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Preface

The Preface to Volume I of the classic treatise, "The Nucleic Acids," by Chargaff and Davidson, which appeared in 1955, concluded with the remark, "If this book helps create an early need for a supplement to its present content, it will have fulfilled one of its purposes." The rapid growth of knowledge in this field and its expansion into what has become known as molecular biology occasioned in 1960 a supplementary volume (III), cutting across the systematic arrangement of Volumes I and II rather than attempting to update or revise their individual chapters. The formidable problems besetting the latter approach to keeping up with the times were also responsible for the initial and continuing guiding concept of this series, expressed in Volume I (1963) in these words: "With the rapid and often seemingly chaotic increase in the advance of knowledge in the field of nucleic acids, the thought has been expressed in several quarters that there is need for a continuing periodical assessment or reassessment of those areas in the field that have arisen or advanced notably since the publication in 1960 of the last of the three volumes of "The Nucleic Acids: Chemistry and Biology," edited by Chargaff and Davidson. Progress in this field is so rapid that there would indeed appear to be room for a publication dealing intensively with timely and significant developments. This is what we have attempted to produce."

It is clear from these statements that this series was intended to be in the nature of an updating of "The Nucleic Acids" by means of periodical assessments or reassessments, and such remains its purpose. It is also clear that such a purpose will give rise over a period of years to similar titles and even to repeat performances by a single author; such will be noted in the list of the titles and authors of earlier volumes at the end of this volume. Occasionally the same subject appears to be covered in two articles appearing in succeeding volumes, but from different vantage points and with different interpretations. This stems also from the charge in the Preface to Volume 1 that "We have encouraged . . . . the expression of points of view that are perhaps controversial and certainly individualistic."

In the present volume, we continue the discussion of eukaryotic RNA polymerases, last explored in Volume 13, with an article by Biswas dealing with such polymerases and the factors controlling them. Bollum, who began Volume 1 with a review of DNA polymerase reactions, returns to describe the biochemical and biological properties of two major DNA polymerases in mammalian cells and to indicate the differences between these and the bacterial polymerases, which raise interesting questions

about DNA replication. Tables of the levels of DNA polymerase in a variety of mammalian tissues are included; these should be useful to those attempting to duplicate classic work on these enzymes.

The reactivity of various classes of alkylating agents toward nucleosides, polynucleotides and nucleic acids *in vitro* and *in vivo* is discussed by Singer (a contributor to Volume 9), with emphasis on the relationship between site-specific alkylations and the subsequent mutagenic and carcinogenic effects, a subject last touched upon in Volume 5. Lomant and Fresco, who appeared in vol. 12, discuss the steric and energetic factors that dispose noncomplementary base oppositions toward extrahelical or intrahelical locations in Watson-Crick type DNA or RNA helices. From studies with synthetic polynucleotides, they conclude that these oppositions can be divided into two distinct classes. In one class are included A;A, U;U, C;C, U;C, and G;G oppositions, which are always extrahelically located in helices whose stereochemistry is dominated by the Watson-Crick pairs, A·U(T) and G·C. In the other class are G;U, A;C, and also those oppositions exclusively relevant to codon-anticodon interaction, I;U and I;A; these "wobble" oppositions all take up intrahelical arrangements at physiological temperature and ionic strength. They note that the significant stability of "wobble"-type base pairs in Watson-Crick helices presents a problem for fidelity in nucleic acid synthesis that is more subtle than has been previously appreciated. A different approach to studying the structure and function of nucleic acids is taken by Zimmer, who indicates how the novel drugs netropsin and distamycin A may be used as probes.

Finally, Gallo *et al.* deal extensively with the rapidly burgeoning field of information transfer in cells infected with RNA-containing tumor viruses and the relationship of this phenomenon to human neoplasia. Structural comparison is made between information-processing elements of the cell and viral components. A search is made for patterns in the virus-cell relationship in normal and neoplastic (infected) states and the extension of these patterns to virus classification. The extent of involvement of RNA tumor viruses in human leukemia (neoplasia) is evaluated. A new nomenclature system for DNA polymerases (also used by Bollum in his article) is proposed.

With respect to chemical and biochemical nomenclature, it has always been and remains the policy of this series to adhere as closely as possible to international recommendations. The most relevant abbreviations and symbols are set out on pp. xiii–xvi and are not, therefore, defined in each article.

Comments and suggestions from readers are desired. As stated in an earlier preface, "We seek to provide a forum for discussion . . . and we welcome suggestions . . . as to how this end may best be served."

W.E.C.

Abbreviations and Symbols

All contributors to this Series are asked to use the terminology (abbreviations and symbols) recommended by the IUPAC–IUB Commission on Biochemical Nomenclature (CBN) and approved by IUPAC and IUB, and the Editor endeavors to assure conformity. These Recommendations have been published in many journals (*1, 2*) and compendia (*3*) in four languages and are available in reprint form from the NAS–NRC Office of Biochemical Nomenclature (OBN), as stated in each publication, and are therefore considered to be generally known. Those used in nucleic acid work, originally set out in section 5 of the first Recommendations (*1*) and subsequently revised and expanded (*2, 3*), are given in condensed form (I–V) below for the convenience of the reader.

I. Bases, Nucleosides, Mononucleotides

1. *Bases* (in tables, figures, equations, or chromatograms) are symbolized by Ade, Gua, Hyp, Xan, Cyt, Thy, Oro, Ura; Pur = any purine, Pyr = any pyrimidine, Base = any base. The prefixes S–, H_2, F–, Br, Me, etc., may be used for modifications of these.

2. *Ribonucleosides* (in tables, figures, equations, or chromatograms) are symbolized, in the same order, by Ado, Guo, Ino, Xao, Cyd, Thd, Ord, Urd (Ψrd), Puo, Pyd, Nuc. Modifications may be expressed as indicated in (1) above. Sugar residues may be specified by the prefixes r (optional), d (=deoxyribo), a, x, l, etc., to these, or by two three-letter symbols, as in Ara-Cyt (for aCyd) or dRib-Ade (for dAdo).

3. *Mono-, di-, and triphosphates of nucleosides* (5′) are designated by NMP, NDP, NTP. The N (for "nucleoside") may be replaced by any one of the nucleoside symbols given in II-1 below. 2′-, 3′-, and 5′- are used as prefixes when necessary. The prefix d signifies "deoxy." [Alternatively, nucleotides may be expressed by attaching P to the symbols in (2) above. Thus: P-Ado = AMP; Ado-P = 3′-AMP.] cNMP = cyclic 3′:5′-NMP; Bt_2cAMP = dibutyryl cAMP; etc.

II. Oligonucleotides and Polynucleotides

1. Ribonucleoside Residues

(a) Common: A, G, I, X, C, T, O, U, Ψ, R, Y, N (in the order of I-2 above).

(b) Base-modified: *s*I or M for thioinosine = 6-mercaptopurine ribonucleoside; sU or S for thiouridine; brU or B for 5-bromouridine; hU or D for 5,6-dihydrouridine; i for isopentenyl; f for formyl. Other modifications are similarly indicated by appropriate *lower-case* prefixes (in contrast to I-1 above) (*2, 3*).

(c) Sugar-modified: prefixes are d, a, x, or l as in I-2 above; alternatively, by *italics* or **boldface** type (with definition) unless the entire chain is specified by an appropriate prefix. The 2′-*O*-methyl group is indicated by *suffix* m (e.g., -Am- for 2′-*O*-methyladenosine, but -mA- for *N*-methyladenosine).

(d) Locants and multipliers, when necessary, are indicated by superscripts and subscripts, respectively e.g., -m^6_2A- = 6-dimethyladenosine; -s^{4}U- or -^{4}S- = 4-thiouridine; -ac^{4}Cm- = 2′-*O*-methyl-4-acetylcytidine.

(e) When space is limited, as in two-dimensional arrays or in aligning homologous sequences, the prefixes may be placed *over the capital letter*, the suffixes *over the phosphodiester symbol*.

2. Phosphoric Acid Residues [left side = 5′, right side = 3′ (or 2′)]

(a) Terminal: p; e.g., pppN . . . is a polynucleotide with a 5′-triphosphate at one end; Ap is adenosine 3′-phosphate; C > p is cytidine 2′:3′-cyclic phosphate (*1, 2, 3*).

(b) Internal: hyphen (for known sequence), comma (for unknown sequence); unknown sequences are enclosed in parentheses. E.g., pA-G-A-C(C_2,A,U)A-U-G-C > p is a sequence with a (5′) phosphate at one end, a 2′:3′-cyclic phosphate at the other, and a tetranucleotide of unknown sequence in the middle. **(Only codon triplets are written without some punctuation separating the residues.)**

3. Polarity, or Direction of Chain

The symbol for the phosphodiester group (whether hyphen or comma or parenthesis, as in 2b) represents a 3′-5′ link (i.e., a 5′ . . . 3′ chain) unless otherwise indicated by appropriate numbers. "Reverse polarity" (a chain proceeding from a 3′ terminus at left to a 5′ terminus at right) may be shown by numerals or by right-to-left arrows. Polarity in any direction, as in a two-dimensional array, may be shown by appropriate rotation of the (capital) letters so that 5′ is at left, 3′ at right when the letter is viewed right-side-up.

4. Synthetic Polymers

The complete name or the appropriate group of symbols (see II-1 above) of the repeating unit, **enclosed in parentheses if complex or a symbol**, is either (a) preceded by "poly," or (b) followed by a subscript "n" or appropriate number. **No space follows "poly"** (*2, 5*).

The conventions of II-2b are used to specify known or unknown (random) sequence, e.g.,

polyadenylate = poly(A) or $(A)_n$, a simple homopolymer;

poly(3 adenylate, 2 cytidylate) = poly(A_3C_2) or $(A_3C_2)_n$, a *random* copolymer of A and C in 3:2 proportions;

poly(deoxyadenylate-deoxythymidylate) = poly[d(A-T)] or poly(dA-dT) or $(dA\text{-}dT)_n$ or $d(A\text{-}T)_n$, an *alternating* copolymer of dA and dT;

poly(adenylate, guanylate, cytidylate, uridylate) = poly(A,G,C,U) or $(A,G,C,U)_n$, a random assortment of A, G, C, and U residues, proportions unspecified.

The prefix copoly or oligo may replace poly, if desired. The subscript "n" may be replaced by numerals indicating actual size.

III. Association of Polynucleotide Chains

1. *Associated* (e.g., H-bonded) chains, or bases within chains, are indicated by a *center dot* (not a hyphen or a plus sign) separating the *complete* names or symbols, e.g.:

poly(A)·poly(U) or $(A)_n\cdot(U)_n$ or $(A\cdot U)_n$

poly(A)·2 poly(U) or $(A)_n\cdot 2(U)_n$ or $(A\cdot 2U)_n$

poly(dA-dC)·poly(dG-dT) or $(dA\text{-}dC)_n\cdot(dG\text{-}dT)_n$.

2. *Nonassociated* chains are separated by the plus sign, e.g.:

$$2[\text{poly(A)}\cdot\text{poly(U)}] \xrightarrow{\Delta} \text{poly(A)}\cdot 2\ \text{poly(U)} + \text{poly(A)} \qquad \text{(II-4a)}$$

or $$2[A_n\cdot U_n] \xrightarrow{\Delta} A_n\cdot 2U_n + A_n. \qquad \text{(II-4b)}$$

3. Unspecified or unknown association is expressed by a comma (again meaning "unknown") between the completely specified residues.

Note: In all cases, each chain is completely specified in one or the other of the two systems described in II-4 above.

IV. Natural Nucleic Acids

RNA	ribonucleic acid or ribonucleate
DNA	deoxyribonucleic acid or deoxyribonucleate
mRNA; rRNA; nRNA	messenger RNA; ribosomal RNA; nuclear RNA
D-RNA; cRNA	"DNA-like" RNA; complementary RNA
mtDNA	mitochondrial DNA
tRNA	transfer (or acceptor or amino acid-accepting) RNA; replaces sRNA, which is not to be used for any purpose
aminoacyl-tRNA	"charged" tRNA (i.e., tRNA's carrying aminoacyl residues); may be abbreviated to AA-tRNA
alanine tRNA or $tRNA^{Ala}$, etc.	tRNA normally capable of accepting alanine, to form alanyl-tRNA. [*Note:* fMet = formylmethionyl; hence $tRNA^{fMet}$ or $tRNA_f^{Met}$]
alanyl-tRNA or alanyl-$tRNA^{Ala}$	The same, with alanyl residue covalently attached.

Isoacceptors are indicated by appropriate subscripts, i.e., $tRNA_1^{Ala}$, $tRNA_2^{Ala}$, etc.

V. Miscellaneous Abbreviations

P_i, PP_i	inorganic orthophosphate, pyrophosphate
RNase, DNase	ribonuclease, deoxyribonuclease
t_m (not T_m)	melting temperature (°C) (T = Kelvin temperature)

Others listed in Table II of Reference 1 may also be used without definition. No others, with or without definition, are used unless, in the opinion of the Editor, they increase the ease of reading.

Enzymes

In naming enzymes, the 1972 recommendations of the IUPAC-IUB Commission on Biochemical Nomenclature (CBN) (*4*), are followed as far as possible. At first mention, each enzyme is described *either* by its systematic name *or* by the equation for the reaction catalyzed *or* by the recommended trivial name, followed by its EC number in parentheses. Enzyme names are not to be abbreviated except when the substrate has an approved abbreviation (e.g., ATPase, but not LDH, is acceptable).

References*

1. *JBC* **241**, 527 (1966); *Bchem* **5**, 1445 (1966); *BJ* **101**, 1 (1966); *ABB* **115**, 1 (1966), **129**, 1 (1969); and elsewhere.†
2. *EJB* **15**, 203 (1970); *JBC* **245**, 5171 (1970); *JMB* **55**, 299 (1971); and elsewhere.†
3. "Handbook of Biochemistry" (H. A. Sober, ed.), 2nd ed. Chemical Rubber Co., Cleveland Ohio, 1970, Section A and pp. H130–133.
4. "Enzyme Nomenclature," Elsevier Scientific Publ. Co., Amsterdam, 1973.
5. "Nomenclature of Synthetic Polypeptides," *JBC* **247**, 323 (1972); *Biopolymers* **11**, 321 (1972); and elsewhere.†

* Contractions for names of journals follow.

† Reprints of all CBN Recommendations are available from the Office of Biochemical Nomenclature (W. E. Cohn, Director), Biology Division, Oak Ridge National Laboratory, Box Y, Oak Ridge, Tennessee 37830, USA.

Abbreviations of Journal Titles

Journals	*Abbreviations used*
Annu. Rev. Biochem.	ARB
Arch. Biochem. Biophys.	ABB
Biochem. Biophys. Res. Commun.	BBRC
Biochemistry	Bchem
Biochem. J.	BJ
Biochim. Biophys. Acta	BBA
Cold Spring Harbor Symp. Quant. Biol.	CSHSQB
Eur. J. Biochem.	EJB
Fed. Proc.	FP
J. Amer. Chem. Soc.	JACS
J. Bacteriol.	J. Bact.
J. Biol. Chem.	JBC
J. Chem. Soc.	JCS
J. Mol. Biol.	JMB
Nature, New Biology	Nature NB
Nucleic Acids Res.	NARes
Proc. Nat. Acad. Sci. U.S.	PNAS
Proc. Soc. Exp. Biol. Med.	PSEBM

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The Mechanism of the Mutagenic Action of Hydroxylamines
E. I. Budowsky

Polyadenylate Polymerases
M. Edmonds and M. A. Winters

Diethyl Pyrocarbonate in Nucleic Acid Research
L. Ehrenberg, I. Fedorcsák and F. Solymosy

Structure and Function of 5-S RNA
V. A. Erdmann

Ribosomal RNA
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Bacterial Ribosomal Proteins
R. A. Garrett, K. Nierhaus and H. G. Wittman

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Information Transfer in Cells Infected by RNA Tumor Viruses and Extension to Human Neoplasia

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I. Introduction

Since the turn of this century, it has been known that members of a particular class of RNA-containing viruses can produce tumors in some animals. These viruses have been called RNA tumor viruses. In the past few years, work with these viruses has dramatically increased. This is in part owing to their increasing availability from several species, but it also results from relatively recent advances in the understanding of their mode of replication and the general conviction that understanding the molecular events leading to neoplastic transformation is now possible. It is fair to say that these particles are rapidly becoming a major interest of modern molecular biology. This review focuses on these molecular studies and attempts particularly to interpret and correlate recent findings that bring us to a working model for their origin, evolution, function, and especially their relationship to neoplasia. Special attention is given to the mammalian viruses. Reviews, more descriptive in nature, have recently appeared (*1–5*).

A. Historical Background

The first observation that an animal neoplasia could be induced by a filtrate was apparently that of Ellerman and Bang in 1908 (*6*). The landmark discovery that chicken sarcomas are inducible by a virus was made by Rous 3 years later (*7*). The next major advance occurred some 10–15 years later with the development of inbred strains of mice by Little *et al.* [cited in Gross (*7a*)]. This led to two critical observations, those of Bittner (*8*), which led to the isolation of the mouse mammary tumor virus and the demonstration that this agent was involved in the etiology of mouse breast cancer, and those of Gross in the isolation of the first mammalian leukemia virus (*9*). A number of other leukemic virus isolates were soon made, e.g., Friend, Moloney and Rauscher mouse leukemia viruses. These may be laboratory variants of the natural mouse (Gross) leukemia virus. Sarcoma viruses of mice were then isolated by Harvey (*10*) and by Moloney (*11*). These were obtained by passing murine (Moloney) leukemia viruses into rats (*10*) or by using high titers of the leukemia virus (*11*) and inoculating newborn BALB/c mice. In these cases, sarcomas were induced. Similarly, Kirsten (*12*) isolated a sarcoma virus from murine erythroblastosis virus (Gross-type), passaged in rats. Almost none of the murine sarcoma viruses were derived from a natural tumor. An exception to this is the osteosarcoma mouse virus isolated by Finkel (*13*). A number of other RNA tumor viruses were subsequently isolated from various species (see Section I, C), including a few from