1953
LA STRUTTURA DEL DNA

AG 10 Novembre 2023
G. Montaudo

PROTEINE e ACIDI NUCLEICI

La struttura tridimensionale di queste macromolecole biologiche fu delucidata nel corso degli anni ’50.

Lo studio della struttura delle proteine era cominciato già nel 1935, allora si pensava che i geni fossero proteine, mentre per il DNA gli studi sistematici erano cominciati intorno al 1946.

Agli inizi degli anni ’50, Quattro Gruppi si dedicavano allo studio della struttura delle macromolecole biologiche.

PROTEINE :

1. **Pauling e Corey al Caltech di Pasadena**
2. **Bragg, Peruz, Kendrew, al Cavendish di Cambridge.**

ACIDI NUCLEICI:

3. **Wilkins e Franklin al King’s College di Londra**
4. **Crick, Watson, al Cavendish di Cambridge.**

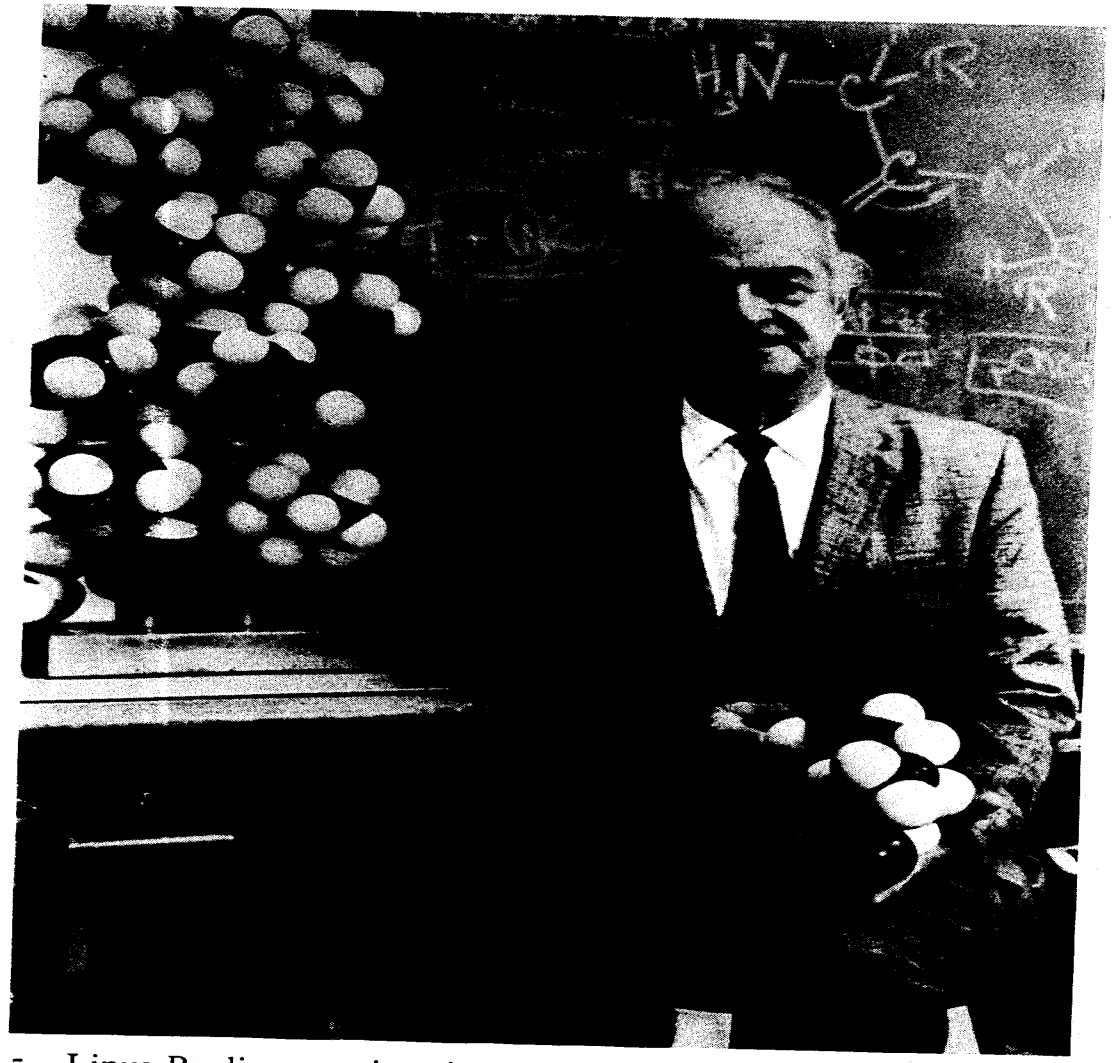
Nel 1951 fu risolta la struttura della CHERATINA
Nel 1953 fu risolta la struttura del DNA
Nel 1958 la struttura della MIO/EMO-GLOBINA

Struttura delle Proteine

1. **Toccò a Pauling di cogliere il primo successo, quando nel 1951 risolse la struttura delle proteine fibrose, proponendo la famosa α-elica.**

- **Egli aveva studiato per lungo tempo la struttura di piccoli peptidi, e risalì alla struttura delle proteine fibrose costruendo dei modelli molecolari molto accurati, basati sui dati di diffrazione ai raggi X dei peptidi.**

2. **Bragg, Peruz e Kendrew, al Cavendish di Cambridge, avevano tentato (1950) di risolvere lo stesso problema, ma la loro struttura risultò sbagliata.**



5 Linus Pauling con i suoi modelli di atomi.

P. NOBEL 1954

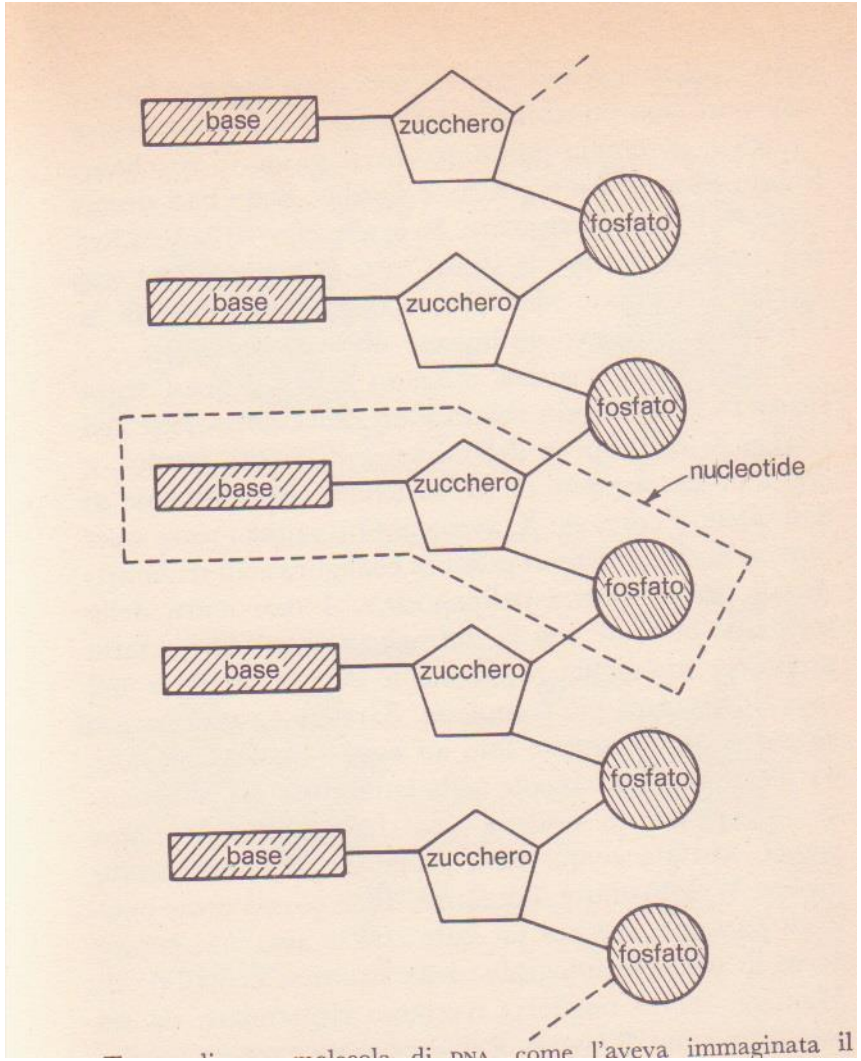
La scoperta di Linus Pauling della struttura ad alfa elica delle proteine fibrose (1950) segnò il primo grande progresso nel campo della struttura delle proteine, ma pose il quesito se anche che altre macromolecole biologiche potevano possedere una

STRUTTURA ELICOIDALE

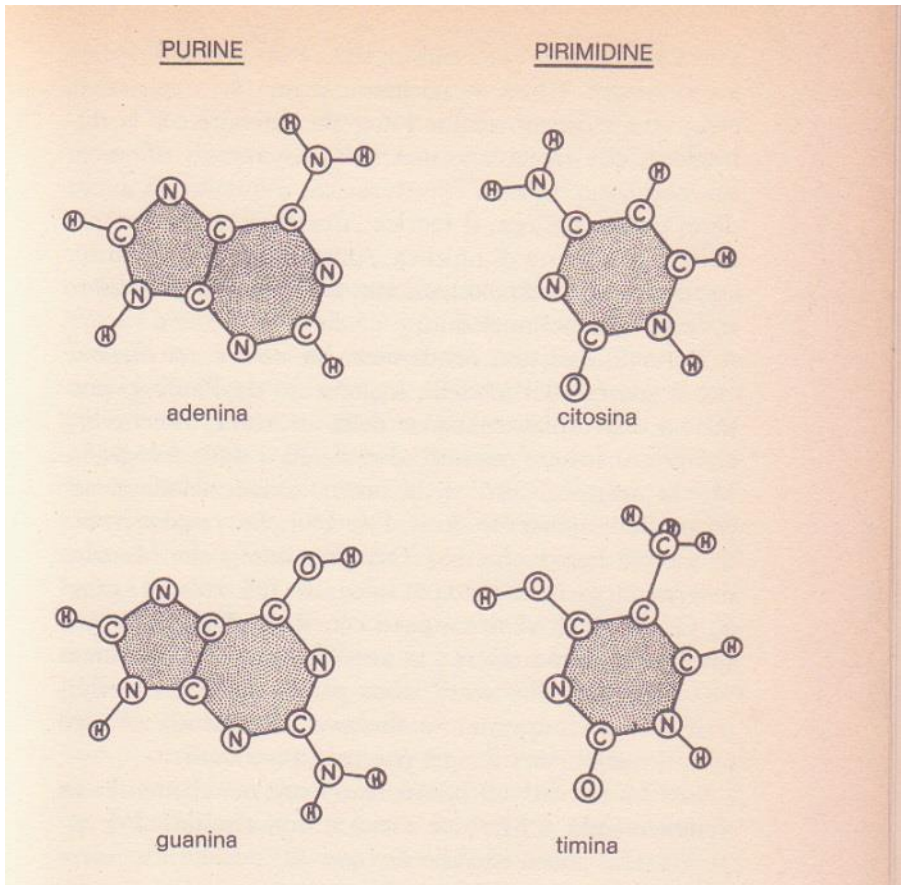
In generale, una struttura elicoidale possiede elementi di simmetria intrinseci (asse elicogiro), per cui può dare luogo a figure di diffrazione ai raggi X (spettri di fibra) che danno qualche indicazione (incompleta) sulla struttura della macromolecola.

Era quindi necessario ricorrere ai modelli molecolari.

Crick formulò per la prima volta (1951) la teoria matematica della trasformata ottica dell'elica discontinua (tramite la funzione di Bessel), e poté disporre di uno strumento teorico a priori che permette di prevedere il diffrattogramma corrispondente ad una qualsivoglia struttura elicoidale.



molecola di DNA come l'aveva immaginata il


PURINE
PIRIMIDINE
adenina
citosina
guanina
timina

STRUTTURA DEL DNA

ATSBURY (1947)
Ottenne spettri di diffrazione ai raggi X di fibre di DNA, dimostrando che questo ha una struttura regolare e ordinata, nonostante che le basi nucleiche siano puriniche e pirimidiniche.

Il DNA usato da ATSBURY non era puro ed i suoi spettri di fibra risultarono di bassa qualità.

Wilkins (1951) usò del DNA purissimo e ottenne diffrattogrammi migliori

Struttura del DNA

1. Wilkins al King's College di Londra ottiene (1951) i diffrattogrammi di fibra della forma A del DNA, che presenta ad un Convegno a Napoli.

Watson li vede e va a Cambridge per studiare la struttura del DNA.

2. Rosy Franklin (1952) ottiene i diffrattogrammi di fibra della forma B del DNA e conclude che lo Scheletro Zucchero-Fosfato sta all'esterno.

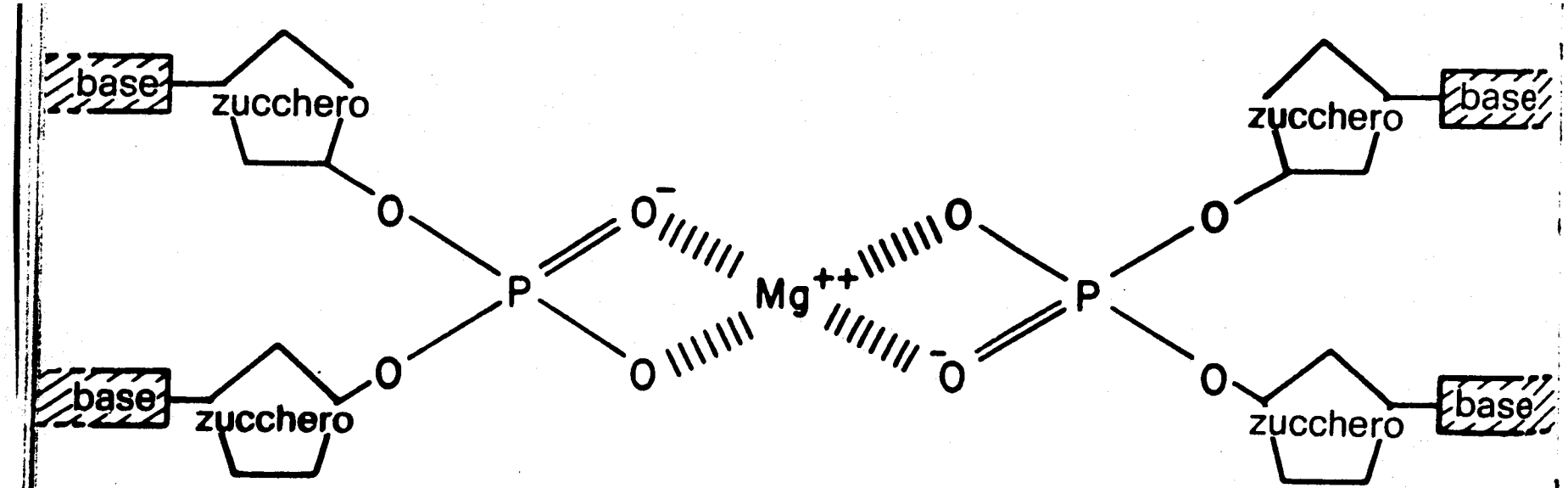
Dissidio fra Wilkins e Rosy Franklin

3. <u>Primo modello di Crick e Watson</u> (Natale 1951). Tripla elica, Scheletro Zucchero-Fosfato interno. Modello errato.

4. Secondo modello di Crick e Watson (Natale 1952).
Doppia elica, scheletro zucchero-fosfato esterno, basi in forma chetonica, accoppiamento A/T, G/C.

5. **Febbraio 1953** , Pauling pubblica sui PNAS il suo **modello per struttura tridimensionale del DNA.**
Il modello risulta errato:
Tripla Elica, Scheletro Zucchero-Fosfato interno.

Pauling utilizzò il suo metodo di costruire modelli molecolari, ma per confrontarli con i dati di diffrazione ai raggi X, si basò sui dati di Atsbury (1947), largamente insufficienti, mentre Watson e Crick poterono usare i dati della Franklin .



Così gli ioni Mg^{++} potrebbero legare gruppi fosforici carichi negativamente al centro di un'elica composta.

F. CRICK e J. WATSON (1953)

Propongono la struttura a Doppia Elica del DNA

Nel criticare (stupidamente) l'approccio dei modelli molecolari usato da W&C per scoprire la struttura del DNA, si dimentica che lo stesso tipo di approccio aveva portato Pauling a scoprire l'alfa elica delle proteine fibrose nel 1950.

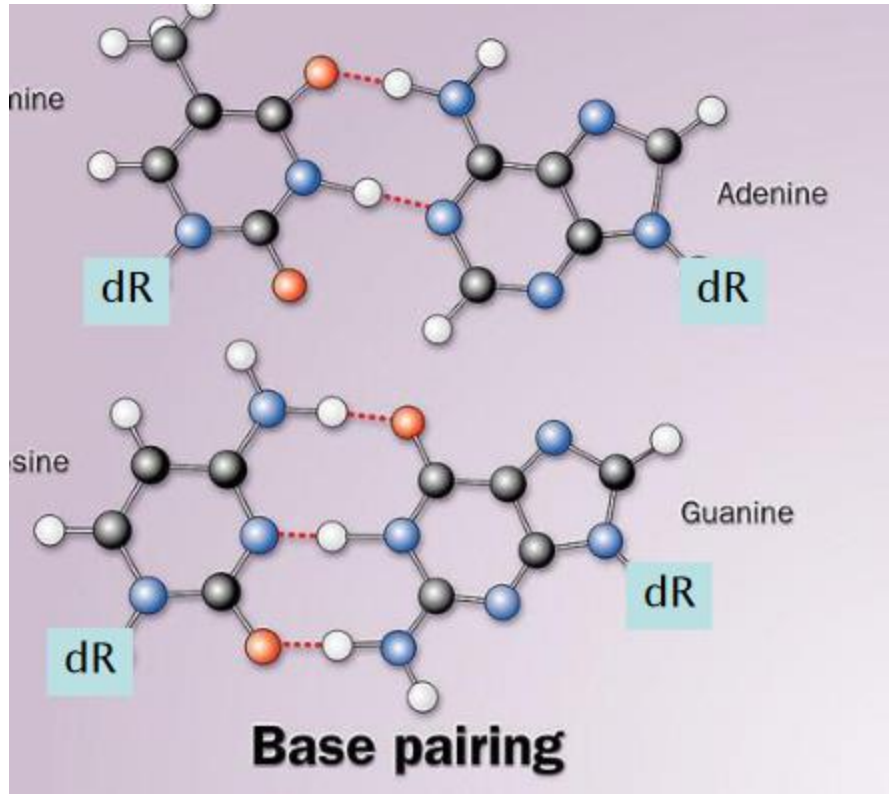
Inoltre, si dimentica che lo stesso Pauling lavorava ora coi modelli molecolari alla struttura del DNA, in concorrenza con W&C.

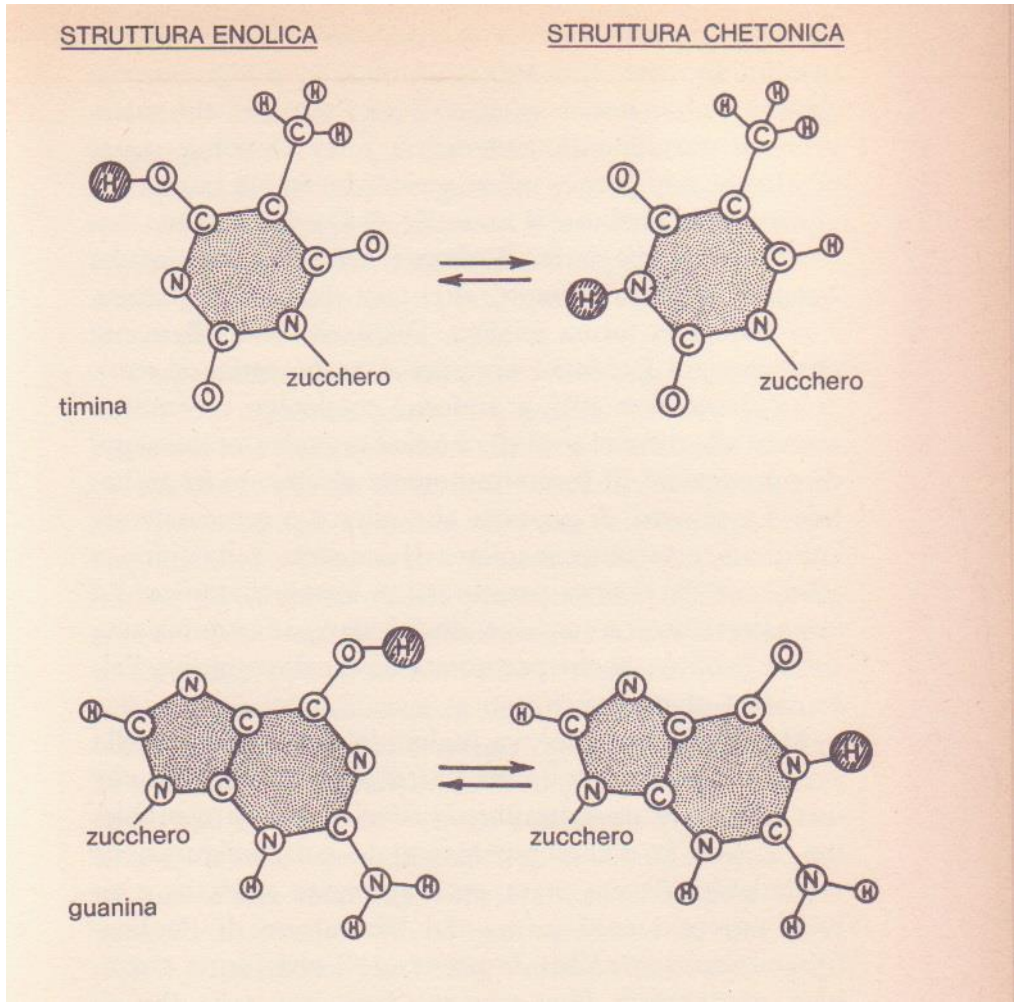
Infatti, Pauling basandosi sui modelli molecolari, propose nel 1952 una struttura a tripla elica del DNA, che risultò errata.

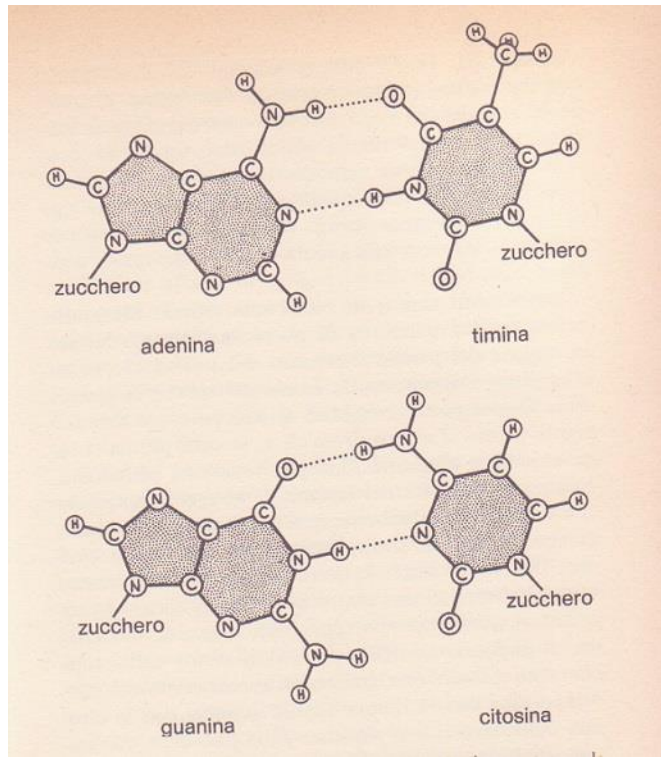
W&C, nell'Aprile del 1953, usando i modelli molecolari e i diffrattogrammi di Rosalind Franklin proposero la struttura vincente.

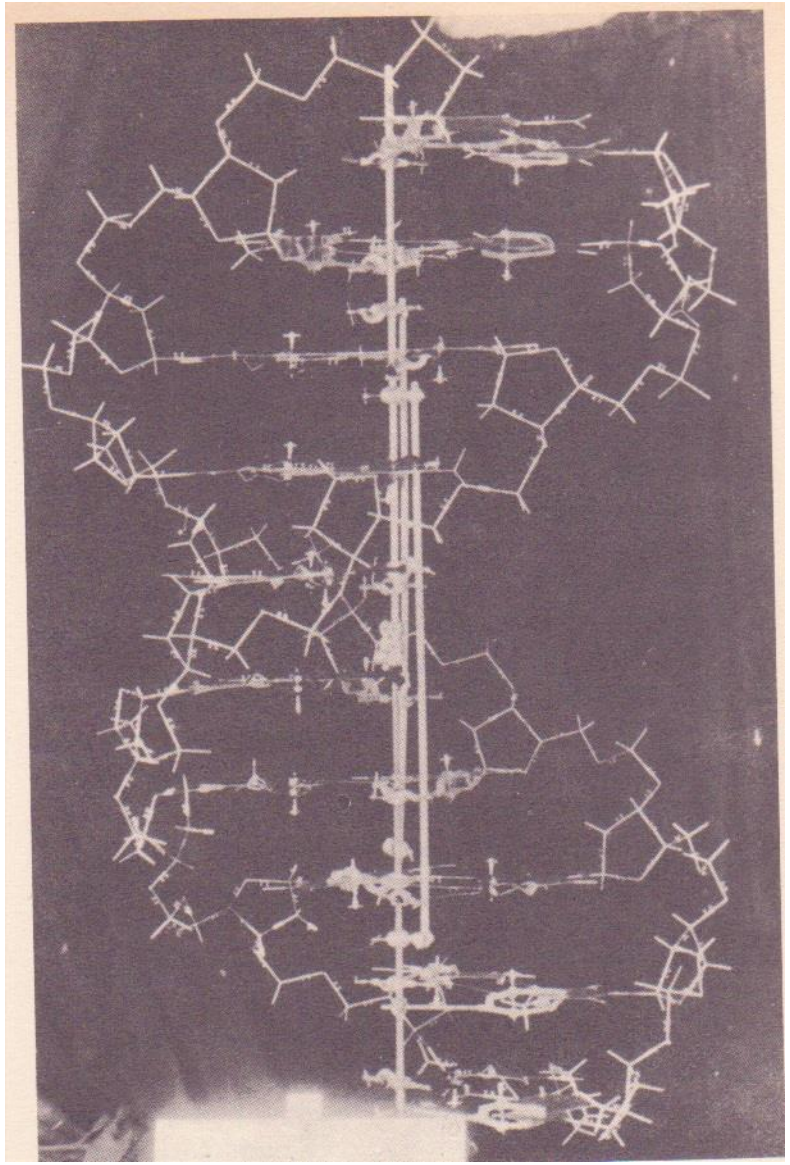
Tra i molti meriti del lavoro di W&C emergono:

l'avere formulato la corretta geometria per l'accoppiamento delle basi nucleiche (Watson)


nine
Adenine
dR
dR
sine
Guanine
dR
dR
Base pairing


STRUTTURA ENOLICA
STRUTTURA CHETONICA
zucchero
timina
zucchero
zucchero
guanina
zucchero


zucchero
zucchero
adenina
timina
zucchero
zucchero
guanina
citosina



Crick formulò per la prima volta (1951) la teoria matematica della trasformata ottica dell'elica discontinua (tramite la funzione di Bessel), e poté disporre di uno strumento teorico a priori che permette di prevedere il diffrattogramma corrispondente ad una qualsivoglia struttura elicoidale.

- **La funzione di Bessel si prestava molto bene a descrivere la trasformata ottica di un'elica discontinua.**

  Se una macromolecola biologica si presenta in forma cristallina elicoidale, si può approntare un modello molecolare a priori, immediatamente confrontabile con i dati di diffrazione di fibra ai raggi-X.

<u>Questa teoria fu poi applicata alla elaborazione del modello della doppia elica.</u>

Questo strumento teorico, nelle mani di Crick e Watson, si rivelò essenziale per la definizione della struttura del DNA.

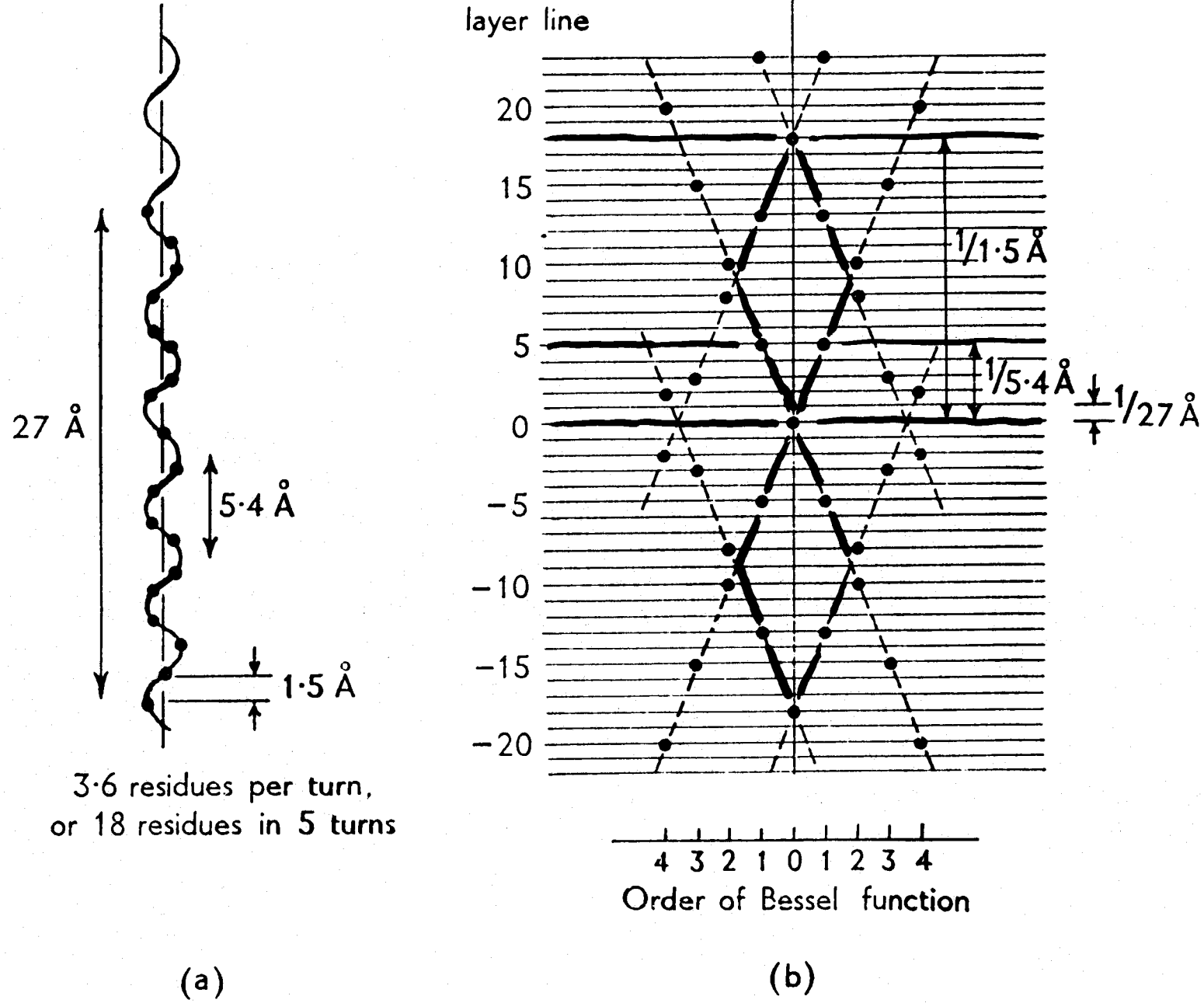
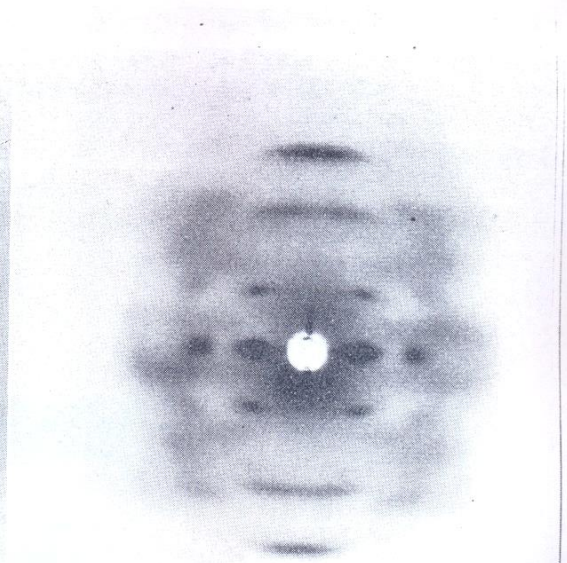
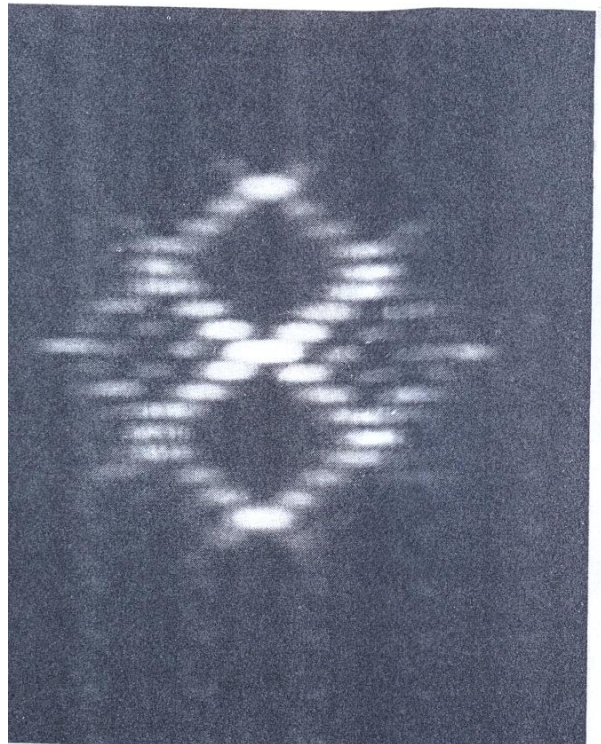
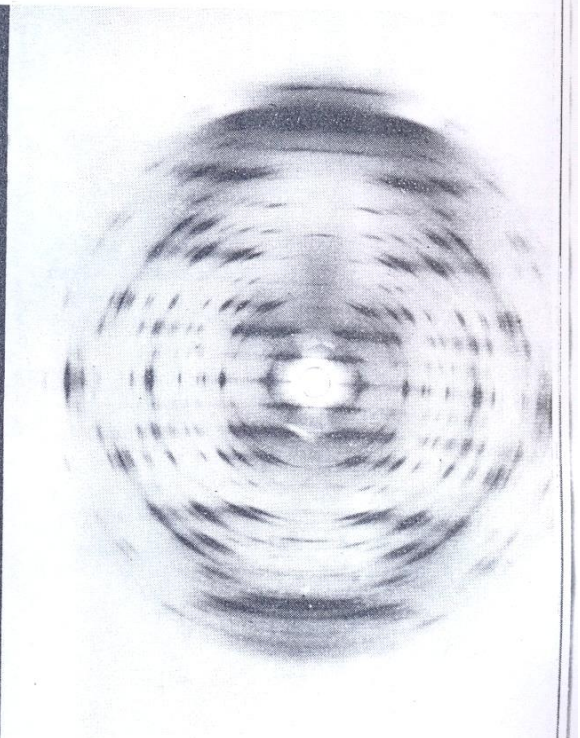
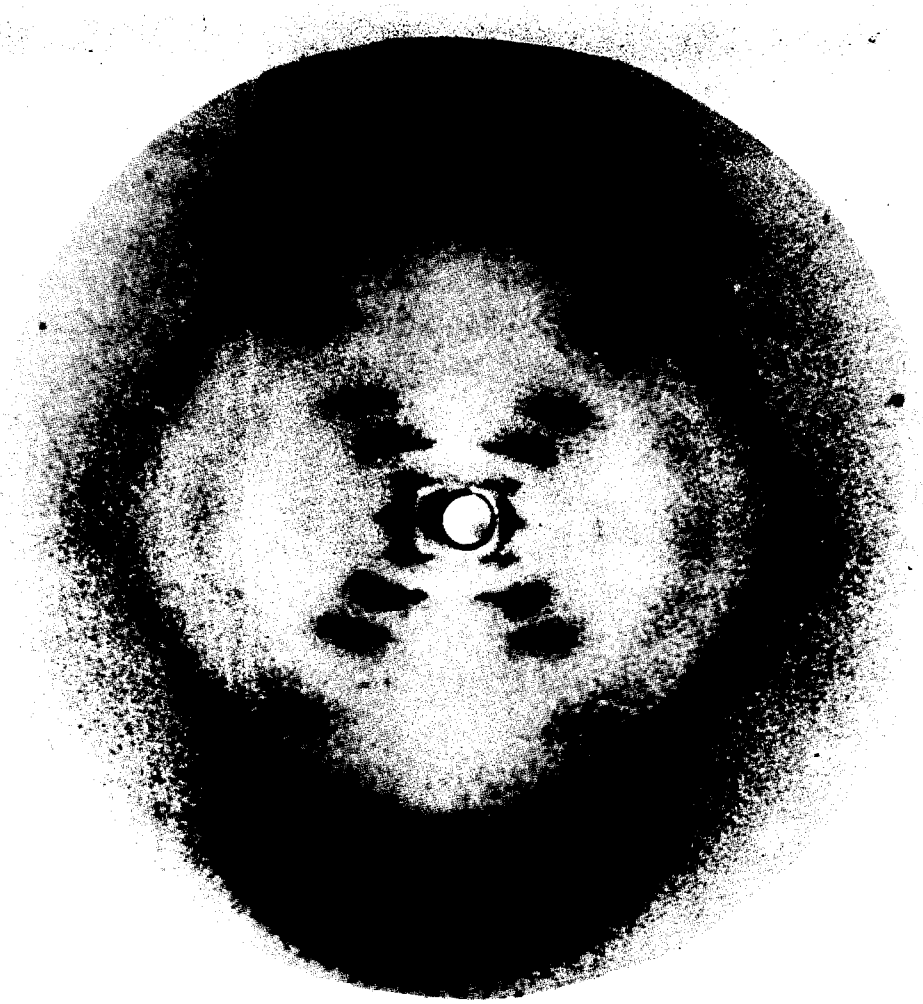


Fig. 3.4 A diagrammatic representation of (a) the α-helix, and (b) the Bessel functions contributing to the x-ray diffraction pattern.









Fotografia del DNA nella struttura « B » ottenuta con i raggi X da Rosalind Franklin nel 1952.

Altro merito è di avere costruito il modello molecolare del DNA usando i corretti dati corrispondenti alle distanze di contatto fra atomi non legati all'interno dell'elica.

equipment, and to Dr. G. E. R. Deacon and the captain and officers of R.R.S. *Discovery II* for their part in making the observations.

[1] Young, F. B., Gerrard, H., and Jevons, W., *Phil. Mag.*, **40**, 149 (1920).
[2] Longuet-Higgins, M. S., *Mon. Not. Roy. Astro. Soc., Geophys. Supp.*, **5**, 285 (1949).
[3] Von Arx, W. S., Woods Hole Papers in Phys. Oceanog. Meteor., **11** (3) (1950).
[4] Ekman, V. W., *Arkiv. Mat. Astron. Fysik.* (Stockholm), **2** (11) (1905).

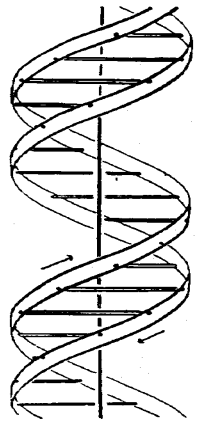
MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A Structure for Deoxyribose Nucleic Acid

WE wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

A structure for nucleic acid has already been proposed by Pauling and Corey[1]. They kindly made their manuscript available to us in advance of publication. Their model consists of three intertwined chains, with the phosphates near the fibre axis, and the bases on the outside. In our opinion, this structure is unsatisfactory for two reasons: (1) We believe that the material which gives the X-ray diagrams is the salt, not the free acid. Without the acidic hydrogen atoms it is not clear what forces would hold the structure together, especially as the negatively charged phosphates near the axis will repel each other. (2) Some of the van der Waals distances appear to be too small.

Another three-chain structure has also been suggested by Fraser (in the press). In his model the phosphates are on the outside and the bases on the inside, linked together by hydrogen bonds. This structure as described is rather ill-defined, and for this reason we shall not comment on it.



This figure is purely diagrammatic. The two ribbons symbolize the two phosphate—sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical

We wish to put forward a radically different structure for the salt of deoxyribose nucleic acid. This structure has two helical chains each coiled round the same axis (see diagram). We have made the usual chemical assumptions, namely, that each chain consists of phosphate diester groups joining β-D-deoxyribofuranose residues with 3′,5′ linkages. The two chains (but not their bases) are related by a dyad perpendicular to the fibre axis. Both chains follow right-handed helices, but owing to the dyad the sequences of the atoms in the two chains run in opposite directions. Each chain loosely resembles Furberg's[2] model No. 1; that is, the bases are on the inside of the helix and the phosphates on the outside. The configuration of the sugar and the atoms near it is close to Furberg's 'standard configuration', the sugar being roughly perpendicular to the attached base. There is a residue on each chain every 3·4 A. in the *z*-direction. We have assumed an angle of 36° between adjacent residues in the same chain, so that the structure repeats after 10 residues on each chain, that is, after 34 A. The distance of a phosphorus atom from the fibre axis is 10 A. As the phosphates are on the outside, cations have easy access to them.

The structure is an open one, and its water content is rather high. At lower water contents we would expect the bases to tilt so that the structure could become more compact.

The novel feature of the structure is the manner in which the two chains are held together by the purine and pyrimidine bases. The planes of the bases are perpendicular to the fibre axis. They are joined together in pairs, a single base from one chain being hydrogen-bonded to a single base from the other chain, so that the two lie side by side with identical *z*-co-ordinates. One of the pair must be a purine and the other a pyrimidine for bonding to occur. The hydrogen bonds are made as follows: purine position 1 to pyrimidine position 1; purine position 6 to pyrimidine position 6.

If it is assumed that the bases only occur in the structure in the most plausible tautomeric forms (that is, with the keto rather than the enol configurations) it is found that only specific pairs of bases can bond together. These pairs are: adenine (purine) with thymine (pyrimidine), and guanine (purine) with cytosine (pyrimidine).

In other words, if an adenine forms one member of a pair, on either chain, then on these assumptions the other member must be thymine; similarly for guanine and cytosine. The sequence of bases on a single chain does not appear to be restricted in any way. However, if only specific pairs of bases can be formed, it follows that if the sequence of bases on one chain is given, then the sequence on the other chain is automatically determined.

It has been found experimentally[3,4] that the ratio of the amounts of adenine to thymine, and the ratio of guanine to cytosine, are always very close to unity for deoxyribose nucleic acid.

It is probably impossible to build this structure with a ribose sugar in place of the deoxyribose, as the extra oxygen atom would make too close a van der Waals contact.

The previously published X-ray data[5,6] on deoxyribose nucleic acid are insufficient for a rigorous test of our structure. So far as we can tell, it is roughly compatible with the experimental data, but it must be regarded as unproved until it has been checked against more exact results. Some of these are given in the following communications. We were not aware of the details of the results presented there when we devised our structure, which rests mainly though not entirely on published experimental data and stereochemical arguments.

It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material.

Full details of the structure, including the conditions assumed in building it, together with a set of co-ordinates for the atoms, will be published elsewhere.

We are much indebted to Dr. Jerry Donohue for constant advice and criticism, especially on interatomic distances. We have also been stimulated by a knowledge of the general nature of the unpublished experimental results and ideas of Dr. M. H. F. Wilkins, Dr. R. E. Franklin and their co-workers at

King's College, London. One of us (J. D. W.) has been aided by a fellowship from the National Foundation for Infantile Paralysis.

J. D. Watson
F. H. C. Crick

Medical Research Council Unit for the Study of the Molecular Structure of Biological Systems,
Cavendish Laboratory, Cambridge.

April 2.

[1] Pauling, L., and Corey, R. B., *Nature*, **171**, 346 (1953); *Proc. U.S. Nat. Acad. Sci.*, **39**, 84 (1953).
[2] Furberg, S., *Acta Chem. Scand.*, **6**, 634 (1952).
[3] Chargaff, E., for references see Zamenhof, S., Brawerman, G., and Chargaff, E., *Biochim. et Biophys. Acta*, **9**, 402 (1952).
[4] Wyatt, G. R., *J. Gen. Physiol.*, **36**, 201 (1952).
[5] Astbury, W. T., Symp. Soc. Exp. Biol. 1, Nucleic Acid, 66 (Camb. Univ. Press, 1947).
[6] Wilkins, M. H. F., and Randall, J. T., *Biochim. et Biophys. Acta*, **10**, 192 (1953).

Molecular Structure of Deoxypentose Nucleic Acids

While the biological properties of deoxypentose nucleic acid suggest a molecular structure containing great complexity, X-ray diffraction studies described here (cf. Astbury[1]) show the basic molecular configuration has great simplicity. The purpose of this communication is to describe, in a preliminary way, some of the experimental evidence for the polynucleotide chain configuration being helical, and existing in this form when in the natural state. A fuller account of the work will be published shortly.

The structure of deoxypentose nucleic acid is the same in all species (although the nitrogen base ratios alter considerably) in nucleoprotein, extracted or in cells, and in purified nucleate. The same linear group of polynucleotide chains may pack together parallel in different ways to give crystalline[1-3], semi-crystalline or paracrystalline material. In all cases the X-ray diffraction photograph consists of two regions, one determined largely by the regular spacing of nucleotides along the chain, and the other by the longer spacings of the chain configuration. The sequence of different nitrogen bases along the chain is not made visible.

Oriented paracrystalline deoxypentose nucleic acid ('structure *B*' in the following communication by Franklin and Gosling) gives a fibre diagram as shown in Fig. 1 (cf. ref. 4). Astbury suggested that the strong 3·4-A. reflexion corresponded to the inter-nucleotide repeat along the fibre axis. The ~ 34 A. layer lines, however, are not due to a repeat of a polynucleotide composition, but to the chain configuration repeat, which causes strong diffraction as the nucleotide chains have higher density than the interstitial water. The absence of reflexions on or near the meridian immediately suggests a helical structure with axis parallel to fibre length.

Diffraction by Helices

It may be shown[5] (also Stokes, unpublished) that the intensity distribution in the diffraction pattern of a series of points equally spaced along a helix is given by the squares of Bessel functions. A uniform continuous helix gives a series of layer lines of spacing corresponding to the helix pitch, the intensity distribution along the nth layer line being proportional to the square of J_n, the nth order Bessel function. A straight line may be drawn approximately through

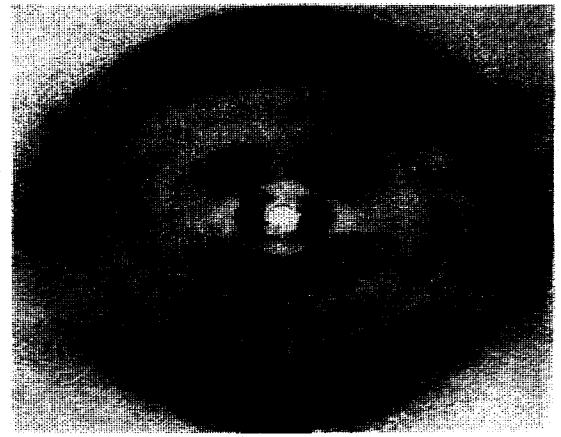


Fig. 1. Fibre diagram of deoxypentose nucleic acid from *B. coli*. Fibre axis vertical

the innermost maxima of each Bessel function and the origin. The angle this line makes with the equator is roughly equal to the angle between an element of the helix and the helix axis. If a unit repeats n times along the helix there will be a meridional reflexion (J_n^2) on the nth layer line. The helical configuration produces side-bands on this fundamental frequency, the effect[5] being to reproduce the intensity distribution about the origin around the new origin, on the nth layer line, corresponding to C in Fig. 2.

We will now briefly analyse in physical terms some of the effects of the shape and size of the repeat unit or nucleotide on the diffraction pattern. First, if the nucleotide consists of a unit having circular symmetry about an axis parallel to the helix axis, the whole diffraction pattern is modified by the form factor of the nucleotide. Second, if the nucleotide consists of a series of points on a radius at right-angles to the helix axis, the phases of radiation scattered by the helices of different diameter passing through each point are the same. Summation of the corresponding Bessel functions gives reinforcement for the inner-

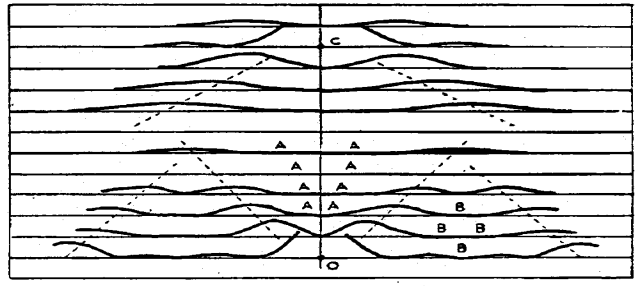


Fig. 2. Diffraction pattern of system of helices corresponding to structure of deoxypentose nucleic acid. The squares of Bessel functions are plotted about 0 on the equator and on the first, second, third and fifth layer lines for half of the nucleotide mass at 20 A. diameter and remainder distributed along a radius, the mass at a given radius being proportional to the radius. About C on the tenth layer line similar functions are plotted for an outer diameter of 12 A.

We wish to thank Prof. J. T. Randall for encouragement; Profs. E. Chargaff, R. Signer, J. A. V. Butler and Drs. J. D. Watson, J. D. Smith, L. Hamilton, J. C. White and G. R. Wyatt for supplying material without which this work would have been impossible; also Drs. J. D. Watson and Mr. F. H. C. Crick for stimulation, and our colleagues R. E. Franklin, R. G. Gosling, G. L. Brown and W. E. Seeds for discussion. One of us (H. R. W.) wishes to acknowledge the award of a University of Wales Fellowship.

M. H. F. Wilkins
Medical Research Council Biophysics Research Unit,
A. R. Stokes
H. R. Wilson
Wheatstone Physics Laboratory,
King's College, London.
April 2.

[1] Astbury, W. T., Symp. Soc. Exp. Biol., 1, Nucleic Acid (Cambridge Univ. Press, 1947).
[2] Riley, D. P., and Oster, G., *Biochim. et Biophys. Acta*, 7, 526 (1951).
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[5] Cochran, W., Crick, F. H. C., and Vand, V., *Acta Cryst.*, 5, 581 (1952).
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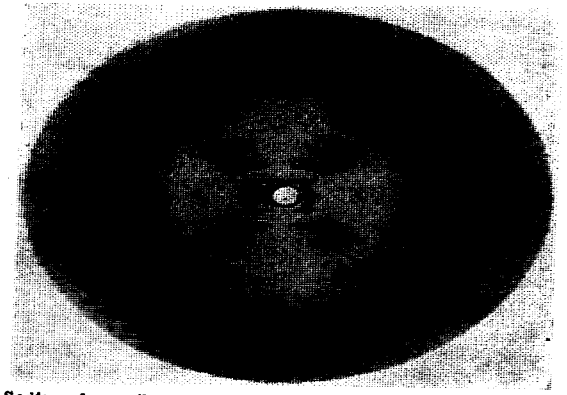
Molecular Configuration in Sodium Thymonucleate

Sodium thymonucleate fibres give two distinct types of X-ray diagram. The first corresponds to a crystalline form, structure *A*, obtained at about 75 per cent relative humidity; a study of this is described in detail elsewhere[1]. At higher humidities a different structure, structure *B*, showing a lower degree of order, appears and persists over a wide range of ambient humidity. The change from *A* to *B* is reversible. The water content of structure *B* fibres which undergo this reversible change may vary from 40–50 per cent to several hundred per cent of the dry weight. Moreover, some fibres never show structure *A*, and in these structure *B* can be obtained with an even lower water content.

The X-ray diagram of structure *B* (see photograph) shows in striking manner the features characteristic of helical structures, first worked out in this laboratory by Stokes (unpublished) and by Crick, Cochran and Vand[5]. Stokes and Wilkins were the first to propose such structures for nucleic acid as a result of direct studies of nucleic acid fibres, although a helical structure had been previously suggested by Furberg (thesis, London, 1949) on the basis of X-ray studies of nucleosides and nucleotides.

While the X-ray evidence cannot, at present, be taken as direct proof that the structure is helical, other considerations discussed below make the existence of a helical structure highly probable.

Structure *B* is derived from the crystalline structure *A* when the sodium thymonucleate fibres take up quantities of water in excess of about 40 per cent of their weight. The change is accompanied by an increase of about 30 per cent in the length of the fibre, and by a substantial re-arrangement of the molecule. It therefore seems reasonable to suppose that in structure *B* the structural units of sodium thymonucleate (molecules or groups of molecules) are relatively free from the influence of neighbouring



Sodium deoxyribose nucleate from calf thymus. Structure *B*

molecules, each unit being shielded by a sheath of water. Each unit is then free to take up its least-energy configuration independently of its neighbours and, in view of the nature of the long-chain molecules involved, it is highly likely that the general form will be helical[3]. If we adopt the hypothesis of a helical structure, it is immediately possible, from the X-ray diagram of structure *B*, to make certain deductions as to the nature and dimensions of the helix.

The innermost maxima on the first, second, third and fifth layer lines lie approximately on straight lines radiating from the origin. For a smooth single-strand helix the structure factor on the nth layer line is given by:

$$F_n = J_n(2\pi rR) \exp i\, n(\psi + \tfrac{1}{2}\pi),$$

where $J_n(u)$ is the nth-order Bessel function of u, r is the radius of the helix, and R and ψ are the radial and azimuthal co-ordinates in reciprocal space[2]; this expression leads to an approximately linear array of intensity maxima of the type observed, corresponding to the first maxima in the functions J_1, J_2, J_3, etc.

If, instead of a smooth helix, we consider a series of residues equally spaced along the helix, the transform in the general case treated by Crick, Cochran and Vand is more complicated. But if there is a whole number, m, of residues per turn, the form of the transform is as for a smooth helix with the addition, only, of the same pattern repeated with its origin at heights mc^*, $2mc^*$ . . . etc. (c is the fibre-axis period).

In the present case the fibre-axis period is 34 A. and the very strong reflexion at 3·4 A. lies on the tenth layer line. Moreover, lines of maxima radiating from the 3·4-A. reflexion as from the origin are visible on the fifth and lower layer lines, having a J_5 maximum coincident with that of the origin series on the fifth layer line. (The strong outer streaks which apparently radiate from the 3·4-A. maximum are not, however, so easily explained.) This suggests strongly that there are exactly 10 residues per turn of the helix. If this is so, then from a measurement of R_n the position of the first maximum on the nth layer line (for n 5≮), the radius of the helix, can be obtained. In the present instance, measurements of R_1, R_2, R_3 and R_5 all lead to values of r of about 10 A.

which has never been since surpassed. Dr. Schonland expressed disappointment that the membership in recent years has been but a little more than a thousand, for South Africa has expanded enormously since 1906 and with this expansion the need for, and potential value of, such a body as the Association. The general aims of the Association have not changed at all with the passing of years: "We exist," he said, "primarily to create and foster a scientific fraternity in South Africa, not to publish original work. We exist to provide a common meeting-ground for South African scientists and a forum for general discussion of the problems of this country from the scientific angle." He defended the use of Afrikaans by those who preferred it, for "we were intended by our founders to be parochial, and we should pride ourselves on being parochial. I would suggest that if we try to be anything else we will have mistaken our real aim".

Having thus firmly and, most people would agree, wisely placed the Association in its proper perspective, Dr. Schonland went on to make some concrete suggestions. The *South African Journal of Science* should have a series of semi-popular articles reviewing and surveying the new ideas of science and so bridge the gap between those who teach and do advanced research work and those who pay for it. This, he thought, is the proper function of the *Journal*, and it is but one aspect of the Association's duty, as representative of all sections of scientific opinion in South Africa, "to take a stronger, a more continuing and a more active interest in all scientific developments, national and university, in South Africa and to study carefully what is being done in other countries".

Besides his plea that the Association needs to form a standing committee to watch over scientific education in schools, Dr. Schonland suggested that the Association might consider taking a part in the formation of a body on the lines of the British Parliamentary and Scientific Committee and also help in the creation of better facilities for advanced research in South Africa. On this last-named point, he cited the instances of the National University in Canberra and the Institute for Advanced Studies in Dublin, but he made the interesting suggestion that a more acceptable solution might be the creation of a number of specialized institutes for advanced study, attached to and forming part of those universities which for one reason or another are best suited for them.

BASIS OF TECHNICAL EDUCATION

GENERAL education to-day should be planned so as to enable the ordinary citizen to adapt himself to the needs of technological society and to understand what is happening and what is required of him. This was the theme of an international conference convened by the United Nations Educational, Cultural and Scientific Organization at Unesco House in June 1950*.

Broadly, the Conference found that organized social foresight is essential to enable the educational system of a country to prepare children for the type of life and work they are likely to encounter, and that a substantial development of technical education is required at all levels: at present it is wholly inadequate for future needs, while the practical content of general education is also inadequate for the needs of future citizens of a technological society. The cultural content of technical education is also generally inadequate; technical education requires special consideration, and training for adaptability is an outstanding requirement in an age of ultra-rapid technological change. The education of women and girls also demands particular attention in view of their dual role as workers and home-makers, and improved administrative arrangements are essential if education is to fulfil its true function in such a society.

The report does not suggest that all these propositions apply equally to every country, though the Conference considered that, so far as its knowledge extended, they are generally valid for the world as a whole. The stress is laid on the need for adapting technology to man, not man to technology. The questions formulated in this report—and which merit attention in current discussions on the expansion of both technical and technological education in Great Britain—are raised in the belief that mastery of the machine by man is not an end in itself: it is a means to the development of man and of the whole society.

The distinction between technician and technologist is not always kept clear in this report, particularly in the chapter on the content of technical education. Nevertheless, the report directs attention to some fundamental issues which no sound policy for either type of education can disregard. In both fields it must be recognized that we are concerned not simply with the efficiency of production, but also with the fundamental attitude which the men and women of to-morrow will adopt in facing the problems of a technological society. Both, too, in seeking to foster flexibility, must recognize that flexibility is determined not only by education and training but also by social, economic and technical conditions; and the administrative measures required to ensure that education becomes more adapted to the needs of a changing technological society are themselves likely to be most effective when they are informal and varied rather than concentrated and uniform. The administrator, no less than the teacher and student, has need of frequent opportunities of contact with the industrial world, and requires experience of the difficulties and problems created by technological development in society; just as the teacher and student should keep abreast of developments in research and of practical applications in industry.

* Education in a Technological Society: a Preliminary International Survey of the Nature and Efficacy of Technical Education. (Tensions and Technology Series.) Pp. 76. (Paris: Unesco; London: H.M.S.O., 1952.) 200 francs; 4s.; 75 cents.

GENETICAL IMPLICATIONS OF THE STRUCTURE OF DEOXYRIBONUCLEIC ACID

By J. D. WATSON and F. H. C. CRICK

Medical Research Council Unit for the Study of the Molecular Structure of Biological Systems, Cavendish Laboratory, Cambridge

THE importance of deoxyribonucleic acid (DNA) within living cells is undisputed. It is found in all dividing cells, largely if not entirely in the nucleus, where it is an essential constituent of the chromosomes. Many lines of evidence indicate that it is the carrier of a part of (if not all) the genetic specificity of the chromosomes and thus of the gene itself.

CODICE GENETICO

Gamow 1953.

Dopo aver letto l'articolo su Nature, Gamow propone un codice a triplette (sovrapposte) per passare da un alfabeto a 4 lettere a quello a 20 lettere.

$$4^3 = 64$$

$$4^2 = 16$$

1. See page 32.

MICHIGAN UNION
Ann Arbor, Michigan

July 8th
1953

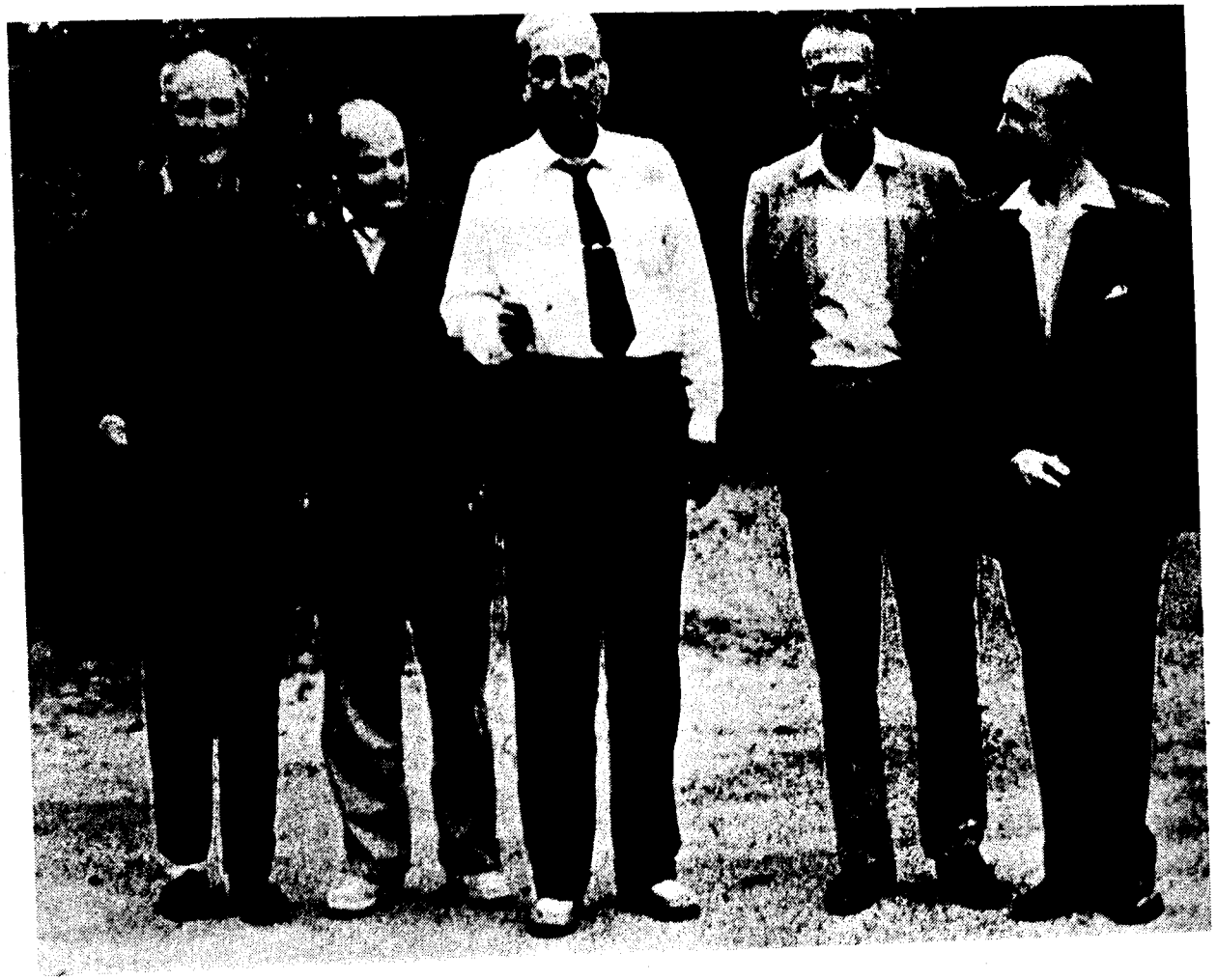
Dear Drs. Watson & Crick,

I am a physicist, not a biologist, and my interest in biology can be justified, if anything, only by my recently published book "Mr. Tompkins Learns to Facts of Life" (Cambr. Univ. Press. 1953). But I am very much excited by your article in May 30th Nature, and think that this brings ~~the~~ Biology ~~over~~ over into the group of "exact" sciences. I plan to be in England through most of September, and hope to have a chance to talk to you about all that; but

(Trs. P.T.O.)

George Gamow's original cutout-paper design for the RNA Tie Club tie

warned us not to publish



At the Cold Spring Harbor Symposium, June 1963: (from left to right) Francis Crick, Alex Rich, George Gamow, JDW, and Melvin Calvin