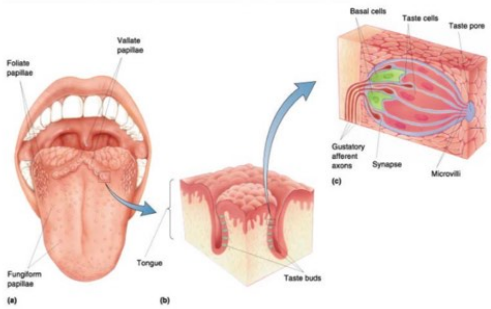
Neurophys – 3.1 – L7 – Olfaction (Smell) and Taste

Sensory receptors

- Almost 50% of the vertebrate GPCR repertoire
- Different types of receptors – have amino acid ECM chain, big extracellular binding domain or intracellular domain (sensitisation)

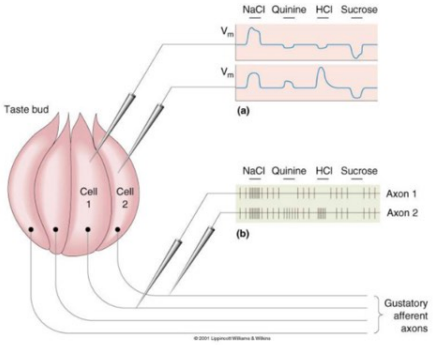


Flavour – **BOTH OLFACTION + TASTE** contribute to flavour

- Taste buds in mouth, diffusion of volatile odorants into nasal cavity → activate afferents
- Ability to discriminate flavours important in survival (salt, sweet, bitter, umami, sour)
- Pharynx and epiglottis (along with tongue, palate) participate in taste

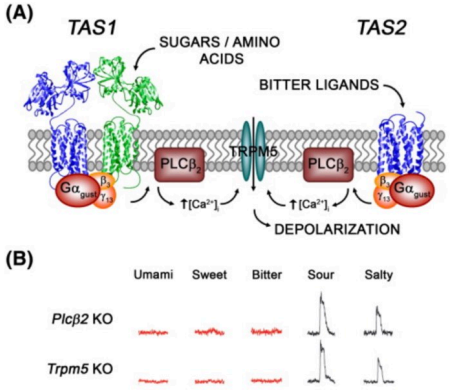
Taste buds – collections of taste-receptive cells → **SENSING ELEMENT NOT NEURON**

- Papillae (different types) = **taste-sensitive** structures with **each cell** having **different sensitivities**
  - **Final output from each taste bud must be integrated centrally** to achieve tongue's regional selectivity
- 2000-5000 in mouth, regularly (bi-weekly) turnover
- **ACCESSORY CELL** which communicates with neuron which is responsible for sending info. to CNS
  - Some taste receptor cells have voltage gated ion channels and can generate APs but they don't need to → these receptor potential changes are sufficient to cause calcium to flow in through VG Ca^{2+} channels and cause transmitter release which then released from cells (1,2) to activate axons of gustatory afferents
  - General perception rule: all sensory information goes to cortex via thalamus (except olfactory/smell)
- Sweet, umami, bitter → GPCR
- Salt, acid detection → direct interaction with ion channels

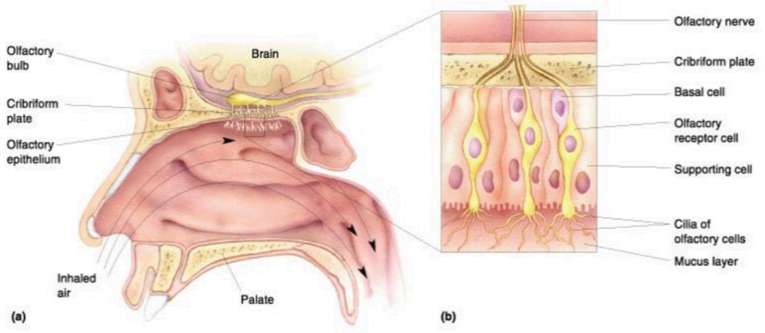


Gustatory receptors – **GPCR – SWEET, UMAMI, BITTER** - 7 transmembrane receptor that is coupled to G protein initiating intracellular signalling pathways

- **TAS1R** – glutamate GPCR family (3 members) → sweet + umami
- **TAS2R** – 25 highly divergent FPCR → bitter (aversive/toxic)
  - Response to binding to ligand, receptor conformation changes across membrane leading to α becoming open to signal molecule, β gamma subunits dissociate and have another effect = 2 potential effects
  - βγ binds to PLC causes increase in intracellular calcium, which binds to transient receptor potential M5 class of ion channel, opening it and allowing positive ions to enter and cause depolarisation
  - TAS1 and TAS2 has same effect - mechanism feed → determine what is what by population effects, sensitivities between neighbouring cells
  - If we knock out enzyme or channel (B) - we lose signalling associated with umami, sweet + bitter *but* retain salt and sour because they're in different pathway



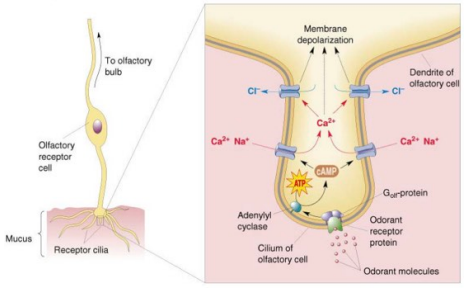
Olfactory system



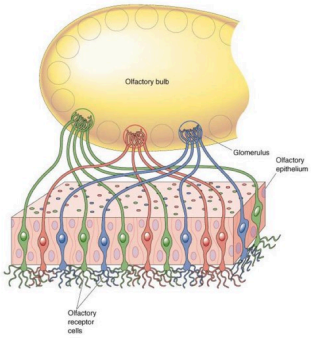
- Epithelium → lies on roof of nasal cavity containing *olfactory receptor cells (CN1)* ***(neurons)*** which are turned over continuously → cells send axons through Cribiform plate to olfactory bulb
    - Neurons are sensing element – no intermediate as with taste
    - Cilia → Production of mucus with polysaccharides, antibodies, binding molecules → odour molecules come in a dissolve in solution - can bind to cilia of olfactory neuron (every 10min turned over - desensitisation)
- Olfactory bulb → primitive, 2nd order olfactory neurons have branching dendritic trees that form glomeruli with terminals of olfactory receptor cells → **where neurons synapse with new neurons**

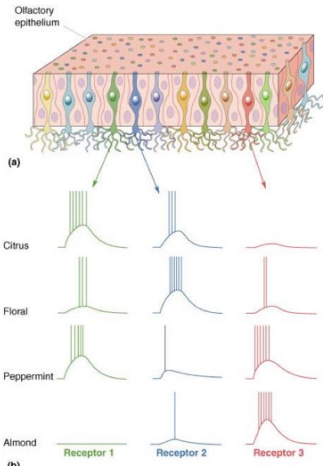
Olfactory axons → bulb → 2nd order neuron → CNS (NOT TO THALAMUS) → multiple steps → olfactory paleo-cortex NOT neocortex

Transduction of smell



- Many different odorants able to be detected → **selectivity depends on odorant receptor molecule**
- **PATHWAY COMMON AFTER ACTIVATION** of receptor
    - Odorant molecules binding to receptor protein (GPCR) which activates adenylyl cyclase causing conversion of ATP to cAMP activating the cAMP pathway (causes influx of Ca^{2+}, Na^{+} and efflux of Cl^{-} - cells have high intracellular Cl^{-}) resulting in **depolarisation**
- **Receptors are coded by ~900 genes** (but many pseudogenes) and **~390 proteins** vs **1500 genes in rodents** (3-5% of all encoded genes) as they're more smell-dependent
    - **NUMBER OF ODORANTS >> RECEPTOR NUMBER** so each odorant affects multiple receptors and each receptor detects multiple odorants
        - **Different receptors have different response profiles to arrays of odorants → determining RECEPTIVE FIELD** – combination = pattern = brain can discern
        - **ALSO, receptor cells with same receptive field synapse TOGETHER in glomerulus** – express same odorant receptor





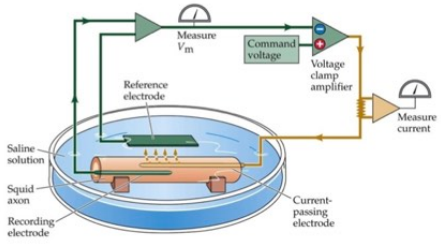
    - Only expresses 1 GPCR in each receptor cell
    - Also existence of pheromone GPCR (3 families) → Verosa nasal organ, a less developed organ in humans than other animals - gives us a sense of smell that we don't perceive - pheromones - responsible for subconscious reactions we have with environments and each other

Functional odorant and taste receptors expressed in **other viscera** other than nasal cavity/mouth – no idea for most but → testis (chemotaxis), GI (organic nutrient sensing), respiratory (response to irritants), kidneys (regulation of renin secretion/GFR) → **bitter GPCRs (TAS1R/TAS2R) expressed in heart** (increase taste receptor = ↑activity of heart = functionally relevant)

Neurophys – 3.2 – L8 – Measuring Neuronal Activity 1

We can measure neural activity at many levels

- Neural activity is defined as a network of activity that is response to defined stimulus and is invariant in response and equal = reflex, something more complex is called a motor pattern - chewing, tap dancing, speaking, repetitive behaviours
    - Behaviour, activity in specific regions/networks associated with behaviour, network activity in networks resulting from a defined stimulus (*in vivo or in vitro*), activity in single cells (individual neurons) or activity in cellular sub-compartments
- **Properties measured at single-cell level**
    - We get **VOLTAGE** (neurons use electrical signals to communicate, ion channels, K^+ flow, so respond to V=IR)**, CURRENT** (current flow produces voltage changes)**, TRANSIENT CHANGES** in intracellular ions (Ca^{2+})

Method	Mechanism	Strengths	Weaknesses
Single Cell Recording	Isolate AP from one unit (cell, axon, dendrite) and measure the extracellular signal only and not all the ones around it → detects currents produced by action potentials → metal or glass capillary microelectrode → the closer to the source, the more powerful	• Can be used anywhere in NS • *In vitro* and *in vivo* possible • Can be used in freely behaving animals/contracting tissues • Can be combined with multiple recordings to allow correlation of activity at different sites • Can be used for a relatively decent time	• Can't identify specific type of neuron recorded in mixed nucleus without other methods • Doesn't give information about neurons that don't fire APs • Does not identify synaptic potentials that lead to changes in firing - Some neurons will respond because inhibition has been removed from cell body - inhibit the inhibition (disinhibition) you get excitation - what you see when current changes is direct excitation, could be disinhibition
Intra-cellular recording	Sharp microelectrode (0.05 – 0.5 µm tip) inserted into individual neuron → electrode glass capillary filled with conducting KCl ~3M	• Records membrane potentials (APs, IPSPs**, EPSPs, synaptic potentials) from cell body NOT single unit • Used *in vitro* but can be *in vivo* • Allows injection of intracellular markers to identify neuron morphology + neurochemistry	• If require long (days) recordings – need very stable situations, so *not* freely behaving animals • Prolonged periods limited to hourly if drug testing for synaptic transmission • *Allows study of membrane mechanisms that determine excitability* but is **hard** • Does not identify sites within a neuron that generate a signal (treats whole neuron as one)
Voltage clamp	Records current needed to keep membrane potential constant - with one electrode and passes current with other	• Determines current passing through membrane after a stimulus	

SNS and visceral primary afferents innerve whole length. SNS modulates circuits and contraction. Visceral afferents are made of dorsal root afferents (splanchnic and pelvic nerves for pain) and vagal afferents (CNS interaction, reflexes). PNS everywhere via vagus except jejunum and ileum.

Functions of ENS

- Controls movement of intestinal content
  - Absence of ENS = no movement of food = gut swelling
- Regulation of water and electrolyte transport across mucosa
  - Movement of H_2O + NaCl into body from lumen = absorption
  - Movement of H_2O + NaCL from body to lumen = secretion
- Contributes to control of acid secretion in stomach, mucus secretion along length and bicarbonate secretion in duodenum (to neutralise acid for enzymes)
- Indirectly controls differentiation of epithelium, interaction with immune system, affecting endocrine system

Experiment in intestinal movements show contractions seen **only if nutrient is in lumen**. Shows that **contractions are blocked by nicotinic/muscarinic ACh antagonists** (hexamethonium) or **voltage dependent sodium channels hence skeletal muscle** (tetrodotoxin – doesn't affect smooth muscle)

Shows that contractions **independent of CNS**, can be **confined to local or long segments**, contractions **can propagate (move along)** and **jejunum contains entire circuit** for generation of complex behaviour (two types of cholinergic neurons)

To produce nutrient induced motor patterns:

- Need intrinsic sensory neurons to **sense presence of nutrients in lumen** according to experimental result
- Need excitatory motor neurons supplying **circular muscle and longitudinal muscle**
- Need inhibitory motor neurons supplying **circular muscle and longitudinal muscle**
- **DO NOT NEED orally directed interneurons** (as inhibition not required to produce motor patterns)
- **DO NOT NEED vagal efferent neurons** (can modulate activity but not required to produce)

Neurons **that MUST** be in the ENS

- **INTRINSIC SENSORY NEURONS** because we need sensitivity to luminal nutrients (small intestine), mucosal deformation (stretch in neurons) and distension (swell by pressure inside)
- **EXCITATORY MOTOR NEURONS** to circular and longitudinal muscle to churn and propagate food
  - Smooth muscle has latch mechanism which is unique (skeletal muscle doesn't) = need to unlatch with neuronal response to cause relaxation smooth muscle
- **INHIBITORY MOTOR NEURONS** to circular and longitudinal muscle to stop contractions
- **INTERNEURONS** to **run both orally (ascending) and anally (descending)** for inhibition
- **SECRETOMOTOR NEURONS** for water and electrolyte secretion, also vasodilator neurons, also other neurons functions unidentified