Umami: Fifth Taste? Flavor Enhancer?

A neuroscientist's view of the most complex of taste qualities

Alexander Bachmanov, Monell Chemical Senses Center

Umami substances, especially when they are present in food, increase the sensation of mouthfullness (thickness, continuity), which is sometimes described by the Japanese word kokumi *and probably involves tactile sensation; this mouthfeel effect also contributes to one's liking of food.*

Like most people, I firmly knew in my childhood that there are four tastes: sweet, salty, sour and bitter. I first learned this in my native language, Russian, then in German, and finally in English. I was quite comfortable with this concept until I became interested in taste science. Then, it appeared to me that some foods have a taste quality that could not be described by any of these four sensations. What was this other taste sensation? It turns out that I was not the first person who wondered about this. Over a century ago, a Japanese chemist, Kikunae Ikeda, was trying to explain "the peculiar taste" arising, for example, from fish or meat, which he believed was distinct from the four known tastes. He called this fifth taste "umami" (loosely: deliciousness/savory) and found that it is evoked by glutamic acid and its salts.

What is Umami?

Because I am a neuroscientist writing for flavorists, let me start with terminological conventions, which sometimes differ between these two fields.

Flavor and taste: For a neuroscientist, flavor is a complex sensation arising from stimulation of several distinct sensory systems: gustatory, olfactory and somatosensory (touch, temperature, pain, etc.). Each system has its unique anatomical and functional organization. The gustatory system in mammals includes taste receptor cells that are organized in taste buds. Most of the taste buds are located within gustatory papillae on the tongue, but some buds are present in other parts of the oral cavity, for example on the soft palate. Taste stimuli interact with the taste receptor cells, and this activates gustatory nerves and subsequently brain structures involved in gustation. Some brain structures that receive sensory information from taste receptor cells also receive input from olfactory and/or somatosensory systems. Integration of the input from these three distinct sensory systems results in the complex perception of flavor. We consider umami a taste sensation because known umami taste stimuli activate all levels of the gustatory system.

Taste qualities: Each of the sensory systems contributing to flavor perception can generate qualitatively different sensations. For example, somatosensation includes perception of temperature or touch. Stimulation of the gustatory system evokes sensations of different taste qualities. Most taste neuroscientists now agree that there are five primary taste qualities: sweet, bitter, salty, sour and umami. However, for much of the history of taste science there was a debate over whether primary taste qualities exist at all, how many of them are genuine and what exactly they are. This debate is documented in works of ancient Greek philosophers, including Democritus, Plato, Aristotle and Theophrastus. Some of them believed that there is an endless number of tastes along a continuum, while others thought there are only a few primary tastes. This debate continued until the end of the 20th century.

There was a good reason why scientists could not agree; these discussions were based on data obtained using the limited techniques available at the time. These techniques included psychophysical evaluation of taste responses in humans, and behavioral and neurophysiological experiments with animals. It often happened that different scientists obtained conflicting results or that results could be interpreted in different ways. If scientists could not agree on whether classical primaries of sweet, bitter, sour and salty exist, it was even more difficult to accept a fifth primary taste of umami.

It turns out that the key information needed to resolve this debate was missing. The way we perceive different sensations is determined to a large degree by interactions of stimuli with sensory receptors. However, the identity of taste receptors remained elusive for a long time. The situation has changed within the last decade, as the molecular

At a Glance

It is now proven that umami is one of the primary taste qualities, although a complex one. Its complexity is due to synergistic interactions among different umami-tasting substances, interactions among umami taste and other flavor components that influence palatability, and individual variation in umami taste sensitivity. Umami tasting compounds, such as glutamate, not only influence food flavor, but also have beneficial nutritive and health effects. These post-ingestive effects could contribute to development of liking of glutamate. The recent discovery of umami taste receptors has opened new avenues in a quest for new umami compounds.

identities of some taste receptors were discovered. The identification of these taste receptors revealed a correspondence between chemical stimuli for what we perceive as taste primaries and the specific receptors that generate these sensations. Importantly, it was shown that there is a taste receptor that responds to umami-tasting stimuli (**F-1**), which is undeniable evidence for umami being a primary taste quality.

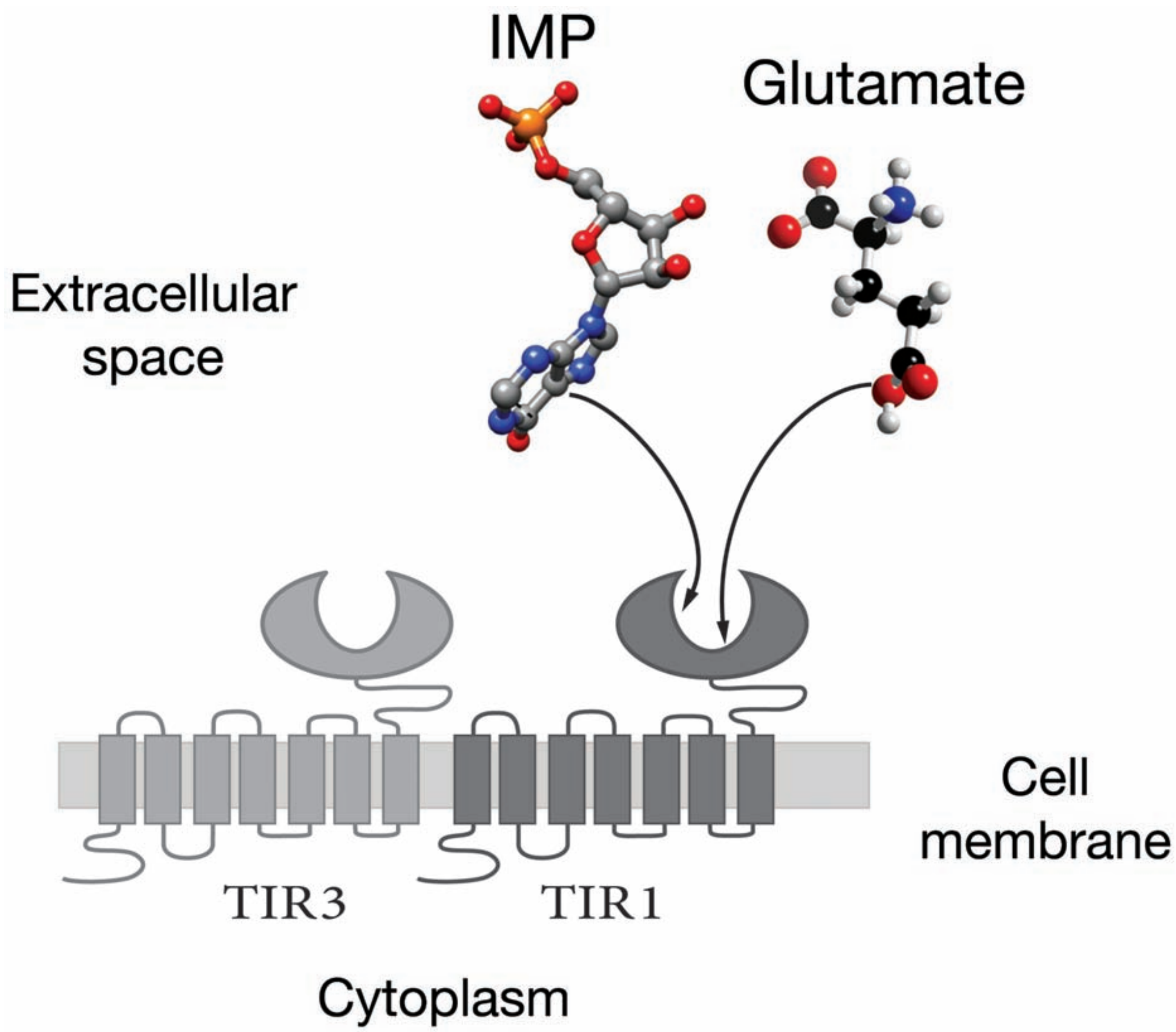
Taste stimuli: The function of the taste system is to detect chemicals in the environment and to evaluate whether they should be consumed or not. We call chemicals that interact with taste receptor cells and evoke taste sensations taste stimuli. For the four classical primary taste qualities, representative taste stimuli evoke sensation of only one taste quality. For example, it is accepted that sucrose has a purely sweet taste, sodium chloride tastes salty, acids taste sour, and compounds such as quinine or caffeine evoke bitter taste. However, many substances, even when they are chemically very simple, evoke complex taste sensations. For example, potassium chloride has a bitter-salty taste and saccharin tastes bitter-sweet. Moreover, a single compound can stimulate different chemosensory systems: many taste stimuli also have an odor or act as chemosensory irritants.

Although many compounds have an umami taste component, none have a pure umami taste. One representative umami taste stimulus, glutamate, is a salt of glutamic acid. While the anion of glutamate generates umami taste, the cation also contributes a different taste. For example, the cation in monosodium glutamate (MSG), Na^+, contributes a salty taste to MSG. Because of its acidic pH, glutamic acid itself is strongly sour, masking its weaker umami taste. Umami taste stimuli from the other umami stimulus group, purine 5'-ribonucleotides, also exist in the form of sodium salts, and therefore also have a salty taste component.

The important point to bear in mind is that although a single taste stimulus can sometimes evoke a sensation of a single taste quality, this often is not the case, particularly for umami-tasting compounds.

How humans perceive umami: It is important to make a distinction between how we perceive umami taste quality and how we perceive umami tastants. From the discussion thus far, it follows that when humans sense an umami-tasting food or even a pure umami-tasting compound, they perceive more than umami taste quality. Therefore, to discern pure umami taste from other flavor components evoked by umami stimuli, humans need to make some comparisons. The inventor of the umami concept, Ikeda, described umami taste quality as "something common in the complicated taste of asparagus, tomatoes, cheese and meat" that cannot be classified under sweet, bitter, sour or salty taste qualities. A good way to experience umami is to compare tastes of equimolar solutions of MSG and NaCl. Both solutions have saltiness, which is attributed to sodium, but MSG also has another taste component not present in NaCl solutions. This component is umami. But even in this simple test, some people cannot discern the umami component (see ***Does Umami Taste the Same to Everyone?***).

Anatomy of the umami taste receptor **F-1**



The human umami taste receptor is composed as a heterodimer of T1R1 and T1R3 proteins. T1R1 and T1R3 are G protein-coupled receptors. Each consists of ~850 amino acids, and has seven transmembrane helices forming a heptahelical domain. The large extracellular N-terminus is composed of a "Venus flytrap" (VFT) domain and a cysteine-rich domain connected to the heptahelical domain.[1] Both glutamate and IMP interact with the VFT domain of T1R1, but at different binding sites. Glutamate induces the closure of the VFT domain, whereas IMP further stabilizes the closed conformation, which determines the synergistic effect between glutamate and purine 5'-ribonucleotides.[9] In rodents (mice and rats), the T1R1+T1R3 heterodimer functions as a broadly tuned L-amino acid receptor. Some scientists proposed that in addition to T1R1+T1R3, several other molecules could function as mammalian taste receptors for umami or glutamate taste. These additional candidate receptors include splice variants of metabotropic glutamate receptors mGluR4 and mGluR1, and the ionotropic N-methyl-D-aspartate (NMDA)-type glutamate receptor; all of these are involved in glutamatergic synaptic transmission in the brain. There is also evidence that glutamate and purine 5'-nucleotides may activate different taste receptors.

Defining "umami": Ikeda derived the word umami from the Japanese adjective *umai* (旨い). Umai has two levels of meaning; one includes a hedonic aspect (delicious, nice or palatable) and the other involves a qualitative description of sensation (brothy, meaty or savory). Both meanings convey important aspects of umami taste perception. At the same time, the word umai is not equivalent to the taste quality discovered by Ikeda: other tastes and flavors (e.g., sweet) can also be described as umai (palatable), and "brothy, meaty or savory" represents multiple flavor components.

To make a distinction between umai and the taste quality illustrated by MSG that he discovered, Ikeda invented the word umami.[a] When he first reported his findings in English, he referred to this taste quality as "glutamate taste." In the contemporary English scientific literature, both "umami taste" and "glutamate taste" are used interchangeably to describe the same taste quality. Umami is appropriate for describing human taste perception. However, glutamate taste or "glutamatelike taste" are more appropriate terms for describing taste responses in non-human animals for two reasons—first, the ways different species perceive the same taste stimulus may be different, and second, even taste receptors that are related across different species may be tuned to detect different sets of substances.

The term "savory" is also used to describe umami taste, but it has the same disadvantage as umai, i.e., both are not strictly limited to umami taste quality. Since the Japanese word umami is already established in the scientific literature as a taste quality descriptor, there is no need to invent an equivalent word in English or other languages.

The Fifth Taste or Flavor Enhancer?

Umami taste is probably the most complex of the five taste qualities. We usually recognize it as one of many flavor components in foods we eat, and there are several types of interactions among different sapid substances and the percepts they evoke. Within the umami taste quality, interactions exist in the form of synergism between glutamate and purine ribonucleotides (**F-1**). In addition, umami substances are known to enhance food palatability. How exactly this works is not completely understood, but there are several mechanisms that can contribute to this flavor enhancing effect. First, umami compounds may change how the flavor of other food ingredients is perceived (e.g., they can suppress unpleasant flavors). Second, umami substances, especially when they are present in food, increase the sensation of mouthfullness (thickness, continuity), which is sometimes described by the Japanese word *kokumi* and probably involves tactile sensation. This mouthfeel effect also contributes to one's liking of food. Third, the palatability of glutamate itself depends on the form in which it is presented. Humans typically dislike or are indifferent to MSG solutions in water, but like MSG when it is present in a more complex medium, such as soup or broth.

[a] "Umami" is spelled 旨味 in kanji, or うま味 in a mixed hiragana-kanji spelling; 味, pronounced as "mi," means taste.

Umami Taste: Nature or Nurture?

Because humans experience umami taste within a context of complex effects of savory food, their perception may be modified by learning an association of umami taste with other properties of food, e.g., its satiating or other rewarding effects. But what is our inborn response to umami taste stimuli? Gary Beauchamp, Leslie Stein, Julie Mennella and their colleagues at Monell are looking for an answer to this question by studying taste responses in infants.[2,4] They found that infants as young as two months old had taste responses to MSG similar to those of adults: MSG decreased palatability of water but increased palatability of soup. MSG did not change palatability of a NaCl solution in infants, which suggests that, to be palatable, MSG needs to be presented in a more complex vehicle. Thus, it seems that to like umami taste, one needs to perceive it in the context of other chemosensory stimuli; this response is present at a very early age. On the other hand, it may be difficult to find the inborn response to umami taste stimuli because human milk has a high glutamate content, and therefore associations between glutamate taste and other chemosensory, nutritive and psychological aspects of breast feeding may form as early as within the first hours after birth. It is interesting that unlike humans, rodents (e.g., laboratory mice and rats) prefer water solutions of MSG at certain concentrations.

Does Umami Taste the Same to Everyone?

Individual variation in taste sensitivity is well known, and umami taste is no exception. Several scientists have noticed that while most people can discriminate between the tastes of MSG and NaCl, some individuals are unable to do this, which suggests that these people are insensitive to glutamate taste. But what is the reason for this apparent insensitivity? Monell scientist Paul Breslin and his colleagues decided to examine whether this differential MSG taste sensitivity depends on the genetic makeup of the umami taste receptor proteins T1R1 and T1R3.[6] They found that both proteins differ among individuals at certain amino acid positions; however, only polymorphisms in the T1R3 protein are associated with variation in MSG taste perception. This study established that some people have difficulty recognizing umami taste and revealed that this taste insensitivity has a genetic basis. Furthermore, these data are consistent with results of molecular studies *in vitro* showing that the umami taste receptor involves both T1R1 and T1R3 proteins (**F-1**).

The role of T1R3 in umami taste was confirmed in another study conducted in Paul Breslin's lab. He and his colleague, Veronica Galindo-Cuspinera, studied whether lactisole, a potent sweetness inhibitor that binds *in vitro* to human T1R3 receptor protein, also inhibits umami taste.[7] They reasoned that if T1R3 is a part of both the sweet and umami receptors, and if lactisole binds to T1R3, then it should inhibit both sweet and umami taste. And they were correct: Lactisole indeed suppressed a significant portion of the perception of umami taste from MSG. Lactisole is used by food manufacturers to reduce excess sweetness of sugar-containing products, but Breslin's study shows that if the food has a desirable umami component, lactisole may decrease that as well.

Can Other Creatures Taste Umami?

For several reasons it is useful to understand whether non-human animals also taste umami. First, much knowledge about taste mechanisms stems from experiments with laboratory animals. Second, if umami taste stimuli can be useful for improving the flavor of human food, they also could be useful for making food for companion and farm animals more palatable. It appears that human umami taste originates from the ability of our remote ancestors to detect the taste of amino acids. Studies at Monell in the laboratory of Joe Brand have shown that the fish taste system is specialized to detect many amino acids, which probably signal the location of food sources.[8] Rodents seem to use their T1R1+T1R3 receptor to detect not only glutamate, but also a wide range of other L-amino acids. In humans and their closest relatives, apes, the T1R1+T1R3 taste receptor apparently became specialized to detect the taste of glutamate and its potentiation by ribonucleotides.

The role of amino acids as attractive taste stimuli is particularly important for cats. Early studies of Gary Beauchamp, current director of Monell, revealed that cats are indifferent to sweeteners but display a preference for several amino acids.[5] A recent study conducted at Monell by Joe Brand, Xia Li and their colleagues explained the molecular basis for cat's indifference toward sweeteners.[10] A cat gene encoding the T1R2 protein is nonfunctional, so that sweet taste receptor dimer T1R2+T1R3 cannot be formed and cats cannot detect sweet stimuli. Only the amino acid receptor dimer T1R1+T1R3 is able to detect taste stimuli and these stimuli are palatable to cats.

Glutamate: More Than a Taste Stimulus

Glutamate is one of the most abundant amino acids available in animal and plant proteins that we eat; it is also present in a free form in many food products. Glutamate has multiple functions in our bodies. It serves as building blocks for proteins, is a major source of energy in the intestine, can be converted into other molecules (e.g., glucose), can stimulate gastric secretion and is one of the major neurotransmitters in the central nervous system.

Our bodies have several independent systems that regulate glutamate metabolism. Most dietary glutamate is metabolized by the intestine as soon as it is absorbed. Any glutamate not utilized by the intestine is metabolized by the liver. As a result, under natural conditions the level of glutamate in the general circulation does not increase after consumption of glutamate-containing food. In addition, the central nervous system cannot use glutamate circulating in the blood because the blood-brain-barrier is not permeable to glutamate. Thus, all glutamate used for neurotransmission is produced in the brain.

Adding glutamate to food not only improves its organoleptic properties, but also could have beneficial health effects, especially in certain groups of people such as elderly individuals or patients with certain gastrointestinal problems. Experiments with laboratory animals also show that supplementation with glutamate can reduce body fatness.

Studies in my laboratory have shown that mice with different genetic makeups vary in how their bodies utilize dietary glutamate, and that this affects glutamate preference. My colleagues and I have studied mice from different inbred strains[b] using preference tests and found that mice from the C57BL/6 strain voluntarily consume more MSG than do mice from the 129P3/J strain. We first examined whether these differences could be due to variations in taste responsiveness but found that mice from both strains have similar taste responses to MSG, as measured in gustatory nerves. These mice were also similar in behavioral tests designed to evaluate their perception of the taste quality of MSG.

Because we could not find any differences in taste responsiveness to MSG, we thought that mice from these two strains may differ in how their bodies process glutamate after it is ingested. To test this, we delivered MSG into their stomachs and then measured several metabolic parameters, including blood glucose level and body temperature. We found that intragastric administration of MSG raised blood glucose in the MSG-preferring C57BL/6 strain, but raised body temperature in 129P3/J mice. These data suggest that when glutamate is preferentially turned into glucose (this process is called gluconeogenesis and mostly occurs in the liver), this generates a rewarding stimulus, which stimulates MSG intake. On the contrary, when glutamate is preferentially used to generate heat (this process is called thermogenesis and can occur in the intestinal wall that uses glutamate as a source of energy, as well as in other tissues), this generates a stimulus that limits glutamate intake.[3] These data suggest that the postingestive effects of glutamate could also contribute to its attractiveness to humans, and that individual humans may also vary in glutamate metabolism in a manner that influences their glutamate liking.

Do Humans Need More Umami Taste Stimuli?

Analyses of organic substances present in our food have detected a substantial number of compounds that have umami taste. They include some L-amino acids (e.g., glutamate and aspartate), purine 5'-ribonucleotides [e.g., monophosphates of inosine (IMP), guanosine (GMP) and adenosine (AMP)], ibotenic, tricholomic, succinic and gallic acids, theogallin, theanine and a number of peptides. Despite this abundance of umami taste substances, there is an interest in developing new umami tastants and taste enhancers.[11] There are several factors that stimulate this interest. MSG has a negative connotation with some consumers, especially in Western countries. It is sometimes regarded as an "artificial" or "chemical" additive and, even though scientific evidence is lacking, is commonly associated with the "Chinese restaurant syndrome." In addition,

[b]Animals within each inbred strain are genetically identical. Differences between inbred strains are attributed to allelic variation of polymorphic genes.

MSG contains sodium, increased consumption of which elevates the risk for cardiovascular diseases. Finding new umami compounds with no or less sodium and suitable for a variety of types of food processing would be beneficial from a health perspective—not to mention product development.

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Address correspondence to Alexander Bachmanov, Monell Chemical Senses Center, 3500 Market St., Philadelphia, PA 19104-3308; tel: 1-267-519-4760; bachmanov@monell.org.

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