

Contents

Preface

About the authors

Summary of contents

Reviewer acknowledgements

Figure acknowledgements

Chapter 1 History and basic concepts

■ Box 1A Basic stages of *Xenopus laevis* development

The origins of developmental biology

1.1 Aristotle first defined the problem of epigenesis and preformation

1.2 Cell theory changed the conception of embryonic development and heredity

1.3 Two main types of development were originally proposed

■ Box 1B The mitotic cell cycle

1.4 The discovery of induction showed that one group of cells could determine the development of neighboring cells

1.5 The study of development was stimulated by the coming together of genetics and development

1.6 Development is studied mainly through selected model organisms

1.7 The first developmental genes were identified as spontaneous mutations

Summary

A conceptual tool kit

1.8 Development involves the emergence of pattern, change in form, cell differentiation, and growth

■ Box 1C Germ layers

1.9 Cell behavior provides the link between gene action and developmental processes

1.10 Genes control cell behavior by specifying which proteins are made

1.11 The expression of developmental genes is under tight control

■ Box 1D Tracking gene expression in embryos

1.12 Development is progressive and the fate of cells becomes determined at different times

1.13 Inductive interactions can make cells different from each other

1.14 The response to inductive signals depends on the state of the cell

v	1.15 Patterning can involve the interpretation of positional information	25
vii	■ Box 1E Signal transduction and intracellular signaling	26
ix	1.16 Lateral inhibition can generate spacing patterns	27
xix	1.17 Localization of cytoplasmic determinants and asymmetric cell division can make daughter cells different from each other	27
xx	■ Box 1F When development goes awry	28
1	1.18 The embryo contains a generative rather than a descriptive program	29
2	1.19 The reliability of development is achieved by a variety of means	30
4	1.20 The complexity of embryonic development is due to the complexity of cells themselves	30
4	1.21 Development is intimately involved in evolution	31
5	Summary	32
6	Summary to Chapter 1	32
7		
8		
8	Chapter 2 Development of the <i>Drosophila</i> body plan	35
8	<i>Drosophila</i> life cycle and overall development	36
9	2.1 The early <i>Drosophila</i> embryo is a multinucleate syncytium	36
11	2.2 Cellularization is followed by gastrulation and segmentation	38
13	2.3 After hatching, the <i>Drosophila</i> larva develops through several larval stages, pupates, and then undergoes metamorphosis to become an adult	38
13	2.4 Many developmental genes have been identified in <i>Drosophila</i> through induced large-scale genetic screening	39
14	Setting up the body axes	40
15	2.5 The body axes are set up while the <i>Drosophila</i> embryo is still a syncytium	40
17	2.6 Maternal factors set up the body axes and direct the early stage of <i>Drosophila</i> development	41
17	■ Box 2A Mutagenesis and genetic screening strategy for identifying developmental mutants in <i>Drosophila</i>	42
19	2.7 Three classes of maternal genes specify the antero-posterior axis	43
20	2.8 Bicoid protein provides an antero-posterior gradient of a morphogen	44
21		
23		
25		

2.9 The posterior pattern is controlled by the gradients of Nanos and Caudal proteins	46	2.24 Segmentation genes stabilize parasegment boundaries and set up a focus of signaling at the boundary that patterns the segment	74
2.10 The anterior and posterior extremities of the embryo are specified by cell-surface receptor activation	47	2.25 Insect epidermal cells become individually polarized in an antero-posterior direction in the plane of the epithelium	77
2.11 The dorso-ventral polarity of the embryo is specified by localization of maternal proteins in the egg vitelline envelope	48	■ Box 2F Planar cell polarity in <i>Drosophila</i>	78
2.12 Positional information along the dorso-ventral axis is provided by the Dorsal protein	49	2.26 Some insects use different mechanisms for patterning the body plan	79
■ Box 2B The Toll signaling pathway: a multifunctional pathway	50	Summary	80
Summary	50	Specification of segment identity	81
Localization of maternal determinants during oogenesis	51	2.27 Segment identity in <i>Drosophila</i> is specified by Hox genes	81
2.13 The antero-posterior axis of the <i>Drosophila</i> egg is specified by signals from the preceding egg chamber and by interactions of the oocyte with follicle cells	52	2.28 Homeotic selector genes of the bithorax complex are responsible for diversification of the posterior segments	82
2.14 Localization of maternal mRNAs to either end of the egg depends on the reorganization of the oocyte cytoskeleton	53	2.29 The Antennapedia complex controls specification of anterior regions	84
2.15 The dorso-ventral axis of the egg is specified by movement of the oocyte nucleus followed by signaling between oocyte and follicle cells	54	2.30 The order of Hox gene expression corresponds to the order of genes along the chromosome	84
Summary	56	2.31 The <i>Drosophila</i> head region is specified by genes other than the Hox genes	85
Patterning the early embryo	56	Summary	85
2.16 The antero-posterior axis is divided up into broad regions by gap-gene expression	57	Summary to Chapter 2	86
2.17 Bicoid protein provides a positional signal for the anterior expression of zygotic <i>hunchback</i>	57	Chapter 3 Vertebrate development I: life cycles and experimental techniques	93
2.18 The gradient in Hunchback protein activates and represses other gap genes	58	Vertebrate life cycles and outlines of development	94
2.19 The expression of zygotic genes along the dorso-ventral axis is controlled by Dorsal protein	59	3.1 The frog <i>Xenopus laevis</i> is the model amphibian for developmental studies	96
■ Box 2C P-element-mediated transformation	60	3.2 The zebrafish embryo develops around a large mass of yolk	101
■ Box 2D Targeted gene expression and misexpression screening	61	3.3 Birds and mammals resemble each other and differ from <i>Xenopus</i> in some important features of early development	103
2.20 The Decapentaplegic protein acts as a morphogen to pattern the dorsal region	63	3.4 The early chicken embryo develops as a flat disc of cells overlying a massive yolk	103
Summary	65	3.5 Early development in the mouse involves the allocation of cells to form the placenta and extra-embryonic membranes	109
Activation of the pair-rule genes and the establishment of parasegments	66	Experimental approaches to studying vertebrate development	113
2.21 Parasegments are delimited by expression of pair-rule genes in a periodic pattern	66	3.6 Not all techniques are equally applicable to all vertebrates	114
2.22 Gap-gene activity positions stripes of pair-rule gene expression	68	■ Box 3A Gene-expression profiling by DNA microarray	115
Summary	70	3.7 Fate mapping and lineage tracing reveal which cells in the early embryo give rise to which adult structures	117
Segmentation genes and compartments	70	■ Box 3B Insertional mutagenesis and gene knock-outs in mice: the Cre/loxP system	118
2.23 Expression of the <i>engrailed</i> gene delimits a cell-lineage boundary and defines a compartment	70	3.8 Developmental genes can be identified by spontaneous mutation and by large-scale mutagenesis screens	119
■ Box 2E Genetic mosaics and mitotic recombination	73	■ Box 3C Large-scale mutagenesis in zebrafish	120

3.9 Transgenic techniques enable animals to be produced with mutations in specific genes	120	4.15 Members of the TGF- β family have been identified as mesoderm inducers	157
3.10 Gene function can also be tested by transient transgenesis and gene silencing	123	4.16 The zygotic expression of mesoderm-inducing and patterning signals in <i>Xenopus</i> is activated by the combined actions of maternal VegT and Wnt signaling	158
3.11 Gene regulatory networks in embryonic development can be revealed by chromatin immunoprecipitation techniques	124	4.17 Signals from the organizer pattern the mesoderm dorso-ventrally by antagonizing the effects of ventral signals	159
Summary to Chapter 3	124	4.18 Threshold responses to gradients of signaling proteins are likely to pattern the mesoderm	161
Chapter 4 Vertebrate development II: axes and germ layers	128	■ Box 4E A zebrafish gene regulatory network	162
Setting up the body axes	129	4.19 Mesoderm induction and patterning in the chick and mouse occurs during primitive-streak formation	163
4.1 The animal-vegetal axis is maternally determined in <i>Xenopus</i> and zebrafish	129	Summary	165
4.2 Localized stabilization of the transcriptional regulator β -catenin specifies the future dorsal side and the location of the main embryonic organizer in <i>Xenopus</i> and zebrafish	130	Summary to Chapter 4	166
■ Box 4A Intercellular protein signals in vertebrate development	131	Chapter 5 Vertebrate development III: patterning the early nervous system and the somites	173
4.3 Signaling centers develop on the dorsal side of <i>Xenopus</i> and zebrafish blastulas	133	The role of the organizer and neural induction	175
4.4 The antero-posterior and dorso-ventral axes of the chick blastoderm are related to the primitive streak	136	5.1 The inductive capacity of the organizer changes during gastrulation	175
4.5 The definitive antero-posterior and dorso-ventral axes of the mouse embryo are not recognizable early in development	138	5.2 The neural plate is induced in the ectoderm	179
4.6 Movement of the distal visceral endoderm indicates the definitive antero-posterior axis in the mouse embryo	140	■ Box 5A Chromatin-remodeling complexes	182
4.7 The bilateral symmetry of the early embryo is broken to produce left-right asymmetry of internal organs	141	■ Box 5B The FGF signaling pathway	184
■ Box 4B Fine-tuning Nodal signaling	143	5.3 The nervous system is initially patterned by signals from the mesoderm	185
Summary	145	5.4 Neural crest cells arise from the borders of the neural plate	186
The origin and specification of the germ layers	145	Summary	186
4.8 A fate map of the amphibian blastula is constructed by following the fate of labeled cells	146	Somite formation and antero-posterior patterning	187
4.9 The fate maps of vertebrates are variations on a basic plan	147	5.5 Somites are formed in a well-defined order along the antero-posterior axis	187
4.10 Cells of early vertebrate embryos do not yet have their fates determined and regulation is possible	149	■ Box 5C The Notch signaling pathway	190
4.11 In <i>Xenopus</i> the endoderm and ectoderm are specified by maternal factors, but the mesoderm is induced from ectoderm by signals from the vegetal region	150	5.6 Identity of somites along the antero-posterior axis is specified by Hox gene expression	191
■ Box 4C Identical twins	152	■ Box 5D Retinoic acid; a small-molecule intercellular signal	192
■ Box 4D Preimplantation genetic screening	153	■ Box 5E The Hox genes	194
4.12 Mesoderm induction occurs during a limited period in the blastula stage	154	5.7 Deletion or overexpression of Hox genes causes changes in axial patterning	197
4.13 Zygotic gene expression is turned on in <i>Xenopus</i> at the mid-blastula transition	155	5.8 Hox gene expression is activated in an anterior to posterior pattern	198
4.14 Mesoderm-inducing and patterning signals in <i>Xenopus</i> are produced by the vegetal region, the organizer, and the ventral mesoderm	156	5.9 The fate of somite cells is determined by signals from the adjacent tissues	199
		Summary	201
		The initial regionalization of the vertebrate brain	202
		5.10 Local signaling centers pattern the brain along the antero-posterior axis	203
		5.11 The hindbrain is segmented into rhombomeres by boundaries of cell-lineage restriction	203

■ Box 5F Eph receptors and their ephrin ligands	205	Summary	243
5.12 Hox genes provide positional information in the developing hindbrain	206	Ascidians	244
5.13 Neural crest cells from the hindbrain migrate to populate the branchial arches	207	6.15 Animal-vegetal and antero-posterior axes in the ascidian embryo are defined before first cleavage	244
5.14 The embryo is patterned by the neurula stage into organ-forming regions that can still regulate	208	6.16 In ascidians, muscle is specified by localized cytoplasmic factors	246
Summary	209	6.17 Notochord, neural precursors, and mesenchyme in ascidians require inducing signals from neighboring cells	247
Summary to Chapter 5	209	Summary	249
		Summary to Chapter 6	249
Chapter 6 Development of nematodes, sea urchins, and ascidians	215	Chapter 7 Plant development	255
Nematodes	216	7.1 The model plant <i>Arabidopsis thaliana</i> has a short life-cycle and a small diploid genome	256
6.1 The antero-posterior axis in <i>Caenorhabditis elegans</i> is determined by asymmetric cell division	218	Embryonic development	258
■ Box 6A Gene silencing by antisense RNA and RNA interference	220	7.2 Plant embryos develop through several distinct stages	258
6.2 The dorso-ventral axis in <i>Caenorhabditis elegans</i> is determined by cell-cell interactions	221	■ Box 7A Angiosperm embryogenesis	259
6.3 Both asymmetric divisions and cell-cell interactions specify cell fate in the early nematode embryo	222	7.3 Gradients of the signal molecule auxin establish the embryonic apical-basal axis	260
6.4 Hox genes specify positional identity along the antero-posterior axis in <i>Caenorhabditis elegans</i>	223	7.4 Plant somatic cells can give rise to embryos and seedlings	263
6.5 The timing of events in nematode development is under genetic control that involves microRNAs	226	■ Box 7B Transgenic plants	264
■ Box 6B Gene silencing by microRNAs	228	Summary	264
6.6 Vulval development is initiated by the induction of a small number of cells by short-range signals from a single inducing cell	229	Meristems	265
Summary	231	7.5 A meristem contains a small, central zone of self-renewing stem cells	265
Echinoderms	232	7.6 The size of the stem-cell area in the meristem is kept constant by a feedback loop to the organizing center	266
6.7 The sea-urchin embryo develops into a free-swimming larva	232	7.7 The fate of cells from different meristem layers can be changed by changing their position	267
6.8 The sea-urchin egg is polarized along the animal-vegetal axis	235	7.8 A fate map for the embryonic shoot meristem can be deduced using clonal analysis	268
6.9 The sea-urchin fate map is finely specified, yet considerable regulation is possible	236	7.9 Meristem development is dependent on signals from other parts of the plant	270
6.10 The vegetal region of the sea-urchin embryo acts as an organizer	236	7.10 Gene activity patterns the proximo-distal and adaxial-abaxial axes of leaves developing from the shoot meristem	270
6.11 The sea-urchin vegetal region is demarcated by the nuclear accumulation of β -catenin	238	7.11 The regular arrangement of leaves on a stem is generated by regulated auxin transport	272
6.12 The genetic control of the skeletogenic pathway is known in considerable detail	238	7.12 Root tissues are produced from <i>Arabidopsis</i> root apical meristems by a highly stereotyped pattern of cell divisions	273
6.13 The oral-aboral axis in sea urchins is related to the plane of the first cleavage	241	7.13 Root hairs are specified by a combination of positional information and lateral inhibition	275
6.14 The oral ectoderm acts as an organizing region for the oral-aboral axis	242	Summary	276
		Flower development and control of flowering	276
		7.14 Homeotic genes control organ identity in the flower	277
		7.15 The <i>Antirrhinum</i> flower is patterned dorso-ventrally as well as radially	279

■ Box 7C The basic model for the patterning of the <i>Arabidopsis</i> flower	
7.16 The internal meristem layer can specify floral meristem patterning	
7.17 The transition of a shoot meristem to a floral meristem is under environmental and genetic control	
Summary	
Summary to Chapter 7	
Chapter 8 Morphogenesis: change in form in the early embryo	
■ Box 8A Change in cell shape and cell movement	
Cell adhesion	
8.1 Sorting out of dissociated cells demonstrates differences in cell adhesiveness in different tissues	
■ Box 8B Cell-adhesion molecules and cell junctions	
8.2 Cadherins can provide adhesive specificity	
Summary	
Cleavage and formation of the blastula	
8.3 The orientation of the mitotic spindle determines the plane of cleavage at cell division	
8.4 Cells become polarized in the sea-urchin blastula and the mouse morula	
8.5 Fluid accumulation as a result of tight-junction formation and ion transport forms the blastocoel of the mammalian blastocyst	
8.6 Internal cavities can be created by cell death	
Summary	
Gastrulation movements	
8.7 Gastrulation in the sea urchin involves cell migration and invagination	
8.8 Mesoderm invagination in <i>Drosophila</i> is due to changes in cell shape that are controlled by genes that pattern the dorso-ventral axis	
8.9 Germ-band extension in <i>Drosophila</i> involves myosin-dependent remodeling of cell junctions and cell intercalation	
8.10 Dorsal closure in <i>Drosophila</i> and ventral closure in <i>Caenorhabditis elegans</i> are brought about by the action of filopodia	
8.11 Vertebrate gastrulation involves several different types of tissue movement	
■ Box 8C Convergent extension	
Summary	
Neural tube formation	
8.12 Neural tube formation is driven by changes in cell shape and convergent extension	
Summary	
Cell migration	318
8.13 Neural crest migration is controlled by environmental cues	318
Summary	320
Directed dilation	320
8.14 Later extension and stiffening of the notochord occurs by directed dilation	321
8.15 Circumferential contraction of hypodermal cells elongates the nematode embryo	321
8.16 The direction of cell enlargement can determine the form of a plant leaf	322
Summary	323
Summary to Chapter 8	323
Chapter 9 Germ cells, fertilization, and sex	329
The development of germ cells	330
9.1 Germ-cell fate is specified in some embryos by a distinct germ plasm in the egg	331
9.2 In mammals germ cells are induced by cell-cell interactions during development	333
9.3 Germ cells migrate from their site of origin to the gonad	334
9.4 Germ cells are guided to their final destination by chemical signals	334
9.5 Germ-cell differentiation involves a halving of chromosome number by meiosis	335
■ Box 9A Polar bodies	338
9.6 Oocyte development can involve gene amplification and contributions from other cells	338
9.7 Factors in the cytoplasm maintain the totipotent potential of the egg	339
9.8 In mammals some genes controlling embryonic growth are 'imprinted'	339
Summary	342
Fertilization	342
9.9 Fertilization involves cell-surface interactions between egg and sperm	343
9.10 Changes in the egg envelope at fertilization block polyspermy	345
9.11 Sperm-egg fusion causes a calcium wave that results in egg activation	346
Summary	348
Determination of the sexual phenotype	348
9.12 The primary sex-determining gene in mammals is on the Y chromosome	349
9.13 Mammalian sexual phenotype is regulated by gonadal hormones	349

9.14 The primary sex-determining signal in <i>Drosophila</i> is the number of X chromosomes, and is cell autonomous	351	10.15 The differentiated state of a cell can change by transdifferentiation	397
9.15 Somatic sexual development in <i>Caenorhabditis</i> is determined by the number of X chromosomes	353	10.16 Embryonic stem cells can proliferate and differentiate into many cell types in culture	399
9.16 Most flowering plants are hermaphrodites, but some produce unisexual flowers	354	■ Box 10B Testing ES cell potential in tetraploid blastocysts	399
9.17 Determination of germ-cell sex depends on both genetic constitution and intercellular signals	355	10.17 Stem cells could be a key to regenerative medicine	400
9.18 Various strategies are used for dosage compensation of X-linked genes	356	■ Box 10C Induced pluripotent stem cells	401
Summary	359	10.18 Various approaches can be used to generate differentiated cells for cell-replacement therapies	403
Summary to Chapter 9	360	Summary	405
Chapter 10 Cell differentiation and stem cells	365	Summary to Chapter 10	406
The control of gene expression	368	Chapter 11 Organogenesis	411
10.1 Control of transcription involves both general and tissue-specific transcriptional regulators	368	The vertebrate limb	412
10.2 External signals can activate gene expression	370	11.1 The vertebrate limb develops from a limb bud	412
10.3 The maintenance and inheritance of patterns of gene activity depend on chemical and structural modifications to chromatin, as well as on gene-regulatory proteins	371	11.2 Genes expressed in the lateral plate mesoderm are involved in specifying the position and type of limb	413
■ Box 10A Histones and Hox genes	374	11.3 The apical ectodermal ridge is required for limb outgrowth	415
Summary	374	11.4 Patterning of the limb bud involves positional information	416
Models of cell differentiation	375	11.5 How position along the proximo-distal axis of the limb bud is specified is still a matter of debate	416
10.4 All blood cells are derived from multipotent stem cells	375	11.6 The polarizing region specifies position along the limb's antero-posterior axis	419
10.5 Colony-stimulating factors and intrinsic changes control differentiation of the hematopoietic lineages	378	11.7 Sonic hedgehog produced by the polarizing region is likely to be the primary morphogen patterning the antero-posterior axis of the limb	420
10.6 Developmentally regulated globin gene expression is controlled by regulatory sequences far distant from the coding regions	379	■ Box 11A Positional information and morphogen gradients	421
10.7 The epithelia of adult mammalian skin and gut are continually replaced by derivatives of stem cells	382	11.8 Transcription factors might specify digit identity	422
10.8 The MyoD family of genes determines differentiation into muscle	385	■ Box 11B Too many fingers: mutations that affect antero-posterior patterning can cause polydactyly	423
10.9 The differentiation of muscle cells involves withdrawal from the cell cycle, but is reversible	387	■ Box 11C Sonic hedgehog signaling and the primary cilium	424
10.10 Skeletal muscle and neural cells can be renewed from stem cells in adults	388	11.9 The dorso-ventral axis of the limb is controlled by the ectoderm	426
10.11 Embryonic neural crest cells differentiate into a wide range of different cell types	389	11.10 Development of the limb is integrated by interactions between signaling centers	427
10.12 Programmed cell death is under genetic control	392	11.11 Different interpretations of the same positional signals give different limbs	427
Summary	393	11.12 Hox genes establish the polarizing region and also provide a code for limb patterning	428
The plasticity of gene expression	394	11.13 Self-organization may be involved in the development of the limb bud	430
10.13 Nuclei of differentiated cells can support development	394	11.14 Limb muscle is patterned by the connective tissue	431
10.14 Patterns of gene activity in differentiated cells can be changed by cell fusion	396	■ Box 11D Reaction-diffusion mechanisms	432
		11.15 The initial development of cartilage, muscles, and tendons is autonomous	433

11.16 Joint formation involves secreted signals and mechanical stimuli	433	12.2 The development of neurons in <i>Drosophila</i> involves asymmetric cell divisions and timed changes in gene expression	472
11.17 Separation of the digits is the result of programmed cell death	434	12.3 Specification of vertebrate neuronal precursors also involves lateral inhibition	473
Summary	435	■ Box 12A Specification of the sensory organs of adult <i>Drosophila</i>	474
Insect wings and legs	436	12.4 Neurons are formed in the proliferative zone of the vertebrate neural tube and migrate outwards	475
11.18 Positional signals from compartment boundaries pattern the wing imaginal disc	438	■ Box 12B Timing the birth of cortical neurons	478
11.19 A signaling center at the boundary between dorsal and ventral compartments patterns the <i>Drosophila</i> wing along the dorso-ventral axis	439	12.5 The pattern of differentiation of cells along the dorso-ventral axis of the spinal cord depends on ventral and dorsal signals	478
11.20 The leg disc is patterned in a similar manner to the wing disc, except for the proximo-distal axis	441	12.6 Neuronal subtypes in the ventral spinal cord are specified by the ventral to dorsal gradient of Shh	480
11.21 Butterfly wing markings are organized by additional positional fields	442	12.7 Spinal cord motor neurons at different dorso-ventral positions project to different trunk and limb muscles	481
11.22 Different imaginal discs can have the same positional values	443	12.8 Antero-posterior pattern in the spinal cord is determined in response to secreted signals from the node and adjacent mesoderm	482
Summary	444	Summary	483
Vertebrate and insect eyes	445	Axon navigation	484
11.23 The vertebrate eye develops from the neural tube and the ectoderm of the head	448	12.9 The growth cone controls the path taken by a growing axon	485
11.24 Patterning of the <i>Drosophila</i> eye involves cell-cell interactions	450	12.10 Motor neuron axons in the chick limb are guided by ephrin-Eph interactions	486
11.25 Eye development in <i>Drosophila</i> is initiated by the actions of the same transcription factors that specify eye-precursor cells in vertebrates	451	12.11 Axons crossing the midline are both attracted and repelled	488
Summary	451	12.12 Neurons from the retina make ordered connections with visual centers in the brain	489
Internal organs: insect tracheal system, vertebrate lungs, kidneys, blood vessels, heart, and teeth	452	Summary	492
11.26 The <i>Drosophila</i> tracheal system is a model for branching morphogenesis	453	Synapse formation and refinement	493
11.27 The vertebrate lung also develops by branching of epithelial tubes	454	12.13 Synapse formation involves reciprocal interactions	493
11.28 The development of kidney tubules involves reciprocal induction by the ureteric bud and surrounding mesenchyme	455	12.14 Many motor neurons die during normal development	496
11.29 The vascular system develops by vasculogenesis followed by angiogenesis	456	12.15 Neuronal cell death and survival involve both intrinsic and extrinsic factors	497
11.30 The development of the vertebrate heart involves specification of a mesodermal tube that is patterned along its long axis	457	12.16 The map from eye to brain is refined by neural activity	497
11.31 A homeobox gene code specifies tooth identity	459	Summary	499
Summary	461	Summary to Chapter 12	500
Summary to Chapter 11	461	Chapter 13 Growth and post-embryonic development	505
Chapter 12 Development of the nervous system	468	Growth	505
Specification of cell identity in the nervous system	469	13.1 Tissues can grow by cell proliferation, cell enlargement, or accretion	506
12.1 Neurons in <i>Drosophila</i> arise from proneural clusters	470	13.2 Cell proliferation is controlled by regulating entry into the cell cycle	506

13.3 Cell division in early development can be controlled by an intrinsic developmental program	508	Regeneration in <i>Hydra</i>	548
13.4 Organ size can be controlled by both intrinsic growth programs and extracellular signals	509	14.7 <i>Hydra</i> grows continuously but regeneration does not require growth	548
13.5 The amount of nourishment an embryo receives can have profound effects in later life	511	14.8 The head region of <i>Hydra</i> acts both as an organizing region and as an inhibitor of inappropriate head formation	549
13.6 Determination of organ size involves coordination of cell growth, cell division, and cell death	512	14.9 Genes controlling regeneration in <i>Hydra</i> are similar to those expressed in vertebrate embryos	551
13.7 Body size is also controlled by the neuroendocrine system in both insects and mammals	513	Summary	552
■ Box 13A Gradients of signaling molecules could determine organ size		Summary to Chapter 14	552
13.8 Growth of the long bones occurs in the growth plates	514	Chapter 15 Evolution and development	556
13.9 Growth of vertebrate striated muscle is dependent on tension	517	■ Box 15A 'Darwin's finches'	558
13.10 Cancer can result from mutations in genes that control cell multiplication and differentiation	519	The evolution of development	559
13.11 Hormones control many features of plant growth	520	15.1 Genomic evidence is throwing light on the origin of metazoans	559
Summary	522	15.2 Multicellular organisms evolved from single-celled ancestors	560
Molting and metamorphosis	523	Summary	562
13.12 Arthropods have to molt in order to grow	523	The evolutionary modification of embryonic development	562
13.13 Metamorphosis is under environmental and hormonal control	524	15.3 Hox gene complexes have evolved through gene duplication	563
Summary	527	15.4 Changes in Hox genes generated the elaboration of vertebrate and arthropod body plans	565
Aging and senescence	527	15.5 The position and number of paired appendages in insects is dependent on Hox gene expression	567
13.14 Genes can alter the timing of senescence	529	15.6 The basic body plan of arthropods and vertebrates is similar, but the dorso-ventral axis is inverted	568
13.15 Cell senescence blocks cell multiplication	530	15.7 Limbs evolved from fins	569
Summary	531	15.8 Vertebrate and insect wings make use of evolutionarily conserved developmental mechanisms	574
Summary to Chapter 13	531	15.9 The evolution of developmental differences can be based on changes in just a few genes	575
Chapter 14 Regeneration	535	15.10 Embryonic structures have acquired new functions during evolution	576
Limb and organ regeneration	536	Summary	578
14.1 Amphibian limb regeneration involves cell dedifferentiation and new growth	537	Changes in the timing of developmental processes	579
14.2 The limb blastema gives rise to structures with positional values distal to the site of amputation	540	15.11 Evolution can be due to changes in the timing of developmental events	579
14.3 Retinoic acid can change proximo-distal positional values in regenerating limbs	542	15.12 The evolution of life histories has implications for development	581
14.4 Insect limbs intercalate positional values by both proximo-distal and circumferential growth	544	Summary	581
14.5 Heart regeneration in the zebrafish involves the resumption of cell division by cardiomyocytes	546	Summary to Chapter 15	582
14.6 The mammalian peripheral nervous system can regenerate	547	Glossary	587
Summary	547	Index	603