A Primer on Smell

By Elise Hancock

In addition to bringing out the flavor of food, what does the sense of smell do for us?

Smell "gives us information about place, about where we are," says Randall Reed, a well-known Hopkins neuroscientist whose specialty is the sense of smell. And smell tells us about people. "Whether we realize it or not, we collect a lot of information about who is around us, based on smell," says Reed. And about food.

Odors can also warn of trouble--spoiled food and leaking gas (today), cave bears (once), or fire (any eon)--even at a distance. "It's a great alerter," offers Donald Leopold, a Hopkins otolaryngologist. "If someone lights a cigar three offices down, you know it right away."

Smell can also evoke remarkably intense emotion, just with a simple scent. Music stimulates emotion, too, but it typically takes an entire symphony or song to make anyone burst into tears. With music, "I think it's a result of higher processing," says Reed. But fragrance, he points out, can do it to you with a single odorant, by the smell's associations, and the conscious mind need not be involved. Say the smell is purple petunias, which have a rich spiciness no other petunia has, and say your mother died when you were 3. You wouldn't need to identify the smell, or to have conscious memories of your mother or her garden, to feel sad when that sweet tang drifts up to the porch.

Do all creatures have a sense of smell?

That's a good question, if you ask it in another way: Do all creatures directly sense chemical molecules? Seemingly so, even if they lack a nose. Moths have chemical receptors on their antennae, flies on their feet. Even bacteria will cluster around one chemical and avoid others. Salmon and trout find their way back to their original spawning areas by smell.

Smell in that broad sense is thought to be ancient, because its fundamental structures are similar in species all the way from fish to moths to primates. In all species, chemical receptors do their work in a fluid medium (mucus for human smell), as would be expected if this sense formed in primeval seas. All smell receptors are self-renewing (practical, since they're exposed to the world at large, including toxins). And all smell receptors report directly to the brain (in primates to the old part of the cortex), without

intervening synapses in the thalamus.

Compared with other mammals, how well do people detect smells?

That depends what you mean by "how well." We are low on receptors: Current estimates say that humans have roughly five million olfactory receptor cells, about as many as a mouse. A rat has some 10 million, a rabbit 20 million, and a bloodhound 100 million.

"Across species, there is a relatively good correlation between the number of receptor cells and olfactory acuity," says Reed. "You can hardly find the olfactory bulb in a human brain--it's a pea-sized object. In a mouse, it's a little bigger. It's bean- sized in a rat, about the size of your little finger in a rabbit, and the size of your thumb in a bloodhound."

Oh. So our sense of smell is not very acute.

Not exactly. While we may not have the olfactory range of other creatures, the receptors we do have are as sensitive as those of any animal. Several recent papers indicate that humans are capable, at least in experimental conditions, of smelling a single molecule. If so, in that sense not even a bloodhound could hope to do better.

We can also think, making conscious (and successful) efforts to sort smells out. A trained "nose," a professional in the perfumery business, can name and distinguish some 10,000 odors. Reed says that a master perfumer can sniff a modern scent that has a hundred different odorants in it, go into the lab, and list the ingredients. "In a modest amount of time, he comes back with what to you or me would smell like a perfect imitation of that perfume. It's amazing." Similarly, using smell alone, trained wine tasters can tell you a wine's alcohol content, year of production, grape variety, and even the district in which the grapes were grown.

While a few people do have a dramatically better sense of smell, most of us probably just don't pay attention. "Noses" say that their abilities are a matter of training, in which the important thing is to practice, to make the distinctions conscious, and to attach words to each one. That makes sense, given the acute sense of smell found in the few remaining aboriginal peoples of the world, for whom smell remains a matter of survival.

Physically, how does the sense of smell work?

Smell receptors in the innermost parts of the nose bond to gas molecules from the air. The receptors then send electrical signals to the olfactory bulb, which signals the orbitofrontal cortex, where the firing pattern reveals to the rest of the brain what smells so nice (or bad) out there. Most receptors (though not all, according to preliminary research in Don Leopold's lab) are arrayed in two dime-sized patches, one per nostril.

The genetics and biochemistry of the system are a hot field of study, and much of what's known is new. The first gene for a smell receptor was discovered as recently as 1991, by

a team from Columbia. That triumph broke the subject wide open.

One major surprise, discovered in 1992, is how very many receptor types take part in smell--500 to 1,000, researchers infer from genetic evidence. By contrast, color vision uses three receptor types, taste four or five, and hearing only two.

Several hundred receptors sounds like a lot, except that the world has thousands and thousands of different odors. How can we distinguish so many?

Because we don't need a special receptor for each individual odor. Current thinking holds that each receptor type bonds to one or several specific molecules, according to shape. Researchers often describe the system in terms of locks and keys, because only the right odorant will unlock the receptor. The fit must be precise even to the molecule's handedness.

For instance, a left-handed carvone molecule smells like spearmint, while its right-handed twin smells like caraway seeds. Clearly, right- and left-handed versions fit different receptors, therefore send along different signals (as is also true of smell in other animals and bacteria).

Receptors mostly overlap, many of them responding to the same odorants. Researchers infer that from their work with specific anosmias, conditions in which people cannot smell some particular substance because they lack the receptors--which is most likely if the receptor is coded by only one gene. No gene, no receptor, no smell.

But there are only about 30 such anosmias, which means there must be many thousands of smells that are handled either by many receptors, or by combinations of receptors. These are the smells any person with normal olfaction can detect. Reed says, "Take phenyl ethyl alcohol, which smells like rose. If there are 10 different receptors that all detect some level of phenyl ethyl alcohol, you will not find people who cannot smell rose. I'm certainly not aware of any."

Two people may not perceive a scent in the same way, though. Because we all have different genes, including genes for smell receptors, we each have our own combination of receptors, including those for phenyl ethyl alcohol. Each combination makes a different firing pattern in the brain--but we all call it "rose." (Well, sort of. This chemical is the "rose" in drugstore perfume.)

Complex aromas, like a genuine rose or the rose-scented perfume Joy, consist of many different odorant molecules. Therefore they trigger a variety of receptors, giving each of us a unique firing pattern that we can recognize, and name, with practice.

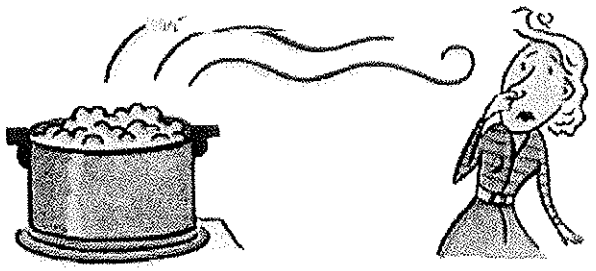
Do we pick up odors equally from both nostrils?

Surprise! Maybe not, according to preliminary, unpublished research by Leopold. He and

his team took CAT scans of 90 patients who said they had lost their sense of smell in either the right or left nostril. The scans showed, however, that regardless of which nostril was supposedly affected, a significant number of patients had anatomical obstructions in the left nostril and the left nostril only.

"What we took this to mean," says Leopold, "was that the majority of these 90 patients were using only the left side of their noses, [at least while their smell was being tested]. They were ignoring their right nostril."

Do most people have one dominant nostril, then, just as most are right-handed? "That's the logical leap we'd like to make," admits Leopold. But the data aren't there yet.



Why is it that even an overwhelming odor--except garlic-- seems to go away after a few minutes?

The system adapts, primarily through a biochemical mechanism discovered by King-Wai Yau, a neuroscientist at the medical school: Calcium cations enter the olfactory receptors and prevent them from sending signals. "Essentially, they turn down the volume," says Reed.

All senses have variations on the theme, ways to damp stimuli, and a good thing, too. We've all had times, such as cleaning up after a child vomits, when that damper is essential. Or imagine walking from a shadowed doorway into sunlight, which can be more than a millionfold brighter--yet we're only dazzled for a few seconds, because our eyes adjust so quickly.

You'd never get anything done if you couldn't ignore most of the sights, sounds, smells, and touches around you, from the sensation of your feet in your shoes to sirens outside. You'd miss new sense signals, too.

What happens to the sense of smell as we age?

Many old people continue to have good olfactory function. That's not the rule, however. Leopold says that olfactory function is generally highest in childhood, plateaus from the teens through the 50s, and drops starting at about 60 for women, 65 for men. "On average, your standard 80-year-old is only able to smell things half as well as your standard 20-year-old," says Leopold.

I've heard of people who experience "phantom smells." What are they?

That's an unusual condition in which people "smell something nobody else is smelling," says Leopold. "It's like a ringing in the ear, and they're miserable," because the odor

never goes away. "They'll wake up and smell burned rubber, or a mixture of burned toast and rotten eggs, and they'll have that taste all day. Breakfast tastes that way, and lunch tastes that way, and dinner tastes that way."

In general, Reed says the most common reasons for olfactory loss are upper respiratory infections and a sharp blow to the head, as in an automobile accident. On their way from brain to nose, the olfactory nerves thread through minute holes in a bony plate, "and during the impact, the plate shears off the nerves."

Unlike hearing or vision, however, the sense of smell can regenerate. It's as if the brain reaches out, sending new nerve fibers down through the plate. The fibers then regrow their proper receptors. When Leopold severs the nerves to cure patients with phantom smell (on one side only), about half the time the fibers grow back--healthy. The patients are cured.

Unfortunately, the openings in the plate can get blocked by scar tissue, especially when the injury is accidental. Leopold is working on a surgical procedure that may someday take out the scar tissue.

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