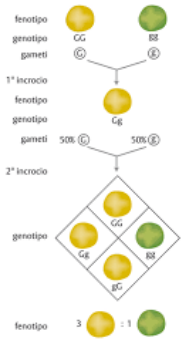
Come nasce la Biologia Molecolare?

Funzioni biologiche

genetica

- Organismo -
Sin un componente:
mutazioni
(1850-)
"olistico"



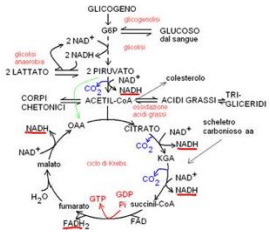
geni

DNA ricombinante

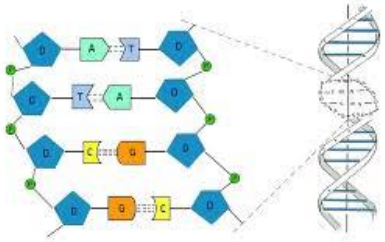
proteine

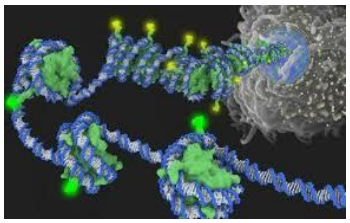
biochimica

componenti individuali
di un organismo (1800-)
"Riduzionistico"



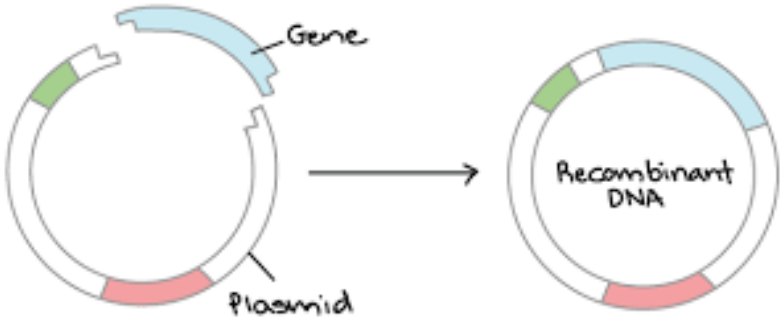
Biologia molecolare





Il termine Biologia Molecolare viene usato per la prima volta nel 1945 per definire lo studio della **struttura chimico-fisica di macromolecole biologiche.**

DNA ricombinante



This obstacle to the progress of molecular biology was overcome by the development of **recombinant DNA technology**, which provided scientists with the ability to isolate, sequence, and **manipulate individual genes derived from any type of cell.**

Recombinant DNA technology comprises altering genetic material outside an organism to obtain enhanced and desired characteristics in living organisms or as their products.

The application of recombinant DNA has thus enabled detailed molecular studies of the structure and function of eukaryotic genes, thereby **revolutionizing our understanding of cell biology**.

Genetica

1866: Mendel pubblica ill suo lavoro sull'ibridazione delle piante
1900: Cromosomi come unità ereditarie
1910: Cromosomi contengono I geni
1930: Le mutazioni identificate come cambiamenti fisici nei geni

Biochimica

368 6 February 1965 BRITISH MEDICAL JOURNAL

Middle Articles

Centenary of Mendel's Paper

At two meetings of the Natural Sciences Society of Brünn (now Brno, in Czechoslovakia) on 8 February and 8 March 1865 Mendel delivered his famous paper on hybridization in the edible pea. It was first printed in the society's transactions, Verhandlungen des naturforschenden Vereines in Brünn, *1865,* **4**, *Abhandlungen (papers) 1–47. The first page of the MS., endorsed by the editor for 40 reprints, opposite, is from the* Life *by H. Iltis, and the first page of the printed paper appears below in facsimile. Some 35 years later the botanists De Vries, Correns, and Tschermak realized its significance and got it republished in* Flora, *1901,* **89**, *364. An English translation prepared by the Royal Horticultural Society was issued in the same year with a note by the Cambridge biologist W. Bateson in the* Journal of the Royal Horticultural Society, *1901,* **26**, *1. Then in 1909 Bateson included this translation, slightly modified and with added notes, in his book* Mendel's Principles of Heredity (*Cambridge University Press*). *With the permission of the Cambridge University Press and the Royal Horticultural Society extensive extracts from this version, together with some of Bateson's notes, are given at p. 370. The portrait is from the same work.*

Biologia mole

1944 : Identificazione del DNA
1953 : Rivelata la struttura a d
1959 : Replicazione semicons

La biologia molecolare nasc
spiegazione del fenomeno
caratteri ereditari in te

Gregor Mendel, aged about 40.

Versuche über Pflanzen-Hybriden.

Von

Gregor Mendel.

(Vorgelegt in den Sitzungen vom 8. Februar und 8. März 1865.)

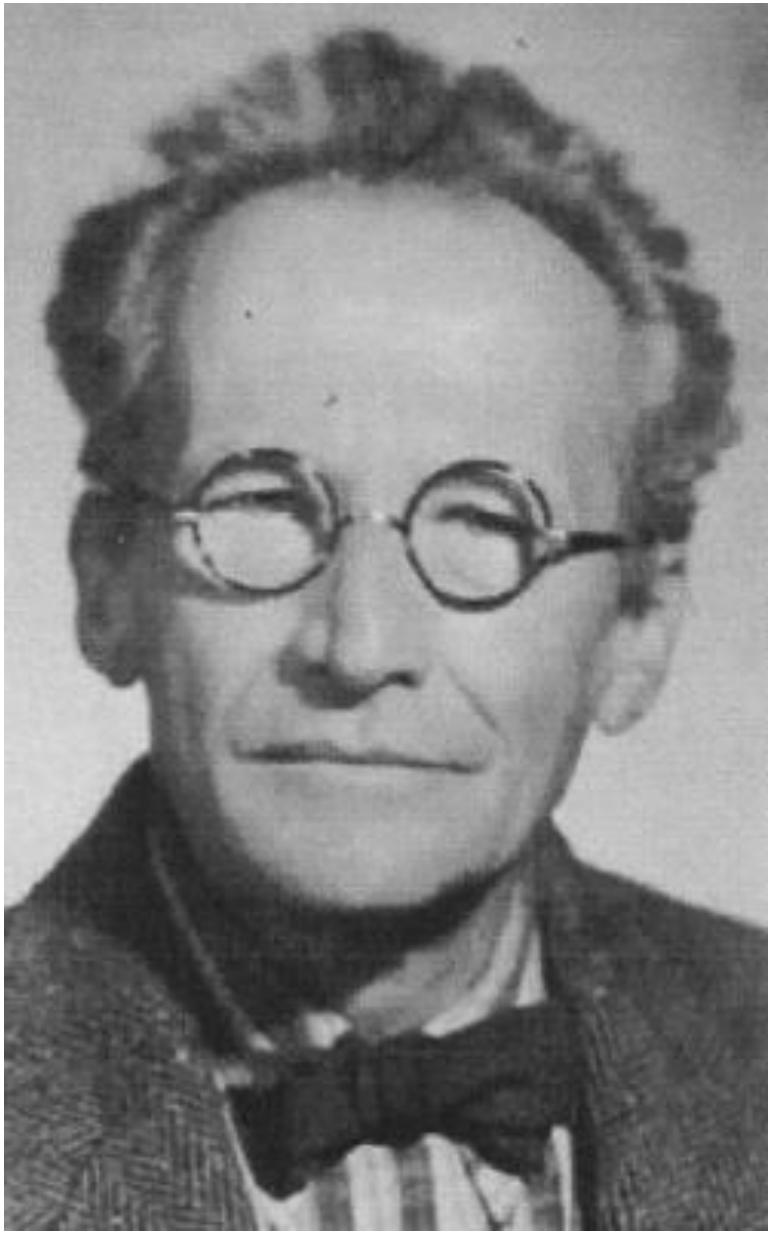
Einleitende Bemerkungen.

Künstliche Befruchtungen, welche an Zierpflanzen desshalb vorgenommen wurden, um neue Farben-Varianten zu erzielen, waren die Veranlassung zu den Versuchen, die her besprochen werden sollen. Die auffallende Regelmässigkeit, mit welcher dieselben Hybridformen immer wiederkehrten, so oft die Befruchtung zwischen gleichen Arten geschah, gab die Anregung zu weiteren Experimenten, deren Aufgabe es war, die Entwicklung der Hybriden in ihren Nachkommen zu verfolgen.

Dieser Aufgabe haben sorgfältige Beobachter, wie Kölreuter, Gärtner, Herbert, Lecocq, Wichura u. a. einen Theil ihres Lebens mit unermüdlicher Ausdauer geopfert. Namentlich hat Gärtner in seinem Werke „die Bastarderzeugung im Pflanzenreiche" sehr schätzbare Beobachtungen niedergelegt, und in neuester Zeit wurden von Wichura gründliche Untersuchungen über die Bastarde der Weiden veröffentlicht. Wenn es noch nicht gelungen ist, ein allgemein giltiges Gesetz für die Bildung und Entwicklung der Hybriden aufzustellen, so kann das Niemanden Wunder nehmen, der den Umfang der Aufgabe kennt und die Schwierigkeiten zu würdigen weiss, mit denen Versuche dieser Art zu kämpfen haben. Eine endgiltige Entscheidung kann erst dann erfolgen, bis Detail-Versuche aus den verschiedensten Pflanzen-Familien vorliegen. Wer die Ar-

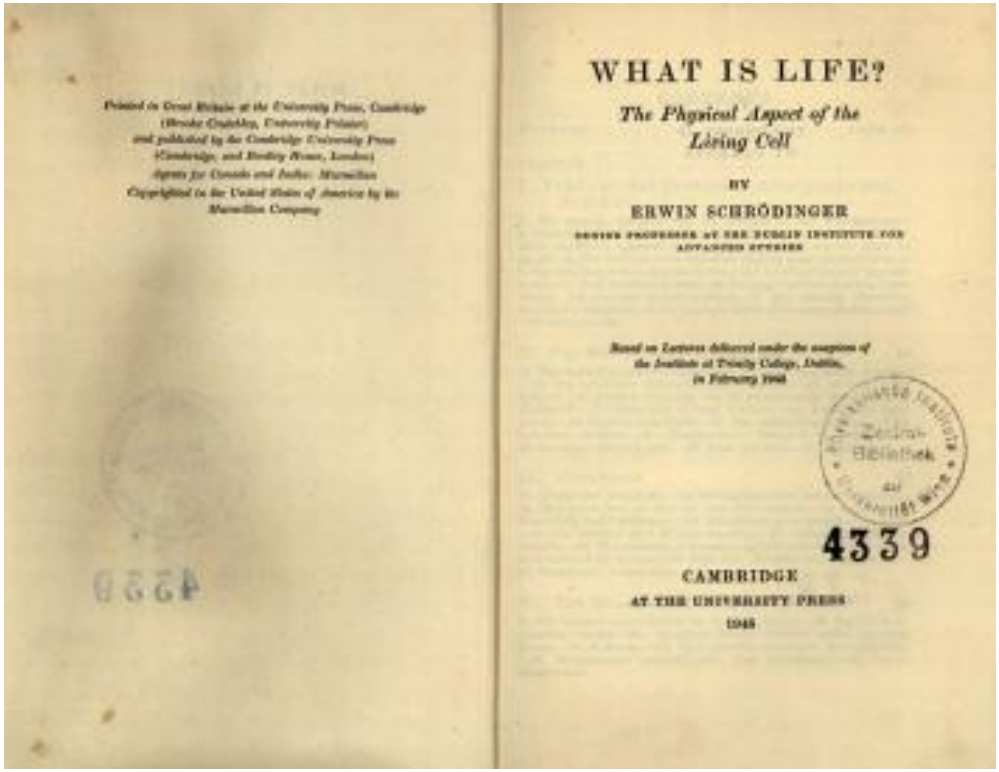
1*

Personaggi, eventi ed esperimenti chiave per la nascita della Biologia Molecolare



Erwin Schrödinger.
(1887-1961) Fisico

"Che cos' è la vita?



WHAT IS LIFE?

The Physical Aspect of the Living Cell

BY

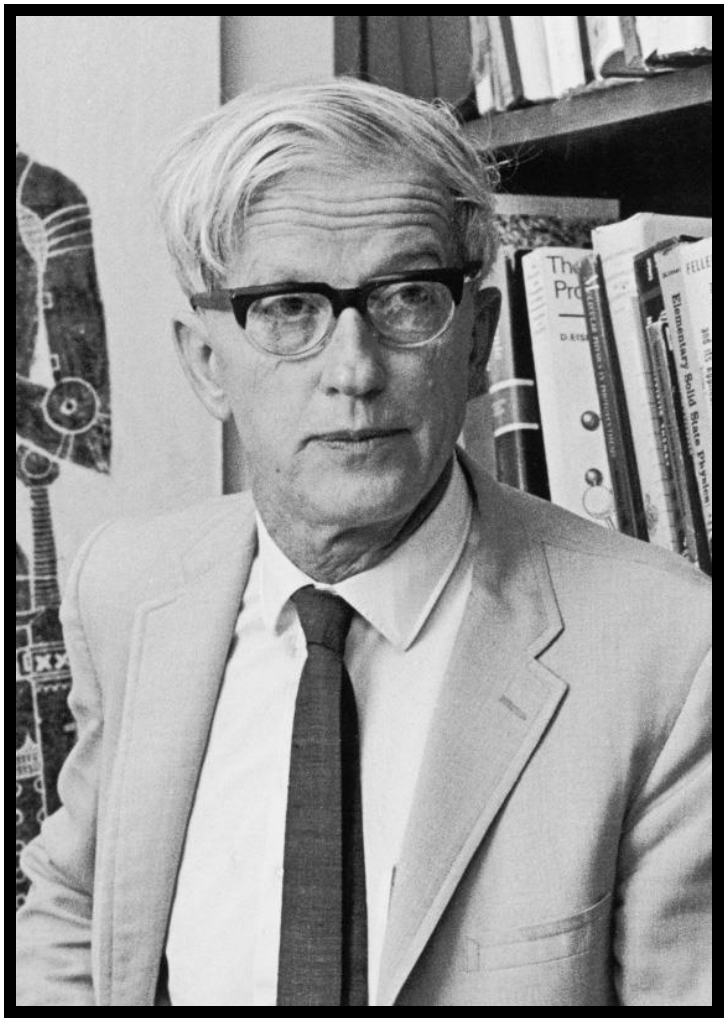
ERWIN SCHRÖDINGER

CAMBRIDGE
AT THE UNIVERSITY PRESS
1948

Solleva il **problema della struttura dei geni**

Genetic code=Morse code?

Fisici che se interessano alla Biologia e al problema biologico della struttura e funzione dei geni (materiale genetico)



Max Delbrűck

(1906-1981) Fisico

Salvador Luria

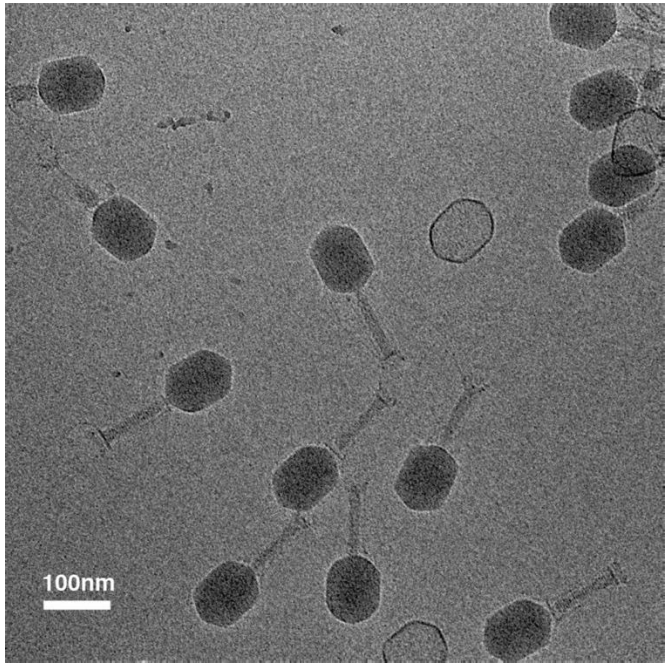
(1912-1991) Medico

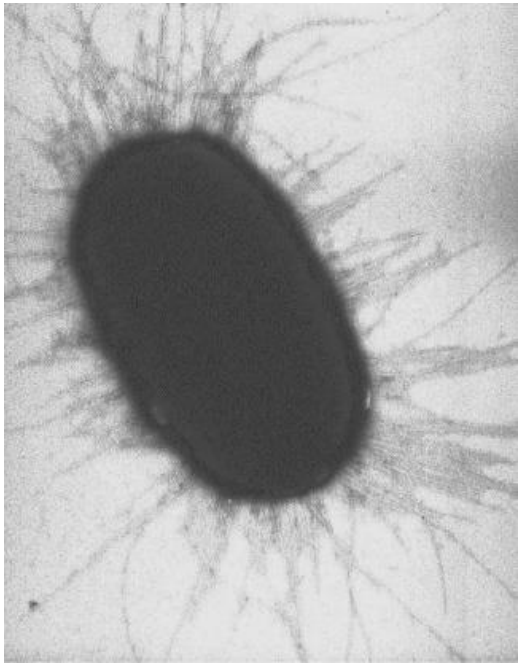
Stati Uniti

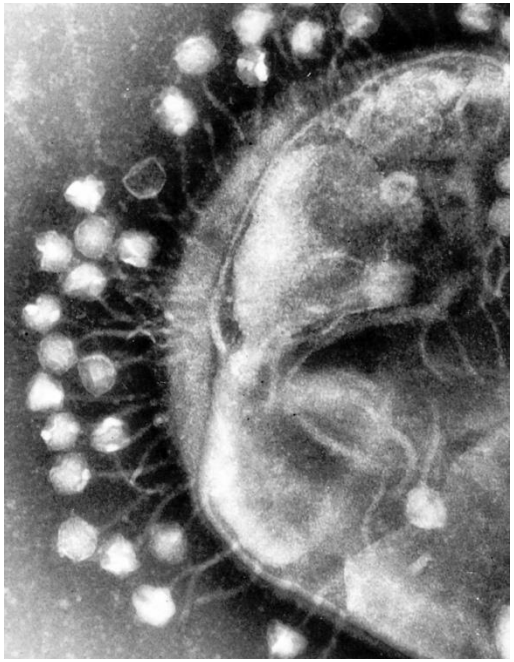
1937

“Gruppo del Fago”

Pensano in studiare un fenomeno complesso come la trasmissione dei caratteri ereditari usando un sistema semplice: BATTERIOFAGI !!



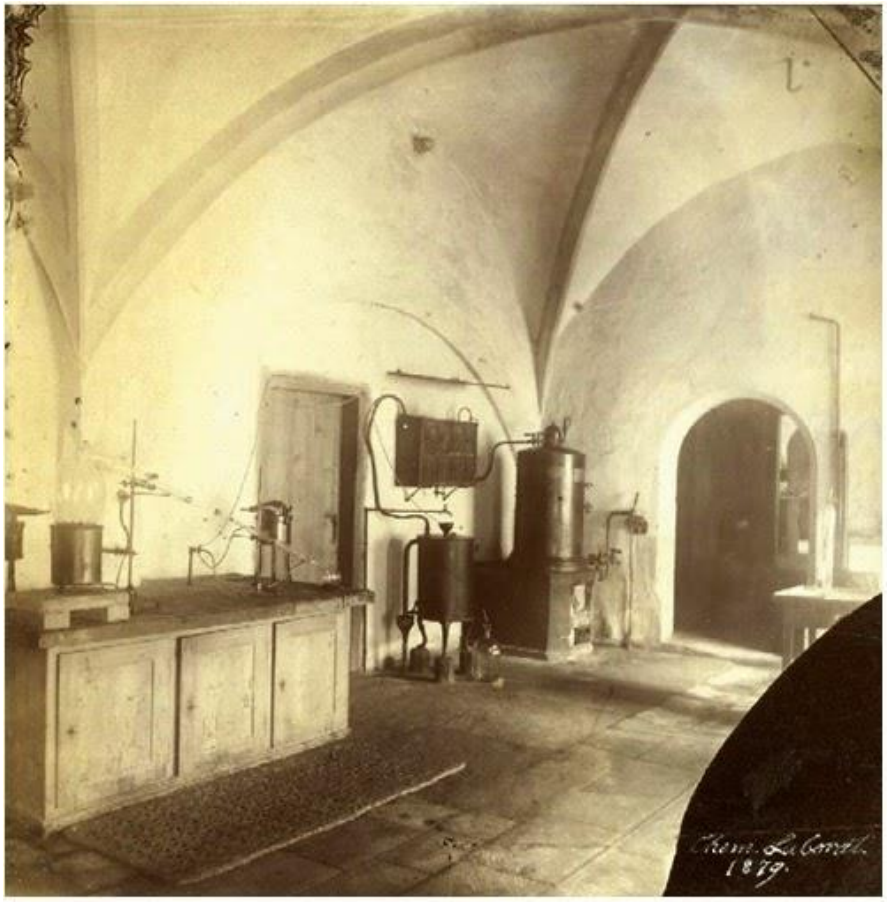




Scoperta del DNA

1869: **Friedrich Miescher**, Biologo Svizzero

- Usando leucociti isola una sostanza resistente a proteasi, la NUCLEINA.
- Studi posteriori rivelarono che la nucleina aveva delle proprietà acide per le quale fu chiamato ACIDO NUCLEICO



Johan Friedrich Miescher
(1844-1895)

Laboratorio en la Universidad Tubingen, en donde Miescher hizo el descubrimiento de la nucleína y un vial con muestras de la nucleína.

Scoperta del “principio trasformante”

1928: **Frederick Griffith,** batteriologo inglese

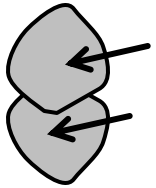
Prima prova che il principio trasformante è il materiale genetico:

“ESPERIMENTO DI GRIFFITH”

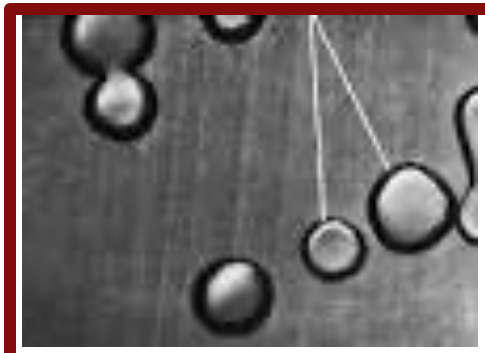
Frederick Griffith
(1879-1941)

Streptococcus pneumoniae

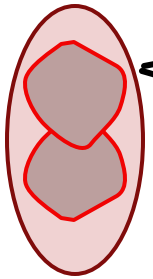
Ceppo **R**_ benigno



Sistema immunitario



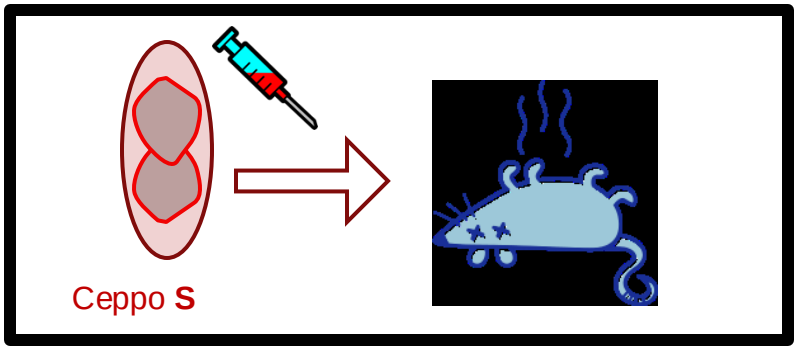
Ceppo **S**_ virulento

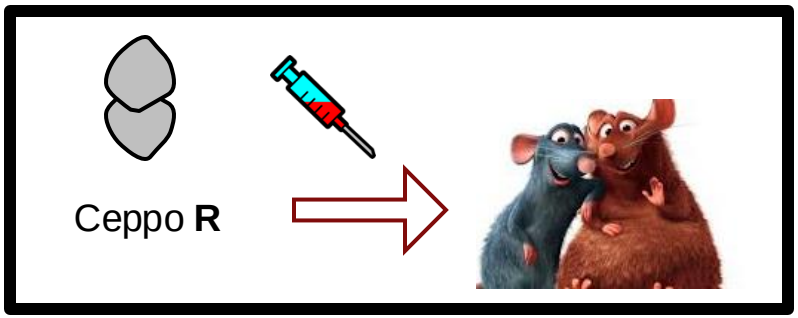


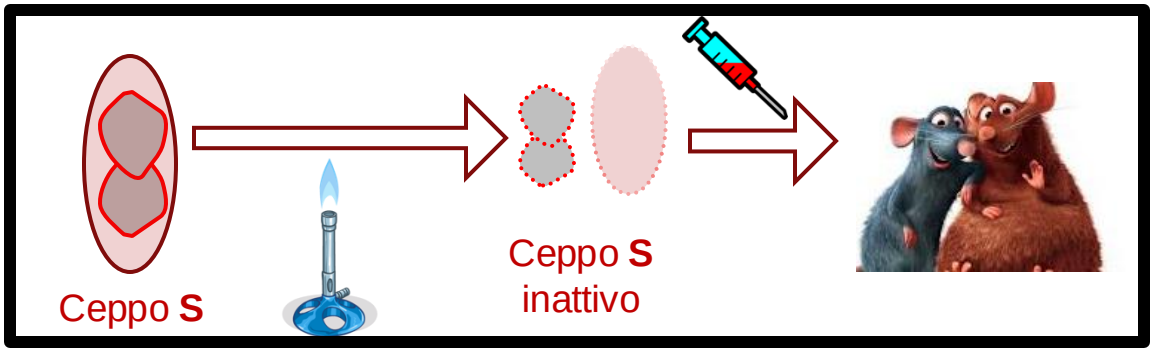
Sistema immunitario

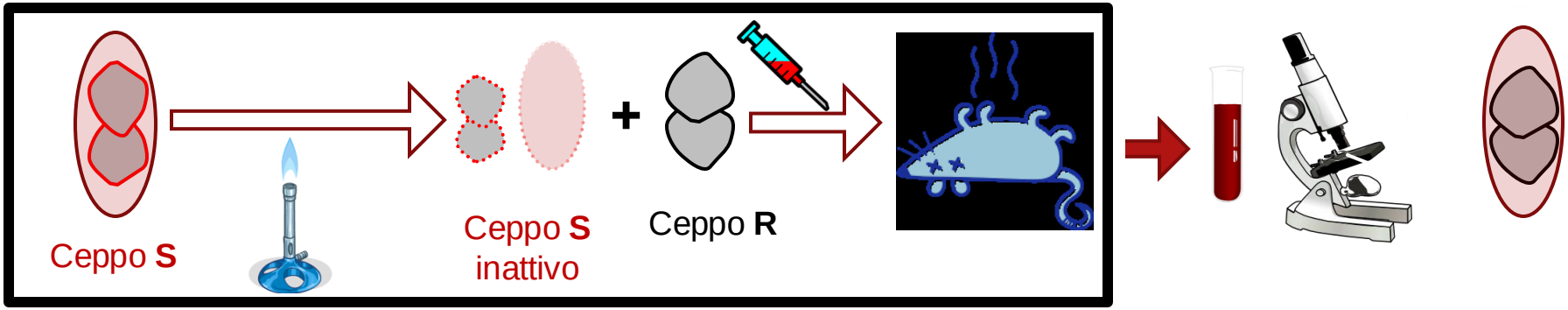
+ Capsula polisaccaridica

“ESPERIMENTO DI GRIFFITH”

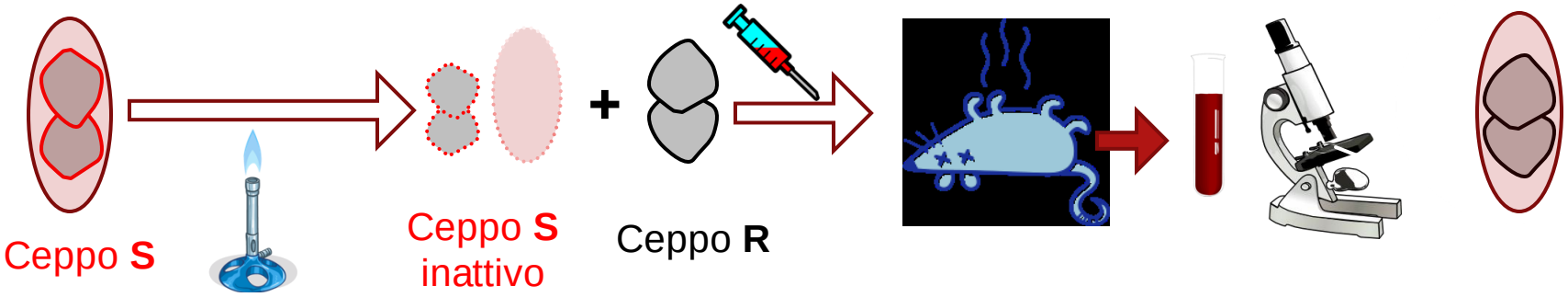








“ESPERIMENTO DI GRIFFITH”



Il Ceppo R acquisisce la capsula polisaccaridica del Ceppo **S**, mantenendo questa caratteristica **per molte generazioni**

Ipotesi: qualcosa del ceppo **S** inattivato viene integrato nel ceppo **R** e lo converte nel ceppo S virulento. Questo elemento sarà chiamato

« PRINCIPIO TRASFORMANTE «

https://www.youtube.com/watch?v=sSa2pHZEwMs

Natura del PRINCIPIO TRASFORMANTE?

Oswald T. Avery
(1877-1955)
Medico canadese

Colin McLeod
(1909-1972)
Genetista

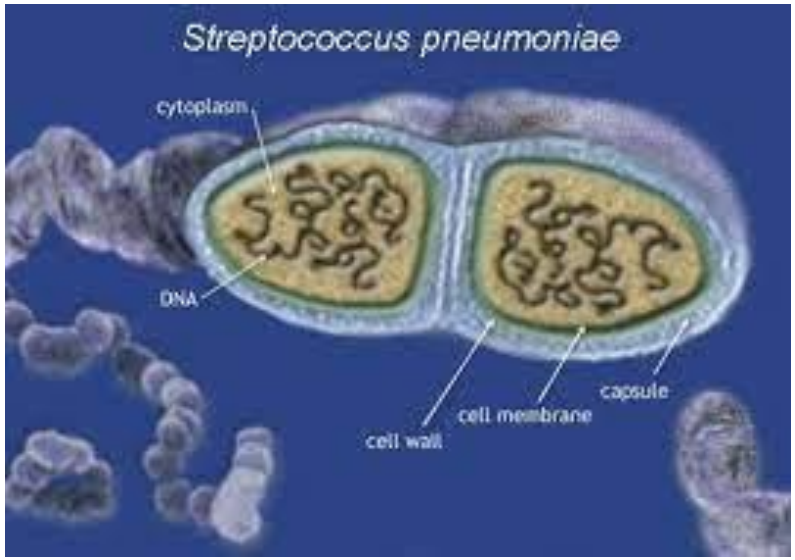
Maclyn McCart
(1911-2005)
Genetista

1944
Dimostrano che il materiale genetico è il **DNA**

« Bomba di Avery «

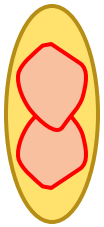
Natura del PRINCIPIO TRASFORMANTE?

Quali dei componenti molecolari presenti nell‘estratto di batteri di ceppo S e’ il responsabile della trasformazione?



« Bomba di Avery «

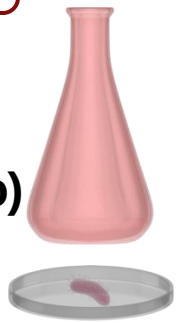
1



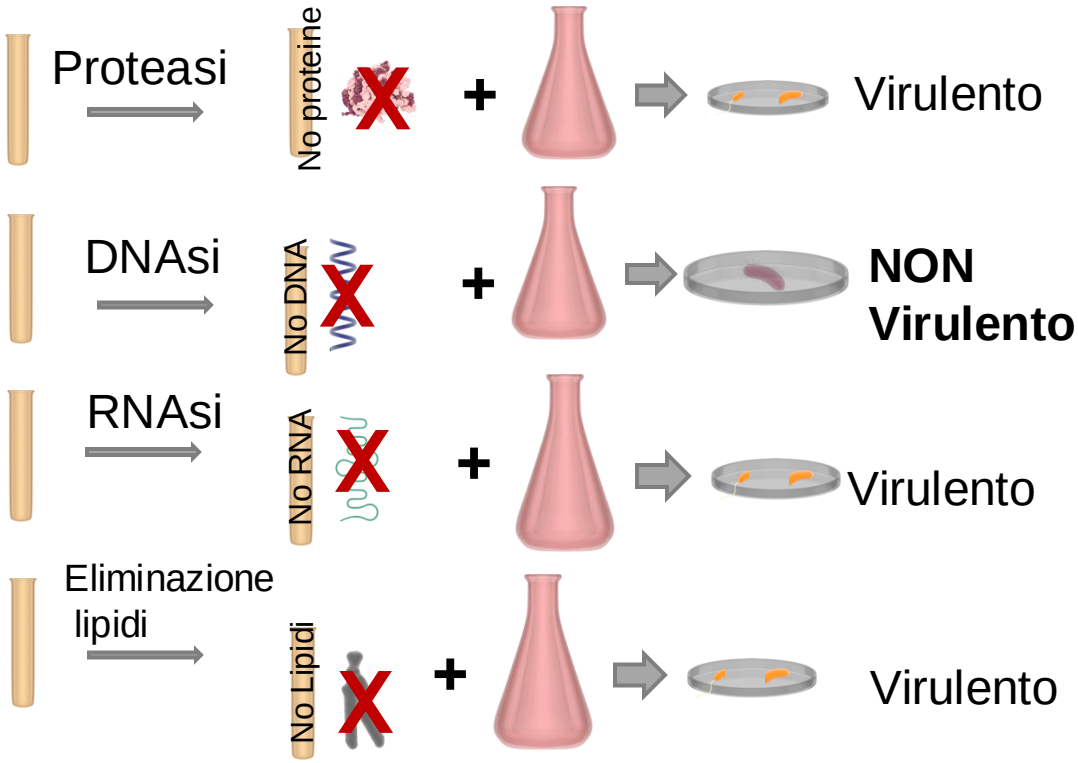
Ceppo **S**
(virulento)

2

Ceppo **R**
(NON virulento)



Estratto Ceppo **S**
(virulento)



Natura del PRINCIPIO TRASFORMANTE

« Bomba di Avery «

Quali dei componenti molecolari presenti nell 'estratto di batteri di ceppo S e' il responsabile della trasformazione?

All'epoca già si conosceva il
DNA e RNA

Dimostrarono che il principio trasformante era il DNA

Non ebbi ripercussione in quanto il DNA era considerata una molecola troppo semplice costituita solo di 4 monomeri. Si pensava più alle proteine, costituite da 20 aa, come linguaggio più efficiente per codificare l'informazione genetica

PRINCIPIO TRASFORMANTE: il DNA

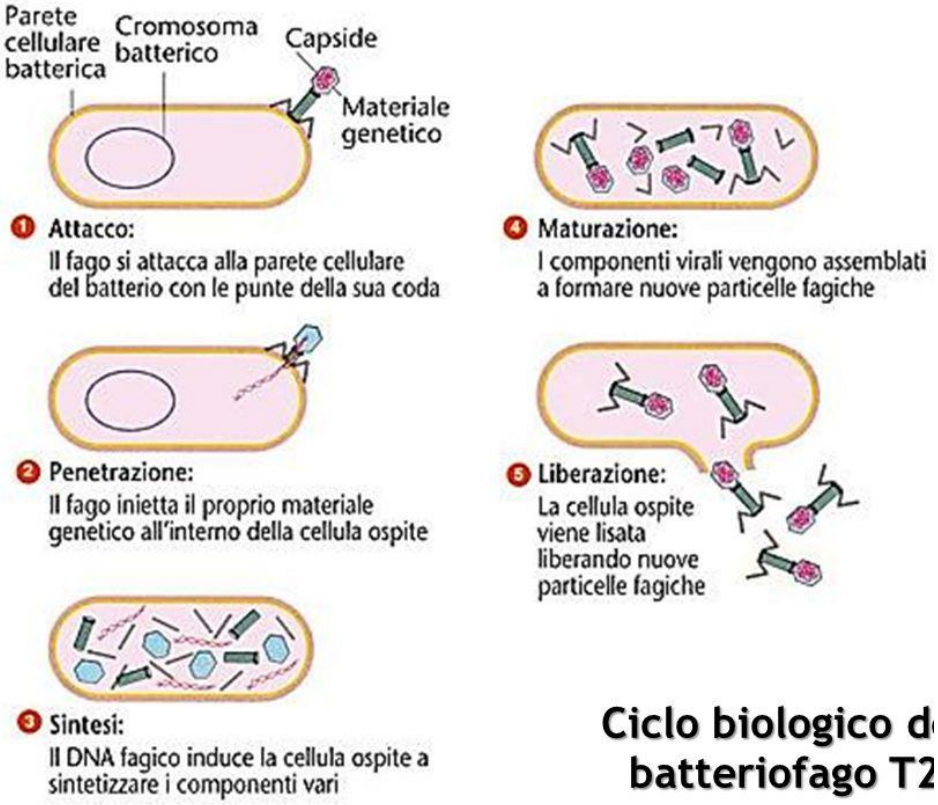
(Gruppo del Fago)

1952

« Esperimento del Frullatore «

Martha Chase
(1927-2003)

Alfred Hershey
(1908-1997)

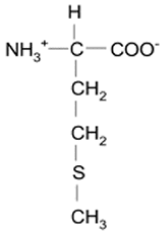


Ciclo biologico d batteriofago T2

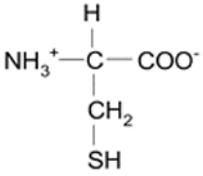
Natura del PRINCIPIO TRASFORMANTE

« Esperimento del Frullatore «

Metionina



Cisteina



https://www.youtube.com/watch?v=hubXqPrslR4

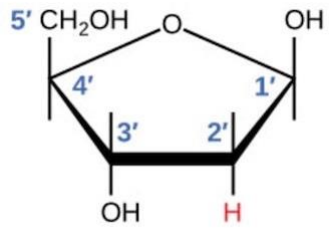
1952: Il DNA è il materiale genetico

Quale è la struttura del DNA?

- Quali **caratteristiche chimiche** permettono al DNA di contenere la informazione genetica?
- Come è questa molecola organizzata dal punto di vista **strutturale** ?

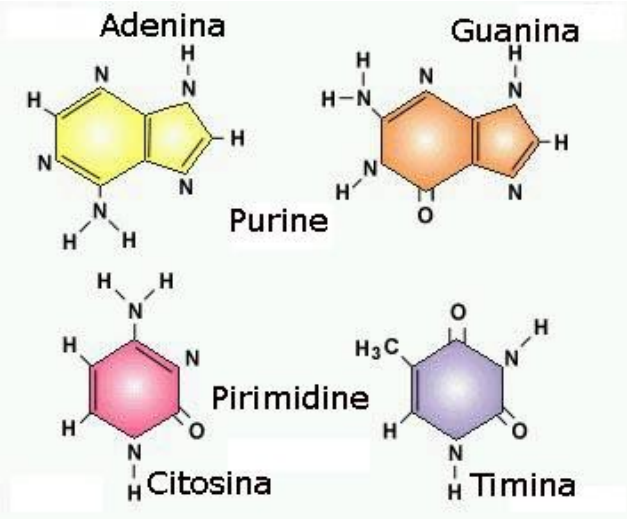
Struttura chimica del DNA

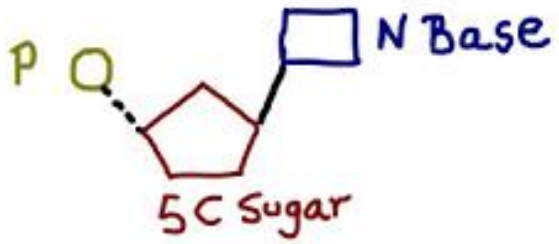
Zucchero: **desossiribosio**



Desossiribosio

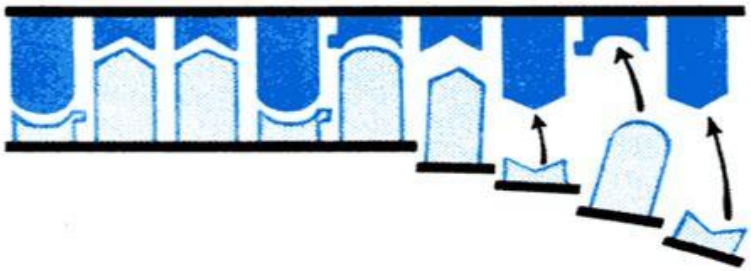
Basi azotate: **A**denina
Guanina
Timina
Citosina

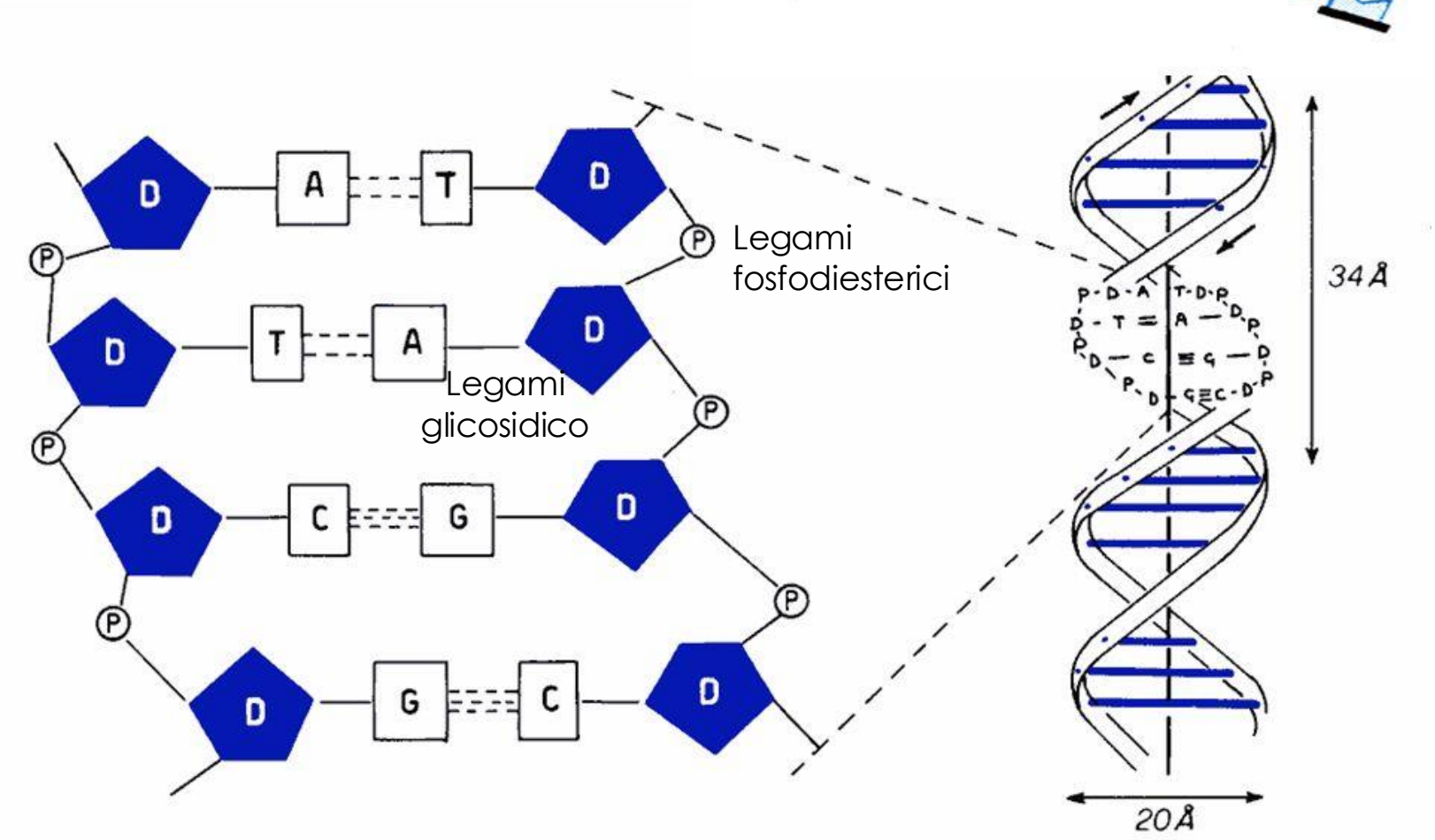




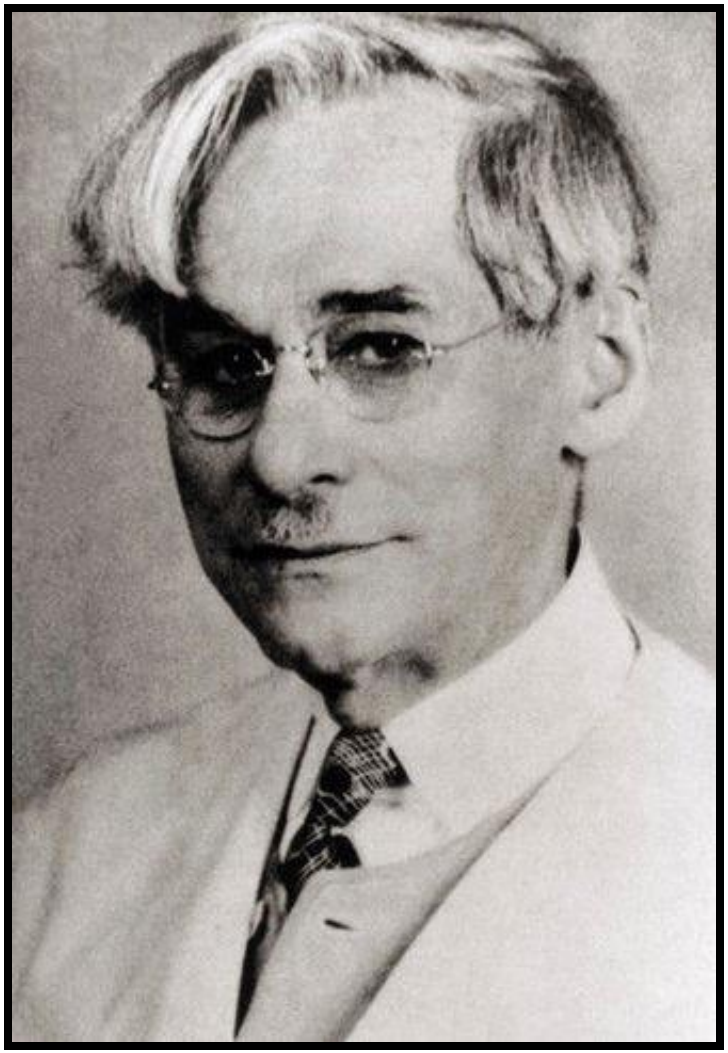
NUCLEO –
SIDE = SUGAR + BASE
TIDE = SIDE + PHOSPHATE

La doppia elica





Struttura chimica del DNA



Phoebus Levene
(1869-1940), Biochimico

- Caratterizzò le molecole di DNA e RNA

- Identificò il ribosio (1909) e il desossiribosio (1929).
- Scoprì che il DNA era formato da:

- 4 basi azotate (adenina, guanina, timina, citosina)
- uno zucchero (desossiribosio)
- fosfato

Scoprì che fosfato-zucchero e base azotate erano legati formando nucleotidi che si univano fra loro attraverso I gruppi fosfato. (Questa struttura era il "backbone" del DNA)

Morì nel 1940 quando ancora non si sapeva che il DNA era il materiale genetico

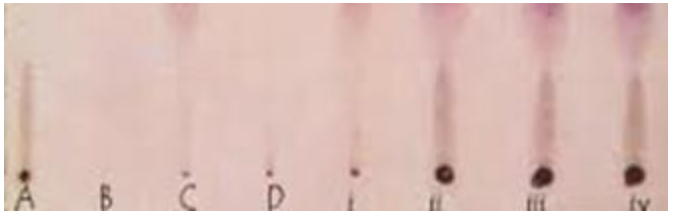
Struttura chimica del DNA

Table 11-1. Molar Properties of Bases* in DNAs from Various Sources

Organism	Tissue	Adenine	Thymine	Guanine	Cytosine
Escherichia coli (K12)	—	26.0	23.9	24.9	25.2
Diplococcus pneumoniae	—	29.8	31.6	20.5	18.0
Mycobacterium tuberculosis	—	15.1	14.6	34.9	35.4
Yeast	—	31.3	32.9	18.7	17.1
Paracentrotus lividus (sea urchin)	Sperm	32.8	32.1	17.7	18.4
Herring	Sperm	27.8	27.5	22.2	22.6
Rat	Bone marrow	28.6	28.4	21.4	21.5
Human	Thymus	30.9	29.4	19.9	19.8
Human	Liver	30.3	30.3	19.5	19.9
Human	Sperm	30.7	31.2	19.3	18.8

* Defined as moles of nitrogenous constituents per 100 g-atoms phosphate in hydrolysate.

SOURCE: E. Chargaff and J. Davidson, eds., *The Nucleic Acids*. Academic Press, 1955.

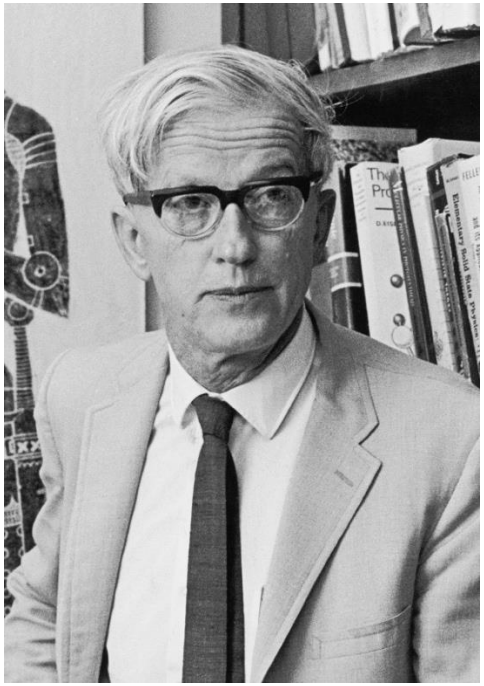


REGOLA DI CHARGAFF (1950)

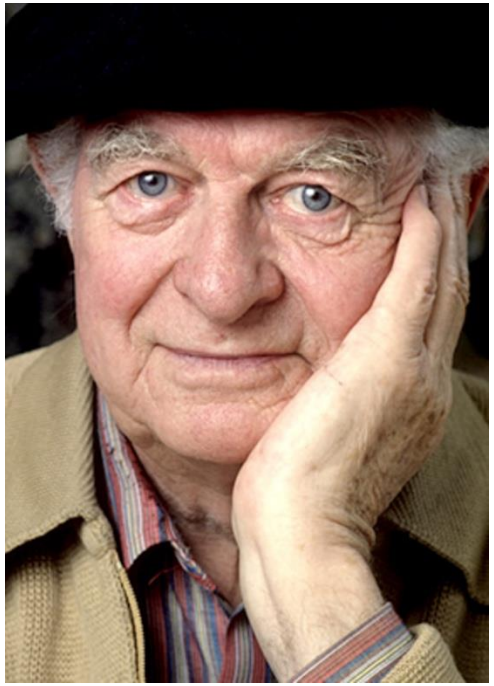
(Regola valida per il DNA, non per il RNA!)

Struttura fisica dei geni

1940



Max Delbrűck
(1906-1981) Fisico



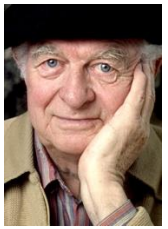
Linus Pauling
(1901-1994)

Alla ricerca del materiale genetico, che ancora si pensava fossero le proteine

Per capire la natura del materiale genetico Delbruck e Pauling ragionarono su 2 proprietà fondamentali che dovrebbe avere il gene:

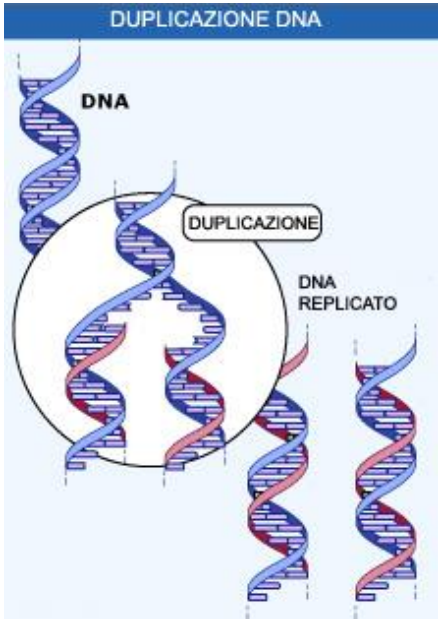
1. Capacità di essere duplicato
2. Deve esprimere un carattere o fenotipo

Struttura fisica del DNA



(1940)

- La duplicazione non è un evento comune in natura a parte la duplicazione del DNA. Non esiste una macchina che sappia duplicarsi.
- Esistono pero stampi che possono produrre il complementare di un oggetto. Ripetendo la procedura otteniamo un oggetto come l'originale.



Propongono che, strutturalmente, un gene deva essere costituito da 2 parti complementari, e che ciascuna possa fare di stampo per la replicazione

THE NATURE OF THE INTERMOLECULAR FORCES OPERATIVE IN BIOLOGICAL PROCESSES

By LINUS PAULING, MAX DELBRÜCK

Science 26 Jul 1940:
Vol. 92, Issue 2378, pp. 77-79
DOI: 10.1126/science.92.2378.77

The examination covers five grades, with salaries ranging from $2,600 to $5,600 a year, less the retirement deduction. Applications should be on file with the Commission's Washington office on August 19. Further information regarding these examinations may be obtained from the Secretary of the Board of U. S. Civil Service Examiners at any first- or second-class post office, or from the U. S. Civil Service Commission, Washington, D. C.

ALPHA EPSILON DELTA, the national honorary premedical fraternity, recently installed a new chapter at the Ohio State University. On May 31 Dr. Emmett B. Carmichael, of the School of Medicine of the University of Alabama, who is executive councilor of the fraternity, installed thirty students and four members of the faculty of the charter group as the Ohio Alpha Chapter. Members of the faculty initiated as honorary members of the fraternity were: Dr. H. E. Setterfield, associate professor of anatomy in the College of Medicine; Dr. Alva W. Smith, associate professor of physics; Dr. Raymond J. Seymour, professor of physiology in the College of Medicine, and Dr. Joseph N. Miller, instructor in parasitology.

THE Desert Laboratory at Tucson, Arizona, has been turned over by the Carnegie Institution of Washington, D. C., to the Forest Service. The Desert Laboratory was concerned with the study of arid and semi-arid regions which comprise almost a fourth of the area of continental United States.

A FELLOWSHIP has been established in the National Research Council for the year 1940–41 through funds provided by the RCA Manufacturing Company, Inc., for the purpose of investigating biological problems such as the structure of viruses, bacteria and other micro-organisms, and tissue cells with the electron microscope. It will carry a stipend of $3,000 and will be known as the RCA Fellowship, to be awarded by the following committee of the National Research Council, who will act also in an advisory capacity to the fellow: Stuart Mudd, *chairman*, M. Demerec, Caryl P. Haskins, J. H. Kempton, C. W. Metz, W. M. Stanley and V. K. Zworykin. The work will be carried on in the Research Laboratories of the RCA in Camden, N. J. In considering candidates, preference will be given to versatile young men of United States citizenship, who have sound training in micro-biology, a doctor's degree and a record of original work. Applications, in quadruplicate, on forms which will be supplied on request, together with supporting documents, should be submitted on or before August 15 to the Division of Biology and Agriculture, National Research Council, 2101 Constitution Avenue, Washington, D. C.

APPROPRIATIONS of the Federal Government to the various states for improvement of game conditions amount to the sum of $2,300,000. Michigan received the largest amount, $127,322; Texas was second with $120,297, and New York third with $120,163. Participating states are required to contribute 25 per cent. of the cost of any project. The total sum available in aid of wild life for the present year is $3,066,667.

DISCUSSION

THE NATURE OF THE INTERMOLECULAR FORCES OPERATIVE IN BIOLOGICAL PROCESSES

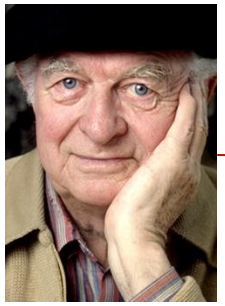
IN recent papers P. Jordan[1] has advanced the idea that there exists a quantum-mechanical stabilizing interaction, operating preferentially between identical or nearly identical molecules or parts of molecules, which is of great importance for biological processes; in particular, he has suggested that this interaction might be able to influence the process of biological molecular synthesis in such a way that replicas of molecules present in the cell are formed. He has used the idea in connection with suggested explanations of the reproduction of genes, the growth of bacteriophage, the formation of antibodies, and other biological phenomena. The novelty in Jordan's work lies in his suggestion that the well-known quantum-mechanical resonance phenomenon would lead to attraction between molecules containing identical groups and to autocatalytic reproduction of molecules. Jordan himself expressed some doubt as to whether resonance attraction could really be operative in this way; after studying the question, we have reached the conclusion that the theory can not be applied in the ways indicated by him, and that his explanations of biological phenomena on this basis can not be accepted. In this note we wish to state our objections to Jordan's hypothesis and to formulate briefly our view of the present status of the chemical problems involved in these phenomena. We shall not discuss here Jordan's biological arguments for the occurrence of autocatalytic reactions, as distinct from the arguments concerning their mechanism.

Let us consider two identical molecules or parts of molecules, A and B, which interact with each other, the interaction being perhaps the electrostatic interaction of electric dipoles in the molecules, as considered by Jordan. If both molecules are in their lowest

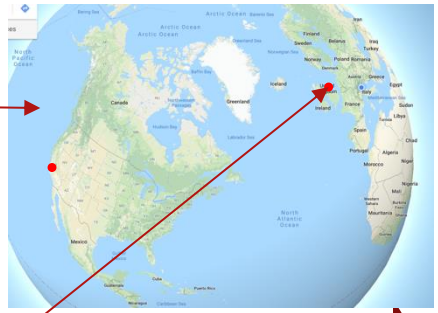
[1] P. Jordan, *Phys. Zeits.*, 39: 711, 1938; *Zeits. f. Phys.*, 113: 431, 1939; *Fundam. Radiol.*, 5: 43, 1939; *Zeits. f. Immun. forsch. u. exp. Ther.*, 97: 330, 1940.

Struttura fisica del DNA

Una volta identificato il DNA come materiale genetico grazie ad Avery, Griffith, and Chase&Hershey, aumenta l'interesse per conoscere la struttura tridimensionale del DNA



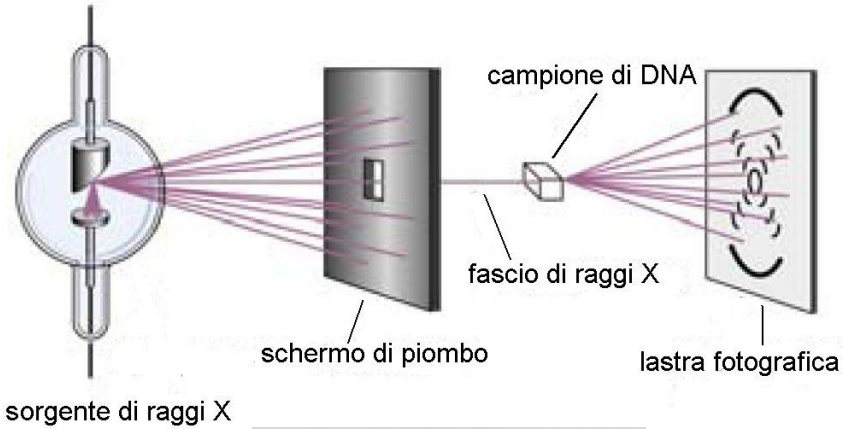
Linus Pauling

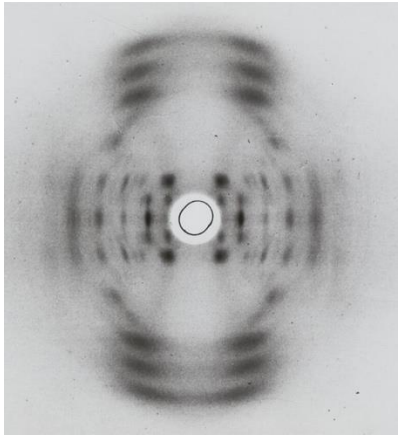


Maurice Wilkins (1916-2004)

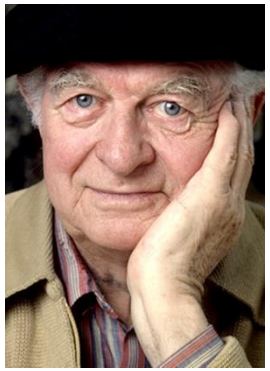
Rosalind Franklin (1920-1958)

Tecnica diffrazione dei raggi X





Struttura a triple elica (1952)



Linus Pauling

A PROPOSED STRUCTURE FOR THE NUCLEIC ACIDS

By Linus Pauling and Robert B. Corey

Gates and Crellin Laboratories of Chemistry,* California Institute of Technology

Communicated December 31, 1952

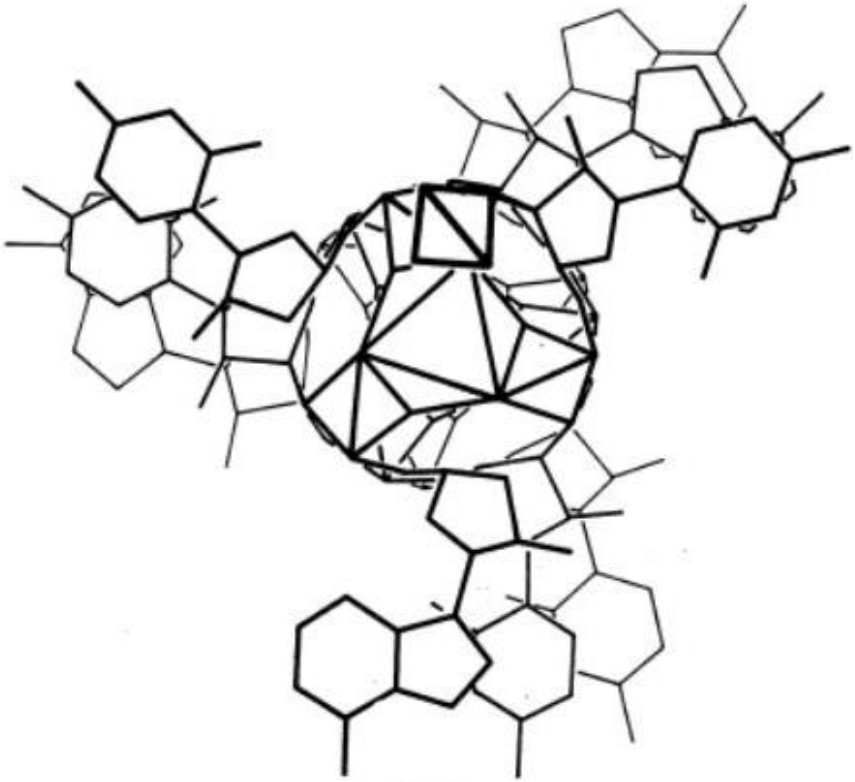


FIGURE 6

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

Propose la **struttura a triple elica con lo scheletro zucchero-fosfato all'interno e le basi al esterno**.

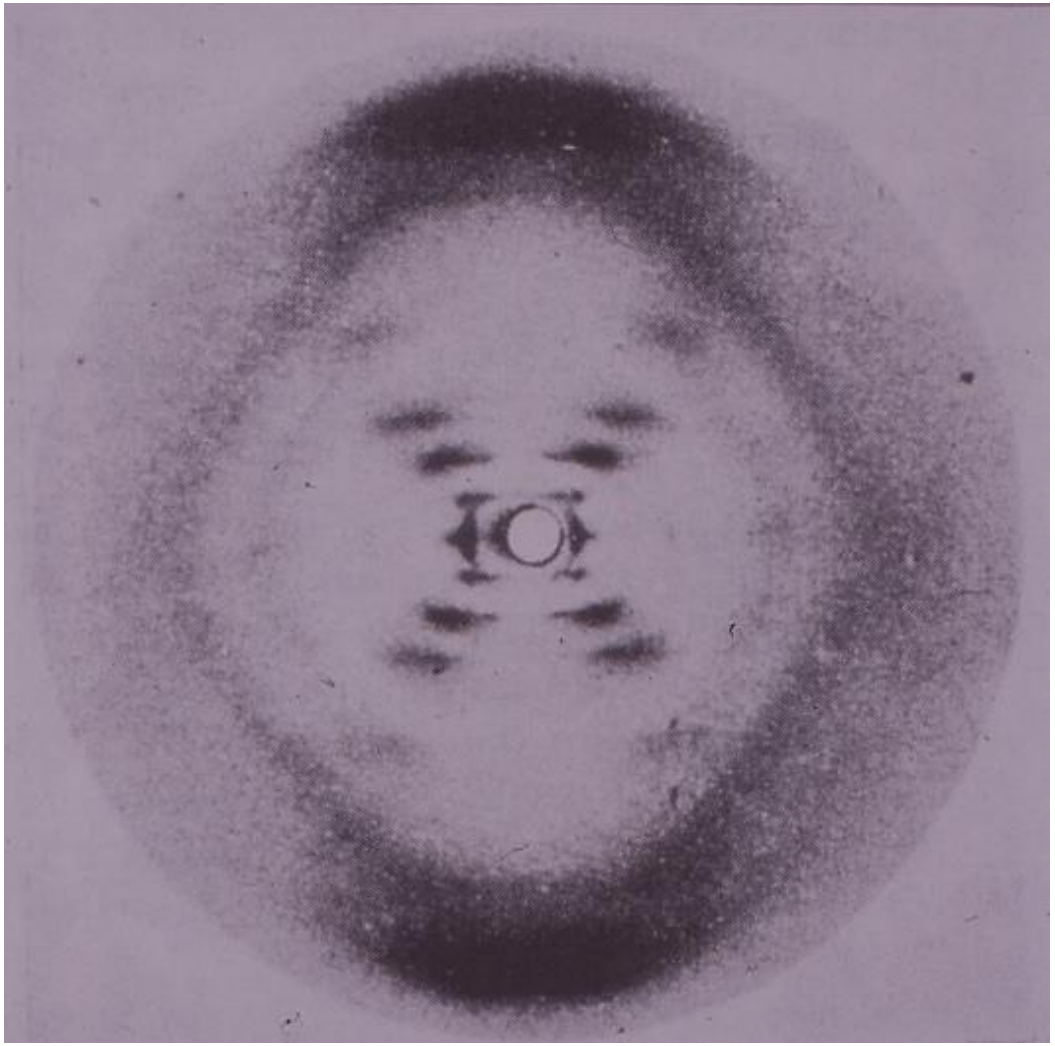
Questo ultimo per dare un senso alla struttura regolare osservata, con un diametro costante, che era difficile da spiegare se le basi fossero state all'interno e considerando che le pirimidine sono più piccole delle purine.

Sbagliata

1952: Rosalind Franklin ottiene la Foto 51

Maurice Wilkins (1916-2004)

Rosalind Franklin (1920-1958)



Crick Watson

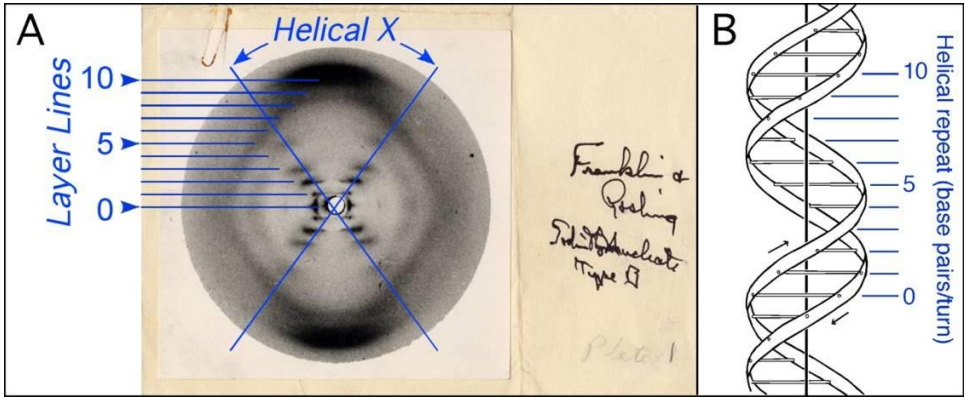
Maurice Wilkins (1916-2004)

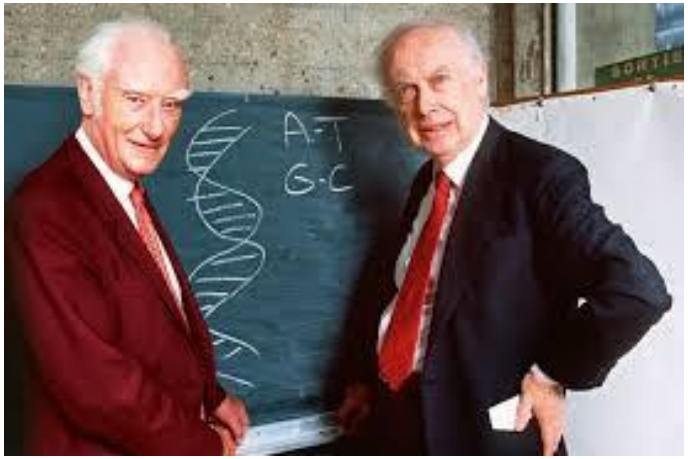
Rosalind Franklin (1920-1958)

Nel fratempo Crick e Watson diventarono collaborator e amici

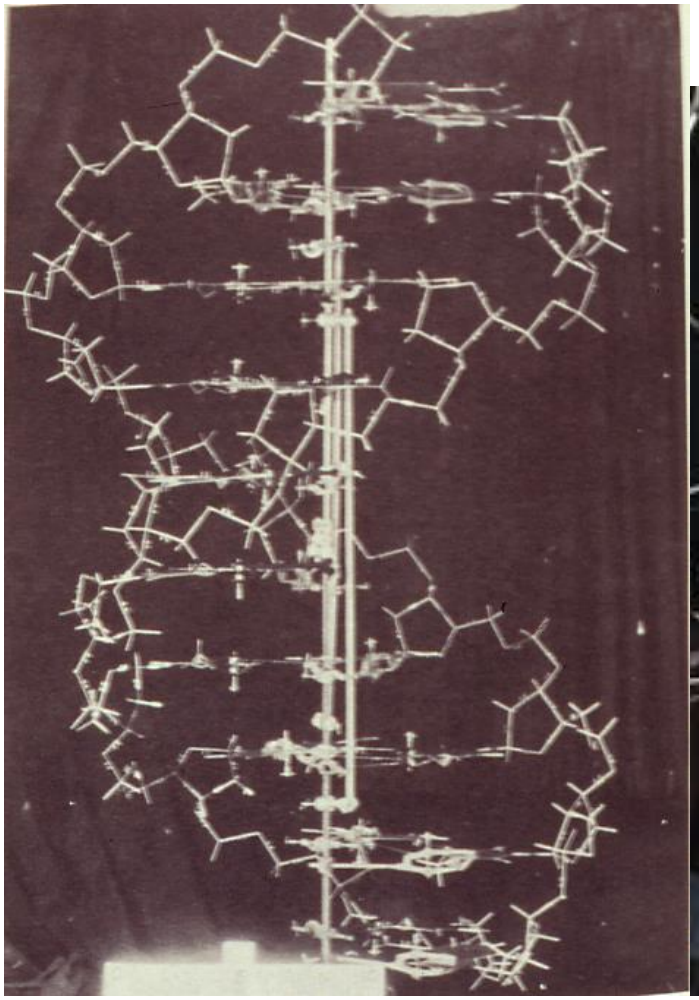
Crick 1962 Watson

Il loro merito fu interpretare l'immagini di Rosalind Franklin, Crick capiì subito che si trattava di una elica. Calcolò i parametri e costruirono dei modelli di cartone.





1993



https://www.dnalc.org/view/15492-Discovering-the-double-helix-structure-ofDNA-JamesWatson-video-with-3D-animation-and-narration.html

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.

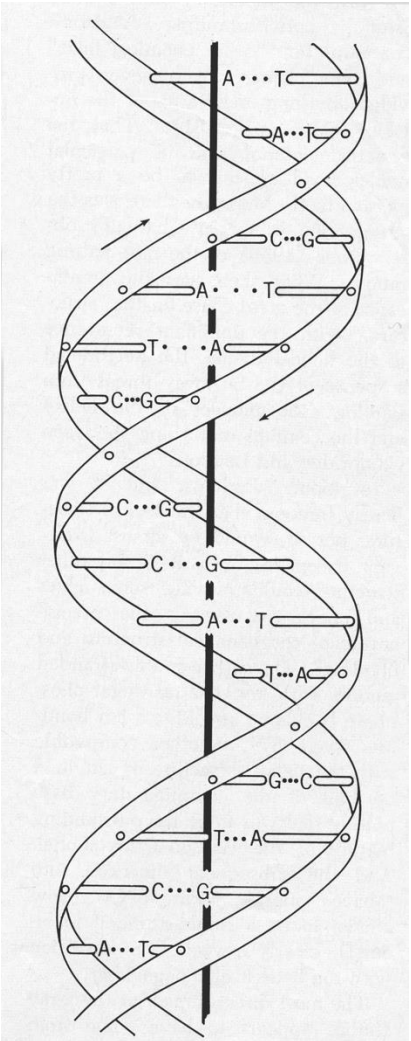
It is probably impossible to build this structure with a ribose sugar in place of the deoxyribose, as the extra oxygen atom would make too close a van der Waals contact.

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



DOUBLE HELIX. The two sugar-phosphate backbones twist about on the outside with the flat hydrogen-bonded base pairs forming the core. With these base pairs as the steps the structure resembles a helical staircase

Nobel Prize in Medicine 1962

Francis Crick

James Watson

Maurice Wilkins

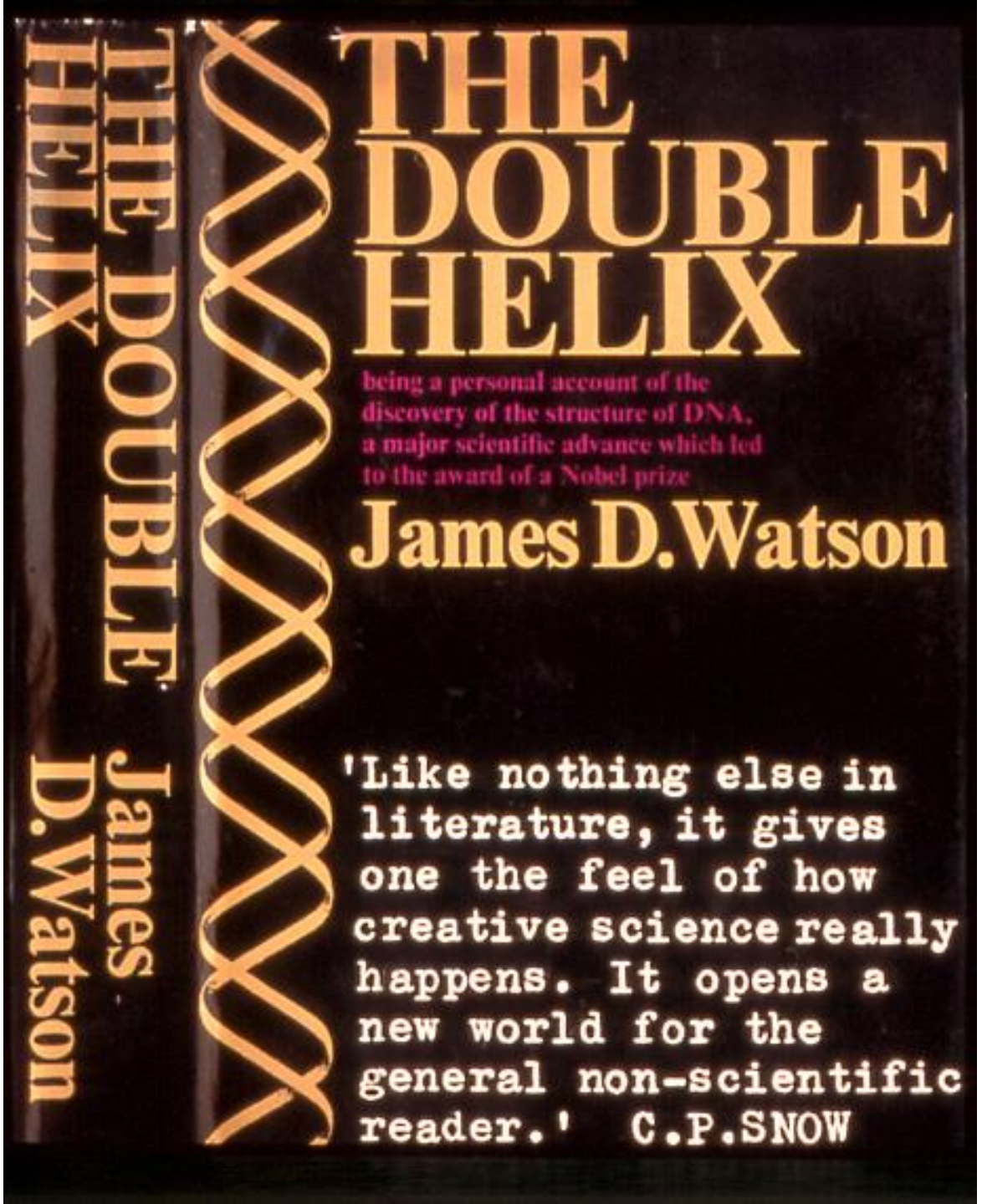
Rosalind Franklin

Qualche anno fa, mentre stava visitando l'Istituto di Medicina Molecolare dell'Università di Oxford University, Jim Watson fu invitato a dare un seminario agli studenti e ai ricercatori.

Alla fine dei suoi discorsi stimolanti sulla etica del Progetto Genoma Umano, un timido giovane studente, con timore reverenziale si alzò in piedi e disse:"Dr. Watson lei ha fatto, nella biologia, la più importante scoperta degli ultimi cento anni e forse di sempre. Di quale natura potrebbe essere una scoperta di uguale importanza per i prossimi cento anni?"

Dopo un interminabile silenzio, durante il quale gli occhi di Watson ruotavano verso il soffitto e 400 futuri scienziati si muovevano nervosamente sul ciglio delle loro sedie, lui replicò:

Mah !! Non credo che ce ne sarà un'altra!


THE DOUBLE HELIX
James D. Watson
THE DOUBLE HELIX
being a personal account of the discovery of the structure of DNA, a major scientific advance which led to the award of a Nobel prize
James D. Watson
'Like nothing else in literature, it gives one the feel of how creative science really happens. It opens a new world for the general non-scientific reader.' C.P.SNOW

1954-1967: una cascata di scoperte

- **1956:** Arthur Kornberg e Severo Ochoa scoprono la **DNA polimerasi** (Nobel nel 1959)
- **1957**: Crick & Gamov: Flusso della informazione
- **1958:** Matthew Meselson e Franklin Stahl producono l'evidenza sperimentale che dimostra l'ipotesi di Watson e Crick sulla **replicazione semiconservativa del DNA**.
- **1960**: Francois Jacob, André Lwoff e Jacques Monod descrivono il **modello dell'operone** definendo le **basi molecolari del controllo dell'espressione genica** (Nobel nel 1965)
- **1961:** Sidney Brenner con Jacob e Meselson e, indipendentemente, Watson con Walter Gilbert scoprono **l'RNA messaggero**
- Brenner (Nobel nel 2002 con Horovitz e Sulston) e Crick svelano le **basi del codice genetico**.

- **1966:** Marshall Nirenberg inizia la **decifrazione del codice genetico**, un lavoro che giungerà al termine 5 anni dopo grazie al contributo di Har Gobind Khorana (entrambi Nobel nel 1968 con Robert W. Holley)
- **1967:** Mark Ptashne e Walter Gilbert, indipendentemente, **isolano le proteine regolatorie predette dagli esperimenti di Jacob e Monod**
- **1970:** Prima avvisaglia della rivoluzione: Howard Temin e David Baltimore isolano la **trascrittasi inversa** (Nobel nel 1975 con Dulbecco), un enzima che apparentemente rovescia il flusso dell'informazione genica affermato dal dogma centrale.
- **1971:** Stanley Cohen, Annie Chang e Herbert Boyer usano i cosiddetti **enzimi di restrizione** (scoperti alla fine degli anni '60: Nobel nel 1978 a Werner Arber, Hamilton Smith e Daniel Nathans) per un *cut and paste* del DNA: viene prodotta la prima molecola di DNA ricombinante. E' l'inizio ufficiale dell'era della biotecnologie.

1972: **Paul Berg** and co-workers create the first recombinant DNA molecule (*PNAS*).

1980:**Allan Maxam** and **Walter Gilbert** at Harvard University and **Frederick Sanger** at the U.K. Medical Research Council (MRC) independently develop methods for sequencing DNA (*PNAS*, February; *PNAS*, December).

1982: **Akiyoshi Wada**, now at RIKEN in Japan, proposes automated sequencing and gets support to build robots with help from Hitachi.

1984: MRC (Medical research Council) scientists decipher the complete DNA sequence of the Epstein-Barr virus, 170 kb (*Nature*).

1972: **Kary Mullis** and colleagues at Cetus Corp. develop **PCR**, a technique to replicate vast amounts of DNA

1985-2001: **Human Genome Project (HGP)**
The HGP consortium publishes its working draft in *Nature* (15 February 2021), and Celera Genomics publishes its draft in *Science* (16 February 2021).