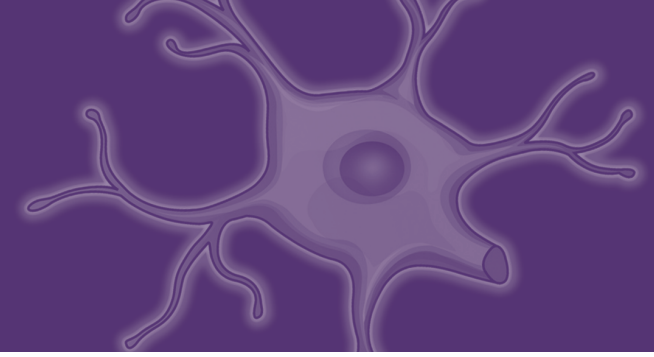

NEUROSCIENCE FUNDAMENTALS

for

Communication Sciences and Disorders

SECOND EDITION

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SECTION 3. Motor Systems

PREFACE

Neuroscience Fundamentals for Communication Sciences and Disorders (NFCSD) was developed with three goals in mind. First and foremost, NFCSD was developed to provide senior undergraduate and graduate students in communication sciences and disorders (CSD) programs (as well as students in Doctor of Audiology [AuD] programs) with a richly illustrated, comprehensive, yet highly readable and accessible textbook covering the neuroanatomy and neurophysiology of the human nervous system. NFCSD was written as a "brain and behavior" style of textbook, while also ensuring comprehensive coverage of essential neuroanatomy in an integrative fashion. My principal goal for producing this book was (and continues to be) to help students develop a deep understanding and appreciation of critical brain-behavior relationships that can impact and help inform their careers as rehabilitation specialists for patients and clients with speech, language, and hearing disorders. Valuing the critical role of the nervous system in the behaviors, perceptions, and cognitive functioning of someone with a communication disorder is something I believe is central to the development and implementation of effective and efficient evidence-based treatments.

Second, this textbook was written with the practicing clinician in mind. I wanted to provide clinical practitioners with a ready resource guide to the inner workings of the nervous system and its processes that was both accessible and comprehensive for their everyday needs. A reference book of this type is always useful in one's professional library. Clinicians need a reference book that can be read, appreciated, and understood without having to take another formal course in the subject matter. My hope is that the accessibility of the writing and the numerous illustrations within the book can allow those who have been out of school for a while to use the material in this textbook directly to inform their practice. Aside from its direct use for informing patient care, the book can also be used for client and caregiver educational purposes; the illustrations and the explanatory analogies are ideal for helping clients better understand the brain-based nature of a disorder.

Lastly, my third goal was to write a textbook for faculty who are responsible for teaching neural bases of speech and language courses, but who do not themselves have specific expertise in this area. Larger programs in CSD usually have someone on their faculty with specific neuroscience experience, but medium- to smaller-sized programs may not. I wanted this textbook to be a resource guide for any faculty colleague of mine who is in the challenging position of having to develop a class in and/or teach a neural bases course but does not feel comfortable or confident in doing so. If this happens to describe your circumstances, then this textbook can certainly be of help to you. For faculty in this position, think of the textbook as a user guide to help you develop lectures and course content. Feel free to use the analogies and examples scattered throughout the book as your own when teaching; customize them as you wish. The lecture slides that are available on the book's PluralPlus companion website provide a framework that you should feel free to customize and change as your circumstances dictate.

For faculty who adopt this book for their own classes, I welcome your thoughts and opinions on its content and organization; *I really mean this!* If there are sections that you feel need to be expanded or reduced, areas that should be organized differently, or areas where my interpretation of the material doesn't conform to your own, please e-mail me. I welcome this kind of feedback and dialogue from those who are choosing to incorporate this textbook into their courses. I want this book to work for you in the best manner possible, and the only way I can accomplish this is by getting your real-use perspectives. As such, to adopting faculty as well as students and clinicians alike, if you find errors in the book, or have comments or questions, please feel free to e-mail me at richard.andreatta@uky.edu and I'll do my best to respond promptly to your messages and take note of your thoughts.

I believe that textbooks should be dynamic and living things that evolve and change as we learn more about our subject matter. As such, the contents of this book are as current as possible, with every effort made to check and cross-check its accuracy against several independent sources. Despite these efforts, there will be errors in the book, and for these I apologize in advance; the fault for these errors is mine, and mine alone.

Using the Textbook in Class: Suggestions to All Faculty Who Adopt NFCSD

To faculty who adopt NFCSD 2E for their courses, the book was written to build a student's understanding and comprehension of neuroscience gradually from the workings of the neuron to the broad functioning of systems underlying behavior and cognition. Let me offer the following suggestions for using and assigning readings from this book to help you and your students get the most out of it.

First, **Chapter 1** sets the stage and rationale for the textbook and provides important study ideas and strategies for student use. In other words, don't skip over **Chapter 1**, as many of us are guilty of doing often. **Chapter 1** will help orient students and contains important insights as to the grand scope of the book's content. **Chapters 2** through **7** (**Section 1**) should be read in the order presented because these chapters lay out the essential groundwork for the remainder of the book's content. **Chapters 2** through **7** should be referenced *continuously* as students proceed through the textbook. It is important to think of **Chapters 2** through **7** as a *"reference core"* within the book. I have intentionally placed throughout all the chapters parenthetical reminders to go back to this reference core to review critical concepts, figures, and descriptions. This was a pedagogical decision that

I believe will help students cross-link different topical areas of information more easily.

For the sensory systems section of the textbook (**Section 2**), **Chapter 8** is a general chapter that provides students with a basic grounding in concepts related to sensation and perception. This chapter needs to be read first because its content cuts across all the sensory systems, equally. After this is accomplished, all other sensory chapters (**Chapters 9** through **12**) can be read in the order that best suits your needs. I ordered the sensory chapters in this textbook solely based on my own view of their importance to CSD, with somatosensory and auditory being the most critical systems to appreciate, followed by the visual and chemical senses.

The motor control section of the textbook (**Section 3**) ideally should be read in the presented order, but it is perfectly fine to move **Chapter 13** on muscle tissue to a different content location if needed. This chapter can also be used as a self-study module if you don't want to spend class time on this material. The motor control systems content in **Chapter 14** should be assigned in four separate segments: (1) direct motor systems, (2) the basal ganglia, (3) the cerebellum, and (4) the visceromotor system. Lastly, **Chapter 15** on motor control theory is another chapter that can be used as a self-study module if so desired.

Finally, **Chapters 16** through **18** (**Section 4**) can be read in any order because each is self-contained. I can envision some faculty using **Chapters 16** through **18** immediately after **Section 1** of the book, or perhaps using **Chapter 18** on the central auditory pathway immediately after the content on the inner ear presented in **Chapter 10**. Although these last three chapters are intended to be the culminating section of the book, use them as you think is best to meet your needs.

In the end, what you use from the textbook will be your decision based upon your needs, the content you think is important to cover, and the realities of class time and scheduling. The textbook was designed to broadly meet the various needs of faculty in different types of CSD programs and thus can easily be adapted to fit any semester or course schedule you are working within. Depending on your department, and how integrated your curriculum is, the book can be conceivably purchased at the start of a student's program and then used throughout the curriculum as needed. Of course, the book is intended for use in neural bases classes, but parts of the book can potentially be adapted for use in several different courses. For example, the auditory system chapters can be held over for audiology courses; the neural bases of speech and language chapters can be used as review material for motor speech and normal language courses; the neuroanatomical content of the textbook can be incorporated into aphasia or neurocognitive classes; and so on and so forth. Regardless of how you choose to creatively use this textbook, I hope that it meets your needs and that your students find it informative and useful in their training.

New to the Second Edition!

Faculty and student insights from the first edition were invaluable as preparations were made for this new edition of NFCSD. Among some of the major changes and updates in the second edition of NFCSD are:

- Reorganization and division of content from **Chapters 4**, **5**, and **6** of the first edition into six new and more digestible chapters in the second edition.
- Creation of a stand-alone chapter on the cranial nerves.
- Addition of more summary tables and process flowcharts to simplify the text and provide ready-made study material for students.
- Addition of over 40 new full-color illustrations to increase the total number of figures in the second edition of the textbook to over 400.
- Revisions to most figures throughout the book to improve their clarity and coherence with the written material.
- For each chapter, a one-stop listing of all abbreviations used in the chapter has been added to improve reader usability.
- Expanded and updated glossary.
- Inclusion of exams and updated lecture slides to PluralPlus for faculty use.
- Addition of a major section and discussion on the neural bases of swallowing.
- Content updates throughout all chapters.
- Corrections to figures and text.

ABOUT THE ILLUSTRATOR: MAURY AASENG

Maury Aaseng graduated from the University of Minnesota Duluth with a BFA in Graphic Design and began working as a freelance illustrator, creating graphics for young adult nonfiction. His work expanded into medical and anatomical illustration as he started collaborating with authors and experts in various medical fields to create vivid figures for publications that illuminate concepts necessary to understand the science of the body. His subject matter in this field includes illustrations of intricate imagery of human anatomy, brain surgery, endoscopic views, cellular level structures, medical devices and technological advancements, and patient education. His style range also includes vector drawn line art, cartooning, mechanical illustration, pen and ink, and watercolor.

Through his emphasis on watercolor, he has created promotional materials for opera productions, illustrative signage for landscaping initiatives focusing on pollinator habitats and botanical gardens, and custom paintings. His watercolor paintings won recognition in the juried exhibition Upstream People Gallery in 2008 and a collection of his watercolor work entitled *Saturated Life* was displayed at the Great Lakes Aquarium gallery in 2016. He teaches classes covering scientific illustration and nature-inspired watercolors, and over the years he has reached into his broad experience of painting and drawing to create books that demonstrate his techniques to other budding artists.

Maury lives in Duluth, Minnesota, with his wife and two children near the shores of Lake Superior. Much of his artistic inspiration is drawn from the outdoors, where he spends time observing and photographing the natural world for subject matter. An online collection of his work can be viewed at mauryillustrates.com

CHAPTER 2

Basic Structure and Function of Neurons

Richard D. Andreatta

Introduction and Learning Objectives

Chapter 2 and the one that follows focus on the structural and general functional factors characterizing the cells of the nervous system. While this topic may seem far removed from speech pathology and audiology, the reality is that an intuitive understanding of basic neurobiological principles and processes will allow you to more fully appreciate how major functional activities of the nervous system, such as motor control and perception, operate. Putting on my "*Mr. Obvious*" hat, speech, language, and hearing (S-L-H) all require the operation of the brain. Performing these behaviors adaptively to support human communication requires the coordinated activity of numerous brain regions underlying cognition, emotion, movement, and sensation. While it might seem satisfactory to simply know the major anatomical regions of the brain operating during S-L-H behaviors, it shouldn't be satisfactory to you at all. We are living in an era where advancements in our appreciation of the brain's functionality, its interconnectivity, and its adaptability are growing at an astoundingly rapid pace, with the majority of these leaps occurring in our understanding of the microstructure of the brain.

The operation of the nervous system as a whole, or what we generally describe in this textbook as "*behavior*," is based on the collective and cooperating function of tens of millions of individual cells. Without an introduction and basic foundation in cellular neurobiology *(a complex-sounding term that simply means the study of how nervous system cells work*), you will be left wondering why and how brain regions communicate with one another to produce their associated behavior or how these same areas change their actions in light of rehabilitation after injury or disease. Here is just one example and justification for why it's worth your time to learn about the neurobiology of the nervous system.

In recent years, the term "*neuroplasticity*" has become a popular buzzword in the media to describe a growing number of commercial products and apps that supposedly allow you to change your brain. Coincidentally, a number of therapeutic techniques, complete with manufactured items you can purchase for a hefty sum of money, are also being developed and sold claiming to be based on the science of neuroplasticity. As a future rehab specialist in S-L-H, one of your key responsibilities will be to select appropriate and scientifically valid treatments for your clients/patients. Without a good appreciation of the neurobiology of the brain, you simply won't have the knowledge and tools needed to independently evaluate new therapy approaches based on neuroplasticity. *Why?* Because understanding the adaptability and plasticity of the brain (*how it changes structurally and functionally*) is all about understanding how neurons change their own structure and function with experience and practice.

The advancements in cellular neurobiology of the nervous system since the early 20th century have led to an explosion in knowledge about the role that nervous system cells have in the complex creation and expression of animal behavior. We now understand that actions, thoughts, perceptions, remembered experiences, emotions, and virtually everything about who you are as an individual or have ever experienced in your lifetime are rooted in the cooperative activity of vast interconnected networks of cells throughout the nervous system. Additionally, our understanding of the cellular bases of complex disease states and debilitating neurological disorders has expanded to a point where neuroscience is on the threshold of finding effective therapies for conditions such as Alzheimer's and amyotrophic lateral sclerosis (Lou Gehrig's disease). The cellular structure and function of the nervous system is thus a crucial body of knowledge to appreciate the operation of the nervous system and the fundamental bases of behavior more fully.

I hope I've convinced you, or at least begun to persuade you, to take the time to learn about these basic cellular principles. The time and effort you spend learning about these ideas will be well worth it as we go forward and discuss other more complex features of the nervous system. In this chapter, we focus on the **cytology** of the neuron: the historical foundations leading to the discovery of this cell type, its general role in behavior, and its basic structure. After completing this chapter, you should be able to meet the following learning objectives:

- Explain the history behind the discovery of the neuron as the essential anatomical building block of the nervous system.
- Identify and describe the functional roles of different structural features of the neuron.
- Understand and explain the concept of population coding and how this mechanism helps form the decision-making unit of the nervous system.
- Understand and explain the significance of the dendrite/soma–axon–dendrite/soma organization of information flow between connected neurons.
- Apply knowledge of a simple reflex circuit to your understanding of how neurons work cooperatively to perform a behavior.

- Identify and define the physical structural features of a neuron and glial cells.
- Describe the function and structural features of major neuronal organelles.
- Explain the basic steps in gene expression (transcription and translation).

Discovery of Two Classes of Cells in the Nervous System

The idea that tissues of the body are made up of individual units called cells seems remarkably obvious and a rather mundane fact by today's standards. But it has been only in the last 200 years (*give or take a couple of decades*) that our understanding of the cellular organization of life has even formally existed. The **cell doctrine**, the notion that animals are comprised of small components called cells, was developed only in the early part of the 19th century. A little-appreciated fact about this doctrine, though, is that it was thought to apply to every part of the body *except* the nervous system. The exclusion of the nervous system from the cell doctrine had much to do with the lack of experimental methods to visually identify the complex structure of nerve cells in their entirety in living tissues. In fact, it took until the turn of the 20th century for neurobiologists to finally develop the methods needed to confirm that the nervous system, like all other parts of the body, is made up of individual cellular units. This accomplishment was by no means trivial. Realizing that the brain and the nervous system are comprised of cells just like all other regions of the body began the era of neurobiological study in which we find ourselves today.

We can thank three influential neurobiologists—Camillo Golgi, Santiago Ramón y Cajal, and Charles Sherrington—who together were largely responsible for the needed technological advancements in nerve cell **histology** (*microscopic study of tissue structure*) that eventually spring-boarded the field into a new era of understanding. Golgi and Ramón y Cajal were chiefly responsible for the development of novel methods to stain or dye nerve cells to reveal their complex shapes and extensive branching. Before these stains existed, the internal structure of the nervous system was a complete mystery because of the visual uniformity of brain tissue (*a generally cream-colored and beige-looking tissue with the consistency of loose Jell-O*) and the inability of rudimentary microscopes of that era to focus clearly on cells with little image contrast. Imagine the excitement of early investigators upon seeing for the first time, through the use of newly developed staining techniques, the enormous complexity and diversity of nervous system cells! Neurobiologists at last had the ability to identify not only the form of nerve cells, but by using different types of staining methods, to also identify intracellular structures. Thus, the histological methods created by these and other early neurobiologists helped to establish critical distinctions both structurally and functionally between cells of the nervous system and any other cell type in the body.

This early histological work led to the discovery that the nervous system is comprised of two distinct families of cells: **neurons** and **glial cells** (Kandel, Barres, & Hudspeth, 2013). If the different parts of the nervous system were a cast of performers in a Broadway musical, neurons would definitely be the stars of the show, the divas that get all the attention and get to sing the best songs. Glial cells, on the other hand, would be the members of the stage crew, working behind the scenes backstage trying to keep everything running smoothly.

Neurons (also called *nerve cells*) are highly excitable cells capable of generating and transmitting electrical signals over a wide range of physical distances. When I say "*electrical signals*," I literally mean the same general form of electricity that runs your cell phone, your laptop, and the lights in a room, albeit on a much smaller scale. Neurons are able to change their electrical state rapidly in response to environmental changes. The quick shifting of electrical activity in a neuron is made possible by the presence of specific protein structures on the neuron's cell membrane that regulate the motion of charged particles, called **ions**, into and out of the cell (more on this in **Chapter 3**). In turn, neurons use these rapid electrical changes to trigger the release of chemical agents from within the cell that operate to interconnect neurons with one another to form functional networks (Hall, 1992). The moment-to-moment state and complexity of these networks of interconnected neurons underlie all behaviors that an animal can produce during its lifetime. We can thank the electrophysiological studies of Charles Sherrington for these fundamental insights because his work was central to the discovery of a nerve cell's communicative abilities at locations called **synapses** (Kandel et al., 2013). (*A little historical fact: Sherrington was the person who first introduced the term "synapse" to identify the physical communication point between neurons.*) In short, neurons participate directly in all activities that we would describe and characterize as a "*behavior*" (Kandel et al., 2013).

In contrast to neurons, glial cells don't directly participate in signaling (the transmission of information from one place to another), but instead form a critical structural, insulating, and metabolic resource for neurons (Allen & Barres, 2009; Guyton & Hall, 2006). A silly way to remember the general role of glial cells is to think of them as packing peanuts or bubble-wrap used to protect and support fragile items when shipping a package. The importance of the structural and supportive roles of glia cells is reinforced by the fact that they outnumber signaling neurons by about 10 to 1. *Absolutely astonishing!* Even though the recognized roles of glial cells are backstage and not terribly glamorous, without them the show could literally not go on. We'll elaborate on the functional and structural details of neurons versus glial cells in much more depth in the next few sections of this chapter.

For now, it's best to appreciate the major distinctions between these two cell classes in the nervous system: *Neurons signal information, and glial cells provide structural and metabolic support to neurons*.

The Neuron

In this next section, we will describe and characterize the major structural and functional features of the neuron. The components we will discuss are key to the way neurons obtain inputs, process information, and share that information with other neurons within highly interconnected collections or networks of cells.

Neurons Are Made for Signaling and Communication

A neuron possesses four functional and associated structural zones necessary to fulfill its role in signal propagation (*a term that neuroscientists frequently use to describe the sending of information over some distance*) and neuron-to-neuron communication. The structural (morphological) features of a typical neuron are (a) the **soma** or **cell body**, (b) **axons**, (c) **dendrites**, and (d) the **presynaptic terminal**. As shown in **Figure 2–1A**, each of the structural features of a neuron is associated with a functional role that allows for the generation of different types of regional signals: an input site (*dendrites and soma*), a region for integrating (*mixing things*) the input signals together (*axon hillock*), a conducting segment (*axon*), and lastly an output site (*presynaptic terminal*). Regardless of whether we are talking about neurons that convey sensory or motor signals (**Figure 2–1B**), these structures and functional roles form the basis by which we can understand how individual neurons operate within the context of larger groups of neurons to generate and change behavior (Carpenter, 1991).

Before we start delving into the fine-grain details of neuronal structure and function, it is beneficial to step back and first develop a more intuitive appreciation of how a single neuron's activity fits into the grand scope of how the nervous system produces the wide range of behaviors animals perform. With this context in place, you'll be better equipped to connect and appreciate how the finer details of neuronal structure contribute to the production of a behavior.

Neurons Never Function Alone

Neurons never work in isolation, but rather are found arranged in functional collections or interconnected populations that share common inputs and outputs. What this means is that a *single* neuron by itself does not directly produce the types of behavior performed by an animal. Rather, it is a group, or more correctly stated, a population of neurons working cooperatively that in reality forms the foundation for all types of sensory, perceptual, motor, cognitive, and emotional behaviors in an animal (Kohn, Coen-Cagli, Kanitscheider, & Pouget, 2016). This notion may seem a little confusing and surprising at first, so here's a good way of thinking about this idea so it makes more intuitive sense. Imagine a population of neurons as a group of citizens in a country, where each person in the group has the ability to cast a vote on a particular issue. During an election, each citizen can cast a "*yea*" or "*nay*" vote for the outcome they would like to see on an issue. All the votes are counted, and the majority vote outcome wins the day. The final action taken on the issue voted upon will be dependent on the sum of all of the votes cast by the citizens. In other words, whether the decision has been approved or rejected is not based solely on a single person's voting choice, but rather on the collective decision made by ALL the citizens who voted. The "*population*" of citizens is therefore the basic "*decision-making unit*" for a democracy. Hopefully, you can see where I'm going with this analogy. Individual neurons (*our citizens*) are participants in the process of generating a behavior (*they can cast a vote either yea or nay*), but it takes large numbers of neurons working together in real time to move the needle sufficiently to produce or observe a change in a behavior (*output of the entire population of citizens decides the final outcome*). In short, when it comes to understanding the neural basis of behavior, it is the activity of *populations* of neurons that matters the most.

Let's further solidify this idea by walking through a more visual and concrete analogy of what we'll refer to as the "*population response*" of a collection of neurons to produce motion in an intended direction. In **Figure 2–2**, a population of 48 neurons is arranged in a grid of 8 columns by 6 rows. Each box in the grid represents a single neuron. The different heights of the colored cylinders extending out of each box represent the levels of activity for each given neuron. On the front border of the grid's columns are drawn arrows that point in different directions. The arrows represent the preferred direction of a reaching movement that will be created by the neurons in that column. For example, all the neurons in the first column (far left) will participate in or "*vote for*" the production of an upward arm motion, whereas the neurons in the third column will participate preferentially in a rightward reaching motion. Neurons in a given column are essentially "*tuned*" or biased to respond preferentially whenever a person is wanting or intending to reach in the direction indicated by the arrows.

If we now take a holistic view of the activity that this specific population of neurons is creating, *can we determine and predict the direction of reaching movement that is being coded for by the entire population?* Let's inspect this population's activity column by column to find the answer to this question. In the first three columns, cell activity for the directions indicated (upward, upper right, and direct right) is variable and relatively low in strength (colored cylinders are short).

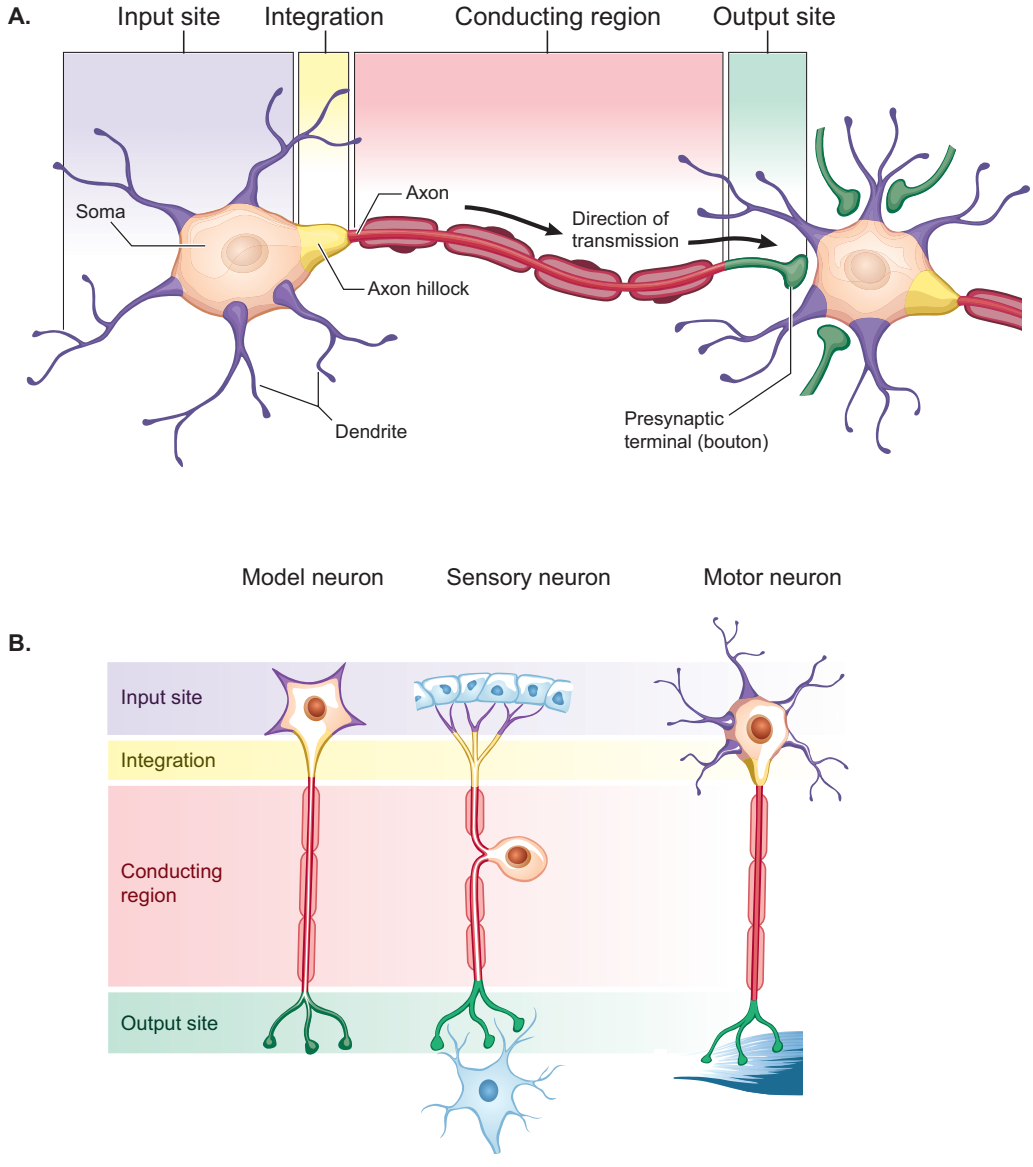


FIGURE 2–1. Basic structure and regional function of the neuron. **A.** A single multipolar neuron is shown synapsing to a target neuron. **B.** Both sensory and motor neurons possess regional functionalization.

In the fourth column, neuron activity for a right-downward reaching action becomes more consistent and is far stronger, as shown by the increasing heights of the colored cylinders for the neurons in that column. In the fifth column, neuron activity for a downward reach is uniformly strong across all the cells in the column. In the sixth column, neuron activity for a left-downward reaching direction begins decreasing and becomes slightly more variable again. Finally, in the seventh and eighth columns, neuron activity for a direct-left or upward-left reach is very low. The take-home point of this example is that by looking at the whole pattern of activity across all the columns, we can predict that this entire population of neurons is coding for a reaching movement that is somewhere in the right-downward to left-downward direction (see red asterisks) (Georgopoulos & Carpenter, 2015). We can make this prediction because the columns that encode right-downward to left-downward directions are the most strongly activated of all the columns (neurons) present.

Let's say that the person performing this behavior suddenly changed his or her mind and decided instead to reach in an upward and right direction. *What would happen to the population's activity then?* What you would see is a shift in the population's response in the following manner: Columns 1 and 2 would suddenly become strongly activated (high cyl-

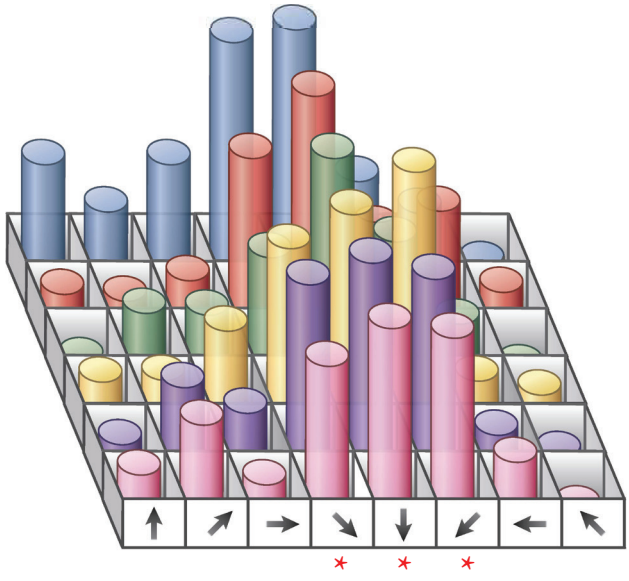


FIGURE 2–2. Schematic illustration of population coding. A collection of 48 neurons, arranged in a grid-like pattern, represents a population of neurons encoding the direction of movement in 360 degrees, as symbolized by the arrows on the front of the grid. Colored cylinder heights represent the relative amount of activation for each neuron in the population. Notice that for motion in the right-downward, downward, and left-downward directions, all cells in those columns are highly active to different degrees. The population of neurons is encoding a specific range of movement direction, as indicated by the columns with the red asterisks.

inder levels), while the neurons in the remaining columns would become far less activated. As such, how a given neuron "*votes*" and how strongly it produces that vote depends on whether the desired action matches the neuron's voting preference. Thus, the direction for any given reaching motion depends on which part of the population is the most strongly activated at any instance in time. No single neuron determined this population's coding for a given direction of reaching motion . . . *the neurons worked cooperatively to decide how the animal reached*. This example highlights what typically happens when the nervous system is performing and regulating a given behavior, albeit on a much larger scale.

Neurons Perform Fundamental Activities

Interconnected groupings of neurons go by several interchangeable terms including **neural ensembles**, **neuronal groups**, **neural networks**, and/or **neural circuits**. Although neural networks vary in size, complexity, and the function being served, they share a common operating plan or strategy. This operating plan ensures that information is distributed among members of the network in such a way as to give each cell an opportunity to "*weigh in*" or vote on the final form of the output being cooperatively created by the population of cells. Regardless of the form and functionality of a given neural network, each participating neuron within the network must perform three fundamental activities to ensure the effective distribution or sharing of information throughout the network: *Neurons must receive an input, integrate that input, and form an output to a target* (Kandel et al., 2013; Vanderah & Gould, 2010).

To satisfy the first activity, neurons must receive an input from other cells at locations such as the dendrites and the soma. Neurons can also receive inputs from real-world signals associated with stimulation from the environment. The nature of these inputs can vary greatly but are generally categorized into those that increase and those that decrease the operation of the neuron. Generally, inputs that increase cellular activity in a neuron are characterized as **excitatory** in nature, while inputs that decrease cell activity are described as **inhibitory**. Excitatory inputs typically drive neurons to boost their signaling output and increase their influence on the operation of the neural network. Inhibitory inputs have the opposite effect, making the neuron less likely to participate in the population's work during behavior.

The second fundamental activity of a neuron is that it must take the sum total of the inputs it receives (excitatory and/or inhibitory) and integrate or "*mix*" them together to generate an overall change in the baseline or resting electrical state of the neuron. All neurons have a "*resting*" electrical state that they maintain when quiet and not activated. Changes in the neuron's baseline or resting state are key to creating many different types of neural signals, each contributing in a unique way to the overall function of the cell (Hall, 1992). One of the most important neural signals generated by the neuron is called the **action potential**. The action potential is initiated at a highly specialized region of the neuron called the **axon hillock**, located at the point where the axon emerges out of the soma (see **Figure 2–1**). The axon hillock is responsible for monitoring changes in the electrical state of the neuron's cell body. If these changes are great enough and of a certain quality, the axon hillock triggers the generation of the action potential. Action potentials are the signals that allow the brain to convey information throughout a network of neurons. Without action potentials, there is little effective communication possible between neurons.

To satisfy the third factor, the newly generated action potential must propagate or transmit down an axon to activate the neuron's communication system located in a region of the axon called the **presynaptic terminal**. Activation of the presynaptic terminal kick-starts a series of chemical activities that will lead to an output event that is passed along to the input site of the next neuron in the neural network.

When you link these three fundamental activities, what arises is a basic organizational scheme for information flow: **dendrite (or soma)–axon–dendrite**. This organization is a key factor in understanding how neurons arrange themselves into functional populations and fits well with the functional

specialization of each region of a neuron (see **Figure 2–1A** for examples of what this basic scheme looks like). Understanding this basic connection scheme between neurons will go a long way toward helping you appreciate how neural signaling arises and how information is shared throughout a population of neurons. This specific topic will be covered in detail in the next chapter.

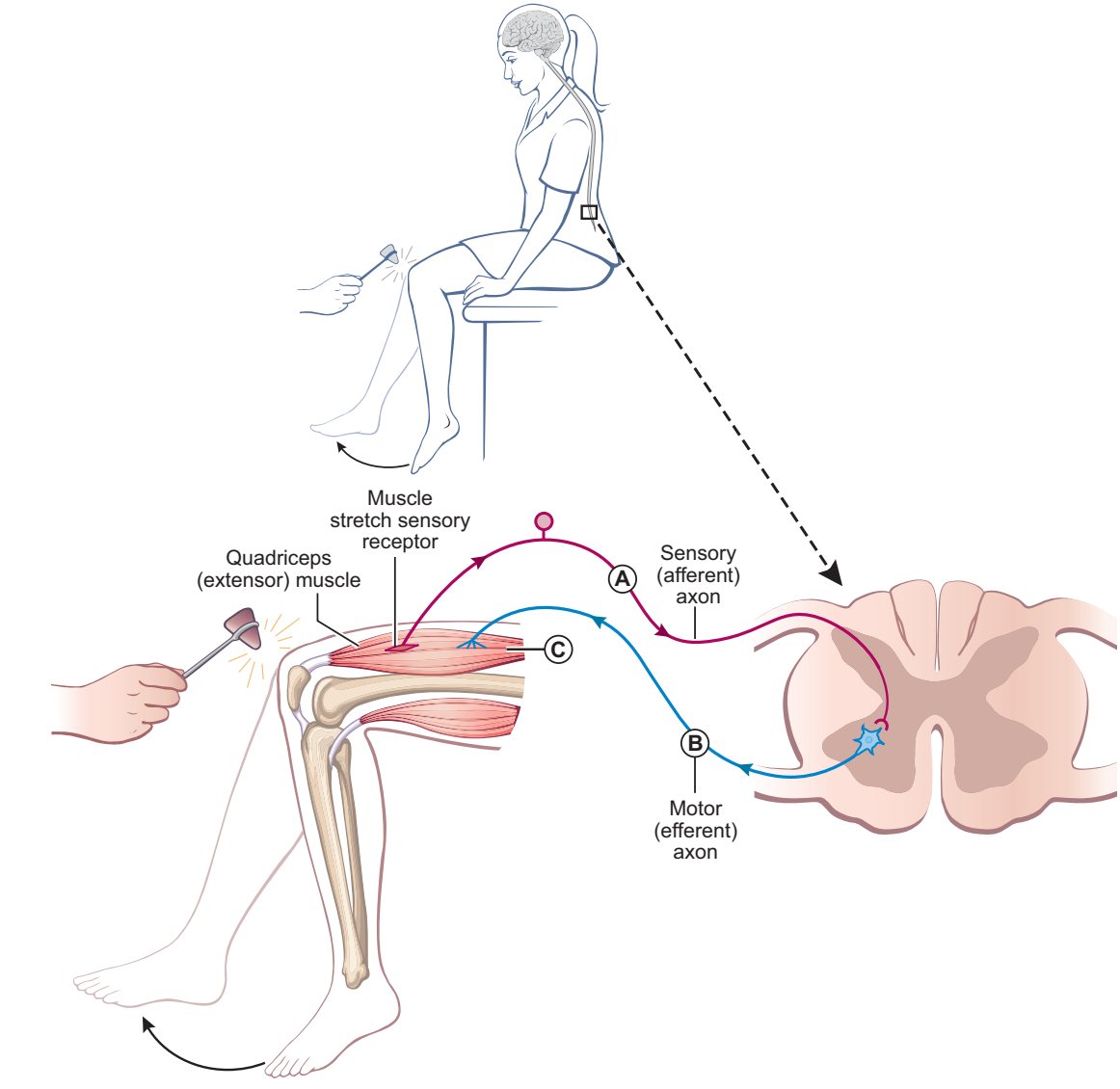
Reflexes Provide a Window Into the Fundamental Operation of Neural Networks

While neural networks can consist of thousands to millions of neurons, regardless of their size, they all operate in a fundamentally similar manner. Because of this fact, we can use a very simple neural network consisting of just two neurons to help us understand the essence of neural network function. For this example, we'll use part of the circuitry of a reflex response we are all familiar with if we've ever had a physical exam by a physician: the knee-jerk response (Purves et al., 2018). Illustrated in the top panel of **Figure 2–3** is a schematic view of the two-neuron pathway that mediates the essential component of your knee-jerk response. To keep things simple and straightforward, in this illustration, only the main segments of the neural circuit that activates the extensor muscle of the thigh are visible.

As illustrated in **Figure 2–3**, the neural network (or in this case a neural circuit) for the knee-jerk response begins with a stretch-sensitive sensor called a muscle spindle embedded in the quadriceps tissue of the thigh. The muscle spindle has an axon (see the red neuron labeled **A**) that leaves the quadriceps and makes its way into the spinal cord (represented as the round slice of tissue on the right side of the top panel). In the spinal cord, the sensory axon coming from the muscle spindle connects to or synapses onto a class of cell called a motor neuron (see the blue neuron labeled **B**). The motor neuron, in turn, projects an axon out of the spinal cord that extends all the way back to the quad muscle of the thigh. The activation or excitation of the motor neuron is responsible for triggering a brief and small contraction of the quadriceps, ultimately causing the lower leg to rapidly extend outward in the direction of the arrow. Given this anatomical description of the knee-jerk response's neural circuity, let's walk through the functional operation of this simple circuit using the bottom panel of **Figure 2–3** as a guide.

In the bottom panel of **Figure 2–3**, the knee-jerk reflex circuit has been laid out linearly. Above the illustrated sensory and motor neurons of the neural circuit are depicted the different forms and types of signals generated by each of the four functional regions (input, integration, conduction, output) of the neurons shown (see **Figure 2–1**). The muscle tissue of the thigh is also shown at the far right with its corresponding signals above it (*muscle tissues are also excitable and behave similarly to neurons*). The reflex response is initiated by striking the patellar tendon of the quadriceps with a mallet. This action causes a small and quick stretching of the tendon that then stretches the thigh muscle to which it is attached. The ensuing stretch of the quad muscle is encoded or "*detected*" by the stretch-sensitive muscle spindle, causing a change in the electrical resting state of the embedded sensory neural ending (labeled as receptor potential in the bottom of **Figure 2–3**). If the tap is strong enough, it triggers an action potential at the axon hillock of the muscle spindle that then travels along the length of the sensory axon into the spinal cord. The action potential reaches the end of the sensory axon where the release of a chemical neurotransmitter from the presynaptic terminal is triggered. At this point, the synapse or connection between the sensory and motor neuron is activated. The neurotransmitter released by the presynaptic terminal of the red sensory neuron initiates electrical changes in the dendrites of the blue motor neuron (the postsynaptic cell), resulting in a change in the electrical resting state of the motor neuron itself (labeled as postsynaptic potential in **Figure 2–3**). Similar to the sensory neuron, if the motor neuron experiences a change of sufficient strength in its electrical state, it will create its own action potential that then travels down the axon of the motor neuron toward the quad muscle of the thigh. The axon of the motor neuron synapses onto the muscle tissue and forms the connection that is responsible for altering the electrical resting state of the muscle. (*Can you detect a theme emerging from these descriptions?*) Muscle cells, like neurons, are excitable and require a driving input via a synaptic structure called the **neuromuscular junction** (NMJ) to generate a contraction. The motor neuron releases a neurotransmitter that causes excitation of the muscle tissue and triggers the muscle cells to contract, causing a quick extension of the lower leg (the observable response). *Phew! Did you expect that the process of creating a knee-jerk response would be comprised of so many steps?*

What have we learned through our discussion on neural networks and the knee-jerk response about the fundamental operating principles of the brain? First, and most critically, generating a behavior (or making a change in one) depends on a population of interconnected neurons working cooperatively to shift the balance of neural activity in any appreciable way (Kandel et al., 2013; Purves et al., 2018). Second, individual neurons comprising a neural network all share a similar functional and structural organization. Finally, there are three basic factors at play in the neural control of behavior: an input from another neuron or the outside world, integration and communication of electrical and chemical signals, and motor output (Kandel et al., 2013; Purves et al., 2018). Through the use of a straightforward analogy on how neural populations are organized (*review the voting and population analogy provided earlier*) and how the knee-jerk response is anatomically structured and functionally generated, you've actually learned a great deal about the fundamental operations of the nervous system thus far. Now that we have a more intuitive appreciation of how neurons generally fit into



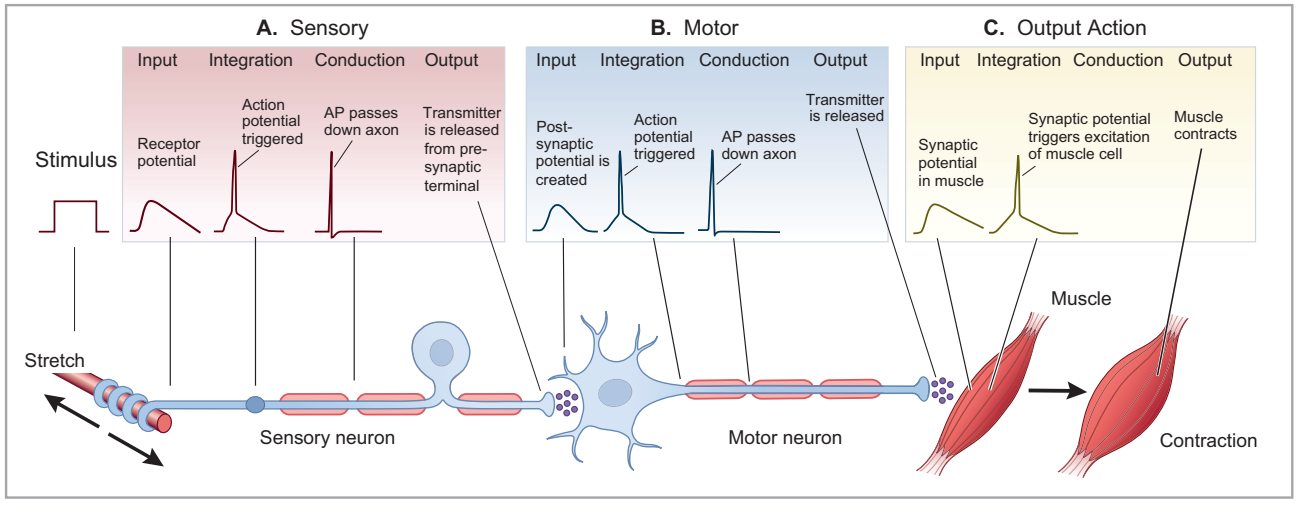


FIGURE 2–3. Knee-jerk reflex circuit. *Top panel:* A simplified version of the knee-jerk reflex circuitry. The red neuron depicts the sensory arm, while the blue neuron represents the motor arm of the circuit. The reflex circuit is activated through a mechanical tap to the patellar tendon that in turn creates a rapid stretch of the thigh muscle. This muscle stretch is encoded by a stretch-sensitive sensory ending, triggering activation of the reflex circuit. *Bottom panel:* The knee-jerk circuity is laid out horizontally with corresponding representations of electrochemical activity that occurs at different locations along the pathway (*see red, blue, and yellow shaded boxes*).

the grand scheme of the nervous system's ability to produce a behavior, let's turn our focus back to the details of neuronal structure and function.

Nerve Cells Have Different Shapes, Sizes, and Functions

Aside from developing histological methods to visualize neurons, Ramón y Cajal was also the first to appreciate that neurons could be sorted into three distinct morphological (structurally defined) groups: **unipolar**, **bipolar**, and **multipolar cells** (Bear, Connors, & Paradiso, 2016; Schwartz, Barres, & Goldman, 2013). As illustrated in **Figure 2–4**, the main factor that determines the classification type of a neuron is the number of cytoplasmic extensions or "*branches*" that come out of the soma or cell body.

Unipolar cells have just one main projection from the soma, with smaller branches extending off this main trunk. Typically, the smaller branches operate as the dendrites or input sites and the larger projection operates as the axon. We find unipolar cell types mostly in simpler nervous systems, such as those of invertebrates like squids and worms. Bipolar cells have two projections typically arising from opposite sides of the soma. Each of the two projections operates as either a dendrite or an axon. A prominent location for bipolar cells in the nervous system is in the retina of the eyes, as we will explore when we discuss the visual system. A variant of the bipolar cell is called the **pseudounipolar** type. This variant is a cross between the unipolar and the bipolar cell shape. Pseudounipolar cells have a single, very short projection from the soma that quickly divides into two segments that project in opposite directions. The sensory nerves that transmit touch from the skin into the nervous system are comprised by this class of cell. The last group is the multipolar cell type. This type of cell has one major extension that operates as the axon and output site, and many smaller extensions emerging from the soma that operate as the input locations or dendrites of the cell. The multipolar cell type is the shape of a neuron that most students envision when thinking about what a typical neuron might look like.

Aside from these structural or morphological categories, neurons can be functionally characterized into **afferent neurons**, **efferent neurons**, and **interneurons** (Carpenter, 1991). Afferent or sensory neurons are those that carry neural signals toward the central nervous system. The signals carried by afferent neurons are used for developing a sensory perception or for providing feedback to motor control regions of the nervous system. Efferent or motor neurons transmit neural signals from the brain, spinal cord, and brainstem to muscle tissues and glands of the body. Efferent signals are responsible, to a large degree, for generating muscle contractions and the release of substances from glandular tissues. The functional grouping known as interneurons can be thought of as cells that help interconnect different regions of the brain,

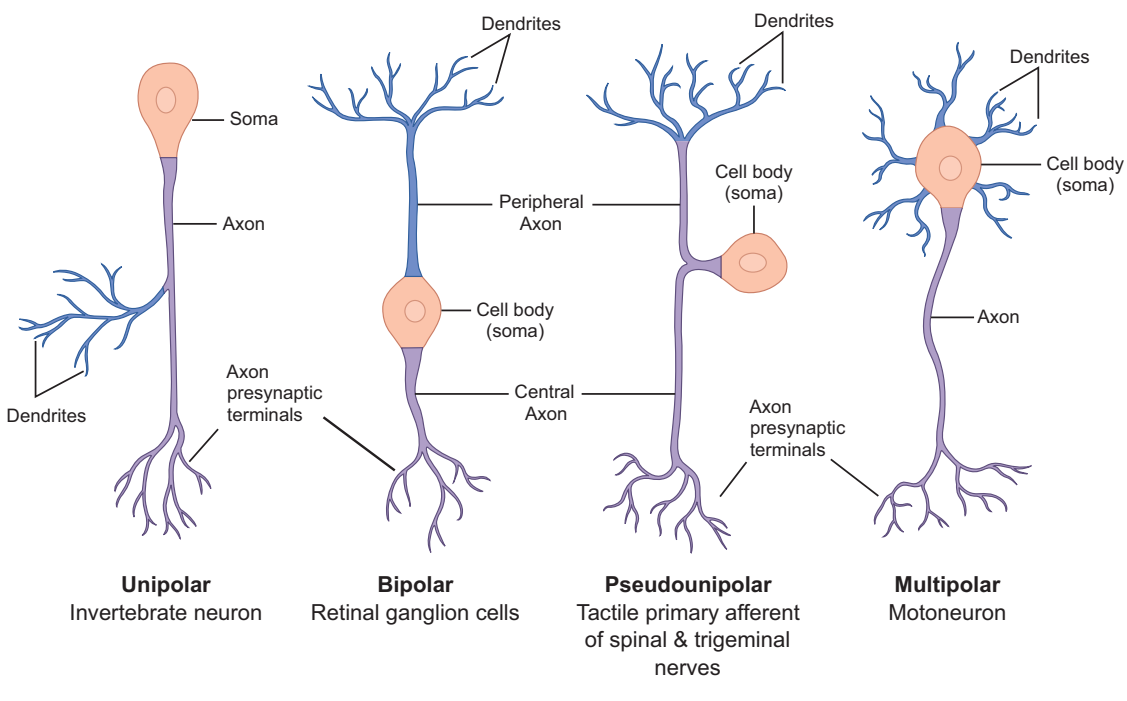


FIGURE 2–4. Neurons are classified based on the number and complexity of processes that extend from the cell's soma. The four different cell forms shown include the unipolar, bipolar, pseudounipolar, and multipolar cell types.

spinal cord, and brainstem. In other words, interneurons (*as the name implies*) are go-betweens that connect one neuron to another. Interneurons are by far the most numerous functional cell type and can link neighboring areas via short axon connections or connect regions of the nervous system that are widely spread apart using longer axons. In summary, afferent neurons bring information into the nervous system; efferent neurons transmit information out of the nervous system to trigger some type of response in muscles and glands; and interneurons help to link groups of neurons, providing a means for the sharing of information.

Before we leave this section, it is important to be aware of and appreciate that methods in **molecular biology** (*analysis of genes, proteins, and chemical cell products*) are now routinely used to classify and categorize neurons on a molecular and genetic level (Crick, 1999). Histology and functional categories still matter and continue to be used, but what we have discovered is that cells that may be identical morphologically may differ in great ways with regard to their molecular features. In fact, most known functional and structural differences between neurons or between neurons and any other cell type in the body can now be reduced to differences in gene expression. Molecular and genetically based differences in neurons can operate to change how these cells respond to an input and how they communicate with other neurons or targets (Crick, 1999). This new understanding was made possible through the extraordinary efforts of scientists who sequenced the entire human genome during the late 1990s and the early 2000s.

Why is this important and why should you care? Well, think about this: Once the genetic profile of a neuron or class of neurons is known, neuroscientists can use bioengineering methods to create what are referred to as transgenic, knockout, or knock-in animals. These animals are genetically altered research subjects that possess phenotypic features (*their physical characteristics*) and physiological processes that mimic those of humans. **Knockout** and **knock-in** animals are those bioengineered to have either a gene deleted or added, while **transgenic** animals have new genes introduced within their nucleus. Because of the evolutionary conservation of genes and mechanisms of protein synthesis between humans and animals, bioengineered animal models can operate as a valid and critical method of discovering the molecular bases of human behavior. Specifically, once molecular and genetic markers are found for a particular human neurological disease, neurobiologists can use that information to develop genetically altered animals that have the exact same deficit or condition. These genetically altered animals can then be used to discover the etiology or cause of a disorder and to understand the effects of new treatments before they are used in humans. The use of molecular and genetic analysis and methods in neuroscience is rapidly changing the landscape of our understanding of the nervous system and offering much hope for the development of efficacious and safe treatments for debilitating neurological conditions (Crick, 1999). Take a look at **Box 2–1** for a more in-depth discussion on the process of creating genetically modified research animals to study human behavior and disease.

Structural Features of the Neuron

Soma, Cell Membrane, and Cytoskeleton

The soma or cell body is the structural, metabolic, and genetic center of the neuron. From the soma, two major extensions of the cell membrane arise: the **dendrites** and **axon**. Both structures can be thought of as highly specialized extensions of the soma that operate as the chief input and output sites of the neuron, respectively. Dendrites form complex branch-like structures that receive information from the axons of other neurons and pass them to the soma. The axon, on the other hand, is often a single element extending from the soma and is dedicated to passing electrical signals to the dendrites and somas of other neurons downstream (see **Figure 2–1A** for an example). It should be noted that axons do divide into smaller branches called **axon collaterals** as the main axon trunk approaches a target (see the output site in **Figure 2–1B** for an example). Axon collaterals from the main axon trunk help to distribute information from a single neuron to multiple output target locations simultaneously.

All these structural components are bound by the cell membrane or the neuron's **plasmalemma**. The terms cell membrane and plasmalemma can be used interchangeably for all intents and purposes. The plasmalemma forms a barrier between the extracellular environment and the intracellular cytoplasm of the neuron. As seen in **Figure 2–5**, the cell membrane is composed of molecules know as phospholipids arranged in two opposing layers, giving the plasmalemma its characteristic moniker of a **phospholipid bilayer**. The

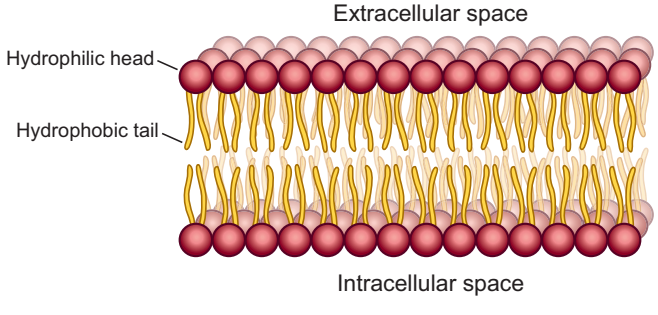


FIGURE 2–5. Phospholipid bilayer that forms the cell membrane of the neuron. The bilayer is comprised of molecules known as phospholipids, which consist of a hydrophilic head (phosphate) and hydrophobic tail (lipid). Bilayer configuration produces a semipermeable barrier because the hydrophobic tails of the phospholipid molecules are arranged pointing inward while the hydrophilic heads face the watery cytoplasm and extracellular fluid.

Box 2–1. Further Interest: **I'm Going to Knock You Out!**

When investigating the function and effects of human genes, scientists have historically turned to model biological systems that possess analogous sets of genes to that of humans. By testing these model systems, we can determine the effect and consequence of a given gene on behavior or on a disease process. Believe it or not, humans happen to share a good deal of their genome with the simple mouse. Approximately 99% of genes in humans have a complement in mice. With this great level of genetic similarity, mice suddenly become ideal candidates for genetic experiments that cannot be performed in humans, but that are nonetheless critically needed to understand human gene functioning. Because mice are rather inexpensive to raise and maintain in colonies, geneticists first attempted to find mice in the wild with genetic alterations and mutations that mimicked human characteristics and diseases. Through lengthy cross-breeding methods, they were able to develop entire strains of mice with a certain gene that was absent or silenced. As you can imagine, such an approach was effective, but painstakingly slow to realize. But what if you suddenly had a way to speed up this process by using molecular biology to directly manipulate the mouse genome to delete or silence any gene you wanted to examine?

In the last couple of decades, scientists have employed the power of molecular biology to generate what are called *knockout mice*. By definition, a knockout mouse is one in which geneticists have intentionally turned off ("knocked out") an existing gene and in its place substituted an inactive or inert segment of DNA. By removing the influence of a given gene, valuable clues about how that gene normally operates can be identified. For example, changes in a mouse's phenotype (set of observable characteristics or traits) created by a gene's absence allows us to understand the effects of the gene on an animal's behavior, or physical or biochemical nature. With this information in hand, measures for a given phenotype in a knockout mouse can be compared to identical metrics in a mouse that has not undergone genetic modification for a given trait. Through this comparison, geneticists can now identify the specific functions that are changed by the knockout. By extension, if the knockout gene has a high degree of similarity to a gene present in humans, geneticists can confidently say that the two genes likely function in similar ways. Effectively, we now have a way to understand a gene's role and contribution to human forms of the condition under study. Some examples of research that use the knockout mouse include studying different forms of cancer, obesity, heart disease, diabetes, arthritis, drug abuse, anxiety, aging, and various neurological disorders. These same mice can also be very useful in testing the effects of novel pharmaceuticals and therapies for various conditions. With the introduction of the knockout mouse, the acceleration rate of genetic research for diagnosing, treating, and preventing human disease has been truly explosive . . . *a fact that always just knocks me out!*

Resources

Miko, I., & Lejune, L. (2004). *Scientists can analyze gene function by deleting gene sequences* [ebook]. Retrieved from https://www.nature.com/scitable/ebooks/essentials-of-genetics-8/119492586#bookContentViewAreaDivID

National Human Genome Research Institute. (2015). *Knockout mice fact sheet.* Retrieved from https://www.genome.gov/12514551

Pilcher, H. R. (2003). It's a knockout. *Nature.* https://doi.org/10.1038/news030512-17

phospholipid molecule consists of a **hydrophilic** (water-loving) "*head*" and **hydrophobic** (water-hating) "*tail*." With these molecules arranged with their hydrophobic tails pointing inward and their hydrophilic heads facing the cytoplasm and extracellular fluid (which happens to be mostly water), you get an effective semipermeable barrier to most substances.

The bilayer arrangement of the plasmalemma is actually very useful and serves an important purpose in maintaining the contents of the neuron separate from the outside world. The bilayer is selectively permeable to substances wanting access through the membrane based on the composition of those substances. As you can predict, molecules that are hydrophobic will be allowed to readily pass through the water-repelling core of the bilayer. On the other hand, hydrophilic substances will be shunted away from the core and prevented from passing through. While the plasmalemma of the neuron might seem like a necessary but albeit boring part of the cell, the truth couldn't be more different. As we'll see in **Chapter 3**, the cell membrane is a key factor underlying the excitable nature of neurons and plays a critical role in the process of neural signaling.

Adding internal support to the cell membrane, the soma, and its associated extensions is the cytoskeleton of the cell. Much like we have a rigid skeletal framework supporting the soft tissues of our bodies, cells possess a cytoskeleton that functions in a similar manner. The cytoskeleton consists of three major classes of filament-like components: **microtubules**, **microfilaments**, and **neurofilaments** (Haines, 2013). These