

Biological Discovery in Woods Hole

Founded in 1888 as the Marine Biological Laboratory

SUMMER 2014 Volume 9, Number 2

IN THIS ISSUE

A Critical Mass in a Closed Space

Eyes on Target

Shoring up the Coastline

Watershed Issue for Earth

at Many Scales





FROM THE DIRECTOR

Dear Friends,

VOLUME 9. NUMBER 2

Ioan V Ruderman

Ionathan Gitlin Pamela Clapp Hinkle

Diana Kenney

Beth Ready Liles

One of the most exciting aspects of the MBL-University of Chicago affiliation, which became official last summer, is the many doors the affiliation opens for scientific and educational collaborations that build on the partners' unique combination of strengths and resources. Faculty, heads of operational units and administrative leaders at the MBL and UChicago have been engaged in a wide variety of activities over the past year that focused on implementing the first phases of the affiliation. This spring, the MBL Board of Trustees welcomed Robert J. Zimmer, president of the University of Chicago, as the new chair of the MBL Board. President Zimmer succeeds Jack W. Rowe, who led the MBL through an exceptionally successful capital campaign and two significant renovation projects that transformed Loeb and Rowe laboratories. The MBL has benefitted tremendously from Jack Rowe's leadership and from the exceptional generosity of the Jack and Valerie Rowe family, for which we are very grateful.

The tremendous promise and energy surrounding the affiliation was evident at the first MBL-UChicago Scientific Retreat, held in February in Chicago, and the second Scientific Retreat, held at the MBL in May (see p. 9). At both meetings, scientists from the MBL, the University, and another of the University's affiliates, Argonne National Laboratory, explored many overlapping research and educational interests. I am grateful for all the hard work that the MBL's resident scientists put into organizing both retreats, as well as the time they have dedicated over the past year to meeting with numerous University of Chicago scientists, staff and leadership who visited the MBL.

The May retreat also provided a great opportunity for scientists from all corners of the MBL—including many visiting investigators and course faculty, as well as resident scientists—to collectively consider, "What are the MBL's greatest strengths?" One answer is the extraordinary diversity of research taking place on the MBL's very small campus footprint: MBL scientists are studying life at all scales, from genes to organisms to ecosystems. This high campus density promotes easy, frequent interactions and crosstalk among scientists in all programs and parts of the institution. Another special strength is that the MBL offers flexible, assignable lab space and housing for visiting scientists, educators and students, making it possible to sponsor new kinds of courses, workshops, conferences and other initiatives. A third strength, and one that is particularly relevant to the affiliation, is our capacity to host courses for UChicago undergraduates during the academic year, as well as a diversity of other scientific activities for our colleagues from all institutions, thus increasing use of the MBL's lab and housing facilities beyond the busy summer season.

This issue of *MBL Catalyst* spotlights several research initiatives at the MBL that, collectively, illustrate the breadth of the lab's scientific commitments. As the MBL-UChicago affiliation enters its second year, we expect this diversity in research and education will continue to cross-pollinate, blossom and grow across the institution and with our colleagues at UChicago and Argonne. There is enormous room for discovery, and opportunities for translation into improved public health and for stewardship of the Earth for all future life.

Joan Rudern

Joan Ruderman, President and Director

IN THIS ISSUE





DEPARTMENTS

8 News & Notes

The latest findings from our laboratories and field sites.

12 MBL MOMENT

Skating Into an Ancient Time Taking cues from chick embryology, Neil Shubin uses the skate to peer into the evolution of the vertebrate limb.

14 GIFTS & GRANTS

14 ACCOLADES

15 COOL TOOL

Fish Out of Water

16 SCIENTIST'S EYE VIEW

Just as a shift in your gut microbes can signal illness, Mitchell Sogin sees how similar changes can predict stress in the environment.

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SUMMER 2014

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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

Founded in Woods Hole, Massachusetts, in 1888, the

MBL is a private, nonprofit institution and an affiliate

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Images: Inside cover: West Creek in the Plum Island Estuary. Massachusetts (David Samuel Johnson); MBL President and Director

Joan Ruderman (Bachrach Studios), P. 1: illustration by Dreamstime

clockwise: illustrations by Dreamstime.com; eye of hatchling squid

(Stephen Senft, George Bell, Lizzie Kripke and Bob Gould); melting ice sheet (John Hobbie); HHMI Summer Institute scientists at MBL (Tom Kleindinst). Pp. 4-5: moon jellyfish (Brad Gemmell) Pp. 6-7: Club Head

Creek in the Plum Island Estuary, Massachusetts (Sarah Wilkins); Tatoos Island, Washington (Dreamstime.com). Pp. 8-9: female Brachionus

Investigator Amy Gladfelter of Dartmouth College leads a breakout

session at the second MBL-University of Chicago Scientific Retreat, May

2014 (Tom Kleindinst); a breakout session at the MBL-UChicago retrea (Tom Kleindinst); Chinonye Nnakwe of the University of Chicago at the

MBL-UChicago retreat (Tom Kleindinst). Pp. 10-11: wetlands landscape

(Dreamstime.com); MBL Distinguished Scientist Jerry Melillo (courtesy of Jerry Melillo); ocean storm (Dreamstime.com). Pp. 12-13: Neil Shubin,

Robert R. Bensley Professor of Organismal Biology and Anatomy, University of Chicago (Nathaniel Chadwick); skate (Dreamstime.com);

model of Tiktaalik roseae (Jellyfish Pictures, Ltd.) P. 14: MBL Physiology course students (Tom Kleindinst); Harvard Forest, Petersham, Mass.

(Harvard Forest LTER). P. 15: zebrafish (Dreamstime.com); zebrafish embryo (Scott Dugan). P. 16: MBL Distinguished Scientist Mitchell Sogin

evolutionary tree diagram from Darwin, Charles, 1872, On the Origin of

Species By Means of Natural Selection. 6th ed. London: John Murray; Blautia oligotypes and their host occurrence patterns. Fig. 5 from Fren

Back cover: Mouse large intestine stained with host cell nuclei (magent

enta objects are host cell nuclei, while magenta dots are bacte Depicts the relationship between mucus layer of gut, food, and host cells

ABOUT THE COVER: MBL research spans many scales, from molecular

the MBL-directed Plum Island Ecosystems Long Term Environmental Research project (David Samuel Johnson); bottom illustration by

Online extras: For full image descriptions, supplemental

materials, and other information related to this issue, visit:

to environmental. Top: West Creek in Rowley, Mass., is a field site within

and two different types of mucus labels (red and green). On the left,

goblet cells containing mucus can be identified as green ovals. Large

(Tom Kleindinst). P. 17: background: Partial reproduction of foldout

AM et al (2014), A single genus in the gut microbiome reflects host preference and specificity. ISME Journal, doi: 10.1038/ismej.2014.97.

maniavacas rotifer with egg (Kristin Gribble): Erik M. Jorgensen (Butch Adams) and Clare Waterman (Tom Kleindinst); MBL Whitman

com; HHMI Summer Institute scientists at MBL (Tom Kleindinst); moon jellyfish (Brad Gemmell); ocean storm (Dreamstime.com). Pp. 2-3,

in biology, biomedicine, and environmental science.



LIFE AT MANY SCALES

FEATURES

2 A Critical Mass in a Closed Space

Taking advantage of rich resources for advanced imaging and collaborative exchange, a big group of MBL visiting scientists pushes into uncharted biological territory.

Eyes on Target

When is a robot like a jellyfish? When it can cover long distances using minimal power. Biologists and engineers team up to design a jellyfish "swim-bot" for the U.S. Navy.

Shoring Up the Coastline

Linda Deegan's team discovered one reason why East Coast salt marshes are falling apart. Now, they seek to understand all the stressors on these critical habitatsand how to prevent them from becoming open ocean.

A Watershed Issue for Earth 10

As a graduate student, Jerry Melillo was surrounded by environmental scientists who wanted to make sure their work made a difference. It's a lesson he never forgot.

17

The Finest of Limbs on the Tree of Life

MEMORABILIA

To record a nearly infinite variety of microbes. MBL scientists multiply the branches on Darwin's evolutionary tree.

The zebrafish isn't marine, but it earns its keep at the MBL

A Universe of Microbiomes

MBL

Life at Many Scales This issue of MBL Catalyst showcases the breadth of MBL research, spanning inquiry from the molecular building blocks of cells to the large-scale forces driving climate change.

A Critical Mass in a Closed Space

AN EXPERIMENTAL COLLABORATION AT THE MBL TACKLES A BIG UNKNOWN IN CELL BIOLOGY

Staking out new territories in cell biology is a signature of MBL visiting research, and this summer a group of 21 scientists from seven different institutions is proving just that. The group is zeroing in on the enigmatic protein "clusters" that scientists have noticed for years in various cells and biological systems, but nobody knows how they form-or why. To tackle these wide-open questions, the scientists are experimenting with new ways of working as collaborative teams.

"These clusters aren't rigidly defined structures, like a building, which has x number of girders, screws and drywall components," says Ron Vale, a principal investigator (PI) on the project and a Howard Hughes Medical Institute (HHMI) Investigator at the University of California, San Francisco. A good analogy for these self-assembling, constantly changing, "loosely held confederates of proteins working together," he says, might be a conference of people. "Sometimes, to get something done, you have to gather a critical mass of the right people into a closed space."

Vale could just as well be referencing the unusually flexible, five-year grant that supports this collaboration in the MBL's Whitman Center for Visiting Research. The grant, from the Howard Hughes Medical Institute, enables new people to be brought into the collaboration each year, and even "allows us to change the nature of the problem we are tackling," Vale says.

Michael Rosen, an HHMI Investigator from University of Texas Southwestern Medical Center at Dallas, and Jim Wilhelm from University of California, San Diego, are two other PIs on the grant. The fourth "PI" isn't a scientist but the MBL itself, "one of the very few places you can get so many labs from so many places together for a couple of months to collaborate," Rosen says.

"Many of us have written grants about collaborations before; we always state that we will be able to do science together that we couldn't do on our own. Very often that works OK; a little bit of synergy comes from working together. But there aren't often fireworks," Rosen says.

"It was frankly shocking to me how well this collaboration at MBL worked

last summer."

- Michael Rosen, HHMI/ University of Texas



"We will need a lot of eyes on the problem."

"But it was frankly shocking to me how well this collaboration at This summer, the HHMI group is looking at another example MBL worked last summer," he continues. "We did a whole bunch of protein clusters: RNA granules, which are thought to play an of experiments we hadn't even thought of until a group of us were important role in RNA metabolism in cells. "Because it's a different sitting at lunch expressing some frustration—this didn't work or molecular system, a different collection of people are coming to the that didn't work-and someone piped up and said, 'Doesn't that MBL to provide the breadth of technical expertise and intellectual mean we can do this experiment? I can bring this reagent, and you frameworks we'll need," Rosen says. They'll have fresh brain can bring that reagent, and we can actually do it this afternoon?' power—and advanced microscopes, different from those required That kind of synergy just happened over and over and over again. last summer-to test their hypothesis that these protein clusters are structurally analogous to oil droplets in water. When collaborators can get together for a significant amount of time, it really changes how the sociology works."

"Once we've figured out how to create these structures, the next key question is, why do cells go to the trouble of doing this?" Last summer, the HHMI group focused in part on the immunological synapse, "a beautiful dance of molecules," Rosen Rosen says. "We will need a lot of eyes on the problem." Joining says, at the interface of a T-cell—a white blood cell central to Rosen, Wilhelm and Vale on the collaborative team this summer fighting infection—and an infected, antigen-presenting cell. When are Clifford Brangwynne (Princeton University), Amy Gladfelter (Dartmouth College), Hao Wu (Boston Children's Hospital/Harvard the immunological synapse forms through this still-undefined Medical School) and Roy Parker (University of Colorado, Boulder) protein clustering process, the T-cell is activated to mount an and their students and postdoctoral fellows. immune response.

The group decided to try and recreate T-cell activation and its downstream signaling in a test tube, for which they had to make about 20 different proteins. "Just at a technical level, that is very, very difficult to do. If I said to someone in my lab, 'Go make 20 different proteins, and then we are going to do this crazy experiment to reconstitute [the immunological synapse],' they'd laugh at me, because it would take about three years and probably wouldn't work," Rosen says. But by divvying up the work between their teams at MBL, they were able to successfully do the experiment-in a matter of weeks.



Rosen expects they'll make good headway, and their MBL experience will be like last summer's, which was "what you always hope collaborations will be: The whole was much, much greater than the sum of its parts." • —DK

Target

MBL BIOLOGISTS TEAM UP WITH ENGINEERS TO MIMIC JELLYFISH MOTION IN ROBOT DESIGN

Marine scientists and the U.S. Navy share a basic need to "see" beneath the ocean waves. While scientists study undersea creatures and processes, and our naval forces watch over the nation's subsea security, both require "eyes on target," something that is hard to come by amid the vast volumes of salt water encircling our Earth.

It seems fitting, then, that marine biologists are working with ocean engineers and naval researchers to develop sensorladen "swim-bots" that can monitor remote underwater activities. One of those robots, under development by a team of MBL visiting scientists including Jack Costello of Providence College, swims a lot like a jellyfish.

"We've been studying jellyfish for the past decade, trying to understand their biomechanics," says John O. Dabiri, Professor of Aeronautics and Bioengineering at Caltech and one of the MBL group's main collaborators. "Along the way we realized that the solutions we've found for efficient swimming might be useful for the Navy. So, in recent years we have been working together to translate the skills of a jellyfish into an underwater vehicle."

"Since animals can move through the ocean better than humans do, we follow nature's lead," Costello says.

The team's jellyfish robot research is part of a multimilliondollar, multi-university program funded by the U.S. Office of Naval Research to create advanced, biomimetic hydropropulsion technology. The MBL provides a meeting place for collaborative research on the project for Costello, Sean Colin of Roger Williams University, and Brad Gemmell of University of Texas at Austin.

The languid jellyfish may not seem like the best pattern model for a smart, self-guided, subsea probe, one that could operate something like a Mars rover for our equally mysterious oceans. But for a certain class of vehicle—palmsized, slow, able to swim extended distances with minimal energy expenditure—the humble jellyfish fits the bill. Umbrella-like jellies called medusas were among the earliest animals to evolve muscle-powered locomotion, and the flatter, disk-like types are still among the most efficient at it, Costello says. Unlike longer-bodied, bell-shaped medusas that use strong sternward squirts to jet around at speed, these blunt-nosed, parasol-shaped jellies lead a more leisurely life, pulsing around in a rather stately fashion pursuing essentially immobile, tiny prey such as crab-like copepods, larvae, and fish eggs suspended in the brine.

"These jellyfish have to swim to explore new waters where they might find prey," Dabiri explains. Predators are usually few, "so for them it's mainly about getting from A to B without wasting too much energy. As a result, they've evolved clever ways to use their flexibility to move the water around them without having to apply too much force."

No members of the jellyfish jet set, the disk-like medusas rely on their membranous bodies to perambulate through the water, almost like they are rowing boats with oars. The thin, flexible umbrella membrane expands to encompass some water and then closes to accelerate the water rearward. Scientists call this low-speed mode of pulse propulsion "rowing."

The slow, cycling gait is elegantly effective for getting around in a fairly viscous medium like seawater, because it addresses energy and power constraints imposed by the animal's small, fragile body and modest metabolism. Similarly constrained would be an analogous sea-going robot, notes Dabiri, who says that pulse propulsion like the sea jellies' could cut the energy consumption of such vehicles by about a third.

The rowing metaphor grows more apt considering how the disk-like jellyfish uses the trailing edges of its umbrella, what the scientists call the margins. With each stroke, the margins precisely sweep through the surrounding water to smoothly send the body forward. In this way, the inward-outward stroke of the jelly's "circular oar" resembles that of an expert boatsman who first pulls the oars through the water for the power stroke, then deftly feathers them for the recovery stroke. Both the rower and the jellyfish leave characteristically smooth swirl wakes that are notably "quiet," that is, they contain a minimum of drag-causing turbulence.

To better understand how these jellies propel so well through the water, Costello and other research divers recorded the animals' swim strokes using a customized, underwater video camera called a particle image velocimeter (PIV). This visualization technology, which traces the paths of particles suspended in water, enabled the team to quantify the 3D flow structure of the jellies' swirling wake vortices.

The fascinating PIV videos, some of which can be viewed on the MBL's YouTube channel (mblwoodshole), show how the jelly's margins entrain the adjacent water during the animal's contractile power stroke. This creates a vortex ring—the equivalent of a wet "smoke ring" that rolls rearward like a tossed yo-yo. Then, as the medusa's umbrella expands during the relaxation phase of its swim cycle, a second, smaller vortex ring appears astern. This ring, which rotates in the opposite direction to its predecessor, spins off the umbrella's margin as it sweeps back through its whip-like trajectory.

"We're exploring the notion that it's the kinematics—the actual motion of the jelly's flexible body—that are most important, rather than its material properties," Dabiri says. The graceful to-and-fro swing of the margins, it turns out, waft out alternating vortices that smoothly flow into each other: swirl, counterswirl, neatly transitioning with minimum energy loss. This is how the jelly sustains the greatest forward thrust with the least amount of effort.

"It's the recovery stroke during the relaxation phase that's important," Costello points out. "The rebound of the flexible membrane is where the jellyfish get an added push, an extra kick." Over millions of years, the membrane margin has evolved to move just so to optimize the momentum transfer to the surrounding fluid, he says. "If we can understand how to use flexible membranes to efficiently generate such vortices in robot vehicles, we'll be on our way to the practical, capable designs we want." • -SA

Shoring Up the Coastline

Just an hour north of the Boston skyline lie the productive salt marshes and tidal waters of Plum Island Sound estuary. Though often tranquil, this landscape is the centerpiece of an ambitious experiment that could help preserve embattled salt marshes across the globe.

"We're studying 300 linear meters of creek and 60,000 square meters of marsh—a whole, true ecosystem," says Linda Deegan, a senior scientist in the MBL's Ecosystems Center and the only person crazy enough, her friends like to say, to tackle an experiment so immense for more than a decade.

Deegan's big-picture approach has been rewarded with big results. In 2012, her team upended decades of wisdom about the resilience of salt marshes with a paper that implicated nutrient loading in the widespread disintegration of marshes along the U.S. East Coast. Now, the team is continuing its work to better understand how salt marshes will fare in the face of continued development and sea-level rise—and how to prevent their conversion to open ocean.

For many Americans, the salt marshes that skirt the East Coast bring to mind summers at the beach and the telltale smell of low tide. They serve as a critical interface between coastal lands and waters, providing storm protection to seaside cities, food and refuge to countless species, and thick root systems for storing carbon. In recent decades, scientists have watched salt marshes and their vital ecosystem services deteriorate, with no clear verdict on the causes. Salt marshes are

disintegrating, and

MBL scientists are

finding out why-

and how to save them

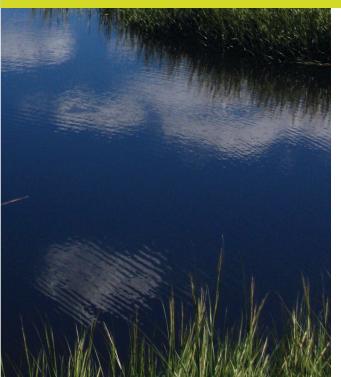


In 2003, Deegan's MBL-based team of scientists set out to change that by zeroing in on a key issue: how excess nutrients like nitrogen and phosphorus, which can enter watersheds from septic systems and agricultural runoff, impact salt marshes at the landscape level.

Salt marshes are effective nutrient filters, but researchers never established how much might be too much. "Much of the way that we thought about nutrient enrichment in salt marshes was based on relatively small, plot-level experiments," Deegan says. Her team's project at Plum Island Sound estuary took an unusual strategy in two regards—they dissolved the nutrients in a way that better mimicked enrichment from septic systems and runoff, and they did so on a grander scale than ever before.

For the first several years, the cordgrass (*Spartina* spp.) that dominates and stabilizes salt marshes grew tall and vibrant in the experimental section, bolstered by nutrient levels similar to those of Cape Cod or Long Island waters. Yet by 2010, a far different—and more surprising—outcome became clear. The results, published two years later in *Nature*, showed marked disintegration and collapse of the nutrient-enriched salt marsh edges compared to the reference marsh, which was not experimentally enriched. The team identified a feedback loop in which increased microbial decomposition and poorly anchored cordgrass plants contributed to the collapse of the marsh banks.





LOCATION IS EVERYTHING: COMPARING NI TROGEN'S FATE IN THE ATLANTIC AND PACIFIC OCEANS

Off the tip of the Olympic Peninsula in Washington, if you look carefully, you can find Tatoosh Island, the first place water hits when it laps in from Japan. Owned by the Makah Tribal Nation, Tatoosh is small, pristine and rarely visited—except for the research sojourns that ecologists Catherine Pfister and Tim Wootton have made to the island for many years.

Tatoosh's relatively untouched state has allowed Pfister and Wootton—both professors in the University of Chicago's Department of Ecology and Evolution—to learn more about natural ecosystems through experiments and long-term observations. One of their interests is right up Linda Deegan's alley: the relationship of animal, microbial and algal populations to the nitrogen cycle. Given their bi-coastal interest in nitrogen cycling, Deegan and Pfister are organizing a workshop at MBL to understand if ecosystems along the edges of the Pacific and the Atlantic respond differently to similar stresses, such as increases in nitrogen loading. The workshop, to be held in September, will address questions that compare across these two oceanic realms.

"Do animal communities living in different ocean temperatures (the Pacific is much colder than the Atlantic) have the same response to rising global temperatures?" Deegan asks. Washington shores are characterized by high nitrogen due to the natural

Now, the project has secured additional funding from the National Science Foundation to confirm whether a

- glut of nitrogen lowers the tipping point beyond which salt marshes degrade into open ocean. Not surprisingly, Deegan and her colleagues are planning experiments that span more disciplines than ever.
- "We want to understand all the integrated responses in this habitat and to know the limits of the change here," Deegan said. "One of the main questions is, will the marsh ultimately accommodate the nutrients and settle down to a new, stable configuration? Or, as the creek bank breaks up into these smaller and smaller pieces, will that just allow the nutrients to dig deeper into the marsh?"

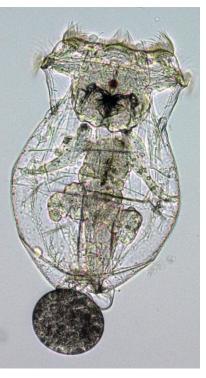
Because commercial fisheries often depend on the nursery and foraging grounds provided by salt marsh banks, the team will investigate nitrogen's influence on animal biomass and coastal food webs. They will continue to look at shifts in the genetic diversity of cordgrass, for which they've already identified intriguing evidence for a genotype that produces fewer roots and rhizomes. They'll also explore the make-up of the marsh's microbial communities, which somehow revved up decomposition in the nutrientrich environment without significant changes to the bacterial assemblages.

Deegan says the diversity of research questions is what makes this long-term study such an exciting project. "Nutrients affect so many different things: food webs, nutrient cycles, carbon storage, geomorphology. We really want to understand all of it." • —EW

> process of upwelling. Pfister asks, "Do the responses of ecosystems that have experienced naturally elevated nitrogen for millennia differ from those that are recently high in nitrogen due to human inputs?"

> The workshop will bring together key researchers from the MBL, the University of Chicago, and other institutions to address how plants, microbes and animals interact to determine the fate of nitrogen in ecosystems. "Ultimately, we want to understand if human disturbances to the nitrogen cycle will play out in the same way on both coasts," Deegan says. •—DK

News & Notes



Negative Impacts of Advanced Maternal Age on Offspring are Preventable, MBL Study Finds

Older mothers give birth to shorter-lived offspring, an observation Alexander Graham Bell made in humans in 1918 that has since been confirmed in several animal and plant species. But are there any beneficial effects of advanced maternal age on offspring? Kristin Gribble and David Mark Welch of the MBL's Bay Paul Center and colleagues studied this question in the rotifer (B. manjavacas), a tiny aquatic animal that is becoming established as a model organism for aging research. Advanced maternal age, they found, reduced the lifespan, fecundity and size of offspring. However, if they put the mothers on a calorierestricted diet during pregnancy, it reduced the severity of these effects to varying degrees, depending on the type of caloric restriction (90 percent reduction in food given or alternating cycles of eating and fasting) and the gender of the offspring (lifespan of female offspring increased by about 17 percent, but lifespan of males did not change). Understanding the basis for these different maternal effects, the scientists say, may one day guide effective interventions to improve human health and life span. (Aging Cell, doi: 10.1111/acel.12217, 2014). •

MBL and University of Chicago Announce First Recipients of Lillie Awards for Collaborative Research

Erik M. Jorgensen and Clare Waterman are the recipients of the first two Frank R. Lillie Research Innovation Awards. This new grant program is the first formal research



opportunity between the University of Chicago and the MBL since their affiliation in 2013. The awards provide funding for scientists to develop novel, collaborative projects based at the MBL that will likely lead to transformative biological discoveries. Jorgensen, a University of Utah neuroscientist, and his colleagues are addressing the fundamental question of how high-level brain processes such as memory are related to changes in the structure and function of neural connections. Waterman. a Distinguished Investigator at the National Institutes of Health, and her multidisciplinary team of cell biologists and advanced microscopists are investigating basic molecular mechanisms of cellular movement, shape and form, which are critical to understanding human disorders such as cancer. The awards support two years of research for a total of \$125,000 per award. Jorgensen, Waterman and their teams are beginning their projects this summer.

Sensing Gravity with Acid: MBL Scientists Discover a Role for Protons in Neurotransmission

While probing how organisms sense gravity and acceleration, scientists at the MBL and the University of Utah uncovered evidence that acid (proton concentration) plays a key role in communication between neurons. The team, led by the late MBL Senior Scientist Stephen M. Highstein, discovered that sensory cells in the inner ear continuously transmit information on the orientation of the head relative to gravity and low-frequency motion to the brain using protons as the key synaptic signaling molecule. "This addresses how we sense gravity and other low-frequency inertial stimuli, like acceleration of an automobile or roll of an airplane," says co-author Richard Rabbitt, Professor of Bioengineering at University of Utah and adjunct scientist in the MBL's Program in Sensory Physiology and Behavior. "These are very long-lasting signals requiring a synapse that does not fatigue or lose sensitivity over time. Use of protons to acidify the space between cells and transmit information from one cell to another could explain how the inner ear is able to sense tonic signals, such as gravity, in a robust and energy-efficient way." (PNAS doi:10.1073/pnas.1319561111, 2014). •

Second MBL-University of Chicago Scientific Retreat Moves Affiliates Toward a New Era in Discovery



Keeping up the momentum after their first retreat in Chicago in February, faculty and scientists from the MBL's resident and visiting scientist communities, the University of Chicago, and Argonne National Laboratory convened for a second retreat at the MBL in May.

Through wide-ranging, lively discussions about the big research questions the MBL-UChicago affiliation is uniquely positioned to address, the 190 retreat participants emerged with several key scientific themes for the institutions to explore. These themes, broadly defined, are Imaging, Computational Biology, Organisms, and Seed/Collaborations, the latter being a cross-cutting request for more opportunities for MBL and UChicago scientists to interact through mechanisms such as seed grants for early research.

"This was an inclusive process in which everyone present had a voice, including a large number of MBL summer investigators," said Steven Zottoli, MBL adjunct senior scientist from Williams College. Zottoli was a member of the retreat planning committee, which was co-chaired by cell biologist Karl Matlin, professor in UChicago's Department of Surgery, and Joel Smith, MBL's associate director of Education and assistant scientist in the Bell Center. "Of the four emerging categories, everybody had a stake in one of them, or part of one," Zottoli said.

The Imaging category embraces imaging life across multiple scales, from atomic to ecosystems, and pulls in scientists from many disciplines, including biologists, physicists, computer scientists, and environmental scientists. The Computational Biology category is also inclusive, with research ideas ranging from gene regulatory networks in developmental retreat weekend. and cancer biology, to neural networks, to microbiomes in human and animal health, to global biogeochemistry networks. While the Organism category focuses on marine animals, it includes other model organisms, such as *Xenopus* frogs and zebrafish, as well as microbial communities.

On the second day of the retreat, the participants identified critical first steps needed to move forward in these emerging scientific areas. Those strategic recommendations will be considered by the MBL and University of Chicago faculty advisory committees, which are responsible for fostering and developing the scientific themes that the affiliates could affiliation. The UChicago faculty advisory committee is led by Neil Shubin, Robert R. Bensley Professor of Organismal Biology and Anatomy and senior advisor to the president of the University of Chicago.

"There is a clear need for focused conferences on imaging, computation, marine resources and other scientific priorities, with white papers as output. These will begin in fall 2014," Shubin said. The MBL and UChicago faculty advisory committees will also start examining the scientific infrastructure at the institutions, he said. "What do we have, and what do we need to move forward in our collaborations?"



The second retreat also served as a welcoming orientation for many UChicago and Argonne faculty who had never visited the MBL before. Tours of the Loeb teaching labs, the National *Xenopus* Resource, the visiting scientists' labs in Rowe and the Marine Resources Center were offered, and a poster session and mixer kicked off the

"These kind of visits leave people energized and transformed, when they see the resources that the affiliation brings to the table. Both Neil Shubin and I want to encourage more of them," said Jonathan Gitlin, MBL's deputy director of Research and Programs. To that end, the University of Chicago has set up an MBL-UChicago Connection Fund that enables visits between the campuses for students, scientists and staff, as well as joint workshops.

En route to achieving broad consensus on address, the retreat yielded an abundance of stimulating research ideas. For example, "how to deal with questions of scale across the sciences" emerged as an important question that the affiliates could effectively investigate, said MBL President and Director Joan Ruderman. "We have an opportunity to look in a large way from genomes to global cycles," she said.

"This retreat was a very positive starting point; not a fait accompli," Zottoli said. To further engage MBL scientists, course faculty and visiting researchers, another retreat is planned for summer 2015 at the MBL. •—DK

<u>A Waters hec ssue</u>

May 6, 2014, was a memorable date for MBL Distinguished Scientist Jerry Melillo



"This was the time of Earth Day; of the idea that your scientific work should make a difference. I was steeped in that."

That morning, he was at the White House to release the Third National Climate Assessment, a towering scientific document detailing the impacts of climate change, current and predicted, in all regions of the country. As chairman of the federal advisory committee that prepared the assessment, Melillo was seeing three years of public service come to fruition. And the report's broad messages—climate change is happening now, all regions in the country are affected, and it is not too late to act, including at the local level were widely covered in the national media. The day fulfilled Melillo's vision of what science can offer-a vision that has guided his entire career.

Science and service

When Melillo was a graduate student at Yale in 1970, an issue of Scientific American came out that "was a life-changer for many of us being educated at the time," he recalls. Titled "The Biosphere," the issue contained early explorations of a very, very big picture: "how the earth's thin film of living matter [the biosphere] is sustained by grand-scale cycles of energy and chemical elements." Years before the term "global warming" would enter the public's awareness in the late 1980s, this issue pointed out that "all of these cycles are presently affected by the activities of man."

For Melillo, "The Biosphere" delineated the mindstretching dimensions of the young discipline of biogeochemistry. It also dovetailed with an intense interest among earth scientists at Yale in "science in the service of society," he says. "This was the time of Earth Day; of the idea that your scientific work should make a difference. I was steeped in that."

One of Melillo's doctoral advisors was F. Herbert Bormann, a leader in identifying acid rain and the environmental damage it inflicts. When The New York Times published Bormann's results from his acid rain research at Hubbard Brook Experimental Forest in New Hampshire, the issue took hold in the public mind. Bormann's testimony on acid rain aided Congress in amending the Clean Air Act in 1977.

"The Hubbard Brook group was very rigorous in all of its analyses, all of its communications. They wanted to make sure policymakers had the best scientific information possible as they thought through a problem," Melillo says.

For his doctoral research at Hubbard Brook, Melillo studied how clearcutting disrupts the nitrogen cycle of a mid-successional forest. Another big influence on his thinking was George Woodwell, then at Brookhaven National Laboratory, who "would come to Yale once or twice a week to give lectures on global issues, such as how humans were influencing the carbon cycle," Melillo says. "There were two areas of concern. One was the burning of fossil fuels and the release of carbon dioxide into the atmosphere, which would lead to a warming earth, since CO₂ is a heat-trapping gas. The second was the emission of carbon from tropical forests, which were being burned to clear land for agriculture."

After Melillo finished his Ph.D., Woodwell invited him to the MBL Ecosystems Center, which Woodwell had founded in 1975. "I thought I would be at the MBL for a year, but it's been nearly four decades now. It's been a surprise, and a wonderful one," says Melillo, who directed the Ecosystems Center from 1989 to 2009. "There is a community of intellectual excitement here that is very special."

At the MBL, Melillo's research on human impacts on nitrogen and carbon cycling has taken him to study sites across the globe—from arctic Sweden to Africa to the Brazilian Amazon. His work has two components: modeling to consider how changes in climate would affect how landscapes function, and long-term field studies to inform and test the models. In the mid-1980s, Melillo and his colleagues developed the first model of land ecosystem dynamics that was both global in scale and projected out for centuries. Called the Terrestrial Ecosystems Model, it spawned a cottage industry of similar models developed by other research groups.

Informing policy

With his research breaking new ground, Melillo soon heard the call of service. In 1988, the United Nations set up the Intergovernmental Panel on Climate Change (IPCC) to assess human impacts on global climate based on current, published scientific research. Melillo was invited to convene a chapter in the first IPCC report, a role he repeated for its second report in 1995.

"Our intention was that these U.N. reports would inform action by policymakers," Melillo says. But consensus on action did not come easily. The IPCC reports led in 1997 to the Kyoto Protocol, an international treaty that binds developed countries that ratify it to reducing their emissions of heattrapping gases. But "there was a conundrum about how to move forward," Melillo says. "Developed countries were very worried about how this would affect their economies. And there were powerful forces, such as the major energy companies, that didn't want their assets threatened. They framed the climate change issue as a choice: *either* the environment or the economy. There was no vision that you could address both and have a win-win. It was a very contentious time. As scientists, we weren't involved in that debate, but we wanted to make sure that everyone who was, knew what we

knew." (To date, the United States has not ratified the Kyoto Protocol. The IPCC and Al Gore, Jr., received the 2007 Nobel Peace Prize for their efforts to inform policymakers on the science of climate change.)

After spending 1996 to 1997 as a scientific advisor in the U.S. President's Office, Melillo was tapped to help prepare climate assessments for the U.S. Global Change Research Program. The Third National Climate Assessment, just released, reports that U.S. average temperature has increased by 1.3 to 1.9 degrees F since 1895, with most of the increase occurring since 1970. "The global warming of the past 50 years is primarily due to human activities, predominantly the burning of fossil fuels," it unequivocally states (www.globalchange.gov).

Many regions are experiencing climate change as an increase in extreme weather, such as longer droughts or more heavy rainfall. The oceans are becoming warmer and more acidic, broadly affecting ocean dynamics and marine life. The "800-pound gorilla," Melillo says, is the melting, disintegration and predicted collapse of the two big polar ice sheets, Antarctica and Greenland, which would cause a dramatic rise in coastal sea levels. In May, two research teams reported that collapse of the West Antarctica Ice Sheet has begun and is now unstoppable.

And yet he remains optimistic that humans will find ways to address climate change and its impacts. Public, private and governmental groups have begun seriously planning to adapt to and mitigate climate change, as described in the third national assessment. "We have choices," Melillo says. "It's not too late to act." • —DK



"That is what keeps me up at night: We are putting into motion these natural processes that will have long-term effects. They have a momentum of their own," Melillo says.

"We have choices. It's not too late to act."

— Jerry Melillo, Chairman, National Climate Assessment Development and Advisory Committee



MBL MOMENT with ...



Neil Shubin

Robert R. Bensley Professor of Organismal Biology and Anatomy, Associate Dean in the Division of Biological Sciences and Senior Advisor to the President, University of Chicago

When the University of Chicago-MBL affiliation was finalized in July 2013, UChicago President Robert J. Zimmer appointed Neil Shubin to provide faculty leadership and build collaborative programs between the two institutions. A paleontologist, evolutionary biologist and former professor of anatomy at UChicago's Pritzker School of Medicine, Shubin received his A.B. degree from Columbia University and his Ph.D. from Harvard University. Shubin is a member of the National Academy of Sciences, the American Academy of Arts and Sciences, and the American Association for the Advancement of Science. He has written two popular science books: The Universe Within: Discovering the Common History of Rocks, Planets, and People (2013) and Your Inner Fish: A Journey into the 3.5-Billion-Year History of the Human Body (2008), which won the 2009 Science Communication Award from the National Academy of Sciences.

Skating Into an **Ancient Time**

Neil Shubin first came to Woods Hole to visit the **MBL** Embryology course in 1985, when he was a

Harvard graduate student interested in visualizing cell movements in limb development. His research is devoted to understanding the evolutionary origin and development of anatomical features, especially appendages such as fins and hands. In 2004, Shubin and his colleagues found a 375-million-year old fossil in the Canadian Arctic that exhibits both fish and amphibian traits. Named Tiktaalik, this "fishapod" was hailed as a transitional creature from the time when marine organisms first ventured onto land. Shubin's book, Your Inner Fish: A Journey into the 3.5-Billion-Year History of the Human *Body*, was recently made into a three-part television documentary by Tangled Bank Studios, a division of the Howard Hughes Medical Institute. This interview took place in April, the morning after Your Inner Fish

premiered nationwide

on PBS.



A model of Tiktaalik roseae, a fossilized fish with limbs.

What was it like to watch yourself on TV?

NS I didn't even see myself! PBS asked me to live-Tweet during the show and answer students' questions. So I didn't have my head up out of the computer the whole time! But it was fun; the kids were very excited and asked a lot of questions.

We were happy to see skate embryo cases (mermaid's purses) from the MBL's Marine Resources Center in Your Inner Fish. Randy Dahn from your lab used skates in the early 2000s to show how the development of fins and of human hands is orchestrated, in part, by the same regulatory gene—providing a clear example of our "inner fish." Are you still using skates in your research?

NS Oh, very much so. Randy's idea was to take the powerful toolkit of chicken embryology, which had been used for a long time, and apply it to studying the skate. You can [cut a] window [in] the mermaid's purse just like you can window a chicken's egg, and manipulate the embryo and see what happens to development. Two other features make the skate a great system to study. It's a cartilaginous fish, so we share an ancient common ancestor with them. And the skate has some unusual features, like its fins grow funny. They essentially surround its head! Any time you have unusual features, you can ask how they get that way. Sometimes the exceptions tell us a lot about how regular things work.

Since Randy's time, we've gotten very interested in the skate. We can apply so many different experimental tools to them now; it gives us access to important biological questions. We are interested in the [genetic] patterning of fins and limbs, the patterning of the gills and the formation of the main body axis. We can now begin to look at the regulatory portions of its genome.

Tetsuya Nakamura from my laboratory is an MBL Whitman investigator this summer, and he is asking, "How does the skate get its unusual fins? What controls how that pattern forms? What genes are active?" We are hoping that will tell us a lot about cartilage patterning in general. It's an exceptional opportunity to be at the MBL this summer, to be part of a community where we can share tools and ideas and really think about skate embryology.

How can studying patterns of embryonic development help you reconstruct how an extinct animal, like Tiktaalik, may have looked?

NS We look for parts of the genome that are highly conserved (nearly identical) in many living animals, and therefore stayed the same

over long periods of time. If you see a certain pattern of gene activity that is characteristic of birds, mice, rabbits and primates, it's a safe assumption that if you find a fossil rabbit, that rabbit also had that pattern of development.

But in reality, we're not so much trying to reconstruct whether an extinct creature had a particular regulatory gene or not. For us, the fundamental question is, "What is the genetic toolkit that builds a hand? And a wrist?" You can answer that question by comparing mice and chickens and fish and asking, "How is the genetic toolkit that patterns a wrist and a hand different from the genetic toolkit that patterns a fin?" You can ask this purely with living creatures; you don't need fossils. The fossils are an added benefit because then we can ask, "When did wrists and fingers evolve? What did those creatures look like when wrists and fingers evolved? What did the world look like at that time?" But, fundamentally, we are interested in how pattern is built in biology.

You are setting out on a new fossil-hunting expedition in the Canadian Arctic this summer. What are you looking for?

NS We're going to northern Ellesmere Island, well north of the site where we found *Tiktaalik*, because the exposed rocks there are of Cambrian and/or Ordovician age (540 to 443 million years old). The Cambrian age is really important because it is when the first vertebrate organisms appear on Earth. It's one of those areas in the fossil record where any new evidence can really impact our understanding. My specific goal is to find [a fossil] of our earliest vertebrate. We'll be doing basic exploration, looking for rocks of the right type that might hold these fossils, like we did in the early days of the *Tiktaalik* expedition. I'm really excited about it.

Do you have a sense of what the earliest vertebrate might look like?

NS I'm thinking it will be a worm-like animal with gill arches, filled with cartilage and maybe a piece of a brain case. A worm with a head, to put it in colloquial terms!

You are known to love new vistas, new places to explore. Does the University of Chicago-MBL affiliation seem like that?

NS Yes, I love new challenges and opportunities. The affiliation offers a great opportunity for the folks in Woods Hole and the folks in Chicago to build something new and unique. The MBL is a remarkable institution, and to be part of it at this time in its history is a true privilege • —DK

GIFTS & GRANTS



ACCOLADES

The National Science Foundation awarded \$1,148,370 for a three-year project titled "Collaborative Research: Ecosystem Evolution and Sustainability of Nutrient Enriched Coastal Saltmarshes." Bruce Peterson is the principal investigator.

The National principal investigator. Institutes of Health awarded \$1,099,195 over five years in support of the Neurobiology course. William Reznikoff is the principal investigator.

The Department of Energy awarded \$1,049,999 for a three-year project titled "Changes in Soil Carbon Dynamics in Response to Long-Term Soil Warming: Integration Across Scales from Cells to Ecosystems." Jerry Melillo is the

The Howard Hughes Medical Institute awarded \$840,926 for a project titled "HHMI Summer Institute (2013-

2016) Polymerization and Partitioning: Mechanisms for **Regulating Protein** Activity." Jonathan Gitlin is the principal investigator.

The National Institutes of Health awarded \$703,219 for a project titled "Spatial investigator. Organization of the Oral Microbiome." David Mark Welch is the principal investigator.

The National Science Foundation awarded \$702,663 for a project titled "ABI Sustaining: A Visualization and Analysis Resource for Comparative Microbial Ecology." David Mark Welch is the principal

Charles M. and **Phyllis Rosenthal** contributed \$500,000 in support of postdoctoral recruitment in the Ecosystems Center. •

The Bay and Paul Foundations

awarded \$500,000

in support of the

Bay Paul Center's

investigation of the

human microbial

expanding

biome.

Mitchell Sogin has been appointed MBL Distinguished Scientist, a rarely bestowed rank that recognizes a career of outstanding scientific achievements and service to the laboratory. Sogin, an international leader in the fields of molecular evolution and microbial diversity, founded the MBL's Josephine Bay Paul Center for Comparative Molecular Biology and Evolution in 1996; the MBL Workshop on Molecular Evolution; and the MBL Strategies and Techniques for Analyzing Microbial Population Structures course.

MBL Distinguished Scientist and Director Emeritus at the Ecosystems Center Jerry Melillo was elected to the National Academy of Sciences. Other members of the MBL research and education community who received the honor include: Larry Abbott, Columbia University; Carolina Barillas-Mury, National Institutes of Health; Bruce P. Bean, Harvard Medical School; Emery N. Brown, Massachusetts General Hospital; Jonathan J. Cole, Cary Institute of Ecosystem Studies; Benjamin F. Cravatt, The Scripps Research Institute; Robert B. Darnell, HHMI/Rockefeller University; Benjamin D. Hall, University of Washington; Richard M. Harland, University of California, Berkeley; Jeff W. Lichtman, Harvard University; Martin M. Matzuk, Baylor College of Medicine; Margaret McFall-Ngai, University of Wisconsin, Madison; Timothy J. Mitchison, Harvard Medical School; Andrew W. Murray, Harvard University.

Robert J. Zimmer, president of the University of Chicago, officially began serving as chairman of the MBL Board of Trustees on April 12, 2014. Zimmer succeeds John W. Rowe, who had served as board chairman since 2006. Other individuals elected to the board's class of 2017 are: Paul R. Dupee, Haddeo Partners, London, England; David B. Fithian, the University of Chicago; Ethan A. Lerner, Massachusetts General Hospital; Edward P. Owens, Wellington Management Company; John W. Rowe, Columbia University; and William T. Speck, New York, N.Y.

Senior Scientist Rudolf Oldenbourg was named director of the MBL's Cellular Dynamics Program.

Senior Scientist Anne Giblin was named a fellow of the American Association for the Advancement of Science.

Edward Leadbetter (emeritus MBL Society member; former course director, Microbial Diversity) received the 2014 D.C. White Research and Mentoring Award from the American Society for Microbiology.

John Hobbie, Ecosystems Center Distinguished Scientist, co-authored Alaska's Changing Arctic: Ecological Consequences for Tundra, Streams, and Lakes, a synthesis of findings from the Arctic Long Term Ecological Research project, a program of the MBL Ecosystems Center. •

Gut of Water



From sharks to clams, sea creatures rule the roost in the MBL's Marine Resources Center. They draw scores of scientists to the MBL every year who appreciate the unique characteristics that make marine organisms excellent models for biological and biomedical research. But one freshwater fish has claimed a place of honor at the MBL: the zebrafish. This small, robust vertebrate even has its own dedicated facility in Rowe Laboratory.

The zebrafish (Danio rerio) is exceptionally valuable to research scientists for several reasons. One is its genome, which is 70 percent identical to the human genome and is fully sequenced, well annotated (biologically interpreted), and easy to manipulate with genetic and pharmacologic techniques. Another is its reproductive cycle: Zebrafish eggs are fertilized and develop outside of the mother, a process that can be replicated in a laboratory dish. Zebrafish embryos are also optically transparent, so high-level microscopy tools can be used to illuminate their early development.

"All of these advantages allow you to create, in the zebrafish, models of many diseases that affect early human development, including congenital heart disease and disorders of the brain, blood, peripheral nervous system, kidney and pancreas," says Jonathan Gitlin, MBL's deputy director of Research and Programs.

COOL TOOL: ZEBRAFISH





Unlike many neural disorders, scientists know a great deal about the retina and retinal diseases due in part to zebrafish research pioneered by John Dowling of Harvard University. Dowling, a former MBL visiting scientist, trustee, and president emeritus of the MBL Corporation, founded the MBL Zebrafish Development and Genetics course. The faculty in this course rely upon the MBL's Zebrafish Facility to



maintain various colonies of the fish for specific studies, as do many other MBL scientists, including those interested in the development of vertebrate species.

On top of all these advantages, zebrafish are easy and cheap to maintain. "The cost is easily a twentieth of what it costs to maintain mice," Gitlin says. Freshwater or not, Danio rerio has earned a place to stay at the MBL. • — DK

SCIENTIST'S EYE VIEW



Mitchell Sogin joined the MBL faculty in 1989 and founded the Josephine Bay Paul Center for Comparative Molecular Biology and Evolution in 1996. Over its short history, the Bay Paul Center has become a focal point for collaborative research between molecular biologists, parasitologists, ecologists, and other colleagues from the MBL's visiting and resident communities. Sogin currently holds the rank of Distinguished Scientist at the MBL and the appointment of Professor (MBL) in the Department of Molecular Biology, Cell Biology and Biochemistry at Brown University. Sogin received his B.S. in Chemistry and Microbiology and his Ph.D. in Microbiology and Molecular Biology from the University of Illinois. In 1976, he joined the faculty of National Jewish Hospital and attained the rank of Associate Professor in the Microbiology Department of the University of Colorado Health Sciences Center. Sogin is a fellow of the American Association for the Advancement of Science. the American Academy of Arts and Sciences, the American Academy of Microbiology and a Miller Professor at the University of California, Berkeley. He was the recipient of the Stoll Stunkard Award from the American Society for Microbiology and the Roger Porter Award from the American Society for Microbiology.

A Universe of Microbiomes

By Mitchell Sogin

Astronomers like to throw out big numbers—400 billion stars in the Milky Way, giant elliptical galaxies with 100 trillion stars, 170 billion observable galaxies—for a grand total of at least 10^{24} or a septillion stars. Yet the number of microbes on Earth eclipses the number of stars by at least one million fold. My favorite estimates of microbial numbers include 10²⁴ microbes that live in association with Earth's 7.1 billion people and 10^{29} microbes that live in the oceans—Would that be a million septillion cells? Why so many? How do they influence our environment? What do they contribute to human health and well-being?

While biomedical scientists leveraged advances in DNA and RNA sequencing to understand how cells orchestrate gene expression and to map each of the three billion letters in the human genome, the microbiologists developed genomic strategies that enable molecular inventories of microbial communities containing thousands of different kinds of microscopic organisms. Initial efforts focused on extreme environments seemingly hostile to all life forms. Studies of hydrothermal vents and terrestrial hot springs encountered microbes capable of growth at 122 degrees C. Discoveries of uncharted diversity in oceans and soils provided astonishing descriptions of metabolic diversity. Recent investments by the National Institutes of Health have revealed unanticipated human microbiome diversity that varies between individuals because of their diet, their age, their state of well-being or a host of other epigenetic factors.

At first blush, investigating the microbiomes of humans, soils, oceans, and marine animals seem like disconnected efforts. Yet they address the same questions in systems made up of an incredible number of moving parts. Microbial ecologists seek to understand how single-cell factories orchestrate all of the major biogeochemical transformations that make Earth habitable, while biomedical scientists explore how the human microbiome influences our nutrition, our physiology, and how beneficial microbes protect us against pathogenic life forms. Both environmental and medical microbiology seek to understand the dynamic response of complex microbial communities to shifts in the environment caused by stressors. For humans, the stressors include unhealthy diets, drugs we ingest, and exposure to new microbial populations. (Having recently returned from Nicaragua, I have first-hand experience with stressors to my gut microbiome.) In a similar way, release of nutrients, sewage, and other toxicants affects the microbiomes of marine organisms and accelerates the decline and loss of animal populations in the oceans.

Early MBL investigators came to Woods Hole to study the rich biodiversity of marine animals off the coast of Cape Cod. Today, we focus efforts on coastal ecology and water quality to understand how stressors threaten long-term survival of our ecosystem. Human microbiome initiatives at the MBL in collaboration with the University of Chicago and studies of marine animal microbiomes address related questions. Just as shifts in human microbiome populations represent responses to stressors, we hypothesize that stressor-induced shifts in the microbiomes of marine animals will occur before we can even detect disease and potential loss of biodiversity in the oceans. This convergence brings us full circle to the goals and aspirations of nineteenth-century science at the MBL

The Finest of Limbs on the Tree of Life When Charles Darwin published On the Origin of Species in 1859 and proposed that all life forms evolved from a common ancestor, he popularized the concept of an evolutionary tree—a branching diagram that visualizes relationships between species. The sixth edition of Darwin's seminal book, a copy of which is in the MBL Archives, contains the simple, hand-drawn diagram partly reproduced on this page. 3

Oligotyping is a computational method for investigating diversity, at an extremely precise level, among closely related organisms using subtle variations in their 16S ribosomal RNA genes. This dendrogram (tree diagram) shows oligotypes within the genus Blautia, a common gut bacterium that is important for nutrient assimilation, and the oligotypes' host occurrence patterns. From Eren AM et al (2014) A single genus in the gut microbiome reflects host preference and specificity. ISME Journal, doi: 10.1038/ismej.2014.97.

COW

TREASURES FROM THE MBLWHOI LIBRARY ARCHIVES

The MBL's copy was originally owned by Alpheus Hyatt, first president of the MBL Corporation, who received it from Darwin. (Darwin forgot to autograph the book, so he later sent his signature to Hyatt, who pasted it on the inside front cover.)

Nearly 150 years later, advances in genomics and computation have vastly improved our ability to make subtle distinctions between living organisms, especially among the microbes that populate every ecological niche on Earth, including our bodies. MBL Assistant Research Scientist A. Murat Eren's tree, at left, uses a novel technique he developed, called oligotyping, to differentiate among hundreds of nearly identical strains within a single genus of bacteria. • ---LH

The diagram in the background, the only illustration to Darwin's original text, represents the divergence of species. From Darwin, Charles, 1872. On the Origin of Species By Means of Natural Selection. 6th ed. London: John Murray.



Biological Discovery in Woods Hole



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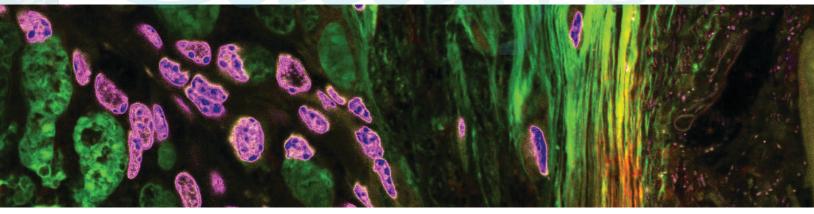
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IN THE NEXT MBL CATALYST



The Convening Power of MBL Imaging

Imaging is seeing, and now is a thrilling time for scientists who are seeing life in much greater detail than was previously thought possible. A crucial component of the MBL's culture of discovery is the ongoing collaboration between scientists exploring new ground, and teams developing microscopes, cameras and image analysis tools that in some cases have never been built before. The MBL's affiliation with the University of Chicago, along with Argonne National Laboratory, brings additional strengths in imaging and computational biology into the picture. The next issue of *MBL Catalyst* explores the MBL's role as an international destination where biologists and instrument developers intermingle, experiment and drive innovation in biological and environmental imaging.