

Contents

Contributors

xvii

Part I

Formation of axons and dendrites

1. Development of neuronal polarity in vivo

F. Polleux

1.1 Introduction	3
1.2 Axon initiation in vitro versus in vivo	4
1.2.1 Axon initiation in vitro	4
1.2.2 Axon initiation in vivo	5
1.3 Distinction between cues regulating axon specification versus axon growth	5
1.4 Extracellular cues regulating neuronal polarization and axon initiation	6
1.4.1 Netrin-1 and Wnt control axon initiation in <i>Caenorhabditis elegans</i>	6
1.4.2 Polarized emergence of the axon in retinal ganglion cells of <i>Xenopus</i>	6
1.4.3 Extracellular cues underlying the emergence of axon and dendrites in mammalian neurons	7
1.5 Intracellular pathways underlying neuronal polarization	8
1.5.1 Role of protein degradation and local translation in axon specification and axon growth	8
1.5.2 Role of cytoskeletal dynamics in axon initiation and growth	9
1.5.3 Major signaling pathways involved in axon initiation and growth	10
1.6 Conclusion and future directions	15
References	16

2. Role of the cytoskeleton and membrane trafficking in axon—dendrite morphogenesis

Kevin C. Flynn and Frank Bradke

2.1 Introduction	21
------------------	----

2.2 Developmental stages	23
2.3 Role of cytoskeleton in establishment of neuronal polarity	24
2.3.1 Actin	24
2.3.2 Actin dynamics during axon formation	27
2.3.3 Microtubules	30
2.3.4 Microtubules dynamics during axon formation	32
2.3.5 Cytoskeletal dynamics during dendritic growth and arborization	35
2.3.6 Subcellular cytoskeletal specializations	37
2.4 The role of (membrane) trafficking during neuronal polarization	39
2.4.1 Trafficking during early neuronal development	39
2.4.2 Motor protein—based transport in axons and dendrites	40
2.4.3 The secretory and endosomal pathway	43
2.4.4 RNA transport and local translation	44
2.4.5 Barriers for the segregation of functional domains	45
2.4.6 Protein stabilization and degradation	46
2.5 Maintaining neuronal polarity	46
2.6 Future work on neuronal morphogenesis	47
References	48

3. Axon growth and branching

Le Ma and Stephen R. Tymanskyj

3.1 Introduction	57
3.2 Cell biological mechanisms	58
3.2.1 Growth cones: structure and function	58
3.2.2 Regulation of cytoskeleton assembly	58
3.2.3 Interaction between F-actin and microtubules	62
3.2.4 Membrane trafficking and axonal transport	63
3.2.5 Protein translation and stability	64

3.3 Extracellular regulation of axon growth and branching during neural development	65	5. Axon guidance: semaphorin/neuropilin/plexin signaling	
3.3.1 Nerve growth factor and neurotrophic factors	65	Marieke G. Verhagen and R. Jeroen Pasterkamp	
3.3.2 Guidance molecules: netrin, slit, semaphorin, ephrin, and wnt	66	5.1 Introduction	109
3.3.3 Cell adhesion molecules: permissive or instructive	68	5.2 Structural features	111
3.3.4 Glial cells and myelination	69	5.3 Mechanisms of intracellular signaling	113
3.3.5 Neural activity	70	5.4 Function in neural circuit development	115
3.3.6 Additional axon branching molecules	71	5.5 Semaphorins, plexins, and neuropilins in neurological disorders	116
3.4 Intracellular signaling mechanisms that mediate axon growth and branching	71	5.5.1 Autism spectrum disorder	116
3.4.1 Rho family small GTPases: linking receptors to the cytoskeleton	71	5.5.2 Kallmann's syndrome	116
3.4.2 Calcium	72	5.5.3 Amyotrophic lateral sclerosis	117
3.4.3 Cyclic nucleotides as second messengers and modulators	72	5.5.4 Late-onset neurodegenerative diseases	117
3.5 Concluding remarks	73	5.6 Conclusions and perspectives	117
References	73	References	118
4. Axon guidance: Netrins		6. Ephrin/Eph signaling in axon guidance	
Marc Tessier-Lavigne		Franco Weth and Artur Kania	
4.1 Introduction	87	Abbreviations	123
4.2 Netrins and their receptors	88	6.1 The setting of the play	124
4.2.1 Netrin discovery and structure	88	6.1.1 Ephs and ephrins	124
4.2.2 Netrin receptors	89	6.1.2 Rules of interaction	124
4.2.3 Interactions with other signaling systems	89	6.1.3 Fundamental action modes	125
4.2.4 Netrin functional domains and interactions with receptors	92	6.1.4 Phylogeny	125
4.3 Netrin function in axon guidance and cell migration	92	6.2 Mechanisms of ephrin/Eph signaling in axon guidance	126
4.3.1 Mammalian spinal cord	92	6.2.1 Biophysical aspects	126
4.3.2 Mammalian hindbrain	95	6.2.2 Biochemical aspects	128
4.3.3 Guidance of other classes of mammalian axons and cells: attraction, repulsion, and modulation	96	6.3 Ephrins and Ephs in invertebrate axon guidance	131
4.3.4 Invertebrate systems	97	6.3.1 <i>Caenorhabditis elegans</i>	131
4.4 Beyond axon and cell guidance: additional roles for Netrins in the nervous system	99	6.3.2 Insects	132
4.5 Involvement of Netrin signaling in disorders of the nervous system	99	6.4 Binary ephrin/Eph signaling—pathfinding	132
4.6 Netrins: players outside the nervous system	100	6.4.1 Peripheral pathfinding—limb bud innervation	132
4.7 Conclusion	101	6.4.2 Pathfinding in the spinal cord	134
References	102	6.4.3 Pathfinding in the brain stem—auditory system	135
		6.4.4 Central pathfinding	135
		6.5 Proportional ephrin/Eph signaling—mapping	136
		6.5.1 Olfactory wiring	136
		6.5.2 Retinotectal/retinocollicular projection	136
		6.5.3 Retinogeniculate projections	139
		6.5.4 Thalamocortical projections	139
		6.5.5 Corticocollicular projections	140
		6.6 Ephrins and Ephs in regeneration	140

6.7 Perspectives and open questions—"curtain down and nothing settled"	140	8.2 Sonic hedgehog in axon guidance	176
Acknowledgments	141	8.2.1 Canonical Shh signaling	176
References	141	8.2.2 Shh is a chemoattractant for spinal cord commissural axons	178
7. Axon guidance: Slit–Robo signaling		8.2.3 Shh binding to Boc attracts commissural axons through a noncanonical signaling pathway to modulate the growth cone cytoskeleton	179
<i>Katrine Iversen, François Beaubien, Janet E.A. Prince and Jean-François Cloutier</i>		8.2.4 Shh guides axons along the longitudinal axis of the spinal cord	180
7.1 Introduction	147	8.2.5 14-3-3 proteins regulate a cell-intrinsic switch from Shh-mediated attraction to repulsion of commissural axons after midline crossing	180
7.2 Slits and their receptors	147	8.2.6 Shh guides contralateral and ipsilateral retinal ganglion cell axons	181
7.2.1 Slit discovery and structure	147	8.2.7 Shh is a chemoattractant for midbrain dopaminergic axons	182
7.2.2 Identification of the slit receptor robo	148	8.2.8 Shh binding to Gas1 repels enteric axons	182
7.2.3 Slit and Robo interactions	149	8.3 TGF-β superfamily members in axon guidance	183
7.3 Slit–Robo function in midline crossing	150	8.3.1 Canonical bone morphogenetic protein signaling	183
7.3.1 Spatial expression patterns of Slit and Robo	152	8.3.2 BMP7:GDF7 repels spinal cord commissural axons	183
7.3.2 Posttranscriptional Robo regulation	152	8.4 Wnts in axon guidance	184
7.3.3 Regulation of Robo protein expression at the midline	152	8.4.1 Canonical and noncanonical Wnt signaling	184
7.3.4 Regulation of Robo signaling at the midline in vertebrates	154	8.4.2 Wnt5 repels commissural axons from the <i>Drosophila</i> posterior commissure via derailed, a Ryk tyrosine kinase family member	186
7.3.5 Slit–Robo signaling for exiting the midline	155	8.4.3 Wnt5, complexed with derailed, repels <i>Drosophila</i> mushroom body axons	187
7.4 Modulation of Slit–Robo signaling	155	8.4.4 Wnt binding to Ryk repels axons of the corticospinal tract and corpus callosum through a Ca^{2+} -dependent mechanism	187
7.4.1 Transcriptional control	155	8.4.5 Wnt binding to Fz attracts postcrossing commissural axons via protein kinase C ζ and planar cell polarity signaling	188
7.4.2 Regulation of Slit–Robo signaling by metalloprotease cleavage	156	8.4.6 Wnt binding to Fz regulates dopaminergic axon guidance through planar cell polarity signaling	189
7.4.3 Regulation of Slit–Robo signaling by ubiquitination	157	8.4.7 Wnt3 mediates mediolateral retinotectal topographic mapping	190
7.5 Signaling downstream of Robo	157	8.4.8 Wnts guide axons of <i>Caenorhabditis elegans</i> mechanosensory neurons and D-type motoneurons via Fz-type receptors	190
7.5.1 Rho family of small GTPases	158		
7.5.2 Abelson tyrosine kinase	158		
7.5.3 Actin-interacting proteins	159		
7.6 Beyond the midline: additional roles for Slit–Robo in the nervous system	159		
7.6.1 Lateral positioning	159		
7.6.2 Cell migration and cell polarity	160		
7.6.3 Dendritic and axonal outgrowth and branching	161		
7.7 Slit–Robo contribution to axon targeting in a complex target field	162		
7.8 Involvement of Slit–Robo in disorders of the nervous system	164		
7.9 Conclusion	164		
References	165		
8. Nonconventional axon guidance cues: Hedgehog, TGF-β/BMP, and Wnts in axon guidance			
<i>Patricia T. Yam and Frédéric Charron</i>			
8.1 Introduction	176		
8.1.1 Morphogens as axon guidance cues	176		

8.4.9	The Wnt ligand CWN2 regulates <i>Caenorhabditis elegans</i> motor neuron axon guidance through a Ror-type receptor CAM-1	192
8.5	Cross-talk between axon guidance cues	192
8.5.1	Shh induces the response of commissural axons to semaphorin repulsion during midline crossing	192
8.5.2	Shh regulates Wnt signaling in postcrossing commissural axons	193
8.5.3	The TGF- β family member unc-129 regulates Unc6/Netrin signaling in <i>Caenorhabditis elegans</i>	193
8.6	Conclusions and perspectives	193
	List of Acronyms and Abbreviations	194
	Glossary	195
	Acknowledgments	195
	References	196

9. Axon regeneration

R.J. Giger

9.1	Introduction	201
9.2	Anatomy of the spinal cord	202
9.3	Spinal cord injury repair: a complex problem	202
9.4	Axon regeneration in the injured central nervous system versus peripheral nervous system	203
9.4.1	Intrinsic mechanisms of dorsal root ganglion neuron axon regeneration	203
9.5	Extrinsic mechanisms: inhibitors of central nervous system axon regeneration	204
9.6	Extrinsic mechanisms: growth factors	205
9.6.1	The anatomical substrate of neurorepair	206
9.7	Axon regeneration in the retinofugal system	207
9.8	Lessons learned from an evolutionary perspective	208
9.8.1	Immune-mediated neurorepair mechanisms	208
9.9	Conclusions	209
	Acknowledgments	210
	References	210

10. Axon maintenance and degeneration

Fan Wang, Jing Yang and Zhigang He

10.1	Introduction	217
10.2	Essentials of axonal transport in axon maintenance	218

10.2.1	Cellular components that are transported along the axons	218
10.2.2	Regulations of microtubule stability and organization during axon maintenance	220
10.2.3	Defects in motor proteins cause axon degeneration	221
10.2.4	Role of mitochondria transport in axon maintenance	221
10.2.5	Membrane transport and insertion are essential for axon maintenance	222
10.3	Proteasome and autophagy pathways in axonal homeostasis	223
10.3.1	Ubiquitin-proteasome system in axon maintenance	223
10.3.2	Role of autophagy/lysosome pathway in maintaining axonal homeostasis	223
10.4	Role of glial cells in axon maintenance	224
10.5	Maintaining axon track positions and other structural features	224
10.6	Axon pruning and axon degeneration	225
10.6.1	Developmental axon pruning	225
10.6.2	Pathological axon degeneration	227
10.6.3	Molecular mechanisms of pathological axon degeneration	227
	References	229

11. Dendrite development: invertebrates

Wesley B. Grueber and Bing Ye

11.1	Structure and anatomy of invertebrate dendrites	232
11.2	Methods for studying dendrite morphology in <i>Drosophila</i>	232
11.3	Anatomical background for key model systems in which dendritic morphogenesis is studied in invertebrates	233
11.3.1	<i>Drosophila</i> dendritic arborization sensory neurons	233
11.3.2	<i>Drosophila</i> motoneurons	233
11.3.3	<i>Drosophila</i> olfactory projection neurons	233
11.3.4	<i>Caenorhabditis elegans</i> PVD neurons	234
11.4	Cell biology of dendritic growth	235
11.4.1	Microtubule polarity differs between dendrites and axons	235
11.4.2	Dynein-dependent trafficking controls dendritic branching	235

12.5.2	Laminar targeting of retinal dendrites is coordinated by adhesive and repellent cues	269	13.2.4	Transformation from multipolar migrating neurons to bipolar locomoting neurons	293
12.5.3	Transcriptional control of laminar-specific targeting of dendrites in retina	271	13.2.5	Departure from the ventricular zone: differences in migratory behavior between direct progeny of the apical progenitors in the VZ and the basal progenitors in the subventricular zone / intermediate zone	294
12.5.4	Local recognition mechanisms to control synapse selectivity	273	13.2.6	Behaviors of the progenitor cells in the subventricular zone	296
12.5.5	An integrated, multistep model for synaptic wiring in the retina IPL	273	13.3	Molecular mechanisms that regulate the initiation of migration and cell polarity during migration	297
12.6	Space-filling mechanisms to optimize dendritic field distribution	273	13.3.1	Coupling between neuronal differentiation and migration	298
12.6.1	Tiling and mosaics	273	13.3.2	Controlling the initiation of radial migration	299
12.6.2	Dendrite self-avoidance	275	13.3.3	Regulation of multipolar migration	299
12.7	Emergence of dendrite compartmentalization	277	13.3.4	Extracellular molecules that affect migrating cells	301
12.7.1	Subcellular patterning of synaptic inputs along dendritic domains	277	13.4	Conclusion	301
12.7.2	Patterning the membrane excitability of dendritic compartments	278		List of abbreviations	301
12.8	Neurodevelopmental disorders: the price of poor dendritic development?	278		Glossary	302
12.9	Conclusion	279		Supplementary data	302
	Abbreviations	279		References	302
	Acknowledgments	280			
	References	280			

Part II Migration

13. Cell polarity and initiation of migration

K. Hayashi, K. Sekine, H. Tabata and K. Nakajima

13.1	Introduction	289
13.2	Migratory behaviors during radial migration in the developing cerebral cortex	290
13.2.1	Bipolar migrating neurons along the radial glial fibers: locomotion	290
13.2.2	Radial glial fiber-independent mode of migration: somal translocation and terminal translocation	290
13.2.3	Multipolar migration	292

14. Nucleokinesis

Only Reiner and Eyal Karzbrun

14.1	Nucleokinesis: introduction	305
14.2	The nucleus	305
14.2.1	The nuclear membrane and nuclear pores	305
14.3	Chromatin	306
14.4	Membraneless organelles in the nucleus	307
14.5	Higher order structure of the nucleus	307
14.6	Diseases	308
14.6.1	Cohesinopathies	308
14.6.2	Affecting the nuclear envelope	309
14.7	Interactions between the nucleus and the cytoskeleton	310
14.7.1	The LINC complex, structure	310
14.8	The LINC complex, function	311
14.9	The LINC complex in nuclear positioning	311
14.10	The link between the nucleus and the centrosome	311

14.11	The LINC complex in nucleokinesis	312	16.2	Molecular cues drawing the path of cortical interneuron migration	347
14.12	Nucleokinesis during interkinetic nuclear movement	312	16.3	Molecular cues controlling the integration of interneurons into the cortical migratory streams	348
14.13	Microtubule binding motors	312	16.4	Molecular cues controlling the intracortical dispersion of interneurons	349
14.13.1	Dynein	313	16.5	Signals dictating the arrest of interneuron migration within the cortical wall	350
14.13.2	Kinesin Kif1a	314	16.6	Role of subpallial transcription factors in the tangential migration of interneurons into the cortex	350
14.14	Cytoskeleton dynamics as nuclear drivers	314	16.7	Cell-intrinsic regulation of cortical interneuron migration	351
14.15	Collective mechanisms for nuclear migration	314	16.8	Dynamic remodeling of the cytoskeleton during interneuron migration	352
14.15.1	Intercellular signaling	314	16.9	Regulation of the tangential migration of interneurons in the rostral migratory stream to the olfactory bulb	352
14.15.2	Mechanical interactions	315	16.10	Molecular regulation of the migration of striatal interneurons	353
14.16	The role of INM during neurodevelopment	315	16.11	Evolutionary perspective of the tangential migration	354
14.17	INM summary	315	16.12	Conclusions and perspectives	354
14.18	Conclusions and future directions	316		List of acronyms and abbreviations	355
	Acknowledgments	316		References	356
	References	316			
15.	Radial migration in the developing cerebral cortex		17.	Migration in the hippocampus	
	<i>Stephen C. Noctor, Christopher L. Cunningham and Arnold R. Kriegstein</i>			<i>Hirofumi Noguchi, Guangnan Li and Samuel J. Pleasure</i>	
15.1	Introduction	323	17.1	Overview of hippocampal structure and lamination	365
15.2	Production of cortical projection neurons	324	17.1.1	Terminology important for studying hippocampal structure	365
15.3	Organization of the neocortex	326	17.2	Developmental specification of hippocampal fields	366
15.4	Trajectory of migrating neurons in the developing brain	326	17.2.1	The basic developmental scheme of the hippocampus	366
15.5	Modes of migration	328	17.2.2	The cortical hem	366
15.6	Radial migration in the developing human neocortex	330	17.2.3	The cortical hem organizes the hippocampal fields	366
15.7	Factors that regulate the radial migration of cortical neurons	330	17.2.4	The role of canonical Wnt signaling in hippocampal development	367
15.7.1	Secreted molecules	330	17.3	Migration of Cajal–Retzius cells in the hippocampus	367
15.7.2	Neurotransmitters	331	17.3.1	What are Cajal–Retzius cells?	367
15.7.3	Adhesion molecules	332			
15.7.4	Cytoskeletal regulators	333			
15.7.5	Transcription factors	335			
15.8	Summary	336			
	References	337			
16.	Mechanisms of tangential migration of interneurons in the developing forebrain				
	<i>Fanny Lepiemme, Carla Silva G. and Laurent Nguyen</i>				
16.1	Birth of distinct interneuron subtypes and onset of their migration from the subpallium	345			

17.3.2	What are the functions of Cajal–Retzius cells?	367
17.3.3	What are the origins of Cajal–Retzius cells?	367
17.3.4	The cortical hem is the major source of Cajal–Retzius cells for the dorsal telencephalon	368
17.3.5	The extent of the cortex covered by hem-derived Cajal–Retzius cells	368
17.3.6	Recruitment of hem-derived Cajal–Retzius cells to the meninges	368
17.3.7	Tangential dispersion of Cajal–Retzius cells in the marginal zone	368
17.4	Migration of hippocampal pyramidal neurons	369
17.5	Migration of hippocampal interneurons	370
17.5.1	Cellular and distributional diversity of interneurons in the hippocampus	370
17.5.2	Origins and migration of hippocampal interneurons	370
17.6	Migration of neural progenitors and granule cells in the dentate gyrus during development	372
17.6.1	The basic developmental scheme of the dentate gyrus	372
17.6.2	Migration of granule neurons to form the granule cell layer	373
17.6.3	Emergence and migration of long-lived neural stem cells and establishment of subgranular zone	374
17.7	Conclusions	375
	References	375

18. Hindbrain tangential migration

Constantino Sotelo and Alain Chédotal

18.1	Introduction	381
18.2	Tangential migration: a historical overview	382
18.3	Molecular mechanisms controlling the tangential migration of precerebellar neurons	384
18.3.1	Influence of the midline on tangentially migrating precerebellar neurons	384
18.3.2	Why do PCN neurons migrate near the pial surface?	388

18.4	Molecular mechanisms controlling the tangential migration of facial motor neurons	389
18.4.1	Origin and migration of facial motor neurons	389
18.4.2	The caudal migration of FBM neurons	390
18.4.3	Role of chemoattraction and chemorepulsion	392
18.4.4	Role of the meninges in the tangential migration of FBM neurons	393
18.5	Ending tangential migration	394
18.6	Conclusion	395
	Acknowledgments	395
	References	395

19. Neuronal migration in the developing cerebellar system

Christophe Laumonnier and David J. Solecki

19.1	Introduction	403
19.1.1	Part I. Diverse migration pathways and guidance cues during cerebellar system development	405
19.1.2	Part II. The cytoskeletal organization of cerebellar granule neurons	411
19.1.3	Part III. The facets of cerebellar granule neuron polarity: timing cell recognition, differentiation, germinal zone exit, and morphogenesis	420
19.1.4	Part IV. Migration deficits in cerebellar medulloblastomas: the effects of perturbed migration pathways are no longer limited to cognitive deficiency	424
	Acknowledgments	427
	References	427

20. Neuronal migration of guidepost cells

Franck Bielle and Sonia Garel

	Chapters cited	435
20.1	An introduction to guidepost cells	436
20.1.1	Neuronal migration in the context of axonal tracts formation	436

20.1.2	Defining the notion of guidepost cells	436	20.5.2	Roles of glial cells in the development of the corpus callosum	447
20.2	Role of neuronal migration in the formation of the lateral olfactory tract	437	20.5.3	Tangentially migrating neurons in the development of the corpus callosum	448
20.2.1	Anatomy and development of the lateral olfactory tract	437	20.6	Neuronal migration of guidepost cells and evolution of brain wiring	449
20.2.2	Diffusible guidance cues in the pathfinding of lateral olfactory tract axons	438	20.6.1	Tangential migration of guidepost neurons: a hallmark of the telencephalon?	449
20.2.3	Roles of guidepost "lot cells"	439	20.6.2	Neuronal migration of guidepost cells in the evolution of the internal capsule	450
20.2.4	Tangential migration of lot cells: specification, routes, and molecular mechanisms	439	20.7	Towards an integration of migrating guidepost neurons in normal and pathological brain development	451
20.2.5	Fate of lot cells	440	20.7.1	Guidepost neurons in the shaping of axonal tract organization and topography	451
20.3	Hippocampal Cajal–retzius cells in the formation of axonal connections	440	20.7.2	Integrating tangential neuronal migration of guideposts in normal and pathological brain development	452
20.3.1	Anatomy and development of the hippocampus and entorhinohippocampal projections	440	20.8	Conclusions	452
20.3.2	Cajal–Retzius cells as putative guidepost neurons for the formation of entorhinal projections	440	References	453	
20.3.3	Toward a more generic role of Cajal–Retzius cells as guideposts?	442	21. Neuronal migration in the postnatal brain		
20.4	Migration of neuronal guidepost cells in the formation of thalamocortical connections	442	<i>Masato Sawada and Kazunobu Sawamoto</i>		
20.4.1	Anatomy and development of thalamocortical and corticofugal axons	442	21.1	Introduction	465
20.4.2	Pioneer cortical subplate axons in the pathfinding of thalamocortical projections	443	21.2	Regulation of neuronal migration in the normal brain	466
20.4.3	Origin and migration of subplate neurons	444	21.2.1	Migratory scaffolds	466
20.4.4	The subpallium is a major intermediate target for thalamocortical axons	444	21.2.2	Directional control from the V-SVZ toward the OB	469
20.4.5	Guidepost cells in the diencephalic and subpallial pathfinding of thalamocortical projections	445	21.2.3	Migration termination in the OB	470
20.4.6	Migration of guidepost corridor cells: routes and guidance cues	446	21.3	Regulation of neuronal migration in the injured brain	470
20.4.7	Fate of guidepost cells for thalamocortical projections	447	21.3.1	Migratory scaffolds in the injured brain	470
20.5	Neuronal migration of guidepost cells in the formation of the corpus callosum	447	21.3.2	Directional control toward a lesion	472
20.5.1	Anatomy and development of the corpus callosum	447	21.3.3	Enhancement of neuronal migration as a strategy for endogenous neuronal regeneration	473
			21.4	Postnatal neuronal migration in primates	473
			21.5	Summary	474
			References	474	

22. Transcriptional and posttranscriptional mechanisms of neuronal migration

Zeljka Krsnik, Tatiana Popovitchenko and Mladen-Roko Rasin

22.1	Introduction to neuronal migration	479
22.1.1	Different ways to migrate: "I did it my way"	480
22.2	Transcriptional and posttranscriptional control of neuronal migration	480
22.2.1	Radial migration	480
22.2.2	Tangential migration: transcriptional and posttranscriptional control	495
22.3	Conclusion and future directions	503
	List of acronyms and abbreviations	503
	References	503

23. Migration of myelin-forming cells in the CNS

Fernando de Castro and Bernard Zalc

23.1	Introduction	515
23.1.1	Genesis of myelin-producing cells during development	516
23.1.2	Oligodendrocyte precursor cells: born to migrate	517
23.2	Migratory paths followed by oligodendrocyte progenitor and precursor cells	518
23.3	Chemokinetic factors: the motility of oligodendrocyte precursors	518
23.4	Adhesion and chemotactic mechanisms: how the movement of oligodendrocyte precursors is guided?	519
23.4.1	Adhesion and surface molecules	519
23.4.2	Secreted factors	521
23.5	Concluding remarks	524
	Acknowledgments	524
	References	524

24. Coordination of different modes of neuronal migration and functional organization of the cerebral cortex

Holden Higginbotham

24.1	Introduction	531
24.1.1	Arealization of the cortex	531
24.1.2	Cortical columns constitute cortical areas	532
24.1.3	Minicolumns constitute columns	532

24.2 Migration of related projection neurons into the same minicolumn

24.2.1	Early lack of evidence that sister projection neurons migrate into the same minicolumn	534
24.2.2	Sister projection neurons migrate into the same minicolumn and intersynapse	535

24.3 Integration of projection neurons into cortical minicolumns

24.3.1	Migratory scaffolds restrict tangential movement of projection neurons	535
24.3.2	Molecular signaling limits tangential movement of projection neurons during multipolar stage	537

24.4 Integration of interneurons into cortical columns

24.4.1	Interneuron subtypes areally distribute via tangential migration	538
24.4.2	Do sister interneurons migrate into the same minicolumn?	540
24.4.3	Sister interneurons preferentially intersynapse	540
24.4.4	Regulating the timing of the shift from tangential to radial migration	541
24.4.5	Projection neurons attract migrating interneurons into cortical plate	542
24.4.6	Radial glial cells trigger a shift in migration mode	543

24.5 Genetic and cellular mechanisms controlling shifts in migratory modes

24.6	Conclusion	544
	List of abbreviations	545
	References	545

25. The impact of different modes of neuronal migration on brain evolution

Fernando García-Moreno and Zoltán Molnár

25.1	Types of neuronal migration in vertebrate brain development—radial and tangential migration shaping vertebrate brains	555
25.2	The impact of radial migration on brain evolution	557
25.2.1	Evolution of radial migration	557

25.2.2	Radial migration on laminar brains	557
25.2.3	Radial migration on elaborated brains	559
25.2.4	The influence of radial migration on pallial internal circuitry	560
25.3	The impact of tangential migration on brain evolution	563
25.3.1	Pallial interneurons and the modulation of brain circuits	565
25.3.2	Glutamatergic tangential contributions as developmental scaffolds	567
25.3.3	Tangential migration shaping brain connections—guidepost neurons in evolution	570
25.3.4	Tangential migrations along the central nervous system	571
25.4	Conclusions	572
	Glossary	572
	References	572

26. Neuronal migration disorders

Joseph J. LoTurco and Jean-Bernard Manent

26.1	Introduction	577
26.2	Types of malformations	578
26.2.1	Pachygyria	578
26.2.2	Lissencephaly	578
26.2.3	Cobblestone lissencephaly	579
26.2.4	Subcortical band heterotopia	579
26.2.5	Periventricular heterotopia	579

26.2.6	Polymicrogyria	579
26.2.7	Mammalian target of rapamycin complex pathway—related malformations	580
26.2.8	Microcephaly	580
26.3	Identified mutations and mechanisms in neuronal migration disorder	580
26.3.1	Mutations in microtubule-associated proteins (LIS1, DCX, KIF5C, KIF2A, DYNC1H1, and EML1)	580
26.3.2	Tubulin mutations (TUBA1A, TUBB2B, TUBB3, TUBG1, TUBA8, and TUBB5)	581
26.3.3	Periventricular heterotopia and mutations in FLNA, ARFGEF2, C6orf70, FAT4, DCHS1, and MOB2	582
26.3.4	Variant lissencephalies and mutations in ARX and RELN	583
26.3.5	Cobblestone malformations and mutations in dystroglycan genes	584
26.3.6	Focal cortical dysplasias and dysplastic megalencephaly and mutations in mTOR, PIK3CA, DEPDC5, AKT3, NPRL3, and PIK3R2	584
26.4	Summary and concluding remarks	585
	References	585

Index	589
--------------	-----