MBL

Catalyst

JANUARY

eptember is a productive season on Cape Cod in many ways. The cranberries are ripe, ready for harvest mid-month. Clams, haddock, and sea scallops are plentiful; the oysters are plump. The schools reopen and fill with students.

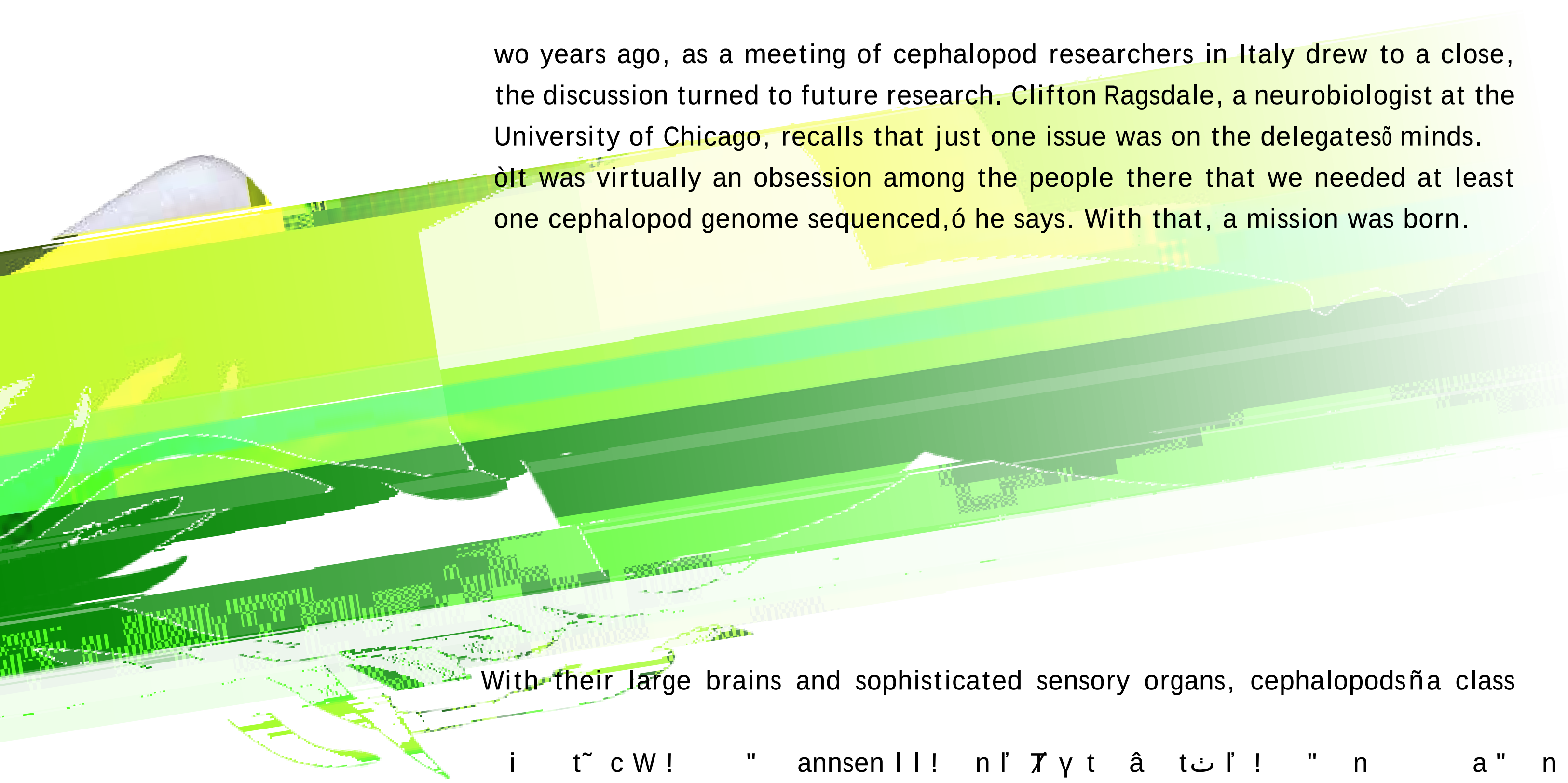
In Woods Hole, amid other comings and goings, the "acorn worm group" reunites at the MBL. Arriving from several places—often Harvard, Stanford, Caltech, and Georgetown—these scientists pursue different research questions, yet congenially share lab space and resources. What draws them to the MBL is the spawning season of the acorn worm.

Throughout the month, mature acorn worms burrow into the sand near Woods Hole, usually in sheltered bays and other brackish sites. "We dig them up, bring them back to the lab, separate the males and females, and keep them alive in seawater," says Jessica Gray of Harvard Medical School. Through time-tested methods, many developed at the MBL, the organisms are stimulated to release their copious eggs or sperm. The scientists can then fertilize the eggs *in vitro* and observe the cascade of changes as the embryo develops.

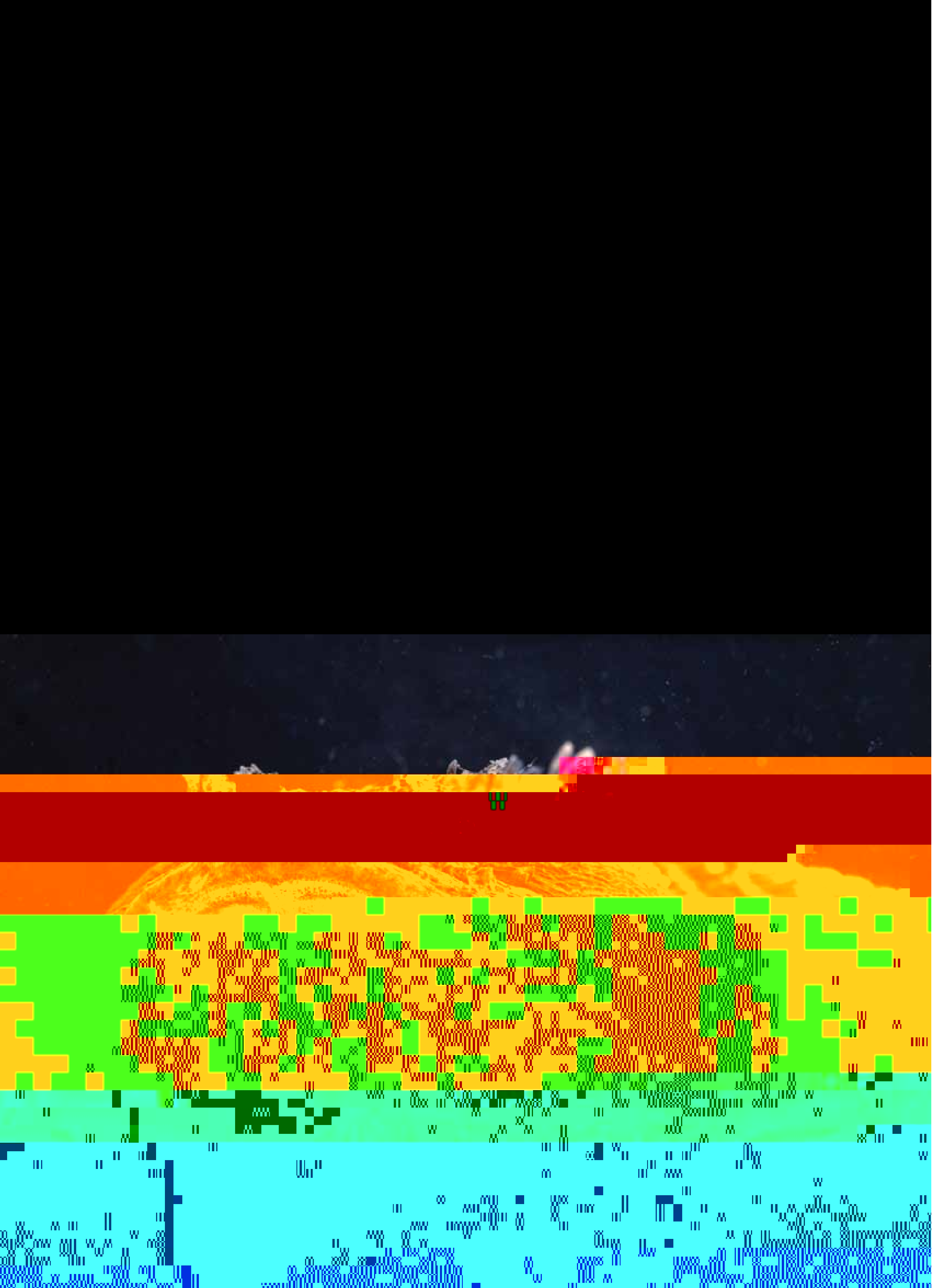
These scientists are interested in the acorn worm not for its own sake,

Genome

wo years ago, as a meeting of cephalopod researchers in Italy drew to a close, the discussion turned to future research. Clifton Ragsdale, a neurobiologist at the University of Chicago, recalls that just one issue was on the delegatesô minds. òIt was virtually an obsession among the people there that we needed at least one cephalopod genome sequenced,ó he says. With that, a mission was born.



With their large brains and sophisticated sensory organs, cephalopodsña class



With their fleshy lips and flat heads, toadfish won't win any marine beauty contests. But what they lack in good looks, they make up for in hardiness. "You can't kill them," Mensinger says. Toadfish hold another advantage over other fish: Their sensory nerves are protected by only the thinnest bit of skull. By removing this plate of bone, researchers can directly access the fish's neural wiring to figure out what makes them tick.

Toadfish have been research subjects at MBL since the laboratory first opened in 1888, when zoologist Cornelia Clapp began studying their development for her doctoral dissertation at the University of Chicago. In the 1960s, MBL researchers prized the animals for research on insulin. In humans, insulin-secreting cells are scattered in islets throughout the pancreas. In the toadfish, however, these cells are largely found within a single islet, making them easy to locate, isolate, and study. This research revealed new ways to stimulate insulin secretion.

Stephen Highstein, now a senior scientist at MBL, began working with the toadfish in the 1970s. He is interested in the vestibular system in the inner ear, which controls equilibrium and balance. "It's a very convenient experimental animal," Highstein says. Because their heads are so broad, "the inner ear organ is quite a distance from the brain, which gives you a long length of nerve to work with." Highstein isn't put off by the fish's appearance. "I think they're handsome," he says.

Mensinger joined Highstein's lab in the 1990s as a postdoctoral associate, and that's when he began working with toadfish. Together they fitted toadfish with electrodes to record their nerve impulses and sent them into space as part of NASA's 1998 NeuroLab shuttle mission. "We wondered how the ear would respond to the lack of normal gravitational stimulus," Highstein says.

How did the space-traveling fish do? In the microgravity of space, the fish's inner ear "turned up" its sensitivity to gravitational stimuli, looking for the missing signal. "This seems to be a general principle in biology," Highstein says. "In Parkinson's syndrome, for example, when the brain decreases its production of dopamine, there is a genetic up-regulation of some dopamine receptors, looking for the missing dopamine." In space, "the perverted inner-ear signal regarding gravity conflicts with other vestibular and visual signals, creating a mismatch in the brain areas responsible for body and head orientation," he says. "We think this mismatch causes motion sickness, or space adaptation syndrome."

Highstein, an MD/PhD, continues to value the fish for basic biomedical research. "A few times in my research career, I've been lucky enough to discover something in the toadfish that, because of my clinical background, I recognized its relationship to human malfunctions of the inner ear," he says.

Mensinger today works in the field of neuroethology, which explores the neural basis of natural animal behaviors. Research in this field has typically been carried out on a single sensory system—hearing, vision, or smell. However, "when fish are out there, they're getting all this sensory information from multiple sources," Mensinger says. He wonders how they absorb and process this wealth of input.

Male toadfish, for example, attract females by producing a long, low sound uncannily like a fog horn. How the fish hear this mournful call is something of a mystery. The hearing organ in fish is internal and [illegible]

Not unique at all, it turns out. "Regeneration is broadly distributed," says Sánchez Alvarado, who today co-directs the Embryology course and is a Howard Hughes Medical Institute investigator at the Stowers Institute for Medical Research. "There are species in every phyla that will do some truly remarkable regenerative feats."

Often considered to be poor regenerators, even mammals can display a robust ability to regenerate. Last year, researchers reported that at least two species of African spiny mice can rapidly replace large patches of skin and hair. But there's little rhyme or reason to the pattern of distribution. Two nearly identical species that inhabit the same environment may not possess the same regenerative capabilities.

When Sánchez Alvarado entered the field, regeneration was not a hot research topic. Many scientists dismissed it as a curiosity, a capacity only a few organisms possess. Others argued that the secrets of regeneration could be revealed simply by studying tissue formation during embryonic development. Sánchez Alvarado didn't buy it. "In an adult animal, [to regenerate], you're asking tissues that are already committed to a particular fate to all of a sudden make a new tissue and then functionally integrate it into the existing tissue," he says. "That never happens in embryogenesis."

One day, while wandering the stacks of the MBL's library, Sánchez Alvarado stumbled across a 1901 book on regeneration by Thomas Hunt Morgan, a longtime MBL visiting scientist, Nobel Prize laureate, and pioneer of genetics. Sánchez Alvarado spent much of that night and the next morning reading. "I couldn't put it down," he says. In the pages of that book he found his model organism: planaria, a tiny freshwater flatworm

The Collector's Net

Which species are most popular, in terms of researchers requesting their suppl from the Marine Resources Department (MRD)?

DR The priority species change with time. When I worked at the MRD in the 1980s, everybody wanted the surf clam ( ). Research on cell division using eggs of these clams was just going gangbusters, and we couldn't collect enough. But that has gone through its gold-rush phase and settled to a low boil. Squid, horseshoe crabs, many of the organisms we collect have been significantly important at different times. Right now, the starlet sea anemone ( ) is really big and the demand for skate embryos ( ) exceeds our ability to supply them. Although we usually just collect wild animals and ship them to researchers, we have started breeding programs for the sea anemone and the skate to ramp up for demand. Both are used for research on embryological development and the evolutionary history of development. Sea urchins, another useful organism for studies of development, are also in high demand.

Ho do ou collect the organisms?

DR We drag a net from our collecting vessel, the , for some species; others are collected by hand. We dive for organisms that are below the surface of the ocean floor or are too delicate to collect by other means. Surf clams and parchment worms ( ) have to be dug by hand, for example.

The MBL can collect an unusuall rich diversit of species ithin a 75-mile radius of Woods Hole. Wh is that?

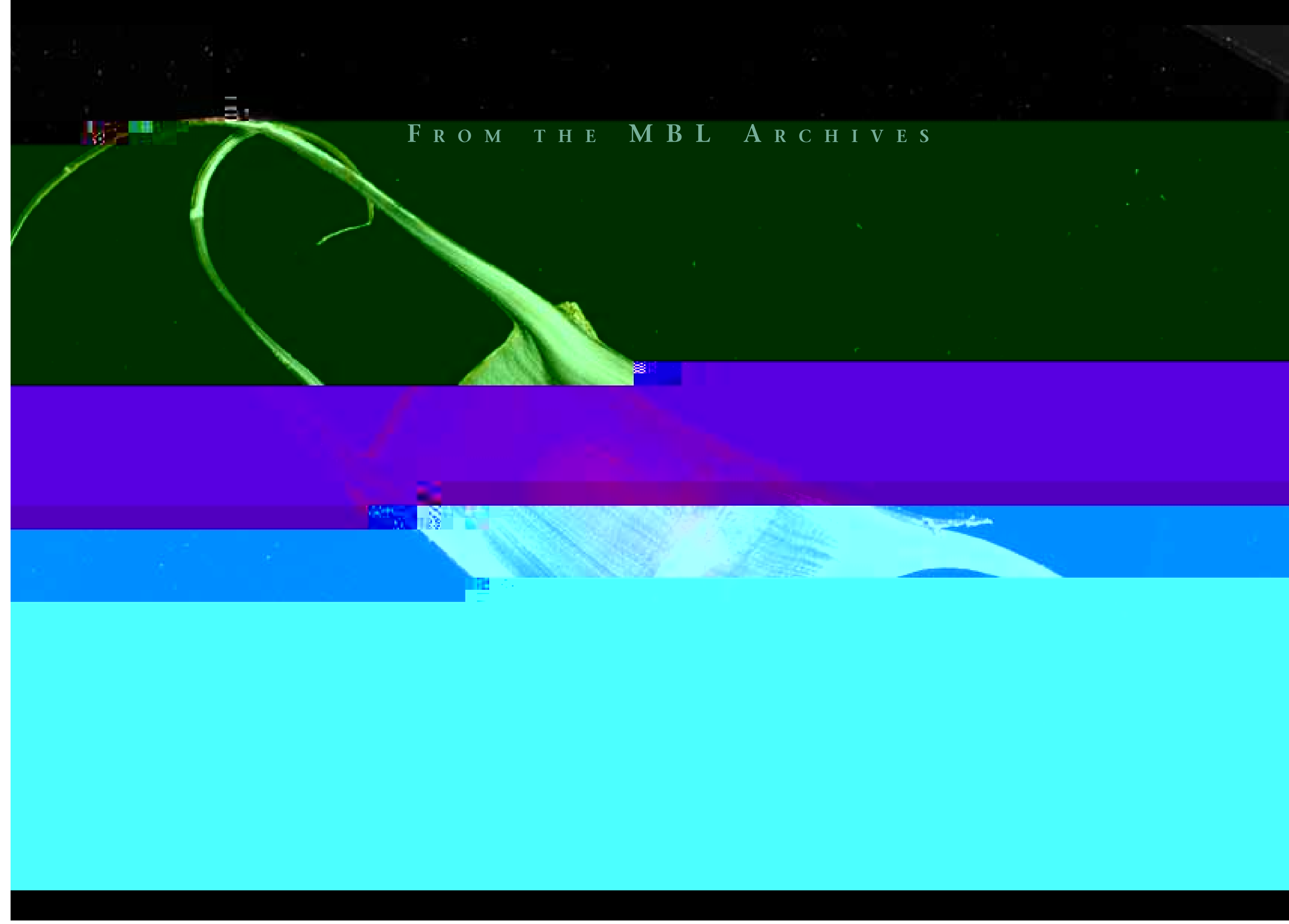
DR The species assemblages you find in the waters north of Cape Cod are very different from those found in the south. The purple-spined sea urchin (A), for example, is found in Woods Hole and south to the Gulf of Mexico, while the green sea urchin ( ) is found in Cape Cod Bay and north into the Arctic. We collect the purple urchin when they are gravid [have eggs] from June through August, and we know how to keep them gravid at the MRD until November. Then the eggs of the green sea urchin come into season from December through February. If we keep them in cooler water at the MRD, rather than letting them warm up in the spring, they will stay gravid through April. That gives us almost ten months of urchin egg availability. Other organisms come into season at other times.

Ho do ou kno here to look for a particular organism?

DR It's an oral tradition

Ecosystems Center senior scholar **B ce Pe e** was awarded the A.C. Redfield Award for Career Achievements in Aquatic Science from the Association for the Sciences of Limnology and Oceanography.

Ecosystems Center senior research scientist **I a Va e a** receive s



A Chaos of Delight

The great Danish physiologist, Nobel laureate, and MBL visiting scientist August Krogh, whose work elucidated the inner workings of capillary flow and function, noted that for every essential question in biology there is an organism ideally designed to provide answers. The truth to this idea lies in the principle of evolutionary adaptation and the "endless forms most beautiful" that have helped scientists unravel many fundamental biological problems. The diversity

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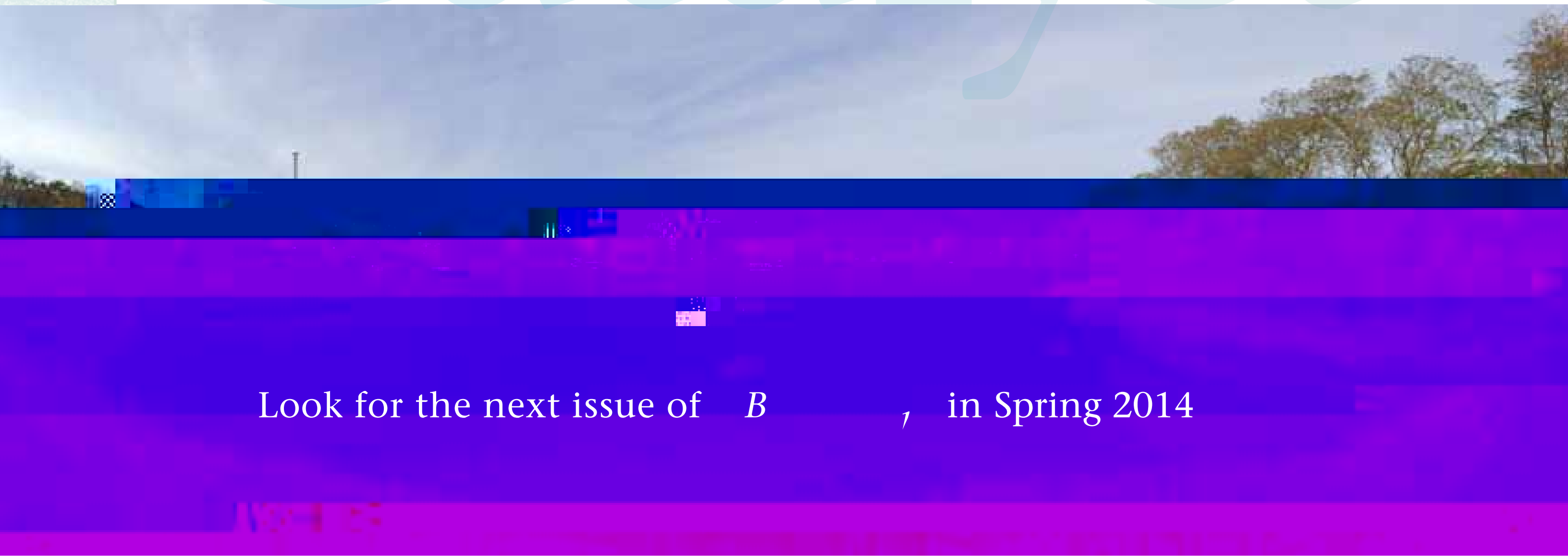

Look for the next issue of *B* , in Spring 2014