

# The Mouse Tap

Researchers have identified 1,100 receptors in a rodent's nose, each occupying a distinct position. Who benefits from this finding? **Emily Anthes** reports

Over the past century, scientists have mapped several of the body's sensory systems in microscopic detail, discovering that the cells that process sight, sound and touch are arranged in predictable spatial patterns.

It has been much harder to navigate the complex landscape of the nose, with its enormous array of scent receptors. For years, many scientists believed that these receptors were distributed mostly at random.

Now, two teams of scientists have managed to map the nose of a mouse. Using advanced genetic sequencing and imaging techniques, the researchers found that each of the 1,100 different types of olfactory receptors in the nose occupied a distinct and predictable position, consistent from mouse to mouse.

The findings, which were published in a pair of papers in *Cell*, represent the first comprehensive, fine-scale maps of odour receptors in the nose. They suggest that topographic maps may be as fundamental to olfaction as they are to other senses.

"The organisation of information in space is a major organising principle for all sensory systems," said Sandeep Robert Datta, a neurobiologist at Harvard University, US, and an author of one of the new papers. "We have, to some extent, unveiled this long lost map for smell."

Scientists have not yet demonstrated that the same sort of map exists in the human nose and do not yet understand why the receptors are arranged the way they are. But the research sheds light on how the olfactory system develops and paves the way for a better understanding of an often overlooked sense.

"Having this broad understanding of the organisation of the olfactory system is absolutely essential to understand how we process scent," said Catherine Dulac, a molecular biologist and neuroscientist at Harvard and author of the other paper.

Topographic maps preserve key sensory information about the world and help the brain process that information more efficiently. In the ear and the auditory cortex, for instance, adjacent cells detect adjacent sound frequencies. In the eye and the visual cortex, neighbouring neurons process information from neighbouring points in the visual field.

But scientists have not been able to detect equivalent maps in the nose, which contains a staggeringly diverse array of olfactory receptors. These receptors are specially shaped proteins that sit on the surface of neurons and bind to complementary odour molecules. Humans have several hundred different types of these receptors but some species, including mice, have 1,000 or more. Each receptor type binds to a different set of odour molecules, and each neuron in the nose carries just one type of receptor.

Scientists had previously discovered that the nose could be divided into several broad zones, containing different sets of olfactory receptors. But within those zones, experts long believed, the receptors were distributed randomly.

In their new study, Datta and his



**ROUGH GUIDES:** A cross-section of the nose of a mouse; the green parts are the smell neurons

colleagues analysed neurons from mouse noses to determine exactly which genes — of the many in the mouse genome — were active, or expressed, in each individual neuron.

That data revealed which particular olfactory receptor each neuron was expressing. But the scientists also identified hundreds of additional genes, with a variety of different functions, whose activity seemed to vary from neuron to neuron, depending on which receptor type was present.

The researchers hypothesised that these genes might help determine which receptor any given neuron expressed — and that they might do so based on where that neuron was located in physical space. To test their hypothesis, the researchers analysed larger samples of mouse nasal tissue, using advanced spatial imaging technology to pinpoint where, in physical space, these various genes were expressed.

Dulac's team used the same imaging technology to map the expression of olfactory receptor genes in tissue samples from both the nose and the olfactory bulb, which is the brain

structure that receives information from the nose.

Ultimately, the teams ended up producing similar maps, with the receptors in consistent locations. They also found that the map of neurons in the olfactory bulb mirrored the map in the nose.

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"I think this is really a highly tenable hypothesis," said James Schwob, a neurobiologist who studies smell at Tufts University, US, and was not involved in the research. The study provides "a deeper molecular understanding of how position in the nose is encoded genetically," he added.

Linda Buck, a neurobiologist who

shared a Nobel Prize in Physiology or Medicine for discovering olfactory receptors and how the olfactory system was organised, described the new research as "groundbreaking". Buck, who now studies olfaction at the Fred Hutchinson Cancer Center in Seattle, US, said that she was particularly excited about the discovery of hundreds of genes that might play a role in regulating the receptors that neurons express. "This is an important discovery that opens the way to future experiments to further understand how the olfactory system develops," she said.

Still, the big question remains — why are certain receptors located where they are and how might that help the brain make sense of odours? One possibility is that adjacent neurons detect odour molecules with similar chemical structures. Another is that the map is organised by meaning, with attractive odours, like the scent of one's own offspring, detected in one area and repellent ones, like the smell of a predator, processed in another.

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