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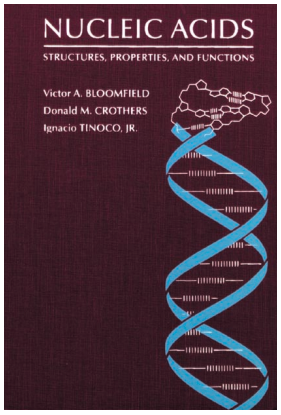

Nucleic Acids: Structures, Properties and Functions

Reviewed by Vadim Demidov

by Victor A. Bloomfield, Donald M. Crothers and Ignacio Tinoco, Jr, University Science Books, 2000. $85.00 (794 pages, hardback), ISBN: 0-935702-49-0

Nucleic acids, DNA and RNA, represent three entities in molecular pharmacology. First, as core elements of genetic machinery, they are a primary target for many drugs, including some antibiotics and anti-cancer chemotherapeutics. Second, nucleic acids and their components and modifications are drugs themselves: manufactured semi-synthetically from fish sperm or produced synthetically, azidothymidine (AZT), which is widely used in the treatment of AIDS, is such an example. Third, nucleic acids are the basis for the development of DNA and RNA molecular diagnostics (such as the PCR assay) for various diseases. Therefore, the design of modern drugs requires a wide knowledge of the structures, properties and functions of nucleic acids.

The book under review is distinguished among other volumes on the subject. In the active, rapidly advancing area of nucleic acid research there is an urgent need for a broad coverage of the latest developments. This work effectively closes a gap in the scientific literature where a comprehensive updated reading on that topic has been long overdue. Written by three recognized worldwide experts in the field, the book acts as an up-to-date encyclopedia of nucleic acids with an emphasis on implications for biological functions.

What is inside

The tome contains a thoroughly referenced characterization of nucleic acids, along with experimental and theoretical approaches commonly used to study the structural and dynamic properties of DNA and RNA and their interactions with drugs, proteins and other ligands. The introductory chapter provides an outline of the entire volume. It also describes:

- methods for the isolation of nucleic acids;
- the periodical literature covering the biophysics and physical chemistry of nucleic acids;
- useful books on these and related topics, including basic texts in molecular biology, nucleic acid biochemistry and physical chemistry with applications to the life sciences;
- historical monographs that describe the revolutionary discovery of the double-helix; and
- literature on computer analysis and databases of sequences and structures.

Each chapter is organized in a uniform manner beginning with an introductory statement that highlights the biological significance of every topic. This is followed by a concise description of the principal ideas underlying each subject and key results from the corresponding studies. All chapters end with an extensive bibliography, which facilitates the use of this book as a reference guide for those involved in drug discovery and development. Some of the sections are written with contributions from an accompanying quartet of experienced scientists: John E. Hearst (*Psoralen photocross-linking*), David E. Wemmer (*NMR methods*), Peter A. Kollman (*Theoretical methods*) and Douglas H. Turner (*Conformational changes*). Special sections and appendices provide quantitative details of theoretical analysis.

Almost one-third of this 14-chapter tome is devoted to the following two chapters:

- *Size and shape of nucleic acids in solution* (a menagerie of macromolecular structures as characterized by sedimentation, electrophoresis, microscopy, light scattering and viscosity; bending and twisting of DNA).
- *Protein–nucleic acid interactions* (biological role and elementary energetics; sequence and structural specificities; kinetics and the search mechanism; twisting, bending and looping of DNA sequences).

Other chapters are shorter and include the study of nucleic acid structure by chemical and enzymatic assays, diffraction and NMR methods, electronic and vibrational spectroscopy, and theoretical approaches. The chapter *Bases, nucleosides, and nucleotides* describes the configurations and conformations of nucleic acid building blocks. *Conformational changes* focuses on the dynamic transitions in oligo- and poly-nucleotides stimulated by the environment. *Supercoiled DNA* considers the major topological form of DNA *in vivo*, *Interaction of nucleic acids with water and ions* is dedicated to two key species that are omnipresent in any nucleic acid environment affecting their form and stability, and *Higher order structure* considers the DNA condensation *in vitro* and its packaging in bacteriophages, bacteria and eukaryotes.

What is missing

Importantly for drug design, Chapter 12 (*Interaction and reaction with drugs*) describes intercalative and groove-binding modes of interaction, the

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kinetics of drug binding, natural products that covalently react with DNA, and synthetic DNA-binding agents. An apparent drawback of this chapter is that it is devoted exclusively to DNA–drug interactions, thus leaving RNA–drug interactions aside. For example, there is not even a brief discussion of significant differences in DNA and RNA chemical reactivity and stability, interaction of RNA with intercalating drugs such as furocoumarins, properties and applications of ribozymes[1,2] (and catalytic DNAs) or use of ribonucleases as antiviral agents.

Also, surprisingly, the sub-chapter on sequence-specific DNA targeting says nothing about the promising antisense/antigene strategy that involves synthetic duplex- and triplex-forming oligonucleotides and their numerous analogues or mimics. The 2000 Galenus Prize-winning anti-cytomegalovirus Vitravene™ (fomivirsen), which is an antisense phosphorothioate-oligonucleotide drug, is the most recent and meaningful illustration. An example of a prospective gene therapy drug is a protein-like biologically stable ersatz oligonucleotide, peptide nucleic acid (PNA)[2–4], that forms exceptionally stable complexes with single-stranded RNA and DNA, and features an unusual ability to selectively invade DNA duplexes.

However, these minor drawbacks do not change the fact that this book is essential treatise and it is definitely top of its class. Furthermore, this book contains only a few typographical errors, which is usually inevitable in printing such a large volume (for errata, see http://www.uscibooks.com/bloomerr.htm). Every chapter in this book (except the introductory one) is excellently illustrated with miscellaneous schematics, diagrams, graphs, tables and molecular structures and includes two dozen color figures as separate plates between Chapters 12 and 13. I therefore strongly recommend reading this book in order to become familiar with the current status of nucleic acid research.

References

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Vadim V. Demidov
Senior Research Scientist
Center for Advanced Biotechnology
Boston University
Boston, MA 02215, USA
tel: +1 617 353 8490
fax: +1 617 353 8501
e-mail: vvd@bu.edu