Preface

A Message From the Authors

Education is not the filling of a pail, but the lighting of a fire.

—William B. Yeats

Flip through this book and you'll see that its pages are chock-full of facts and further looks—just a sampling gleaned from a vast supply that grows too fast for any of us to keep up with and that becomes obsolete just as fast. But sifting through those facts and reporting them is neither the most difficult nor the most important function of a good textbook. A greater challenge is that most students fail to share their instructors' infatuation with learning; perhaps they lack the genes, or the parental role models, or just the idea that learning can be fun. At any rate, they can find a text on a subject like this intimidating, and it is the authors' role to change their minds.

The colorful illustrations, case studies, and research vignettes may capture students' interest, but sparking interest alone is not enough. That's why we've adopted a big-picture approach in writing the text, one that marshals facts into explanations and discards the ones left standing around with nothing to do. When you put facts to work that way, you begin to see students look up and say "That makes sense" or "I've always wondered about that, but I never thought of it that way" or "Now I understand what was going on with Uncle Edgar."

We believe that education has the capacity to make a person healthy, happy, and productive and that it makes a society strong. Education realizes that promise when it leads people to inquire and to question—when they *learn how to learn*. When 45% of the public believes in ghosts, and politics has become a game played by shouting the loudest or telling the most convincing lie, education more than ever needs to teach young people to ask "Where is the evidence?" and "Is that the only reasonable interpretation?"

To those who would teach and those who would learn, this book is for you.

To the Student

Brain & Behavior is our attempt to reach out to students, to beckon them into the fascinating world of behavioral neuroscience. These are exceptionally exciting times, comparable in many ways to the Renaissance that thrust Europe from the Middle Ages into the modern world. According to the American neurologist V. S. Ramachandran in *The Tell-Tale Brain: A Neuroscientist's Quest for What Makes Us Human* (Norton: 2010),

> How can a three-pound mass of jelly that you can hold in your palm imagine angels, contemplate the meaning of infinity, and even question its own place in the cosmos? Especially awe inspiring is the fact that any single brain, including yours, is made up of atoms that were forged in the hearts of countless, far-flung stars billions of years ago. These particles drifted for eons and light-years until gravity and change brought them together here, now. These atoms now form a conglomerate—your brain—that can not only ponder the very stars that gave it birth but can also think about its own ability to think and wonder about its own ability to wonder. With the arrival of humans, it has been said, the universe has suddenly become conscious of itself. This, truly, is the greatest mystery of all. (pp. 4–5)

We know of no scientific discipline with greater potential to answer the burning questions about ourselves than behavioral neuroscience. We hope this textbook will convey that kind of excitement as

you read about discoveries that will revolutionize our understanding of what it means to be human and how we got to where we are.

We want you to succeed in this course, but more than that we want you to learn more than you ever imagined you could and to go away with a new appreciation for the promise of behavioral neuroscience. So, we have a few tips we want to pass along. First, try to sit near the front of the class because those students usually get the best grades. That is probably because they stay more engaged and are encouraged to ask more questions, but to ask good questions, you should always read the text before you go to class. And so that you'll know where you're going before you begin to read, take a look at the Learning Objectives and then skim the chapter subheadings and read the summary at the end of the chapter.

Here are some special tips if you are using a digital form of this text for an online course. First, make sure you ask questions of your instructor as you go through the material and attend the instructor's virtual office hours! An online course is much more challenging—you are responsible for keeping up with the material on your own without the in-person reminders you'd normally get from a physical class. And when answering questions, make sure you document where you got your information; it is all too easy to simply copy and paste information without properly citing your sources (and plagiarism detectors will find it)! Finally, get into a study group with your fellow students. Not everybody understands the material with a single read-through, so discussing the content and exercises with your fellow students can help all of you grasp the complex concepts of behavioral neuroscience. Just like a single brain cell cannot accomplish what the entire brain can do as an organ, a single student cannot possibly learn all the complex nuances of this subject by himself or herself.

As you read, pay special attention to instances of highlighted text; these are definitions of the most important terms, which are defined again in the Glossary at the end of the book. Answer the Concept Check questions at the end of each section and the For Further Thought questions at the end of each chapter, and be sure to check your knowledge with Test Your Understanding (or the Student Study Guide, or take the Sage Vantage quizzes if you have access to them). There are a lot of aids available for this text, and we want you to make use of them. Then don't forget to look up some of the books and articles in For Further Reading; we selected these not only to increase your understanding of a particular topic but hopefully also to be fun to read as well! If you do all these things, you won't just do better in this course; you will leave saying, "I really got something out of that class!" And when it's time to take the GRE (or MCAT or VCAT), or talk to your doctor, or interview for a biomedical job, or simply read the Science section of the *New York Times*, you'll be using the knowledge you gained in this text.

We wrote *Brain & Behavior* with you in mind, so we hope you will let us know where we have done things right and, especially, where we have not. We wish you the satisfaction of discovery and knowledge as you read what we have written *for you*.

To the Instructor

A good textbook is all about teaching, but there is no teaching if there is no learning. Over the years, our students have taught us a great deal about what they need to help them learn. For one thing, we have realized how important it is for students to build on their knowledge throughout the course, so we have made several changes from the organization of other texts. First, the chapter on neuronal physiology precedes the chapter on the nervous system because we believe that you can't begin to understand the brain until you know how its cellular components work. And we reverse the usual order of the vision and audition chapters because audition provides a friendlier context for introducing the basic principles of sensation and perception. The chapters on addiction, motivation, emotion, and sex follow the introduction to neurophysiology; this was done to build student motivation before tackling sensation and perception. Perhaps more significantly, some topics are in different chapters than their original systems so that they can be developed in a more behaviorally meaningful context. For instance, we discuss language along with audition, the body senses with the mechanisms of movement, the sense of taste in the context of feeding behavior, and olfaction in conjunction with sexual behavior.

We also have updated a significant number of concepts in this text to reflect more modern ways of addressing sensitive topics such as gender identity and psychological disorders. Most unique, though,

is the significant revision of the chapter on the biology of cognitive functioning (formerly a chapter on intelligence) and another on consciousness. The former finally sheds the historical framework focused on IQ and instead discusses the biological bases of having an overall high-performing set of cognitive systems (the traditional "high IQ" label) as well as the uniqueness and usefulness of having one or more specialized subsets of cognitive ability (not "impaired" but rather "differently abled"). And the latter is a full treatment of recent developments in the field rather than being limited to the usual topics of sleep and split-brain behavior. These two chapters strongly reinforce the theme that behavioral neuroscience is personally relevant and capable of addressing important questions.

Brain & Behavior has several features that will motivate students to learn and encourage them to take an active role in their learning. It engages the student with interest-grabbing opening vignettes, illustrative case studies, A Further Look features that take an intriguing step beyond the chapter content, and a Concept Check at the end of each section that serves as a reminder of the important ideas. At the end of each chapter, In Perspective emphasizes the importance and implications of what the student has just read, a summary helps to organize that information, and Test Your Understanding questions assess the student's comprehension. For Further Reading suggestions guide the student in exploring each chapter's topics more fully and is suitable for developing individualized assignments that go into more detail about content areas in the chapter. We have found over the years that students who use the study aids in a class are also the best performers in the course and improve their chances of success in neuroscience-related careers.

The process of writing (and revising) a textbook is never completed because new developments arrive faster than we can revise the text. And some topics we would have really liked to include simply could not fit (this text is already getting quite thick)! So do not take an omission of a topic you enjoy as being worth less than those topics we include, and we are always open to instructor feedback on items to be considered in the next edition. Let us know!

New in the Seventh Edition

When we published the sixth edition 3 years ago, we called it "another ambitious revision of *Brain & Behavior*"; the seventh edition continues and refines these changes. As in the previous edition, we consulted literally thousands of research articles and news stories; we selected more than 400 of them in our effort to make sure that *Brain & Behavior* continues to have the most up-to-date coverage possible. One major change you will see from the sixth edition is moving all the references we cite from the giant list in the back of the text to the end of each chapter where the references are cited. This should make it much easier for instructors and students to track down a reference or news story if they wish to learn more. In addition, we continue our effort to update or replace many of the A Further Look features to keep up with current events and research. In all, we have added 28 new features and updated 9 more.

- In Chapter 1 on the history of behavioral neuroscience, we added a new feature on the prehistory of neuroscience, explained the composition of genetic material in more detail, added new research techniques including genome-wide association studies (GWAS), single-nucleotide polymorphisms (SNPs), and bioinformatics, and updated the end of chapter study information. We incorporated 7 new references into the chapter as well.
- In Chapter 2 on the equipment of the nervous system, we simply refined the content throughout by adding a new table on glial cells, more information on the early history of neuroscience and the founders of structural neuroscience (Ramón y Cajal and Golgi), and updated the feature on artificial neural networks.
- In Chapter 3 on neuroanatomy, which was also already in good shape, we further refined the chapter by adding new treatments for spinal cord injuries, explained how radiation during space missions can affect the brain, and updated several figures on cortical synchronization across the hemispheres and effect of radiation on the prefrontal lobe. We added 9 new references as part of the refresh.

- Chapter 4 on research methods saw major changes to reflect advances in techniques over the last 4 years. We added several new methods for studying the brain: additional details on GWAS, SNPs, and CRISPR (clustered regularly interspaced short palindromic repeats) methods for investigating the genetic bases of neural form and function we introduced in Chapter 1, updated the feature on the colorful staining method called Brainbow, added a new feature on stem cell treatments, added more methods used in research to determine connections between brain areas, and addressed the effects of increasing vaccine hesitancy. This chapter added 17 new references and 10 new figures.
- Chapter 5 on pharmacology also saw major changes, with nine new or updated figures, 28 new references, and three new features on the fentanyl crisis, marijuana legalization, and the genetic links to drug abuse risk. We also added many new concepts to the chapter: auto-brewery syndrome, famous deaths due to drugs, links between the COVID-19 epidemic and alcoholism, novel forms of stimulant and hallucinogenic use, and non-pharmacological treatments for pain.
- Chapter 6 on internal states was significantly updated to reflect advances since the last edition. We updated the feature on conditioned taste aversion and added two new features on the new GLP-1 (glucagon-like peptide-1) weight loss drugs and how society is redefining obesity. We also added several new content areas: how some COVID-19 treatments can affect your sense of taste, the effects of COVID-19 on life expectancy and obesity, the new dumping syndrome condition in individuals having had gastric bypass surgery, and more brain changes in anorexia nervosa sufferers. We also updated the glossary to reflect current usage for several key terms. And 24 new references were added
- Chapter 7 on sex and gender saw continued improvement from the major changes made in the prior edition, many of which were to address new concept areas, like maternal behaviors and transgenderism, and updated areas of topical interest, like gender identity, male-female neuroanatomical differences, and effects of hormones on the brain. We added three new feature articles: one on the medial amygdala's role in regulating sex behaviors, one on differences in anatomy and function in transgender individuals, and one on gender differences in juvenile brains. And we added 38 new references to this section. Several figures were updated and added as well.
- Chapter 8 on emotion and health saw significant updates with three new features, new content areas, and 22 new references added. We now talk about the new interoceptive model of emotion, the physiological effects of stress in a novel fish model, and an outstanding new feature on the gut-brain axis. We also updated the content areas about stress and ion channels, sources of immune cells, and sudden cardiac death. We also revised or added four new figures.
- Chapter 9 on hearing and language was updated to discuss several topical areas involving hearing and communication such as the condition called foreign accent syndrome, to add a feature on restoring hearing using bone conduction, and to update the feature on human echolocation. We added new content areas on using genetic screening for language disorders and how cultural immersion can help to learn a second language. We also added three new figures and one table on sound measurements as part of the revision.
- Chapter 10 on vision was improved with many new figures, features, and sources. We added six new figures on thermal imaging, visual connections, spectral sensitivities and distribution of the different receptors in the eye, and additional examples of synesthesia. We also revised two figures and one table for clarity of the information and added an additional table that better explains how the retina processes color. We also added two new features: one on restoring vision using the same materials that are in solar panels and one on how we perceive pain in the faces of others. We also updated the use of artificial intelligence and artificial neural networks on image generation.

- Chapter 11 on body senses and movement saw significant updates: two updated features, nine new figures, one new table, and 40 additional references. New features include one on new spinal cord injury treatments and one on how Parkinson's disease can be triggered by a poor diet. Multiple content areas were added including one on the types of primary nerve fibers and what they do and one on how whisker barrel neurons tell rats where they are and where they are going. We also revised the content in multiple areas: the role of PIEZO2 in telling new neurons where to make their connections, treating motion sickness without drugs, the key role of the posterior parietal cortex, updated medications used for pain, statistics on chronic pain, changes in the brain after losing a limb, how a reflex works, more detail on Huntington's disease and the genetic bases of that disorder, and new treatments for multiple sclerosis.
- Chapter 12 on learning and memory also saw significant updates. We added a new feature about how inhibition can drive learning in the brain and updated the feature on Alzheimer's disease. We added new content about Lewy body dementia and revised several areas of content as well, such as effects of aging on the brain and dietary influences on learning, and updated the Alzheimer's disease section. We also added one new figure and 30 new references.
- Chapter 13 on cognitive functioning and neurodiversity was completely revamped to make the content more current and engaging. Much of the focus on IQ was pared back and reframed to be more inclusive to a modern audience. The benefits of variations in cognitive functioning and emphasis on neurodivergence over disability were our goals in this section. As a result, we have created a new section on variations in cognitive functioning that includes a discussion of autism spectrum disorder and the influences of the brain and biochemistry and how genetics and environment influence cortical functioning. We also included attention-deficit/hyperactivity disorder and Savantism in this section. Then, we reframed the next section as cognitive functioning across the lifespan, where we discuss how aging affects the development and maintenance of the brain and its connections. In this section we discuss intellectual developmental disorders such as Down syndrome, fragile X syndrome, and other conditions that affect the brain. We added a new feature about intelligence in animals and added three new figures and more than 50 new references to the chapter. We hope instructors and students will appreciate the much improved content in this chapter.
- Chapter 14 on psychological disorders saw mostly refinement in the chapter to update treatments and add new findings since the last edition. These included new features on glutamate receptors and schizophrenia and microbial links to obsessive-compulsive disorder, and we updated the receptor targets for psychological disorders. We also added new content on new genes and neural changes associated with symptoms of schizophrenia, types of symptoms for schizophrenia, and new information about suicidal ideation in mood disorders. We also updated the incidence of various disorders and added cognitive symptoms to the key terms. Several tables were revised, and 37 new references were added.
- Chapter 15 on consciousness saw major updates as well. We added nine new figures on effects of sleep deprivation and brain damage on sleep and consciousness, among other areas. We added two new features on sleep as social behavior and treating disorders of consciousness. We updated multiple areas: new functions of sleep in organisms, new treatments for sleep disorders, the use of neural networks to explain levels of consciousness, and determining consciousness in coma patients and in animals. We also added topical areas such as insomnia and sleep apnea, measuring attention through the Stroop task, and the cortical areas involved in the sense of self. We added a new key term in the claustrum and more than 50 new references.

Digital Resources

This text is available in Sage Vantage—an intuitive learning platform you and your students will actually love.

Fully 9 of 10 of your colleagues using Sage Vantage would recommend it!

Sage Vantage for *Brain and Behavior*, Seventh Edition, integrates all the textbook content with assignable multimedia activities and auto-graded assessments to drive student engagement and ensure accountability. Unparalleled in its ease of use and built for dynamic teaching and learning, Vantage offers customizable LMS (Learning Management System) integration and best-in-class support.

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—Aubrey Akins, student, St. Bonaventure University

"This is the **smoothest student onboarding process** I have ever experienced."

—Echo Leaver, instructor, Salisbury University

Analytic Skill Building

Assignable video activities and reading activities in Sage Vantage align with learning objectives, reinforcing fundamental concepts in every chapter. With automatic assessment integration into your gradebook, these resources provide an ideal platform for students to hone their critical thinking and application skills by applying chapter concepts to real-world scenarios.

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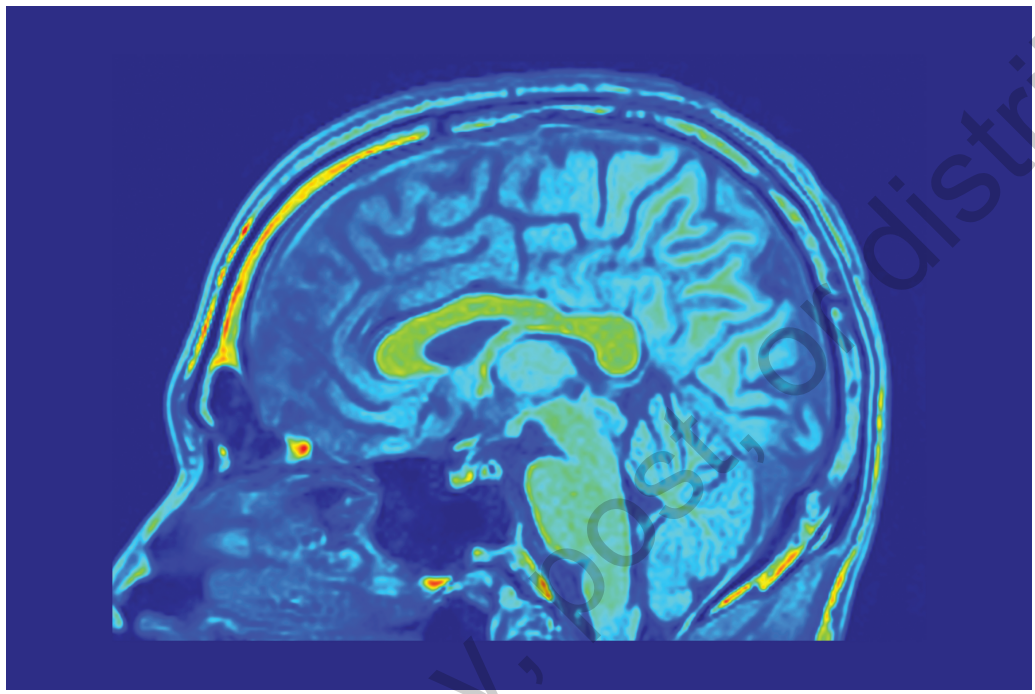
- **Learning management system** cartridges that easily integrate with your course management system so student test results and graded assignments seamlessly flow into your gradebook;
- **Test banks**, aligned to Bloom's Taxonomy, that provide a diverse range of test items, including multiple choice, true/false, and essay questions;
- **Lecture notes** that provide an outline and the key concepts in each chapter to aid in lecture preparation;
- **PowerPoint slides** that offer a flexible, accessible, and customizable solution for creating multimedia lectures;
- **Tables and figures from the book** are available to support lecture preparation and class discussions;
- **Sample course syllabi** include suggested models for structuring your course.

Chapter 1

What Is Behavioral Neuroscience?



FocalFinder/iStockPhoto

Learning Objectives

1.1 Describe the contributions of philosophers, scientists, and physiologists to the development of behavioral neuroscience as a field of study.

1.2 Compare the relative contributions of genes and environment in the development of behavioral characteristics.

That device you carry in your pocket is a wonder of modern technology. It represents a very recent step in the evolution of long-distance communications, which began with smoke signals and drum beats and progressed through the telegraph, the wireless radio, and the landline telephone.

Mobile telephones appeared in vehicles in 1956, but a handheld "cellphone" was not commercially available until 1984; dubbed the "brick," it weighed 1.75 pounds (0.79 kilogram) and cost $3,995 (Figure 1.1a). Your 4- to 6-ounce smartphone operates over a global cellular network to connect you to your friends and family and an estimated 7.5 billion people all around the world (there are actually more mobile devices on Earth than there are people). Assuming you have a smartphone, you have access to many additional people by way of email, text, and live video as well as more than 1.8 billion

websites on the internet. Your phone also allows you to record memories in the form of notes and images, perform calculations, identify a tune or a flower, find your friends, play interactive games with others, and determine the best route for your road trip. In addition, you can use your smartphone as a tablet for your laptop and connect it to other devices to stream music or video.

Figure 1.1 ▪ 40 Years of Cellular Phone Development.

(a) Lead engineer Martin Cooper with the Motorola DynaTAC 8000X. (b) A modern smartphone. When the Motorola DynaTAC 8000X, the first handheld cellular phone, came out in 1984, it cost $4,000 (about $10,000 today), had a battery that took 10 hours to charge, and had only 30 minutes of talk time. Nowadays, modern smartphones like the iPhone can last up to a week and communicate instantly with anywhere on Earth.

Sources: Ted Soqui/Corbis Historical/Getty Images; Matt Cardy/Getty Images.

The brain has many similarities. An iPhone 15 Pro, which has a processor built in a microscopic 3-nanometer framework, has around 19 billion transistors (Figure 1.1b; Shankland & Goldman, 2023). The human brain contains about 80 billion neurons, but each of these in turn connects to thousands of others, forming a network of more than 100 trillion synapses (The Human Memory, 2019) where the brain's work is done. One computational neuroscientist estimated that the brain's storage capability rivals that of the internet; as a psychologist put it, if the brain were a video recorder, it could store 2.5 petabytes (2.5 million gigabytes or 2.5 trillion megabytes) of video information, which would take you about 300 *years* to watch the 3 million hours of content (Reber, 2010). But storage of memories and information is only one of the brain's many tasks. The brain is organized into specialized subnetworks that orchestrate your body's 650 muscles and 206 bones, generate thought and make decisions, perform calculations, keep track of where you are and help you navigate around your world, tell you when and what to drink and eat, and provide your language capability and range of sensory capabilities. Like the smartphone, the brain has evolved over time and across species, but in this case, as its capability has grown, so has its size. Still, all its amazing power is packed into just 3 pounds of tissue that consumes the same amount of energy as a 4-watt LED light bulb, the same as the light bulb in a microwave oven!

Mobile phones came into their own in the last decade of the 20th century in terms of both their capabilities—such as built-in cameras, Bluetooth connectivity, and augmented reality—and their popularity, indicated by more sales worldwide in 1998 than for cars and PCs combined. This period was also seminal for the awakening field of neuroscience, so much so that in the United States the 1990s was designated the "Decade of the Brain." Planned as an effort to increase public awareness of the benefits of brain research, the Decade of the Brain was also a celebration of past achievements and a sober look at the future.

At the threshold of a new millennium, we understood that we had an obligation to expand the horizons of human knowledge and advance the treatment of neurological diseases, emotional disorders,

and addictions that cost the United States a trillion dollars per year in care, lost productivity, and crime (Uhl & Grow, 2004). Since then, in the span of your lifetime, we have produced a map of the human genetic code (later in this chapter), peered into the living human brain to watch it work (Chapter 4), developed agents that block addiction to drugs (Chapter 5), found new treatments for eating disorders (Chapter 6), found ways in which to slow the memory impairment of Alzheimer's and other neurodegenerative disorders (Chapter 12), identified key genes and treatments for schizophrenia and depression (Chapter 14), and even made artificial intelligence and simulated consciousness closer to science fact than science fiction (Chapter 15). This is truly the golden age for neuroscience. These achievements seem remarkable for such a brief span of time, but in fact they have their roots in a 300-year scientific past and more than 22 centuries of thought and inquiry before that. For that reason, we will spend a brief time examining those links to our past.

The Origins of Behavioral Neuroscience

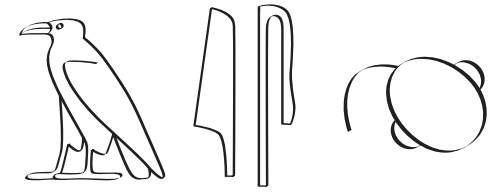
The term *neuroscience* identifies the subject matter of the investigation rather than the scientist's training. A neuroscientist may be a biologist, a physiologist, an anatomist, a neurologist, a biochemist, a psychologist, a psychiatrist—or even a computer scientist or a philosopher. Psychologists who work in the area of neuroscience specialize in **behavioral neuroscience**, the interdisciplinary intersection between biology and psychology that studies the relationships between behavior and the body, particularly the brain. (*Behavioral neuroscience* is the more modern term of *biological psychology*, though sometimes the term *biopsychology, psychobiology*, or *physiological psychology* is also used.) For psychologists, *behavior* has a very broad meaning that includes not only overt acts but also internal processes such as learning, thinking, and emotion. Behavioral neuroscientists attempt to answer questions such as "What changes in the brain when a person learns?" "Why does one person develop depression, another under similar circumstances becomes anxious, while a third seems unaffected?" "What is the physiological explanation for emotions?" "How do we recognize the face of a friend?" and "How does the brain's activity result in consciousness?"

Behavioral neuroscientists use a variety of research techniques to answer these questions, as you will see in the coming chapters. Sometimes they find the links between chemicals in the brain and psychological processes. Other times they investigate how changes in the chemicals of the nervous system affect behaviors. Still other times they develop animal models for human conditions such as aging. You can find success as a behavioral neuroscientist with a background in chemistry, biology, physics, engineering, medicine, public health, human development, psychology, computer science, or even history. Whatever their primary area of study or their strategies for doing research, behavioral neuroscientists try to go beyond the mechanics of how the brain works to focus on an integrated multilevel understanding of the brain's role in behavior.

To really appreciate the impressive accomplishments of today's behavioral neuroscientists, it is useful, perhaps even necessary, to understand the thinking and the work of their predecessors. Contemporary scientists stand on the shoulders of their intellectual ancestors, who made heroic advances with far less information and technology at their disposal than is available to today's students. One of the earliest documented studies of the brain was a written record of treatments for individuals with head injuries and contained the first symbol for and descriptions of the brain (Figure 1.2); although the papyrus of Ebers and Edwin Smith was written around 1550 BCE, there is a chance the original source might be 1500 years older (Haas, 1999). See A Further Look for more about the early history of studying the brain.

Many writers have pointed out that psychology has a brief history but a long past. What they mean is that thinkers have struggled with the questions of the physiological bases of behavior and experience for millennia, but psychology arose as a separate discipline fairly recently; the date most people accept is 1879, when Wilhelm Wundt (Figure 1.3) established the first psychology laboratory in Leipzig, Germany. But behavioral neuroscience would not emerge as a separate science until scientists offered convincing evidence that the biological approach could answer significant questions about psychology

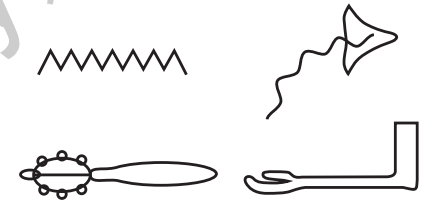
Figure 1.2 ▪ Symbols for Various Brain Areas as Indicated in the Papyrus of Ebers and Edwin Smith.



Brain

Gyri and Sulci

Meninges



Cerebrospinal fluid

Soul/mind

Source: Fountoulakis, K. N. (2022). The Human Connectome. Cham, Switzerland: Springer Nature Switzerland AG.

and behavior. To do so, they would need to come to terms with an old philosophical question about the nature of the mind. Because the question forms a thread that helps us trace the development of modern behavioral neuroscience, we will orient our discussion around this issue.

Figure 1.3 ▪ Wilhelm Wundt (1832–1920).

Weltrundschau zu Reclams Universum 1902

A Further Look

The Earliest History of Neuroscience

Although we cannot say who the first individual was that discovered the importance of the brain in controlling our mental abilities, we do know that the first documented medical cases involving the brain come from a physician's summary of various treatments of skull fractures in ancient Egypt around 3000 BCE. The Smith papyrus (Figure 1.4) documents how the Egyptians treated the Pharaoh Imhotep about a thousand years prior for a head injury, and it describes the brain as well as the nonphysical mind. In addition, it contains the collected wisdom of the ancient Egyptians' medical treatments for various head injuries. But it is probable that prior to the Smith papyrus, the brain's importance (and fragility) was well known to ancient cultures given that skulls found dating to around 5000 BCE show signs of surgical interventions such as drill holes (called trephination; right). And signs of infection around the drilled (or sawed) holes suggest that the patients had survived the surgery and lived for at least some time. Sadly, we do not have any earlier written documents from that time; primitive written language would not exist until around 3500 BCE when cuneiform was invented in the Mesopotamian region of the Middle East.

Figure 1.4 ▪ Edwin Smith Papyrus.

Prescientific Psychology and the Mind-Brain Problem

This issue is usually called "the mind-body problem," but it is phrased differently here to place the emphasis squarely where it belongs—on the brain. The **mind-brain problem** deals with what the mind is and what its relationship is to the brain. There can be no doubt that the brain is essential to our behavior, but does the mind control the brain or is it the other way around? Alternatively, are the mind and the brain the same thing? How these questions are resolved affects how we ask all the other questions of neuroscience.

At the risk of sounding provocative, we argue that there is no such thing as *mind*. It exists only in the sense that, say, weather exists; weather is a concept used to include rain, wind, humidity, and related phenomena. We talk as if there is *a weather* when we say things like "The weather is interfering with my travel plans." But no one really thinks that there is *a weather*. Most, though not all, neuroscientists believe that we should think of the mind in the same way; it is simply the collection of things the nervous system does such as thinking, sensing, planning, and feeling. But when we think, sense, plan, and feel, we get the compelling impression that there is *a mind* behind it all, guiding what we do and how we interpret our world. Most neuroscientists say this is just an illusion; the sense of mind is nothing more than an awareness of what the brain is doing. Mind, like weather, is just a concept; it is not a *something*—it does not *do* anything.

This position is known as monism, from the Greek *monos*, meaning "alone" or "single." **Monism** is the idea that the mind and the body consist of the same substance. Idealistic monists believe that everything is a nonphysical mind (like the simulated world of *The Matrix* movies), but most monists take the position that the body and mind and everything else are physical; this view is called **materialistic monism**. The idea that the mind and the brain are separate is known as **dualism**. For most dualists, the body is material and the mind is nonmaterial. Most dualists also believe that the mind influences behavior by interacting with the brain.

This question did not originate with modern psychology. Ancient Egyptian texts about life after death support a dualistic perspective well before two millennia BCE (Figure 1.2), and the Greek philosophers were debating it in the fifth century BCE (Murphy, 1949) when Democritus proposed that everything in the world was made up of atoms (*atomos*, meaning "indivisible"), his term for the smallest particle possible. Even the soul, which included the mind, was made up of atoms, so it too was material. Plato and Aristotle, considered the two greatest intellectuals among the ancient Greeks, continued the argument into the fourth century BCE. Plato was a dualist, whereas his monistic student Aristotle joined the body and soul in his attempt to explain memory, emotions, and reasoning.

Defending either position was not easy. The dualists needed to explain how a nonphysical mind could influence a physical body, and monists had the task of explaining how the physical brain could account for mental processes such as perception and conscious experience. But the mind was not observable, and even the vaguest understanding of the nervous system was not achieved until the 1800s, so neither side had much ammunition for the fight.

Descartes and the Physical Model of Behavior

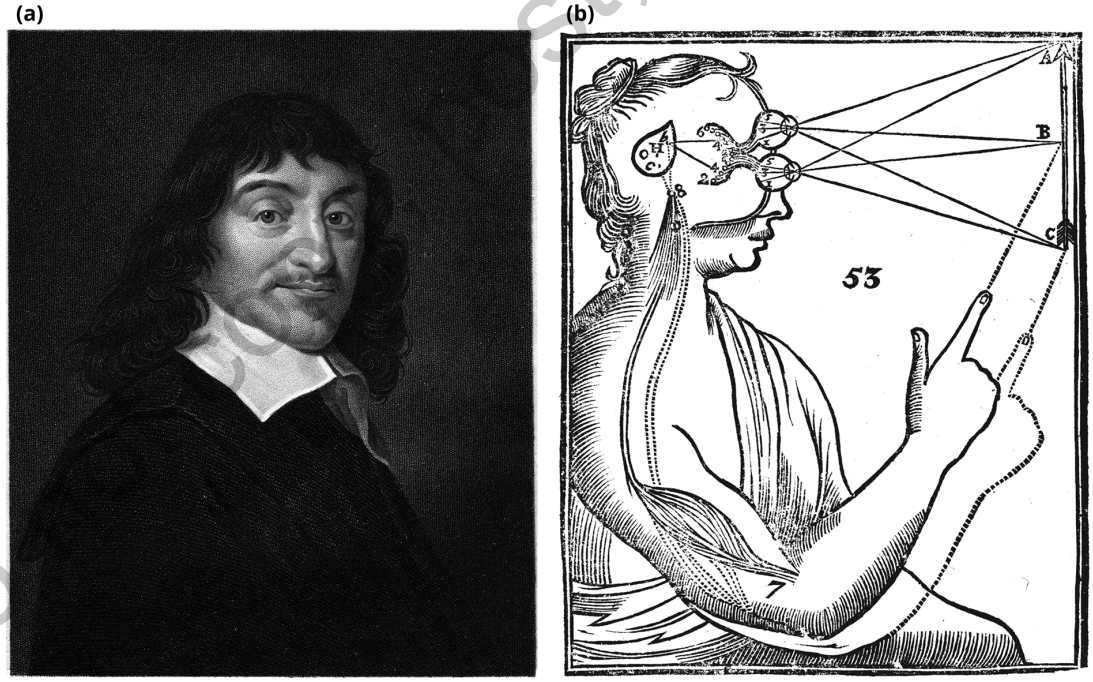
Scientists often resort to the use of models to understand whatever they are studying. A **model** is a proposed mechanism for how something works. Sometimes a model is part of a larger theory, which is a general explanation for observed phenomena. One such **theory** is Charles Darwin's explanation that a species can develop new capabilities because variations in that capability enhanced survival and opportunity to reproduce in individuals with that variation compared with other variations. Other times a model is a simpler organism, simulation, or system that scientists study in an attempt to understand a more complex one or part of a larger theory. For example, researchers have used the rat to model everything from learning to Alzheimer's disease in humans, and the computer is increasingly used to simulate models of cognitive processes. Historically, theories and models tended to follow technological advancements in society, especially in early attempts to understand the nervous system. But as we discuss

in Chapter 2 with respect to human-exclusive processes, models may never duplicate the complexity of the human mind.

In the 17th century, the French philosopher and physiologist René Descartes (Figure 1.5a) used a hydraulic model to explain the brain's activity (Descartes, 1662/1984). Descartes's choice of a hydraulic model was influenced by his observation of the statues in the royal gardens at Saint Germain. When a visitor stepped on certain tiles, the pressure forced water through tubes to the statues and made them move. Using this model, Descartes then reasoned that nerves were also hollow tubes. The fluid they carried was not water but rather what he called "animal spirits"; these flowed from the brain and inflated the muscles to produce movement. Sensations, memories, and other mental functions were produced as animal spirits flowed through "pores" in the brain. The animal spirits were pumped through the brain by the pineal gland (Figure 1.5b). Descartes's choice of the pineal gland (named because it resembled a pine cone) was based on his conclusion that it was at a perfect location to serve this function. Attached just below the two cerebral hemispheres by its flexible stalk, it appeared capable of bending at different angles to direct the flow of animal spirits into critical areas of the brain. It also was, to Descartes, the only part of the brain that was a single organ and not split into left and right sides (Berhouma, 2013). Thus, for Descartes, the pineal gland became the "seat of the soul," the place where the mind interacted with the body. Although Descartes assigned control to the mind, his unusual emphasis on the physical explanation of behavior foreshadowed the physiological approach that would soon follow.

Figure 1.5 ▪ René Descartes (1596–1650) and the Hydraulic Model.

Descartes (a) believed that behavior was controlled by animal spirits flowing through hollow nerves and pumped by the pineal gland (b). He also believed that changes in behaviors were due to the tube diameters expanding and contracting.



iStockphoto.com/traveler1116; Photo 12/Contributor/Getty Images

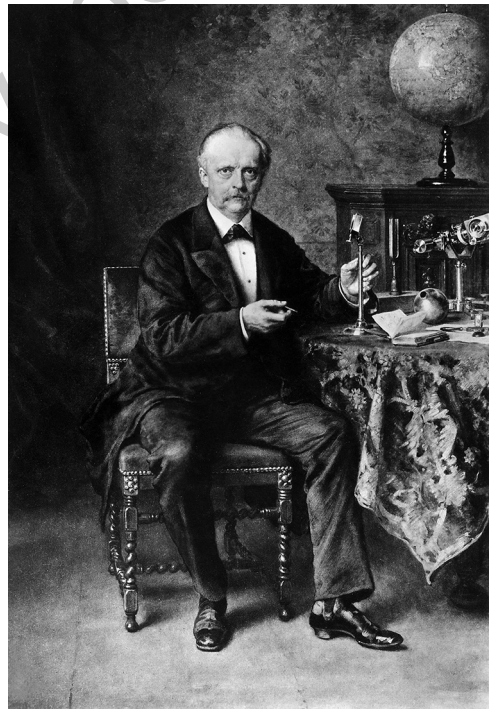
Descartes lacked an understanding of how the brain and body worked, so he relied on a small amount of anatomical knowledge and a great deal of speculation. His hydraulic model not only represented an important shift in thinking, it also illustrates how a model or a theory can lead us astray, at least temporarily. Fortunately, this was the age of the Renaissance, a time not only of artistic expansion and world exploration but also of scientific curiosity. Thinkers began

to test their ideas through direct observation and experimental manipulation as the Renaissance gave birth to science. In other words, they adopted the method of **empiricism**, which means that they gathered their information through observation and evidence rather than logic, intuition, or other means. Progress was slow, but two critically important principles would emerge as the early scientists ushered in the future.

Helmholtz and the Electrical Brain

Ancient Egyptians had known that the human body was sensitive to strong sources of electricity like lightning and electric fish. But it was not until the late 1700s when the Italian physiologist Luigi Galvani demonstrated that he could make a frog's leg muscle twitch by stimulating the attached nerve with electrical current even after the nerve and muscle had been removed from the frog's body. A century later in Germany, Gustav Fritsch and Eduard Hitzig produced leg movement in dogs by electrically stimulating their exposed brains (Fritsch & Hitzig, 1870). What these scientists showed was that animal spirits were not responsible for movement; instead, the cause was *nerves operated by electricity*! But the German physicist and physiologist Hermann von Helmholtz (Figure 1.6) demonstrated that nerves do not behave like wires conducting electricity. He was able to measure the speed of conduction in nerves, and his calculation of about 90 feet/second (27.4 meters/second) fell far short of the speed of electricity in wires, which is about 90% of the speed of light (186,000 miles/second or 299,000 kilometers/second). It was obvious that researchers were dealing with a biological phenomenon and that the functioning of nerves and of the brain was open to scientific study. Starting from this understanding, Helmholtz's studies of vision and hearing gave "psychologists their first clear idea of what a fully mechanistic 'mind' might look like" (Fancher, 1979, p. 41). As you will see in later chapters, Helmholtz's ideas were so insightful that even today we refer to his theories of vision and hearing as a starting point before describing the current ones (see Chapter 10).

Figure 1.6 ▪ Hermann von Helmholtz (1821–1894).



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The Localization Issue

The second important principle to come out of this period—localization—emerged over the first half of the 19th century. **Localization** is the idea that specific areas of the brain carry out specific functions. Fritsch and Hitzig's studies with dogs gave objective confirmation to physicians' more casual observations dating as far back as 17th-century BCE Egypt (Breasted, 1930), but it was two medical case studies that really grabbed the attention of the scientific community. In 1848, a railroad construction foreman named Phineas Gage was injured when a dynamite blast drove an iron tamping rod through his skull and the frontal lobes of his brain (see Chapter 3). Amazingly, he survived with little impairment of his intelligence, memory, speech, or movement. But he became irresponsible and profane and was unable to abide by social conventions (Damasio et al., 1994). Then, in 1861, the French physician Paul Broca (Figure 1.7) performed an autopsy on the brain of a man named Tan who had lost the ability to speak after a stroke (see Chapter 9). The autopsy showed that damage was limited to an area on the left side of Tan's brain now known as Broca's area (Broca, 1861).

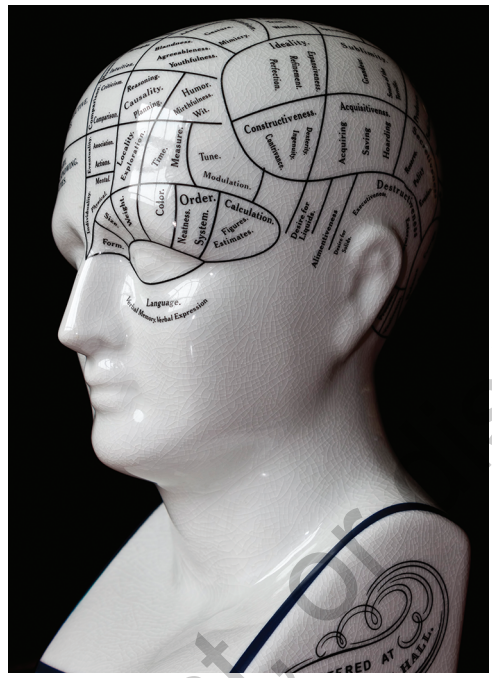
Figure 1.7 ▪ Paul Broca (1824–1880).

Wikimedia Commons

By the mid-1880s, additional observations like these had convinced researchers about localization. But a few brain theorists were already taking the principle of localization too far, and we should be on guard lest we make the same mistakes. At the end of the 18th century, when interest in the brain's role in behavior was really heating up, German anatomist Franz Gall had come up with an extreme and controversial theory of brain localization. According to **phrenology**, each of 35 different "faculties" of emotion and intellect—such as combativeness, inhabitiveness (love of home), calculation, and order—was located in a precise area of the brain (Spurzheim, 1908). Gall and his student J. G. Spurzheim determined this by feeling bumps on people's skulls and relating any protuberances to the individuals' characteristics; because these scientists knew the personality traits of their subjects, each phrenology map was as unique as the people they studied and did not stand up to the test of time (Figure 1.8 shows a later map from American L. N. Fowler). Others such as Karl Lashley took an equally extreme position at the other end of the spectrum; **equipotentiality** is the idea that the brain functions as an undifferentiated whole (Lashley, 1929). According to this view, the extent of damage, not the location, determines how much function is lost.

Figure 1.8 ▪ A Modern Reproduction of the Phrenologist L. N. Fowler's Map of the Brain.

Phrenologists believed that the psychological characteristics shown here were controlled by the respective brain areas. Fowler was an American who came up with his own map different from the British map of Gall and Spurzheim.



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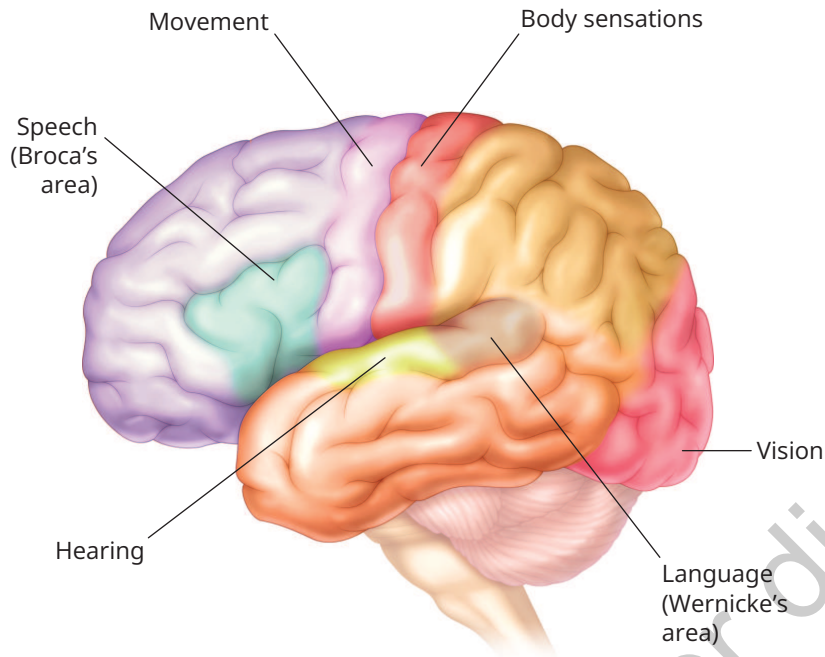
Obviously, bumps on the skull have nothing to do with the size of the brain structures beneath, and most of the characteristics Gall and Spurzheim identified have no particular meaning at the physiological level. But we also know that the brain is not equipotential. The truth, as is often the case, lies somewhere between these two extremes.

Today's research tells us that functions are as much *distributed* as they are *localized*; behavior results from the interaction of many widespread areas of the brain. In later chapters, you will see examples of cooperative relationships among brain areas in language, visual perception, emotional behavior, motor control, and learning. In fact, you will learn that neuroscientists these days are less likely to ask where a function is located than to ask how the brain integrates activity from several areas into a single experience or behavior. Nevertheless, the localizationists strengthened the monist position by showing that language, emotion, motor control, and so on are controlled by *relatively* specific locations in the brain (Figure 1.9). This meant that the mind ceased being *the explanation* and became *the phenomenon to be explained*.

Understand that the nature and the role of the mind are still debated in some quarters. For example, some neuroscientists believe that brain research will be unable to explain how a material brain can generate conscious experience and that this will spell the final doom of materialism. These nonmaterial neuroscientists interpret the brain changes that occur during behavior therapy for obsessive-compulsive disorder symptoms as evidence of mental states during therapy were changing the brain directly (Schwartz et al., 1996; see Chapter 14). Of course, what material neuroscientists see is incoming experiences processed by the brain modifying circuits within the brain. Neuroscience has been able to explain a great deal of behavior without any reference to a nonmaterial mind, and as you explore the rest of this text, you will begin to see why most brain scientists would describe their research as materialistic monism.

Figure 1.9 ▪ Some of the Brain's Functional Areas.



Concept Check

Take a Minute to Check Your Knowledge and Understanding

- What change in method separated science from philosophy?
- What were the important implications of the discoveries that nerve conduction is electrical and that specific parts of the brain have (more or less) specific functions?
- Where do scientists stand on the localization issue?
- Why is neuroscience considered to be materialistic monism?

Nature and Nurture

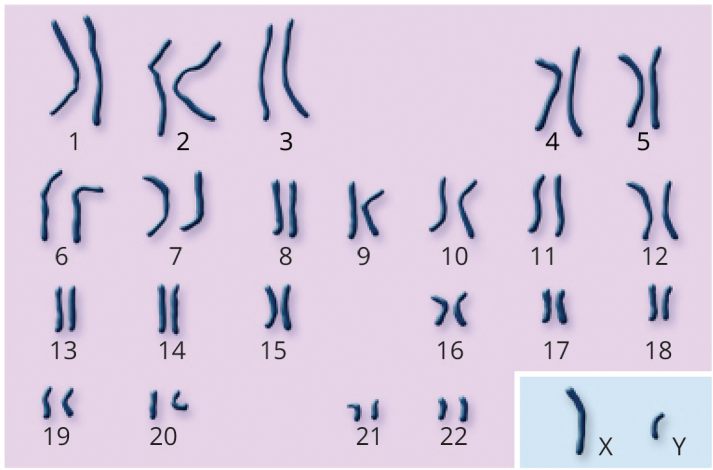
A second extremely important issue in understanding the biological bases of behavior is the **nature versus nurture** question, or how important heredity and genetics are relative to environmental influences in shaping behavior. Like the mind-brain issue, this is one of the more controversial topics in psychology, at least as far as public opinion is concerned. The arguments are based on emotion and values almost as often as they appeal to evidence and reason. For example, some critics complain that attributing behavior to heredity is just a form of excusing actions for which the person or society should be held accountable. A surprising number of behaviors are turning out to have some degree of hereditary influence, so you will encounter this issue again in later chapters. Because there is so much confusion about heredity, we need to be sure you understand what it means to say that a behavior is hereditary before we go any further.

The Genetic Code

The **gene** is the fundamental biological unit that directs cellular processes and transmits inherited characteristics. Most genes are found on the chromosomes, which are located in the nucleus of each cell, but there are also a few genes in structures outside the nucleus, called mitochondria, that are inherited from the mother. Each body cell in a human has 46 chromosomes arranged in 23 pairs (Figure 1.10).

Each pair is identifiably distinct from every other pair. This is important, because genes for different functions are found on specific chromosomes. The chromosomes are referred to by number from longest to shortest except for the sex chromosomes; in mammals, females have two X chromosomes, whereas males typically have an X and a Y chromosome. Notice that the members of a pair of chromosomes are similar to each other, again with the exception that the Y chromosome is much shorter than the X chromosome.

Figure 1.10 ▪ A Set of Human Chromosomes.



U.S. National Library of Medicine

Unlike the body cells that have paired chromosomes, the male's sperm cells and the female's ova (egg cells) each have 23 chromosomes—one of each. When these sex cells are formed by the division of their parent cells, the pairs of chromosomes separate, so that each daughter cell receives only one chromosome from each pair. Whereas every ovum contains a single X chromosome, sperm cells can contain either an X or a Y chromosome. When the sperm enters the ovum during fertilization, the chromosomes of the two cells merge to restore the number to 46, and the combination of XX or XY will determine the biological sex of either female or male, respectively. The fertilized egg, or **zygote**, then undergoes rapid cell division and development on its way to becoming a functioning organism. For the first 8 weeks (in humans), the new organism is referred to as an **embryo**, and from then until birth is referred to as a **fetus**.

The mystery of how genes carry their genetic instructions began to yield to researchers in 1953, when James Watson and Francis Crick published a proposed structure for the deoxyribonucleic acid that genes are made of (Watson & Crick, 1953). **Deoxyribonucleic acid (DNA)** is a double-stranded chain of chemical molecules that looks like a ladder that has been twisted around itself; this is why DNA is often referred to as a *double helix* (Figure 1.11). Each rung of the ladder is composed of two of the four nucleotides: adenine, thymine, guanine, and cytosine (A, T, G, and C, respectively). Adenine and thymine are always together on a rung, and guanine and cytosine are always together; this matched base arrangement makes separating and duplicating the DNA strand using complementary bases both easy and highly accurate during cell division. The order in which these nucleotides appear on the ladder forms the sequences of genes that carry all our genetic information. The four-letter alphabet these nucleotides provide is adequate to spell out the instructions for every structure, function, and protein in your body.

We only partially understand how genes control the development of the body and its activities as well as how they influence many aspects of behavior. However, we do know that genes exert their influence in a deceptively simple manner: They provide the directions for making proteins. Some of these proteins are used in the construction of the body, and others are enzymes that act as catalysts, modifying chemical reactions in the body. It is estimated that humans differ among each other in the sequences of nucleotides that make up our DNA by only about 0.5% (Levy et al., 2007); however, you will see throughout this text that this variation leads to enormous differences in development, traits, and behavior.

Because all but two of the chromosomes are paired, most genes are as well; a gene on one chromosome is paired with a gene for the same function on the other chromosome. The exception is that the shorter Y chromosome has only 1/25th as many genes as the X chromosome. Although paired genes have the same type of function, their effects often differ; each different version of a gene is called an **allele**. In some cases, the effects of the two alleles blend to produce a mixed result; for example, a person with the allele for type A blood on one chromosome and the allele for type B blood on the other will have type AB blood (Figure 1.12).

Figure 1.11 ▪ Structure of a Strand of DNA.

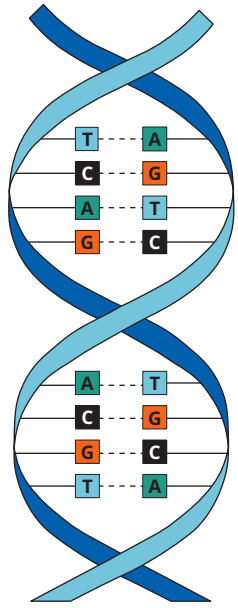
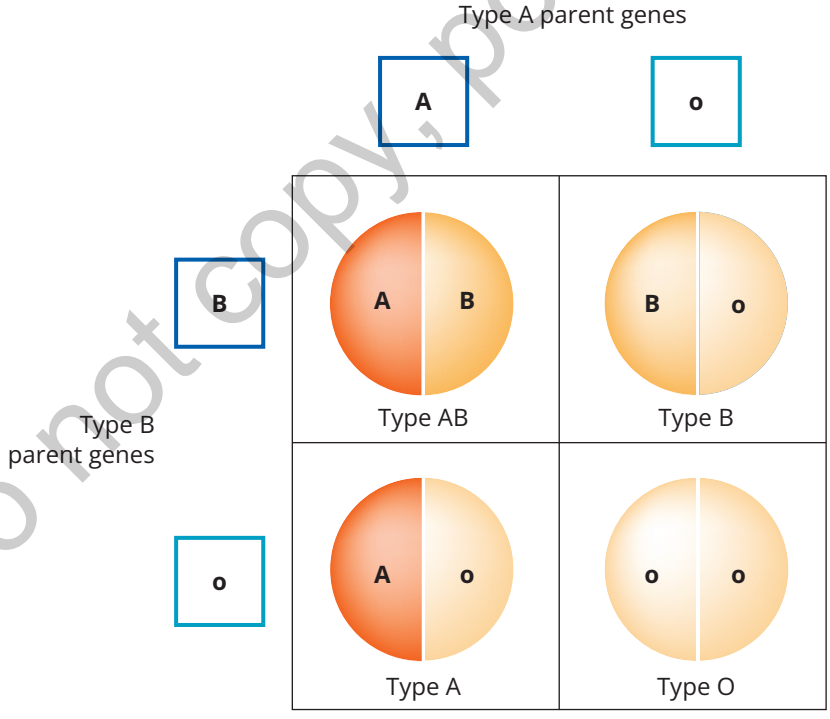


Figure 1.12 ▪ Blood Types in the Offspring of Heterozygous Parents.

The small boxes indicate the alleles of two parents; because A and B alleles are dominant over the o allele, the parents' phenotypic blood types are A and B, respectively. Each offspring receives one allele from each parent; the circles show the four possible combinations of alleles (genotypes) in the offspring, each of which has an equal chance of occurring. The text under the circles indicates the blood types (phenotypes) of the offspring. Note that type O blood occurs only when the child receives two recessive o alleles.



In other cases, one allele of a gene may be dominant over the other. A **dominant** allele will produce its effect regardless of which allele it is paired with on the other chromosome; a **recessive** allele will have an influence only when it is paired with the same allele. Figure 1.12 illustrates this point. In the

example, note that one parent is **heterozygous** for the blood type B allele, which means that the two alleles are different; the other parent is heterozygous for the blood type A allele. The A and B alleles are dominant over the o allele (present but hidden in each parent in this hypothetical example); as a result, each blood type (A, B, AB, or O) has an equal chance (one in four) of occurring in an offspring. Individuals with the same **phenotype** (an observable characteristic such as blood type B) may differ by **genotype** (combinations of alleles such as B and B or B and o). You can see in the figure that type A and B parents have a one in four chance of having a child with different blood types, one of which will be **homozygous** (receiving two identical alleles) for the recessive o allele.

In the case of unpaired genes on the X chromosome, a recessive gene alone is adequate to produce an effect because it is not opposed by a dominant gene. A characteristic produced by an unpaired gene on the X chromosome is referred to as **X-linked**. With such a large discrepancy in the number of genes on the X and Y chromosomes, you can understand the potential for sex-specific effects from X linkage genes. One example is that males are eight times more likely than females to have a deficiency in red-green color vision. See Chapter 10 for more on this deficiency. Another trait is androgen insensitivity syndrome, which is a form of 46,XY intersex disorders that disrupt normal male sexual development (see Chapter 7).

Some characteristics—such as blood type and color vision deficiency—result from a single pair of genes, but many characteristics are determined by several genes; they are **polygenic**. Height and skin color are polygenic, and most behavioral characteristics such as intelligence and psychological disorders are also controlled by a large number of genes.

We have known from ancient times that animals could be bred for desirable behavioral characteristics such as hunting ability and a mild temperament that made them suitable as pets. Darwin helped establish the idea that behavioral traits can be inherited in humans as well, but the idea fell into disfavor as an emphasis on learning as the major influence on behavior became increasingly fashionable. In the 1960s and 1970s, however, the tide of strict environmentalism began to ebb and the perspective shifted toward a balanced view of the roles of nature and nurture (Plomin et al., 1994). Konrad Lorenz, one of the founders of the field of ethology (the study of natural behaviors), strongly advocated that natural selection was driven by differences in behavior (Lorenz, 1963). By 1992, the American Psychological Association was able to identify genetics as one of the themes that best represent the present and the future of psychology (Plomin & McClearn, 1993).

Of the behavioral traits that fall under genetic influence, intelligence is the most investigated and the most controversial (see Chapter 12). Most of the behavioral disorders, including alcoholism and drug addiction, schizophrenia, major mood disorders, and anxiety, are partially hereditary as well (McGue & Bouchard, 1998). The same can be said for some personality characteristics (Bouchard, 1994) and sexual orientation (J. M. Bailey & Pillard, 1991; J. M. Bailey et al., 1993; Kirk et al., 2000).

However, you should exercise caution in thinking about these genetic effects. Genes do not provide a script or instructions for behavior. They control the production of proteins; the proteins in turn affect the development of brain structures, the production of neurotransmitters and the receptors that respond to them, and the functioning of the glandular system. In addition, the environment can also exert influences on genes to turn them off or on, an "epigenetic" effect we will discuss in more depth in Chapter 6. We will offer specific examples in later chapters, where we will discuss this topic in more depth.

The Human Genome Project

After geneticists have determined that a behavior is influenced by genes, the next step is to discover which genes are involved. The various techniques for identifying genes boil down to determining whether people who share a particular characteristic also share a particular gene or genes that people without the characteristic do not have. This task is extremely difficult if the researchers do not know where to look because the amount of DNA is so great. However, the gene search received a tremendous boost in 1990, when a consortium of geneticists at 20 laboratories around the world began a project to identify all the genes in our chromosomes, or the human **genome**.

The goal of the **Human Genome Project** was to map the location of all the genes on the human chromosomes and to determine the genes' codes—that is, the order of bases within each gene. In 2000—just 10 years after the project began—the project group and a private organization simultaneously announced they had produced "rough drafts" (International Human Genome Sequencing Consortium, 2001; Venter et al., 2001); within another 5 years, the entire human genome had been sequenced (Gregory et al., 2006).

But when it comes to gene functioning, there is still more mystery than enlightenment. Only 21,000 of our genes—just 3% of our DNA—have turned out to be protein encoding (ENCODE Project Consortium, 2012). The lowly roundworm has 19,735 protein-coding genes (Hillier et al., 2005), so clearly the number of genes is not correlated with behavioral complexity. However, the amount of noncoding DNA—which we used to call "junk DNA"—*does* correlate with behavioral complexity (Andolfatto, 2005; Siepel et al., 2005). So what is important about "junk" DNA? Some of it is, in fact, nonfunctional, remnants left behind during evolution. But 80% of the non-protein-coding DNA is biochemically active. Much of it controls the functioning of other genes by altering **gene expression**—the translation of encoded information into the production of proteins (Pennacchio et al., 2006). For example, when a stretch of noncoding DNA known as *HACNS1*—which is unique to humans—is inserted into a mouse embryo, it turns on genes in the "forearm" and "thumb" (Figure 1.13; Prabhakar et al., 2008). DNA taken from the same area in chimpanzees and rhesus monkeys does not have that effect. The researchers speculate that the genes that *HACNS1* turns on led to the evolutionarily important dexterity of the human thumb.

Figure 1.13 ▪ Human Junk DNA Turns on Genes in a Mouse Embryo's Paw.

To determine where the DNA was having an effect, it was paired with a gene that produces a blue protein when activated. The blue area indicates that HACNS1 is targeting genes in the area analogous to the human thumb.

From "Human-specific Gain of Function in a Developmental Enhancer," by S. Prabhakar et al., ***Science***, 321, p. 1348. Reprinted with permission from AAAS.

Recently, scientists have developed a group of methods that can quickly analyze large and complex biological and psychological datasets. This area of study, called bioinformatics, is a powerful research area that can rapidly identify genes that are correlated to biological and psychological differences between individuals and can identify candidate genes that can then be further studied in animal and computer models to determine the role of individual genes (and groups of genes) in the development and symptoms of the disorders. Scientists can now identify individuals who have one nucleotide inside a gene that is different from others (such as a thymine where normally there should be a guanine). This single change is called a **single-nucleotide polymorphism (SNP)**, and scientists have linked specific

SNPs to individuals with symptoms of psychological and eating disorders, autism, and other behaviors. Another type of genetic screening is called a **genome-wide association study (GWAS)**, which uses whole-genome sequencing to compare a large number of SNPs across a large number of individuals who have donated their DNA for testing; these sorts of tests can discover how likely it is that individual SNPs contribute to behavioral variation and can quickly identify for further exploration genes that may be unknown or associated with other, unrelated traits (Figure 1.14; Stranger et al., 2011). The advancement and speed of genetic studies continues to amaze us; the Human Genome Project was a Herculean task that took 13 years and billions of research dollars to complete, but today you can get your own genome sequenced from a company like 23andMe or AncestryDNA in less than 10 weeks for under a hundred dollars.

Figure 1.14 ▪ Genome-Wide Association Study.

The entire genome of individuals with and without symptoms of schizophrenia was sequenced, and genetic differences (SNPs) found in the affected individuals (a), but not in the unaffected control group (b), are identified for further testing (a significant difference in the affected group has more SNPs and is identified with a red circle).

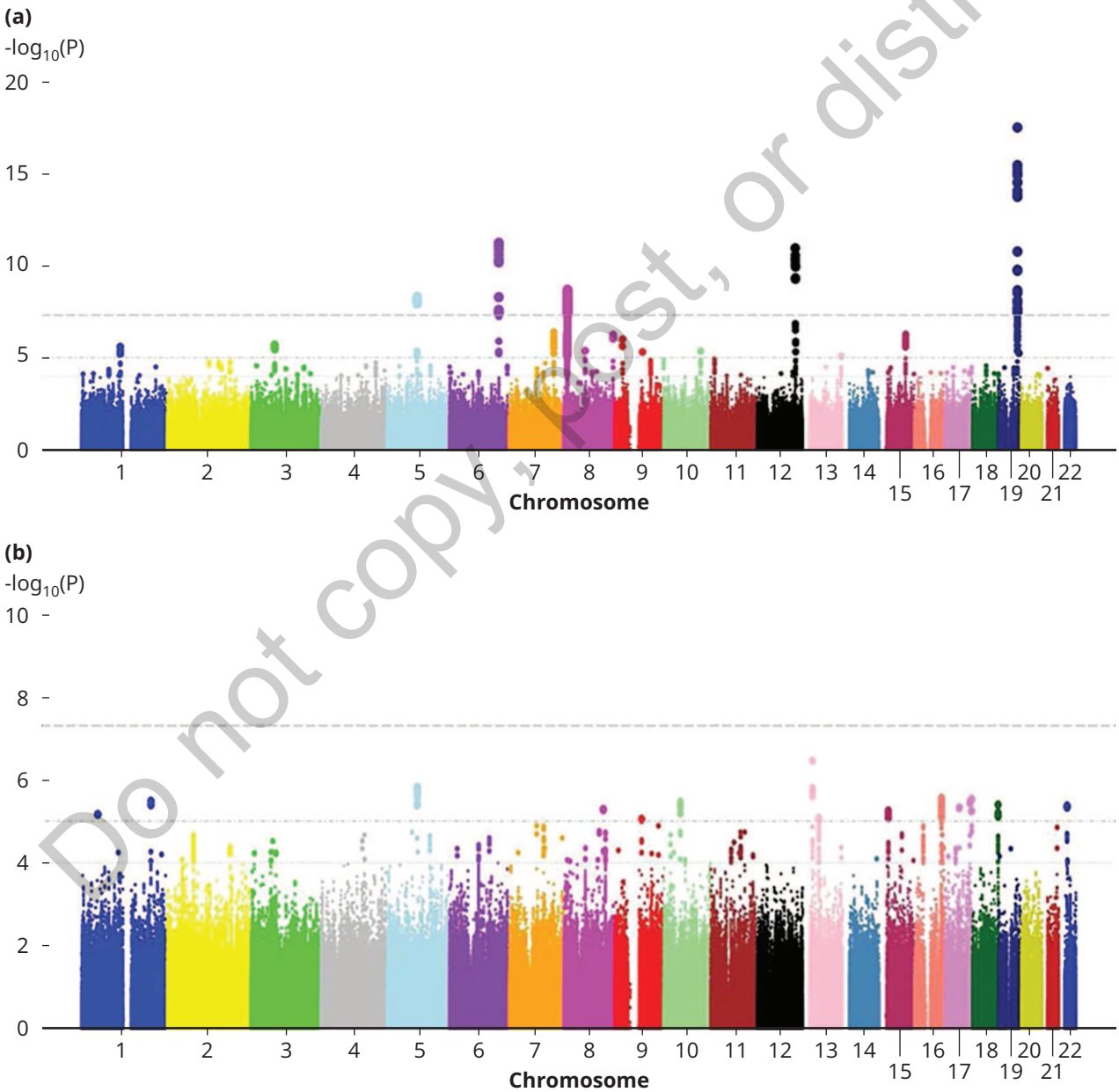


Figure 2A from "Shared Genetic Loci Between Body Mass Index and Major Psychiatric Disorders" by S. Bahrami et al., 2020, *JAMA Psychiatry*, 77(5), 503–512.

A second question is what the genes do. The gene map does not answer that question, but it does make it easier to find the genes responsible for a particular disorder or behavior. For example, when geneticists were searching for the gene that causes Huntington's disease in the early 1980s, they found that most of the affected individuals in a large extended family shared a couple of previously identified genes with known locations on chromosome 4, whereas the disease-free family members did not. This meant that the Huntington's gene was on chromosome 4 and near these two *marker* genes (Gusella et al., 1983). Actually finding the Huntington's gene still took another 10 years; now the gene map is dramatically reducing the time required to identify genes.

Identifying the genes and their functions will improve our understanding of human behavior and both psychological and medical disorders. We will be able to treat disorders genetically, counsel vulnerable individuals about preventive measures, and determine whether a patient will benefit from a drug or have an adverse reaction, thus eliminating delays from trying one treatment after another.

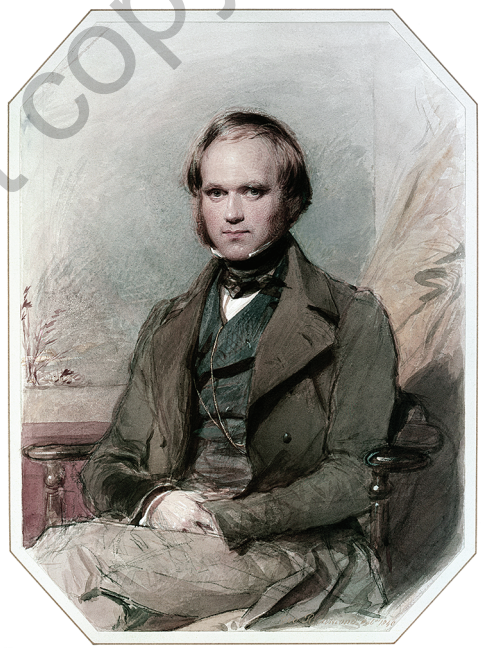
Heredity: Destiny or Predisposition?

To many people, the idea that several, if not most, of their behavioral characteristics are hereditary implies that they are merged forms of their parents and their future is engraved in stone by their genes. This is neither a popular nor a comfortable view, and it creates considerable resistance to the concept of behavioral genetics. The view is also misleading; a hallmark of genetic influence is actually *diversity*.

Genes and Individuality

Although family members do tend to be similar to each other, children share only half of their genes with each of their parents or with each other. A sex cell receives a random half of the parent's chromosomes; as a result, a parent can produce 2^{23}, or 8 million, different combinations of chromosomes. Add to this the uncertainty of which sperm will unite with which egg, and the number of genetic combinations that can be passed on to offspring rises to 60 or 70 trillion! So sexual reproduction increases individuality in spite of the inheritability of traits. This variability powers what Darwin (Figure 1.15) called **natural selection**, which means that those whose genes endow them with more adaptive capabilities are more likely to survive and transmit their genes to more offspring (Darwin, 1859).

Figure 1.15 ▪ Charles Darwin (1809–1882).



From Origins, Richard Leakey and Roger Lewin.

The effects of the genes themselves are not rigid; they can be variable over time and circumstances. Genes are turned on and turned off, or their activity is upregulated and downregulated, so that they produce more or less of their proteins or different proteins at different times. If the activity of genes were constant, there would be no smoothly flowing sequence of developmental changes from conception to adulthood. And a large number of genes change their functioning late in life, apparently accounting for many of the changes common to aging (Ly et al., 2000) as well as the onset of diseases such as Alzheimer's (Breitner et al., 1986). The functioning of some genes is even controlled by experience, which explains some of the changes in the nervous system that constitute learning (C. H. Bailey et al., 1996). For the past half century, researchers have puzzled over why humans are so different from chimpanzees, our closest relatives, considering that 95% to 98% of our DNA sequences are identical (Britten, 2002; King & Wilson, 1975; Varki & Altheide, 2005). Part of the answer appears to be that we differ more dramatically in which genes are *expressed*—those actually producing proteins—in the brain (Suntsova & Buzdin, 2020).

Genes also have varying degrees of effects. Some determine a person's characteristics, whereas others only influence them. A person with the mutant form of the *huntingtin* gene *will* develop Huntington's disease, but most behavioral traits depend on many genes (see Chapter 11 for more on this disorder). For instance, a single gene will account for only a slight increase in intelligence or in the risk for schizophrenia (see Chapter 14). The idea of risk raises the issue of vulnerability and returns us to our original question, the relative importance of heredity and environment.

Heredity, Environment, and Vulnerability

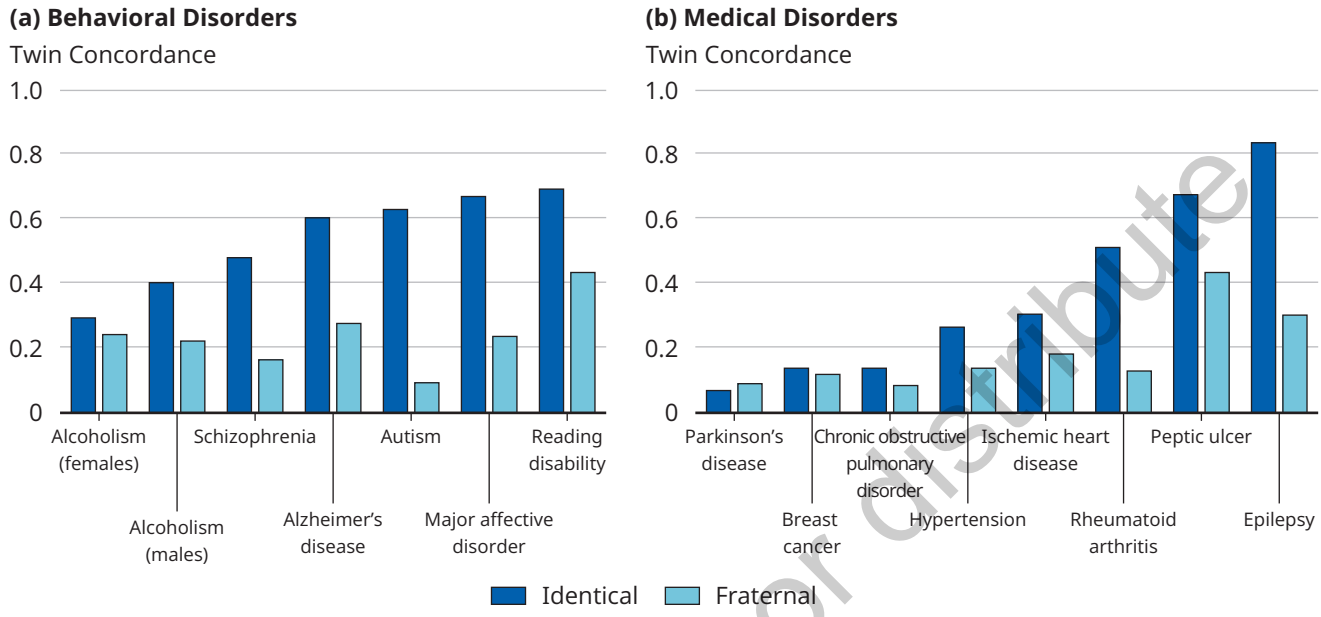
To assess the relative contributions of heredity and environment, we need to be able to quantify the two influences. **Heritability** is the percentage of the variation in a characteristic that can be attributed to genetic factors. There are various ways of estimating heritability of a characteristic. One technique involves a comparison of how often identical twins share the characteristic with how often fraternal twins share the characteristic. The reason for this comparison is that identical twins develop from a single egg and therefore have the same genome, whereas fraternal twins develop from separate eggs and share just 50% of their genomes like nontwin siblings. Heritability estimates are around 60% for intelligence (Plomin & Deary, 2015), which means that about half of the population's differences in intelligence are due to heredity. Heritability has been estimated at 70% to 90% for schizophrenia (Sullivan et al., 2003) and 40% to 50% for personality characteristics (Power & Pluess, 2015). By way of comparison, an older study demonstrated that the genetic influence on behavioral characteristics is typically stronger than it is for common medical disorders, as Figure 1.16 shows (Plomin et al., 1994).

Because about half of the differences in behavioral characteristics among people are attributable to heredity, approximately half are due to environmental influences. Keep in mind that heritability is not an absolute measure but rather tells us the proportion of variability that is due to genetic influence; the measure depends on the environmental circumstances of the group we are looking at as much as its genetic characteristics. For example, adoption studies tend to overestimate the heritability of intelligence because adopting parents are disproportionately from the middle class. Because the children's adoptive environments are unusually similar, environmental influence will be lower and heritability will be higher than in the general population (McGue & Bouchard, 1998). Similarly, heritability will appear to be lower if we look only at a group of closely related individuals.

Researchers caution us that "we inherit dispositions, not destinies" (Rose, 1995, p. 648). This is because the influence of genes is only partial. This idea is formalized in the vulnerability model, which has been applied to disorders such as schizophrenia (Zubin & Spring, 1977). **Vulnerability** means that genes contribute a predisposition for a disorder, which may or may not exceed the threshold required to produce the disorder; environmental challenges such as neglect and emotional trauma may combine with a person's hereditary susceptibility to exceed that threshold. The general concept applies to behavior and abilities as well, though we would not use the term *vulnerability* in those contexts. For example, the combination of genes a person receives determines a broad range for the person's potential intelligence; environmental influences then will determine where in that range the person's capability will fall. Psychologists no longer talk about heredity versus environment, as if the two are competing

Figure 1.16 ▪ Twin Studies of Behavioral and Medical Disorders.

The concordance of behavioral disorders (a) and medical disorders (b) in identical and fraternal twins is shown. Concordance is the proportion of twin pairs in which both twins have the disorder. Note the greater concordance in identical twins and the generally higher concordance for behavioral disorders than for medical disorders.



From "The Genetic Basis of Complex Human Behavior," by R. Plomin, M. J. Owen, and P. McGuffin, ***Science***, 264, p. 1734. © 1994 American Association for the Advancement of Science. Reprinted with permission from AAAS.

with each other for importance. Both are required, and they work together to make us what we are. As an earlier psychologist put it, "To ask whether heredity or environment is more important to life is like asking whether fuel or oxygen is more necessary for making a fire" (Woodworth, 1941, p. 1).

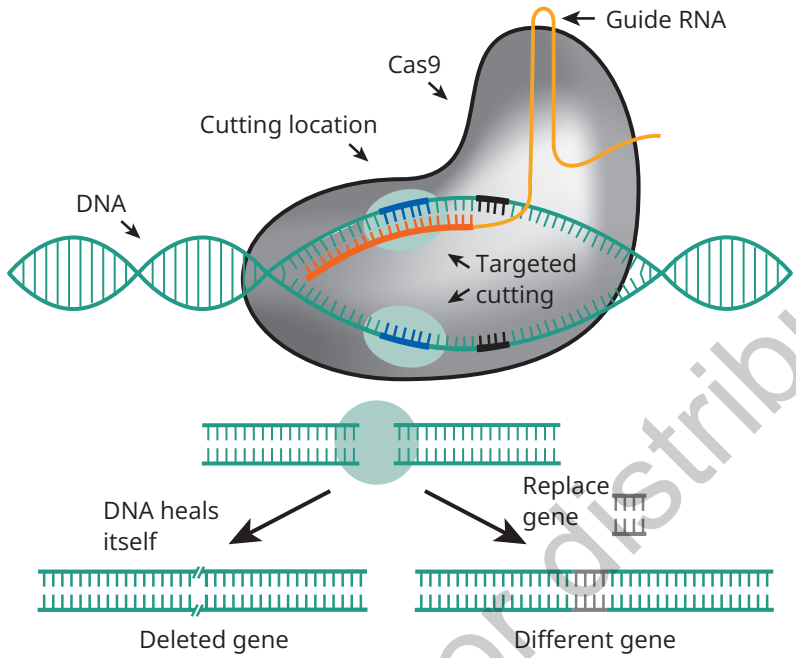
With an increasing understanding of genetics, we are now in the position to change our very being. This kind of capability carries with it a tremendous responsibility. The knowledge of our genetic makeup and the ready availability of genetic testing through companies such as AncestryDNA and 23andMe raise the question of whether it is better for a person to know about a risk that may never materialize such as susceptibility to Alzheimer's disease or another mental disorder. In addition, many people worry that the ability to do genetic testing on our unborn children means that some parents will choose to abort a fetus because it has genes for a trait they consider undesirable (see A Further Look for more about genetic editing of fetal genes). This rationale is increasingly cited as a reason to ban elective abortions. Our ability to plumb the depths of the brain and the genome is increasing faster than our grasp of either its implications or how to resolve the ethical questions that will arise. We will consider some of the ethical issues of genetic research in Chapter 4.

A Further Look

CRISPR—A New Tool to Edit Genes

A DNA passes through a protein labeled Cas9. Inside the protein, the DNA splits and targeted cutting of the gene takes place at specific cutting locations on the strand. The proteins in the guide ribonucleic acid (RNA), present in Cas9, pair with the proteins of one of the DNA strands. The cut DNA either heals itself, resulting in a deleted gene, or replaces the gene, resulting in a different gene.

Figure 1.17 ▪ The CRISPR Process.



As we gain an increased understanding of the role, timing, and location of gene actions through efforts such as the Human Genome Project, it is only a matter of time before we will be routinely replacing defective genes in humans with healthy functioning ones. Replacing or repairing a gene requires three key procedures at the DNA level: (1) identifying key genetic sequences that indicate the start and end of the defective DNA, (2) developing enzymes that can remove the DNA from the genome while leaving the rest of the genetic material intact, and in some cases (3) inserting an alternative form of DNA into the genome.

CRISPR stands for *clustered regularly interspaced short palindromic repeats*, which were discovered in bacteria. These repeats are fragments of previous viral infections that the bacterial cell uses to recognize and destroy similar invading viruses. Scientists employ various CRISPR-associated (Cas) proteins, which use an RNA sequence generated by the scientist as a guide to recognize DNA to be removed; the enzyme then acts like molecular scissors, cutting the ends of the DNA. The cell then patches the break or inserts replacement DNA carried by the Cas enzyme. This technology has the power to revolutionize our understanding of the genetic effects on physiology, behavior, and cognition as well as to treat genetic diseases.

Although CRISPR is still in its infancy, its early successes have raised fears that this technique will eventually be used for editing human traits and creating designer babies. This fear was heightened in November 2018, when the Chinese scientist He Jiankui admitted that he had edited the genomes of two female embryos to make them immune to HIV infection (Marchione, 2018). HIV viruses require the CCR5 receptor to enter white blood cells, and He was trying to replace the normal receptor gene with the gene for the CCR5 delta 32 receptor, which is HIV resistant. Although the technique was unsuccessful (the girls have one normal and one resistant gene, leaving them susceptible to HIV infection), the use of CRISPR technology on human embryos was universally condemned, and He was sentenced to 3 years in jail (Normile, 2018).

Concept Check

Take a Minute to Check Your Knowledge and Understanding

- Why is it inappropriate to ask whether heredity or environment is more important for behavior and mental illness?
- When we say that a person inherits a certain personality characteristic, what do we really mean?

- Explain how two parents who have the same characteristic produce children who are different from them in that characteristic. Use appropriate terminology.
- What are some negative outcomes if individuals know the contents of their genome?

In Perspective

In the first issue of the journal *Nature Neuroscience* in 1998, the editors observed that brain science still had a "frontier" feel to it. The excitement of exploration is real and tangible, and the discoveries and accomplishments are remarkable for such a relatively young discipline. The successes come from many sources: the genius of our intellectual ancestors, the development of new technologies, the adoption of empiricism, and, we believe, a coming to terms with the concept of the mind. Evidence of all these influences will be apparent in the following chapters.

Behavioral neuroscience still has a long way to go. For all our successes, we do not fully understand what causes schizophrenia, exactly how the brain is changed by learning, and why some people are more intelligent than others. The 1990s was declared the Decade of the Brain; Torsten Wiesel (whose landmark research in vision you will read about later) scoffed at the idea of dedicating a decade to the brain as "foolish. . . . We need at least a century, maybe even a millennium" (as cited in Horgan, 1999, p. 18). As you read the rest of this book, keep in mind that you are only halfway through that century's journey and just starting that millennium of discovery.

Chapter Summary

The Origins of Behavioral Neuroscience

- Behavioral neuroscience (or biopsychology) developed out of physiology and philosophy as early psychologists adopted empiricism.
- Most psychologists and neuroscientists treat the mind as a product of the brain, believing that mental activity can be explained in terms of the brain's functions.
- Localization describes brain functioning better than equipotentiality, but a brain process is more likely to be carried out by a network of structures than by a single structure.

Nature and Nurture

- We are learning that a number of behaviors are genetically influenced. One does not inherit a behavior itself, but genes influence structure and function in the brain and body in a way that influences behavior.
- Behavior is a product of both genes and environment. In many cases, genes produce a predisposition and environment further determines the outcome.
- With the knowledge of the genome map, we stand on the threshold of unbelievable opportunity for identifying causes of behavior and diseases, but we face daunting ethical challenges as well.

Study Resources

For Further Thought

- Why, in the view of most neuroscientists, is materialistic monism the more productive approach for understanding the functions of the mind? What will be the best test of the correctness of this approach?

- Scientists were working just as hard on the problems of the brain a half century ago as they are now. Why were the dramatic discoveries of recent years not made then?
- What are the implications of knowing what all the genes do and of being able to do a scan that will reveal which genes an individual has?
- If you were told that you had a gene that made it 50% likely that you would develop a certain disease later in life, what should you do with that knowledge?

Test Your Understanding

1. What is behavioral neuroscience, and how does it relate to psychology?
2. How would a monist and a dualist pursue the study of behavioral neuroscience differently?
3. What is a model in science, and how is it useful?
4. What was the impact of the early electrical stimulation studies and the evidence that specific parts of the brain were responsible for specific behaviors?
5. How are characteristics inherited?
6. The allele for type B blood is, like the one for type A, dominant over the allele for type O. Make a matrix like the one in Figure 1.12 to show the genotypes and phenotypes of the offspring of an AO parent and a BO parent.
7. A person has a gene that is linked with a disease but does not have the disease. We mentioned three reasons why this could occur; describe two of them.
8. Discuss the interaction between heredity and environment in influencing behavior, including the concept of vulnerability.
9. Why do males more often show characteristics that are caused by recessive genes?
10. What are some of the inheritable behaviors?
11. What is the Human Genome Project, and how successful has it been?
12. Do genes lock a person into a particular outcome in life?

Select the Best Answer

1. The idea that the mind and brain are both physical is known as
   - **a.** idealistic dualism.
   - **b.** materialistic dualism.
   - **c.** idealistic monism.
   - **d.** materialistic monism.
2. A model is
   - **a.** an analogy not intended to be entirely realistic.
   - **b.** a plan for investigating a phenomenon.
   - **c.** an organism or a system used to understand a more complex one.
   - **d.** a hypothesis about the outcome of a study.
3. Descartes's most important contribution was in
   - **a.** emphasizing the importance of nerves.
   - **b.** explaining how movement is produced.
   - **c.** increasing knowledge of brain anatomy.
   - **d.** suggesting the physical control of behavior.
4. Helmholtz showed that

a. nerves do not conduct animal spirits.
b. language, emotion, movement, and so on depend on the activity of nerves.
c. nerves are not like electrical wires because they conduct too slowly.
d. nerves operate electrically.

5. In the mid-1800s, studies of brain-damaged patients convinced researchers that
a. behaviors originated in specific parts of the brain.
b. the pineal gland could not serve the role Descartes described.
c. the brain's activity was electrical.
d. the mind was not located in the brain.

6. Localization means that
a. any part of the brain can take over other functions after damage.
b. brain functions are located in widespread networks.
c. specific functions are found in specific parts of the brain.
d. the most sophisticated functions are located in the highest parts of the brain.

7. X-linked characteristics affect males more than females because
a. the responsible gene is not paired with another gene on the Y chromosome.
b. the male internal environment exaggerates effects of the genes.
c. the X chromosome is shorter than the Y chromosome.
d. unlike males, females have only one X chromosome.

8. Two parents are homozygous for a dominant characteristic. They can produce a child with the recessive characteristic
a. if the child receives two dominant genes.
b. under no circumstance.
c. if the child receives a dominant gene and a recessive gene.
d. if the child receives two recessive genes.

9. The Human Genome Project has
a. determined the functions of most genes.
b. cloned most of the human genes.
c. counted the number of human genes.
d. made a map of the human genes.

10. Heritability is greatest for
a. personality.
b. schizophrenia.
c. intelligence.
d. occupational interest.

11. If we all had identical genes, the estimated heritability for a characteristic would be
a. 100%.
b. 50%.
c. 0%.
d. impossible to determine.

Answers:

1. d, 2. c, 3. d, 4. c, 5. a, 6. c, 7. a, 8. b, 9. d, 10. b, 11. c

For More Information

The following journals are major sources of neuroscience articles (those that are not *open* access may require a subscription or university access). These may be of use to you as you progress through the textbook and your scholarly pursuits in behavioral neuroscience:

Brain and Behavior (open access)

Brain, Behavior and Evolution

Frontiers in Neuroscience (open access; see also related journals)

Journal of Neuroscience

Nature

Nature Neuroscience

Nature Reviews Neuroscience

New Scientist (for the general reader)

PLoS Biology and *PLoS Genetics* (open access)

Scientific American Mind (for the general reader)

The Scientist (for the general reader)

Trends in Neurosciences

General information sites:

BrainFacts (various topics in neuroscience)

Brain in the News (neuroscience news from media sources)

The Human Brain (a collection of brain-related articles published in the magazine *New Scientist*)

Neuroguide (a small but growing offering of resources)

Science Daily (latest developments in science; see "Mind & Brain" and "Health & Medicine")

For Further Reading

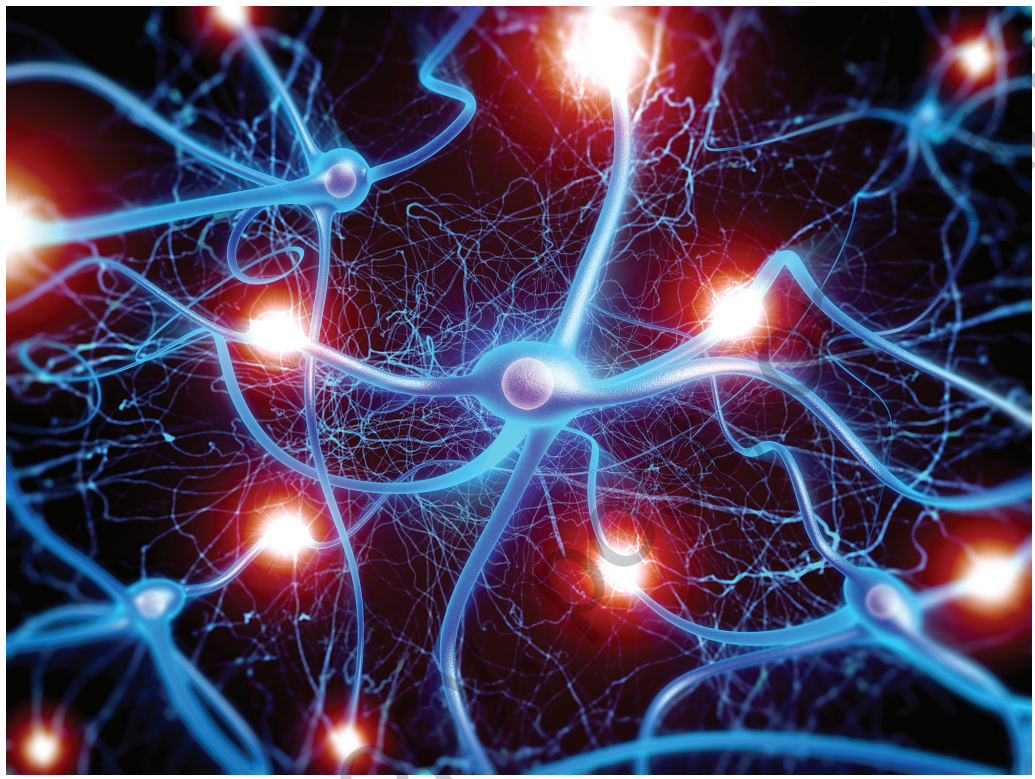
1. "The Emergence of Modern Neuroscience: Some Implications for Neurology and Psychiatry," by W. Maxwell Cowan, Donald H. Harter, and Eric R. Kandel (*Annual Review of Neuroscience*, 2000, *23*, 343–391), describes the emergence of neuroscience as a separate discipline in the 1950s and 1960s and describes some of its important accomplishments in understanding disorders.
2. Neuroscientist Michael Gazzaniga calls Mitchell Glickstein's *Neuroscience: A Historical Introduction* (MIT Press, 2014) "authoritative, highly readable, wonderfully illustrated, and just plain interesting."
3. *The Scientific American Brave New Brain*, by Judith Horstman (Jossey-Bass, 2010), describes how today's scientific breakthroughs will in the future help the blind see and help the deaf hear, allow our brains to repair and improve themselves, help us postpone the mental ravages of aging, and give the paralyzed control of prosthetic devices and machinery through brain waves.
4. *Behavioral Genetics*, by Valerie Knopik, Jenae Neiderhiser, John DeFries, and Robert Plomin (Worth, 2017, 7th ed.), is a textbook on that topic; another text, *Evolutionary Psychology*, by William Ray (Sage, 2013), takes a neuroscience approach to the evolution of behavior.
5. "Tweaking the Genetics of Behavior," by Dean Hamer (*Scientific American*, April 1999, 62–67), is a fanciful but thought-provoking story about a female couple in 2050 who have decided to have a child cloned and the decisions available to them for determining their baby's sex and physical and psychological characteristics through genetic manipulation.

Key Terms

allele
behavioral neuroscience
deoxyribonucleic acid (DNA)
dominant
dualism
embryo
empiricism
equipotentiality
fetus
gene
gene expression
genome
genome-wide association study (GWAS)
genotype
heritability
heterozygous
homozygous
Human Genome Project
localization
materialistic monism
mind-brain problem
model
monism
natural selection
nature versus nurture
phenotype
phrenology
polygenic
recessive
single-nucleotide polymorphism (SNP)
theory
vulnerability
X-linked
zygote

Chapter 2

Communication Within the Nervous System



Henrik5000/iStockPhoto

Learning Objectives

2.1 Identify the two major types of cells of the nervous system and their locations, types, and signals.

2.2 Explain the roles of ions, the cell membrane, neurotransmitters, and networks in nervous system communication and generating your experiences of the world.

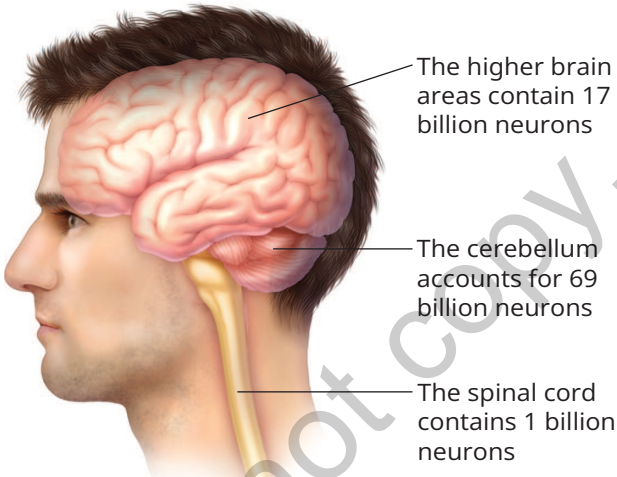
Things were looking good for Jim and his wife. She was pregnant with their first child, and they had just purchased and moved into a new home. After the exterminating company treated the house for termites by injecting the pesticide chlordane under the concrete slab, Jim noticed that the carpet was wet and there was a chemical smell in the air. He dried the carpet with towels and thought no more about it, not realizing that chlordane can be absorbed through the skin. A few days later, he developed headaches, fatigue, and numbness. Worse, he had problems with memory, attention, and reasoning.

His physician referred him to the toxicology research center of a large university medical school. His intelligence test score was normal, but the deficiencies he was reporting showed up on more specific tests of cognitive ability. Jim and his wife needed to move out of their home; at work, he needed to accept reduced responsibilities because of his difficulties in concentration and adapting to novel situations. The chlordane had not damaged the structure of his brain as you might suspect, but it had interfered with the functioning of the brain cells by impairing a mechanism called the sodium-potassium pump (Zillmer & Spiers, 2001). Jim's unfortunate case reminds us that the nervous system is as delicate as it is intricate. Only by understanding how it works will we be able to appreciate human behavior, to enhance human performance, and to treat behavioral problems such as drug addiction and psychosis.

The Cells That Make Us Who We Are

To understand how the brain works, you must first have at least a basic understanding of the two categories of cells that carry messages back and forth in the brain and throughout the rest of the body. A **neuron** conveys sensory information into the brain; carries out the operations involved in thought, feeling, and action; and transmits commands out to the body to control muscles and organs. It is estimated that there are about 86 billion neurons in the human brain (Figure 2.1; Azevedo et al., 2009). This means that there are more neurons in your brain than stars in our galaxy. But as numerous and as important as they are, neurons make up only half of the brain's cells (von Bartheld et al., 2016). There are also nearly as many glial cells and, as we will see later in the chapter, they are almost as important.

Figure 2.1 ▪ Estimated Numbers of Neurons in the Brain and Spinal Cord.



Neurons

Neurons are responsible for all the things we do—our movements, our thoughts, our memories, and our emotions. It is difficult to believe that anything so simple as a cell can measure up to this task, and the burden is on the neuroscientist to demonstrate that this is true. As you will see, the neuron is deceptively simple in its action but impressively complex in its function.

Basic Structure: The Motor Neuron

First, let's look inside a neuron because we want to show you that the neuron is a cell, very much like other cells in the body. Figure 2.2 is an illustration of the most prominent part of the neuron, the **cell body** or soma. The cell body is filled with a liquid called cytoplasm and contains a number of *organelles*. The largest of these organelles is the *nucleus*, which contains the cell's chromosomes and the mechanisms for reading them. Other organelles are responsible for converting nutrients into fuel for the cell, constructing proteins and lipids, removing waste materials, and other important biological functions. So far, this is the description of any cell; now, let's look at the neuron's specializations that enable it to carry out its unique role. Figure 2.3 illustrates a typical neuron. We use "typical" guardedly here because there are three major kinds of neurons and many variations within those types. The figure illustrates a **motor neuron**, which transmits commands to the muscles and organs. It is particularly useful for demonstrating the structure and functions that all neurons have in common.

Dendrites are extensions that branch out from the cell body to receive information from other neurons. Their branching structure allows them to collect information from many sources. The **axon** extends like a tail from the cell body and carries information to targets, sometimes across great distances. The myelin sheath that wraps around the axon supports the axon and provides other benefits that we will consider later. Branches at the end of the axon culminate in swellings called **axon terminals**.

Figure 2.2 ▪ Cell Body (Soma) of a Neuron.

Part of the membrane has been removed to show interior features. The different types of organelles have unique colors.

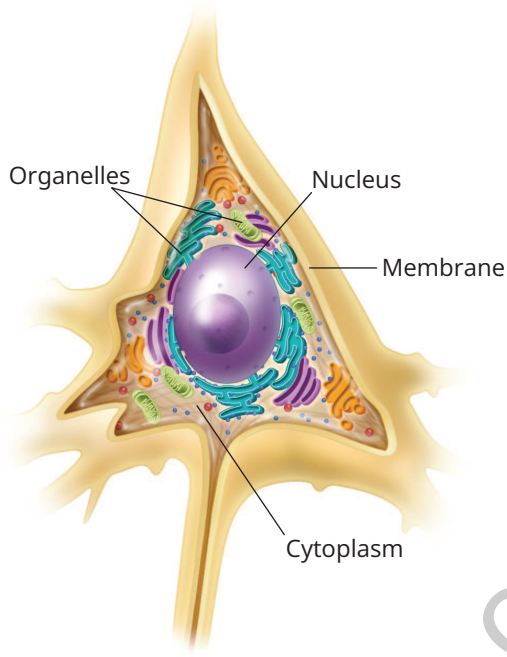
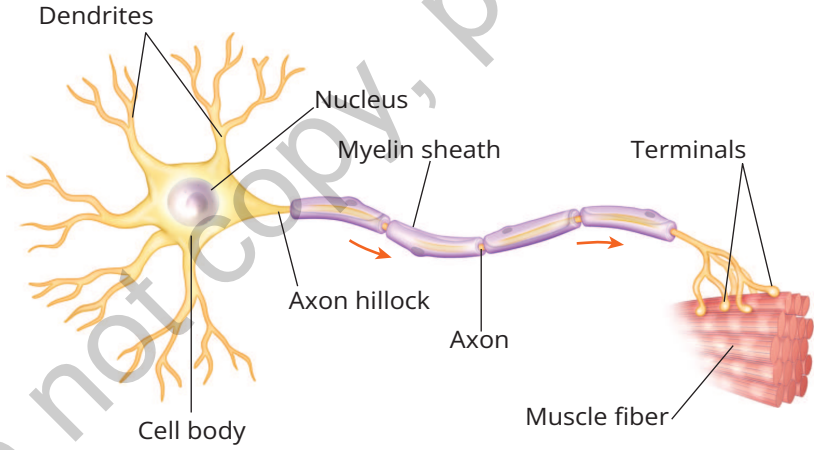


Figure 2.3 ▪ Components of a Neuron.

The illustration is of a multipolar motor neuron.



The terminals contain many molecules of a chemical **neurotransmitter**, which the neuron releases to communicate with a muscle, an organ, or the next neuron in a chain. In our examples, we will talk as if neurons form a simple chain, with one cell sending messages to a single other neuron and so on; in actuality, a single neuron receives input from many neurons and sends its output to many others.

Neurons are usually so small that they can be seen only with the aid of a powerful microscope. The cell body is the largest part of the neuron, ranging from 0.005 to 0.1 millimeter (mm) in diameter in mammals. (In case you are unfamiliar with metric measurements, a millimeter is about the thickness of a dime.) Even the giant neurons of the squid, favored by researchers for their conveniently large size, have axons that are only 1 mm in diameter. Typical axons are smaller; in mammals, they range from

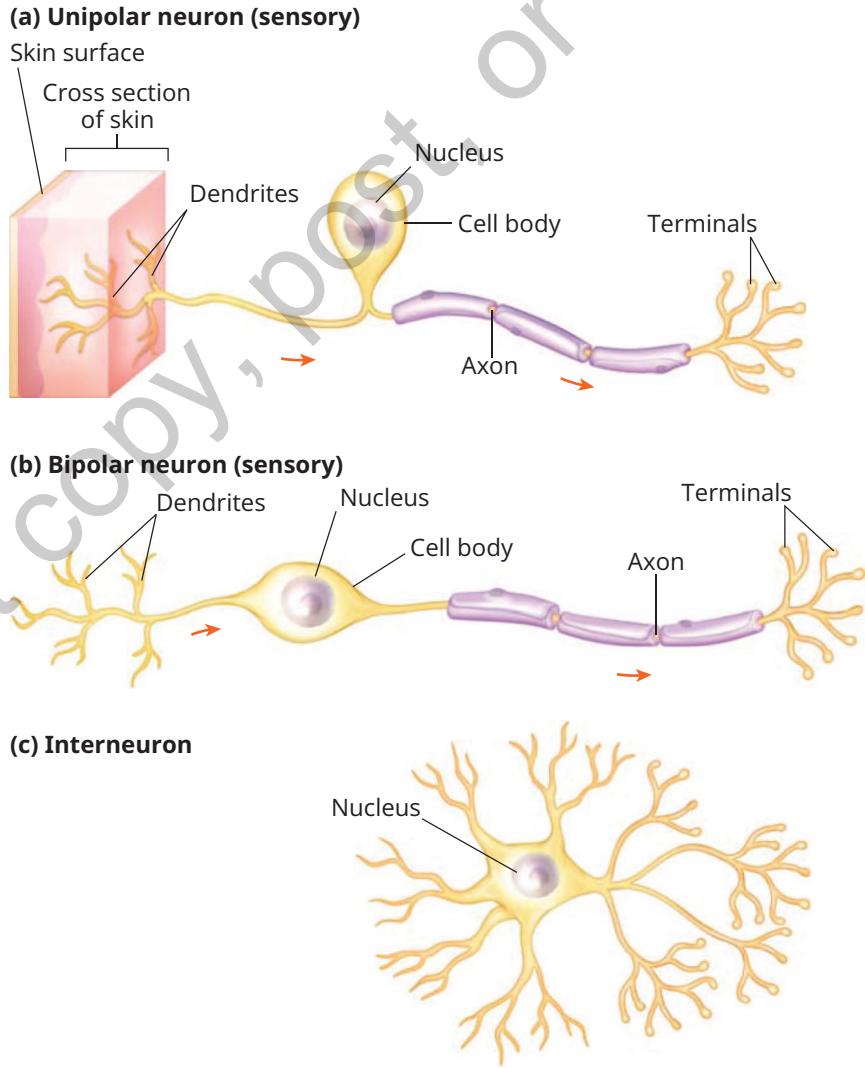
0.002 to 0.02 mm in diameter. Axons may be absent, as short as 0.1 mm, or as long as 30 m in the blue whale (Smith, 2009).

Other Types of Neurons

The second type of neuron is the sensory neuron. A **sensory neuron** carries information from the body and the outside world into the brain and spinal cord. Motor and sensory neurons have the same components, but they are configured differently. A motor neuron's axon and dendrites extend in several directions from the cell body, which is why it is called a *multipolar* neuron. Sensory neurons can be either *unipolar* or *bipolar*. The sensory neuron in Figure 2.4a is called a unipolar neuron because a single short stalk from the cell body divides into two branches, with dendrites on one side and the axon and terminals on the other. (In the pseudo-unipolar subtype, both connections to the cell body are axons; that is because its sensory information must travel over a longer distance, from the periphery of the body to the spinal cord and the brain.) Bipolar neurons have an axon on one side of the cell body and a dendritic process on the other (Figure 2.4b). Motor and sensory neurons are specialized for transmission over long distances; their lengths are not shown here in the same scale as the rest of the cell.

Figure 2.4 ▪ Sensory Neurons and an Interneuron.

Compare the location of the soma in relation to the dendrites and axon in these neurons and in the motor neuron.



Carolina Hrejsa/Body Scientific Intl.

The third type is neither motor nor sensory. An **interneuron** connects one neuron to another in the same part of the brain or spinal cord. Notice in Figure 2.4c that this neuron is also multipolar, but its axon appears to be missing; this is true for some interneurons, and when they do have axons they are often so short that they are visually indistinguishable from dendrites. Because interneurons make connections over very short distances, they do not need the long axons that characterize their motor and sensory counterparts. In the spinal cord, interneurons bridge sensory neurons and motor neurons to produce a reflex. In the brain, they connect adjacent neurons to carry out more complex processing tasks. Considering the major roles each type plays, it should come as no surprise that interneurons are by far the most numerous type.

The different kinds of neurons operate similarly; they differ mostly in their shape, which fits them for their specialized tasks. We will examine how neurons work in the next few sections. The types of neurons and their characteristics are summarized in Table 2.1.

Table 2.1 ▪ The Major Types of Neurons.

Type	Function	Form and Soma Location	Description
Motor	Conducts messages from brain and spinal cord to muscles and organs	Multipolar; central nervous system	Axon, dendrites extend in several directions from cell body
Sensory	Carries information from body and world to brain and spinal cord	Unipolar; peripheral nervous system, cranial nerves	Single short stalk from cell body divides into two branches
		Bipolar; peripheral nervous system	Axon and dendritic processes are on opposite sides of cell body
Interneuron	Conducts information between neurons in same area	Multipolar; central nervous system	Has short or no axon; communicates locally (with nearby neurons)

The Neural Membrane and Its Potentials

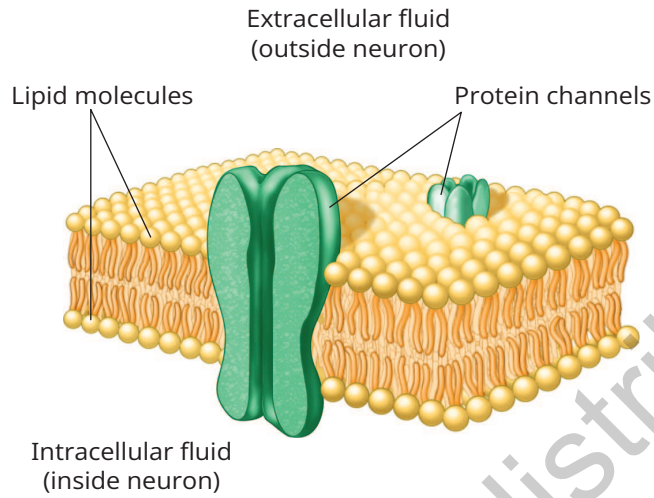
The most critical factor in the neuron's ability to communicate is the membrane that encloses the cell. The membrane is exceptionally thin—only about 4 nanometers (billionths of a meter) thick—and is made up of lipid (fat) and protein (van Meer et al., 2008; Figure 2.5). Each lipid molecule has a water-soluble "head" end and a water-insoluble "tail" end. The heads are attracted to the seawater-like fluid around and inside cells, whereas the tails are repelled by the fluid. Therefore, as the heads orient toward the fluid and the tails orient away from the fluid, the molecules point their tails toward each other and form a double-layer membrane.

The membrane not only holds a cell together but also controls the environment within and around the cell. Some molecules, such as water, oxygen, and most gases, can diffuse through the membrane freely. Many other substances are barred from crossing the membrane. Still others are allowed limited passage through protein channels (shown in Figure 2.5 in green) that open and close under specific circumstances. This selective permeability contributes to the most fundamental characteristic of neurons, **polarization**, which means that there is a difference in electrical charge between the inside and outside of the neuron. A difference in electrical charge between two points, such as the poles of a battery or the inside and outside of a neuron, is also called a **voltage**.

The Resting Potential. Just as you can measure the voltage of a battery, you can measure a neuron's voltage (Figure 2.6). By arbitrary convention, the voltage is expressed as a comparison of the inside of the neuron with the outside. The difference in charge between the inside and outside of the membrane of a neuron at rest is called the **resting potential**. This voltage is negative and varies anywhere from –40 to –80 millivolts (mV) in different neurons but is typically around –70 mV. You should understand

Figure 2.5 ▪ Cross Section of the Cell Membrane of a Neuron.

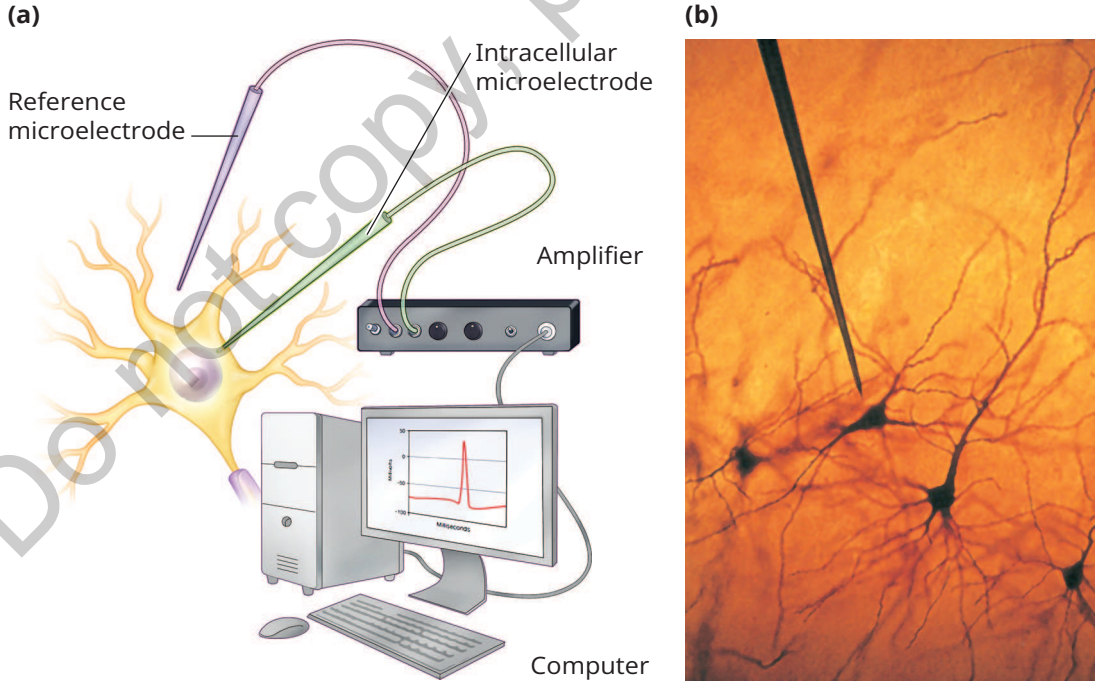
Notice how the lipid molecules form the membrane by orienting their heads toward the extracellular and intracellular fluids.



that neither the inside of the neuron nor the outside has a voltage because a voltage is a *difference* and is meaningful only in comparison with another location. Note that this voltage is quite small—the voltage of a standard 1.5-V battery is many times greater. No matter; we are moving information, and very little power is required.

Figure 2.6 ▪ Recording Potentials in a Neuron.

(a) Potentials are being recorded in the axon of a neuron, with an electrode inside the cell and one in the fluid outside. Due to the size of neurons, the electrodes have microscopically small tips. (b) A highly magnified view shows the size of a microelectrode relative to that of neurons. Electrodes for recording inside neurons are even smaller.

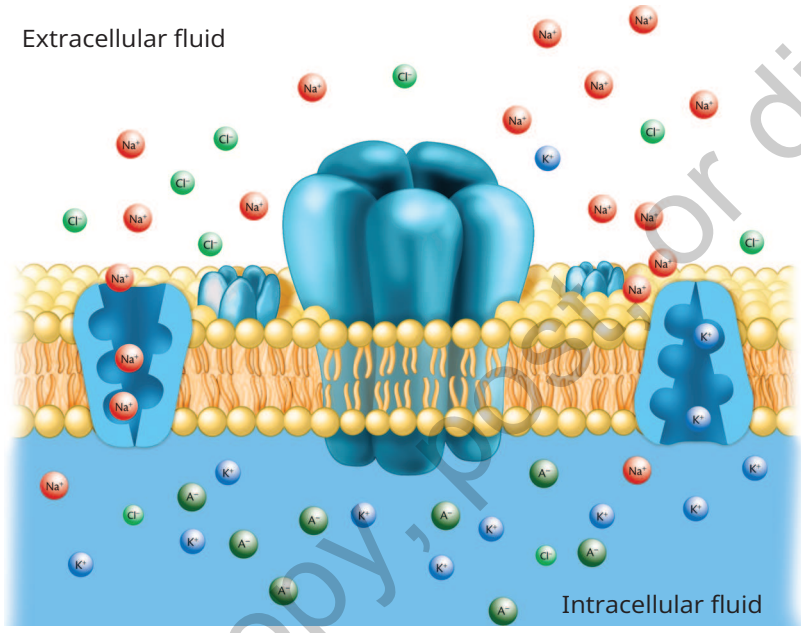


Right Photo: Bob Jacobs, Colorado College

The resting potential is due to the unequal distribution of electrical charges on the two sides of the membrane. The charges come from groups of particles called an **ion** (an atom that has lost or gained one or more electrons in its outer shell). Sodium ions (Na^+) and potassium ions (K^+) are positively charged (both lost one electron), along with calcium ions (Ca^{2+}, lost two electrons; not shown in Figure 2.7 but will be important later in this chapter). Chloride ions (Cl^-) are negative (has an extra electron), as are certain proteins and amino acids that make up the organic anions (A^-). The fluid outside the neuron contains mostly Na^+ and Cl^- ions, and the ions inside the neuron are mostly K^+ and A^- (Figure 2.7). The inside of the neuron has more negative ions than positive ions, whereas the ions on the outside are mostly positive, and this makes the resting potential slightly negative.

Figure 2.7 ▪ Distribution of Ions Inside and Outside the Resting Neuron.

Ions on the outside are mostly Na^+ (red) and Cl^- (green) ions; inside, the ions are mostly K^+ (blue) ions and organic (dark green) anions. In the middle of the membrane is an ion channel, which is closed and not allowing ions through; on the left a sodium-potassium pump is discharging three Na^+ ions outside the neuron, whereas on the right an identical pump is returning two K^+ ions to the inside.



If you remember from grade school science that molecules tend to diffuse from an area of high concentration to one of low concentration, then you are probably wondering how this imbalance in ion distribution can continue to exist. In fact, two forces do work to balance the location of the ions. The first is the **force of diffusion**, where ions want to move through the membrane to the side where they are less concentrated. The second force is **electrostatic pressure**, where ions are repelled from the side that is similarly charged and attracted to the side that is oppositely charged. This is similar to how the positive side of one magnet will be attracted only to the negative side of another magnet.

In spite of these two forces, a variety of other influences keep the membrane polarized. Both forces would normally drive negatively charged anions (A^-) like proteins out, but they are too large to pass through the membrane. The negative charges inside the membrane also repel the external chloride (Cl^-) ions, so the force of diffusion is unable to move those ions inside. As a result, the "real player" then becomes the potassium ions. Potassium's force of diffusion is stronger than its electrostatic pressure, and although the potassium and sodium channels both are closed during resting, potassium can slip through the membrane itself more readily than the other ions.

Another significant contributor to polarity is the **sodium-potassium pump**, which consists of large protein molecules that move sodium ions through the cell membrane to the outside and potassium ions back inside (the blue channels on the outside of Figure 2.7). It moves three sodium ions out for every

two potassium ions it moves inside, which helps keep the inside of the membrane more negative than the outside. The pump's operation is an active metabolic process, which means that it uses energy; in fact, it accounts for an estimated 40% of the neuron's energy expenditure. But you will soon see that this energy is well spent because the resting potential stores the energy to power the action potential, the major signal in the nervous system.

Ion Channels and Local Potentials. Before we move on, we need a better understanding of how the ion channels work. These are pores in the membrane formed by proteins, and they gate the flow of ions between the extracellular and intracellular fluids. Chemically gated channels can be opened by ligands (neurotransmitters or hormones), and electrically gated channels are opened by a change in the electrical potential of the membrane.

A neuron is usually stimulated by inputs that arrive on the neuron's dendrites and/or cell body from another neuron or from a sensory receptor. The effect may be excitatory or inhibitory, depending on the ligand and the characteristics of the receptors. An excitatory signal causes a slight partial depolarization, which means that the polarity in a small area of the membrane is shifted toward zero. This partial depolarization disturbs the ion balance in the adjacent membrane, so the disturbance flows down the dendrites and across the cell membrane. This looks at first like the way the neuron might communicate its messages through the nervous system; however, because a partial depolarization is decremental—it dies out over distance—it is effective over only very short distances. For this reason, the partial depolarization is often called the *local potential*. The ion channels in the axon are electrically gated, and they have unique physical properties. If the local potential exceeds the threshold for activating those channels, typically about 10 mV more positive than the resting potential, it will initiate an action potential. This normally occurs at the base of the axon, called the axonal hillock, where local potentials arrive from the dendrites through the soma.

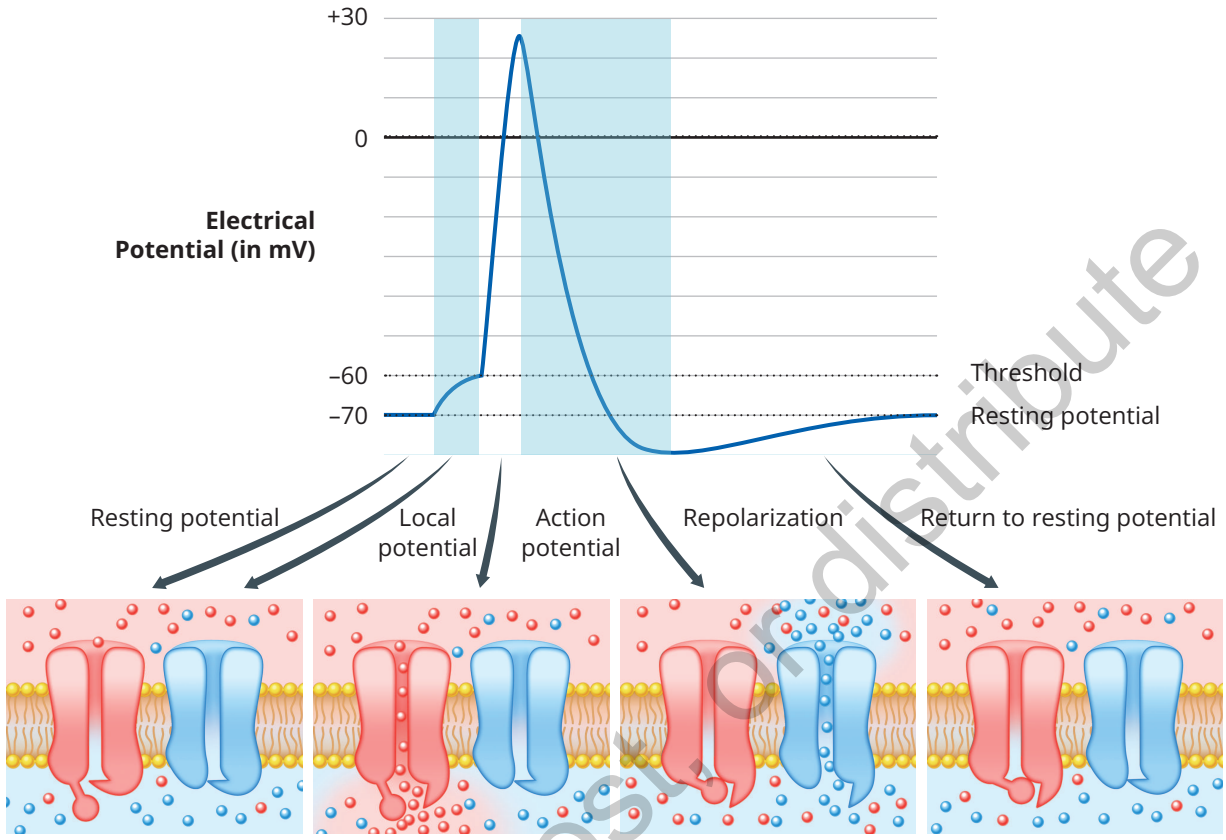
Action Potentials. The **action potential** is an abrupt depolarization of the membrane that allows the neuron to communicate over long distances. The voltage across the resting neuron membrane is stored energy, just as the term resting *potential* implies. Imagine countless sodium ions being held outside the neuron against the combined forces of diffusion and electrostatic pressure (Figure 2.8a). A stimulus that partially depolarizes a segment of membrane causes voltage-gated sodium ion channels to open; this allows nearby sodium ions to rush into the axon at a rate 500 times greater than normal (Figure 2.8b). They are propelled into the cell's interior so rapidly that the movement is often described as explosive. A small area inside the membrane becomes fully depolarized to zero; the potential even overshoots to around +30 or +40 mV, making the interior at that location temporarily positive.

Just as abruptly as the neuron "fires," it begins to recover its resting potential. At the peak of the action potential, voltage sensors in the sodium channels detect the depolarization and close a gate, inactivating the channel and preventing further sodium ion influx (Catterall, 2010). The depolarization also causes voltage-gated potassium ion channels to open; the positive charge and the higher concentration of potassium ions inside the membrane combine to force potassium ions out. This outward flow of positive potassium ions lowers the axon voltage to its resting potential and sometimes a bit beyond (Figure 2.8c). In total, the action potential lasts about 1 millisecond (one thousandth of a second); the actual duration varies among individual neurons. (Obviously, these channels are what make the neuron operate.)

Only a relatively few ions very near the two sides of the membrane have participated in the action potential; these dislocated ions quickly diffuse into the surrounding fluid, and the membrane potential returns to its resting level (Figure 2.8d). Eventually, though, the ions must be returned to their original locations or the neuron cannot continue firing; the sodium-potassium pump takes care of this. (Perhaps you can see now why Jim was in such a bad way after his bout with chlordane.)

The depolarization that occurs during the action potential triggers nearby sodium channels to open as well. Thus, a new action potential is triggered right next to the first one. That action potential in turn triggers another farther along, creating a chain reaction of action potentials that move across the axon; thus, a signal flows from one end of the neuron to the other. Nothing physically moves down the axon. Instead, a series of events occurs in succession along the axon's length, much as a line of dominoes standing on end knock each other over when you tip the first one. When the action potential reaches

Figure 2.8 ▪ Ion Movement and Voltages During the Neural Impulse.



(a) Sodium channels (red) and potassium channels (blue) are closed and the membrane is at resting potential. Arrival of a local potential partially depolarizes the membrane but does not cause the channels to open unless it reaches threshold.

(b) As the local potential reaches the neuron's threshold, the sodium channels' activation gates open. Sodium ions (red) rush in, producing an action potential. The membrane in that area depolarizes and overshoots to positive.

(c) Sodium channels' inactivation gates close. Potassium channels' activation gates open; potassium ions (blue) move out, repolarizing the membrane. Polarity overshoots beyond resting potential.

(d) Potassium channels close. The "excess" displaced ions drift away and the potential returns to resting level. (The sodium channel gates will return to their original state later.)

the terminals, they pass the signal on to the next neuron in the chain (or to an organ or a muscle). The transmission of signals from neuron to neuron is covered later; for now, the action potential needs to be examined a bit further.

The action potential differs in two important ways from the local potential that initiates it. First, the local potential is a **graded potential**, which means that it varies in magnitude with the strength of the stimulus that produced it. The action potential, by contrast, is *ungraded*; it operates according to the **all-or-none law**, which means that it occurs at full strength or it does not occur at all. A larger graded potential does not produce a larger action potential; like the fuse of a firecracker, the action potential depends on the energy "stored" in the neuron, in this case, due to the difference in ion concentrations between the two sides of the membrane. A second difference is that the action potential is **nondecremental**; it travels down the axon without any decrease in size, propagated anew and at full strength at each successive point along the way. The action potential thus makes it possible for the neuron to conduct information over long distances.

However, because the action potential is all-or-none, its size cannot carry information about the intensity of the initiating stimulus. One way stimulus intensity is represented is in the number of neurons generating action potentials. The voltage sensitivity of sodium channels varies among neurons, resulting in different thresholds; a more intense stimulus will recruit firing in neurons with higher thresholds and,

therefore, in more neurons. There is, though, a way in which the individual neuron can encode stimulus strength, as you will see in the discussion of refractory periods.

Refractory Periods

If you remember a few paragraphs back, we stated that the flow of an action potential down the axon was like knocking down a line of dominoes. And just as you must go through and reset the dominoes so that they can fall again, the ion channels must be reset before the neuron can fire again. During the action potential and initial recovery, the sodium ion channels are open but unresponsive to further stimulation, no matter how intense, due to the closing of a gate preventing ions from entering the neuron (see Figure 2.8c); this time is referred to as the **absolute refractory period**. This delay in responsiveness has two important effects. First, the 1- to 2-millisecond duration of the absolute refractory period limits how fast the neuron can generate new action potentials; a study of cortical *fast-spiking neurons* found maximal rates of 453 per second in humans, 611 in monkeys, and 342 in mice (Wang et al., 2016). Second, because the ion channels behind the action potential are still recovering, the impulse can propagate only down the axon toward the dendrites, not back toward the cell body. This makes neural transmission unidirectional, which has the secondary effect of preventing the neuron from "locking up." If recovery were immediate, activity would self-propagate in both directions from an ongoing action potential; this would result in impulses moving repeatedly back and forth along the axon, which would block the ability to respond to newly arriving messages.

At the end of the absolute refractory period, the gates blocking the sodium channels have relaxed, so the neuron is able to fire again. But the potassium channels remain open for an additional 3 or 4 milliseconds, and as potassium ions continue to exit the neuron, the polarity is driven slightly more negative than the resting potential (the "dip" in Figure 2.8). During the resulting **relative refractory period**, another action potential can be generated, but only by a stronger-than-threshold stimulus. A stimulus that is slightly greater than this temporarily higher threshold will cause the neuron to fire again before the end of the relative refractory period; with progressively stronger stimuli, the neuron will fire increasingly earlier and, therefore, at a higher rate. Thus, the axon encodes stimulus intensity not in the size of its action potential but rather in its firing rate, an effect called the **rate law**.

Glial Cells

A **glial cell** is a nonneural cell that provides a number of supporting functions to neurons (Table 2.2). The name *glia* is derived from the Greek word for "glue," which gives you some idea of how the role of glial cells has been viewed in the past. However, glial cells do much more than hold neurons together. One of their most important functions is to increase the speed of conduction in neurons (these are the purple cells wrapping segments of the axon in Figure 2.4).

Table 2.2 ▪ Major Types of Glia and Their Functions.

Brain and Spine				Periphery
Oligodendrocytes	Radial glia	Microglia	Astrocytes	Schwann cells
Insulate segments of multiple axons	Provide scaffold for neurons migrating to final targets during development	Provide energy to neurons and remove waste products and pathogens	Provide metabolic and physical support to brain and spine	Insulate segments of peripheral axons

Myelination and Conduction Speed

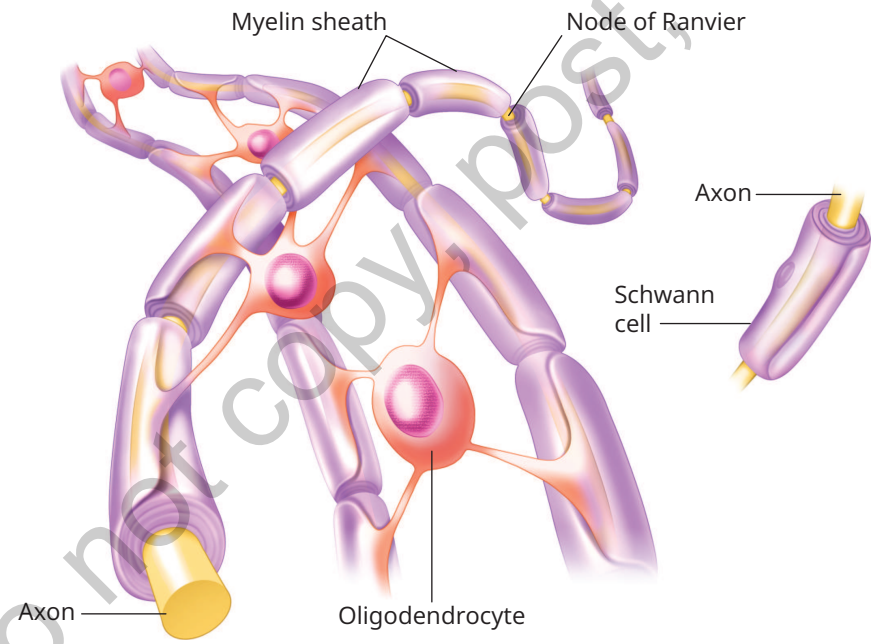
Survival depends in part on how rapidly messages can move through the nervous system, enabling the organism to pounce on its prey, outrun a predator, or process information quickly. The speed with which the fastest neurons conduct their impulses approaches 120 meters (m) per second (s), or about 270 miles

per hour (435 km/hr). This seems fast, but the speed of electricity flowing through a wire, the analogy sometimes used to describe neural conduction, is up to 690 times faster. Because conduction speed is so critical to survival, strategies have evolved for increasing it. One way is to develop larger-diameter axons, which provide less resistance to the flow of electrical potentials. By evolving motor neurons with 0.5-mm-thick axons, the squid has achieved conduction speeds of 30 m/s compared with 1 m/s in the smallest-diameter neurons.

However, conduction speed increases not in direct proportion to axon size but rather closer to the square of the diameter (Rushton, 1951). To reach our four-times-greater maximum conduction speed of 120 m/s, our axons would need to be $4^2 = 16$ times larger than the squid axon, or 8 mm in diameter (the size of a large pea). Obviously, your brain would be larger than you could carry around and your spine would be thicker than a giant sequoia tree trunk! In other words, if axon diameter were the only way to achieve fast conduction speed, *you* would not exist. Vertebrates (animals with backbones) have developed another solution, myelination. Two types of glial cells produce **myelin**, a fatty tissue that wraps around the axon (like a jelly roll) to insulate it from the surrounding fluid and from other neurons. Only the axon is covered, not the cell body. Myelin is produced by billions of glial cells; in the brain and spinal cord by a glial cell called an **oligodendrocyte** and in the rest of the nervous system by a cell called a **Schwann cell** (Figure 2.9). Nearly 75% of the glial cells in the brain are myelin-producing oligodendrocytes (Pillay & Manger, 2007).

Figure 2.9 ▪ Oligodendrocytes Produce Myelin for Axons.

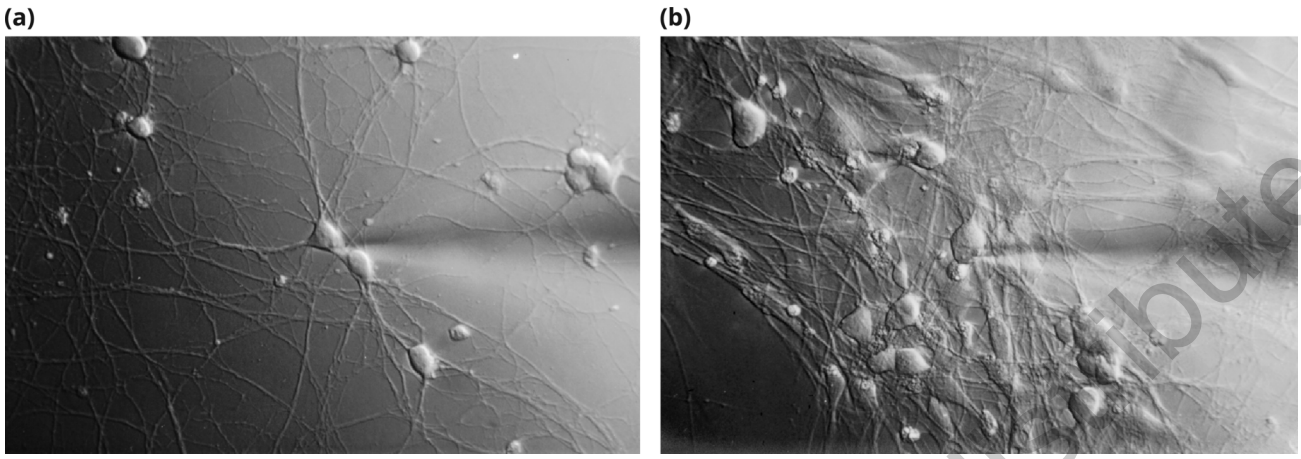
A single oligodendrocyte provides myelin for multiple segments of the axon and for multiple neurons. A Schwann cell covers only one segment of an axon (see Figure 2.4).



Because there are very few sodium channels under the myelin sheath, and there is no way for ions to move through them even if there were more, action potentials cannot occur there; conduction under myelinated areas is by local graded potential only (Waxman & Ritchie, 1985). However, myelin appears in segments about 1 mm long, with a gap of one or two thousandths of a millimeter between segments; this gap in the myelin sheath is called a **node of Ranvier** (see Figure 2.9). At each node of Ranvier, where the membrane is exposed and there are plenty of sodium and potassium channels, the graded potential (which is still above threshold even after traveling underneath the myelin) triggers an action potential. Action potentials thus appear to jump from node to node in a form of transmission called **saltatory conduction**.

Figure 2.10 ▪ Glial Cells Increase the Number of Connections Between Neurons.

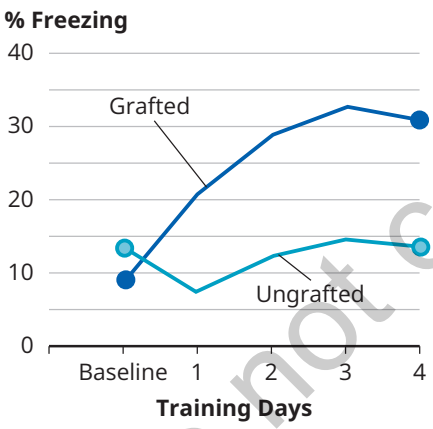
Neurons were cultured for 5 days in the absence of glial cells (a) and in the presence of glia (b). The number of neurons was similar in both cultures; the greater density on the right is due to increased connections among both neurons.



Source: From F. W. Pfrieger and B. A. Barres, "Synaptic Efficacy Enhanced by Glial Cells In Vitro," *Science*, Vol. 277, p. 1684, 1997. Reprinted with permission from AAAS.

Figure 2.11 ▪ Human Glial Cells Enhance Conditioning in Mice.

Mice receiving brain grafts of human glial cells rapidly learned a fear response ("freezing" to a tone that signaled an upcoming electric shock), whereas ungrafted controls showed little or no improvement.



Source: Adapted from Figure 6B of "Forebrain Engraftment by Human Glial Progenitor Cells Enhances Synaptic Plasticity and Learning in Adult Mice," by Xiaoning Han et al., 2013, *Cell Stem Cell*, 12, p. 350.

This arrangement has three benefits. First, the insulating effect of myelin reduces an electrical resistance of the membrane to electricity called capacitance. Because capacitance slows the movement of ions down the axon, the graded potential gets a big boost in speed. The overall effect of myelination is the equivalent of increasing the axon diameter 100 times (Koester & Siegelbaum, 2013). Second, the breaks in the myelination mean that the signal is regenerated by an action potential at every node of Ranvier. Third, myelinated neurons use much less energy because there is less work for the sodium-potassium pump to do.

Some diseases, such as multiple sclerosis, leukodystrophy, and myelitis, destroy myelin. As myelin is lost, the capacitance rises, reducing the distance that graded potentials can travel before dying out. The individual is worse off than if the neurons had never been myelinated; because there are few voltage-sensitive sodium channels under the myelin sheath (Ritchie & Rogart, 1977), action potentials may not be generated in the previously myelinated area. Therefore, conduction slows or stops in affected neurons. And because neuronal energy use also goes up, neurons can deplete their energy stores and lose the ability to survive.

Other Glial Functions

There are several types of glial cells, and they make numerous contributions to neural functioning. During fetal development, *radial glia* form scaffolds that guide new neurons to their destinations. Later on, *microglia* provide energy to neurons and act as the brain's immune system by responding to injury and disease by removing cellular debris and damaged cells. Neurons form seven times as many connections in the presence of the type of glia called *astrocytes*, and they start to lose their synapses if astrocytes are removed from the culture dish (Pfrieger & Barres, 1997; Ullian et al., 2001; see Figure 2.10). Astrocytes also appear to play a key role in learning, as Figure 2.11 demonstrates (Han et al., 2013; Suzuki et al., 2011). A recent study suggests that an additional function of oligodendrocytes is to supplement very active axons with glucose, an important sugar in the brain (Fletcher & Young, 2024). Later in this chapter, you will see that glial cells play a direct role in neural activity.

Concept Check

Take a Minute to Check Your Knowledge and Understanding

- How is information conducted in the axon?
- How does the all-or-none law limit information transmission?
- What benefits do the refractory periods provide?
- What are the major types and functions of glial cells?
- How does myelin speed up conduction in axons?

How Neurons Communicate With Each Other

Before the late 1800s, we did not really know what was inside our brains because scientists who examined brain tissue under the primitive microscopes of the time (like Descartes) could not see any discernible structures other than blood vessels and gross brain areas. In the late 1800s, however, the Italian biologist Camillo Golgi developed a new tissue-staining method that applied a silver technique invented to develop photographic film to brain tissue; he helped anatomists see individual neurons given that the silver would randomly stain some entire cells without staining others (see the discussion of staining methods in Chapter 4). Because microscopy was also in its infancy, all he could see was an interconnected web of tissue, which he dubbed the neural reticulum. Later, the Spanish anatomist Santiago Ramón y Cajal looked at similarly stained brain tissue with a more powerful microscope; he was able disprove Golgi's reticulum theory when he saw that each neuron was a separate cell (Ramón y Cajal, 1937/1989; see For Further Reading at the end of this chapter for more information about Ramón y Cajal's seminal work on describing the nervous system). The connection between two neurons is called a **synapse**, a term derived from the Latin word meaning "to grasp." The neurons are not in direct physical contact at the synapse but rather are separated by a small gap called the **synaptic cleft**. Two terms will be useful to us in the following discussion: The neuron that is transmitting to another is called the **presynaptic** neuron; the receiving neuron is the **postsynaptic** neuron (Figure 2.12).

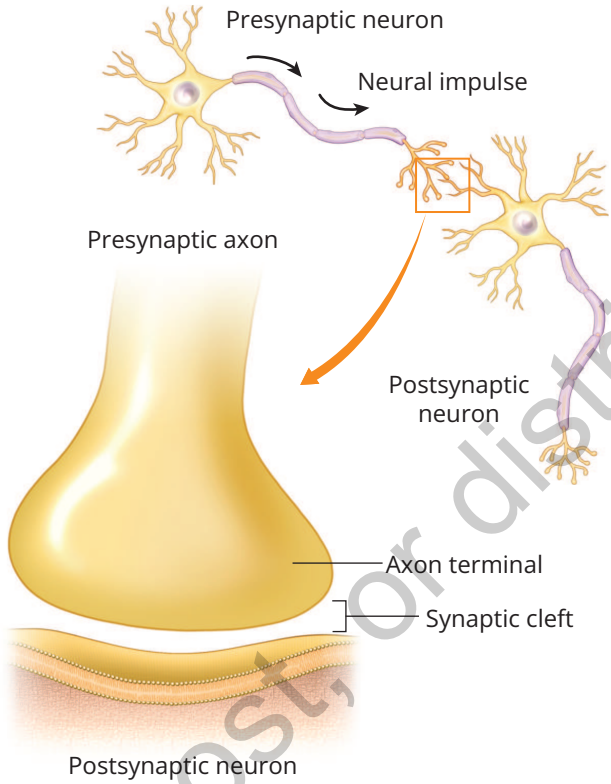
Chemical Transmission at the Synapse

Until the 1920s, physiologists were not sure whether neurons communicated at the synapse by an electrical current or by releasing a chemical. The German physiologist Otto Loewi believed that synaptic transmission was chemical, but he did not know how to test his hypothesis. One night, Loewi suddenly awoke from sleep with the solution to his problem (Loewi, 1953). He wrote his idea down so that he would not forget it, but the next morning he could not read his own half-awake scribblings. He recalled that day as the most "desperate of my whole scientific life" (p. 33). But the following night, he awoke again with the same idea; taking no chances, he rushed to his laboratory. There he dissected out the beating hearts of two frogs and bathed each in a separate salt solution. He applied electrical stimulation to the vagus nerve attached to one of the hearts, which slowed the heartbeat. Then he extracted some of the salt solution, which he assumed would have captured any chemical that might have been released. When he applied this salt solution to the solution bathing the second heart, that heart slowed too, just as Loewi predicted. Then he stimulated the accelerator nerve of the first heart, which caused the heart to beat faster. When he transferred the solution from the first heart to the second, this time it sped up (Figure 2.13). So Loewi demonstrated for the first time that transmission at the synapse is chemical and that neurons can release at least two different chemicals with opposite effects.

It turned out later that some neurons do communicate electrically by passing ions through channels that connect one neuron to the next; their main function appears to be synchronizing electrical activity in nearby neurons (Bennett & Zukin, 2004). In addition, some neurons release a gas transmitter. Still, Loewi was essentially correct because the vast majority of synapses are chemical. (By the way, if this example suggests to you that although sometimes the best way to solve a problem is to "sleep on it," keep in mind that such insight occurs only when people have paid their dues in hard work beforehand!)

Figure 2.12 ▪ The Synapse Between a Presynaptic Neuron and a Postsynaptic Neuron.

Notice the separation between the presynaptic axon terminal and the postsynaptic neuron.



At chemical synapses, neurotransmitters are stored in the terminals inside groups of a tiny membrane-enclosed organelle called a **vesicle**; this term means, appropriately, "little bladders." When the action potential arrives at a terminal, it opens channels that allow calcium ions to enter the presynaptic membrane from the extracellular fluid. The calcium ions cause the vesicles clustered nearest the membrane to fuse with the membrane. The membrane opens there, and the neurotransmitters spill out and diffuse into the cleft in a process called *exocytosis* (Figure 2.14).

On the postsynaptic neuron, the neurotransmitter docks with specialized protein receptors that match the molecular shape of the transmitter molecules like a key in a lock (see Figure 2.14). Activation of these receptors opens the ion channels, allowing ions to flow across the membrane. An **ionotropic receptor** forms the ion channel and opens quickly to produce the immediate reactions required for muscle activity and sensory processing. A **metabotropic receptor** opens the channel indirectly through an internal second messenger system; it acts slowly and produces the longer-lasting effects needed for learning and memory. Opening the channels is what sets off the graded potential that initiates the action potential. You will see in the next section that the effect this has on the postsynaptic neuron depends on which receptors are activated.

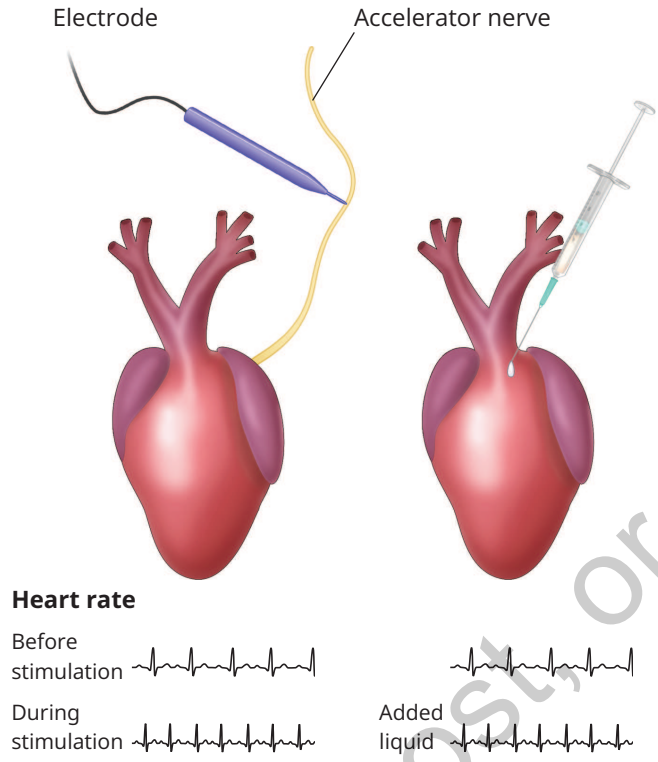
The chemical jump across the synapse takes a couple of milliseconds; that is a significant slowing compared with electrical transmission down the axon. In a system that places a premium on speed, inserting gaps that slow down transmission in the neural pathway must have some compensating benefit. As you will see in the following sections, synapses add important complexity to the simple all-or-none response in the axon.

Excitation and Inhibition

Opening ion channels on the dendrites and cell body has one of two effects; it can cause the local membrane potential to shift in a positive direction toward zero, partially depolarizing the membrane,

Figure 2.13 ▪ Otto Loewi's Experiment Demonstrating Chemical Transmission in Neurons.

Loewi stimulated the first frog heart. When he transferred fluid from it to the second heart, it produced the same effect there as the stimulation did in the first heart.



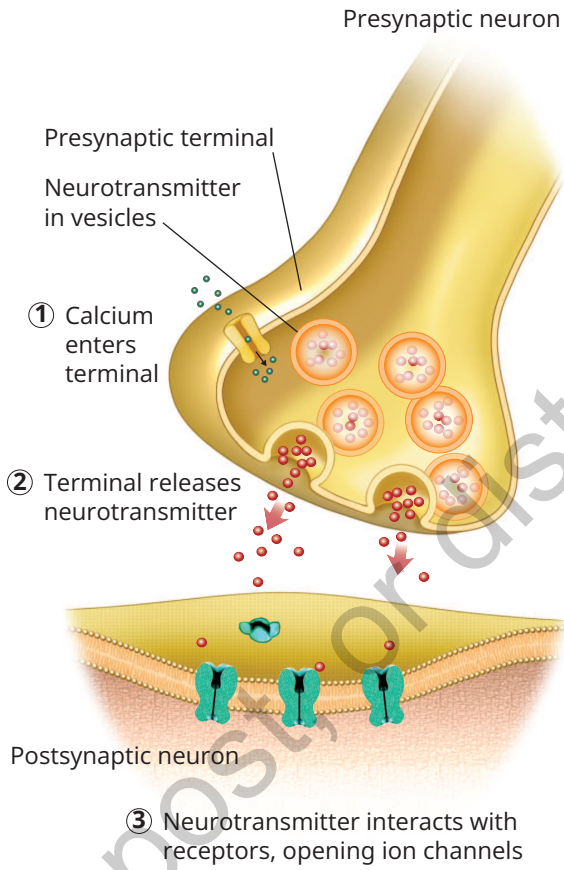
or it can shift the potential farther in the negative direction. **Partial depolarization** is excitatory and facilitates the occurrence of an action potential; increased polarization, or **hyperpolarization**, is inhibitory and makes an action potential less likely to occur. The value of excitation is obvious, but inhibition can communicate just as much information as excitation does. Also, the message becomes more complex because input from one source can partially or completely negate input from another. In addition, inhibition helps prevent runaway excitation; one cause of the uncontrolled neural storms that sweep across the brain during an epileptic seizure is a deficiency in receptors for the inhibitory transmitter gamma-aminobutyric acid (GABA; Baulac et al., 2001). Lithium, which is used to reduce manic symptoms of bipolar disorder, decreases excitatory neurotransmitters while increasing GABA transmission (Malhi et al., 2013). A Further Look describes an intriguing new finding about the importance of inhibition.

What determines whether the effect on the postsynaptic neuron is exciting or inhibiting? It depends on a combination of which transmitter is released and the type of receptors on the postsynaptic neuron. A particular transmitter can have an excitatory effect at one location in the nervous system and an inhibitory effect at another; however, some transmitters typically produce excitation, and others most often produce inhibition. If the receptors open positively charged channels like sodium, this produces a partial depolarization of the dendrites and cell body, which acts as an **excitatory postsynaptic potential (EPSP)**. Other receptors open potassium channels, negatively charged ion channels like chloride, or both; as potassium ions move out of the cell or chloride ions move in, they produce a hyperpolarization of the dendrites and cell body called an **inhibitory postsynaptic potential (IPSP)**.

At this point, there is only a graded local potential in a very small location. This potential can spread down the dendrites, merge or cancel out other potentials across the dendrites and cell body, and eventually reach the *axon hillock* (where the axon joins the cell body). Here, a positive graded potential

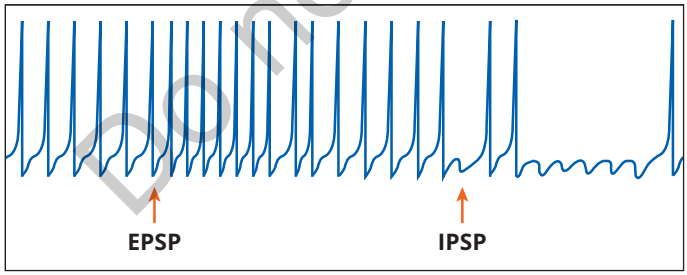
Figure 2.14 ▪ A Presynaptic Terminal Releases Neurotransmitters at the Synapse.

The neurotransmitters then interact with receptors embedded in the postsynaptic membrane.



that surpasses threshold will produce an action potential, whereas a negative graded potential will make it less likely to be generated. Most neurons have a baseline rate of spontaneous action potential generation; EPSPs will increase this rate, whereas IPSPs will decrease the rate of firing (Figure 2.15). So now another form of complexity has been added at the synapse; the message to the postsynaptic neuron can *modulate* the rate of firing, not just turn it on or off.

Figure 2.15 ▪ Effect of Excitation (EPSP) and Inhibition (IPSP) on Spontaneous Firing Rate.



Source: Adapted from *Principles of Neural Science*, 5th ed., by E. R. Kandel et al., p. 213. © 2013, McGraw-Hill Companies, Inc.

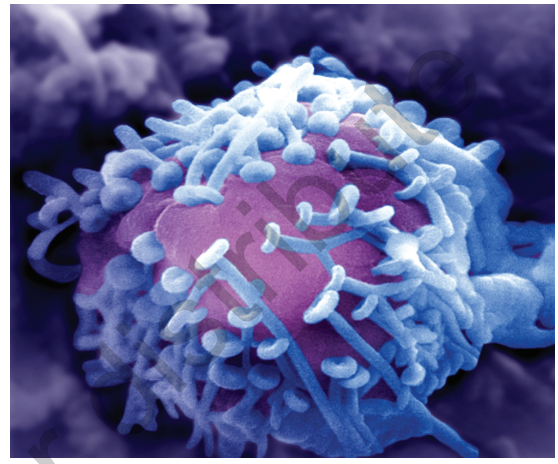
You should not assume that excitation of neurons always corresponds to activation of behavior or that inhibition necessarily suppresses behavior. An EPSP may activate a neuron that has an inhibitory effect on other neurons, and an IPSP may reduce activity in a neuron that has an inhibitory effect on other neurons, increasing their activity. An example of this paradox at the behavioral level is the effect of Ritalin. Ritalin and many other medications used to treat attention-deficit/hyperactivity disorder (ADHD) in children are in a class of drugs called stimulants, which increase activity in the nervous system (we will talk about this in more detail in Chapter 13). Yet in low doses, they calm hyperactive individuals and improve their ability to concentrate and focus attention (Cox et al., 2000; Mattay et al., 1996). They do this by increasing stimulating neurotransmitters in frontal areas of the brain that normally restrain behavior, where activity has been found to be abnormally low in people with ADHD (Berridge et al., 2006; Faigel et al., 1995).

Next, you will see that the ability to combine the inputs of large numbers of neurons expands the synapse's contribution to complexity even further.

Postsynaptic Integration

The output of a single neuron is not enough by itself to cause a postsynaptic neuron to fire or to prevent it from firing. In fact, an excitatory neuron may depolarize the membrane of the postsynaptic neuron by as little as 0.2 to 0.4 mV (Siegelbaum et al., 2013); remember that it takes an approximately 10-mV depolarization to trigger an action potential. However, a typical neuron receives input from approximately 1,000 other neurons (Figure 2.16); because each neuron has numerous terminals, this amounts to as many as 10,000 synaptic connections in most parts of the brain and up to 100,000 in the cerebellum (Siegelbaum & Kandel, 2013).

Figure 2.16 ▪ A Cell Body Virtually Covered With Axon Terminals.



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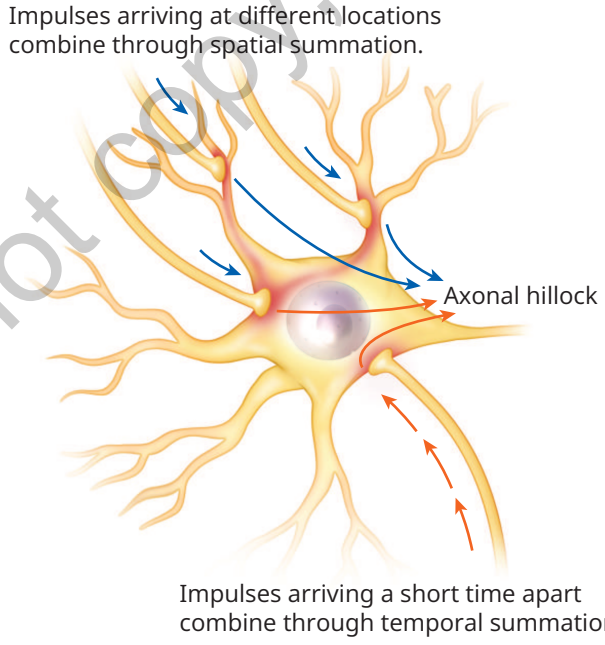
Because a single input neuron has a relatively small effect, the postsynaptic neuron must combine potentials from many neurons to fire. This requirement is actually advantageous; it ensures that a neuron will not be fired by the spontaneous activity of a single presynaptic neuron, and it allows the neuron to combine multiple inputs into a more complex message. These potentials are combined at the axon hillock in two ways. **Spatial summation** combines potentials occurring simultaneously at different locations on the dendrites and cell body. **Temporal summation** combines potentials arriving a short time apart from either the same or separate inputs. Temporal summation is possible because a local potential persists for a few milliseconds. Spatial summation and temporal summation occur differently, but they have the same result. Summation is illustrated in Figure 2.17.

Figure 2.17 ▪ Spatial and Temporal Summation.

The axonal hillock is on the right side of the neuron.

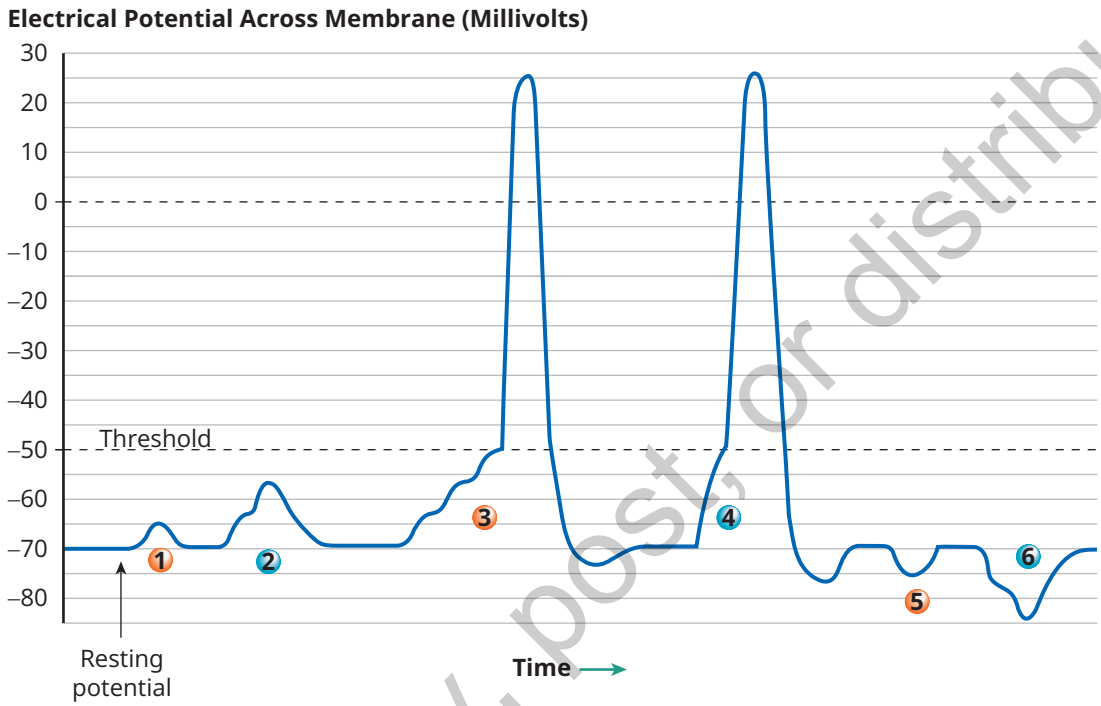


As you can see in Figure 2.18, summation combines EPSPs so that an action potential is more likely to occur. Alternatively, summation of IPSPs drives the membrane's interior even more negative and

makes it more difficult for incoming EPSPs to trigger an action potential. When both excitatory and inhibitory impulses arrive on a neuron, they will summate algebraically. The combined effect will equal the difference between the sum of the partial depolarizations and the sum of the hyperpolarizations. Spatial summation of two excitatory inputs and one inhibitory input is illustrated in Figure 2.19. The effect from temporal summation would be similar.

Figure 2.18 ▪ Temporal and Spatial Summation.

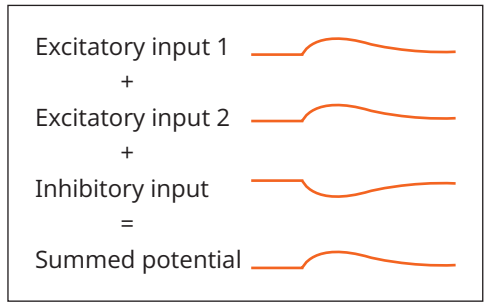
An EPSP (Point 1); summation of two EPSPs (2); summation of three EPSPs reaches threshold (3); summation of EPSPs reaches threshold (4); an IPSP (5); and summation of two IPSPs (6).



Because the neuron can summate inputs from multiple sources, it rises above the role of a simple message conductor—it is an *information integrator*. And using that information, it functions as a *decision maker*, determining whether to fire or not. Thus, the nervous system becomes less like a bunch of electrical wires and more like a computer. In subsequent chapters, you will come to appreciate how important the synapse is in understanding how we experience the world, how we learn and process information, and how we succumb to mental illness.

Figure 2.19 ▪ Summation of Excitatory and Inhibitory Potentials.

Note that inhibitory potentials cancel out excitatory potentials of equal strength (and vice versa).

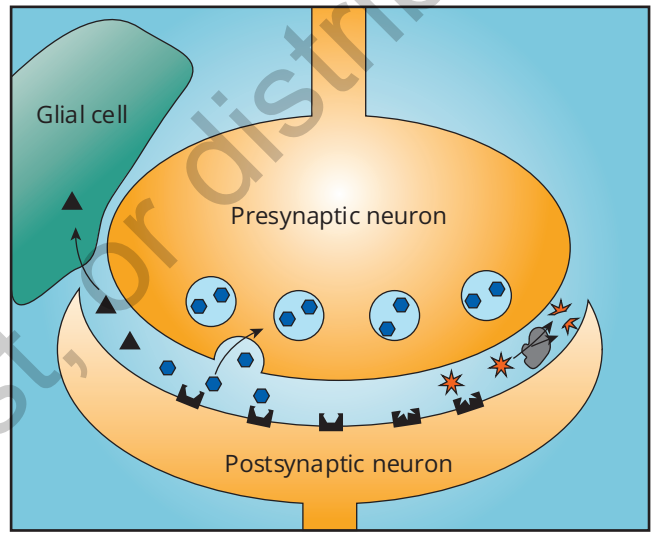


Terminating Synaptic Activity

Usually, the transmitter must be inactivated; otherwise, it will continue to stimulate postsynaptic receptors or leak over to other synapses and interfere with their functions. Typically, transmitters are taken back into the terminals by membrane proteins called transporters in a process called **reuptake**; they are repackaged in vesicles to be used again by the presynaptic neuron (Figure 2.20). The neurotransmitter serotonin, for example, is selectively removed through reuptake. At some synapses, the transmitter in the cleft is absorbed by nearby astrocytes. In others, transmitters are partially broken down through a process called *inactivation*. The neurotransmitter acetylcholine, for example, is inactivated by the enzyme acetylcholinesterase, which splits the molecule into its components of choline and acetate. Choline is then taken back into the terminals and used to make more acetylcholine.

Controlling how much neurotransmitter remains in the synapse is one way to vary behavior, and many drugs capitalize on this mechanism. Cocaine blocks the reuptake of dopamine; some antidepressant medications block the reuptake of serotonin (*selective serotonin reuptake inhibitors* or SSRIs), norepinephrine, or both, whereas others (*MAO inhibitors*) prevent the enzyme monoamine oxidase from inactivating those transmitters as well as dopamine and epinephrine; and drugs for treating the muscular disorder myasthenia gravis increase acetylcholine availability by inhibiting the action of acetylcholinesterase.

Figure 2.20 ▪ Reuptake, Glial Absorption, and Inactivation.



Regulating Synaptic Activity

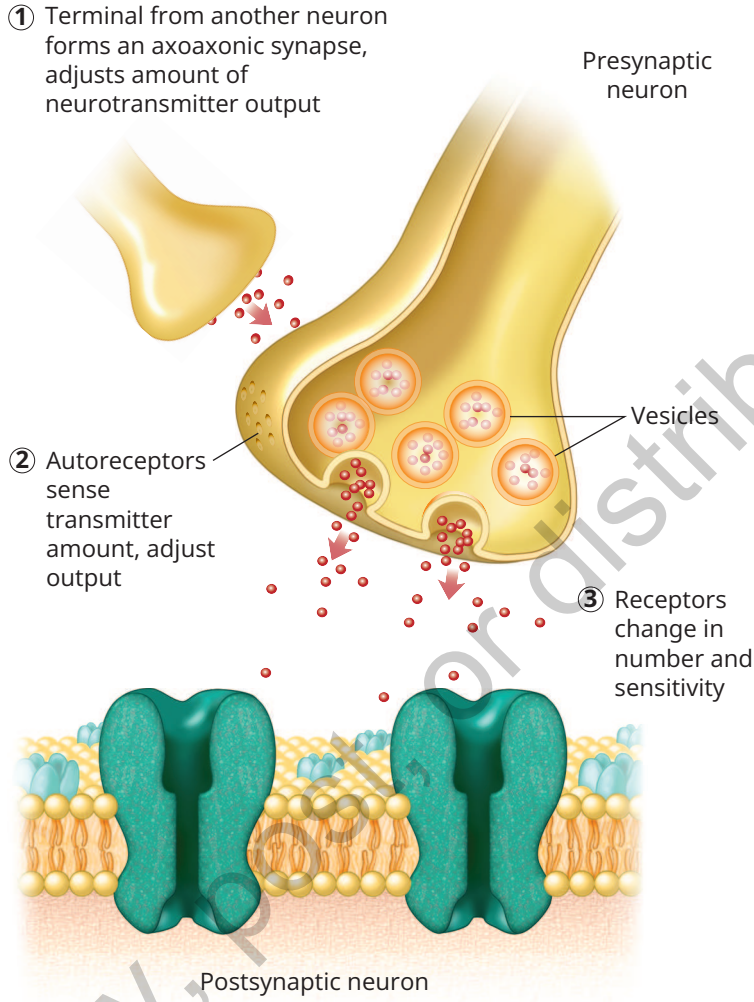
The previous description has been of a linear system that amounts to "*neuron A stimulates neuron B, neuron B stimulates neuron C,*" and so on. However, such a simple system cannot transmit the complex information required to solve a math equation, write a symphony, or care for a newborn. Not only that, but as messages flow from neuron to neuron, activity would soon drift out of control; some activity would fade out, whereas other activity would escalate until it engulfed an entire area of the brain. A nervous system that controls complex behavior must have several ways in which to regulate its activity.

The synapses described so far are referred to as *axodendritic* and *axosomatic* synapses because their terminals connect to dendrites and cell bodies. At *axoaxonic* synapses, a third neuron releases transmitter onto the terminals of the presynaptic neuron (see Point 1 in Figure 2.21). The result is **presynaptic excitation** *or* **presynaptic inhibition**, which increases or decreases, respectively, the presynaptic neuron's release of neurotransmitter onto the postsynaptic neuron. One way an axoaxonic synapse can adjust a presynaptic terminal's activity is by regulating the amount of calcium entering the terminal, which, you will remember, triggers neurotransmitter release.

Neurons also regulate their own synaptic activity in two ways. An **autoreceptor** on the presynaptic terminal senses the amount of transmitter in the cleft; if the amount is excessive, the presynaptic neuron reduces its output (Figure 2.21, Point 2). Postsynaptic neurons participate in regulation of synaptic activity as well. When there are unusual increases or decreases in neurotransmitter release, postsynaptic receptors change their sensitivity or even their numbers to compensate (Figure 2.21, Point 3). You will find in Chapter 14 that receptor changes figure prominently in some psychological disorders such as schizophrenia.

Glial cells also contribute to the regulation of synaptic activity. They surround the synapse and prevent neurotransmitter from spreading to other synapses, but some also remove neurotransmitter from the synaptic cleft and recycle it for the neuron's reuse (Figure 2.22). By varying the amount of transmitter they remove, glial cells influence postsynaptic excitability (Oliet et al., 2001). They can even respond to the neurotransmitter level in the synapse by releasing transmitters of their own. These gliotransmitters regulate transmitter release from the presynaptic neuron or directly stimulate the postsynaptic neuron

Figure 2.21 ▪ Regulating Activity at the Synapse.



to excite or inhibit it (M. Anderson & Hanse, 2010; Newman, 2003). Thus, rather than simply being neural "glue" as the name implies, glia should be considered active partners in neural transmission.

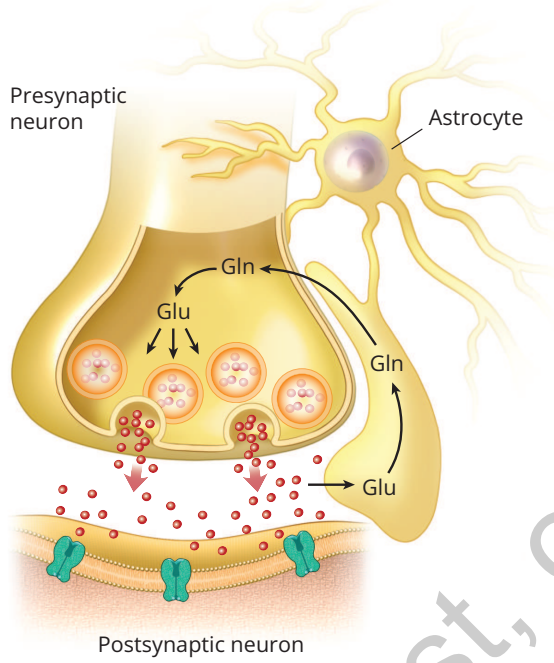
Neurotransmitters

Table 2.3 lists 12 transmitters, grouped according to their chemical structure. This is an abbreviated list; there are other known or suspected transmitters, and undoubtedly there are additional transmitters yet to be discovered. This summary is intended to illustrate the variety in neurotransmitters and to give you some familiarity with the functions of a few of the major ones. You will encounter most of them again in the discussion of various behaviors in later chapters.

Having a variety of neurotransmitters multiplies the effects that can be produced at synapses; the fact that there are different subtypes of the receptors adds even more. For example, two types of receptors detect acetylcholine: the nicotinic receptor, so-called because it is also activated by nicotine, and the muscarinic receptor, named for the mushroom derivative that can stimulate it. Excitatory nicotinic receptors are found predominantly in muscles. Muscarinic receptors are more frequent in the brain, where they have an excitatory effect at some locations and an inhibitory one at others. Other transmitters have many more receptor subtypes than acetylcholine does. An example of this is the serotonin receptor, where there are at least 15 different subtypes organized in seven major families (Kroeze et al., 2002).

Figure 2.22 ▪ Glial Cell Interacting With Neurons at the Synapse.

An astrocyte, a type of glial cell, encloses the synapse, where it absorbs the neurotransmitter glutamate (Glu) from the synaptic cleft. It recycles the transmitter into its precursor glutamine (Gln) and returns the Gln to the presynaptic terminal for reuse. The glial cell can influence synaptic activity by granting or withholding transmitter absorption and by releasing its own transmitter in response to the neurotransmitter level in the synapse.



Source: Adapted with permission from "Energy on Demand," by P. J. Magistretti et al., 1999, *Science*, 283, p. 497. Copyright © 1999. Reprinted with permission from AAAS.

Table 2.3 ▪ Some Representative Neurotransmitters.

Neurotransmitter	Function
Acetylcholine	Transmitter at muscles; in brain, involved in learning, etc.
Monoamines	
Serotonin	Involved in mood, sleep and arousal, aggression, depression, obsessive-compulsive disorder, and alcoholism.
Dopamine	Contributes to movement control and promotes reinforcing effects of food, sex, and abused drugs. Dysregulation is involved in schizophrenia and Parkinson's disease.
Norepinephrine	A hormone released during stress. Functions as a neurotransmitter in the brain to increase arousal and attentiveness to events in the environment. Diminished norepinephrine transmission is involved in depression.
Epinephrine	A stress hormone related to norepinephrine; plays a minor role as a neurotransmitter in the brain.
Amino Acids	
Glutamate	The principal excitatory neurotransmitter in the brain and spinal cord. Vitally involved in learning; glutamate dysfunction is implicated in schizophrenia.

(*Continued*)

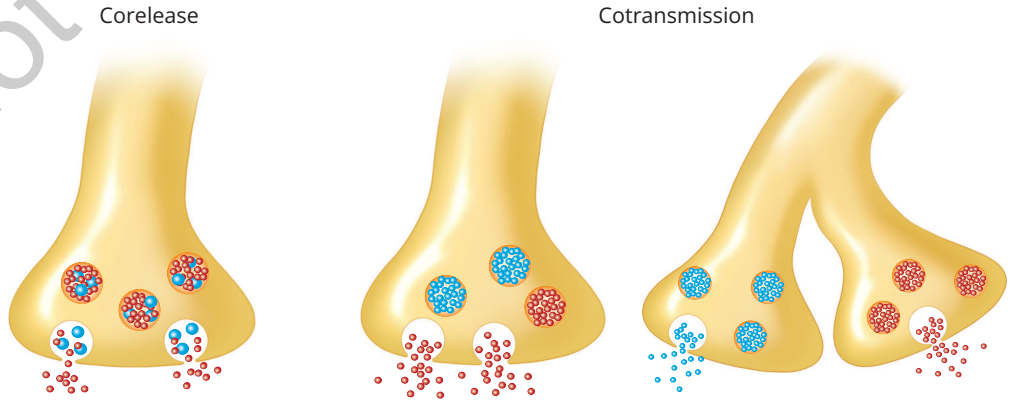
Table 2.3 ▪ Some Representative Neurotransmitters. (*Continued*)

Neurotransmitter	Function
GABA	The predominant inhibitory neurotransmitter. Its receptors respond to alcohol and the class of tranquilizers called benzodiazepines. Deficiency in GABA or receptors is one cause of epilepsy.
Glycine	Inhibitory transmitter in the spinal cord and lower brain. The poison strychnine causes convulsions and death by affecting glycine activity.
Neuropeptides	
Endorphins	Neuromodulators that reduce pain and enhance reinforcement.
Substance P	Transmitter in neurons sensitive to pain.
Neuropeptide Y	Initiates eating and produces metabolic shifts.
Gas	
Nitric oxide	One of two known gaseous transmitters along with carbon monoxide. Can serve as a retrograde transmitter, influencing the presynaptic neuron's release of neurotransmitter. Viagra enhances male erections by increasing nitric oxide's ability to relax blood vessels and produce penile engorgement.

For decades, neurophysiologists labored under the erroneous belief, known as **Dale's principle**, that a neuron was capable of releasing only a single transmitter. We now know that many neurons ply their postsynaptic partners with more than one chemical messenger (Vaaga et al., 2014). These neurons may release two fast-acting neurotransmitters, a fast-acting neurotransmitter and a slow-acting monoamine, or a fast-acting neurotransmitter and a neuromodulator, which alters the effect of the transmitter. There is even evidence that some neurons release more than two neurotransmitters, for example, dopamine, GABA, and glutamate. And some neurons can release one transmitter in response to weak stimulation and another during strong stimulation. As you can now see, synaptic transmission vastly increases the complexity of the nervous system.

Figure 2.23 ▪ Neural Corelease and Cotransmission.

(a) In corelease, the neuron can limit exit of larger chemical messengers by partially opening the fusion pore. (b) When the messengers are in different vesicles in the same terminal, the vesicles' differential Ca^{2+} sensitivity provides release selectivity. (c) Packaging the transmitters in separate terminals allows the neuron to have different effects at the terminals' destinations.



(a) Partial vesicle opening **(b) Differential Ca^{2+} sensitivity** **(c) Spatial segregation**

Source: Adapted from "Dual-transmitter Neurons: Functional Implications of Co-release and Co-transmission," by C. E. Vaaga, M. Borisovska, and G. L. Westbrook, 2014, *Current Opinions in Neurobiology*, 29, 25–32.

The release can occur in three ways. In *corelease*, the transmitters are packaged in the same vesicles. However, this does not mean they are always released equally; in the example in Figure 2.23a, the fusion pores between the vesicle and terminal membranes have opened only partially, impeding the release of the larger messenger molecules while allowing the smaller molecules to exit freely (see Braun et al., 2007). In *cotransmission*, the transmitters are in separate vesicles. Vesicles containing different transmitters in the same terminal differ in sensitivity to calcium (Ca^{2+}); a low rate of neural impulses will trigger release of only one of the messengers, whereas a higher rate will release both of them (Figure 2.23b). Finally, the neuron may release different transmitters from its various terminals to produce different effects at separate destinations (Figure 2.23c).

Corelease and cotransmission are not well understood, but we do know they play a significant role in neural functioning. For example, release of inhibitory GABA dampens the excitatory effects of glutamate during seizures (Trudeau, 2004) and counters the arousing effects of histamine to prevent hyperactivity and sustained wakefulness (Yu et al., 2015). In addition, direction-detecting cells in the retina of the eye release acetylcholine and GABA in response to any movement of a visual object, but they release only GABA when the movement is in the cell's "preferred" direction (Lee et al., 2010).

A Further Look

Agonists and Antagonists in the Real World

Neurotransmitters are not the only substances that affect the nervous system. A drug or other compound that mimics or increases the effect of a neurotransmitter is called an **agonist**. Any substance that reduces the effect of a neurotransmitter is called an **antagonist**. Practically all drugs that have a psychological effect interact with a neurotransmitter system in the brain, and many of them do so by mimicking or blocking the effect of neurotransmitters (Snyder, 1984).

Amazonians tip their blowgun darts with the plant neurotoxin curare.

Source: By Jialiang Gao, https://commons.wikimedia.org/wiki/File:Yahua_Blowgun_Amazon_Iquitos_Peru.jpg, licensed under CC BY-SA 4.0 https://creativecommons.org/licenses/by-sa/4.0.

You have already seen that the effect of acetylcholine (ACh) is duplicated by nicotine and muscarine at the two kinds of acetylcholine receptors (nicotinic-ACh and muscarinic-ACh, respectively). Opioid drugs such as heroin and morphine also act as agonists, stimulating receptors for opiate-like transmitters in the body. The drugs naloxone and naltrexone act as antagonists to opiates, occupying the receptor sites without activating them; consequently, naloxone and naltrexone can be used to counteract an overdose. The plant toxin curare blocks nicotinic acetylcholine receptors at the muscle, causing paralysis (Trautmann, 1983). Indigenous tribes of Central and South America put curare on the tips of their darts and arrows to disable their game. A synthetic version of curare was used as a muscle relaxant during surgery before safer and more effective drugs were found (Goldberg & Rosenberg, 1987). It was even used occasionally in the past to treat the muscle spasms of tetanus (lockjaw), which ironically is caused by another **neurotoxin**.

Neural Codes and Neural Networks

Underlying this discussion has been the assumption that we can explain behavior by understanding what neurons do. But we cannot make good on that promise as long as we talk as if neural communication

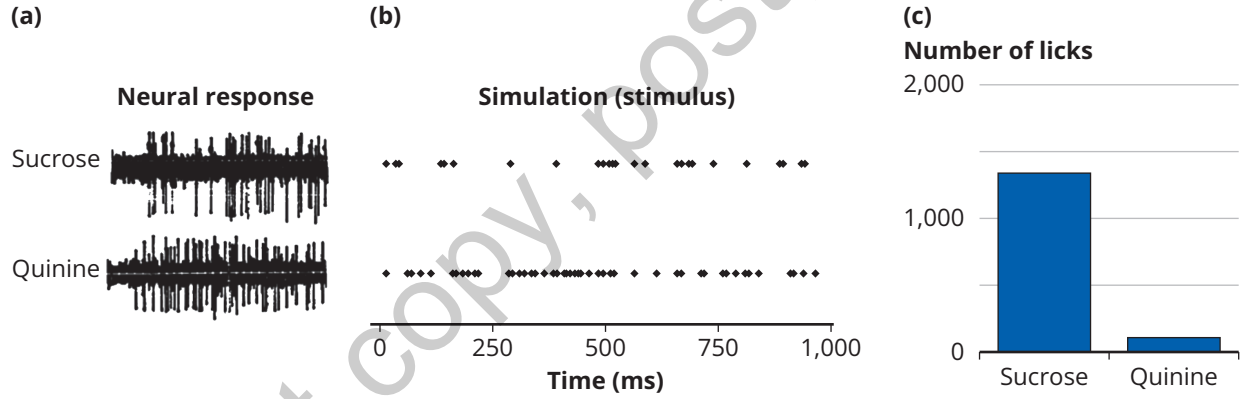
is limited to single chains of neurons that either fire or do not fire. In fact, neurons are capable of generating complex messages, which they send across intricate networks.

Coding of Neural Messages

Neurons do not just produce a train of equally spaced action potentials; they vary the intervals between spikes, they produce bursts of varying lengths, and the bursts can be separated by different intervals (Cariani, 2004). But do these temporal (time-related) variations in firing pattern form a code that the brain can use, or are they just "noise" in the system? The best way to answer this question is to look at sensory processes because the researcher can correlate firing patterns with sensory input on one end and behavior on the other. A good example is an early study done by Patricia Di Lorenzo and her colleague Gerald Hecht. First, they recorded the firing patterns in individual taste neurons of rats during stimulation with a sucrose (sugar) solution and quinine (the flavoring in tonic water). As you can see in Figure 2.24a, these flavors produce different neural activity. Then they duplicated the temporal patterns in the form of electrical pulses (Figure 2.24b) and used these to stimulate the cortical taste centers of other rats. The assumption was that if the brain *uses* this information, the unanesthetized rats would behave as if they were actually *tasting* sweet sucrose or bitter quinine. As Figure 2.24c shows, that is exactly what happened: The rats licked a water tube at a high rate when they were receiving stimulation patterned after sucrose but almost stopped licking—even though they were water deprived—when the stimulation was patterned after quinine (Di Lorenzo & Hecht, 1993).

Figure 2.24 ▪ Response of Rats to Neural Stimulation Simulating the Taste of Sucrose and Quinine.

(a) Recordings from individual neurons during stimulation with sucrose and quinine. (b) Electrical stimulation mimicking the recorded neuronal activity; each dot represents a signal neural impulse. (c) The average number of times the rats licked a drinking tube for water during delivery of the quinine simulation and the sucrose simulation.



Sources: (a) and (b) Adapted from Figure 7 of "Temporal Coding in the Gustatory System," by R. M. Hallock and P. M. Di Lorenzo, 2006, *Neuroscience and Biobehavioral Reviews*, 30, p. 1156. Used with permission from Elsevier. (c) Adapted from Figure 4 of "Perceptual Consequences of Electrical Stimulation in the Gustatory System," by P. M. Di Lorenzo and G. S. Hecht, 1993, *Behavioral Neuroscience*, 107, p. 135.

However, this coding apparently is not sufficient to carry the complex information involved in brain communication. An additional opportunity for coding is provided by the fact that neural information often travels over specialized pathways. For example, taste information is carried by at least five types of specialized fibers; Di Lorenzo and Hecht (1993) recorded the sucrose firing pattern from a "labeled line" specialized for sweet stimuli and recorded the quinine pattern from another one specialized for bitter stimuli. Stimulating the labeled line from sweet receptors will always result in the perception of sweetness even if the pattern mimics the bitter pattern. In later chapters, you will see that not only taste but also information about color and the higher sound frequencies is transmitted over a limited number of labeled lines. However, even with temporal coding and labeled lines, a significant burden remains for the brain if it is to make sense of this information. This leads us to the topic of neural networks.

Neural Networks

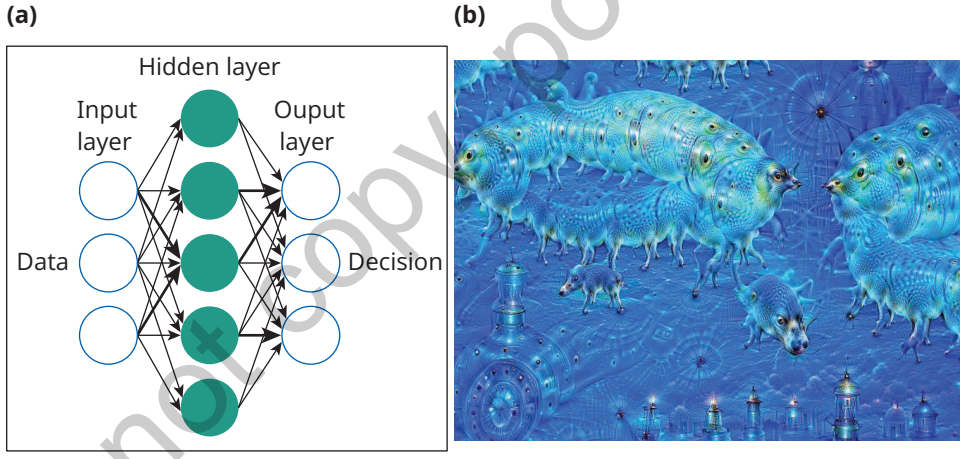
Individual neurons cannot carry enough information to determine the taste of a bite of food or the color of an object. Color processing, for example, depends on four "labeled lines" carrying information about red, green, blue, and yellow light; we can distinguish millions of colors by comparing the relative activity in these four pathways. This kind of analysis requires complex interactions among a network of neurons. A **neural network** is a group of neurons that function together to carry out a process; it is where the most complex neural processing—the "computing" work of the brain—occurs. Sometimes these networks involve a relatively small number of neurons in a single area such as groups of neurons in a part of the brain called the hippocampus. When rats navigate a maze, these networks store their preceding choices and calculate their next choice. The networks perform so reliably that the researcher can use their activity to predict which way the rats will turn after a delay (Pastalkova et al., 2008). As you will see in later chapters, other networks combine the activity of widespread brain areas to perform language functions (Chapter 9), to identify an object visually and locate it in space (Chapter 10), and, some researchers believe, to produce conscious awareness (Chapter 15). We go into more detail about other uses of neural networks, such as in the creation of art and in deceptive video editing, in A Further Look.

A Further Look

Uses and Abuses of Artificial Neural Networks

Figure 2.25 ▪ Neural Network and an Image Derived From It.

(a) Example of a simple artificial neural network. (b) DeepDream image produced from a picture of jellyfish after 50 iterations, by a network trained on pictures of dogs.



Custom art (G. Hough, 2019); Artwork by Martin Thoma (2015, Creative Commons Public Domain)

Artificial neural networks are computer programs that mimic the brain's neural networks; rather than being programmed to perform in a specific way, these networks *learn* how to carry out their task by trial and error, much as humans do. The networks consist of multiple layers of simulated neurons: an input layer, one or more hidden layers where the processing is done, and an output layer. The network is trained by repeatedly feeding it data and then giving it correct results to compare with its own output. At first, the network's performance is random, but it improves over time by adjusting the strength of connections among its simulated neurons. For example, an early network that was designed to read and speak English text initially produced random sounds, which were replaced with babbling and then pseudowords, but after just 10 training trials the speech was intelligible and sounded like that of a small child (Sejnowski & Rosenberg, 1987).

Artificial neural networks can be used to identify people through facial recognition, control a self-driving car, and detect alterations to an image or video (Coldeway, 2019). In fact, if you have flown on an airplane, unlocked your smartphone, or got your driver's license renewed, your face has likely already been used to identify you. Artificial neural networks are especially useful in tasks requiring decision making, such as in finance, but also as far afield as in art. DeepDream software, which was created to recognize faces and other patterns in images, can be run in reverse to produce "psychedelic" and surreal art. The two photographs here were created from a picture of jellyfish by a network that was trained to perceive dogs, so it gave the jellyfish image "dog" characteristics. Nowadays, even people with no art training can create surprisingly realistic images that mimic photographs, videos, and even styles of art using these artificial neural networks.

But anything this powerful is subject to abuse; one good example is *deepfake* videos. These originated as fake pornographic videos of celebrities, created by collecting multiple photos of the person from around the web and using artificial intelligence (AI) to superimpose them on the body of an actor. More recently, a deepfake video appearing to show Facebook's Mark Zuckerberg saying he has "total control of billions of people's stolen data" went viral on the web. The frightening potential exists to create convincing fake evidence of a person committing a crime or a video of a political opponent making reprehensible statements. As a means of warning about the risks of such "fake news," director Jordan Peele and BuzzFeed's former chief executive officer, Jonah Peretti, created a deepfake video of Barack Obama calling Donald Trump a "complete and utter dips__t" (Chivers, 2019). Another abuse is in how the programs generate the images given that the networks need to be trained using large existing datasets that are sourced by scouring the internet. Recently, one group won a copyright lawsuit against Stable Diffusion in federal court, claiming that the company violated the Digital Millennium Copyright Act (Cho, 2024). This makes legal use of AI-generated content more difficult, especially because image generation is now included with just about every major internet browser, office software, and image creation software.

While we are waiting for neuroscientists to explain how the brain works, the idea of neural networks provides a useful way of thinking about mental processes. The next time you are trying to remember a person's name that is "on the tip of your tongue," imagine your brain activating individual components of a neural network until one produces the name you are looking for. If you visualize the person's face as a reminder, imagine that the name and the image of the face are stored in connected networks, so that activating one memory activates the other. This is not just speculation: Electrode recordings from patients preparing for brain surgery show that the information triggered by the photo of a familiar person and by the person's written name converge on the same neurons in a critical memory area of the brain (Quian Quiroga et al., 2009)—thanks, of course, to neural networks.

Concept Check

Take a Minute to Check Your Knowledge and Understanding

- How is information transmitted at the synapse?
- It can be said that integration transforms neurons from a "telephone line" into a computer. Explain.
- What difference would it make if there were no regulation of activity at the synapse?
- What is Dale's principle, and in what way is it incorrect?
- Explain why researchers' focus is shifting from localized neural activity to brainwide connections and activity.
- What are artificial neural networks?

In Perspective

It is impossible to understand either the brain or the behavior without first knowing the capabilities and the limitations of the neuron. Although more complexity is added at the synapse, a relatively simple

device is the basis for our most sophisticated capabilities and behaviors. However, what happens at the individual neuron is not enough to account for human behavior; neurons work in concert with each other in both local and brainwide networks. With modern tools and large cooperative efforts, researchers hope to understand how neurons work together to produce thought, memory, emotion, and consciousness. In Chapter 3, you will learn about some of the functional structures in the brain that are formed by the interconnection of neurons.

Chapter Summary

The Cells That Make Us Who We Are

- There are three major kinds of neurons: motor neurons, sensory neurons, and interneurons. Although they play different roles, they have the same basic components and operate the same way.
- The neural membrane is electrically polarized. This polarity is the resting potential, which is maintained in the short term by the effects of selective membrane permeability in combination with the forces of diffusion and electrostatic pressure and in the long term by the sodium-potassium pump.
- Polarization is the basis for the neuron's responsiveness to stimulation in the form of the graded potential and the action potential.
- The neuron is limited in firing rate by the absolute refractory period and in its ability to respond to differing strengths of stimuli by the all-or-none law. More intense stimuli cause the neuron to fire earlier during the relative refractory period, providing a way to encode stimulus intensity (the rate law).
- Glial cells provide the myelination that enables neurons to conduct rapidly while remaining small. They also help regulate activity in the neurons and provide several supporting functions for neurons.

How Neurons Communicate With Each Other

- Transmission from neuron to neuron is usually chemical in vertebrates, involving neurotransmitters released onto receptors on the postsynaptic dendrites and cell body.
- The neurotransmitter can create an excitatory postsynaptic potential, which increases the chance that the postsynaptic neuron will fire, or it can create an inhibitory postsynaptic potential, which decreases the likelihood of firing.
- Through temporal and spatial summation, the postsynaptic neuron integrates its many excitatory and inhibitory inputs.
- Regulation of synaptic activity is produced by axoaxonic synapses from other neurons, adjustment of transmitter output by autoreceptors, and change in the number or sensitivity of postsynaptic receptors.
- Leftover neurotransmitters may be taken back into the presynaptic terminals, absorbed by glial cells, or broken down by an enzyme.
- The human nervous system contains a large number of neurotransmitters, which are detected by an even greater variety of receptors. A neuron can release combinations of two or more neurotransmitters.
- The computing work of the brain is done in complex neural networks.

Study Resources

For Further Thought

- What would be the effect if there were no constraints on the free flow of ions across the neuron membrane?
- Sports drinks replenish electrolytes that are lost during exercise. Electrolytes are minerals or elements that carry an electric charge like sodium. What implication do you think selective electrolyte loss of sodium from sweating might have for the nervous system?
- Imagine what the effect would be if the nervous system used only one neurotransmitter.
- How similar to humans do you think computers are capable of becoming? How much is your answer based on how you think human behavior is controlled versus how capable you think computers are?

Test Your Understanding

1. Describe the ion movements and voltage changes that make up the neural impulse, from graded potential (at the axon hillock) to recovery.
2. What is the role of the sodium-potassium pump in both resting and action potentials?
3. How is an action potential different from a graded potential?
4. What are the absolute and relative refractory periods?
5. What are the three ways of regulating synaptic activity?
6. Discuss the ways in which the synapse increases the neuron's capacity for transmitting information.
7. Describe how neurons regulate neurotransmitter amounts in the synapse and what might happen to behaviors if those processes work too well or too poorly.
8. Describe neural networks and explain their importance.
9. What are the functions of glial cells?

Select the Best Answer

1. The inside of the neuron is relatively poor in _____ ions and rich in _____ ions.
   a. chloride; phosphate
   b. sodium; potassium
   c. optassium; sodium
   d. calcium; sodium

2. The rate law
   a. explains how the intensity of stimuli is represented.
   b. does not apply to neurons outside the brain.
   c. describes transmission in myelinated axons.
   d. describes the process of postsynaptic integration.

3. Without the sodium-potassium pump, the neuron would become
   a. more sensitive because of accumulation of sodium ions.
   b. more sensitive because of accumulation of potassium ions.
   c. overfilled with sodium ions and unable to fire.
   d. overfilled with potassium ions and unable to fire.

4. There is a limit to how rapidly a neuron can produce action potentials. This is due to
- **a.** inhibition.
- **b.** facilitation.
- **c.** the absolute refractory period.
- **d.** the relative refractory period.

5. Saltatory conduction results in
- **a.** less speed with the use of more energy.
- **b.** greater speed with the use of less energy.
- **c.** less speed with the use of less energy.
- **d.** greater speed with the use of more energy.

6. General anesthetics open potassium channels, allowing potassium ions to leak out of the neuron. This
- **a.** increases firing in pain-inhibiting centers in the brain.
- **b.** increases firing in the neuron until it is fatigued.
- **c.** depolarizes the neuron, preventing firing.
- **d.** hyperpolarizes the neuron, preventing firing.

7. When the action potential arrives at the terminal button, entry of _____ ions stimulates release of transmitter.
- **a.** potassium
- **b.** sodium
- **c.** calcium
- **d.** chloride

8. All the following neurotransmitters are deactivated by reuptake except
- **a.** acetylcholine.
- **b.** norepinephrine.
- **c.** serotonin.
- **d.** dopamine.

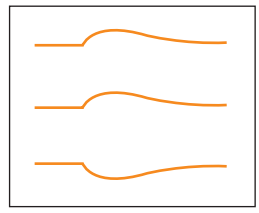
9. An inhibitory neurotransmitter causes the inside of the postsynaptic neuron to become
- **a.** more positive.
- **b.** more negative.
- **c.** more depolarized.
- **d.** neutral in charge.

10. Excitatory postsynaptic potentials are typically produced by movement of _____ ions, whereas inhibitory postsynaptic potentials are typically produced by movement of _____ ions.
- **a.** potassium; sodium or chloride
- **b.** potassium; sodium or calcium
- **c.** sodium; calcium or chloride
- **d.** sodium; potassium or chloride

11. Which of the following is not an example of regulation of synaptic activity?
- **a.** A neuron has its synapse on the terminals of another and affects its transmitter release.
- **b.** Autoreceptors reduce the amount of transmitter released.
- **c.** A presynaptic neuron inhibits a postsynaptic neuron.
- **d.** Postsynaptic receptors change in numbers or sensitivity.

12. Figure 2.26 shows three graded potentials occurring at the same time. Assume that the resting potential is –70 mV and that each graded potential individually produces a 5-mV change. What is the membrane's voltage after the graded potentials arrive?

Figure 2.26 ▪ Graded Potentials for Question 12.



a. –65 mV
b. –70 mV
c. –75 mV
d. +75 mV

13. The presence of synapses in a neuron chain provides the opportunity for
a. increases in conduction speed.
b. modification of neural activity.
c. two-way communication in a pathway.
d. regeneration of damaged neurons.

14. Neural networks
a. are groups of neurons that function together.
b. are where the most complex work of the brain occurs.
c. must connect at least two brain areas to be considered a network.
d. All of these are true.
e. Not all of these are true.

Answers:

1. b, 2. a, 3. c, 4. c, 5. b, 6. d, 7. c, 8. a, 9. b, 10. d, 11. c, 12. a, 13. b, 14. e

For Further Reading

1. *Synaptic Self*, by Joseph LeDoux (Penguin Books, 2003), takes the position that "your 'self,' the essence of who you are, reflects patterns of interconnectivity between neurons in your brain." A good read by a noted neuroscientist.

2. "From Cajal to Connectome and Beyond" (*Annual Review of Neuroscience*, 2016, *39*, 197–216) reviews the "long history of attempts to understand how the brain operates as a system," dating as far back as the fifth century.

3. Two books by Olaf Sporns, *Discovering the Human Connectome* (MIT Press, 2016), which discusses the **Human Connectome Project**, and *Networks of the Brain* (MIT Press, 2016), elaborate on topics in this chapter.

4. Sebastian Seung's book *Connectome* (Mariner Books, 2013) describes the effort to map the brain using computers and artificial intelligence (AI); you can read a summary and review in *New Scientist*, February 4, 2012, p. 46.

5. Ethan Mollick's book *Co-Intelligence: Living and Working With AI* (Portfolio, 2024) is a good introduction to artificial intelligence and how we can safely and effectively use AI to improve our world while avoiding the trap of allowing AI to "do the work" for us.

6. *Beautiful Brain: The Drawings of Santiago Ramón y Cajal* (Abrams Books, 2017), by Larry Swanson, Eric Newman, Alfonso Araque, and Janet M. Dubinsky, presents Ramón y Cajal's drawings as beautiful art in their own right.

Key Terms

absolute refractory period
action potential
agonist
all-or-none law
antagonist
autoreceptor
axon
axon terminal
cell body
Dale's principle
dendrites
electrostatic pressure
excitatory postsynaptic potential (EPSP)
force of diffusion
glial cell
graded potential
Human Connectome Project
hyperpolarization
inhibitory postsynaptic potential (IPSP)
interneuron
ion
ionotropic receptor
metabotropic receptor
motor neuron
myelin
neural network
neuron
neurotoxin
neurotransmitter
node of Ranvier
nondecremental
oligodendrocyte
partial depolarization
polarization
postsynaptic
presynaptic
presynaptic excitation
presynaptic inhibition
rate law
relative refractory period
resting potential
reuptake
saltatory conduction
Schwann cell
sensory neuron
sodium-potassium pump
spatial summation
synapse
synaptic cleft
temporal summation
vesicle
voltage