

TOWARD 'MOLECULAR GASTRONOMY,' OR WHAT'S IN A TASTE?

Flavor is the quality that most often distinguishes excellent food from that which is just ordinary. Most of us are aware of the remarkable gifts a chef must have to create a multicourse meal that presents a progression of complementary flavors without repetition. However, the flavor of even the simplest dish presents a daunting challenge to scientific analysis. A food item that is particularly appealing may have hundreds or even thousands of chemical and micronutrient constituents that stimulate either the tongue's taste receptors or the nose's olfactory receptors—often at a sensitivity of parts per billion. As creators or consumers of fine cuisine, each of us exhibits different taste and olfactory receptors at different stages of the life cycle. These differences are coupled with different neuronal circuits and together produce our highly individualized perceptions of taste.

WHAT'S IN A TASTE OR, MOLECULAR GASTRONOMY?

Artists mix paint and color on a canvas to create delicate and intriguing textures and images. Chefs use foods and techniques that produce extracts, dialysates and concentrates to create delicate and intriguing meals. And physical, chemical and biological scientists use principles, concepts, facts and technology to determine the constituents of solids, liquids and gases. In recent years, these scientific investigations have advanced toward a "molecular gastronomy."

When we consider the hundreds and thousands of small and large molecules and micronutrients that are found in foods, how do we identify and discriminate between tastes and smells during a gourmet meal created by a talented chef? To begin to address this complex set of issues, a group of scientists supported by the

National Institutes of Health recently has made significant progress toward "molecular gastronomy." It is becoming increasingly common for scientists from various universities, federal laboratories and private industries, as well as from different scientific disciplines, to form collaborative groups to address complex problems. The following is just one example of the remarkable scientific progress that can be made through cross-disciplinary and multidisciplinary approaches to complex problem solving.

HUMAN TASTE RECEPTORS

Our senses of taste and smell exist for pleasure, health and well-being. For example, sweetness is a signal that we are consuming nutrients that will provide us with energy, whereas bitterness often is an alarm that we may be eating something toxic. These very fundamental sensory perceptions

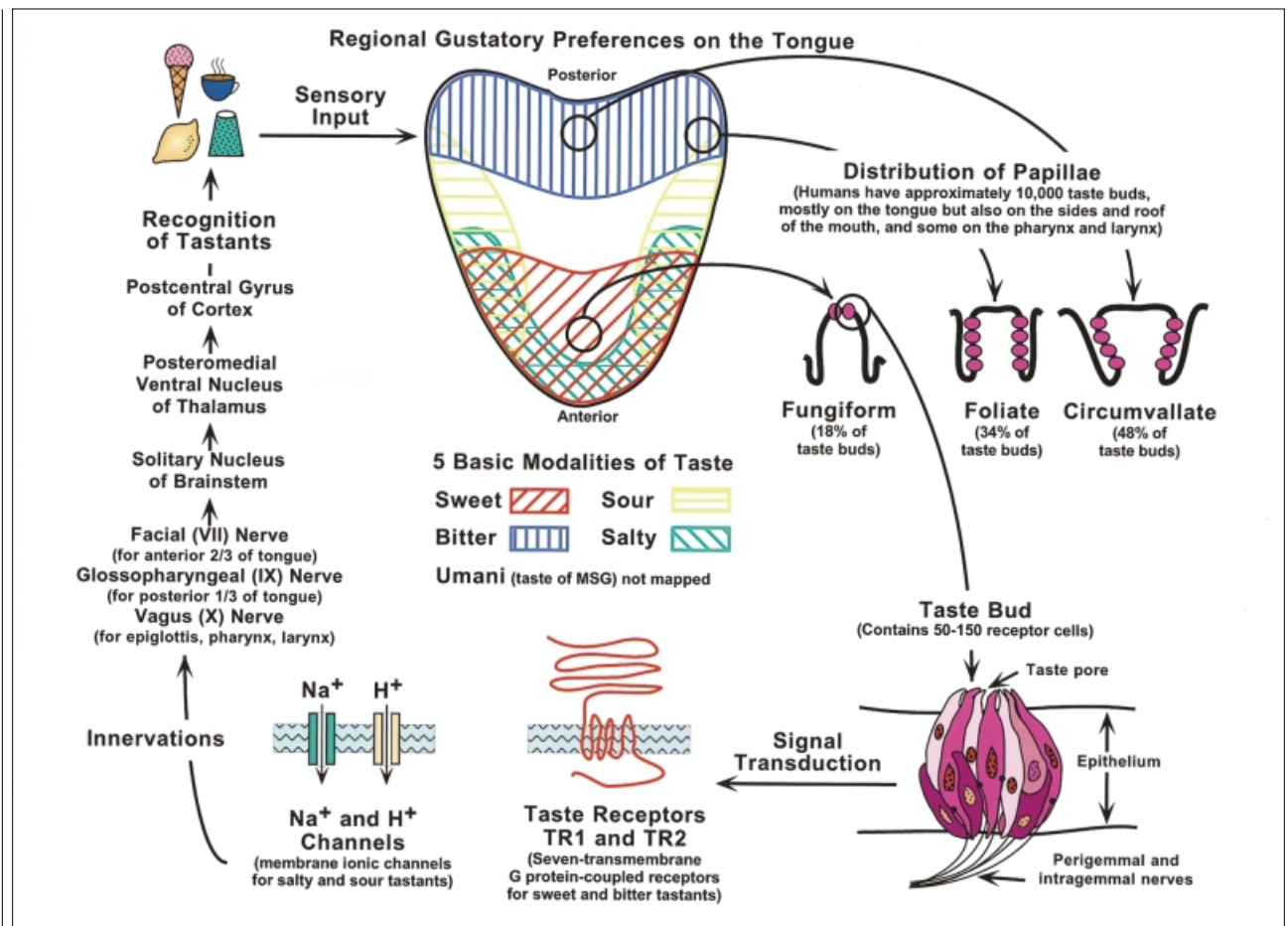


Figure. Scheme of the regional gustatory preferences nested within the 10,000 taste buds distributed on the human tongue. This scheme also shows the recent discovery of two taste receptor genes—TR1 and TR2—that appear to facilitate sweet and bitter taste signals.

have been highly conserved through evolution and have proven to be essential for survival and well-being.

In mice and humans, taste receptors are organized into onion-shaped clusters within taste-bud structures. Knowledge in this scientific area dates back to the description of the lingual papillae by Malpighi¹ in 1664, and to Schwalbe² and Loven,³ who both reported detailed descriptions of taste buds as taste receptors in 1867. More recently, scientists have discovered that taste buds first appear on the human fetus' tongue during the fifth month of gestation.^{4,5} In fact, it has been estab-

lished that infants born in the seventh month of gestation have the ability to detect sourness.⁵

From before birth and throughout the life span, 10,000 taste buds reside in papillae, which are small protuberances that predominantly cover the upper and lateral surfaces of the tongue, as well as the palate, larynx and pharynx in sparse numbers. Different types of papillae are positioned on different regions of the tongue (Figure). At the very back are circumvallate papilla that appear to be sensitive to bitter ligands or signals. Along the sides are foliate papilla that are sensitive to both sourness and

bitterness. Fungiform papillae are located at the front of the tongue and are most sensitive to salty, sour and sweet ligands or signals. Most of these taste buds register several tastes and, therefore, send sensory information in polyphony to the central nervous system for processing and interpretation.⁶

MOLECULAR BIOLOGY OF TASTE

Earlier this year, a scientific team from the National Institutes of Health discovered two genes that encode proteins and that appear to function as taste receptors.⁷ Using numerous types of DNA technology,

cloning and screening techniques, these scientists sifted through many thousands of possibilities for candidate genes and discovered two. They identified these genes as TR1 and TR2 because they resembled other types of sensory receptor genes; TR stands for taste receptor. They selected these candidate genes based on the homology found within the nucleic acid sequence that characterizes each of these genes. Computer-assisted searching of gene databases can be very informative (for example, see GenBank at "<http://www.ncbi.nlm.nih.gov/Web/Search/index.html>"). The development of molecular tools and information technology have allowed for recent and rapid advances—such as the capability to screen millions of genes and identify a needle in a haystack. Earlier studies of the molecular biology of olfaction provided the proof of principle for the recent successes in discovering taste receptor genes.⁸

If TR1 and TR2 are indeed functional taste receptors, they should be located within one or more of these strategically placed types of taste buds on the tongue's surfaces. One way of knowing is to visualize the location of TR1 and TR2's messenger RNA, or mRNA. This can be done by using highly sensitive and specific complementary nucleic acid probes that will bind to the TR1 or TR2 transcripts in the right cells at the right time and that will have a "reporter molecule" attached so that the binding reaction can be directly visualized in the taste buds—so-called *in situ* hybridization or whole-mount hybridization.

When scientists used such an

approach, they found that TR1 was expressed in nearly all fungiform papillae and was exceedingly rare in the taste buds of the bitter-sensitive circumvallate papillae.¹ TR2 was localized in the opposite distribution.¹ It was expressed rarely in fungiform papillae but was expressed essentially always in circumvallate papillae. In addition, both TR1 and TR2 were expressed in foliate taste buds, but both were not expressed in the very same cell of a specific taste bud.

The next step in this scientific investigation was to deter-

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mine precisely where these two genes' mRNAs were located. Scientists asked themselves if the TR1 and TR2 mRNAs were expressed only in taste receptor cells. Previous scientific research established the general principle that each sensory mechanism—such as the visual or olfactory system—receives stimuli from the external environment, and these stimuli are translated into signals that eventually are sent to the brain for interpretation. I discussed the scheme for visualization in a recent article.⁹

In taste sensation or percep-

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tion, the mechanism begins in the taste pores of the taste receptor cells, where sweet, sour, salty or bitter ligands bind to specific receptor transmembrane molecules and invoke signal transduction processes. These processes eventually present patterns of electric information within the central nervous system, where a perception of taste and flavor assembles. Using highly specific antibodies directed against either TR1 or TR2, immunolocalization studies that used

serial histology sections of tongue demonstrated that TR1 was found only in the taste pores of foliate and fungiform taste buds, and TR2 was localized in the taste pores of circumvallate and foliate taste buds. At this stage of the investigation, the TR1 and TR2 gene products were localized in the right place at the right time.

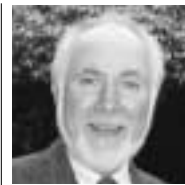
The next step will be to test whether these putative taste receptors can detect and bind specific ligands or taste stimuli. The outcome of this step will be extraordinarily important, as many molecules—such as carbohydrates, proteins, certain amino acids, inorganic salts and artificial sweeteners—can invoke a “sweet” perception. How do we perceive the subtle flavors around “sweet” or any other special taste perception? What do we mean when we describe a person as having a “sweet tooth”?

CONCLUSION

Let's revisit a chef's gourmet creation. Clearly, we savor it with our sensory sight and

smell. Then, as we begin to eat, we employ our senses of sight, smell, taste and touch to fully integrate the experience. The tongue facilitates our delight with food and flavors, and it helps us chew and swallow, which we do about nine times a minute during our gourmet delights and once a minute when we are not eating. Saliva provides a lubricant loaded with hundreds of molecules—such as enzymes, enzyme inhibitors and antibodies—to coat food and microbes and to even inactivate microbes and initiate digestion in the oral cavity. With the help of our tongues, we swallow these microbes along with the gourmet delights, and then gastric acids hydrolyze or fragment these products of the gastronomy experience.

I remain impressed with the remarkable taste receptors that line the taste pore within each of the 10,000 taste buds that each of us uses to appreciate the flavor of artistically prepared foods. And we all can admire and appreciate fully the remarkable curiosity of the intellectual quest



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to eventually understand a molecular gastronomy. ■

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