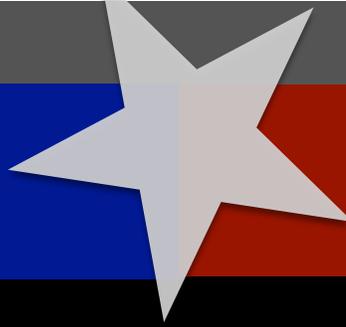
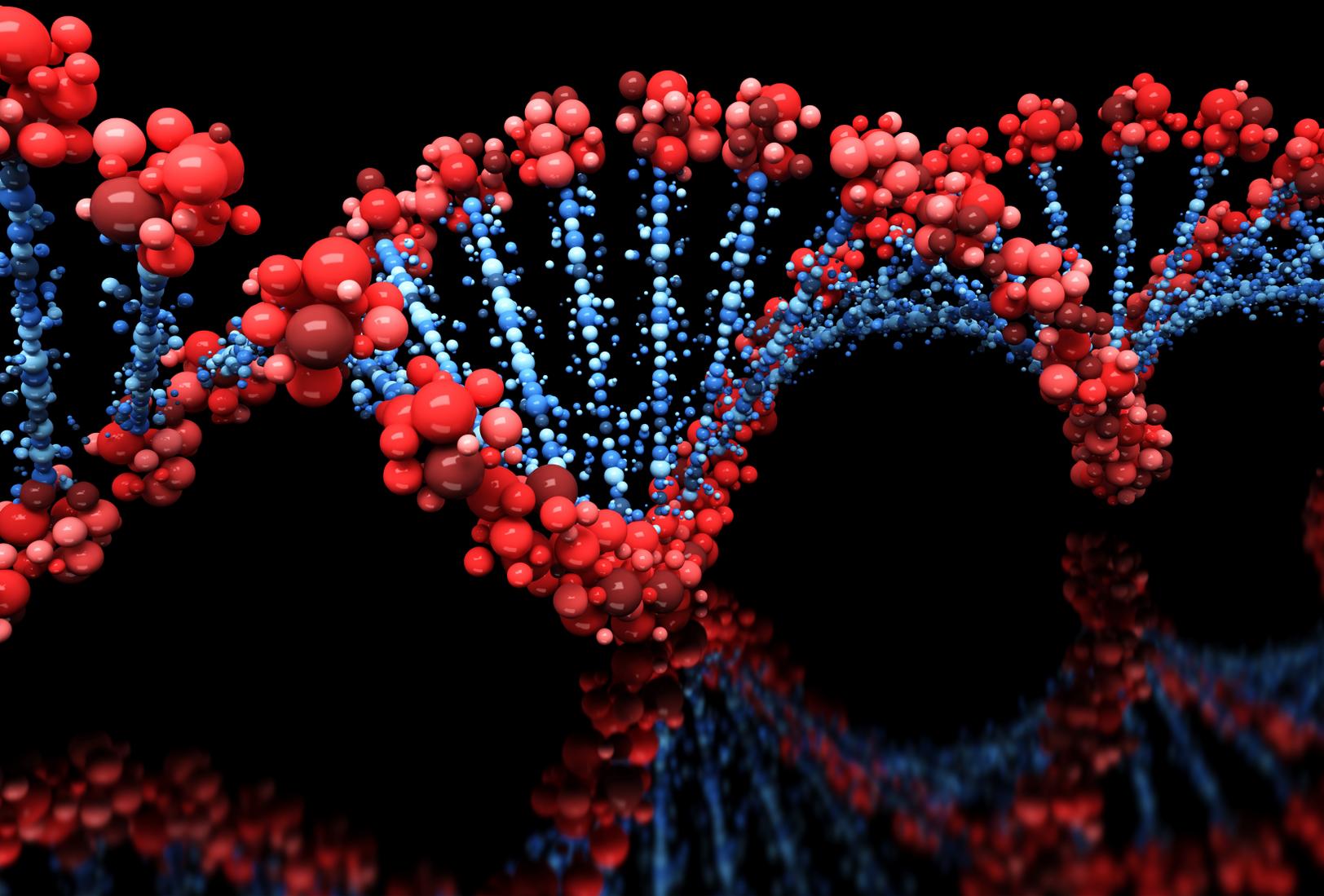


Presidential Series
Field Trip Enhancement Program



Race for the Double Helix



Presented by the
Eisenhower Foundation



Race for the Double Helix

A month after President Eisenhower was inaugurated, one of the most important discoveries in the scientific field occurred. The discovery of DNA's chemical structure — the double helix — by Francis Crick and James Watson altered molecular biology forever. However, that race for the double helix discovery was peppered with competition and sexism.

In this program, students will first be introduced to people behind the discovery of DNA's chemical structure and the roles they played. Next, students will recreate Watson's discovery of the hydrogen bonding between nucleotides. Finally, students are encouraged to use this lesson about past scientific discoveries and presidential support to connect with current scientific news and how governmental decisions can impact scientific research.

Objectives: The student will:

- Analyze a variety of primary and secondary sources to gain knowledge of the past
- Recognize the contributions of Pauling, Rosalind Franklin and Maurice Wilkins, Watson and Crick that led to uncovering the structure of DNA
- Learn the base-pairing rule, its underlying reason and its effect on the DNA structure.
- Explain how Watson and Crick combined their modeling approach with other sources of data to solve the structure of DNA
- Link current scientific committees/research to past departments and agencies created by President Eisenhower

Acknowledgements:

This unit was produced in June 2017 by the Eisenhower Foundation.

Shannon Heintz, writer

Mitzi Bankes Gose, editor

Thanks to the Eisenhower Presidential Library, Museum and Boyhood Home for support.



Contents:

- 2-4 Lesson Plan
- 5-7 Glossary of Key Scientific Terms
- 8 Background Information
- 9-10 Race for the Double Helix Puzzle Pieces Table
- 11-12 Answer Key to Puzzle Pieces Table
- 13 Primary Documents List
- 14-37 Primary Documents
- 38-40 D.N.A. Puzzle Pieces Activity & Key
- 41 In Conclusion
- 42 Extension

Target Grades: High School: 9-12

Common Core State Standards		
Grades 9-12	RI - Reading Informative Text	9-10:1,4,5,7 11-12: 1,2,3,4,7
	RST - Science and Technical Subjects	9-10:1,2,4,5,6,8 11-12: 1,2,4,7,8,9
	SL - Speaking and Listening	9-12: 1a,1d,2,4
	RH - History/Social Studies	9-10:1,2,4,6,7,8 11-12: 1,2,6,7,8

Natl. Curriculum Standards for Social Studies		
High School	Time, Cont., and Change	Theme 2
	Ind., Groups, and Inst.	Theme 5
	Science, Tech and Society	Theme 8

Next Generation Science Standards		
High School	Life Sciences : Molecules to Organisms/ Structures and Processes	HS-LS 1-1, 1-6



Lesson Plan

1. Show a segment of the HHMI documentary, “The DNA Double Helix Discovery” in order to give background information about the key players and the competition involved in the race to deduce the chemical structure of DNA. This video can be found at: www.youtube.com/watch?v=ivm3od_UmFg&t=235s. Show the first 12 minutes and 34 seconds of the video.

12 minutes

Stop the video before Jim Watson goes to the lab on a Saturday morning and analyzes cardboard cut outs of the base pairs. (The last few minutes of the video are basically the answer to the D.N.A. puzzle piece activity later in the lesson, so this part of the video should be shown after the puzzle activity)

Teacher Note: It may be helpful if students have a basic knowledge of D.N.A. and its structure prior to this lesson.

2. Discuss the term “primary source.”
3. Assign each student or a small group of students (2-3) one of the primary documents listed below and provide copies for them. These primary sources can be found on pages 14-37.

3 minutes

- Frederick Griffith’s “Significance of Pneumococcal Types”
- Maclyn McCarthy and Oswald Avery’s “Studies on the Chemical Nature of the Substance Inducing Transformation of Pneumococcal Types”
- Erwin Chargaff’s “Chemical Specificity of Nucleic Acids and Mechanism of the Enzymatic Degradation”
- Linus Pauling and Robert B. Corey’s “A Proposed Structure for the Nucleic Acids”
- A.D Hershey and Martha Chase’s “Independent Functions of Viral Protein and Nucleic Acid in Growth of Bacteriophage”
- R. E. Franklin’s D.N.A. Crystallography Calculations (Lab Notebook)
- M.H.F Wilkins and R.G. Gosling’s “Physical Studies of Nucleic Acid”
- J.D. Watson and F.H.C. Crick’s “Genetical Implications of the Structure of Deoxyribonucleic Acid”

4. This exercise will provide students with the perspective of scientists and the race to deduce the structure of D.N.A. Direct students to read and examine their assigned primary document using the “Race for the Double Helix: Pieces of the Puzzle” worksheet. Emphasize to students two things: 1). They are reading dense, scientific literature, so if they don’t understand every word, that is fine. They are trying to extract a small nugget of big picture knowledge from the document. 2). Explain to them to pay special attention to the “sticky notes” on each document, these guide the reader to the specific passage in the article that details each scientists’ contribution.

15 minutes

5. After students or groups have analyzed their assigned primary document and completed their portion of the “Race for the Double Helix” worksheet, have students/groups report their findings to the entire class. As students are detailing their assigned scientists’ findings, other students should complete that section of the worksheet. It may be helpful for teachers to add to the discussion using the included answer key if students are struggling.

10 minutes

6. It is now time for students to step into James Watson and Francis Crick’s shoes. One of their dilemmas was how the base pairs of D.N.A. are bonded together. Provide students with templates of D.N.A base pairs Adenine, Thymine, Cytosine and Guanine along with four deoxyribose, four phosphates (P) and five hydrogen bonds (H bond). Share with students that they are going to imagine they are James Watson walking into the Cavendish Lab early Saturday morning February 28, 1953 at the University of Cambridge in England. They should attempt to solve the base pairing dilemma by rearranging the pieces of the puzzle to correctly create a small portion of D.N.A. with knowledge gained from scientists discussed earlier in the lesson. Again, it is perfectly acceptable for students to struggle and some may not obtain the correct answer, but this can then be an opportunity for teachers to explain to students they are in a scientific role, trying to figure out a problem, which is not always easy.

20 minutes

7. After students have attempted the D.N.A. puzzle activity, show the last 4 minutes and 36 seconds of the video showing James Watson’s explanation of how the bases (A, T, C and G) pair together. This explanation, along with the provided answer key will provide students the correct arrangement of their D.N.A. template pieces. This last portion also explains the impact of this discovery for the future of science.

10 minutes

8. To conclude the activity, teachers should read the “In Conclusion” information to students. Ask students to listen as the teacher reads the information and to pick out at least three to four scientific contributions that President Eisenhower and his administration helped to achieve. This establishes the importance of President Eisenhower’s creation of the Department of Health, Education and Welfare, the Advanced Research Project Agency, the National Defense Education Act, and NASA to historical scientific discoveries and their link to current scientific advancements

5 minutes

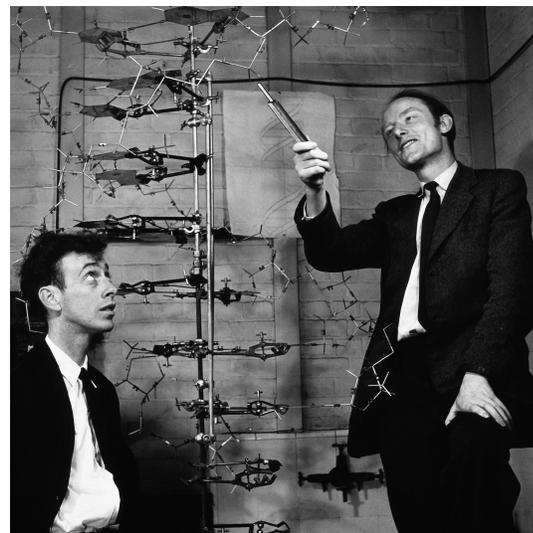


“Templates from Crick and Watson's DNA molecular model, England, 1953”

From: www.sciencemuseum.org.uk/broughttolife/objects/display?id=92854

“Race for the Double Helix” Watson and Crick’s 1953 model of D.N.A.

From: <http://dataphys.org/list/watson-and-cricks-3d-model-of-dna/>



Glossary of Scientific Terms

This glossary may assist teachers in facilitating the lesson. Key vocabulary terms from each primary document are defined below. Terms are in alphabetical order and are sorted according to the document in which they are located.

Document 1: Griffith's Experiment:

Inoculation - The process of introducing an antigenic substance or vaccine into the body to trigger immune response against a specific disease.

(from: <http://www.biology-online.org/dictionary/Inoculation>)

Pneumococcus - Bacteria that can cause pneumonia, sinusitis, middle ear infections, meningitis. formal name for this bacteria today is *Streptococcus pneumoniae*.

(from: <http://www.medicinenet.com/script/main/art.asp?articlekey=4957>)

Septicemia - Systemic disease associated with the presence and persistence of pathogenic microorganisms or their toxins in the blood.

(from: <http://www.biology-online.org/dictionary/Septicaemia>)

Strain - A genetic variant or subtype of a micro-organism (e.g., virus or bacterium or fungus)

(from: [https://en.wikipedia.org/wiki/Strain_\(biology\)](https://en.wikipedia.org/wiki/Strain_(biology)))

Virulent - Of a pathogen, especially a virus; highly infectious

(from: <http://en.oxforddictionaries.com/definition/virulent>).

Document 2: Avery's Experiment:

Deoxyribonucleic acid - A double-stranded nucleic acid that contains the genetic information for cell growth, division, and function (D.N.A.)

(from: <http://www.biology-online.org/dictionary/DNA>)

Enzymatic - Referring to enzymes (a biological catalyst) ability to degrade the molecule.

Pneumococcus (appears as pneumococcal in article) - Bacteria that can cause pneumonia, sinusitis, middle ear infections, meningitis. formal name for this bacteria today is *Streptococcus pneumoniae*.

(from: <http://www.medicinenet.com/script/main/art.asp?articlekey=4957>)

Transforming substance/Transformation - Refers to the ability of the biological molecule (D.N.A. or protein) to transform the bacteria (in this case) into a different version (transform the R strain into the S strain).

Document 3: Chargaff's Experiment:

Adenine - One of the bases that form part of a nucleotide, the structures that are present in D.N.A. chains; pairs with thymine.

(from: <http://www.biology-online.org/dictionary/Adenine>)

Cytosine - A nitrogen base found in D.N.A. and R.N.A. that pairs with guanine.

(from: <http://www.biology-online.org/dictionary/Cytosine>)

Deoxyribonucleic acid - A double-stranded nucleic acid that contains the genetic information for cell growth, division, and function (D.N.A.).

from: <http://www.biology-online.org/dictionary/DNA>

Guanine - A nitrogen base found in D.N.A. and RNA; pairs with cytosine.

(from: <http://www.biology-online.org/dictionary/Guanine>)

Thymine - A nitrogen base found in DNA; pairs with adenine

(from: <http://www.biology-online.org/dictionary/Thymine>)

Document 4: Pauling's Experiment:

Axis - Central portion of the D.N.A. molecule

Helical - Referring to helix (a spiral staircase or coil structure)

Tetrahedra - (plural form of tetrahedron) Triangular pyramid, is a polyhedron composed of four triangular faces.

(from: <https://en.wikipedia.org/wiki/Tetrahedron>)

Trigonal - Referring to a group of three.

Document 5: Hershey and Chase's Experiment:

Bacteriophage - (or phage) A virus capable of infecting a bacterial cell, and may cause lysis to its host cell.

(from: <http://www.biology-online.org/dictionary/Bacteriophage>)

Progeny - Referring to the offspring or descendants of the bacteriophage.

Document 6: Franklin's Experiment:

Nucleotide - The basic building block of nucleic acids, such as DNA and RNA. It is an organic compound made up of nitrogenous base, a sugar, and a phosphate group.

(from: <http://www.biology-online.org/dictionary/Nucleotide>)

Document 7: Wilkin's Experiment:

Phosphate backbone - Referring to the alternating sugar and phosphate backbone or "side pieces" of a DNA molecule.

Purine - Referring to the nitrogen bases adenine and guanine.

Pyrimidine - Referring to the nitrogen bases thymine and cytosine.

Document 8: Watson and Crick's Experiment:

Deoxyribonucleic acid - A double-stranded nucleic acid that contains the genetic information for cell growth, division, and function (D.N.A.)

(from: <http://www.biology-online.org/dictionary/DNA>)

Nitrogenous base - Nitrogenous bases are one of the fundamental components of nucleic acids, such as DNA. (adenine/thymine and cytosine/guanine are nitrogenous bases)

(from: http://www.biology-online.org/dictionary/Nitrogenous_base)

All that and a sense of humor: Rosalind Franklin's "obituary" for Watson and Crick's first model of D.N.A.

(from: http://blogs.discovermagazine.com/fire-in-the-mind/2013/04/25/on-dnas-anniversary-how-roosalind-franklin-missed-the-helix/#.WXE3_dPyuRs)

IT IS WITH GREAT REGRET THAT WE HAVE
TO ANNOUNCE THE DEATH, ON FRIDAY 18TH JULY 1952
OF D.N.A. HELIX (CRYSTALLINE)

DEATH FOLLOWED A PROTRACTED ILLNESS WHICH
AN INTENSIVE COURSE OF BESSERISEB INJECTIONS
HAD FAILED TO RELIEVE.

A MEMORIAL SERVICE WILL BE HELD NEXT
MONDAY OR TUESDAY.

IT IS HOPED THAT DR. M.H.F. WILKINS WILL
SPEAK IN MEMORY OF THE LATE HELIX

R. E. Franklin

Rhoslin

Race for the Double Helix

Background Information

*Teachers may choose to read this to students if there is sufficient time available.
It is not necessary to read this to students in order to complete the lesson.*

Science in the 1950s ushered in some significant events. In 1952, Jonas Salk produced the polio vaccine, effectively saving millions of lives, Russia pioneered space travel with its' launch of Sputnik in 1957 and a year later, in 1958, the United States joined the space race by launching its first satellite, Explorer 1. The "Race for the Double Helix" was a race peppered with competition and sexism among scientists to deduce the structure of D.N.A..

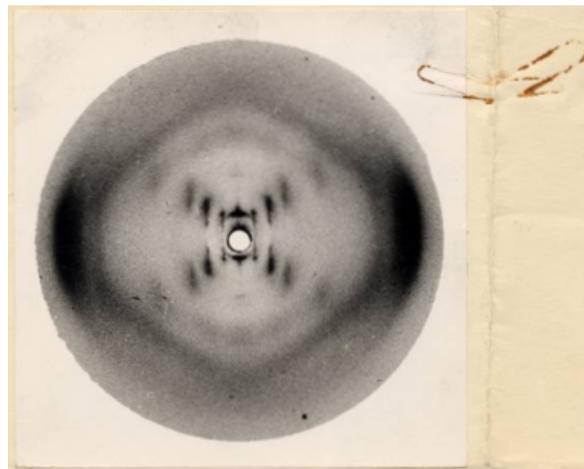
Rosalind Franklin, a notable scientist in this quest, was a female facing 1950s' gender inequalities. Instead of being viewed as leading her own research, she was often thought of as an assistant by a male colleague, Maurice Wilkins. Rosalind was not even allowed to eat lunch with males in the cafeteria at King's College in London. The strained relationship between Franklin and Wilkins might have contributed to Wilkins giving Watson and Crick Franklin's x-ray crystallography picture of D.N.A. without her permission.

In early 1953, Watson and Crick discovered the structure of D.N.A., which would pave the way for molecular biologists to eventually conduct gene cloning experiments, personal genomics and gene editing (C.R.I.S.P.R.). This discovery would not have been possible without the work of several scientists before them trying to solve their piece of the D.N.A. puzzle.

In this program, students will first be introduced to people behind the discovery of DNA's chemical structure and the roles they played. Next, they will recreate Watson's discovery of the hydrogen bonding between nucleotides. Finally, students will use this lesson about past scientific discoveries and connect them with President Eisenhower's support of scientific research and education, as well as how these governmental decisions can impact the future of scientific research.

"Race for the Double Helix" Rosalind Franklin's Photo 51

Image from: <http://scarc.library.oregonstate.edu/coll/pauling/dna/pictures/sci9.001.5-large.html>



Race for the Double Helix

Pieces of the Puzzle

Examine the primary documents that helped provided Watson and Crick with all the pieces of the puzzle to solve the chemical structure of DNA. Fill out the following table for the document(s) provided. Be prepared to share your findings with the whole class so that all of the scientists' contributions will be known.

Scientist	Document #	What was his/her contribution?	Year indicated by Document
 <hr/>			
 <hr/>			
 <hr/>			
 <hr/>			

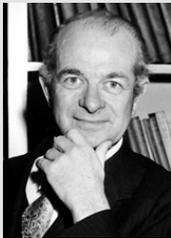
Scientist	Document #	What was his/her contribution?	Year indicated by Document
 <hr data-bbox="110 590 418 596"/>			
 <hr data-bbox="110 898 418 905"/>			
 <hr data-bbox="110 1241 418 1247"/>			
 <hr data-bbox="110 1585 418 1591"/>			

Race for the Double Helix



Pieces of the Puzzle, Answer KEY

Examine the primary documents that helped provide Watson and Crick with all the pieces of the puzzle to solve the chemical structure of DNA. Fill out the following table for the available documents provided for you. You will then discuss as a large group so that all scientists' contributions will be completed.

Scientist	Document #	What was his/her contribution?	Year indicated by Document
 Fredrick Griffith	1	<p>Virulence of a bacteria deprived of its' characteristics can be restored. There is an "intermediate stage" that helps this transformation.</p> <p>Heat killed S strain is still capable of transforming R strain into infective, virulent bacteria that kills mice.</p>	1928
 Oswald Avery	2	<p>Wanted to establish what the "transforming principle" was.</p> <p>He concludes that it is not protein or R.N.A. that transforms the R bacteria but D.N.A. from the heat killed S strain.</p>	1945
 Erwin Chargaff	3	<p>Tables indicate that there are similar amounts of Adenine and Thymine; Cytosine and Guanine.</p> <p>(Example data from Table III: Adenine=0.29 and Thymine=0.31 and Cytosine=0.18 and Guanine=0.18)</p>	1950
 Linus Pauling	4	<p>Concluded there were three helixes and the phosphates are located toward the axis (middle) of the molecule.</p>	1953

Scientist	Document #	What was his/her contribution?	Year indicated by Document
 <p><u>Alfred Hershey and Martha Chase</u></p>	5	D.N.A. was found inside the bacteria but protein was not. So, they concluded that D.N.A. was the infective part of the bacteriophage, not the protein.	1952
 <p><u>Rosalind Franklin</u></p>	6	Lab notebook indicates it is a chain of nucleotides. Students may or may not be able to deduce that D.N.A's structure is a helix from her "Photo 51."	1953
 <p><u>Maurice Wilkins</u></p>	7	The components of D.N.A. are oriented with a 45 degree rotation about the "fiber" or D.N.A. axis.	1951
 <p><u>James Watson and Francis Crick</u></p>	8	D.N.A. is a double helix with two chains and the phosphates are along the backbone of the molecule.	May 30, 1953

Primary Documents

1. Griffith, Frederick. "Significance of Pneumococcal Types". *Journal of Hygiene*. Volume XXVII. (January 1928): 8, 113-157. <http://learning.hccs.edu/faculty/r.ramakrishnan/lecture-notes/additional-readings-historical-biographical-scientific/griffiths-original-transformation-paper-chp9/view> (Visual from: https://upload.wikimedia.org/wikipedia/commons/thumb/6/6a/Griffith_experiment.svg/450px-Griffith_experiment.svg.png)
2. McCarthy, Maclyn and Avery, Oswald. "Studies on the Chemical Nature of the Substance Inducing Transformation of Pneumococcal Types". *Journal of Experimental Medicine*. (October 1945): 89-96. <https://profiles.nlm.nih.gov/ps/access/CCGM CZ.pdf> (Visual from: <https://www.slideshare.net/thelawofscience/historical-experiments-related-to-dna>)
3. Chargaff, Erwin. "Chemical Specificity of Nucleic Acids and Mechanism of the Enzymatic Degradation". *Experientia*. Volume 6. (1950): 201-240. http://modelisationsvt.free.fr/activites/adn_epistemologie/chargaff_1950.pdf
4. Pauling, Linus and Corey, Robert B. "A Proposed Structure for the Nucleic Acids". *Proceedings of the National Academy of Sciences*. Volume 39. No 2. (February 1953): 84-97. : <http://scarc.library.oregonstate.edu/coll/pauling/dna/papers/1953p.9-090.html>
5. Hershey, A.D. and Chase, Martha. "Independent Functions of Viral Protein and Nucleic Acid in Growth of Bacteriophage". *J. Gen. Physiol.*, 36 (1): (September 20, 1952). 39-56. <http://scarc.library.oregonstate.edu/coll/pauling/dna/papers/hershey-independent-54.html> (Visual from: <http://hersheychasednaexperiment.weebly.com/uploads/4/6/3/8/46380507/118481362.jpg?1423424620>)
6. Franklin, R. E. Randall Institute. King's College, London, England. D.N.A. Crystallography Calculations, 1953. <https://wellcomelibrary.org/item/b19832059#c=0&m=0&s=0&cv=44&z=0.6035%02C-0.0841%02Co.4995%02Co.3351> (Visual from: <http://scarc.library.oregonstate.edu/coll/pauling/dna/pictures/sci9.001.5-large.html>).
7. Wilkins, M.H.F and Gosling, R.G. "Physical Studies of Nucleic Acid". *Nature* 167. (May 12, 1951): 1-7. <https://wellcomelibrary.org/item/b20048622#c=0&m=0&s=0&cv=5&z=-0.5572%02C-0.0112%02C2.2265%02Cl.5933>
8. Watson, J.D. and Crick, F.H.C. "Genetical Implications of the Structure of Deoxyribonucleic Acid" *Nature* 171. (May 30, 1953). 964-967. <https://www.nature.com/nature/dna50/watsoncrick2.pdf>

Table III²

Composition of desoxyribose nucleic acid of man (in moles of nitrogenous constituent per mole of P).

Constituent	Sperm		Thymus	Liver	
	Prep. 1	Prep. 2		Normal	Carcinoma
Adenine . . .	0.29	0.27	0.28	0.27	0.27
Guanine . . .	0.18	0.17	0.19	0.19	0.18
Cytosine . . .	0.18	0.18	0.16		0.15
Thymine . . .	0.31	0.30	0.28		0.27
Recovery . . .	0.96	0.92	0.91		0.87

Erwin Chargaff's data Table III

From: http://modelisationsvt.free.fr/activites/adn_epistemologie/chargaff_1950.pdf

THE SIGNIFICANCE OF PNEUMOCOCCAL TYPES.

By FRED. GRIFFITH, M.B.

(A Medical Officer of the Ministry of Health.)

(From the Ministry's Pathological Laboratory.)



You do not need to read the article, only note the Author and Date from this page. Turn to the next page for more directions.

CONTENTS.

OBSERVATIONS ON CLINICAL MATERIAL		
Types in Lobar Pneumonia		117
Variety of Types in Sputum from the same Case		
Rough Virulent Strain		119
A Strain agglutinating specifically with two different Group IV Sera		119
II. EXPERIMENTAL MODIFICATION		120
Attenuation in Culture		120
(1) Growth in Immune Serum		120
(2) Growth on Solid Media		121
(3) Differences between Individual R and S colonies		122
Reversion from Rough to Smooth		125
A. Origin of the R Strains used		125
B. Passage of R II Strains		126
C. Massive Dosage with R II		129
Inoculation of living R and killed S cultures		129
Preliminary Experiments		129
Group IV S culture + R I and II		132
Type I S culture + R II and I		134
Type III S culture + R I and II		141
Type II S culture + R I		144
Types I and II S cultures + R Group IV		146
Inoculation of living and dead R cultures		147
III. DISCUSSION		148
IV. SUMMARY		157

I. OBSERVATIONS ON CLINICAL MATERIAL.

SINCE communicating my report¹ on the distribution of pneumococcal types in a series of 150 cases of lobar pneumonia occurring in the period from April, 1920 to January, 1922, I have not made any special investigation of this subject. In the course, however, of other inquiries and of the routine examination of sputum during the period from the end of January, 1922, to March, 1927, some further data have been accumulated².

Table I gives the results in two series and, for comparison, those previously published.

¹ Reports on Public Health and Medical Subjects (1922), No. 13.

² I owe many thanks to Dr J. Bell Ferguson, formerly Medical Officer of Health for Smethwick, for sending me many specimens from cases of lobar pneumonia.

which serves indifferently as a foundation for the building up of either Type II or a Group IV strain.

The R form derived from a Group IV strain, viz. Type II A, can be transformed into the S forms of Type I or Type II or changed back to its original S form according to the particular S substance which is injected along with it. On the other hand, another Group IV strain which was incompletely attenuated invariably reverted to its original S form no matter what type of S culture was injected with it. It seems that, if a pneumococcus has a moderately well-developed S structure, there is no tendency to develop into an S variety of any other type.

The method by which transformation of type has been secured consists in heating to 60° C. for 15 minutes up to 3 hours a virulent culture of one type and inoculating a large amount of the heated culture under the skin of a mouse together with a small dose of the R strain derived from another type.

Experiments with culture heated at temperatures higher than 60° C. have rarely been successful in causing transformation of type. In one instance the S form of Type I was obtained from a mouse which had been inoculated with the R form derived from Type II together with a suspension of Type I heated to 70° C. for 15 minutes, in a second the S form of Type II was obtained from a mouse inoculated with the R form of Type I together with a virulent Type II culture heated to 65° C. for 15 minutes.

The question arises whether heating at the above temperatures had in fact killed all the individual pneumococci in the mass of virulent type. I have given this question careful consideration and I have concluded that, by the ordinary methods of culture and animal inoculation, the presence of viable organisms in the heated cultures. So far as I know, there is no reason to suppose, and I have had no evidence to show, that the cultures used were mixed, there seems to be no alternative to the hypothesis of transformation of type.

A few years ago the statement that a Type I strain could be changed into a Type II or a Type III would have been received with greater scepticism than at the present day. Since, however, it has been shown that a pneumococcus can readily be deprived of its type characters and virulence, and that under favourable conditions these can be restored, the possibility appears less unlikely.

The apparent transformation is not an abrupt change of one type into another, but a process of evolution through an intermediate stage, the R form, from which the type characters have been obliterated. Mutation of type among disease-producing bacteria is a subject of obvious importance in the study of epidemiological problems. If it can be proved to occur in the pneumococcus group with its sharply defined immunological races, the possibility can hardly be denied to other bacterial groups where the serological

Read the last 2 paragraphs on this page what are Griffith's observations?

Note:
pneumococcus is a type of bacteria.

Having trouble? You may want to refer to the graphic about Griffith's experiment on page 17.

Read #10 and the sentence after. What are Griffith's observations?

F. GRIFFITH

159

10. The inoculation into the subcutaneous tissues of mice of an attenuated R strain derived from one type, together with a large dose of virulent culture of another type killed by heating to 60° C., has resulted in the formation of a virulent S pneumococcus of the same type as that of the heated culture.

The newly formed S strain may remain localised at the seat of inoculation, or it may disseminate and cause fatal septicaemia.

The S form of Type I has been produced from the R form of Type II, and the R form of Type I has been transformed into the S form of Type II.

The clear mucinous colonies of Type III have been derived both from the R form of Type I and from the R form of Type II, though they appear to be produced more readily from the latter. The newly formed strains of Type III have been of relatively low virulence, and have frequently remained localised at the subcutaneous seat of inoculation.

Virulent strains of Types I and II have been obtained from an R strain of Group IV.

11. Heated R cultures injected in large doses, together with small doses of living R culture have never caused transformation of type, and only rarely produced a reversion of the R form of Type II to its virulent S form.

12. The results of the experiments on enhancement of virulence and on transformation of type are discussed and their significance in regard to questions of epidemiology is indicated.

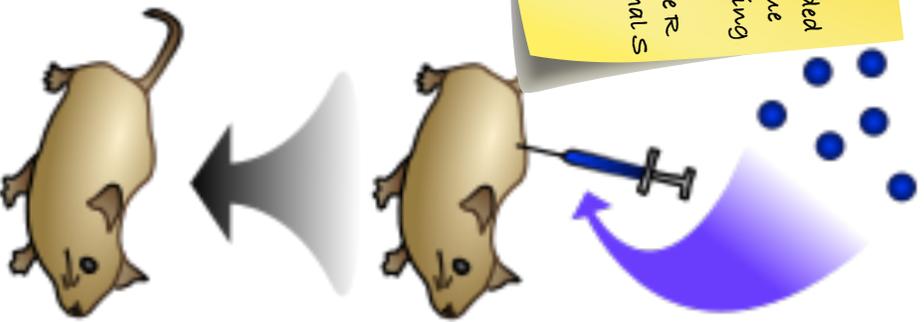
(MS. received for publication 26. VIII. 1927.—Ed.)

Having trouble getting it? Use the visual on the next page to help.

“Race for the Double Helix” Fredrick Griffith’s Experiment

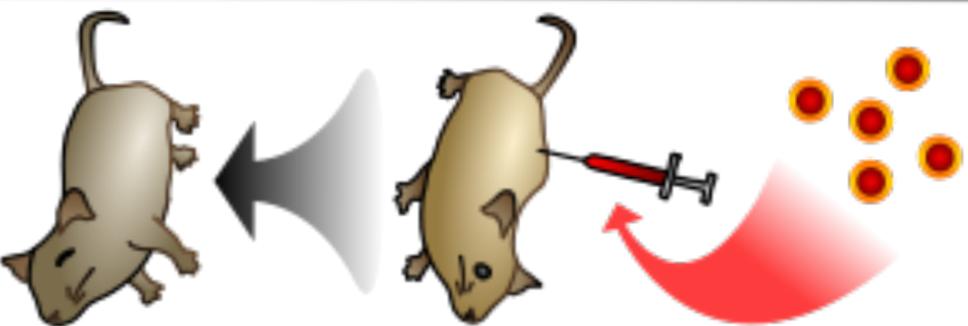
Note: Griffith's experiment concluded that there was some sort of "transforming principle" ^{transforming the R strain into the lethal S strain.}

rough strain
(nonvirulent)



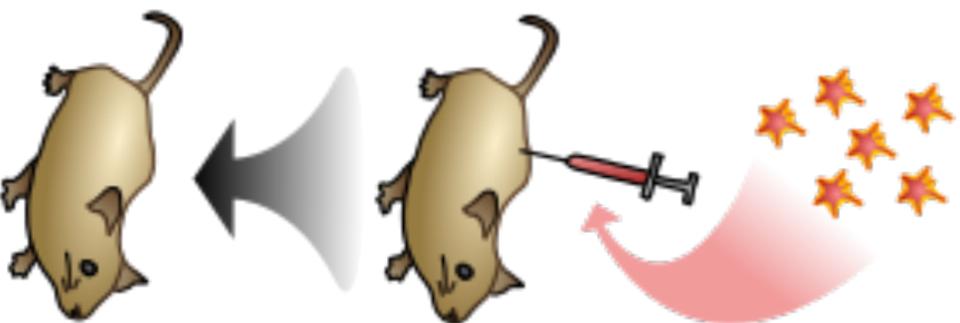
mouse lives

smooth strain
(virulent)



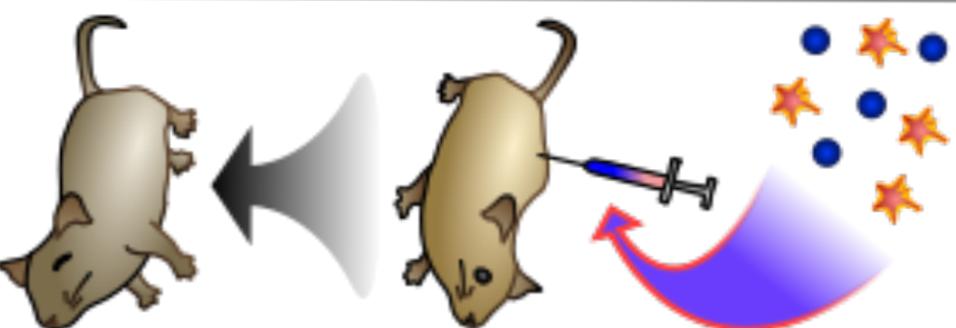
mouse dies

heat-killed
smooth strain



mouse lives

rough strain &
heat-killed
smooth strain



mouse dies

Note the Author and Date from this page



STUDIES ON THE CHEMICAL NATURE OF THE SUBSTANCE INDUCING TRANSFORMATION OF PNEUMOCOCCAL TYPES

II. EFFECT OF DESOXYRIBONUCLEASE ON THE BIOLOGICAL ACTIVITY OF THE TRANSFORMING SUBSTANCE*

By MACLYN McCARTY, M.D.,

Lieutenant Commander, Medical Corps, United States Naval Reserve,

AND OSWALD T. AVERY, M.D.

(From the United States Navy Research Unit at the Hospital of The Rockefeller Institute for Medical Research)

(Received for publication, October 10, 1945)

Read both paragraphs on this page.

What was Avery trying to establish?

What molecule does he suggest as the "transforming principle"?

Having trouble? You may want to refer to the graphic about Avery's experiment on page 20.

The substance inducing transformation of pneumococcal types has been isolated from *Pneumococcus* Type III in the form of a desoxyribonucleic acid fraction (1). The data obtained by chemical, enzymatic, and serological analysis, as well as by electrophoresis and ultracentrifugation of the purified material strongly suggest that the nucleic acid is itself responsible for the biological activity.

The enzymatic analysis was begun early in the course of the attempts to determine the nature of the transforming substance. Relatively unpurified pneumococcal extracts were subjected to enzymatic study in the hope that by this approach some clue might be obtained as to the identity of the biologically active constituent. Crystalline trypsin, chymotrypsin, and ribonuclease had no effect on the transforming substance, but it was found that certain crude enzyme preparations were able to bring about complete loss of transforming activity. When the possible importance of desoxyribonucleic acid was suggested by chemical fractionation, the experiments with crude enzyme preparations were extended to determine whether their ability to destroy the activity of the transforming principle could be correlated with any enzymatic action on authentic samples of desoxyribonucleic acid of non-bacterial origin. A variety of crude enzymes were tested both for their ability to inactivate the transforming substance, and for their effect on desoxyribonucleic acid from animal tissues (1). Of the enzyme preparations tested only those capable of depolymerizing authentic desoxyribonucleic acid were effective in destroying the transforming activity of pneumococcal extracts. Other parallelisms between the two actions were observed: for example, sodium fluoride inhibited both the depolymerizing action and the inactivation of the transforming sub-

* The Bureau of Medicine and Surgery of the U. S. Navy does not necessarily undertake to endorse the views or opinions which are expressed in this paper.

as substrate. However, the qualitative effect was readily recognizable, and in those tubes in which complete enzymatic destruction of the transforming activity had occurred, there was a corresponding loss in viscosity when compared with the control tube containing no enzyme.

DISCUSSION

The fact that a purified preparation of desoxyribonuclease in exceedingly low concentration is capable of destroying irreversibly the Type III transforming substance provides strong confirmatory evidence for the view that biological activity is a property of the desoxyribonucleic acid. In this connection it is of interest that irreversible inactivation of the transforming agent by enzymatic digestion differs from that form of inactivation brought about by ascorbic acid and certain related compounds, since in the latter instance, the reaction is reversible and full activity can be restored by the use of sulfhydryl compounds (3).

The possibility has been recognized that the activity of the transforming agent might be referable to minute amounts of some other substance such as protein in the purified preparations. The results of the present investigation show that in order to detect proteolytic activity, it is necessary to use an amount of purified desoxyribonuclease 100,000 times greater than that required to cause rapid and complete destruction of activity of the transforming substance. This evidence, in conjunction with the data previously reported on the chemical and physical properties of the active principle, leaves little doubt that the ability of a pneumococcal extract to induce transformation depends upon the presence of a highly polymerized and specific form of desoxyribonucleic acid, and that this constituent is the fundamental unit of the transforming principle.

The objection can be raised that the nucleic acid may merely serve as a "carrier" for some hypothetical substance, presumably protein, which possesses the specific transforming activity. Depolymerization of the nucleic acid would according to this hypothesis, destroy the effectiveness of the essential carrier and thus result in loss of biological activity. There is no evidence in favor of such a hypothesis, and it is supported chiefly by the traditional view that nucleic acids are devoid of biological specificity. On the contrary, there are indications that even minor disruptions in the long-chain nucleic acid molecule have a profound effect on biological activity. Thus, treatment of the transforming substance with concentrations of desoxyribonuclease so small that only a slight fall in viscosity occurs causes a marked loss of biological activity. It is suggested that the initial stages of enzymatic depolymerization which are reflected only by minimal changes in the physical properties of the nucleate are sufficient to bring about destruction of specific activity.

Although the results of enzymatic studies provide additional evidence for

Read the three paragraphs under "Discussion".

Note: The suffix -ase refers to enzymes that in this case destroy the molecule.

(e.g.

desoxyribonuclease destroys D.N.A.)

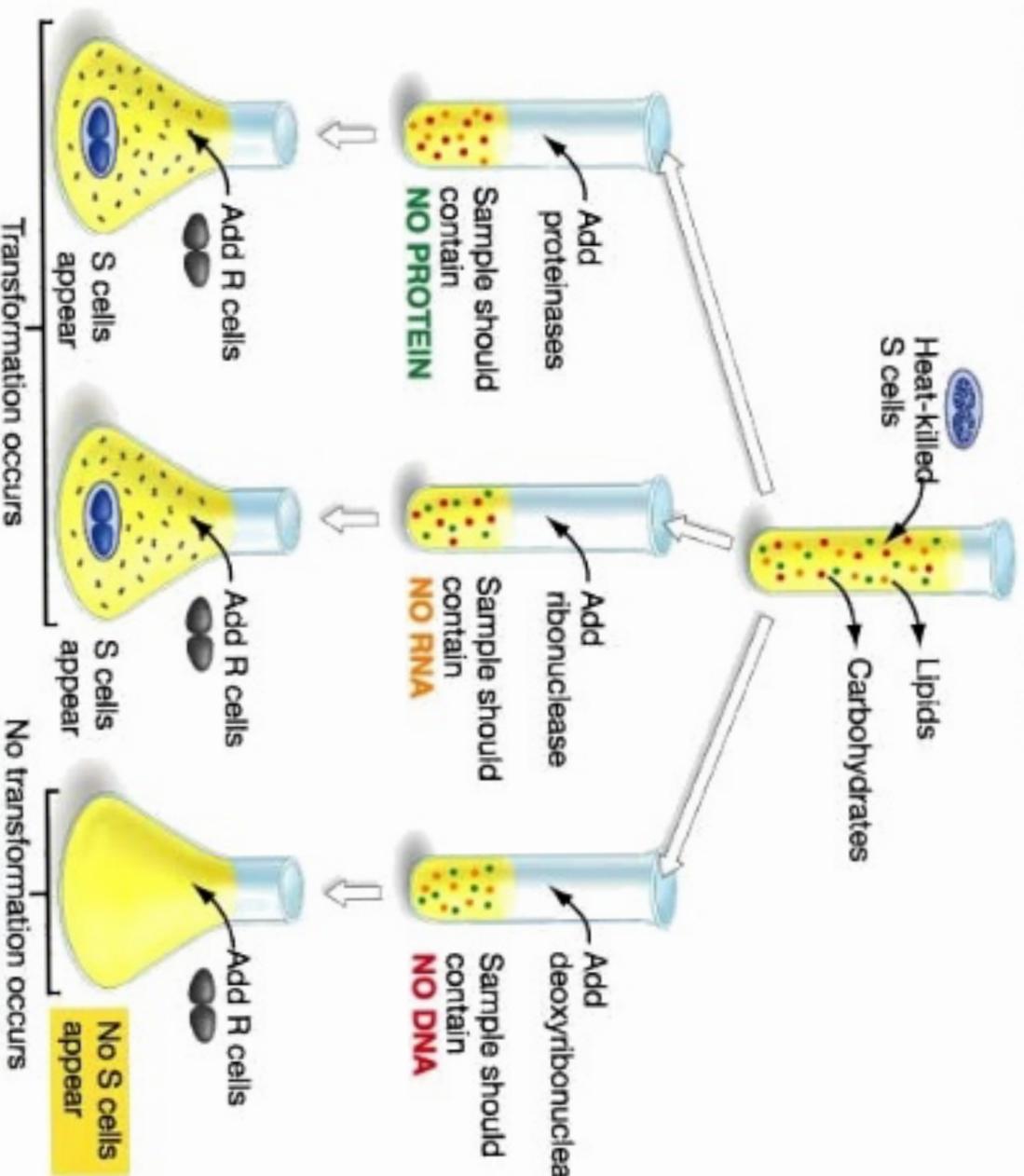
What did Avery's experimental data conclude about the "transforming principle"?

Is it protein or D.N.A.?

Having trouble getting it? Use the visual on the next page to help.

“Race for the Double Helix” Oswald Avery’s Experiment

DETERMINING THAT DNA IS THE HEREDITARY MATERIAL



1. Remove the lipids and carbohydrates from a solution of heat-killed S cells. Proteins, RNA, and DNA remain.

2. Subject the solution to treatments of enzymes to destroy either the proteins, RNA, or DNA.

3. Add a small portion of each sample to a culture containing R cells. Observe whether transformation has occurred by testing for the presence of virulent S cells.

From: <https://www.slideshare.net/helawofscience/historical-experiments-related-to-dna>

Chemical Specificity of Nucleic Acids and Mechanism of their Enzymatic Degradation¹

By ERWIN CHARGAFF², New York, N.Y.



You do not need to read the article, only note the Author and Date from this page. Turn to the next page for more directions.

Introduction

We have witnessed an enormous renaissance in the chemical and biological properties of nucleic acids. These are components essential for the life of the cell. It is not particularly surprising, therefore, that the study of nucleic acids represents one of the most important unsolved problems in biochemistry. It is not easy to say what provided the impulse for this rather sudden rebirth. Was it the fundamental work of E. HAMMARSTEN³ on the highly polymerized deoxy-ribonucleic acid of calf thymus? Or did it come from the biological side, for instance the experiments of BRACHET⁴ and CASPERSSON⁵? Or was it the very important research of AVERY⁶ and his collaborators on the transformation of pneumococcal types that started the avalanche?

It is, of course, completely senseless to formulate a hierarchy of cellular constituents and to single out certain compounds as more important than others. The economy of the living cell probably knows no conspicuous waste; proteins and nucleic acids, lipids and polysaccharides, all have the same importance. But one observation may be offered. It is impossible to write the history of the cell without considering its geography; and we cannot do this without attention to what may be called the chronology of the cell, i. e. the sequence in which the cellular constituents are laid down and in which they develop from each other. If this is done, nucleic acids will be found pretty much at the beginning. An attempt to say more leads directly into empty speculations in which almost no field

abounds more than the chemistry of the cell. Since an ounce of proof still weighs more than a pound of prediction, the important genetical functions, ascribed—probably quite rightly—to the nucleic acids by many workers, will not be discussed here. Terms such as “template” or “matrix” or “reduplication” will not be found in this lecture.

II. Identity and Diversity in High Molecular Cell Constituents

The determination of the constitution of a complicated compound, composed of many molecules of a number of organic substances, evidently requires the exact knowledge of the nature and proportion of all constituents. This is true for nucleic acids as much as for proteins or polysaccharides. It is, furthermore, clear that the value of such constitutional determinations will depend upon the development of suitable methods of hydrolysis. Otherwise, substances representing an association of many chemical individuals can be described in a qualitative fashion only; precise decisions as to structure remain impossible. When our laboratory, more than four years ago, embarked upon the study of nucleic acids, we became aware of this difficulty immediately.

The state of the nucleic acid problem at that time found its classical expression in LEVENE's monograph¹. (A number of shorter reviews, indicative of the development of our conceptions concerning the chemistry of nucleic acids, should also be mentioned².) The old tetranucleotide hypothesis—it should never have been called a theory—was still dominant; and this was characteristic of the enormous sway that the organic chemistry of small molecules held over biochemistry. I should like to illustrate what I mean by one example. If in the investigation of a disaccharide consisting of two different hexoses we isolate 0.8 mole of one sugar and 0.7 mole of the other, this will be sufficient for the

¹ This article is based on a series of lectures given before the Chemical Societies of Zürich and Basle (June 29th and 30th, 1949), the Société de chimie biologique at Paris, and the Universities of Uppsala, Stockholm, and Milan.

² Department of Biochemistry, College of Physicians and Surgeons, Columbia University, New York. The author wishes to thank the John Simon Guggenheim Memorial Foundation for making possible his stay in Europe. The experimental work has been supported by a research grant from the United States Public Health Service.

³ E. HAMMARSTEN, *Biochem. Z.* **144**, 383 (1924).

⁴ J. BRACHET in *Nucleic Acid*, Symposia Soc. Exp. Biol. No. 1 (Cambridge University Press, 1947), p. 207. Cp. J. BRACHET, in *Nucleic Acids and Nucleoproteins*, Cold Spring Harbor Symp. Quant. Biol. **12**, 18. (Cold Spring Harbor, N.Y., 1947).

⁵ T. CASPERSSON, in *Nucleic Acid*, Symp. Soc. Exp. Biol., No. 1 (Cambridge University Press, 1947), p. 127.

⁶ O. T. AVERY, C. M. MACLEOD, and M. McCARTY, *J. Exp. Med.* **79**, 137 (1944).

¹ P. A. LEVENE and L. W. BASS, *Nucleic Acids* (Chemical Catalog Co., New York, 1931).

² H. BREDERECK, *Fortschritte der Chemie organischer Naturstoffe* **1**, 121 (1938). — F. G. FISCHER, *Naturwissensch.* **30**, 377 (1942). — R. S. TIPSON, *Adv. Carbohydrate Chem.* **1**, 193 (1945). — J. M. GULLAND, G. R. BARKER, and D. O. JORDAN, *Ann. Rev. Biochem.* **14**, 175 (1945). — E. CHARGAFF and E. VISCHER, *Ann. Rev. Biochem.* **17**, 201 (1948). — F. SCHLENK, *Adv. Enzymol.* **2**, 455 (1949).

Table I

pyrimidines to treatment with strong acid. A mixture of known concentration was dissolved in the acids and heated at 175° in a bomb tube. The concentration of the individual pyrimidines were determined through the recoveries of separated pyrimidines before and after the heating of the mixture.

Acid	Heating time min.	Concentration shift, per cent of starting concentration		
		Uracil	Cytosine	Thymine
HCOOH + HCl (1:1)	90	+62	-63	+3
	60	+3	-5	0
	120	+24	-19	0
HCl (98 to 100%)	60	0	-1	-2
	120	0	+2	+1

Observe Table III and Table IV. What do you notice about the relationship between the amount of adenine/thymine and guanine/cytosine in Chargaff's prepared samples?

analysis of the pyrimidine nucleotides by means of concentrated formic acid. For the liberation of the purines, concentrated sulfuric acid (100°, 1 hour) is employed; for the liberation of the pyrimidines, the purines are first precipitated as the hydrochlorides by treatment with dry HCl gas in methanol and the remaining pyrimidine nucleotides cleaved under pressure with concentrated formic acid (175°, 2 hours). This procedure proved particularly suitable for the investigation of the desoxypentose nucleic acids. For the study of the composition of pentose nucleic acids a different procedure, making use of the separation of the ribonucleotides, was developed more recently, which will be mentioned later.

VII. Composition of Desoxypentose Nucleic Acids

It should be stated at the beginning of this discussion that the studies conducted thus far have yielded no indication of the occurrence in the nucleic acids examined in our laboratory of unusual nitrogenous constituents. In all desoxypentose nucleic acids investigated by us the purines were adenine and guanine, the pyrimidines cytosine and thymine. The occurrence in minute amounts of other bases, e.g. 5-methylcytosine, can, however, not yet be excluded. In the pentose nucleic acids uracil occurred instead of thymine.

A survey of the composition of desoxyribose nucleic acid extracted from several organs of the ox is provided

Table II¹

Composition of desoxyribonucleic acid of ox (in moles of nitrogenous constituent per mole of P).

Constituent	Thymus			Spleen		Liver
	Prep. 1	Prep. 2	Prep. 3	Prep. 1	Prep. 2	
Adenine . .	0.26	0.28	0.30	0.25	0.26	0.26
Guanine . .	0.21	0.24	0.22	0.20	0.21	0.20
Cytosine . .	0.16	0.18	0.17	0.15	0.17	
Thymine . .	0.25	0.24	0.25	0.24	0.24	
Recovery . .	0.88	0.94	0.94	0.84	0.88	

in Table II. The molar proportions reported in each case represent averages of several hydrolysis experiments. The composition of desoxypentose nucleic acids from human tissues is similarly illustrated in Table III. The preparations from human liver were obtained from a pathological specimen in which it was possible, thanks to the kind cooperation of M. FABER, to separate portions of unaffected hepatic tissue from carcinomatous tissue consisting of metastases from the sigmoid colon, previous to the isolation of the nucleic acids¹.

Table III²

Composition of desoxypentose nucleic acid of man (in moles of nitrogenous constituent per mole of P).

Constituent	Sperm		Thymus	Liver	
	Prep. 1	Prep. 2		Normal	Carcinoma
Adenine . . .	0.29	0.27	0.28	0.27	0.27
Guanine . . .	0.18	0.17	0.19	0.19	0.18
Cytosine . . .	0.18	0.18	0.16		0.15
Thymine . . .	0.31	0.30	0.28		0.27
Recovery . . .	0.96	0.92	0.91		0.87

In order to show examples far removed from mammalian organs, the composition of two desoxyribonucleic acids of microbial origin, namely from yeast³ and from avian tubercle bacilli⁴, is summarized in Table IV.

Table IV⁵

Composition of two microbial desoxyribonucleic acids.

Constituent	Yeast		Avian tubercle bacilli
	Prep. 1	Prep. 2	
Adenine	0.24	0.30	0.12
Guanine	0.14	0.18	0.28
Cytosine	0.13	0.15	0.26
Thymine	0.25	0.29	0.11
Recovery	0.76	0.92	0.77

The very far-reaching differences in the composition of desoxypentose nucleic acids of different species are best illustrated by a comparison of the ratios of adenine to guanine and of thymine to cytosine as given in Table V. It will be seen that in all cases where enough material for statistical analysis was available highly significant differences were found. The analytical figures on which Table V is based were derived by comparing the ratios found for individual nucleic acid hydrolysates of one species regardless of the organ from which the preparation was isolated. This procedure assumes that there is no organ specificity with

¹ Unpublished experiments.

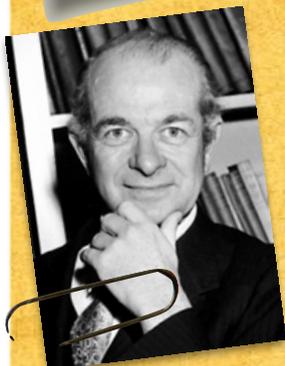
² From E. CHARGAFF, S. ZAMENHOF, and C. GREEN, *Nature* (in press); and unpublished results.

³ E. CHARGAFF and S. ZAMENHOF, *J. Biol. Chem.* 173, 327 (1948).

⁴ E. CHARGAFF and H. E. SNEY, *J. Biol. Chem.* 177, 417 (1949).

A PROPOSED STRUCTURE FOR THE NUCLEIC ACIDS

Note the Author
and Date from
this page



By

LINUS PAULING AND ROBERT B. COREY

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

Reprinted from the Proceedings of the NATIONAL ACADEMY OF SCIENCES,
Vol. 39, No. 2, pp. 84-97. February, 1953

the similar α helix, in which the atoms are packed in a satisfactorily close manner about the axis, is an important protein structure.) There are three possibilities as to the composition of the core: it may consist of the purine-pyrimidine groups, the sugar residues, or the phosphate groups. It is found by trial that, because of their varied nature, the purine-pyrimidine groups cannot be packed along the axis of the helix in such a way that suitable bonds can be formed between the sugar residues and the phosphate groups; this choice is accordingly eliminated. It is also unlikely that the sugar groups constitute the core. The shape of the ribofuranose group and the deoxyribose group along a helical axis, such that close packing of these groups along a helical axis, shows the difficulty of packing them has been found. It is shown that starch, which achieves close packing is a helical molecule. Iodine molecules can form helices with a hole at the center. We conclude that the core is probably formed of the phosphate groups.

A close-packed core of phosphoric acid residues, HPO_4^{--} , can easily be constructed. At each level along the fiber axis there are three phosphate groups. These are packed together in the way shown in figure 1. Six oxygen atoms, two from each tetrahedral phosphate group, form an octahedron, the trigonal axis of which is the axis of the three-chain helical molecule. A similar complex of three phosphate tetrahedra can be superimposed on this one, with translation by 3.4 \AA along the fiber axis, and only a small change in azimuth. The neighborhood of the axis of the molecule is then filled with oxygen atoms, arranged in groups of three, which change their azimuthal orientation by about 60° from layer to layer, in such a way as to produce approximate closest packing of these atoms.

The height (between two opposite edges) of a phosphate tetrahedron is about 1.7 \AA . If the same distance were preserved between the next oxygen layers, the basal-plane distance along the fiber axis would be 3.4 \AA . This value is the spacing observed for the principal meridional reflection.

It is to be expected that the outer oxygen atoms of the complex of three phosphate groups would be attached to the ribofuranose or deoxyribofuranose residues, and that the hydrogen atom of the HPO_4^{--} residues

Read the first four sentences
in the second paragraph.

According to Pauling, how
many chains compose the
"helical molecule"?



FIGURE 2

would be attached to one of the two inner oxygen atoms, and presumably would be involved in hydrogen-bond formation with another of the inner oxygen atoms, of an adjoining phosphate group. The length of the O—H \cdots O bond should be close to that observed in potassium dihydrogen phosphate, 2.55 Å. The angle P—O—H should be approximately the tetrahedral angle. It is found that the spacing 3.4 Å is not compatible with this bond angle, if the hydrogen bonds are formed between one phosphate group

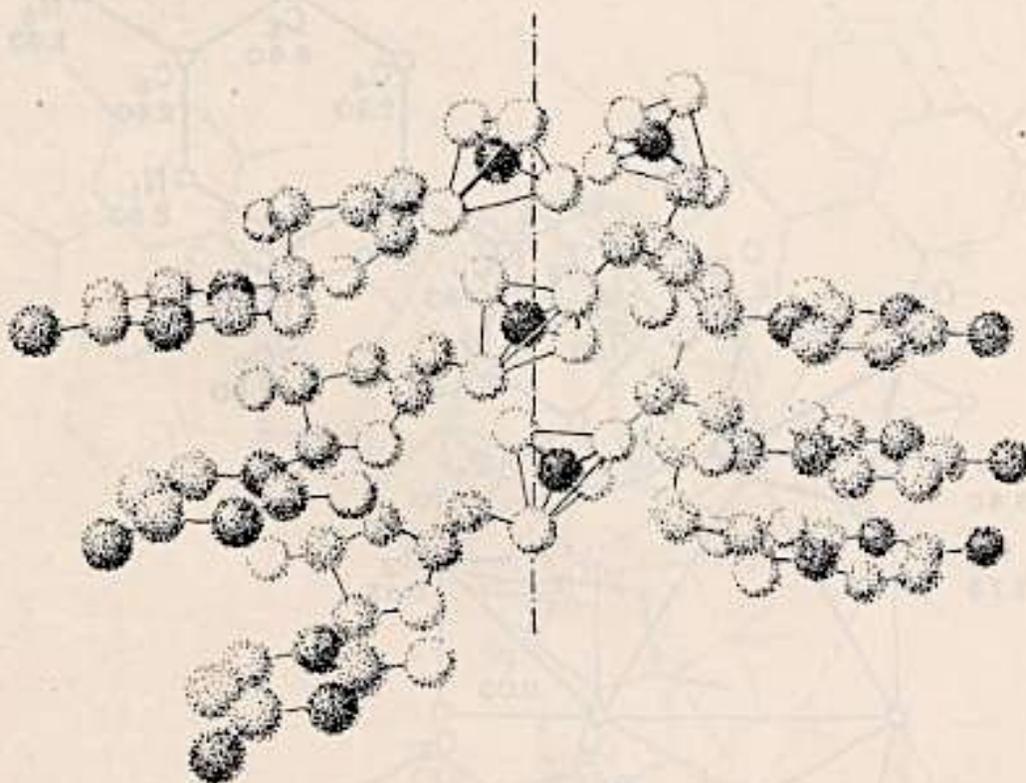


FIGURE 4

Perspective drawing of a portion of the nucleic acid structure, showing the phosphate tetrahedra near the axis of the molecule, the β -D-ribofuranose rings connecting the tetrahedra into chains, and the attached purine and pyrimidine rings (represented as purine rings in this drawing). The molecule is inverted with respect to the coordinates given in table 1.

Hard to read? The above paragraph is retyped below for visual clarity.

Perspective drawing of a portion of the nucleic acid structure, showing the phosphate tetrahedra near the axis of the molecule, the β -D-ribofuranose rings connecting the tetrahedra into chains, and the attached purine and pyrimidine rings (represented as purine rings in this drawing). The molecule is inverted with respect to the coordinates given in table 1.

the minimum distortion required by the five-membered ring, one atom of

Use Figure 4 to confirm your answer to the number of chains in the "helical molecule".

Read the caption to Fig. 4. Where does Pauling hypothesize the phosphates are located in the molecule (in the outer rings or toward the axis/middle)?

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 reason-

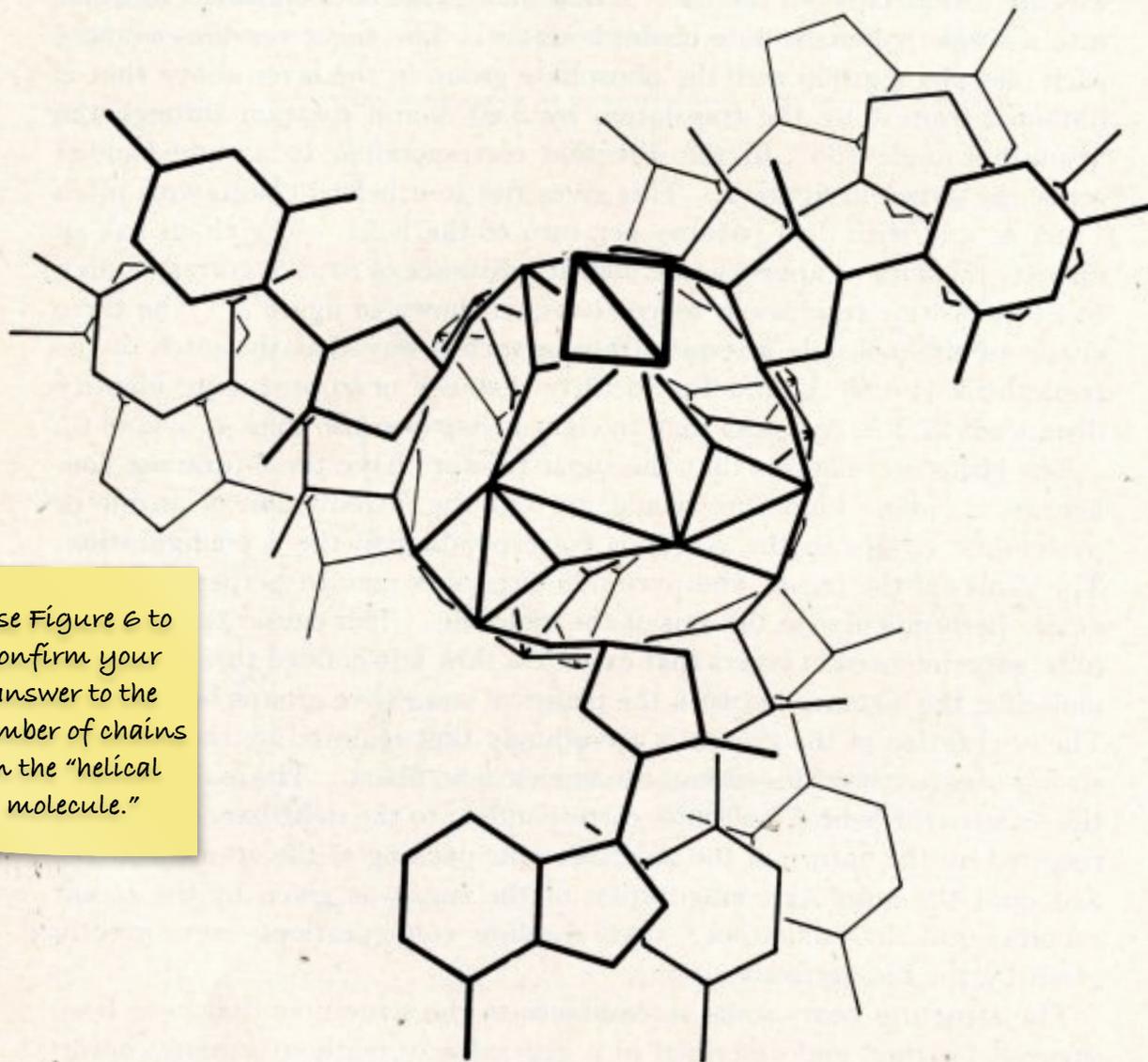


FIGURE 6

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

able 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

Use Figure 6 to confirm your answer to the number of chains in the "helical molecule."

INDEPENDENT FUNCTIONS OF VIRAL PROTEIN AND NUCLEIC ACID IN GROWTH OF BACTERIOPHAGE*

BY A. D. HERSHEY AND MARTHA CHASE

(From the Department of Genetics, Carnegie Institution of Washington, Cold Spring Harbor, Long Island)

(Received for publication, April 9, 1952)

You do not need to read the article, only note the Author and Date from this page. Turn to the next page for more directions.

Doermann (1948), Doermann and Dissosway (1952) has shown that bacteriophage T2 can be grown in a non-infective form. The phage is released from the bacterial cell by certain lysogenic bacteria (Lwoff and Gauthier, 1951). Little is known about the vegetative phase of these viruses. The experiments reported in this paper show that one of the first steps in the growth of T2 is the release from its protein coat of the nucleic acid of the virus particle, after which the bulk of the sulfur-containing protein has no further function.



Materials and Methods.—Phage T2 means in this paper the variety called T2H (Hershey, 1946); T2*h* means one of the host range mutants of T2; UV-phage means phage irradiated with ultraviolet light from a germicidal lamp (General Electric Co.) to a fractional survival of 10^{-6} .

Sensitive bacteria means a strain (H) of *Escherichia coli* sensitive to T2 and its *h* mutant; resistant bacteria B/2 means a strain resistant to T2 but sensitive to its *h* mutant; resistant bacteria B/2*h* means a strain resistant to both. These bacteria do not adsorb the phages to which they are resistant.

“Salt-poor” broth contains per liter 10 gm. bacto-peptone, 1 gm. glucose, and 1 gm. NaCl. “Broth” contains, in addition, 3 gm. bacto-beef extract and 4 gm. NaCl.

Glycerol-lactate medium contains per liter 70 mM sodium lactate, 4 gm. glycerol, 5 gm. NaCl, 2 gm. KCl, 1 gm. NH_4Cl , 1 mM MgCl_2 , 0.1 mM CaCl_2 , 0.01 gm. gelatin, 10 mg. P (as orthophosphate), and 10 mg. S (as MgSO_4), at pH 7.0.

Adsorption medium contains per liter 4 gm. NaCl, 5 gm. K_2SO_4 , 1.5 gm. KH_2PO_4 , 3.0 gm. Na_2HPO_4 , 1 mM MgSO_4 , 0.1 mM CaCl_2 , and 0.01 gm. gelatin, at pH 7.0.

Veronal buffer contains per liter 1 gm. sodium diethylbarbiturate, 3 mM MgSO_4 , and 1 gm. gelatin, at pH 8.0.

The HCN referred to in this paper consists of molar sodium cyanide solution neutralized when needed with phosphoric acid.

* This investigation was supported in part by a research grant from the National Microbiological Institute of the National Institutes of Health, Public Health Service. Radioactive isotopes were supplied by the Oak Ridge National Laboratory on allocation from the Isotopes Division, United States Atomic Energy Commission.

Read the first 2 paragraphs under "Discussion".

What did Hershey-Chase's experimental data conclude about what was "infecting" the progeny cell?

Having trouble?
You may want to refer to the graphic about Hershey/Chase's experiment on page 29.

These properties show that T2 inactivated by formaldehyde is largely incapable of injecting its DNA into the cells to which it attaches. Its behavior in the experiments outlined gives strong support to our interpretation of the corresponding experiments with active phage.

DISCUSSION

We have shown that when a particle of bacteriophage T2 attaches to a bacterial cell, most of the phage DNA enters the cell, and a residue containing at least 80 per cent of the sulfur-containing protein of the phage remains at the cell surface. This residue consists of the material forming the protective membrane of the resting phage particle, and it plays no further role in infection after the attachment of phage to bacterium.

These facts leave in question the possible function of the 20 per cent of sulfur-containing protein that may or may not enter the cell. We find that little or none of it is incorporated into the progeny of the infecting particle, and that at least part of it consists of additional material resembling the residue that can be shown to remain extracellular. Phosphorus and adenine (Watson and Maaløe, 1952) derived from the DNA of the infecting particle, on the other hand, are transferred to the phage progeny to a considerable and equal extent. We infer that sulfur-containing protein has no function in phage multiplication, and that DNA has some function.

It must be recalled that the following questions remain unanswered. (1) Does any sulfur-free phage material other than DNA enter the cell? (2) If so, is it transferred to the phage progeny? (3) Is the transfer of phosphorus (or hypothetical other substance) to progeny direct—that is, does it remain at all times in a form specifically identifiable as phage substance—or indirect?

Our experiments show clearly that a physical separation of the phage T2 into genetic and non-genetic parts is possible. A corresponding functional separation is seen in the partial independence of phenotype and genotype in the same phage (Novick and Szilard, 1951; Hershey *et al.*, 1951). The chemical identification of the genetic part must wait, however, until some of the questions asked above have been answered.

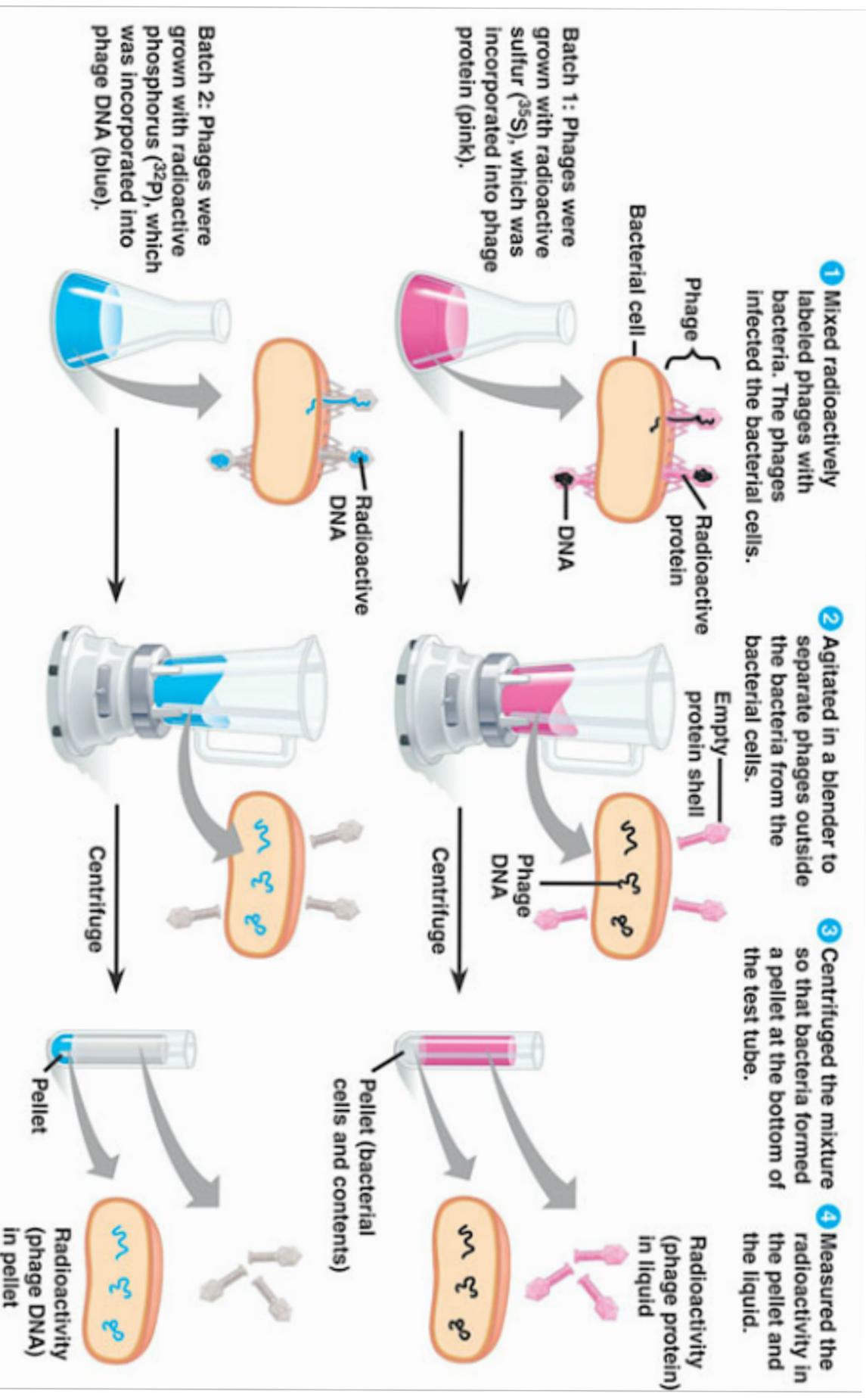
Two facts of significance for the immunologic method of attack on problems of viral growth should be emphasized here. First, the principal antigen of the infecting particles of phage T2 persists unchanged in infected cells. Second, it remains attached to the bacterial debris resulting from lysis of the cells. These possibilities seem to have been overlooked in a study by Rountree (1951) of viral antigens during the growth of phage T5.

SUMMARY

1. Osmotic shock disrupts particles of phage T2 into material containing nearly all the phage sulfur in a form precipitable by antiphage serum, and capable of specific adsorption to bacteria. It releases into solution nearly all

“Race for the Double Helix”

Martha Chase & Alfred Hershey’s Experiment



From: <http://hershychasednaexperiment.weebly.com/uploads/4/6/3/8/46380507/118481362.jpg> 21423424620

Rosalind Elsie Franklin's hand-written lab notebook

6

R. E. F.

DNA. Crystallographic Calculs. etc 1953

Note the Author
and Date from
this page



Look at the figure on this page and read the text.

What sort of shape/structure did Rosalind Franklin attribute to D.N.A.?

Peak at longit 0. lies on axis.

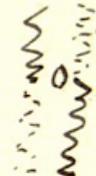
2 P atoms attached to similar nucleotides

apart from this, symmetry does not control nucleotide sequence

except that is a "back to back" pair of chains top half of

one is similar to bottom half of other

each chain only peaks in unit cell



can't reconcile nucleotide sequence with Chargaff's analysis

~~if all chains are the same, sequence must be ABCDDCB~~

N.B. Symmetry run does not effect sequence within one chain.

Distance between neighboring peaks 5.7 Å (in 3 dimensions)

Nearer to agreement with Chargaff's analysis would be

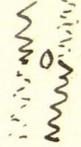
4 purines, 3 pyrimidines, with 2 purines < 2 pyrimidines

or applying equal positions

-c.f. Broomehad, v similar x total structures of adenine and guanine.

Peaks at height 0 lies on axis

\therefore 2 P atoms attached to similar nucleotides
- apart from this, symmetry does not control nucleotide sequence
except that = a "back-to-back" pair of chains top half of
one is similar to bottom half of other



Each chain (of) peaks = unit cell

can't reconcile nucleotide sequence with Chargaff's analysis

~~if all chains are same, sequence must be~~ ABCDDCB

N.B. Symmetry axis does not affect sequence within one chain

Distance between neighboring peaks 5.7A (= 3 dimensions)

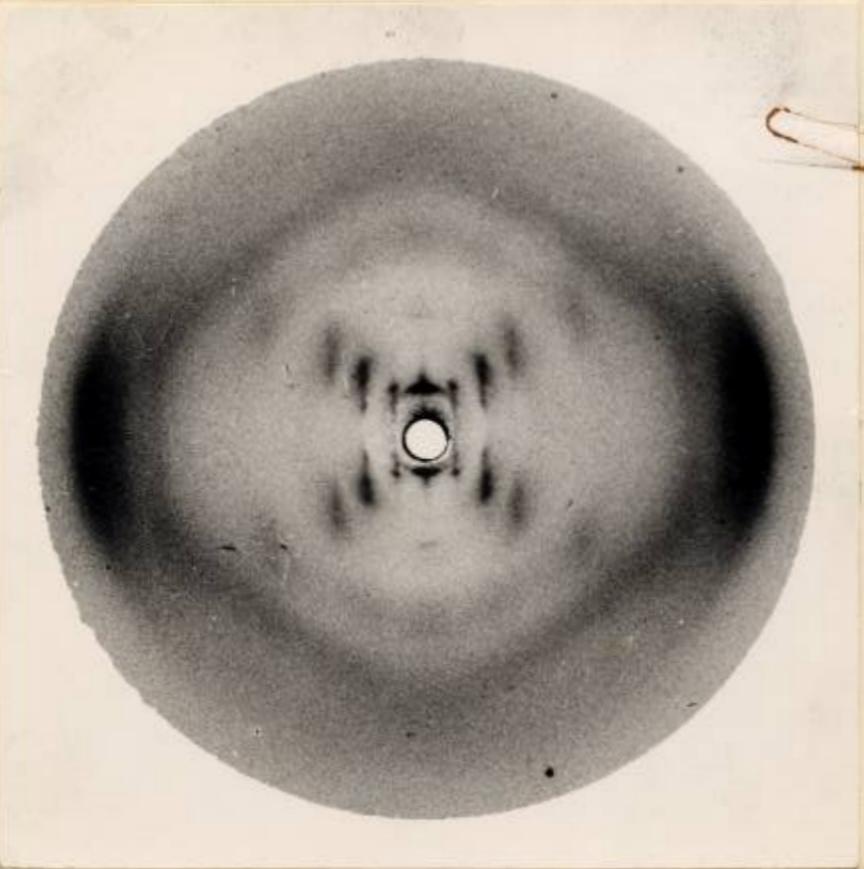
Nearest to agreement with Chargaff analysis would be

4 purines, 3 pyrimidines, with 2 purines & 2 pyrimidines
occupying equivalent positions

- c.f. Broomhead, & similar X-ray structures of adenine & guanine

“Race for the Double Helix” Rosalind Franklin’s Photo 51

Look at this X-ray
crystallography photo of
D.N.A. taken by Rosalind
Franklin.
What sort of shape for
D.N.A. can you deduce
from this photo?



Franklin &
Pauling
with
Rosalind
Franklin
Type B

Photo 1

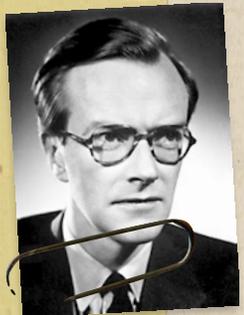
From: <http://scarc.library.oregonstate.edu/coll/pauling/dna/pictures/sci9.001.5-large.html>

PHYSICAL STUDIES OF NUCLEIC ACID

By Dr. M. H. F. WILKINS, R. G. GOSLING and W. E. SEEDS ; Mrs. MARY J. FRASER and ROBERT D. B. FRASER

Reprinted from Nature, Vol. 167, p. 759, May 12, 1951

You do not need to read the article, only note the Author and Date from the bottom of the front cover (above) and the first page of the article. Turn to the next page for more directions.



PHYSICAL STUDIES OF NUCLEIC ACID

Nucleic Acid: an Extensible Molecule ?

THE negative birefringence and ultra-violet dichroism of streaming solutions and fibres of sodium thymonucleate¹⁻³ has been taken as indicating a long molecule with purine and pyrimidine rings roughly at right-angles to the length. Astbury⁴ has observed by X-ray diffraction a 3.4-A. spacing along the length of the fibres, and has suggested that the nucleotides are flat and lie 3.4 A. apart. We have studied in more detail the properties of sodium thymonucleate fibres and have confirmed the above general conception, but have observed an unusual stretching phenomenon in the fibres which suggests that the long molecules may be extended into a second form.

The main experimental facts may be summarized as follows: Fibres in air of 50 per cent humidity are

There is little change in X-ray spacing along the length of the fibre on drying, and, in view of the great length of the molecules, which is probably at least 1000 A., it would appear likely that most of the increase of length of the fibre on hydration is associated with the change from the amorphous to the crystalline state, and is not due to water packing between crystallites. Presumably, on dehydration, the backbone of phosphate ester linkages in the molecule becomes crumpled and the purine and pyrimidine rings tilted; and, on hydration, the molecules pack regularly together and become extended in length with the purine and pyrimidine rings approximately at right-angles to the length. It is also unlikely that the reversible extension of the fibre on stretching is due to reversible slipping of molecules over one another, and it is difficult to avoid the conclusion that these molecules have been extended in length during the necking process. The optical observations show that the purine and pyrimidine rings have rotated during this process and lie on the average at about 45° to the length of the fibre.

Read the last sentence, starting with "The optical ..."

When one considers the general form of the nucleic acid structure, a hypothesis which could explain these observations comes to mind. Nucleic acid consists broadly of large flat rings closely packed together^{4,6}, each nucleotide being joined to the next by a single chain of bonds. Such a system might be deformed very easily, and the rings might slide over one another from one equilibrium position to another (corresponding to the discontinuous process of necking) while keeping their separation roughly constant. If the general direction of the phosphate backbone of the molecule is kept straight during this process, extension of the backbone-length in the ratio of 1 to $\sqrt{2}$ would mean tilting the rings from 90° to 45° as observed. The extension could take place by rotations of the bonds in the backbone-chain relative to one another, the bond-angles being kept roughly constant.

Read the last two sentences, starting with "If the ..."

From these three sentences, what does Wilkins' observe about the shape/orientation of components of D.N.A.?

Whatever the precise mechanism of the necking process, its study may well cast light on the structure of nucleic acid. So far the X-ray diffraction picture of the positive phase shows only diffuse rings, but in the case of infra-red dichroism the change of orientation of the units in the molecule gives much extra information⁵.

We wish to thank Prof. R. Signer for sodium thymonucleate, Dr. K. A. Smith for nucleoprotein, and Prof. J. T. Randall and Dr. R. E. Franklin and colleagues for discussion. A fuller account of this work will be published later. We are indebted to the

which has never been since surpassed. Dr. Schonland expressed disappointment that the membership in recent years has been more than a little diminished enormously. The need for, and the Association. The Association have not been years: "We and foster a not to publish a common problems of this defended the it, for "we parochial, and we on being parochial. I would suggest if we try to be anything else we will have mistaken our real aim".

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

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

BASIS OF TECHNICAL EDUCATION

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

Broadly, the Conference found that organized social foresight is essential to enable the educational system of a country to prepare children for the type of life and work they are likely to encounter, and that a substantial development of technical education

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

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 likely to be most effective when they are varied rather than concentrated. The administrator, no less than the student, has need of frequent contact with the industrial world, and the difficulties and problems of development in society; just as the student should keep abreast of research and of practical applications.



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.

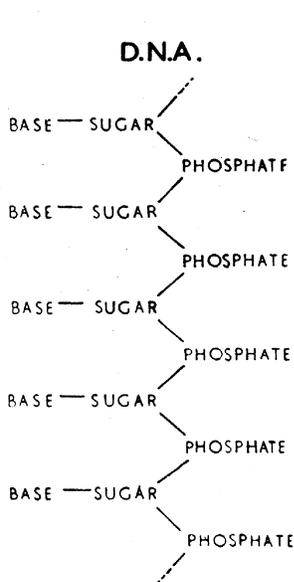


Fig. 1. Chemical formula of a single chain of deoxyribonucleic acid

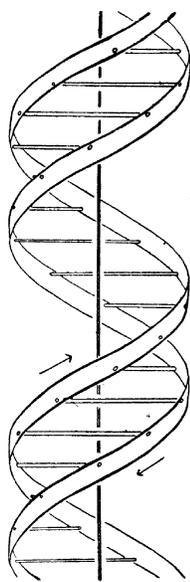


Fig. 2. This figure is purely diagrammatic. The two ribbons symbolize the two phosphate-sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis

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 structure¹ 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, London², and presented at the same time, gives qualitative support to our structure and is incompatible with all previously proposed structures³. 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 evidence², 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.

First, examine Fig. 1 and Fig. 2 (top left).

Then, read the two paragraphs that begin "The chemical ..." and "The first ..."

1). How many chains are in D.N.A. according to Watson and Crick?

2). Where do Watson and Crick hypothesize the phosphates are located in the molecule (in the outer rings or in the "backbone"?)

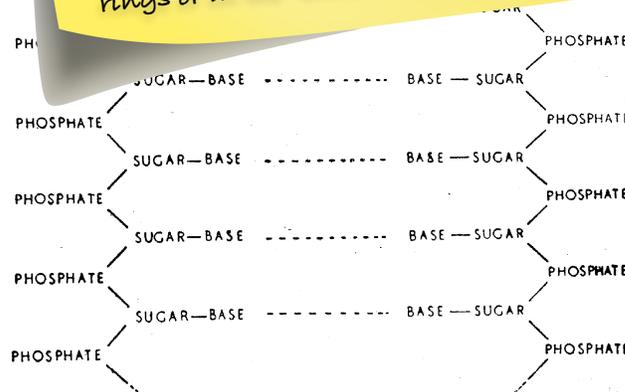


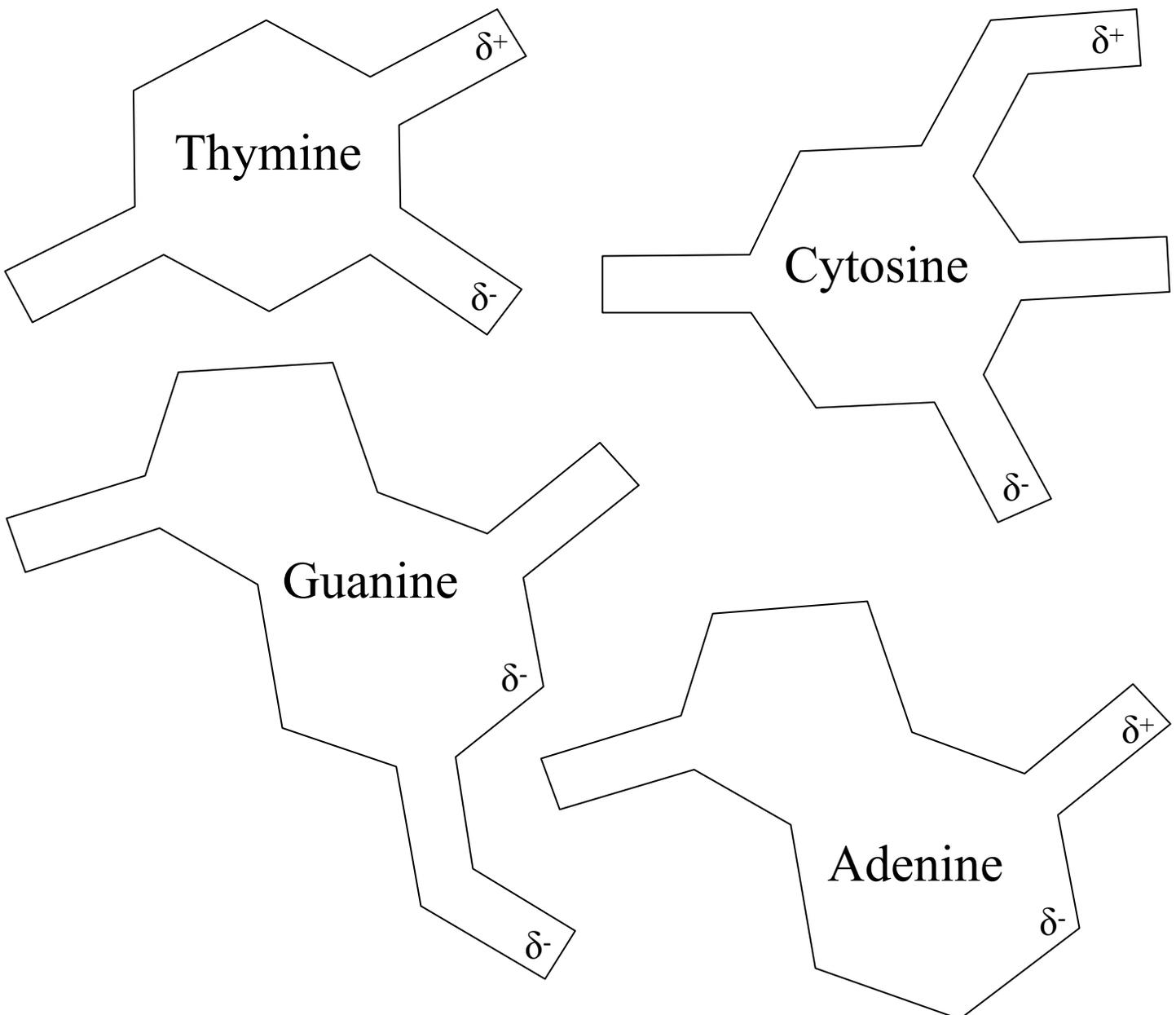
Fig. 3. Chemical formula of a pair of deoxyribonucleic acid chains. The hydrogen bonding is symbolized by dotted lines

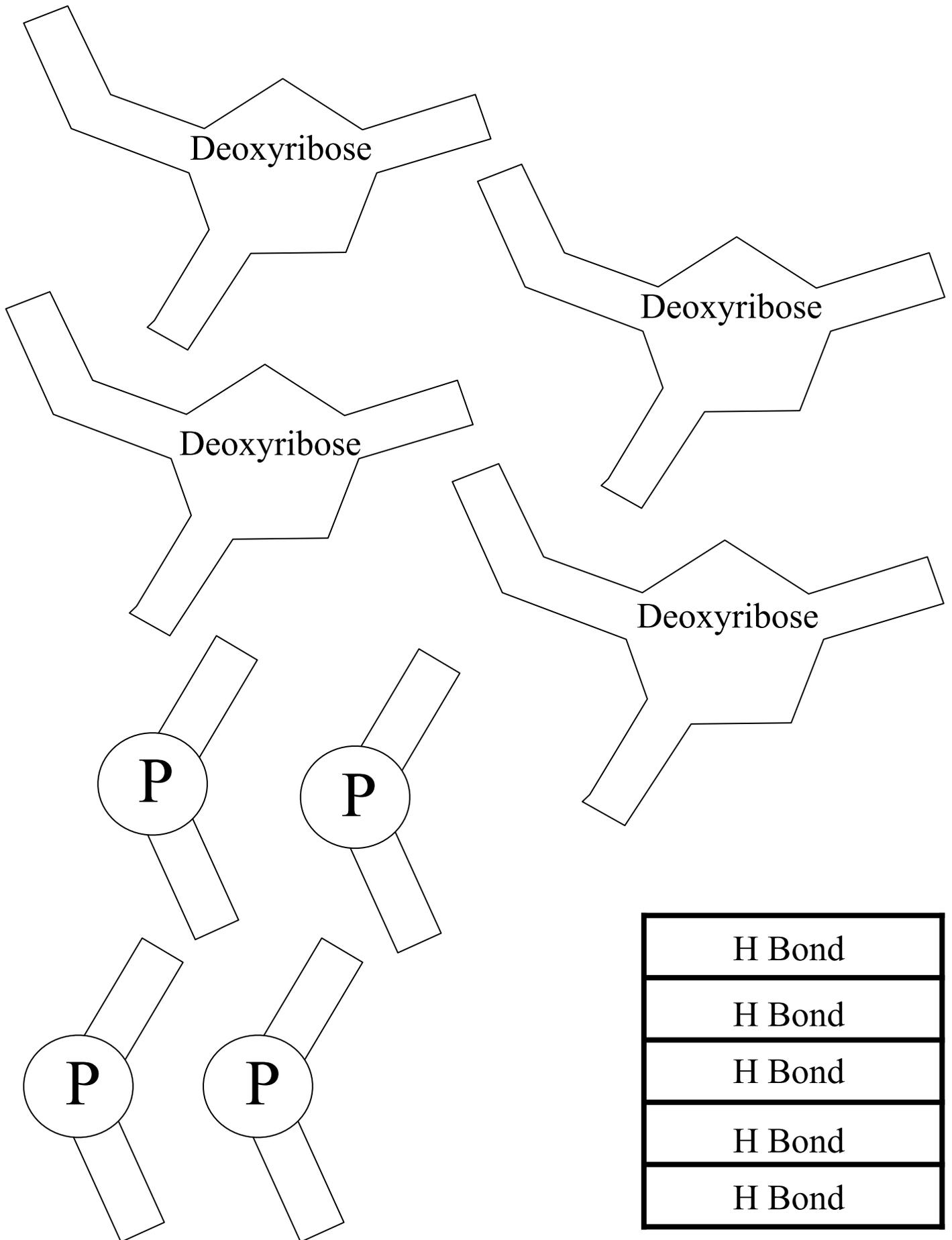
“Race for the Double Helix”

DNA model pieces

Directions: Recreate James Watson and Francis Crick’s struggle to deduce the bonding between base pairs. Rotate each base and pair it with its correct corresponding base. Use the hydrogen bonds (H bonds) on page 36 and lay them over the correct locations where hydrogen bonds would be created between the bases. You must also use the deoxyribose sugar pieces and phosphate (P) pieces on page 36 and correctly connect them to the base pairs to make an alternating sugar-phosphate backbone.

Note: The pieces are shaped with ‘connectors’ to show the bonds they can form. Sites marked with symbols ($\delta+$ or $\delta-$) can ONLY form weak hydrogen bonds, others only covalent bonds. Pieces can be rotated but must stay writing side up.







DNA model pieces **KEY**

Students should have Adenine paired with Thymine using two Hydrogen bonds and Cytosine paired with Guanine using three Hydrogen bonds. The backbone (or side pieces) should be composed of deoxyribose connected directly to the nitrogen base (Adenine, Thymine, Cytosine or Guanine) alternating with a Phosphate (P). Note: Students should have one of each pair of bases turned upside down as DNA runs antiparallel (one side runs in the opposite direction compared to the other).



In Conclusion

After completing the D.N.A. model piece activity where students are in the role of James Watson, the teacher should wrap up the lesson by completing the following.

1. Show the last 4 minutes and 36 seconds of the video showing James Watson's explanation of how the bases (A, T, C and G) pair together. This explanation, along with the provided answer key will provide students the correct arrangement of their D.N.A. template pieces. This last portion also explains the impact of this discovery for the future of science.
2. **Read the following paragraphs to students and ask them to listen for 3-4 scientific advancements President Eisenhower and his administration assisted in developing.**

President Eisenhower helped develop America's leadership role in scientific research and education. In March 1953, President Eisenhower established the Department of Health, Education and Welfare (which later became the Department of Health and Human Services). He appointed Oveta Culp Hobby as the secretary of this new department, the only woman in the cabinet. It was under her direction that millions of children were administered the life saving polio vaccine.

In a memorandum of a conference with President Eisenhower in October, 1957, Eisenhower expressed the need to further scientific research so that we would not be out distanced by Russian scientific advancements. To assist him he appointed James Rhyne Killian as his Presidential Science Advisor, the first position of its' kind. To further address the Russian missile crisis, The Advanced Research Project Agency (ARPA, renamed DARPA in 1972) was established under President Eisenhower in February 1958. Its' primary goal was to advance United States missile supremacy, but research broadened and eventually helped develop our current Global Positioning System (GPS) technology and the internet. And, on September 2, 1958, he signed into law the National Defense Education Act which authorized funding for scientific research and development of scientific curricula. President Eisenhower also signed the National Aeronautics and Space Act in July of 1958 establishing the National Aeronautics and Space Administration (NASA).

These departments and agencies developed during President Eisenhower's administration helped pave the way for further scientific advancements.

3. **Ask students to share (for 1 minute) with a partner the 3-4 scientific advancements President Eisenhower and his administration assisted in developing.** Teachers can then ask a few students to share their responses.

Answer: Polio vaccine, Global Positioning System (GPS), internet (lead to the development) and NASA.

Executive Order 10510—Establishing a Seal for the Department of Health, Education, and Welfare
December 17, 1953
<http://www.presidency.ucsb.edu/ws/?pid=106560>



Extension



Courtesy of Cold Spring Harbor Laboratory Archives and Svenskt Press Photo, Stockholm, Sweden.
Noncommercial, educational use only.

WANT TO LEARN MORE?

There is more drama to this story. To read more about the discovery and people involved, visit: PBS: www.pbs.org/wgbh/aso/databank/entries/do53dn.html or D.N.A. from the beginning: www.dnafb.org/19/index.html where teachers can find animations, concept elaborations, videos, photo galleries and other links.

Excerpt from an interview with Lynne Osman Elkin, a professor of biological sciences at California State University, Hayward.

From: <http://www.pbs.org/wgbh/nova/tech/rosalind-franklin-legacy.html>

There is no way without her data that Watson and Crick could have figured out the structure before [her March 17th draft] got published. Now, if that had gotten published first and *then* they figured it out—remember, she talked about the double helix in that paper—then even though they had figured out the actual structure, they would have had to incorporate her information and credit her properly, and she would not have been written out of history.

After Watson saw Photo 51, he went out to dinner with [Wilkins](#) and pressed him for the interpretation of it—the [34-angstrom measurements](#) and so on. At that early date Watson didn't know how to interpret a diffraction photo, other than that an "X" meant helix. In terms of getting measurements out of it, he hadn't the foggiest—at that point. It was Wilkins who told him how to interpret it.

So the big question is, if Franklin had lived, would she or should she, instead of Wilkins, have received the Nobel Prize with Watson and Crick?

There's a big difference between "would" and "should." Should she have? Absolutely. One of the things I proposed last year at AAAS [the American Association for the Advancement of Science annual meeting] is that I think it should be called the Watson-Crick-Franklin structure. As far as I'm concerned, she was a de facto collaborator. Maybe she didn't give them her information directly. But every time they hit a stumbling point, it was her information that they got from Wilkins that straightened it out. So do I think should she have? Absolutely.

Would she have? I'm not so sure. The Nobel Prize could be very political, and often the Nobel Committee would put great emphasis on those who started the research, which in this case was Wilkins. But even Watson begrudgingly says that she should have gotten it.