ABRAMS IMAGE
NEW YORK

THE
CURIOUS,
EXCITING,
AND
SLIGHTLY
DISTURBING
SCIENCE
OF
SQUID

KRAKEN

BY
WENDY WILLIAMS

CHAPTER SEVEN

DIAPHANOUS AND DELICATE

The biology of the mind will be to the twenty-first century what the biology of the gene was to the twentieth century.

—ERIC KANDEL

For more than a century, the summertime village of Woods Hole, Massachusetts, has been a world-renowned center of intellectual excitement as well as a fashionable watering hole for the scientific elite. Some of the world's best biologists, including a liberal salting of Nobel Prize winners, have come to sit on the beach and play tennis, to work in the research facilities of the Marine Biological Laboratory, to give and attend lectures, and to exchange ideas. The village's sidewalks overflow with scientists, students, and tourists. There's rarely a place to park your car, even on Albatross Street, and you can count on the Water Street drawbridge, which lets boats leave their Eel Pond moorings for destinations like Martha's Vineyard or Nantucket, being raised and lowered many times throughout the day.

But in the winter, the village can be awfully forlorn. Water Street has a distinctly dowdy look, as though it's down on its luck. Slate-gray skies hang heavy over the silent, institutional buildings. The renowned science library, where you can hold in your own hands scientific journals from the mid-1800s, is almost deserted. If you walk down the main street on the wrong November day, you could easily think that the village is on the skids.

But if you're there on the right November day, there's an intellectual Indian summer. That's when the neurosurgeons arrive, ready to bone up on the latest discoveries in their field. Among the many skills they learn is how to dissect a live axon from a decapitated squid. Or, at least, they *try* to learn that skill.

On the particular day I went to observe, it was chilly and wet. Sheets of rain flooded the streets. Farther north in New England,

it was snowing. The first crew of confident neurosurgeons made their way, heads down against the downpour, to the research building where so many Nobel scientists have worked and where squid and other marine life-forms have been studied for nearly a century.

Course teacher Bruce Andersen, a neurosurgeon from Idaho, picked up an eight-inch squid, a common *Loligo pealei*, in one hand. He held a pair of scissors in the other. The animal's chromatophores were showing. It flushed a deep, rich red.

Andersen held on to the squid body. The animal's one head, eight arms, and two tentacles writhed.

"We'll start with the gross dissection," he said.

Then he snipped off the head.

A deep, anguished groan came from the thirty mostly male surgery residents.

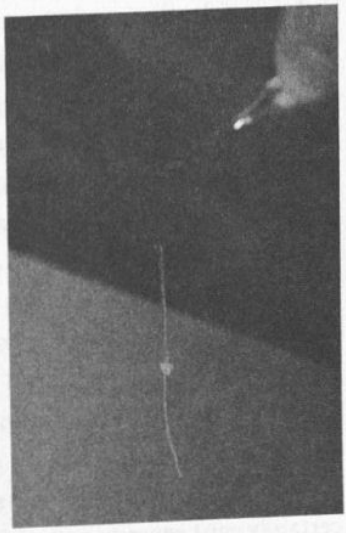
"Neurosurgeons are surprisingly squeamish," Andersen told me later.

"And it's all for the good of science," he told them.

"This is all the guts 'n' stuff," he said as he cleaned the body out.

Next, he demonstrated how to lay out the squid's body, find the giant axon that allowed the animal to swim, and gently remove it.

Andersen gave each student a squid and ordered the students to begin their own fine dissection—the removal of the squid axon from the animal's flesh. Properly handled, an axon can continue to function for hours after the animal is dead, even when completely removed from the specimen. The point of the exercise was to remove the axon without harming it.



Loligo's giant axon

This turned out to be more difficult than the neurosurgeons expected. *Loligo*'s axon is large and easily visible, but it's also diaphanous, like a beautiful bridal veil or a thin sheet of water cascading over rocks. It's as delicate as gossamer and as easily destroyed as the filament spun by a small spider.

Nick the axon cell membrane and you're toast.

All the surgeons tried. All failed.

Their axons died on the operating table.

"You'll all have to go talk to the families now," Andersen instructed. "Luckily, few squid have good lawyers."

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It may seem strange that medical doctors practice their neuroscience skills on squid, but it turns out that the squid's neuron with its axon, so diaphanous and delicate, behaves quite like a neuron in our own brains. These nerve cells, or neurons, are "the workhorse of the nervous system," in the words of one particularly articulate neuroscientist, Robert Sapolsky. Without the neuron, we wouldn't function. It allows us to move our muscles, to meditate on the meaning of life, to read books and talk about what we've read. Yet in humans, neurons are ineffably tiny. "Few things in clinical neurosurgery approach the scale and delicacy of dissecting a 300-micron human axon," Andersen said.

We humans have very roughly 100 billion such cells. And as unlovely and nonmammalian as *Dosidicus* and *Architeuthis* and other squid may be, we share this important cell with them. Because of this, scientists suspect that the neuron in one form or another has been around on our planet for quite a while, possibly since the days of *urbilateria*.

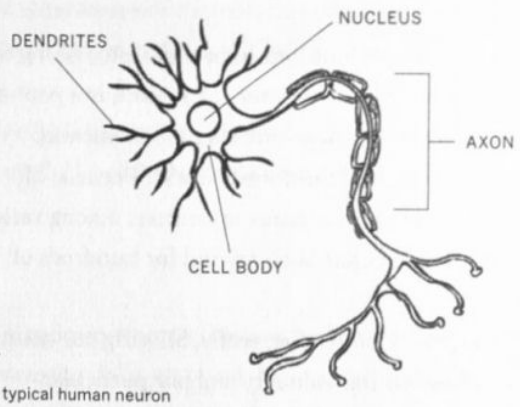
For us, neurons are not easy to come by. In general, we get all the neurons we'll ever have soon after birth, although under the right circumstances the human brain may be able to grow a few absolutely spanking new neurons in a few locations in the brain during adulthood. This process is called "neurogenesis," and it remains poorly understood and somewhat controversial. We certainly can't generate new neurons on a large scale, though.

Human neurogenesis pales next to the ability of the cephalopod to continue to create neurons throughout much of its life. In many cephalopod species, if an arm or tentacle is lost, the animal is able to grow a new one. No one understands exactly how this happens, but scientists consider it a fertile avenue for future study.

But there is one overarching and somewhat astonishing truth, a marvelous fact of evolutionary history: A neuron is a neuron is a neuron. The neuron is a near-universal phenomenon, existing throughout much of the animal world. Because life is flexible, there are some differences in neurons among various species, but the basic idea has been around for hundreds of millions of years.

I find this thrilling. Comforting, really. Sharing our neuron—the cell that gives us our individuality and our particular personality—with so many other species makes our planet a little less lonely. The foundation of our ability to think is the same foundation that allows the cuttlefish to change color and shape instantly, or the Humboldt to swim in the ocean or fly through the air at super-high speeds. (Yes, Humboldt and some other squid species can "fly" by shooting out of the water at very high speeds, although they don't flap their fins the way birds flap their wings.) The neuron allows the giant squid to live in the deepest parts of our ocean and the colossal squid to hunt by using its "headlights." It allows birds to navigate our skies. There were neurons in dinosaurs that allowed them to eat, and neurons in the first tiny proto-mammals that allowed them to survive the destruction that killed the dinosaurs and eventually to become—us. As evolution continues and we disappear from the universe, as we certainly will sooner or later, the neuron will probably go on, blossoming in some other intelligent being's brain and, hopefully, creating a life-form that finally figures out how to stop fighting and just enjoy being alive.

The neuron is the main cell in the cephalopod's brain, and in my brain, and in your brain. As you read these words, your neurons are hard at work, assembling the black ink on the page into very large concepts, like the universality of life.



A typical human neuron

The neuron has three basic parts that you need to know about: the cell body, the dendrites, and the axon.

The first is the cell body, a kind of a torso, in a sense. Like your own torso, the cell body contains most of the parts necessary to keep the cell alive. The body of a neuron, an extremely busy place, is like the manufacturing hub of a large city. The nucleus, where most of the neuron's DNA resides, performs a kind of executive function, directing the building of all kinds of molecules the neuron needs in order to thrive and help you accomplish goals like moving muscles, reading a book, and thinking about science.

The second major part of a neuron is the network of dendrites leading into the cell body. Dendrites extend from the cell body like little hairs and are there to absorb information from the world outside the neuron and take it into the cell body for consideration. Dendrites are roughly the equivalent of e-mail in-boxes. Some scientists call dendrites the "antenna systems" of the neuron, because they absorb signals and then send those signals to the cell body. The absorbed information might come from another neuron, or it might come from the world outside. There are special neurons, called "sensory neurons," with unique

types of dendrites that allow you to see, to hear, to smell, to touch, and to taste. The number of sensory neurons differs greatly from species to species. A dog does not see the array of colors that we see, but has many, many more neurons and dendrites devoted to smell than we humans do. We are limited to roughly 5 million such smell receptors, while some dogs may have more than 200 million. While the dog misses the glorious world of color that we see, we enjoy only a fraction of the odiferous universe that the dog gets high on when it rides in the back of the car. There are even sometimes immense differences in breeds. German shepherds have twice as many neurons devoted to smell than do dachshunds.

Sometimes the dendrites leading into a nonsensory neuron are so plentiful that, under a microscope, they look very much like a richly branched coral, or perhaps like a piece of finely tatted lace. This is a good thing. In the case of dendrites, complexity is what you want. The more dendrites a neuron has, the better connected that neuron is with other neurons in the brain. Dendrites are constantly growing and changing. The more reading, thinking, information gathering, and just plain experiencing a person enjoys, the richer his or her dendritic connections.

Human infants are born with some, but not a lot, of dendrites. There is, however, plenty of space for dendrites to develop, and if the infancy is normal, that's exactly what happens. The process of growing up is the process of developing more and more dendrites. This is why kids shouldn't spend all their time playing with their electronic toys: They're missing out on building all the other dendritic connections they will need to live a full life as an adult. Experience-deprived kids have many fewer dendrites (and the consequent interconnections with other neurons) than do humans who were fortunate enough to enjoy a highly enriched childhood.

Nurture—experience—intertwines with nature. As important as our DNA is, our lives are not genetically predetermined, because the genes we are born with interact constantly with the world we live in.

The third main part of the neuron is the axon, which performs its main function after the neuron's cell body assembles all the information brought in by the dendrites; if conditions are correct, the information is sent down the axon to another cell. The axon is huge compared to the rest of the neuron. It's often more than 99 percent of the whole cell. Each axon is essential to your body because you don't constantly grow new ones. Moreover, many neurons have only one axon, only one pathway through which they can send information or instructions out of the cell. And that's pretty much it. For life. If you damage that axon, forget about the cell. Eventually the axon will die back all the way to the cell body, and the cell itself will die. Nerve injuries are actually destroyed axons, and researchers have learned that the cause of many neurological diseases is a slowly disintegrating axon.

Neural axons vary greatly in length. The axon may carry information to other neurons located right next door in the brain. In that case, the axon may be very short, perhaps only a little more than a hair's width. Or it may send instructions, like "run away from the crab that just bit you," to muscles all the way down your torso and then connect with other neurons in your spinal cord that pass the message on to your leg and, ultimately, to your toe.

Human axons like these may be several feet in length. A giraffe may have an axon that's as long as 15 feet, while the blue whale, currently the planet's largest animal, may have an axon as long as 60 feet. The blue whale's axon extends from its brain down much of the length of its body. The final result: the flexing of its tail muscles. It takes a blue whale a longer time to send a message to its tail than it takes your brain to send a message to your toe. But the time difference is not one that we'd notice easily, since responses to our environmental surroundings happen, often, much more quickly than we are able to consciously think about them. In other words, we are likely to have already run away from the crab by the time we get around to thinking, *Stupid crab!*

Just as all neural axons are not the same length, neither are they the same diameter. The thickness of an axon is species-dependent. Humans have axons that are too thin to see without a microscope. Instead, what we see are *bundles* of axons, what we commonly call "nerves." The nerve bundle that leads from our eye to our brain, called the optic nerve, has about one million axons. Neurosurgeons rarely operate on individual axons, but instead often work on these bundles when they try to repair nerves. Individual human axons are too small and too delicate to work with under normal circumstances.

But there is one very special group of animals that turns out to have a very thick axon: squid, including little *Loligo pealei*. This tiny animal, which Bruce Andersen held in his hand that rainy November afternoon, is only a few inches in length. Yet it possesses a "giant axon," that, if you look carefully, is visible to the naked human eye. Little *Loligo*'s giant axon is not particularly

A handful of little *Loligos*

long, but it is very thick. It's sometimes said to be "as thick as a pencil lead," but most specimens are not. However, many are about a thousand times thicker than a human axon.

Loligo's axon evolved in order to protect the animal from predators. Squid are among the fastest swimmers in the sea, and the purpose of this very thick axon—also possessed by *Dosidicus*—is to help the squid jet away from danger at lightning speed. Most of us cannot send messages to our arms and legs with anything like the speed of this little squid, although I did that day see Bruce Andersen, after several tries, catch a *Loligo* in a tank with his bare hands. His feat was quite impressive.

For obvious reasons, this thick axon is much easier to study than a human axon. If you are highly skilled—and even neurosurgeons with their super-steady hands need to practice this delicate task—you can remove this axon from the squid and insert tools in it to discover what's going on inside.

This is fortuitous. But what's equally as convenient is that these small animals are abundant. It's not so easy to find a giant squid, but at the right time of year—spring and summer around Woods Hole, as it happens—*Loligo pealei* are as thick as gnats. Traveling only a few miles away from home port, Cape Cod fishermen catch them by the boatload, either to sell to a fish market to be turned into calamari, to use as fish bait, or to send to a research lab for study.

CHAPTER EIGHT

SOLVING FRANKENSTEIN'S MYSTERY

It's the squid they really ought to give the Nobel Prize to. . . .

—ALAN HODGKIN, NOBEL LAUREATE

On the streets of Woods Hole, there's a fellowship of souls in the peaceful hour of darkness before dawn. "Mornin'" is the preferred greeting at this special hour, along with a polite but reserved acknowledging nod when two bodies pass each other. There's a sense of community. Most of the people up at this hour are finishing their caffeine and heading out on the water.

One promising August morning in 2009, squid lover Joe DeGiorgis, professor of neuroscience at Providence College and a Marine Biological Laboratory researcher who studies the inner workings of the squid axon, was carrying enough coffee and pastry to keep the crew of the fishing boat *Gemma* well buzzed for hours. Joe was looking forward to a fruitful trip. The *Gemma* looks quite like any of the Cape's fleet of commercial fishing trawlers, but it's actually the collecting boat for the Marine Biological Laboratory. For decades, the *Gemma* has gone out most summer mornings with the first raising of the Water Street drawbridge. The mission: collect enough squid, clams, sea urchins, monkfish, and whatever other marine animals are needed to fill the day's research needs of the institution's scientists.

For Joe, this particular morning was a kind of homecoming, since he'd started his career at MBL as a collecting diver whose job was to hunt for animals like the sea urchin and the common surf clam. Along with the cephalopods, these sea animals, like so many other sea species, have contributed greatly to medical research. Both the sea urchin and the surf clam are extremely practical as research specimens, since they are abundant and easy to harvest, and consequently, cheap.

Various sea species have specific qualities that make medical research easier. The eggs of sea urchins, for example are large and develop quickly. They're also transparent, so that, unlike in a hen's egg, for example, scientists can watch the process of the animal growing and developing inside the egg.

Victorian scientists used sea urchin eggs to learn about human fetal development. In 1899, MBL summer scientist Jacques Loeb made an important discovery: He could get unfertilized sea urchin eggs to divide and form new animals by putting the eggs in certain kinds of liquids. The ease of initiating the development process meant that researchers could—and did—make astounding progress in understanding this very early stage of the development of a living organism.

Surf clams, the diced-up bits of flesh you're probably eating when your dip your spoon into a bowl of clam chowder, have also contributed to the progress of human medicine. Surf clams are mollusks, like squid, but much less complicated. The surf clam's life consists mostly of hiding in its shell, buried deep in the sand, sucking water in and filtering out whatever nourishment is around.

While Joe was a diver, scientists were using surf clams and sea urchins to do basic research that ultimately ended up improving cancer treatments.

Almost all cells in the human body divide into two, then regrow. This is why skin heals, fingernails grow, and hair gets long. Growing new cells is an essential process: Out with the old, bring in the new. But the body usually controls that process very carefully. Under normal circumstances, the cell divides only after a certain time period.

Promiscuous activity resulting in lots of cell division is unwelcome. Cells are not supposed to keep dividing. Various types of cells in your body routinely divide at different rates, but most of the new cells are supposed to undergo a kind of rest period, before they wear out and are cast off. A cancer occurs when the cells continue to divide and divide, never taking time to relax and just smell the roses.

To better understand why some cells become cancerous, researchers need to better understand the basic biology of cells.

What makes normal cells divide in the first place? Without understanding the normal process, it's harder to control the abnormal process. Using some of the species of animals collected by Joe, researchers learned that two different complex molecules in a cell—called "cyclin" and "ubiquitin"—control the basic divide-then-rest routine.

Cyclin and ubiquitin are a yin-and-yang pair. They work as a duo, balancing each other out in a wonderful example of teamwork. Cyclin builds up over the life of a cell, then, when the correct time comes, the ubiquitin attacks the cyclin. It breaks up the complicated molecule so that when the cell divides, the new cells don't have as much. Then the cycle of buildup and breakdown begins anew in the just-divided cells.

Nature is often organized in this pleasantly logical way. The compound cyclin was discovered by MBL summer scientist Tim Hunt of Great Britain in 1982, while he was studying sea urchins. Hunt learned that the amount of cyclin in a cell increases gradually over the life of that cell. Finally, it reaches a peak. The peak is the signal for action. The cell divides. For finding this clue in the mystery of why cells divide, which provided a completely new strategy for treating cancer, Hunt and several colleagues won a Nobel Prize in 2001. Later, Joan Ruderman, one of the students who worked with Hunt in 1982, found that some breast cancer cells do indeed have too much cyclin, which could possibly initiate too much cell division.

The discovery of ubiquitin came around the same time. Ubiquitin is so named because it is ubiquitous—present, like cyclin, in nearly all animal cells, even in tiny algae. It is ubiquitin that destroys cyclin so that the new cells don't have too much. What goes up must come down. If the amount of cyclin were high in the new cells, the cells would keep dividing. Ubiquitin ensures that this doesn't occur by breaking apart the cyclin, so that the healthy, well-measured dividing of cell growth can begin again. The discovery of ubiquitin earned MBL summer researcher Avram Hershko (who, as a six-year-old, narrowly escaped an Auschwitz gas chamber) and several other colleagues the Nobel Prize in 2004.

One of the most marvelous things about cyclin and ubiquitin is that these molecules are present in almost all living cells—in plants, in yeasts, in most animals, and in humans. Across all these species, the compounds are similar enough that scientists believe they must have been present in very early life-forms. In scientific jargon, the genetic recipes for these molecules have been "conserved" throughout much of evolution.

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While Joe was diving for research purposes, he began to learn about the natural behavior of squid. He learned that *Loligo pealei* has elaborate courtship behaviors, and that when a male mates with a female, he sticks around afterward, trying to keep the other males away.

"It's like a bar scene, when a guy has one eye on his girlfriend and another on every other guy in the room," Joe explained.

When the first female of a shoal of squid lays her eggs, the second comes along and lays her eggs in the same place. The second female attaches her eggs to the first batch of eggs, and so on and so forth, until all the females have left their gifts to the sea. "It finally looks like a huge anemone," Joe said. "There are hundreds of fingers, all containing eggs, physically linked together. It's an event. They reproduce as an event." From then on, the development of the baby squid is synchronous. They develop together, watching with their eyes all the others in their group. They hatch together. They school together, swimming as a group throughout their very short life span (less than a year). Thus, one shoal of hundreds of squid may go through a complete life cycle together, as though, in some ways, they are one living being.

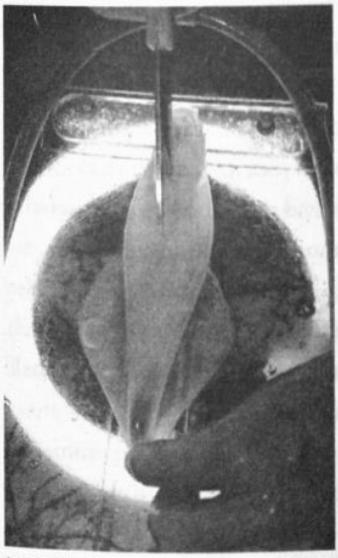
Joe was also fascinated by the braininess of the little animals. "Besides the fact that they're very beautiful, they're very intelligent," he said. "The point is—they're thinking. Does a mouse think on their level? Probably not. Does a dog? Depends on the dog."

For a while Vineyard Sound *Loligo* were in great demand in laboratories around the world. Joe started a business called

Calamari Inc. Laboratories put in their orders for a variety of squid parts—eyes and axons and fin nerves and brains—and Joe would dissect the squid and send the scientists what they needed. A scientist from the National Institutes of Health called him one day and asked for 2,000 squid eyes. The scientist was studying how eyes actually see. Joe sat down and removed squid eyes, one every five minutes at $5.00 an eye, froze them, and sent them to Washington.

At $5.00 an eye and twelve eyes an hour, Joe was making pretty good money for a kid. But he eventually realized he was bored sitting on the sidelines. He was interested in the neuroscience itself. He went on to earn a doctorate in neurobiology. These days, he heads his own MBL lab, and is working on squid science that he hopes will help lead toward a cure for Alzheimer's disease.

But he's always happy for a chance to ride on the *Gemma*. As we crossed the Sound that August morning, basking in the early morning sun, we headed for a prime fishing spot near the island of Martha's Vineyard. I asked DeGiorgis about his most unusual dive in these waters when he was still working for the collections department. He said it was the sudden appearance one day of hundreds and hundreds of salps, strange jellyfish-like organisms that make long chains and float through the water, eating and growing along the way. On that particular dive, he had to part the strands as he moved through the water. "It was like walking through a beaded curtain," he said. "It was a virtual sea of salps. Then, the next day, they were all gone. Vanished. It was a place where I've dived more than anywhere else in the world. I've never seen them again. Bizarre."



Joe DeGiorgis dissecting a squid

The squid fishing wasn't great that warm late-summer

day, but after a series of runs with the trawling nets, the crew had brought up enough *Loligo pealei* to call it a day. Back at the dock, scientists and their lab assistants dropped by to pick up their orders for another day of research.

After the trip, Joe dissected an axon to show how it's done.

"The neuron is shaped like a tree," he explained later. "It has 'branches'—the dendrites; a 'trunk'—the axon; and 'roots'—the terminal end of the axon. The axon, the trunk of the tree, is what I'm interested in."

He tied off both ends of the axon using thread, black on one end and white on the other, like you might tie the end of a balloon. Then he gently lifted the axon out of the squid's body and placed it on a petri dish. He peeled away the unnecessary tissue clinging stubbornly to the outside of the axon. It was kind of like peeling a banana. That left the naked axon, containing only the goo—the "axoplasm"—that filled up the axon's insides.

It took him about five minutes. In Joe's experienced hands, the task looked easy.

To prove the axon was still doing its job, he put an electrode inside it.

The clicking sound, the buzz of electricity, was clear as a bell.

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As nerves, bundles of axons produce the river of power that runs through your body. Electricity, the same physical force that turns on your electric lights or makes your computer work, is the force that enables you to think and dream and play baseball and drive a car. That's why many medical textbooks equate the nervous system to a system of electrical wiring. "Life exists because of a delicate dance of electrons," wrote author Joseph MacInnis. Without *Loligo pealei*, we might not have several basic facts that led us to this understanding.

For thousands of years, we've known that some sea animals produce electric shocks. Torpedo rays, capable of stunning their victims with as much as 220 volts of electricity, found their way into Plato's *Dialogues*. Early Roman physicians used these

animal-generated electric shocks to treat human ailments like headaches and gout, presumably with some success. But while ancient cultures understood that some animals were capable of emitting shocking levels of electricity, they did not understand that *all* muscles—including our own—contain and discharge electricity.

The fact that our muscles work because of electricity was discovered around the time of the American Revolution. Other scientists had played around with the phenomenon of electrical interaction with animal muscle, but it was Italian scientist Luigi Galvani who did the first series of solid experiments in the field, in the 1780s. During a storm, Galvani saw that a severed frog's leg, hung outside on a copper hook on an iron balcony, twitched when lightning appeared in the sky. He also found that he could make the severed leg twitch with static electricity, as well as when he sent electric current from a Leyden jar, a kind of very primitive battery, into the dead leg. He thought about this a great deal and finally suggested that the muscles themselves created their own unique kind of electricity, which he called "animal electricity."

While Galvani was studying "animal electricity," other scientists were independently studying electricity more generally. Ben Franklin, of course, established that lightning bolts were bolts of electricity, and also coined many of today's basic electrical terms, like "positive," "negative," and "current." The impish Franklin liked to show off for his dinner guests by killing turkeys with bolts of static electricity.

Franklin and other researchers imagined that electricity was rather like water, only invisible. Yet while Franklin and others were able to work out a bit about *what* electricity did, they did not understand *why* electrical phenomena occurred. The discovery of what was actually flowing—energy from the bouncing around of negatively charged electrons—would not occur for another century.

At first glance, the discoveries of Galvani and Franklin and many other scientists seemed contradictory. Too much electricity could, obviously, kill. On the other hand, a jolt of electricity

seemed, from Galvani's experiments with frogs, to give life. How could this be?

Scientists proposed the existence of two different kinds of electricity and suggested that the electricity in a frog's muscle differed in some basic way from the electricity Franklin discovered. The electricity that moved muscles became "animal electricity." Franklin's lightning-bolt electricity became "natural electricity."

This may seem silly to us today, but then many scientists thought it reasonable. After all, how could bolts of static electricity kill a turkey but also, apparently, give life to a dead frog's leg? The whole thing seemed very odd.

The public was both confused and fascinated. An "electrical frenzy" swept Europe, writes neuroscientist and historian Stanley Finger. For much of the nineteenth century, people imagined that electricity could do all kinds of things. Percy Shelley, the great English poet, tried to cure his sister's skin disease by using electrical shocks and, explained Finger, "managed to electrocute the family cat in the process."

Smatterings of what the scientists had learned gradually entered the popular culture. The verb "to galvanize" entered the vernacular, and some people claimed to be able to use electricity to encourage people to become more active. (And indeed, it does turn out that when you administer an electric shock to someone, you do "galvanize" them into action.) Other people began to wonder if the electrical force wasn't what created the human "spirit," which seemed to disappear when a person died. Could you use electricity to bring back the dead?

As often happens, this scientific breakthrough caused a popular uproar. To many people, it seemed as though scientists were eating apples from the Garden of Eden, usurping knowledge and abilities that should belong only to God. And thus was born *Frankenstein; or, The Modern Prometheus*, perhaps the first-ever novel to be written in the mad scientist genre. Mary Shelley, a bored English teenager, was hanging around the resort of Lake Geneva with friends, including the poet Lord Byron and her lover, Percy Shelley, in the extremely cold and very rainy summer of 1816. Because of the weather, Mary and her companions were

stuck inside, forced to huddle around a warm fireplace, swaddled in layers of clothing.

On one of those chilly evenings, Mary listened to Percy and Lord Byron explore the essence of the word "galvanize." Was it really possible, they wondered, to assemble body parts and create a living being? Would it ever be possible to discover "the nature of the principle of life"? In Mary's fertile imagination then appeared the fictional character Frankenstein, a scientist who did just that. In her novel, after building the technology and assembling the body parts, the professor brought to life a humanlike monster. "It was on a dreary night in November," Mary wrote in chapter five, "I collected the instruments of life around me, that I might infuse a spark of being into the lifeless thing that lay at my feet." Powered by electrical shocks, the monster opened its dull yellow eyes, breathed, and began to move its muscles.

It wasn't until the end of the nineteenth century that scientists finally resolved the confusion. The physicist J. J. Thompson proved the existence of electrons, particles even smaller than atoms. Scientists then understood that what was flowing through nerves and axons were really electrical charges created by the activity of these electrons.

If the discovery of electrons helped physicists understand a bit more about electricity, it also helped neuroscientists get back on track regarding the work of the brain's neurons by putting to rest the idea that electricity could bring the dead back to life.

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Enter *Loligo pealei*. In the middle of the 1800s, scientists discovered that an electrical impulse travels along an axon at a speed of about 90 feet per second, much more slowly than it would travel through a metal wire. By that time, scientists were able to understand the concept of electrical flow through a wire, and imagined that the body was filled with continuous "wiring" that seemed to have something to do with these long strands of fibers that ran down the spinal cord. It wasn't until the 1880s that a Spanish scientist was able to draw the neuron and explain

what the various parts of the neuron, including the axon, actually did. By finally clarifying that the neuron with its axon is the basic unit of the brain and that the body does not have a continuous system of wires running through it, Santiago Ramón y Cajal became one of neuroscience's most famous researchers.

Progress continued, although slowly by the standards of modern science. Once science accepted that the neuron had a beginning (the dendrites), a middle (the cell body), and an end (the tip of the axon), researchers were able to learn that all electrical impulses traveling along an axon have exactly the same strength. That is to say, there are not some very powerful electrical pulses and some very weak electrical pulses flowing along an axon. This seemingly uninteresting fact had considerable implications: It meant that the electrical message being sent down the axon was charmingly simple. It was binary, like the telegraph. Either dots or dashes, on or off. Or in terms of computer language, either zeros or ones. The pulse either traveled down the axon—or it didn't.

When scientists attached some simple technology to human nerve fibers, they could hear a characteristic "buzz" when electrical messages traveled down those nerves. But they still couldn't understand the details of what was happening. One of their biggest handicaps was that they were not able to look *inside* a human axon as it was firing. It was simply too small and too delicate for the technology that existed in the decades after Cajal's momentous discovery. For decades, scientists were stumped. It seemed as though it just wasn't going to be possible to study the interior workings of a neuron. How the cell did what it did was apparently going to remain a mystery.

Then British biologist and cephalopod fanatic John Zachary Young came across the Atlantic in the summer of 1936 to enjoy Woods Hole. Young had been interested in cephalopod anatomy from the beginning of his career. That summer at the Marine Biological Laboratory, he worked with *Loligo*.

Young began studying a long, delicate strand of squid tissue believed by most scientists to be a blood vessel. Young stimulated one end of this bit of tissue and heard the characteristic static

that showed that electrical impulses were traveling down the pathway. He determined that the tissue was not a blood vessel at all. It was actually a very large axon.

Back in Britain, he continued his research for a while, but not for long enough. Call it a quirk of fate. He decided not to pursue this line of research to its ultimate end—figuring out how the cell managed to create the electrical impulse and send it from one end of the axon to the other. Thus this great scientist gave up an opportunity to earn a Nobel Prize.

He instead handed the research on to Alan Hodgkin and Andrew Huxley. Hodgkin had worked on squid with Young, and he asked Huxley, his onetime student, to work with him to continue to solve the mystery. The two formed the exceptionally powerful bond of two scientists who work well together. Their first job was to develop an appropriate approach. Removing the axon from the squid, they placed it in seawater. They took a finely honed electrical probe and placed it inside the axon and placed another probe outside. They already knew from earlier experiments by other scientists that the inside of the axon, when at rest, had a comparatively negative charge and that the outside of the axon had a comparatively positive charge. Scientific consensus theorized that the charge inside the axon would move from negative to neutral.

Instead, Hodgkin and Huxley discovered, much to their amazement, that there was a big jump inside the axon, much bigger than anyone had anticipated. In fact, the inside of the axon changed to strongly positive. By comparison, the outside became negative. Then, when the axon returned to its resting state, the charges returned to their original charges.

"We have recently succeeded in inserting micro-electrodes into the giant axons of squids," the scientists wrote triumphantly in a short note to other scientists, published in *Nature*, a prestigious British science journal. The pair mentioned in the note that although they had succeeded in one respect, there were many questions they still wanted to try to answer.

Ultimately, they were able to watch the flow of electricity

down the axon as though they were watching the flow of a twig down a stream. They realized that one type of charged molecule moved from outside the cell axon to inside the cell axon, while the other type moved from inside to outside.

Then the pair found something even more intriguing. While many of the molecules involved in keeping a cell alive are rather large and complicated, those involved in keeping the electricity flowing were comparatively simple and very common: sodium (like the sodium in table salt or seawater) and potassium (found in foods like tomatoes and bananas). Both the sodium and the potassium lacked one electron, so they became positively charged "ions." When the axon is at rest, the scientists found, there are a lot more positive ions outside the cell than inside the cell. When electricity flows down the axon, some of these ions outside the cell are in fact moving into the cell. When the electrical impulse passes, the ions move back outside. The inside of the axon returns to its original, comparatively negative state.

By studying the giant axon of little *Loligo*, Hodgkin and Huxley had made this profound discovery: Our ability to think is based on this marvelously simple process—the movement of electrical charges, ions, into and out of the axon.

But like many scientific discoveries, this one raised questions. Why were potassium and sodium moving into and out of the cells at only the appropriate times? Why didn't they move back and forth randomly?

In turned out that there were gates, or channels, in the axon that opened and closed at only the appropriate times. In science, the more questions you answer, the more questions materialize. This is part of the fun. Once Hodgkin and Huxley revealed the basics of how electricity flows down an axon cell wall, other scientists wanted answers to questions about exactly how these gates or channels operated.

Scientist Clay Armstrong, one of Huxley's students, tackled the question. Armstrong sometimes used the "giant" axons of the little squid found near Woods Hole, but he also traveled to South America, where fishermen provided him with Humboldt squid.

Armstrong discovered that individual ions like potassium have their own specific gates that open and close only for them. These gates control passages through the cell wall that have come to be called "ion channels" and that are voltage-sensitive. In other words, the flow of electricity down the axon involves the opening and closing of these various channels.

This complicated-seeming idea is quite simple: Imagine a field filled with horses and cows. The horses can only enter and leave by one gate; the cows only enter and leave by another gate. "We are what we are because of ion channels," Armstrong explained to one interviewer. To another, he explained that "every perception is encoded in electrical form. All of our thoughts, all of our emotions, involve the action of millions of ion channels. Billions."

Since then, scientists have learned that there are many different kinds of channels leading into and out of an axon, and, indeed, into and out of all kinds of cells in the body. The reason some tranquilizers work is that they block the flow of ions through these channels, and thus the flow of electricity down the neuron's axon. The axons or nerves become quiet.

Armstrong's squid-based discovery has had immense consequences for human medicine. A whole new class of medications—channel blockers—has saved countless human lives. A common channel blocker called a calcium channel blocker is routinely prescribed to lower blood pressure and prevent heart attacks. Other medications help to control some forms of diabetes by influencing the opening and closing of potassium channels. Some forms of epilepsy seem to be the result of the malfunctioning of the ion channels in neurons; researchers hope to eventually find medications to improve life for epileptics by controlling the channel malfunctions.

In fact, Armstrong's work on squid has led to a whole new field of medical research—the study of channelopathies, or the study of the malfunction of channels in the axon. It's not hard to see why Hodgkin and Huxley's discovery using *Loligo*'s giant axon has been called one of the most important breakthroughs in the twentieth century. The pair received the Nobel Prize in

1963. Many people expected Clay Armstrong also to win a Nobel, but sadly, he was never so honored.

It seems incredible to me that nature has worked out such a system, so consistent across species, at once brilliantly simple—based on the tiny ions of sodium and potassium, and on simple binary code—and yet so complex, in that it controls so many different processes in our bodies. And yet this is why we can think, birds can fly, and cephalopods can change their colors in only milliseconds.

CHAPTER NINE

SERENDIPITOUS SQUID

Chance favors only the prepared mind.

—LOUIS PASTEUR

Around the time Ben Franklin was killing wild turkeys with electricity in the colonies, Horace Walpole, an English public intellectual and the Fourth Earl of Orford, was contemplating the phenomenon of accidentally finding out about things you weren't necessarily trying to understand. Walpole realized that these accidental achievements were more common than you might think—common enough, in fact, to deserve their own unique term.

Thus did Walpole coin the word "serendipity." There is more serendipitous science than you might at first suspect. Until the early 1950s, scientists mistakenly believed that humans had forty-eight chromosomes in their cell nucleus. Then a solution of chemicals accidentally spilled on a dish of human cells. Soaked by the unique chemical solution, the chromosomes swelled and were each clearly, individually visible for the first time. It turned out that humans have forty-six chromosomes, two less than was thought. Moreover, by making individual chromosomes easily visible, the scientist, T. C. Hsu, paved the way for medical research that would eventually save the lives of countless people suffering from chromosome-based diseases.

The most often cited example of serendipity involves the Scottish biologist Alexander Fleming, who won a Nobel Prize for discovering the curative abilities of penicillin in 1928. The commonly told story is that Fleming discovered the organism from which penicillin is made. He didn't. Other scientists had seen the fungus before. But it was Fleming who realized the importance of what he was seeing and who did something about it. It was Fleming who discovered that *Penicillium* fungi could be used to cure an infection of *Staphylococcus*, a bacterium often

deadly to humans. Fleming is therefore considered the founder of the field of antibiotics.

The story goes this way: Returning to his lab after a brief trip, Fleming saw that he had forgotten to put away a petri dish containing the *Staph* he had been studying. When he looked at the dish, he found that some of the bacteria had been killed. He also saw that some other life-form was growing there instead. It turned out to be a fungus. He began working with this material and, after much persistence, created the world's first antibiotic medicine—penicillin.

Which goes to show: Serendipitous discovery isn't entirely accidental. You have to be in tune enough with what you're looking at to know that you're seeing something important.

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"My brain feels like Jell-O" is sometimes used, tongue in cheek, to describe a feeling of mental exhaustion, but in fact scientists do use the word Jell-O to describe the texture of the goo inside your axons. "You can pick up clumps of it with forceps," Joe DeGiorgis told me, "and you can squeeze it out of the axon the way you squeeze toothpaste out of a toothpaste tube."

When Joe was in high school, the axoplasm in a neuron was described as a "soup," he said, "but it's not like that really. It's thicker. You can pick it all up, and it stays together." The material is a fluid, but a very sticky fluid, perhaps just a bit thicker than Jell-O. It's so difficult to describe that many scientists have adopted a highly technical description—"goo." The term appears not uncommonly in the scientific literature.

While some scientists were studying the flow of electricity along the axon, others were looking at what went on in the goo. How did the "Jell-O" function? What, exactly, was this plasma? What kinds of molecules were in there? If most of the manufacturing and maintenance work occurred in the cell body, under the direction of the executive DNA in the nucleus, how did the packages of information get "mailed"? How did food—

that is, energy—get from one place in the neuron to another? One purpose of the axon is to send an electrical pulse from one point to another, but many other support functions also need to happen in your neurons in order for you to be able to contemplate the words printed on this page.

Scientists have known for quite a while that the axon was filled with a gelatinous substance, and speculated quite reasonably that the substance must have some important job in helping us think. By the end of the nineteenth century, they were able to use simple materials to stain the insides of the neurons and look at a few of the structures there. They could, for example, see the DNA in the cell nucleus, although they had no idea how it worked.

They could also see, with the proper technology, the strange, tiny, sausagelike mitochondria, where energy is made ready for the cell to use. When you eat a jelly bean for breakfast, your body does all kinds of things with that food, but ultimately some of that energy reaches your neurons. In the neural cell body, a portion of that energy goes into the mitochondria, which are little power plants. In these power plants, the energy of food is changed into ATP, which is the form of energy that your cells need to keep functioning.

Some cells in your body have only a few mitochondria, but neurons contain hundreds. This is why kids need to eat breakfast before they go to school: Without food, the mitochondria remain unemployed and kids don't have the mental energy—ATP—that helps them think.

Although scientists had known for quite a while that these structures existed inside the neuron, they had little understanding as to what exactly they were or why they were there. The only way to see them was to kill the cell, stain it, then study it under a microscope. You could see the mitochondria along with other structures, but you could not watch them work. As microscopes became more and more powerful and as staining

techniques improved, scientists could with ever greater clarity look at the structures inside the neuron. But they could never see those structures *moving*—never see the living manufacturing plants, or watch their packaged exports travel through the axoplasm.

In the late 1940s, medical research, spurred by the nerve injuries of World War II, concentrated on improving the understanding of how axons worked. A pair of researchers performed an impressively simple experiment. They took some silk and tied it around a bundle of axons, a nerve. After creating this "dam," they saw that the part of the axons closest to the cell bodies gradually "ballooned." Looking at this bulge on one side of the silk tie but not on the other, they realized that something *inside* the axon was flowing, just as the electrical pulse flowed down the cell wall. So it turned out that there were at least two flow systems in the axon—the flow of electricity and a flow of axoplasm, with its various smaller structures, within the axon itself. The flow of axoplasm inside the axon, however, was much, much slower than the electrical pulse. Researchers estimated that the axoplasmic flow might be only a millimeter or so a day. In comparison, the electrical pulse zips along the cell wall.

By the second half of the twentieth century, scientists could use radioactivity to follow some of the movements. But the details were still mysterious. Exactly how did these packages—tiny organelles, including the sausagelike mitochondria—move? Did they just drift along? Was there some kind of system? It clearly wasn't just random chance that got essential proteins and energy from one part of the cell to another. But how organized could something like that be?

In the 1970s, the field of cell biology was somewhat stymied, in part because the tools available to researchers were not up to the task. Light microscopy—the traditional kind of microscope that we used in high school that relies on visible light—had gone about as far as it could go, at least when it came to resolution limits. At a certain point, when scientists tried to look at smaller components inside a cell, the image would become confused. It was somewhat as though you were looking at those old-fashioned stereoscopes when the tool wasn't the right distance from your eyes.

I called up Scott Brady, an expert on the secret life of the axon. Now a senior scientist and lab head at the University of Illinois, Brady in the early 1980s was a young and ambitious researcher spending summers at Woods Hole.

Progress on understanding the axon had come to a standstill, he told me, because the light microscopes of the day were inadequate. "You started not being able to tell whether it was one versus two objects you were looking at. We were basically stuck, because the kinds of questions we wanted to explore were below that size limitation."

Some researchers suggested adopting the newest video technology, but many of the older scientists remained skeptical. "The reigning paradigm was that TV would never be something you would want to use," cell biologist Nina Strömgren Allen told me. Strömgren Allen was part of a group of researchers who would overturn that paradigm. Her father, a Danish astrophysicist and formerly a student of Neils Bohr, told her about the new high-powered, high-resolution telescopes that had recently been developed for astronomy. Could some of that technology be transferred to the world of microscopy? Strömgren Allen and her husband, Robert Day Allen, began working on a new idea—Video-Enhanced Microscopy—that they hoped would be able to show the inner life of a living neuron. By 1979, they had made some progress, and by 1981 they had published a paper on their breakthrough.

Then one of those key moments of serendipitous science occurred. The couple was teaching a course in Woods Hole about how to use microscopes. They placed a common *Loligo* squid axon under a light microscope, to which was connected a video camera and a television screen. When they switched on the technology, the image didn't seem quite clear.

Allen turned a knob, hoping to bring the image into focus. Twisting the knob controlled how much light was let in and, therefore, how much you could see. Allen was explaining

this principle to his students, and he wanted them to see the problem.

Continuing to look through his microscope, he twisted the knob.

"See," he said. "You can't see anything anymore."

Hands waved in the audience of students.

"The image isn't washed out. We're looking right at it," the students said. "In fact," they continued, "we can see it *better* than before."

"Of course it goes away," Allen said. "I can't see anything."

Then he stepped away from the eyepiece of his microscope and looked at the image on the television screen.

Suddenly, right in front of everyone, appeared the movement of tiny little components *inside* the squid axon. A whole new world was revealed. Word of the amazing sight spread quickly on the streets of Woods Hole. Scientists passing each other on the sidewalks buzzed with excitement.

"Suddenly, the veil was lifted," Strömgren Allen remembered when we spoke on the phone. "We knew they were there, but we couldn't see them before this."

When Allen followed up on what had happened, he found out that the new microscope that had been sent to him had been tuned incorrectly by the manufacturer. Serendipitously, it was this incorrect tuning that revealed for the first time this whole new avenue of exciting scientific research.

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The accident created a revolution in medicine, just as the creation of penicillin had decades earlier. Scott Brady was there the day it happened. He said: "It provided us with a means to visualize these very tiny objects in living preparations. You could resolve things that were smaller with electron microscopy, but you also had to impregnate what you wanted to see with metals, so that you weren't then seeing much in the way of direct objects, but depositions of metal stains. All of that was dead, and if you're interested in movement, it's not going to do you much good. It was really quite remarkable. No one knew there was so much

movement. And no one had realized that all this movement was almost continuous."

Suddenly you could look at a lot more than the electrical pulse flowing along the squid axon. You could see that *inside* little *Loligo*'s axon was a beehive of activity. Or, to use the analogy provided in one scientific paper, it was "as engrossing as the ant farms of our childhood."

Scientists had never imagined that the world inside the axon was so dynamic. And the first thing they noticed—what was stunningly obvious—was that this activity was much more than just a lackadaisical "drift" of organelles. There seemed to be roadways and pathways, lots of stop-and-go traffic, and much more organization that anyone had previously imagined. There was a whole universe in there. It was as though you were looking at a model train set, the very elaborate kind you see in department stores at Christmas. There were engines going in all sorts of directions, lots of different tracks, and loaded-up flatbed cars and stop-and-go points where things were loaded and unloaded. It was all highly orchestrated so that (usually) none of the moving parts, the molecules, collided with each other. Some of the engines seemed to be zipping along, much faster than the one millimeter a day that had been estimated. Others crept along at a pace that would have made a snail look high-powered.

There were even, occasionally, accidents. Sometimes scientists could see collisions. Every once in a while, the molecules pulling their loads would inexplicably (or so it seemed) jump the tracks.

The movements the scientists saw that day were breathtakingly sophisticated. "It was a jaw-dropping experience for those guys, and started a whole new flurry of activity. It's a very famous story," Joe DeGiorgis explained. Worlds within worlds, right there, in each and every neuron. Many of these organelles were being tugged along trackways, out of the cell body and into the axon, traveling some-times all the way to the axon tip. In the 60-foot blue whale axon, this is quite a trip.

What soon became obvious was that various molecules had specific jobs. Using the new technology, a number of younger scientists began studying the intricacies of the activity. Intriguingly, they learned that they could squeeze the axoplasm out of the squid axon, and that, under proper conditions, it would continue to do its job of shuttling the tiny packages around for quite a while. This made their task much easier, because they could look directly at the tracks and cars, rather than having to look at them through the semitranslucent cell wall.

Almost immediately the scientists began looking at the chemistry of the miniature railroad system. Scott Brady was in on the action right from the beginning. The senior scientist he was working with in Woods Hole told him about the news as soon as it happened. For a young scientist, to be present at a revolution is like receiving manna from heaven. This moment of video-enhanced clarity provided Brady, in an instant, with his life's work, with a whole new wide-open field of research where no other scientist had yet staked out territory.

It was like being the first prospector to find gold at Sutter's Mill.

"There was so much excitement," Brady remembered. "Then we started asking questions: How can we make use of this?"

The race was on among the young scientists in Woods Hole that summer to be the first to find out what the various molecules inside the squid axon were up to. Thrilled with the new technology, Brady set about trying to find how the larger molecules were pulled along the tracks in the axon.

Both Brady and a competing young researcher, Ron Vale, found a kind of "motor," eventually called "kinesin," that was responsible for moving packages up and down the axon. It turned out that kinesin was a kind of "slave" molecule that "walked" along one of the tracks, putting one foot in front of the other, pulling its loads behind it.

Eventually, after decades of research, researchers, including Joe DeGiorgis, had found many different kinds of hardworking kinesins in squid and other animals, including humans.

There are multiple motors in the same neuron. Humans may have nearly fifty different kinds.

I asked Joe why we need so many.

"We're trying to figure that out," he answered. "We don't know yet what all these motors do. We know it's a trafficking issue. We want to know that if there's a problem with some of this transport, does that lead to neurological disease?"

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So, inside the axon is a city that never sleeps.

Thanks to the squid, we understand this. But how does an axon die? What happens to brain cells when we develop diseases like Alzheimer's or Parkinson's? Brady and a number of colleagues across the country and around the world have devoted much of their research during the first decade of the twenty-first century to answering that question. And once again, they've used the squid axon in some of their research.

"Neurons have some very special challenges," Brady explained. "You have to remember that neurons are, many of them, extremely long. When you start stretching a cell over a meter [a meter is a bit more than three feet] or more, we're talking about large as well as long. Especially when all the proteins needed all along the axon have to be packaged and transported to where they're going."

Recently, scientists have learned that the trackways inside the axon run in both directions. Packages put together in the cell body must sometimes travel all the way to the end of the axon. And materials at the far end of the axon sometimes must travel all the way back to the cell body. This two-way transport is mandatory. It's also sometimes mandatory for the packages to be dropped off at points in between both ends. "These things are essential for the survival of the cell. It turns out that you have to have particular proteins at particular places all along the neuron," Brady said.

So, Brady and others wondered, what makes the proteins inside the neurons start and stop? How do the kinesins "know" when to dump their loads and relax? How do they know when to keep on truckin' just a little bit farther? One of the triggers, or switches, that flips the kinesins on and off turned out to be

another molecule, called a "kinase." It's the kinase's job to give kinesins their marching orders. Kinases are like the switchmen positioned along railroad tracks, managing traffic.

"What happens when the kinase doesn't do its job?" I asked.

"You get a perfect storm," Brady answered. "The axon starts dying back. And if the axon dies back far enough, then the whole neuron dies."

In 2009, Brady and others published papers that tied at least part of the problem in patients suffering from various types of neurological diseases to the malfunction of the kinases in the neuron that give the kinesins their orders.

It reminded me of the story Yale's Vincent Pieribone had told me about the different characters—"amazing little guys"—inside the axon. Using squid and other animals, scientists keep finding more and more such characters, all with their own individual, highly specialized jobs to do.

By studying kinases, the switchmen, Brady and his lab team believe they have discovered an important part of what happens in the human axon when Huntington's disease debilitates a human body. Researchers have long known that the disease has a genetic, inherited basis. Because of this genetic problem, a long chain reaction or a cascade of errors occurs. The kinase does not do its job properly. Which means the kinesins do not keep on truckin'. The packages that need to be carried back and forth between the tip of the axon and the cell body do not get where they need to go in the correct quantities or in the correct time frames. Eventually, the very existence of the neuron itself becomes an issue.

Brady believes that there are a number of common neurological malfunctions that have their roots in the malfunction of the axon's shuttle system, and that Alzheimer's and Parkinson's disease may be among them. He and his lab have even created a name for this group of illnesses: dysferopathy.

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It took several decades and many, many scientists to decipher this puzzle, and the success of the endeavor stretches all the way

back to J. Z. Young and the discovery of the giant axon in little *Loligo pealei*. It's been nearly a century of scientists standing upon the shoulders of the generation that preceded them.

I asked Brady about that history, and about how odd it seemed to me that so much of our own brains have been revealed by studying an animal that's so incredibly different from us.

"The squid was designed by Mother Nature for neuroscientists by making everything so big that it allows us to see things and have access to things that we just really can't get to in an intact mammalian system," he answered. "These kinds of experiments can only be done with squid. We share a surprisingly large number of features with the squid. The kinesin motors, for example. There are big chunks of our kinesin motors that are remarkably similar to those of the squid. We both have the same basic mechanisms. The choices [about how the neuron would develop] were made before we split [on the evolutionary tree], perhaps 700 million years ago. And we both took advantage of those choices to re-create the remarkable signaling that is the nervous system. So far, everything that we've identified in the squid, we've been able to confirm in the mammalian system."

I asked him the question I asked everyone: If squid have such complex brains, are they smart?

"Squid are the jocks of the cephalopod world. They swim very fast. They're designed for speed," he said. "The octopus is the intellectual. They can solve problems and learn quite remarkable things."

We may share many things with squid—a similar eye, a similar neuron, neurotransmitters like dopamine, perhaps even certain intellectual proclivities—but there is one biological area in which our styles decidedly differ: sex.