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Smell is 'noisy' and 'in shades of grey': Scientists debunk ancient lock-and-key theory

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University of Manchester scientists have overturned the 2,500-year-old theory that smell is detected by simple lock-and-key codes – using maggots with only one working olfactory sensory neuron (OSN), a nose with one nerve cell.

It was thought that smells are detected by simple lock-and-key codes. Instead it appears that there is a combination of precise and 'fuzzy' coding that allows organisms to sharpen their response to odours, rather like the dither that is famously used to improve computer performance. Whilst fuzzy coding is known to occur in the central brain, this is the first time it has been shown in the periphery.

Dr Matthew Cobb, at the University's Faculty of Life Sciences, explains: "We have been able to address a problem that people have been trying to resolve for 2,500 years, since the Greek philosopher Democritus suggested that nice smells came from smooth, round atoms and bad smells came from spiky atoms.

"Until now, people have thought that smell works by a simple lock-and-key code where each smell molecule fits into one or more receptors that recognise it. If the smell is there, then the receptors will respond.

"However we have found this to be an over-simplification. It is not just a lock-and-key system. Sometimes a smell comes along and doesn't 'turn

the lock'.

"We first set out thinking we would crack the code of locks and keys but we were driven to a new conclusion by the data. We tested for everything, controlled everything, but we found our starting place was wrong. It was a very exciting turn of events."

Dr Cobb and his colleague Dr Cathy McCrohan, together with their PhD student Derek Hoare, have published their study in *Journal of Neuroscience.* They used Drosophila larvae (maggots) with only one working olfactory sensory neuron (OSN) – a nose with one nerve cell. Although it might seem an unlikely animal to study, the "wiring diagram" of a maggot's nose is exactly the same as that in a human, but much simpler. The scientists recorded the activity in the maggot's nose, to see exactly how smells were detected. The test group was compared to a control group of normal maggots with a full complement of twenty-one working OSNs.

As expected, some OSNs showed consistent, precise lock-and-key responses - either excitation or inhibition - in response to a given odour. But to the scientists' surprise, most cells also showed variable responses - "fuzzy coding"; sometimes they responded to a given odour and sometimes they did not. This variability was real: it was not related to odour type, concentration, stimulus duration, or the genetic make-up of the individual maggot, and it was seen in both test and control groups. They concluded that the peripheral code combines precise coding with fuzzy, stochastic responses in which neurons show apparent unpredictability in their responses to a given odour.

They now believe that fuzzy coding occurs in other organisms, is translated into differing degrees of activation in the brain, and forms a key component of odour recognition in the first stages of olfactory processing.

Dr McCrohan explains: “The nose gives us insight into the brain - it’s not a computer, it’s not precise, it’s fuzzy. This may be a consequence of way the receptors are built and must be used in some way as part of the process by which the brain perceives an almost infinite variety of odours.

She adds: “These data explained previously mysterious findings that people had reported but were unable to fit into the ‘lock and key’ model.

“These findings had people scratching their heads, now we can explain them. Fuzziness is true, a real phenomenon that forms a key part of how we detect smells.”

The pair now plans to take the research further. So far they have been using pure smells but real smells are highly complex mixtures of chemicals. In addition the single cell maggot nose is extremely simple; many animals possess hundreds of thousands of OSNs and humans have millions.

Dr Cobb says: “We’ve been using pure smells but real smells are complicated blends; for example a cherry has 200 different molecules. Maybe when you detect a real smell, you use a combination of precise and fuzzy responses – to give yes/no/maybe – forming overall recognition. This is rather like face recognition in which you recognise the same face, even from different angles. So we would like to see how maggots respond with blends.

“We also want to extend the study to other organisms such as beetles, which have nearly as many olfactory receptor types as humans. Other scientists who work with mice or humans could rise to the challenge. I presented this study to a scientific meeting on the sense of smell in Slovenia. It was controversial but well received. People went away convinced they need to look again at data that they have thrown away or

ignored.

“Science works by analogy. In the past, people believed the body was like a machine. Then, with the advent of technology, we first thought the brain was like a computer, then like the worldwide web. What we’ve found here is that these analogies can be misleading. Animals are not machines: information processing in the nervous system involves a huge amount of unpredictability – even in a maggot.”

A copy of the paper ‘Precise and Fuzzy Coding by Olfactory Sensory Neurons’ by Derek J. Hoare, Catherine R. McCrohan and Matthew Cobb is available at www.jneurosci.org/cgi/content/ … 0&resourcetype=HWCIT

Provided by University of Manchester