Molecular structure of a double helix that has non-Watson–Crick type base pairing formed by 2-substituted poly(A) and poly(U)

(x-ray diffraction/nucleic acid/alternative complementarity/molecular evolution/gene processing)

TOSHIO HAKOSHIMA, TOSHIKAZU FUKUI, MORIO IKEHARA, AND KEN-ICHI TOMITA

Faculty of Pharmaceutical Sciences, Osaka University, Suita, Osaka 565, Japan

Communicated by Alexander Rich, August 5, 1981

ABSTRACT X-ray fiber diffraction studies of duplexes formed by 2-substituted poly(A) and poly(U) provide evidence for the existence of a double helical structure of poly(A)·poly(U) held together by Hoogsteen-type base pairing with parallel chain polarity.

A variety of observations on duplex structures of polynucleotides have been interpreted by the single base-pairing scheme proposed by Watson and Crick (1) in 1953, and many biological phenomena are analyzed in the context of the molecular structure of the double helix. The precise manner by which guanine pairs with cytosine has been established by numerous experiments, but it is not always clear exactly how adenine pairs with uracil or thymine. Actually, base-pairing schemes other than the Watson–Crick type (Fig. 1 *b–d*) have been observed in cocrystals of adenine and uracil or thymine derivatives (2) and in tRNA crystals (3, 4). There is renewed interest in the possibility that polynucleotides may form a complementary double-stranded structure that has non-Watson–Crick pairing. Indeed, it is not clear whether other base-pairing schemes are incapable of existence in a double-stranded structure or whether they exist but are separated from the most stable one by relatively large differences in energy.

Recently, it has been argued from spectroscopic experiments that a poly(A)·poly(U) duplex having non-Watson–Crick base pairs could be formed by introducing a substituent [e.g., methyl (5), methylthio (6), ethylthio (6), or dimethylamino (7)] group into the C(2) position (Fig. 1) of the poly(A) to control the geometry of the base pairing by sterically blocking one side of the adenine ring [i.e., the N(1) side, which is used in the Watson–Crick and the reverse Watson–Crick pairings (Fig. 1 *a* and *b*)]. UV absorption, circular dichroism, and infrared absorption spectra of the duplexes of these chemically modified poly(A)·poly(U)s have been examined, but little is known about the actual base-pairing fashions and the secondary structures.

Here, we report x-ray fiber diffraction studies on the sodium salts of the double helices formed by poly(2-methylthioadenylic acid) [poly(ms²A)] and poly(U) [poly(ms²A)·poly(U)] and poly(2-methyladenylic acid) [poly(m²A)] and poly(U) [poly(m²A)·poly(U)]. We have obtained the similar diffraction patterns shown in Fig. 2 *Upper* and *Lower* for the two duplexes and have developed molecular models corresponding closely to the observed diffraction. It is shown that, in these duplexes, the two sugar-phosphate backbones are running in the same direction and held together by Hoogsteen-type hydrogen bonds between the 2-substituted adenine and the uracil bases (Fig. 1*c*) in a manner similar to that of the double-helical portion having non-Watson–Crick base pairing of the triple-stranded helix, poly(U)·poly(A)·poly(U) (9).

MATERIALS AND METHODS

The synthesis and physicochemical properties of poly(m²A) and poly(ms²A) have been described (5, 6). Fibers were drawn from a sticky pellet made by dissolving ≈0.1 mg of the polymer in 20 μl of 0.01 M NaCl and allowing the solution to dry in a closed dish containing saturated KNO₃ (96% relative humidity) for several hours at 4°C. All diffraction diagrams were obtained with nickel-filtered CuKα radiation using a flat-film microcamera in which the temperature was kept at 0–2°C by a cooling apparatus and the relative humidity was controlled at ≈88% by helium gas constantly flushed through saturated KCl. The specimen-to-film distances were ≈30 mm and were calibrated by reference to the spacings of NaCl powder reflexions.

Molecular models were built by using the Kendrew wire model (a scale of 5 cm = 0.1 nm), and the validity of these models was tested by comparing the cylindrical average of the squared Fourier transforms from their coordinates with the observed intensities. Scattering from water molecules in the fiber was allowed by modifying the scattering factors of all atoms of the model as suggested by Langridge *et al.* (10). All calculations were carried out on an ACOS series NEAC ACOS-700 computer at the Crystallographic Research Center, Institute for Protein Research, Osaka University.

RESULTS

Diffraction Patterns. As shown in Fig. 2, the most ordered forms of the fibers are not fully crystalline and give the mixtures of Bragg reflexions and continuous diffraction. The pattern of poly(ms²A)·poly(U) is characterized by three intense meridional arcs having Bragg spacings of 0.314, 0.345, and 0.373 nm; two off-meridional arcs, a medium one at 0.44 nm and a medium strong one at 0.59 nm; and a strong maximum on the first layer line with an axial spacing of 3.16 nm, which is obtained from the mean ℓ of 10 Bragg reflexions on the first three layer lines. In the pattern of poly(m²A)·poly(U), the corresponding reflexions and arcs are three meridional arcs at Bragg spacings of 0.310, 0.340, and 0.370 nm; two off-meridional arcs at 0.44 and 0.57 nm; and a strong maximum on the first layer line with an axial spacing of 3.11 nm.

The diffraction patterns of the two duplexes are strikingly similar. Indeed, the principal differences between them are the slight contraction of the spacings and somewhat more diffuse diffraction of poly(m²A)·poly(U). This broadening of diffraction by poly(m²A)·poly(U) may be due to the fact that its thermal stability is poorer than that of poly(ms²A)·poly(U) [compare their melting temperatures at 0.15 M NaCl of 21°C (5) and 31°C (6), respectively]. The remarkable correspondence in both the spacings and the distribution of intensity demonstrates that the secondary structures of the two duplexes are essentially similar.

FIG. 1. Base-pairing schemes for adenosine and uridine. (a) Watson-Crick type. (b) Reverse Watson-Crick type. (c) Hoogsteen type. (d) Reverse Hoogsteen type. The substituent R is as follows: H for adenosine and CH_3 or SCH_3 for 2-methyl- or 2-methylthioadenosine.

Both of the diffraction patterns, which are clearly those of helical molecules, are unusual when compared with those of any DNA (11, 12) or RNA (13, 14) double helices. A peculiar feature of the patterns is the absence of strong intensity close to the meridian on the second and third layer lines with the existence of very strong intensity on the first layer line. In contrast to this feature, the first maximum on the second layer line is the strongest among the first, second, and third layer lines in the diffraction patterns given by the A and B forms of DNA and the members of A RNA groups (14). Since this region of fiber diffraction is at a resolution of >0.7 nm, such characteristic distribution of intensity indicates that the fundamental framework of the helical structures must be quite different from those of DNA and RNA double helices studied so far.

FIG. 2. X-ray diffraction patterns of the sodium salts of poly(ms^2A)·poly(U) (Upper) and poly(m^2A)·poly(U) (Lower). When fibers of poly(m^2A)·poly(U) were made without additional salt or with addition of a few microliters of 0.01 M NaCl, their diffraction patterns were different from those shown in Lower and could not be interpreted by a single structural model (see ref. 8). From our results, which can deduce a single model from the well-defined diffraction patterns given by both complexes, we conclude that, at low salt concentration, disproportionation between single- and double-stranded molecules might occur to give a mixed diffraction pattern.

To allow meridional reflexion on the 10th–12th layer lines, fibers were photographed at different angles away from normal to the x-ray beam: three intense meridional arcs on the 8th, 9th, and 10th layer lines (see Fig. 2) and extremely weak arcs, like a kind of discontinuous background, assignable to the 11th and 12th layer lines were recorded. Among them, the only spot splitting detected with certainty is that on the 8th layer line.

Helical Parameters and Lattice Parameters. In general, the layer line upon which the first meridional reflection occurs is used to define the residue repeat number of the helix. However, this is not well-delimited in the current poly(ms^2A)·poly(U) and poly(m^2A)·poly(U) patterns, very likely because the upper layer lines are so diffuse. On the basis of the following arguments, it seems reasonable to assign the strong arc on the 10th layer line to the true meridional reflection. This implies a 10-fold helix with an axial rise per residue of 0.316 nm for poly(ms^2A)·poly(U) and of 0.311 nm for poly(m^2A)·poly(U).

In the diffraction patterns of helical polynucleotides, axial spacings of intense near-meridional diffraction are related to the tilt angle of the nucleotide bases: on the lower layer lines, intense near-meridional diffraction appears the more the bases tilt—for example (14), it appears at spacings of 0.400 nm for A'-RNA (a base tilt of 10°), of 0.441 nm for A-RNA (16°), and 0.470 nm for A-DNA (20°). This relationship is so quantitative that it might be possible to estimate an appropriate value for the base tilt without model building. Therefore, the three intense meridional arcs at axial spacings of 0.316–0.395 nm for poly(ms^2A)·poly(U) and 0.311–0.389 nm for poly(m^2A)·poly(U) suggest that the bases are not perpendicular to the helix axes nor tipped at angles $>10^\circ$. The axial rises per turn of 0.316 and 0.311 nm would actually cause a base tilt of 10° .

Additional support for the 10-fold helical symmetry hypothesis was obtained from the tentative unit cell dimensions. For example, poly(ms^2A)·poly(U) is a monoclinic lattice with $a = 2.26$ (4) nm, $b = 2.63$ (4) nm, $c = 3.16$ (1) nm (fiber axis), and $\gamma = 108$ (2°). In the unit cell, one duplex could be packed and the possible space group is $\text{P}2_1$ only. This would require the helix to have an even number of residue repeats and, therefore, 10-fold helical symmetry is compatible. In addition, γ is close to an integral multiple of 36° . Thus this may be a case in which the molecular symmetry is reflected in the crystal packing arrangement.

Although the number of nucleotide pairs per turn could not be established with certainty, the allowed variation of helix twist is small enough to derive the fundamental secondary structure of these duplexes and, in this sense, the conformation of the molecules could be fairly well defined. Therefore, we focused our analysis on a 10-fold helix.

Model Building. The four possible base-pairing schemes having two hydrogen bonds between the bases shown in Fig. 1 were examined. The geometry of the base pairs was derived from the results of single-crystal analyses (15–18) and the sugar conformation was assumed to be a standard C(3')-endo pucker (19) but some modifications were allowed if necessary.

The reverse Watson–Crick pair (Fig. 1*b*) was ruled out *a priori* because this pair has no stereochemical advantage over the Watson–Crick pair (Fig. 1*a*). Both pairs have the identical short contact between the substituent at the C(2) position of adenine and a keto [O(2) for the Watson–Crick and O(4) for the reverse Watson–Crick] oxygen atom of uracil. The lengthening required for relaxing the short contacts to the extent of the sum of their van der Waals radii is 0.06 nm for the Watson–Crick and 0.08 nm for the reverse Watson–Crick.

In the Hoogsteen and reverse Hoogsteen pairs (Fig. 1*c* and *d*), the substituent on adenine ring is placed on the opposite side of the hydrogen bonding [N(6) and N(7)] atoms and, therefore, has no direct steric effect on the geometry of the base pairs.

Calculated Fourier Transforms. Because poly(ms²A)·poly(U) and poly(m²A)·poly(U) give almost identical diffraction patterns, one of the principal arguments for the detailed molecular models was provided by poly(ms²A)·poly(U).

The best model was obtained with the Hoogsteen pair. Comparison of the calculated and observed intensities showed a satisfactory correspondence, with the closest agreement being in the low angle region in which the characteristic intensity distribution described above was observed (Fig. 3). The interpre-

tation of the intensity distribution on the first, second, and third layer lines clearly agrees with the stereochemical consequences of the model, in which the two sugar-phosphate backbones run in the same direction, on the basis of the following consideration.

If there are $2N$ atoms in the repeating unit of a helical molecule that has a pitch length of c , the cylindrical average of the squared Fourier transform can be written (20) as

$$\langle FF^* \rangle_\psi = \sum_n G_{nl2N} G_{nl2N}^*, \quad [1]$$

where

$$G_{nl2N} = \sum_j f_j J_n(2\pi r_j \xi) \exp i(-n\phi_j + 2\pi l z_j / c) \quad [2]$$

and f_j and r_j , ϕ_j , z_j are the atomic scattering factor and the cylindrical polar coordinates of the j th atom, respectively. J_n is a Bessel function of the first kind of order n , and ξ , ψ , l/c are the cylindrical polar coordinates on the l th layer line in reciprocal space. If we assume that one chain is related to the other by a rotation of α around the helix axis, this relationship allows us to derive from Eq. 2 that

$$G_{nl2N} = G_{nlN} [1 + \exp(in\alpha)], \quad [3]$$

and then Eq. 1 can be rewritten as

$$\langle FF^* \rangle_\psi = 2 \sum_n G_{nlN} G_{nlN}^* [1 + \cos(n\alpha)]. \quad [4]$$

This equation means that, if $\alpha = 90^\circ$, the amplitude contribution from Bessel functions of order $n = 2, 6, \dots$ is zero. Exactly speaking, the double helix that has the Hoogsteen pair and the sugar-phosphate backbones running in the same direction possesses no symmetrical relationship between the two glycosidic bonds and, therefore, the two backbones are nonequiva-

FIG. 3. Observed and calculated intensities for poly(ms²A)·poly(U). (a) The best model (see Fig. 4) has Hoogsteen-type base pairing and parallel chains. (b) Excluded models: Watson–Crick (---) and Hoogsteen (····) type base pairing and antiparallel chains. (c) Models that have Hoogsteen-type base pairing and parallel chains but alternative helical symmetries: ---, 11-fold; ···, 9-fold. Observed intensities: vw, very weak; w, weak; m, medium; s, strong; vs, very strong.

lent. Nevertheless, it is fair that the backbones are related to each other by a pseudo-rotation around the helix axis to such an extent that Eq. 4 is virtually applicable to the backbones. The best model for poly(ms²A)·poly(U) shown in Fig. 4 has $\alpha = 74^\circ$, the angle between the two C(1') atoms of the base-paired nucleotides. This value is adequate to cause the absence of the first maxima on the second layer line and, in part, on the third layer line.

The remaining possibilities of alternative models are even less plausible because antiparallel backbones in both the Watson–Crick and Hoogsteen pairs would give calculated intensities that are too strong on the second and third layer lines (Fig. 3b) and in the reverse Hoogsteen pair both parallel and antiparallel backbones would have radii too small to reconcile the calculated intensities with those observed on the equator. It is clear that, in the reverse Hoogsteen pair, parallel backbones are incompatible with the observed diffraction because they imply a dyad axis coincident to the helix axis and would require odd layer lines to be absent.

In the Hoogsteen pair with parallel backbones, the possibility of residue repeats other than 10 were examined by comparing the calculated and observed intensities (Fig. 3c). As described above, models with 9-, 11-, and 12-fold helical symmetry are less satisfactory than the 10-fold model on the 7th–12th layer lines.

FIG. 4. Projection of part of poly(ms²A)·poly(U) structure. (a) Down the helix axis; (b) perpendicular to it. Deviations of bond distances and angles from observed values (ref. 18) are <0.004 nm and 4° , respectively. The helix axis is represented by a cross in a and a line in b. —, Hydrogen bond. The distances O(4)–N(6) and N(3)–N(7) are 0.305 and 0.293 nm, respectively. The bases are tipped to the horizontal by 13° for poly(ms²A) and 10° for poly(U). ..., Unfavorable contacts between the two backbones.

DISCUSSION

Molecular Structure. As shown in Fig. 4, poly(ms²A)·poly(U) has a double helical structure that is characterized by parallel backbones held together by Hoogsteen-type hydrogen bonding. Like the Watson–Crick pair, the glycosidic bonds protrude from one side of the base pair, although the interglycosidic distance, 0.863 nm, is smaller than that of the Watson–Crick pair, 1.05 nm (18). The Watson–Crick pair has a dyad axis on the base-pair plane relating the two glycosidic bonds and, with them, the attached sugar–phosphate backbones of the complexed nucleotides (10, 12, 21): the angle between the glycosidic bond and a line passing through the two C(1') atoms of the base-paired nucleotides is the same for the two glycosidic bonds, 52° . However, no such an axis is present in the Hoogsteen pair: the glycosidic bonds with the sugar–phosphate backbones are not equivalent to each other. For the best model of poly(ms²A)·poly(U), the angles are 51° for the glycosidic bond of poly(ms²A) and 57° for that of poly(U).

Each chain of poly(ms²A)·poly(U) has a similar, but not identical, conformation that can belong to the A family of nucleotide structure (14). For quantitative comparison, the torsion angles of the best model are presented in Table 1, together with the corresponding values obtained for the related polynucleotides. In terms of the pseudorotation phase angle P (19), the puckering of the final model is C(3')-endo ($P = 23^\circ$ and $\tau_m = 38^\circ$) for poly(ms²A) and C(3')-endo-C(2')-exo ($P = 5^\circ$ and $\tau_m = 30^\circ$) for poly(U). The puckering of poly(U) is twisted and less puckered to relax the contact between the O(2) and O(1) atoms (see Fig. 4) by changing the orientation of the uracil base relative to the phosphate oxygen atom. In any case, both are members of the C(3')-endo type pucker ($0^\circ < P < 36^\circ$) and no model of C(2')-endo type pucker could be found for this helix.

Not only are the backbone conformations similar to the A conformation, but the pattern of base stacking (Fig. 4a) also is similar to those of poly(A)·poly(U) (22) and poly(U)·poly(A)·poly(U) (9). Further, the radius of the poly(ms²A)·poly(U) helix is similar to that of poly(U)·poly(A)·poly(U). The atoms C(1') and P in the non-Watson–Crick pair of the triplex are located on radii of

Table 1. Comparison of torsion angles observed in poly(ms²A)·poly(U) and the related polynucleotides

Chain	Angle, * degrees							Ref.
	ω	ϕ	ψ	ψ'	ϕ'	ω'	χ	
Poly(ms ² A)	-102	153	100	79	-132	-72	4	
Poly(U)	-93	-177	76	85	-149	-72	8	
A-RNA	-62	180	48	83	-151	-74	15	22
A'-RNA	-65	-167	44	83	-168	-70	20	22
Poly(U) [†]	-59	-171	44	80	-165	-59	26	9
Poly(A)	-82	180	80	80	-154	-78	16	9
Poly(U)	-40	140	51	80	-124	-105	6	9
Poly(s ² U) [‡]	-37	156	41	81	-139	-94	26	23
Poly(s ² U)	-47	164	53	72	-141	-73	15	23
B-DNA	-46	-147	39	157	155	-96	83	24

* Angles are defined as $P-O(5')-C(5')-C(4')-C(3')-O(3')-P$ for the main chain, $O(4')-C(1')-N(9)-C(8)$ for the purine bases, and $O(4')-C(1')-N(1)-C(6)$ for the pyrimidine bases with zero at the *cis* position and positive clockwise rotation of the farther pair of atoms.

[†] Values are for the 11-fold model of poly(U)·poly(A)·poly(U) in ref. 9. The first poly(U) is the one involved in the Watson–Crick pair.

[‡] Values are for the poly(2-thiouridylic acid) duplex. The former is α -chain and the latter is β -chain; see ref. 23.

0.738 and 0.919 nm in the poly(A) chain and 0.793 and 0.875 nm in the poly(U) chain, respectively, compared with 0.697 and 0.934 nm in the poly(ms²A) chain and 0.779 and 0.844 nm in the poly(U) chain of this duplex, respectively.

It is surprising that the remarkable conservatism of nucleotide conformation (9, 25, 26) is observed in poly(ms²A)-poly(U), which has significant structural differences from all double helices of the Watson-Crick type—i.e., relatively short interglycosidic distances and nonequivalent and parallel sugar-phosphate backbones. It is noteworthy that the conservatism observed in poly(ms²A)-poly(U) was also seen in double helices with homo-pairing—i.e., poly(2-thiouridylic acid) (23) and poly(U)-spermine complex (27). In duplexes involving poly(ms²A)-poly(U) and other double helices of the Watson-Crick type, the glycosidic bonds protrude from one side of the base pairs. This feature may be essential for formation of a stable structure of polynucleotide helix; these base-pairing arrangements allow freedom of position of their helix axes so that the backbones can be in a stable conformation in which all of their torsion angles fall into the narrow ranges of the standard values (25). Note that the double helices of poly(A⁺) (28) and poly(C)-poly(C⁺) (29), both of which have glycosidic bonds protruding from opposite sides of the base pairs, exist only as inner salts. The molecules have negatively charged phosphate groups and protonated bases.

Relationship Between X-Ray Structure and Results of Spectroscopic Experiments. The sugar-phosphate backbones of poly(ms²A)-poly(U) are parallel and, consequently, closer together than the antiparallel backbones of double helices of the Watson-Crick type. Some of the stereochemically unfavorable contacts are found around the oxygen atom O(I) of the phosphate group of the poly(ms²A) chain (Fig. 4); 0.284 nm for the uracil O(2)...O(I) distance and 0.283 and 0.303 nm for the poly(U) ribose O(4')...O(I) and C(1')...O(I) distances, respectively. These contacts would force the torsion angles ω , ψ , and ϕ' of the poly(ms²A) chain to be rather near the eclipsed conformation (Table 1) and the sugar puckering of poly(U) chain to be twisted. These conformations and the contacts, especially between oxygen atoms, are probably responsible for the rather low thermal melting temperatures of these duplexes (5, 6). Furthermore, the fact that the thermal stability of poly(ms²A)-poly(U) is higher than that of poly(m²A)-poly(U) can be explained by the base stacking containing the interaction (see Fig. 4a) between the S atom at the C(2) position and the N(3) atom of the adjacent base in the poly(ms²A) chain. A similar sulfur-nitrogen interaction has been found in the poly(2-thiouridylic acid) duplex (23) and has been shown to have a stabilizing effect on the structure.

Because the methyl group in poly(m²A) has little effect on the π -electron system of the adenine ring, the fact that the circular dichroism spectrum of poly(m²A)-poly(U) closely resembles that of poly(A)-poly(U) suggests that the base arrangements of the two double helices may be similar. Since the diffraction pattern of poly(m²A)-poly(U) shows that the structure must be closely related to that of poly(ms²A)-poly(U), the similarity between the base stacking of poly(ms²A)-poly(U) and that of poly(A)-poly(U) (22) is compatible with the similarity of the circular dichroism spectra of poly(m²A)-poly(U) and poly(A)-poly(U).

A Better Understanding of the Molecular Biology and Physical Chemistry of Nucleic Acids. The present analysis suggests that poly(A) may interact with poly(U) to form a double helical structure constructed by complementary base pairs of the Hoogsteen type, although the existence of the structure has not

been observed and may be difficult to detect because of its poor thermal stability.

From the viewpoint of molecular design or molecular evolution, it is of interest that the 2-keto oxygen atom of the uracil base plays an important role in separating the alternative structure from the more stable one, although this oxygen atom does not participate in any hydrogen bonding interaction to form complementary base pairs of the Watson-Crick type and seems to have little biological importance.

Because the chain polarity is reverse to that of the double helix of the Watson-Crick type (antiparallel), there is no possibility that such a structure of poly(A)-poly(U) bears a part in transfer of genetic information in living systems. This may be responsible for the strong inhibitory effect of poly(ms²A) and poly(m²A) against oncogenic virus reverse transcriptase (6).

We are grateful to Prof. H. Tadokoro and Dr. Y. Chatani for the use of their computer programs. We also thank Prof. D. M. Blow and Dr. A. G. W. Leslie for their comments.

1. Watson, J. D. & Crick, F. H. C. (1953) *Nature (London)* **171**, 737-738.
2. Sobell, H. M. (1972) *Jerusalem Symp. Quantum Chem. Biochem.* **4**, 124-148.
3. Quigley, G. J. & Rich, A. (1976) *Science* **194**, 769-806.
4. Jack, A., Ladner, J. E. & Klug, A. (1976) *J. Mol. Biol.* **108**, 619-649.
5. Ikehara, M., Hattori, M. & Fukui, T. (1972) *Eur. J. Biochem.* **31**, 329-334.
6. Fukui, T. & Ikehara, M. (1979) *Biochim. Biophys. Acta* **562**, 527-533.
7. Ishikawa, F., Frazier, J., Howard, F. B. & Miles, H. T. (1972) *J. Mol. Biol.* **70**, 475-490.
8. Hakoshima, T. & Tomita, K. (1980) in *Biomolecular Structure, Conformation, Function and Evolution*, ed. Srinivasan, R. (Pergamon, Oxford), pp. 313-324.
9. Arnott, S. & Bond, P. J. (1973) *Nature (London) New Biol.* **244**, 99-101.
10. Langridge, R., Marvin, D. A., Seeds, W. E., Wilson, H. R., Hooper, C. W., Wilkins, M. H. F. & Hamilton, L. D. (1960) *J. Mol. Biol.* **2**, 38-64.
11. Langridge, R., Wilson, H. R., Hooper, C. W., Wilkins, M. H. F. & Hamilton, L. D. (1960) *J. Mol. Biol.* **2**, 19-37.
12. Fuller, W., Wilkins, M. H. F., Wilson, H. R., Hamilton, L. D. & Arnott, S. (1965) *J. Mol. Biol.* **12**, 60-80.
13. Fuller, W., Hutchinson, F., Spencer, M. & Wilkins, M. H. F. (1967) *J. Mol. Biol.* **27**, 507-524.
14. Arnott, S. (1970) *Prog. Biophys. Mol. Biol.* **21**, 267-319.
15. Hoogsteen, K. (1963) *Acta Crystallogr.* **16**, 907-916.
16. Katz, L., Tomita, K. & Rich, A. (1966) *Acta Crystallogr.* **21**, 754-764.
17. Sakore, T. D., Taval, S. S. & Sobell, H. M. (1969) *J. Mol. Biol.* **43**, 361-374.
18. Seeman, N. C., Rosenberg, J. M., Suddath, F. L., Kim, J. J. P. & Rich, A. (1976) *J. Mol. Biol.* **104**, 109-144.
19. Altona, C. & Sundaralingam, M. (1973) *J. Am. Chem. Soc.* **94**, 8205-8212.
20. Franklin, R. E. & Klug, A. (1955) *Acta Crystallogr.* **8**, 777-780.
21. Crick, F. H. C. & Watson, J. D. (1954) *Proc. R. Soc. London Ser. A* **223**, 80-96.
22. Arnott, S., Hukins, D. W. L., Dover, S. D., Fuller, W. & Hodgson, A. R. (1973) *J. Mol. Biol.* **81**, 107-122.
23. Mazumdar, S. K., Saenger, W. & Scheit, K. H. (1974) *J. Mol. Biol.* **85**, 213-229.
24. Arnott, S. & Hukins, D. W. L. (1973) *J. Mol. Biol.* **81**, 93-105.
25. Arnott, S. & Hukins, D. W. L. (1969) *Nature (London)* **224**, 886-888.
26. Sundaralingam, M. (1969) *Biopolymers* **7**, 821-860.
27. Zimmerman, S. B. (1976) *J. Mol. Biol.* **101**, 563-565.
28. Rich, A., Davies, D. R., Crick, F. H. C. & Watson, J. D. (1961) *J. Mol. Biol.* **3**, 71-86.
29. Langridge, R. & Rich, A. (1963) *Nature (London)* **198**, 725-728.