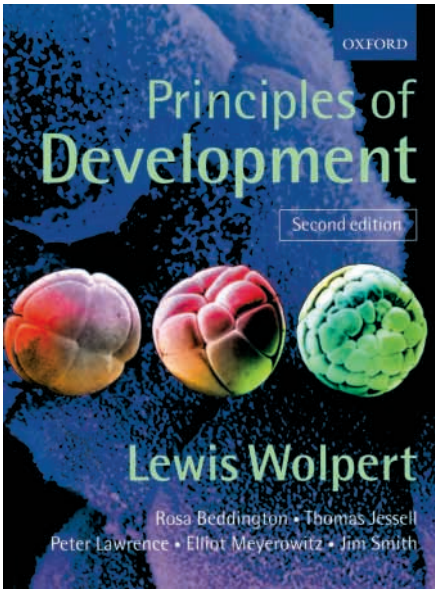
# Developmental biology comes of age




## Principles of Development, 2nd edn

**by Lewis Wolpert, Rosa Beddington, Thomas Jessell, Peter Lawrence, Elliot Meyerowitz and Jim Smith**

Oxford University Press (2002) 542 pages. ISBN 0-19-879291-3
£29.99

The last thirty years have witnessed seismic changes in biology, in its methods and in many ways also its goals. Where genetics had been dealing with one or a handful of genes at a time, now it deals with whole genomes. Where neurobiologists looked in detail at small neuronal circuits with three or four elements, now they can analyze emerging properties of large-scale neural networks. Not surprisingly, all this has had an impact on the way the different disciplines are taught and in the way they deal with each other. These changes have been most dramatic in the area of developmental biology, and *Principles of Development* by Wolpert et al., now in its second edition, is a tribute to these advances, a landmark in a field that has come of age and a guide for the future.

Developmental biology is about the miracle that transforms one cell into many and organizes them in space following creative and appealing design principles. In the 1970s we knew that genetics was about genes, neurobiology about neurons, the immune system about lymphocytes and immunoglobulins, but we had very few clues about what drives the development of embryos. Was every organism a tailor-made recipe with special ingredients and specific instructions? We knew for sure that genes and proteins played a role but what were those proteins? What did they do? It was this mystery that teased and challenged the curious mind. At that time, textbooks of developmental biology struggled to find some common thread in detailed descriptions of the embryology of different organisms, which in the best cases (e.g. Balinski's textbook) were interspersed with experimental interludes. These books, largely a collection of remarkable responses of developing systems to injury, simply enhanced and deepend the mystery. Things had not changed much since the 1930s and it showed. A book like Huxley and de Beer's *The Elements of Experimental Embryology*, first published in 1934 and reprinted in 1963, still attracted some interest in the 1970s. But all this changed in the mid-seventies and has not stopped changing ever since. There were two reasons for this. First of all, genetics and molecular biology brought new angles, perspectives and analytical tools. This allowed biologists to get to the nuts and bolts of the system. In addition, some individuals brought different ways of thinking and new questions that kept the important items in focus. Among these Lewis Wolpert caused an important inflection. His concept of 'positional information' and the way he applied it to concrete problems - for example, limb development and patterning - has had a crucial impact on several generations of young developmental biologists. In addition, it has provided an essential framework in which to think about development and pattern formation and more importantly to organize the information that has been accumulating at an accelerating pace.

There were, and are, a few good textbooks in developmental biology, but almost all of them tread a classic path in which embryological descriptions are interspersed with experiments and crash courses in molecular biology. One exception is, perhaps, Ede's little known *An Introduction to Developmental Biology* (1978), which very early in the modern era tried a more conceptual approach to the subject. A few years ago Wolpert decided to make the effort of extending his conceptual skills to the whole of developmental biology and, with the editorial assistance of a selective group of colleagues, wrote and framed the elegant *Principles of Development* (1998). When I first saw this work I was immediately taken by the way it presents the field. I was particularly struck by the linearity of the argument. This was no collection of facts but a true attempt to show that a field had found maturity and that the conservation of molecular mechanisms revealed by the application of genetics to the subject underpinned the existence of general strategies that operate in different systems. There might be principles in developmental biology after all. The text is simple and makes easy reading, putting concepts first. The illustrations are not only appealing but also conceptually superb, conveying in a direct and clear manner complex ideas. I welcomed the appearance of this much needed book. Now we get its second edition, which, in essence, is an updated version of the first. There are no radical changes to the layout or to the thread of the argument, simply a few more examples that help consolidate what had been so clearly expounded in the first edition. And perhaps this is right. Why alter what is good? For the special thing about Wolpert's book is that it represents Wolpert's way of looking at the field, and this is one in which elegance and simplicity of argument are used not to hide anything but rather to bring out what is important.

Does the book have any flaws? All textbooks with the scope of this one will get this or that detail wrong and, within some very reasonable limits, one should not blame the author for that. Also, inevitably, the interest in stating principles and generalities leads to idiosyncratic choices of example and perspective, which may irritate detail-oriented readers or members of different ideological churches. Probably this is

also good because debate and discussion is the essence of science. If there is one problem with both the old and the new edition it is that Wolpert's view does not rely too much on molecular mechanisms. The essentials are there - the concepts, the signals and the transcription factors, etc. - but the emphasis is not. Once again, having stated this, in the context of the book it maybe alright. Developmental biology has its roots in embryos, and Wolpert's views are and have always been deeply rooted in that realm. Nonetheless, if anything is missing in this second edition it is 'taking in' the increasingly dramatic changes in the cell and molecular biology of development. If the book is seen as an introductory textbook, which in many ways it is, this may not be a problem, simply another reflection of the influential views of the author.

This book is, by far, the best introductory textbook in existence for an interesting but complex subject. I am aware that the book has already influenced the teaching and the thinking of more than one class, and this edition will continue to do so. The book is also a useful reference for researchers because it helps us to focus the questions. If we agree with the notions put forward in the text, it will reinforce them. If we do not agree with them, it will challenge us to f.ind similarly clear arguments to rebut them. Above all the textbook will remind us of the need to search for principles. This is no small reminder in these days in which biology sometimes gets diluted in a sea of information, while we wait for someone or something to give it a framework. And for students, it will give them an interesting flavour and perspective of an area of biology that is rapidly coming of age.

### References

**Wolpert, L., Beddington, R., Brockes, J., Jessell, T., Lawrence, P. and Meyerowitz, E.** (1998). *Principles of Development.* Oxford: Current Biology Ltd, Oxford University Press.

**Huxley, J. S. and De Beer, G. R.** (1934). *The Elements of Experimental Embryology.* Cambridge: The University Press.

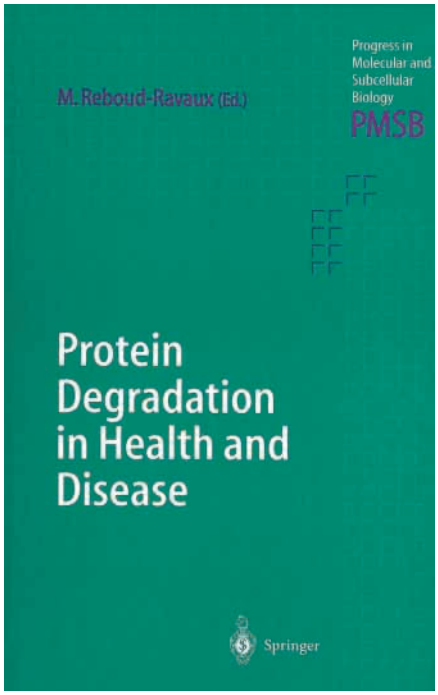
**Ede, D. A.** (1978). An Introduction to Developmental Biology. Glasgow: Blackie & Son.

**Alfonso Martinez Arias**
Department of Genetics, University of Cambridge, Cambridge, UK

*Journal of Cell Science 115, 2623-2625 (2002)*


---

# Ageing due to tired proteolysis




## Progress in Molecular and Subcellular Biology: Protein Degradation in Health and Disease

### edited by Michèle Reboud-Ravaux

Springer-Verlag (2002) 130 pages. ISBN 3-540-42594-2
£45.50/$75

What determines the levels of a functionally active protein inside a cell? If biologists had been asked this question ten years ago the answer would probably have been very different from that given now. Then, the likely response would have been mRNA levels and/or degree of post-translational modification. Now, control of protein degradation would be a key factor to consider. Consequently, an intensive research effort is underway to identify those components and pathways that regulate this latter process.

This book presents a series of independent reviews that have a readable style and cover different aspects of protein degradation within normal and diseased cells and tissues. Our knowledge of this biological process has been increasing at an exponential rate. This book can, therefore, only hope to give a flavour of the different areas covered. Nevertheless, it provides a good starting reference for many of the topics covered through excellent up-to-date review articles.

The opening chapter enforces the concept that protein degradation in cells is not a random process. It provides examples of the complexity of selecting proteins for ubiquitin-mediated degradation. The emphasis is on the SCF-type of ubiquitin-protein ligases and, in particular, on the function of the tumour suppressor protein VHL. This was perhaps not surprising given the authors' research interests. The underlying theme of the next four chapters is the various aspects of the relationship between protein degradation and ageing in normal and diseased tissues. They describe how the removal of misfolded, mutant, oxidatively damaged or inappropriately modified proteins is dependent on the appropriate functioning of these pathways. The importance of protein degradation is also indirectly highlighted by the observation that mutations to components of these pathways include tumour suppressor proteins and proteins associated with neurodegenerative diseases. What is not generally realised, perhaps, is that targeting of proteins for degradation apparently decreases with age.

The final two chapters are concerned with describing the characteristics of the 26S proteasome and the design and use of inhibitors of proteasomal activity. Such reagents could be used to control the rates of protein degradation. This information may be particularly stimulating for those in the pharmaceutical industry seeking drug targets. Components regulating protein turnover could be considered as

potential targets for novel therapeutic strategies. So, for example, the therapeutic use of specific inhibitors of the proteasome for the treatment of muscle-wasting diseases or activators of proteasomal activity for treatment of diseases associated with ageing, such as the neurodegenerative diseases. Promoting the interaction between components of E3 ligases, such as between mutated VHL and its interacting partners, may provide novel approaches for the treatment of cancer. The design of such molecules will be aided as the three-dimensional structures of components of these systems are described. At present, these include the proteasome and SCF complexes.

I would recommend this book particularly to those new to the field, such as graduate students. Those already working in this area of research, will find a number of the sections to be thought provoking and a useful reference. However, there is a danger that the rapid advances being made in this research area will quickly date its contents. The timing of this book is therefore appropriate. Those readers not familiar with the ubiquitin-26S proteasome pathway may find the repeated description of this process in many chapters useful. Others, however, may find it rather repetitive!

**Philip A. Robinson**
Molecular Medicine Unit, St. James's University Hospital, Leeds, UK

*Journal of Cell Science 115, 2623-2625 (2002)*