Taste (Gustation)

A tutorial on the sense of taste

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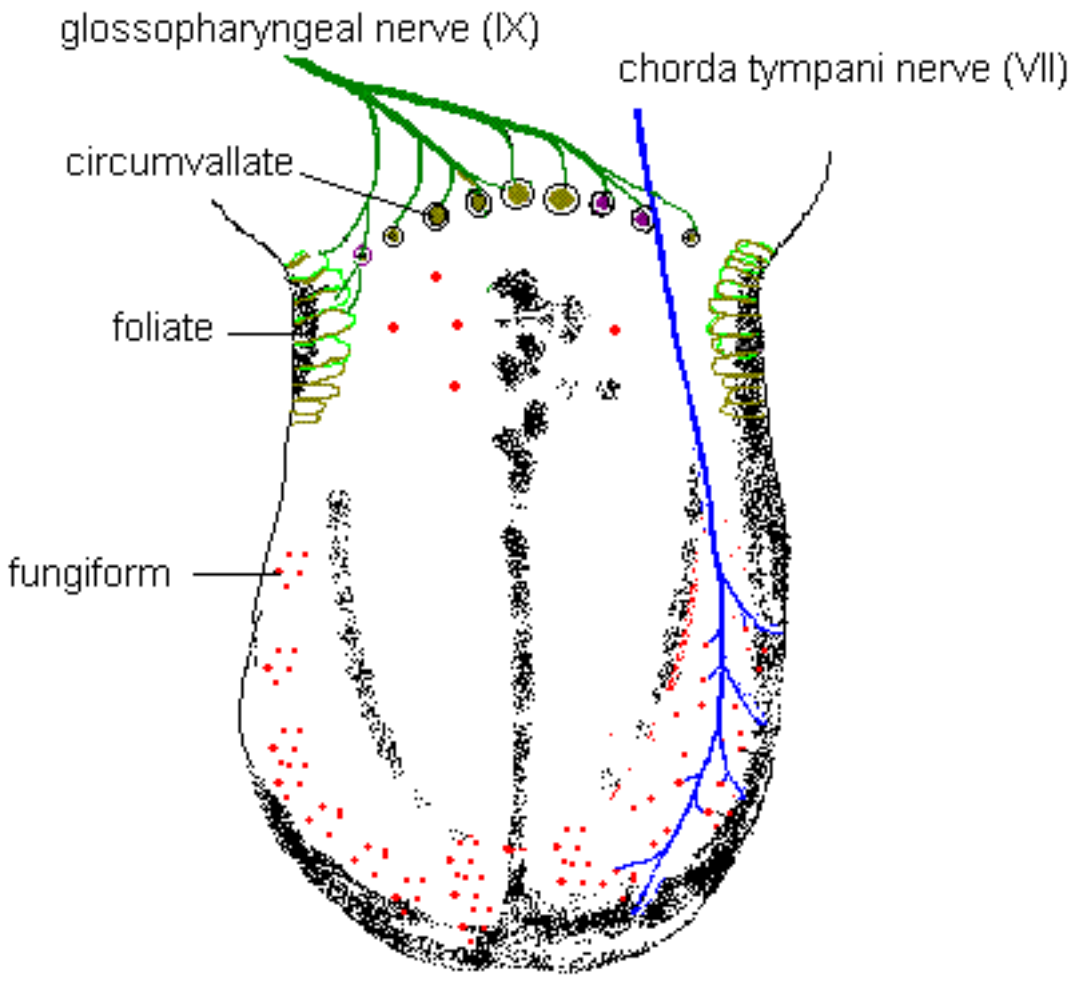

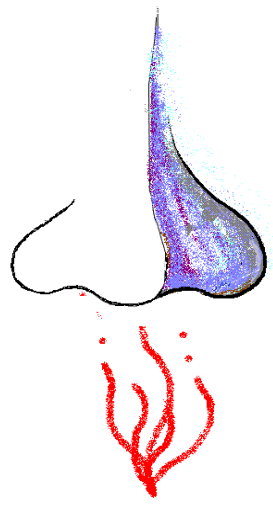

go to companion Smell site

Why taste?

Taste drives appetite and protects us from poisons. So, we like the taste of sugar because we have an absolute requirement for carbohydrates (sugars etc.). We get cravings for salt because we must have sodium chloride (common salt) in our diet. Bitter and sour cause aversive, avoidance reactions because most poisons are bitter (most bitter substances are bad for you - certainly in excess) and off food goes sour (acidic). Why do medicines all taste bitter? Because they are, in fact, poisons and if you take too much they will harm you. We have an absolute need for protein, and amino acids are the building blocks for proteins, so the "new" taste quality umami (pronounced: oo-marmi) which is the meaty, savoury taste drives our appetite for amino acids. This taste has been known to the Japanese for a long time - but has only recently been recognised by the West. Bacon really hits our umami receptors because it is a rich source of amino acids.

Anatomy and Physiology of Gustation (taste)

In mammals, taste buds are groups of 30-100 individual elongated "neuroepithelial" cells (50-60 microns[1] in height, 30-70 microns in width), which are often embedded in special structure in the surrounding epithelium, termed papillae (see Fig. 1 below). At the apex of the taste bud, microvillar processes protrude through a small opening, the taste pore, into the oral milieu. Just below the taste bud apex, taste cells are joined by tight junctional complexes that prevent gaps between cells. Food molecules cannot therefore squeeze between taste cells and get into the taste bud.

[1] a micron is a thousandth of a millimetre (or 10^{-6}m for maths people)

Taste buds and taste papillae.

Taste papillae can be seen on the tongue as little red dots, or raised bumps, particularly at the front of the tongue. These ones are actually called "fungiform" papillae, because they look like little button

mushrooms. There are three other kinds of papillae, foliate, circumvallate and the non-gustatory filiform. Taste buds, on the other hand, are collections of cells on these papillae and cannot be seen by the naked eye. To illustrate the point, have a look at the diagram below. You can see that the taste buds are collections of cells situated on top of, or on the sides of, the different papillae.

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Figure 1.Papillae and taste buds (often mixed up - papillae are visible with the naked eye, taste buds are not)

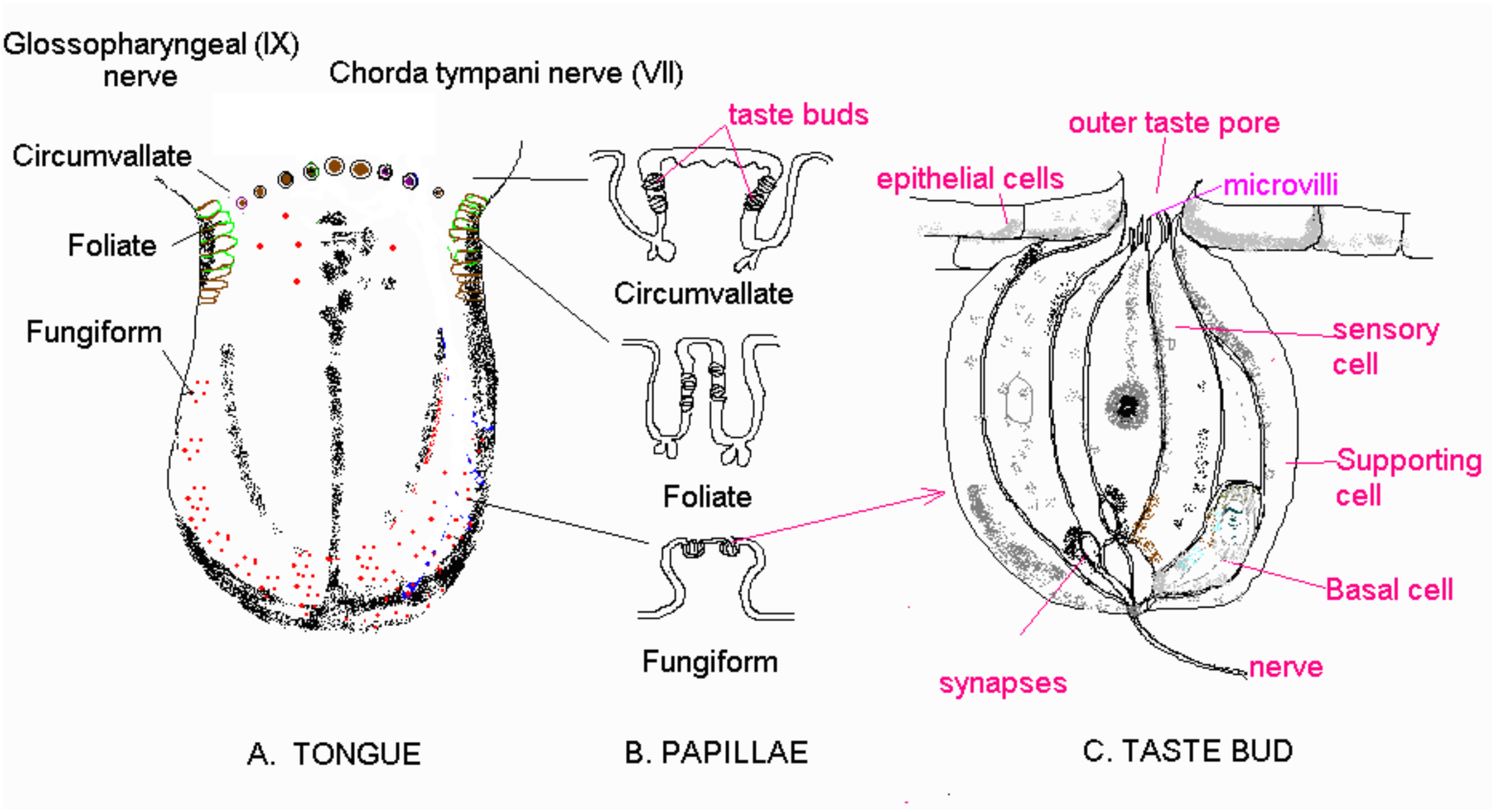

Figure 1 shows the taste **papillae** (on the left) - there are fungiform, foliate and circumvallate papillae. **Taste buds** are situated on the taste papillae (middle section). At the base of the taste bud, afferent taste nerve axons invade the bud and ramify extensively, each fibre typically synapsing with multiple receptor cells within the taste bud .

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In mammals taste buds are located throughout the oral cavity, in the pharynx, the laryngeal epiglottis and at the entrance of the eosophagus. Taste buds on the dorsal lingual epithelium are the most numerous (total number of taste buds, all classes, = 4600 per tongue) and best-studied taste end-organs. Here, taste buds are contained within four major classes of papillae.

- *Fungiform papillae* are located on the most anterior part of the tongue and generally contain one to several taste buds per papilla. They are innervated by the chorda tympani branch of the facial (Vllth cranial) nerve. They appear as red spots on the tongue - red because they are richly supplied with blood vessels. The total number of fungiform papillae per human tongue is around 200. Papillae at the front of the tongue have more taste buds (1-18) compared to the mid-region (1-9). It has been calculated that there are 1120 fungiform taste buds per tongue.
- *Foliate papillae* are situated on the edge of the tongue slightly anterior of the circumvallate line. They are predominantly sensitive to sour tastes. Innervated by the glossopharyngeal (lXth cranial) nerve. On average 5.4 foliate papillae per side of the tongue, 117 taste buds per foliate papillae, total = 1280 foliate taste buds per tongue.
- *Circumvallate papillae* are sunken papillae, with a trough separating them from surrounding wall. The tase buds are in tiers within the trough of the papillae. They are situated on the circumvallate line and confer a sour/bitter sensitivity to the posterior 2/3 of the tongue. Innervated by the glossopharyngeal (lXth cranial) nerve. 3-13 circumvallate papillae per tongue with 252 taste buds per papillae, total = 2200 circumvallate taste buds per tongue
- 

Filiform papillae (left) are mechanical and non-gustatory.

In addition there are 2500 taste buds on the epiglottis, soft palate, laryngeal and oral pharynx. Many of these taste buds are innervated by the facial nerve (Vllth cranial nerve).

The number of taste buds declines with age.

Cells in taste bud (figure 1)

- *Supporting cells* - contain microvilli, appear to secrete substances into lumen of taste bud.
- *Sensory receptor cell* - has peg-like extensions projecting into lumen. These contain the sites of sensory transduction.
- *Basal cells* - these differentiate into new receptor cells. They are derived from surrounding epithelium. The cells are continuously renewed every 10 days or so.

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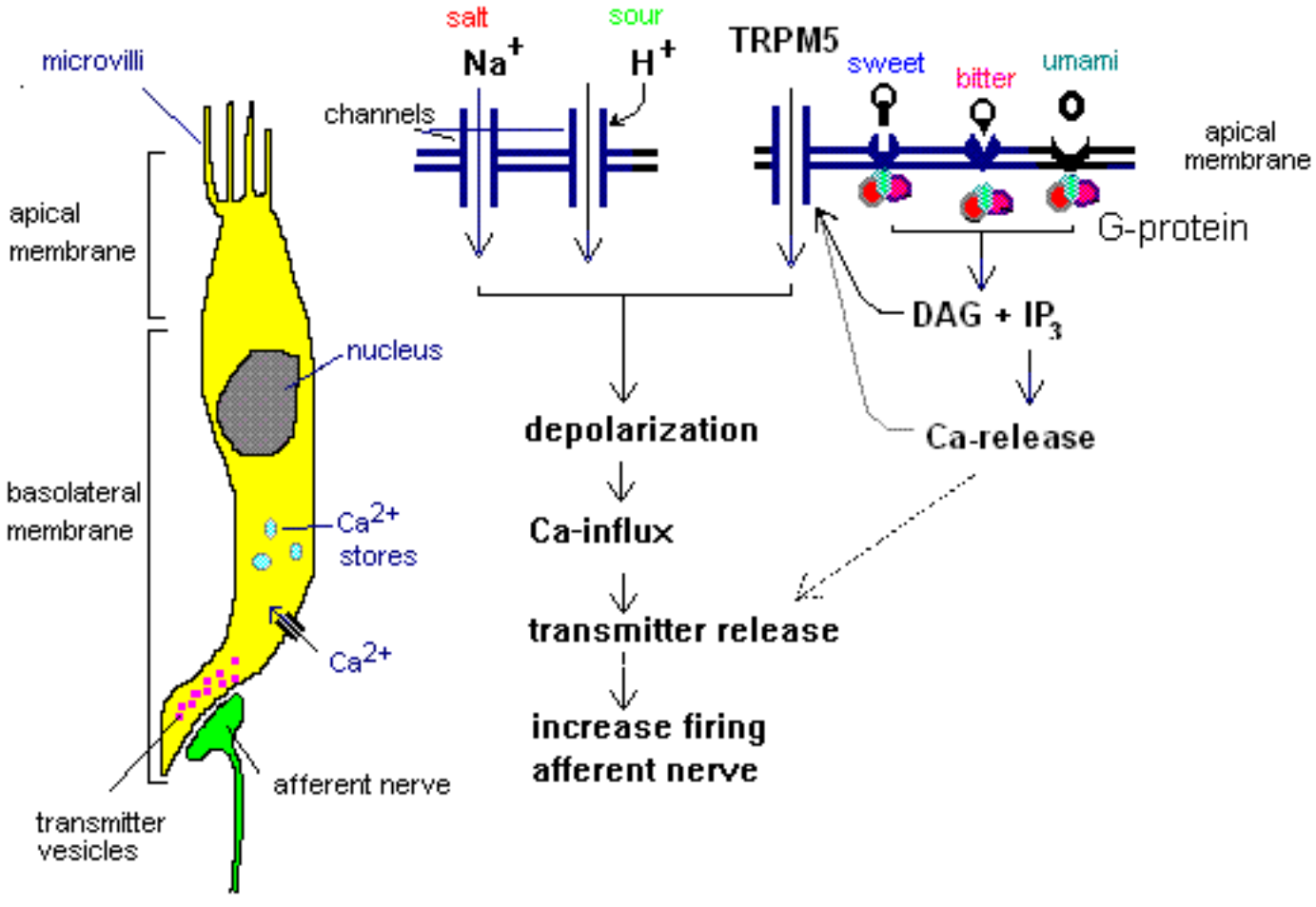
Figure 2. A taste receptor cell



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Taste transduction

There are five basic tastes: salt, sour, sweet, bitter and umami.

The current (as of 2008) thinking[1] is that sweet, amino acid (umami), and bitter taste converge on a common transduction channel, the transient receptor potential channel TRPM5, via phospholipase C (PLC) (see Figure 2). TRPM5 is a newly discovered TRP related to other channels in sensory signalling systems.

It has been shown[2] that PLC, a major signaling effector of G-protein coupled receptors (GPCRs), and TRPM5 are co-expressed with T1Rs and T2Rs and are vital for sweet, amino acid, and bitter taste transduction. Activation of T1R or T2R receptors by their respective tast molecules would stimulate G proteins, and in turn PLC (PLC-ß2). The activation of PLC generates two intracellular messengers - IP_3 and diacylglycerol (DAG) - from the hydrolysis of phosphatidylinositol-4,5-bisphosphate (PIP_2) and opens the TRPM5 channel, resulting in the generation of a depolarizing receptor potential. Other additional pathways may modulate sweet, amino acid, or bitter taste reception but would not, themselves, trigger a taste response. It is not at present known how PLC activates TRPM5 or whether DAG is involved. Future experiments should help reveal the G proteins for the various taste modalities and the mechanism of TRPM5 gating.

It is suggested that the TRPM5 channels are calcium sensitive, thus IP_3 would activate the TRPM5 channels by releasing Ca^{2+} from internal stores - depolarization would follow and this would release the transmitter (ATP - see "Transmitter" below) an increase the firing rate of the gustatory nerve..

1. Chandrashekar, J., Hoon, M.A., Ryba, N.J.P. and Zuker, C.S. (2006) The receptors and cells for mammalian taste. *Nature* **444** 288-294
2. Zhang, Y, Hoon, M.A., Chandrashekar, J., Mueller,K.L. , Cook,B., Wu, D., Zuker, C.S. and Ryba, N.J.P. (2003) Coding of Sweet, Bitter, and Umami Tastes Different Receptor Cells Sharing Similar Signaling Pathways *Cell* **112**, 293-301.

1. *Salt taste*

   Salt is sodium chloride ($Na^+ Cl^-$). Na^+ ions enter the receptor cells via Na-channels. These are amiloride-sensitive Na^+ channel (as distinguished from TTX-sensitive Na^+ channels of nerve and muscle). The entry of Na^+ causes a depolarization, Ca^{2+} enters through voltage-sensitive Ca^{2+} channels, transmitter release occurs and results in increased firing in the primary afferent nerve.
2. *Sour taste*

   Sour taste is acid and acid is protons (H^+). There is exciting new evidence that there is an acid-sensing channel - the PKD2L1 channel[1].This channel is a member of the transient receptor potential channel (TRP) family and is a non-selective cation channel. The activity of PKD2L1 is gated by pH (H^+ ion concentration). This new discovery displaces the previous ideas that H^+ ions block K^+ channels causing a depolarization, or that H^+ ions enter the cell through ENaC channels. These mechanisms may exist but do not lead directly to sour perception.
3. *Sweet taste*

   There are receptors T1R2 + T1R3) in the apical membrane that bind glucose (sucrose - a combination of glucose and fructose - and other carbohydrates). Binding to the receptor activates a G-protein which in turn activates phospholipase C (PLC-ß2). PLC generates IP_3 and diacyl glycerol (DAG). These intracellular messengers, directly or indirectly, activate the TRPM5 channel and depolarization occurs. Ca^{2+} enters the cell through depolarization-activated Ca^{2+} channels, transmitter is released increasing firing in the primary afferent nerve.
4. *Bitter taste*

   Bitter substances bind to the T2R receptors activating the G-protein and causing activation of PLC. The second messengers DAG and IP_3 are produced (by hydrolysis of phosphatidylinositol-4,5-bisphosphate) activating TRPM5 and mediating release of Ca^{2+} from internal stores. The elevated Ca^{2+} causes transmitter release and this increases the firing of the primary afferent nerve.
5. *Umami taste*

   Umami is the taste of certain amino acids (e.g. glutamate, aspartate and related compounds). It was first identified by Kikunae Ikeda at the Imperial University of Tokyo in 1909. It was originally shown[2,3] that the *metabotropic* glutamate receptor (mGluR4) mediated umami taste. Binding to the receptor activates a G-protein and this elevates intracellular Ca^{2+}. More recently it has been found that the T1R1 + T1R3 receptors mediate umami taste[4] . Binding to the receptors activates the non-selective cation channel TRPM5 as for sweet and bitter receptors (i.e. via G-protein, PLC, IP_3 and DAG - see above). Guanosine 5'-monophosphate (GMP) and inosine 5'-monophosphate (IMP) potentiate the effect of umami tastes by binding to another site of the T1R1 receptor.

   Monosodium glutamate, added to many foods to enhance their taste (and the main ingredient of Soy sauce), stimulates the umami receptors. But, in addition, there are *ionotropic* glutamate receptors (linked to ion channels), i.e. the NMDA-receptor, on the tongue. When activated by these umami compounds or soy sauce, non-selective cation channels open, thereby depolarizing the cell. Calcium enters, causing transmitter release and increased firing in the primary afferent nerve

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[1]The cells and logic for mammalian sour taste detection. Huang et al., (2006) Nature 442, 934-8.

[2]Chaudhari et al, (1996) The taste of monosodium glutamate: membrane receptors in taste buds. J. Neurosci. 16, 3817-3826.

[3]Kurihara & Kashiwayanagi (1998) Introductory remarks on umami taste. Annals NY Acad Sci 855, 393-397.

[4]Nelson, G. et al (2002) An amino-acid taste receptor. Nature 416, 199-204.

6. *Monosodium glutamate*

   Monosodium glutamate is the main ingredient of Soy sauce. This is added to foods to enhance their flavour. As well as activating umami receptors, it probably works by activating NMDA receptors which are found in taste cells. NMDA receptors are integral receptor-ion channel complexes and when they open they allow an influx of Na^+ and Ca^{2+} ions. This will depolarise the taste receptor cell and act as an excitatory influence. Then, far less of a particular taste will be required to cause the further depolarisation necessary to bring about transmitter release.

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Transmitter

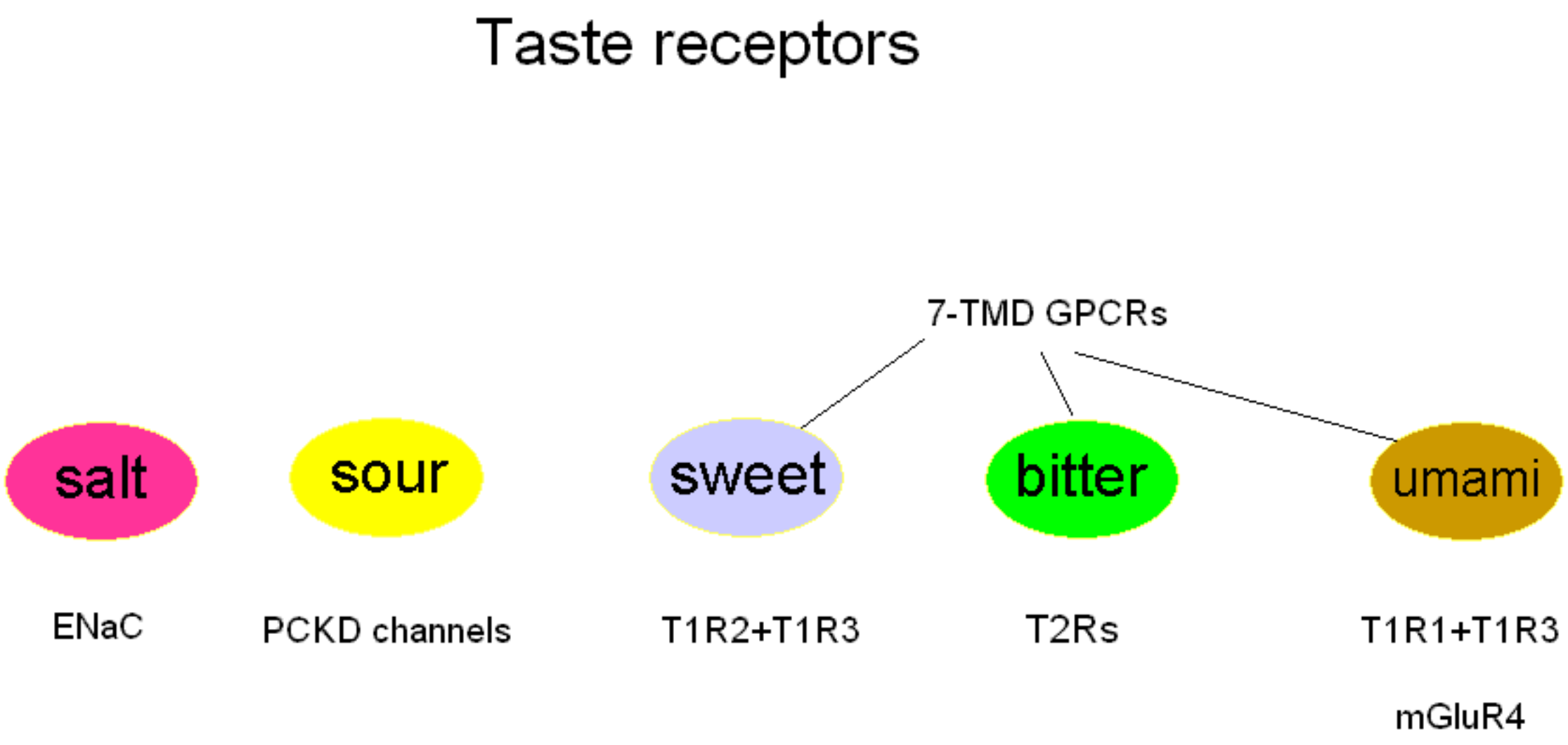
Finger and colleagues[1] showed that all sweet, bitter, sour, salty and umami nerve responses were lost in the purinergic double-knockout mouse. This suggests that ATP (a purinergic agonist) is the taste neurtransmitter, released by the receptor cells to activate the primary afferent nerve. The taste receptor cells release ATP in a non-vesicular fashion to activate the gustatory nerve fibres[2]. Because the ATP is released via pannexin hemichannels rather than by vesicular fusion, Ca-influx is not necessary[3].

1. Finger et al., (2005) ATP signalling is crucial for communication from taste buds to gustatory nerves. *Science* **310**, 1495-1499.
2. Romanov, R.A. et al. (2007) Afferent transmission mediated by hemichanneks in mammalian taste

cells. *EMBO J* **26(3)**, 657-667.
3. Huang, Y.J. et al. (2007) The role of pannexin 1 hemihannels in ATP release and cell-cell communication in mouse taste buds. *PNAS (USA)* **104(15)**, 6431-6441.

Receptors

Sweet, bitter and sour taste receptors have recently been cloned. A summary of the different types of receptor responsible for each of the 5 taste modalities is given below.



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Salt receptor

- ENaC (Epithelial Sodium (Na) channel)
- ubiquitously expressed

Bitter receptor family - T2Rs

- 50-80 members
- expressed in small subset of all taste papillae
- expressed in cells that also express a-gustducin
- 70% of gustducin cells in circumvallate & foliate papillae express T2Rs

Sweet and umami receptors

Heteromeric receptors made up of a combination of different subunits, coded for by a small gene family - T1Rs - have a look at their structure

- T1Rs (3 genes distantly related to mGluRs)
- By in situ hybridization, Liao and Schultz (2003) found that all 3 T1R genes are expressed selectively in human taste receptor cells in the fungiform papillae, consistent with their role in taste perception.
- T1R1+3 = amino acid receptor (umami)
- T1R2+3 = sweet receptor
- T1R3 - on its own may be the sweetner receptor
- Umami is possibly mediated by both mGluR4 and T1R1+3 receptors

Liao, J.; Schultz, P. G. Three sweet receptor genes are clustered in human chromosome 1. Mammalian Genome 14: 291-301, 2003.

Sour receptors

Sour is the taste of acid, i.e. protons (H^+).

In August 2006, Huang et al[4] published a paper showing that mice in which cells expressing PKD2L1 (polycycstic kidney disease-like channel) were ablated (knocked out) were completely unable to detect sour substances. PKD2L1 is a member of the TRP (transient receptor potential) superfamily of ion channels. They are non-selective cation channels. PKD2L1 is gated by pH (H^+ ion concentration), a decrease in pH (acidity) openingthe channel and causing a depolarizing receptor potential. This activates voltage-dependent Ca^{2+} channels, evelating intracellular Ca^{2+} . This in turn causes the release of transmitter (now thought to be ATP).

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2. An amino-acid taste receptor. Nelson, G. et al (2002) Nature 416 (14 March), 199-204
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4. The cells and logic for mammalian sour taste detection. Huang et al., (2006) Nature 442, 934-8.

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Artificial Sweetners

Have a look at the structure of sweetners - most sweetners have a structure very different from that of sweet tasting compounds, e.g. glucose.

Saccharin - Discovered in 1879 when a Johns Hopkins worker inadverently licked his fingers. Saccharin is only sweet to humans. Bees/butterflies which normally crave the sweetness of nectar, do not treat it as a desirable substance.

Cyclamate - Discovered by accident. A graduate student at the University of Illinois in 1937 was smoking a cigarette that came into contact with some.

Aspartame - James Schlatter licked fingers in preparing to pick up a peice of weighing paper. It is a combination of two naturally occurring amino acids (aspartic and phenylalanine). Alitame, similar to aspartame in that it combines two amino acids (alanin and aspartic acid) into a dipeptide, is about 2,000-times sweeter than sugar.

Sucralose - A chloride-containing carbohydrate product some 600-times sweeter than sugar. Discovered when a foreign student (Shashikant Phadnis) working in Prof Leslie Hough's lab at King's College, London, misunderstood a request for "testing" as "tasting".

Some plant proteins, e.g. Monellin and Thaumatin, taste 10,000 times as sweet as sucrose (a disaccharide made up of a glucose and a fructose molecule). Salts of lead and beryllium also taste sweet.

Certain artifical sweetners (e.g. saccharin) lead to the generation of IP_3 and a rise in intracellular Ca^{2+} due to release from internal stores.

> Similar to other G protein-coupled receptors of family C, the N-terminal venus flytrap domain ofT1R2 is required for recognizing sweeteners, such as aspartame and neotame - look at structure of T1Rs - . The G protein coupling requires the transmembrane domain of T1R2. Surprisingly, the C-terminal transmembrane domain of T1R3 is required for recognizing sweetener cyclamate and sweet taste inhibitor lactisole. Because T1R3 is the common subunit of the sweet taste receptor and the umami taste receptor, Xu et al. (2004) tested the interaction of lactisole and cyclamate with the umami taste receptor. Lactisole inhibited the activity of the human T1R1/T1R3 receptor and, as predicted, blocked the umami taste of L-glutamate in human taste tests. Cyclamate did not activate the T1R1/T1R3 receptor by itself, but potentiated the receptor's response to L-glutamate. Taken together, these findings demonstrated the different functional roles of T1R3 and T1R2 and the presence of multiple ligand binding sites on the sweet taste receptor (Xu et al., 2004).
>
> Xu, H.; Staszewski, L.; Tang, H.; Adler, E.; Zoller, M.; Li, X. Different functional roles of T1R subunits in the heteromeric taste receptors. Proc. Nat. Acad. Sci. 101: 14258-14263, 2004.

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Modifying taste

Taste exhibits almost complete adaptation to a stimulus - perception of a substance fades to almost nothing in seconds. Taste can be suppressed by local anaesthetics applied to the tongue. Amiloride, a blocker of epithelial Na channels, reduces salt taste in humans and adenosine monophosphate (AMP) may block the bitterness of several bitter tasting agents. Naturally occuring compounds include, gymnemic acid (a product of the Indian tree/shrub Gymnema sylvestre) decreases the sweet perception by competitive

inhibition of the sweet receptor. Artichokes have the opposite effect, enhancing sweet taste (the active compounds in this case are chlorogenic acid and cynarin) by suppression of sour and bitter taste receptors. Miracle fruit turns sour tastes sweet. The active ingredient, "miraculin", binds to a site near the sweet receptor. When sour substances then are tasted, a conformational change in the taste cell membrane occurs in such a way as to bring the miraculin molecule into contact with the sweet receptor, activating it.

Regional localisation of taste on the tongue (Taste maps)

There has been some controversy as to whether the familiar taste maps of the human tongue, which appear in every textbook, are correct. Taste sensation can be localised on the tongue but does the tongue have regions that are more sensitive to one taste modality than another? Fungiform papillae are concentrated on the anterior tip of the tongue and anterior lateral margins in humans and it has been demonstrated that NaCl threshold was inversely related to the number of fungiform papillae (more papillae = more sensitivity, lower threshold). In a study of human fungiform papillae it was found that taste buds can respond to NaCl only or to both NaCl and sucrose. The responses to NaCl and sucrose occurred in different cells within the taste bud. Thus, one can infer that fungiform papillae are salt-sensitive but this does not mean they are insensitive to other tastes. Bitter receptors are not uniformly distributed over the tongue. In rats the bitter receptors are expressed in a subset of taste cells in all papillae but they are more concentrated in foliate and circumvallate papillae situated at the sides and the back of the tongue. Furthermore, alpha-gustducin, which is the G-protein coupled to the T2R bitter receptors (see below), is expressed more in circumvallate than fungiform papillae in the rat. One rather more empirical approach to resolving this question is to stimulate the different areas of the tongue directly. Thermal stimulation of the anterior sides of the tongue in humans (fungiform papillae and the chorda tympani nerve) evokes sweet and salt/sour taste. While thermal stimulation of the rear of the tongue (foliate/circumvallate papillae and glossopharyngeal nerve) causes a different relationship between temperature and taste to the anterior stimulation. One can conclude that the classical "taste map" is an over simplification. Sensitivity to all tastes is distributed across the whole tongue and indeed to other regions of the mouth where there are taste buds (epiglottis, soft palate), but some areas are indeed more responsive to certain tastes than others.

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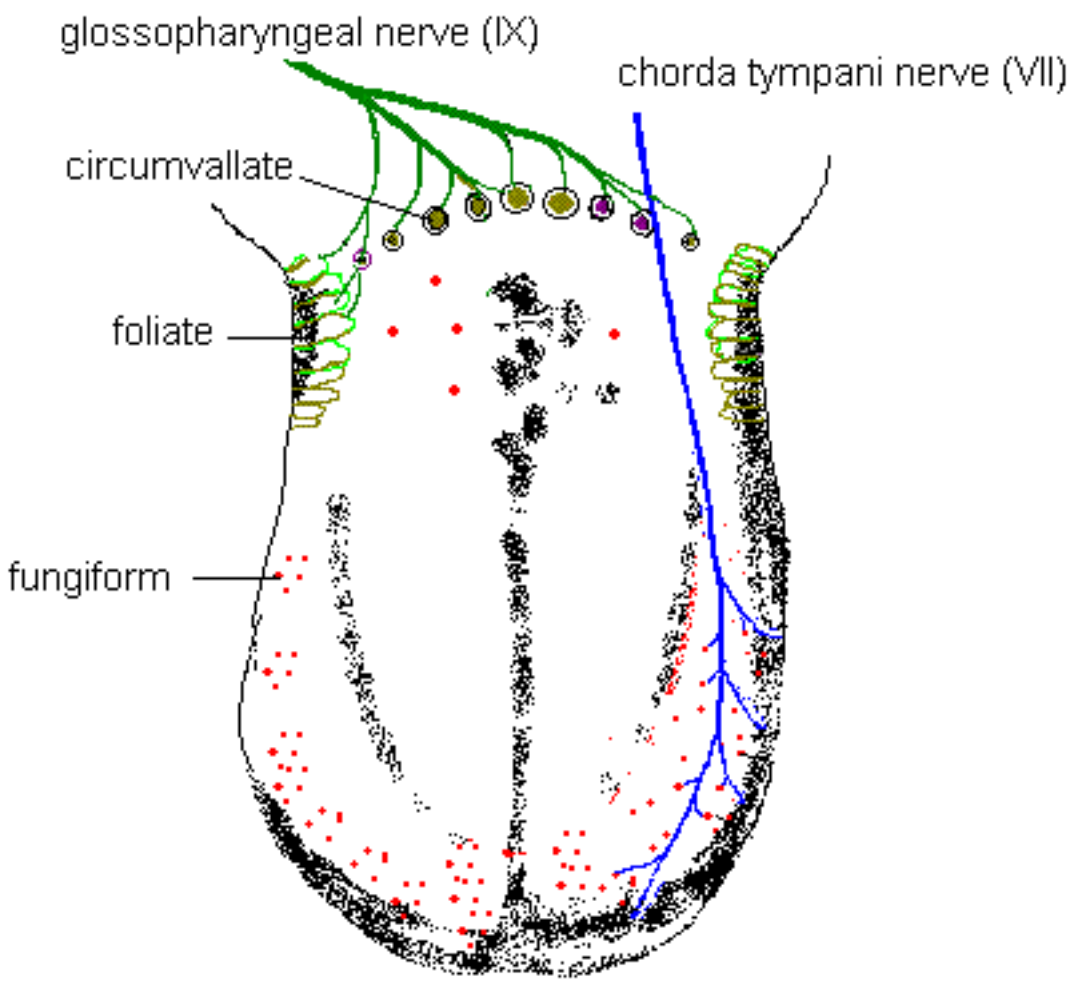
Relay to the brain

Figure 3. Innervation of the tongue



Taste receptor cells do not have an axon. Information is relayed onto terminals of sensory fibres by transmitter. These fibres arise from the ganglion cells of the cranial nerves Vll (facial - a branch called the chorda tympani)) and lX (glossopharyngeal) (see Figure 3).The first recordings from sensory fibres showed an optimal response to one stimuli, but a smaller response to other taste stimuli.

There was been much evidence that taste is determined by the pattern of active (firing) fibres, i.e. by "across-fibre pattern" rather than "labelled-line". However, the molecular biologists have provided some fairly convincing evidence that taste operates by the "labelled-line" mechanism - knocking out specific taste receptor genes rendered mice completely insensitive to that taste modality - can't argue with that! But, the fact remains that many phenomena can only be explained by cross fibre patterns of activity. The pedulum swings between these two theories - the answer (?) - probably lies in-between!

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Central pathways
Primary gustatory fibres synapse centrally in the medulla (in a thin line of cells called the nucleus of the solitary tract). From there the information is relayed (1) to the somatosensory cortex for the conscious perception of taste and (2) to the hypothalamus, amygdala and insula, giving the so-called "affective" component of taste. This is responsible for the behavioural response, e.g. aversion, gastric secretion, feeding behaviour.

Supertasters

It has been found that some people have more than the normal number of taste papillae (and taste buds). They are distinguished by their increased density of fungiform papillae and their exterme sensitivity to the chemical *n*-propylthiouracil (PROP). Supertasters - 25% of the population (and more women than men) - tend not to like green vegetables and fatty foods.

	% of population	*density of taste papillae cm^{-2}
supertasters	25	165
normal tasters	50	127
non-tasters	25	117

* at the tip of the tongue (from Yackinous & Guinard, *Appetite* (2000) **38**, 201-209).

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Strange taste facts

Taste is mainly smell. Hold your nose, close your eyes, and try to tell the difference between **coffee** or **tea**, **red** or wine, **brandy** or **whisky**. In fact, with blocked nose (clothes peg or similar) you can't tell the difference between grated apple and grated onion - try it! Of course, this is because what we often call taste is in fact flavour. Flavour is a combination of taste, smell, texture (touch sensation) and other physical features (eg. temperature).

Smelly fruit

The durian fruit smells horrible. Some people cannot bear to eat it because it smells so foul. But it is called the "King of Fruits" and tastes delicious. It is very large (can be the size of a football) and comes from South East Asia.

Links to other sites:

- Notes on smell
- Chemoreception, a vaste resource of everything to do with taste and smell, wierd and mainstream.

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