MBL CEPHALOPOD RESEARCH

Octopus, squid, and cuttlefish never cease to fascinate. And no wonder – they are large-brained and perceptive, tentacled and skillful, brilliantly colorful and quick. Famous for engaging in elaborate decision-making and problem-solving behaviors, these animals can instantly camouflage in any environment and achieve dexterous escapes from predators or tanks. All told, these spineless marine creatures, called cephalopods, display far more advanced behavior than all other invertebrates on Earth.

CEPHALOPODS AT THE MBL

The Marine Biological Laboratory (MBL) has a long, deep history of studying cephalopod biology, yielding many significant discoveries and even a Nobel Prize (see sidebar).

Building on this expertise, the MBL launched a groundbreaking effort in 2017 to culture cephalopods in the laboratory—which is notoriously difficult—so they can be available to researchers at all life stages at any time of year. As part of the MBL's New Research Organisms Initiative, the first genetically tractable squid species was recently developed at MBL, meaning scientists can manipulate its genes and study the effects over multiple generations. This provides essential information on gene function relative to the animals' anatomy, physiology, advanced behavior, and evolution.

MBL's expertise in cephalopod camouflage attracts collaborators in engineering, materials science, and art

Elaine L. Bearer

WHY STUDY SUCH STRANGE ANIMALS, SO DIFFERENT FROM HUMANS?

The MBL is committed to comparative biology: investigating a wide range of species to compare how they carry out fundamental life processes, such as reproduction, aging, sensory processing, or regeneration.

Grounded in comparative genetics, this approach opens a vast landscape for discovery. With potential applications in numerous fields from medicine to artificial intelligence, comparative biology is also a framework for understanding the evolution of species, from microbes to humans.

Cephalopods open up unique avenues for study and application. Just a few examples:

- MBL's expertise in cephalopod camouflage attracts collaborators in engineering, materials science, and art, with applications such as programmable, 3D materials inspired by octopus skin.
- MBL scientists are learning how to manipulate the prolific RNA editing they discovered in the squid nervous system. If applied in humans, targeted RNA editing could provide safe therapies for genetic diseases as well as for nonheritable conditions, such as inflammation and pain.
- Cephalopods have evolved a sophisticated nervous system from a different brain architecture than vertebrates, offering an alternative model for artificial intelligence design.
- Octopuses have eight, flexible, sucker-lined arms that can be operated independently, which is of interest to robotics design.
- Cephalopods have evolved unique proteins, including some that produce iridescence and others that make their tough but flexible sucker rings. These proteins are being studied for biomaterial applications.
- Some squid live symbiotically with glowing marine bacteria, providing an excellent model for studying the beneficial co-evolution and interactions of microbes and animals.

CEPHALOPOD FACTS

Cephalopods have evolved many striking traits since diverging from the human lineage 500 million years ago, including:

- the largest brain among the invertebrates
- keen senses and cognitive ability
- large, image-forming eyes
- skin that instantly changes color, pattern, and texture for camouflage and communication
- short-term and long-term memory; ability to learn
- exceptional navigation and spatial memory skills
- fast, jet-propulsion swimming
- distributed nervous system radiating through sucker-lined arms or tentacles
- high rate of precision editing of their own RNA, enabling them to fine-tune proteins that control electrical impulses in the nervous system

HIGHLIGHTS FROM A CENTURY OF MBL CEPHALOPOD RESEARCH

This research was conducted in the MBL Whitman Center by visiting investigators, unless indicated otherwise.

THE SQUID GIANT AXON AND A NOBEL PRIZE

1910s to 1930s: Leonard Williams discovers giant nerve cells, sometimes visible to the naked eye, in the local Woods Hole squid , Doryteuthis pealeii. These "giant axons" turn out to be excellent preparations for studying how nerve cells work.

Late 1930s: Using the squid giant axon, scientists at MBL including Alan Hodgkin and Andrew Huxley record the electrical impulse (the action potential) from inside the nerve cell.

1940s to 1950s: Back in England, Hodgkin and Huxley mathematically describe how the action potential is generated. They will receive the 1963 Nobel Prize in Physiology or Medicine for this work, which lays the foundation for understanding electrical activity in the nervous system.

1960s to 1990s: The MBL is "squid central" as researchers convene to describe fundamental mechanisms of neurotransmission, including ion transport across the axonal membrane and properties of the squid giant synapse.

DISCOVERY OF KINESIN

1980s: Scott Brady and Ray Lasek see tiny objects zipping around inside the squid giant axon for the first time, using new, video-enhanced microscopy developed by Nina and Robert Allen and Shinya Inoué. Inspired by these videos, Ron Vale and colleagues discover the motor protein kinesin in squid axoplasm. Kinesins are essential for critical cell processes, such as cell division and molecular transport.

1990S TO THE PRESENT

MBL Senior Scientist Roger Hanlon establishes octopus and cuttlefish as research organisms for quantifying the amazing camouflage abilities of cephalopods.

Scott Brady and Rodolfo Llinás establish the squid as a research organism for studying Alzheimer's disease and other neurodegenerative disorders.

2015: Joshua Rosenthal and colleagues discover extensive recoding of genetic information in the squid nervous system, which the animal accomplishes by precision RNA editing. This research is under development for potential biomedical applications. Rosenthal's team later confirms extensive recoding of genetic information within mRNA across squid, octopus and cuttlefish, which influences the rate at which genes can evolve.

2015: Caroline Albertin (then at the University of Chicago) and colleagues publish the first cephalopod genome (the California Two-Spot Octopus). Albertin later collaborates on the first description of the giant squid genome (2020). Ongoing efforts to generate and characterize cephalopod genomes, including for Doryteuthis pealeii, are essential for establishing them as new research organisms.

The MBL Cephalopod Program is founded in 2017 to develop cephalopod species as genetically tractable experimental organisms. Bret Grasse joins the MBL to lead the cephalopod culturing and breeding effort. To date, Grasse's team has successfully cultured seven distinct cephalopod species through multiple generations, including the pygmy zebra octopus, which was a world first. They have also raised the first gene-edited cephalopods to reproductive adulthood.

In 2019, the Hanlon lab discovered the protein reflectin in the pigment-containing organs in cephalopod skin, demonstrating a unique combination of dynamic pigmentary and structural coloration.

2020: Joshua Rosenthal and colleagues discover in squid that genetic information can be finely tuned between different parts of a neuron.

2020: MBL scientists create the first gene knockout in a cephalopod (Doryteuthis pealeii). The team is led by Joshua Rosenthal and includes Caroline Albertin and Whitman scientist Karen Crawford.

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