Organization of Nervous System:

Nervous system

Integration

Central nervous system (CNS)

Brain

Spinal cord

Peripheral nervous system (PNS)

Motor output

Motor division (efferent)

Sensory division (afferent)

Autonomic nervous system (involuntary; smooth & cardiac muscle)

Sympathetic division

Peripheral Nervous System

The peripheral nervous system links the brain to the “real” world

Nerve Types:

1) **Sensory nerves** (contains only afferent fibers)
2) **Motor nerves** (contains only efferent fibers)
3) **Mixed nerves** (contains afferent / efferent fibers)

Most nerves in the human body are mixed nerves
Nerve Structure:
A. Epineurium:
   • Outside nerve covering
   • Dense network of collagen fibers
B. Perineurium:
   • Divides nerve into fascicles
   • Contains blood vessels
C. Endoneurium:
   • Surrounds individual axons and ties them together

Classification of Nerve Fibers:
• Classified according to conduction velocity

<table>
<thead>
<tr>
<th>Classification</th>
<th>Type</th>
<th>Relative diameter</th>
<th>Relative conduction velocity</th>
<th>Myelination</th>
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<td>B</td>
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<td>C</td>
<td>Smallest</td>
<td>Slowest (0.2 m/s)</td>
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<td>Largest</td>
<td>Fastest</td>
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<td>IV</td>
<td>Smallest</td>
<td>Slowest</td>
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Organization of Nervous System:

Nervous system

Central nervous system (CNS)
- Brain
- Spinal cord

Peripheral nervous system (PNS)
- Motor division (efferent)
- Sensory division (afferent)

Autonomic nervous system (involuntary; smooth & cardiac muscle)
- Sympathetic division
- Parasympathetic division

Somatic nervous system (voluntary; skeletal muscle)

Sensory Systems

“Nothing is in the mind that does not pass through the senses”

Aristotle (~ 350 B.C.)

- Sensory receptors provide the only channels of communication from the external world to the nervous system:
  - **Detect**ions: Electrical impulses - triggered by receptor cells
  - **Sen**sations: Electrical impulses - reach brain via neurons
  - **Per**ceptions: Interpretation of electrical impulses by brain

Sensations / perceptions are not inherent in stimuli themselves; instead they depend on the neural processing of the stimuli
Sensory Pathways in NS:

1) **Receptor:**
   - Converts stimuli to electrochemical energy
   - Structure variable
     - Specialized epithelial cells (e.g., vision)
     - Modified neurons (e.g., olfaction)

2) **First-order afferent neuron:**
   - Cell body located in ganglion (PNS)

3) **Second-order afferent neuron:**
   - Synapse with first-order neuron at relay nuclei
   - Many first-order synapse with one second-order
   - Interneurons present (signal processing)
   - Cross at midline (decussate)

4) **Third-order afferent neuron:**
   - Reside in thalamus (relay nuclei)
   - Interneurons present (signal processing)

5) **Fourth-order afferent neuron:**
   - Reside in appropriate sensory area

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### Sensory Receptors:

<table>
<thead>
<tr>
<th>Type of Receptor</th>
<th>Modality:</th>
<th>Location:</th>
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<tbody>
<tr>
<td><strong>Mechanoreceptors</strong></td>
<td>Touch, Audition, Vestibular</td>
<td>Skin (touch), Inner ear (audition), Inner ear (vestibular)</td>
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<tr>
<td><strong>Photoreceptors</strong></td>
<td>Vision</td>
<td>Eye (vision)</td>
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<tr>
<td><strong>Chemoreceptors</strong></td>
<td>Taste, Olfaction, Osmolarity</td>
<td>Tongue (taste), Nose (olfaction), Vessels (osmolarity)</td>
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<tr>
<td><strong>Thermoreceptors</strong></td>
<td>Temperature</td>
<td>Skin (temperature)</td>
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<tr>
<td><strong>Nociceptors</strong></td>
<td>Pain</td>
<td>Skin (pain)</td>
</tr>
</tbody>
</table>
Sensory Receptors: Sensory transduction: The process by which environmental stimuli activates a receptor and is converted into electrical energy

- Receptor excitation = Change in membrane potential (Receptor potential)
  (usually via opening of ion channels)

Example: Pacinian corpuscle

1) Pressure causes a change in the membrane properties (e.g., mechanical deformation)
2) Ion channels open; receptor potential develops
   - Amplitude correlates with stimulus size
3) Receptor potential triggers action potential

Receptor Potential \(\rightarrow\) Threshold \(\rightarrow\) Action Potential

\(\uparrow\) Intensity = \(\uparrow\) Receptor potential = \(\uparrow\) AP frequency

Receptor Fields: An area of the body that when stimulated results in a change in firing rate of a sensory neuron

Receptor fields exist for first-, second-, third-, and fourth-order neurons

Receptor fields may be excitatory or inhibitory

Excitatory receptor fields increase firing rate
Inhibitory receptor fields decrease firing rate

The smaller a receptor field, the more precisely the sensation can be localized

Lateral inhibition defines boundaries and provides a contrasting border
Sensory Receptors:

**Sensory coding:** Various aspects of perceived stimuli are encoded and sent to the proper location in the CNS.

**Features encoded:**

1) **Modality**
   - Labeled Line Principle:
   - Receptors respond to single modality

2) **Location**
   - Somatosensory cortex
   - Receptor fields

3) **Threshold**
   - Threshold of Detection:
   - Weakest signal that will produce a receptor response 50% of the time
   - Vision: 1 photon of light
   - Hearing: Bending of hair equal to diameter of H atom

4) **Intensity**
   - Number of receptors activated
   - Firing rate of sensory neurons
   - Types of receptors activated

5) **Duration**
   - Length of time a sensory neuron fires
   - During prolonged stimulus, receptors “adapt” to the stimulus

**Sensory adaptation:** When a constant stimulus is applied to a receptor, the frequency of action potentials generated declines over time.

**Tonic receptors** (slowly adapting receptors)
- Transmit impulses as long as stimulus present
- Keep brain appraised of body status

Pattern of adaptation differs among different types of receptors

Guyton & Hall – Figure 46.5
Costanzo – Figure 3.7
Sensory Receptors:

**Sensory adaptation:** When a constant stimulus is applied to a receptor, the frequency of action potentials generated declines over time.

- **Phasic receptors** (rapidly adapting receptors)
  - Transmit impulses only when change is taking place
  - Important for predicting future position/condition of body

- Pattern of adaptation differs among different types of receptors

Costanzo – Figure 3.7

Somatosensory System:

- Processes information about touch, position, pain, and temperature

**Mechanoreceptors:**

- **Pacinian corpuscle**
  - Location: Subcutaneous; intramuscular
  - Detection: Vibration; tapping
  - Adaptation: Very rapidly

- **Meissner’s corpuscle**
  - Location: Non-hairy skin
  - Detection: Tapping; fluttering
  - Adaptation: Rapidly

- **Hair plexus**
  - Location: Hairy skin
  - Detection: Velocity; movement direction
  - Adaptation: Rapidly

- **Ruffini’s corpuscle**
  - Location: Skin; joint capsules
  - Detection: Stretch; joint rotation
  - Adaptation: Slowly

Costanzo – Figure 3.8
Somatosensory System:

• Processes information about touch, position, pain, and temperature

Mechanoreceptors:

- Merkel's receptor / Tactile disc
  Location = Non-hairy skin / Hairy skin
  Detection = Vertical indentation
  Adaptation = Slowly

Thermoreceptors:

- Slowly adapting receptors; located in skin

  • Cold receptors vs. warm receptors
    • Overlap in response ranges
    • Do not respond at extreme ranges (nociceptors)

Nociceptors:

• Respond to noxious stimuli that can produce tissue damage

  Mechanical nociceptors:
  • Respond to mechanical stimuli
  • A delta (A\(\delta\)) afferent neurons (myelinated)

  Polymodal nociceptors:
  • Respond to multiple stimuli:
    • High-intensity chemical stimuli
    • Hot / Cold stimuli
  • C afferent neurons (unmyelinated)

Hyperalgesia:

Process where axons of nociceptors release substances that sensitize the nociceptors to stimuli that were not previously painful

Chemical cues released at damaged:

- H\(^+\)
- K\(^+\)
- ATP
- Substance P
- Prostaglandins
- Bradykinins
Somatosensory Pathways:

1) **Dorsal column system**
   - Information transmitted:
     a) Discriminative touch
     b) Pressure / Vibration
     c) Two-point discrimination
     d) Proprioception
   - Consists mainly of groups I and II fibers
   - Fibers decussate in brain stem (second-order neurons)
     - Nucleus gracilis = Info from lower body
     - Nucleus cuneatus = Info from upper body

2) **Anterolateral (spinothalamic) system**
   - Information transmitted:
     a) Pain
     b) Temperature / Light touch
   - Consists mainly of groups III and IV fibers
     - Fast pain (e.g., pin prick)
       - A delta fibers; group II & group III fibers
       - Rapid onset / offset; precisely localized
     - Slow pain (e.g., burn)
       - C fibers; group IV fibers
       - Aching / throbbing; poorly localized

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Marieb & Hoehn – Figure 12.33
Somatosensory Pathways:

2) Anterolateral (spinothalamic) system

Referred Pain:

Dematomal rule:
Sites on the skin are innervated by nerves arising from the same spinal cord segments as those innervating the visceral organs

Vision:

Contained in orbit of skull:
1) Orbital fat (cushions / insulates eye)
2) Extrinsic eye muscles (6)
3) Lacrimal gland: Produces tears
   - Lubricates eye
   - Supplies nutrients / oxygen
   - Provides antibacterial enzymes

Strabismus:
A condition in which an eye rotates medially / laterally

Marieb & Hoehn – Figure 14.8

Marieb & Hoehn – Figure 15.3
Vision:

Layers of the Eye:

1) **Fibrous Layer**: (outermost)
   - Offers structurally support / protection
   - Acts as anchoring point for muscles
   - Assists in light focusing

2) **Vascular Layer**: (middle)
   - Contains blood vessels / lymph vessels
   - Regulates light entering eye
   - Controls shape of lens

3) **Retina**: (innermost)
   - Pigmented layer (light absorption)
   - Neural layer (light detection)
   - Photoreceptors (light detectors)
     - **Rods** (light sensitive - ~ 125 million / eye)
     - **Cones** (color sensitive - ~ 6 million / eye)

Cones clustered in fovea of macula lutea (sharp focus)

Cornea is the only tissue that can be transplanted with limited rejection issues.
Vision:

Segments of the Eye:

**Aqueous Humor:**
Circulating fluid in anterior segment
- Nutrient / waste transport
- Cushioning of eye
- Retention of eye shape

**Vitreous Humor:**
Gelatinous mass in posterior segment
- Transmits light
- Stabilize eye shape
- Holds retina firmly in place

Intraocular Pressure = 12 – 21 mm Hg

**Glaucoma:**
Disease where intraocular pressure becomes pathologically high (~ 70 mm Hg)

For clear vision, light must be focused on the retina

**Refraction:**
The bending of light when it passes between mediums of different density
1) Cornea: 85% of refraction (fixed)
2) Lens: 15% of refraction (variable)
   - Composed of lens fibers (cells)
   - Crystallins (transparent proteins)

**Accommodation:**
Changing the shape of a lens to keep an image in focus (constant focal length)

Glucoma:
Disease where intraocular pressure becomes pathologically high (~ 70 mm Hg)
**Vision:**

**Accommodation:**

- Lens flattens for distant object focus; Ciliary body **RELAXES**
- Lens bulges for near object focus; Ciliary body **CONTRACTS**

**Near point of vision:**

Inner limit of clear vision

- Children = 7 – 9 cm
- Young Adults = 15 – 20 cm
- Elderly Adults = 70 – 85 cm

**Loss of lens elasticity**

- Pupils constrict
- Eyeballs converge

**Sensory Systems**

**Vision:**

**When Things Go Wrong:**

- **Emmetropia**
- **Myopia**
- **Hyperopia**

**Astigmatism:**

Warping of the lens or cornea leading to image distortion

- Diverging lens Correct with diverging lens
- Converging lens Correct with converging lens

**20 / 20** = Standard visual acuity

**20 / 200** = Legally blind
Vision:

Photon:
Basic unit of visible light

Retinal Layers:

- Pigment cell layer
  - Absorbs stray light
  - Storage site for retinal pigments

- Photoreceptor layer
  - Rods / cones

- Outer nuclear layer
  - Nuclei of receptor cells

- Outer plexiform layer
  - Synapses between receptors and interneurons

- Inner nuclear layer
  - Nuclei of interneurons

- Inner plexiform layer
  - Synapses between interneurons and ganglion cells

- Ganglion cell layer
  - Nuclei of ganglion cells

- Optic nerve layer
  - Leave eye via optic disc

Horizontal cells / Amacrine cells
(facilitate / inhibit serial links – retinal processing)
Vision:

Retinal Layers:

Cones demonstrate high acuity and low sensitivity
- Only a few cones synapse on a single bipolar cell
  - In fovea, a single cone synapses on a single bipolar cell
  - A single bipolar cell synapses on a single ganglion cell

Rods demonstrate low acuity and high sensitivity
- Many rods synapse on a single bipolar cell
  - Light striking any one rod will activate the bipolar cell
  - Multiple bipolar cells may synapse on a single ganglion cell

Photoreception:

A single photon of light can activate a rod; several hundred photons of light are required to activate a cone

Rod Structure:
- Double-membrane discs
- Cytoplasm / cytoplasmic organelles
- Connection to neural elements
- Light-sensitive photochemicals (more abundant in rods)

Cone Structure:
- Membrane infoldings
- Connected via individual cilium
Vision:

Photoreception:

Photochemistry of Vision:

- Rods and cones contain chemicals that decompose on exposure to light
  - Rods = **Rhodopsin** (visual purple)
  - Cones = **Cone pigments** (color pigments)

Example: Rhodopsin

Structure:

- **Opsin** = membrane protein
- **Retinal** = light-absorbing pigment (aldehyde of vitamin A)

Two sterically distinct retinal states in the retina

---

Vision:

Photoreception:

Rod Receptor Potential:

- At rest (in dark...), rod receptor potential ~ - 40 mV (receptor average = - 80 / - 90 mV)
  - **Cause:** Outer segment highly permeable to Na⁺

**Dark Current**

Rhodopsin decomposition triggers **hyperpolarization** of receptor cell

The greater the amount of light, the greater the hyperpolarization

**NT = Glutamate**
Photoreception:

**Rhodopsin Activation:**

1. Conformational change in opsin
2. Activation of transducin (G protein)
3. Activation of phosphodiesterase (enzyme)
4. Closure of ion channels

**Photoreception:**

**Photopigment:**

1. Light
2. Trans-retinal detaches from opsin
3. Trans-retinal is converted to all-trans-retinal
4. All-trans-retinal is converted to 11-cis-retinal
5. 11-cis-retinal is converted to all-trans-retinal
6. All-trans-retinal is converted to all-trans-retinol

**Regeneration of Rhodopsin:**

**Storage location:**

- Storage location is picked up from blood
- Nutritionally dependent on vitamin A

**Bleaching:** The fading of photopigment upon absorption of light

**Night Blindness:**

Reduced photosensitivity of eyes (nutritional deficiency of vitamin A)
Vision:
Photoreception:

Color Vision:

- Three classes of cones recognized
  - Trichromacy Theory
  - Humans: Blue, Green, Orange
  - Sensation of color = CNS processing
- Color sensitivity depends on opsin structure, not light-absorbing molecule
  - Humans (~50% analogy with a.a. of rods)
  - Blue = autosomal chromosome
  - Red / Green = X chromosome
    - ↑ similarity (gene duplication)

Colorblindness:
Defect in cone opsin gene

Test Yourself…

Sex-linked (1% of males affected)
8% of women carriers

Very rare (autosomal recessive)

Normal
Protanopia (lacking red cones)
Deuteranopia (lacking green cones)
Tritanopia (lacking blue cones)
**Vision:**

**Optic Pathways:**

**Hemianopia:**
Loss of vision in half the visual field of one or both eyes

**Visual Field**

<table>
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<tr>
<th>Left</th>
<th>Right</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Left Field" /></td>
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</tbody>
</table>

1) ![Deficit](image)
2) ![Deficit](image)
3) ![Deficit](image)

Costanzo – Figure 3.17

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**Auditory:**

**Sensory Systems**

**Auditory:**

- **Auricle**
- **Tympanic membrane**
- **Oval window**
- **Middle ear**
  - Converts sound waves into mechanical movements (amplification)
- **External ear**
  - Collect / direct sound waves
- **Cochlea** (hearing)
- **Semicircular canals / Vestibule** (equilibrium)
- **Malleus**
- **Incus**
- **Stapes**

Martin & Nath – Figure 13.18
Cochlea ("snail"): Spiral-shaped chamber that houses the receptors for hearing.

Scala media (contains endolymph)
Scala Vestibuli (contains perilymph)
Scala tympani (contains perilymph)

Organ of Corti
Basilar membrane

As basilar membrane vibrates, hair cells bump up against tectorial membrane

Sensory Systems
Auditory:

The Nature of Sound:

Sound: A pressure disturbance produced by a vibrating object

Frequency:
Number of waves passing a given point in a given time
Pitch = Sensory perception of frequency

Amplitude:
Intensity of sound
Loudness = Sensory perception of amplitude

Average human speech = 65 dB
Potential damage = > 100 dB
Pain = > 120 dB
Sound waves enter auditory meatus

- Tympanic membrane vibrates
- Ossicles vibrate
- Oval window vibrates
- Pressure waves develop in scala vestibuli
- Organ of Corti vibrates

Amplification of signal:
1) Lever action of ossicles
2) Large window → small window

Pressure waves exit via round window

- Shear force bends hairs
- $K^+$ conductance changes
- Depolarization leads to NT release

Organ of Corti (Oval window) vibrates

- Shear force bends hairs
- $K^+$ conductance changes
- Depolarization leads to NT release

Cochlear microphonic potential

- Oscillating NT release produces intermittent firing of afferent nerves

Basilar membrane differs in stiffness along length

- High frequency sounds displace basilar membrane near base
- Medium frequency sounds displace basilar membrane near middle
- Low frequency sounds displace basilar membrane near end

Hearing Range:
20 Hz to 20,000 Hz
(most sensitive = 2000 – 5000 Hz)

Conduction Deafness:
Sound is not able to be transferred to internal ear

Sensorineural Deafness:
Damage occurs in neural pathway (e.g., hair cells)
Auditory:
Auditory Pathways:

Central lesions do not cause deafness because fibers from each ear are intermixed in CNS.

Vestibular System:

- Provides stable visual image for retina
- Adjust posture to maintain balance

Vestibule:
Region of inner ear housing receptors that respond to gravity sensation / linear acceleration (static equilibrium)

Maculae:
Sensory receptors for static equilibrium
For every position of the head, there is a unique pattern of AP activity for the utricle & saccule

Head acceleration (e.g., forward) causes otolith membrane to slide; subsequent bending of hair cells modifies AP firing rate.
Sensory Systems

Vestibular System:

Semicircular canals:
Region of inner ear housing receptors that respond to rotational movements of head (dynamic equilibrium)

Crista ampullaris anatomy:
Head rotation (e.g., spinning) causes endolymph to push against cupula; subsequent bending of hair cells modifies AP firing rate

Crista ampullaris:
Sensory receptor for dynamic equilibrium

Vestibular System:

Example:
Counter clockwise rotation of head
1) Cupula begins to move; endolymph is stationary
2) Eventually, endolymph catches up with cupula (hair cells quiescent)
3) When stopped, endolymph briefly moves hair cells in opposite direction (reverses firing rates)

Rotation of head stimulates semicircular cells on same side rotation is occurring

Modified hair cell
(stereocilia bent toward kinocilium)

Costanzo – Figure 3.23
Vestibular System:
Vestibular Pathways:

Nucleus
- Medial nucleus
- Superior nucleus
- Lateral nucleus
- Inferior nucleus

Input
- Semicircular canals
- Vestibule (utricles)
- Vestibule / Semicircular canals

Output
- Extraocular muscles
- Spinal cord (vestibulospinal tract)

Sensory Systems
- Visual reflexes (e.g., nystagmus)
- Postural reflexes
- Midline
- Cerebral cortex
- Thalamus
- Brain stem
- Vestibular nuclei (medulla)
- Spinal cord
- Vestibulospinal tract

Olfaction:

Olfactory Organ: (nasal cavity)

- Olfactory receptor cells (~ 1 million / cm²)
  - Primary afferent neurons (bipolar)
  - Ciliated (~ 20 cilia / cell)
  - Odorant-binding proteins
- Supporting cells
- Basal cells (stem cells → new receptors)
- Continuous neurogenesis

- Odorants must by water / lipid soluble
  - ≥ 4 molecules = receptor activation
  - ~ 1000 receptor types (discriminate ~ 10,000)

Nasal epithelium
- Basal cell
- Nasal epithelium
- Olfactory epithelium
- Ciliated
- Odorant-binding proteins
- Olfactory receptor cell
- Supporting cell
- Olfactory nerve fibers (I)
- Olfactory tract
- Cribriform plate of ethmoid
- Olfactory bulb

Olfactory Organ:

• Odorant-binding proteins
• Olfactory receptor cells (~ 1 million / cm²)
• Primary afferent neurons (bipolar)
• Ciliated (~ 20 cilia / cell)
• Odorant-binding proteins
Olfaction:

Olfactory Transduction:
- G protein ($G_{olf}$) coupled to adenylate cyclase
  - ATP $\rightarrow$ cAMP
  - cAMP triggers ligand-gated Na$^+$ channels

Olfactory Encoding:

We don’t exactly know how…

- What is known:
  1) Olfactory receptors are not dedicated to a single odorant
  2) Olfactory receptors are selective (variable response…)
  3) Different receptor proteins have different responses to the same odors

Olfactory Pathways:

- ~ 1000 receptor cells synapse with a single mitral cell
- Glomeruli (Olfactory bulb)
- Cribiform plate
- Nasal epithelium
- Mitral cells (olfactory tract)
- Olfactory bulb
- Olfactory cortex
- Cerebral cortex
- Thalamus
- Limbic system
- Midline
- Spinal cord
- Brain stem
Gustation:

- Taste buds on lingual papillae:
  - Circumvallate (majority of taste buds)
  - Fungiform (anteriorly located)
  - Foliate (laterally located)

- Taste bud: (~ 10,000 / tongue)
  - Gustatory cells (taste receptors)
  - Slender microvilli (taste hairs)
  - 10 day lifespan
  - Basal cells (stem cells → new receptors)

Taste Transduction:

- Taste buds spread across tongue; different thresholds in different regions

- Bitter
  - Binds G protein-coupled membrane receptor
  - $\uparrow$ $\text{IP}_3$, $\text{Ca}^{2+}$
  - Opens TRP channels
  - Depolarization

- Sweet, umami
  - Binds G protein-coupled membrane receptor
  - $\uparrow$ $\text{IP}_3$, $\text{Ca}^{2+}$
  - Opens TRP channels
  - Transient receptor potential
  - Depolarization

- Sour
  - $\text{H}^+$
  - Blocks $\text{K}^+$ channels
  - $\downarrow$ $\text{K}^+$
  - $\downarrow$ $\text{Na}^+$
  - $\downarrow$ $\text{Cl}^-$
  - Enters through membrane
  - $\downarrow$ $\text{H}^+$
  - $\downarrow$ $\text{Na}^+$
  - $\downarrow$ $\text{Cl}^-$
  - $\downarrow$ $\text{K}^+$
  - $\downarrow$ $\text{Ca}^{2+}$
  - $\downarrow$ TRP channels
  - $\downarrow$ Depolarization

- Salty
Gustation:
Taste Pathways:

Second-order neurons project ipsilaterally

Posterior 1/3 of tongue (bitter/sour):
Glossopharyngeal nerve (IX)

Anterior 2/3 of tongue (sweet/salty/umami):
Facial nerve (VII)

Taste bud

Brain stem

Spinal cord

Taste cortex

Cerebral cortex

Ventral posteromedial nucleus (thalamus)

Solitary nucleus (medulla)

Sensory Systems

midline