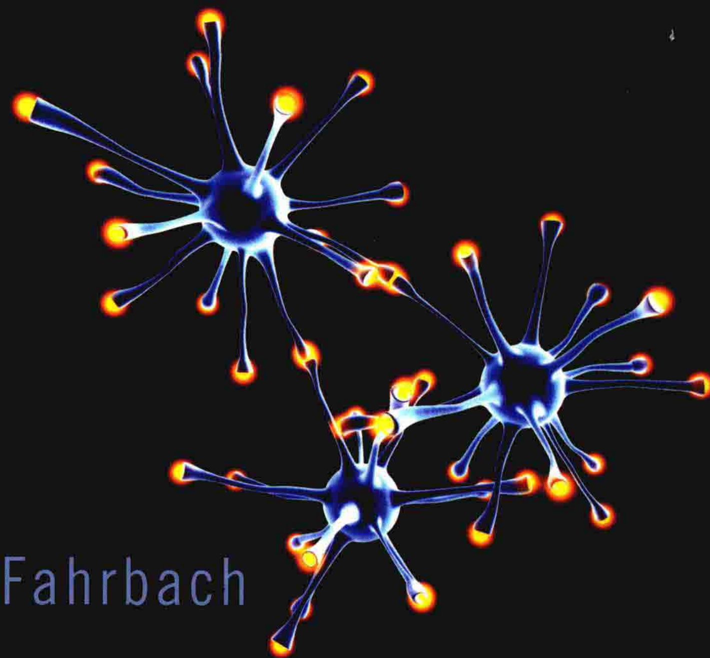
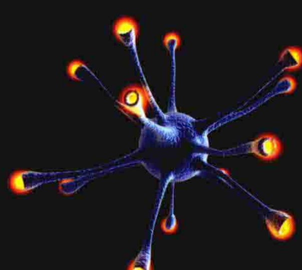


Susan E. Fahrbach

DEVELOPMENTAL NEUROSCIENCE

A Concise Introduction



Developmental Neuroscience

A CONCISE INTRODUCTION

Susan E. Fahrbach

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Developmental Neuroscience

To Jon, for reminding me that it's an adventure

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.

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WHAT ARE INVESTIGATIVE READING QUESTIONS?

Investigative reading questions are found at the end of each chapter. These questions offer students the chance to test their understanding by thinking about experiments based on material presented in the chapter. The most difficult of these questions are highlighted as *Challenge Questions*. Answers can be checked by carefully reading the recommended article that is provided, although you should be open to the possibility that you will come up with a better answer than the original investigators did. Full citations for each article are given at the end of the book. All of the articles used as the basis of investigative reading questions can be accessed free of charge by anyone with an Internet connection, regardless of institutional affiliation. Some of the articles are accessible because the journal publishers (in particular, scientific societies) make their archives freely available. Many articles are archived in PubMed Central (PMC), a free, full-text online library of over 2 million biomedical and life sciences articles maintained by the U.S. National Institutes of Health's National Library of Medicine (http://www.ncbi.nlm.nih.gov/pmc/). All research supported by the National Institutes of Health, the major public funder of research in the United States, is required to be made available to the public via PMC no later than 12 months after initial publication. Other articles that serve as the basis for investigative reading questions were originally published by choice of the authors in an Open Access format. That is, some publishers routinely restrict access to newly published material to subscription holders but give authors the option of paying an Open Access fee to make their articles immediately available to all.

TEACHING USING THE PRIMARY LITERATURE AND INVESTIGATIVE READING QUESTIONS TO COMPLEMENT THE TEXT

Many neuroscience instructors introduce primary literature into their undergraduate classes, but the fact that this practice is common does not mean that it is easy for either instructor or student. My own teaching of the primary literature has been heavily influenced by the C.R.E.A.T.E. method developed by Sally Hoskins and colleagues. C.R.E.A.T.E. stands for **C**onsider, **R**ead, **E**lucidate the hypotheses, **A**nalyze and interpret the data, and **T**hink of the next **E**xperiment. This method has been described in several journal articles, and useful sample teaching modules are available on the C.R.E.A.T.E. Web site (www.teachcreate.org). Another effective approach modifies the familiar journal club format to teach undergraduates a systematic method for reading primary literature. A method to accomplish this, described by Katherine Robertson (2012), can be incorporated into existing courses and takes about four class sessions to complete.

Teaching References

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Developmental Neuroscience

CONTENTS

List of Illustrations xi
Preface xv
Acknowledgments xix
What Are Investigative Reading Questions? xxi
Teaching Using the Primary Literature and Investigative Reading Questions to Complement the Text xxiii

Chapter 1 **Introduction**
What Do We Mean When We Say "Neural Development"? 1
What Is in This Book and How to Use It 1
Methods for Studying Development of the Nervous System 3
Human Brain Imaging 17
The Future 19
Notes 20
Investigative Reading 20

Chapter 2 **Overview of Nervous System Development in Humans**
How Do We Know What We Know? 23
Start by Working Backward 24
The Carnegie Stages of Embryonic Development 26
Development of the Fetal Brain 31
Neural Tube Defects 33
Notes 34
Investigative Reading 35

Chapter 3 **Animal Models**
Model Organisms 37
Some Helpful Concepts for Thinking about Animal Models 38
Practical Considerations 40
The Mouse, *Mus musculus* 41
The Zebrafish, *Danio rerio* 44
The Fruit Fly, *Drosophila melanogaster* 48
The Nematode Worm, *Caenorhabditis elegans* 52

Typical Neurons 55
Gray Matter and White Matter 57
Phylogenetic Relationships 57
Notes 60
Investigative Reading 61

Chapter 4 **Early Events**

Axis Determination and Neural Induction 63
Defining *Anterior* and Making a Head 63
Neural Induction 74
Notes 77
Investigative Reading 79

Chapter 5 **Neurogenesis**

Production of Neurons by Neural Progenitors 81
Neurogenesis in *C. elegans* 83
Neurogenesis in *Drosophila* 88
Neurogenesis in Zebrafish 97
Neurogenesis in the Mouse 99
Neurogenesis in Humans 106
Adult Neurogenesis 110
Notes 116
Investigative Reading 118

Chapter 6 **Later Events**

Not All Animals Are Segmented 121
Regionalization in the *Drosophila* Nervous System 121
Regionalization in the Vertebrate Nervous System 128
Histogenesis of the Mammalian Cortex 135
Notes 140
Investigative Reading 141

Chapter 7 **Becoming a Neuron**

Axons, Dendrites, and the Formation of Synapses 143
The Decision to Grow a Process 145
Microtubules, Actin, and Growth Cones 147
Axon Path Finding 152
Synaptogenesis 160
Notes 164
Investigative Reading 166

Chapter 8 **Glia**

Glia and Neurons 169
Glia in *C. elegans* 170

Glia in *Drosophila* 171
Glia in Zebrafish 176
Glia in Mice 179
Glia in Humans 189
Fruit Flies and Glioblastoma 192
Notes 194
Investigative Reading 195

Chapter 9 **Maturation**
Growing Up 197
Metamorphosis 197
Adolescence 206
Summary 209
Notes 210
Investigative Reading 211

Chapter 10 **Thinking about Intellectual Disability in the Context of Development**
Neuroscience and Intellectual Disability 213
Perturbations of Neuronal Migration 215
Dendritic Abnormalities 219
Neonatal Hypothyroidism 221
Rett Syndrome 222
Fragile X Syndrome 225
Down Syndrome 228
Fetal Alcohol Syndrome 231
Nonmammalian Models 234
Reality Check 237
Notes 238
Investigative Reading 239

Abbreviations 241
References 251
Online Resources 271
Full Citations for Investigative Reading Exercises 277
Index 281

ILLUSTRATIONS

1.1 Determining neuronal birthdates by immunodetection of BrdU 5
1.2 Use of the Cre-*LoxP* system for cell lineage tracing 8
1.3 Use of immunolabeling to study neuronal gene expression 12
1.4 Use of real-time qRT-PCR to study neuronal gene expression 14
1.5 Use of in situ hybridization to study neuronal gene expression 16

2.1 Organization of the human nervous system 25
2.2 Early stages of development of the human embryo 27
2.3 Origins of human embryonic tissues 28
2.4 The neural tube of the human embryo 30
2.5 Vertebrate rhombomeres 32
2.6 Origins of neural tube defects in humans 34

3.1 Comparison of forward and reverse genetics 40
3.2 The egg cylinder stage of mouse embryonic development 43
3.3 Early development of zebrafish embryos 47
3.4 External view of development of *Drosophila* embryos 50
3.5 Larval and adult central nervous system of *Drosophila* 51
3.6 Life cycle of *C. elegans* 54
3.7 Nervous system of *C. elegans* 55
3.8 Typical neurons 56
3.9 Animal phylogeny 59

4.1 Development of asymmetry in the *C. elegans* oocyte 65
4.2 Polarization of the *Drosophila* oocyte 65
4.3 Wnt, β-catenin, and Bmp signaling pathways 69
4.4 Retinoic acid action in zebrafish embryos 71
4.5 Default model of neural induction in vertebrates 76

5.1 Eukaryotic cell cycle 82
5.2 V ectoblast lineages in *C. elegans* 84
5.3 bHLH proteins 85

5.4 Neurogenesis in tail of *C. elegans* males 87
5.5 A chordotonal organ in *Drosophila* 89
5.6 Bristles in *Drosophila* 91
5.7 Notch signaling 92
5.8 Neuroblast ablation in grasshopper embryos 94
5.9 Asymmetrical partitioning of Numb in the lineage of *Drosophila* bristle sensory organs 96
5.10 Misexpression of neurogenin1 (*ngn1*) in zebrafish embryos 98
5.11 Histogenesis of the mouse cortex 103
5.12 Radial glial cells in the developing mouse cortex 105
5.13 The outer subventricular zone (OSVZ) of humans 108
5.14 Adult neurogenesis in the mouse brain 113
5.15 The subventricular zone (SVZ) of the adult mouse brain 114

6.1 Expression of segmentation genes in *Drosophila* embryos 123
6.2 Parasegments in *Drosophila* embryos 124
6.3 The *Antennapedia* and *bithorax* complexes in *Drosophila* 127
6.4 Organization of the vertebrate spinal cord 129
6.5 Sources of Shh and Bmps in the neural tube 132
6.6 Rhombomeres in the hindbrain of a 9.5 dpc mouse embryo 133
6.7 Structure of the mammalian neocortex 137

7.1 The polarized structure of neurons 144
7.2 Regulation of the stability of β-catenin by Wnt 146
7.3 Structure of microtubules 148
7.4 Actin filaments 149
7.5 Example of a multipolar sensory neuron associated with the body wall of larval *Drosophila* 152
7.6 Outgrowth of PDE neurons in *C. elegans* 154
7.7 Outgrowth of commissural axons in the developing vertebrate spinal cord 155
7.8 Reduction of the ventral commissure in netrin-1-deficient animals 156
7.9 Expression of fasciclinI and fasciclinII by developing interneurons in the segmental ganglia of insect embryos 157
7.10 Agrin, MuSK, and Lrp4 at the vertebrate neuromuscular junction 161
7.11 Ephrin-EphB signaling in hippocampal neurons 163

8.1 Amphid sensory organ of *C. elegans* 171
8.2 Glial cell requirement for wild-type intracellular calcium responses in *C. elegans* amphid sensory neurons 172
8.3 Distribution of the major categories of *Drosophila* glia in the embryonic ventral nerve cord 172
8.4 Septate junction in a *Drosophila* nerve 174