocative challenges are why a research-based course on artificial intelligence, called "Brains, Minds and Machines" made its MBL debut last year, joining an unparalleled roster of summer courses in neuroscience that annually attract the field's top investigators to serve as faculty.

Although early computer scientists were optimistic when artificial intelligence began growing into an academic field in the mid-1950s, succeeding years taught them that emulating the operations of 100 billion highly evolved, networking neurons is much harder than it first seemed. Harder than winning championship chess matches, it turned out, or teaching machines to recognize voices and translate texts by analyzing huge numbers of labeled training examples, as do Apple's Siri and IBM's Watson.

"These recent achievements only underscore the limitations of computer science and artificial intelligence," says Tomaso Poggio, Professor of Brain Sciences and Human Behavior at MIT and co-founder of the Brains, Minds and Machines course at MBL. "We do not yet understand how the brain gives rise to intelligence, nor do we know how to build machines that are as broadly intelligent as we are," he says.

Poggio, who heads up the Center for Brains, Minds and Machines (CBMM) at MIT, thinks it's high time to renew the quest to achieve the field's grand goal: to explain the brain. Success in this endeavor should bring not only improved therapies for neurological diseases but computers with robust and sophisticated algorithms that exhibit human-like intuition and understanding of social nuance.

What's more interesting to you than you—and how you work?

"We know much more today than we did before about biological brains and how they produce intelligent behavior," he states. "We're now at the point where we can start applying that understanding from neuroscience, cognitive science, and computer science to the design of intelligent machines."

Poggio and two dozen other researchers from MIT, Harvard University and elsewhere are collaborating to do just that at CBMM, which was founded on the premise that faster progress toward understanding human intelligence will come if computational, biological, and psychological approaches are combined. As part of the Obama Administration's BRAIN Initiative, the National Science Foundation funded the center with a $25 million grant in 2013.

The course of the mind

Not long thereafter, Poggio, neurobiologist Gabriel Kreiman of Harvard Medical School, and several other center principals began to consider where to conduct CBMM's first summer course. "Given the MBL's strong outreach efforts, its broad-umbrella approach to science, and its long history in fundamental neuroscience research, it was the obvious choice," says L. Mahadevan, an applied mathematician, biologist, and physicist at Harvard University and CBMM, and co-director of the first summer course in 2014.

"We approached MBL Education Director Bill Reznikoff, who was very enthusiastic, particularly because our course would complement MBL's popular Methods in Computational Neuroscience course, which approaches the subject from the cellular scale," Mahadevan says.

The group scheduled Brains, Minds and Machines to overlap with other MBL special topics courses to take advantage of the spectacular gathering of neuroscientists and other experts that the courses draw to Woods Hole. "We hoped that we would get good synergy because of the courses' complementary nature and all the good people from many fields that would be there to cross-lecture," Kreiman says.

Brains, Minds and Machines attracted immediate attention in the academic community and admission proved highly competitive. "From about 200 high-level applicants, we selected 25 graduate students from a variety of fields including biology, neuroscience, cognitive sciences, technology, mathematics, machine learning, and software," Mahadevan says. The course lecturers were "top people from five or six institutions … whose expertise spanned the broad range of areas under this topic," he says.

The "hugely integrative" talks focused on the theoretical and mathematical foundations of the biology of vision concurrently with the social aspects of cognition. The first part of the two-week class addressed theoretical foundations and computational methods in intelligence research, and introduced students to empirical methods used in neuroscience and cognitive science to probe the function of neural circuits and emergent behavior. The latter part of the course examined research topics now under investigation at CBMM.

BRAINS, MINDS AND MACHINES COURSE

August 13–September 3, 2015

DIRECTORS: Gabriel Kreiman, Harvard University and Tomaso Poggio, MIT

"Our post-docs also worked with the students on independent projects covering areas that ranged from intuitive physics to understanding aspects of image recognition," Mahadevan says.

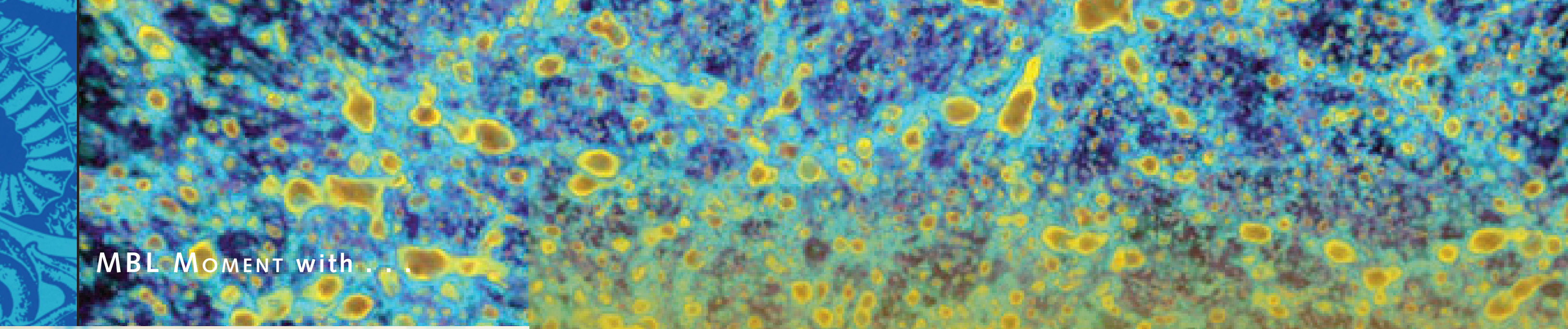
Some students worked on "building computational models to visually recognize objects and faces with the goal of achieving human performance levels in complex recognition tasks—asking questions such as 'What is there?' 'Who is there?'" Kreiman says. These projects "took inspiration from studies of the underlying neurobiological circuitry in the brain." Other students investigated the roots of social interactions by studying situations in which social inferences—guessing what other people are thinking based on sparse data—are key, and attempted to emulate that process using probabilistic programming techniques. Another team "examined at the behavioral level how infants learn fundamental physical concepts, such as mass and momentum, from experience, and tried to embed those ideas into computer algorithms," he says.

Hello, iCub

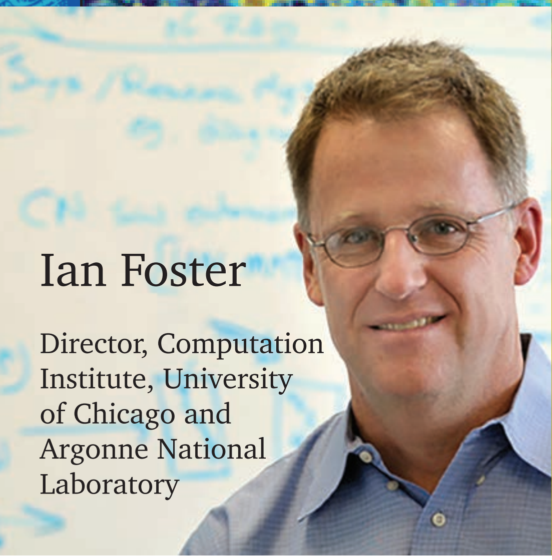
This summer, in addition to continuing with last year's projects, cognitive robotics projects will be introduced in the course, Kreiman says. Some will use the iCub robot, a meter-tall, humanoid robotic test-bed developed by several European universities for research on how human-like manipulation of objects and the environment play a major role in human cognition.

The MBL classroom for the oversubscribed course last year was jam-packed with students, faculty, and a few fortunate onlookers. "I think it was a little unusual how many faculty members from partner institutions ended up auditing the course," Mahadevan notes. "It seemed that after everybody sat through the day lectures, many attended the traditional ad hoc evening lecture sessions, some of which went on late into the night," he says, laughing. "That's always a good sign."

Did the researchers make any advances in demystifying how intelligence is created? "It was only the first year, of course, so there's been precious little chance for any 'Ah, ha!' moments just yet," Mahadevan observes. "But the course is a fantastic opportunity to get the views of one's colleagues—from physics, biology, cognitive neuroscience—about what, to be honest, is a terribly hard question." • —SA



MBL Moment with . . .



Ian Foster

Director, Computation Institute, University of Chicago and Argonne National Laboratory

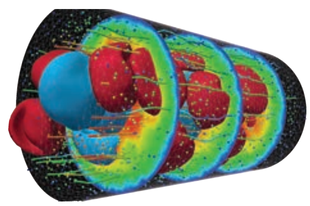
From Climate Change to Fish Eyes to Microbes: Make Way for Supercomputing

Ian Foster is the director of the Computation Institute, a joint institute of the University of Chicago and Argonne National Laboratory. He is also an Argonne Distinguished Fellow and the Arthur Holly Compton Distinguished Service Professor of Computer Science. Foster received a B.Sc. degree from the University of Canterbury, New Zealand, and a Ph.D. from Imperial College, United Kingdom, both in computer science. He is a fellow of the American Association for the Advancement of Science, the Association for Computing Machinery, and the British Computer Society. Foster has won numerous professional awards, including most recently, the 2015 Institute of Electrical and Electronics Engineers (IEEE) TCSC Award for Excellence in Scalable Computing. He was a co-founder of Univa UD, Inc., a company that delivers grid and cloud computing solutions.

Ian Foster likes to think big.

As director of the University of Chicago/Argonne Computation Institute (CI), he says, “a lot of my work is about bringing the power of big computing to bear on scientific problems. I meet with scientists who have incredibly exciting ideas and projects, and I try to think of ways to help them move forward.”

In 1999, Foster co-invented grid computing (now commonly called cloud computing), a system that allows large-scale computing services to be reliably delivered to users at distributed sites. He has developed methods and software that underpin many large national and international cyberstructures, including the U.S. Department of Energy’s Earth System Grid. Among Foster’s successful current projects is Globus, which helps tens of thousands of scientists and other users to move, share, and archive large volumes of data between distributed sites around the globe.



What are the promises and challenges of applying big computing to scientific problems?

IF It's exciting, because when you can build data-analysis or computational-simulation systems that are a thousand times bigger than what people had built before, you can tackle scientific problems that were previously inaccessible. You can ask and answer questions that perhaps people had not even thought of asking, because they were viewed as impossible to address with existing techniques. It's also a challenge, because every time you scale things up by an order of magnitude or more, you run into new sorts of technical problems. A lot of my work is trying to understand how to address those technical problems.

In what fields is big computing gaining traction?

IF Climate science is largely computational. Genomics is vastly computational. It's proving harder to find genetic causes of diseases than people thought, so no one would say we should stop collecting and analyzing genomes.

Climate scientists would like to downscale climate predictions to smaller geographic areas, so the information can be used at local levels to prepare for impacts such as sea-level rise. Can supercomputing help with that?

IF Yes. First, you need to do a reasonably high-resolution climate-change simulation. Then, we often want to combine the results of the simulation with historical data about climate variability in the area to which we are downscaling. That is a computational problem: how to integrate those data sets. One application we have been discussing with people at the MBL, UChicago, and Argonne—and this can't be done at the moment—but if we can acquire and aggregate a wide variety of data about historical weather, results of climate model simulations, and perhaps ecosystem observations, and put them all on one large computer system, it would make it easy for people to start to perform computations over the ensemble of that data. They could look at how ecosystem behavior varies with historical weather and how it might vary in the future as climate changes occur, as predicted by climate models.

What is the focus of the Computation Institute's work in genomics?

IF We are very involved in developing what I call "discovery engine systems" to hold and analyze large amounts of genomic data. As data volumes grow too large for individual labs to hold them, I think we will see more systems like these that support a whole community of scientists. For example, our fellows built MG RAST, an online resource where you can submit sequence data from your microbial sample. The system will perform automated analysis, report back on the nature of your sample, and then integrate the result into its collection of metagenomic data. The system has a continuous process of analysis that derives new knowledge from the ensemble of metagenomic samples. Another system here, called SEED, does the same thing with bacterial genomes. And CI fellow Bob Grossman built a system called Cancer Genomic Commons to hold all the cancer genomic data being produced by National Institutes of Health-funded studies.

Is the CI applying computational power to help scientists "visualize" molecules or cells?

IF Historically, computation was just used to take your three-dimensional imaging data and turn it into a picture. But CI fellow Gordon Kindlemann and others are working on tools that go beyond that to automatically extract additional information from very high-resolution images. Say you want to know how many rods and cones are in the zebrafish eye. Historically, you might try to image the eye and go through and count the rods and cones by hand. Gordon is making these incredibly high-resolution pictures of zebrafish heads and building mechanisms to extract from this very noisy data where the rods and cones are, and then automatically count them. He is also using Argonne's X-ray source (Advanced Photon Source) for high-throughput imaging of zebrafish to understand the effect of genetic mutations on various aspects of the fish's growth and development.

What opportunities do you see arising from the MBL-UChicago affiliation?

IF The MBL seems to be a very exciting place with an amazing amount going on. There's lots of pent-up demand for computational expertise at the MBL and a lot of interesting opportunities for scientific collaboration. • —DK

Big Computing Demystified

Definitions for computation terms can be fluid, Ian Foster says, but here are some of his:

Supercomputer: "Very fast computers that, nowadays, are usually built by tying together a large number of computer processors. The supercomputer Mira at Argonne, for example, has 800,000 computer cores. To put it simply, it is 800,000 times faster than your desktop computer."

Big/Scalable/High Performance/Parallel Computing: "All these terms refer to methods that allow you to deal with very large amounts of data using many computers at once. So your methods, algorithms, and software can scale to deal with thousands or hundreds of thousands of processors and with terabytes or petabytes of data."

Grid or Cloud Computing: "This is the notion of giving people access to the power of advanced computers by giving them access to a network. Amazon Web Services, for example, is a big, commercial, on-demand cloud computing provider that will give you access to a computer for ten cents an hour. The word 'cloud' is also used informally to indicate any large computer cluster, such as the systems that the Computation Institute runs both at Argonne and at the University of Chicago."

RESOURCES FOR RESEARCHERS:
University of Chicago Research Computing Center: **rcc.uchicago.edu**;
Computation Institute's Beagle supercomputer: **beagle.ci.uchicago.edu**;
Argonne Leadership Computing Facility: **alcf.anl.gov**

The Leona M. and Harry B. Helmsley Charitable Trust awarded $3,242,194 for Advanced Training at the Interface of Biology and Computational Science.

Burroughs Wellcome Fund awarded $1,000,000 to establish the endowed Advanced Education Fund, to support the MBL's Discovery courses.

The National Institutes of Health awarded $620,205 for a project titled "Mapping Neuronal Chloride Microdomains." George Augustine is the principal investigator.

Robert A. Prendergast contributed $531,578 to the Catherine N. Norton Fellowship, the Annual Fund, and for a Planned Gift Fund.

Edward P. and Linda Owens contributed $350,000 in support of the Tau Project, the Joan V. Ruderman Fund for Science, and the Annual Fund.

The G. Unger Vetlesen Foundation awarded $350,000 in general support for MBL research in the Bay Paul Center. •

ACCOLADES

The following members of the MBL research, education, and alumni community were elected to the National Academy of Sciences: **Eric Betzig**, HHMI, Janelia Farm Research Campus; **Sue Biggins**, Fred Hutchinson Cancer Research Center; **Marianne E. Bronner**, California Institute of Technology; **Scott V. Edwards**, Harvard University; **Alfred L. Goldberg**, Harvard Medical School; **Harvey J. Karten**, University of California, San Diego; **Jeannie T. Lee**, Harvard Medical School; **James C. Liao**, University of California, Los Angeles; **Satyajit Mayor**, National Centre for Biological Sciences, Bangalore; **Randall T. Moon**, University of Washington; **Karel Svoboda**, HHMI, Janelia Farm Research Campus; **Leslie B. Vosshall**, The Rockefeller University.

The following members of the MBL research, education, and alumni community were elected to the American Academy of Arts & Sciences: **Jean Bennett**, University of Pennsylvania; **Carlos J. Bustamante**, University of California, Berkeley; **Joseph L. DeRisi**, University of California, San Francisco; **Howard Eichenbaum**, Boston University; **David D. Ginty**, Harvard Medical School; **David M. Karl**, University of Hawaii; **David Kleinfeld**, University of California, San Diego; **Michael J. Lenardo**, National Institutes of Health; **Margaret Livingstone**, Harvard Medical School; **Frank P. McCormick**, University of California, San Francisco; **Philip Needleman**, Washington University; **Karl J. Niklas**, Cornell University; **Jenny Saffran**, University of Wisconsin; **Cristian Samper**, Wildlife Conservation Society; **Alejandro Sánchez Alvarado**, Stowers Institute for Medical Research.

Methods in Computational Neuroscience course alumnus **Emery N. Brown** (Harvard Medical School/Massachusetts General Hospital; MIT) was elected to the National Academy of Engineering. Brown, now a member of all three branches of the National Academies, was recognized "for development of neural signal processing algorithms for understanding memory encoding and modeling of brain states of anesthesia."

Former Biology of Aging course director **Gary Ruvkun** (Harvard Medical School/Massachusetts General Hospital) was one of six recipients of the 2015 Breakthrough Prizes in Life Sciences, which honor transformative advances toward understanding living systems and extending human life. Co-recipient **C. David Allis** is a former Physiology course faculty member. •

Dianne K. Newman

Microbial Diversity Course Alumna (1995)
and Co-Director (2014-present)

Dianne K. Newman is a Professor of Geobiology at California Institute of Technology and a Howard Hughes Medical Institute Investigator. Her research focuses on understanding the coevolution of microbial metabolism and environmental chemistry. The contexts that motivate her research span ancient sedimentary deposits to chronic infections. Her work is helping to reshape interpretations of ancient molecular fossils as well as redox-active "secondary" metabolites.

A Diversity of Gifts

When the mantle of "Microbial Diversity course co-director" was placed on Dianne Newman's shoulders last summer, she welcomed the chance to "help shape the field, working with some of the best and most motivated students out there." But equally as important, she was happy to give back to a course that has benefitted her profoundly for more than 20 years.

Newman first got hooked on microbiology when she was an engineering graduate student at MIT, after she met a Microbial Diversity alumna who was isolating bacterial strains from a Boston watershed. Newman's MIT advisor generously said, "'Look, if you are really excited about bacteria, you should go to Woods Hole and take that course,'" Newman says. "I did, and it completely changed my life."

Microbial Diversity was then directed by the late Abigail Saylers of University of Illinois and Ed Leadbetter of University of Connecticut. Saylers had done "pioneering work on gut bacteria using genetics," Newman says. "She made me aware of the power of genetic approaches, which I found elegant and captivating, and went on to pursue in graduate school and beyond." Ed Leadbetter, who died last year, would become Newman's lifelong mentor. Newman now co-directs the course with Leadbetter's son, Jared, also of Caltech, which makes the experience all the more poignant and significant for her.

While continuing some of "the great course traditions that Ed, Holger Jannasch and others started over 40 years ago"—such as collecting microbial samples from Eel Pond, Sippewissett Marsh, and all over Woods Hole—Newman and Leadbetter are revitalizing the course with the latest approaches, as is expected of all MBL course directors. In homage to Sayler, they are incorporating a significant genetics component into the program for the first time, including complete genome sequencing.

"We are showing the students just how easy it is these days to isolate novel species that are biologically fascinating, and how to rapidly make them tractable to genetic analysis," Newman says. Last summer, using sophisticated microscopy and free DNA sequencing offered by companies that partner with the course, "we were able to start literally from dirt samples and get a fully sequenced genome in three weeks," she says. "By the end of the course, some of the students had completed genetic screens on two isolates, using chemical or transposon mutagenesis. They recently presented their work at the general meeting of the American Society for Microbiology. It was remarkably successful."

After her student experience in Microbial Diversity, Newman came back as a teaching assistant and later as faculty. On several occasions she obtained isolates in Woods Hole that became important model organisms in her Caltech lab. The course has also introduced her to students that she hired as post-docs and many enduring, long-term friendships.

Of all the gifts Microbial Diversity has provided, Newman says, perhaps the most profound is deeply influential role models. Saylers, Leadbetter, and "all the course's former instructors were excellent scientists who also engaged the scientific community in a generous way," she says. "They were willing to donate their time to teaching young people. Through them, I developed an enduring respect for making that choice: to have a meaningful impact on science beyond one's own lab. The MBL inspires that in multiple ways." • —DK

The Wisdom of the Unexpected

By William Reznikoff

William (Bill) Reznikoff is the MBL's Director of Education. He is also a senior research scientist in the MBL's Bay Paul Center for Comparative Molecular Biology and Evolution, where his research interests are in the fields of bacterial and molecular genetics.

Renzikoff received a B.A. in biology from Williams College and a Ph.D. in biology from The Johns Hopkins University. He was appointed an MBL senior research scientist in 2007, after nearly four decades as a professor in the Department of Biochemistry at the University of Wisconsin-Madison, where he currently holds the position of professor emeritus. He is a member of the American Academy of Arts and Sciences and the American Academy of Microbiology.

The MBL Education Program encompasses a broad range of students, from high-school biology teachers to university faculty. The MBL's intensive summer courses are world-renowned and attract graduate and postdoctoral students from around the world.

After 6 years as Director of Education, Reznikoff will retire in 2015.

One day at the MBL, I heard Ron Vale, an extraordinary biologist and Howard Hughes Medical Institute Investigator, discussing his scientific motivations with a few undergraduates. What was most exciting to him, Ron said, were the experiments that failed. He then explained that "failed" meant experiments that did not turn out the way he had predicted. That discussion had a profound effect on me because it helped explain why I became a scientist. I enjoy life the most when it is a bit unpredictable, when I see things I don't expect or meet unusual people or get unanticipated experimental results. Those are the events that tell me the most about places, people, or the real basics of life.

At first glance, the story of how I got into science is much more prosaic. My father was a physician-scientist who began spending summers in Woods Hole in the mid-1920s. I was two months old when I was first brought to Woods Hole, and I came for many summers thereafter. Of course, I picked up shells and crabs on the beach and attended the Children's School of Science, but in retrospect that was only part of the story. Woods Hole was a bit bohemian. All sorts of people were here—and were accepted. My father, without intending to, got me interested in genetics by taking me to his hematology lab and showing me blood smears (I remember thinking, "Is leukemia a genetic disease?") It was not just science classes that hooked me on science; it was also enjoying the unpredictable and interesting in general.

One story will exemplify a lifetime of wonderful, unpredicted experiences. On a lark, I spent my junior year abroad at the new University of Ghana in West Africa. How on earth could this relate to my future scientific career? My home institution had insisted I take a course in organic chemistry in Ghana, and it turned out to be an imaginative class taught by a professor with an Oxford Ph.D. With whom had he studied? Dorothy Crowfoot Hodgkins, soon to receive a Nobel Prize for her work in X-ray crystallography. Hodgkins came to Ghana and gave a seminar and, for me, it was "love at first sight." I began hoping I could study molecular mechanisms and macromolecular structures.

This hook on the unexpected was reinforced by the company I kept during graduate school and postdoctoral training, and by great, unpredictable science. My career included detailed studies of the lactose operon in bacteria and chasing down mobile genetic elements. This was done with a lot of interesting and "different" colleagues. When I moved to to the MBL's Bay Paul Center, I was in heaven. The center's founder, Mitchell Sogin, had created a fantastic environment filled with interesting, out-of-the-box scientists (perhaps by design). Then I had the very good luck of becoming the MBL's Director of Education. Here, I am in the midst of an orchestra of interesting and different people, and unexpected things pop up all the time. I will miss that, after I retire this year. Unpredictable personal and scientific discoveries are what make the MBL such an inspiring place for science. •

The School of Life

When Cornelia Clapp arrived for the MBL's inaugural session in 1888 — one of seven investigators, four of them women—she was working on her Ph.D. from Syracuse University and was a highly regarded teacher of zoology and embryology at Mt. Holyoke College in Massachusetts. Known for her enthusiasm for direct observation of organisms from amoebae to mollusks, earthworms to chicks, Clapp, like MBL founding Director C.O. Whitman, had been deeply influenced by Harvard zoologist Louis Agassiz to "Study Nature, Not Books."

Whitman suggested that Clapp study toadfish development, which she did for the next several summers; in 1891 she published her observations in Whitman's *Journal of Morphology*. Like many early MBL researchers, Clapp delved into comparative embryology; her article also detailed the orientation of early cell divisions relative to the embryo's axis. Whitman introduced Clapp to the idea of original research and to the dictum, as she later wrote, "that persistent and completely absorbed attention to one subject will lead to comprehension of much besides that." Encouraged to press into new scientific territory, she began studying the lateral line, a system of sense organs in fish then barely described or understood. Clapp took a leave of absence from Mt. Holyoke to complete her second Ph.D. in 1896 with Whitman at the University of Chicago; her thesis provided the first description of the lateral line system of the adult and developing toadfish.

Clapp's research is lasting, yet she is best remembered as a "spellbinding" teacher. "Her bounding vitality and search for knowledge were contagious," wrote her contemporary Louise Baird Wallace. "I felt I was never fully alive until I knew her." • — DK

Cornelia Clapp came to the MBL nearly every summer from 1888 until her death in 1934. She served as the MBL's first librarian (1893-1907), taught in the MBL Embryology Course (1897-1903), and in 1910 was elected to the MBL Board of Trustees.

(Background) Illustration from Cornelia Clapp's doctoral dissertation at the University of Chicago (1896), "The Lateral Line System of *Batrachus tau*." The lateral line is now known to enable fish to detect weak water motions and pressure gradients and is still studied today.

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