Cellular Neuroanatomy I
The Prototypical Neuron: Soma

Reading:
BCP Chapter 2
The functional unit of the nervous system is the neuron.

Neurons are cells specialized for the reception, conduction, and transmission of electro-chemical signals.

Many sizes and shapes

~100 billion neurons

~100 trillion connections
A typical neuron has a soma (or cell body) and neurites (i.e., dendrites and an axon).

Flow of information:
1. dendrites receive inputs from other neurons
2. the soma integrates (processes) information
3. the axon transmits the output of processing to other neurons
Major Internal Features of a Neuron

The internal features of neurons are similar in most respects to those of other cells. In particular, neurons:

• have a soma which contains a nucleus (that holds genetic information) and organelles that support the life of the cell (including ribosomes and mitochondria)
• are enclosed by a membrane that protects the cell

Neurons differ from other cells in that they:

• stop dividing (reproducing) after birth
• have dendrites and axons, specialized structures designed to receive and transmit information
The soma of a typical neuron is between 10-20 μm in diameter (average width of a human hair = 100 μm).

The watery fluid inside the cell is called cytosol. It is a salty, potassium-rich solution separated from the outside by the plasma membrane.

Everything inside the membrane, excluding the nucleus, is called the cytoplasm.
The nucleus of a neuron is spherical, centrally located, and about 5-10 \( \mu \text{m} \) across.

Within the nucleus are chromosomes, which contain the genetic material DNA (deoxyribonucleic acid). DNA is a molecule composed of two chains (made of nucleotides consisting of a phosphate group, five-carbon sugar and a nitrogenous base) which coil around each other to form a double helix. The nitrogenous bases of the two chains are bound together, according to the rules (A with T and C with G).

The DNA within every cell in the body is the same; what distinguishes a neuron from for example a liver cell are the specific parts of the DNA that are used to assemble the cell. These segments of DNA are called genes.

Number of chromosomes: 46  
Total length of DNA: 2 m  
Width = 2 nm  
Gene length: 0.1-2 mm  
Number of genes: \(~25,000\)
Gene Transcription 1

The “reading” of DNA is known as gene expression. The final product is the synthesis of molecules called proteins.

Protein synthesis occurs in the cytoplasm. Because DNA does not leave the nucleus, an intermediary called messenger ribonucleic acid (mRNA) must be formed (single-stranded, and complementary where uracil replaces thymine).

The process of assembling a piece of mRNA is called transcription. The resulting mRNA is called the transcript.
Gene Transcription 2

Genes include non-coding and coding regions:
• promoter, where RNA-synthesizing enzyme, RNA polymerase, binds to initiate transcription. **Binding is regulated by transcription factors.**
• terminator (stop sequence), end point of transcription.
• exon, codes for proteins
• introns, interspersed regions that do not code for proteins.

Initial transcripts contain introns and exons. Final transcripts are created by a process called RNA splicing. Usually, one gene ➔ one protein. In some cases, exons are also removed, creating “alternatively spliced” mRNA (one gene ➔ multiple proteins).
Ribosomes are dense globular structures found in the cytoplasm that serve as the site of biological protein synthesis (translation).

Ribosomes consist of two major components (which join to translate): the small subunits, which read the mRNA, and the large subunits, which join amino acids to form a polypeptide chain. Each subunit comprises one or more ribosomal RNA (rRNA) molecules and a variety of ribosomal proteins.

Ribosomes may be found floating freely in the cytosol or bound to stacks of membrane called rough endoplasmic reticulum (rough ER; Nissl bodies).
Translation is the process in which ribosomes synthesize proteins after the process of transcription of DNA to mRNA in the cell's nucleus. The polypeptide later folds into an active protein and performs its functions in the cell.

The ribosome facilitates decoding by inducing the binding of complementary tRNA anticodon sequences to mRNA codons (64 possible 3-nucleotide codon sequences code for 20 different amino acids). The tRNAs carry specific amino acids that are chained together into a polypeptide as the mRNA passes through and is "read" by the ribosome.
Protein synthesis starts on free ribosomes. Depending on the initial (ER) sequence, signal recognition particles (SRPs) may direct the ribosome to the rough ER for completion.

Proteins synthesized on free ribosomes are destined for internal structures including the cytosol, nucleus, mitochondrion.

Proteins synthesized on the rough ER are destined to be inserted into the plasma membrane (giving neurons their special information-processing abilities) or enclosed in vesicles to be released from neurons as neurotransmitters.
The Golgi apparatus is a stack of membrane-enclosed disks in the soma. It is a site of extensive “post-translational” chemical processing of proteins released from the rough ER. Another important function of the Golgi apparatus is to direct transmembrane and secretory proteins to their destination (soma, dendrites, or axon).
Mitochondria are abundant organelles (1 μm in length) in the soma that are the site of cellular respiration.

They import pyruvic acid and oxygen, and via a complex series of biochemical reactions called the Krebs cycle and electron-transport chain, produce adenosine triphosphate (ATP), the energy source of the cell.

The breakdown of ATP to ADP provides the energy to fuel most of the biochemical reactions of the neuron (e.g., protein synthesis, establishing chemical makeup of cytosol).
The Neuronal Membrane

The neuronal membrane serves as a barrier to enclose the cytoplasm and to exclude certain substances that float in the fluid that bathes the neuron.

The membrane is composed of a phospholipid bilayer with embedded proteins. Phospholipids have a polar phosphate group at one end that is hydrophilic ("water-loving head") and two long non-polar chains of carbon atoms bonded to hydrogen atoms that are hydrophobic.

The protein composition of the membrane varies depending on the whether it is located in the soma, the dendrites or axon.
Genetic Engineering I

Neurons differ from other cells in the body because of the specific genes that they express as proteins.

The entire length of DNA that comprises the genetic information in human chromosomes has been sequenced. The Human Genome project, completed in 2003, identified approximately 25,000 genes.

DNA microarrays can be used to determine which genes (via relative abundance of mRNAs) are expressed uniquely in neurons (shown at right), or which genes are more-or-less abundant in normal vs. diseased brains.
To determine the function of “neuron-specific” genes, genetic engineering methods can be used to “edit” the genes in an organism:

- delete (knockout)
- insert (knock-in)
- mutate (single nucleotides)

Genetic engineering methods have two important properties:

- target specificity (strand break)
- temporal control (inducible-drugs)

Current methods

- Cre-Lox
- Zinc Finger proteins (ZNFs)
- Transcription activator-like effector nucleases (TALENs)
- CRISPR/Cas

**Overview of genome editing by TALEN and CRISPR-Cas9**

![Diagram of genome editing by TALEN and CRISPR-Cas9](image)

- **Knockout**
  - (double-strand break)
  - (non-homologous end-joining)

- **Knock-in**
  - (homologous recombination using donor DNA)

**One-step generation of mice with genome modifications**

- Zygote
- Micro injection
- NHEJ or HR
- Blastocyst
- Embryo transfer
- Mutant