The Eleven
Women Nobel Laureates

In the Sciences 1903-2004

(and five who should/could have been)

Rita Levi-Montalcini 1909-

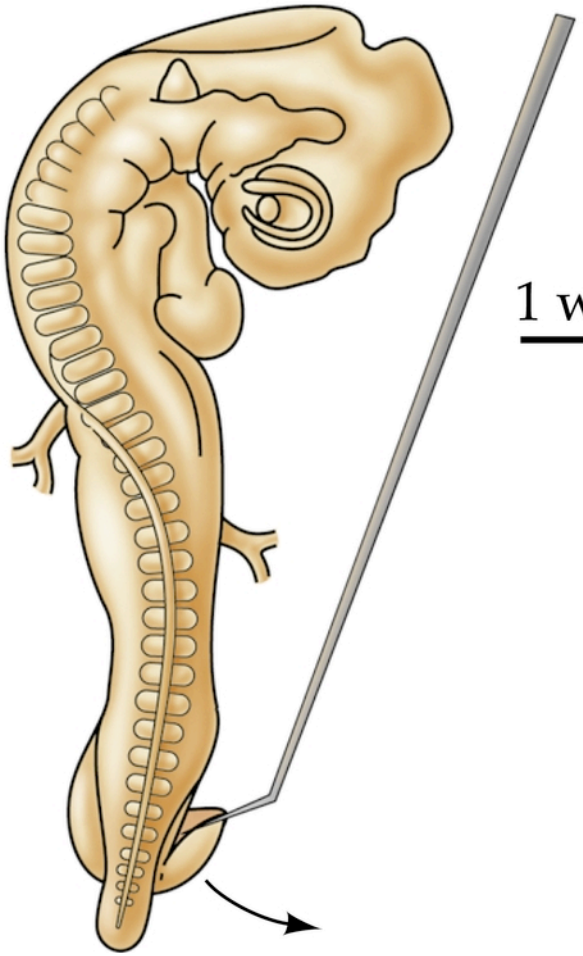
Physiology or Medicine 1986

"For their discoveries of growth factors."

(A)

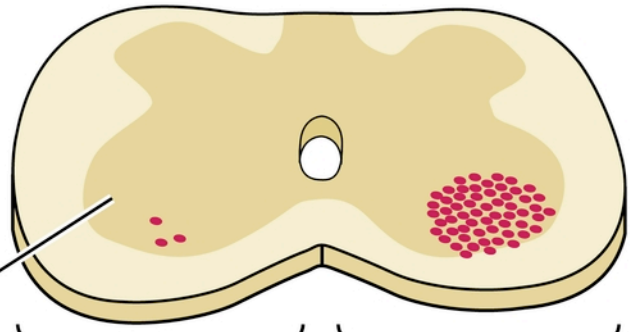
(B)

Limb bud ablation



1 week later

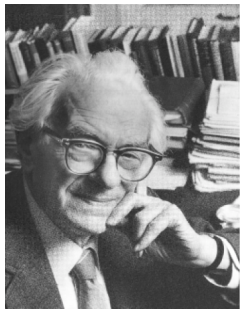
Spinal cord section



Ventral horn

Missing limb

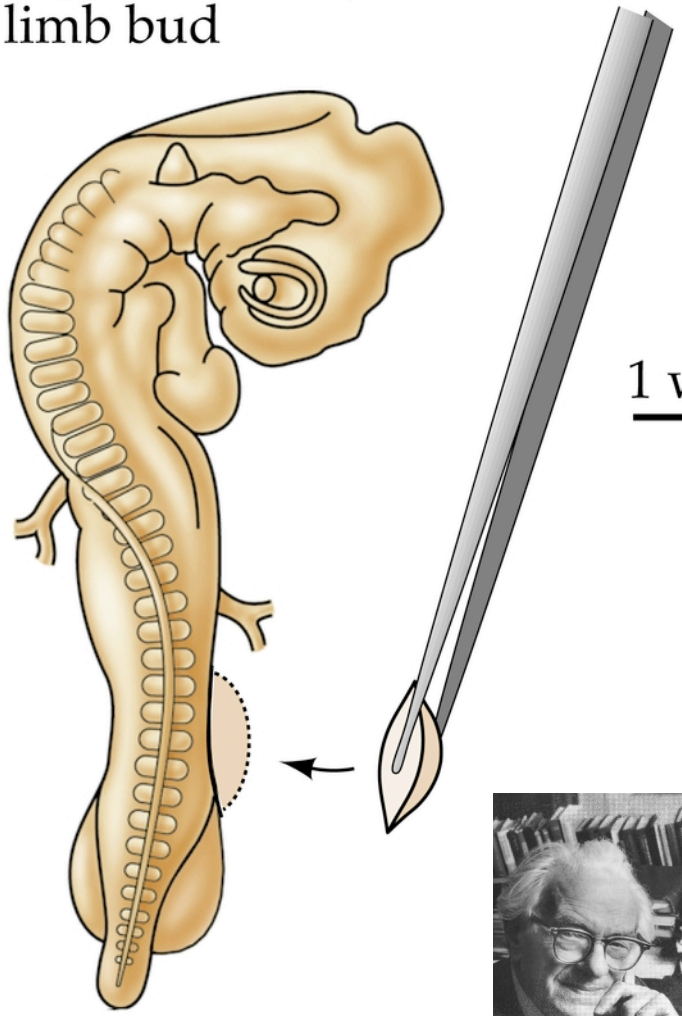
Normal



1934: Victor Hamburger discovered that removal of a limb bud resulted in reduced numbers of sensory and motor neurons in the spinal cord.

(C)

Transplantation of supernumerary limb bud



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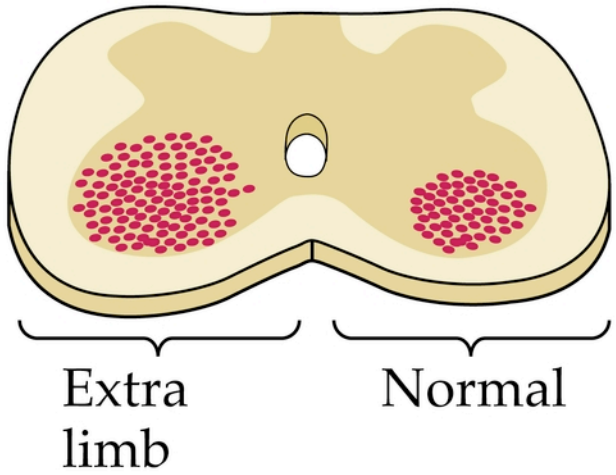
(D)

Spinal cord section

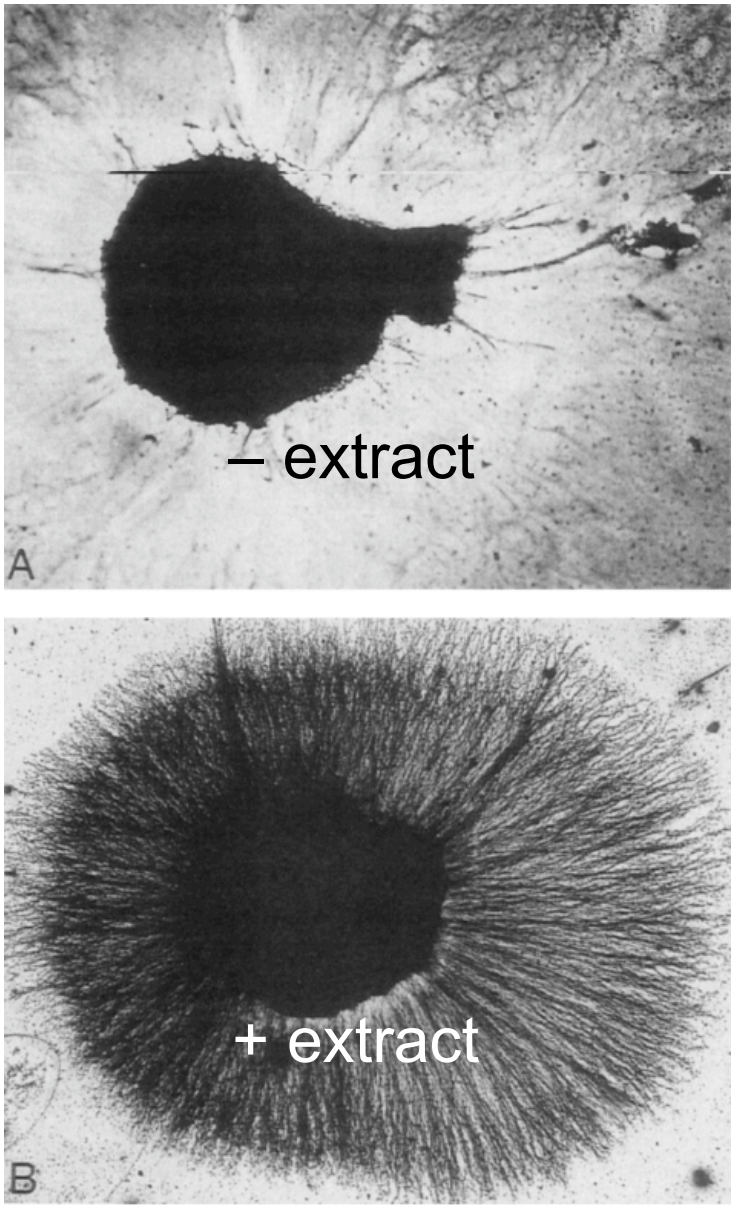


1939: Victor Hamburger showed that transplantation of a supernumerary limb resulted in increased numbers of sensory and motor neurons in the spinal cord.

"La giungla che mi si presenta davanti in quel momento era più affascinante di una foresta vergine: si trattava del sistema nervoso con i suoi miliardi di cellule aggregate in popolazioni le une differenti dalle altre e rinserrate nel viluppo apparentemente inestricabile dei circuiti nervosi che si intersecano in tutte le direzioni nell'asse cerebrospinale. Si aggiungeva, al piacere che pregustavo, quello di attuare il progetto nelle condizioni proibitive create attorno a noi dalle leggi razziali. Se Cajal, con il suo passo da gigante e il suo eccezionale intuito, aveva usato addentrarsi in quella giungla, perché non avventurarmi a mia volta nella strada aperta da lui?"

(Rita Levi Montalcini da "Elogio dell'imperfezione")

1954: neurite outgrowth assay



1960: NGF purified

1969: NGF purified to homogeneity

Stanley Cohen

Rita Levi-Montalcini

1986: Levi-Montalcini and Cohen split the Nobel prize for Physiology or Medicine

"for their discovery of growth factors"

THE NERVE GROWTH FACTOR: THIRTY-FIVE YEARS LATER

Nobel lecture, December 8, 1986

by

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Rosalind Franklin 1920-1958

Physiology or Medicine (DNA)

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).

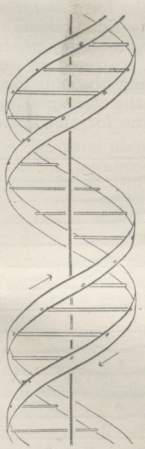
MOLECULAR STRUCTURE OF NUCLEIC ACIDS

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

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.

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.

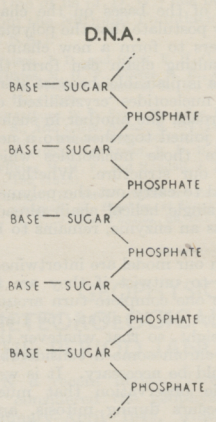


Fig. 1. Chemical formula of a single chain of deoxyribonucleic acid

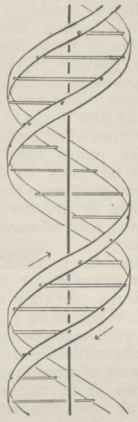


Fig. 2. This figure is purely diagrammatic. The two ribbons symbolize the two phosphate-sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis

Until now, however, no evidence has been presented to show how it might carry out the essential operation required of a genetic material, that of exact self-duplication.

We have recently proposed a structure[1] for the salt of deoxyribonucleic acid which, if correct, immediately suggests a mechanism for its self-duplication. X-ray evidence obtained by the workers at King's College, London[2], and presented at the same time, gives qualitative support to our structure and is incompatible with all previously proposed structures[3]. Though the structure will not be completely proved until a more extensive comparison has been made with the X-ray data, we now feel sufficient confidence in its general correctness to discuss its genetical implications. In doing so we are assuming that fibres of the salt of deoxyribonucleic acid are not artefacts arising in the method of preparation, since it has been shown by Wilkins and his co-workers that similar X-ray patterns are obtained from both the isolated fibres and certain intact biological materials such as sperm head and bacteriophage particles[2,4].

The chemical formula of deoxyribonucleic acid is now well established. The molecule is a very long chain, the backbone of which consists of a regular alternation of sugar and phosphate groups, as shown in Fig. 1. To each sugar is attached a nitrogenous base, which can be of four different types. (We have considered 5-methyl cytosine to be equivalent to cytosine, since either can fit equally well into our structure.) Two of the possible bases—adenine and guanine—are purines, and the other two—thymine and cytosine—are pyrimidines. So far as is known, the sequence of bases along the chain is irregular. The monomer unit, consisting of phosphate, sugar and base, is known as a nucleotide.

The first feature of our structure which is of biological interest is that it consists not of one chain, but of two. These two chains are both coiled around a common fibre axis, as is shown diagrammatically in Fig. 2. It has often been assumed that since there was only one chain in the chemical formula there would only be one in the structural unit. However, the density, taken with the X-ray evidence[2], suggests very strongly that there are two.

The other biologically important feature is the manner in which the two chains are held together. This is done by hydrogen bonds between the bases, as shown schematically in Fig. 3. The bases are joined together in pairs, a single base from one chain being hydrogen-bonded to a single base from the other. The important point is that only certain pairs of bases will fit into the structure. One member of a pair must be a purine and the other a pyrimidine in order to bridge between the two chains. If a pair consisted of two purines, for example, there would not be room for it.

We believe that the bases will be present almost entirely in their most probable tautomeric forms. If this is true, the conditions for forming hydrogen bonds are more restrictive, and the only pairs of bases possible are:

adenine with thymine;
guanine with cytosine.

The way in which these are joined together is shown in Figs. 4 and 5. A given pair can be either way round. Adenine, for example, can occur on either chain; but when it does, its partner on the other chain must always be thymine.

This pairing is strongly supported by the recent analytical results[5], which show that for all sources of deoxyribonucleic acid examined the amount of adenine is close to the amount of thymine, and the amount of guanine close to the amount of cytosine, although the cross-ratio (the ratio of adenine to guanine) can vary from one source to another. Indeed, if the sequence of bases on one chain is irregular, it is difficult to explain these analytical results except by the sort of pairing we have suggested.

The phosphate-sugar backbone of our model is completely regular, but any sequence of the pairs of bases can fit into the structure. It follows that in a long molecule many different permutations are possible, and it therefore seems likely that the precise sequence of the bases is the code which carries the genetical information. If the actual order of the

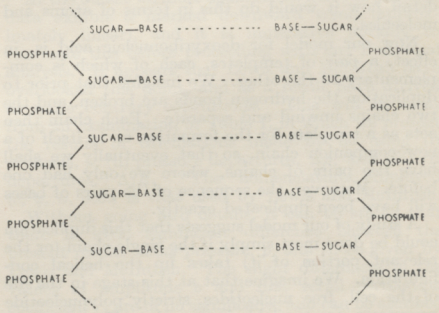
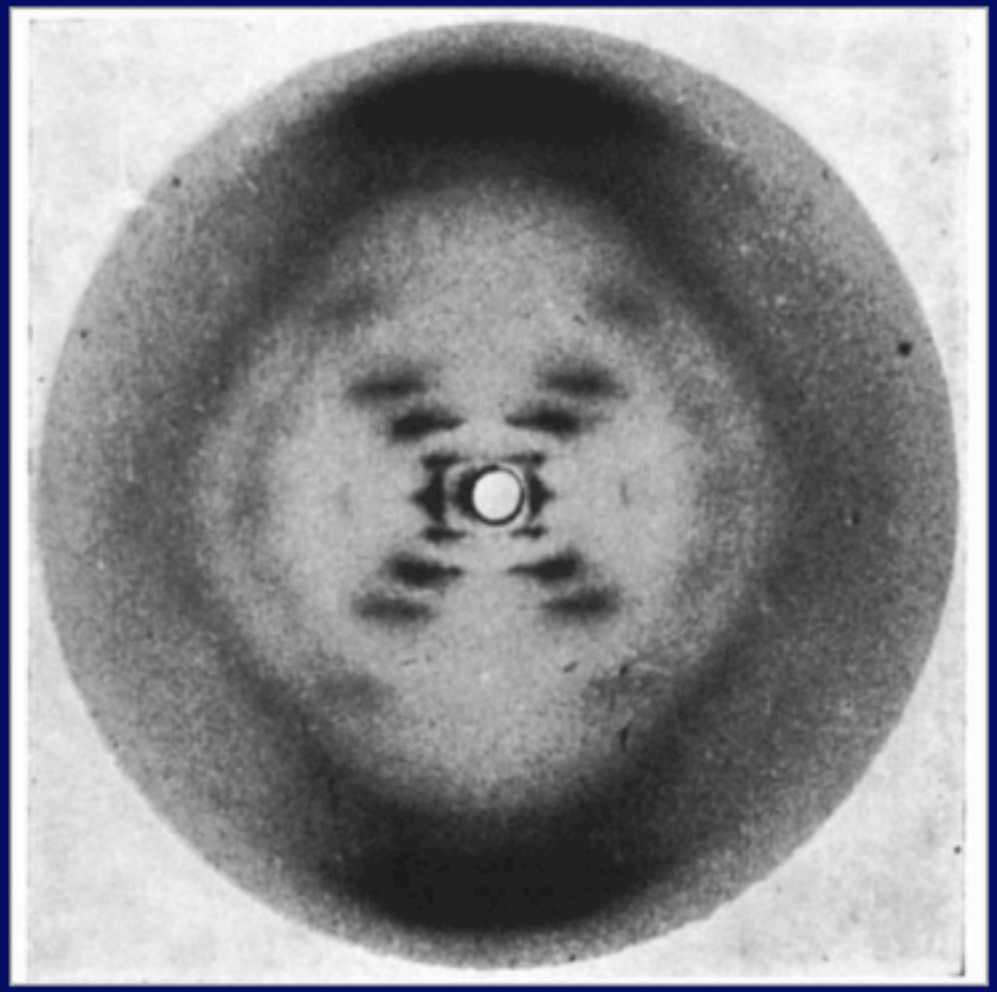
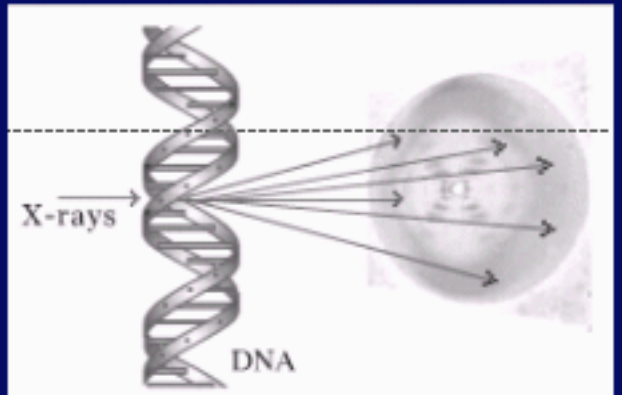


Fig. 3. Chemical formula of a pair of deoxyribonucleic acid chains. The hydrogen bonding is symbolized by dotted lines

Photo 51

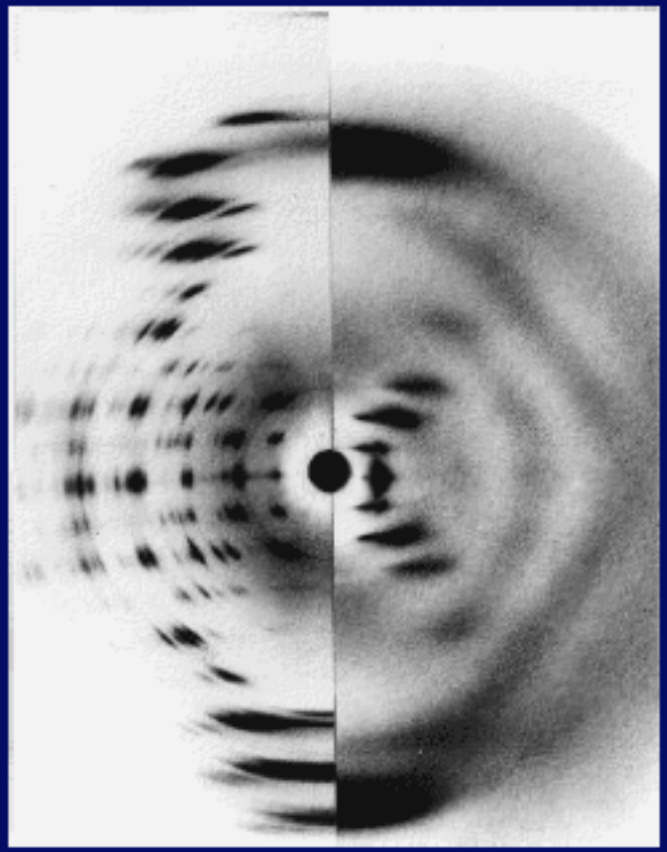


Rosalind Franklin



Franklin aimed X-rays at a vertically suspended fiber the thickness of a single hair that contained millions of strands of the "B" or wet form of DNA from the thymus of a calf. First discovered by Franklin, the B form of DNA is the form found within a living cell.

Francis Crick



Rosalind Franklin

James Watson

Maurice Wilkins

Amare il proprio lavoro costituisce la migliore approssimazione concreta alla felicità sulla terra
(Rita Levi Montalcini)