

General Biology

Ch 10: The Structure and Function of DNA (Ref Book Chapter 8)



The discovery of “The secret of Life”

General Biology

Ch 10: The Structure and Function of DNA (Ref Book Chapter 8)



“DNA Replication”

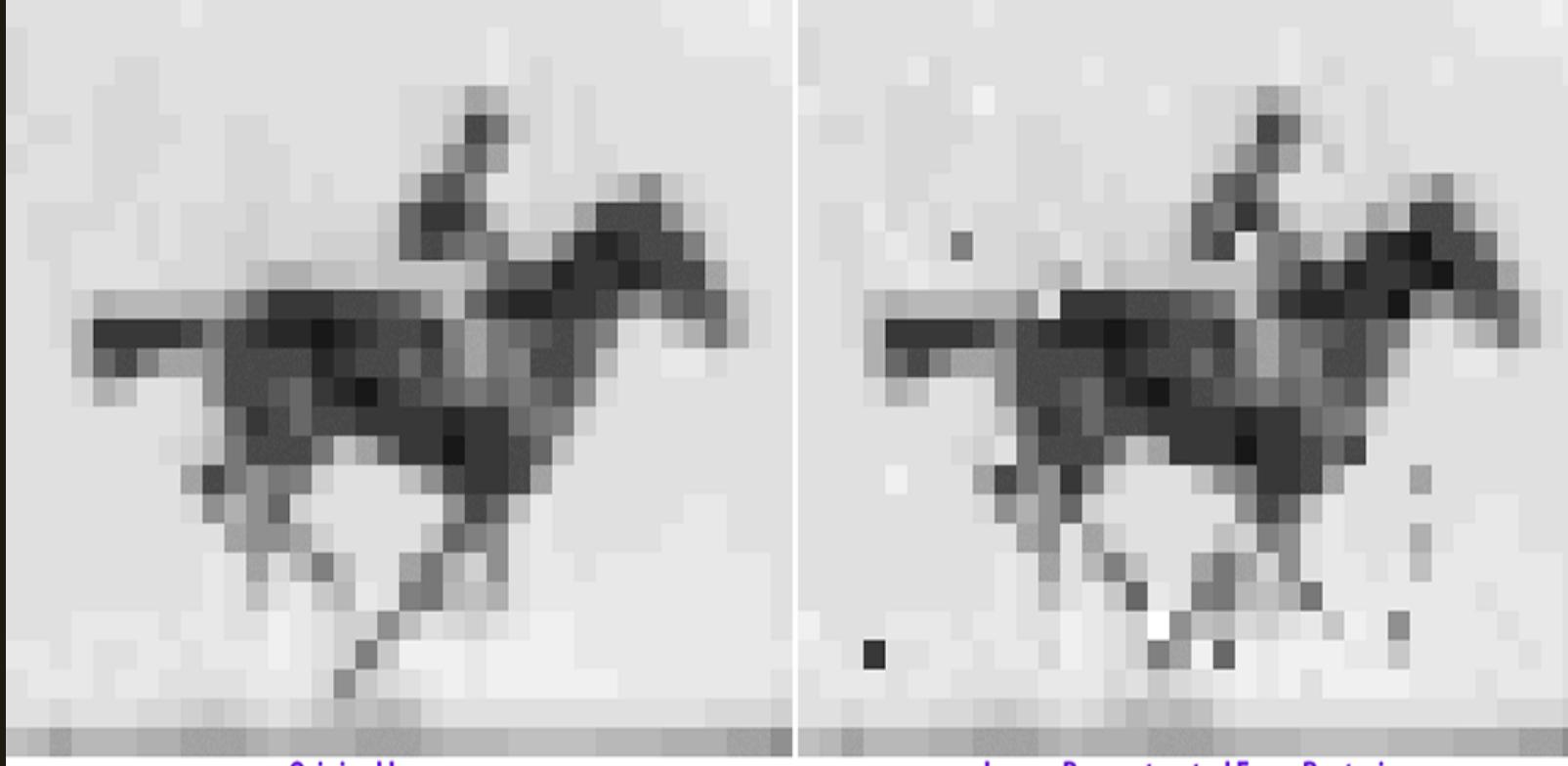
Learning Objectives

- How investigators pinpointed DNA as the genetic material
- The discovery of DNA, the double helix
- Chargaff's Rule
- The elegant Watson-Crick model of DNA structure
- Introduction to DNA replication

Who Needs Hard Drives? Scientists Store Film Clip in DNA

[Leer en español](#)

By GINA KOLATA JULY 12, 2017



Original Image

Image Reconstructed From Bacteria

It was one of [the very first motion pictures ever made](#): a galloping mare filmed in 1878 by the British photographer Eadweard Muybridge, who was trying to learn whether horses in motion ever become truly airborne.

More than a century later, that clip has rejoined the cutting edge. It is now the first movie ever to be [encoded in the DNA of a living cell](#), where it can be retrieved at will and multiplied indefinitely as the host divides and grows.

The advance, reported on Wednesday in the journal *Nature* by researchers at Harvard Medical School, is the latest and perhaps most astonishing example of the genome's potential as a vast storage device.

Scientists already have managed to translate all of [Shakespeare's sonnets into DNA](#). George Church, a geneticist at Harvard and one of the authors of the new paper, also has helped develop "DNA data storage," which

2017

DNA can hold a staggering amount of information. Researchers have stored as much as 700TB of data in a single gram of DNA. If scaled properly, all of the information in the entire world – media, papers, the internet, EVERYTHING – would fit in the back of a single van, according to computational biologist Nick Goldman.

What is the script to different life forms and activities!!!!



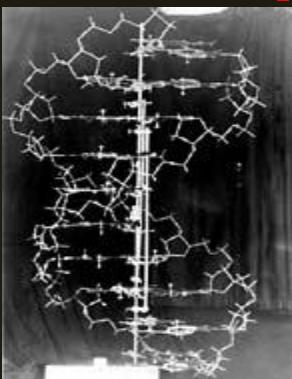


**Crick and
Watson**

**Rosalind
Franklin**

**Maurice
Wilkins**

**Erwin
Chargaff**



**Lets take a journey through the
discovery of DNA, the double helix**

1865: The search to the molecule of inheritance started with Gregor Mendel



Gregor Mendel

- Carried out breeding experiments with peas.
- Used pure strains of round, wrinkled, green and yellow peas.
- Cross bred the peas and counted the different offspring.
- Found that characteristics were inherited in clear predictable patterns.

GREGOR MENDEL

- Mendel stated that physical traits are inherited as “**particles**”
- Mendel did not know that the “particles” were actually **Chromosomes & DNA**



Who identified DNA?

1869: Friedrich Miescher, a Swiss biologist FIRST identified DNA



On February 26, 1869 –
Friedrich Miescher
extracted a weakly
acidic, phosphorous
rich material from
nuclei of human white
blood cells which he
named **nuclein**.

The Discovery of DNA



Figure 1
Friedrich Miescher first investigated nuclein, now known as DNA.

- 1869 – Friedrich Miescher investigated chemical composition of DNA using pus cells.
- At the time, proteins were thought to be hereditary material.
- Miescher discovered the nuclei of cells contained a substance that does not act like protein. He called this substance nuclein.
- This caused debate – Is protein or nuclein the hereditary material?

The Timeline.....

Scientists that determined DNA's Structure and Importance

- 1866 Gregor Mendel – demonstrated that parents pass traits to offspring-thought traits contained in a molecule
- 1869 Friedrich Meisher – Isolated DNA from cell nucleus – named it nucleic acid
- 1889 R.A. Altman-determined the chemical composition of DNA

1928: Frederick Griffith, the “Transforming Principle”

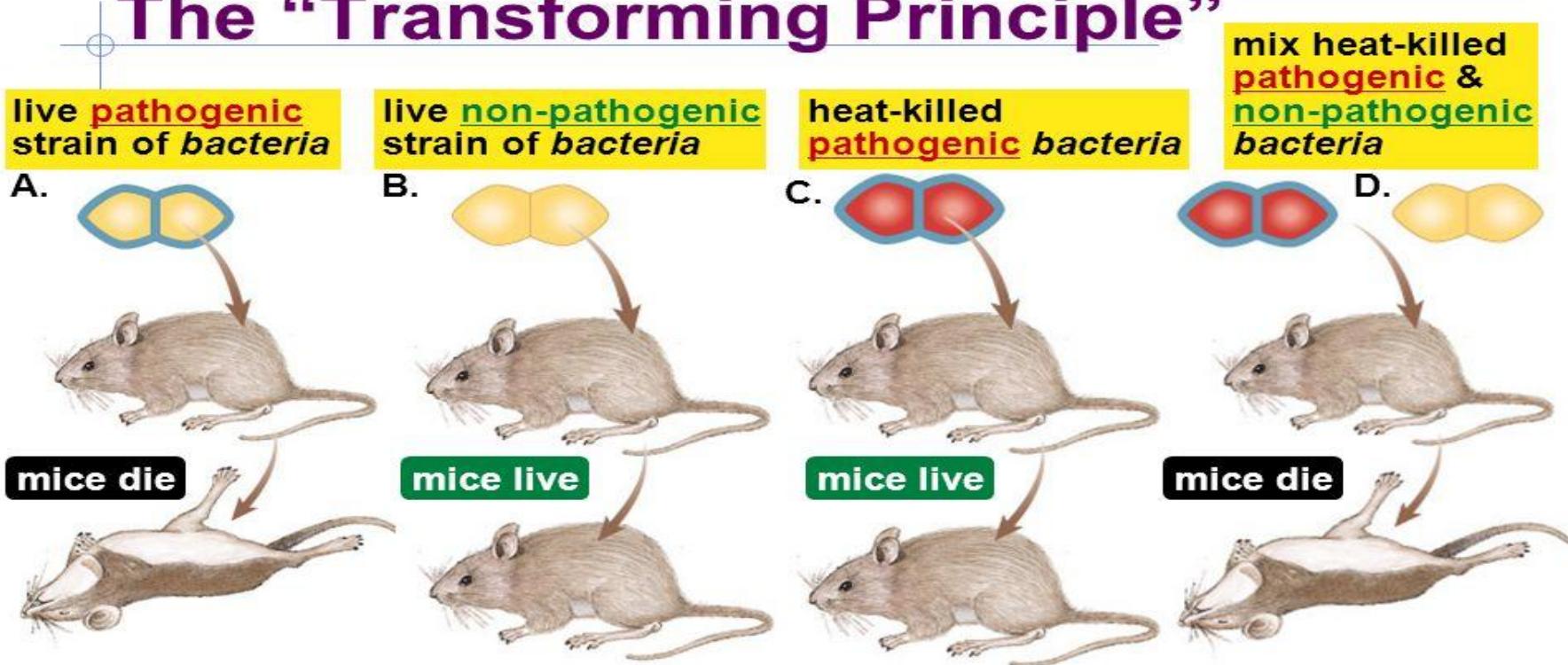
Identifying that DNA is the genetic material



- 1928 (Frederick Griffith) – transforming principle – experiments with *Streptococcus pneumoniae*- ‘R’ and ‘S’ strains (differ in virulence)

What did Griffith determine with his 1928 experiment?

The “Transforming Principle”



Transformation = change in phenotype
something in heat-killed bacteria could still transmit disease-causing properties



What is your conclusion?

Avery, McCarty & MacLeod - 1944

DNA is the transformation material



Oswald Avery



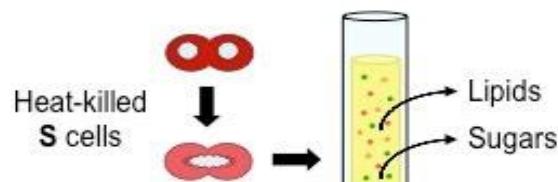
Maclyn McCarty



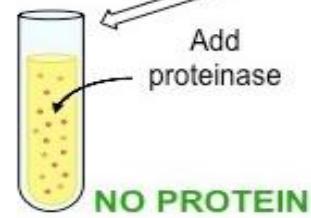
Colin MacLeod

1944: Illustration of the classic experiment by Avery, MacLeod, and McCarty

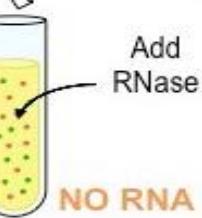
Hypothesis: The genetic material of the cell is either protein or nucleic acid (DNA or RNA)



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

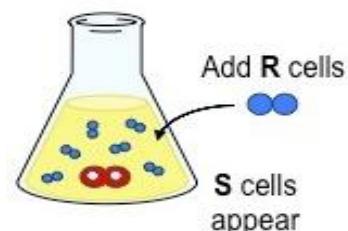
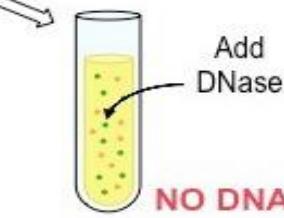


Treat solutions with enzymes to destroy protein, RNA or DNA

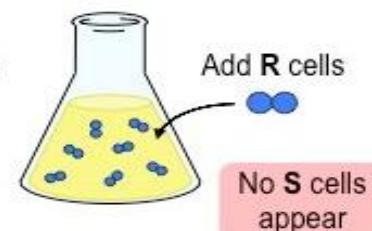
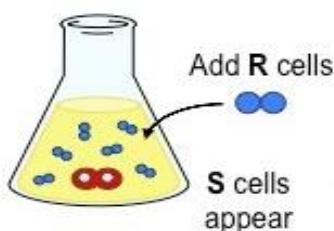


NO DNA

NO RNA



Add to culture containing living R cells. Observe for transformation by testing for the presence of virulent S cells



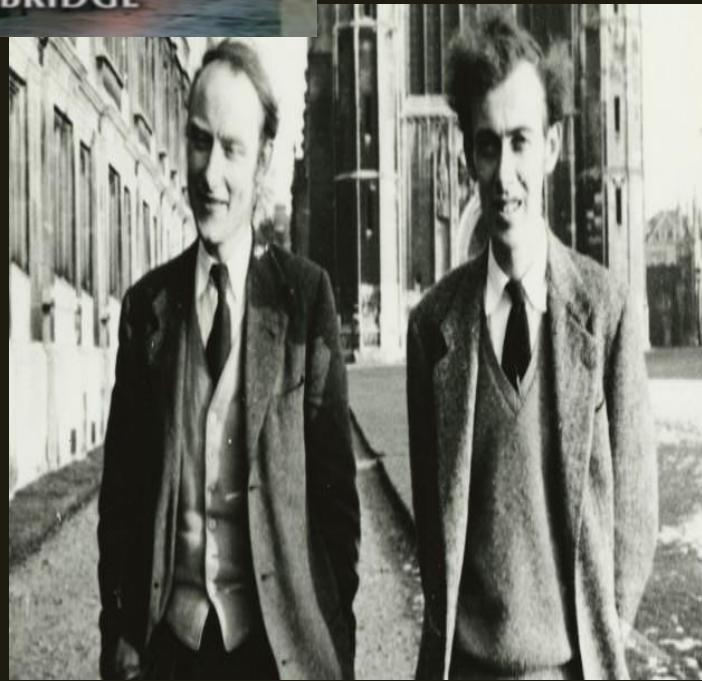
Conclusion: Transformation requires DNA, therefore it is the genetic material of the cell

So, around late 1940's, scientific community became aware that DNA was most likely the molecule of life, even though many were skeptical since it was so **"simple."** They also knew that DNA included different amounts of the four bases (A, T, G and C), but nobody had the slightest idea of what the molecule might look like.

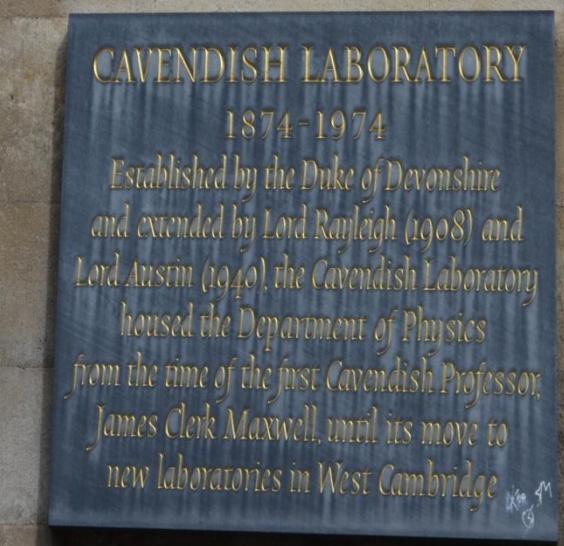
The Race for DNA

Solving the puzzle.....

Cavendish Lab, University of Cambridge



FRY ARCHIVES



King's College, London



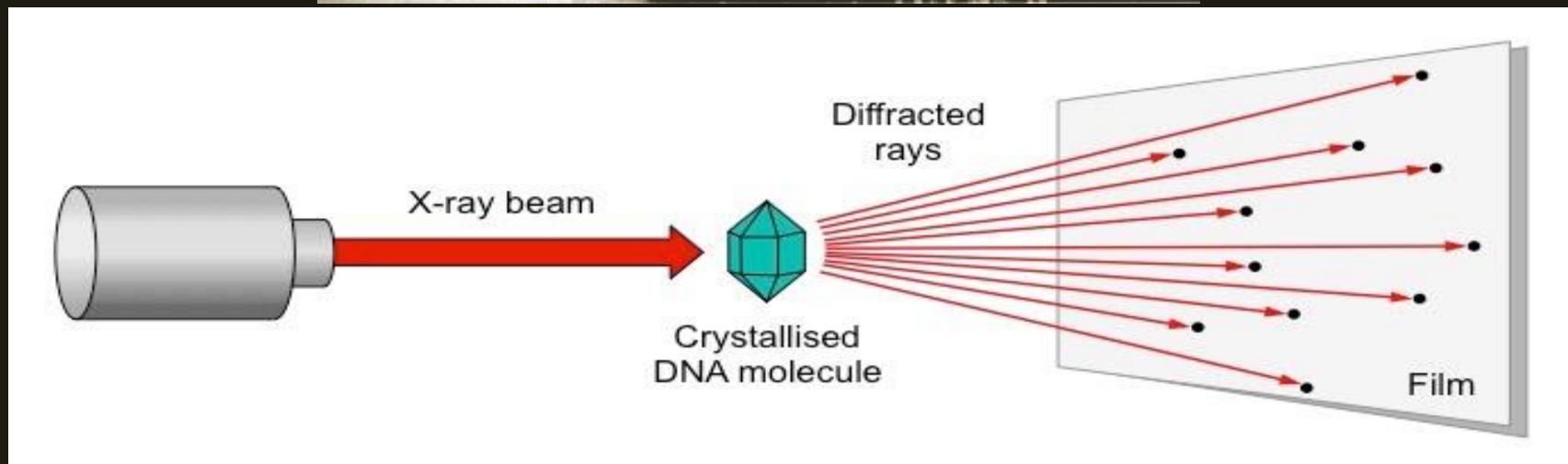
Maurice
Wilkins



Rosalind
Franklin



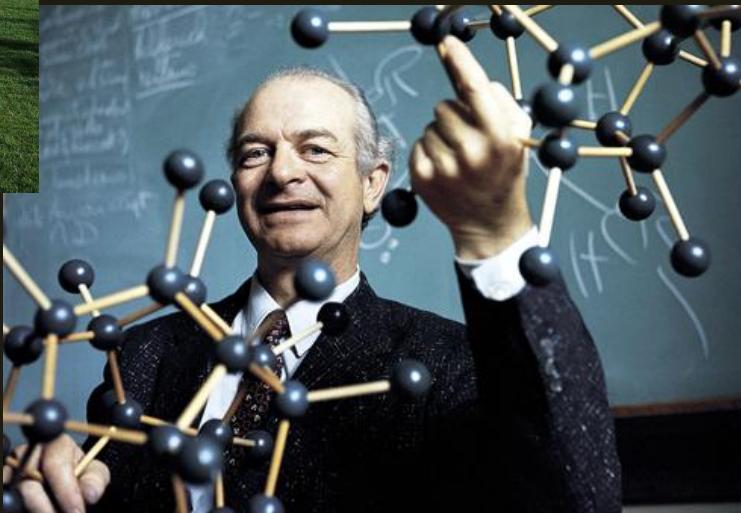
X-Ray Crystallography



At California University of Technology, USA



Linus
Pauling



Nobel Prize, Chemistry

Nobel Prize, Peace



Awarded to Linus Pauling, 1954



Awarded to Linus Pauling, 1962

1951: Rosalind Franklin: The “Dark Lady of DNA”



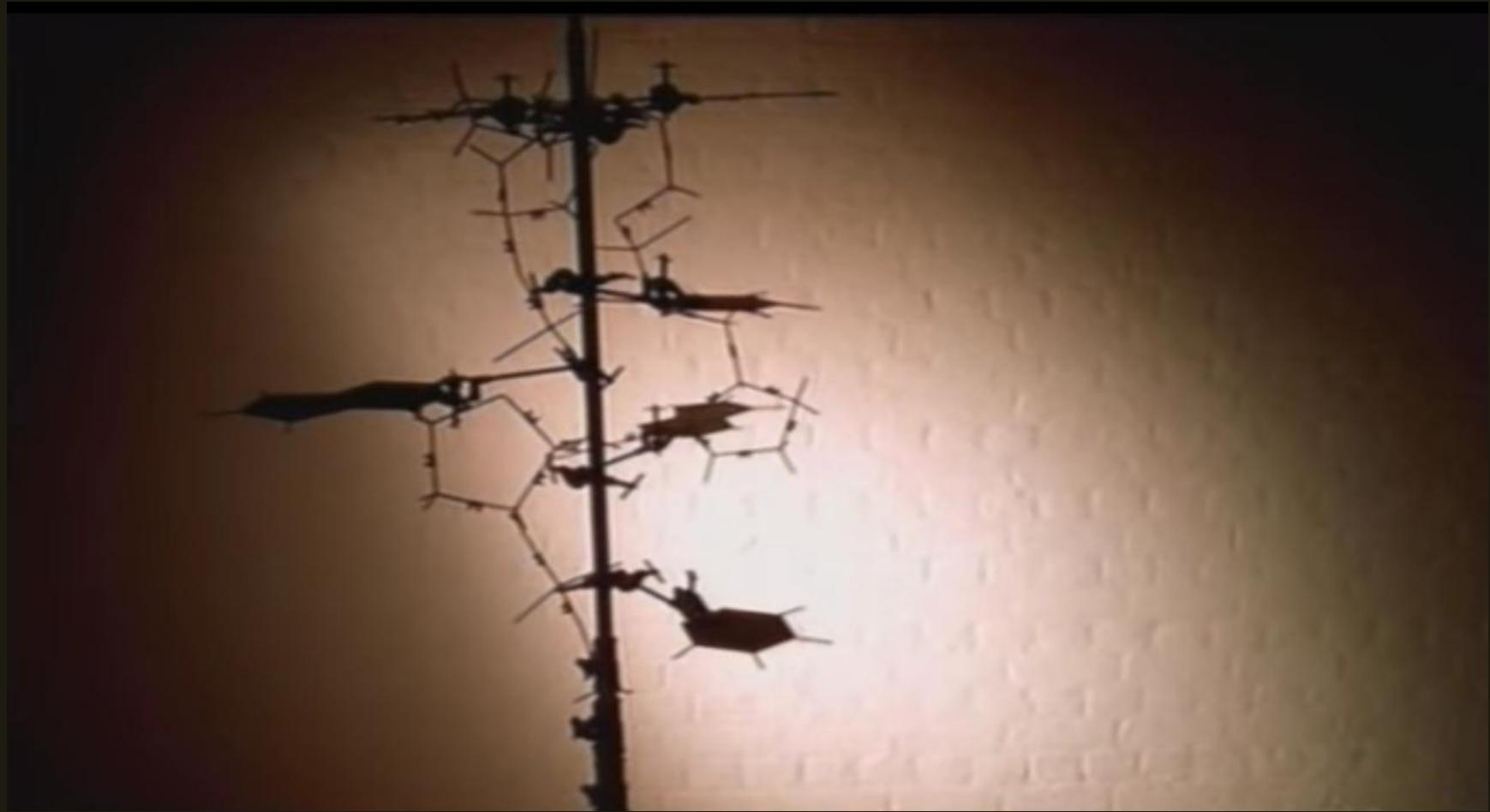
9. Rosalind Franklin
A biophysicist. Produced the first X-Ray diffraction images of DNA.

Rosalind Franklin



Raymond Gosling

Nov 28th 1951- Watson and Crick announced that they have the structure to the secret of life



Tell what is wrong with the model

You have got it inside out---
Rosalind Franklin

Their model was a complete disaster

**Watson and Crick were officially barred
from the race**

1952: Watson and Crick came up with a three stranded helix, with the base rings located on the outside of the molecule and the phosphate groups found on the inside.

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

L. H. C. S. L.

Franklin--noted that DNA soaks up a large amount of water, which indicates that the phosphate groups must be on the outside of the molecule

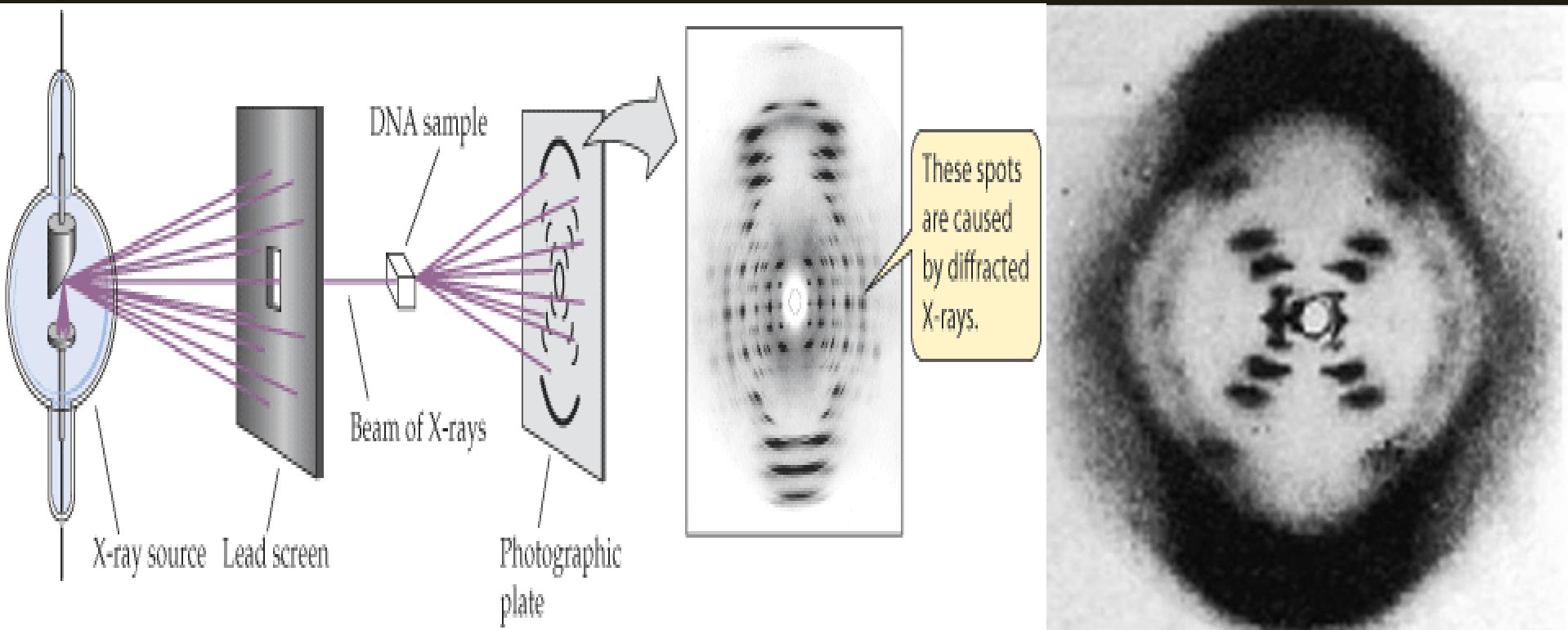


Photo No 51

1950: Erwin Chargaff's Rule



Erwin Chargaff



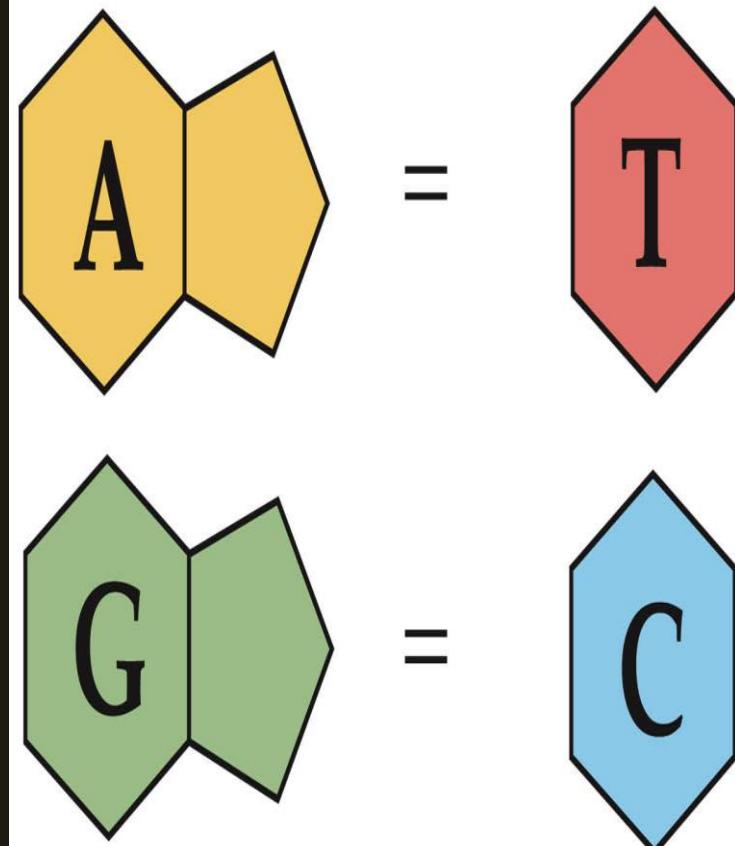
1950: The First Parity Rule

While DNA composition varies among species, the following two equalities are observed:

- (1) $A\% \approx T\%$
- (2) $G\% \approx C\%$

Chargaff's values for humans:

$G = 19.9\%$, $C = 18.8\%$, $A = 30.9\%$, and $T = 29.4\%$



Purines = Pyrimidines

Chargaff's Data

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TABLE 6.1 **Chargaff's Data on Nucleotide Base Composition in the DNA of Various Organisms**

Organism	Percentage of Base in DNA				Ratios	
	A	T	G	C	A:T	G:C
<i>Staphylococcus afermentans</i>	12.8	12.9	36.9	37.5	0.99	0.99
<i>Escherichia coli</i>	26.0	23.9	24.9	25.2	1.09	0.99
Yeast	31.3	32.9	18.7	17.1	0.95	1.09
<i>Caenorhabditis elegans</i> *	31.2	29.1	19.3	20.5	1.07	0.96
<i>Arabidopsis thaliana</i> *	29.1	29.7	20.5	20.7	0.98	0.99
<i>Drosophila melanogaster</i>	27.3	27.6	22.5	22.5	0.99	1.00
Honeybee	34.4	33.0	16.2	16.4	1.04	0.99
<i>Mus musculus</i> (mouse)	29.2	29.4	21.7	19.7	0.99	1.10
Human (liver)	30.7	31.2	19.3	18.8	0.98	1.03

*Data for *C. elegans* and *A. thaliana* are based on those for close relative organisms.

Note that even though the level of any one nucleotide is different in different organisms, the amount of A always approximately equals the amount of T, and the level of G is always similar to that of C. Moreover, as you can calculate for yourself, the total amount of purines (A plus G) nearly always equals the total amount of pyrimidines (C plus T).

1953 – Linus Pauling

- Proposed the alpha helix secondary structure in proteins

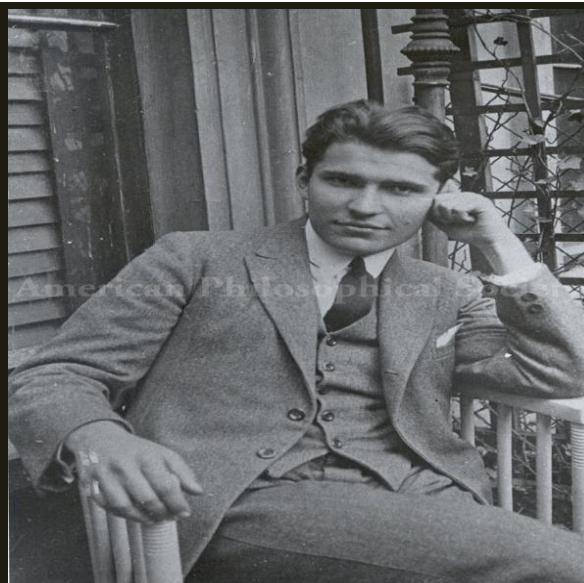
✗ Triple helix DNA model: 3 strands intertwined





10

1953: The great minds put together



The Old



The Current



1953: The ultimate famous article in “Nature”

with compliments of Maurice Wilkins
Oliver R. Stokes

(Reprinted from *Nature*, Vol. 171, p. 737, April 25, 1953)

James D. Watson

Francis Crick

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 Corey¹. They kindly made their manuscript available to us in advance of publication. Their model consists of three inter-twined 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.

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 di-ester 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's² 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 Å. in the z-direction. We have assumed an angle of 36° between adjacent residues in the same

740

NATURE

April 25, 1953

VOL. 171

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

M. H. F. WILKINS

Medical Research Council Biophysics
Research Unit,

A. R. STOKES
H. R. WILSON

Wheatstone Physics Laboratory,
King's College, London.

April 2.

¹ Astbury, W. T., Symp. Soc. Exp. Biol., 1, Nucleic Acid (Cambridge Univ. Press, 1947).

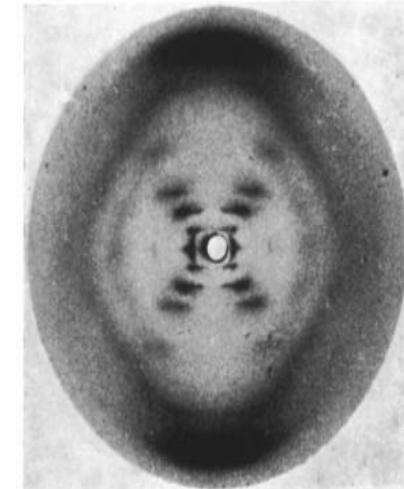
² Riley, D. P., and Oster, G., *Biochim. et Biophys. Acta*, 7, 526 (1951).

³ Wilkins, M. H. F., Gosling, R. G., and Seeds, W. E., *Nature*, 167, 759 (1951).

⁴ Astbury, W. T., and Bell, F. O., *Cold Spring Harb. Symp. Quant. Biol.*, 8, 109 (1938).

⁵ Cochran, W., Crick, F. H. C., and Vand, V., *Acta Cryst.*, 5, 581 (1952).

⁶ Wilkins, M. H. F., and Randall, J. T., *Biochim. et Biophys. Acta*, 10, 192 (1953).



Sodium deoxyribose nucleate from calf thymus. Structure B

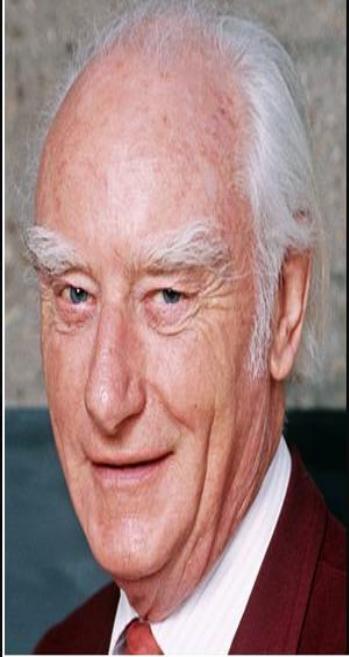
molecules, each unit being shielded by a sheath of water. Each unit is then free to take up its least-energy configuration independently of its neighbours and, in view of the nature of the long-chain molecules involved, it is highly likely that the general form will be helical³. If we adopt the hypothesis of a helical structure, it is immediately possible, from the X-ray diagram of structure B, to make certain deductions as to the nature and dimensions of the helix.

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

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

Molecular Configuration in Sodium Thymonucleate

SODIUM thymonucleate fibres give two distinct types of X-ray diagram. The first corresponds to a crystalline form, structure A, obtained at about 75 per cent relative humidity; a study of this is described in detail elsewhere⁴. At higher humidities a different structure, structure B, showing a lower degree of order, appears and persists over a wide



I think she [Rosalind Franklin] was a good experimentalist but certainly not of the first rank. She was simply not in the same class as Eigen or Bragg or Pauling, nor was she as good as Dorothy Hodgkin. She did not even select DNA to study. It was given to her. Her theoretical crystallography was very average.

— Francis Crick —

AZ QUOTES

The double helix and the ‘wronged heroine’

Brenda Maddox

9 Pitt Street, London W8 4NX, UK (e-mail: bmaddox@pitt.demon.co.uk)

In 1962, James Watson, Francis Crick and Maurice Wilkins received the Nobel prize for the discovery of the structure of DNA. Notably absent from the podium was Rosalind Franklin, whose X-ray photographs of DNA contributed directly to the discovery of the double helix. Franklin's premature death, combined with misogynist treatment by the male scientific establishment, cast her as a feminist icon. This myth overshadowed her intellectual strength and independence both as a scientist and as an individual.

"Science and everyday life cannot and should not be separated. Science, for me, gives a partial explanation of life. In so far as it goes, it is based on fact, experience and experiment." Rosalind Franklin, in a letter to her father, summer 1940.

In late February 1953, Rosalind Franklin, a 33-year-old physical chemist working in the biophysics unit of King's College in London, wrote in her notebooks that the structure of DNA had two chains. She had already worked out that the molecule had its phosphate groups on the outside and that DNA existed in two forms.

Two weeks later James Watson and Francis Crick, at the Cavendish Laboratory at Cambridge, built their now-celebrated model of DNA as a double helix. They did it not only through brilliant intuition and a meeting of compatible minds, but also on the basis of Franklin's unpublished experimental evidence, which had reached them through irregular routes. She did not know that they had seen either her X-ray photograph (Fig. 1), showing unmistakable evidence of a helical structure, or her precise measurements of the unit cell (the smallest repeating unit) of the DNA crystal.

As Watson was to write candidly, "Rosy, of course, did not directly give us her data. For that matter, no one at King's realized they were in our hands." When this admission appeared in Watson's best-selling, much-acclaimed book of the discovery, *The Double Helix*, published in 1968 (ref. 1), he was a Harvard professor and Nobel laureate (he had shared the prize for medicine and physiology in 1962, with Crick and Maurice Wilkins of King's College). By then Franklin had died — in 1958, at the age of 37, from ovarian cancer.

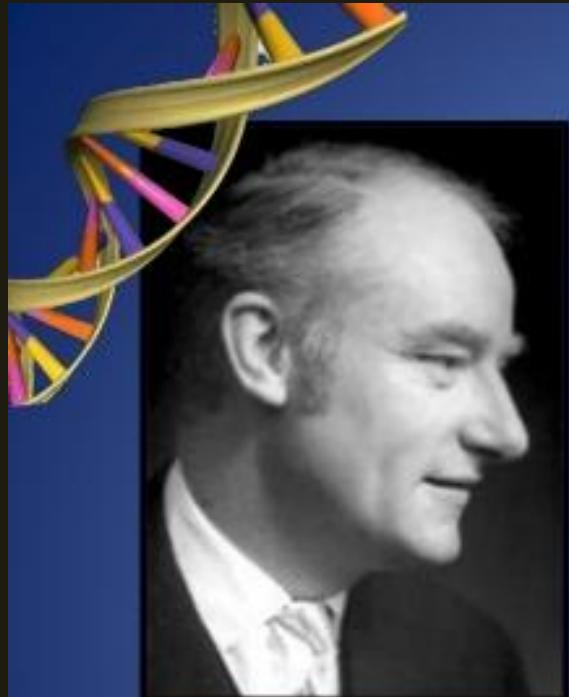
Other comments dismissive of "Rosy" in Watson's book caught the attention of the emerging women's movement in the late 1960s. "Clearly Rosy had to go or be put in her place [...] Unfortunately Maurice could not see any decent way to give Rosy the boot". And, "Certainly a bad way to go out into the foulness of a [...] November night was to be told by a woman to refrain from venturing an opinion about a subject for which you weren't trained."

A feminist icon
Such flan boyantly chauvinist phrases were sufficient to launch the legend of Franklin, the wronged heroine. So too was Watson's insistence on judging Franklin by her appearance rather than by her performance as a scientist. (She was, when she came to King's from the French government laboratory where she had worked from 1947 to the end of 1950, a recognized expert on



the structure of coals, carbons and disordered crystals, with many publications to her credit.)

The Franklin myth has continued to grow, abetted by the fact of her tragically early death. Franklin has become a feminist icon — the Sylvia Plath of molecular biology — seen as a genius whose gifts were sacrificed to the greater glory of the male. Her failure to win the Nobel prize has been given as a prime example



Francis Crick



James D. Watson

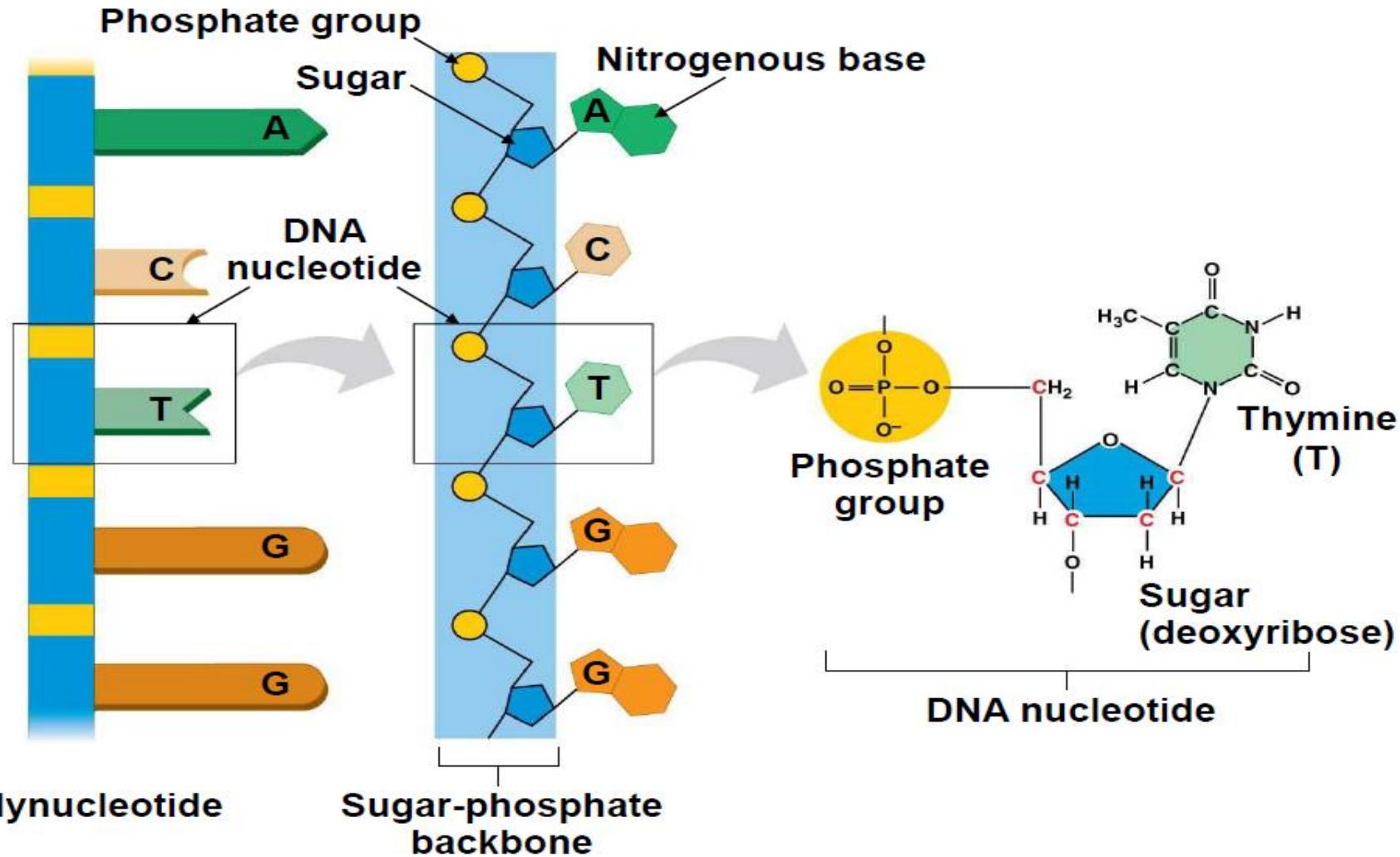


Maurice Wilkins

- The Nobel Prize in Physiology or Medicine 1962 was awarded jointly to Francis Harry Compton Crick, James Dewey Watson and Maurice Hugh Frederick Wilkins "for their discoveries concerning the molecular structure of nucleic acids and its significance for information transfer in living material" (1953).

**What did the world learn about
DNA from their research?**

The essence of the “Watson and Crick’s Research”- 1-Sugar and Phosphate Backbone

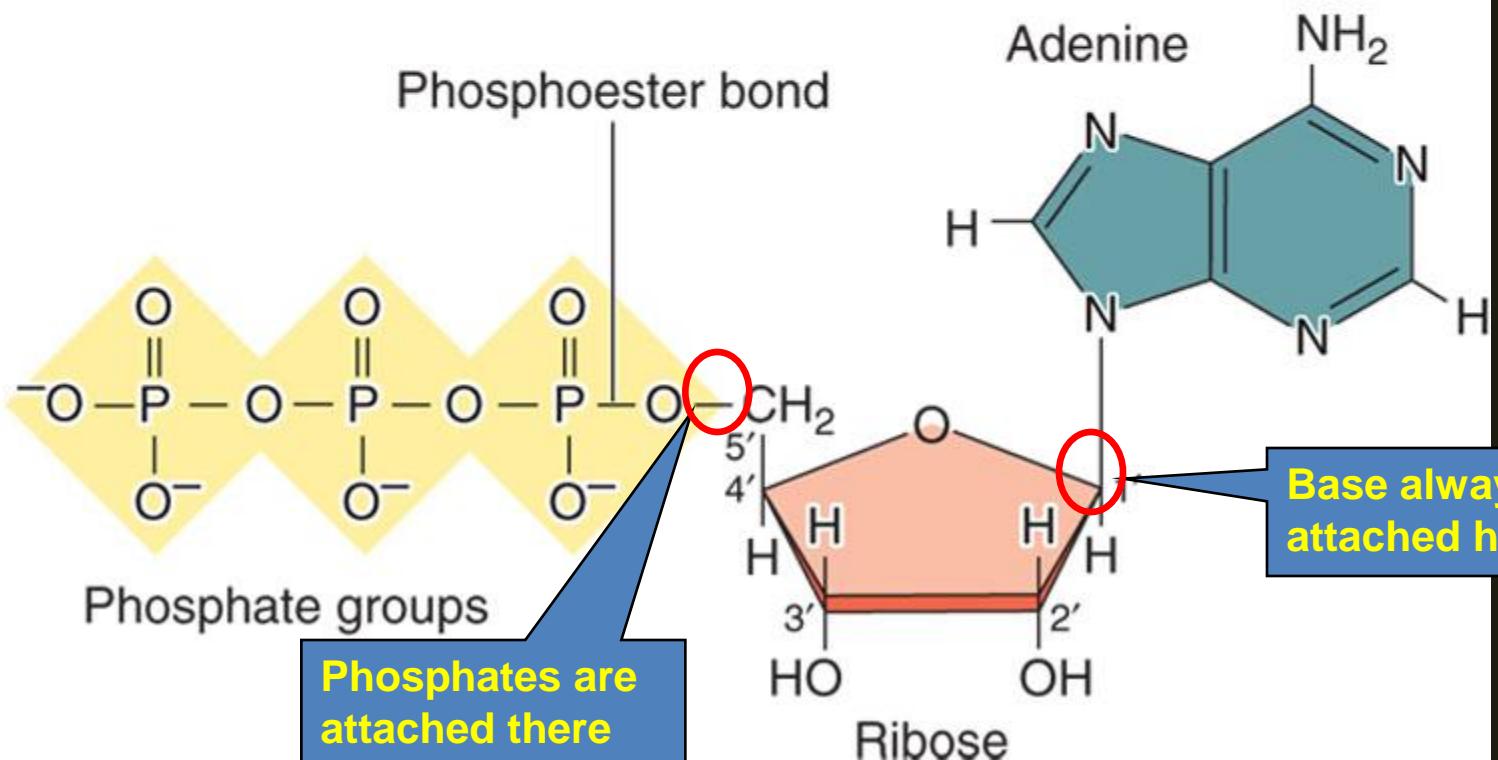


Adenosine triphosphate

Adenosine diphosphate

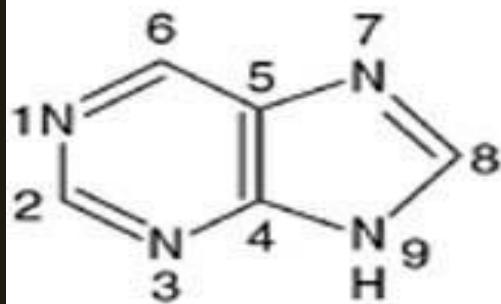
Adenosine monophosphate

Adenosine



The essence of the “Watson and Crick’s Research”-

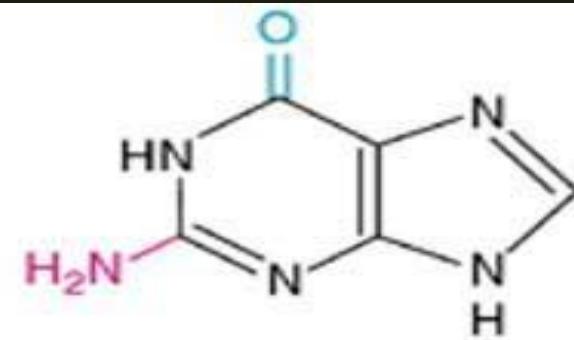
2- Pairing of bases



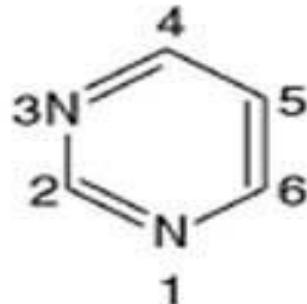
Purine



Adenine



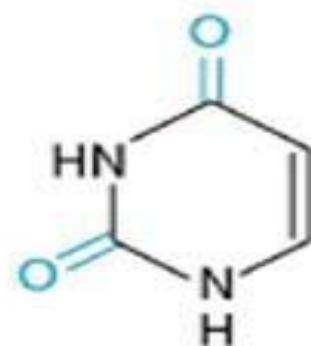
Guanine



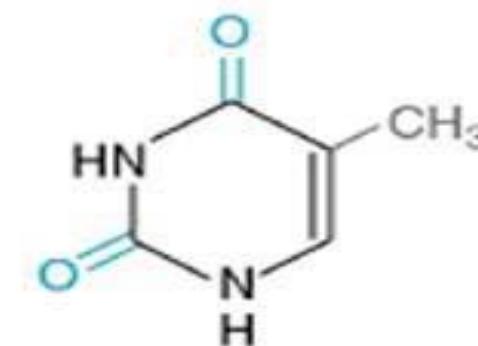
Pyrimidine



Cytosine



Uracil

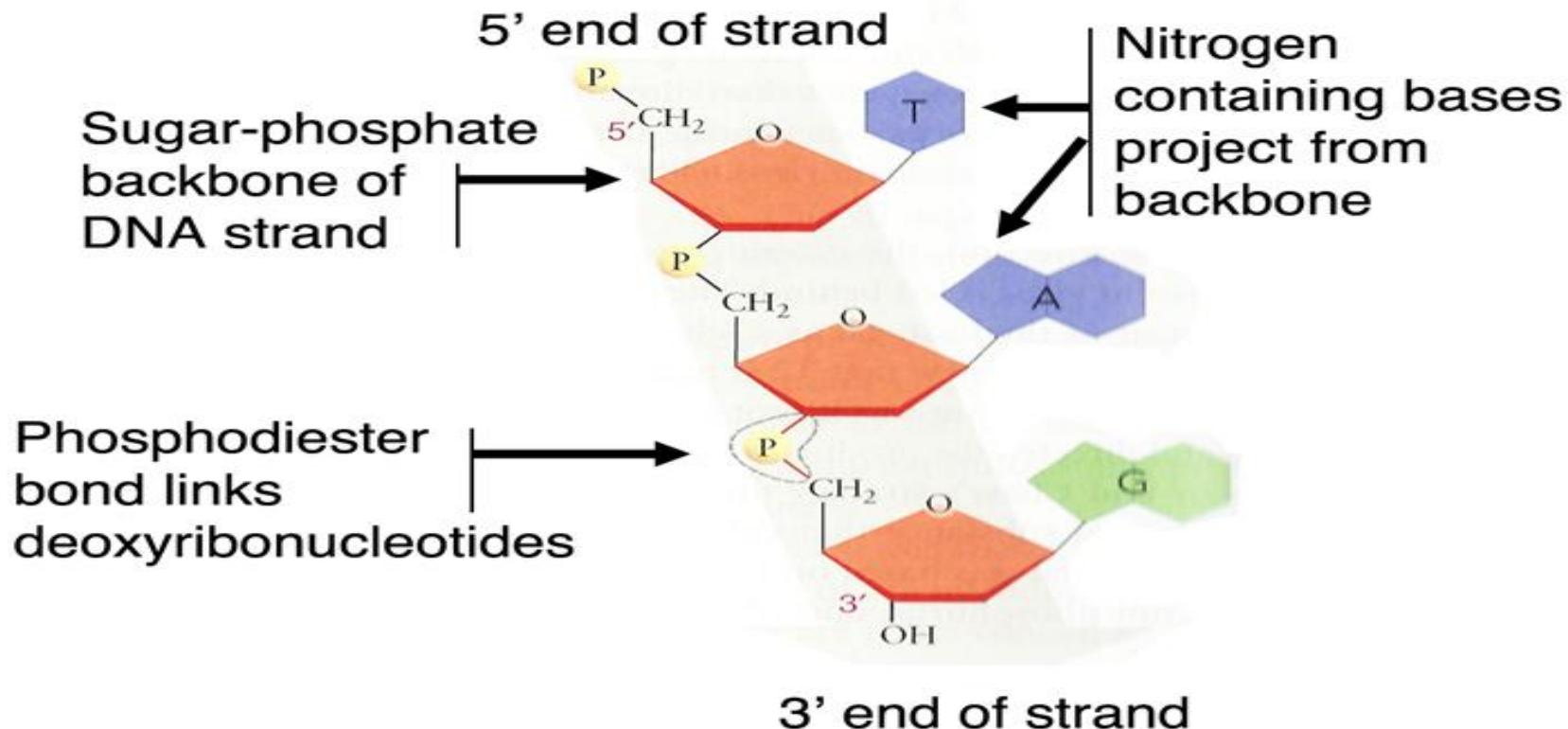


Thymine

Adenine and Guanine are double ring base called Purines
Cytosine, thymine, and uracil are single-ring base called Pyrimidines

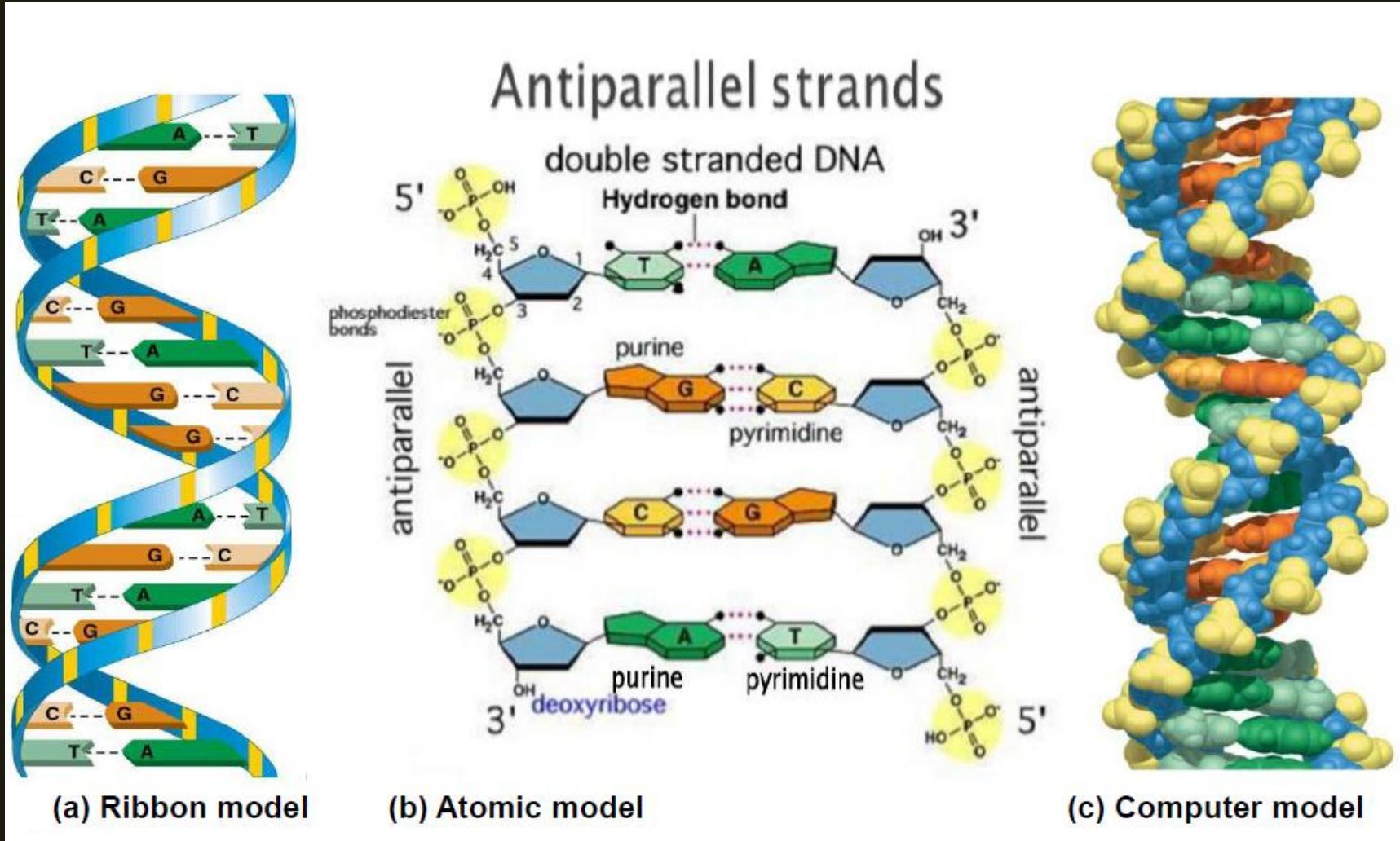
The essence of the “Watson and Crick’s Research”- 3- Polarity of the structure

Primary structure of DNA

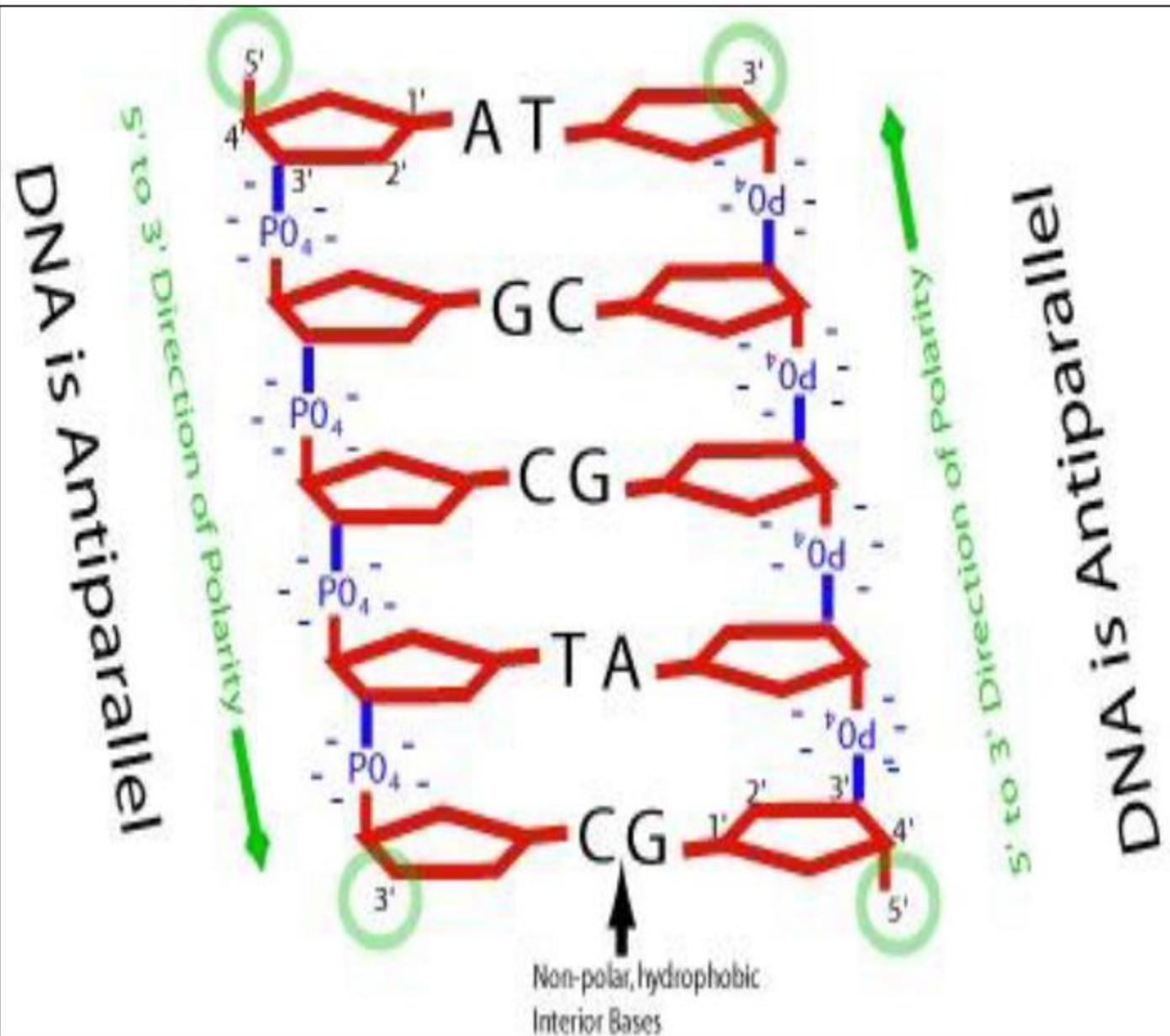


The essence of the “Watson and Crick’s Research”-

4- The two strands run anti-parallel

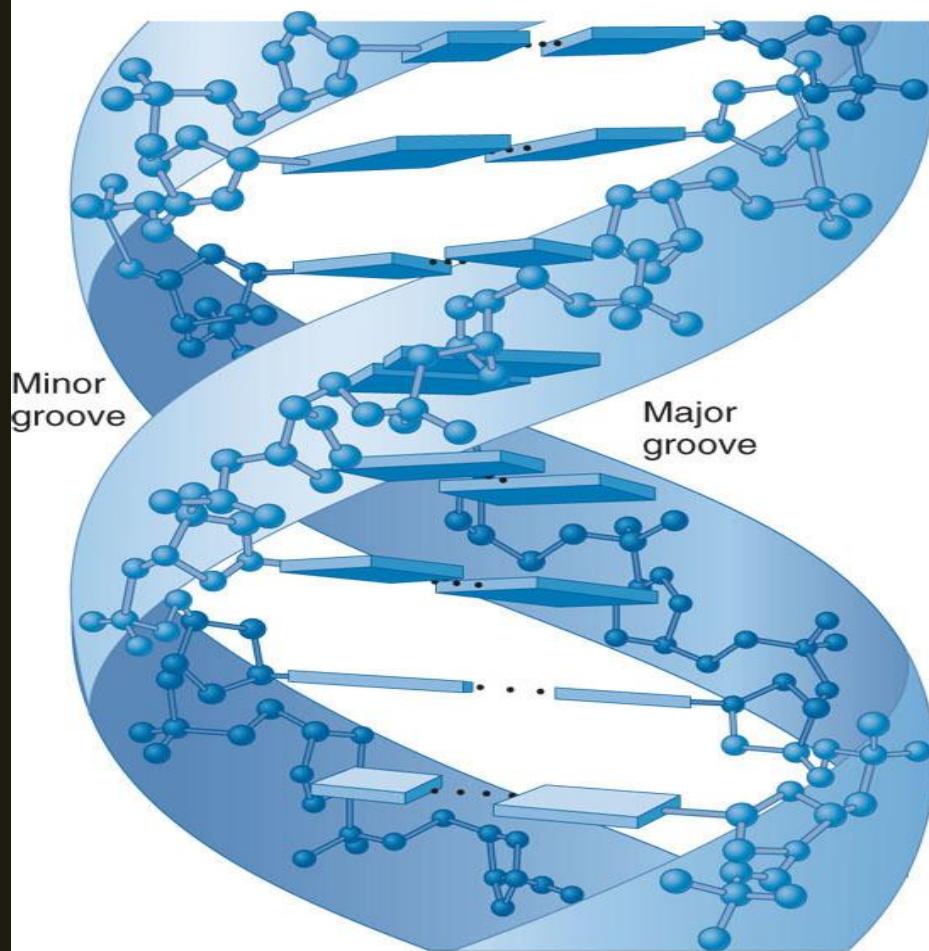


5' and 3' ends of the DNA molecule

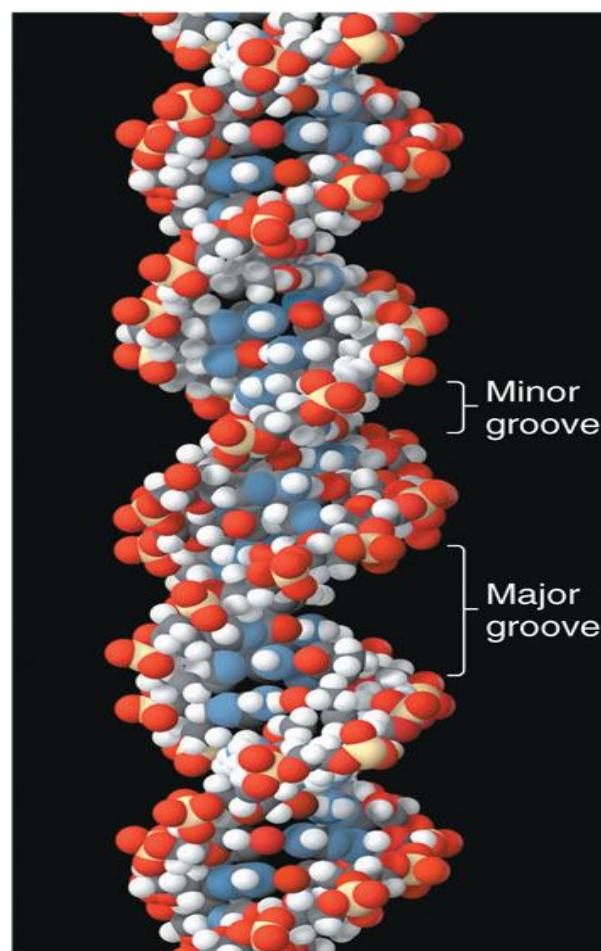


The essence of the “Watson and Crick’s Research”- 5- DNA is Helical (Double Helix)

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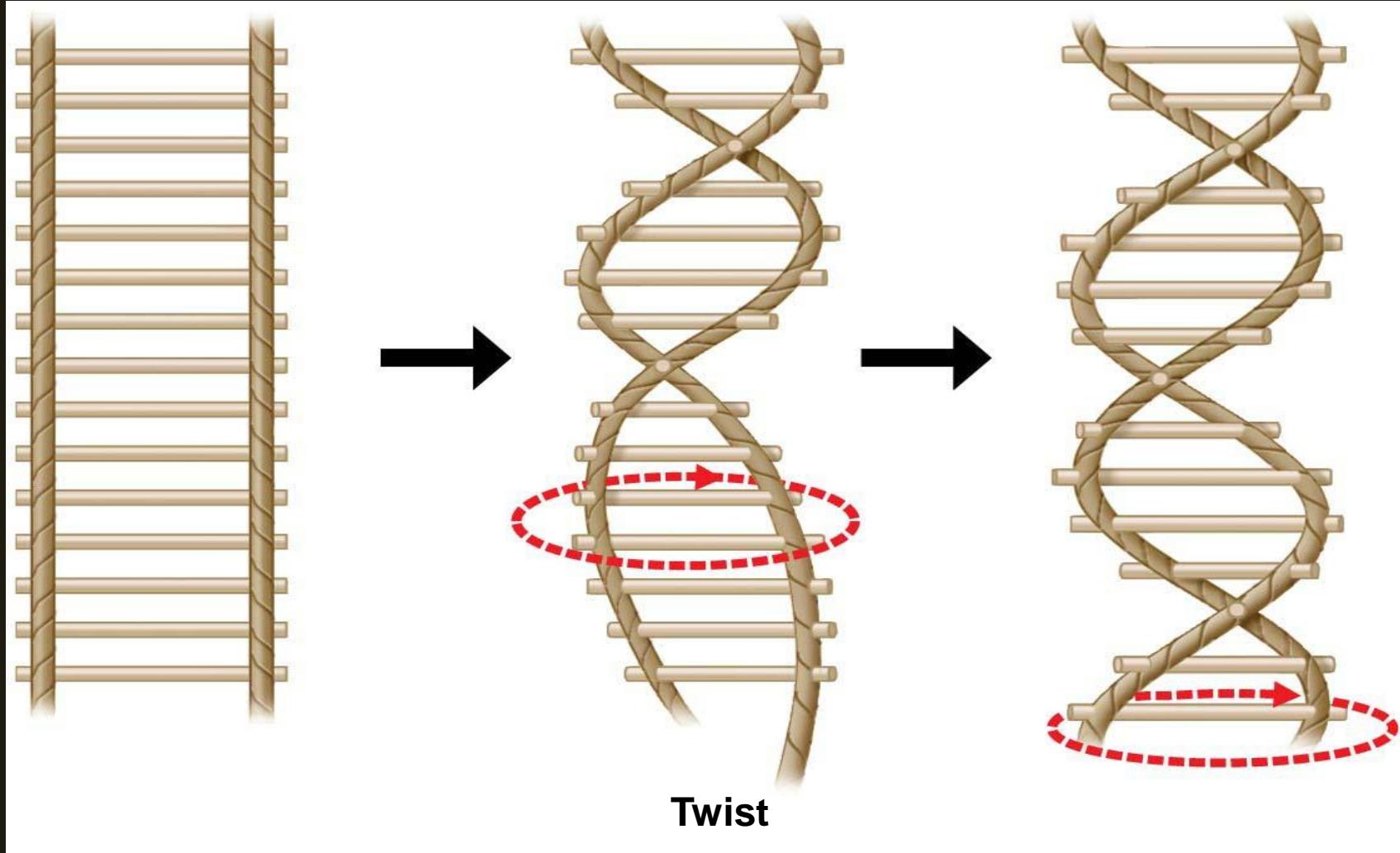


(a) Ball-and-stick model of DNA



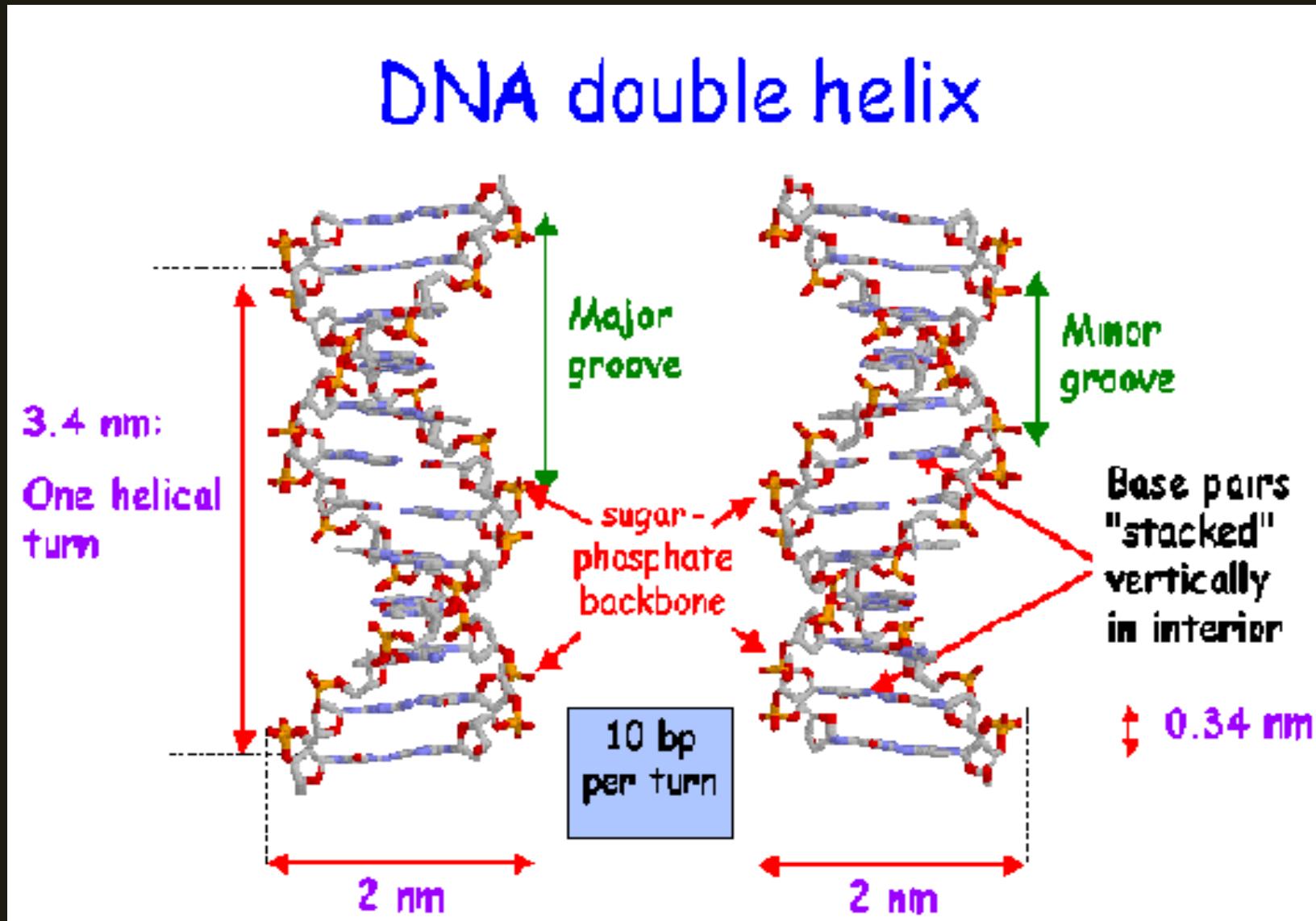
(b) Space-filling model of DNA

Figure 10.4

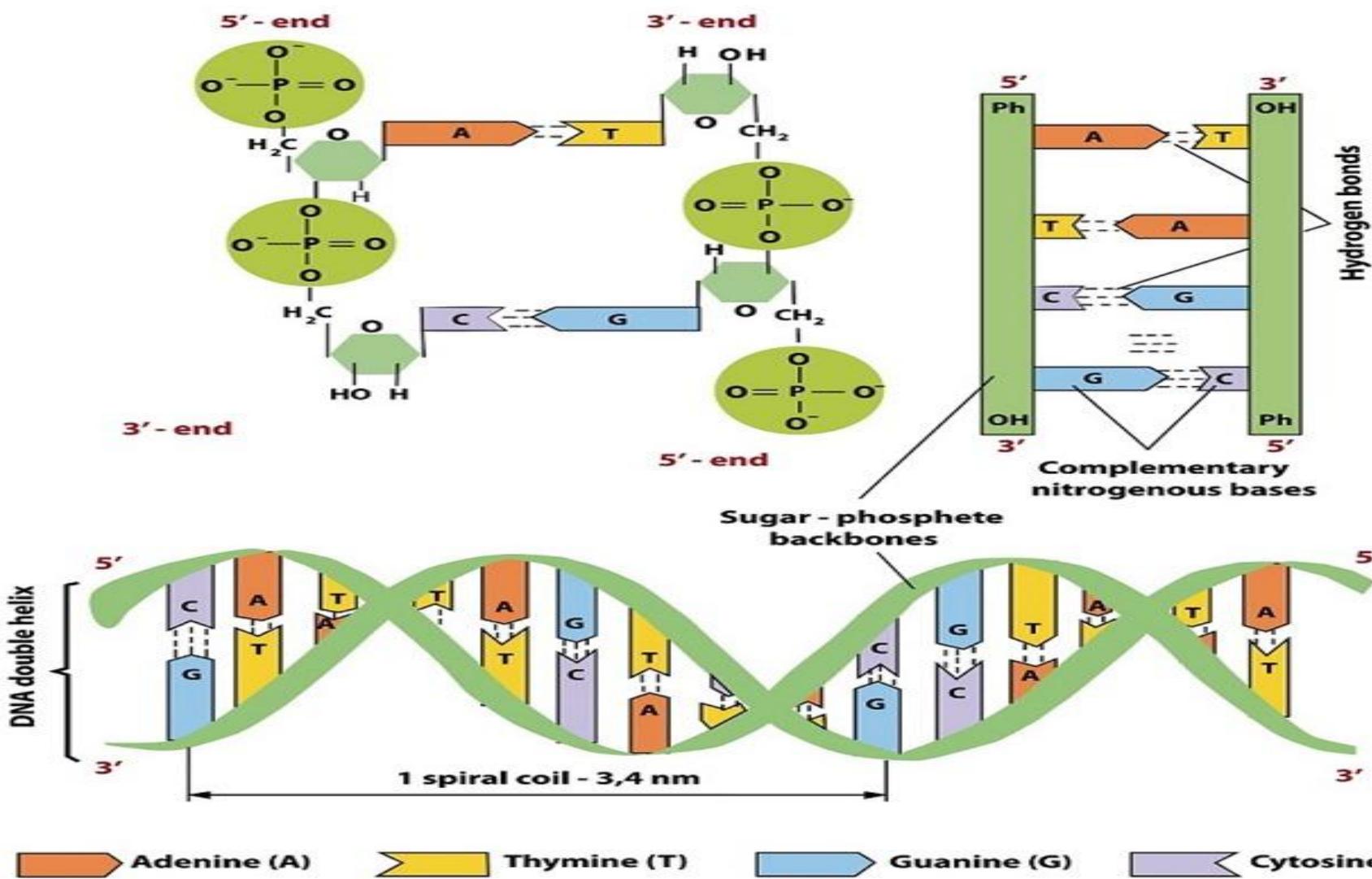


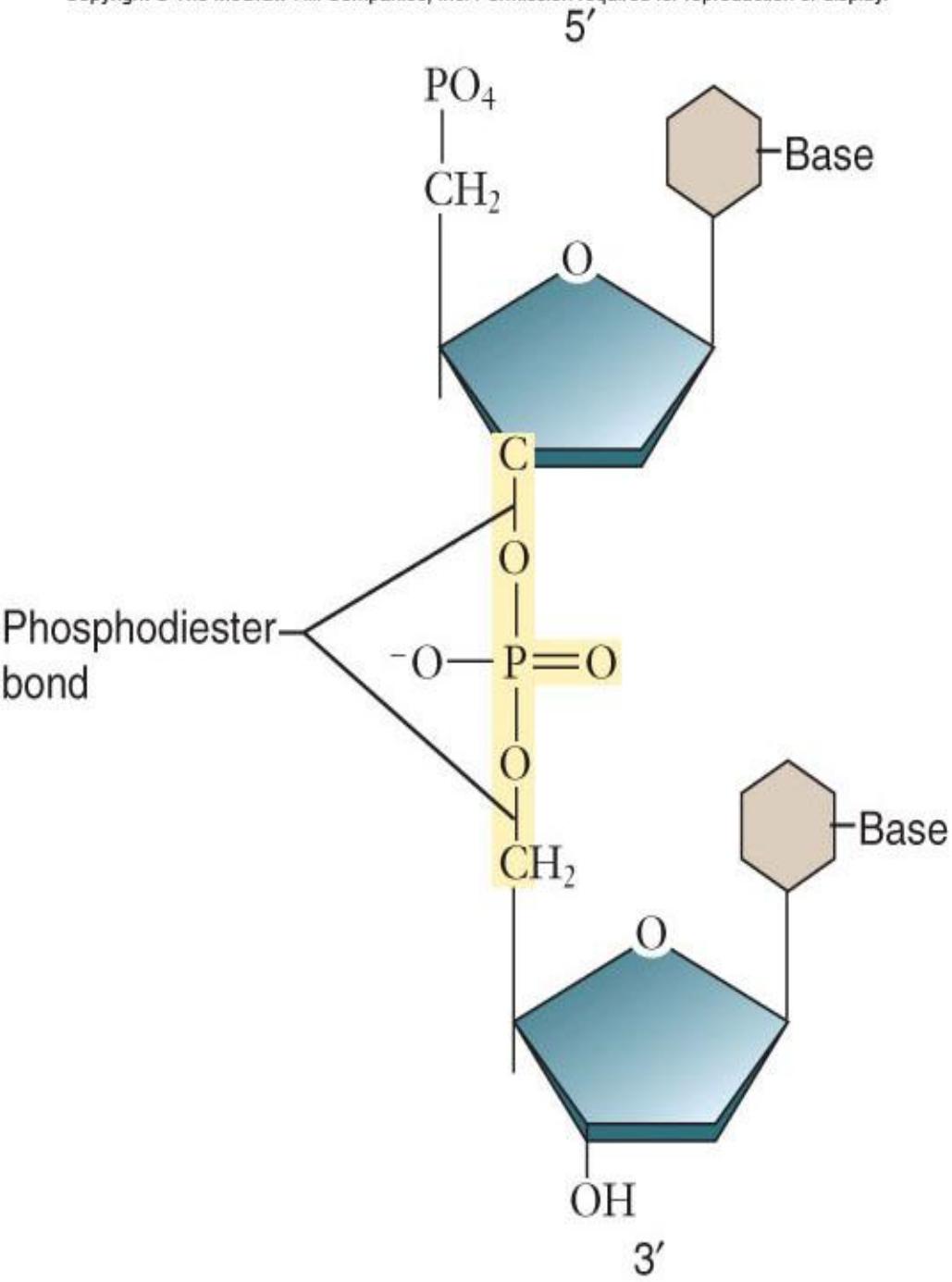
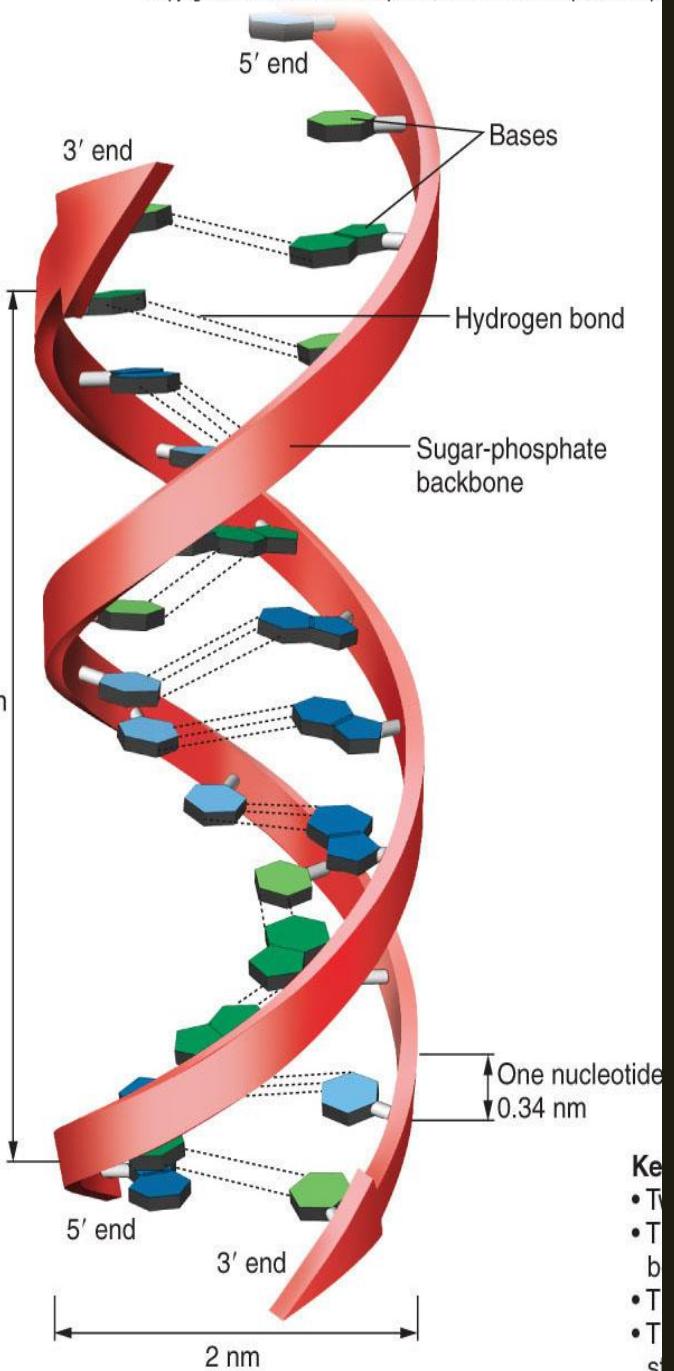
The essence of the “Watson and Crick’s Research”-

6- The measurements



DNA Structure

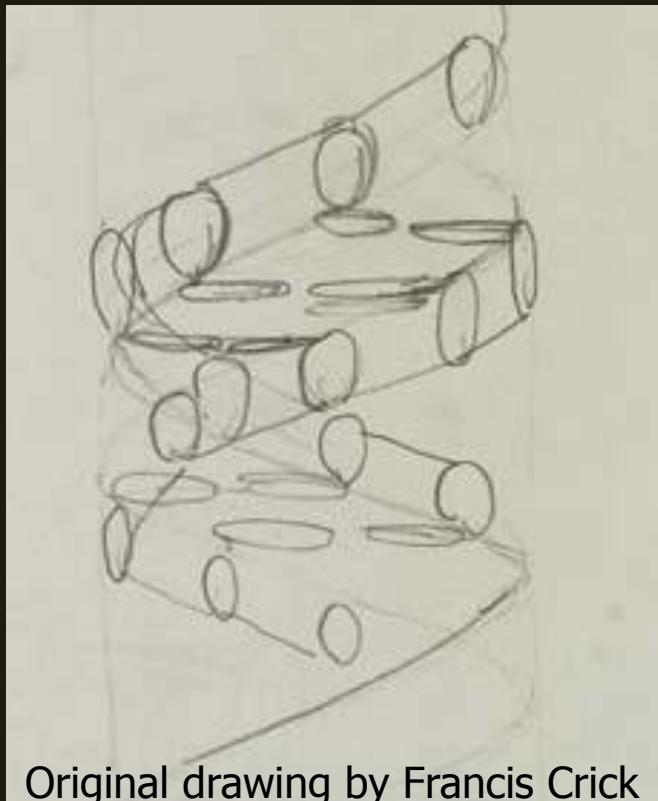




DNA REPLICATION

Watson and Crick wrote:

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



Original drawing by Francis Crick

Learning Objectives

DNA replication

- Why
- How- Mechanism, Speed, Fidelity

Replication Facts

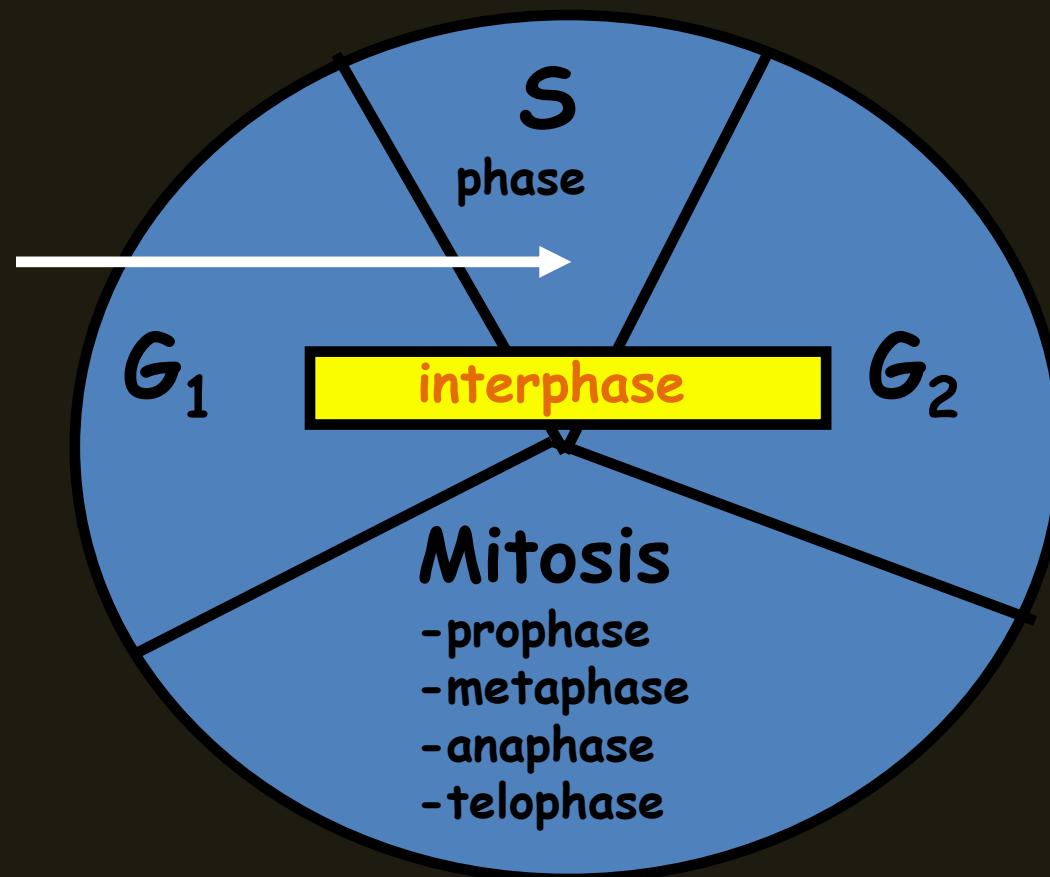


- DNA has to be copied before a cell divides
- New cells will need identical DNA strands

Why do we need to replicate our DNA?

- Growth
- Repair
- Reproduction

At which phase of cell cycle does DNA replication happen?



The modes of DNA replication– the views in 1954

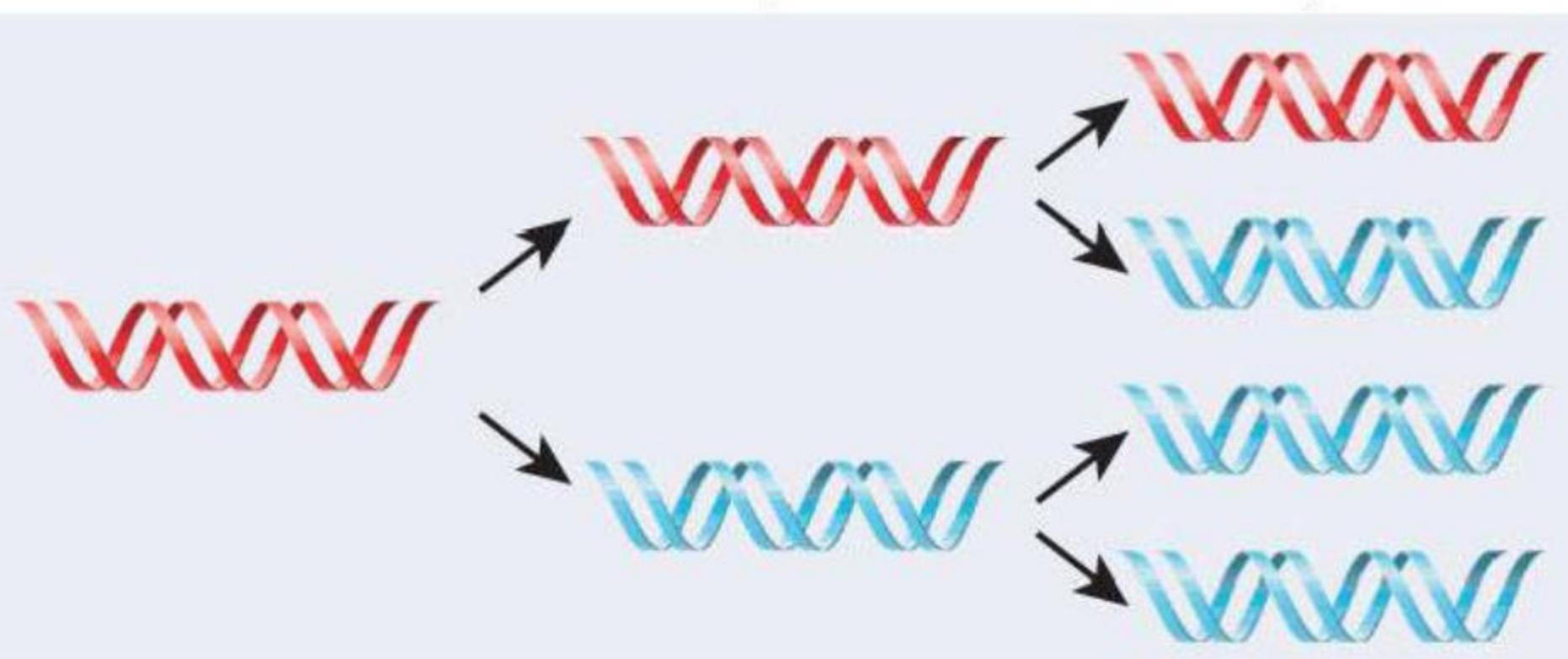
The Conservative mode of Replication

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**Original
double helix**

**First round
of replication**

**Second round
of replication**



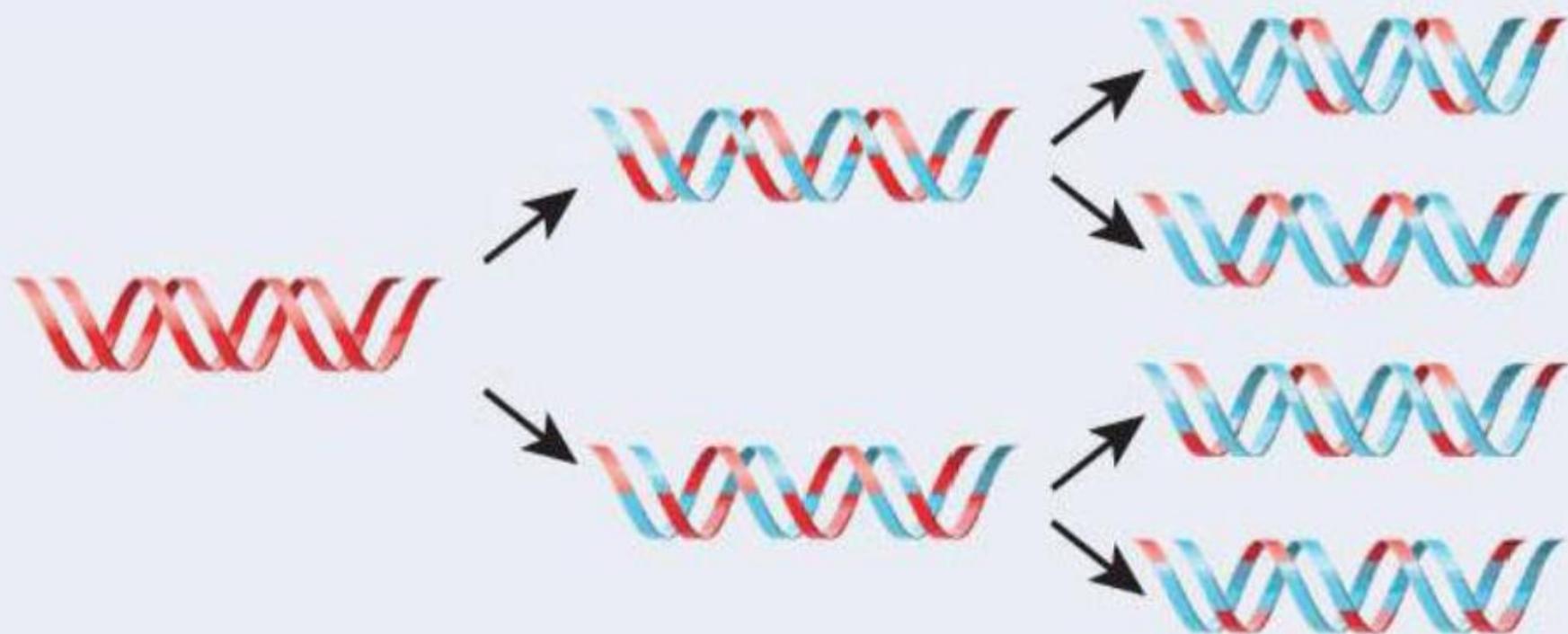
The Dispersive mode of Replication

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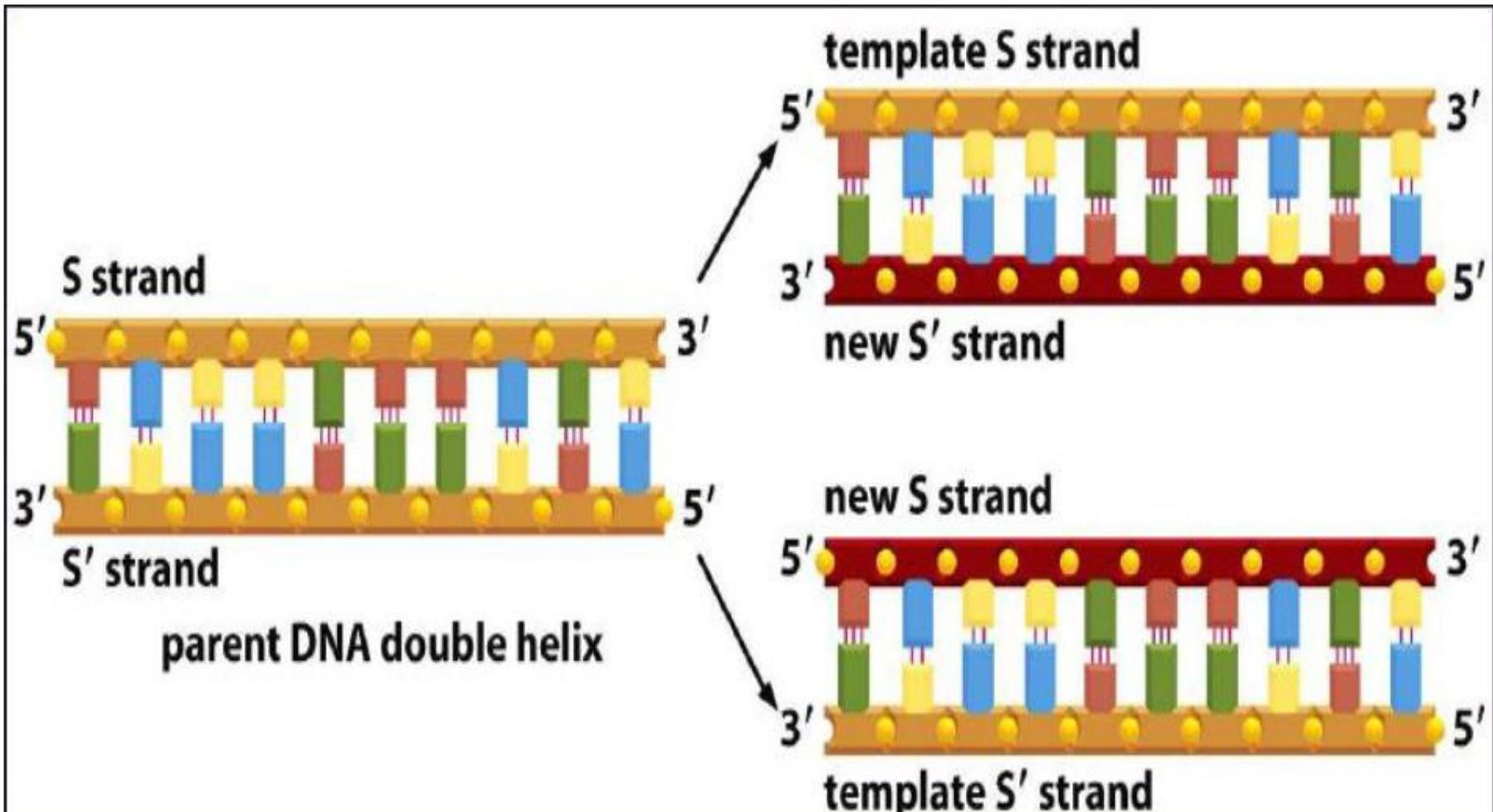
**Original
double helix**

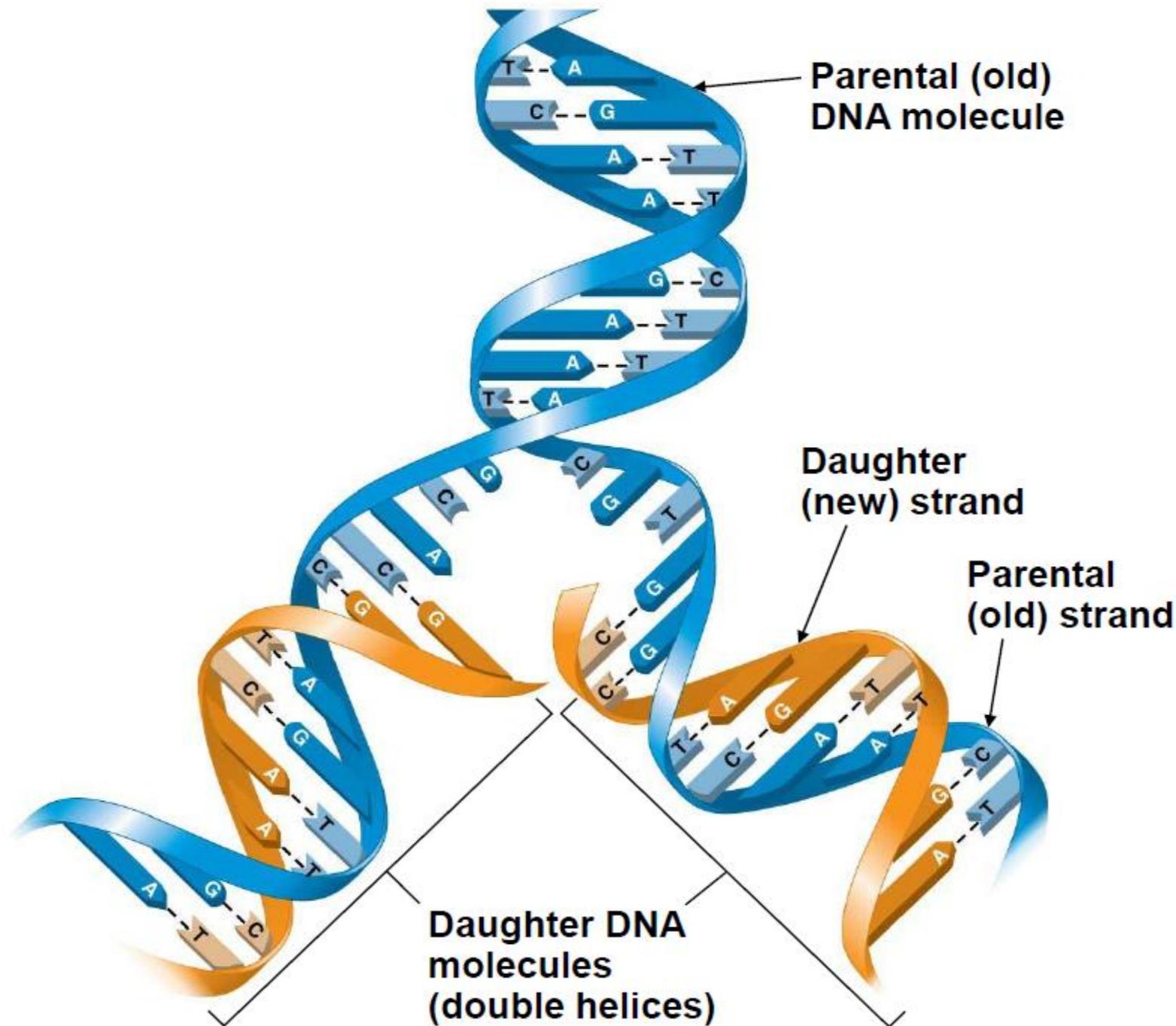
**First round
of replication**

**Second round
of replication**



The semi-conservative mode of DNA replication

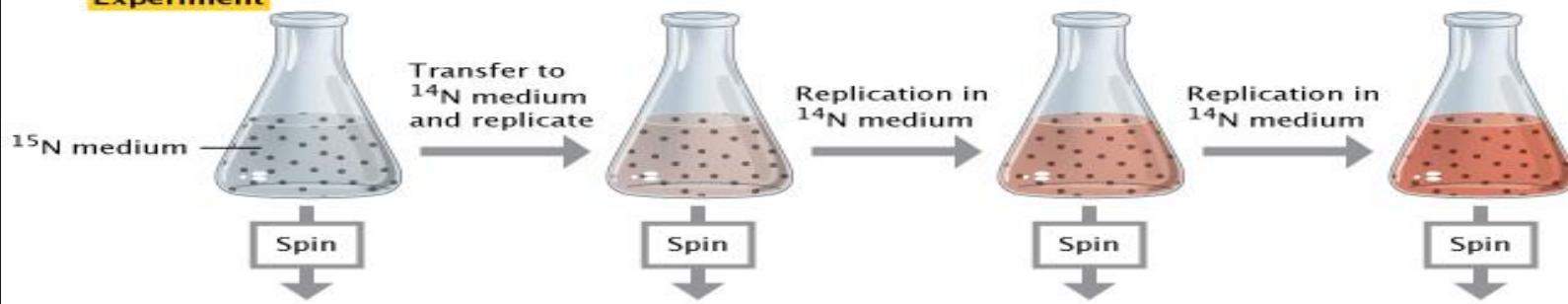




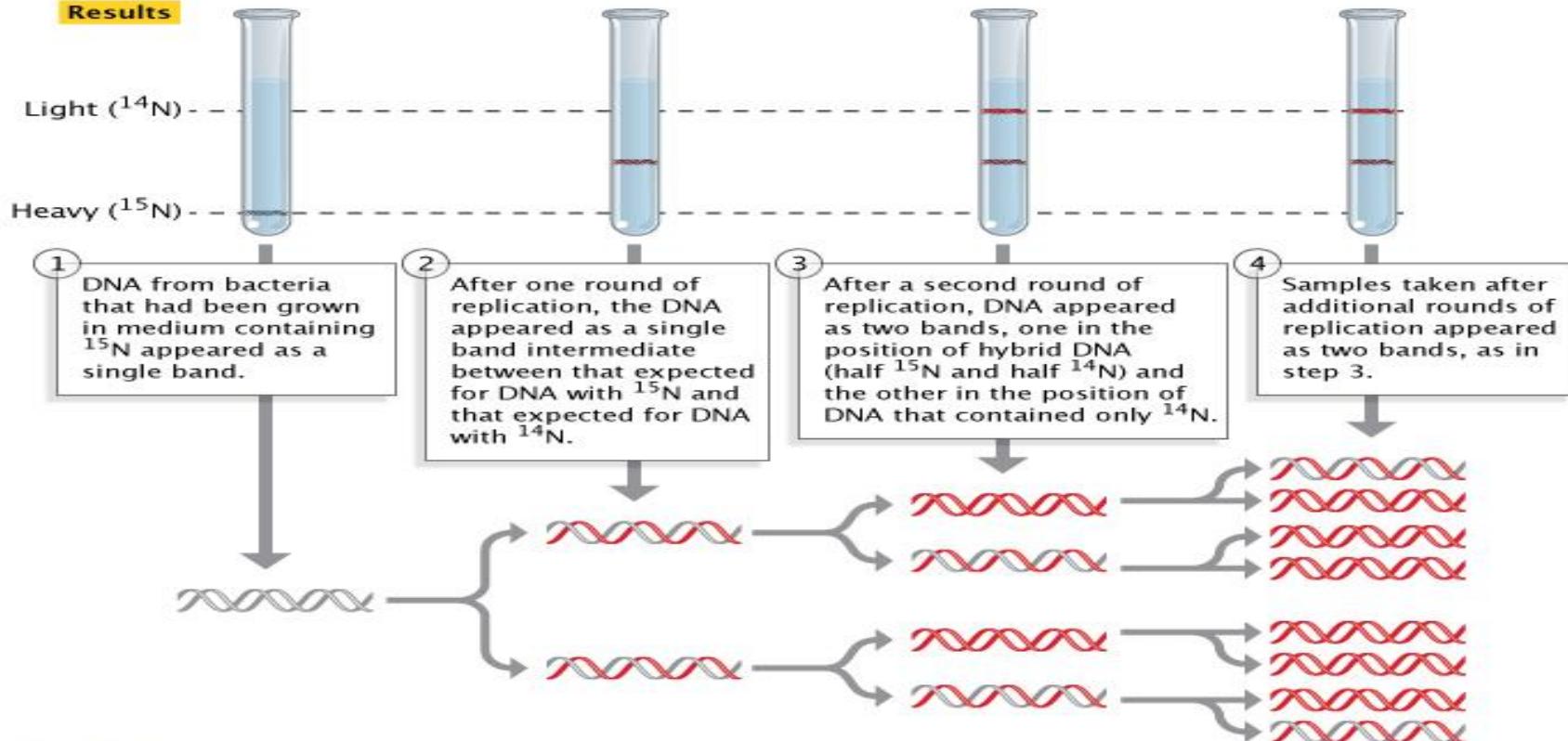
Messelson and Stahl's Exp 1958

Question Which model of DNA replication – conservative, dispersive, or semiconservative – applies to *E. coli*?

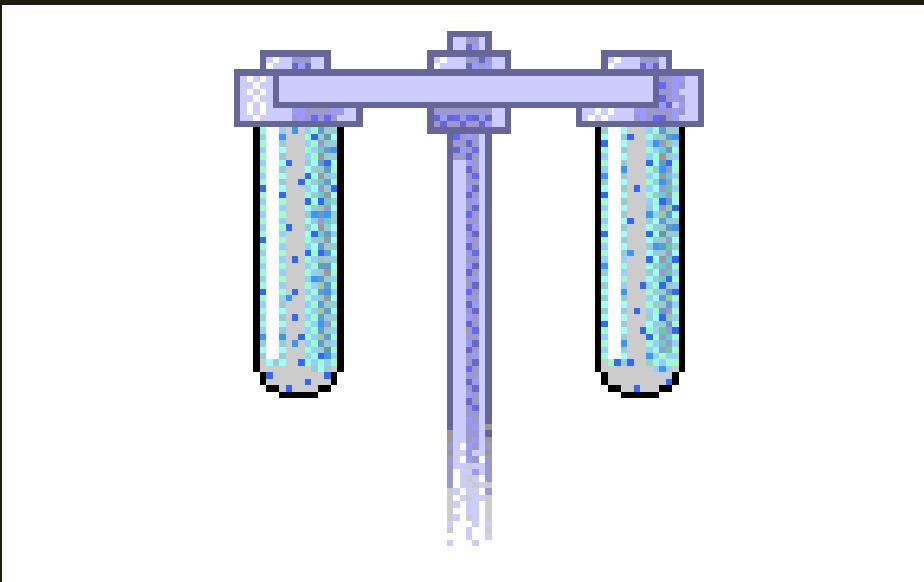
Experiment



Results



Conclusion DNA replication in *E. coli* is semi-conservative.



To separate DNA based on density, DNA is mixed with CsCl and centrifuged at very high speeds (**e.g., 50,000 rpm**) in an ultracentrifuge for many hours. As the tubes spin, a stable, linear gradient of CsCl with the lightest density at the top and the heaviest density at the bottom is formed. As the CsCl gradient forms, the DNA comes to equilibrium in the gradient where its density equals the density of the surrounding CsCl. **If DNA of only one density is present, the result will be a single band of DNA. If two DNAs are present with different densities, the result will be two bands of DNA.**



**In Meselson and Stahl's
Experiment in 1958 they opted
for two isotopes of nitrogen.
Why Nitrogen?**

Messelson and Stahl were locked up in a room for two weeks and asked to write up their experiments and publish

Thus, the discovery of the structure of DNA in 1953 was only the beginning. They provided the scientific community with a challenge to determine exactly how DNA functioned in the cell, including how this molecule was replicated.

**The next obvious question
was to know the key
events responsible for the
physical copying of the
genome.**

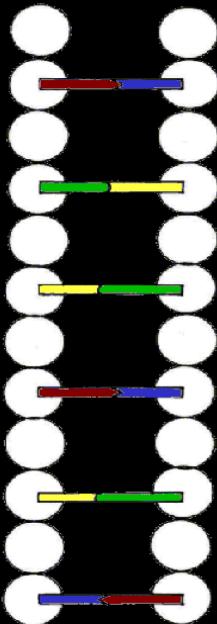


**What is your assumption
to what raw materials you
need for DNA replication?**

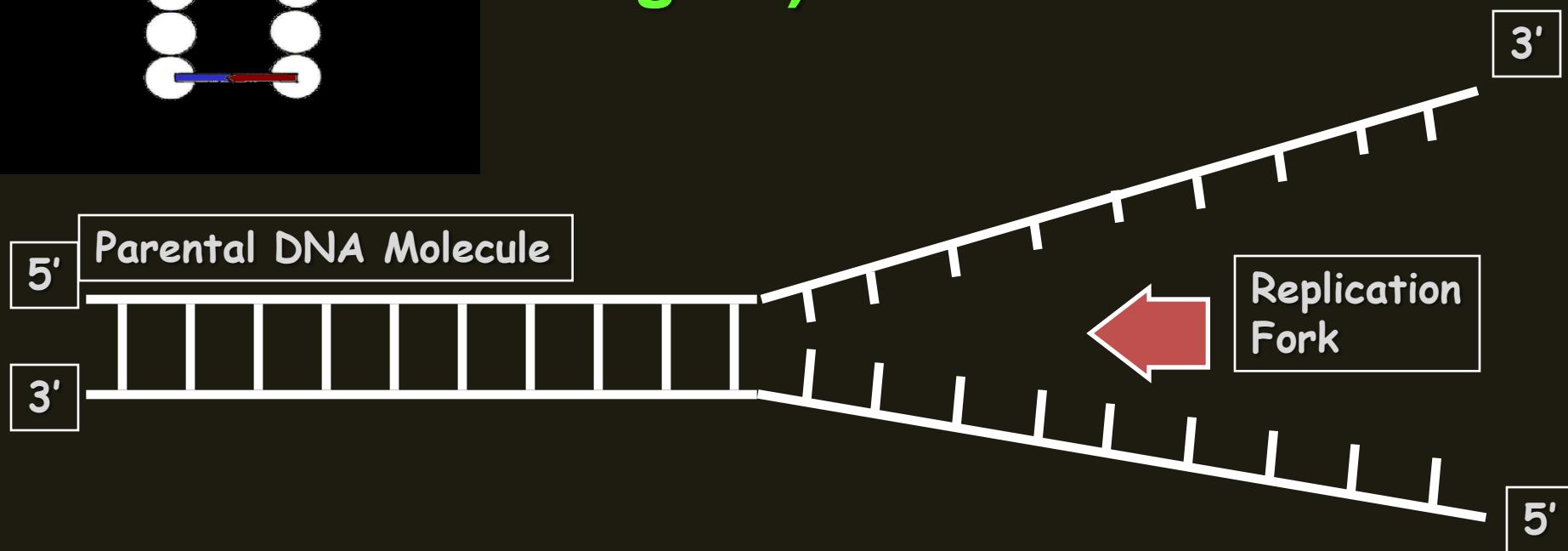
The mechanism of DNA replication!!!!

- begins on a double helix at specific sites, called **origins of replication**, and then
- proceeds in both directions, creating what are called **replication “bubbles”**.

Origin of DNA replication

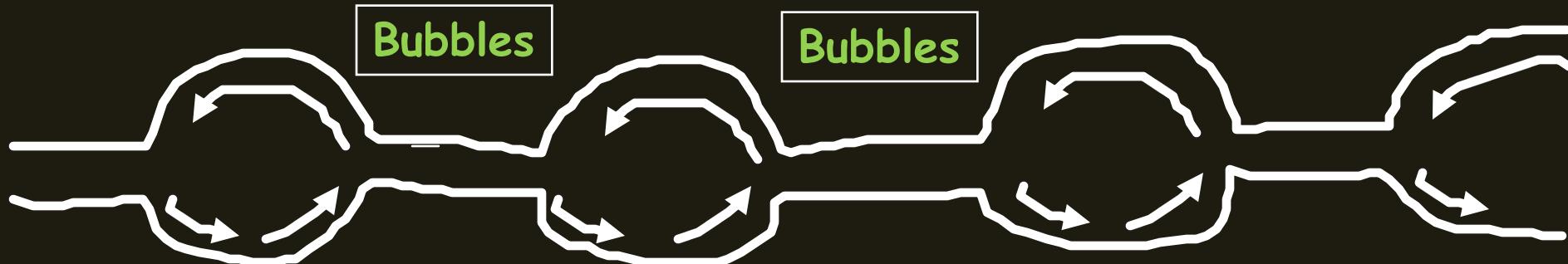


- Begins at **Origins of Replication**
- Two strands open forming **Replication Forks (Y-shaped region)**



Replication Bubble

- As the 2 DNA strands open at the origin, **Replication Bubbles** form
- **Prokaryotes (bacteria)** have a **single** bubble
- **Eukaryotic chromosomes** have **MANY** bubbles



Origin of replication

Origin of replication

Parental strands

Origin of replication

Parental strand

Daughter strand

Bubble



Two daughter DNA molecules

Can you predict the number of origins in Human DNA replication?

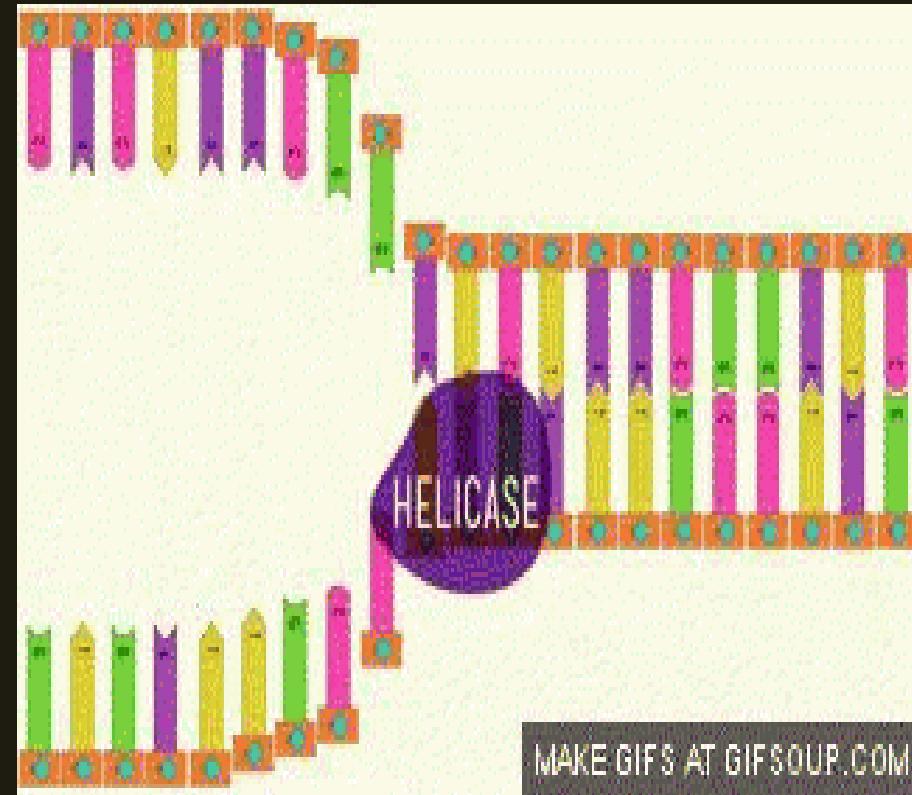
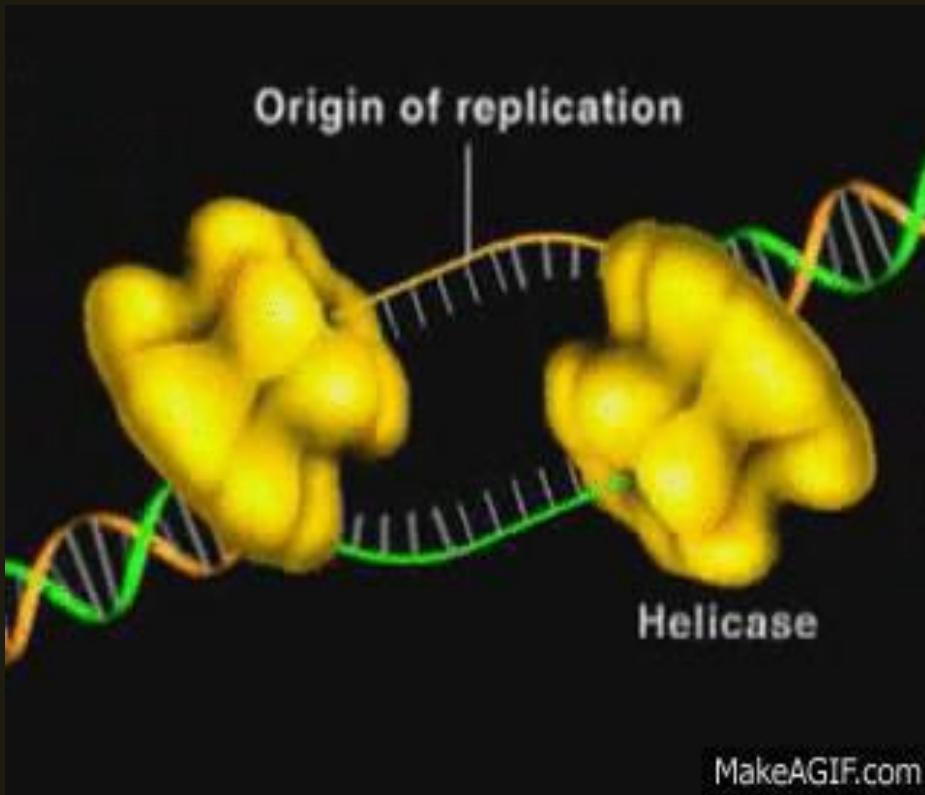
Number of Origins

Organism	# of replicons
<i>Escherichia coli</i> (bacteria)	1
<i>Saccharomyces cerevisiae</i> (yeast)	500
<i>Drosophila melanogaster</i> (fruit fly)	3,500
<i>Xenopus laevis</i> (frog)	15,000
<i>Mus musculus</i> (mouse)	25,000
<i>Homo sapiens</i>	10,000 to 100,000

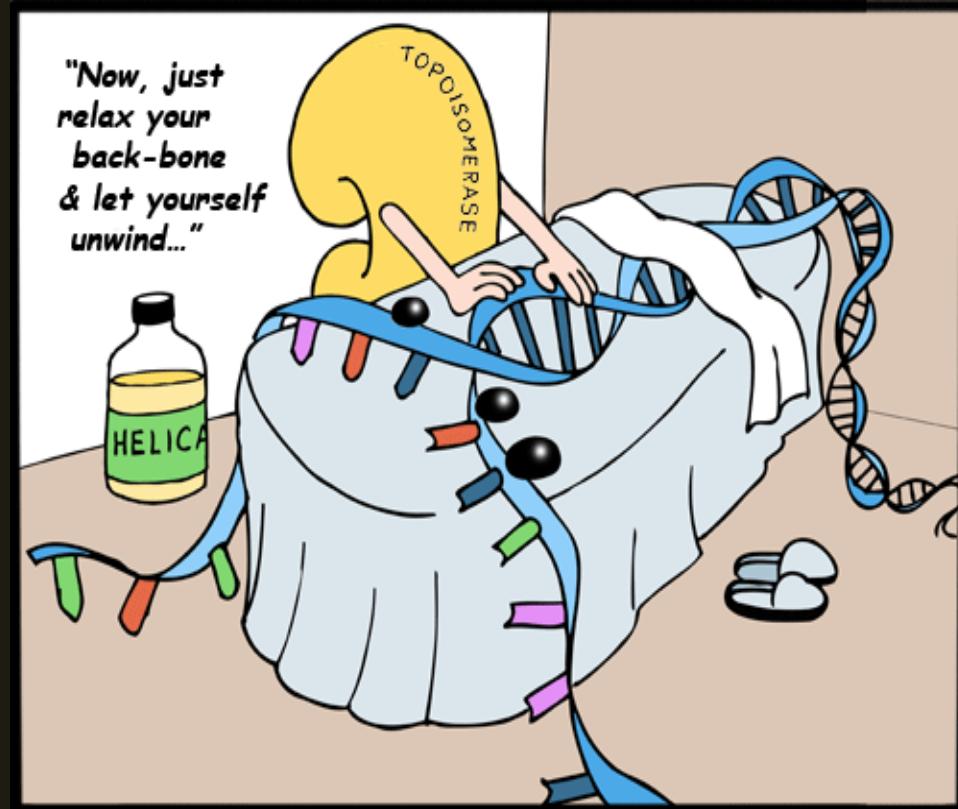
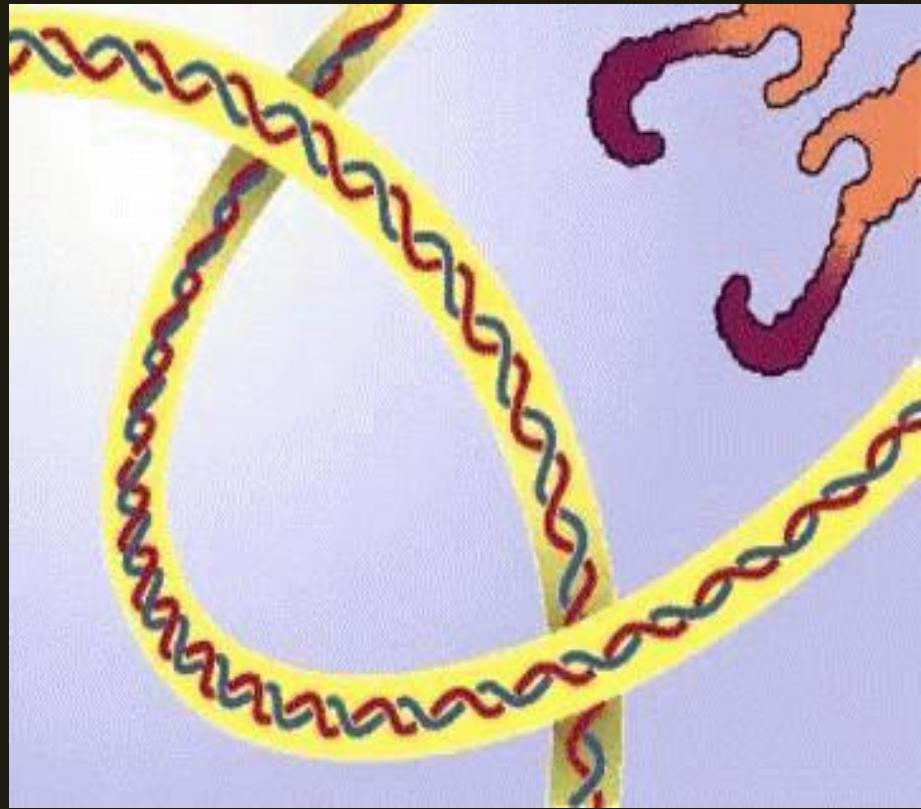


Replication generally starts at “AT” rich region. Why?

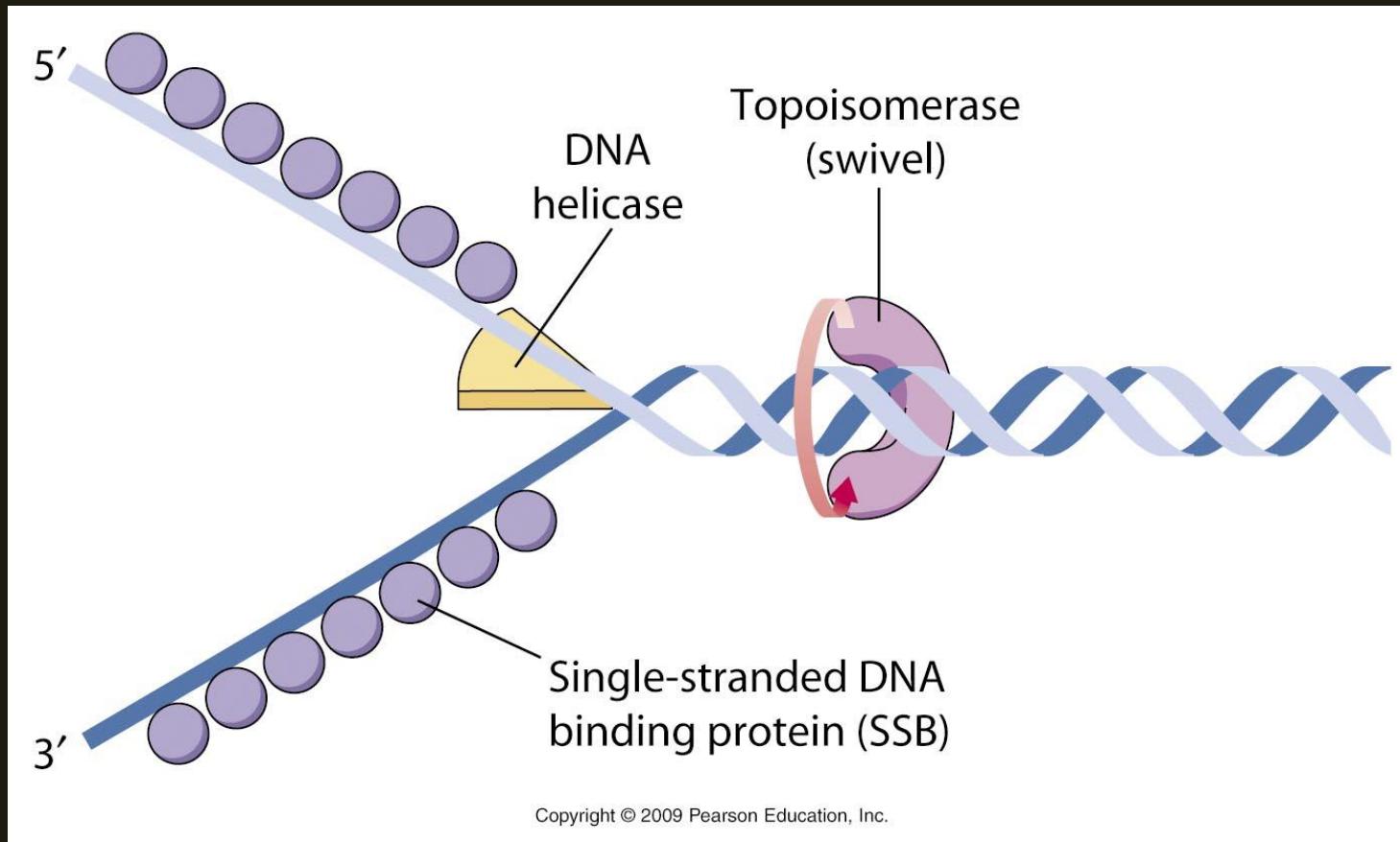
DNA replication- Protein-1: Helicase



DNA replication- Protein-2: Topoisomerase/Gyrase



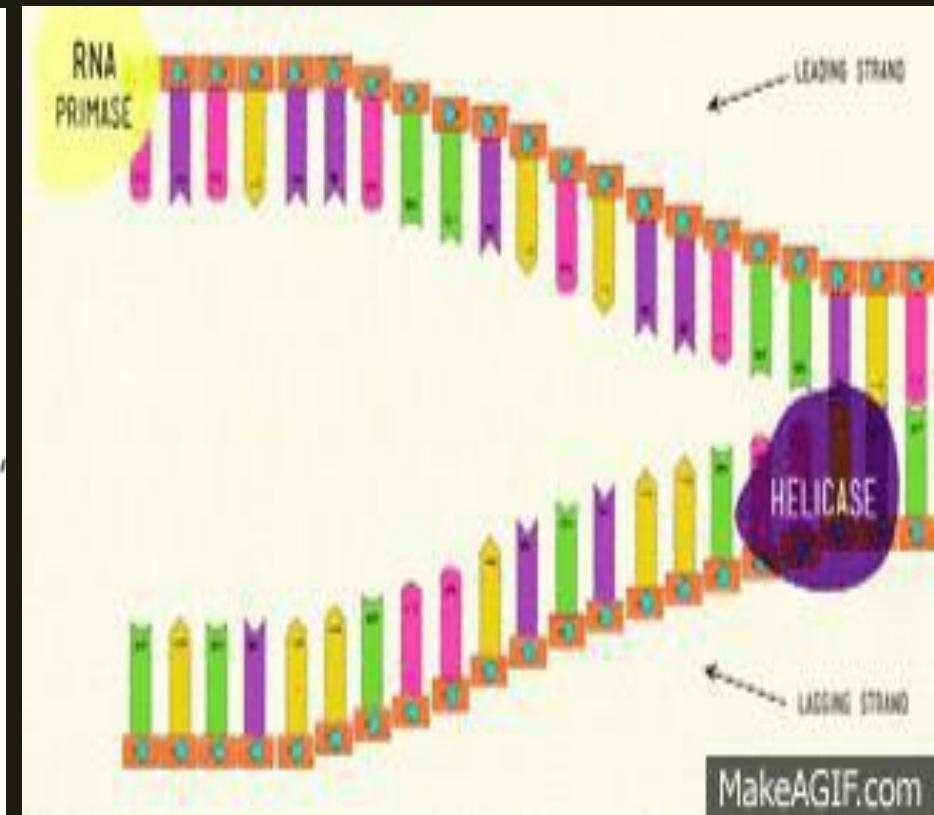
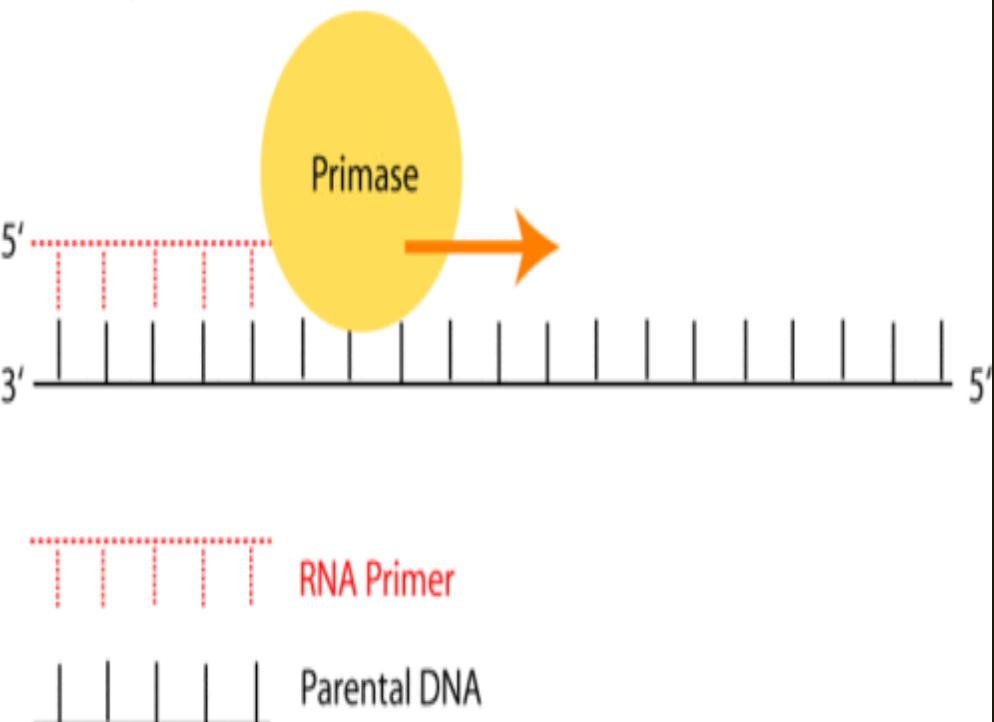
DNA replication- Protein-3: Single strand Binding Proteins



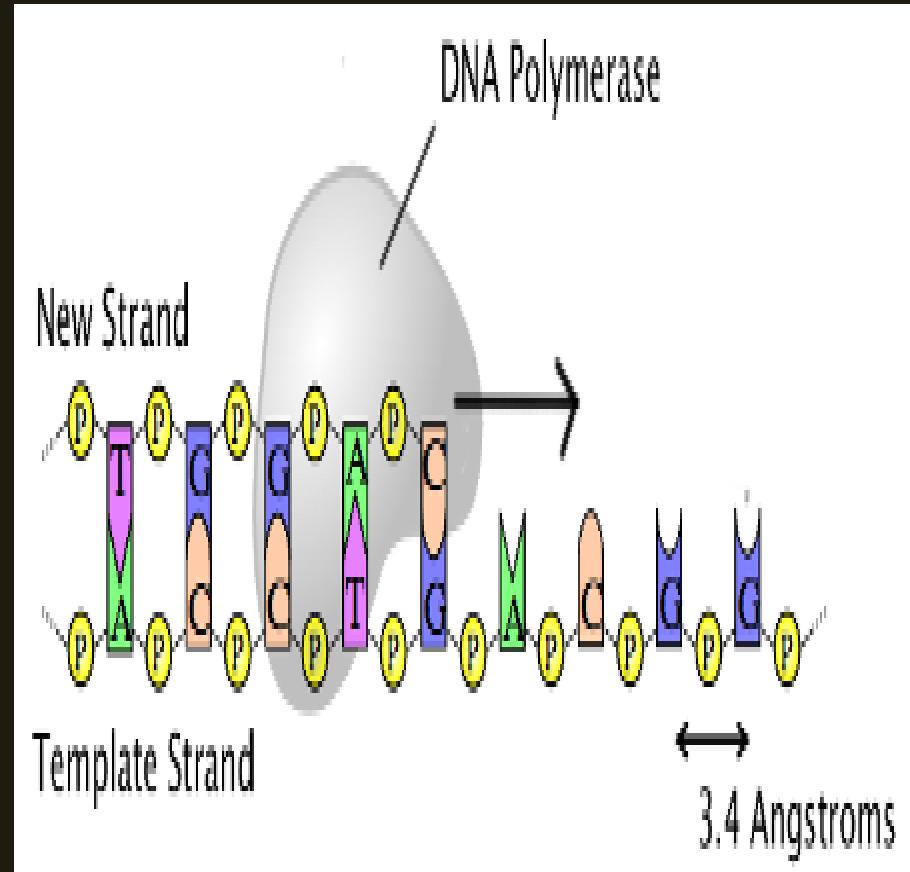
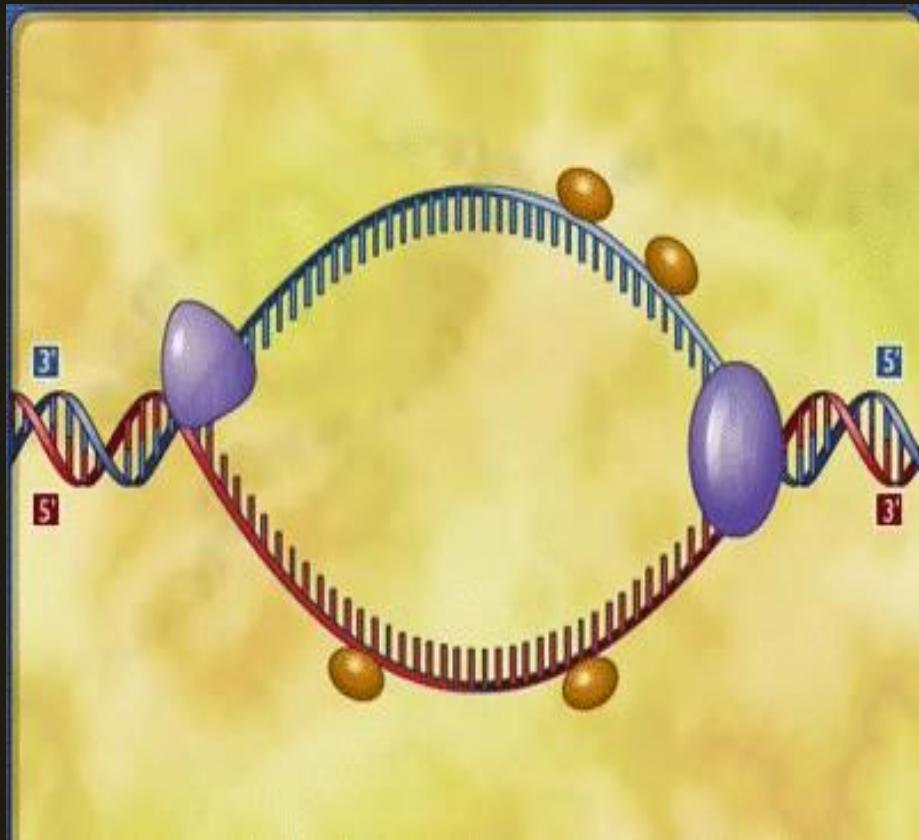
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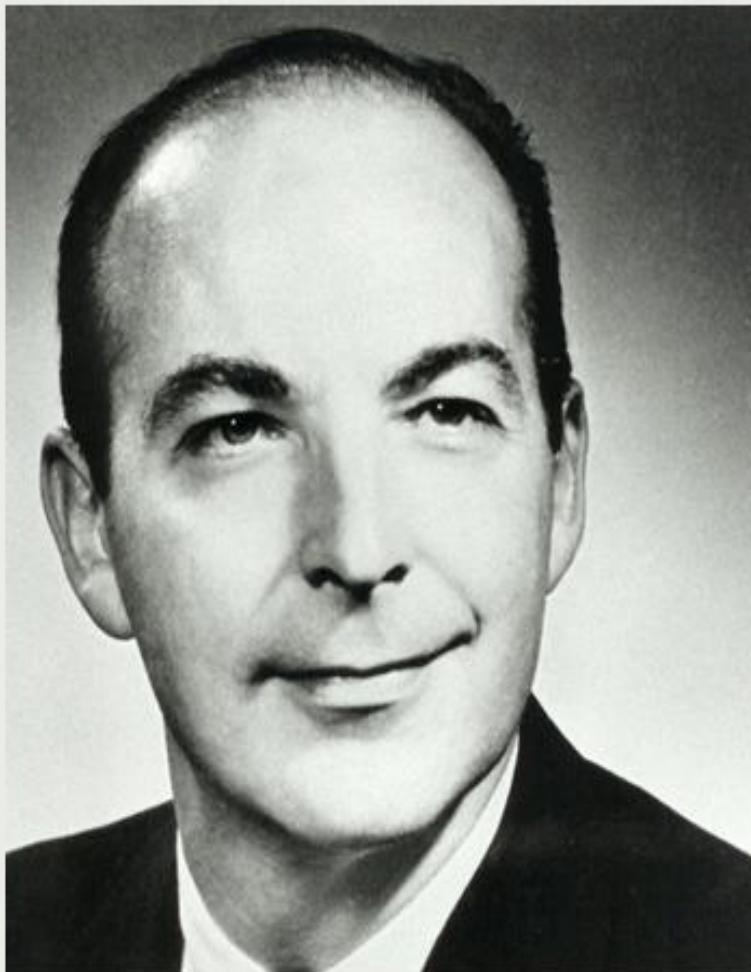
DNA replication- Protein-4: RNA Primase

DNA Synthesis Requires a RNA Primer



DNA replication- Protein-5: DNA polymerase





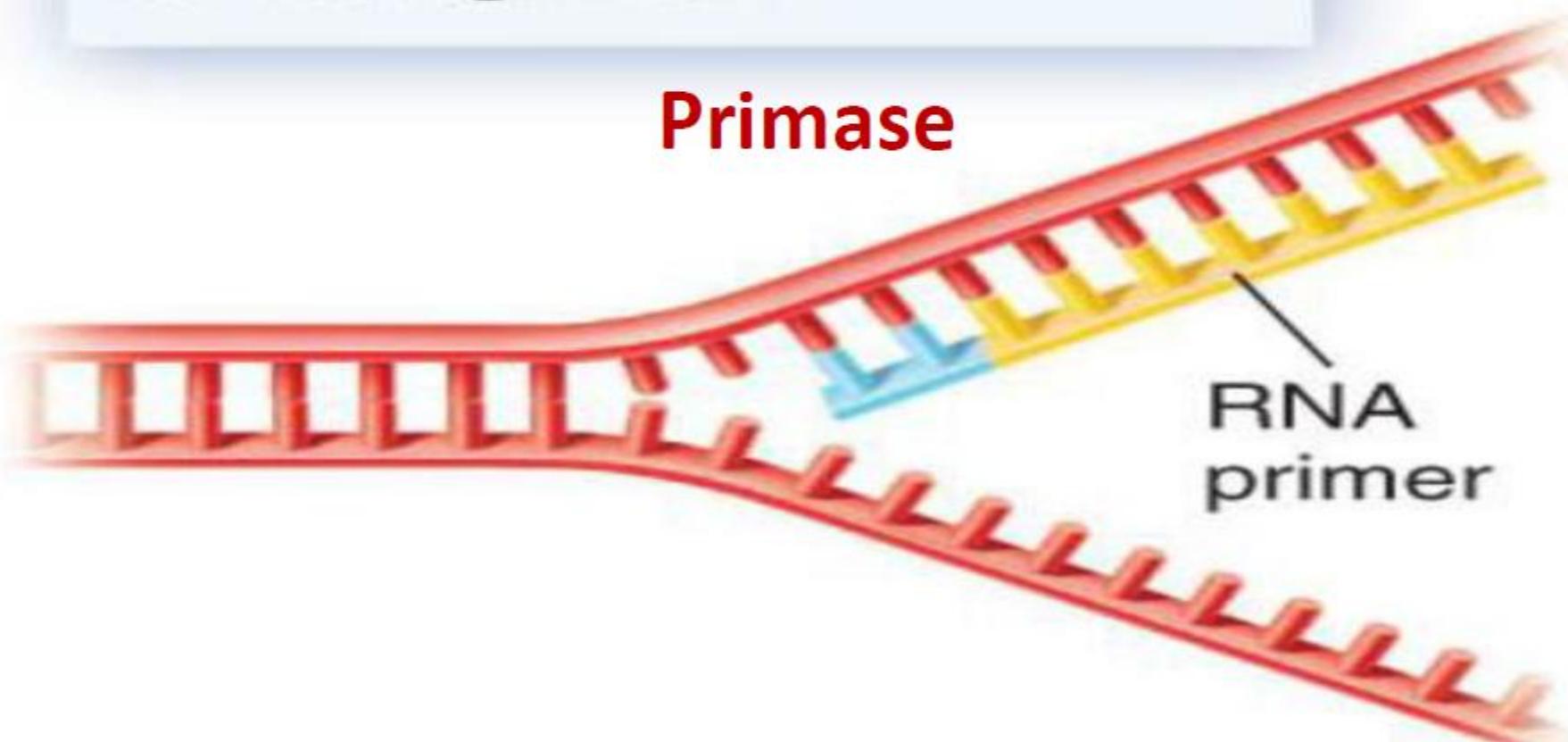
Arthur Kornberg

Nobel Prize for Medicine
1959

City College
Class of 1937

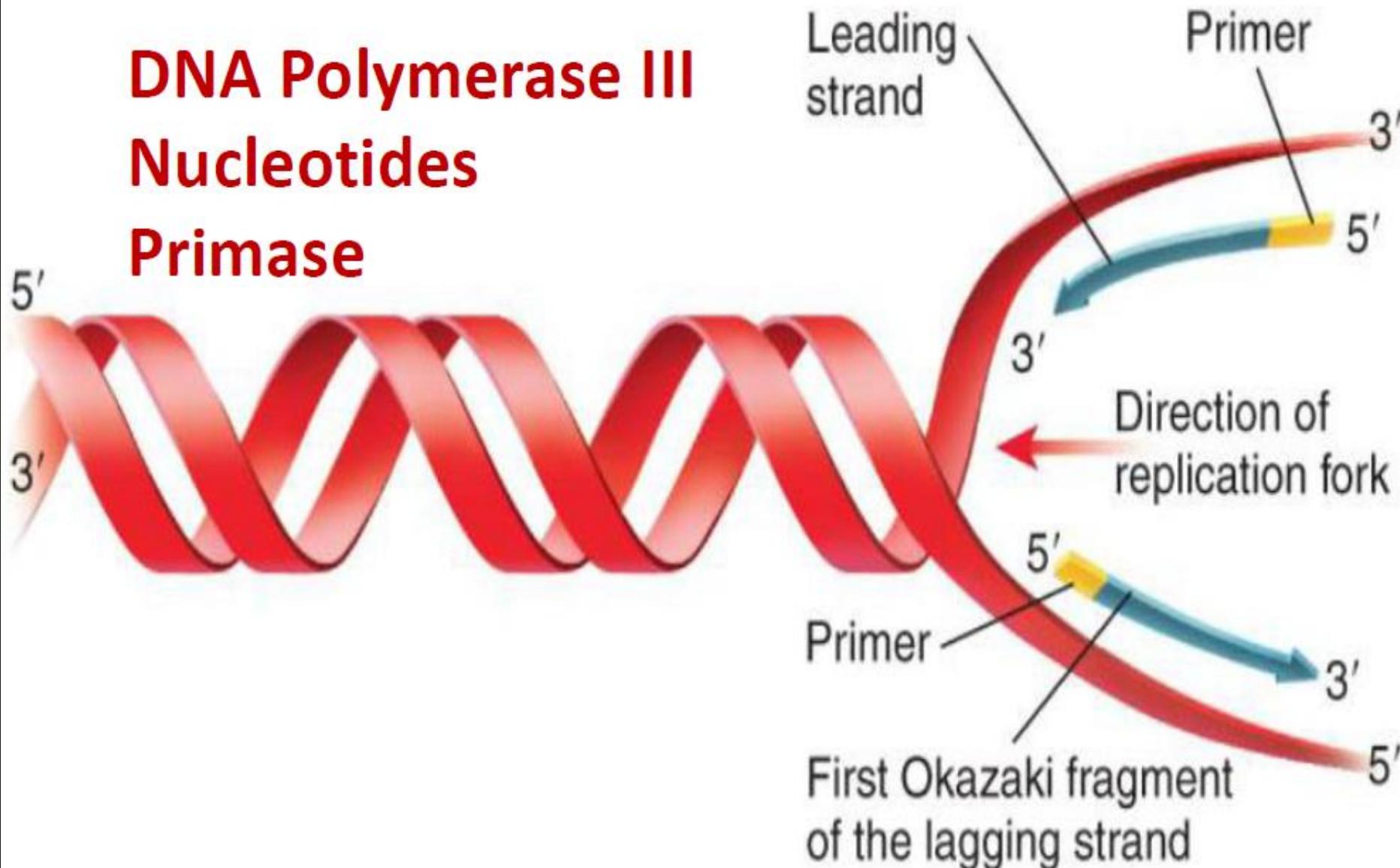
Replication: replication fork

DNA polymerase is able to covalently link nucleotides together from a primer.



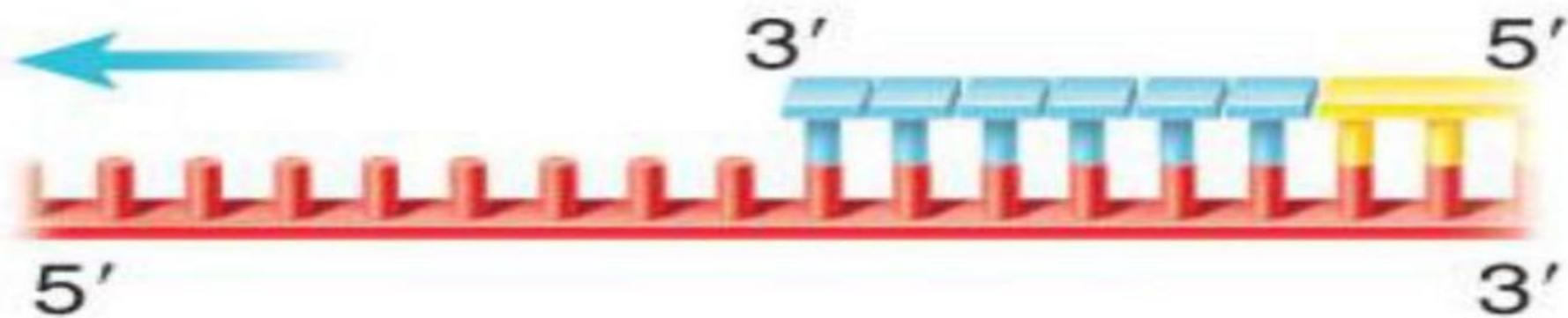
Formation of Leading Strand

DNA Polymerase III
Nucleotides
Primase



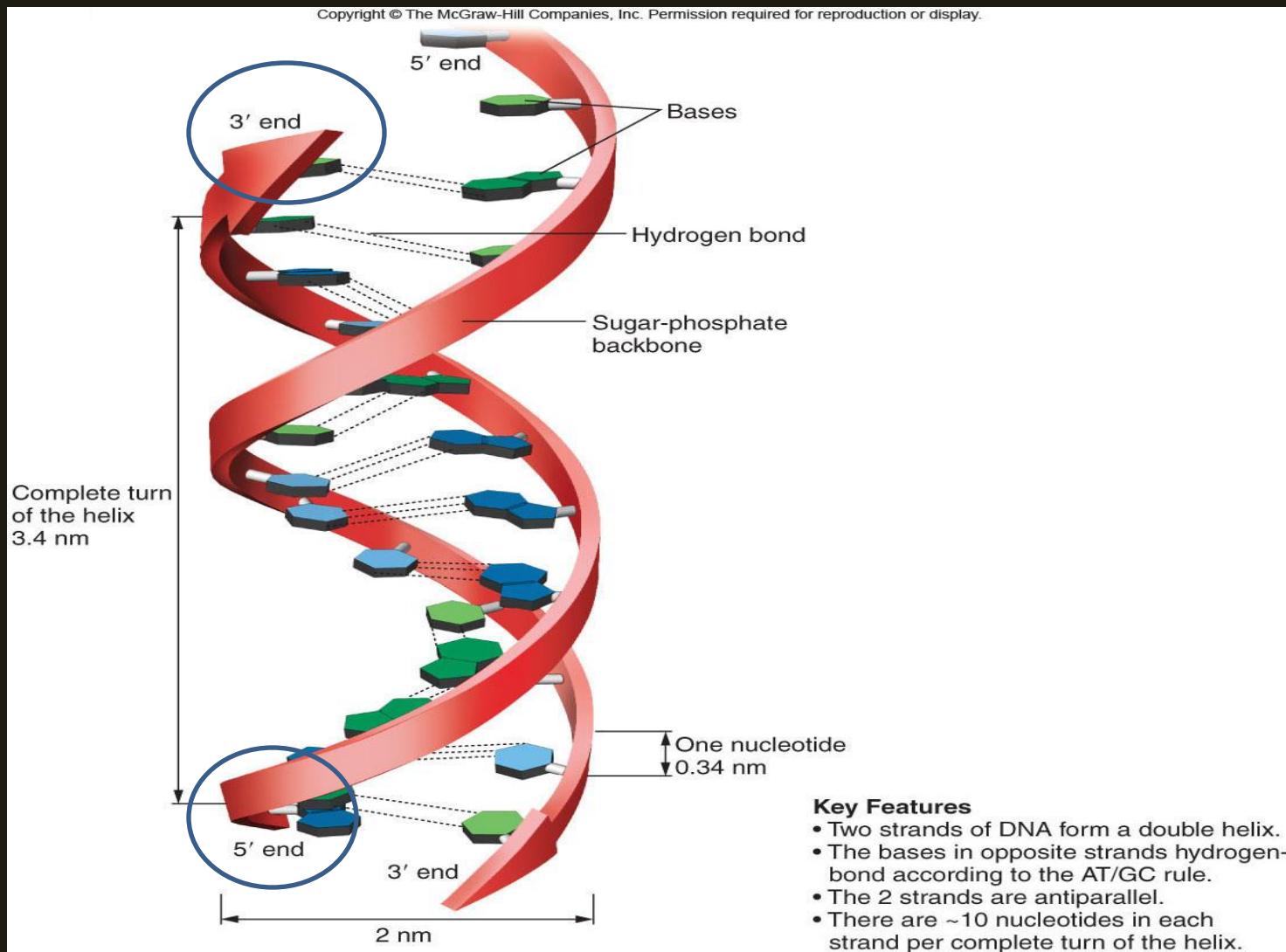
Direction of Replication

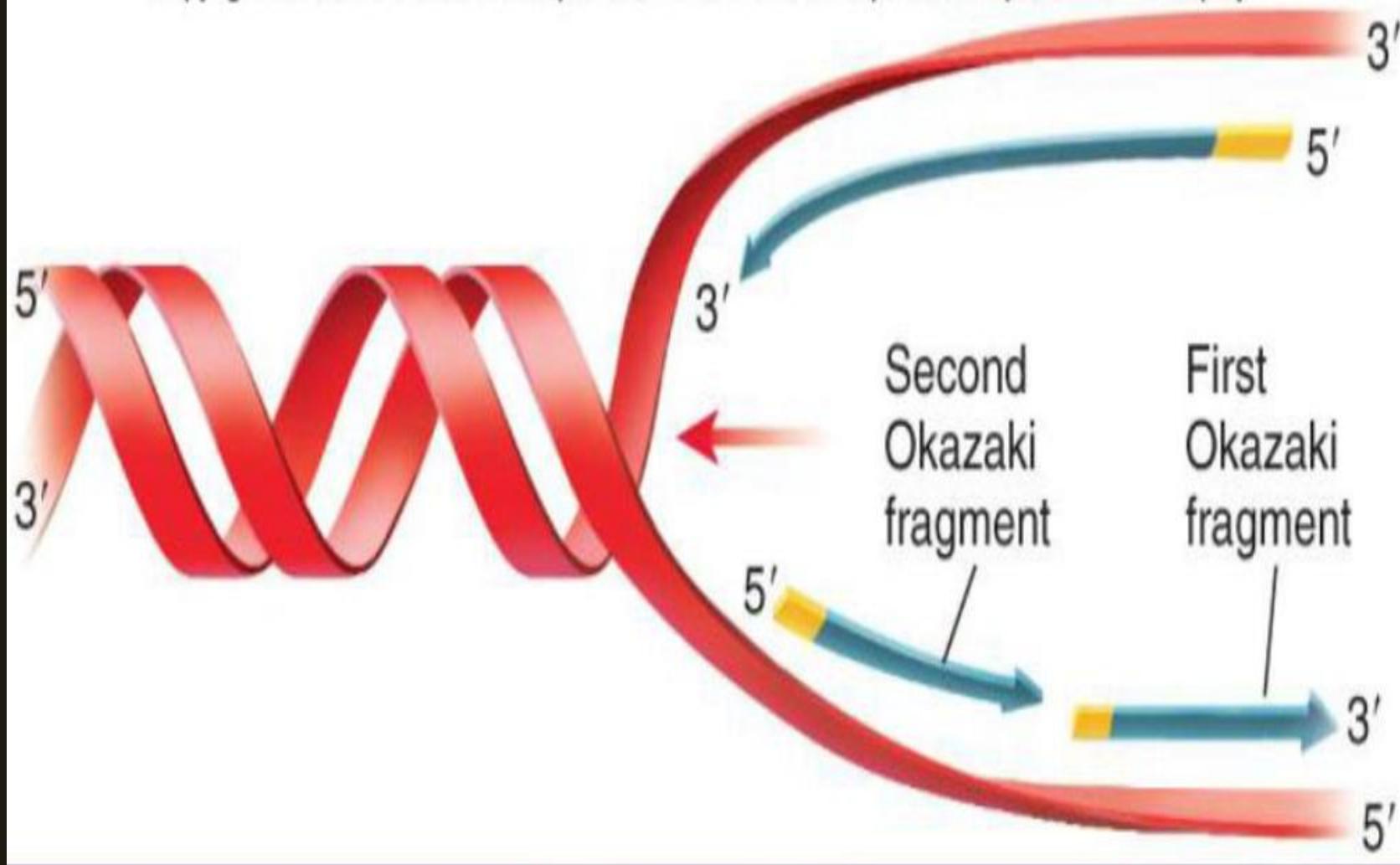
DNA polymerase can only link nucleotides in the 5' to 3' direction.

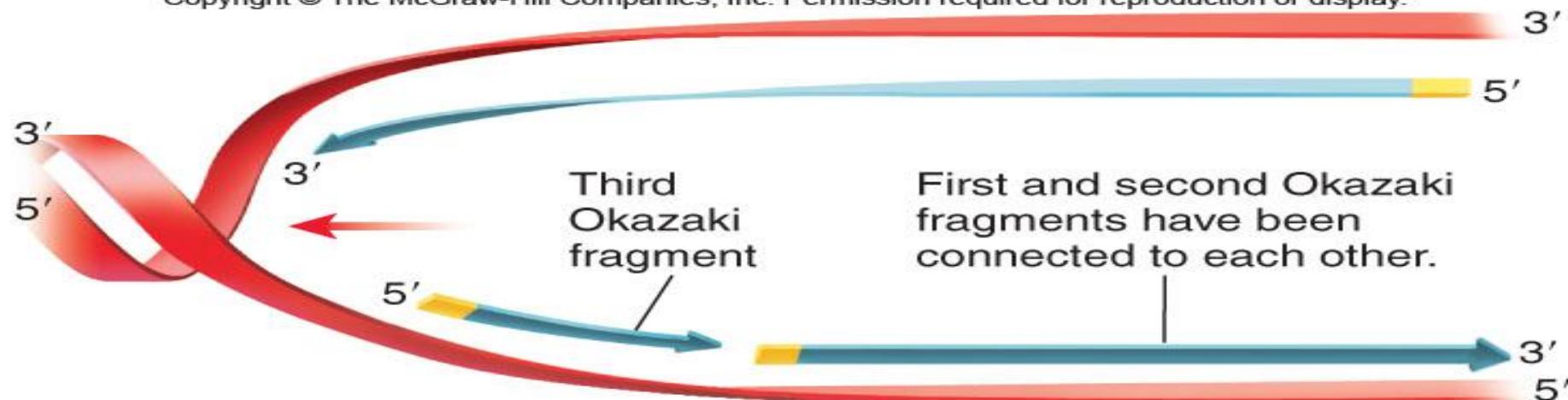
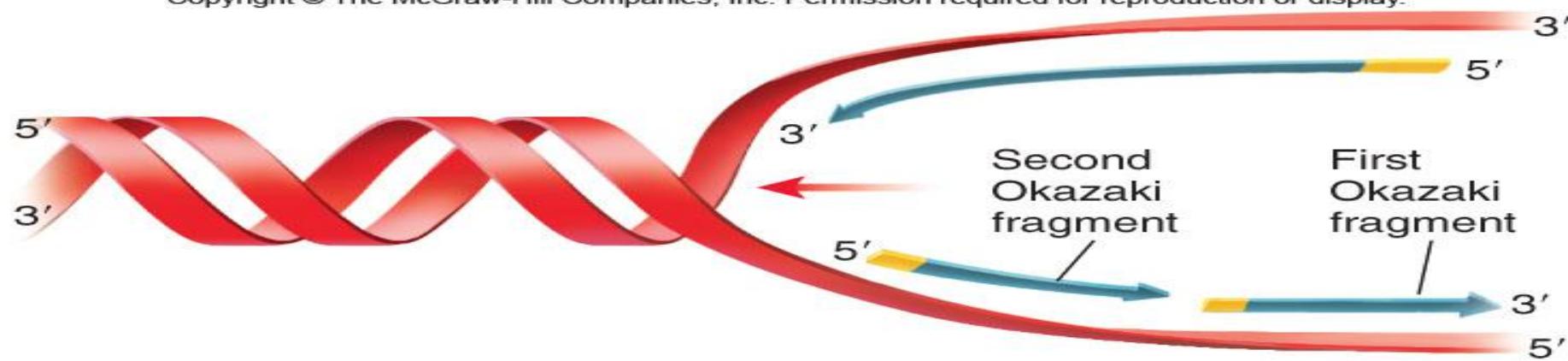


How to solve the problem then?

How to synthesize the lagging strand?







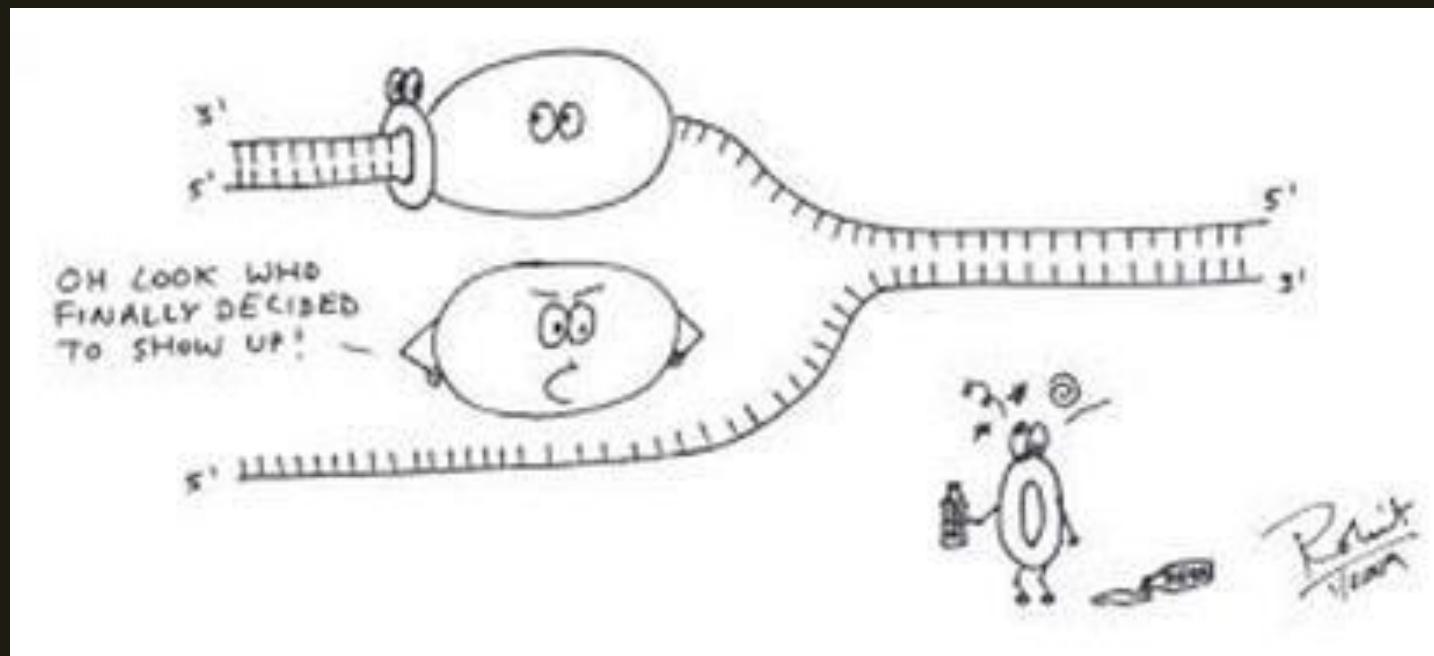
Leading and Lagging Strand in DNA Replication

@AmoebaSisters

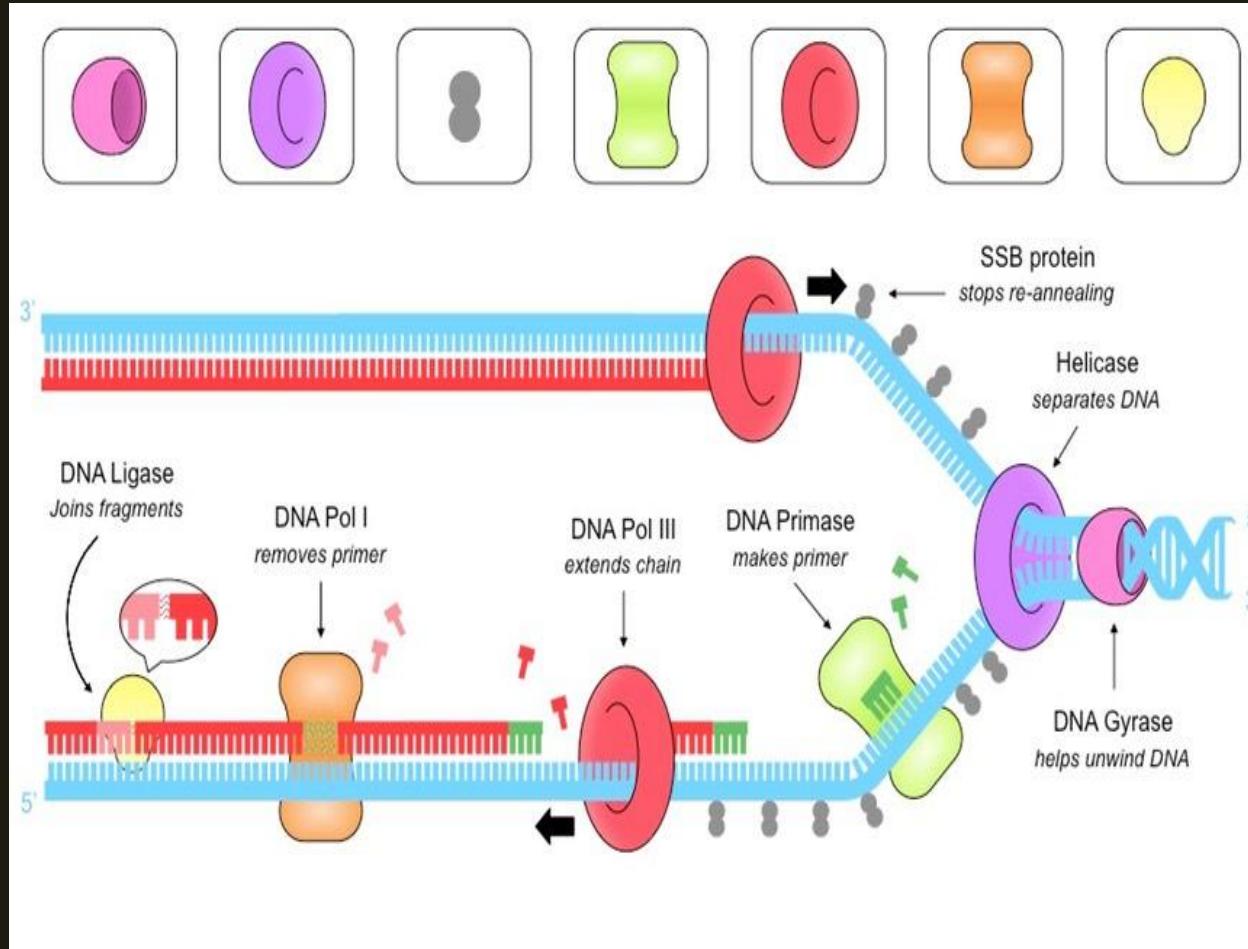
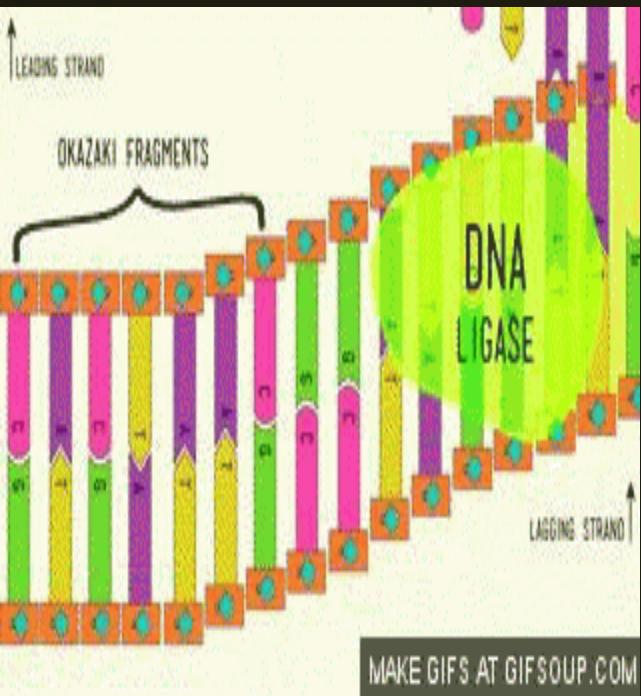


**What would happen to the
DNA replication process if
the growing DNA chain did
not have a free 3' end?**

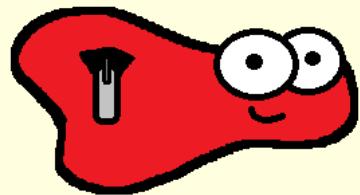
What is left?



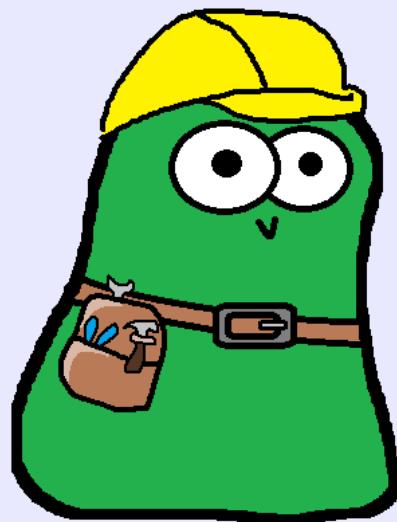
DNA replication- Protein-6: DNA ligase (The glue)



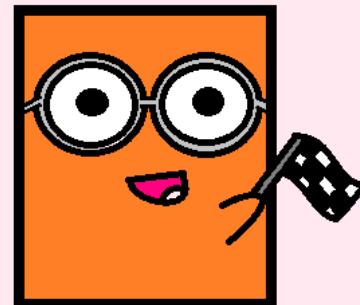
DNA Replication Key Players



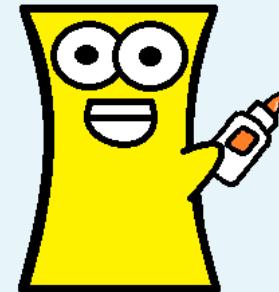
Helicase



DNA Polymerase



Primase

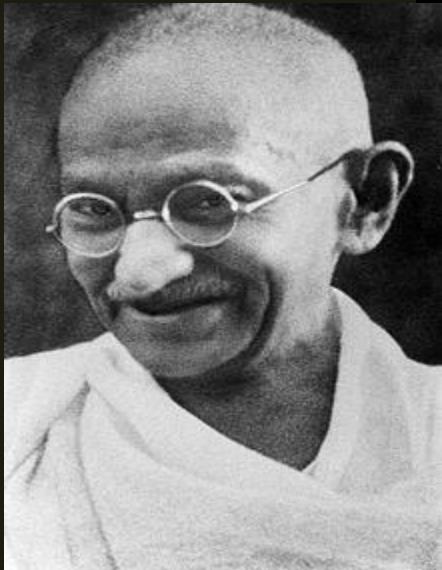


Ligase

- Primase – Synthesizes RNA primer for DNA Polymerase to act
- DNA helicase – Unwinds DNA helix by cleaving Hydrogen bonds
- DNA topoisomerase (gyrase) – relieves the strain in DNA helix (due to supercoiling)
- Single-strand binding (SSB) proteins - Keep parental strands open to act as templates
- DNA Ligase – Finally joins DNA strands via phosphodiester bonds

DNA replication occurs with great fidelity

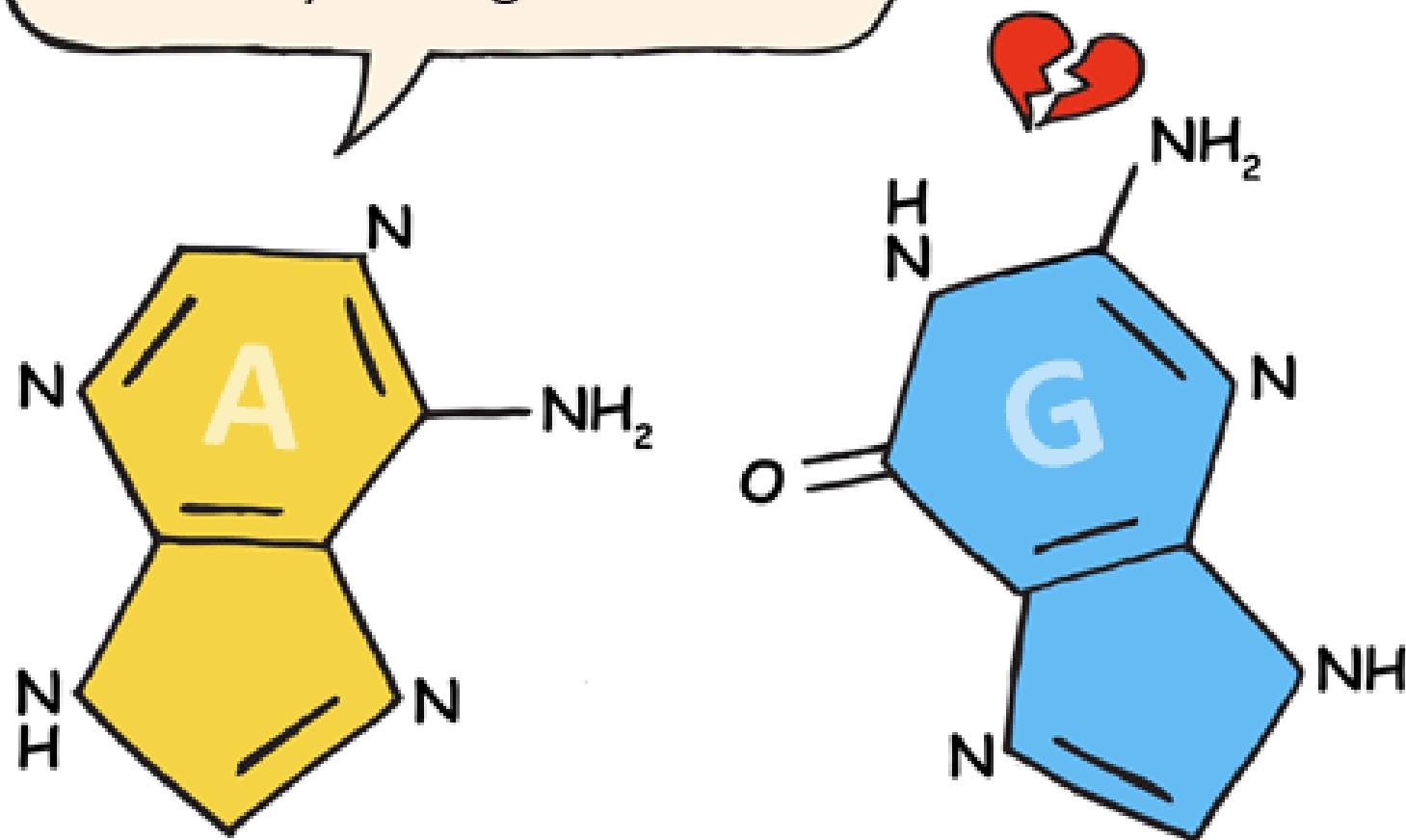
Somatic cell DNA stability and reproductive-cell DNA stability are essential. Why?



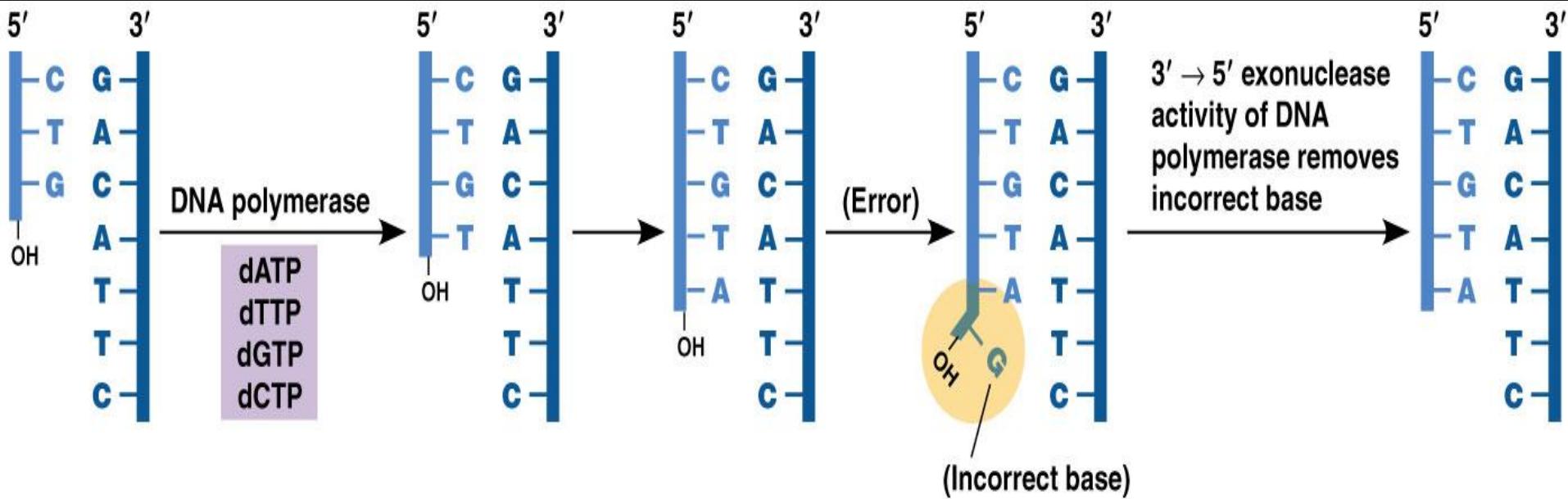
Homo sapiens sapiens
99.9% sequence identity

Pan troglodytes (Chimp)
99% sequence identity

I'm sorry G, but we're
base-ically not a good match...



Proofreading & exo-nuclease activity of DNA Polymerase



Mistakes in replication are rare

- DNA polymerase initially makes about **1 in 10,000 base pairing errors**
- Enzymes **proofread** and correct these mistakes
- The new error rate for DNA that has been proofread is **1 in 1 billion base pairing errors**
- One strand provides information to correct the mistake on the other strand

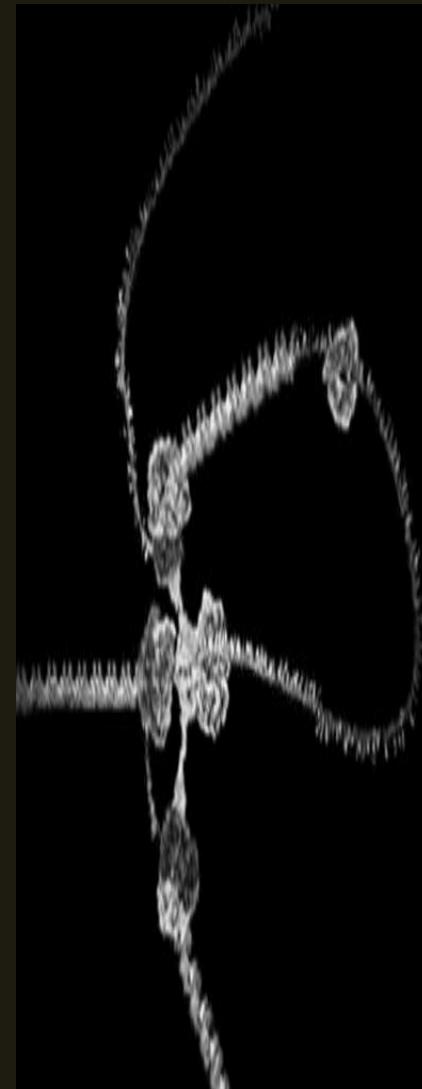
**Replication rate in eukaryotes
is slower resulting in a higher
fidelity/accuracy of
replication in eukaryotes**

Speed of replication any assumption?

SPEED OF REPLICATION

Prokaryotes : Genome size of *E.coli* is 4.7×10^6 nucleotide pairs. Replication proceeds from single origin of replication at the speed of 1000 nucleotides per sec completing replication of whole genome in 40 minutes.

Eukaryotes : Speed is very slow in comparison to prokaryotes. The average human chromosome contains 150×10^6 nucleotide pairs which are copied at about only 50 bp per sec. But because there are multiple origins of replication present along the linear DNA, it is completed in a hour.



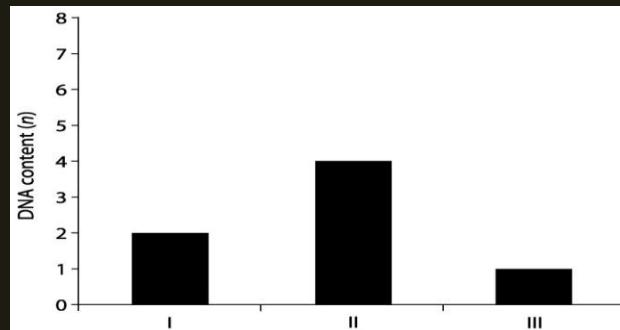
1. If there is 30% Adenine, how much Cytosine is present?

2. Given below are the base (nucleotide) compositions of genomic DNA obtained from different animal species. Which of the following pair/s (a-f) are likely to come from the same species? Explain your answer briefly.

a) 22.4% T b) 29.5% G c) 15.3% C d) 34.7% A e) 25.6% C f) 29.9%T

3. It has been found that at a certain locus of the human genome, 20 different alleles exist in the population. Each person has at most _____ alleles.

4. Consider the following diagram representing the DNA content of 3 cell types I, II and III at different stages, for the same considered organism. Find which of these cell types is actually a gamete, G₂ cell, normal cell. Also briefly write at which alternative phase cell type II could possibly be in.



5. The fruit fly *Drosophila melanogaster* has four pairs of chromosomes, whereas the house fly *Musca domestica* has six pairs of chromosomes. Other things being equal, in which species would you expect to see more genetic variation among the progeny of a cross? Explain your answer.

Review question

- DNA polymerase is the enzyme that
 - A) unzips the DNA strands.
 - B) adds new nucleotides to the growing DNA strand.
 - C) forms a short stretch of ribonucleotides to begin the process of replication
 - D) ties together new pieces of DNA.

Take a careful look...

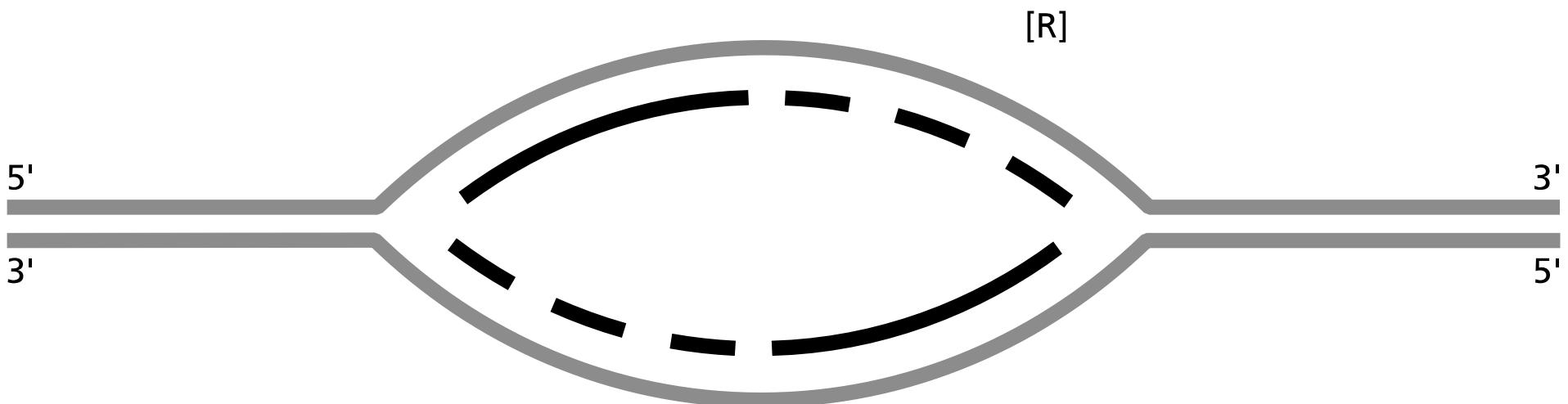
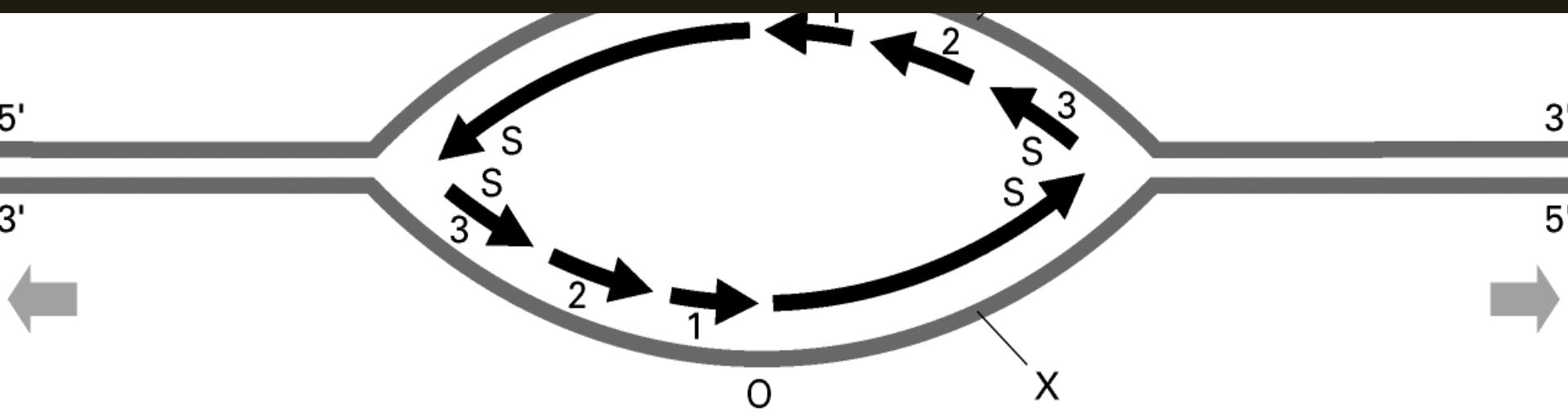
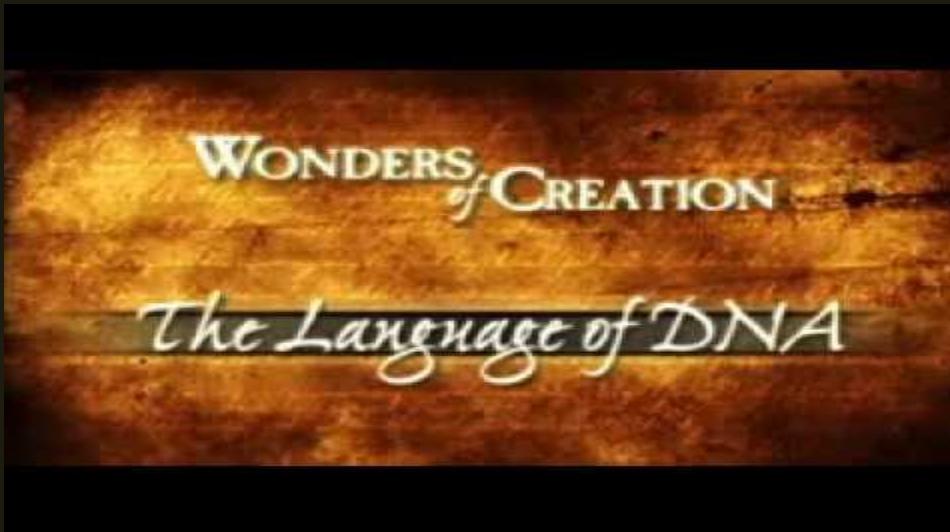


Figure-based review questions

- Mark the Okazaki fragments in the order in which they were synthesized (use 1, 2, 3).
- Indicate the direction of replication using arrows.
- For the right fork, indicate the leading and lagging strand templates by X and Y.





**With every cell reading the programs
encoded in our DNA—its like a hundred
trillion computers reading a hundred
trillion hard drives, every second of
every day of our life**

“We are fearfully and wonderfully made”