

Engineers pave way to 'artificial nose'

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MIT biological engineers have found a way to mass-produce smell receptors in the laboratory, an advance that paves the way for "artificial noses" to be created and used in a variety of settings.

The work could also allow scientists to unlock the mystery of how the sense of smell can recognize a seemingly infinite range of odors.

"Smell is perhaps one of the oldest and most primitive senses, but nobody really understands how it works. It still remains a tantalizing enigma," said Shuguang Zhang, associate director of MIT's Center for Biomedical Engineering and senior author of a paper on the work appearing online this week in the *Proceedings of the National Academy of Sciences (PNAS)*.

Artificial noses could one day replace drug- and explosive-sniffing dogs, and could have numerous medical applications, according to Zhang and his colleagues. DARPA recently approved funding for the team's MIT (microfluidic-integrated transduction) RealNose project.

Until now, efforts to understand the molecular basis of smell have been stymied by the difficulty in working with the proteins that detect odors, known as olfactory receptors.

"The main barrier to studying smell is that we haven't been able to make enough receptors and purify them to homogeneity. Now, it's finally available as a raw material for people to utilize, and should enable many new studies into smell research," said Brian Cook, who just defended his

MIT PhD thesis based on this work.

Smell is one of the most complex and least-understood senses. Humans have a vast olfactory system that includes close to 400 functional genes, more than are dedicated to any other function. Animals such as dogs and mice have around 1,000 functional olfactory receptor genes.

That variety of receptors allows humans and animals to discern tens of thousands of distinct odors. Each odor activates multiple receptors and this pattern of activation creates a signature that the brain can recognize as a particular scent.

The olfactory receptors that bind to odor molecules are membrane proteins, which span the cell surface. Since cell membranes are composed of a bilayer of fatty lipid molecules, the receptor proteins are highly hydrophobic (water-fearing).

When such proteins are removed from the cell and placed in water-based solutions, they clump up and lose their structure, said Liselotte Kaiser, lead author of the *PNAS* paper. That makes it very difficult to isolate the proteins in quantities large enough to study them in detail.

Kaiser and others spent several years developing a method to isolate and purify the proteins by performing each step in a hydrophobic detergent solution, which allows the proteins to maintain their structure and function.

The technique reported this week in *PNAS* involves a cell-free synthesis using commercially available wheat germ extract to produce a particular receptor, then isolating the protein through several purification steps. The method can rapidly produce large amounts of protein — enough to start structural and functional studies.

The team has also demonstrated a similar method that uses engineered mammalian cells to produce the receptors. That method, reported in *PLoS One* in August, takes more time and labor than the cell-free approach, but could have advantages in that the receptor is processed more naturally.

In future work, the team plans to work with researchers worldwide, including MIT's Media Lab and Department of Biology, to develop a portable microfluidic device that can identify an array of different odors. Such a device could be used in medicine for the early diagnosis of certain diseases that produce distinctive odors, such as diabetes and lung, bladder and skin cancers, Zhang said. There are also a wide range of industrial applications for such a smell-based biosensing device, he said.

Source: Massachusetts Institute of Technology

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