ANALYSIS OF POSSIBLE HELICAL STRUCTURES FOR POLY(DINUCLEOTIDES). EVIDENCE FOR LEFT-HANDED Z-DNA AND Z-TYPE HELICES

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ABSTRACT

The helical parameters n (number of dinucleotide residues per turn) and h (height per dinucleotide) have been evaluated for single stranded poly(dinuclectide) helices comprising a variety of dinucleotide conformational repeats. The (n—h) plots as in poly(mononucleotide) case reveal a single phosphodiester as the helix forming domain which shows a strong dependence on the nature and sequence of sugar ring and C4′—C5′ bond conformations and the phosphodiester within the repeat. The results together with conformation energy calculations uniquely characterise the recently discovered left-handed Z-DNA[1] and predict the possibility of other Z-type helices. These are correlated to the occurrence of *trans* C4′—C5′ bond conformation on 5′-side or a C2′-*endo* pucker on 3′-side or both, in the repeating dinucleotide and may manifest in structures crystallised under slightly different salt concentrations or growing conditions.

INTRODUCTION

USING the idea of "dinucleotide", instead of "mononucleotide", as the helix repeat, recently we reported[2,3] the helical parameter analysis for certain poly(dinucleotides) comprising the preferred C3′-*endo* and C2′-*endo* geometries for the nucleotides and the g^-g^- for the phosphodiester. The results of these studies revealed the stereochemical possibility of single as well as double-stranded helices, possessing alternating g^-g^- and tg^- phosphodiesters in succession concomitant with alternating C3′-*endo* and C2′-*endo* nucleotides similar to proposals[4,5] made independently from experimental considerations. The results also suggested the importance of this structure in understanding the dynamical aspects of DNA conformations. In continuation of our studies to probe possible alternative helical structures for nucleic acids, we have been carrying out helical parameter analysis, model building studies and conformational energy calculations by considering a variety of conformations for the repeating "dinucleotide" moieties which include variation in backbone C4′—C5′ bond torsion and sugar puckers as well as their sequences. We describe here briefly the results obtained in relation to the recently observed Z-form[1,6-8] of DNA which is characterised by a left-handed twist with a "dinucleotide" repeat instead of the commonly found form of right-handed duplex with mononucleotide repeat. The helical parameter analysis using (n—h) plots as well as conformational energy surfaces readily predict the left-handed Z-form rather uniquely, but in addition also predicts stereochemical possibility of other forms of Z-DNA possessing essentially similar configurational features but with different conformations for the nucleotides and the junction phosphodiester which link the repeating "dinucleotide" moieties.

METHOD

Figure 1 shows the section of a polynucleotide chain depicting "dinucleoside triphosphate" as the helical repeat along with notations for various torsion angles. The helical parameters, *viz.*, the number of repeating dinucleotide moieties per turn (n) and the height per dinucleotide residue along the helical axis (h), have been computed using the application of matrix methods similar to those used in the study of helical parameters of poly(mononucleotides)[9]. The helical parameters so determined as a function of the P—O bonds between the dinucleotide repeats are represented in the form of curves of constant n- and h-values and is termed the (n—h) plot. The radii (r) of the various helical structures also computed as a function of P—O bonds are superimposed on the n—h plots. Such (n, h, r) plots have been obtained for a variety of single stranded poly(dinuclectide) helices which differ in the conformation of the repeating "dinucleotide". Also conformational energies which include van der Waals, electrostatic, torsional and anomeric interactions[10] have been estimated as a function of phosphodiester P—O bonds both within and between the repeating units to assess the energetics of helix forming phosphodiester conformations. Energies have been estimated by considering sugar-phosphate–sugar backbone interactions alone as in earlier cases to study the intrinsic behaviour of polynucleotide backbone and also by including base interactions. The average geometrical parameters and the nature of potential functions used in all these calculations are the same as reported earlier[11]. Model building is carried

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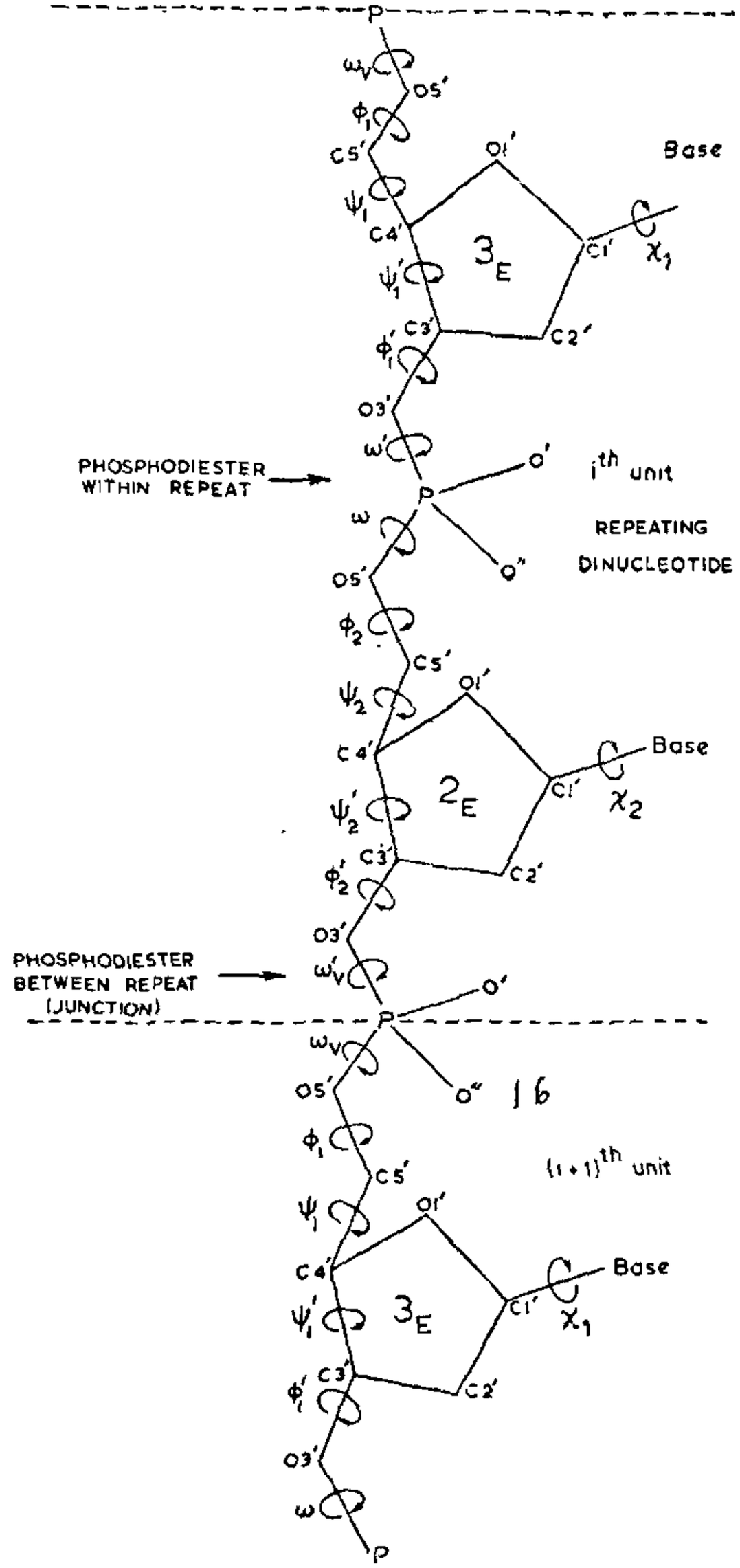

FIG. 1. Section of a deoxy polynucleotide chain depicting the notations[16] for various backbone and side chain torsions. The concept of dinucleotide helical repeat is indicated by horizontal dotted lines. Mixed sugars are indicated by marking 3_E and 2_E. Actual sequences used in the study are discussed in the text.

out using Labquip models and checked by computer simluated procedures at various levels.

CONFORMATIONAL VARIABLES

The idea of proposing dinucleotide as the helix repeat is to exploit its inherent flexible framework to obtain non-classical helical models distinctly different from the familiar A- or B-form of helices. In the present calculations 'dinucleotide' repeats possessing *gauche*$^+$ (g^+) and *trans* (t) conformations around the C4′—C5′ bond and g^-g^-, tg^-, tg^+ g^-t and g^+g^+ for the phosphodiesters are considered with different combinations of C3′-*endo* (3_E) and C2′-*endo* (2_E) mixed as well as similar sugar puckers. The *gauche*$^-$ (g^-) conformation is likely to be less favoured in helical structures and hence not considered here. The phosphodiesters considered above possess the ability to permit the bases to be on same side and show tendency to provide at least partial overlap between adjacent bases with appropriate modifications in the polynucleotide backbone conformations.

RESULTS AND DISCUSSION

(*n*—*h*) *Plot for Poly(dinucleotide) Helices of the Z-type*

Figure 2 shows the helical parameters obtained as a function of (ω'_v, ω_v) at 10° intervals for poly (dinucleotide) helices possessing "dinucleotide" repeats (Fig. 1) characterised by the experimentally observed conformation[1], *viz.*, $(\psi_1, \psi'_1) = (g^+, 2_E)$ and $(\psi_2, \psi_2') = (t, 3_E)$ in the successive nucleotides.

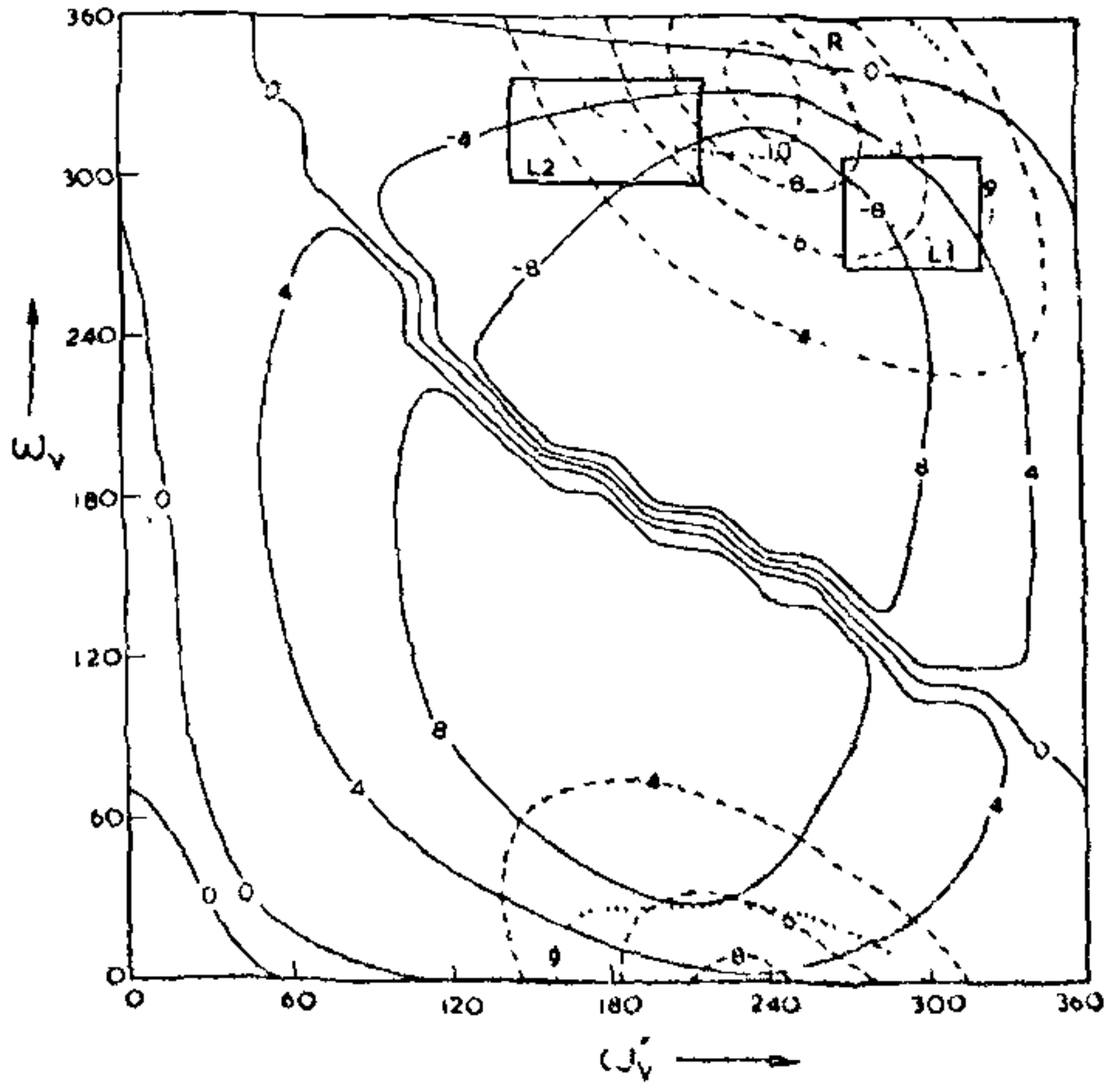

FIG. 2. Curves of iso n (----) and iso h (——) as a function of ω_v' and ω_v for single stranded poly (dinucleotide) helices comprising the dinucleotide conformational repeat similar to Z DNA (1): $(\psi_1, \psi'_1) = (g^+, 2_E)$, $(\omega', \omega) = (g^+, g^+)$ and $(\psi_2, \psi'_2) = (t, 3_E)$. Curves of iso r (. . . .) equal to 9 Å alone are shown. L1, L2 and R describe regions of possible left- and right-handed helices. Note that virtually only left-handed helices are possible in the g g ($/g^-$) phosphodiester domains.

The preferred value of 180° has been assigned for the two C5′—O5′ bond torsions (ϕ_1 and ϕ_2) while C3′—O3′ torsions (ϕ'_1 and ϕ'_2) are assigned values of 270° instead of the generally favoured value of 210° for reasons mentioned later in the discussion. It is noteworthy that the sugars have alternating 2_E and 3_E conformations. Similarly, the backbone C4′—C5′ bond orientation alternates *gauche*$^+$ (g^+) for 5′-sugar and *trans* (t) for 3′-sugar. The phosphodiester within the repeating dinucleotide possesses the $g^+g^+ = (\omega', \omega) = (90°, 90°)$ conformation. This phosphodiester is energetically not favourable with the preferred nucleotide geometry due to stereochemical restrictions imposed by i and $(i+2)$ phosphates[12]. But energy calculations show (Fig. 3) that it is found to be energetically favoured now mainly due to the occurrence of *trans* orientation around C4′—C5′ bond on 3′-side and C2′-*endo* pucker for 5′—sugar which displace the i and $(i+2)$ phosphates considerably apart relieving the steric and electrostatic repulsive interactions between them. Indeed the g^+g^+ phosphodiester is found to be energetically more favoured than the g^-g^- by about 1·5 Kcals/mole despite the absence of base-backbone and base-base interactions. Inclusion of these is found to greatly stabilise the g^+g^+ conformation[12]. Conformational energy calculations also show that the occurrence of g^+ conformation for C4′—C5′ bond on 3′-sugar render the g^+g conformation to be of high energy suggesting the importance of *trans* conformation for C4′—C5′ bond on 3′-side to obtain Z-type helices.

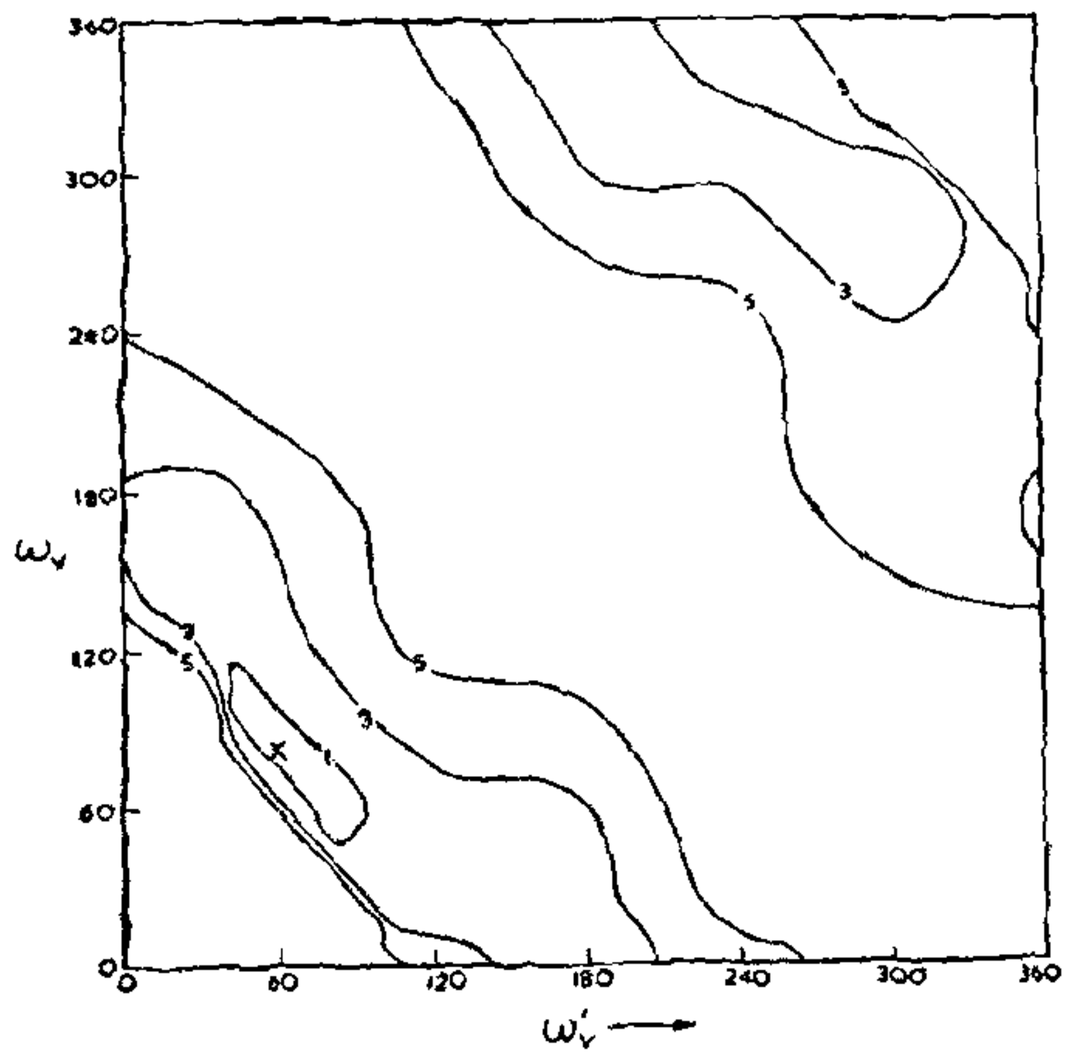

FIG. 3. Conformational energy map obtained as a function of P—O3′ (ω') and P—O5′ (ω) bonds within the repeating dinucleoside triphosphate backbone. The nucleotide on 5′-side possesses g^+ for C4′—C5′ bond with 2_E sugar while on 3′-side t for C4′—C5′ and 3_E sugar. The ϕ'_1 and ϕ'_2 torsions are assigned values of 270°. The energy minimum is marked X. With ϕ' angles of 210°, both g^-g^- and g^+g^+ are nearly equally favoured.

The helical parameter plot (Fig. 2) clearly depicts that curves of constant n-values greater than 4 occur only in the g^-g^-/tg^- and tg^+ regions. Computation of radii also suggests that helical structures with radii between 7 to 9 Å could be generated only in these phosphodiester domains. Other phosphodiesters lead to structures having radii much smaller than (7 Å) and therefore are not likely to be physically meaningful. Thus the important helix forming domain corresponds only to these broad phosphodiester regions. $h = 0$ curve divides the region of phosphodiester conformations which characterise left (L) and right-(R) handed helical structures. As earlier[9] h-curves intersect n-curves at two distinct regions marked L1 and L2 in Fig. 2 demonstrating the possibility of helical structures possessing different types of phosphodiester conformations (g^-g^- or tg^-) between the *repeating dinucleotides but with* identical helical parameters.

The most striking observation in the (n—h) plot is that both the g^-g^- and tg^- phosphodiester domains correspond almost exclusively to the left-handed helical structures since only negative values of h occur here. This is in contrast to all the earlier (n—h) plots obtained for poly(mononucleotides)[9] as well as poly(dinucleotides)[2,3]. Conformational energies computed as a function of P—O bonds (ω'_v, ω_v) between the repeating dinucleotides is shown in Fig. 4. Interactions involving only the adjacent nucleotides flanking the P—O bonds are taken into account. It is clear that the g^-g^- phosphodiester corresponding to the L1 region of (n—h) plot (Fig. 2) is energetically preferred and the tg^- phosphodiester domain which corresponds to the L2 region (Fig. 2) is found to be energetically unfavourable. The energies in the tg^+ phosphodiester corresponding to the right-handed structures and also the g^+g^+ domain are rendered relatively high (> 5 Kcals/mole). This readily suggests that the helix forming phosphodiester domain predicted by the (n—h) plot indeed corresponds to the energetically favoured domains as in poly(mononucleotides)[9]. The phosphodiester between the "dinucleotide" repeat in Z-DNA indeed occurs in the preferred L1 domain indicating that polynucleotide helices comprising even "dinucleotide" as helical repeat can be characterised and predicted rather uniquely by theoretical considerations. The experimentally observed Z-DNA structure[1] possesses $n = 6$ and $h = -7{\cdot}4$ Å and this corresponds to values of (ω'_v, ω_v) $\simeq$ (290°, 280°) in the (n,h) plot. It is clear from Fig. 2 that minor rotational varia-

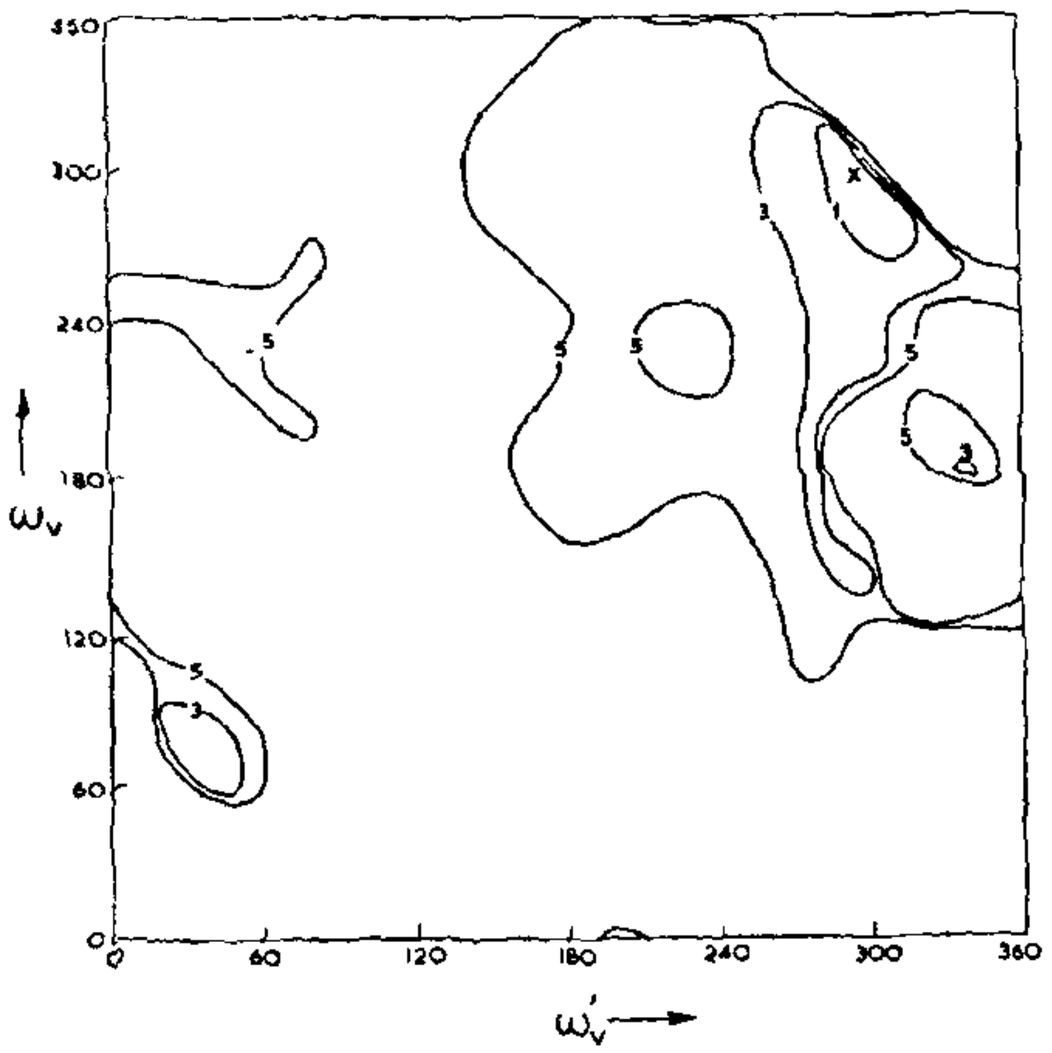

FIG. 4. Conformational energy map obtained as a function of P—O3′ (ω'_v) and P—O5′ (ω_v) bonds between the repeating dinucleoside triphosphate backbone. The nucleotide on 5′-side possesses the *trans*-conformation for C4′—C5′ bond with a 3_E sugar while on 3′-side, g^+ for C4′—C5′ with a 2_E sugar. Note the shift in the global minimum marked X towards g^-g^- compared to Fig. 3.

tions around the inter "dinucleotide" phosphodiester bonds (ω'_v, ω_v) can lead to polymorphs differing in helical parameters.

Effect of Base Sequence and Orientations

The (n, h, r) plot discussed above corresponds to single stranded poly(dinucleotide) helices and the computed helical parameters depend only on backbone conformations. It appears then that occurrence of the left-handed helical structures are as a result of conformational modifications along the backbone (which are of course attributable to the base and base sequence effects). Model building studies show that both *syn* and *anti* conformations for purine as well as pyrimidine bases generate stereochemically permissible left-handed Z–DNA like single stranded helices. But the requirement of double stranded helix with Watson–Crick base pairing mode imposes severe constraints on the energetically favoured base sequence as well as their orientations. Alternating *anti* and *syn* orientations for the 5′- and 3′-bases respectively alone lead to Z-form of double helical conformations as exemplified by the X-ray structures[1,6-8] and model studies[14]. Interchange of purine and pyrimidine bases (*i.e.*, 5′-base purine and 3′-base pyrimidine) would lead to essentially similar left-handed helices although the experimentally observed[1,6-8] pyrimidine-purine sequence is likely to be energetically favoured because of better stacking interactions within the repeating unit besides purines can assume *syn* conformation relatively easily[15]. Energetic preference of pyrimidine-purine and purine-pyrimidine sequences in forming left-handed Z-type duplex structures are being analysed by conformational calculations. On the other hand, interchange of base orientatons, *viz.*, 5′-base (*syn*) and 3′-base (*anti*) instead of the experimentally observed 5′-base (*anti*) and 3′-base (*syn*) does not lead to intertwined double helical structures irrespective of base sequence but results in a sheet or ribbon like structure with a small left-handed twist.

Correlation Between the Helix-forming Phosphodiester and the Dinucleotide Conformational Repeat

To explore possible other helical structures for poly (dinucleotides), analysis has been carried out using a variety of conformations for the repeating "dinucleotide". The effect of *trans* (t) and *gauche*$^+$ (g^+) conformations around C4′—C5′ bonds with C2′-*endo* and C3′-*endo* sugar puckers and also the influence of their occurrence on 5′- or 3′-side of the repeating dinucleotide has been examined. Similarly other phosphodiester conformations like g^-g^-, tg^-, g^-t and tg^+ have been considered for (ω', ω) in addition to g^+g^+ phosphodiester discussed above. The results are summarised in Table I.

Helical parameters have been computed with *trans* conformation around the C4′—C5′ bonds on both 5′- and 3′-sides of the 'dinucleotide' repeat, instead of alternating *gauche*$^+$ and *trans* found in the repeating unit of Z–DNA[1]. The phosphodiester within the repeat is assigned the g^+g^+ conformation which is found to be again energetically preferred. The $(n—h)$ plot so obtained is shown in Fig. 5. It is clear that the helix-forming domain corresponds to (ω'_v, ω_v) values in the g^-t phosphodiester region rather than g^-g^- obtained earlier (Fig. 2). This is suggestive of other possible helical structures with alternative phosphodiester conformations. L1 and L2 and R1 and R2 in Fig. 5 correspond to regions of possible left and right-handed helical structures. Model building studies together with conformational energy calculations[13] indicate that the phosphodiester conformations in the L1 region alone lead to overlap of the adjacent bases at the junction of the repeating dinucleotide residues. Adoption of this phosphodiester between the repeating dinucleotide leads to stereochemically feasible intertwined Watson Crick base paired left-handed double helix. A Labquip molecular model with approximately half-a-turn of helix is shown in Fig. 6. The structure possesses alternating *anti* and *syn* conformations for the 5′- and 3′-sugars and the phosphate groups follow zig-zag path similar to Z–DNA[1]. Other features in this model have

TABLE I

Correlation between the helix-forming phosphodiester and the "dinucleotide" repeat

Models	Conformation of repeating dinucleotide backbone*					Helix-forming Phosphodiester domain	Helix type
	ψ_1	ψ'_1	(ω', ω)	ψ_2	ψ'_2	(ω_p', ω_p)	
I	g^-	2_E	g^+g^+	t	3_E	$g^-g^-(tg^-)$	Z (1)
	g^+	2_E	g^+g^+	t	2_E	g^-t	Z' (8)
	g^+	2_E	g^+g^+	t	1_E	$g^-g^-(g^-t)$	Z' (7)
	t	2_E	g^+g^+	t	3_E	g^-t	Z''
	t	2_E	g^+g^+	t	2_E	g^-g^+ (g^-t)	Z'''
II	t	3_E	g^+g^+	g^+	2_E	Structure not likely	
	t	2_E	g^+g^+	g^+	3_E	due to small radii	
	g^+	3_E	g^+g^+	t	2_E	and/or h values	
	t	3_E	g^+g^+	t	2_E		
	t	3_E	g^+g^+	t	3_E		
III	t	2_E	tg^+	t	3_E	g^-t	Alternating type
	t	2_E	g^-t	t	3_E	g^+g^+ (tg^+)	
IV	g^+	3_E	g^-g^-	g^+	2_E	tg^-	Alternating type (2–5)
	g^+	2_E	g^-g^-	g^+	3_E	tg^-	
V	g^+	3_E	g^-g^-	g^+	3_E	g^-g^-	A-type
	g^+	2_E	tg^-	g^+	2_E	tg^-	B-type

* For notations used for different bond rotations see Fig. 1.

close resemblance to those found in Z–DNA[1]. The important difference between Z–DNA[1] and the theoretically predicted model (Z''–DNA) is that the successive phosphodiesters exhibit g^+g^+ and g^-g^- in the former and g^+g^+ and g^-t in the latter (Table I). Similarly the C4′—C5′ bond torsions alternate from g^+ to t in Z–DNA[1] while it is *trans* throughout in Z''–DNA. It may not be surprising if this new polymorph is found experimentally in crystals grown under different salt concentrations and growing conditions. It is noteworthy that the terminal deoxycytosine in the orthorhombic crystal of CpGpCpG[7] exhibits the *trans* conformation for the C4′—C5′ bond providing indirect credence to our arguments.

Interestingly, it is found that occurrence of *trans* conformation around C4′—C5′ bonds on both 3′- and 5′-sugars facilitate the formation of left-handed helices even with interchange of base orientations, *viz.*, 5′-base pyrimidine (*syn*) and 3′-base purine (*anti*). The helix so formed is wider and the phosphate group separations are relatively larger. There are differences in the nature of overlap of bases within and between the repeating dinucleotide units. However, interchange of base orientations together with base sequence, *viz.*, 5′-base purine (*syn*) and 3′-base pyrimidine (*anti*) does not lead to intertwined double helical structures.

Calculations performed with 2_E conformations for both 5′- and 3′-sugars, with other conformations same as in Z–DNA[1], also predict g^-t as the helix-forming phosphodiester. The g^-t domain almost exclusively suggests left-handed helical structures. Model building studies reveal that use of these conformational combination for the polynucleotide backbone concomitant with alternating *anti* and *syn* bases for 5′- and 3′-sugars yield left-handed duplex structure very similar to Z–DNA configuration[1]. While this work was completed, we found to our pleasant surprise the existence of similar conformational combination in the crystal structures of tetranucleotide CpGpCpG by two independent groups[7,8]. It is most gratifying that our theoretical predictions are in excellent agreement with experimental findings. Thus, it is possible to obtain a small number of Z–DNA

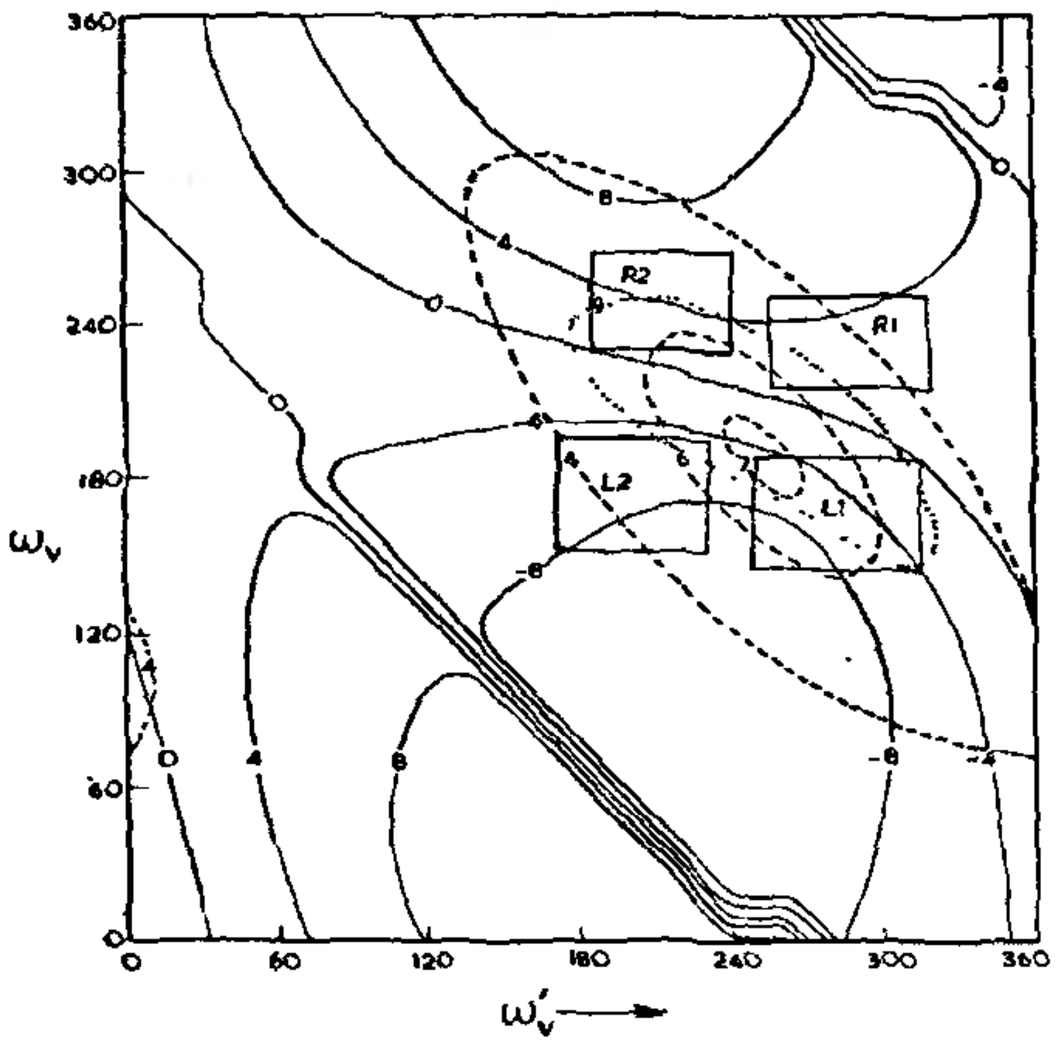

FIG. 5. Curves of iso n (– – -- –) and iso h (——) obtained as a function of ω_v' and $-\omega_v$ for single stranded poly(dinucleotide) helices comprising the dinucleotide repeat with $(\psi_1, \psi_1') = (t, 2_E)$, $(\omega', \omega) = (g^+, g^+)$ and $(\psi_2, \psi_2') = (t, 3_E)$. Curves of iso r (·····) equal to 9 Å alone are shown. Note that $\psi_1 = t$ here compared to g^+ found in Z-DNA[1] and this alone shifts the helix-forming phosphodiester to $g^- t$. The two possible regions of left (L1 and L2) and right-handed (R1 and R2) are shown. L1 region is found to be energetically favoured.

type structures which differ in the backbone conformations of the dinucleotide repeat and the phosphodiester linking them while the overall configuration remaining essentially similar. The relative importance of these structures from energy considerations is being examined.

It is found that dinucleotide repeats possessing either g^+ conformation for C4′–C5′ bond associated with 3′-sugar or 3_E conformation for 5′-sugar or both do not lead to any stereochemically feasible helical structures (Models II of Table I) because of extremely small radii or h-values and also due to steric interactions between the terminal 3′-phosphate and 5′-sugar. Thus, it seems the *trans* orientation of C4′–C5′ bond on 3′-sugar[14] and 2_E for 5′-sugar are crucial for the dinucleotide backbone repeat in forming left-handed Z-DNA type of structures[1].

Similarly, it is found that the helix-forming domain shows a strong dependence on ϕ' values. Use of ϕ' values around 210° for ϕ_1' and ϕ_2' predicts the energetically unfavourable tt phosphodiester as the helix-forming domain[18]. Values around 270° shift the helix-forming domain to $g^- g^-$ phosphodiester. Conformational energy calculations also show that the preference for g^+g^+ and g^-g^- phosphodiesters depend on ϕ' values[13]. The maximum and minimum values of n are also dependent on ϕ' values.

Helical parameter calculations using either $g^- g^-$ or $g^- t$ phosphodiesters within the repeating dinucleotide moiety with appropriate sequence of sugar pucker and C4′–C5′ bond conformations found in Z-type structures[1,6–8] predict in turn the g^+g^+ phosphodiester to be the helix-forming domain as shown in Fig. 7. Although repetition of g^+g^+ phosphodiesters themselves does not lead to either left-handed or right-handed structure, use of this in combination with other phosphodiesters lead to novel helical structures like Z-DNA. The shift in the helix-forming domain from $g^- g^-$ to $g^- t$ when ψ_1 changes from g^+ to t discussed earlier is also shown in Fig. 7.

Models III given in Table I correspond to stereochemically possible double helical structures of the alternating type wherein the bases have *anti* conformations. The details of these are to be discussed elsewhere. Models IV in Table I are also of the alternating type already described[2–5] and possess

FIG. 6. A representative left-handed double helical model (half-a-turn) of Z-DNA with pyrimidine (*anti*)-purine (*syn*) base sequences constructed using L1 phosphodiesters between the dinucleotide repeats suggested in Fig. 5. See text for other details.

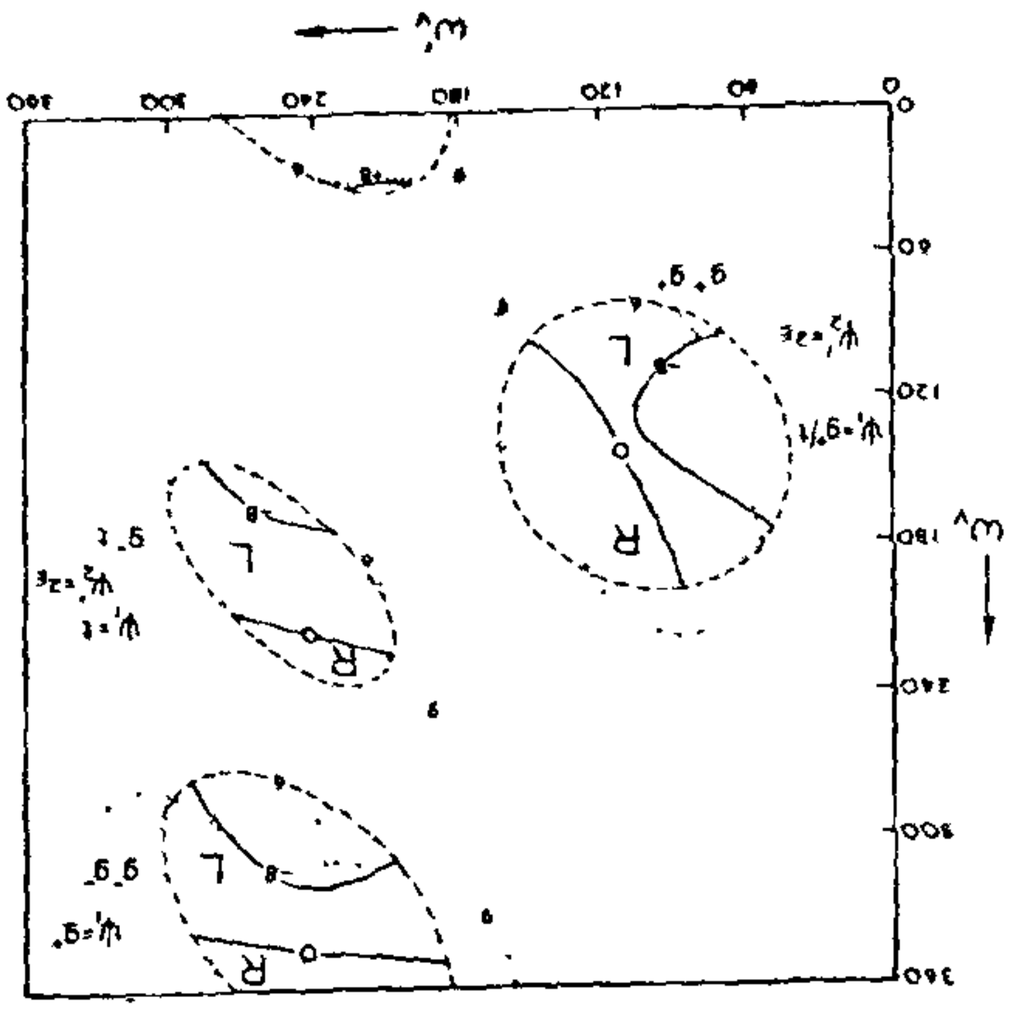

FIG. 7. Curves of iso $n = 6$ (– – – –) and iso $h = -8$ (——) and iso $r = 9$ (·····) obtained as a function of ω_0' and ω_0 for conformationally different dinucleotide repeats. $h = 0$ divides the left (L) and right-handed (R) helical domains. The three important helix-forming domains appear at g^-g^-/tg^-, g^-t and g^+g^+ phosphodiesters corresponding to (ω_0', ω_0) $=(300°, 300°), (180°, 300°), (300°, 180°)$ and $(90°, 90°)$ respectively depending on the nature and sequence of sugar ring and C4′–C5′ bond conformations of the dinucleotide repeat. Note the shift in the helical domain from g^-g^- to g^-t (only ω changes by $-120°$) as ψ_1 is changed from g^+ to t (a change of $+120°$). Similar change appears when 3′-sugar assumes 2_E instead of 3_E in the dinucleotide repeat even with $\psi_1 = g^+$.

preferred nucleotide geometries. Helical structures possessing similar sugar puckers in the dinucleotide repeat but slightly different backbone torsions in the two nucleotides are characterised by Models V in Table I.

Conclusions

One of the important outcomes of the present studies is the ability of theoretical calculations to characterise the experimentally observed Z–DNA structure[1], in addition to predicting other possible helices belonging essentially to the same family but with different conformational features. A striking finding is the prediction of an alternative Z″–DNA structure wherein the successive phosphodiesters possess alternate g^+g^+ and g^-t instead of g^+g^+ and g^-g^- found in Z–DNA[1]. This is correlated to the occurrence of *trans*. orientation for the C4′—C5′ bond on both 5′- and 3′-sugars instead of alternating *gauche*$^+$ and *trans* conformation found in Z-DNA. Calculations also predict similar alternation of g^+g^+ and g^-t phosphodiesters when the 3′-sugar exhibits C2′-*endo* conformation instead of C3′-*endo*. The latter has indeed been found in the most recent crystal structure determinations[7,8]. The importance of characteristic backbone geometry for the dinucleotide repeat, namely, the occurrence of C2′-*endo* for 5′-sugar the *trans* conformation for C4′—C5′ bond on 3′-sugar and the g^+g^+ conformation for the phosphodiester between them, for obtaining Z-type helices is clearly borne out from this analysis. The g^+g^+ phosphodiester itself is rendered energetically favoured by these backbone modifications. While this is true with respect to single stranded helical structures, it is found that the sequence of bases and their orientations play a crucial role in determining stereochemically and energetically preferred Watson–Crick base-paired left-handed double helical structures. Results from both theoretical as well as experimental investigations[1,6–8] have provided evidence for existence of a few left-handed helical structures possessing different geometry for the dinucleotide repeat as well as inter "dinucleotide" phosphodiester while belonging to the same Z-family. Further combined efforts by experimental and theoretical studies would sharpen our understanding of helix $\rightleftarrows$ helix transition and also other possibilities of helical structures obtainable by exploiting the flexible framework of "dinucleotide" helix repeat[2].

Acknowledgement

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SOME MORE KEYS AND RULES FOR A PROGRAMMABLE CALCULATOR

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ABSTRACT

The standard system of keys[1] has been enlarged to incorporate the various concepts of programming. A set of rules governing arithmetic operations and display is also given.

The Blank Key

THIS key, designated as β, is a null key which does nothing other than passing the control to the next step.

Effect of a DR Control Key Followed by the I or D Key

In such cases, the machine will first perform the indicated operation on the memory whose address is given by the content of the concerned IR and *then* increment/decrement its content. Hence SIϕ is equivalent to SRϕ Iϕ and SDϕ to SRϕ Dϕ. The other keys F, M and Z also work similarly.

Relational Operators

These are keys which cause the machine to take a decision depending upon the relation between two numbers. They are $\leqslant$ and $\equiv$ which stand for *less than or equal to* and *equal to*. The role of $\leqslant$ has already been defined[1]. In view of the convenience to the programmer, we redefine its role and similarly define the role of $\equiv$. Both the keys will cause the display to be copied in the internal register. The general form of these keys are $a \leqslant b\,(sss\ldots s)$ and $a \equiv b$ $(sss\ldots s)$, where a and b are the displays before and after encountering the operator key. $sss\ldots s$ is a sequence of steps which will be executed only if the indicated relation is true. The bracket need not be put if there are only four steps inside it.

The Inverse Key

The inverse key V performs the inverse/complement operation of the key succeeding it. Hence V $\leqslant$ stands for *not less than or equal to* and V $\equiv$ for *not equal to*.

These ideas are illustrated in the example given below:

Example 1. Write a programme for finding the greatest absolute value of $x_1, x_2, \ldots x_n$.

The programme is given in Table I. The inputs are n, $x_1, x_2, \ldots, x_n$ and output, the greatest absolute value. Spaces have been provided at appropriate places.

TABLE I

Programme for finding the greatest absolute value

Programme steps		Comment
$\phi\phi\phi$	AG4 HP Sϕ = A	n is stored in DRϕ
$\phi\phi$9	1 Tϕ 3 T1	
ϕ15	HP SI1 Iϕ	Steps ϕ15 to ϕ3ϕ form a loop to store $x_1, \ldots, x_n$ in DR3 onwards
ϕ22	R$\phi\leqslant$ Mϕ $\rightarrow\phi$15	
ϕ31	3 T2 ϕ S2 =	DR2 is initialised to zero
ϕ38	ϕ V$\leqslant$ M2 ($\pm$)	Nos. are called one by one
ϕ47	V$\leqslant$ M2 E S ϕ2	Sign of a negative no. changed and compared with the content of DR2. The greater no. being retained in it
ϕ55	R1 V$\leqslant$ R2 $\rightarrow\phi$38	
ϕ65	A M2 P	
ϕ69	Halt	End of programme