Sniffing out success

Engineers mass-produce smell receptors in lab; 'artificial noses' to follow?

Anne Trafton
News Office

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.

Other authors of the PNAS paper are Johanna Graveland-Bikker, a postdoctoral fellow at MIT, visiting graduate students Dirk Steuerwald and Melanie Vanberghem, and Kara Herlihy of GE Healthcare Biacore.

The research was funded by the ROHM Corporation (Japan), the Knut and Alice Wallenberg Foundation (Sweden), the Netherlands Organization for Scientific Research, and a John Simon Guggenheim Fellowship. Joyce and Roger Kiley '60, MS '61 provided pure odorants.

Renewable energy regulations may miss the mark

Research shows different approach is needed

David Chandler
News Office

Well-intentioned rules passed by many states to combat climate change through the development of renewable energy technologies may not achieve the intended effects and may even be counterproductive, according to research by an MIT graduate student. But the problem is easy to fix: A modified set of regulations could be much more effective, the study found.

At least 25 states have enacted renewable portfolio standards (RPS), which require electric utilities to obtain a certain percentage of their power from renewable sources by a certain date (such as "20 percent from renewables by 2020"). But these standards will not achieve the desired effects and may actually end up delaying some of the most promising renewable-energy technologies, the study found.

Michael Hogan, the student who carried out the study as part of his master's thesis work in MIT's Environmental Technology and Public Policy Program, says that such standards push investments much too heavily toward technology that is already well proven and close to being economically competitive, especially land-based wind power. In the process, technologies that may have much more potential to replace coal plants in the longer term, such as solar thermal systems and offshore wind, get short shrift.

Current RPS programs, Hogan found, "are likely to play at best a very marginal role at an unnecessarily high cost in delivering the necessary reductions in greenhouse gases, with little in the way of long-term technological development benefits."

But by introducing a few refinements to these programs, he says, it is possible to greatly improve the chances that they will achieve the desired results.

Hogan's professional background is tailor-made for this line of research: He spent 28 years in the energy business, including leading roles in starting and running a number of energy companies and organizations, before deciding to resume his education with the MIT Department of Urban Studies and Planning master's program. During his years in the energy business he was responsible for the development of more than $8 billion in energy-related assets in seven countries.

The central problem, Hogan says, is that 80 percent of U.S. carbon dioxide from electricity generation, and about a third of the nation's overall emissions, come from just 620 coal-burning power plants. Thus, any attempt to reduce greenhouse gas emissions must focus squarely on addressing these plants. "In a very real sense," he writes, "nothing else matters."

While RPS tends to foster investment in wind farms, these almost never displace baseload coal-fired plants, he says, which is the key objective. Among other changes, he proposes that the rules be modified to create "bands" of technologies, based on their degree of commercial readiness, and that the regulations should strongly favor promising but still early stage technologies. Encouraging investment in technology that won't produce results until later in the process could actually foster much more significant progress, he says. "We have to bet on all the horses," he says.

In addition, it is important to recognize that rules should be tailored to the conditions in particular parts of the country, he says. For example, while land-based wind dominates the upper Midwest, solar thermal systems should be favored in the Southwest, deep-offshore wind in the Northeast, and biomass in the Southeast.

Lawrence Susskind, Ford Foundation Professor of Urban and Environmental Planning and Hogan's thesis adviser, says his student has demonstrated that renewable portfolio standards "are not working as well as they should."

Susskind says that in carrying out this study, Hogan "builds on his long experience developing energy facilities in many parts of the world" and through his analysis "offers a detailed package of reforms that could make a difference."

Hogan said the research changed his own perspective. "I went in thinking I would reaffirm things I already believed," he says, but that turned out not to be the case. For example, he said, "I went in very negative about offshore wind in the near term," but the study "completely changed my mind."

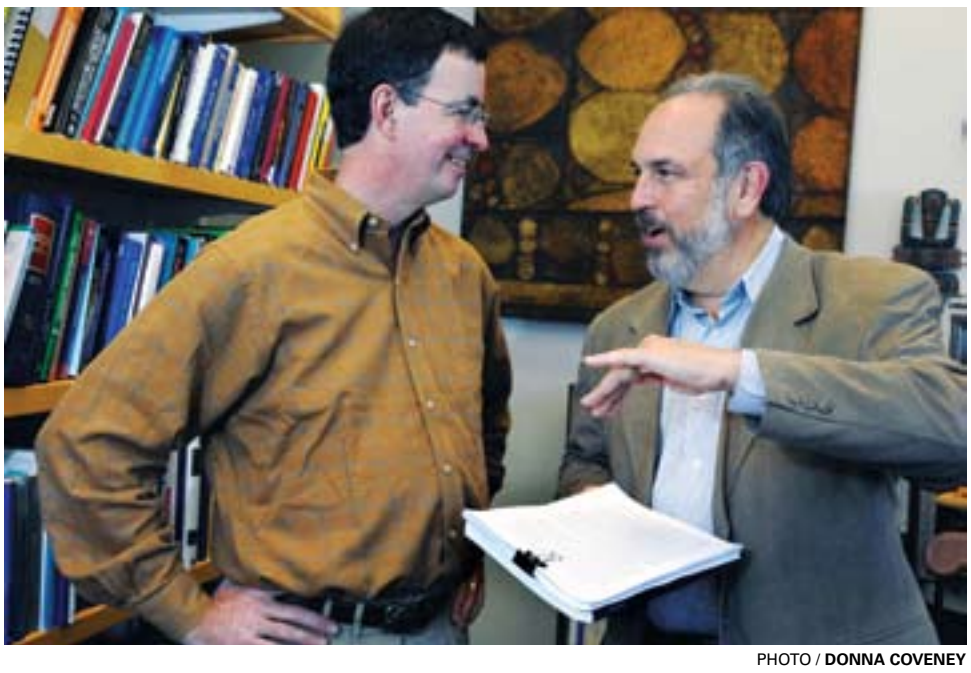

PHOTO / **DONNA COVENEY**

Graduate student in urban studies and planning Michael Hogan, left, and Larry Susskind, Ford Professor of Urban and Environmental Planning, discuss Hogan's thesis on government rules and renewable energy technologies.