CHEMISTRY

Order-conserving Reaction Schemes

A NEW class of reactions, with no counterpart in organic chemistry, has been elucidated in recent years in biological systems; it comprises the template-directed polymerizations of nucleic acids and amino-acids. Results of the intensive work in this area of polymer biochemistry indicate that these reactions involve two concurrent events at each step in polymerization. A free derivative of the monomer specifically complements with the template, and, in the presence of a suitable catalyst, when adjacent to the terminal monomer of a growing chain this is followed by a non-specific coupling reaction. Configuration order, in the form of specified linear arrays of monomers, is thereby recovered from the energy entropy expended in polymerization[1]. This derived order is not transmutable to free energy, nor is the total entropy subject to restriction by the second law of thermodynamics according to Davis. The balance of entropies attained in polydeoxyribonucleic acid synthesis has been evaluated in this report, so far as present data will permit such an analysis; and based on what is at present known of these processes, reaction schemes have been devised that aim at maximizing the diminution of configuration entropy.

Polynucleotide replication involves, in the main, a bijective complementation transform, from template to new polymer, of a sequence of four varieties of nucleotides and condensation of triphosphates into phosphodiester bonds with production of pyrophosphate. The decrease in nucleotide mixing entropy for polymers of equal base composition, the most probable composition, is then given by:

$$\Delta S_{\text{mix}} = -R \ln 4 \qquad (1)$$

$$\Delta S_{\text{mix}} = -2{\cdot}75 \text{ cal/mol deg.}$$

R is the gas constant. The designation of heat entropy units to this magnitude is only symbolic; it cannot physically represent heat entropy. The reaction entropy is of the usual form:

$$\Delta S_r = R \ln q\bar{K}^{-1} \qquad (2)$$

K, the equilibrium constant, is $0{\cdot}36 \times 10^{-2}$ for pyrophosphorolysis of polydeoxyribonucleic acid at pH 6·5 and 37° C (ref. 2). From statistical mechanical considerations it appears that the molar entropy ($R \ln q$) changes by -8 cal/mol deg. Whence the reaction entropy becomes

$$\Delta S_r = -22 \text{ cal/mol deg.}$$

Environmental entropy must rise by at least 22 cal/mol deg. to dissipate the reaction entropy.

It is evident that in the duplication of double-stranded polynucleotides composed of four varieties of monomers, the reaction entropy is approximately 90 per cent of the total entropy change. While the use of four varieties of nucleotides diminishes copying errors, there seems no reason why it should not be possible to synthesize polymers of high order, involving several types of nucleotide complementation. Toward this end it may be observed that three positions are involved in hydrogen bonding guanine and cytosine, and that adenine and thymine pairing demonstrates that only two of such bonds are necessary for specific complementation. Taking into account that two types of groups are involved in hydrogen bonding, proton donors and proton recipients, it is, therefore, possible to conceive twelve sets of complementation, each between a purine- and pyrimidine-like base. A necessary assumption is that hydrogen bonding is sufficiently effective in each of the three available positions to permit specific pairing. With the use of these bases, it may prove possible to construct polymers composed of an extended array of Watson–Crick pairings. The respective entropies would be:

$$\Delta S_{\text{mix}} = -6{\cdot}31 \text{ cal/mol deg.}$$

$$\Delta S_r = -21{\cdot}5 \text{ cal/mol deg.}$$

In such a system the reaction entropy is at the 80 per cent level of total entropy.

Relatively larger decreases in monomer-mixing entropy can be achieved with protein biosynthesis than with polynucleotide replication. However, it is not yet possible to estimate reaction entropy to total entropy ratios with any degree of assurance, as the reaction has not been entirely clarified. The role of guanine triphosphate, in particular, remains to be determined[3]. Recent experiments from the laboratory of Nirenberg[4], in which amino acyl transfer polyribonucleic acid (t-RNA) was bound to ribosomes programmed with oligonucleotides, provide direct evidence that the complementation unit is a sequence of three nucleotides. My exploratory investigations[5] with this system also favoured a triplet-coding unit. In this event, 64 complementation elements are obtained in 4 base polymers and 13,824 are possible in 24 base polymers. To utilize fully the coding potential of such polymers, it is necessary that the polymerization transform between both sets of complementation elements be isomorphic. Hence, each species of t-RNA would have to be purified and then loaded with amino-acids which have distinctive isotope labels, followed by removal of the loading enzymes to prevent transacylation during protein synthesis. In this manner, a system with a coding capacity of about 60 elements may be obtained. To increase further the coding capacity, it would be necessary to synthesize t-RNA molecules and incorporate anti-codons complementary to the unaccounted sequences. As naturally-occurring amino acyl synthetases could not be expected to load these artificial t-RNA's, this step may be included in synthesis. In like manner, a 24-base array of t-RNA molecules could be prepared. It would, of course, only be necessary to use these bases in the anti-codon region. The most probable mixing entropies are:

$$\Delta S_{\text{mix}} \begin{cases} \text{20 element system:} & -5{\cdot}95 \text{ cal/mol deg.} \\ \text{60 element system:} & -8{\cdot}13 \text{ cal/mol deg.} \\ \text{13,824 element system:} & -18{\cdot}92 \text{ cal/mol deg.} \end{cases}$$

Should it prove possible to construct systems with codons of more than three bases, further decreases in mixing entropy would accrue. Flawless complementation has been assumed throughout the calculations.

The magnitudes by which the monomer mixing entropies diminish in protein biosynthesis and polynucleotide replication are such that an experimental assessment is warranted of the order producing propensity of those reactions which permit it.

B. K. DAVIS*

Department of Chemistry,
Harvard University,
Cambridge, Massachusetts.

* Present address: Medical Research Council Laboratory of Molecular Biology, University Postgraduate Medical School, Cambridge, England.

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Novel Chemiluminescence Methods for Determination of Absolute Rate Constants for Elementary Radical Reactions in the Liquid Phase

THE recombination of peroxide radicals is usually accompanied by luminescence (see, for example, refs. 1 and 2). In the presence of certain luminescent substances (activators) that do not affect the reaction rate the luminescence will increase due to energy transfer[3].

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