PREFACE

> The best investigators recognize interesting questions that don't fit into a predefined paradigm and follow the biology for its own sake. These curiosity-driven experiments are the ones that lead to truly surprising discoveries. We can expect that studies of seemingly exotic developmental events will continue to provide new perspectives on evolution and human biology.
>
> Anderson and Ingham (2003), 285

It is long-established tradition that beginning biology students learn to identify the four categories of animal tissue: epithelial, connective, muscle, and nervous. The student learns that nervous tissue contains two cell types: neurons and glial cells. The glial cells are then immediately set aside as the focus shifts to the stars of the nervous system, the neurons. It will be noted that neurons are electrically excitable cells that integrate information and transmit it to other cells (most often, to other neurons), primarily by chemical signals; that neurons are unlike other cells in that they possess long, thin extensions of the cytoplasm called axons and dendrites; and that neurons form polarized cell junctions called synapses. Following this reductionist line of thought helps students understand that the study of nervous system development is the story of how newly born cells differentiate a neuronal phenotype: how they come to express voltage-gated ion channels, assemble an extended cytoskeleton, and position synaptic proteins in just the right locations. In the twenty-first century, the story of how cells acquire a neuronal phenotype can be told in terms of molecular signals and the cellular receptors for those signals. An introductory account of these signals fills major parts of the chapters in this book. The molecular story of neuronal differentiation can in fact be told over and over again, with subtle variations and surprising plot twists, because there are so many different types of neurons. It's been estimated that as many as 100 billion neurons make up the human brain, collectively representing thousands, maybe even tens of thousands, of different ways to be a neuron.

But molecular signaling is only part of our story. The ability of the nervous system to integrate environmental cues and internal signals such as hormones with remembered experience to produce thoughts and behavior depends on its wiring diagram. Information flows through the nervous system via polarized neural circuits (by *polarized* I mean simply that there are distinct input and output sides to the circuit). These sophisticated circuits have built-in feedbacks, delays, and convergences that collectively enable a single circuit to produce multiple outputs. The second part of our story therefore involves understanding how connections within neural circuits are formed and sustained. If the diversity of neuronal phenotypes in the human brain is surprising, the targeting of the estimated 100 trillion connections (synapses) in the brain to form circuits is absolutely astonishing.

The third part of our story is the plasticity of the nervous system. In a sense, the development of the nervous system is a never-ending story. Across the life span, nervous systems respond to internal and external signals by altering neuronal phenotype and refining neural circuits. Familiar examples of neural plasticity are the seasonal behaviors of temperate-zone animals, acquisition of a skill such as playing the violin or a new video game, and formation of long-lasting memories of life events such as our first day of school. Nervous systems also have the capacity to recover from many (but not all) injuries. Does lifelong plasticity reflect reengagement of the mechanisms that supported the formation of the embryonic nervous system? Until we have a fuller understanding of both development and plasticity, this fascinating question is impossible to answer. This book does not avoid topics related to plasticity, but its primary goal is to give the reader a thorough grounding in the earliest stages of development.

While some readers of this book will be interested in learning about the nervous system so that they can better understand brain evolution and animal behavior, others will want this information so that they can be better physicians and educators and, eventually, parents. The latter category of readers may be disappointed that so many chapters focus on species other than humans. These species—some of which play such an important role in studies of development that they are referred to as *model organisms*—have contributed so much to our understanding of development that it would be impossible to write a meaningful book without reference to them. But readers primarily interested in humans can take heart, because advances in our knowledge of the human genome and proteome paired with new techniques of noninvasive brain imaging mean that direct studies of the development of the human nervous system are increasingly informative. For example, studies of teenagers using noninvasive brain imaging have revealed surprising and useful information about brain development during adolescence (Chapter 9).

Some readers of this book may be considering careers in neuroscience research. In the early 1980s, I chose to investigate the changes that occur in insect nervous systems during metamorphosis because I did not foresee the rapidity with which exciting studies of the developing mammalian nervous system would become possible. I love insects and have never been unhappy with my choice, but students interested in research on development of the nervous system can now choose from a longer menu of enticing options.

Many of these new models and areas of research are described in this book. Is it a good time to choose a career in neuroscience research? I think that most neuroscientists would agree with me when I say that the answer to this question is always *yes*.

It is my hope that this introductory account of nervous system development inspires all readers, but it is particularly dedicated to undergraduates encountering the subject of development for the first time. I assume that most such readers will have completed an introductory biology course (or courses) covering the basics of physiology, cell biology, genetics, and molecular biology. Students ready for more information can consult the notes and source lists for each chapter. Many of the references cited are review articles. A well-written review is often fun to read because it provides a concise summary of an interesting topic, but the savvy student appreciates that every such article is also a database. The opinions expressed in a review eventually become dated, but the curated list of references at the end of the article is timeless. In other words, use review articles (the secondary literature) as your portal to the primary literature (research reports published as journal articles).

By the way, my surname is easier to pronounce than to spell: just say *far*-bock, and you've got it.