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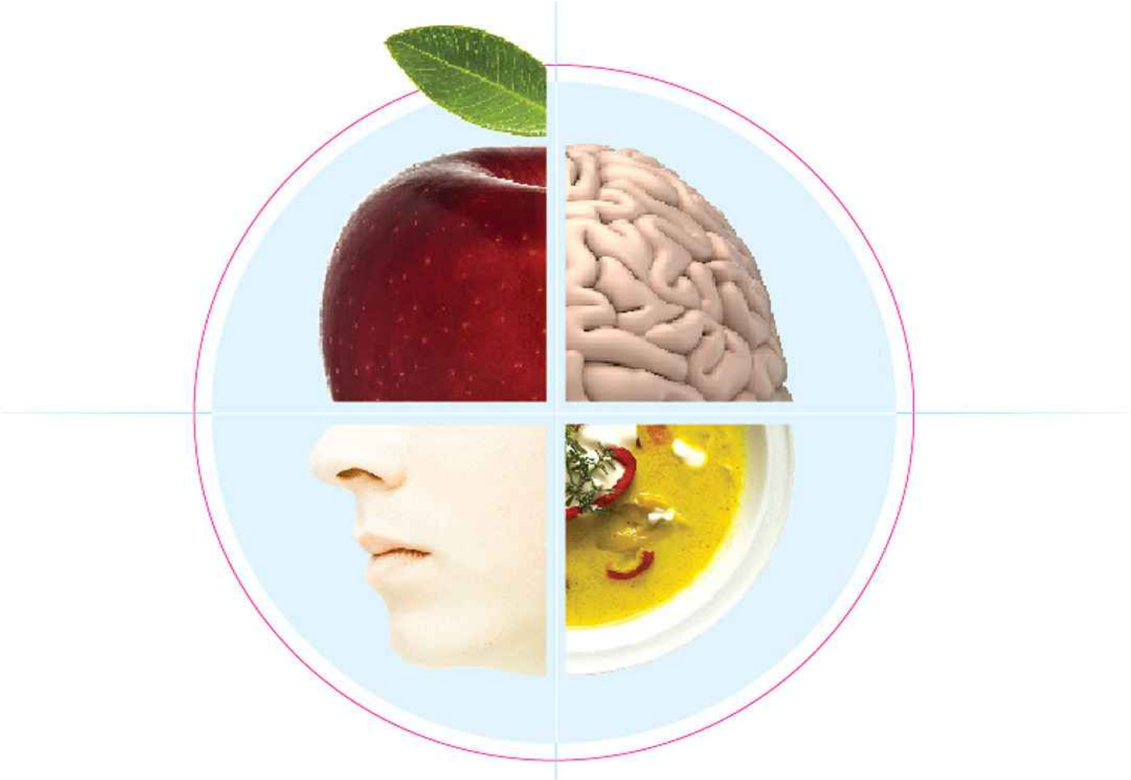
The flavour factory: Hijacking our senses to tailor tastes

Hacking our smell receptors will allow us to create delicious, tailored food flavours. Chocolate cauliflower anyone?



Who makes the flavour?

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IT WAS certainly an unconventional dish, but as Gina Mullins poured another spoonful of apple cider reduction over her tortilla, and sprinkled goji berries on top, she figured she had nothing to lose. She was used to being repulsed by food by this point and was game to try anything.

Mullins, who has lost much of her appetite and sense of taste as a result of chemotherapy, was at the University of Kentucky to judge an unusual cook-off. Chefs, neuroscientists and doctors had joined forces at the inaugural meeting of the International Society of Neurogastronomy. Their challenge? To create a dish that would rekindle the pleasure of eating for people with taste impairments.

The teams tickled the judges' taste buds with a spicy scallop tortilla accompanied by carrots, yogurt, goji berries and blackberry jam, and a hearty potato soup served with pungent, intensely flavoured garnishes. The two dishes were designed to appeal not just to the five basic tastes – sweet, sour, salty, bitter and umami – but also the other senses, which in recent years scientists have come to discover play an important part in how we experience flavour. But that was the extent of their toolbox. In reality, figuring out what might work was largely guesswork.

“We’re talking about modifying ingredients so the brain perceives them differently“

But what if we could remove the guesswork? One scientist at the meeting is trying to do just that. Instead of altering the food, Tim McClintock, a molecular biologist at the University of Kentucky, wants to change the way food tastes by manipulating signals in the brain. Our taste buds play only a small part in the way we perceive flavour – the biggest contributor is smell. If we could mimic or hijack the way the aroma of food creates flavours, we could not only tailor odours to stimulate the smell receptors of people who have trouble tasting, but it would also open the door to Willy Wonka-style gastronomic possibilities for all of us. We could tinker with the way natural ingredients taste or even create new smells and flavours.

Odours are volatile chemicals and so are gases at room temperature. When we sit down to a meal, smells enter our nose either as we inhale or, more powerfully, when we chew food, and odorous chemicals waft up through the back of the throat. When a smell hits the roof of the nose, it comes into contact with about 350 odour receptors – proteins that convert the chemicals they detect into an electrical signal.

Each smell triggers a unique pattern of receptors that some scientists refer to as a kind of “odour barcode”. This barcode is then transmitted to the olfactory cortex, where it is shared with other parts of the brain that handle factors like memory, emotion and reward. Together, they form the brain’s interpretation of the smell.

“Almost all the systems in the brain are affected,” says Gordon Shepherd, a neuroscientist at Yale University who coined the term “neurogastronomy” in 2006 to describe the study of the interaction between the brain and food.

Future flavours

People have been trying to isolate the molecules responsible for odour in food since the 1960s, initially using gas chromatography. This can identify the compounds that make up a smell, but not what happens when it hits the nose. Deciphering that precise odour barcode has so far been impossible, but it’s necessary if you really want to be able to tinker with the brain’s perception of flavour. “Receptor identification is the future of flavour development,” says McClintock.

So he and a handful of other researchers around the world have set about trying to crack the problem. Some 10 years ago, he became interested in the function a gene called *S100A5*, so he genetically engineered mice in which he exchanged *S100A5* for a green fluorescing protein.

At the time, *S100A5* was one of several newly discovered genes expressed in olfactory sensory neurons, but its exact function was unknown. We now know that it is activated when olfactory receptors in the nose are stimulated. McClintock’s *S100A5*-deleted mice provided the perfect way to unlock the secrets of the olfactory system. “I realised that we could use this mouse to reveal which odorant receptors respond to any odour that we chose,” he says. If a receptor responds to an odour smelled by one of these mice, the replaced gene will make fluorescent protein instead of making the *S100A5 protein*. So each neuron activated by a particular odour is tagged with a green fluorescent label.

James K Morris

Inside his lab, McClintock uses a set-up that he calls the Kentucky assay. A series of straw-like tubes pump clean air from a nearby compressor into clear containers containing his engineered mice. After 26 hours without food (to reduce the number of smells around), half of the mice are intermittently exposed to an odour for 14 hours. The other half inhale a more neutral substance.

After each session, all the olfactory sensory neurons are removed from the noses of the mice, mixed with an inert liquid and poured through a giant cell-sorting machine. This equipment detects the presence of the green protein and separates the fluid accordingly.

Every receptor is encoded by a unique gene. By sequencing the RNA of the cells in the green-fluorescing tube, McClintock identifies the exact pattern of receptors activated by an odour.

Gina Mullins tries new flavours at the International Society of Neurogastronomy

Last year, McClintock published his receptor barcodes for muscone – or musk – and eugenol, a chemical prominent in many spices, including clove. His company, Odorcept, provides receptor barcodes for private clients. He cannot disclose who his clients are, but says the system could be used by any firm seeking to create new odours, to alter how we perceive odours, or even to block them altogether.

Although mice have about 1000 odour receptors, far more than humans, research has shown that humans and mice share many similar odour receptor genes, and McClintock is confident that the Kentucky assay translates to our own species. He also envisions engineering a mouse with a human receptor system several years from now.

It is still early days, but if the system does work in human cell receptors, it wouldn't just tell us what the barcode is for a particular odour, it could also be used to test a manufactured smell to see if it hits that same pattern of receptors. This set-up and similar systems in development in other labs will enable us to build an encyclopedia of odour barcodes. These will tell us which receptors need to be activated in order to know that any new chemical is having the desired sensory effect, says Joel Mainland at the Monell Chemical Senses Center in Philadelphia. “Once you have that you can start creating any odour you want,” he says.

But the ultimate goal of McClintock’s system is to reverse-engineer the barcode and create odours for a specific purpose, which means we could craft food to match our receptors. “We’re talking about modifying ingredients through science so that the brain perceives it differently,” says neuropsychologist Dan Han at the University of Kentucky in Lexington, who co-founded the neurogastronomy society and organised the meeting. “Foods that don’t taste good can be manipulated so patients can stomach them better.”

And McClintock hopes it would be possible to determine the patterns of receptors that evoke the most powerful, appealing flavour sensations, so you might use the system to drive people towards better diets. Healthy but unappetising foods could be given a whole new flavour, or delicious smells could be made more potent, thereby stimulating the appetites of people with taste and smell deprivation.

Take fruit and vegetables. The sweetest tomatoes don’t necessarily contain the most sugar – rather, they contain a volatile compound that stimulates a pattern of receptors that our brains read as “sweet”. If we know those receptors, says Mainland, then a vegetable can be bred to contain more of that particular volatile compound, therefore tasting sweeter. “If you’re breeding and having consumers rate them, it’s a very slow process,” says Mainland. “If you’re breeding and doing chemical analysis, that’s much faster.”

The usefulness of the findings extend beyond the dinner table. Knowing the receptor proteins responsible for any aroma – the smell of a new car, freshly cut grass, vanilla – raises the prospect of producing cheaper or improved versions of that smell, or creating artificial versions that evoke certain memories. Others see the technology going even further with visions of smells to accompany movies, cellphones that spray scents on demand and smell-emitting e-books.

Being able to decipher the receptor barcode could also be the key to finding out how dogs can sniff out specific chemicals linked to certain types of cancer so that artificial noses could one day do the same job.

Custard dreams

But for those gathered at the meeting in Kentucky, the most immediate goal is to manipulate the brain’s perception of flavour to bring relief to the people who need it most.

Sid Kapoor, a neurologist at the University of Kentucky, is hoping to use the Kentucky assay, in combination with food technology and culinary creativity, to find a more palatable approach for the ketogenic diet, a high-fat diet used to prevent epileptic seizures. “It’s literally like having to drink oil,” says Kapoor at lunch before the cooking contest. “It can be very difficult to follow.” Kapoor would like to see a greater range of flavours introduced to high fat foods, so that patients are not overloaded with the taste of “butter and meat”.

Across the table, chef Fred Morin is already crafting recipes. “Custards of egg yolks and cream, geared for different flavours?” he suggests.

That vision is still some way off. McClintock is refining the system to be able to analyse more odours faster. “We are just in our infancy of understanding the patterns of receptors that respond to odours,” he says. “Quite frankly, the vast majority of the odour universe is unexplored."

In the meantime, the scientists and chefs cooking for Mullins and her co-judge, Jen Cooper, whose sense of taste was also altered by chemotherapy, are awaiting the result of their educated guesswork. There can be only one winner, and it is the pungently garnished potato soup. "I just don't do scallops," says Mullins, hoping to soften the blow for the losers. For now, scallops still taste like scallops. But in the future, they could taste like pumpkin pie. Or chocolate.