Lecture 14. Insect nerve system (II)

• Structures (Anatomy)
  – Cells
  – Anatomy

• How NS functions
  – Signal transduction
  – Signal transmission
Overview

- **More on neurons:** ions, ion channel, ligand receptor

- **Signal transduction:** convert various incoming sense signals into *electric signals*
  - Chemotransduction: chemical signals (smell, taste)
  - Phototransduction: visual cues (see)
  - Mechanotransduction: mechanical signals (hear, feel touching)

- **Signal transmission**
  - Axon transmission
  - Synaptic transmission
Neuron: ions and resting potential

- **Asymmetrical distribution of ions**: more Na+ (>10-fold), Ca2+ (10,000-fold), and Cl- but less K+ (<20-fold) outside the cell. EXCEPTION: some intracellular membrane-bounded compartments (ER) may have high Ca2+

- **Two ion pumps** (Na+/K+ ATPase, Ca2+ ATPase) and the presence of “leaky” K+ channels (red arrow): Na+/K+ ATPase pumps 3 Na+ out and 2K+ into the cell at the expense of 1 ATP; Ca2+ ATPase pump Ca2+ out the cell. [http://highered.mcgraw-hill.com/olc/dl/120107/bio_a.swf](http://highered.mcgraw-hill.com/olc/dl/120107/bio_a.swf)

- **A resting potential** of about -70 millivolts (mv) for neurons: an electrical charge across the plasma membrane, with the interior of the cell negative with respect to the exterior.

- Cells are polarized
Neuron: ion channels

- **Ion Channels** are pore-forming transmembrane proteins. Channels are closed at the resting state.

- **Stimulus** can open ion channels.

- Ions may flow in or out in downhill directions when their corresponding channels are open.

- Cross-membrane movements of ions lead to potential changes across membrane—electrical signals.
Ion channels: gating mechanisms

- **Mechanically-gated channels**: open or close in response to mechanical forces that arise from local stretching or compression of the membrane around them.

- **Voltage-gated ion channels**: open in response to the transmembrane potential changes. E.g. voltage-gated Na+, K+, and Ca2+ channels.

- **Ligand-gated channels (=receptor of ligand)**: open in response to a specific ligand molecule on the external face of the membrane.

- **Second messenger-gated channels**: open in response to internal second messengers (cAMP, cGMP, IP3, Ca2+) on the internal face of the membrane.
1. **Selectivity filter**: Na+ only (Sodium channel).
2. **Gate**: closed at a resting potential (-70 mV)
3. **Voltage sensor**: when **depolarize** the membrane potential sufficiently (e.g., to -50 mV), the voltage sensor moves outward and the gate opens.
4. **Inactivation gate**: limits the period of time the channel remains open, despite steady stimulation
Ligand-gated channel = ionotropic receptors

- Ligand-gated channel is the receptor of a ligand.
- Binding leads to immediate opening of channels and potential changes.
- Nicotinic acetylcholine (Ach) receptor = Ach-gated cation (Na+ and Ca2+) channel.
- γ-aminobutyric acid (GABA) receptor: GABA-gated Cl- channel.
Second messenger-gated channels

- The receptor of the extracellular ligand ≠ ion channel
- Metabotropic receptor = G-protein coupled receptor (GPCR)
- Ligand binding leads to G-protein activation and then increase or decrease of second messengers
- 2\textsuperscript{nd} messengers bind to 2\textsuperscript{nd} messenger-gated ion channels, channel open and potential changes. Thus 2\textsuperscript{nd} messenger-gated channel = 2\textsuperscript{nd} messenger receptor
- Slow potential changes
GPCR: G-protein

- G-protein has three subunits: α, β, γ
- Alpha unit is critical in function
- Three important classes of alpha units
  - $G_s$: stimulate adenyl cyclase (AC), cAMP increase
  - $G_i$: inhibit AC, cAMP decrease
  - $G_q$: stimulate phospholipase C (PLC), leading to increase of DAG (diacylglycerol), IP3 (inositol 1,4,5-triphosphate), and intracellular Ca2+
GPCR signaling pathway: regulate AC and cAMP level

Examples

- Biogenic amine receptors in synaptic transmission
- Odorant receptors in chemotransduction
GPCR signaling pathway: PLC activation & Ca\textsuperscript{2+} increase

Examples
- Rhodopsin in phototransduction
- Odorant receptors in chemotransduction
- Muscarinic Ach receptor
Signal transduction

- **convert** incoming sense (hear, see, smell, taste, touch) signals (visual, chemical, mechanical) to electric signals, namely, potential changes on the dendritic tip.

- The resulted potential changes is known as **receptor potential**.

- The amplitude of receptor potential is **graded** and vary with the intensity of stimuli.
Signal transduction: mechanotransduction

- Mechanosensory transduction: touch, balance, and hearing.

- The dendritic tip of sensory neuron is directly resided below the thin cuticle or hollow hair.

- Various mechanical forces compress the dendritic tip and open the mechanically-gated ion channels that transduces sound, pressure, or movement into potential changes—receptor potential.
Signal transduction: mechanotransduction

Directional sensitivity of a ventral notopleural bristle.
Walker et al., 2000. Science
Signal transduction: chemotransduction

- Chemotransduction underlying **smell** and **taste**

- **Airborne (smell)** or **water-borne** chemical (taste) molecule directly bind to its receptor, i.e. GPCR in the dendrite membrane

- The coupled G protein regulates AC or PLC rather than directly open or close ion channels

- The resulted intracellular 2\(^{nd}\) messengers (cAMP, IP3, Ca2+) then open 2\(^{nd}\) messenger-gated cation channels--receptor potential

*Figure 1* Schematic diagram of an olfactory sensillum trichodeum with one receptor cell and three auxiliary cells. The cuticular hair is 5 \(\mu\text{m}\) thick and 300 \(\mu\text{m}\) long (by courtesy of T. A. Keil).
Phototransduction: a compound eye
Phototransduction: ommatidium

- Typically contains **8 sensory neurons** called retinal cells or visual cells

- **Rhabdom**: central photoreceptive region, formed of specialized portion of each retinal cell, called **rhabdomere (dendrite?)**

- Rhabdom membrane contains photoreceptive pigments, **Rhodopsin**, the photon receptor protein
Rhodopsin is a G-protein coupled photo receptor

**Rhodopsin**
G-protein-coupled photopigment

**Light**

→ **Metarhodopsin, active state**

↓

- G protein activation

↓

- PLC (phospholipase C)

↓

- PIP2

↓

- IP3 and DAG

↓

- Ca²⁺ channel, Ca²⁺ influx

↓

- Receptor potential

**IP3:** inositol 1,4,5-triphosphate

**DAG:** diacylglycerol

**PIP2:** phosphatidylinositol 4,5-biphosphate
Phototransduction: detection of colors

- About 3 rhodopsins, each with different spectral sensitivity
- Insects can see ultra-violet, blue, green, yellow, but not red
Signal transmission: Axon transmission

How is receptor potential transmitted to the terminal arborization of the axon in CNS?

http://highered.mcgraw-hill.com/olc/dl/120107/anim0013.swf
Axon transmission: generation of action potentials

- If a RP > Na+ gate threshold, Na+ channels open
- Na+ rush into the axon depolarizing it further, the membrane potential becomes positive (+ve) very rapidly, producing a spike
- The Na spike does not last long. Two things bring the voltage back to negative values (repolarization)
  1. Na+ channels close when +ve
  2. K+ channels open when +ve. K+ flows outward making the membrane potential more negative
- Hyperpolarization = negative afterpotential

Action Potential (AP)
Axon transmission: propagation of action potential

- A local current flows away from the AP point in both directions.
- This current results in a potential change sufficient to trigger another AP at the next point. In the same way, a AP wave is produced towards the axon terminal.
- But this current can not trigger an AP at the point that AP has just passed through because of inactivation of Na+ channel and hyperpolarization. [http://highered.mcgraw-hill.com/olc/dl/120107/bio_d.swf](http://highered.mcgraw-hill.com/olc/dl/120107/bio_d.swf)
Axon transmission: AP is conducted in an All-or-None manner

- The "none" part: if \( \text{RP} < \text{Na}^+ \) gate threshold, there will be a little local electrical disturbance, but no action potential.

- The “all” part: if \( \text{RP} > \text{Na}^+ \) gate threshold, an action potential of the same size—i.e., it does not get larger for stronger stimuli. So how do axons indicate stronger stimulus?

- Higher frequency: more action potentials per second

- As the action potential travels along the axon it does not die out, but stays the same size

- This is called the all-or-none law
Signal transmission: Synaptic transmission

- At the synaptic gap the action potential ends
- In most cases further transmission of the signal requires a chemical transmitter. Only a few electrical synapses
- Synapses delay the signal: chemical transmission is slower than electrical transmission
Synaptic transmission: transmitter release

- Neurotransmitters are stored in membrane bound vesicles
- Arrival of action potential leads to opening of voltage-gated Ca\(^{2+}\) channels at the presynaptic terminal
- Influx of Ca\(^{2+}\) cause vesicles to fuse to the membrane, open up, and release transmitters
Synaptic transmission: transmitters diffuses across the synaptic cleft

- Travel across the gap by **simple diffusion**
- Part of molecules reach the postsynaptic membrane and bind to specific **receptors**, which may be **ionotropic** (transmitter-gated ion channels) and **metabotropic** (GPCR)
Synaptic transmission: EPSP or IPSP

- Binding of ionotropic receptors leads to Fast opening of ion channels and influx of Na\(^+\), Ca\(^{2+}\) or Cl\(^-\) or outflow of K\(^+\)
- Binding of GPCRs leads to production of 2\(^{\text{nd}}\) messenger (e.g. cAMP, IP3, or Ca\(^{2+}\)), which then open ion channel—Slow
- Influx of Na\(^+\) and Ca\(^{2+}\) produces an excitatory postsynaptic potential (EPSP)
- Influx of Cl\(^-\) or outflow of K\(^+\) produces an inhibitory postsynaptic potential (IPSP)
- Postsynaptic potential is graded and vary with the number of transmitter molecules released which in turn rely on the presynaptic AP frequency
Synaptic transmission: Axon hillock

- Axon hillock: locate at the beginning of axons and is the site for postsynaptic AP generation
- has no synapses of its own and thus is able to evaluate the total picture of EPSPs and IPSPs created in the dendrites
- It has a lower Na⁺ gate threshold than elsewhere on the cell.
- Only if $\sum{\text{EPSPs}} - \sum{\text{IPSPs}} \geq \text{Na⁺ gate threshold}$ will an action potential be generated.
Synaptic transmission: integration of EPSPs and IPSPs

- IPSPs make the membrane potential more negative (hyperpolarization) and cancel out EPSPs
Synaptic transmission: breaking down and recycling of transmitters

- The transmitter must be **removed** once the signal is delivered
- **Broken down by an enzyme.** e.g. acetylcholinesterase (AchE) breaks down acetylcholine (Ach) to acetate and choline.
- **recycled**--transported back into the presynaptic neuron
- **Combine** enzyme degradation and recycling
### Diversity of chemical synapses

<table>
<thead>
<tr>
<th>Groups</th>
<th>Neurotransmitter</th>
<th>Receptor &amp; Channel</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acetylcholine (Ach)</strong></td>
<td>Acetylcholine</td>
<td>Nicotinic: Ach-gated Na+ channel</td>
<td>Fast Excitatory</td>
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<tr>
<td></td>
<td></td>
<td>Muscarinic: GPCR, IP3-gated Ca2+ channel</td>
<td>Slow excitatory</td>
</tr>
<tr>
<td><strong>Biogenic amines</strong></td>
<td>Dopamine</td>
<td>GPCR, cAMP-gated channel</td>
<td>Excitatory or inhibitory (salivary gland, mushroom body, learning and memory)</td>
</tr>
<tr>
<td></td>
<td>octopamine</td>
<td>GPCR, cAMP-gated cation channel, Ca2+ release</td>
<td>Excitatory (learning and behavior)</td>
</tr>
<tr>
<td></td>
<td>tyramine</td>
<td>GPCR, cAMP-gated cation channel</td>
<td>inhibitory</td>
</tr>
<tr>
<td></td>
<td>Serotonin (5-HT)</td>
<td>GPCR, cAMP-gated cation channel</td>
<td>Excitatory or inhibitory</td>
</tr>
<tr>
<td></td>
<td>Histamine</td>
<td>GPCR, ?</td>
<td>?</td>
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<tr>
<td><strong>Amino acids</strong></td>
<td>glutamate</td>
<td>Glutamate-gated cation or Cl-channel</td>
<td>Excitatory or inhibitory (nerve-muscle)</td>
</tr>
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<td>γ-Amino butyric acid (GABA)</td>
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