Lecture 9:

DNA:

The double helix structure

Readings (chapters 3,6)

Course 371

AIMS

- Introduce the experiments that are related to the discovery of DNA structure.
- Introduce the molecular structure of DNA (the double helix).
- Highlight the biological significance of the DNA structure and its details.

Structure?

Now the chemical composition is understood

What about the structure?

Experiments and findings

Structure?

What are the nucleotides within a given cell/ tissue/organism?

Do organisms vary in the combination of nucleic acids within their cells?

What does knowing the proportions of nucleotides have to do with structure?

Erwin Chargaff

ON THE NUCLEOPROTEINS OF AVIAN TUBERCLE BACILLI*

BY ERWIN CHARGAFF AND HELEN F. SAIDEL

(From the Department of Biochemistry, College of Physicians and Surgeons, Columbia University, New York)

(Received for publication, July 28, 1948)

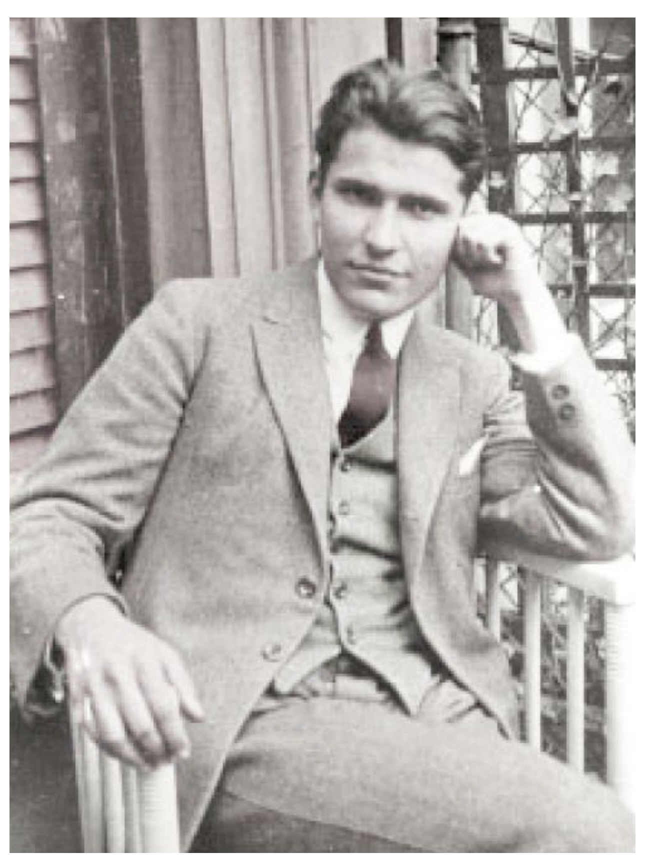
The nucleic acids of tubercle bacilli have formed the subject of several studies, among which may be mentioned those by Ruppel (1), Levene (2), and Johnson and his associates (3–5). The work of Menzel and Heidelberger (6) on the fractionation of the proteins of the tubercle bacillus revealed the presence of several protein fractions, rich in phosphorus and in purines, which appeared to be nucleoproteins. The studies of Seibert *et al.* on tuberculin (7, 8) have included experiments on the separation of nucleic acid, present in the crude preparations, from the biologically active protein. The main portion of the nucleic acid preparations studied appears to have belonged to the desoxypentose type; the presence of pentose nucleic acid does not seem to have been recorded.

In connection with work carried out in this laboratory on bacterial glycogen (9) it was observed that borate buffer extracts of ground avian tubercle bacilli contained, in addition to glycogen, a nucleoprotein fraction giving strong color reactions for desoxypentose. This observation provided an opportunity to study a nucleoprotein obtained from the bacterial cells by a mild extraction process at a low temperature that probably suppressed autolytic reactions. Several other disintegration and extraction methods either were unsuccessful or gave inferior results.

The crude nucleoprotein preparations were slightly yellow; they contained a yellow pigment with a blue-green fluorescence and exhibited an absorption peak at 410 mμ, in addition to the typical ultraviolet spectrum of nucleic acids (Fig. 1). Further fractionation made use of the fact that the principal nucleoprotein fraction was insoluble around pH 4 and could not be precipitated by half saturation with ammonium sulfate. By this procedure a desoxypentose nucleoprotein which contained 3.2 per cent P, and was only slightly contaminated with pentose nucleic acid, could be prepared. The crude preparations, however, contained a much larger proportion of pentose nucleic acid which was removed in the course of the fractionation. The spectra of a crude and of a purified specimen are compared in Fig. 2.

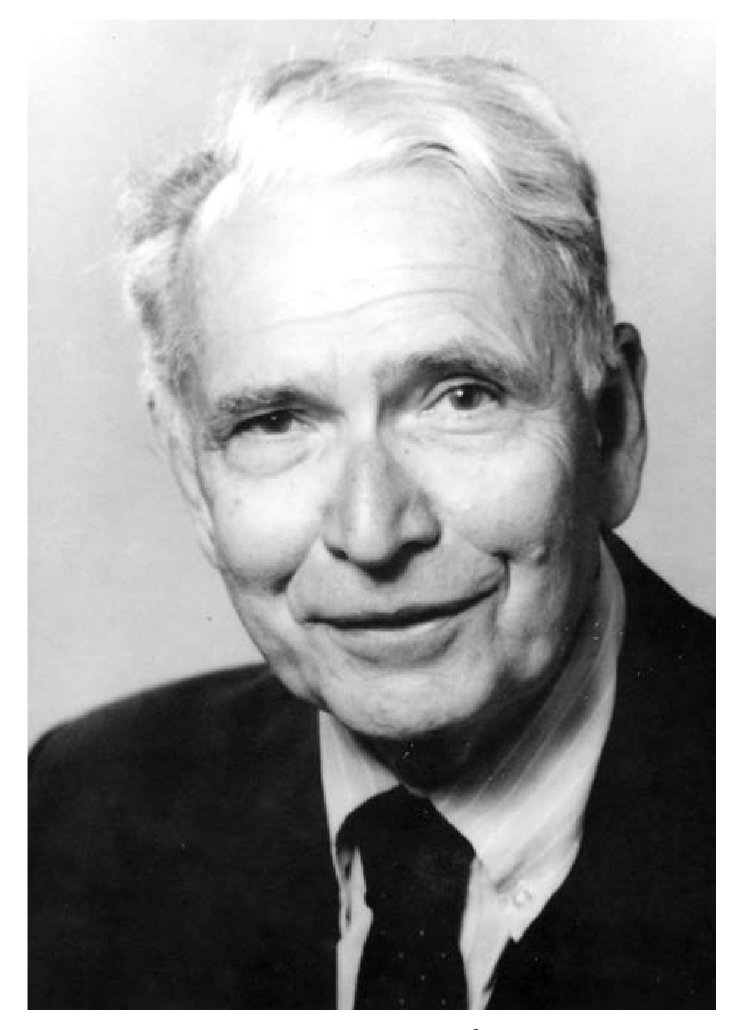
Not much can be said as yet about the nature of the proteins combined

* This work has been supported in part by a research grant from the United States Public Health Service.



Erwin Chargaff

- Chargaff studied the nucleotide proportions within different living systems.
- The question was how much As, Ts, Cs, Gs in X, Y, Z species?
- Are they the same across taxa?



Chargaff's findings

THE COMPOSITION OF THE DESOXYRIBONUCLEIC ACID OF SALMON SPERM*

By ERWIN CHARGAFF, RAKOMA LIPSHITZ, CHARLOTTE GREEN, AND M. E. HODES

(From the Department of Biochemistry, College of Physicians and Surgeons, Columbia University, New York, New York)

(Received for publication, April 25, 1951)

Several studies from this laboratory have in the past few years dealt with the chemistry of nucleic acids. (For recent summaries, see Chargaff (1, 2).) The development of precise micromethods for the separation and quantitative estimation of the purines and pyrimidines has made possible the investigation of a large number of different nucleic acid preparations. These studies led to the conclusion that the desoxypentose nucleic acids (DNA) exhibited a composition that in many cases differed very considerably (3, 4) from that of calf thymus DNA (5). The present paper provides information on the composition of the highly polymerized DNA from the spermatozoa of the salmon (*Salmo salar*) and compares the results obtained with two different hydrolysis methods employed in this laboratory.

Why did Chargaff use salmon sperm as a DNA source?

Chargaff's findings

- Notice the ratios of the bases in each experiment and procedure.
- A = G or A = T?

Table II

Purine and Pyrimidine Contents of Salmon Sperm DNA

The results are expressed in moles per mole of P in the hydrolysate.

Experiment No.*	Preparation No.	Hydrolysis procedure	Nitrogenous constituent				Recovery of nitrogenous constituents		
			Adenine	Guanine	Cytosine	Thymine	Purines	Pyrimidines	Total
1	1	1	0.27	0.18			0.45		
2		1	0.26	0.19			0.45		
3		1			0.17	0.28		0.45	
4		1			0.18	0.28		0.46	
5		2	0.28	0.20	0.21	0.27	0.48	0.48	0.96
6		2	0.30	0.22	0.20	0.29	0.52	0.49	1.01
7		2	0.27	0.18	0.19	0.25	0.45	0.44	0.89
8		2	0.28	0.21	0.20	0.27	0.49	0.47	0.96
9	2	1	0.25	0.18			0.43		
10		1	0.29	0.20			0.49		
11		2	0.29	0.18	0.20	0.27	0.47	0.47	0.94
12		2	0.28	0.21	0.19	0.26	0.49	0.45	0.94
13		2	0.30	0.21	0.20	0.30	0.51	0.50	1.01

* In each experiment between twelve and twenty-four determinations of individual purines and pyrimidines were performed.

Chargaff's findings

TABLE III

Salmon Sperm DNA; Proportions (in Moles of Nitrogenous Constituent per Mole of P in Hydrolysate)

Constituent	Procedure 1			Procedure 2			All analyses	
	No. of hydrolyses*	Mean proportion	Standard error	No. of hydrolyses*	Mean proportion	Standard error	Mean proportion	Standard error
Adenine	4	0.267	0.007	7	0.287	0.005	0.280	0.005
Guanine	4	0.186	0.004	7	0.200	0.006	0.196	0.004
Cytosine	2	0.175	0.001	7	0.197	0.003	0.192	0.006
Thymine	2	0.279	0.002	7	0.273	0.006	0.274	0.005
Total		0.907			0.957		0.942	

* In each hydrolysis between twelve and twenty-four determinations of individual nitrogenous constituent were performed.

TABLE IV

Salmon Sperm DNA; Molar Relationships

Molar ratio*	
Adenine to guanine	1.43
Thymine " cytosine	1.43
Adenine " thymine	1.02
Guanine " cytosine	1.02
Purines " pyrimidines	1.02
P accounted for, % P in hydrolysate†	95.8 (1.6)
Average gm. atoms N per mole constituent	3.7
Atomic N:P ratio in nucleic acid preparations	3.6, 3.7

* The computations of the molar ratio are based on the mean proportions of each nitrogenous constituent found in all analyses (Table III).

† The recovery figure (standard error in parentheses) is based on the average of the total recoveries recorded in all hydrolysis experiments carried out by Procedure 2 (last column, Table II).

- Pyrimidines and purines have equal ratios.
- 50% of nucleotides were purines and 50% were pyrimidines.

Chargaff's findings

- Chargaff's findings were consistent across species.
- The number of As,Cs,Gs,Ts vary between species but the ratios are always the same.

BOX 2-1 TABLE 1 Data Leading to the Formulation of Chargaff's Rules

Source	Adenine to Guanine	Thymine to Cytosine	Adenine to Thymine	Guanine to Cytosine	Purines to Pyrimidines
Ox	1.29	1.43	1.04	1.00	1.1
Human	1.56	1.75	1.00	1.00	1.0
Hen	1.45	1.29	1.06	0.91	0.99
Salmon	1.43	1.43	1.02	1.02	1.02
Wheat	1.22	1.18	1.00	0.97	0.99
Yeast	1.67	1.92	1.03	1.20	1.0
Hemophilus influenzae	1.74	1.54	1.07	0.91	1.0
Escherichia coli K2	1.05	0.95	1.09	0.99	1.0
Avian tubercle bacillus	0.4	0.4	1.09	1.08	1.1
Serratia marcescens	0.7	0.7	0.95	0.86	0.9
Bacillus schatz	0.7	0.6	1.12	0.89	1.0

After Chargaff E. et al. 1949. *J. Biol. Chem.* 177: 405.

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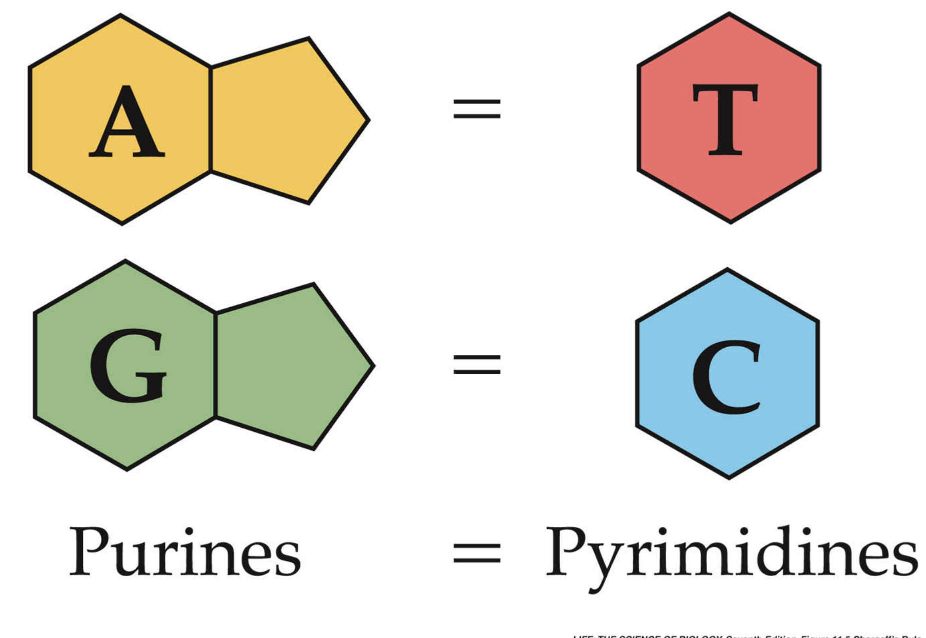
Chargaff's rule



- The amount of Adenine = the amount of Thymine.
- The amount of Guanine = the amount of Cytosine.
- Indicated that DNA is symmetrical.

Chargaff’s rule

He failed to make a connection to the structure of DNA

ERWIN CHARGAFF FOUND:

1. THE COMPOSITION OF DNA VARIED FROM ONE SPECIES TO ANOTHER, IN PARTICULAR IN THE RELATIVE AMOUNTS OF THE BASES A, C, T, G.
2. IN ANY DNA, **THE NUMBER** OF A'S WAS **THE SAME AS THE NUMBER** OF T'S; SIMILARLY, THE NUMBER OF C'S WAS EQUAL TO THE NUMBER OF G'S.

WHAT DID THIS MEAN? CHARGAFF COULDN'T SAY...

(Gonick & Whellis 1991)

Chargaff’s rule

What would have been the ratios if Chargaff analyzed the ribonucleotides instead of deoxyribonucleotides?

The Race to DNA structure

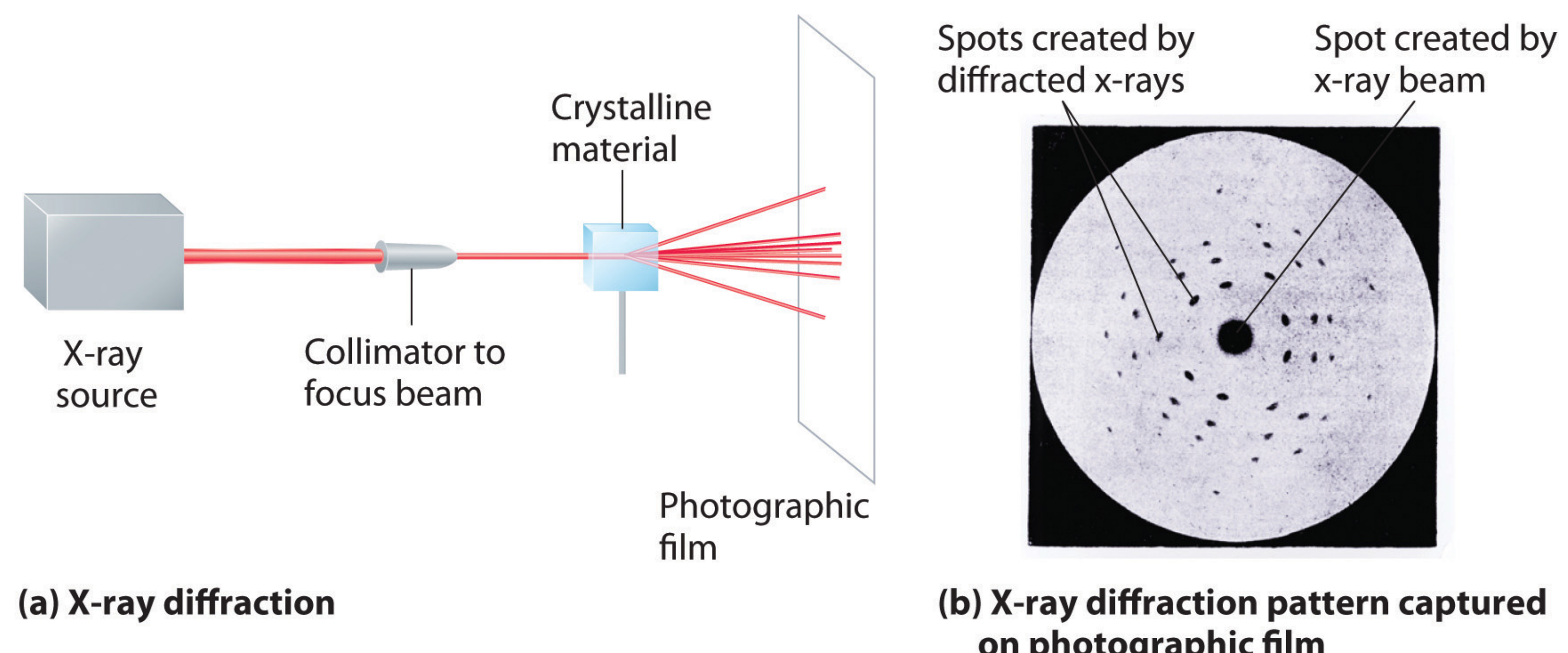
The story of the discovery of the double helix involves these key actors

Molecular structure

How can we learn about the structure of molecules?

X-ray diffraction

X-ray diffraction was the method to study the fine structure of molecules. DNA was no different!

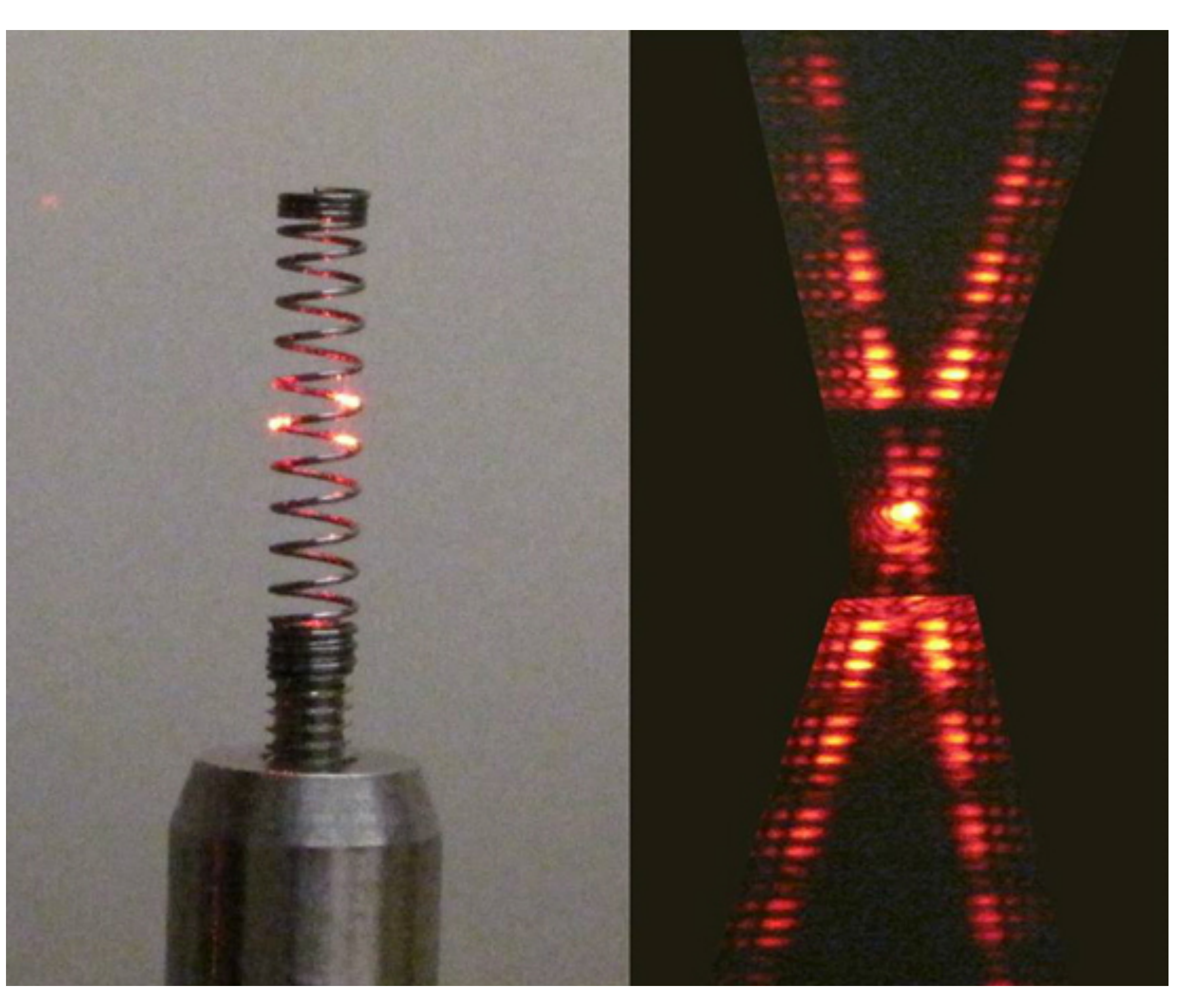


(a) X-ray diffraction

(b) X-ray diffraction pattern captured on photographic film

X-ray diffraction

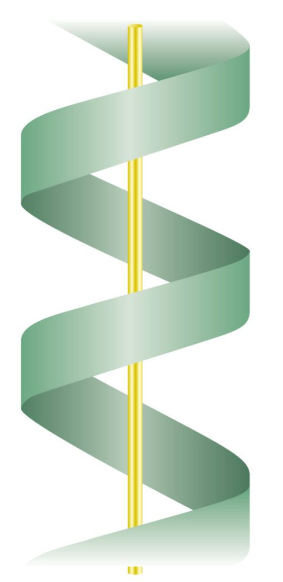
Look at the pattern resulting!

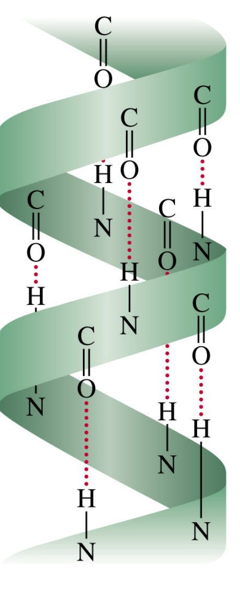


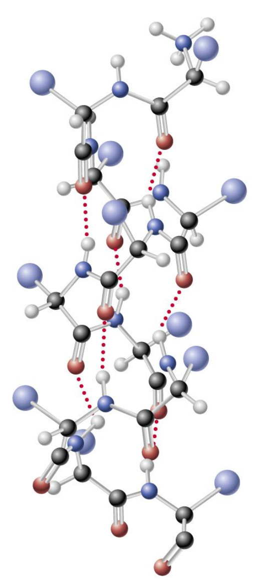
X-ray diffraction

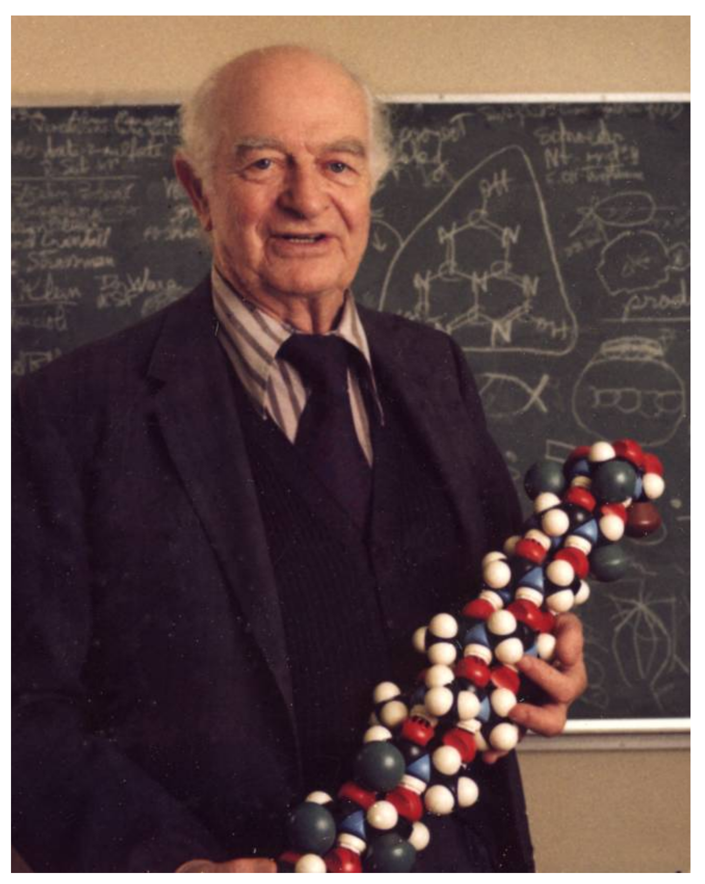
Pauling protein modeling

Linus Pauling discovered the alpha helix protein structure through modeling and x-ray diffraction.









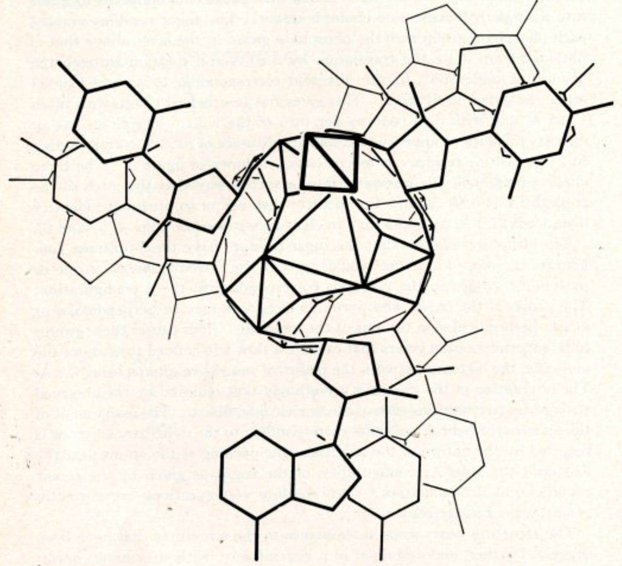
Pauling protein modeling

- Entering the race to find the structure of DNA was a blessing.
- His alpha helix is similar to that of DNA.
- His son Peter was a friend of James Watson and Francis Crick.
- They knew Pauling was after the structure so they wanted to win.

Pauling DNA modeling

- Worked on the DNA structure but not very smart findings.

- Proposed three helices with bases pointing outside and phosphate-sugar backbone pointing inside.



92 *CHEMISTRY: PAULING AND COREY* PROC. N. A. S.

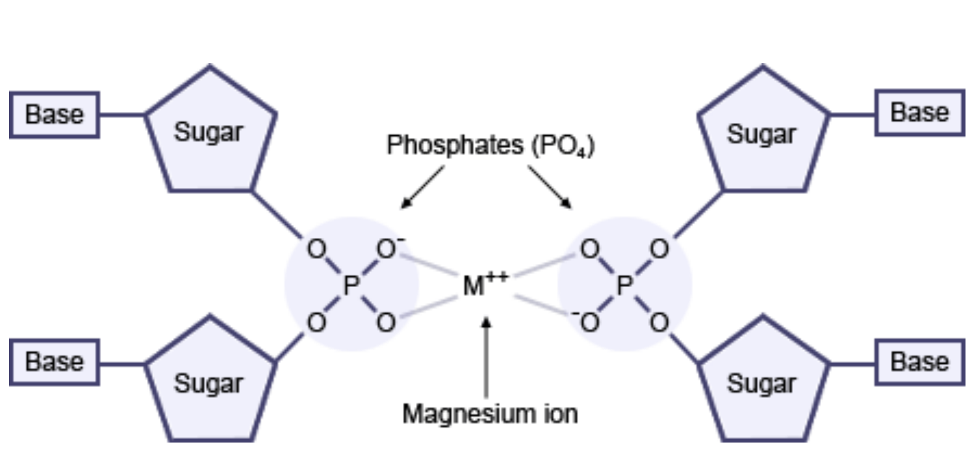
which are involved in ester linkages. This distortion of the phosphate group from the regular tetrahedral configuration is not supported by direct experimental evidence; unfortunately no precise structure determinations have been made of any phosphate di-esters. The distortion, which corresponds to a larger amount of double bond character for the inner oxygen atoms than for the oxygen atoms involved in the ester linkages, is a reasonable one, and the assumed distances are those indicated by the observed values for somewhat similar substances, especially the ring compound S_3O_9, in which each sulfur atom is surrounded by a tetrahedron of four oxygen atoms, two of which are shared with adjacent tetrahedra, and two unshared. The O—O distances within the phosphate tetrahedron are 2.32 Å (between the two inner oxygen atoms), 2.46 Å, 2.55 Å, and 2.60 Å. The

FIGURE 6

Plan of the nucleic acid structure, showing several nucleotide residues.

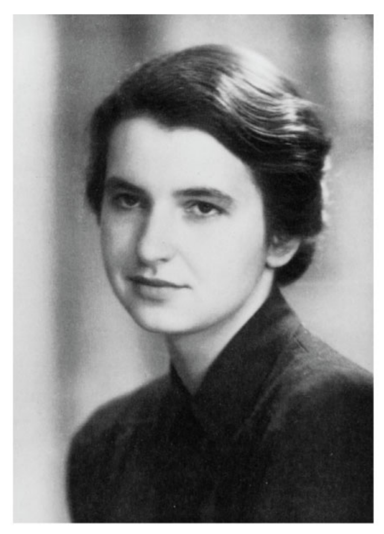
Pauling DNA modeling

Why did Pauling and also Watson and Crick, independently, propose a triple helix with bases facing outside?



Franklin/Wilkin

- At King’s College London, Rosalind Franklin and Maurice Wilkin were working on X-ray diffraction of DNA.



(a) Rosalind Franklin

(b) Franklin’s X-ray diffraction photograph of DNA

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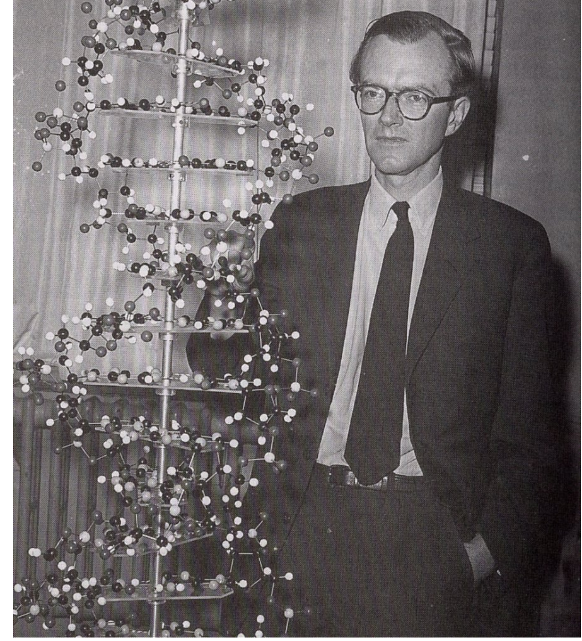


Rosalind Franklin

Franklin/Wilkin

- R. Franklin produced the best diffraction photo (called photo 51).
- Her findings were shared (with or without her approval) Watson and Crick by Wilkin.

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 internucleotide 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

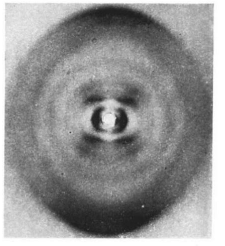


Fig. 1. Fibre diagram of deoxypentose nucleic acid from *B. coli*. Fibre axis vertical

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_0^2) 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-

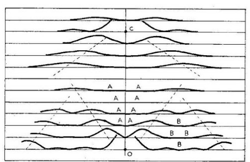
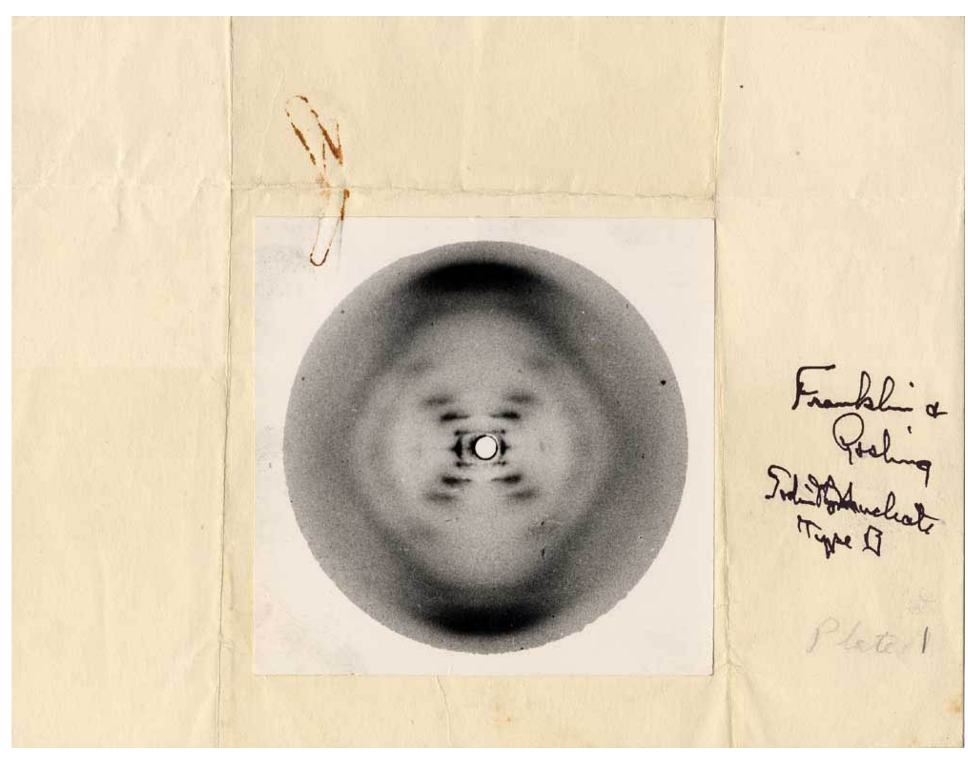


Fig. 2. Diffraction pattern of system of helices corresponding to structure of deoxypentose nucleic acid. The squares of Bessel functions are plotted about 0 on the equator and on the first, second, third and fifth layer lines for half of the nucleotide mass at 20 A. diameter and remainder distributed 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.

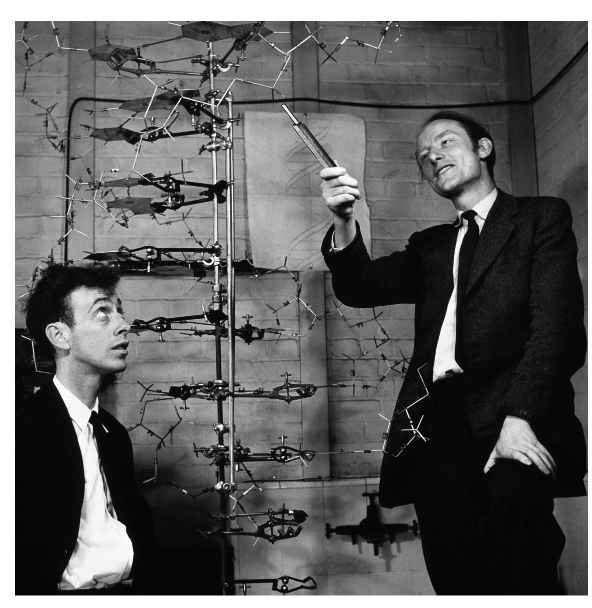


DNA X-ray diffraction

- The X-ray diffraction pattern is indicative a helical structure.
- What about the structure?
- How was it all put together?

Watson and Crick

- Watson and Crick used the empirical data of Franklin, Wilkin, and Chargaff to come up with a model of the DNA structure.
- It was an important finding to the field of molecular biology and genetics.



Watson and Crick

- They published a 900 words paper and Franklin and Wilkin also published on the same issue of Nature.

No. 4356 April 25, 1953 NATURE 737

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).

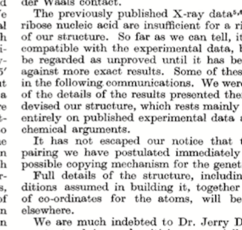
MOLECULAR STRUCTURE OF NUCLEIC ACIDS

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 line marks the fibre axis

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

Watson and Crick

Not only another structure of a molecule

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 line marks the fibre axis

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 chemical 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.

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

The structure of DNA (the genetic material) open the door for us to understand ourselves and life!

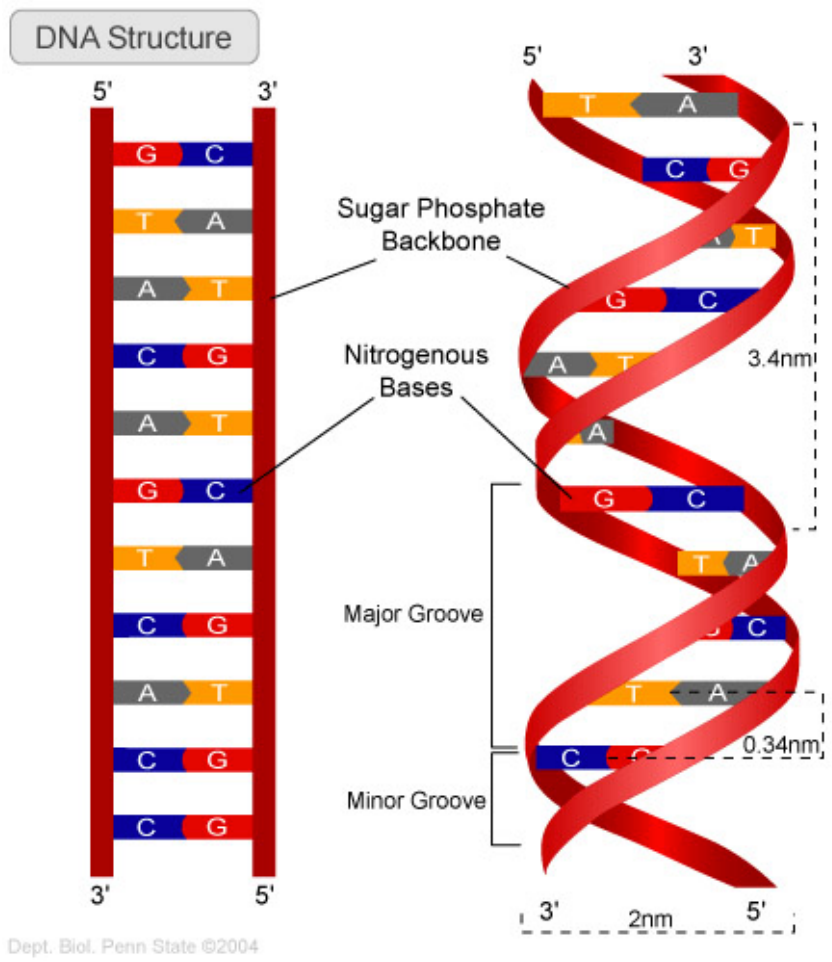
It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material.

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.

DNA structure

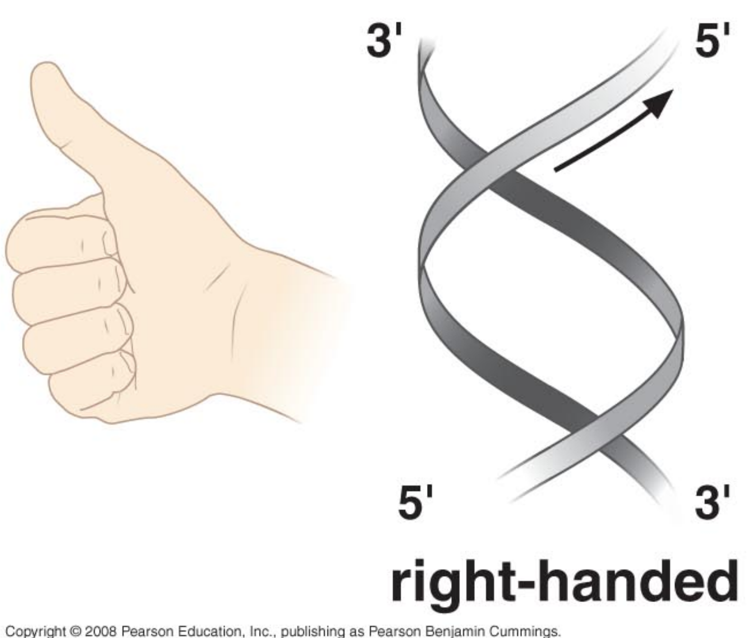
1) DNA is a double helix.

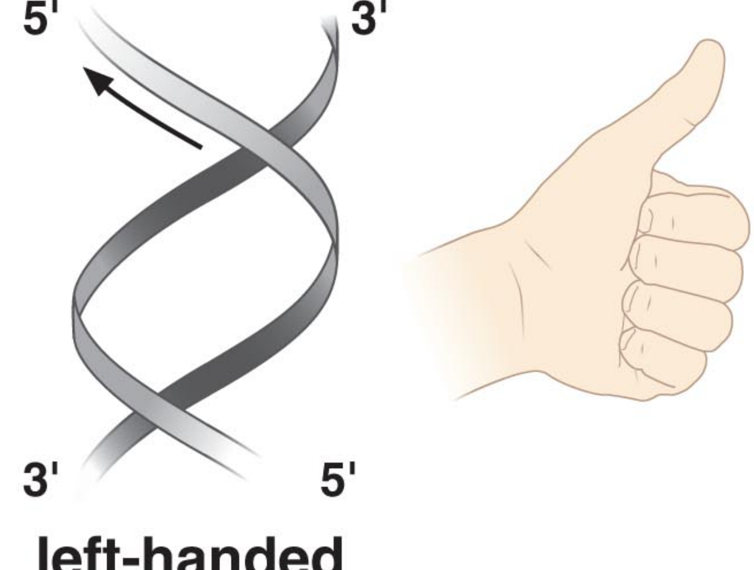
2) Two polynucleotides chains.



DNA structure

3) The two chains wind around right handedly - right handed double helix.





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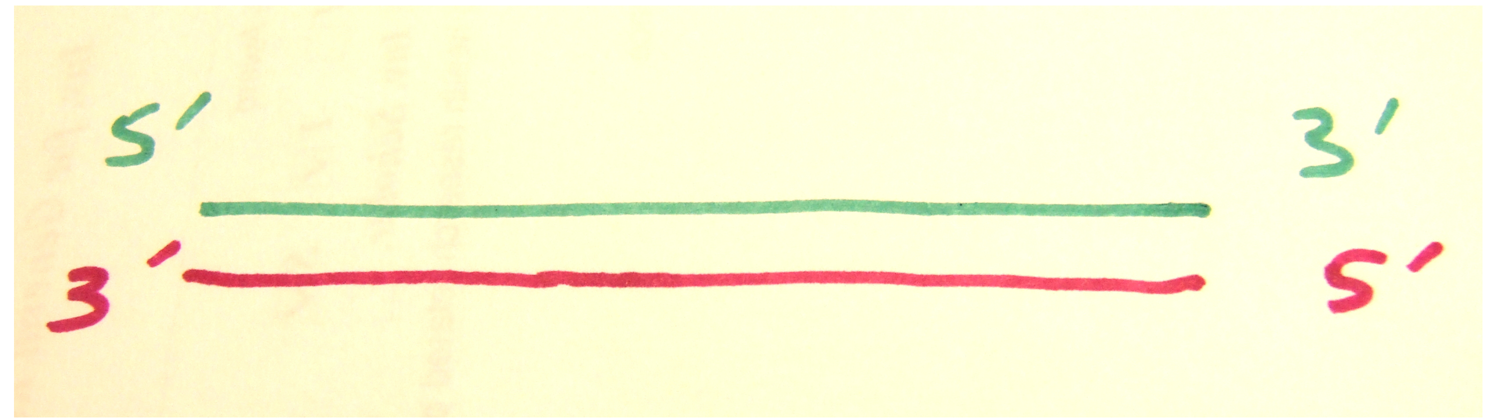
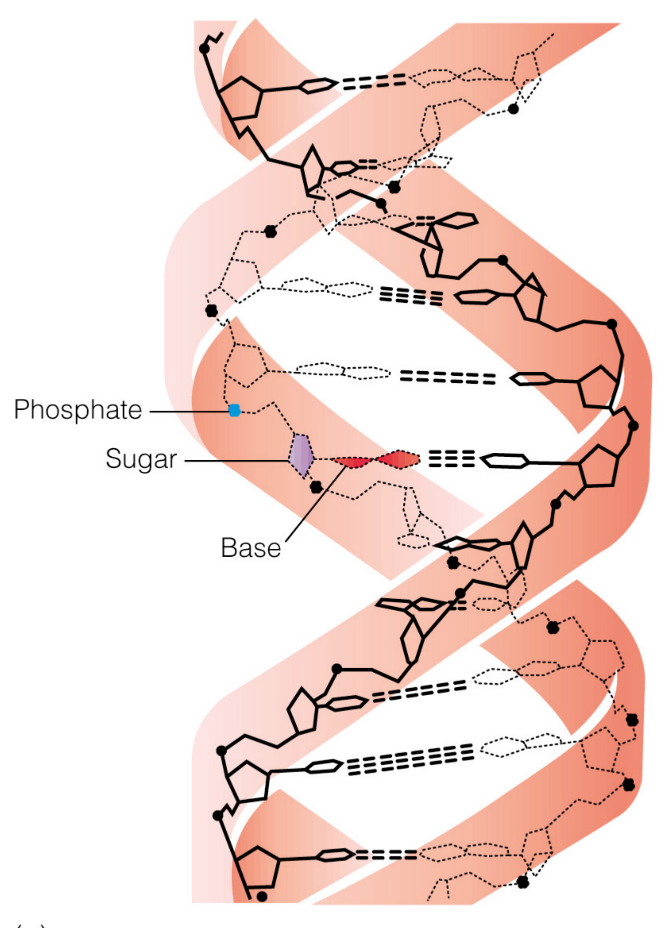
DNA structure

4) The two chains are in an anti-parallel orientation. One strand 5’ – 3’ orientation and the other 3’ – 5’).



DNA structure

5) Sugar-phosphate backbone is located on the outside of the helix.

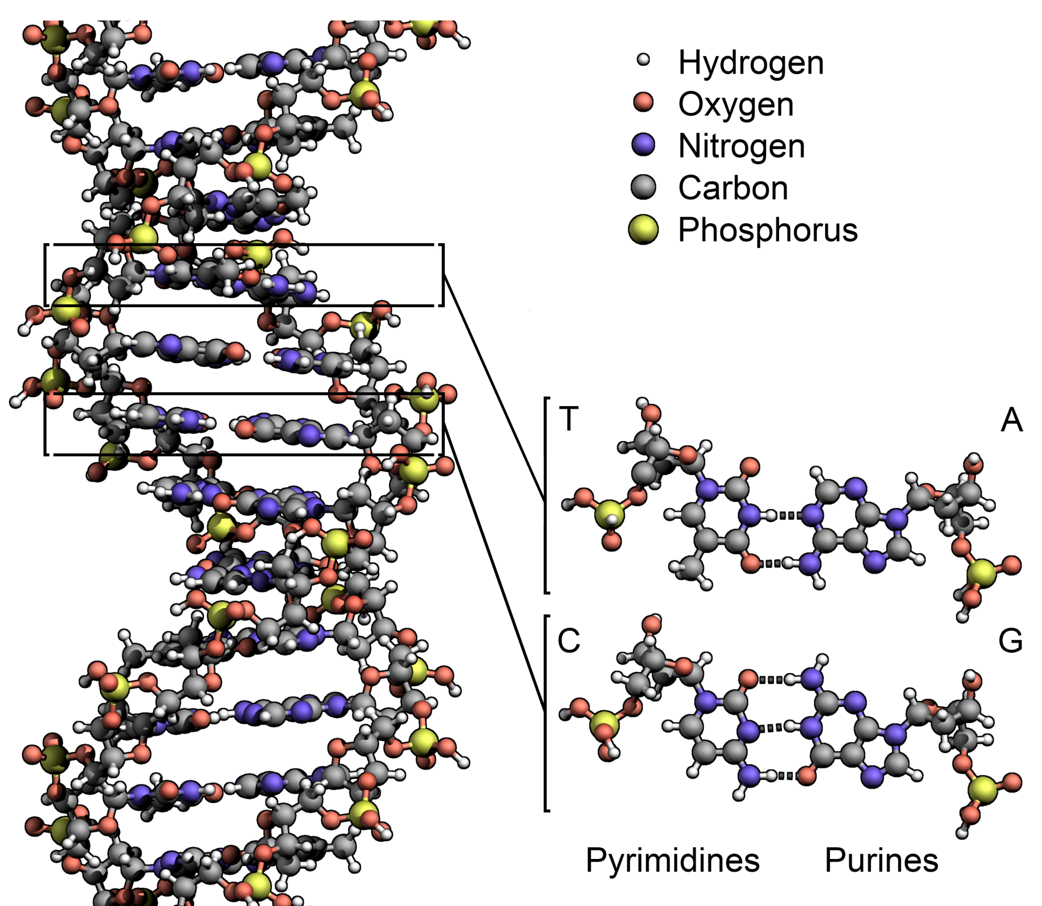


(a)

(b)

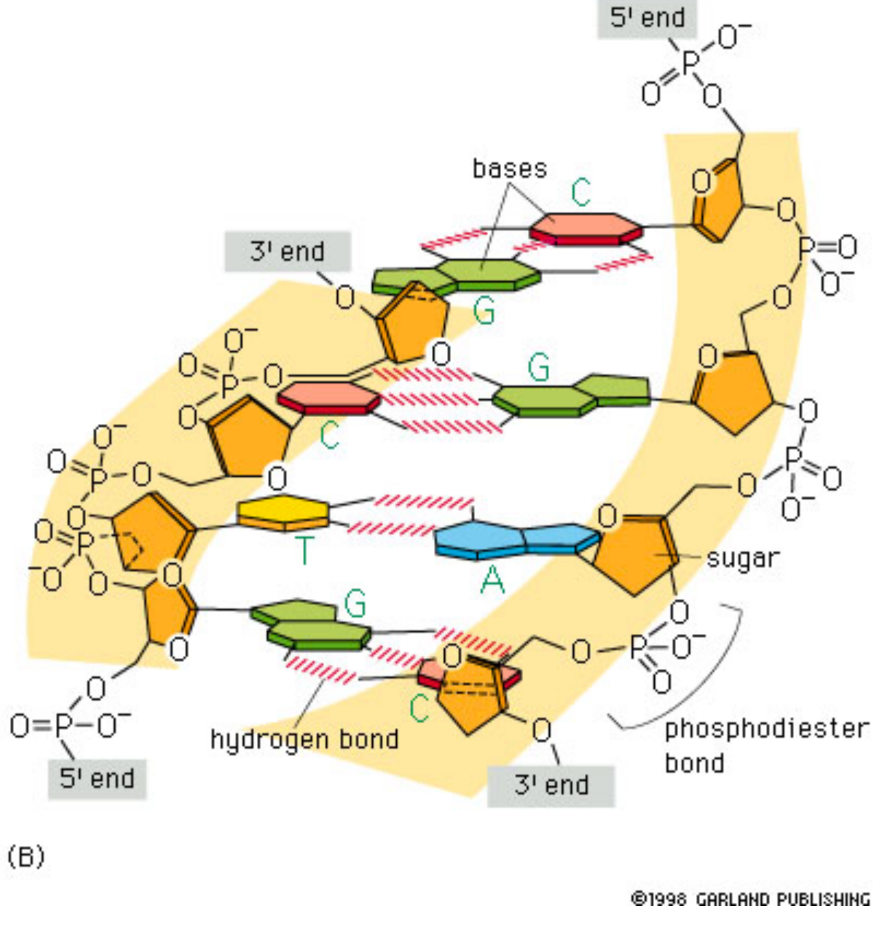
DNA structure

6) The nitrogenous bases located on the inside of the helix.



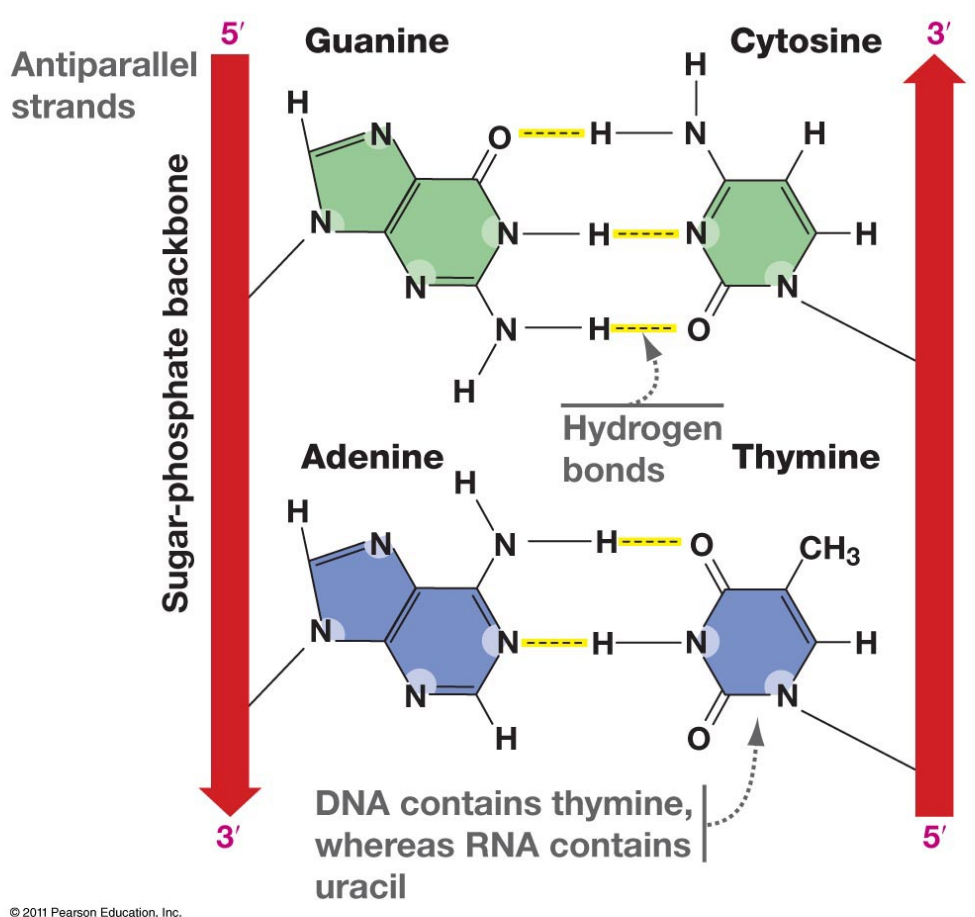
DNA structure

7) The bases are stacked flat and perpendicular to the axis of the helix. The bases are on top of each other following the twist of the helix.



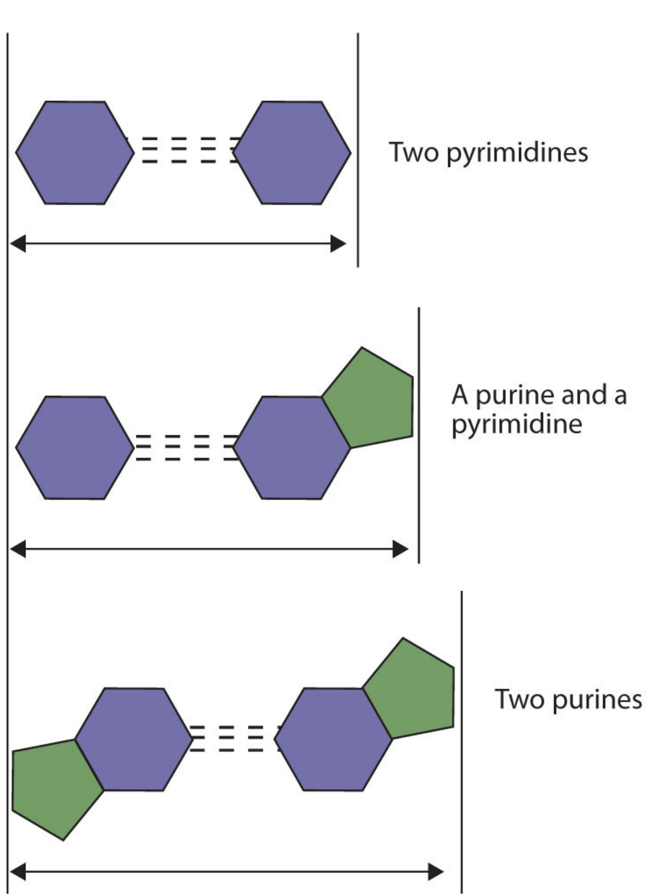
DNA structure

8) The bases of the two polynucleotides are bonded together via hydrogen bonds on the inside of the helix.



DNA structure

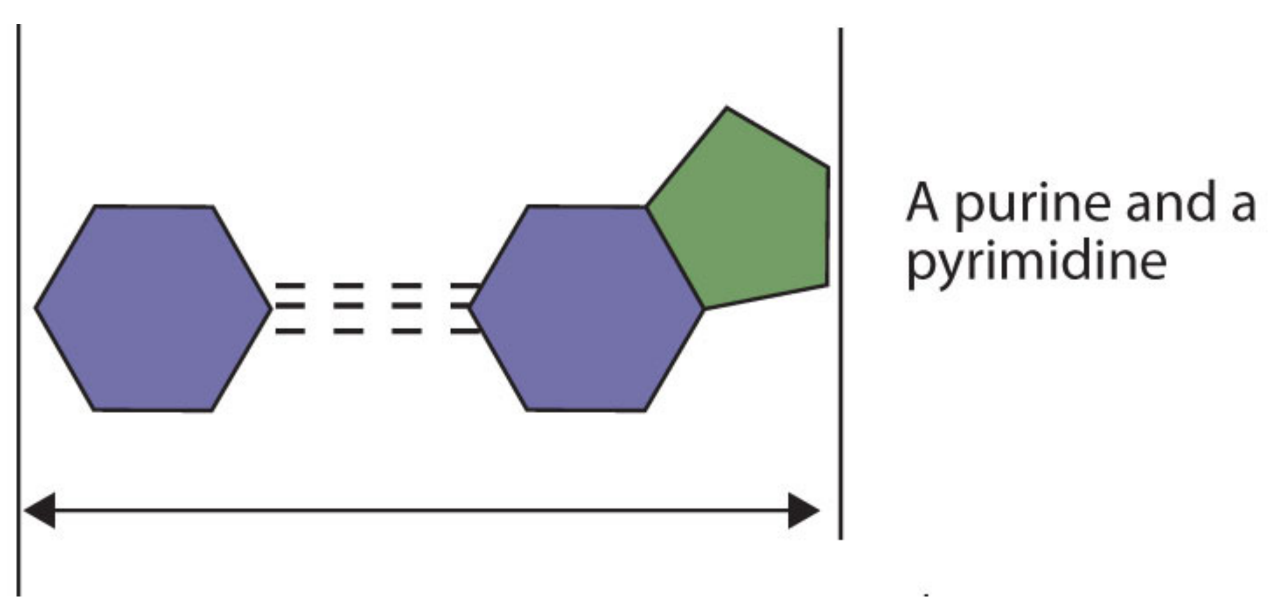
9) Bases of the two polynucleotide chains are base-pairing in a combination that maintains similar diameter of the double helix.



What happens if we have more combinations?

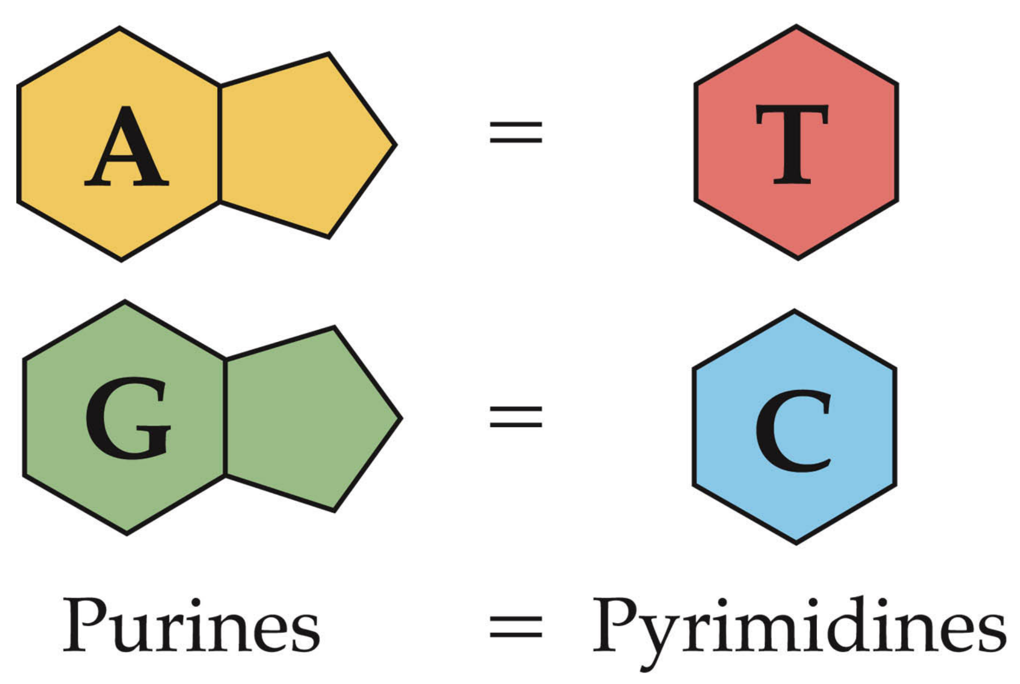
DNA structure

10) A Pyrimidine always basepair with Purine forming **complementary base pairs.**



DNA structure

11) Thymine (T) basepair with Adenine (A), and Cytosine basepair with Guanine (G). Chargaff rule !!!!



DNA structure

12) Two hydrogen bonds involve the base-pairing of (A and T) and three hydrogen bonds between (G and C).

Weak bonds

What are hydrogen bonds?

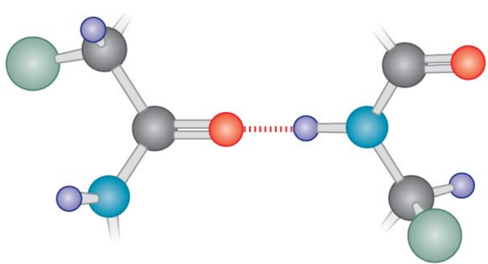
What are their functions?

Real chemical bond?

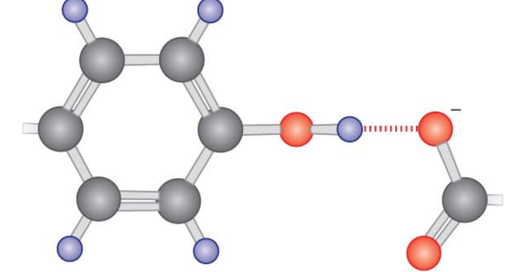
Permanent or temporary?

Weak bonds

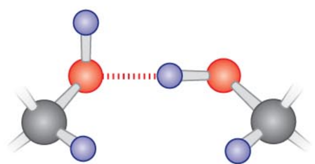
Hydrogen bonds form between a hydrogen attached to electronegative atom and another electronegative atom.



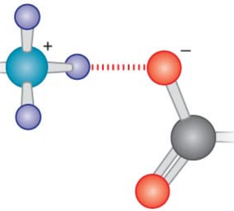
hydrogen bond between peptide groups



hydrogen bond between a charged carboxyl group and the hydroxyl group of tyrosine



hydrogen bond between two hydroxyl groups



hydrogen bond between a charged amino group and a charged carboxyl group

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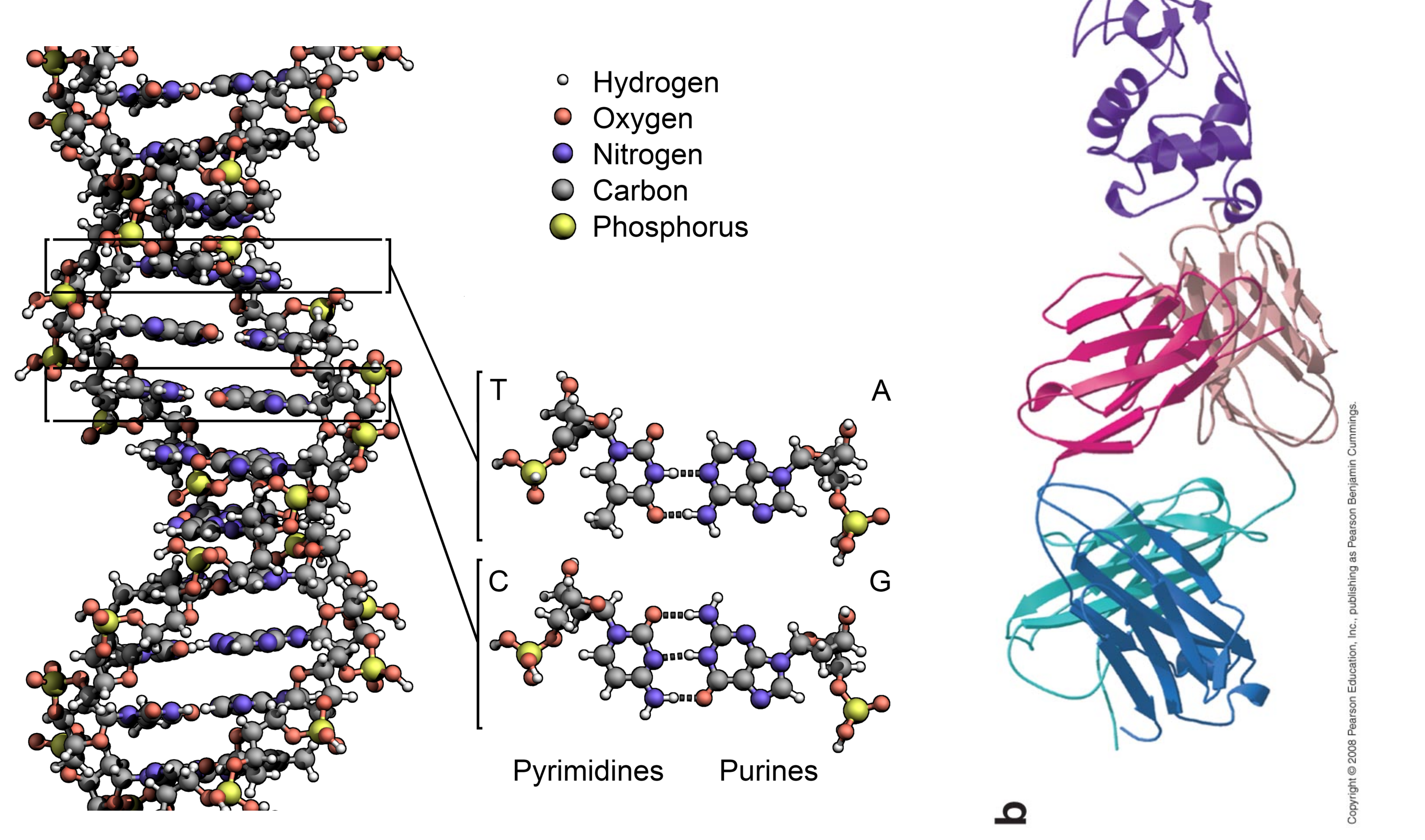
Weak bonds

Allows the formation of complex structures

Allows the specific interactions between molecules



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DNA structure

13) The sequence of one chain (strand) is enough to predict the complementary one in the other orientation.

Original DNA

Original DNA strands pried apart

Two identical DNA molecules: half new, half from original

Quiz

What is the complementary sequence of the following?

5’ A-T-G-C-G-G-G-A-A-A-T-T-T-C-C-C ‘3

a) 5’ A-T-G-C-G-G-G-A-A-A-T-T-T-C-C-C ‘3

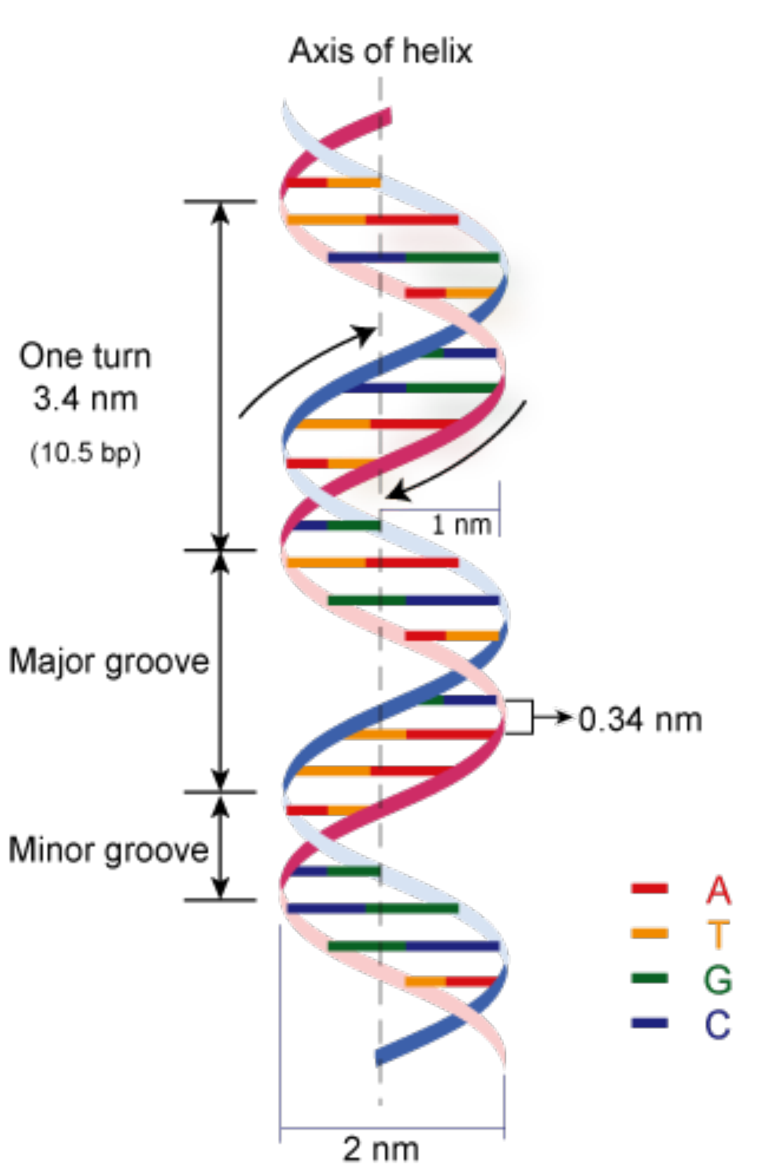
b) 3’ T-A-C-G-C-C-C-T-T-T-A-A-A-G-G-G ‘5

c) 5’ G-G-G-A-A-A-T-T-T-C-C-C-G-C-A-T ‘3

d) a and b

e) b and c

DNA structure



14) The bases are 0.34 nm apart (nm = 10^{-9}).

15) One turn of the helix is achieved (360°) every 10 basepairs or 3.4 nm.

16) The double helix external diameter is 2nm.

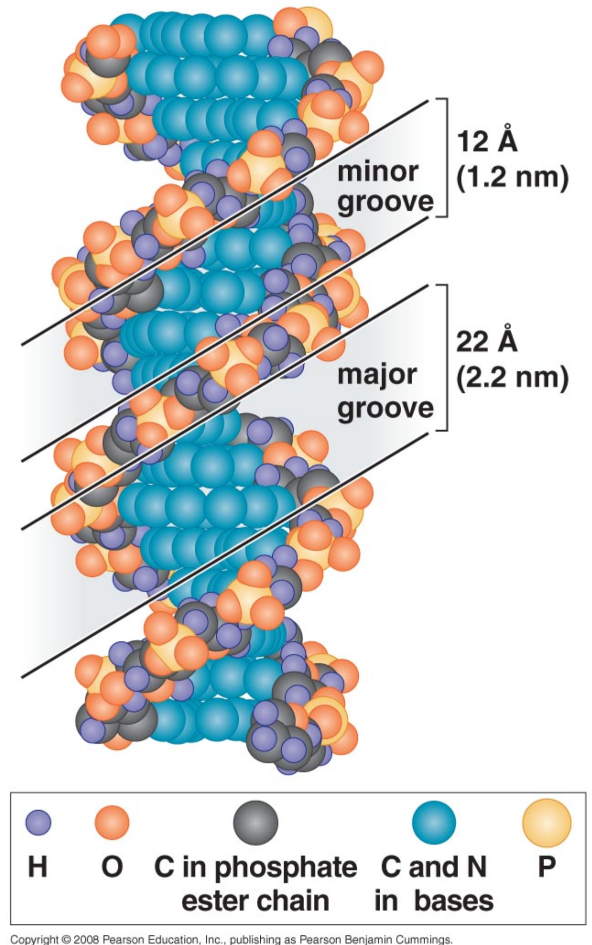
DNA structure

Why is the distance between the basepairs the same despite the identity of the basepairs?

What makes the external diameter of the DNA double helix uniform (2nm)?

DNA structure

17) A major and minor groove result from the unequal spacing of the phosphate-sugar backbone.



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Major and minor grooves

Why the major and minor groove matter?

Major and minor grooves

a

Major groove

Minor groove

b

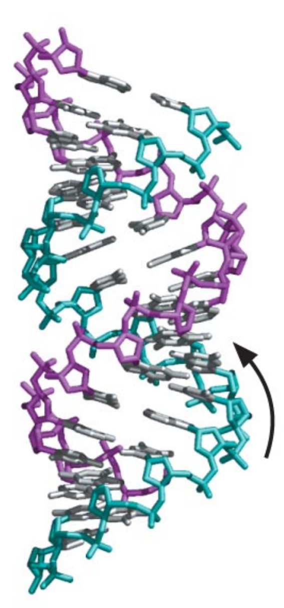
DNA-binding protein

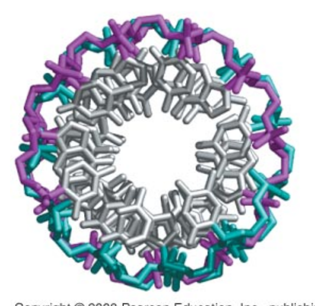
DNA structural forms

b A DNA

A-DNA:

- 11bp/turn.
- Diameter 2.2 nm.
- Right handed double helix.
- Short and wide.
- Found in low humidity.





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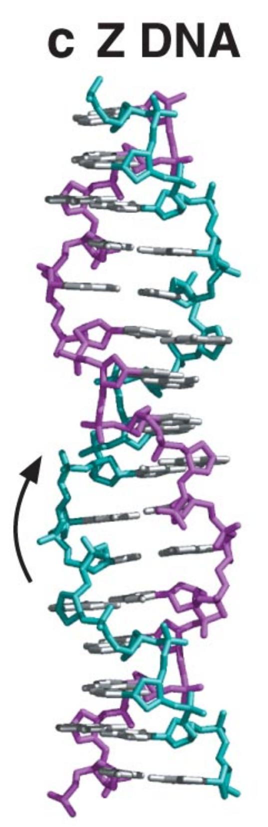
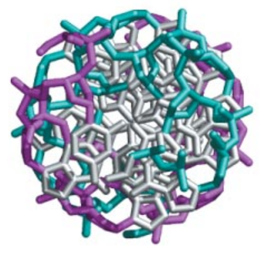
DNA structural forms





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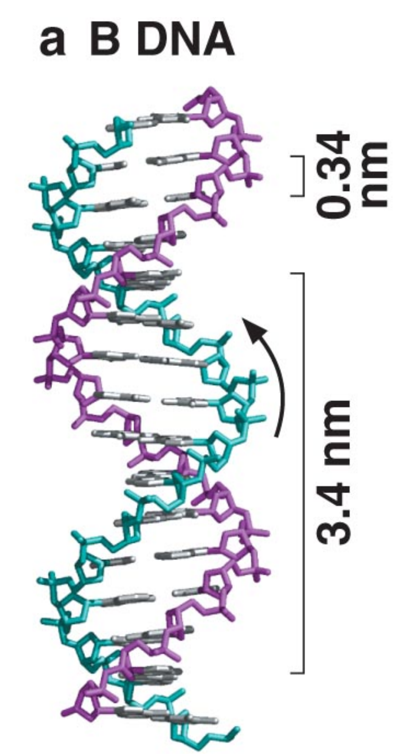
Z-DNA:

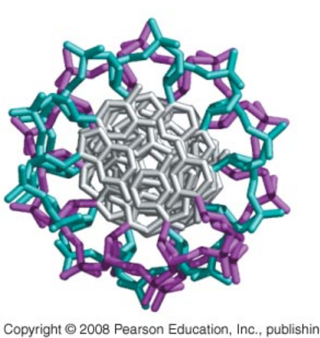
- 12bp/turn.
- Diameter 1.8nm.
- Left handed double helix.
- Thin and elongated.

DNA structural forms



B-DNA:

- 10bp/turn.
- Diameter 2nm.
- Right handed double helix.
- High humidity conditions
- **The one found in the most cells!**



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DNA structural forms

TABLE 6-2 A Comparison of the Structural Properties of A, B, and Z DNAs as Derived from Single-Crystal X-ray Analysis

	Helix Type		
	A	**B**	**Z**
Overall proportions	Short and broad	Longer and thinner	Elongated and slim
Rise per base pair	2.3 Å	3.32 Å	3.8 Å
Helix-packing diameter	25.5 Å	23.7 Å	18.4 Å
Helix rotation sense	Right-handed	Right-handed	Left-handed
Base pairs per helix repeat	1	1	2
Base pairs per turn of helix	~11	~10	12
Rotation per base pair	33.6°	35.9°	–60° per 2 bp
Pitch per turn of helix	24.6 Å	33.2 Å	45.6 Å
Tilt of base normals to helix axis	+19°	–1.2°	–9°
Base-pair mean propeller twist	+18°	+16°	~0°
Helix axis location	Major groove	Through base pairs	Minor groove
Major-groove proportions	Extremely narrow but very deep	Wide and of intermediate depth	Flattened out on helix surface
Minor-groove proportions	Very broad but shallow	Narrow and of intermediate depth	Extremely narrow but very deep
Glycosyl-bond conformation	*anti*	*anti*	*anti* at C, *syn* at G

Adapted, with permission, from Dickerson R.E. et al. 1982. *Cold Spring Harbor Symp. Quant. Biol.* 47: 14. © Cold Spring Harbor Laboratory Press.

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DNA structure

I think this much is enough for one day ☺

Summary

2 nm

Minor groove

Major groove

3.4 nm

0.34 nm

Purine

Pyrimidine

(a) Double helix

5′ end

3′ end

5′ to 3′ direction

Adenine

Thymine

Thymine

Adenine

Cytosine

Guanine

Guanine

Cytosine

3′ end

5′ end

(b) Antiparallel orientation of strands

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Expectations

- You know the story behind the discovery of the structure.
- You the experiments that collectively led to proposing the double helix.
- You know the details of the structure and the biological significance.
- You share your knowledge with people around you. Try to make it simple for them.