

# CONTENTS

## Volume I

Foreword	vii
Figure 1. Pieter D. Nieuwkoop with Richard Gordon...	viii
Figure 2. Pieter D. Nieuwkoop with Natalie K. Björklund...	xii
Preface	xiii
Flip Animation of the Ectoderm Contraction Wave	xxi
Proposition Page Numbers	xlix
<b>1.00 Introduction</b>	<b>1</b>
1.01 Consider a Spherical Cow	1
Figure 3. A scanning electron micrograph (SEM) of a fertilized human egg...	3
1.02 The Epigenetic Problem	7
1.03 Wholeness and the Symmetry of the Early Embryo	10
1.04 Wholeness through the Ruse of Organicism	12
1.05 The Grip of Vitalism	16
1.06 The Rise and Fall of Physics in Embryology	20
1.07 Can We Restore the Physics of the Youth of Embryology?	24
1.08 Avoiding the Spatial Component of Embryogenesis	26
1.09 Wholeness, the Environment, and Symmetry Breaking	30
1.10 Wholeness through Surface Tension	34
1.11 Nonmaterial Physics as the Entelechy of Vitalism	36
1.12 Towards a New Physics of Embryos	38
1.13 New Tools of the Trade	40
1.14 Are We Headed for Reductionism?	46
1.15 Chemical or Mechanochemical Instabilities?	49
1.16 Critique of the Theory of Self-Organizing Systems	53

1.17	Protein Folding as a Deluding Paradigm	56
1.18	A Word on Language	59
1.19	The Embryology/Psychology Merry-go-round (Carrousel)	64
1.20	The Cosmic Context	66
<b>2.00</b>	<b>Neural Induction and the Organizer</b>	<b>69</b>
2.01	A Moment of Discovery	69
	Figure 4. The stages of embryonic development of a urodele salamander...	70
2.02	Origins of the Idea of Induction	71
2.03	Preformationism versus Epigenesis: To Be or To Become? That is the Question	75
2.04	The Hunting of the Snark (The Inducer Molecule)	80
2.05	A Cornucopia of Inducers	83
2.06	The Snark Was a Boojum	88
2.07	Limb Induction: A Parallel Case?	93
2.08	Mesoderm and Other Inductions	95
2.09	Regional Induction	99
2.10	The Cell State Splitter	101
2.11	Meet the Axolotl	105
	Table 1: Timing of early stages of the axolotl embryo...	106
2.12	A History of Sexism in Science Whodunit: Hilde Mangold or Hans Spemann?	112
<b>3.00</b>	<b>Theory of the Cell State Splitter</b>	<b>120</b>
3.01	Overview	120
	Figure 5. Classical model of differentiation...	121
	Figure 6. Alternative classical model for differentiation...	122
	Figure 7. Our new view of differentiation...	122
	Figure 8. State of determination...	123
	Figure 9. Determination tree...	125
	Figure 10. A differentiation tree...	126

3.02	How to Stop a Wave on a Sphere	128
	Figure 11. The contraction wave... in the simple 'shell' model...	129
	Figure 12. The spherical ectoderm of a urodele embryo... in the 'shell' model...	129
	Figure 13. In the 'shell' model... when... a full hemisphere...	130
3.03	How the Ectoderm Contraction Wave Actually Stops: the Lens Model	133
3.04	Internal Pressure May Synchronize Preparation of the Cell State Splitters	136
3.05	The Right Place, at the Right Time, into the Right Kinds	139
3.06	The Intracellular Mechanics of the Cell State Splitter Yields Ectodermal Differentiation	140
	Figure 14. A pressure P inside an embryo...	147
3.07	Force Generating and Load Bearing Cytoskeletal Components: Microtubules (MT)	149
3.08	Force Generating and Load Bearing Cytoskeletal Components: Microfilaments (MF)	152
3.09	Force Generating and Load Bearing Cytoskeletal Components: Intermediate Filaments (IF)	155
3.10	Combinations of Cytoskeletal Components	158
<b>4.00</b>	<b>Development and Genetics</b>	<b>164</b>
4.01	The General Cell State Splitter (Propositions 1-9)	164
4.02	Differentiation Trees (Propositions 10-20)	183
	Figure 15. A few simple differentiation trees...	184
	Figure 16. Terminology for parts of a differentiation tree...	189
	Figure 17. When the cell state splitter mechanically resolves...	208
	Figure 18. Smooth propagation of a contraction differentiation wave...	214
	Figure 19. Propagation of a 'bull's-eye' wave...	214
	Figure 20. Propagation of a spacing pattern wave...	215
	Figure 21. The epigenetic landscape...	217
4.03	Genetics and Differentiation Trees (Propositions 21-29)	221
4.04	A New Definition of 'Tissue' (Propositions 30-39)	241
	Table 2: Positional information and induction vs differentiation waves...	252

4.05	The Relationship between Cells and Tissues in Regulating Embryos (Propositions 40-54)	263
4.06	The Relationship between Cells and Tissues in Mosaic Embryos (Propositions 55-66)	301
	Figure 22. Four dimensional geometry of the development of a mosaic organism...	313
	Figure 23. Four dimensional geometry of the development of a regulating organism...	314
<b>5.00</b>	<b>Development and Evolution</b>	<b>354</b>
5.01	Evolution of Cell State and Tissue Splitting (Propositions 67-73)	354
	Figure 24. DNA basis for a differentiation tree branch duplication...	361
	Figure 25. State of the DNA after a duplication...	362
	Figure 26. Coevolution of DNA after a duplication...	363
5.02	The Secondary Importance of Embryonic Induction (Propositions 74-92)	368
	Figure 27. Hierarchical differentiation cascade...	374
	Figure 28. Differentiation cascade as a web...	375
	Figure 29. Induction is secondary...	376
	Figure 30. Unbreakable inductions...	378
5.03	Dedifferentiation and Redifferentiation (Propositions 93-107)	412
	Figure 31. Two models for transdifferentiation...	414
5.04	The Selfish Differentiation Tree (Propositions 108-112)	436
5.05	The Ciliate Origin of Multicellular Organisms (Propositions 113-127)	447
<b>6.00</b>	<b>Macroevolution</b>	<b>505</b>
6.01	Redefining Microevolution and Macroevolution (Propositions 128-133)	505
	Figure 32. Nematode macroevolution...	509
	Figure 33. How to delete a middle subtree of a differentiation tree...	518
	Figure 34. Simplification of a differentiation tree by fusion...	519

6.02	Possible DNA Mechanisms for Macroevolutionary Change of Differentiation Trees (Propositions 134-157)	520
	Figure 35. Reducing developmental time discrepancies...	528
	Figure 36 Genes per cascade vs number of kinds of cells...	550
	Table 3: Estimated numbers of genes per differentiation cascade...	551
	Table 4: Isochore correlations...	552
	Figure 37. A differentiation tree showing a terminal branch and a subtree...	557
6.03	Differentiation Trees in Punctuated Equilibrium (Propositions 158-170)	573
	Figure 38. The lineage tree of the nematode...	606
6.04	The Grand Sweep of Evolution (Propositions 171-194)	609
	Figure 39. Bonner's Law...	629
	Figure 40. Computer simulation of a... phylogenetic tree...	633
	Figure 41. Evolution of brain size in mammals...	642
6.05	Neutralist Theory (Propositions 195-197)	658
6.06	A Universe Aware of Itself: Differentiation Waves and the Brain (Propositions 198-205)	668
<b>7.00</b>	<b>The Biogenetic Law</b>	<b>701</b>
7.01	'Ontogeny Recapitulates Phylogeny' Revisited via Differentiation Trees (Propositions 206-218)	701
	Figure 42. Differentiation tree of a common ancestor...	708
	Figure 43. Differentiation tree of an archetype...	709
	Figure 44. Heterotropy...	720
	Figure 45. Heterochrony and differentiation trees...	725
7.02	Organisms with Two Differentiation Trees (Propositions 219-229)	726
	Figure 46. In <i>continuing differentiation metamorphosis</i> ...	733
	Figure 47. In <i>pulsatile metamorphosis</i> ...	733
	Figure 48. In <i>single tissue metamorphosis</i> ...	734
	Figure 49. In <i>dedifferentiation metamorphosis</i> ...	735
	Figure 50. <i>Deferred metamorphosis</i> ...	736

7.03 Winding Up Evolution (Propositions 230-240)	747
<b>8.00 The Homeobox</b>	<b>764</b>
8.01 Why Insects and Vertebrates Share Homeobox Domains (Propositions 241-250)	764
Figure 51. The <i>Drosophila</i> morphogenetic furrow...	794
Figure 52. Variogram analysis...	796
8.02 The Development of Bilateral Asymmetry (Propositions 251-258)	803
Figure 53. Microtubule/wave colored symmetry...	818
Figure 54. Bilaterally symmetric shear couples...	823
Figure 55. Torque applied to a cell on the left side...	824
Figure 56. Torque applied to a cell on the right side...	824
8.03 Facets of Embryogenesis (Propositions 259-272)	830

## Volume II

<b>9.00 A Cornucopia of Differentiation Waves</b>	<b>865</b>
9.01 Activation Wave	865
9.02 Cleavage Waves	867
9.03 The Compaction Wave	874
9.04 Mitotic Waves	875
9.05 Quantal Mitoses and a Model for Limb Morphogenesis	881
9.06 Head and Tail Duplications	884
9.07 First Sitings of the Differentiation Waves of the Axolotl	893
9.08 Differentiation Waves of the Neural Plate	895
9.09 A Possible Pair of Differentiation Waves in the Later Epidermis	898
9.10 Neural Crest	901
9.11 Differentiation Waves in Plant Meristems	902
9.12 Differentiation Waves in Fly and Fish Eyes	908
9.13 Single Cell versus Multiple Cell Differentiation Waves	914
9.14 Repetitive Waves	917

9.15	<i>Drosophila</i> Bristles: A Wave/Mechanical Reinterpretation	920
9.16	The American Shorthair Tabby Domestic Cat and Pigment Patterns	925
9.17	Butterfly Eye Spots	928
9.18	The Milk Line	936
9.19	Waves in Assorted Tissues	938
9.20	Waves on Anuran Embryos	943
	Figure 57. A nearly sagittal section of a Stage 10 1/2 axolotl embryo...	951
	Figure 58. Enlargement of one wave profile of the ectoderm contraction wave...	952
9.21	Hints of Other Differentiation Waves	953
9.22	Uninvited Waves	956
	Figure 59. First observations of what may be waves on explants of axolotl ectoderm...	963
9.23	Are Others' Waves Our Waves?	967
	Table 5: Classes of calcium waves...	977
9.24	Are Differentiation Waves Merely Epiphenomena?	980
9.25	Mutant Waves	984
9.26	Wave Parallels between Mosaic and Regulating Organisms	988
9.27	Launching Domains May Have Specific Electrical, Mechanical and Molecular Properties	990
<b>10.00</b>	<b>Conclusion</b>	<b>993</b>
10.01	The Logic of Evolution	993
10.02	Is Evolution Progressive?	995
10.03	Were We Inevitable?	1002
10.04	The Living Ghost of Orthogenesis	1012
10.05	On Purpose and Progress	1017
10.06	The Beads-on-a-String 'New Synthesis'	1022
10.07	Gene Duplication as the Essence of Macroevolution	1026
10.08	The Blessings of Ever Increasing Dimensionality	1030
	Figure 60. Differentiation tree space...	1030

10.09 The Fractal Tree of Life	1035
Figure 61. Darwin's schematic tree of life...	1038
Figure 62. A tissue lineage tree...	1040
10.10 The Novel Unification of Development, Genetics and Evolution	1042
10.11 Exploring the Higher Order Structure of the Genome	1047
10.12 How to Find a GEM	1055
10.13 A Clockwork Universe Within: Nuclear Tensegrity Mechanics (Wurfels) as a Foundation for the Nuclear State Splitter	1058
Figure 63. Wurfel model for chromosomes...	1064
10.14 The Top Ten Questions	1070
10.15 Paradigms for Developmental Biology	1078
10.16 A New Curriculum for Biologists	1083
Appendix I	1085
Gordon, R. & G.W. Brodland (1987). The cytoskeletal mechanics of brain morphogenesis: cell state splitters cause primary neural induction. <i>Cell Biophysics</i> 11, 177-238.	
Appendix II	1147
Brodland, G. W., R. Gordon, M. J. Scott, N. K. Björklund, K. B. Luchka, C. C. Martin, C. Matuga, M. Globus, S. Vethamany-Globus & D. Shu (1994). Furrowing surface contraction wave coincident with primary neural induction in amphibian embryos. <i>J. Morph.</i> 219 (2), 131-142.	
Appendix III	1159
Pursued by the Differentiation Wave	
Appendix IV	1168
Björklund, N. K. & R. Gordon (1993b). Nuclear state splitting: a working model for the mechanochemical coupling of differentiation waves to master genes (with an Addendum). <i>Russian J. Dev. Biol.</i> 24 (2), 79-95.	

Appendix V	1185
Gordon, R., N. K. Björklund & P. D. Nieuwkoop (1994). Dialogue on embryonic induction and differentiation waves. <i>Int. Rev. Cytol.</i> 150, 373-420.	
Appendix VI	1233
Björklund, N.K. & R. Gordon (1994). Surface contraction and expansion waves correlated with differentiation in axolotl embryos. I. Prolegomenon and differentiation during invagination through the blastopore, as shown by the fate map. <i>Computers &amp; Chemistry</i> 18 (3), 333-345.	
Appendix VII	1246
Gordon, R. & N.K. Björklund (1996). How to observe surface contraction waves on axolotls. <i>Int. J. Dev. Biol.</i> 40 (4), 913-914.	
Appendix VIII	1248
Gordon, R. (1992d). Physicist to biologist: A first order phase transition. <i>Bulletin of the Canadian Society for Theoretical Biology</i> (10), 4-5.	
Index of Propositions	1252
References	1266
Glossary and Abbreviations	1584
Citation and Subject Index	1643
Permissions and Note Added in Proof	1833