Flavor R&D Frontiers

From nutrigenomics to biotech

With the advent of relatively inexpensive genetic mapping, one can envision a time in which infants are mapped at birth. This information, aside from medical implications, could have consequences for food and beverage choices, notes Bob Eilerman, Givaudan's head of innovation programs. "At some point I can envision going into a food store where you can purchase food designed for your genetic makeup," he explains, highlighting the growing field of nutrigenomics—the study of the relationship between gene expression and diet. For example, this could potentially address varying sensitivities to tastants or allergens among consumers. "Certain food [constituents] can turn genes on and off and you want to be able to do that to your best interest."

Bob Eilerman

Eilerman is quick to note that research in this emerging area is underway in "a very modest way so far at Givaudan," particularly through a research partnership with the US National Institutes of Health (*www.nih.gov*) that focuses on genetics and sweet and umami perception. "Our interest was initially in seeing if we could map the [human] sweet receptor by understanding demographic differences in sweet taste," he says of one recent study.[a] "We took a group of about 250 people and compared their sensitivity to sucrose and other sweeteners with their sweet taste genetics. What we found was genetic differences (polymorphisms) in the sweet taste receptor that could be extended to the world population. Interestingly, perceived intensity is tied to control of the quantity of sweet receptors on the tongue. So not all groups are equally sensitive to sweetness, and this could clearly influence food choices."

Eilerman adds, "We're doing similar work with umami. We have an interest in mapping these characteristics. There are a lot of different groups working on different pieces. Eventually we're going to have a nice data file on various traits from a taste or smell point of view."

Health and wellness: Such genetic efforts support a key pillar of Givaudan's R&D efforts—health and wellness—in service of reducing obesity and controlling blood pressure. Eilerman, who has 37 years of industry experience and came to Givaudan by way of Fritzsche, Dodge and Olcott, notes that Givaudan currently invests 8.5% of its revenues in its "discovery and development engines." For flavor science and technology, a complement of 145 scientists carry out research at primary sites in Cincinnati; Naarden, Netherlands; and Dubendorf, Switzerland, with a growing component in Shanghai.

"The customer demand is there," says Eilerman of the health and wellness market. Yet his global network of scientists is now faced with finding solutions that are not only effective, but also natural. The low-hanging fruit, in other words, has already been picked. "The consumer goods market and consumers in general are more focused on natural solutions. That ups the ante in terms of challenges for finding natural materials that are as performant. We've spent a lot of our time moving into high throughput screening to look for new molecules … which is much easier for synthetic libraries. Now we've had to build up our natural libraries. You don't have the same flexibility with naturals that you do with synthetics. You can't build [natural] analogs for materials that don't exist in nature. You can't make an analog for something that is not natural."

Efforts in this area, as mentioned, are centered on sweet and salt taste, particularly solutions that reduce or eliminate sugar while enhancing sweet taste palatably. "We've focused some energy on improving the taste profiles of high potency artificial sweeteners," Eilerman says. "That has led to a fairly strong interest in taste masking because a lot of the artificial and natural high-potency sweeteners have some sort of a bitter component to their taste profile. It's something we would obviously like to eliminate or suppress to the extent that we can."

Meanwhile, he says, "Salt reduction is … a different kind of challenge because there's less known about the biology [of salt taste/preference] and a lot of confusion around the absolute mechanism for salt sensing. If you're looking at it from a research perspective … there's some interest to replace MSG with more acceptable umami agents."

Sequential flavor release: "We have a fairly broad-based encapsulation technology base," says Eilerman. "Over the past few years we've embarked on a research program [for] advanced release technologies. Our ultimate goal is to be able to control the way a flavor is displayed in any kind of environment or to be able to trigger a release in any kind of environment—pH, water, enzyme—whatever way you can imagine to trigger a release. We've developed some products that give you a flavor and then you [reach] a break point and you see

[a]AA Fushan, CT Simons, JP Slack, A Manichaikul and D Drayna, Allelic Polymorphism within the *TAS1R3* Promoter Is Associated with Human Taste Sensitivity to Sucrose. *Current Biology*, **19**, 1288–1293 (2009).

another flavor displayed. We've done it with citrus products followed by mint products or one fruit flavor followed by another." The technology has been applied primarily to novelty systems, including gums or even fruit bars, in which sequencing a flavor release can be advantageous. "Being able to build encapsulation systems that let you do that can be very interesting and important," says Eilerman. Such release can occur by chewing, as mentioned, or even osmotically (as water comes in contact with encapsulated flavors, the capsules expand and burst). The strategy, Eilerman notes, is to time release by using different types of encapsulating materials that will dissolve or slough off in stages for timed release under delayed conditioning, such as in a pharma application.

Biotech: Biotech is nothing new for the flavor and fragrance industry, but today's natural ingredient palette is increasingly reliant on such approaches. "On the aroma chemical side we have targets," says Eilerman. "We're looking at materials that we want, from a natural perspective, and [use] fermentation and enzyme-catalyzed processes to create natural versions. We've spent a lot of energy on a natural approach to nootkatone (FEMA# 3166; CAS# 4674-50-4), which is found in citrus fruit. We take valencene (FEMA# 3443, 4630-07-3), which is also found in citrus, and use an enzymatic process to oxidize that to nootkatone." In addition, he says, "A lot of the work we do on the taste side involves fermentation to create complex mixtures. We look at naturally occurring raw materials and biotransform them into a complex mixture that is designed to have certain concentrations of certain materials that we know are effective in, for example, sweetness enhancement, bitterness masking or salt reduction."

Sustainability: R&D activities have also encompassed the company's growing sustainability efforts, including green processes such as fermentation and enzymatic transformations eschewing environmentally harmful chemicals, as for example for oxidations. Eilerman adds, "We have processes that improve the whole vanilla curing process so you get a more consistent product and eliminate a lot of the bulky parts of the process—the sweating and field processing that normally takes place where the growers produce the beans. We've found ways to improve those processes."

Improving the flavor design process: Eilerman sees the company's flavor design tools, including the trademarked Virtual Aroma Synthesizer (VAS) technology, as key pillars of R&D. "Originally the [VAS] was developed to support a paradigm shift in the flavor creation process, making it a more efficient one," he says. "We've actually expanded the utilization of these tools way beyond that." Eilerman notes that every supplier has its own sensory language, making a shared vocabulary for customers elusive. And so, the VAS began to serve as a Rosetta Stone of sorts for sensory language, allowing customers to demonstrate, through smelling, what they're looking for, while also translating consumer understanding for more desirable flavor profiles. This has given formulators greater flexibility and responsiveness in a rapid product development cycle.

"The classical way [to make a new flavor] is to physically combine a set number of ingredients in some metered way such as weighing," says Eilerman. With most flavors containing 20 to 40 ingredients, he notes, even fast, efficient workers would need 30 to 40 minutes to whip up a test batch. Using the VAS, he argues, allows flavorists to limit the number of iterations needed to reach a winning formula. "We rapidly prototype formulations in a way that doesn't use the traditional approach to flavor compounding," he says. "It allows you to take the various aroma components and mix them in a number of ways while storing the results on a computer. So a flavorist can actually dial in a certain concentration of each component and keep changing that on the fly. It lets them look at the impact of different components on a formulation very quickly and arrive at something that they think is [effective]. You can do it with the customer so they can say 'I like this' or 'add more of that.' It allows them to aggressively participate in the development process if they wish, and it allows us to get to a solution much more rapidly." And, he explains, "We've got the formulation in the system so anyone can recreate it in an instant. We can give them the basic rules and let them create whatever they think the greatest grape flavor is."