mation are not very likely to occur in DNA. However, energy calculations indicate that *syn* conformation for purines (especially for guanine) is as favourable as the *anti* conformation[8–9]. Also, a few single crystal structures of nucleosides and nucleotides of guanine[10–13] indicate *syn* conformation for this base. This prompted us to look into the possibility of double helical structures with all purines in *syn* conformation. For this purpose, we have chosen a poly-nucleotide duplex with alternating purine and pyrimidine sequence as the model system. A trinucleoside diphosphate then turns out to be a typical repeating unit instead of dinucleoside monophosphate. Note that the exact repeating unit in such a case is a dinucleotide.

Model Building with Trinucleoside Diphosphate as the Repeating Unit

Use of a trinucleoside diphosphate as the repeating unit, leads to two topologically distinct types of duplexes, the *uniform* and *zig-zag* helices. In the *uniform*

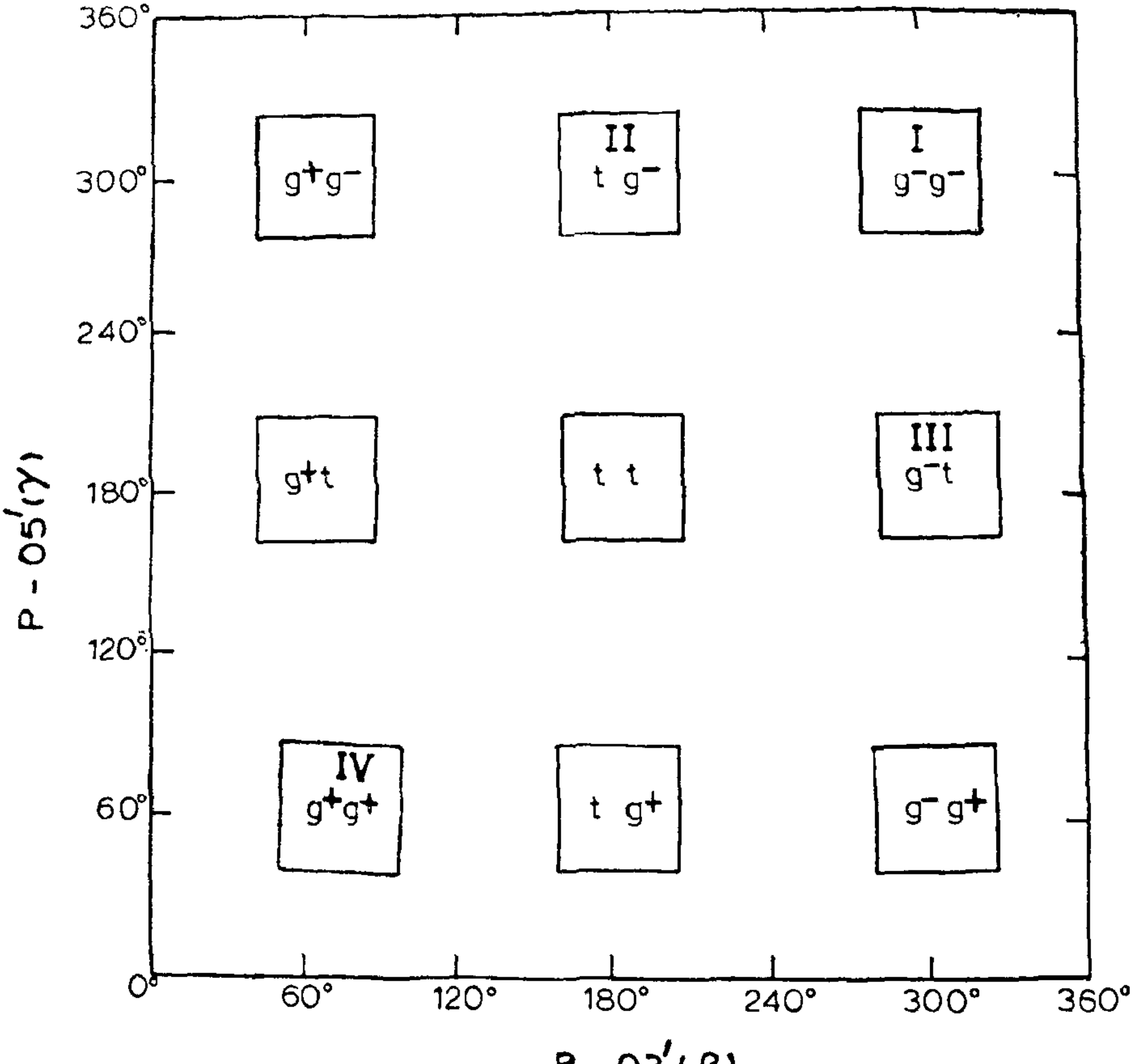


Fig. 1. Schematic representation of the helical domains in the (β–γ) space. The conformational features of the various domains are summarized in Table I. The helical domains are (g^-g^- and tg^-), (g^-t and tt) and (g^-g^+ and tg^+) for gg, gt and tg conformations respectively about the C4′–C5′ bond. The remaining three are non-helical domains. We have only investigated the helical domains I, II and III and the non-helical domain IV as shown. We have found that the (C3′-*endo*, g^-g^+) domain is stereochemically unsatisfactory. The helical domain (C2′-*endo*, tt) and (C2′–*endo*, tg^+) and the non-helical domains g^+g^- and g^+t are not considered here, as these conformations have not been observed so far, for nucleotides and higher oligomers.

TABLE I

Results of the conformational domains investigated in the (β–γ) space with dinucleoside monophosphate as repeating unit

Domain	Torsion (C4′–C5′) ϵ	Puckering (C4′–C3′) ζ	03′–P–05′ torsions (β, γ)	Glycosyl torsion χ	
				Right handed duplex	Left handed duplex
I	gg (55°≤ ϵ≤ 75°)	C3′-*endo* (75°≤ ζ≤ 100°)	g^-g^- (270°≤ β, γ≤ 305°)	low *anti* (10°≤ χ≤ 40°)	near *syn* (310°≤ χ≤ 340°)
II	gg (40°≤ ϵ≤ 65°)	C2′-*endo* (135°≤ ζ≤ 155°)	tg^- (195°≤ β≤ 220°) (280°≤ γ≤ 315°)	*anti* (55°≤ χ≤ 75°)	low *anti* (0°≤ χ≤ 30°)
III	gt (150°≤ ϵ≤ 195°)	C3′-*endo* (75°≤ ζ≤ 100°)	g^-t (280°≤ β≤ 310°) (155°≤ γ≤ 195°)	low *anti* (10°≤ χ≤ 40°)	near *syn* (310°≤ χ≤ 340°)
IV	gg (50°≤ ϵ≤ 75°)	C3′-*endo* C2′-*endo*	g^+g^+ (50°≤ β, γ≤ 90°)	Structure not possible	Structure not possible
	gt (150°≤ ϵ≤ 195°)	C3′-*endo* C2′-*endo*	g^+g^+ (50°≤ β, γ≤ 90°)	Structure not possible	Structure not possible

The alphabetical nomenclature of the torsion angles are adopted from Seeman *et al.*[14]. The molecular models were generated using modified LALS method wherein flexibility in the furanose ring was incorporated.

helices, the helical twist and the vertical displacement between successive phosphate groups are approximately the same. In the *zig-zag* helices the phosphate groups go around the helix axis in a non-uniform (*zig-zag*) fashion. In what follows, we describe the conformational features of the *uniform* and the *zig-zag* helices. We also show that one can join alternate right and left handed segments of the *uniform* helix to form a RL model of DNA, so also for the *zig-zag* helix. The common feature of these two kinds of RL models is that the left variety of both of them has either near-*syn* or pure *syn* conformation for all the purine bases.

The Uniform Helix

It is stereochemically possible to join two dinucleoside monophosphates with conformations in two helical domains and the resulting trinucleoside diphosphate can be used as a repeating unit to generate *uniform* helices. For example, we could link up alternately (C3′-*endo*, g^-g^-) and (C2′-*endo*, tg^-) conformations to obtain both right and left helical duplexes for B-DNA. In such structures, all the purines are attached to sugars with C3′-*endo* sugar puckering while the pyrimidines are attached to sugars with C2′-*endo* puckering. For the right handed duplexes the bases (both purines and pyrimidines) are in *anti* conformation while for the left handed duplexes the purines are in near *syn* conformation (*see* Fig. 2*a*). Such right and left handed double helical segments (each 5 base-pairs in length) could be combined to arrive at a RL model of B-DNA. A space filling model so constructed is shown in Fig. 2*b*. In this model although the back-bone conformation is almost identical in the left and right helical segments, the purines in the right helical segment are in low *anti* conformations while in the left segment they are in the near-*syn* conformation.

The Zig-Zag Helix

Zig-zag helices were generated when two dinucleoside monophosphates, one with conformation in a helical domain and the other with conformation in a non-helical domain or both with conformations in the non-helical domains were joined. We have chosen (C3′-*endo*, g^+g^+) or (C2′-*endo*, g^+g^+) conformation as representative of a non-helical domain (domain IV in Fig. 1). g^+g^+ conformations were found in the single crystal structures of ApApA and UpA[12–13]. Therefore, the role of g^+g^+ conformation around P O bonds in a polynucleotide duplex was investigated in detail. For example, a tri-nucleoside diphosphate with (C3′-*endo*, g^-t-C2′-*endo*, g^+g^+-C3′-*endo*) conformation (*see* Fig. 3*a*) led to both right and left helical duplexes. For the left handed duplex all the purines are attached to sugars with C3′-*endo* puckering and have pure *syn* conformation. For the right handed duplex, although the purines are attached to sugars with C3′-*endo* puckering all of them have *anti* conformation. The dispositions

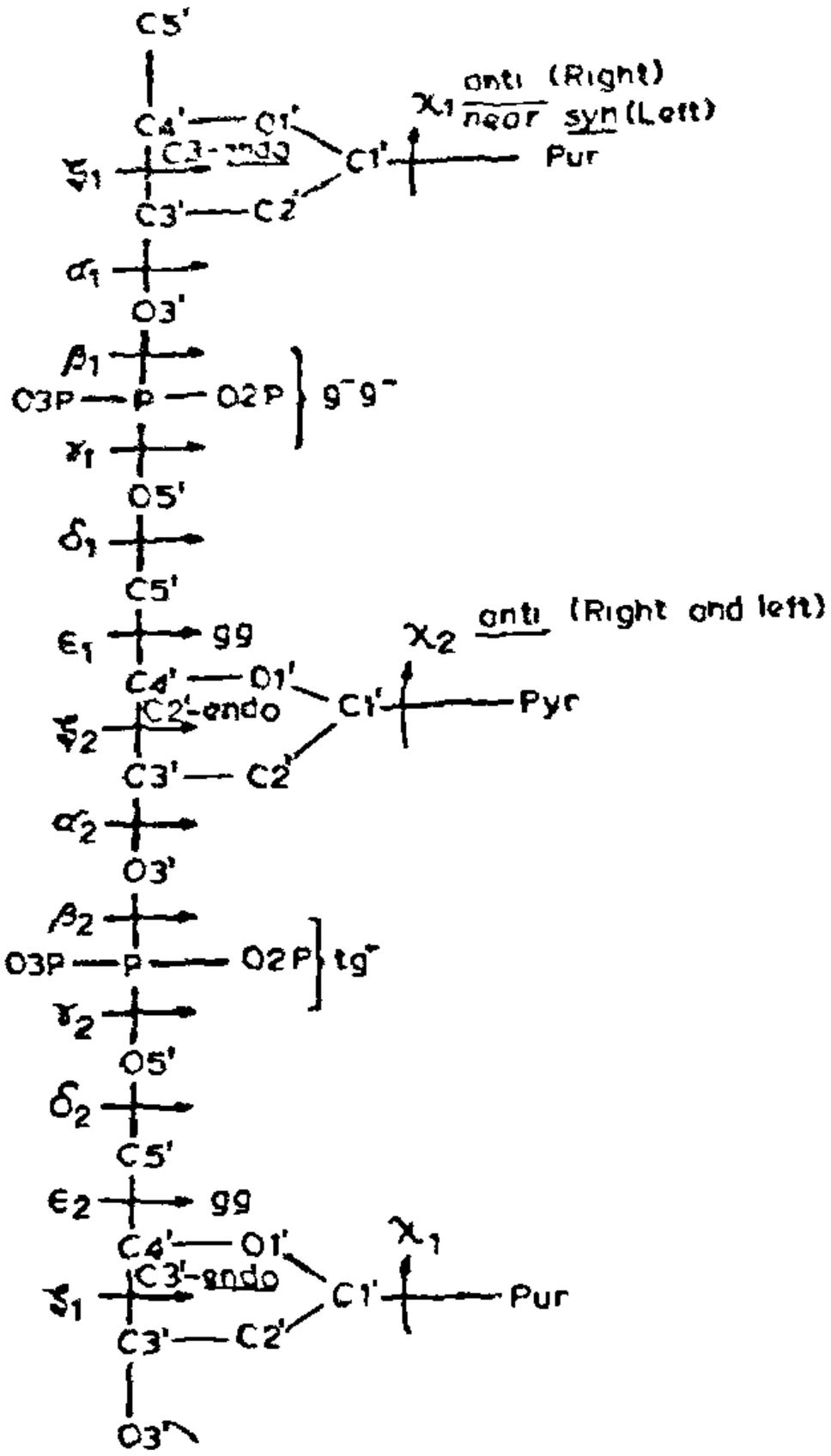


FIG. 2 *a*. Trinucleoside diphosphate as the repeating unit which leads to *uniform* helix. The glycosyl torsion regions are indicated for right and left handed duplexes.

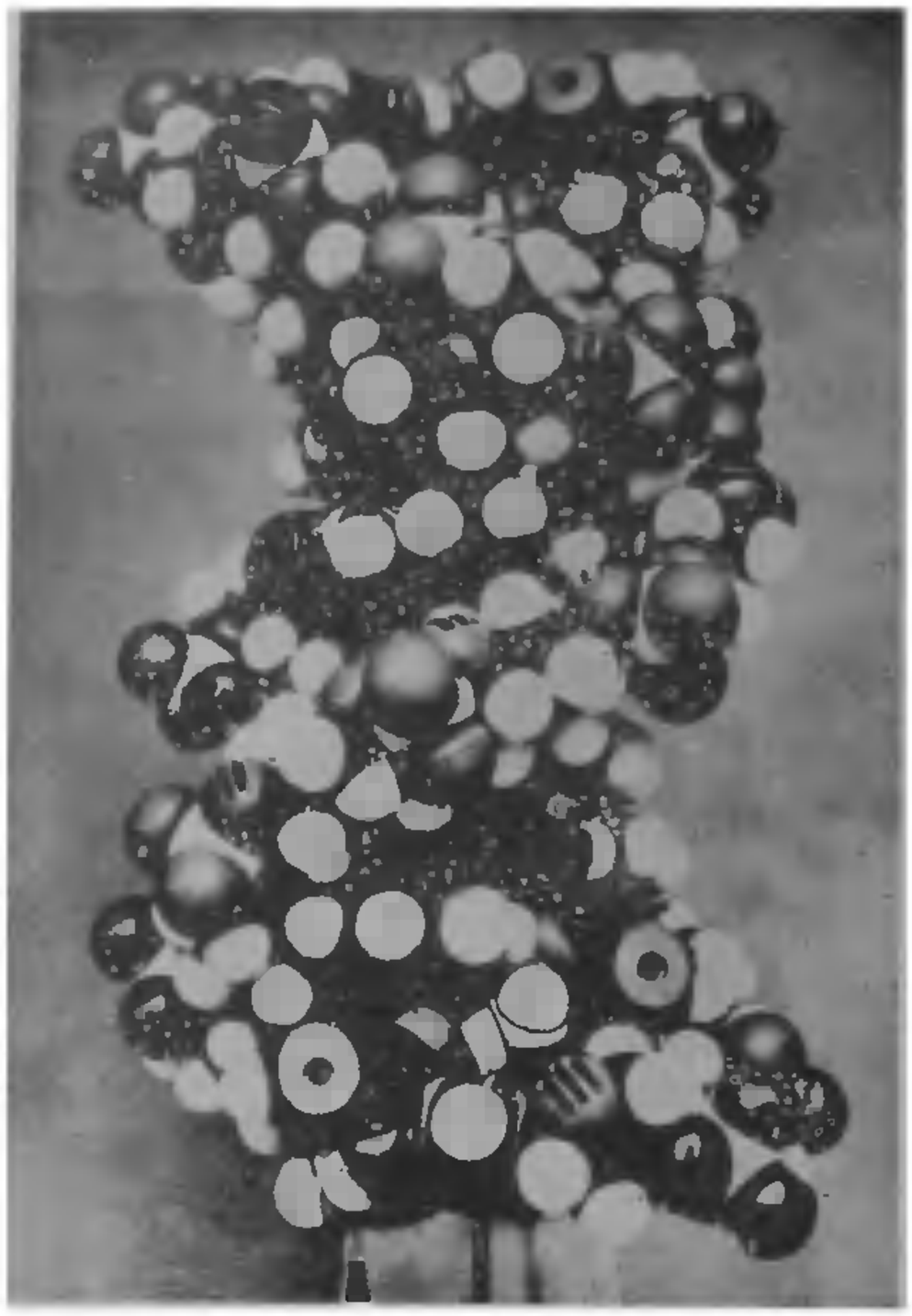


FIG. 2 *b*. Space-filling (CPK) model of a RL model obtained by joining alternately right and left helical segments of the *uniform* helix.

of the phosphate groups for such structures are schematically shown in Fig. 3 *b* and 3 *c*. It is seen that around each phosphate group, the two neighbouring ones are not symmetrically situated; one of them is horizontal while the other is vertically down. Such a left handed duplex can be joined smoothly with a right handed counterpart, within a repeat of 10 base-pairs of B-DNA. Such space filling model for B-DNA is shown in Fig. 4. Here all the purines in the left handed helical segments have pure *syn* conformations.

In a similar fashion, right handed and left handed duplexes with *zig-zag* progression of the phosphate groups were arrived at when the (C3′-*endo*, g^+g^+-C2′-*endo*, g^+g^+–C3′-*endo*) conformation for the trinucleoside diphosphate is adopted. For the right handed duplex, both the sugars have gt conformation about the bond C4′–C5′ (see Fig. 3) while the left handed duplex has gt conformation only for the C3′-*endo* sugar. The left handed *zig-zag* duplex so constructed has greater chain separation than the models with (C3′-*endo*, g^-t–C2′-*endo*, g^+g^+–C3′-*endo*) conformation. Here again all the purines in the left handed duplex have pure *syn* conformation, while in the right handed duplex they are all in *anti* conformation. However, in the case of the left handed duplex, adjacent sugars in the same chain point in opposite directions while the sugars attached to a given base pair point in the same direction. This is in striking contrast to right handed structures. The right and left helical segments, can be joined to obtain a *RL model of B-DNA*, a space filling representation of which is shown in Fig. 5. A left handed segment with either (C3′-*endo*, g^-t–C2′-*endo*, g^+g^+–C3′-*endo*) or (C3′-*endo*, g^+g^+–C2′-*endo*, g^+g^+–C2′-*endo*) conformation can easily be joined to any right handed segment generated from (C3′-*endo*, g^-g^-) or (C2′-*endo*, tg^-) conformation. In such an arrangement, the phosphate groups in the left handed segment have a zig-zag progression while those in the right handed segment are uniformly wrapped around the helix surface.

CONCLUSIONS

These studies clearly indicate that *syn* conformation of the bases is possible only for the left handed duplexes. In such cases, the purines will have only the *syn* conformation and the sugar attached to them should necessarily have C3′-*endo* and not C2′-*endo* puckering. As a result, if left stacking of the bases is preferred to

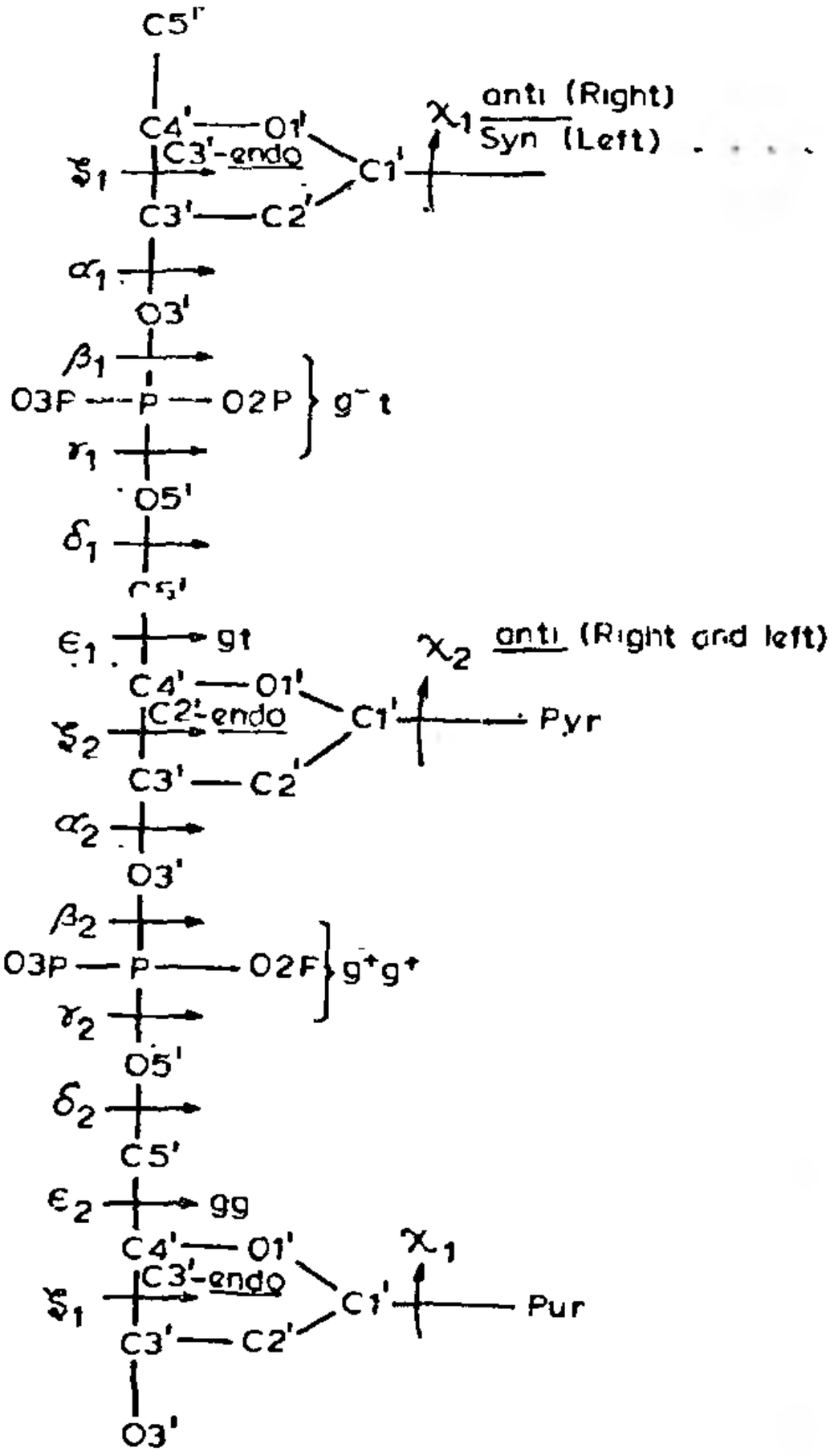
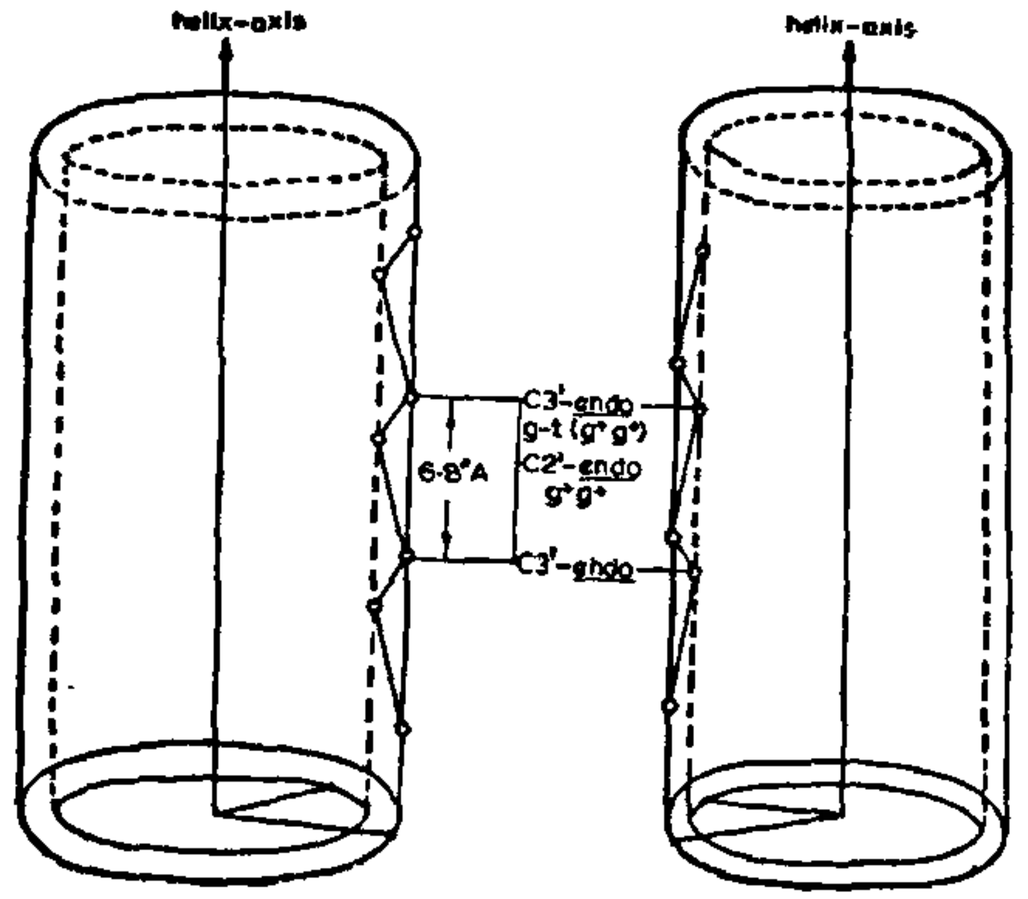


FIG. 3 *a*. Trinucleoside diphosphate which leads to a *zig-zag* helix.* The glycosyl torsion regions are indicated for right and left handed duplexes.

* It was noted that gt conformation around C4′–C5′ bond can be interchanged between sugar with C2′-*endo* puckering and the one with C3′-*endo* puckering. It was also found that (C3′-*endo*, g^-g^-–C2′-*endo*, g^+g^+–C3′-*endo*) and (C3′-*endo*, tg^-–C2′-*endo*, g^+g^+–C3′-*endo*) conformations led to similar *zig-zag* helices. Note that the phosphodiester conformation refers to the phosphate group attached to the 3′-end of the sugar.

right stacking in duplexes with alternate purine-pyrimidine sequences, the *syn* conformation for the purines becomes inevitable. After this work was completed, it has come to our notice that experiments by Wang *et al.*[15], bear out this prediction: In the $(dC\text{–}dG)_3$ crystal structure, internal G's are in *syn* conformation and sugars attached to them have C3′-*endo* puckering. The resulting structure, because of the reasons cited above, is a left handed *zig-zag* helix.

In all the RL models discussed above, the bases are turned over (or flipped over) each other at the



3 *b* 3 *c*

FIGS. 3 *b–c*. *b*. Schematic representation of a right handed *zig-zag* helix showing the progression of the phosphate groups. *c*. Schematic representation of a left handed *zig-zag* helix.

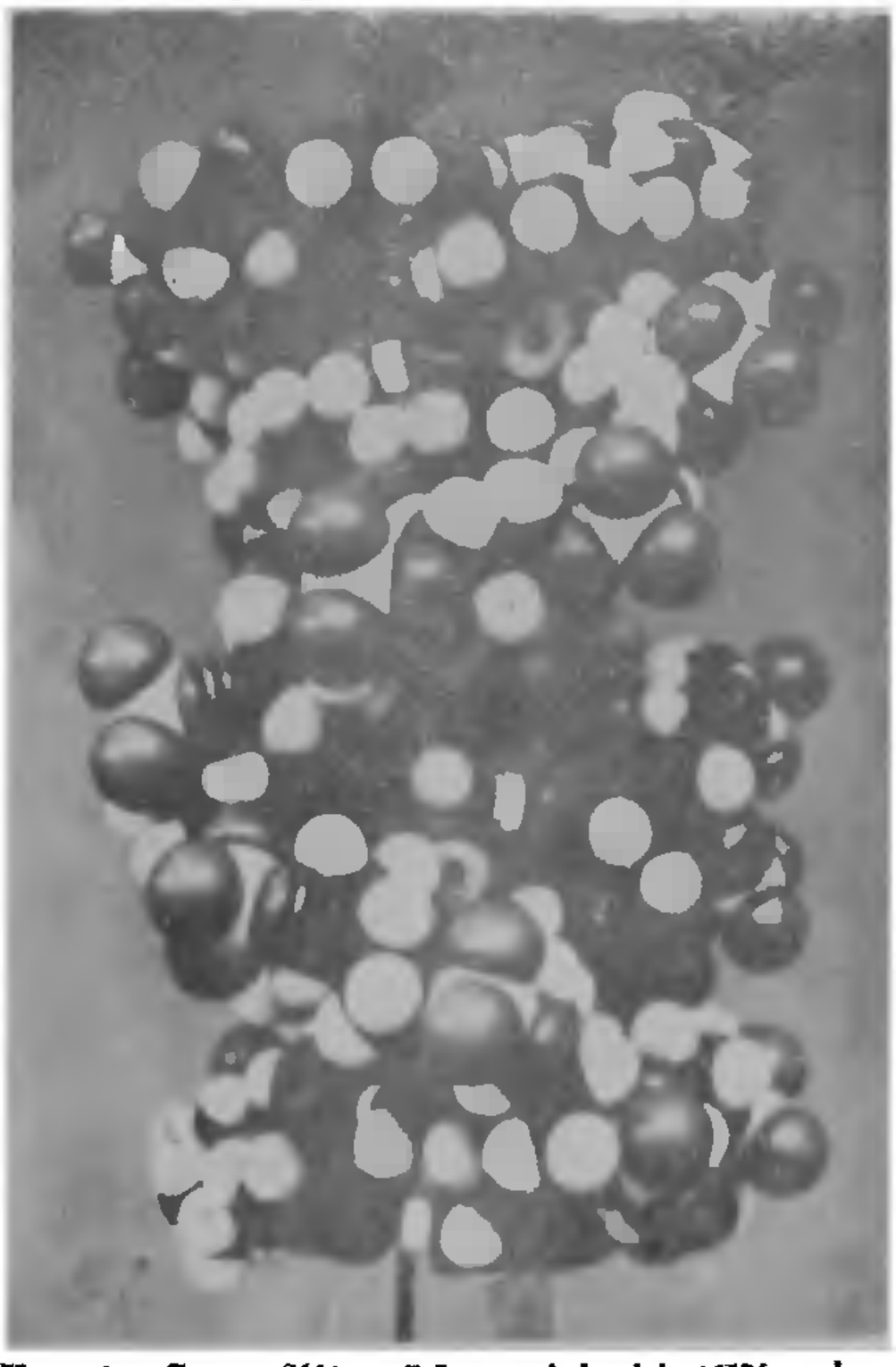


FIG. 4. Space-filling RL model with (C3′-*endo*, g^-t–C2′-*endo*, g^+g^+–C3′-*endo*) conformation.

bend region where the right and left helical segments join together. This inverted stacking arrangement, at the bend region, is a characteristic feature of the type II model published earlier[1–4]. The alternative

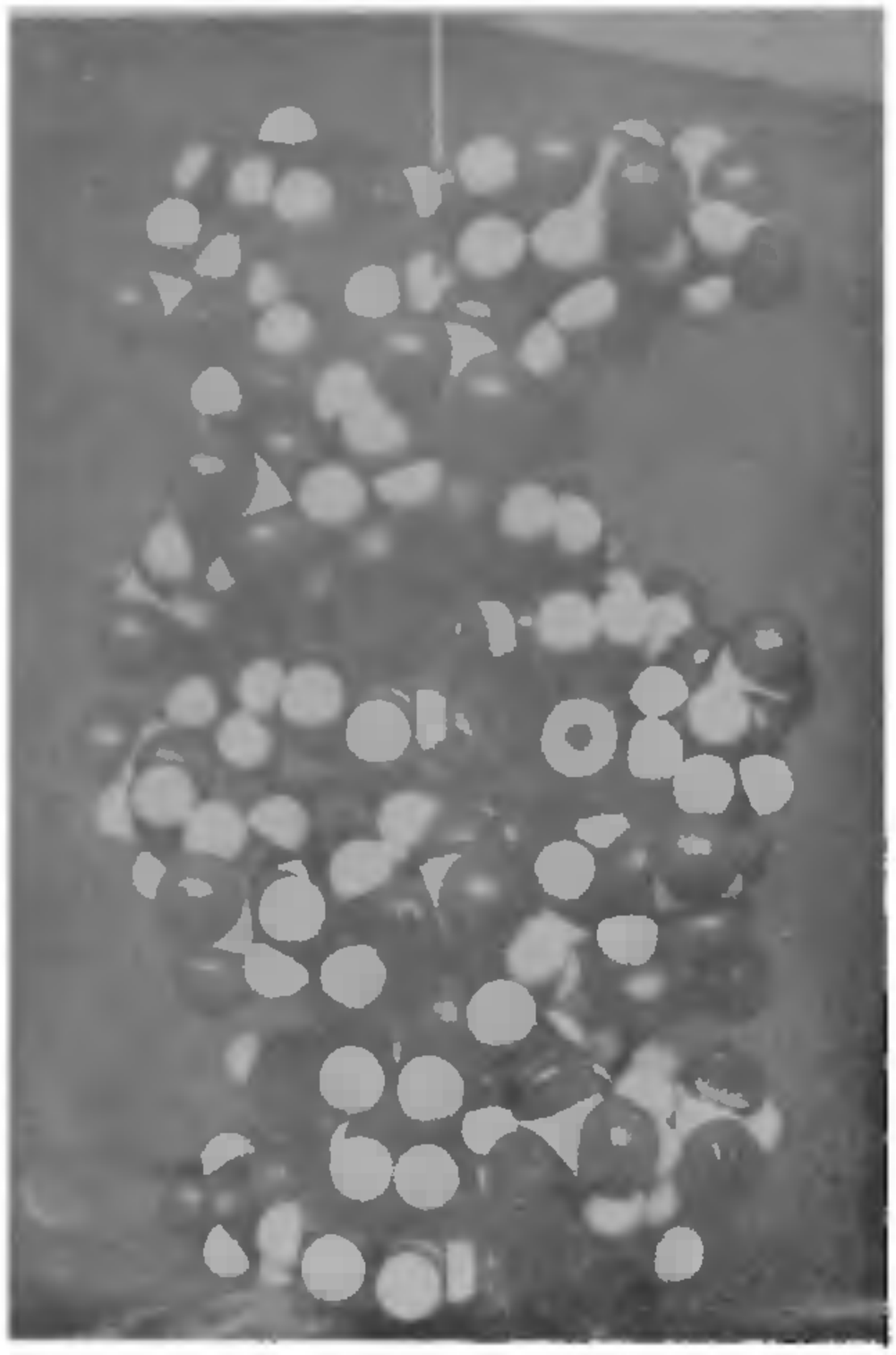


FIG. 5. Space-filling RL model with (C3′-*endo*, g^+g^+ C2′-*endo*, g^+g^+–C3′-*endo*) conformation.

models of DNA considered in this article are minor modifications of the type II structure. It is interesting to note that in the model of Wang *et al.*[15], a segment of left handed *zig-zag* DNA is combined with right handed B-DNA. The resulting structure is again a variant of the type II structure proposed by us[1–4]

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