Contents

1 The Brain and Behavior

1.1 The Brain Has Distinct Functional Regions

The Central Nervous System Has Seven Main Parts

- **Spinal cord**: most caudal part of the central nervous system. It is subdivided into cervical, thoracic, lumbar, and sacral regions.
- **Brain stem**: consists of the medulla oblongata, pons, and midrain. Relays input from the spinal cord and back, and controls input to and from the head.
- **Medulla oblongata**: rostral to spinal cord and includes several centers responsible for vital autonomic functions.
- **Pons**: rostral to medulla and conveys information about movement.
- **Cerebellum**: lies behind pons, modulates force and range of movement, and involved in learning motor skills.
- **Diencephalon**: lies rostral to midrain and contains two structures, thalamus (processes information reaching cerebral cortex) and hypthalamus (regulates autonomic, endocrine, and visceral functions).
- **Cerebrum**: comprises two cerebral hemispheres, each consisting of wrinkled outer layer (the cerebral cortex), and three deep lying structures (basal ganglia, the hippocampus, and the amygdaloid nuclei).
- **Cerebral cortex**: divided into four distinct lobes— frontal, parietal, occipital, and temporal. The frontal lobe is largely concerned with short-term memory and planning, as well as movement; the parietal lobe with somatic sensation, forming a body image, and relating it to extrapersonal space; the occipital lobe with vision; and the temporal lobe with hearing—combined with deeper structures—with learing, memory, and emotion.

2 Nerve Cells, Neural Circuitry, and Behavior

2.1 The Nervous System Has Two Classes of Cells

- There are two main classes of cells in the nervous system: nerve cells, or neurons, and glial cells, or glia.
- A neuron has four defined regions:
  - **Cell body**: or *soma*, is the metabolic center of the cell, containing normal cell organelles.
  - **Dendrites**: branch out in tree-like fashion and are main apparatue for receiving signals.
  - **Axon**: extends some distance from a cell and carries signals to other neurons.
  - **Presynaptic terminals**: specialized enlarged regions of it's axon's branches and is responsible for tranfer of signals.
- **Principle of dynamic polarization**: electrical signals only forlow in one direction in neurons.
- **Connectional specificity**: nerve cells do not connect randomly with one another in these formation of networks.
- Neurons are classified into three groups:
  - **Unipolar**: simpiliest due to single primary process, which gives rise to many branches. One branch as axon and others as receiving structures. These cells predominate invertebrates; they orccur in the autonomic nervous system in vertebrates.
  - **Bipolar**: oval soma that gives rise to two processes: a dendritic structure that receives signals and an axon that carries information towards the central nervous system. Many sensory cells are bipolar, and pain receptors are pseudo-unipolar.
  - **Multipolar**: predominate nervous system of vertebrates and vary greatly in shape; typically containing a single neuron and many dendritic points emerging from various points around the cell body.

- Glial cells support nerve cells and greatly outnumber neurons.
- Glial cells surround the cell bodies, axons, and neurons and can be divided into two major classes:
  - **Microglia**: immune system cells that become phagocytes during injury, infection, or degenerative diseases.
  - There are three main types of **macroglia**: oligodendrocytes, Schwann cells, and astrocytes. About 80% of all brain cells are macrogalia.

3 Genes and Behavior

This chapter has been intentionally left blank, see genetic notes for more information.

4 The Cells of the Nervous System

This chapter was intentionally left blank, see cell biology notes for more information.

5 Ion Channels

5.1 Rapid Signaling in the Nervous System Depends on Ion Channels

- Up to 100 million ions can pass through a single channel each second, comaprable to the turnover rate of the fastest enzymes, catalase and carbonic anhydrase.
- Each channel allows only one or a few types on ions to pass.
- Many open and close, however, some remain open resulting in significant contribution to resting potential.
- Ions pumps maintained gradients and are 100 to 100,000 times slower than channels.
- Questions for this chapter:
  - Why do nerve cells have channels?
  - How can channels conduct ions at such high rates adn still be selective?
  - How are channels gated?
  - How are properties of theses channels modified by various intrinsic and extrinsic conditions?

5.2 Ion Channels are Proteins That Span the Cell Membrane

- Cells have channels in order the transport ions across lipid bilayer easily and eliminate the need to be stripped of waters of hydration.
- The smaller the ion, the greater attraction to water, and the lower its mobility. This partially explains selection, but does how does the inverse selection, that selecting of lower mobility, occur?
- Some ions bind to proteins that can transport them, but this is far to slow for some cases.

- An extension of pore theory says that channels have narrow regions that act as molecular sieves, where the ion sheds most of it's water and only is let through by a binding to a specifically charged selectivity filter.

5.3 Ion Channels in ALl Cells Share Several Characteristics

- The opening and closing of a channel invole conformational changes.
- *Gating*: the transition of a channel between theses stable functional states.
- Three major gating mechanisms:
    - Ligand: binding of chemical ligands known as agonists at either cellular site; transmitters on the extracelluar; others that activate signaling cascades; and more.
    - Voltage-gated: changes in electrochemical changes as often as temperature sensors.
    - Mechanical stretch or physical changes in the membrane.

6 Electrical Properties of the Neuron

This chapter was intentionally left blank. No alternatvie notes, but may need to review chemistry and physics if this chapter is needed.

7 Propagated Signaling

7.1 Personal Notes

- The variety of voltage-sensitive ion channels and the influence of cytoplasmic factors may be analogous to bias/weights or other hyperperamters in neural networks.
- Genetic changes thus change change these networks and may be how transfer learning takes place instead of starting from complete scratch for every organism.
- Innate abilities could represent earlier layers in the network and heavily genetically promgrammed, while later layers are given more time to develop based on environment.
- Can epigenetics have a relatively fast acting change on inherited intelligence?

The rest of this chapter has been left blank, as it is more of an extension of molecular gentics, which I may need to return to later to answer questions like those listed above.

8 Overview of Synaptic Transmission

8.1 Synapses Are Either Electrical or Chemical

- ▷ Average neuron forms and receive several thousand synaptic connections each, with the Purkinje cell of the cerebellum receiving up to 100,000.
- ▷ Both forms of transmission can be enhanced or diminished by cellular activity.
- ▷ Electrial synapses are used to send rapid stereotyped depolarizing signals.
- ▷ Chemical synapses are capable of more complex behaviors due to vairable signaling.
- ▷ Most synapses are chemical.

8.2 Electrical Synapses Provide Instantaneous Signal Transmission

- ▷ Presynaptic terminals must be big enough for its membrane to contain many ion channels to trigger initial depolarization.
- ▷ Postsynaptic terminals must be relatively to small in due to Ohm's law.
- ▷ Even weak subthreshold depolarizing currents can be carried to the postsynaptic neuron and depolarize it.
- ▷ Electrical synapses have a specialized region of contact called the gap junction, with seperation of only 4 nm, bridged by gap-junction channels specialized to conduct ionic current.
- ▷ Electrical transmission can be used to orchestrate actions or large groups of neurons.
- ▷ Groups of electrically coupled cells allows for explosive reactions.
- ▷ Gap junctions are formed between glial cells as well as neurons.

8.3 Chemical Synapses Can Amplify Signals

- Chemical synapses are used to amplify or inhibit signals.
- The synaptic cleft is 20-40 nm wide and depend on the diffusion of neurotransmitters to carry out signaling.
- Neurotransmitters are clustered at speclizied regions called *active zones*, which allow for selective activate of nearby postsynaptic receptors, which lead to the opening or closing of ion channels.
- Chemical synapses can be as short as 0.3 ms but often last several ms.
- Weak activations of chemical synapses can activate larger electrial synapses.
- The action of a transmitter depends on the properties of the postsynaptic receptor, not the chemical properties of itself.
- Neurotransmitters control the opening of ion channels in the postsynaptic cell either directly or indirectly.
- Indirect effects tend to last seconds to minutes and often modulate behavior due to alterations in the excitability of neurons and their synaptic connections.

9 Directly Gated Transmission

This chapter has been intentionally left blank. Unlikely to return to this chatper.

10 Synaptic Integration in CNS

10.1 Central Neurons Receive Excitatory and Inhibitory Inputs

- ▷ Generation of an action potential often requires the near-synchronous firing of a number of sensor neurons.
- ▷ Small inhibitory postsynaptic potential (ISPS), if strong enough, can counteract the sum of the excitatory actions and prevent membrane potential from reaching threshold potential.
- ▷ **Sculpting** function of synaptic inhibition that exerts control over action potentials in neurons that are spontaneously active due to intrinsic pacemaker channels, often completely shaping the firing patterns of cells.
- ▷ Most transmitters usually are inhibitory or excitatory despite being able to be either type.

10.2 Inhibitory Synaptic Action

- ▷ Inhibitory synapses play an essential role in the nervous system both by preventing too much excitation and by helping coordinate activity among networks of neurons.
- ▷ Inhibitory inputs that hyperpolarize the cell perform subtraction on the excitatory inputs, where those that *shunt* perform division.
- ▷ Adding or removing nonshunting inhibitory inputs results in summation, while the combination or excitatory with the removal of inhibitory shunt produces a multiplication.

11 Second Messengers

This chapter has been intentionally left blank. Molecular focused chapters may be reviewed later when a more narrow question needs to be ansewered.

12 Transmitter Release

This chapter has been intentionally left blank. More on the chemistry and molecular function of transmission. Such information May answer questions in the future, but it's not the focus of inquiry at the moment.

13 Neurotransmitters

13.1 Four Criteria of a Neurotransmitter

- ▷ Four steps of synaptic transmission:
    1. Synthesis and storage of a transmitter.
    2. Release of the transmitter.
    3. Interaction of the transmitter with receptors and postsynaptic membrane.
    4. removal of the tranmitter from the synaptic cleft.
- ▷ First approximation of a neurotransmitter can be defined as a substance released by a neuron that affects a specific target in a specific manner.
- ▷ Neurotransmitters typically act on targets other thanthe releasing neuron itself, unlike autacoids.
- ▷ Neurotransmitter interaction with receptors is typically transient, lasting from milliseconds to minutes.
- ▷ General criteria for neurotransmitters:
    - It is synthesized in the presynaptic neuron.
    - It is present in the presynaptic terminal and is released in amounts sufficient to exert a defined action on the postsynaptic neuron or effector organ.
    - When administered exogenously in a reasonable concentrations it mimics the action of the endogenous transmitter.
    - A specific mechanism usually exists for removing the substance from the synaptic cleft.

13.2 Only a Few Small-Molecule Substances Act as Transmitters

- ▷ **Acetylcholine (ACh)**:

  - Only low weight amine transmitter substance that is not an amino acid or derived directly from one.
  - Nervous tissue cannot synthesize choline, which limits ACh biosynthesis due to choline acetyltransferase being the only enzymatic reaction.
  - ACh is released by spinal motor neurons.
  - In the autacoids nervous system it is the transmitter for all preganglionic neurons and for parasympathetic postganglionic neurons as well.
  - ACh is the principle neurotransmitter of the reticular activating system, which modulates arousal, sleep, wakefulness, and other critical aspects of human consciousness.

- **Biogenic Amines**:
  - **Catecholamine Transmitters**:
    - **Dopamine** — Tyrosine
    - **Norepinephrine** — Tyrosine
    - **Epinephrine** — Tyrosine
    - Tyrosine hydroxylase is the rate-limiting for synthesis of bothdopamine and norepinephrine.
    - β-hydroxylase converts dopamine to norepinephrine and is membrane-associated.
    - Norepinephrine is the only transmitter synthesized within vesicles.
    - In order for epinephrine to be formed, then its immediate precursor, norepinephrine, must exit from vesicles into the cytoplasm.
    - In order to be released, epinephrine must be taken up into vesicles.
    - Three of four dopaminergic nerve tracts arise in the midrain, with the last arising in the arcuate nucleus of the hypothalamus.

    - Synthesis of biogenic amines is highly regulated and ca be rapidly increased.

  - **Serotonin** — Tryptophan
  - **Melatonin** — Serotonin
    - Typtophan hydroxylase is the limiting reaction and the first enzyme in the pathway.
    - Cell bodies with serotonergic neurons are found around the midline raphe nuclei of the brain stem and are involved in regulating attention.
    - Productions of serotonergic cells are widely distrubted throughout the brain and spinal cord.
    - Antidepressant mediacation inhibit the uptake of serotonin, norepinephrine, and dopamine.
  - **Histamine** — Histidine
    - Long been recognized as a autacoid, active when released from mast calls in the inflammatory reaction.
    - Concentrated in the hypothalamus.
- **Amino Acid Transmitters**:
  - **Apartate** — Oxaloacetate
  - **γ-Aminobutyric acid (GABA)** — Glutamine:
    - Presnet at high concentrations thoughout the central nervous system and detectable in other tissues.
  - **Glutamate** — Glutamine:
    - Most frequently used at excitatory synapses throughout the central nervous system.
  - **Glycine** — Serine:
    - Major transmitter used by inhibitory interneurons of the spinal cord.
- **ATP and Adenosine**

- Can act as transmitters at some synapses.
- Adenosine has an inhibitory effect in the central nervous system.
- Caffeine's stimulatory effect depends on inhibition of adenosine binding to its receptors.
- ATP released by tissue damage acts to transmit pain sensation in some cases.

13.3 Small-Molecule Transmitters Are Actively Taken up into Vesicles

- *Tranmitter* glutamate must be kept separate from *metabolic* glutamate; this is done through compartmentalization in synaptic vesicles.
- Drugs that are sufficiently similar to the normal transmitter substance can act as false transmitters, tho they often bind weakly decreasing efficacy of of transmission.

13.4 Removal of Transmitter from teh Synaptic Cleft Terminates Synaptic Transimission

- If transmitter molecules released in one synaptic action were allowed to remain in the cleft after release, then they would prevent ner signlas from getting through, the synapse would become refractory due to desensitization.
- Transmitters are removed by three mechanisms: diffusion, enzymatic degradation, and reuptake.
- Degradation is only used by cholinergic synapses.
- Degradation allows for single use signaling and for the lingering choline to be reused.