where to start. The point was to reduce the 64 codons to a total of 20, one for each amino acid (although I can't see why three codons per amino acid wouldn't have been more likely). Objections soon arose. The comma-free code had no evolutionary flexibility among organisms with varying guanine and cytosine content of DNA. Another objection, which was not mentioned, is that 70% of possible single nucleotide substitutions produced by point mutations will give rise to nonsense codons, so evolution would be virtually impossible. In the universal code, only 4.2% of possible point mutations produce stop codons. The comma-free code met a swift death when Nirenberg and Matthaei found that polyuracil coded for phenylalanine so that apparently the translation process could start anywhere. Later, of course, ribosome binding sites and start signals were discovered.

Crick obtained great satisfaction from his experiments in establishing the triplet nature of the code by using addition and deletion mutants of T4 bacteriophage as described on pp. 122–142. One (or two) additions would put the reading frame out of phase. If one (or two) deletions were made a short distance further along, the reading frame would start again. This was beautiful work, but it did not provide a surprise. By contrast, the wobble theory, proposed by Crick in 1966, was entirely unexpected, and was based on striking deductions from a handful of data obtained through model-building. It says, for example, that guanine in first anticodon positions pairs with both uracil and cytosine in third codon positions. Therefore, all pairs of codons ending in uracil or cytosine are synonymous; each of the 16 pairs of codons ending in a pyrimidine should code for a single amino acid, which prediction was promptly confirmed by biochemical studies with synthetic polynucleotides. All anticodons that have been discovered confirm the wobble rules.

Readers are given quite a lot of good advice. Crick says, "Most of the book is fairly easy. Don't give up hope just because a few paragraphs seem a little hard to follow." On p. 142, discussing theorists, "It is amateurs who have one big bright beautiful idea that they can never abandon. Professionals know that they have to produce theory after theory before they are likely to hit the jackpot." And "Theorists almost always become too fond of their own ideas. It is difficult to believe that one's cherished theory, which really works rather nicely in some respects, may be completely false."

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Chromatin Research Surveyed

Chromatin. KENSAL E. VAN HOLDE. Springer-Verlag, New York, 1988. xii, 497 pp., illus. $98. Springer Series in Molecular Biology.

Though the study of chromatin began in 1871 with the work of Miescher on "nuclein," in the past 15 to 20 years investigations of the complex of DNA, histones, and other proteins that make up the genetic material of eukaryotic cells have proliferated at an incredible rate. Milestones marking this development include the first chromatin Gordon Conference in 1972, the Cold Spring Harbor meeting in 1977, and now van Holde's monograph. Though reviews of progress in areas of chromatin research appear at least yearly, this book is the first comprehensive overview of this important field.

In the preface, the author compares his effort, which began eight years ago, to that of Sisyphus. Indeed, the task van Holde took on was gigantic and could have been unending—the book includes about 2000 references, and this list is quite selective—but he wisely set an end to it. The result, though not totally current, is a major contribution for the expanding scientific community that needs to have a background in chromatin.

Chromatin begins with two historical chapters, the first tracing early studies that defined DNA as the genetic element and described its association with structural proteins in the cell nucleus, and the second documenting efforts in the 1970s that led to the paradigm of nucleosomal organization of chromatin. The author then provides three chapters that succinctly but appropriately describe features of DNA, histone, and nonhistone chromatin protein composition and structure. This section of the book is invaluable to a chromatin scientist, a critical compilation of a lot of information for application to research.

With composition established, the second half of the book addresses chromatin structure and function. As the author notes, the time is ripe for some meaningful conclusions about the former topic, but premature for such analysis of the latter. Van Holde, one of the major contributors to the development of ideas about histone–DNA interactions, first deals with nucleosome structure. He recounts how, having a biochemically defined substrate for study, chemists were able to glean much information about the detailed organization of the nucleoprotein complex, culminating in the crystal structure of the core particle, that "precarious marriage of basically incompatible partners," DNA and the histone octamer. The second chapter on structure addresses organization from the chromatin fiber to metaphase chromosomes—again it is critical and illuminates controversies in this area of investigation and the current uncertainties in interpretation of data.

The final two chapters of the volume address the more difficult subject of chromatin function in transcription and replication. As van Holde acknowledges, these are areas where developments are occurring with great rapidity and, as he predicted in the preface, the chapters are already somewhat out of date. He has elected to review a limited subset of transcriptionally active or competent gene structures and reviewed them in detail (an approach I applaud, as opposed to an encyclopedic but shallow compilation of all studied systems). His chapter on replication addresses a complex subject that is of great interest; unfortunately, it has fallen from favor largely because the questions are so difficult and the answers often ambiguous. This chapter is one of the best examinations of replication of chromatin I have read.

What are the weaknesses in the book? Unfortunately, there are not infrequent mechanical errors. References are current only through 1985, with some from 1986 and only a few from 1987. The volume is not meant to be equivalent to a journal mini-review—rather, it provides a foundation for assessing the current literature.

What is the major strength of *Chromatin*? The author has provided a critical evaluation of a mass of data that have never before been reviewed in such detail. Admittedly personal, his ideas are well thought out and usually solid. He is willing to take a stand on some controversial issues while admitting he might be shown wrong in the future. He consistently points out limitations in interpretation of data and eschews overly speculative thinking.

Finally, who should read this volume? Not surprisingly, almost anyone who is involved in research directly or peripherally related to its topic. It will be a marvelous springboard for a graduate-level course in eukaryotic protein-DNA interactions. All those interested in *trans*-acting factors, who run mobility shift gels or do footprints, should read it to discover features of the in vivo milieu in which DNA really exists. Those of us who have been around through the nearly two decades of modern chromatin research should read it to relive the excitement and to take heart in still working at the admittedly more difficult current questions involved in relating composition, structure, and function in the eukaryotic genome.

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