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.

14 Diseases of the Nerve and Motor Unit

This chapter has been intentionally left blank. Might revisit, reading comprehension was low.

15 Organization of the Central Nervous System

15.1 The Central Nervous System Consists of the Spinal Cord and the Brain

- The spinal cord is divided into a core of central gray matter and surrounding white matter.
- The gray matter is divied into *dorsal* and *ventral* horns.
- *Dorsal horn*: contains orderly sensory relay neurons that receive input from periphery.
- *Ventral horn*: contains group of motor neurons and interneurons that regulate motor neural firing patterns.
- The brain stem(*Medulla, pons, and midbrain*) has five distinct functions:
    1. Spinal cord mediate sensation and motor control of trunk and limbs, but the brain stem control the head, neck and face.
    2. Site of entry for information from several specialized sites such as hearing, balance, and taste.
    3. Mediation of parasympathetic reflexes, such out cardiac output, pupil constriction, and more.
    4. Contains ascending and descending pathways that carry sensory and motor information to other parts of the CNS.
    5. Contains the *reticular formation*, which receives a summary of incoming sensory information and regulates alertness and arousal.

15.2 The Major Functional Systems Are Similarly Organized

- The central nervous system consists of several functional systems that are relatively autonomous and much work together using numerous interconnected anatomical sites throughout the brain.
- Information is transformed at each synaptic relay, with the output rarely being the same as the input.

- Neurons at each synaptic relay are organized into a neural map of the body.
- Most sensory systems inputs are arranged topographically through out successive stages of processing.
- Each functional system is hierarchically organized.
- *Decussations*: crossing of second order fiber from the brain stem and the spinal cord.

15.3 The Cerebral Cortex is Concerned with Cognition

- Increasing the surface area due to sulci and gyri allow for greater number of cortical neurons which provide a greater capacity for information processing.
- Neurons in the cerebral cortex are organized in layers and columns which helps computational efficiency.
- The neocortex receives inputs from the thalamus, other cortical regions on both sides of the brain, and other structures then output to other various regions.
- The input-output relation is organized into orderly layering of cortical neurons, with most containing six layers.
    - Layer I: the *molecular layer*, is occupied by dendrites of cells located in deeper layers and axons that make connections to other areas of the cortex.
    - Layer II: the *external granule cell layer*, one of two layers that contain small spherical neurons.
    - Layer III: the *external pyramidal cell layer*, second layer of small spherical neurons, typically larger that layer II.
    - Layer IV: the *internal granule cell layer*, contains much larger number of spherical neurons and is main recipient of sensory input from the thalamus.
    - Layer V: the *internal pyramidal cell layer*, contains pyramidal neurons

that are also larger than it's external layer. Theses neurons give rise to major output pathways of the cortex.

- Layer VI: the *multiform layer*, a blend neurons into white matter that forms the deep limit of the cortex and carries axons to and from areas of the cortex.

- Thickness of the layers vary throughout the cortex.
- The cerebral cortex has a large variety of neurons, more than 40 different types based only on the distribution of their dentrites and axons.
- Most neurons are either principal (projection) neurons or local interneurons.

15.4 Subcortical Regions of the Brain are Functionally Organized into Nuclei

- Three major structures lie deep within the cerebral hemisphere: the basal ganglia, the hippocampal foramtion, the amygdala, and the basal ganglia. These subcortical structures act to regulate the cortical activity.
- Basal ganglia regulates movement and certain cognitive functions such as learning of motor skills.
- THe basal ganglia has five major functional subcomponents: the caudate nucleus, putamen, globus pallidus, subthalamic nucleus, and substantia nigra.
- The hippocampal formation includes the hippocampus, dentate gyrus, and subiculum. Together theses structures are responsible for the formation of long-term memories episodic memories, but not responsible for storage.
- The amygdala is involved in analying the emotional significance of sensory stimuli.

15.5 Modulatory Systems in the Brain Influence Motivation, Emotion, and Memory

- ▷ Some brain areas are neither sensory nor motor, but instead modify specific functions.
- ▷ Distinct modulatory systems within the brain stem modulate attention and arousal.

15.6 The Peripheral Nervous System is Anatomically Distinct from the Central Nervous System

- ▷ The peripheral nervous system supplies the central nervous system with a continuous stream of information about both externala and internal environments. It is split into two divisions.
- ▷ The *somotic division* includes the sensory neurons that receive information from skin, muscles, and joints and provide information about position and pressure.
- ▷ The *autonomic division* mediates visceral sensation as well as motor control of the viscera, vascular, and exocrine glands. It consists of sympathetic (response to stress), parasympathetic (restores homeostasis), and enteric (controls smooth muscle of the gut) systems.