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BOOK REVIEWS

Gene Activity in Early Development

Eric H. Davidson
Third Edition, 670 pp.
New York: Academic Press, 1986

In 1925, Edmund Wilson published the now classic third edition of his book *The Cell in Development and Heredity*, in which he laid out most of the important questions about developmental biology that we are still attempting to answer. In 1986, Eric Davidson published the third edition of his book *Gene Activity in Early Development*, in which the progress toward answering Wilson's questions is described. Wilson (1896) is quoted: "If chromatin be the idioplasm ... in which inheres the sum total of hereditary forces, and if it be equally distributed at every cell division, how can its mode of action so vary in different cells as to cause diversity of structure, *i.e. differentiation*?" How indeed. It would be fascinating to hear Wilson's responses after informing him of enhancers and RNA splicing. Davidson is clearly an admirer of Wilson, and like Wilson has a broad perspective on the field which brings to the new edition the strengths of a profound knowledge of classical developmental biology together with an appreciation of the power of the new molecular methods.

There are themes that run through the presentation and help to tie together a barrage of facts. Genes (usually) are not altered during development, transcription is the major form of regulation at some stages but perhaps not at others (e.g. early mouse embryogenesis), the localization of maternal products can be important, position-specific (and in some cases lineage-specific or tissue-specific) gene expression is crucial, and cells may be determined long before the determination is evident from 'morphological indices of differential function.' Molecular probes have pushed back the time when cells in an apparently homogeneous population can be recognized as different, raising anew the question of what constitutes differentiation. There is documentation of some of the major problems on which there has been rather little progress in many years, such as the molecular mechanisms through which maternal mRNA is sequestered and eventually activated. These sorts of issues are abstracted to a different level in the extraordinarily good chapter on development in *Molecular Biology of the Cell* by Alberts *et al.* There, no original data are shown and most of the experiments are not described. In contrast Davidson has excerpted the literature, including much original data and selective descriptions of key experiments In many cases the original data are reorganized, or calculations are made, so as to make the story more coherent. This is a great help.

Davidson's book is an extremely useful reference. The tables and appendices provide a large amount of digested and therefore digestible data that is otherwise only available in papers scattered through an immense literature. The reference list is extensive and thorough. The index is reasonably good but could be more detailed. The production of the book was exacting; there are unusually few typographical errors and the printing quality does justice to the subject material. The illustrations are well chosen and in some cases, particularly the colourful showcase in the centre of the book, are exceedingly beautiful. Conklin's drawings, made in 1897, are examples of a lost art, and stand well beside some of the aesthetic triumphs, such as immunofluorescence pictures of the cytoskeleton, of the modern era. (Conklin, as Davidson points out, deduced the existence of the cytoskeleton and named it the 'persistent framework' or the 'spongioplasm' in 1917.)

Davidson's new book has as little relation to previous editions as restriction enzymes have to deoxyribonuclease. The book serves as an extensive review of what has been learned, mostly during the seventies, from analyses of populations of mRNA molecules using Rot curves and analyses of genome organization using Cot curves, and goes on to incorporate much that has been learned using more recently applied methods. The precloning era, to which Davidson made so many important contributions, is well represented in the text and in the references. These global pictures of DNA and RNA complexities are useful for putting in perspective the expression of the many individual genes that are now being studied using cloning methods. In some cases, the new methods have yet to provide important answers to some curious mysteries first discovered using the older methods, such as the enormous complexity of brain RNA. The third edition of the book traces the transition from studying the masses to appreciating the individual; rather than talking only about populations of thousands of genes and their products it is possible to discuss the peculiarities of particular genes.

Another critical transition in developmental biology is in progress and is documented: the individual genes being studied most intensively are not merely those with abundant products or those that for some other reason are most accessible. Rather, there is increasing focus on genes that have been shown through genetics to be critically important to the control of embryogenesis. The importance of this transition is underemphasized in the book, in my opinion. Case studies of genes with abundant products can, of course, provide extremely important information, take haemoglobin and the thallasaemias as one instance, but previously such studies were the only game in town and now we can add to them the studies of the genes that *cause* genes for specialized products such as haemoglobin to be active in only the right cells and at only the right time.

The book is divided into six massive chapters: I. From genome to embryo: The regulation of gene activity in early development, II. The nature and function of maternal transcripts, III. Transcription in the embryo and transfer of control to the zygotic genomes, IV. Differential gene function in the embryo, V. Gene activity during oogenesis, and VI. Cytoplasmic localization. As is evident from the titles, there is overlap between the subject material in the different chapters. The order of the chapters is somewhat surprising. One might have expected the juxtaposition of the issue of maternal transcripts with cytoplasmic localization, for example, or of gene activity during oogenesis with maternal transcripts. The chapters would stand well individually as major reviews or as monographs, and one has the feeling that they were written as separate units. I found the last two chapters to be the best. They are interesting, well-organized, and integrate the old with the new especially smoothly.

Both of the common modes of organization of a developmental biology book, with chapters arranged in order of developmental events or divided according to organism, are largely rejected in favour of an 'issue-driven' organization. This allows a comparative discussion, something that is too rarely attempted. The number of transcription units in the embryos of a variety of species can, for example, be compared in one section. The nongenerality of certain phenomena can be addressed; one example is the apparent nongenerality of the midblastula transition (p. 139). Davidson states: 'it becomes evident that many of the special devices utilized during early development can be interpreted in terms of their adaptive value, given the special biological constraints to which each species is exposed, for example, the time available for oogenesis or embryogenesis, and the conditions in which these processes must occur' (p. 3). This is a very different attitude from that of those searching for relatively universal mechanisms. The comparative approach fosters broader thinking and is likely to lead to a heightened appreciation of the different strategies used by different organisms, but it does make the book more difficult for the uninitiated student. The amount of data and its complexities becomes overwhelming, especially in cases where the experiments have been done in somewhat different ways with the different species. It is also sometimes difficult to know where to find some topics. The discussion of the *Xenopus* transcription factor TFIIIA, for example, is within the lampbrush chromosome section (p. 376–380). Especially in Chapters III–V, subjects are often intermingled in ways that make assimilation of the material more difficult than it could be.

It must have been a special challenge to Dr Davidson to try to select important material for inclusion from the onslaught of publications in the *Drosophila* and *Caenorhabditis* fields. It is impossible for rapidly published reviews to keep up with the current results in these areas and, therefore, it would be completely unfair to expect such a polished book to include the latest about *C. elegans* cell lineages or new 'striped' *Drosophila* genes. It is good, for this reason, that much of the *Drosophila* and *Caenorhabditis* work described addresses issues that have, in some sense, matured Thus, measurements of mRNA complexity at different stages are presented, there is a fold-out copy of the complete *C. elegans* cell lineage, and there is a survey of the different classes of *Drosophila* genes that have been studied for their involvement in embryogenesis. The classes of fly genes are presented in terms of differential gene expression rather than from the perspective of interacting gene networks that control development; as in most of the book, genetic circuitry is not emphasized. Considering its length (about 35 pages) the review of *Drosophila* developmental genetics covers a lot of ground. However, it is my blatantly biased view that in future editions of the book this section would have to be expanded dramatically. The molecular analysis of development has progressed from bulk measurements of transcripts to the study of individual genes and, now, using *Drosophila* and *Caenorhabditis*, from the question of *which* individual genes to study to the goal of studying *all* of the genes involved in a particular developmental process.

There are some errors that may mislead and some unnecessary jargon. Calling something 'interspersed cytoplasmic RNA' (p. 364) is confusing. The striped expression of the *ftz* gene is not reduced to half the usual number of stripes in progeny of mutant *bicoid* mothers, contrary to the statement on p. 289. Nor is the control of *Ubx* expression by the abdominal genes of the BX-C a *cis* effect as is stated on p. 297. These latter issues are ones with which I am especially familiar; I suspect there are fewer slips in some of the other areas that are closer to Dr Davidson's own work. There are other cases where either I miss the reasoning or perhaps the statement is as controversial as it sounds. In *C elegans*, development differential zygotic genome function is observed when the embryo has only a few hundred cells, and it is claimed that 'This property directly predicts the importance of *early cell lineage* in determining the fate of the descendant blastomeres' (p. 194). I do not understand the reasoning behind this claim. Elsewhere it is stated, in reference to the flexibility of early amphibian development, 'Nor can the initial specification processes depend on sequential cascades of genomic regulatory events' (p. 257). Yet why should such a cascade be incapable of flexibility?

The massive amount of material discussed makes the book an imposing task to read, and I see its usefulness more as a reference source than for a course text. How could the amount of material have been usefully reduced to make the remaining text more easily consumed? There are occasional sections where the information presented is of unclear importance and could have been condensed. On pages 58–69, for example, there is a lengthy discussion of the symmetric transcription of repetitive DNA sequences in *S. purpuratus* (and *Xenopus*) embryos that comes to the conclusion that no function can be ascribed to the RNAs. In this instance, the drive to be comprehensive could have been reigned in and a number of others. However, there is no escaping the basic difficulty that the field is vast and therefore the book has to be long. The absence of other books that have the same sorts of goals is probably due at least in part to a lack of authors willing to rise to the task. Other books such as Adam Wilkins' *Genetic Analysis of Animal Development* cover only some of the issues discussed in Davidson's book, although Wilkins' book does much more justice to the power of genetics.

Despite the large amount of material, is there anything missing that should be there? I looked for more advice and guidance from an author with such an exceptional historical perspective. History should help to guide the experimentalist. We would like to hear how to recognize which of the current approaches to developmental biology are most likely to be successful, based on lessons from the past. Wilson (1925, p. 1041) quotes R. Lankester (1877) as stating 'Though the substance of a cell [an egg] may appear homogeneous under the most powerful microscope, it is quite possible, indeed certain, that it may contain *already formed and individualized*, various kinds of physiological molecules.' Of the mass of available data, how are the important facts and ideas to be distinguished from the details? Are we indeed focusing too much on just a few organisms and how are we likely to err in doing so? The implicit answers to some of these questions lie within the book, but a direct assessment of where we stand and how we should best proceed would have been useful. Perhaps science is so different now that what worked for E. B. Wilson would not be as effective anymore, but I suspect that Dr Davidson would agree that Wilson would be every bit as successful in science now as he was 90 years ago. The integrated discussion of classical experimentation and modern developmental biology research is unique to Dr Davidson's and guarantees its lasting value.

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Teratocarcinomas and Embryonic Stem Cells: A Practical Approach

E. J. Robertson (editor)
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Thirty years ago teratocarcinomas were little more than pathological oddities, of passing interest to some oncologists but quite unknown to most biologists. Their emergence from obscurity was largely due to the work of Roy Stevens and Barry Pierce who, between them, gradually impressed on their audiences the special features of these obscure tumours. At a gross level, there was something immediately fascinating in the monstrous form of some teratocarcinomas, the jumble of hair and teeth, skin and brain tissue, intestine and skeletal elements all chaotically cohabiting in a single tumour. But it was the 'life cycle' of teratocarcinomas that was especially intriguing, particularly in the context of the major advances in manipulating early mammalian embryos which occurred in the 1960s.

The stem cells of teratocarcinomas (embryonal carcinoma cells, EC, cells) share many morphological, biochemical and behavioural characteristics with their natural progenitors: germ cells and early