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Building Electronic Bridges to Bionics: The Basic Science of Neural Prosthetics

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Building Electronic Bridges to Bionics: The Basic Science of Neural Prosthetics

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COVER: The development of neural prosthetics, which can help restore hearing, sight and movement to those who have lost these functions, is a culmination of centuries of basic research. Biologists, bioengineers, and physicists have pieced together the underlying circuitry of the nervous system, and are using that knowledge to bring bionic medical advances, once the stuff of science fiction, to those who need them most. *Images from SPL/Photo Researchers, Anna Knott, and Department of Energy.*

Building Electronic Bridges to Bionics: The Basic Science of Neural Prosthetics

Margie Patlak

At first sight Rachel looks like a typical teenager—she spends endless hours on her cell phone talking to her friends, and enjoys rap music and the television show *American Idol*. It is only after talking to her mother about Rachel's medical history, that the amazement sets in. Despite appearances to the contrary, Rachel is deaf.

Born with a birth defect that destroyed a portion of both of her inner ears, Rachel cannot hear anything without her cochlear implant. This electronic device enables most sounds entering Rachel's ear to complete the neural pathway to Rachel's brain where they are perceived as voices, birdsongs or a panoply of other auditory features that the hearing take for granted. Surgically inserted when she was just a year old, the cochlear implant has enabled Rachel to lead a normal life free of the disability of deafness.

Rachel is one of a growing number of people with a missing function that has been restored with a neural prosthetic device. The oldest and most widely used of these electrical, and often computerized, devices is the cochlear implant, which has provided hearing to thousands of congenitally deaf people in this country. Recently, the use of the cochlear implant is expanding to the elderly, who frequently suffer major hearing loss. More cutting edge are artificial retinas, which are helping dozens of blind people see, and "smart" artificial arms and legs that amputees can maneuver by thoughts alone, and that feel more like real limbs.

Such pioneering devices are brought to us by the collaborative efforts of a myriad of scientists from a diverse range of fields including biomedical engineering, physics, biology, neuroscience, and computer sciences. These researchers, whose curiosity led them to explore frog legs dancing during thunderstorms, a snail-shaped organ in the inner ear, and how various eye cells react to light, have fostered an understanding of how to "talk" to the nervous system. That understanding combined with the miniaturization of electronics and enhanced computer processing has enabled prosthetic devices that often can bridge the gap in nerve signaling that is caused by disease or injury.

Electrifying Experiments

Today's neural prosthetics can trace their origin, in part, to a pair of frog legs that caused quite a laboratory sensation in Mozart's time (c.18th century). The lab belonged to the Italian anatomy professor and physicist Luigi Galvani, who was dissecting a frog at a table. Also on the table was a wheel that generated static electricity for Galvani's physics experiments. Just as Galvani put a scalpel to the sciatic nerve, which connects to the muscles in the frogs' legs, his assistant happened to discharge a spark of electricity from the wheel. Galvani noticed that when the spark was released, the legs of his dissected frog jerked. Apparently the static electricity released into the air was picked up by the metal scalpel and passed to the nerve (Figure 1).

This led Galvani to conduct other experiments, including one in which the static electricity of a thunderstorm prompted frog legs on a rooftop to dance, and another one in which touching the exposed nerve to a frog leg muscle was enough to cause the muscle to twitch. The results of these experiments led Galvani to conclude that there was "animal electricity" stored in the nerves of all living creatures, and literally sparked the notion that nerves use electrical energy to trigger muscle movement. (Galvani's experiments also apparently inspired Mary Shelley, who read about them shortly before writing her famous novel Frankenstein, in which electricity is used to bring to life Dr. Frankenstein's monster [Figure 2].)

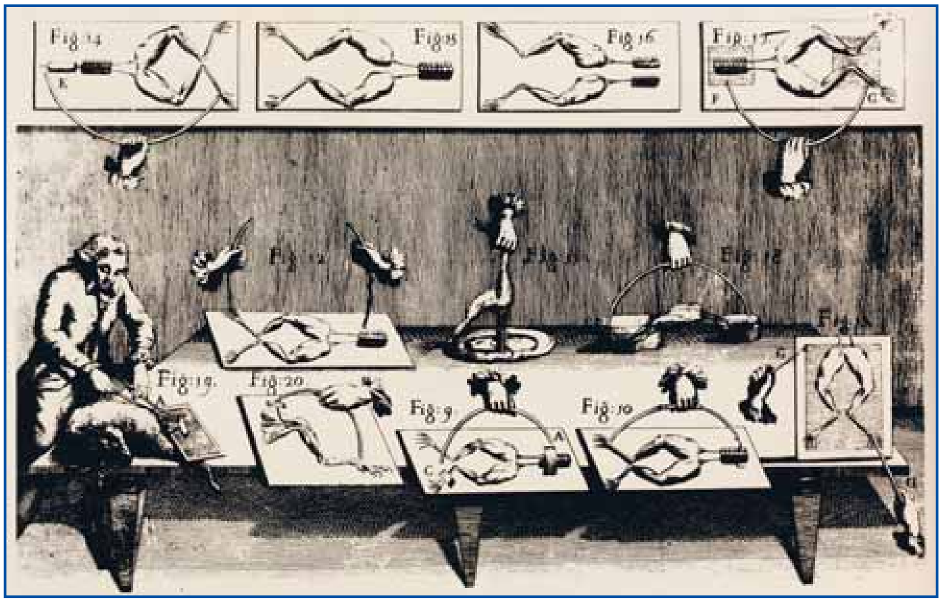

Figure 1 – Galvani's frog experiment: Illustration showing the various experiments conducted by Italian physicist Luigi Galvani in 1791 on frog muscle and electricity. The result was that the muscles in the frog's leg twitched, indicating the presence of electricity. This engraving was taken from Galvani's *De viribus electricitatus in motu musculari commentarius*, 1791. *Credit: SPL/Photo Researchers, Inc.*

In the 19th century, the invention of an amplifier of electric current called the galvanometer (named after Galvani), enabled several basic science researchers to eavesdrop on the electrical chatter of muscles and nerves. The experiments these European physicists did on frogs revealed that an electrical current applied to the nerve can briefly reverse the charge emitted by that section of the nerve. This flip-flop in charge from positive to negative quickly spreads down the length of the nerve and to the muscle where it causes the muscle to contract. In other words, by exploring the innate electrical activity of tissues and how that changes in response to electrical stimulation, these researchers had collectively stumbled upon the electrical nerve impulse, which is the basic signaling mechanism that nerves use to communicate with tissues and organs (Figure 3).

Figure 2 – Frankenstein's monster: Galvani's experiments showing that electrical impulses are carried through nerves to trigger muscle movement helped inspire Mary Shelley's novel, *Frankenstein,* later popularized in film.

Later, studies in the 1920's revealed that the electrical activity runs on a two-way street—it can pass not just from the motor nerve to the muscle, but in the reverse direction from the muscle to a sensory nerve. The brain uses motor nerves to tell the muscle to contract or relax. But the muscle can talk back to the brain via sensory nerves that convey the amount of tension in the muscle.

One particularly telling experiment was that of the British physiologist (and later Nobel Prize winner) Edgar Douglas Adrian. He had suspended a frog leg from a brass hook and was surprised by the spike of irregular electrical activity coming from nerves in the leg. He first thought that this was due to faulty equipment used to record the electrical activity and frustratingly expected that he would have to spend months rebuilding it. But then he noticed that when the frog leg was placed on a glass plate, the irregular electrical activity stopped only to come back when the leg was suspended again. That's when it dawned on him that the electrical activity was actually an electrical signal being passed from muscle to nerve to tell the nerve (and ultimately the brain in an intact animal) that the muscle in the frog leg was being stretched. (Such stretching didn't occur when the leg was merely laying on the plate.)

These "electrifying" findings opened up a whole new way of understanding how the body works, and led investigators to electrically explore how a cacophony of sounds that pass through our ears become music to our minds.

Journey into Inner Space

Meanwhile, by the middle of the 19th century, anatomists had mapped out the inner ear.

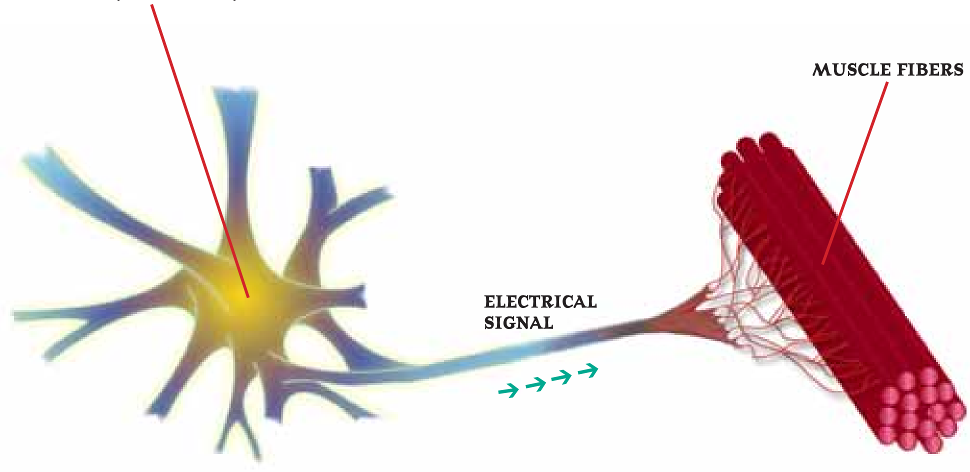

Figure 3 – Nerve Impulse: Electrical impulses travel through motor neurons, or nerve cells, to signal muscle contraction. As described in later figures, electrical signals can also be carried from tissues back through sensory neurons to the brain to communicate the amount of tension in the muscle. *Figure designed by Corporate Press.*

Their dissections revealed that in addition to a thin membrane, called the ear drum, and some of the tiniest bones in the body, the inner ear had a strange snail-shaped structure called the cochlea. The cochlea was filled with fluid and carpeted with thousands of tiny hairs. Because these hair cells connected with the auditory nerve that travelled from the ear to the brain (Figure 4), it was assumed that the cochlea played a crucial role in hearing. But there was no experimental evidence to confirm this. Also, ear dissections did not answer a key puzzle—how the cochlea could transform the multitude of sounds that entered the ear into distinct tones (frequencies) that the brain uses to tell the difference between a vowel and a consonant, or between various notes in the musical scale. Fortunately, insight in this regard was provided in 1928 by Georg von Bekesy, a physicist who had an ingenious way of *seeing* sound.

While working for the Hungarian Post Office on how to improve telephone communications, von Bekesy turned to the inner ear for guidance. In order to best transform the human voice into meaningful signals, he first wanted to know how the human ear processes sound. So he dissected the inner ears of animals and human cadavers such that the cochlea remained intact and functioning—not an easy feat given that the cochlea is encased in the bones of the skull. He then sprinkled light-sensitive silver flakes on the hair cell lining and used strobe photography to mark how the hair cells moved in response to various tones. His basic research revealed that not all hair cells were alike—those close to the base of the cochlea moved more in response to high-pitched tones, whereas hair cells at the tip of the cochlea were more swayed by low-pitched tones. For this research von Bekesy later won the Nobel Prize (Figure 5).

A year after von Bekesy photographically saw the cochlea's

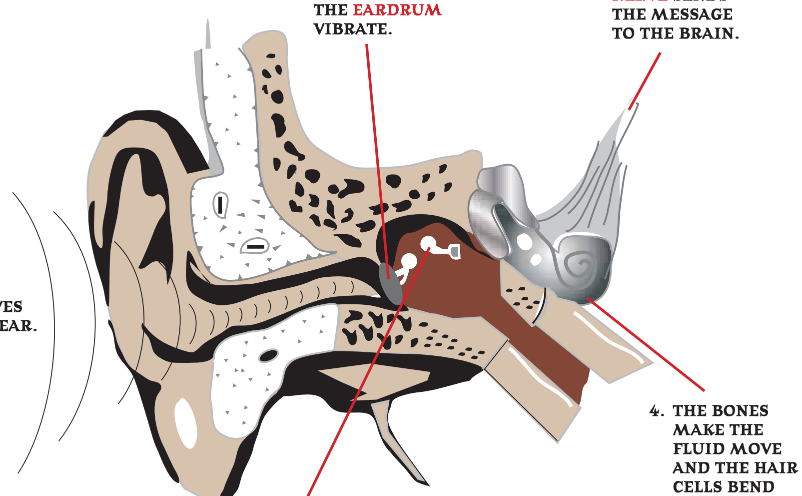

Figure 4 – Anatomy of the ear: The discovery that the cochlea was critical for hearing led scientists to explore the way in which this snail -shaped organ helped translate sound waves to nerve impulses. This, in turn, led to the breakthrough finding that electrical signals could be used to stimulate the auditory nerve, and ultimately resulted in the development of cochlear implants. *Figure designed by Corporate Press.*

response to sound, Princeton psychologists E. Glen Wever and Charles Bray electrically heard speech from this organ. Wever was trying to discover if the ear codes the different tones heard by how often electric nerve impulses land on the auditory nerve, much like the clicks and pauses of Morse code are used to represent the various letters in the alphabet. To assess this, the researchers put electrodes on the auditory nerve of an anesthetized cat, and the signals they picked up were amplified and sent via cables to a telephone receiver in another room down the hall. Wever spoke into the cat's ear while Bray listened to the receiver.

Bray expected to hear the typical monotone staccato of discharging nerves. But instead he heard exactly what Wever was saying! That was because the researchers overheard the complex electrical chatter of the cochlea. This electrical signaling conveyed minute differences in frequencies across

Figure 5 – Nobel Prize stamps honoring von Bekesy: Georg von Bekesy observed that hairs inside the cochlea move in response to different tones, helping to explain the physical mechanism by which sound was interpreted by the ear. For this he won a 1961 Nobel Prize and was later honored on a Swedish stamp set together with other scientists who had made discoveries related to the biology of senses.

a span of five octaves enabling it to preserve all the frequency variations that comprised Wever's speech. The Princeton finding solidified the importance of the cochlea as an organ of hearing and inspired some scientists to consider restoring hearing in those with damaged cochleas by electrically stimulating the auditory nerve.

An Electronic Bridge to Hearing

The next step on the way to an electronic bridge to hearing was taken by a physician who spent most of his time dabbling in electrophysiology, the study of the effects of electricity on the body that Galvani accidentally invented. Andre Djourno began his scientific career at Paris University, like most electrophysiologists at the time, by studying how electricity stimulates frog nerves. Seeing those powerful effects prompted Djourno to explore the possibility of using electric shocks to revive electrocution victims and regular electrical discharges to prompt nerves to trigger contraction of the breathing muscles in people paralyzed by polio.

As part of these investigations, Djourno did numerous experiments on rabbits (Figure 6). He buried under the skin of these anaesthetized animals an electrical device that was connected to a nerve or muscle he wanted to stimulate with electricity. That electricity was created by a wire coil placed outside the skin of the animal but attached to a source of electricity. When electrical current passed through this external coil it produced a matching current in the implanted device that was passed to the animal's nerves or muscles. In this way Djourno was able to trigger a rabbit to jump with just the flick of a switch.

The electrical frequency Djourno used to stimulate muscle contractions was in the same range as that of speech, so he often checked the effectiveness of his implanted electrical stimulators by using his own voice as the activating trigger. (A microphone was used to translate his speech into electrical signals.) This is probably what led Djourno to note, in 1954, that one possible application of his implantable device would be to stimulate the auditory nerve to restore hearing. Three years later he had a chance to see if this was so.

Charles Eyries, a Parisian ears, nose, and throat surgeon, was treating a patient who had gone deaf due to tumors that destroyed both his inner ears (including the cochleas) and facial nerves, but left his auditory nerve somewhat intact. This patient, who was an engineer, noticed he heard sounds when Eyries used electrically induced heat in his ear to repair his damaged facial nerve. Desperate to have his hearing back, the patient asked Eyries if a similar device might be used to let him hear again. A mutual colleague aware of Djourno's experiments put the surgeon in touch with the electrophysiologist. So

Figure 6 – Animal models: Animal models, including rabbits, cats, and frogs, were vital to discoveries that led to the development of neural prosthetics such as the cochlear implant. Laboratory animals still play an important role in biomedical research, allowing researchers to study how cells and tissues interact inside the body or how disease affects living systems. *Credit: Getty Images.*

when Eyries' deaf patient underwent surgery to try to relieve facial paralysis, he implanted Djourno's electrical stimulator just above the patient's ear and threaded a wire from it to the auditory nerve. The external coil was placed nearby on the patient's head.

Much to the patient's delight, he experienced some hearing following his surgery. After years of silence, he could once again hear doors opening and closing, and make out a few words spoken to him. But his hearing couldn't distinguish the different frequencies of vowels and consonants so that he could understand conversations.

Encouraged by his initial results, Djourno tried to improve his hearing device, but when he was denied a grant to support this work, he turned to other lines of research. However, his findings inspired researchers around the world to take up the torch, including an Australian group, and three separate groups in California, whose work was mainly funded by the National Institutes of Health. This governmental support enabled them to conduct basic research on how exactly the cochlea transmits speech sounds to the brain, as well as to do animal and clinical studies on the safety and effectiveness of the cochlear implants they devised to restore hearing. By the early 1970's, the first cochlear implant made its debut.

All contemporary cochlear implants work by having microphones that pick up sound, computer chips that code that sound by frequency, and a series of electrodes that electronically convey frequency information to the auditory nerve (Figure 7). Sound is filtered into different frequency channels in these implants because of the work of Bekesy and others that revealed that this is what happens in a normal cochlea via the hair cells. The first cochlear implant only had one electrode and channel. But studies revealed that speech perception greatly improved with the multichannel devices that surfaced shortly thereafter.

Today more than 23,000 adults and 15,000 children in the United States have cochlear implants, including a Miss America and a radio talk show host, according to the National Institute on Deafness and Other Communication Disorders (NIDCD, one of the National Institutes of Health). Success of these implants varies depending on how long patients were deaf prior to the implant, how intact their nerves are in their inner ear, whether they had some hearing before they went deaf, and how successful their post-implant training was. Cochlear implants often enable deaf or severely hearing impaired people to understand speech without the aid of lip reading, and to speak clearly with the right volume. Some people with the implants can also enjoy music, birdsongs, and hear many other environmental sounds besides speech.

In deaf children, the devices work best the younger the age at implant. About 2 or 3 out of every 1,000 children in the United States are born deaf or hard-of-hearing, and more lose their hearing later during childhood, according to NIDCD.

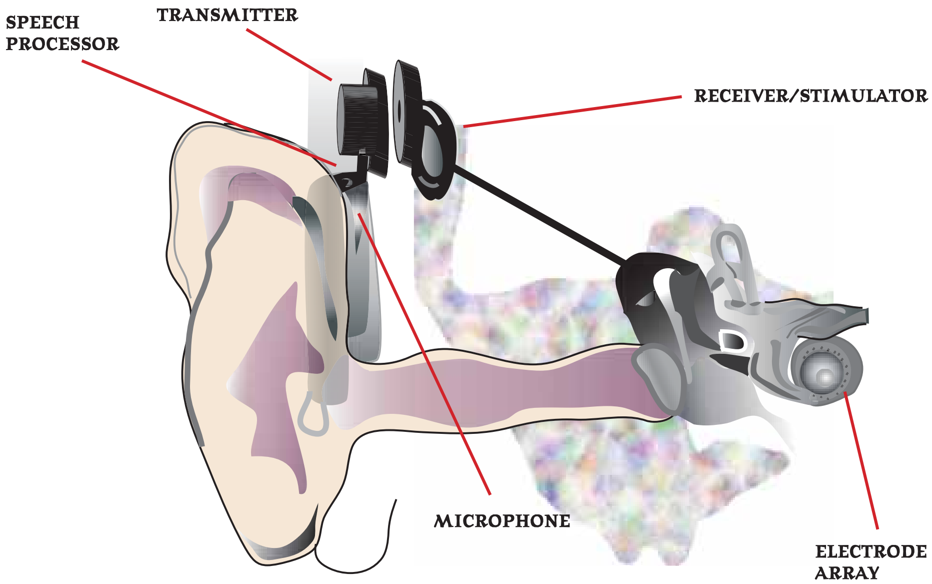

Figure 7 – Diagram of cochlear implant: A microphone placed above the ear converts sounds to electrical signals, which it sends to a speech processor worn behind the ear or attached to a belt. The speech processor is a computer chip that divides up and encodes the electrical signals by frequency, which our brains interpret as pitch. This frequency data and the power needed to activate the cochlea implant are sent, often via radio waves, to a receiver-stimulator implanted near the ear. This device decodes the sound information back into electrical impulses, with each of the frequency groups (channels) sent to eight or more different electrodes placed in the cochlea. These electrodes convey the signals to various portions of the auditory nerve, which then carries them to the brain (the ultimate processor) where they are perceived as speech and environmental sounds. *Image designed by Corporate Press.*

When such congenital hearing loss is not effectively treated early, it can lead to permanent problems with language development and linked learning and social difficulties. The Institute recommends screening newborns within the first month of life for hearing loss because children begin learning speech and language in the first 6 months of life. Most children who receive the cochlear implant and training before age 5 or 6 are able to speak and understand speech as well as their normal hearing peers, and those who receive the implant as infants or toddlers tend to develop language at the same pace as those with normal hearing.

Some experts in hearing were surprised by the success of the cochlear implants. How could a small number of electrodes mimic the sensitivity to sounds of the 15,000 hair cells seen in the ears of those who can hear adequately? That challenging question sent basic researchers scurrying back to the lab to try to find answers. What they discovered not only furthered understanding of how we hear, but made the prospects of giving sight to the blind an attainable goal.

From Redundancy to Artificial Retinas

It turns out that when it comes to hearing, only a fraction of the information on the frequency of sounds sent to the brain is needed to understand speech. Recent studies indicate that the normal cochlear divides frequencies into the equivalent of 28 channels before sending them to the auditory nerve, but we can hear with far fewer channels. Researchers at Arizona State University used processors to divide and compress the frequency bands in speech listened to by people with normal hearing. (The processing of the speech mimicked what is done by a cochlear implant.) Their studies reveal that as few as 8 channels are needed to discern speech adequately. Presumably, a lot of the complex sound information sent to the brain is redundant, experts now think, so one doesn't have to capture it completely to provide adequate hearing.

Part of the success of cochlear implants is also due to the amazing ability of the brain to see the big picture from sketchy information. For example, consider those personalized license plates that, due to the limited number of characters they can have, omit vowels yet are still understandable to the person reading them during a traffic jam. We see "LVMYDG" yet realize it stands for "Love my dog." Our brain is able to fill in the missing letters so we can read the license plate. Similarly, our brain can fill in missing frequencies so we can hear what people are saying to us.

Those of us with years of experience listening to people talk are better able to fill in the missing sounds. This may explain why people who have been deaf for a short time do better with cochlear implants than those with long-term deafness. But with proper training, many people who have been deaf for most of their lives can learn how to make sense of what they are hearing with their cochlear implants. Studies show that people with the implants do better at discerning speech over time as they gain more experience with them. This shows the remarkable plasticity of the brain that refutes the notion that the brain is permanently hard-wired.

However, studies in cats reveal that there does appear to be a critical window of time during which the part of the brain that processes sounds and fosters language skills develops most readily. These studies have mapped the sensitivity of various regions of the brain to various sound frequencies and found that when it comes to hearing, its all about location—high frequency pitches activate different minute sections of the brain than low tones. When kittens are deafened shortly after birth, their brains never develop this sound specialization unless their hearing is restored within a short period of time. Yet when these deafened kittens are given cochlear implants, the sound-processing regions of their brains appear to develop normally. This probably explains why cochlear implants are often so successful in young children, and has important clinical implications now that universal screening of newborns makes it possible to detect deafness by one month of age.

Battling Blindness

Encouraged by the success of cochlear implants and the findings on redundancy of nerve signaling and brain plasticity, researchers began to tackle in earnest the possibility of creating electronic eye prosthetics for people blinded by various diseases. Their efforts were not a literal stab in the dark, but hinged on more than a century's worth of basic research on the eye. This research had solved the intriguing puzzle of how light entering our eyes is transformed into images in our brain.

In early studies, anatomists discovered and drew in painstaking detail all of the eye's cellular components and the nerve pathway from the eye to the brain. But the functions of these eye components remained hidden until biochemists and electrophysiologists in the 20th century showed how the various cells in the eye responded chemically or electrically to light or darkness. Their research revealed that the kingpin of sight is the retina, the light-sensitive inner lining at the back of the eye. It is there that light encodes the scene before us into an image that is sent to the brain, much like film encodes an image captured by a camera.

The retina has a layer of cells called rods and cones that contain special pigments. When light strikes these pigments, it triggers a chemical reaction that creates electrical signals. These signals are passed to a layer of nerve cells called ganglion cells, which convey them to the optic nerve. The nerve travels from the eye to the brain, where the electrical signals are transformed into recognizable images (Figure 8). Throughout this visual pathway, the spatial configuration of all the elements seen is maintained. In other words, an American flag will be encoded in both the retina and the brain with stars on the upper left and stripes beside and below it. Because the retina plays such a key role in sight, damage to it can cause blindness. More than one million people in the United States are blind due to diseases of the retina that destroyed their rods and cones, according to the National Eye Institute (another one of the National Institutes of Health). There are no effective treatments for these disorders, which take a tremendous toll on patients. They need significant aid to carry on their daily tasks, let alone adjust to the psychological burden of no longer being able to have an independent lifestyle. With a growing aging population, the number of people affected by blinding diseases may triple by 2025, some experts predict, creating a future pandemic of vision loss. (Macular degeneration is a blinding vascular disorder in the eye that damages the retina and affects more than one-third of people 75 years of age and over.)

Until recently, it was assumed that destruction of the rods and cones would cause the ganglion cells to deteriorate as well. This frequently happens to tissues no longer fed signals from nerves. Eager to see if that was the case

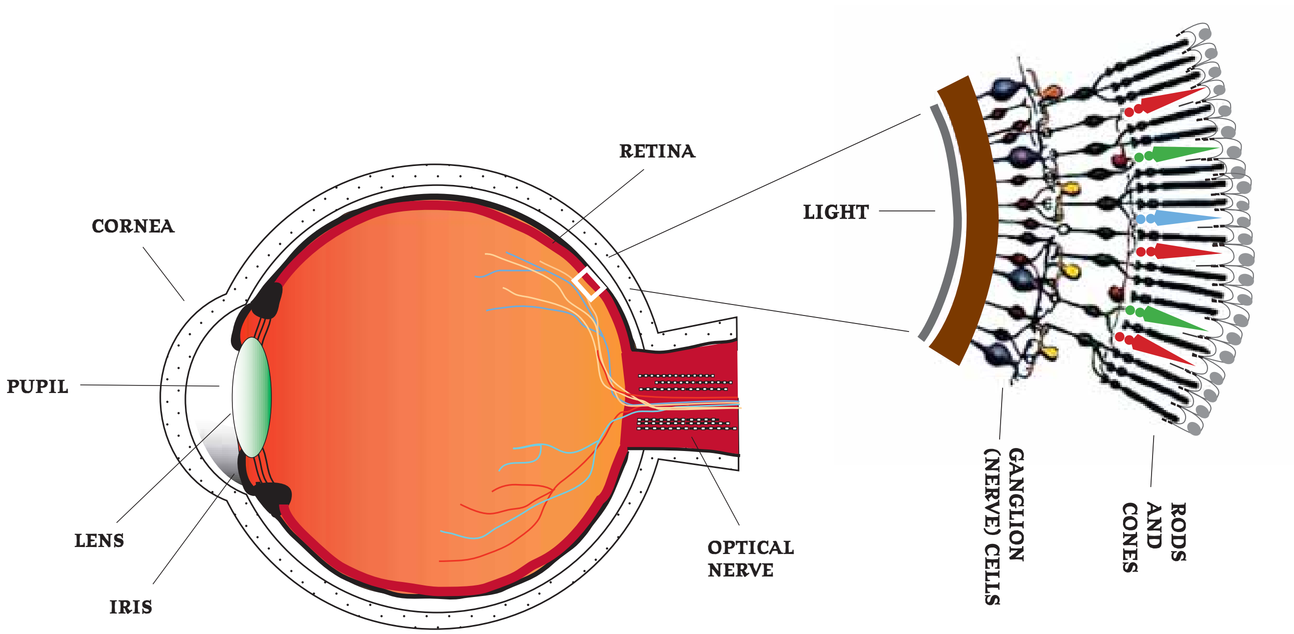

Figure 8 – Anatomy of the eye: Light entering the eye passes through to the retina, where specialized vision cells, called rods and cones, will be stimulated to set off a chain of reactions converting light to electrical impulses. These impulses are conveyed via ganglion cells, a type of nerve cell, to the optic nerve, which ultimately transmits them to the brain, where visual input is translated. Understanding how this circuitry works helped scientists create an artificial retina to restore some sight in those suffering from retinal damage. *Image designed by Corporate Press.*

was ophthalmologist and bioengineer Mark Humayun. Inspired by his grandmother, whose blindness developed during his teenage years and contributed to her demise, Humayun's doctoral research was a blueprint for a device that could act as a signaling rescue operation in eyes with damaged rods and cones. The success of that device hinged on having enough ganglion cells in the retina still working.

In the early 1990s, Humayun and his colleagues dissected the eyes of people with retinal diseases that were donated after death. He was thrilled to discover that even people with severe disease still had more than one-quarter of their ganglion cells and those with milder disease had most of these cells intact. But did those remaining ganglion cells still work? To test this, Humayun gave volunteers blinded by retinal disease a local anesthetic and then put tiny electrode probes in their eyes. These individuals all had major loss of their rods and cones. But when Humayun electrically stimulated different parts of their retina with the probe, the patients reported seeing streaks or dots of light. When two probes stimulated the retina at two different sites, patients reported seeing two different light bursts with the same position in space as the electrodes were on their retinas. This suggested that evenly spaced electrical stimulation of the remaining retina cells could preserve the spatial configuration of retinal signaling that is so important for sight.

Creating the Bionic Eye

But creating an implantable array of electrodes in the retina was a daunting task. Thinner than the tip of a pen and with the strength of a wet Kleenex, the retina could be easily torn by an inflexible device, or damaged by the heat released by the numerous electrodes needed to activate sufficient nerve cells. (More than a million nerve cells comprise the optic nerve compared to the 30,000 cells that make up the auditory nerve.) To top it off, any device implanted in the eye has to survive the corrosive effects of a salty world and deliver information to the brain quickly, so a person doesn't realize they are seeing a curb a minute after they trip over it.

To meet these bioengineering challenges, Humayan is collaborating with several engineers, materials scientists, ophthalmologists, neuroscientists and other experts funded by the Department of Energy, the National Science Foundation and the National Eye

Institute. The first artificial retina these researchers created is showing promise in tests on blind people. This device consists of a tiny camera and computer chip mounted on sunglasses that capture, code, and convert what is "seen," into electrical signals that are relayed to the ganglion cells via an electrode-studded computer chip. This chip is implanted in between the retina and the jelly-like inner portion of the eyeball (Figure 9). The minor amount of heat given off by the chip is carried away by the fluid in the inner eye so it doesn't build up and harm the retina.

After extensive testing of the implant in dogs and rabbits, Humayan finally implanted the first model of this artificial retina in 6 blind volunteers in 2002. Humayan didn't expect much from his pilot retinal implant model, which after all only has only 16 electrodes that are a far cry from the million nerve cells in the optical nerve. But, in what he has described as a defining moment in his life, testing of the patients revealed that they were able to distinguish a cup from a plate or a knife and detect movement of objects across a screen. This crude vision is helping some of these patients better maneuver in their environment—they can avoid a tree branch blocking their way because it appears to them as a bright white line, and they can discern a table or a door.

Such surprisingly good results were unexpected and attributed to the remarkable ability of the brain to learn and fill in the blanks when given sketchy signals. And to the patient volunteers, some of whom had been blind for 50 years, those sketchy signals were immensely rewarding. One patient was thrilled when he could see the shadow of his 18 year-old son, whom he hadn't seen since the boy was 5 years old. None of these volunteers have experienced surgical complications or damage to their eyes caused by the implant so far. The devices were not intended to last indefinitely, but in one patient it has continued to operate for more than 5 years.

By taking advantage of the recent advances in microelectronics, which enable more electrodes and processing power to be packed into smaller spaces, (see side bar) the Humayan group created a newer version of its artificial retina. This model has 60 electrodes and is currently being tested in a larger number of volunteers with the expectation that it will improve their unaided mobility. They have also developed an artificial retina with 200 electrodes that has many improvements over the previous two models. Thanks to innovative technology developed by collaborators at Lawrence Livermore

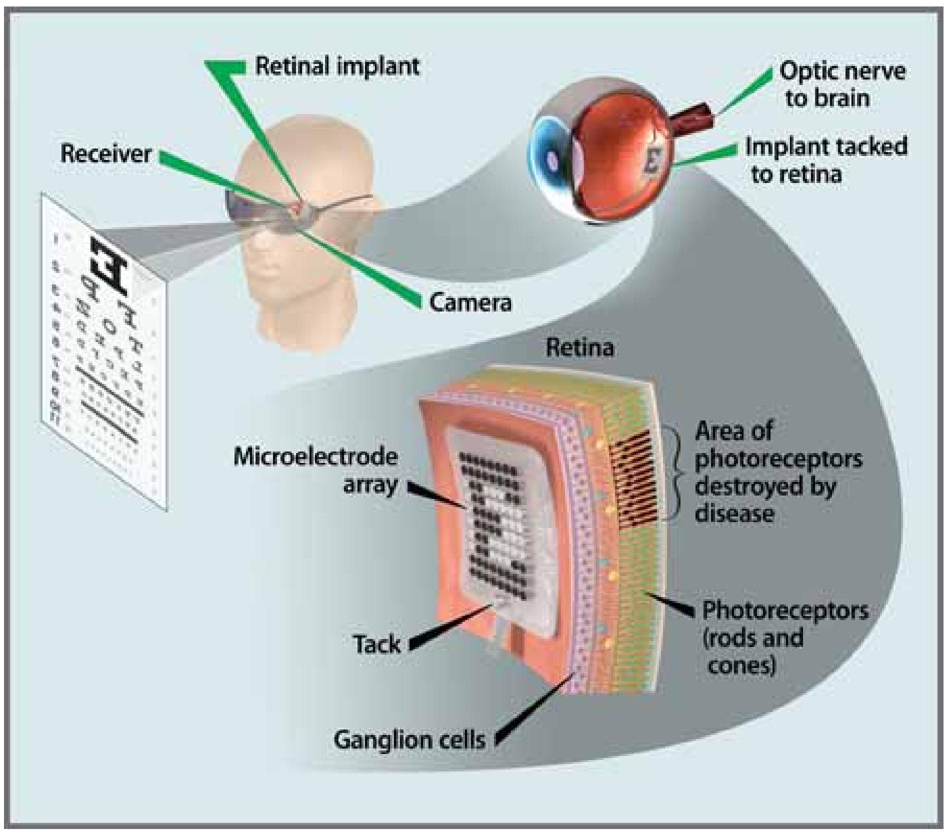

Figure 9 – Artificial retina: The camera and microprocessor substitute, in part, for the missing light-sensitive cells in the retina. The camera videotapes the patient's surroundings and sends a digital black and white version of the scene to the microprocessor. This computer chip compresses and simplifies the data it receives, and converts them into electrical signals. These signals are sent to the receiver and its attached wires that connect to the retinal implant, which is about an inch long and tacked to the retina. There the signals are passed on to the ganglion cells and the optic nerve, which carries them to the brain. A wireless battery pack, worn on a belt, powers the device. *Image courtesy of U.S. Department of Energy Artificial Retina Project, artificialretina.energy.gov*

National Laboratory, the most latest version of the implant is made of flexible silicon rubber with the thinness and consistency of plastic food wrap so that it can conform to the shape of the retina. It is also protected from salt corrosion by microscopically thin packaging developed by Argonne National Laboratory.

By 2011, the research team expects to start clinically testing a version that will up the number of electrodes in the artificial retina to 1000, which should enable reading and face recognition. The electrodes in this device are less than one percent the thickness of a human hair. Additional improvements will include a miniature video camera embedded in a contact lens that will be permanently implanted and replace the natural lens of the eye. This will enable users to more easily scan their environments by just moving their eyes. With the current model, users have to continually shift their heads to take in the whole picture (Figure 10).

Like the cochlear implant, the artificial retina requires some experience and training so patients learn to interpret what they are seeing. It is not expected to help people who were born blind and whose visual processing areas of the brain did not develop due to a lack of stimulation during that critical time in early childhood when the "if you don't use it you lose it" rule tends to govern brain development. It also isn't expected that an artificial retina—even one with 1000 electrodes—will provide the same detailed vision that a normal sighted person will see. But the hope is that it will enable most blind people to maneuver in their environment independently. There are more than twenty other research teams throughout the world who have developed other types of artificial retinas, and several of these models are currently being tested in people.

Closing the Gap for Amputees

The innovative technology that is helping the deaf hear and the blind to see is also being used in artificial limbs to make them much more functional and closer to the real thing than the standard models used by the thousands of people in this country who have had their arms or legs amputated due to injury or disease. This number is increasing with the return of American soldiers from Iraq, whose body armor kept them alive but did not always prevent them from losing limbs.

Most prosthetic limbs are quite limited in what they can do.

Engineering Sight, Hearing and Mobility

The development of artificial retinas, modern cochlear implants and smart artificial limbs has been spurred to a large degree by remarkable advances in microfabrication that is packing more electronics and processing power into smaller devices. This microelectronics revolution began in the 1960's when integrated circuits (silicon chips) were born. These are made by using light or x-rays to etch onto a thin silicon wafer a pattern of integrated transistors, which act as on-off switches in computers. Then a chemical process dissolves away everything but the etched circuit. Because this technique can squeeze together more transistors into tighter spaces, processing speed increases. This almost instantaneous "real-time" processing is critical for neural prosthetics that aim to imitate the nervous system.

Also spurring smart prosthetics are advances in computer sciences and mathematical modeling that can digest the tremendous amount of sound, visual or tactile data collected into key elements that are used to transform electrical signaling so it is meaningful to the brain. More recently engineers introduced a microfabrication technique to create micro-electro-mechanical systems (MEMS) including electrically driven motors smaller than the width of a human hair and microscopic electrodes. These microdevices are typically embedded in integrated circuits to add some "brains" (processing power) to the miniature machines.

Retinal implant: Advances in bioengineering and microelectronics have enabled the development of devices like the retinal implant shown in this picture. *Image courtesy of U.S. Department of Energy Artificial Retina Project, artificialretina.energy.gov*

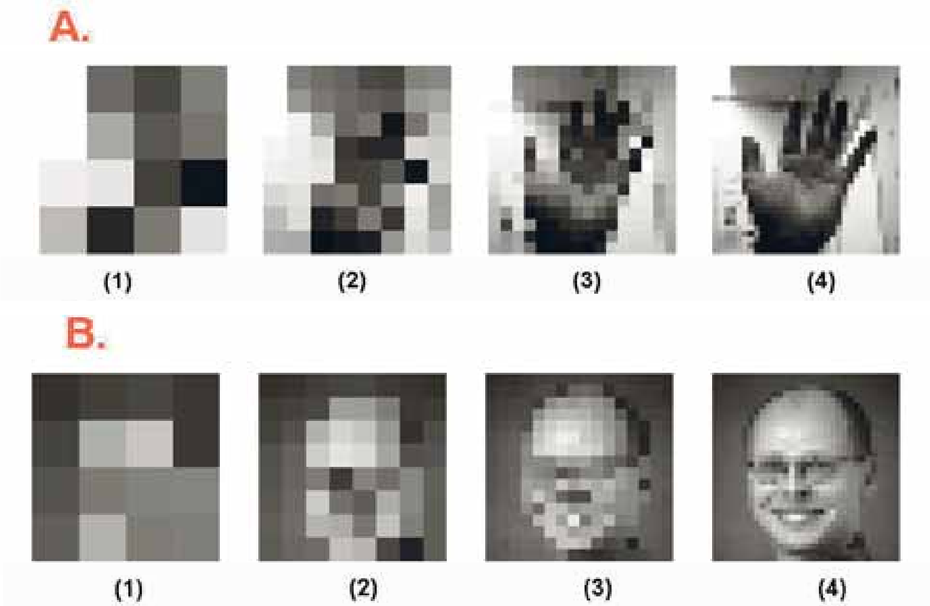

Figure 10 –What you see with an artificial retina: These images of a hand (A) and head (B) approximate what patients with retinal devices see. Increasing the number of electrodes (moving from 1 to 4) will result in enhanced visual perception and higher resolution vision. Scientists work with patients who receive artificial retinas for about one month after surgery to help them interpret what they see. Deaf individuals with cochlear implants also need such guidance to understand sounds they are hearing for the first time. Technology is also helping to improve processing of signals from retinal implants: the Artificial Vision Support System (AVSS), devised and developed by Dr. Wolfgang Fink and associate Mark Tarbell at the California Institute of Technology, performs real-time image processing/enhancement of the video-stream provided by the external camera to improve on the limited vision afforded by these implants for the benefit of the blind subjects. *Image courtesy of Dr. Wolfgang Fink and Mark Tarbell, Visual and Autonomous Exploration Systems Research Laboratory, California Institute of Technology*

Artificial arms, for example, use a system of pulleys and cables or electronic motors to enable them to bend at the elbow or pick up items with a hook that opens and closes. These prosthetics cannot restore the full range of motion and capabilities of a real arm—they may let you pick up a fork, but they don't let you feed yourself with it. They also require a lot of concentration to use—you have to not only manipulate the device with your other arm or nearby muscles, but you have to continually watch the prosthetic in action so it can pick up an Object or carry out some other function.

This is no surprise when you consider what our nervous system does every time we drink a cup of coffee. Our brain sends electric signals that travel to the motor nerves of our arm and hand. There they simultaneously trigger our hand and arm muscles to contract or extend so we can grasp the cup. At the same time, thousands of nerve cell sensors in our skin, muscles and joints of our hand and arm signal to sensory nerves and then the brain so we can feel the cup in our hand, gauge if we are grasping it tight enough or lifting it with enough force, as well as let us know where our arm/hand is in space. This information is quickly sent back to the brain which then uses it to guide our arm and hand motor nerves so we can lift the cup and precisely position it to our lips. Such a simple action requires our nervous system to instantly coordinate millions of electrical nerve impulses with a precision that we take for granted, and at which bioengineers marvel (Figure 11A).

When someone loses a limb or finger, the portion of the brain and motor nerves that once governed its movements continues to send signals to the missing body part, despite the fact that these signals never reach their target. Even the sensory nerves once connected to the amputated limb or finger will send signals back to the brain if they are stimulated any place along their pathway. For example, if a sensory nerve for touch that once was connected to the thumb of a missing hand is electrically stimulated at the arm level, the person will report feeling that something just brushed against his or her missing thumb. This lingering nerve signaling is why about three-quarters of amputees report that they still feel their missing limbs and have the urge to move them (Figure 11B). For example, when a motorcycle accident severed the left arm of Claudia Mitchell, she didn't even realize it was missing and couldn't understand why it wasn't working when she tried to use it to push herself up off the ground.

Fortunately, bioengineers are helping Mitchell and a handful of others by connecting the still

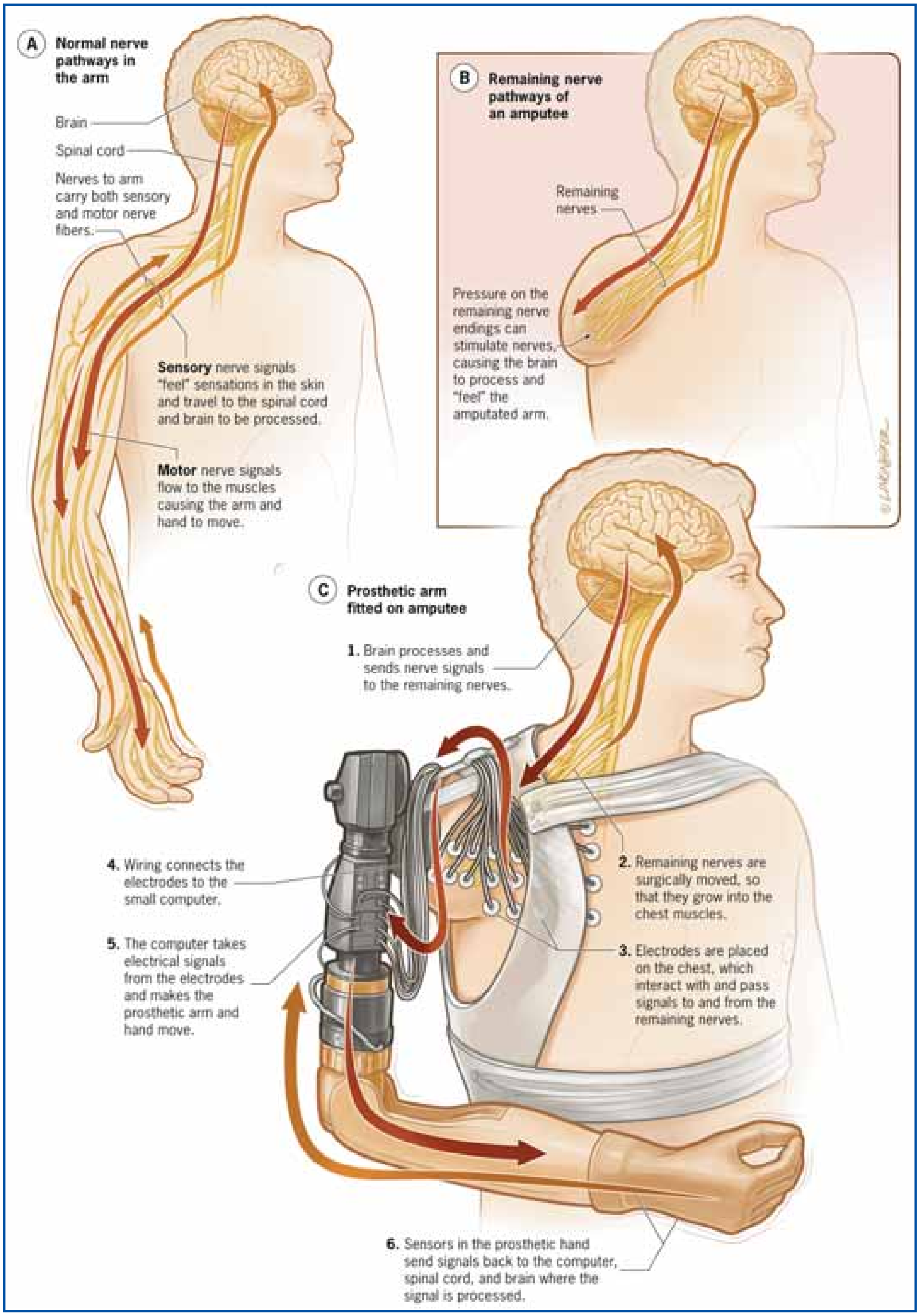

Figure 11 – Nerve signal transmission in a healthy arm (A), amputee (B), and neural prosthetic arm (C). *Images designed by Michael Linkinhoker, Link Studios, LLC.*

signaling nerves in their stumps to artificial mechanical arms fitted with pressure sensors. To do this, researchers funded by the Department of Defense and the National Institute of Neurological Disorders and Stroke attach superfine electrode arrays to the residual nerves of the missing arm to complete the electrical signaling communication loop from the brain to an arm prosthetic and back in volunteer amputees. Some of these electrodes connect with motor nerves and send their electrical signals to a computer that directs motors in an attached artificial arm to move the prosthetic appropriately. Other electrodes connect with the sensory nerve cells to convey

Figure 12 – Claudia Mitchell: After losing her arm in a motorcycle accident, Claudia Mitchell became the first woman to be outfitted with a bionic arm developed by the Rehabilitation Institute of Chicago. The neural prosthetic operates by detecting the movements of muscles in her chest that have been rewired to the stumps of nerves that once went to her amputated arm. *Credit: Anna Knott Photography.*

the signals sent from silicon-based touch pressure sensors on the prosthetic arm. These sensory signals are also sent to the computer and then the brain (Figure 11C). The end result is that amputees feel that the artificial arms are more a part of their bodies because they can control them intuitively, and they can sense what the arm prosthetics are touching and where they are in space.

For example, as soon as Mitchell thinks about opening her left hand, her artificial hand opens. She has been effectively able to use it to peel a banana, and cut a steak (Figure 12). Other amputees fitted with the new artificial arms can pull credit cards from their back pockets, or with their eyes closed have their "fake" arm mimic the position of their real arm. Researchers expect to eventually produce a prosthetic arm model with a plastic sleeve that not only looks and feels like skin, but has the feelings of skin as well, thanks to numerous sensors scattered throughout it. Bioengineers are also pursuing similar smart prosthetic legs. These are bound to benefit many of the nearly two million people in the United States living without a limb.

Galvani could not have imagined his basic research on nerve signaling in frogs would eventually blossom into artificial eyes, cochleas, and arms for people. But none of these smart prosthetics would have been possible if basic researchers from such diverse disciplines as physics, physiology, ophthalmology, computer sciences, mathematics and engineering hadn't explored how we hear and see and how the nervous system works. Collectively these scientists fostered the development of bio-engineered devices that can close crucial gaps in nerve signaling so that the deaf can hear, the blind can see, and amputees can have artificial limbs that feel and act like their missing limbs.

Biographies

Margie Patlak writes about biomedical research and health from the Philadelphia region. She has written for *Discover, Glamour, Physician's Weekly, Consumer Reports on Health, The Washington Post, Los Angeles Times, Dallas Morning News* and numerous other publications. She also writes frequently for the National Institutes of Health and the National Academy of Sciences. This is her seventh article in the Breakthroughs in Bioscience series.

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