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BRIGHT IDEAS

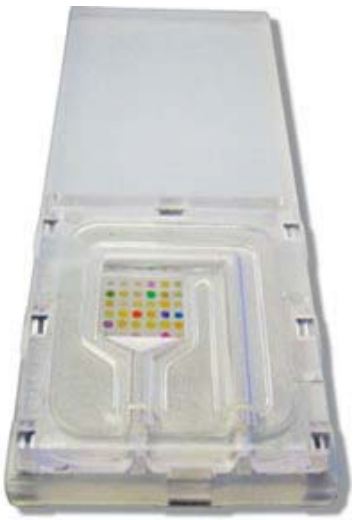
What the e-Nose Knows

A whiff of the future.

BY SANDRA A. SWANSON

IMAGINE A BREATHALYZER-TYPE device that could detect cancer in its earliest stages, by smell alone without invasive blood draws and body scans. It's not a new idea. Centuries ago, Hippocrates linked patients' musty breath with liver disease. And a handful of studies suggest that dogs, with their sensitive snouts, can be trained to sniff out tumors.

This puff-of-air diagnostic tool isn't a pipe dream. It already exists, courtesy of iSense, a company founded by Kenneth Suslick, PhD '78, and Paul Rhodes, MS '83.

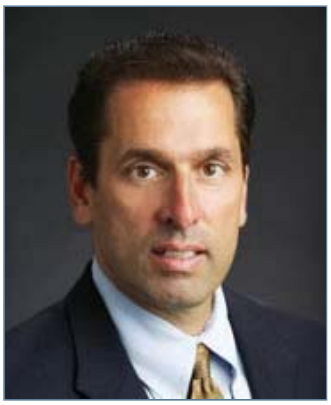


NOSE ON A CHIP: The iSense chemical sensor, developed by Rhodes (below left) and Suslick (below right), mimics nature's design.

Courtesy iSense

"Cancer cells are a little different in their metabolism," Rhodes explains. Their rapid reproduction creates byproducts, some of which are airborne, producing a distinct odor undetectable by humans.

Preliminary results of a study conducted by the Cleveland Clinic suggest that the iSense device can correctly diagnose early-stage lung cancer in three out of four patients. Other health conditions that might be put to the smell test include pulmonary disease, diabetes and kidney disease. In addition to health care, the technology could have implications for homeland security, food safety and more. Rhodes expects iSense's medical-diagnostic device will be commercially available in 2011. "Every doctor's office on earth could end up having one," he says.



Courtesy Evolved Machines

At the core of the device is a sophisticated array of chemical sensors that mimics what the nose does naturally. When you catch a whiff of, say, the malodorous *Mephitis mephitis*, airborne molecules become trapped in the mucus lining your nasal membranes. There they interact with specialized cells that respond to particular chemical properties. In mammals, there are a few hundred different types of these olfactory receptors, and the human nose has somewhere around 30 million of them. (Fido, by comparison, has upwards of 1 billion.) The particular combination of cell types triggered gives rise to a pattern that the brain recognizes, in this case, as *eau de skunk*.

A chemistry professor at University of Illinois at Urbana-Champaign, Suslick has spent the past 12 years tweaking Mother Nature's design. To visualize odor patterns—an approach he calls "smell-seeing"—he devised an array of 36 colored dots, small enough to fit on

a fingernail. The dots are dyes that change color in response to various chemical characteristics and include pH indicators and doughnut-shaped molecules called metalloporphyrins that trap metal ions in their center. (This class of molecule was the focus of Suslick's PhD work at Stanford.)

Courtesy iSense

The disposable array is printed on one end of a piece of translucent plastic about the size of an iPod Nano. It's inserted into a brick-sized device equipped with a bare-bones 1-megapixel camera. (Suslick expects to shrink the reader to cell-phone size by next year.) The device takes a picture of the array's default state for reference. Then, a tiny pump sucks air over the surface and within seconds some of the dots change color as they react with molecules in the sample. The device snaps another picture. After subtracting the "before" photo, the result is a unique pattern, which an onboard microcomputer analyzes and compares to a large library of odor images.

Depending on the odor analyzed, iSense's array can detect chemical levels ranging from parts-per-million to parts-per-billion (the degree of color change indicates the concentration). With funding from the National Institute of Environmental Health Sciences, Suslick demonstrated that his device could accurately detect 19 toxic industrial chemicals, such as ammonia and sulfur dioxide. Factory workers might someday wear badges that would sense toxic gases and alert them before harmful exposure occurred.

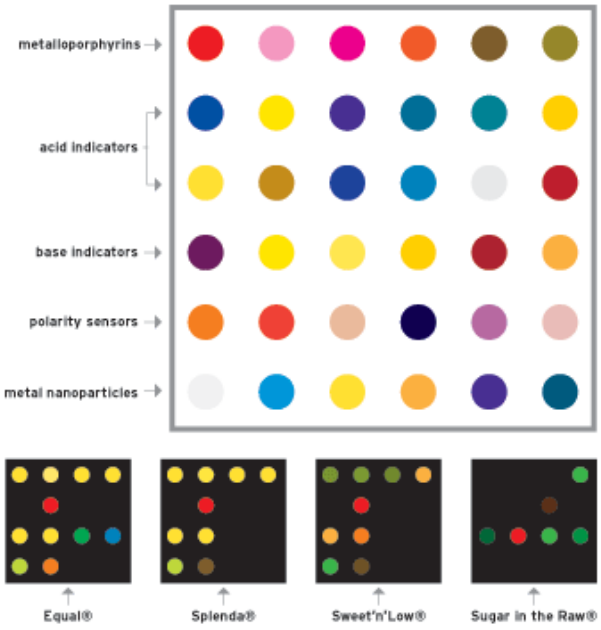
Food and beverage manufacturers have shown interest in the array, too, says Suslick. Sensors could address food safety concerns, identifying spoilage or harmful pathogens in products before they reach consumers. They could also check product consistency on the fly, confirming that the chemical fingerprint in one giant vat of black-cherry soda matches the next.

The array can also function as an "electronic tongue," detecting molecules dissolved in a liquid, rather than suspended in the air. Suslick showed that the iSense device could distinguish among 14 different commercial sweeteners. And, just for fun, he and his son, who plans to major in chemistry, compared 10 coffee brands with the array. "We could determine each one, without error, in 50 trials," he says.

Of all the senses, smell is the most mysterious. How is it that humans can differentiate thousands of aromas? Why can you detect the smell of a ripe banana when other fragrances are present in the room—what keeps those scents from being a muddled, indecipherable mess? To build a better nose, it helps to understand how the real thing functions.

That's one goal at Evolved Machines, a company Rhodes founded in 2005 while a visiting professor at Stanford. (iSense, founded in 2007, is an affiliate.) Using ultra-high-speed computing, Evolved Machines simulates the human olfactory system's response to various odors. This allows researchers to study how all the components work together. "It can open up a new way to gain real insight into biological function," Rhodes says.

The answer to the banana puzzle, he says, may have something to do with the strength of connections between olfactory neurons—how those connections fade with use, and then rapidly recover. He's writing a paper about how humans classify odors when background smells are present, based on data gleaned from simulations.



SWEET SPOTS: Dots of dye react to particular molecular features to produce a unique pattern for each compound.

Data courtesy of iSense

These insights could lead to better chemical detection systems. In 2008, Evolved Machines was chosen as a contractor for a Defense Advanced Research Projects Agency initiative called RealNose that aims to create an artificial nose from biological components. Such a sensor could address the military's need to detect explosives and chemical or biological weapons. (Another Rhodes-founded company, Nanosense, receives funding from DARPA to develop reusable carbon nanotube sensors.)

Of course, not all of the potential applications for artificial olfaction are mission critical. One Japanese company contacted iSense about adding an array to cell phones to let the user check for bad breath or body odor. And there was the lawyer who called Suslick, wanting to use the array to help defend his client, a pig farmer. Apparently, the client's neighbors deemed his operation an olfactory affront. By quantifying the pig odor, the lawyer hoped to show the stink was really in the neighbors' heads—not in their noses. Says Suslick: "I told him we weren't ready yet for that particular application."

SANDRA A. SWANSON *is a science writer based in the Chicago area.*

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