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Book Reviews

A Chromatin Retrospective (1871–1989)

Chromatin.
By K. E. van Holde.
New York: Springer-Verlag. (1989). 497 pp. $98.00.

This is a very readable book on the structure and function of chromatin, which provokes a personal perspective on the field of chromatin research. Dr. van Holde brings a physical chemical bias to his writing, which is appropriate for a field heavily dependent upon physical techniques and models. In one sense, the purpose of the book is to bring the physical chemistry and molecular biology of chromatin to the biochemist or cell biologist who might have a disrespect for the ambiguities that surround studies of DNA complexed with protein. Another group in critical need of knowledge are those many students of DNA sequences, DNA structures, transcription factors, and in vitro transcription, as well as others who study genes sans nucleosomes. They should be curious about how their studies might relate to genetic material that is subject to the constraints imposed by nucleosomes, chromosome fibers, and nuclear matrix. After reading the book, such readers might have more appreciation for the goals and difficulties of the experiments on chromatin. To devotees of chromatin, the book serves to unify all facets of chromatin knowledge. It is an indispensable reference for anyone who studies the eukaryotic genetic apparatus.

A chromatin review is timely. This is the first comprehensive book on chromatin—preceded only by a handful of edited volumes, notably *The Nucleohistones* (edited by J. Bonner and P. Ts'o, Holden Day, 1964), *Chromatin* (Volume XLII of the Cold Spring Harbor Symposia on Quantitative Biology, 1978), *Chromatin Structure and Function* (edited by C. A. Nicolini, Plenum Press, 1978), and Volumes 1–12 of *The Cell Nucleus* (edited by H. Busch, Academic Press, 1974–1982).

Although van Holde maintains that studies of chromatin are expanding, I don't think this is true. The total number of publications in the area is actually decreasing, and many former chromatin investigators have found productive employment in other fields. The first era of chromatin research is coming to a close, and van Holde's eulogy is in order. Studies of the canonical nucleosome, gene, chromatin fiber, and chromosome are becoming less and less relevant, as it is realized that diversity of chromatin structure is the inevitable consequence of diversity of genetic function.

The situation is reminiscent of the first era of DNA research, which was based on the canonical forms of DNA, and the recent resurgence of interest in DNA structure brought about by methods that make feasible the study of the sequence specificity of DNA structure. Chromatin research awaits such a resurgence, which will probably come from transcriptional, biochemical, and structural studies of specific-sequence chromatin fragments in vitro.

In fact, the new wave of understanding about gene-specific chromatin is presaged by recent innovative studies, such as those on scaffold-associated regions (e.g., Gasser and Laemmli, Cell *46*, 521–530, 1986), the interactions of transcription factors with nucleosomes (e.g., Workman and Roeder, Cell *51*, 613–622, 1987), the mechanism of nucleosome positioning (e.g., Thoma and Zatchej, Cell *55*, 945–953, 1989), the changes in nucleosomes during transcription (e.g., Nacheva et al., Cell *58*, 27–36, 1989), and the heterogeneity of rRNA chromatin (Conconi et al., Cell *57*, 753–761, 1989). van Holde documents the past failures and successes of the chromatin field and points out many of the useful future approaches.

Chromatin reviews the results from about 2000 research articles. Chapters are devoted to a history of the pre-nucleosome era, the discovery of the nucleosome, the structure of DNA, the histones, the nonhistones, the nucleosome, higher order structure, transcription, and replication. In reading the last six chapters, I was depressed by how much effort it has taken to unsuccessfully approach the critical questions. Whenever yet another study of nuclease sensitivities of specific genes appears, I am reminded of people wishfully searching the woods for footprints and other ephemeral evidence of the yeti. In fact, neither the structure nor the function of histones, nonhistones, nucleosomes, or higher order fibers is known to useful resolution. What do we actually know of the roles of DNA methylation, histone modification, and DNA topology in gene structure or function? What we think we know really amounts to imaginative models and cartoons—blurred images of the real quarry.

Relevant to the recent discussions of the role that journals should play in publishing unexpected results, Chapter 2 begins with a referee's damning comments about what should have been a seminal paper by C. L. F. Woodcock in 1973: "A eukaryotic chromosome made out of self-assembling 70 Å units, which could perhaps be made to crystallize, would necessitate rewriting our basic textbooks on cytology and genetics! I have never read such a naive paper purporting to be of such fundamental significance. Definitely it should not be published anywhere!" Reviewers beware! Reports of cold fusion, absurd dilution experiments, and polywater (remember when?) seem to be a small price to pay for the freedom to publish innovative work.

A more thorough review of Chapter 8 on chromatin structure and transcription will illustrate van Holde's approach. It begins with a series of questions that are important to the understanding of the mechanism of gene regulation. The experimental techniques, such as electron microscopy, nuclease digestion, and chromatin fractionation, and their shortcomings are described. There are sections on tRNA, 5S, and ribosomal genes, as well as on pol II–transcribed genes. The chapter includes a table summarizing the nuclease digestion results from 39 genes and detailed discussions of the hemoglobin, heat shock, and ovalbumin genes. van Holde then weighs the often conflicting evidence that transcriptional activity is correlated with histone stoichiometry, histone modifications, nonhistone proteins, or DNA torsion. The domain model for gene activation is explained. van Holde is aware of the difficulties in designing, performing, and interpreting the experiments. His emphasis is upon the mechanism and theoretical principles, rather than phenomenology and ad hoc explanations. As an experienced chromatineer who has seen the alchemy of new experiments turn fact into forgotten reference, he is cautious in his interpretations.

This book is meant to be read from cover to cover. The style is conversational and very easy to understand. This style is sometimes abused, however, by phrases in the first person, such as "it seems to me" and "recent results from our laboratory." The lack of detail in the table of contents, subtopic headings, and index is a serious problem, which makes the book difficult to use as a reference text. In addition to omission of obvious index entries (e.g., NMR, histone exchange, magnesium, and nucleoplasmin), the page references are often incomplete. The extensive reference list of publications before 1985 is a very useful resource for chromatinologists. However, the sevenfold reduction in the number of references between 1985 and 1986 and the virtual lack of results after 1986 are serious shortcomings of the book. The usefulness of this unified treatment of the diverse subject of chromatin far outweighs the shortcomings.

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Microtubule-Based Motility: Two-Way Traffic Ahead

Cell Movement. The Dynein ATPases. Volume 1.
Edited by F. D. Warner, P. Satir, and I. R. Gibbons.
New York: Alan R. Liss, Inc. (1989). 337 pp. $88.00.

Cell Movement. Kinesin, Dynein, and Microtubule Dynamics. Volume 2.
Edited by F. D. Warner and J. R. McIntosh.
New York: Alan R. Liss, Inc. (1989). 478 pp. $98.00.

Turning the wrong way onto a one-way street is both embarassing and dangerous. The typical reaction is to pull into the nearest driveway and turn around, all the while to the sound of honking horns from cars going in the right direction. Until recently, models to explain motile events suspected of being based on microtubules (MTs) were constrained by an analogous one-way sign, because the only protein known to generate force along a MT was axonemal dynein. Because dynein can power movement only toward the (−) end of MTs, interpretation of data that implicated MTs in cellular movements had to heed the one-way sign or face the honking horns of colleagues.

Work in the last five years has led to a series of striking developments that have fundamentally changed our views of MT-based motility. In *Cell Movement*, a nearly comprehensive collection of articles describes these advances. The book has been divided into two volumes that could be subtitled *The Old* and *The New*, depending on when the motor proteins discussed in each were initially discovered. *The Dynein ATPases* (Volume 1) covers about 20 years of research on axonemal dynein, the archetypal MT-based motor. The topics in this volume range from the largely unanswered questions about dynein's composition, overall structure, and cross-bridge cycle to present concerns about the domain substructure of its heavy chains, the regulation and coordination of its activity in the axoneme, and the conversion of linear sliding force into the complicated bending of the axoneme.

Kinesin, Dynein, and Microtubule Dynamics (Volume 2) is a more eclectic mix. While it focuses on the recent work on kinesin and nonaxonemal or cytoplasmic dynein, it also includes sections on MT structure and dynamics and MT movements in mitosis. Although these latter sections stray from the focus of the second volume, their inclusion is warranted. The section on MT structure reminds us of the importance of understanding both the engine(s) and the track(s); that on mitosis provides us with an example of how the discovery of cytoplasmic motors has influenced other fields. It is curious that a section exploring the impact of the discoveries of kinesin and cytoplasmic dynein on other areas was not included, because there is considerable evidence that the intracellular motility of many secretory organelles (e.g., Golgi, ER, etc.) is MT based; although the motor proteins for these organelles have not been identified, it is likely that they will be similar or perhaps identical to kinesin and dynein. A discussion of current research in this area would have extended the general appeal and usefulness of the books.

The chapters of *Cell Movement* were contributed by top researchers in the field and range from extensive *Annual Reviews*-type articles to efforts largely concerned with research in the author's lab. Most of the articles are targeted to the general audience of cell biologists, and the short "Perspective" articles that begin each section should be useful in orienting the unfamiliar to a particular topic. The volumes will also appeal to the specialist, because they draw together a body of work previously unavailable in a single reference. This is especially true of the volume on axonemal dyneins, a cover-to-cover reading of which gives one an appreciation for the development of our knowledge about this fascinating protein. However, some of this extensive coverage of axonemal dynein would have benefited from heavier editing—reading about which polypeptides belong to outer and inner arm dynein for the fourth or fifth time was an effective yawn inducer.

Although the articles understandably contain little previously unpublished data, there are some new data, as well as a number of novel provocative ideas that make these