Book Reviews

The Human Genome Project. Deciphering the Blueprint of Heredity. Edited by N. G. Cooper. University Science Books, Mill Valley, California. 1994. x + 360 pp. 22.5 cm × 29 cm. ISBN 0-935702-29-6. $38.00.

The Human Genome Project is unprecedented in that it is the first very large international effort in biological research with an estimated 15-year budget of approximately 3 billion dollars. Although other "big science" projects exemplified by the Hubble space telescope and the now abandoned supercollider may be of great importance in advancing our understanding of the macroscopic and submicroscopic universe, the Human Genome Project will undoubtedly yield much more immediate and tangible rewards for mankind. The ultimate goal of the project is to completely sequence the nearly 3 billion base pairs that constitute the human genome and identify the nearly 100 000 genes that define the human species. In addition, the genomes of several model organisms are also being sequenced, the bacterium *Escherichia coli* (3 million base pairs), the yeast *Saccharomyces cerevisiae* (14 million base pairs), the nematode *Caenorhabditis elegans* (80 million base pairs), the fruit fly *Drosophila melanogaster* (165 million base pairs), and the mouse *Mus musculus* (3 billion base pairs). The major reason for including these species is that many important genes and their protein products are highly conserved, thus allowing the function of human genes to be identified in easily manipulated test organisms.

The goal of the Human Genome Project is to provide an infrastructure for scientists so that they can determine the function of every gene, including those that are responsible for human diseases. Constructing a detailed map of human DNA could be compared to mapping a transcontinental highway starting with relatively few landmarks. The strategy is to first identify short unique sequences spaced evenly along the 3-billion base pair genome and then fill in the intervening stretches. At its present resolution, the map is comparable to a 3000-mi highway in which a 2-ft stretch has been mapped at 1-mi intervals. Critics of the Human Genome Project complain that identifying the position of every base pair is wasteful since less than 10% of human DNA actually codes for proteins, the remainder being termed "junk" DNA. However, portions of the "junk" are known or speculated to have important functions in gene regulation, cell division, DNA packaging, and protection of the genetic message. Obviously, many research groups are not waiting for information from the Human Genome Project but are identifying genes of potential pharmaceutical interest by using messenger RNA expressed in cells to produce complementary DNA via reverse transcriptase.

Several books about the Human Genome Project have been published. This one is particularly suited for those who are relatively unfamiliar with the strategies and techniques involved in gene mapping and sequencing. The text is divided into eight sections; the first two, "Understanding Inheritance: An Introduction to Classical and Molecular Genetics" and "Mapping the Genome: The Vision, the Science, the Implementation" (67 and 114 pages, respectively), are particularly informative. Sections two and eight have an unusual format in that they are based on round table discussions with some of the important contributors to the field of molecular genetics such as James Watson, David Baltimore, and Leroy Hood. Most of the sections contain numerous sidebars which clearly explain concepts and techniques referred to in the text. These are well illustrated with high-quality drawings and photographs. While there are no references in the body of the text or sidebars, most have a "Further Reading" section at the end with references as current as 1992. Photographs of contributors and brief biographical sketches are also included. The book contains a very useful glossary containing definitions for arcane acronyms and terms such as PCR, RFPL, STS, YAC, centimorgan, contig, and cosmid that are used throughout the text. The index is very complete.

In general, this is a very readable, well-illustrated volume that covers a topic of immense importance to a number of disciplines. For medicinal chemists, information contained in the human genome can help unravel the underlying molecular mechanism of disease processes so that more effective therapeutic agents can be designed. Potential targets may be at the level of DNA, messenger RNA, or the expressed protein. While thousands of human diseases have been defined as having a genetic origin, finding the gene, sequencing it, discovering the specific defect, and determining the function of its expressed protein product require a very significant effort. Even more difficult to dissect are diseases caused by more than one gene. In reality, there is no single human genome. We are all genetically unique, except for homozygous (identical) twins. Such individual differences are of interest to scientists studying human cognition and behavioral traits. Since these characteristics have a large genetic component, detailed molecular information may eventually impact policies with respect to our educational and criminal justice systems. DNA differences between racial and ethnic groups are of interest to population geneticists and anthropologists who want to trace human evolution at the molecular level. DNA fingerprinting has proved to be a powerful tool for forensic work and is being used by the military as a molecular dog tag. Therefore, this book will be of interest to a rather wide audience for which it is highly recommended.

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Advanced Organic Chemistry of Nucleic Acids. Zoe A. Shabarova and Alexey A. Bogdanov. VCH, Weinheim, Germany. 1994. xv + 588 pp. 18 × 24.5 cm. ISBN 3-527-28921-4. DM 249.00.

This is an updated version of a text that was originally published in Russian in 1978 and was used by the authors to teach organic chemistry students about nucleic acids. In general the organic chemistry of the various classes of molecules that make up living organisms, including specifically the nucleic acids, is largely ignored in standard biochemistry textbooks, just as the biochemistry of these compounds generally receives very little attention in standard organic chemistry textbooks. Thus, this work is a laudable attempt to fill a void in the pedagogical literature.

The book is divided into 11 chapters, of which the first six, as well as parts of two others, are by Professor Shabarova whereas the rest are written, in their entirety or jointly, by Professor Bogdanov. The first chapters are devoted to very elementary topics such as the structures, physical properties, and chemical reactions of nucleosides (including a few examples of natural nucleoside antibiotics) and nucleotides. Also covered here are the composition, primary structure, and chemical and enzyme-catalyzed reactions of nucleic acids. Chapter 6 deals in detail with strategies for DNA and RNA mapping, both in solution and on solid supports. Likewise presented in the chapter are an introduction to the use of polymerase chain reaction (PCR) technology and a discussion of the use of computers in nucleic acid sequencing. Chapters 7 and 8 are devoted to the three-dimensional conformation of the sugars and bases in single- and double-stranded DNA and RNA, the base stacking interactions in double-stranded polynucleotides, the physical chemistry of double-stranded DNA denaturation and renaturation, the interaction of various types of double-stranded DNA with oligonucleotides to form triple-helical structures, and the secondary and tertiary structures of the various species of RNA. Chapter 9 covers the chemical reagents that may be used to modify the structure of DNA and RNA in various ways and probe their structure. Chapter 10 deals very briefly with the organic chemistry of ribozymes. Chapter 11 teaches the strategies and techniques of nucleic acid synthesis, starting from a thorough review of the fundamentals (i.e., blocking groups and coupling reagents) and culminating in some of the most up to date applications such as the preparation of synthetic genes.

While this book is clearly among the most comprehensive treatises available on this subject, one of its weaknesses is that whereas the first half if obviously a primer for students who may have never heard of nucleic acids at all (perhaps undergraduates with one year of organic chemistry), the second half is clearly targeted to professionals who are already well acquainted with, or are actively working in, this field. Thus, both groups of readers may be somewhat disappointed, that is, the novice will be left in the dust while the expert will feel patronized, for example, by the lengthy expositions of Ingold's principles of electronic structure. Indeed, one can even argue about whether or not the organic chemistry covered in the book should be characterized in the title as 'advanced' by contemporary standards. To compound the problem, literature references at the end of many of the chapters merely cite other well-known European and American textbooks or monographs, some of which are more than 30 years old. Finally, this reviewer was greatly disappointed in the overall 'production values' of the book. Many structural formulas and equations, especially in the early chapters, look as though they had simply been borrowed from other works published in the 1950's. In some chapters, chemical structures appear to have been generated with the help of a software program of marginal quality or perhaps by someone not very proficient in its use. Furthermore, there is an irritating lack of consistency in the typography throughout the book as well as innumerable spelling errors (e.g., 'formiate' for 'formate', 'hypoxantine' for 'hypoxanthine', '*Cordyceps militaries*' for '*Cordyceps militaris*', '*Streptomyces tubecidiens*' for '*Streptomyces tubercidicus*', '*ribite*' for 'ribitol', 'ribosse' for 'ribose', 'primery' for 'primary', and on and on in a similar vein). Awkward and pedantic translations are likewise ubiquitous. As a grating example, consider the sentence on p 38: "If one proceeds from the assumption that the electron density in unsubstituted nuclei of pyrimidine and purine is diccontinuous [sic], or split (see above), as well as from the data on the most preferable tautomeric forms of existence of the major pyrimidine and purine bases in nucleosides, one can draw conclusions about the distribution of electron density in the corresponding substituted heterocyclic systems." Or consider this example on p 42: "The alkyl radical in molecules of both substances [referring to the three compounds diazomethane, methyl iodide, and dimethyl sulfate] is associated with electronacceptor [sic] groups which are substituted when interacting with sufficiently strong nucleophiles, and act as departing groups." Annoying colloquialisms are also endemic: on p 12, "The mechanisms of such reactions seem to *boil down* to...", on p 43, "quite contrary, its role *boils down* to giving the unit a universal trait inherent in every monomer.", and on p 89, "Such restructuring is not accompanied by cleavage on the phosphorus-substituted bonds and *boils down* to changes in bond angles and lengths in a sufficiently persistent transient state, as represented by the trigonal bipyramid."

In summary, this book is a well-meaning attempt to pull together a prodigious amount of information into a single resource that can be used by scientific readers with widely diverse levels of sophistication. By attempting to reach too broad an audience, it can be argued that the authors have, to some extent, done both themselves and their readers a disservice. Further, considering the numerous editorial lapses, the price of the book does not seem justified.

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