DOUBLE STRANDED POLYNUCLEOTIDES: TWO TYPICAL ALTERNATIVE CONFORMATIONS FOR NUCLEIC ACIDS

V. SASISEKHARAN AND N. PATTABIRAMAN

Molecular Biophysics Unit, Indian Institute of Science, Bangalore 560012

ABSTRACT

Two typical alternative conformations for double stranded polynucleotides with Watson-Crick base pairing scheme are presented. These types avoid tangling of the two chains. Representative models of these types with two different views, to show the similarity and dissimilarity between these models and the Watson-Crick model, are given.

INTRODUCTION

THE well-known Watson and Crick model[1] for DNA is a right handed double helix. Our extensive work, carried out on the analysis of helical conformations for double stranded polynucleotides with antiparallel chains revealed that both right and left handed double helices are stereochemically possible. Based on our analysis, a type I model, employing Watson-Crick base pairing and conformations for the nucleotides, as observed in single crystals, was presented* in which the polynucleotide chain had both right and left handed segments. This immediately avoids the tangling of the two chains and hence has, in addition, other advantageous features over the Watson-Crick model. Since then a detailed conformational analysis carried out by using an IBM 360/44 computer has revealed two typical conformations based on the orientations of the sugars of the chain. These two types of conformations are energetically more favourable than the Watson-Crick double helix. The present paper outlines these two alternative conformations.

RIGHT AND LEFT HANDED DOUBLE HELICES

Figure 1 (*a*) shows the schematic diagram for right and left handed double helices (with antiparallel chains) with base pairing shown as dotted lines. The dihedral angles (which are restricted)[2] about the various single bonds in the backbone and the side chain (base) dihedral angle about the glycosidic

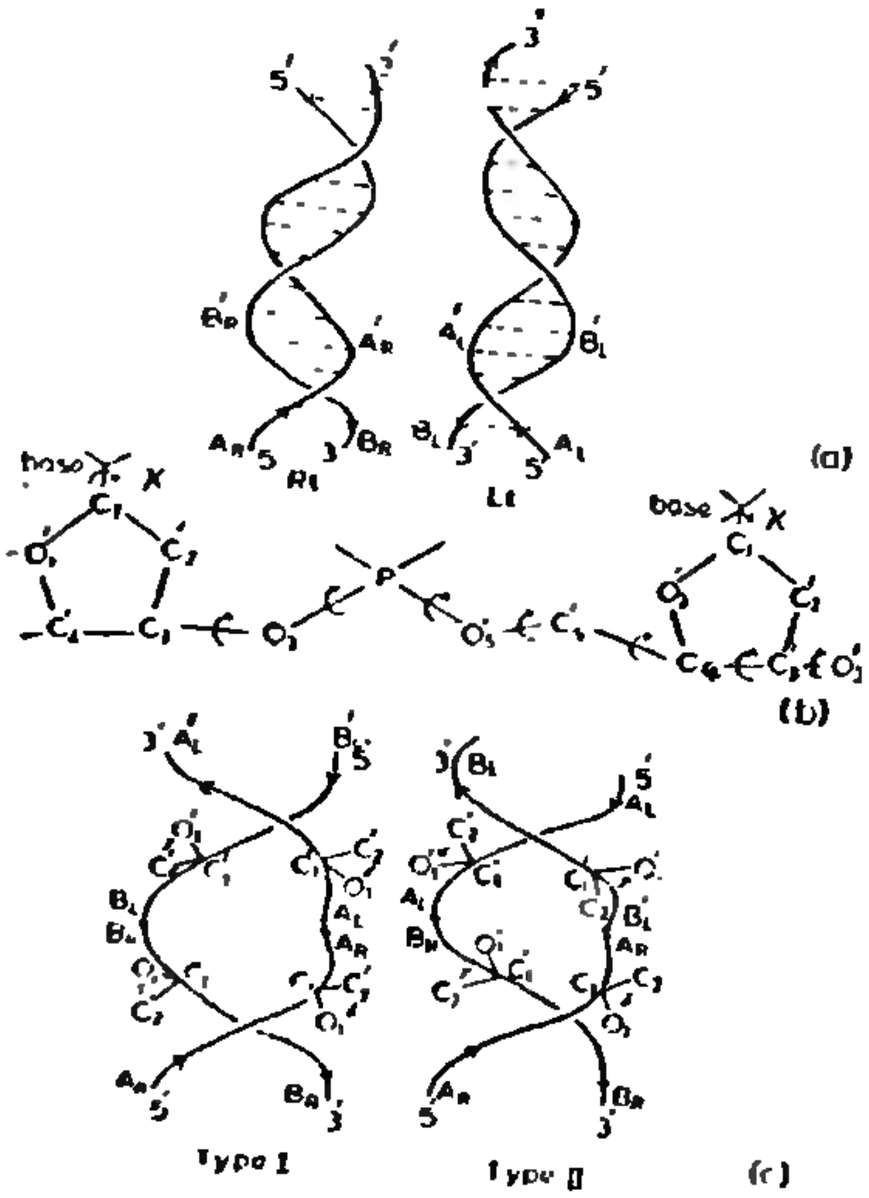


FIG. 1. (*a*) Schematic diagram of right and left handed helices; (*b*) Polynucleotide backbone; (*c*) The two types of linking right and left segments

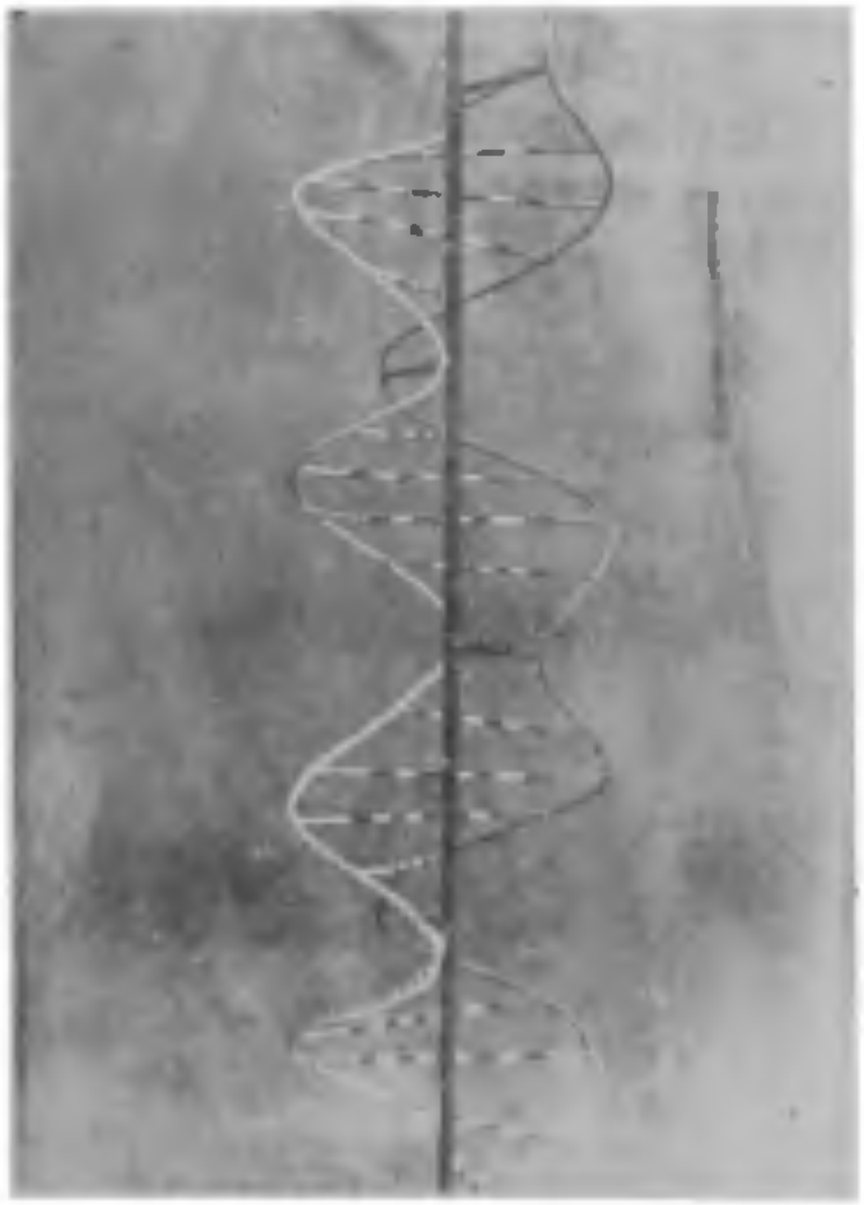


FIG. 2. Shematic view of the models (Types I and II) to show lateral separation of the two chains.

bond are shown in Fig. 1 (*b*). The regions of backbone dihedral angles for the possible right and left handed double helical conformation have already

* At the Divisional Review of the Chemical and Biological Sciences, Indian Institute of Science, Bangalore, February 23, 1976.

been given[2]. Further analysis of the regular helices with antiparallel chains and with the number of residues per turn $n \simeq 10$ and height per turn $h \simeq 3{\cdot}4$, restricted these possibilities to a few. Suffice it to say, that sterically both left and right handed conformations can be obtained with *gg*, *gt* and *tg* conformations about the C_4'–C_5' bond with the corresponding conformations about the P–O bonds. Most interestingly, our analysis of the conformation about the glycosidic bond (for a nearly perpendicular orientation of the bases as in B DNA) indicates two alternating regions for right and left handed helices. These are (*a*) for the right handed helix (1) normal *anti* region $\chi < 90°$ and (2) *syn* region $180° < \chi < 240°$, and (*b*) for the left handed helix (1) low *anti* region $\chi \lesssim 0°$ and (2) high *anti* region $\chi > 90°$. The exact value in each case would depend on the backbone dihedral angles as well as the puckering of the sugar. The flexibility of the sugar puckering was taken into account as described earlier[2]. It may be worthwhile to mention here that right and left handed helices can have the same radius for the phosphorus atom ($\sim$ 9 Å) but at the same time have different radii for the C_1' atom. In such a case the radius of C_1' atoms in the left handed helix is larger by 0·5 Å than the radius of the C_1' atoms in the right handed helix. However, the Fourier transforms of both the models are very similar. The other features of the right and left handed double helices will be discussed in greater detail elsewhere.

The Two Types of Conformations : I and II

There are two typical ways [Fig. 1 (*c*)] by which the right and left handed segments can be joined to form a double stranded polynucleotide chain having Watson-Crick base pairing but which would avoid tangling. For a repeating unit of ten base pairs, roughly half a turn of the right handed double helix can be linked to the corresponding half a turn of the left handed double helix. In type I, the right handed segments A_RA_R' and B_RB_R' are joined to the left handed segments A_LA_L' and B_LB_L' respectively. If the left and right handed segments are joined this way, the orientations of the sugars of the chain are in the same direction (shown in the diagram by the vectors $C_2' \rightarrow O_1'$). In the type II structure, the right handed segments A_RA_R' and B_RB_R' are joined to the left handed segments $B_L'B_L$ and $A_L'A_L$ by an inversion of the left handed segment such that the chain directions 5′ to 3′ and 3′ to 5′ are preserved. In such a structure the sugars in the right handed segment are pointing roughly opposite to the sugars in the left handed segment (shown by the vectors $C_2' \rightarrow O_1'$).

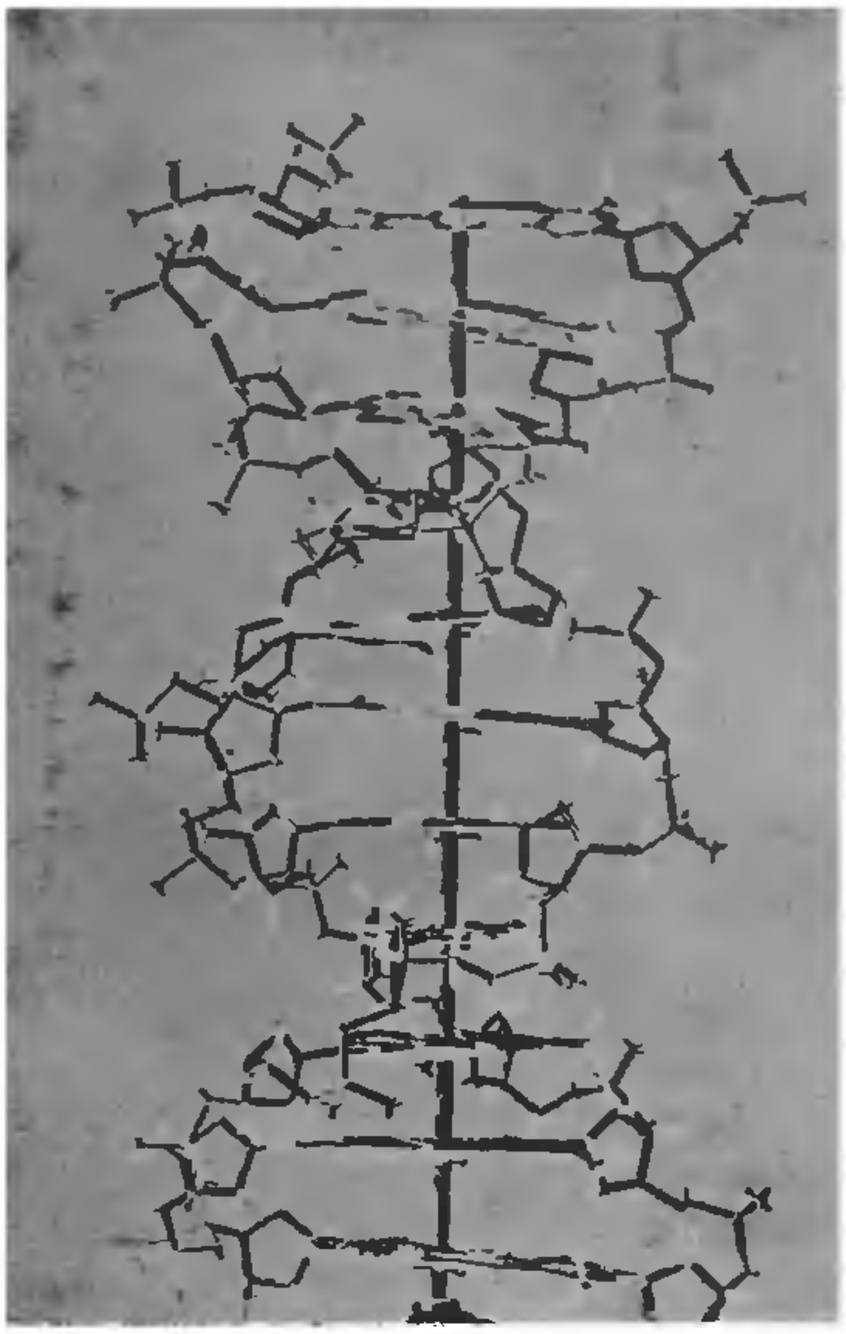
Both the type I and type II structures involve 'folds' or 'bends' along the chain and these folds occur in pairs approximately after every five base pairs. Since there is flexibility about the backbone of the polynucleotide chains[2], there can be a family of folds. In the representative models for each type shown, we have used the types of fold which we consider as plausible. Apart from the types of folds, the main feature of both the structures is the value of χ for the base pair. In the type I structure, if a normal *anti* conformation ($\chi < 90°$) is used for the right handed segment, then the left handed segment has a value for $\chi > 90°$ (high *anti* region). In type II, for the normal *anti* conformation of the right segment, the left segment has $\chi \lesssim 0$ (low *anti* region). Similarly, for the *syn* conformation of the bases in the right handed segment, both types I and II are possible, but with the χ values interchanged for the left handed segments. The *syn* conformation was not investigated further.

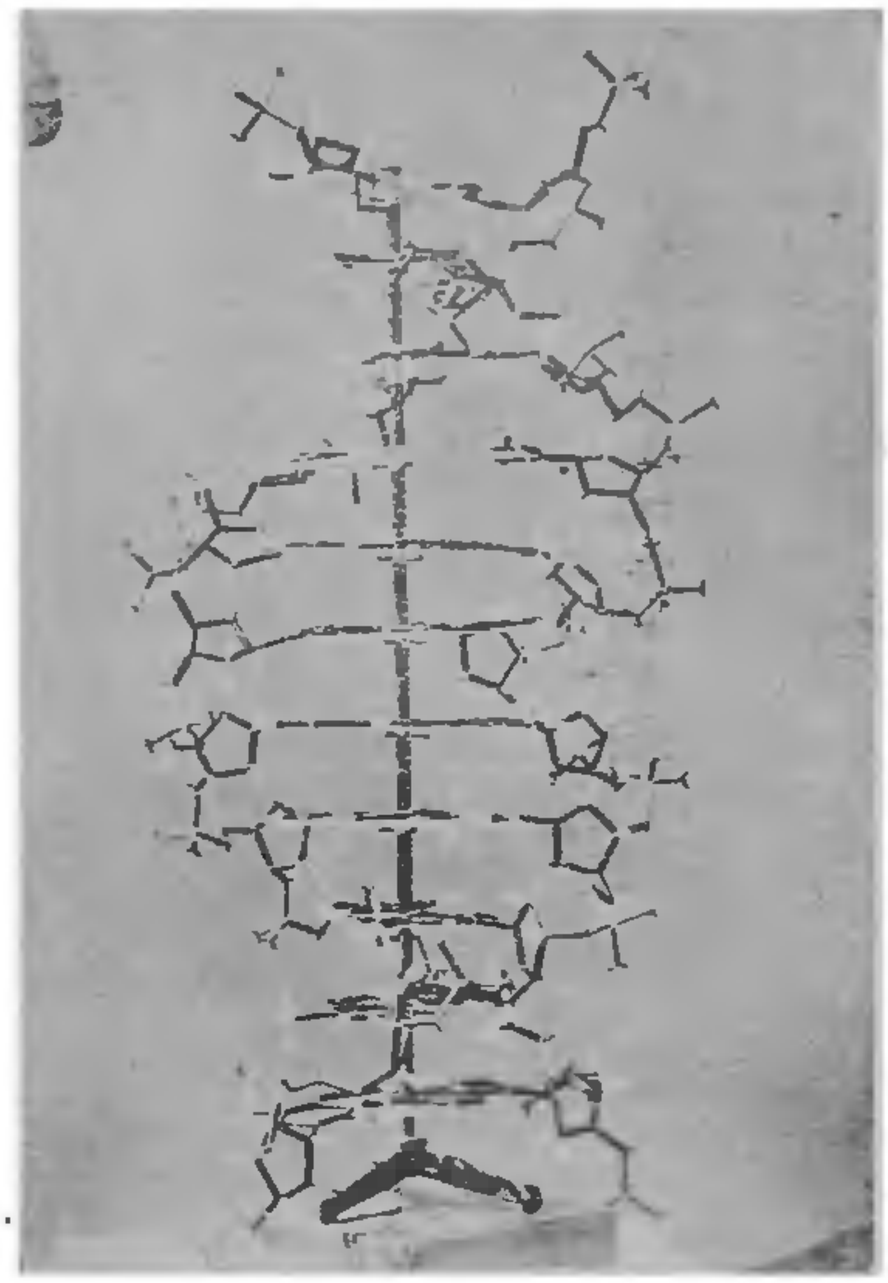
Thus in both types I and II, the two polynucleotide chains have a wavy structure and avoid intertwining (Fig. 2). Both have alternating right and left segments along the length of the chain and have a pair of folds in each repeating unit. In type I, the sugars point roughly in the same direction in both the segments which have normal bases stacked. In type II, the sugars in the adjoining segments are inverted ; that is, point in opposite directions. This structure has the base in the adjoining segments in inverted positions and stacked accordingly.

The Need for Folding

It is clear that as the conformational energy difference between the various types of backbone conformations of the monomer unit of the polynucleotide chain is small[3,4], the conformations of the chains are mainly determined by the base-base interactions apart from hydrogen bonds. As the Watson-Crick base pairing has been maintained in our models, the essential difference between our two structures and the Watson-Crick model lies in the mode of stacking of bases. The stacking energy between any two bases in different orientations and when separated by various distances was therefore investigated. A detailed report is under preparation (Sasisekharan and Gautam Gupta). The results of interest to us are the following : In the case of cytosine (C), stacking is achieved only for interactions between normal C and inverted C. The normal base-base interaction is repulsive and becomes attractive only when one C inverted. This agrees with the calculations reported earlier[5] ; similar conclusions hold for G–G interactions. Thus a G–C pair followed by another G–C pair will be highly stable when one of the G–C pairs is inverted ; the energy difference is more than 10 kcals/mole. Thus a C–C (or G–G) base sequence along the polynucleotide chain can bring about a fold in type II.

(3 *a*)

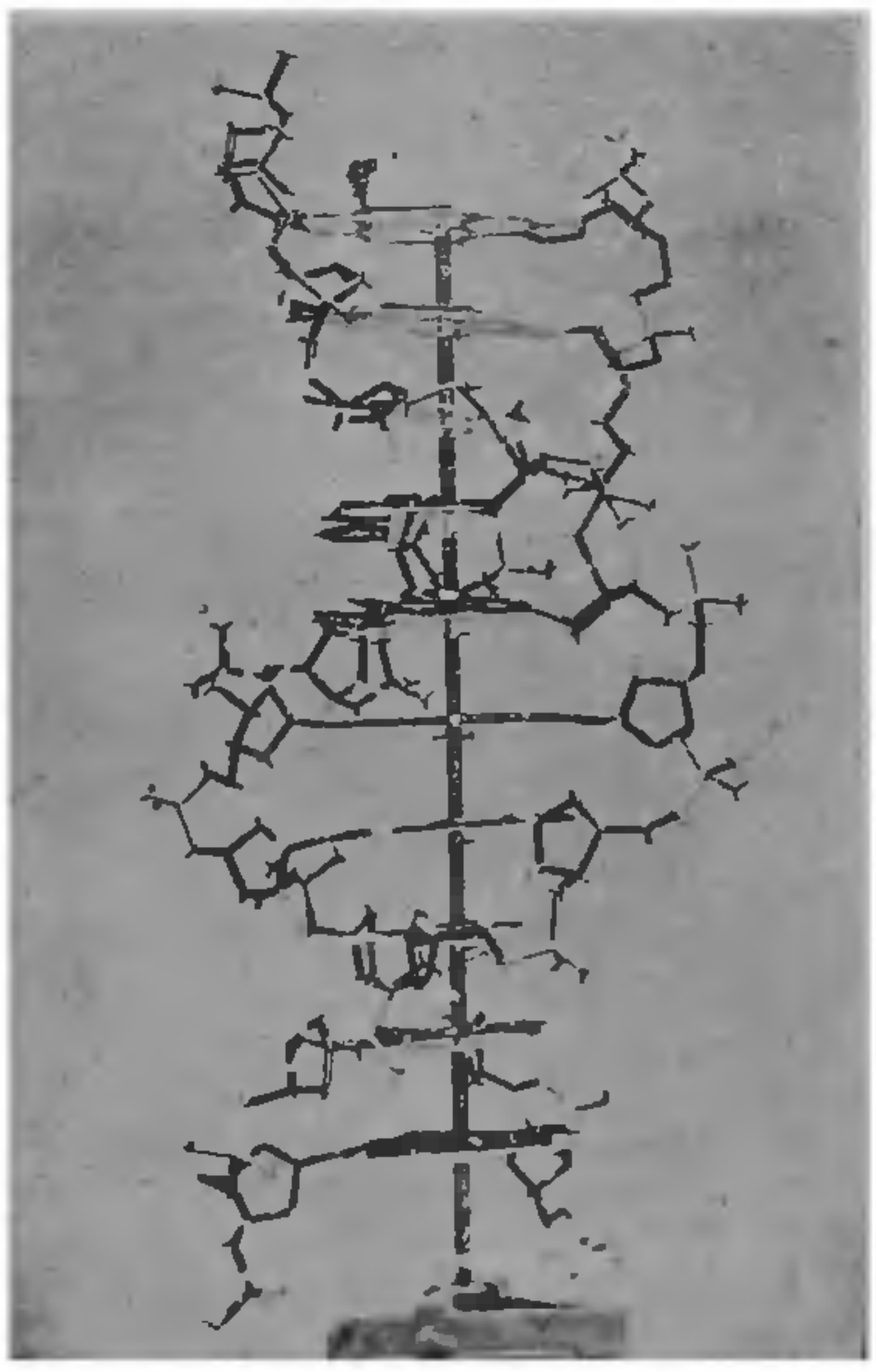


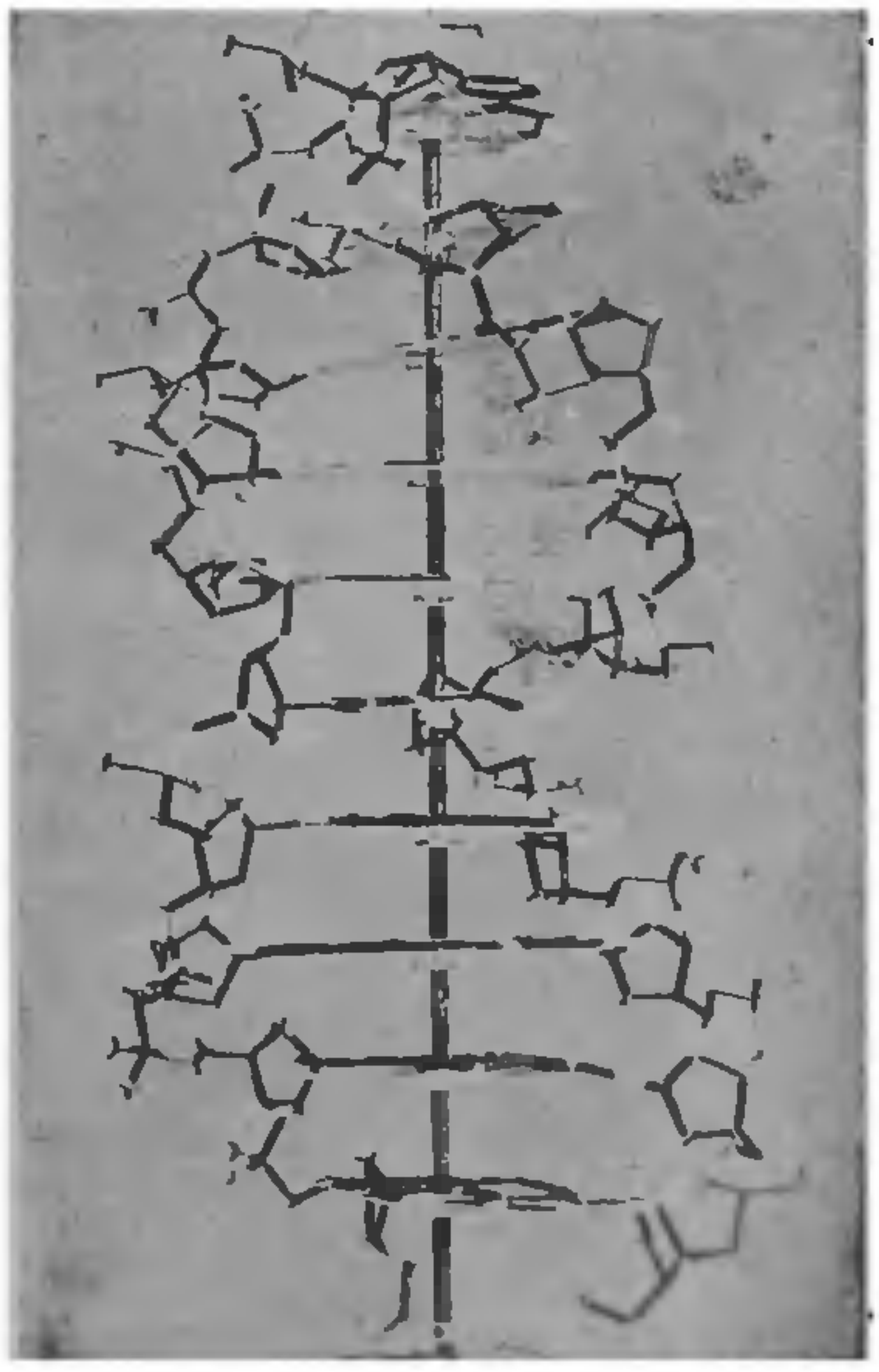


(3 *b*)

FIG. 3. A Model of type I—Two views.

(4 *a*)





(4 *b*)

FIG. 4. A Model of type II—Two views.

For A–A, both (normal base)–(normal base) interactions and (normal base)–(inverted base) interactions have nearly the same energy. For T–T, the normal (base)–(base) interaction is small; however, it is lower than the interaction energy between a normal base and an inverted base.

In the case of purine-pyrimidine (or pyrimidine-purine) sequences (normal base)-(normal base) stacking is favoured. However, depending upon the sequence, either a right or a left stacking of bases is preferred. Thus, in a sequence GpC, the stacking is right handed whereas in CpG the stacking is left handed. As a consequence, sequences like CpG can involve a right to left fold in type I. Similarly, for ApT and TpA respectively, right and left stacking of bases can occur; however, the energy difference is small.

Representative Models of Types I and II

A representative model for type I with two different views is shown in Fig. 3. Here, we have used the *gg* conformation about the C_4'–C_5' bond for the right handed segment of the chain[6] and *gt* conformation for the left handed segment of the chain. The *gt* conformation has already been observed in a crystal structure[7]. It may be worthwhile to mention that the *gg* conformation for the left handed segment is also possible for this model. As regards the two types of folds, one involves a change from *gg* to *gt* conformation about the C_4'–C_5' bond as has been used in the kinky helix[8]. The other involves a change from *gg* to *tg* conformation. Again, the *tg* conformation has also been observed in a crystal structure[9]. For the right handed segment, the C_2' endo conformation for the sugar has been used. For the left handed segment the C_3' endo sugar has been used.

A model for type II with two different views is shown in Fig. 4. The conformation employed about the C_4'–C_5' is *gg* for both the right and the left handed segments. The sugar puckering employed is C_2' endo in the right handed segment and C_2' endo –C_1' exo for the left segment. Here one fold is achieved by employing g^+g^+ conformation about the P–O bonds. This conformation has been observed in two crystal structures[10,11]. The other fold is achieved by slight modifications of the conformations about the various single bonds that are employed for the right handed segment. One view of both the types resembles the typical Watson-Crick model. However, the other view, taken at 90° from the first one, reveals marked differences and clearly shows the lateral separation of the two chains without intertwining.

Other types of puckering could be employed in both these models. Also, the puckering of the sugars at the folds could be different. In both the models we have maintained the radius of the phosphorus atom to be very nearly 9 Å. This could also be varied if necessary, and the width of the two segments could also differ.

The Fourier transform of these models has not been computed, as the mathematics of the same has to be worked out. However, the Fourier transforms of the corresponding left handed and right handed helices are similar. It is clear that these types of structures could be built with folds at other levels and not necessarily after every five base pairs. These types of arrangements have more degrees of freedom and hence flexible. As the models presented here are tentative, we do not wish to discuss their geometrical properties. Full details of the two structures will be published elsewhere.

Conclusions

The purpose of the present paper is to show that double-stranded polynucleotide chains having base orientation as in B DNA can be constructed in two typical ways without tangling. The two types of arrangements appear to bend more readily than the conventional double helix. The preliminary model building indicates that a minimum of three base pairs are necessary between any two folds. In a nucleic acid chain, where we have a sequence of bases, we believe that both the types could be present in a single molecule. In such a case DNA need not be a double helix throughout and such a structure has a number of attractive features and these will be dealt with elsewhere.

Note: A paper "A possible conformation for double-stranded polynucleotides" has just appeared in the *Proceedings of the National Academy of Sciences*, USA, Vol. 73, No 9, 1976, pp. 2959-2963) which describes a model similar to the type I structure presented here. We thank Professors H. Sharat Chandra and O. Siddiqi for drawing our attention to this report.

Acknowledgements

We wish to thank Prof. G. N. Ramachandran for his keen interest. We thank the Science and Engineering Research Council, of the Department of Science and Technology, Government of India, for financial support. One of us (N. P.) acknowledges financial assistance from the University Grants Commission in the form of a Junior Research Fellowship.

1. Watson, J. D. and Crick, F. H. C., *Nature*, 1953, 171, 737.
2. Sasisekharan, V., *The Jerusalem Symposium on Quantum Chemistry and Biochemistry*, Vol. V, 1972, p. 247.
3. Lakshminarayanan, A. V. and Sasisekharan, V., *Biopolymers*, 1969, 8, 489.

4. Sasisekharan, V. and Lakshminarayanan, A. V., *Ibid.*, 1969, 8, 505.
5. Pullman, A. and Pullman, B., *Advances in Quantum Chemistry*, 1968, 4, 267.
6. Arnott, S., Dover, S. D. and Wonacott, A. J., *Acta Cryst.*, 1969, B 25, 2192.
7. Seshadri, T. P. and Viswamitra, M. A., *Pramāna*, 1974, 3, 218.
8. Crick, F. H. C. and Klug, A., *Nature*, 1975, 255, 530.
9. Viswamitra, M. A., Seshadri, T. P. and Post, M. L., *Ibid.*, 1975, 258, 542.
10. Suck, D., Manor, P. C., Germain, G., Schwalbe, C. H., Weimann, G. and Saenger, W., *Nature New Biology*, 1973, 246, 161.
11. Rubin, J., Brennan, T. and Sundaralingam, M., *Biochemistry*, 1972, 11, 3112.

KINETICS OF DECOMPOSITION OF NITROUS OXIDE OVER NICKEL TITANATE

G. NAGASUBRAMANIAN, B. VISWANATHAN AND M. V. C. SASTRI
Department of Chemistry, Indian Institute of Technology, Madras 600 036

ON account of their greater chemical stability, structural reproducibility and catalytic activity than their parent binary oxides, ternary oxides of transition metals have generated wide-spread interest in recent years as catalysts of choice for a diverse variety of catalytic reactions. As part of a general study of the catalytic properties of these oxides, the kinetics of decomposition of nitrous oxide were studied on a series of titanates, with a view to evaluating the usefulness of this reaction for comparative assessment of their catalytic activities for oxidation reactions. No report is available of any previous study of this reaction over ternary oxides. The results obtained with nickel titanate are reported in the present communication. Similar results were obtained with the titanates of cobalt, manganese, magnesium, barium, strontium and calcium.

Nickel titanate was prepared by the method of Saikali *et al.*[1]. Its composition ($NiTiO_3$) and ilmenite structure were established by chemical analysis and X-ray diffraction. BET surface area determined with nitrogen at — 198° C = 3·14 m^2/gm. Nearly pure N_2O, was further purified by selective freezing at — 78° C.

The kinetics of N_2O decomposition over nickel titanate were studied in the temperature range 440–510° C in a quartz reactor, with closed circuit recirculation using an all-glass electromagnetic pump. The decomposition rate was followed by noting the increase in pressure as a function of time. After each kinetic run, the catalyst was "prepared" for the next run, by evacuation at 520° C for 6 hours followed by 8 hours exposure to oxygen (100 torr) at the temperature of the next run and a short evacuation at the same temperature for 3 minutes. This procedure for surface restoration was found to yield reproducible results in repeat runs.

Winter[2], who studied the decomposition of nitrous oxide over rare earth oxides, noted that different rate equations were to be used to express the kinetics of the decomposition at high and low pressures, namely,

$$-\frac{dP_{N_2O}}{dt} = \frac{kP_{N_2O}}{(P_{O_2})^{1/2}},$$

at N_2O pressures > 200 torr (I)

and

$$-\frac{dPN_2O}{dt} = k'.P_{N_2O},$$

at N_2O pressures < 50 torr (II)

The same duality of kinetic behaviour at high and low N_2O pressures was observed in the present work also, as may be seen from the consistency of the k values (low standard deviations) calculated with the appropriate rate expressions (*vide* Table I).

TABLE I

Values of rate constants deduced from differential equations I and II

Temp. °C	Values of rate constants (k)			
	k ($cm^{1/2}$ min^{-1} m^{-2}) 10^{14} (above 200 Torr)		k (min^{-1} m^{-2}) $\times$ 10^{14} (below 50 Torr)	
	Equation I	Equation II	Equation I	Equation II
440	2·24±0·182	5·44±1·71	3·66±0·76	9·7±0·036
460	3·85±0·1	6·59±1·41	4·37±0·92	13·7±0·7
490	5·29±0·1	4·49±0·8	7·76±1·85	15·7±0·04
510	8·3±10·27	11·9±2·92	12·99±4·14	27·1±0·11