Book Reviews

Molecular Biology of the Chromosome

Cold Spring Harbor Symposia on Quantitative Biology. Vol. 38, Chromosome Structure and Function. Papers from a symposium, Cold Spring Harbor, N.Y., May 1973. Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y., 1974. xxii, 1010 pp., illus. $30.

While the central role of the chromosomes is fundamental to our concepts of development and heredity, these organelles have, until recently, been disappointingly inaccessible to attempts to elucidate their basic structural and functional organization. The physical and chemical complexities of eukaryotic chromosomes have made difficult the successful application of the sophisticated techniques of molecular biology that were so powerful in contributing to our understanding of simpler genetic systems.

Chromosome Structure and Function shows clearly that more than a beginning has been made toward a description, if not yet a full understanding, of chromosomes at the molecular level. Most of the 95 papers included in this symposium volume, covering topics ranging from operator regions in bacteriophage lambda and *Escherichia coli* to B chromosomes in grasses and grasshoppers, consider in various ways problems of the organization of DNA and proteins in chromosomes, transcription of chromosomal DNA, and, to a lesser extent, duplication of chromosomes. While almost overwhelming quantities of data, some of which have been published previously, are presented, there is general agreement on several aspects of the chromosome and no lack of speculation on others that are less well understood.

One long-standing problem that now appears to be resolved is that of chromosome strandedness. The hypothesis that each unduplicated chromosome contains only one double helix of DNA is very strongly supported by the demonstration that cells contain DNA molecules of molecular weights almost exactly equivalent to the estimated DNA contents of individual chromosomes. This is elegantly shown by Kavenoff *et al.*, using chromosomally different strains and species of *Drosophila*, and by Petes *et al.* and Cryer *et al.*, using aneuploid strains of yeast.

From the large number of papers in this symposium describing work in which nucleic acid hybridization techniques are used, it is apparent that these are the most popular, and probably also the most powerful, probes currently available for the analysis of the organization and transcription of chromosomal genes. Many of the data obtained by such techniques support the hypothesis that there is a large proportion of unique sequences of DNA in the eukaryotic genome, many of which are interspersed with shorter, repeated sequences. The use of RNA to elucidate the arrangement of sequences in the DNA from which it is transcribed is especially impressive; the results are interpreted by several authors as showing that the transcriptional unit consists of repeated sequences adjacent to the coding sequence of the structural gene. Some of the repeated sequences are transcribed and may even be retained in messenger RNA (mRNA) molecules, although the latter does not seem to be the case with the hemoglobin mRNA discussed by Bishop and Freeman. Whatever the fate of the transcribed repetitive sequences, the data support the attractive hypothesis of Britten and Davidson that repeated sequences may be involved in regulation of transcription or translation.

The origin and maintenance of the tandemly linked repeated sequences coding for ribosomal RNA are discussed at some length, and mechanisms for amplification, magnification, and rectification are suggested. Speculation on the role of simple-sequence DNA's is noticeably absent, and more attention is paid to evolutionary aspects of these highly repeated sequences than to their function; it is clear, however, that the unfortunate tendency to assign repeated-sequence DNA's without known function to categories of "redundant," "nonsense," or "junk" DNA is much less prevalent than before.

The one-to-one relationship between bands of polytene chromosomes and units of genetic function appears to be well established, as is illustrated in papers by Judd and Young, Hochman, and Lefevre. Especially fascinating is the fate of the DNA of individual bands of polytene chromosomes of the ciliate *Stylonychia*; Prescott and Murti review the evidence that this DNA is degraded to "gene-sized" fragments which then undergo multiple replications to form the mature macronucleus. Clearly the maintenance of a linear chromosome is not required in this specialized type of nucleus.

Neither the nature nor the functions of the associations of chromosomal proteins with DNA have been established. Speculative models of chromosome fiber organization are again presented here, but the differences in interpretation are sufficient to illustrate the lack of understanding in this field. Both histone and nonhistone proteins are implicated in regulation of gene expression, although the significance of the complex modifications shown to be undergone by these proteins is not yet clear.

The large number of papers included makes for considerable variation in style of presentation and ease of reading. Overall, however, this volume succeeds not only in illustrating the major areas of chromosome research but also in pointing out that, despite the enormous gaps in our knowledge, the "sense of excitement" mentioned in the foreword is fully justified.

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Cells in Culture

Biology of Fibroblast. Proceedings of a symposium, Turku, Finland, Aug. 1972. E. KULONEN and J. PIKKARAINEN, Eds. Academic Press, New York, 1973. xiv, 690 pp., illus. $35.50.

The title of this book is not only awkward, it is misleading, since only a small fraction of the 60 chapters deal specifically with fibroblasts. Most of the chapters (which are authored by a total of 127 investigators) discuss results of research on cells other than fibroblasts concerning such matters as cell metabolism, collagen biosynthesis, biochemistry of the extracellular matrix and the cell surface, tissue inflammation, repair and fibrosis, and components of the vascular wall.

The book derives from a conference sponsored by the Sigrid Jusélius Foundation, which, it is said, has supported most of the medical research done in postwar Finland.

The book is broadly representative of research done on the subjects listed above and furthermore has the advantage of incorporating the views of many of the recognized authorities in these fields.

As is common among cell biologists generally, most of the authors of papers purportedly dealing with fibroblasts either are not dealing with fibroblasts or are not, as they seem to imply, dealing with normal fibroblasts. Studies done in vitro on such "fibroblast" populations as 3T3, BHK21, and mouse L cells suffer from the fact that the populations are clearly abnormal in at least one property yet are regarded either as consisting of typical normal fibroblasts or as providing normal controls for virus-transformed cells. The use of these cells is usually predicated on their common availability and the ease with which they may be cultured; but this is hardly a convincing rationale in view of the likelihood that any similarities between them and normal fibroblasts may be purely coincidental. Since such cell populations resemble no known in vivo cell type, their use can be likened to a kind of extraterrestrial biology. How disconcerting it is to realize that so much good science, carefully reasoned and technically sophisticated, rests on the use of cell populations twice removed from reality. Normal mouse, hamster, rabbit, and human fibroblasts are as easily available and as simply cultivated as are the continuously propagable abnormal cell populations now in wide use. Why do cell biologists resist using the genuine articles, which would make data extrapolation, with its inherent dangers, unnecessary?

Equally troublesome is the apparent assumption on the part of several of the authors represented in this book that a primary cell population consists entirely of fibroblasts. Surely this assumption is erroneous and the chapters based on it must be reevaluated. Several authors also base their experimental design on the notion that "normal cells in culture stop dividing after growing to confluent monolayers," a "fact" again widely accepted by cell biologists but patently false, as has been shown in several publications and as one should expect from the three-dimensional distribution of normal fibroblasts and other normal cell types in vivo.

Despite these deficiencies, this book is a unique collection of information on connective tissue, ancillary cell types, and biosynthesis of the extracellular matrix. Those readers who are cell culturists might very well conclude that the fibroblast, long regarded as analogous to a weed pest, is fast approaching deserved recognition as an important cell species which, in addition to being the archetype of proliferative capacity in vitro, is capable of several complex and important functional activities.

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Metal-Ammonia Solutions

Electrons in Fluids. The Nature of Metal-Ammonia Solutions. J. JORTNER and N. R. KESTNER, Eds. Springer-Verlag, New York, 1973. xii, 494 pp., illus. $44.10.

Although most of the 37 papers in this volume are concerned with metal-ammonia systems (including both liquid- and solid-phase systems), at least 12 of them deal with nonammoniacal systems such as metallic vapors and excess electrons in hydrocarbons. About half the papers present new experimental data; the others are either theoretical expositions or interpretive reviews.

One gets the impression on reading this book that the last few years have produced no major breakthroughs in our understanding of metal-ammonia solutions. Of course, the nature of dilute metal-ammonia solutions is now fairly well understood; this understanding has come through the application of a wide variety of physical techniques, including optical spectroscopy, nuclear magnetic resonance, electron spin resonance, calorimetry, magnetic susceptibility studies, electrical conductivity studies, and density measurements. Perhaps the principal remaining perplexity regarding these dilute solutions is an unexplained 400-cm^{-1} shift in the infrared absorption band that accompanies a change in concentration from $10^{-3}M$ to $10^{-1}M$.

Most of the current research on metal-ammonia systems is concerned with relatively concentrated solutions and with metal-ammonia solid compounds. Evaporation of ammonia from a dilute, blue, electrolytically conducting metal-ammonia solution produces a concentrated, bronze-colored, highly conducting solution. This "nonmetal-to-metal" transition has fascinated many experimentalists and theoreticians and has not yet been explained completely. One approach toward understanding the phenomenon, described in this volume, is the study of the properties of compressed metal vapors as a function of density. Such one-component disordered systems show analogous transitions and serve as simple models of the more complicated ammonia system.

By low-temperature evaporation of ammonia from the appropriate metal-ammonia solutions, one can isolate the solid compounds $Li(NH_3)_4$, $Ca(NH_3)_6$, $Sr(NH_3)_6$, and $Ba(NH_3)_6$. These materials exhibit unusual magnetic behavior and phase transitions that deserve further study. Unfortunately, the compounds are very difficult to prepare in a pure state, and reliable data are obtained only with extreme difficulty.

Only four of the papers are concerned with chemical reactions of metal-ammonia solutions. Chemical reactions definitely deserve more attention. It is remarkable that the kinetics of reactions of the short-lived aqueous electron (which must be studied by ultrafast techniques) have been much more extensively studied than the kinetics of the ammoniacal electron (which can be studied by many conventional techniques).

The book will be of interest to a wide spectrum of readers, from theoretical physicists to chemical kineticists, and it can be recommended as a summary of recent activity in the field.

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Scattering

Chemical Applications of Molecular Beam Scattering. M. A. D. FLUENDY and K. P. LAWLEY. Chapman and Hall, London, 1973 (U.S. distributor, Halsted [Wiley], New York). x, 400 pp., illus. $24.95.

Chemists have long recognized that they could find out much about molecular interactions if they could observe the scattering of a beam of molecules from a target of other molecules. Many of the techniques developed by physicists to learn about the nucleus should enable chemists to learn in detail about