farms into rivers.

Crop plants aren't the only culprits: 40% of the world's grain goes to feed livestock, which produces mountains of nitrogen-rich manure. The Netherlands illustrates the challenges: There, strict rules since 1986 have required steps such as keeping manure covered or plowing it into fields. But nitrogen still escapes, wafting off the fields as ammonia or washing into streams, says Jan Willem Erisman of the Netherlands Energy Research Foundation: "You can put it in the soil, but it comes out anyway."

The best way to address that problem—other than decreasing meat consumption—would be to reduce the amount of nitrogen animals release in the first place by feeding them a precise amino acid ratio, said Henry Tyrrell, an animal scientist at the U.S. Department of Agriculture; it's unneeded proteins that wind up as the nitrogen-rich urea in an animal's urine. But such precision feeding would be expensive.

Indeed, cost is a factor in many of the technological fixes suggested at the meeting, such as capturing NO_x produced by power plants for fertilizer. As long as energy prices stay low, making synthetic fertilizer will always be less costly, researchers said. "It's much too cheap," Erisman says. Confronting the unyielding economics of the Haber-Bosch process may be policy-makers' biggest challenge. —JOCELYN KAISER

OLFACTION

Smell's Course Is Predetermined

New studies suggest a high level of hardwiring in the olfactory system, perhaps explaining instinctual reactions to some scents

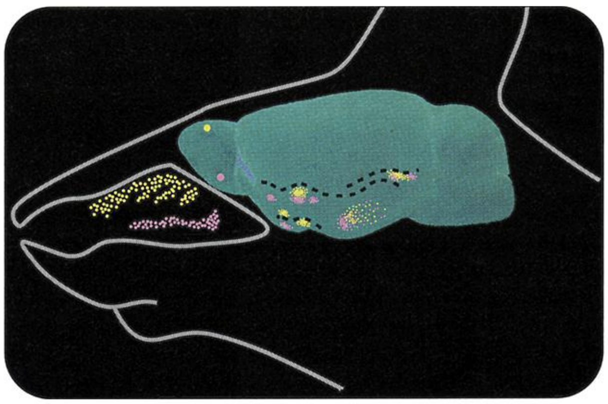
From the aroma of coffee enticing us to rise and shine to the alarm we feel at the acrid smell of smoke, our brains are constantly responding to odors. The brain can differentiate the smells of thousands of chemicals, should they happen to waft into our noses and tickle sensory neurons located there. But how those neurons pass information to the brain, and how the brain processes it to discern, say, the scent of an orange from that of a tangerine, has remained a mystery.

Two papers in the 8 November issue of *Nature* provide new insights into how the brain is structured for sorting out smells. In one study, Linda Buck and her colleagues at Harvard Medical School in Boston traced the connections of odor-responsive neurons in the brains of mice, providing the first glimpse of how the olfactory cortex, the part of the brain that processes odors, organizes incoming signals. In separate work, Liqun Luo's team at Stanford University revealed how links form between odor-responsive neurons and the brain.

Both papers suggest that the olfactory system is highly genetically programmed, or hardwired, perhaps more so than vision and other sensory systems, says olfaction researcher Leslie Vosshall of Rockefeller University in New York City. And that may help smells to directly trigger instinctual behavior, some researchers speculate.

The sensation of a smell begins when odor molecules bind to receptor proteins on sensory neurons in the nose. Mice have millions of sensory neurons, each bearing one of about 1000 different types of receptors on its surface. Those neurons send extensions called axons to a brain area called the olfactory bulb. Whereas neurons that bear the same receptor type are scattered rather randomly inside the nose, their axons sort out neatly, converging in each half of the bulb onto one or two structures called glomeruli, each of which receives input from only one receptor type. Most smells consist of multiple odor chemicals; the receptors they trigger send signals to a small subset of the 2000 or so glomeruli in the olfactory bulb.

But what happens to the signals at the next step—the olfactory cortex—has been unclear. "The olfactory cortex has been terra incognita," says neuroscientist Lawrence Katz of Duke University Medical Center in Durham, North Carolina. Some researchers have speculated that the connections linking the olfactory bulb to the cortex may be random and that the brain may learn to recognize the pattern each odor produces. Others suspected that there must be some predetermined order in the olfactory cortex; now Buck's team has found that to be true.



Connect the dots. Buck's team traced the connections of sensory neurons bearing two different olfactory receptors (yellow and pink) from sites in the nose (left), to one glomerulus on each side of the olfactory bulb (near the nose), to multiple spots in the olfactory cortex.

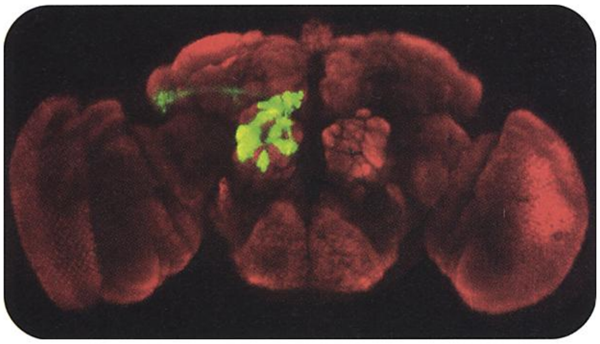
CREDIT: Z. ZOU AND L. BUCK

The team discovered the organization of connections by marking the pathway of neurons that receive signals from an individual type of odor receptor. Zhihua Zou and Lisa Horowitz in Buck's lab inserted the gene for a marker protein called barley lectin next to the gene for an olfactory receptor protein in mice. Neurons bearing that receptor made barley lectin and transferred the marker to connecting neurons, enabling the team to trace the olfactory neurons' connections through the olfactory bulb to the olfactory cortex.

The researchers did this with two odor receptor genes. In each case, they found one or two stained glomeruli on each side of the olfactory bulb, as expected, and multiple clusters of stained neurons in the olfactory cortex. And the pattern of staining was clearly not random: For each receptor type the pattern was the same in all the mice. That shows for the first time "that there is order in the projection from the bulb to the cortex," Katz says.

What's more, the data suggest that pathways from different receptors converge in the cortex, an important feature if their signals are to be compared and processed. Buck's group deduced this because in the olfactory bulb, each receptor is represented in 1 out of 1000 glomeruli in each half of the bulb, or 0.1% of the bulb's area. But when a receptor's projections reach the cortex, they occupy about 5% of the area, suggesting that individual olfactory cortex neurons receive input from up to 50 different olfactory receptors. "Those signals have to be brought together," says Harvard olfaction researcher Catherine Dulac, to enable the brain to analyze and distinguish among the patterns triggered by different smells.

Luo's team, meanwhile, has filled in information about how neurons form the links that carry olfactory signals. In fruit flies, so-called "projection neurons" pick up the signal in the glomeruli and carry it to the fly's equivalent of the olfactory cortex. But what determines which connections those neurons make? The neurons might have no special instructions but wait for sensory



Marked. Stained projection neurons (green) in a fruit fly brain connect to glomeruli (bright green, foreground) and to higher brain areas (fainter green lines to the left).

input to guide them, as happens in the visual cortex. Alternatively, instructions may be programmed into the projection neurons from their birth—which is what Luo's team found.

The 150 or so projection neurons are born sequentially from cells called neuroblasts. Graduate students Greg Jefferis and Lisa Marin marked projection neurons, using a shock of heat to turn on a marker gene in only those neurons being born during the heat shock. By varying the timing of the heat shock, the researchers could label different neurons in the birth sequence.

The researchers heat-shocked thousands of fly larvae at various times in development. They found that the neurons that made connections with particular glomeruli always seemed to be born at roughly the same time. That suggested that, from the time a projection neuron is born, it knows which glomerulus to connect to. In a separate analysis, the team labeled neuroblasts, which then transferred the label to all of their progeny born after that time. In flies labeled early, a full set of glomeruli showed up. As the labeling time moved later, one by one the marked glomeruli disappeared. "They drop out in a defined sequence," says Luo. "There is no exception." The two analyses, Katz states, provide "absolutely compelling" evidence that the projection neurons get their marching orders at birth, based on when during development the neuron emerges.

Indeed, the picture drawn by both papers is that "the organization of this very complicated sensory system seems to be highly predetermined," says Rockefeller's Vosshall. And to many researchers, that makes a lot of sense. Smells are tightly linked to many instincts. If a young mouse had to learn from experience that the smell of coyote urine means danger, Vosshall notes, it may not get a second chance to use that information. It would be much more adaptive, she argues, for the coyote-urine smell to be hardwired into the animal's fear center by natural selection.

—MARCIA BARINAGA

ZOO BIOLOGY

A Fertile Mind on Wildlife Conservation's Front Lines

Renowned for getting captive elephants to breed, Thomas Hildebrandt and his team are extending their prowess to scores of other rare species

BERLIN—Few people in the world are as intimately familiar with the elephant cervix as Thomas Hildebrandt. That particular knowledge may not make the 37-year-old veterinarian a hit at a cocktail party, but it has won him admirers in zoos around the world. Hildebrandt and his colleagues at the Institute for Zoo Biology and Wildlife Research (IZW) in Berlin have pioneered an innovative approach—artificial insemination (AI) technology aided by ultrasound—to impregnate half a dozen elephants, raising hope that zoos will be able to maintain their populations of these hard-to-breed creatures.

Hildebrandt's ultrasound techniques "have revolutionized our ability to assess elephant reproductive health," says Janine Brown of the Smithsonian National Zoological Park in Washington, D.C., where an elephant named Shanthi is expected to give birth next month—thanks to the "Berlin Boys," as the IZW team is known.

These days, the team's prowess at making babies is in high demand. Scores of zoo elephants are nearing the end of their life-spans, while recent laws have made it nearly impossible to import endangered species from the wild. Without AI, say several experts, zoo elephants could all but disappear within 2 decades. Other rare animals are also falling for the charms of these high-tech love doctors. Hildebrandt and colleagues Frank Göritz and Robert Hermes have used their ultrasound instruments to probe the internal organs of more than 200 species, including giant pandas, Komodo dragons, endangered European brown hares, and even invertebrates: Hildebrandt has used his technique to sex an octopus at Washington's National Zoo. "He'll ultrasound just about anything that lives or crawls," says Richard Montali, head of the National Zoo's pathology department.

The face of elephant husbandry. Thomas Hildebrandt and his probe have become intimate with the reproductive systems of animals ranging from Komodo dragons to octopuses.

The team is currently working its charms on the rare white rhinoceros. This rhino has been hunted nearly to extinction for its horn, rumored to have aphrodisiac powers. Such power has sadly eluded white rhinos in captivity, where they have managed to breed successfully only a handful of times. The IZW researchers have pioneered techniques for both sperm collection and artificial insemination in the rhino, and they are waiting to hear whether an animal that they treated last month is pregnant. The Berlin Boys "are a sterling example of how science can work to the benefit of endangered species," says Michael Keele of the Oregon Zoo in Portland, coordinator of the national species survival program for elephants in the United States.

Key to the team's success is ultrasonic imaging, used in human medicine to visualize organs without penetrating the skin. A probe emits high-frequency sound waves, which tissues absorb or reflect to different degrees depending on their density. Although technicians can image a fetus by moving the probe outside a woman's abdomen, an elephant's skin and muscle layers are so thick that the sound waves cannot penetrate to the internal organs. Researchers can glimpse the animal's reproductive tract only from a closer vantage point: inside the digestive tract. Donning a shoulder-length glove, one of the team members inserts the specially designed ultrasound probe through the rectum and more than a meter into an elephant's colon and points it toward the reproductive organs. Although endoscopy exams are noto-

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