No one knows whether these kinds of changes to nuclear structure trigger aging and disease or result from them, or both. In any case, it is clear "that if you mess around with the [nuclear] architecture, you can get disease," Misteli says. It might one day be possible to diagnose diseases and age-related problems simply by looking at nuclear snapshots, he adds.

Perhaps the biggest remaining mystery is how the nucleus gets organized in the first place. Do molecular scaffolds tether nuclear constituents in a deterministic way, or does genome activity affect positioning in a probabilistic manner? Evidence supports both theories, and Spector posits that RNA may play an important role. This past March he and his colleagues identified an RNA that helps to structure nuclear compartments called paraspeckles. Undoubtedly, the mechanisms controlling nuclear organization will prove to be varied and complex. As Spector puts it: "Things in biology tend to not be in black and white."

Melinda Wenner is based in New York City.

Technology

Tasting the Light

Device lets the visually impaired "see" with their tongues BY MANDY KENDRICK

The late neuroscientist Paul Bach-y-Rita hypothesized in the 1960s that "we see with our brains not our eyes." Now a noninvasive device trades on that thinking and aims to partially restore the experience of seeing for the visually impaired by relying on the nerves on the tongue's surface to send light signals to the brain.

First demonstrated in 2003 by neuroscientists at Middleton, Wis.–based Wicab (a company co-founded by Bach-y-Rita), the device could finally be ready for sale at the end of the year. Called BrainPort, it tries to substitute for the two million optic nerves that transmit visual signals from the retina to the brain's primary visual cortex. Visual data are collected through a small digital video camera mounted on the center of sunglasses worn by the user. Bypassing the eyes, the data go to a handheld base unit, which houses such features as zoom control and light settings as well as a central processing unit (CPU), which converts digital signals into electrical pulses.

From the CPU, the signals are sent to the tongue via a "lollipop," an electrode array about nine square centimeters that sits directly on the tongue, which seems to be an ideal organ for sensing electric current. (Saliva is also a good conductor.) Moreover, the tongue's nerve fibers are densely packed and are closer to the surface relative to other touch organs. The surfaces of fingers, for example, are covered with a layer of dead cells called the stratum corneum.

Each electrode on the lollipop corresponds to a set of pixels. White pixels yield a strong electrical pulse, whereas black pixels translate into no signal. The nerves at the tongue surface receive the incoming electrical signals, which feel a little like Pop Rocks or champagne bubbles to the user.

Typically within 15 minutes of using the device, blind people can begin interpreting spatial information via BrainPort, says William Seiple, research director at the nonprofit vision health care and research organization Lighthouse International. The electrodes spatially correlate with the pixels so that if the camera detects light fixtures in the middle of a dark hallway, electrical stimulations will occur along the center of the tongue. "It becomes a task of learning, no different than learning to ride a bike," says Wicab neuroscientist Aimee Arnoldussen, adding that the "process is similar to how a baby learns to see. Things may be strange at first, but over time they become familiar."

COURTESY OF WICAB

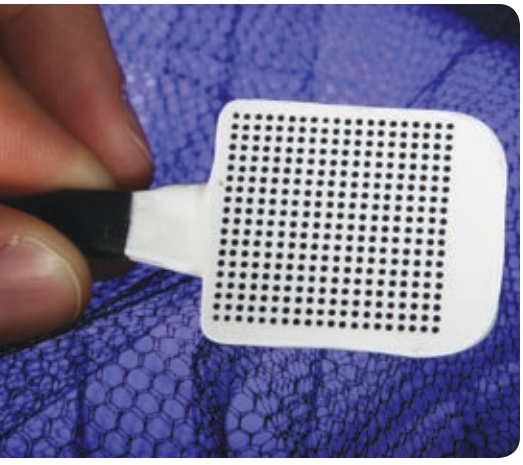
TASTE SENSATION: In a device called BrainPort, a sunglasses-mounted camera sends data to a handheld unit, which converts light to electrical signals that can be detected by the tongue.

Seiple works with four patients who are training with BrainPort once a week. He notes that his patients have learned how to quickly find doorways and elevator buttons, read letters and numbers, and pick out cups and forks at the dinner table without having to fumble around. "At first, I was amazed at what the device could do," he says. "One guy started to cry when he saw his first letter." The researchers have yet to figure out if the electrical information is transferred to the brain's visual cortex, where sight information is normally sent, or to its somato-

sensory cortex, where touch data from the tongue are interpreted.

To develop criteria for monitoring the progress of artificial sight, optometrist Amy Nau of the University of Pittsburgh Medical Center's Eye Center will further test BrainPort, along with other devices such as retinal and cortical implant chips. "We can't just throw up an eye chart. We have to take a step back and describe the rudimentary precepts that these people are getting," she says. Nau is particularly interested in BrainPort because it is noninvasive, unlike implants.

"Many people who have acquired blindness are desperate to get their vision back," she points out. According to the National Institutes of Health, at least one million Americans older than 40 are legally blind, with vision that is 20/200 or worse or that has a field of view of less than 20 degrees. Adult vision loss costs the country about $51.4 billion a year.



"LOLLIPOP" DEVICE is an electrode array that stimulates the tongue in a pattern based on the light intensity picked up by a camera.

Although sensory substitution techniques cannot fully restore sight, they do provide the information necessary for spatial orientation. Wicab had planned to submit BrainPort to the U.S. Food and Drug Administration for approval at the end of August, says Robert Beckman, president and chief executive officer of the company. He notes that the device could be approved for market by the end of 2009 for about $10,000 a machine.

Going with Golgi

Scientists create an artificial organelle for the first time

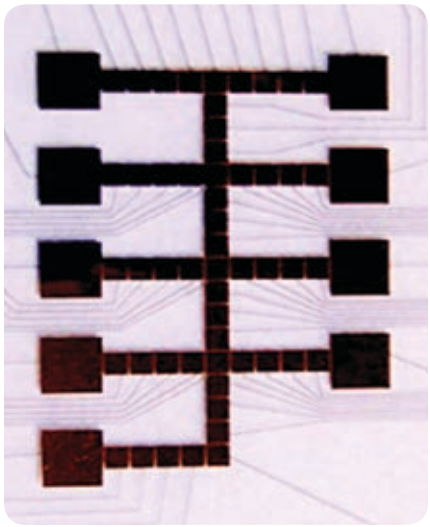
BY CHARLES Q. CHOI

In recent years scientists have made synthetic versions of key parts of the cell, such as chromosomes and ribosomes. Now researchers have developed the first working artificial prototype of an "organ" of a human cell—the Golgi apparatus.

Made up of a network of sacs piled together like a stack of pancakes, the Golgi apparatus chemically modifies proteins to help make them stable and functional, and it helps to manufacture complex sugars. But it remains one of the most poorly understood organelles. "The sacs are fluid and constantly change shape, so it's difficult to get a handle on," explains Robert Linhardt, a chemist at Rensselaer Polytechnic Institute. "And while we know the general direction of the flow of vesicles between stacks, we don't really know what cargoes they're carrying."

To better dissect how the Golgi apparatus works, Linhardt and his colleagues created a synthetic version of it, designing a square-millimeter-size lab-on-a-chip to mimic the assembly line of enzymes that modify a biomolecule within the Golgi apparatus. The sample molecules are attached to magnetic particles suspended in a watery droplet 300 billionths of a liter in size and placed on the chip. When the desired location on the chip for those molecules is electrically charged, it attracts the droplet and causes it to flow there. A larger magnet under that spot can keep in place the magnetic particles attached to the biomolecules. In this way, the drop can be moved through chambers loaded with an assembly line of enzymes, sugars and other raw materials.

In experiments with an inactive precursor of heparin, a widely used blood thinner, the scientists discovered their device could quickly and efficiently modify the anticoagulant to make it functional, findings they detail in the August 12 *Journal of the American Chemical Society*. The researchers suggest that an artificial Golgi could lead to a faster, safer method of producing heparin than current techniques, which employ animal tissue.



ARTIFICIAL GOLGI APPARATUS uses voltage to shuttle molecules among nine electrodes, where they are modified by enzymes.

Scientists have experimented with building up cells piece by piece for decades, including the creation of simple artificial cells in the form of bubbles made of synthetic cell membranes, to better understand how life on earth might have began. In 1997 researchers devised the first artificial human chromosome. And earlier this year molecular technologist George Church of Harvard University and his colleagues developed artificial ribosomes—bodies inside each cell that make proteins based on instructions from DNA—that functioned under cell-like conditions.

Linhardt and his co-workers plan on creating a synthetic endoplasmic reticulum (ER) as well, the organelle into which ribosomes are studded and where protein synthesis and folding take place. "We'd even like to integrate an artificial Golgi and ER together," Linhardt says. "We're basically taking pieces of a cell and making them on electronic chips," with the hope of moving to even more complex systems.

Charles Q. Choi is a frequent contributor based in New York City.

COURTESY OF WICAB ("*lollipop*" *device*); COURTESY OF ROBERT LINDHART *Rensselaer Polytechnic Institute (artificial Golgi)*