History lesson

Benno Müller-Hill

A History of Molecular Biology

by Michel Morange

translated by Matthew Cobb

Harvard University Press, Cambridge, MA,

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Michel Morange, a French professor of biochemistry, has written a history of molecular biology in 21 chapters that is now available in a paperback version in English. Molecular biology arose when geneticists, physicists and biochemists came together and moved DNA into the centre of their interest. 'A molecular biologist is a biochemist without a licence' was a description by Erwin Chargaff, a biochemist who discovered the base-pairing regularity of DNA.

Morange's historical overview begins with a description of the 'roots of the new science', i.e. *Drosophila* genetics and protein chemistry. From there, it took a long time until the structure and function of DNA and proteins became finally known. In this context, Morange mentions briefly the colloid theory of proteins, which claimed that amino acids are non-covalently connected, adding that several Nobel prizes were awarded for this work. Unfortunately, he does not include their names and discoveries.

In fact, there are many details not mentioned that would be interesting to know. When writing about the One Gene–One Enzyme hypothesis, Morange does not mention Adolf Butenandt and Alfred Kühn. They made the discovery, but indeed they did not spell it out. Oswald Avery's work is then discussed in detail and the reason why he did not get a Nobel prize. Morange mentions the claim of a French bacteriologist, André Boivin, to have repeated Avery's experiment with *Escherichia coli* but nobody could repeat Boivin's experiments. This is followed by chapters on the phage group, the role of

physicists in molecular biology and in bacterial genetics: how lucky Joshua Lederberg was to have used *E. coli* K12, the only *E. coli* strain that contained an F factor!

The next chapters are on the double helix, messenger RNA and the genetic code. All this is written in a rather abstract manner. I would have liked to read, for example, what happened to Heinrich Matthaei after his discovery that poly-U makes polyphenylalanine. It is as if the people who did the experiments are shadows, who did not exist before and after their discoveries. However, the chapters on the 'French School' are different, i.e. describing André Lwoff, François Jacob and Jacques Monod. Indeed, Morange gives strong emphasis to their work and life. Monod has a footnote of about half a page on his political and literary activities. According to Morange, 'the work of the French school...made it possible at last for molecular biology to come of age'. However, 'molecular biology made little progress between 1965 and 1972'. So the isolation, functional analysis and protein sequence of the Lac and Lambda repressors is just boring science that does not need to be discussed. Would he have come to a different conclusion had scientists from the Institut Pasteur isolated these repressors? Furthermore, Morange seems to believe that Gunther Stent was by and large right when he wrote in 1968 that molecular biology had come to an end. What a mistake! Cloning of DNA in *E. coli*, DNA sequencing and synthesis, large scale X-ray and NMR analyses were still to come, and are indeed aptly described in later chapters.

But Morange includes only a few recent works in molecular biology in his book. For example, he does not mention Jeffrey Miller's mutant analysis of the Lac repressor, Roger Kornberg's and others' work on the structure of the nucleosome, or Mark Ptashne's work on transcriptional control by Gal4 in yeast. Apoptosis, prions and conditional knock-out mutants of the mouse do not seem to exist. Admittedly, inclusion of all these items would have changed the size and structure of the book.

A book becomes exciting when even experts learn things they did not know before. The most troubling news for me was that Pauling published two papers announcing *in vitro* proof of his instructive theory of antibody formation [*Science*, **95**, 440–441 (1942) and *J. Exp. Med.*, **76**, 211–220 (1942)]—discoveries that he could not repeat. According to Morange, Pauling and other immunologists never quoted these results again. There are more of these stories in the book that will be of interest to the general reader.

Although there are occasional misprints, the book is well translated. And despite its emphasis on the work of the French school and the gaps in the history of recent molecular biology, the book is certainly a must for historians as well as for biochemists interested in the roots of their science. However, I do not think that this book will appeal to the younger molecular biologists, who will have already learned the early history during their lectures on biochemistry and molecular genetics. Such a history of molecular biology is yet to be written.

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Aging stochastically

Suresh I.S. Rattan

A Means to an End. The Biological Basis of Aging and Death

by William R. Clark

Oxford University Press, Oxford, UK.

233 pages, US\$ 27.50

ISBN 0-19-512593-2

I have read this book twice. Not because it is, as it claims on its cover, '... a highly readable, provocative account of some of the most far-reaching and controversial

questions we are likely to ask in the next century...,' but because I was desperately trying to find something positive, something praiseworthy to say about it. One good thing I found is the Greek mythological story of the three sisters Klothos, Lachesis and Atropos who spin, apportion and cut the thread of life, respectively. There is more imagination, vision and suggestion in this 250-word myth mentioned in the opening pages of the book than in the remaining 233 pages.

In recent years, the market has been flooded with books on aging, covering the whole range from serious discussions of the theories and mechanisms of aging to self-help, quick-fix anti-aging miracles. Fortunately, this book does not belong to the latter category of books that give a bad name to the field of aging research. On the other hand, it does not contribute anything new to the field of biogerontology either. I could not find out to what 'End' this book is 'A Means'!

In his brief introduction, Clark compares the state of aging research with that of cancer research and expresses his hope for unified DNA-based answers to the complex phenomenon of aging. In the rest of the book, the author treads a well-trodden path of reviewing the whole field of biogerontology in 10 chapters. The book starts with a description of lifespan curves, maximum lifespans for selected species, and outdated correlations of body weight with maximum lifespan, before it goes on to a superficial discussion of the nature and evolution of senescence and death. What could have been an important discussion of the developmental genetics of senescence and lifespan, and the nature of senescence repressor and senescence effector genes is marred by an almost mystical presentation of 'death is the default state' kind of ideas. Clark briefly discusses premature aging syndromes, before he returns the reader's attention to Leonard Hayflick's discovery that somatic cells can undergo only a limited number of replications. It would have been instructive if the author had expanded on the important role of telomeres and telomerase. Even the chapter on the immunology of aging, which is supposedly the author's field of research, is superficial and uncritical. The remaining chapters are just general overviews of the research on the anti-aging and life-prolonging effects of calorie restriction, the role of

free radicals and other oxidative stress in the occurrence and accumulation of macromolecular damage, and the aging of the brain. In the final chapter, 'A Conditional Benefit', William Clark makes an unsuccessful attempt to reduce aging and longevity to the genome, and to argue for life style modulations to achieve a healthy old age.

'A Means to an End' serves nobody's purpose. It neither quenches the public's thirst for scandal, miracle cures and false hopes, nor does it strike an intellectual chord with scientists. Indeed, the author is certainly not going to make either money or his name from the book. Although factually correct, the overall tone of the book is impersonal, uncritical and unexciting. The limited bibliography at the end does no justice to the vast literature available in the field of gerontology. In my view, the author of four previous books on immunology, sex and molecular medicine could and should have done much better in his fifth book on aging and death.

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Brain history

Norman Saunders

Mechanisms of Cortical Development.

by David J. Price and David J. Willshaw

Oxford University Press, Oxford, UK.

328 pages, £69.50

ISSN 0-19-262427-X

Single author, or as in this case, dual author textbooks are becoming rare in today's world of increasing specialization and explosion of factual knowledge. The big advantage of this type of book is that the reader gets a unified view of a field. This is difficult to achieve in multi-authored books, which even with the most diligent editors are likely to be a mosaic with gaps and style changes. However, the uniformity of single/dual authors may be at the cost of detail and

accuracy when they stray from their areas of expertise.

David Price and David Willshaw join a select group of distinguished authors who have shown their breadth of expertise by providing specialist monographs on topics as diverse as 'Secretory Mechanisms of the Gastro-Intestinal Tract' and 'Human Baro-reflexes in Health and Disease'. Those interested in the development of the cerebral cortex should be grateful to the authors for providing a largely up-to-date book that seeks to explain what is known today about the fundamental mechanisms that underlie the development of the mammalian neocortex. The scope is broad indeed, covering topics at the cellular and molecular levels including: the early development of the telencephalon, its molecular regulation, axon guidance and the control of cortical connections. The general coverage of the monograph makes it useful not only to the non-expert who wants an entry into or update on the field, but the wide range of the book makes it also of benefit to experts, who want a view of related aspects in the context of their own work.

The introduction mentions future challenges, which helps to establish the scope of the volume. The authors make the case that understanding the mechanisms of cortical development will have a great impact on our ability to comprehend and eventually treat neurological disorders. They make the conscious (*sic*) decision, however, not to deal with the nature of consciousness on the grounds that it is not directly observable, but can only be inferred from behaviour—a view that may not be shared by cognitive neurobiologists. The one concession to this view of neurobiology is in the last chapter, which deals very briefly with face perception and language, both of which require consciousness.

Much of the authors' description of cortical development is based on what is known about the mouse. They reason that future use of molecular biology techniques and studies of mutant mice will substantially increase our understanding of human neurological disorders. As the authors demonstrate, this is already bearing fruit in understanding the earliest stages of neural tube development and the etiology of certain neurological disorders. But proper understanding of human conditions requires knowledge of development of the