
Contents

<i>Preface</i>	<i>xi</i>
<i>Abbreviations</i>	<i>xii</i>
1 Introduction	1
What are growth cones?	1
Growth cone morphology and behaviour	3
Appearance and behaviour under the light microscope	4
Methodological advances	12
Factors influencing growth cone shape	15
Decision regions	17
Fasciculation	19
Developmental age and type of substratum	19
Growth cone collapse/contact inhibition	20
Leader (pioneer) and follower growth cones	21
Appearance under the electron microscope: organelles of the growth cone	21
Membrane-bounded organelles	22
Cytoskeletal elements	26
Axonal versus dendritic growth cones	27
2 Motility and Neurite Extension: The Growth Cone Cytoskeleton	30
Introduction	30
	vii

viii CONTENTS

Organisation of the growth cone cytoskeleton	31
Microtubules	31
Microtubule organisation in neurites and growth cones	32
Neurite extension and microtubule dynamics	33
Location of microtubule assembly	39
Direct visualisation of microtubule dynamics	40
Post-translational modifications of tubulin	42
Assembly competent tubulin in growth cones	44
A model for the organisation of microtubules in neurites and growth cones	45
A role for microtubules in growth cone pathfinding	46
Microtubule-associated proteins	49
Microfilaments	52
Microfilament organisation in neurites and growth cones	53
Growth cone motility and actin filament dynamics	59
Do growth cones 'push' or 'pull'?	64
Differential adhesivity and growth cone pathfinding	65
Actin binding proteins	68
Neurofilaments	70
Neurite extension and surface membrane growth	71
Membrane recycling in growth cones	74
3 Pathfinding	75
Introduction	75
Decision regions and pathfinding	76
Suitable animals and appropriate techniques	78
Pathfinding is a property of growth cones	79
Guidance cues	80
Pioneers	81
How can guidance cues be identified?	86
Channels and tunnels	87
Electric fields	88
Extracellular matrix molecules	90
Laminins	93
Laminin receptors: integrins	96
Tenascins	100
Proteoglycans	102
Do extracellular matrix molecules have permissive or instructive roles in pathfinding?	102
Cell surface molecules	103
Neural cell adhesion molecule and the immunoglobulin superfamily	104
The labelled pathways hypothesis	109
Molecules mediating growth cone–cell surface interactions in invertebrates	110

	CONTENTS	ix
Fasciclins		111
Cadherins		112
Growth cone collapse and retraction		114
Collapsing factors		116
Collapsins/semaphorins		116
Collapsin/semaphorin receptors		119
Eph receptors and their ligands (ephrins)		120
Chemotropic (diffusible) factors		123
Nerve growth factor		124
Can growth cones detect chemical gradients and with what steepness?		126
Demonstration of chemotropic factors <i>in vitro</i>		126
Molecular characterisation of chemotropic factors		130
Netrins and their receptors		130
Summary		136
4 Intracellular Signalling in Growth Cones		137
Introduction		137
Calcium		139
Calcium is implicated in neurite growth		139
The calcium 'set-point' hypothesis		141
Calcium regulation in growth cones		141
Do changes in growth cone calcium regulate pathfinding events?		143
Physiological agents affecting growth cone calcium levels		144
Down-stream targets for calcium in growth cones		149
Growth cone calcium concentration and the cytoskeleton		150
Growth-associated protein 43		151
Widespread expression of GAP-43 in the developing nervous system		151
GAP-43 is a calmodulin and actin-binding phosphoprotein		152
GAP-43 regulates phosphatidylinositol-4-phosphate kinase and G protein activity		153
GAP-43 function		154
Non-receptor tyrosine kinases and phosphatases		155
Heterotrimeric G proteins, small GTP-binding proteins and GTPases		157
Rho subgroup of the Ras superfamily		158
5 Synaptogenesis		160
Introduction		160
Morphological differentiation of synapses		161
Acquisition of synaptic properties by growth cones		163
Neurotransmitter release from growth cones		163
Neurotransmitter storage in growth cones		165

x CONTENTS

Neurotransmitter receptors	165
Molecular mechanisms underlying synaptogenesis at the neuromuscular junction	166
Motoneuron growth cones release factors that induce synaptogenesis	170
Agrin induces neurotransmitter receptor aggregation at the synapse	171
MuSK and rapsyn	172
<i>References</i>	<i>174</i>
<i>Index</i>	<i>255</i>