PREFACE

"Whenever a new scientific concept comes into prominence, it sends shock waves of surprise to the scholars contributing to that field" (Carlson, 1966).

It is my intention to describe a phenomenon that I seem to be the first to have stumbled across with understanding: a quiet wave that forms our very minds. It will crest as it crashes over and forever intertwines the three fields of development, genetics and evolution. The wave forming the brain is there, and many others, perhaps determining every tissue of which we are made. These waves are easily seen with simple tools in common embryos, by anyone who will take the trouble to look. This book is an interpretation of these waves. You may not agree with my interpretation, and are most welcome, and indeed encouraged, to invent other interpretations. But you will not be able to ignore these waves, which will color your view of biology from here on, as they have mine. With the discovery of differentiation waves, it is no longer true that...

"The determination or chemodifferentiation of any given part, i.e. the decision as to what any cell or group of cells shall develop into, takes place invisibly some time prior to the process itself" (Needham, 1931b).

We can now watch it happening.

This book was inspired by a lecture by Lionel (Jim) Johnson given in my Pollution Biology class in February, 1989. (The manuscript was started on June 9, 1989.) When Lionel opened my eyes to fundamentally unsolved and exciting problems in evolution and ecology, he showed how one could leap from population data on arctic charr to possible explanations of the grand sweep of evolution (Vanriel & Johnson, 1995).

I would like to thank Guenter Albrecht-Buehler, Thomas F.H. Allen, Hilary Alto, Karl J. Aufderheide, Penniman B. Austin, Lev V. Beloussov, Teresa C. Binstock, John Tyler Bonner, G. Wayne Brodland, Chris Chetland, Simon Conway Morris, James Cummins, Marc R. Del Bigio, Graham Dellaire, Daniel C. Dennett, Wim J.A.G. Dictus, Hadass Eviatar, Sergei V. Evsikov, David H.A. Fitch, Srecko Gajovic, Helen Gordon, the late Paul B. Green, Gary W. Grimes, Gerhard Grössing, Efroim Gurman, Max K. Hecht, Lewis I. Held Jr., Michael Keller, Glen R. Klassen, James A. Lake, Keith E. Latham, Michael Levin, John A. McCoshen, Andrew D. McCulloch, Ross McGowan, Leonard E. Munstermann, Vidyanand Nanjundiah, Stuart Nelson, the late Henriette C.M. Nieuwkoop-Beukers, Hugh E.H. Paterson, Andrey Polezhaev, Bruce Ratcliffe, Robert Rosen, Cynthia M. Ross, Sharon Y. Roth, Nancy D. Rumph, Tsvi Sachs, Charles B. Schom, Verner L. Seligy, Stanley K. Sessions, William Silvert, Mark Solomonovich, Roland Somogy, Arlin Stoltzfus, Stephen A. Stricker, Michael Sumner, Patrick P.L. Tam, Edward Theriot, Yuri Trusov, Leigh M. Van Valen, Michael W. Vannier, Carey Vigor-Zierk, S. Randal Voss, Richard J. Wassersug, Donald I. Williamson and Kenneth H. Wolfe for critical comments and suggested improvements of draft sections. Thanks are due to Margo Kautz, Kim Nozick, Lana M. Hunstad and Alan W. Hunstad for library assistance, and to Daniel W. Rickey for assistance with digitizations. The following people have bravely tackled reading of whole draft manuscripts: Russell W. Anderson, Natalie K. Björklund, Diana Gordon, C. Cristofre Martin, Stephen P. McGrew, the late Pieter D. Nieuwkoop, and Przemko Tylzanowski. I would not wish to suggest that any of these people endorse all the ideas put forward here. To some extent, this book has become a dialog with them.

The research behind this book was consistently supported by grants from the Spina Bifida Association of Canada (SBAC), an enlightened group of parents who see in fundamental research a possible understanding of their children's condition, which might help the next generation. Partial support was also offered by Abbott Laboratories/Winnipeg Health Sciences Centre, Children's Hospital of Winnipeg Research Foundation (especially through its former Director, Victor Chernick), Departments of Botany and Radiology and Harley Cohen and Nick Anthonisen, Deans of Science and Medicine at the University of Manitoba, Easter Seal Research Institute, Employment and Immigration Canada Challenge Program, Manitoba CareerStart, Manitoba Hydro, Manitoba Schools Science Symposium, Natural Sciences and Engineering Research Council of Canada, Spina Bifida Association of Manitoba, Spina Bifida and Hydrocephalus Association of Ontario, and the University of Manitoba Research Grants Committee of Senate. The University of Manitoba, especially my former colleagues in the Department of Botany (1984-1994, during which much of the writing of this book occurred), John Stewart and David Punter, and in Radiology, Martin H. Reed, E. (Ted) A. Lyons, I. David Greenberg, and Blake M. McClarty, provided an atmosphere of academic freedom that made this study possible. This book was written in part in the midst of a strike by professors at the University of Manitoba in defense of academic freedom (Gordon, 1996c). My predoctoral, doctoral, and postdoctoral mentors, Edward Anders, Terrell L. Hill, and Robert Rosen, respectively, taught me the importance of academic freedom by their examples.

Two of my students, Kurt B. Luchka and C. Cristofre Martin, provided much of the momentum for the underpinnings of this work. I would also like to thank the innumerable colleagues who responded to my appeals for their reprints, many of whom heard me out in seminars, conversations, and e-mail exchanges, whose ideas are woven into the fabric presented here. I would especially like to thank the staff of the Medical Library of the University of Manitoba, including Ruth Holmberg and Ju-Dai Chuang in Interlibrary Loan (over 300 items), Beverley Brown, Carol Cooke and Bill Poluha in Reference, and Jovy Beltran, Erlinda Erjavec, David Howe, Thomas Quinlan and Moira Raglan in Circulation, and their then Acting Head, Michael Tennenhouse, for their immense effort, along with Ginette Wright and Hung-Hsueh Shao in the Science Library. Thanks are also due to Oeke Kruythof, Librarian, Hubrecht Laboratory, Netherlands Institute for Developmental Biology, who supplied many of Pieter Nieuwkoop's papers, and to Sook Cheng Lim and Yolande Koh of World Scientific Publishing

for their patience and editorial and production assistance in bringing this to fruition.

I have been dragged kicking and screaming by our axolotl embryos back into a now matured molecular biology which I had abandoned in 1964 as an immature graduate student. That approach did not seem to me then (nor yet, alone) to be capable of divulging 'the secret of life'. Not that it didn't make an impression on me being surrounded by the enthusiasm of Aaron Novick (Novick & Szilard, 1950), Jack Sadler (Sadler, Sasmor & Betz, 1983), Frank W. Stahl (1964), Sid A. Bernhard (1968) and the late George Streisinger (Streisinger et al., 1981) at the Institute of Molecular Biology at the University of Oregon. At that time the genetic code was being delivered by emissaries day by day, codon by codon ("Crick (1966b, 1988a) provides engaging accounts of this exciting period of biochemical sleuthing": Mange & Mange, 1990). I now understand part of what was lacking: the very physics and chemical physics I was then drawn to, with skills honed under Susan Meschel (Handler & Meschel, 1993) and Edward Anders in quantitative chemistry. As an undergraduate in his lab, I considered organic matter in meteorites and their relevance to the origin of life (Anders et al., 1964; Anders & Lewis, 1987). Under the eye of my graduate mentor, Terrell L. Hill (1956b, 1960, 1963, 1964, 1969, 1977, 1985a, 1987, 1989), I investigated equilibrium (Gordon, 1968a) and nonequilibrium (Gordon, 1968b) phase transitions and was given the freedom and encouragement to delve into embryogenesis (Gordon, 1966) while earning a Ph.D. in Chemical Physics. On my recent journey back to molecular biology, my constant guide and companion has been Natalie K. Björklund, friend, collaborator, spouse, believer in 'the wave' when it was a 'mere' prediction, and first discoverer of the ectoderm contraction wave in explants and *in vivo*.

Seven embryologists had major impacts on me. (While I nominally postdoced under Conrad H. Waddington around 1970: Waddington, 1972, he was primarily immersed in futurism at that time.) An exciting lecture on embryonic cell sorting by Aaron A. Moscona while I was an undergraduate at the University of Chicago initiated me into the fascination of embryology and the possibilities for its explanation (cf. Moscona, 1957, 1974). While I was a graduate student at the University of Oregon, I corresponded with and visited Max Braverman in Pittsburgh, who was working on hydroid colonies (Braverman, 1962, 1963; Braverman & Schrandt, 1966). We concluded at that time that it was indeed possible to generate biologically realistic patterns from 'rules' of cell behavior and interaction (cf. Gordon, 1966; Held Jr., 1992). The next problem was to figure out how embryos actually did it (a distinction that unmade leads to arguments even today: cf. Bird & Hoyle, 1994, vs. Niklas, 1994a). During my postdoc with Robert Rosen (1967, 1970, 1991), he set examples of clear and independent thinking in dissecting morphogenesis (Goel et al., 1970, 1975; Rosen, 1970, 1972a,b). I tried my hand at modelling gradients in hydra with the inspiring civil engineer turned biologist, Lewis Wolpert (Wolpert, Hicklin & Hornbruch, 1971; Wolpert, 1991a), in 1969, getting nowhere. After meeting at the 1969 Woods Hole Embryology course organized by Malcolm S. Steinberg, with whom I also later had the pleasure of collaborating (Gordon et al., 1972, 1975), Antone G. Jacobson and I then had the exhilarating and thought sharpening experience of working out how the newt neural plate changes shape (Jacobson & Gordon, 1976a; Gordon & Jacobson, 1978). More recently, I have had the honor and enjoyed the friendship, company and collaboration of that late master of classical embryology, Pieter D. Nieuwkoop (Nieuwkoop & Faber, 1956, 1975, 1994; Nieuwkoop & Sutasurya, 1979, 1981; Nieuwkoop, Johnen & Albers, 1985; Gerhart, 1987; Appendix V: Gordon, Björklund & Nieuwkoop, 1994; Nieuwkoop, Björklund & Gordon, 1996).

Three superb cell biologists, the eclectic diatom electron microscopist Ryan W. Drum (Drum, Pankratz & Stoermer, 1966; Gordon & Drum, 1970, 1994), the late Robert D. Allen (Allen & Kamiya, 1964; Allen & Allen, 1983; Allen, 1987), and the late James F. Danielli (Danielli, 1955; Stein, 1986), gave me a firm foundation in intracellular phenomena and their visualization, while early efforts at what we now call computed tomography of ribosomes with my friend Robert Bender (Bender, Bellman & Gordon, 1970; Bellman et al., 1971), started in the lab and at the suggestion of Cyrus Levinthal (1968), gave me some practical experience in biological image processing, which I parlayed into a second career in medical imaging. Lewis E. Lipkin introduced me to digital imaging in light microscopy (Lemkin et al., 1976).

While I am not an historian of science, I have a curiosity about intellectual history, which I attribute to my so inclined friend John B. Musgrave. If I am right, this work culminates a search that has been going on for well over a century, for the essence of explanation in embryology, representing a vast, worldwide intellectual effort, which I think must be acknowledged. This is why the text is woven through with quotations. I prefer to let previous and contemporary researchers, reviewers and textbook writers speak in their own words, and to retrace the history of ideas. This will exasperate or delight you, depending on your expectations of a scientific monograph. It also allows you to see if you can devise alternative interpretations to mine of what has been said by others. My interest in history does not make me skilled at it, and I have noticed subtle differences in accounts by scientists who turned late in their careers to writing about history versus professional historians of science. Thus the reader should be warned that I take accounts much at face value, only here and there noting contradictions or situations warranting further historical digging. I have not gone to primary sources (unpublished letters, etc.), the way a proper historian does.

The quotes are often extensive to add information beyond my text, and thus generally should not be skipped. Keep in mind that these quotes are selected to support (or occasionally contradict) my thesis, so they may not fully represent the authors' viewpoints. (To enhance readability, I used a colon for a full stop before a quotation, and '...' to indicate no break. If I chose to change the capitalization of a word from the original, the first letter is underlined. I have corrected obvious misspellings rather than using *sic.*) This practice of massive quotation leads to many secondary references, which I have checked when accessible. Any emphases (italics, etc.) are as in the original, unless otherwise indicated (except that genera and species names are always italicized). My connecting or explanatory words, and editorial comments, are in square brackets (although occasionally, as in [Ca^{2+}], square brackets designate 'concentration of').

I use the common scientific reference style, which gives credit to each idea one builds on directly in line in the text, cumbersome as it may be. Sometimes annoying long strings of references are given, not so much to support my argument by the weight of authority, but to give the reader a broad entry into the literature. I see this text as a beginning of an explanation of embryogenesis, not the final word. There is much work yet left to do, and with a literature so vast and far flung, I prefer to pass on the benefit of my labor by pulling the literature together (nearly 7000 references). For each reader, different aspects will seem tutorial and elementary. Just skip what seems obvious.

An animated set of flip through figures of the ectoderm contraction wave has been prepared by artist and medical artist K. Jack Butler (1996).

It took six starts to decide on a style for this book. It is hard to cross so many fields and keep one's wits. I finally devised a format consisting of propositions, each followed by its justification and corollaries, by rough analogy with Martin Luther's 95 Theses posted in Wittenberg. As the jargon of the many fields is incomprehensible for the uninitiated, as I once was, I have provided a partial glossary, including repeated abbreviations. The reader should note that many common words have specialized meanings in biology, so confusion may sometimes be cleared up by checking the glossary.

I throw a wide net, one with gaping holes due to the uneven state of our intellectual successes in biology. If I seem to claim too much, it is because I am casting for a very large fish, and hope the net holds:

"Aristotle... reports that the Pythagoreans found that acoustical 'harmonies' only depend on (commensurate) ratios of lengths and on nothing else, and that they generalized from this experience in acoustics to physics and knowledge in general.... It is true that, against their own background, the Pythagoreans were recklessly imprudent when concluding so much from so little. But Isaac Newton was also 'reckless' when proposing that there is a universal gravitational law which subsumes both terrestrial falls of bodies and celestial orbitings of planets" (Bochner, 1966).

I will be accused of trying, but will not attempt, to solve everything at once in this book: there are those brave souls who have tried to see in morphogenesis (Sinnott, 1963; Edelman, 1989, 1992a) or the cytoskeleton (Penrose, 1994, 1995) a solution to the problem of self-awareness and consciousness (cf. Dennett, 1995). I have but little to offer towards the solution of this higher problem, other than perhaps a fresh look at how the brain is built, which may or may not help understand how it functions.

The ideas here are roughly hewn, for that is the imperfect nature of our science of biology and my own understanding. If fragments survive the test of time, and the scorn and mislaid praise of my peers, I will be satisfied with my efforts. If you are dusting off this quaint document a century hence, as I have admiringly done to those of my predecessors, may I wish you the best. Carry on.

Winnipeg, 1998.