Making Sense of Our Senses

When people express their love of life, they often describe corporeal sensations—the taste of dark chocolate, the rapture of listening to Mozart’s complex symphonies, or the radiant vision of the sun rising above the sea. While the emotions our senses elicit have moved our souls for ages, sensory neuroscientists are only now beginning to understand how the brain encodes and processes the information inundating our bodies. Understanding the basic mechanisms underlying our perceptions is only one area of sensory science in which scientists are building their careers. Others are translating these research findings into innovations that improve how we experience life, from restoring hearing loss to dampening pain to enriching the scents and flavors of every day products. By Amy Maxmen

Technological advances in areas such as induced pluripotent stem (iPS) cell systems, DNA sequencing, and optogenetics have been accelerating every aspect of sensory science over the past decade. Ruth McKernan, the chief scientific officer of the pain and sensory disorder unit at Pfizer’s Neusentis, based in Cambridge, U.K., is well aware of the recent technological tidal wave. Having entered sensory science in the early 1980s as a graduate student studying neuroscience at the University of London, McKernan has seen the trends change from her studies of neurotransmitter release at single synapses in the rat brain to the ability to now analyze the activity of hundreds of neurons at once.

“This field has been revolutionized by technology,” McKernan says. “We can now answer questions using very large datasets,” drawn from the genetic analyses of hundreds of people and from electrophysiological experiments measuring the output from many neurons synchronously, in real time. Researchers are beginning to learn how the brain integrates thousands of scattered bits of information into recognizable smells, tastes, and objects. And industry scientists are markedly more focused on applying this knowledge and learning to manipulate receptors that respond to the external environment or transmit information.

At Pfizer, for example, McKernan’s team puts the bulk of their sensory science efforts into pain research. With a prescription painkiller market worth more than $40 billion (according to the research report “Pain Management Review and Outlook 2011”), many major pharmaceutical companies are working to develop treatments that are superior to ones that currently exist. Smaller, yet significant efforts in industry also go toward developing treatments for hearing loss and vision problems. “Vision and hearing are more minor industry research areas compared to pain,” says McKernan, “but they will be growing in the future as we learn more about how these senses work, and develop ways to treat disorders with small molecules, antibodies, and stem cells.”

In addition to designing treatments for sensory system malfunctions, jobs are available in the private sector for neuroscientists who want to enrich the lives of our sentient selves. Companies built around this goal serve a sustained need, says Ahmet Baydar, the vice president of global research and development at International Flavors & Fragrances, based in Union Beach, New Jersey. He says, “Our industry will be around as long as people eat and drink, and want to smell nice.”

—Ahmet Baydar

Designer Tastes and Smells

Scientists moved closer to understanding the neurological mechanisms of olfactory perception after Richard Axel and Linda Buck’s 1991 Nobel-winning discovery of about 10,000 genes that encode odorant receptors. Each receptor detects a discrete number of odorous molecules in the air and sends signals to the brain for processing.

Researchers can grow their careers around expanding upon this basic knowledge or finding creative applications for this research. For example, there are about 60 scientists who focus exclusively on taste and smell at the Monell Chemical Senses Center in Philadelphia, Pennsylvania. There, sensory neurophysiologist Johannes Reisert seeks to understand fundamental questions about how smell works through recording the electrophysiological properties and analyzing the gene expression of olfactory cells while mice are exposed to a variety of scents. Other Monell researchers investigate questions geared toward real-world solutions since some

Upcoming Features

Regional Focus: China—November 15
Faculty—February 7
Postdoc—February 28

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Investigating how mosquitoes seek out their hosts using olfaction. Learning about the genetics of their projects is funded by food, fragrance, and drug companies that are looking for advice. For example, a company may be interested in how to mask the bitter taste of a medicine. To address this, Monell researchers investigate how bitter taste receptors function or how bitterness interacts with other sensory information. Reisert enjoys talking about real-world problems with people who visit Monell from industry, because “it puts us into a more translational mindset so that we seriously consider how our work could be applied in the real world,” he explains.

With a world full of people buying food, wine, shampoo, and other sundries based on taste and smell, scientists will find no shortage of opportunities in companies that cater to the senses. Baydar, at International Flavors & Fragrances, says the company’s sales continue to increase in both developed and emerging markets. The company employs a few hundred scientists with neuroscience, molecular biology, and chemistry backgrounds who focus on a variety of questions, such as how to reduce a food’s salt content without changing its taste. The company’s researchers must design creative, noninvasive ways to assess how people’s brains respond to taste and smell. For that reason, when interviewing job candidates Baydar looks for signs of creativity and the ability to design and run research projects. A good publication record or the ownership of patents often indicates these qualities, he says. Baydar does not assign projects, but asks scientists to come up with their own using the company’s resources. For example, the company’s impressively large database of color-odor associations can be used by researchers, he says, to “look for correlations … to understand why certain fragrance mixtures relax people, energize them, or make them happy or sad.”

Not all taste and smell research is geared toward improving products for human consumption; some research is designed to help with disease interventions. At Rockefeller University in New York City, neuroscientist Leslie Vosshall has dedicated her career to studying how olfaction affects behavior in a variety of animal models. With funding from the Bill and Melinda Gates Foundation and the Howard Hughes Medical Institute, she has been investigating how mosquitoes seek out their hosts using olfaction. Learning how to disrupt this ability could lead to interventions that end mosquito-transmitted diseases, such as malaria and dengue fever. In another project, Vosshall studies how hunger in Drosophila melanogaster intersects with their perception of smell. The Boston-based nonprofit organization, The Klarman Family Foundation, supports the project because such avenues of research could shed light on the biological basis of eating disorders.

The diverse portfolio of Vosshall’s funding stream is no accident. “Food intake and appetite are sensory issues,” Vosshall says. Although researchers should never pursue projects that do not interest them scientifically, she advises, scientists should think about how their interests might coincide with those of foundations willing to support basic sensory science. After all, grants from the National Institutes of Health (NIH) have become quite difficult to get as federal budgets tighten. “The secret recipe for staying in the business is to diversify your funding portfolio,” Vosshall explains.

**AMPLIFYING THE SOUNDS AROUND US**

How slight vibrations within the eardrum communicate all of the qualities of sound continues to intrigue scientists, who are still working toward more fully understanding the inner workings of the auditory system. Much research is specifically focused on the causes and repair of inner ear hair cell damage, a common cause of deafness.

**Jim Hudspeth,** a neuroscientist at Rockefeller University studying hair cell development sees sound research moving in two directions: molecular and integrative. “One line of research focuses on how [hair] cells change sound into electrical signals and how they amplify inputs,” he says. The other direction asks questions such as “how are complex sounds analyzed and converted into language?” Or, “how do we lock in on a conversation and avoid the noises going on around it?” he explains. Neither research avenue is linked to a single technique, and both typically require specialized laboratory equipment to conduct hearing research.

Hudspeth uses a zebrafish model because the hair cells are more accessible than those found in mammals. His research uses gene expression analysis, mechanical and electrical recordings, and mathematical modeling of how vibrations are amplified through the auditory system. Hudspeth recommends that early career scientists who are interested in the field find laboratories equipped with soundproof rooms and tools for measuring sound, or look for positions that offer generous startup grants and access to a skilled technician since it may be necessary to build and equip a specialized space.

While hair cell regeneration remains a subject for basic research, technologies that improve hearing, such as cochlear implants, have been in use for decades. These implants replicate hair cell-induced auditory nerve transmission using stimulators and an electrode array. **Jim Patrick,** the chief scientist at Cochlear, a company for cochlear implant products based in New South Wales, Australia, was hooked on the technology from the moment his team placed the first cochlear implant in a deaf volunteer in 1978. With the implant, the patient was able to hear sounds, just well enough to make out what people’s lips were saying. “It’s the most amazing feeling to help change people’s lives,” Patrick says. Since then, the company has developed five generations of implants that have provided progressively better hearing.

**Abhijit Kulkarni,** the vice president of research and technology at Advanced Bionics, a cochlear implant company based in Valencia, California, says that scientists at the company benefit from skills in biomedical, electrical, or biomechanical engineering that continued>
CONSTRUCTING VISUAL REALITIES

To understand how the brain converts patterns of light into images, scientists often study individual components of the visual system. For example, to study object recognition, Margaret Livingstone, a neurobiologist at Harvard Medical School in Boston, measures the neuronal activity in the temporal lobe of monkeys as they look at different items. Livingstone figures out how that information is processed into object recognition using specialized software programs. For this type of research, she explains, a background in computer programming is necessary since her team performs a lot of data analysis. She recommends that scientists who want to grow their career in vision science take programming classes or workshops, which are routinely held at various universities.

Beyond studying how the brain integrates visual information, some scientists in academia and industry are using visual neuroscience in ways that might not have been predicted 20 years ago. For instance, Nicola Rohrseitz, the founder of ViSSee, based in Zurich, Switzerland, and his team have developed a software platform that makes cameras function like a fly eye, which can measure speed and distance between obstacles while in motion. In graduate school, Rohrseitz modeled how the fly eye recognizes and assesses this information, and his team at ViSSee now uses these models to program software that will translate the data into action. The technology has been used to create “touchless screens” that can detect the hand gestures of surgeons, for instance, to control high-tech equipment, such as CT scanners.

TOUCHING UPON TREATMENTS

Touch may be the first sense that humans develop in the womb, although it might also be the least understood of the senses, says Richard Vickery, a neuroscientist at the University of New South Wales in Australia who studies how the cat brain responds to touch.

Perhaps the lack of information on touch might account for the dearth in adequate pain medications in the United States. Even though over $40 billion worth of prescription pain medications are sold each year in the United States, the drugs do not provide relief for more than half of the 100 million Americans living in chronic pain. These drugs also come with risks like addiction and liver damage. Recently, Congress requested that the NIH and the U.S. Food and Drug Administration increase their focus on pain research.

In order to discover more effective pain medications, Clifford Woolf at Harvard Medical School examines how the nervous system processes injuries to sensory fibers, and how the extent of that processing differs among people with different genetic backgrounds. Using this information, he also hopes to create better animal models for pain research by inserting mutations underlying specific pain-inducing diseases in humans into the mouse genome. “There have been many failures in Phase 2b studies of pain medications that looked wonderful in rodent models,” Woolf says, “which raises the worry that the mouse models we are currently using are not good predictors of human efficacy.” Funders apparently agree with him. Recently his project to create better mouse models was supported by a neuroscience consortium funded by the Massachusetts Life Sciences Center that involves scientists from universities in Massachusetts and seven international pharmaceutical companies.

Many biopharmaceutical companies support research and development in the area of pain management. Pfizer’s McKernan says the company focuses on the different ways in which pain works, and on genomic analyses of patients with genetic pain disorders like erythromelalgia—linked to mutations in a gene encoding a sodium channel, causing sufferers to feel as though their limbs are burning—so that they might develop more personalized treatments. While one person might benefit from a drug that blocks ion channels, for example, another might be better off with one that activates opioid receptors. When hiring, McKernan explains, “We are interested in people with expertise in bioinformatics, electrophysiology, genetics, and iPS cell technology.” She adds that Pfizer often collaborates with scientists in academia, and students who are curious about drug discovery might consider a postdoctoral fellowship at the company. “Learning something that no one knows is a privilege, but to then turn that into something that helps people, that’s just the best thing you could hope for out of your job,” says McKernan.