Science of Living System (BS20001)

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- **Research interests:**

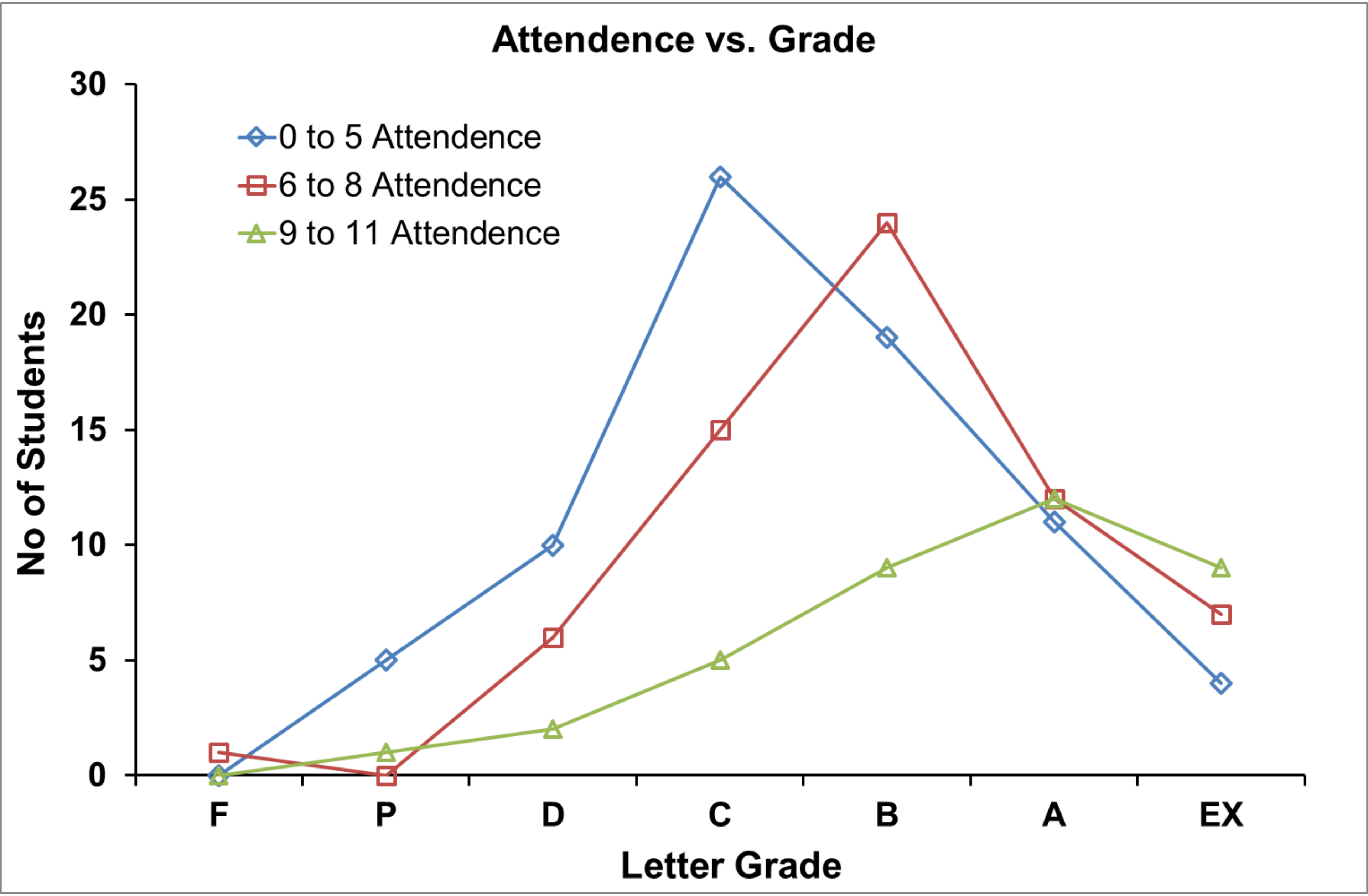
  Biophysics

  Nuclear Magnetic Resonance (NMR) Spectroscopy

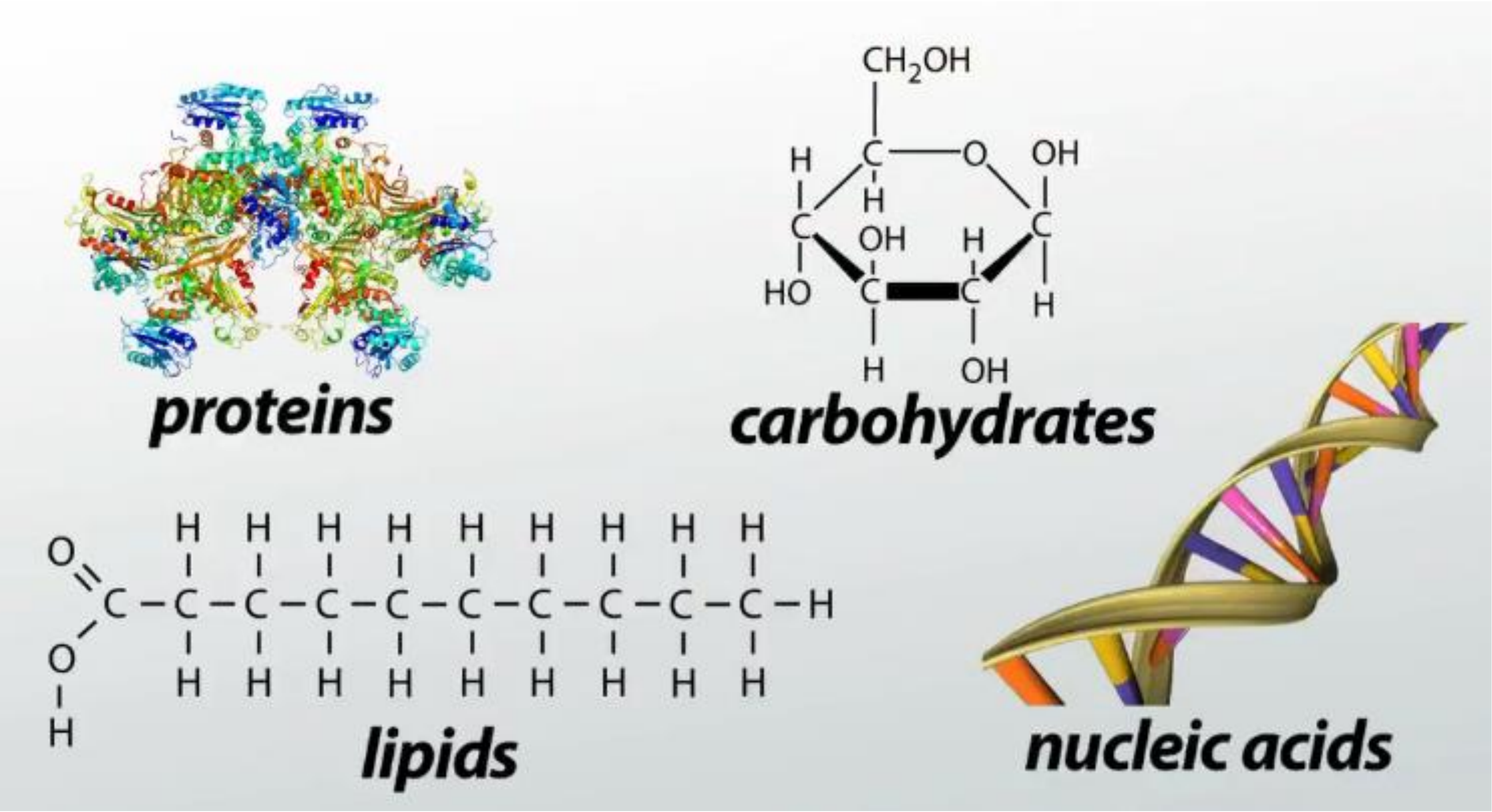
  Protein Engineering

  Signal Transduction and Gene Expression

  Enzymology


Attendence vs. Grade
0 to 5 Attendence
6 to 8 Attendence
9 to 11 Attendence
30
25
20
15
10
5
0
No of Students
F
P
D
C
B
A
EX
Letter Grade

Molecules of Life
Biological Macromolecules



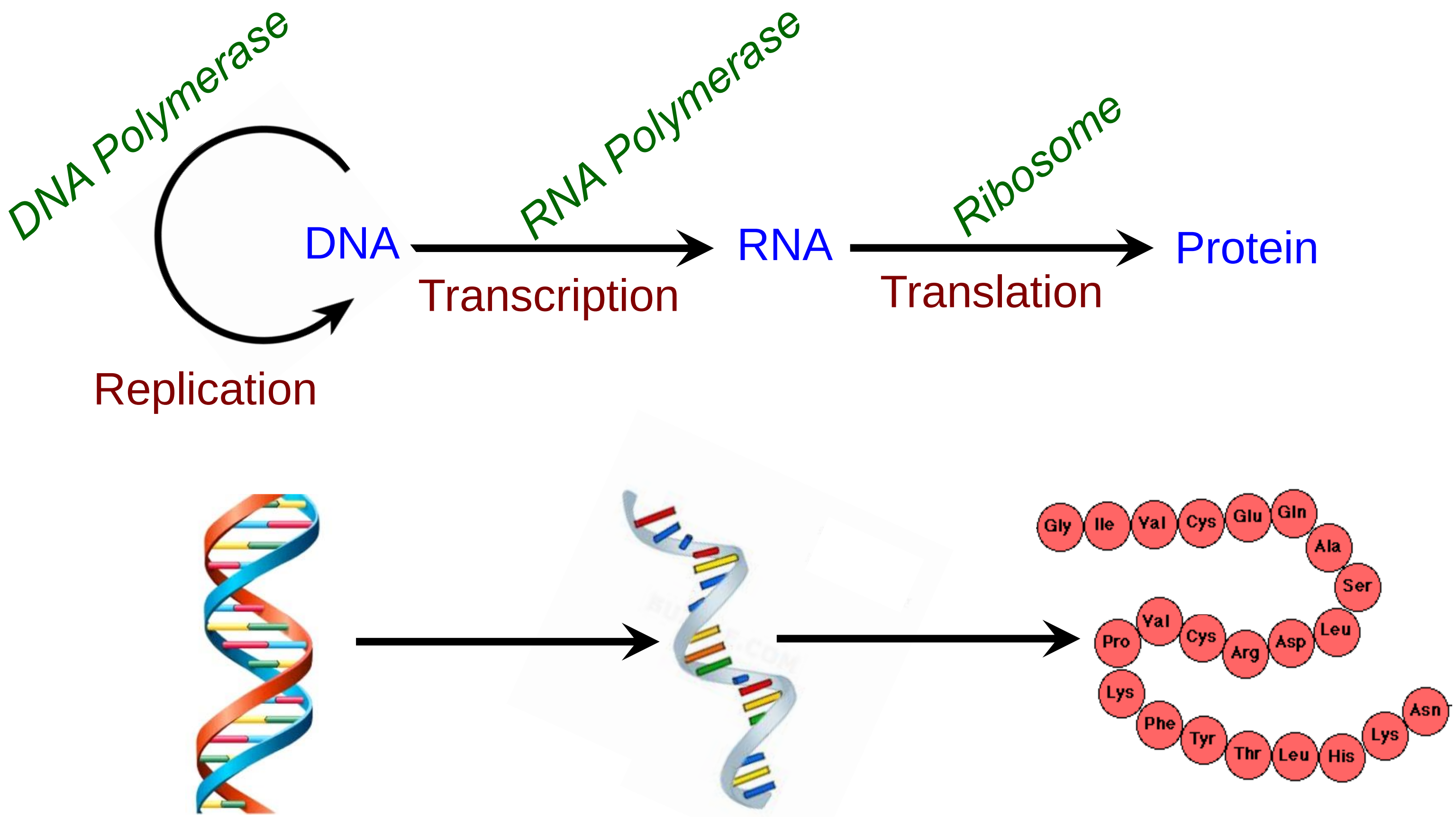
Nucleic Acid

Nucleic Acid

RNA: <u>R</u>ibo<u>n</u>ucleic <u>A</u>cid

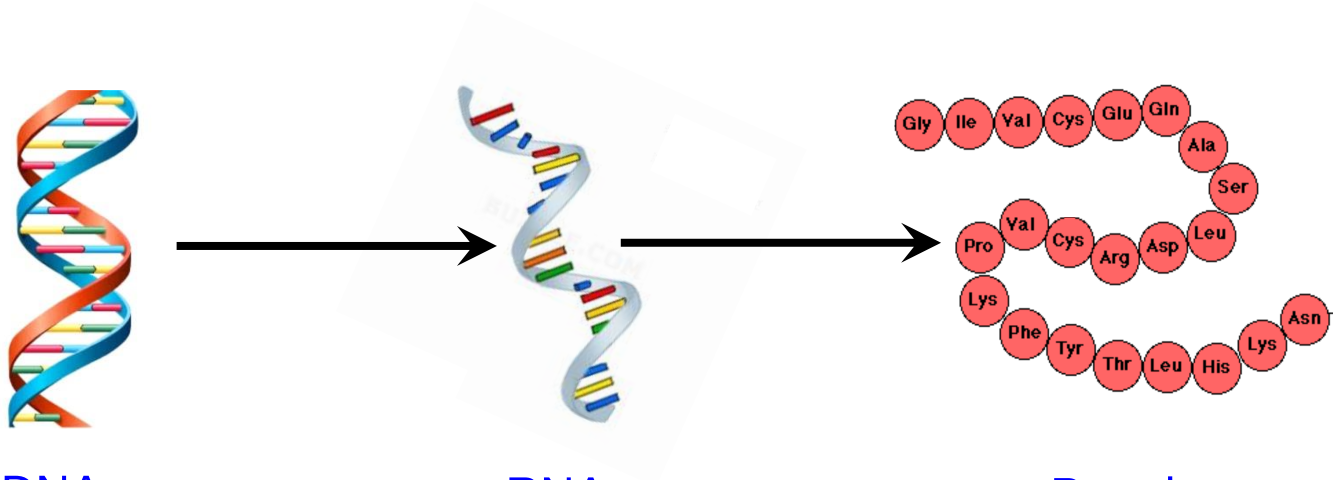
DNA: <u>D</u>eoxyribo<u>n</u>ucleic <u>A</u>cid

Flow of Genetic Information:
The Central Dogma of Molecular Biology



DNA	RNA	Protein
Polymer of nucleotides	Polymer of nucleotides	Polymer of amino acids

DNA is a long thread that stores information



DNA

Polymer of nucleotides

RNA

Polymer of nucleotides

Protein

Polymer of amino acids

Cassette Tape

Why study Living System?

STORAGE LIMITS

Estimates based on bacterial genetics suggest that digital DNA could one day rival or exceed today's storage technology.

	Hard disk	Flash memory	Bacterial DNA
Read–write speed (µs per bit)	~3,000–5,000	~100	<100
Data retention (years)	>10	>10	>100
Power usage (watts per gigabyte)	~0.04	~0.01–0.04	$<10^{-10}$
Data density (bits per cm^3)	$\sim10^{13}$	$\sim10^{16}$	$\sim10^{19}$

©nature

455 Exabyte/gm

Microsoft Corporation – DNA Storage Research

A DNA-Based Archival Storage System Bornholt J, et. al. ASPLOS 2016 (International Conference on Architectural Support for Programming Languages and Operating Systems)

Microsoft Store Products Support

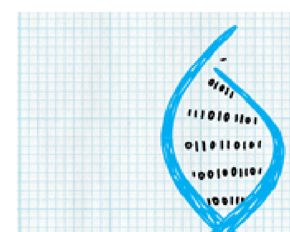
Research Research areas Products & Downloads Programs & Events People Careers About

DNA Storage

Established: January 1, 2015

https://ieeexplore.ieee.org/document/7948677

The amount of digital data produced has long been outpacing the amount of storage available. This project enables molecular-level data storage into DNA molecules by leveraging biotechnology advances in synthesizing, manipulating and sequencing DNA to develop archival storage. Microsoft and University of Washington researchers are collaborating to use DNA as a high density, durable and easy-to-manipulate storage medium.



PCMag India | News

Microsoft Is Using DNA to Solve Our Impending Data Storage Crisis

BY MATTHEW HUMPHRIES MARCH 22, 2019, 7:02 P.M.

The data stored in a warehouse-sized datacenter today would fit into 'a space roughly the siz few board game dice.'

Microsoft device stores digital info as DNA

It translated “HELLO” into DNA and back again -- and it only took 21 hours.

istine Fisher, @cfisherwrites
21.19 in Internet

Comments

1399
Shares

Microsoft and University of Washington demonstrate automated DNA data storage

BY ALAN BOYLE on March 21, 2019 at 6:00 am

Microsoft's DNA storage breakthrough could pave way for exabyte drives

Scientists develop a more efficient way to find and selectively retrieve files stored on DNA.

DNA Storage is robust and has high storage density

Tweet

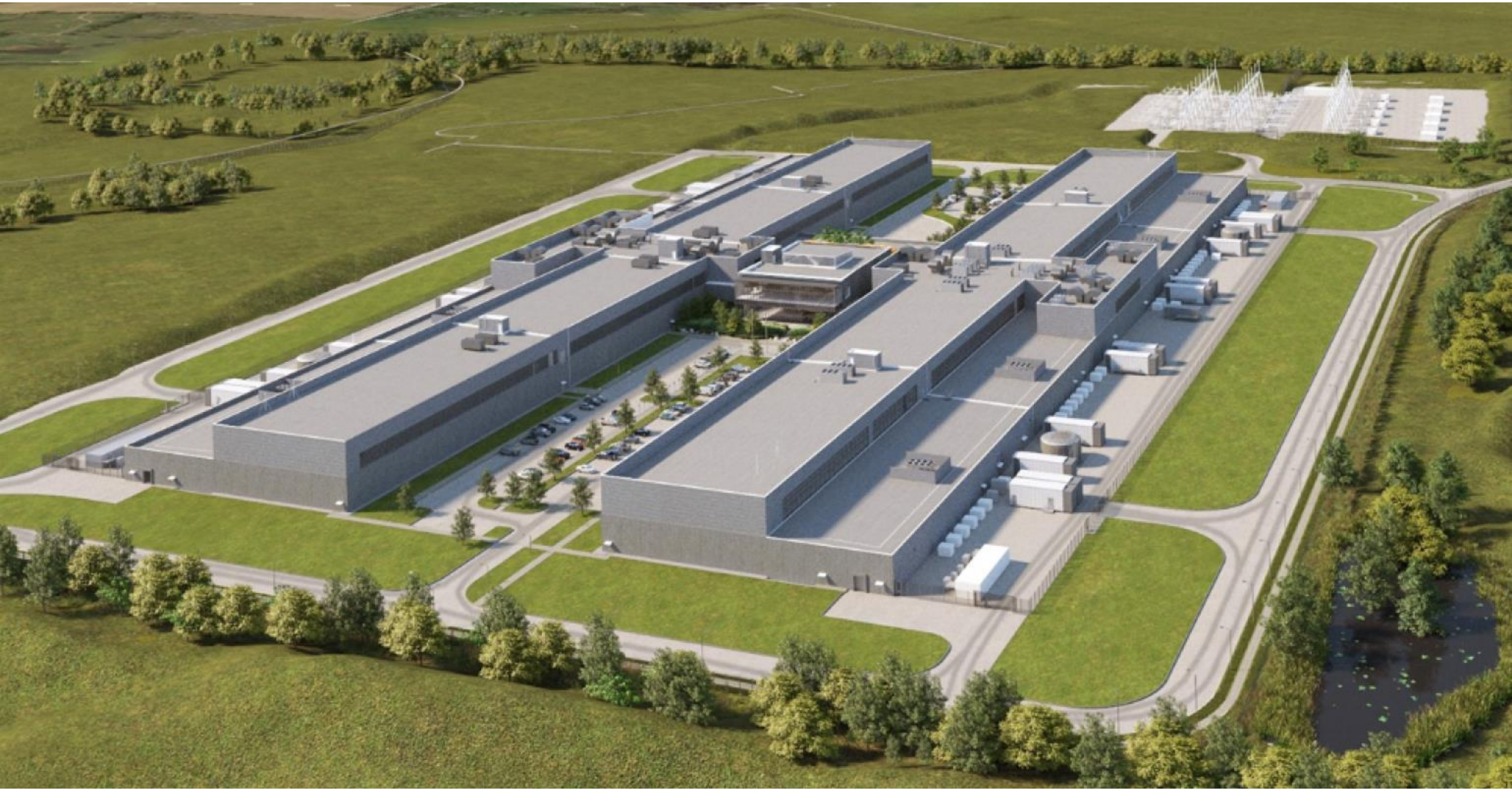
ETH Zurich
@ETH_en

The ETH spin-off Turbobeads has stored the @NetflixDE series #Biohackers in #DNA. In the Making of, the researchers explain how the digital record was translated into a sequence of the four DNA building blocks adenine, guanine, cytosine and thymine.

youtube.com
Biohackers | First Original Series stored in DNA | Netflix
Biohackers is a gripping science thriller about biotechnologies. We have turned the series itself into a ...

2:43 PM · Aug 17, 2020 · Falcon Social Media Management

DNA Storage has high storage density



$800 million data center in Gallatin, a small town just outside of Nashville, Tennessee. Facebook acquired the 809 acres of land for this data center in 2020. One cricket ground is ~ 4 acres. Storage capacity is several Exabyte of data. 1 gm of DNA can store 455 Exabyte of data.

DNA Storage is robust

https://en.wikipedia.org/wiki/Otzi

https://www.bbc.com/news/science-environment-58191123

- Otzi the mummy was discovered in 1991 in the Ötztal Alps on the border between Austria and Italy.
- He lived from 3275 BC to 3230 BC i.e. 5000 years ago.
- Otzi's full genome has been sequenced and published on February 2012.
- DNA analysis also showed him at high risk of atherosclerosis and lactose intolerance.
- DNA of over 3,700 Tyrolean male blood donors revealed that Otzi has living relatives in Austria today.
- Oldest DNA sequenced: DNA extracted from the tooth of 1.2 million year old mammoth. (Feb 2021) https://www.nature.com/articles/d41586-021-00436-x
- In 2016, researchers reported protein sequences from 3.8-million-year-old ostrich eggshells from Tanzania.

Nucleic Acid

- **Nucleic acids are polymers**

- **Monomer---nucleotides**
  - **Nitrogenous bases**
    - **Purines**
    - **Pyrimidines**
  - **Sugar**
    - **Ribose**
    - **Deoxyribose**
  - **Phosphates**

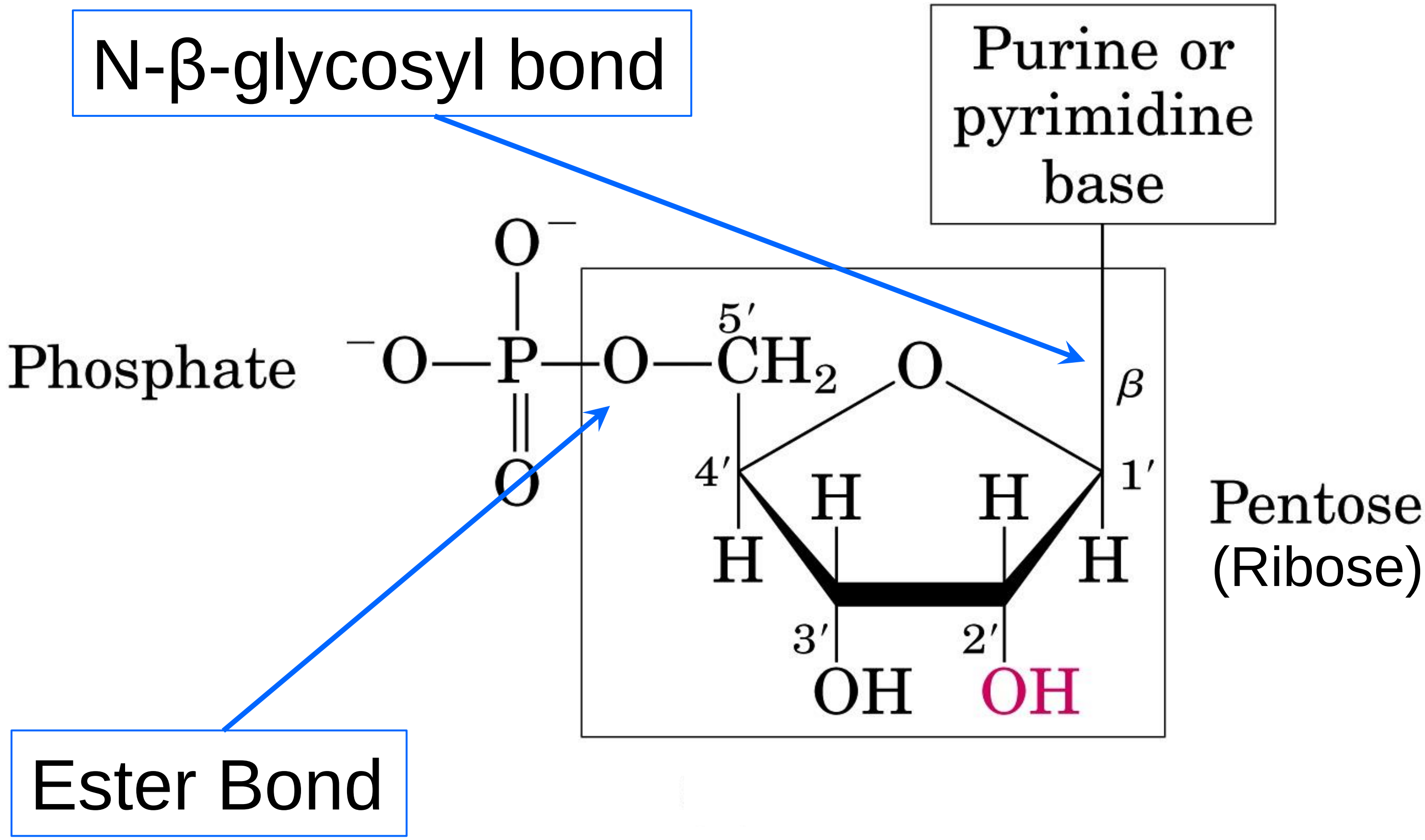
Nucleosides

Nucleotides

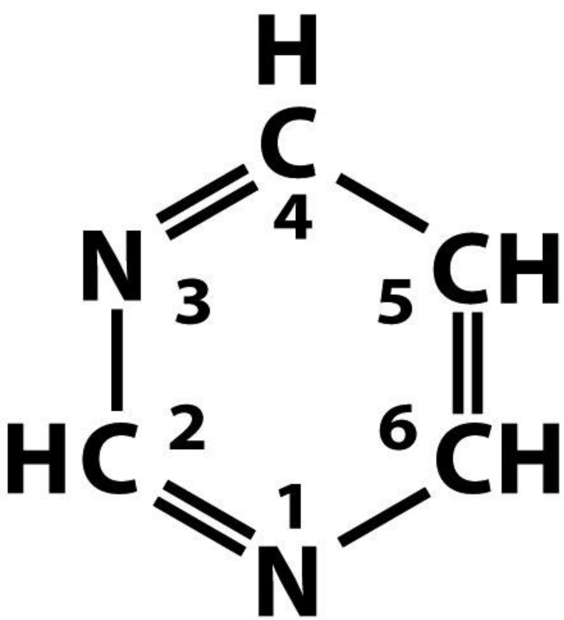
Nucleic Acid monomer structure

RNA - Ribonucleic Acid **(OH)**

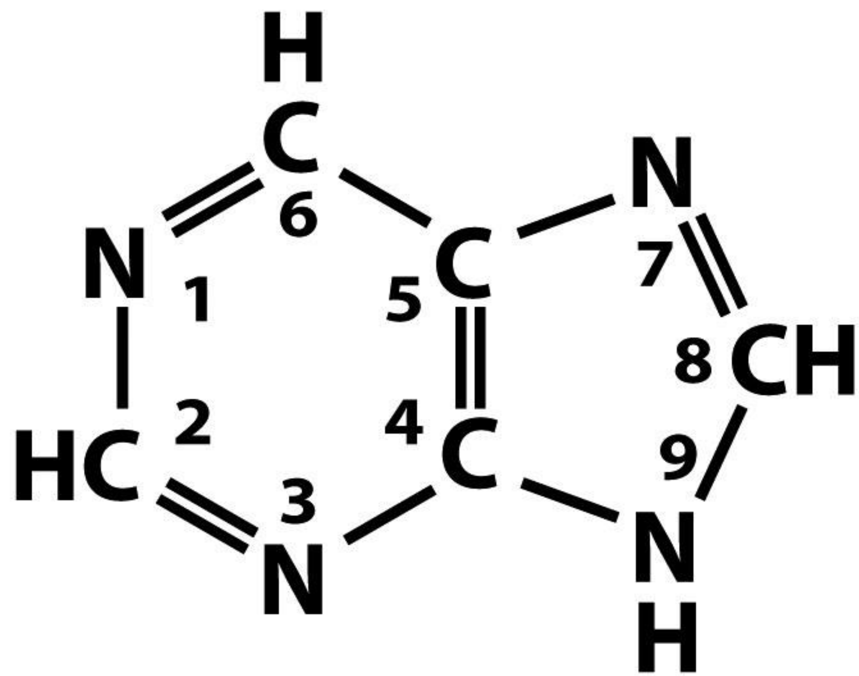
DNA - Deoxyribonucleic Acid **(H)**



Two Types of Nitrogenous Bases



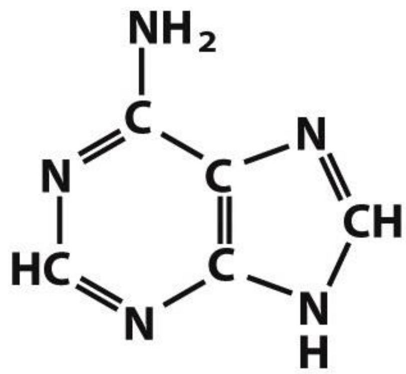
Pyrimidine



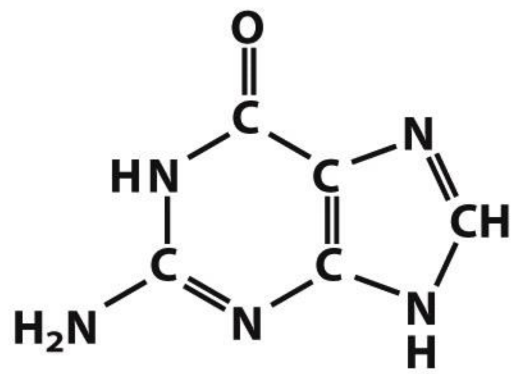
Purine

Figure 8-1b
Lehninger Principles of Biochemistry, Fifth Edition

Purine and Pyrimidine Bases

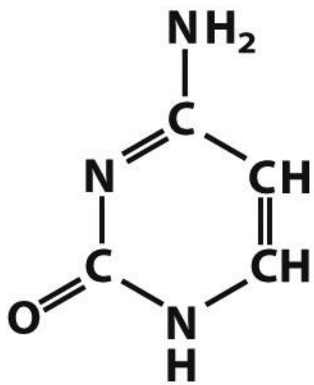


Adenine

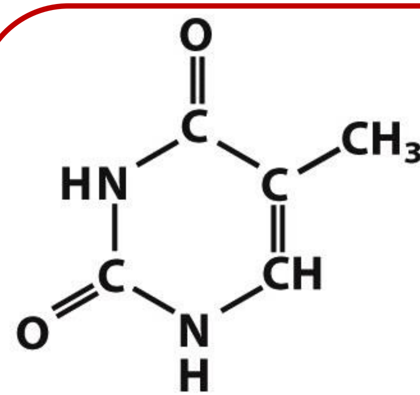


Guanine

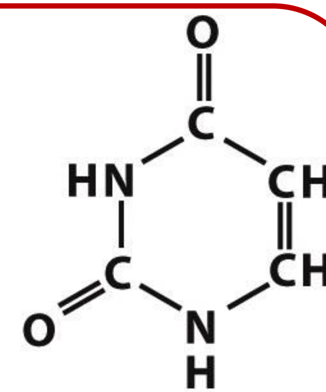
Purines



Cytosine



Thymine
(DNA)

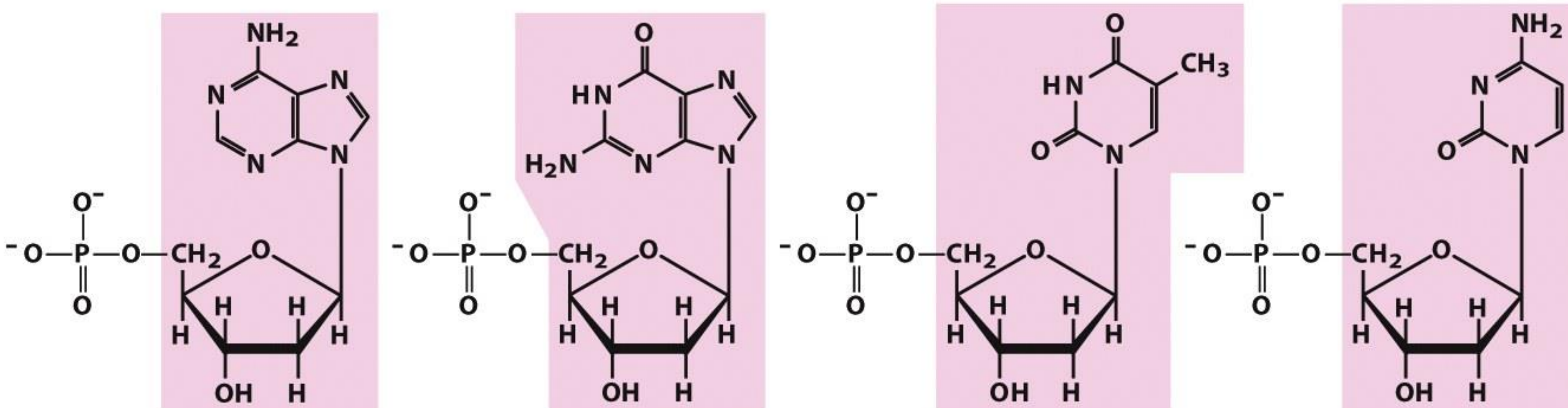


Uracil
(RNA)

Pyrimidines

Nucleotide = Nucleoside + Phosphate

(Nucleoside = Sugar + Base)



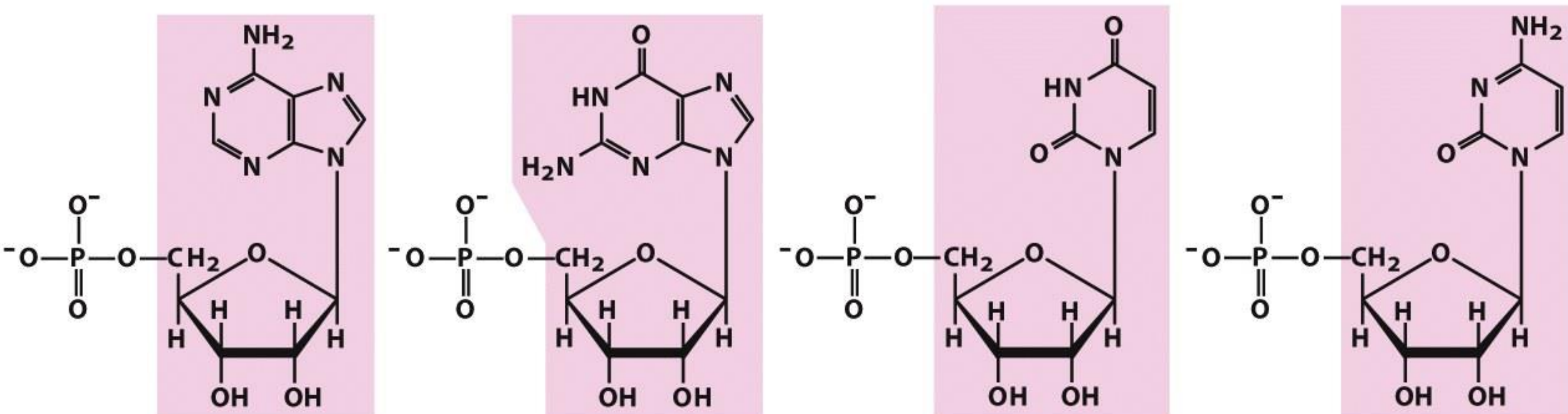
Nucleotide:	Deoxyadenylate (deoxyadenosine 5′-monophosphate)	Deoxyguanylate (deoxyguanosine 5′-monophosphate)	Deoxythymidylate (deoxythymidine 5′-monophosphate)	Deoxycytidylate (deoxycytidine 5′-monophosphate)
Symbols:	A, dA, dAMP	G, dG, dGMP	T, dT, dTMP	C, dC, dCMP
Nucleoside:	Deoxyadenosine	Deoxyguanosine	Deoxythymidine	Deoxycytidine

Deoxyribonucleotides

Figure 8-4a
Lehninger Principles of Biochemistry, Fifth Edition

Nucleotide = Nucleoside + Phosphate

(Nucleoside = Sugar + Base)



Nucleotide:	Adenylate (adenosine 5′-monophosphate)	Guanylate (guanosine 5′-monophosphate)	Uridylate (uridine 5′-monophosphate)	Cytidylate (cytidine 5′-monophosphate)
Symbols:	A, AMP	G, GMP	U, UMP	C, CMP
Nucleoside:	Adenosine	Guanosine	Uridine	Cytidine

Ribonucleotides

Figure 8-4b
Lehninger Principles of Biochemistry, Fifth Edition

Phosphodiester Linkages in the Covalent Backbone of Nucleic Acid

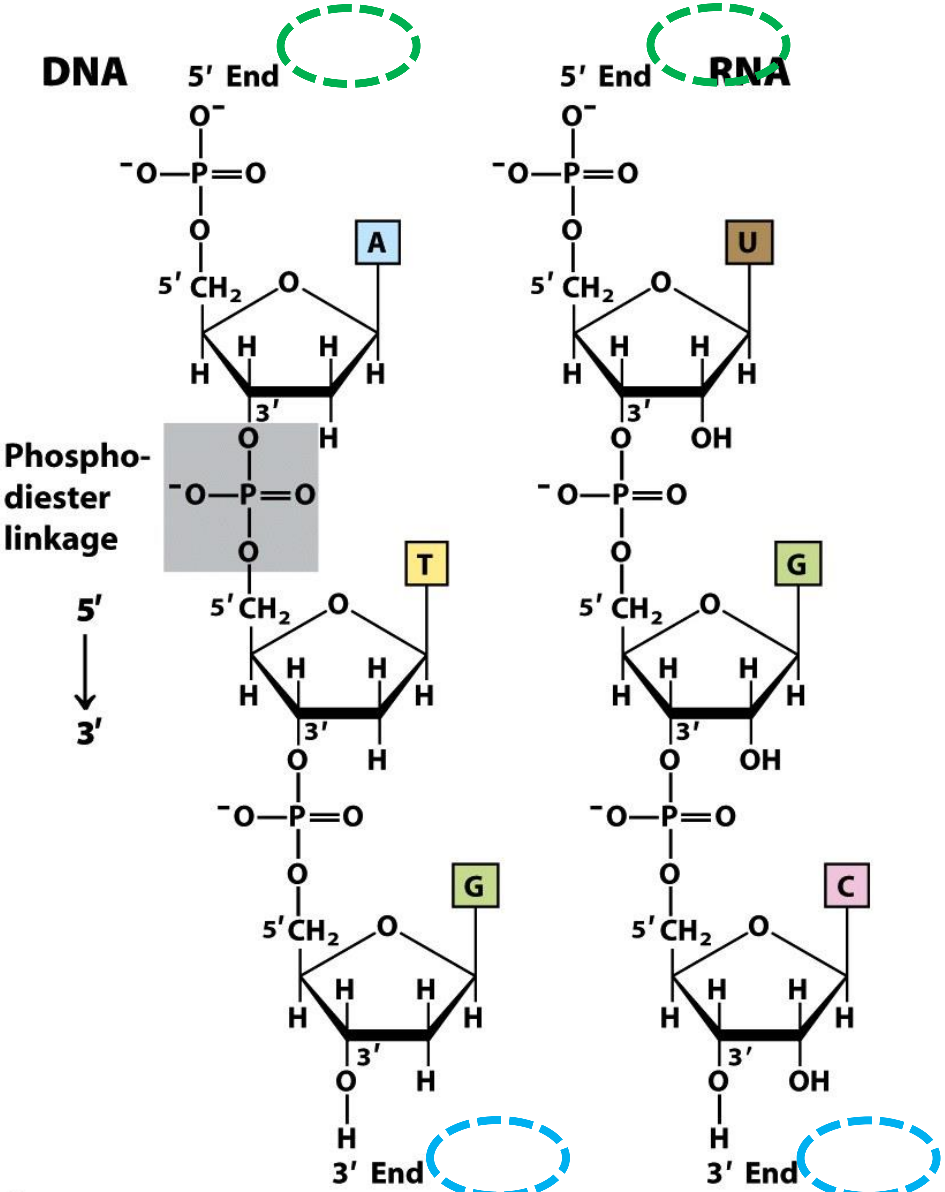
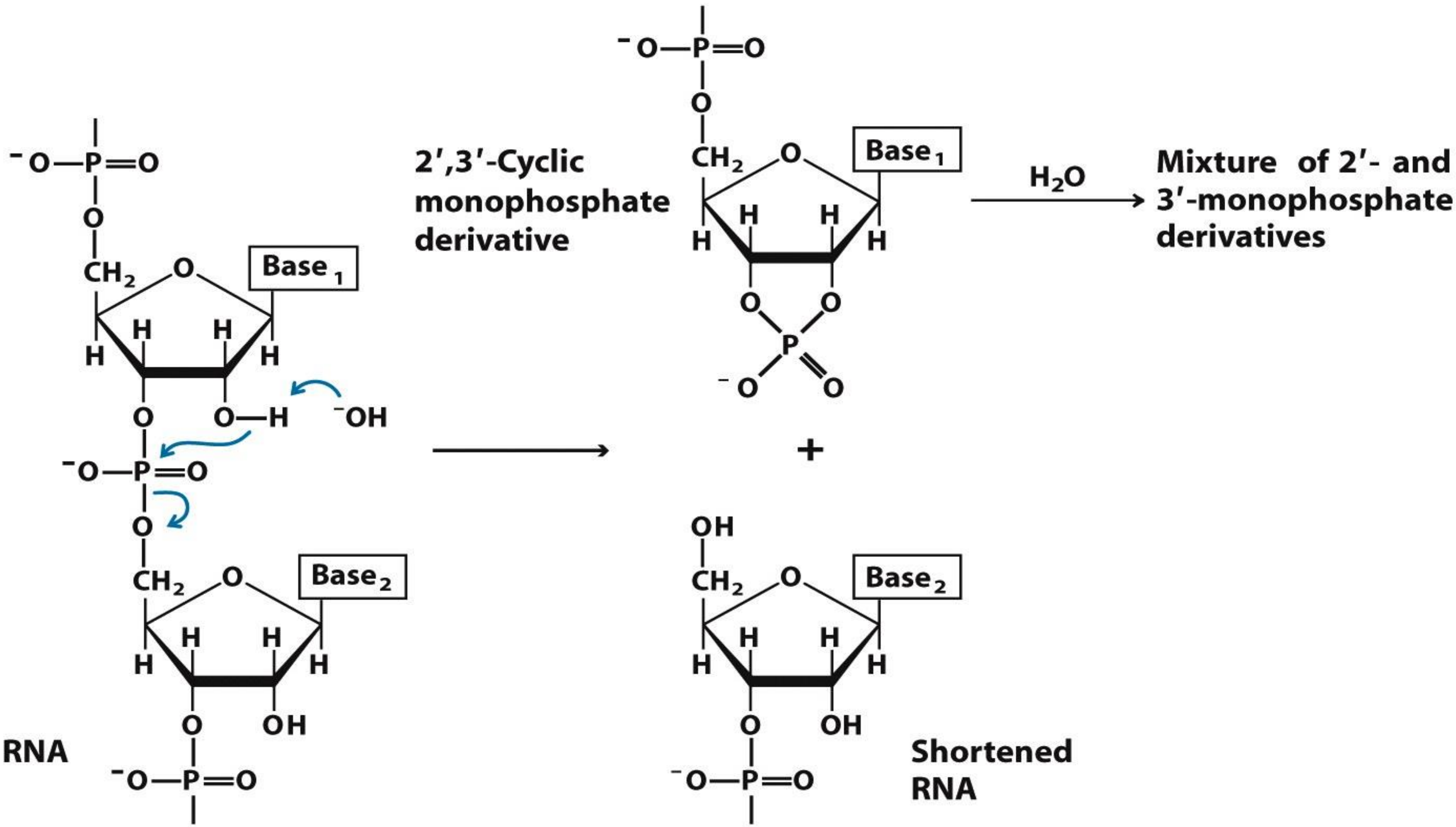


Figure 8-7
Lehninger Principles of Biochemistry, Fifth Edition

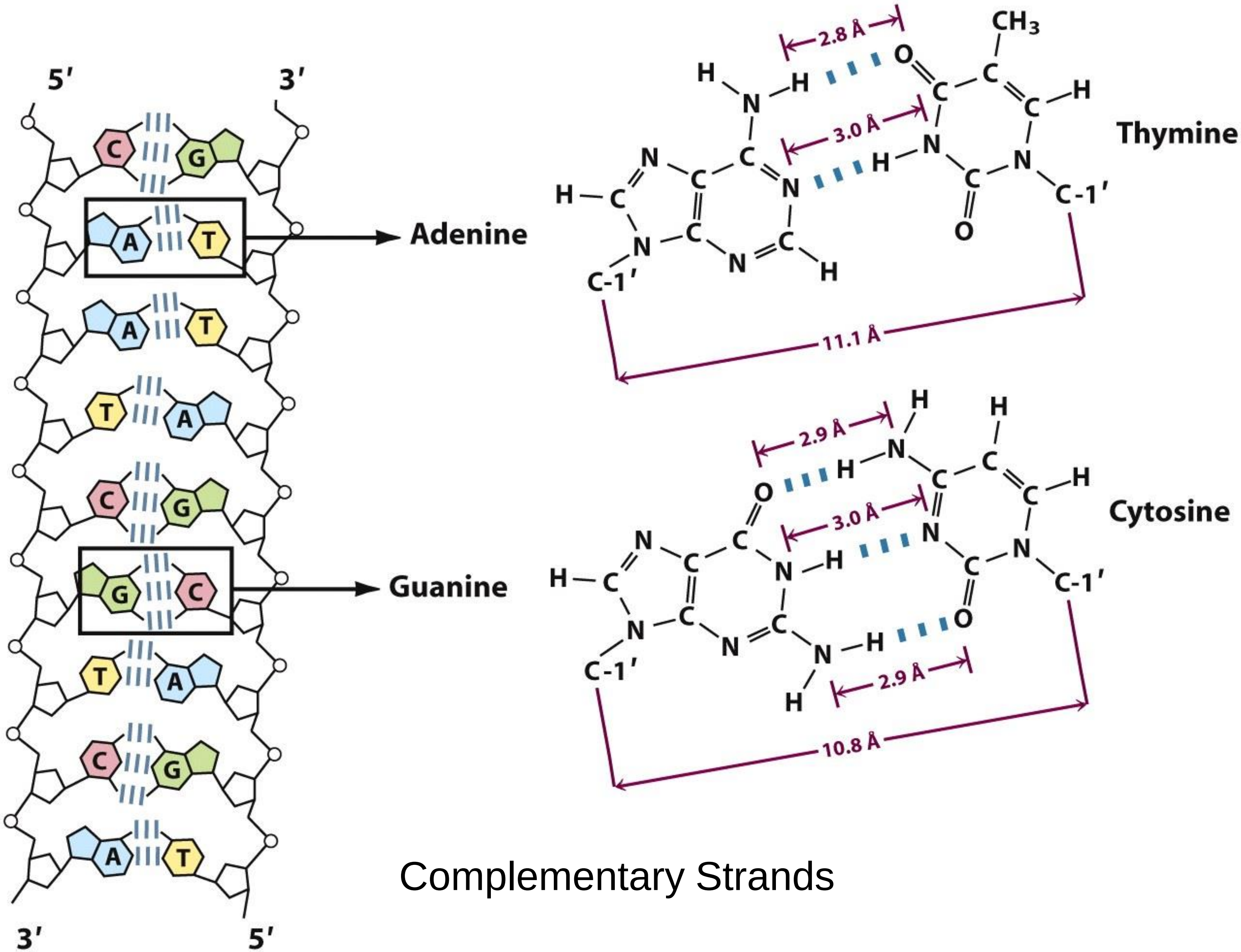
How information is stored in DNA or RNA?

5′-**ATG**-3′	5′-**ATC**-3′	5′-**ATA**-3′	5′-**ATT**-3′
5′-**TTG**-3′	5′-**TTC**-3′	5′-**TTA**-3′	5′-**TTT**-3′
5′-**GTG**-3′	5′-**GTC**-3′	5′-**GTA**-3′	5′-**GTT**-3′
5′-**CTG**-3′	5′-**CTC**-3′	5′-**CTA**-3′	5′-**CTT**-3′
5′-**AGG**-3′	5′-**AGC**-3′	5′-**AGA**-3′	5′-**AGT**-3′
5′-**TGG**-3′	5′-**TGC**-3′	5′-**TGA**-3′	5′-**TGT**-3′
5′-**GGG**-3′	5′-**GGC**-3′	5′-**GGA**-3′	5′-**GGT**-3′
5′-**CGG**-3′	5′-**CGC**-3′	5′-**CGA**-3′	5′-**CGT**-3′
5′-**ACG**-3′	5′-**ACC**-3′	5′-**ACA**-3′	5′-**ACT**-3′
5′-**TCG**-3′	5′-**TCC**-3′	5′-**TCA**-3′	5′-**TCT**-3′
5′-**GCG**-3′	5′-**GCC**-3′	5′-**GCA**-3′	5′-**GCT**-3′
5′-**CCG**-3′	5′-**CCC**-3′	5′-**CCA**-3′	5′-**CCT**-3′
5′-**AAG**-3′	5′-**AAC**-3′	5′-**AAA**-3′	5′-**AAT**-3′
5′-**TAG**-3′	5′-**TAC**-3′	5′-**TAA**-3′	5′-**TAT**-3′
5′-**GAG**-3′	5′-**GAC**-3′	5′-**GAA**-3′	5′-**GAT**-3′
5′-**CAG**-3′	5′-**CAC**-3′	5′-**CAA**-3′	5′-**CAT**-3′

RNA is Less Stable than DNA



DNA: Deoxyribonucleic Acid

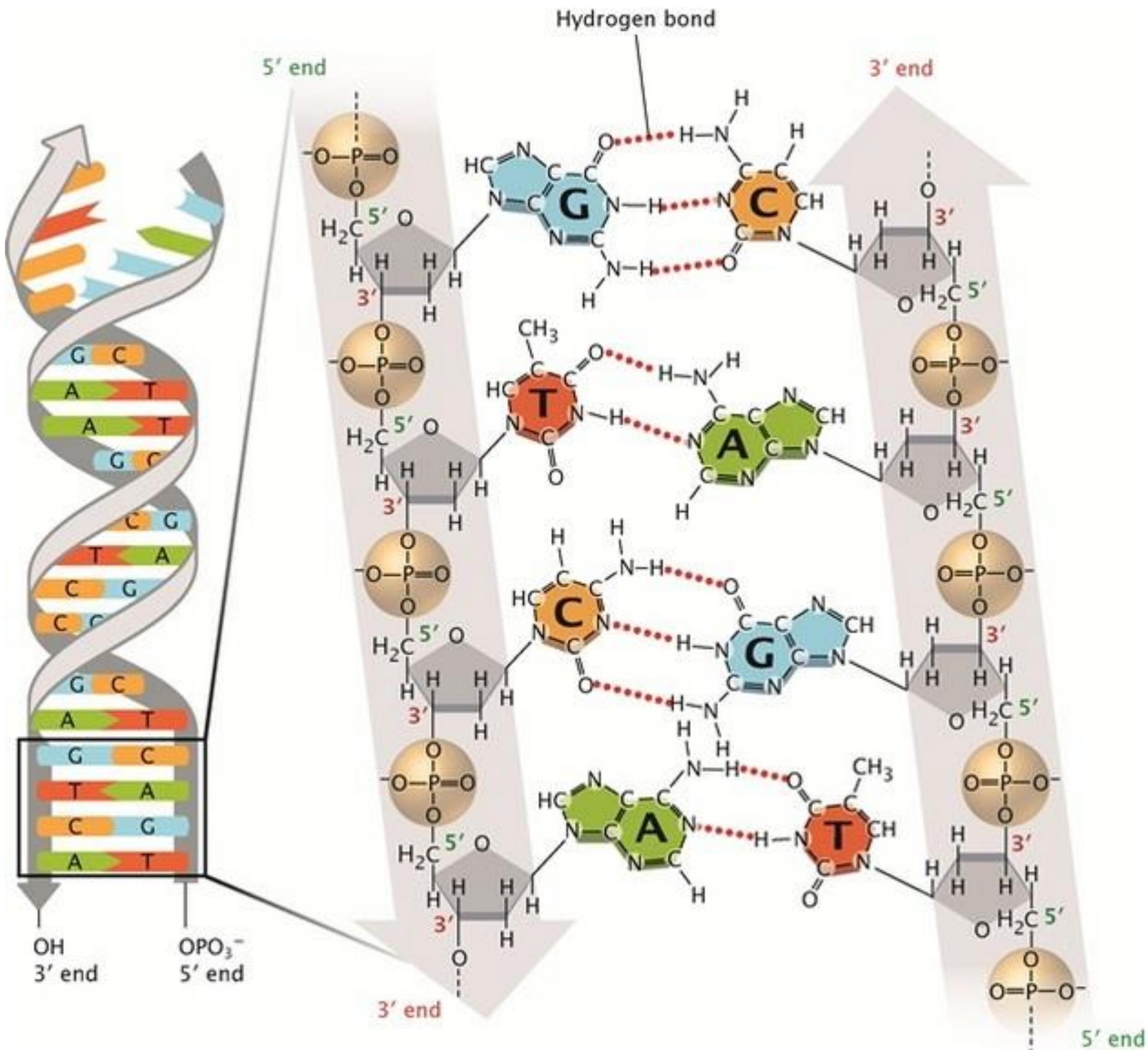


Complementary Strands

Some key features of DNA

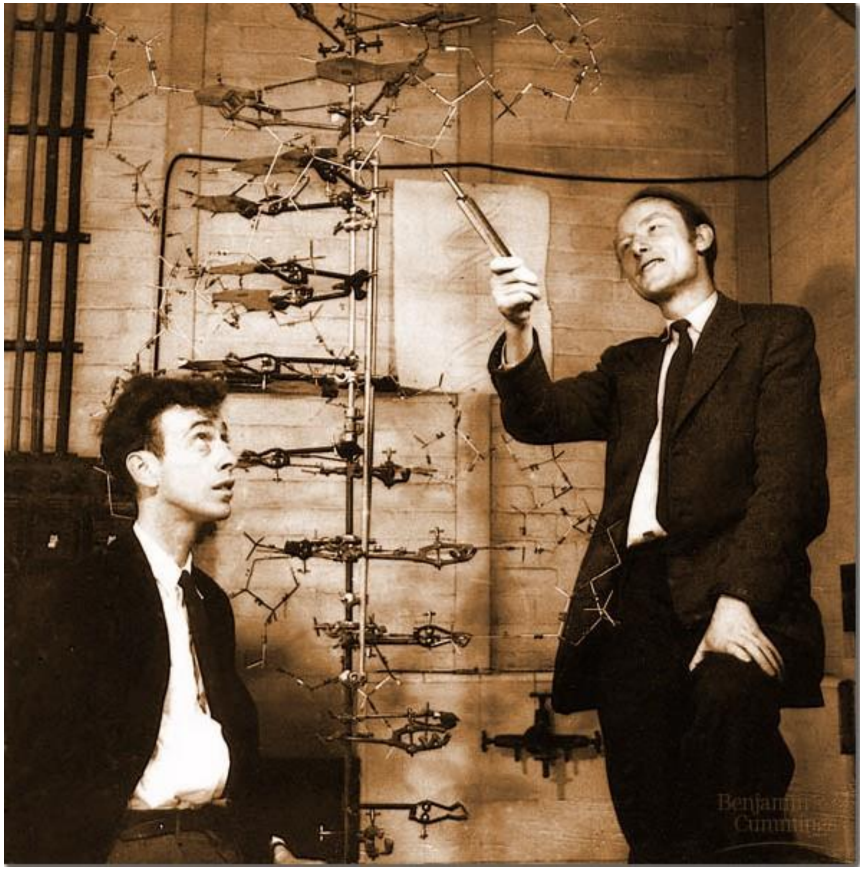
- In **DNA,** two nucleic acid strands anneal together through extensive **inter-strand H-bonding** between the bases**.** This **base pairing** follows the rule proposed by Watson and Crick.
- **Chargaff's rule: A always pairs with T and G pairs with C**
- Hence the two strands become **complementary** to each other
- **Directionality** of two strands is **opposite:** one is **5'-3'** and another **is 3'-5'**
- Hence complementary DNA strands are **antiparallel**

DNA: Deoxyribonucleic Acid



Discovery of the DNA Structure

- Structure was discovered in 1953 by James Watson and Francis Crick
- Awarded **<u>Nobel Prize in 1962</u>**



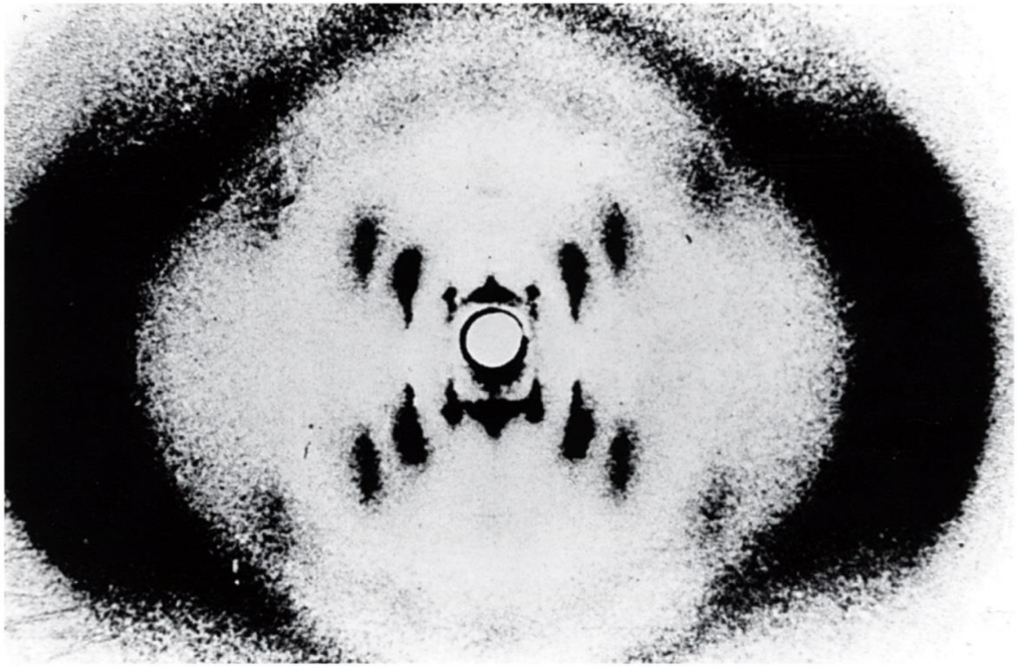
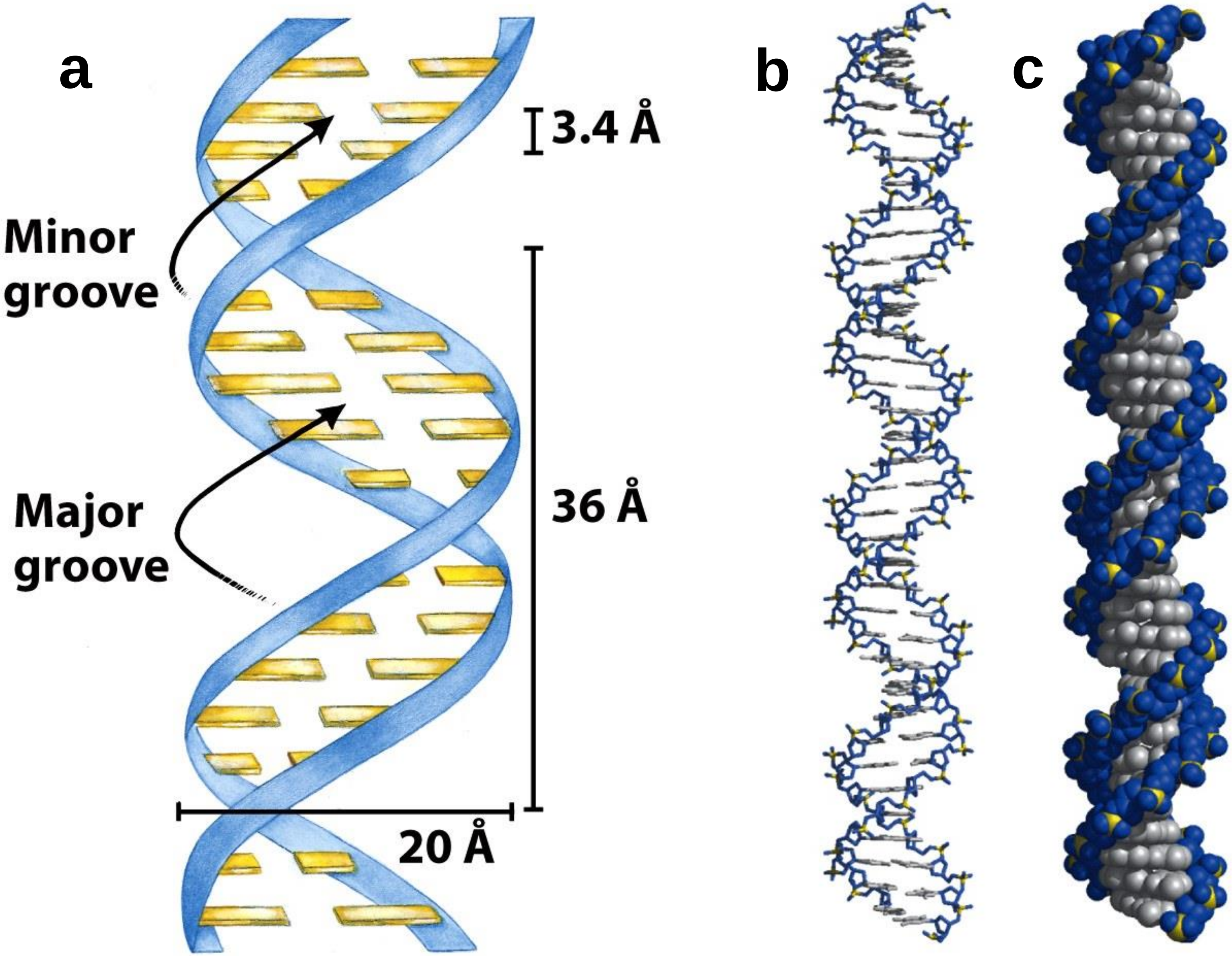


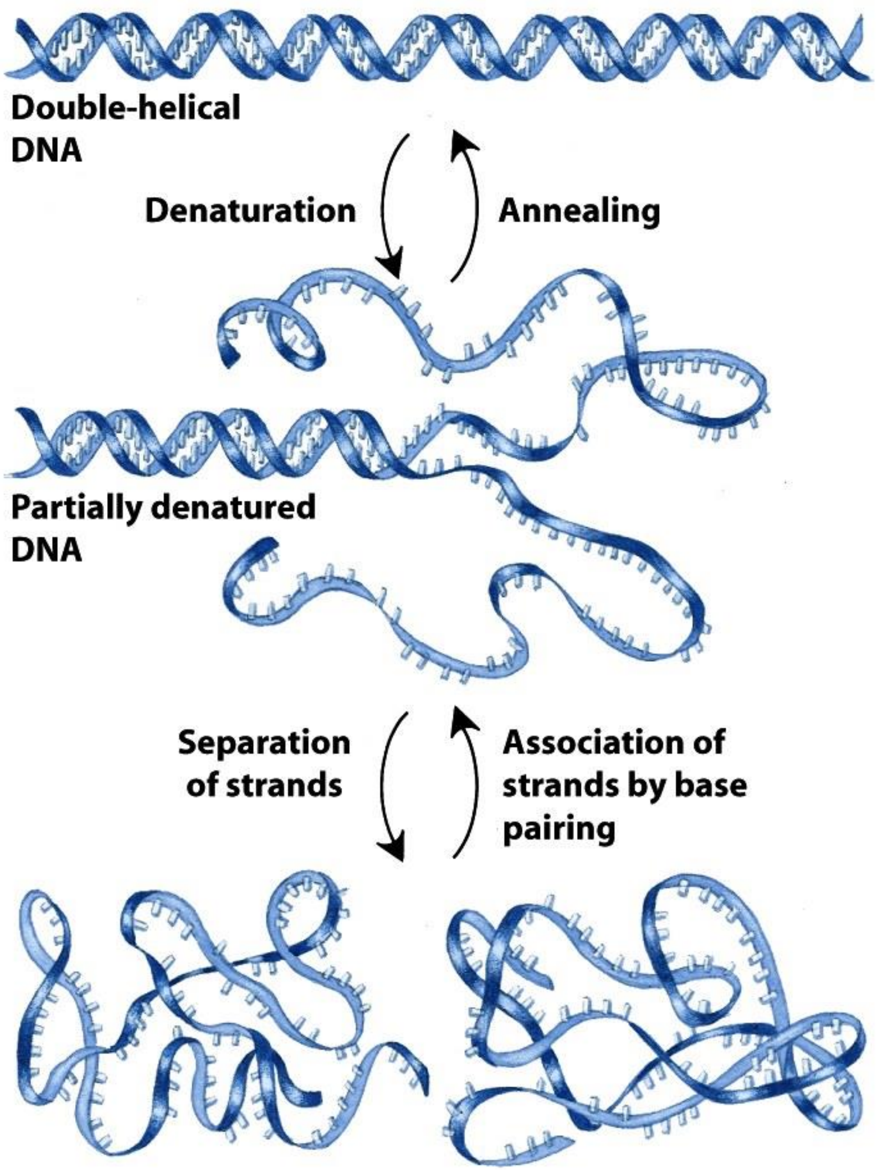
Figure 8-12
Lehninger Principles of Biochemistry, Fifth Edition

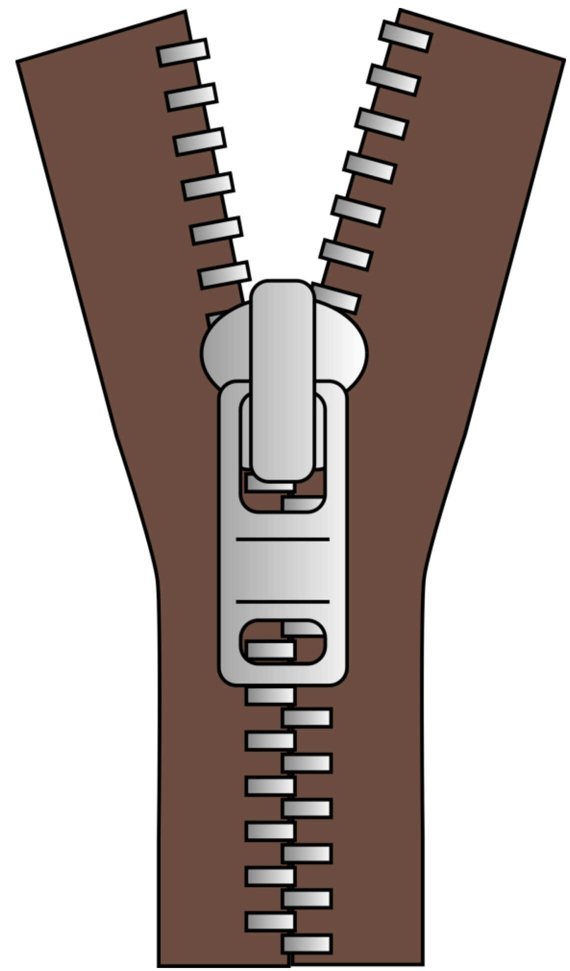
Rosalind Franklin

Watson-Crick Model for the Structure of DNA

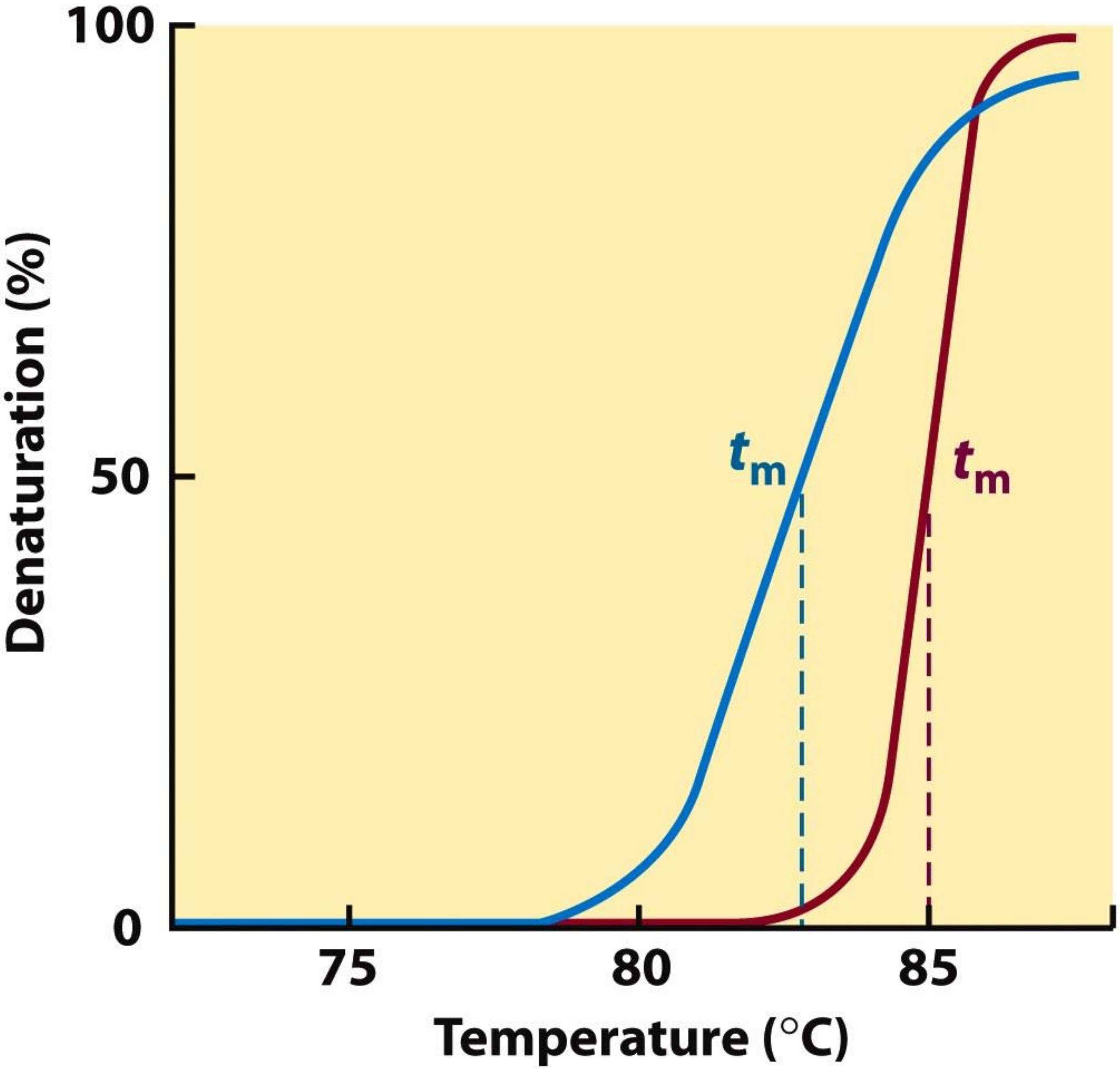


Reversible Denaturation and Annealing (Renaturation) of DNA

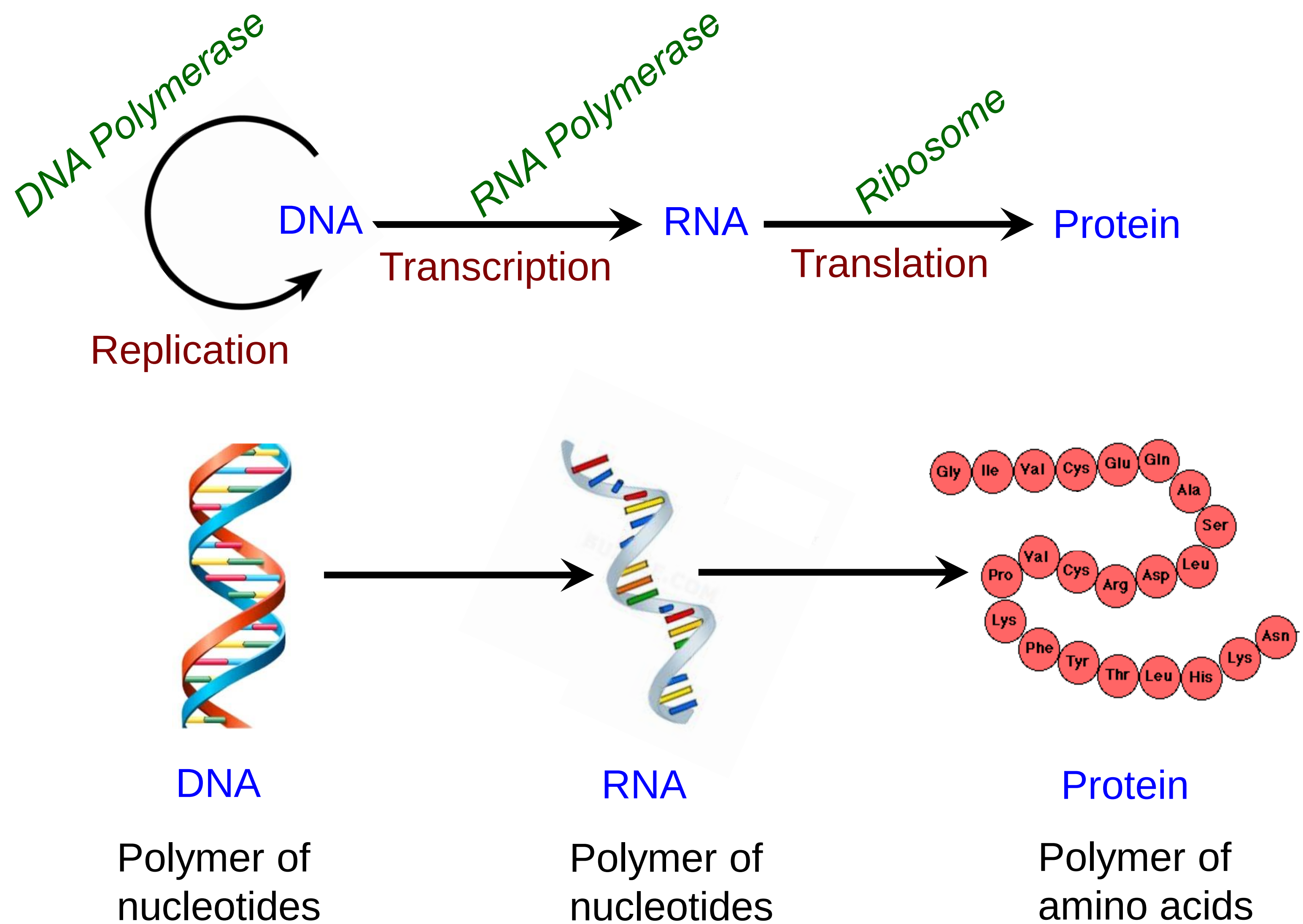




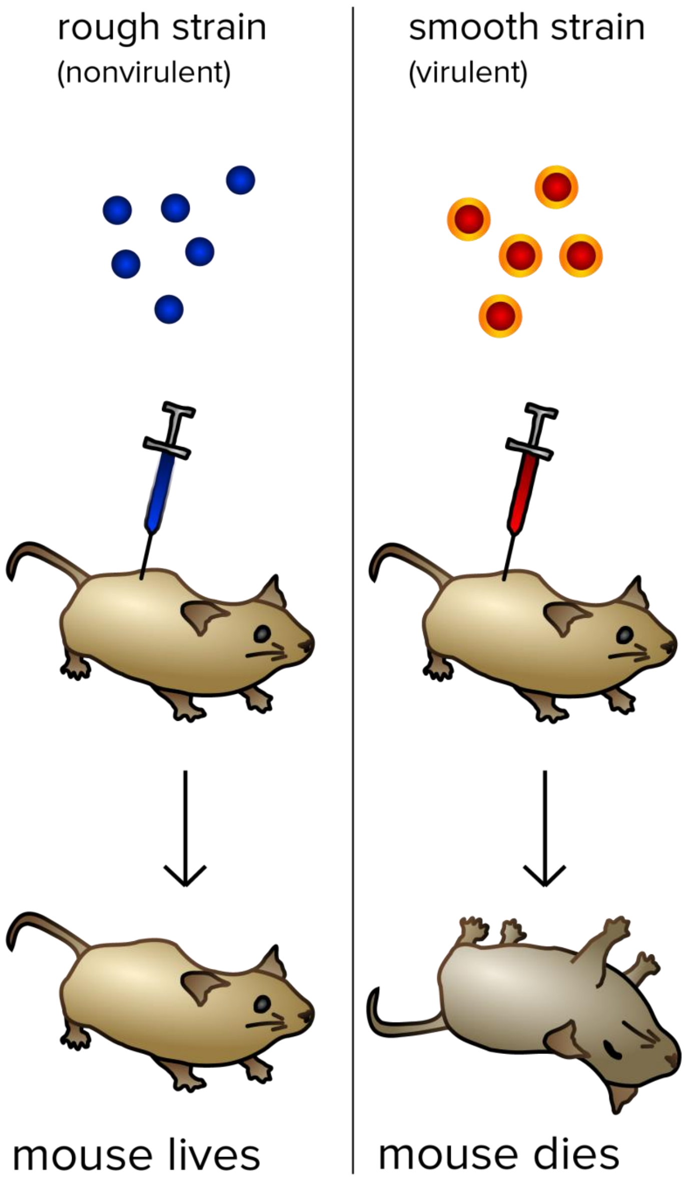
Heat Denaturation of DNA



Flow of Genetic Information: The Central Dogma of Molecular Biology

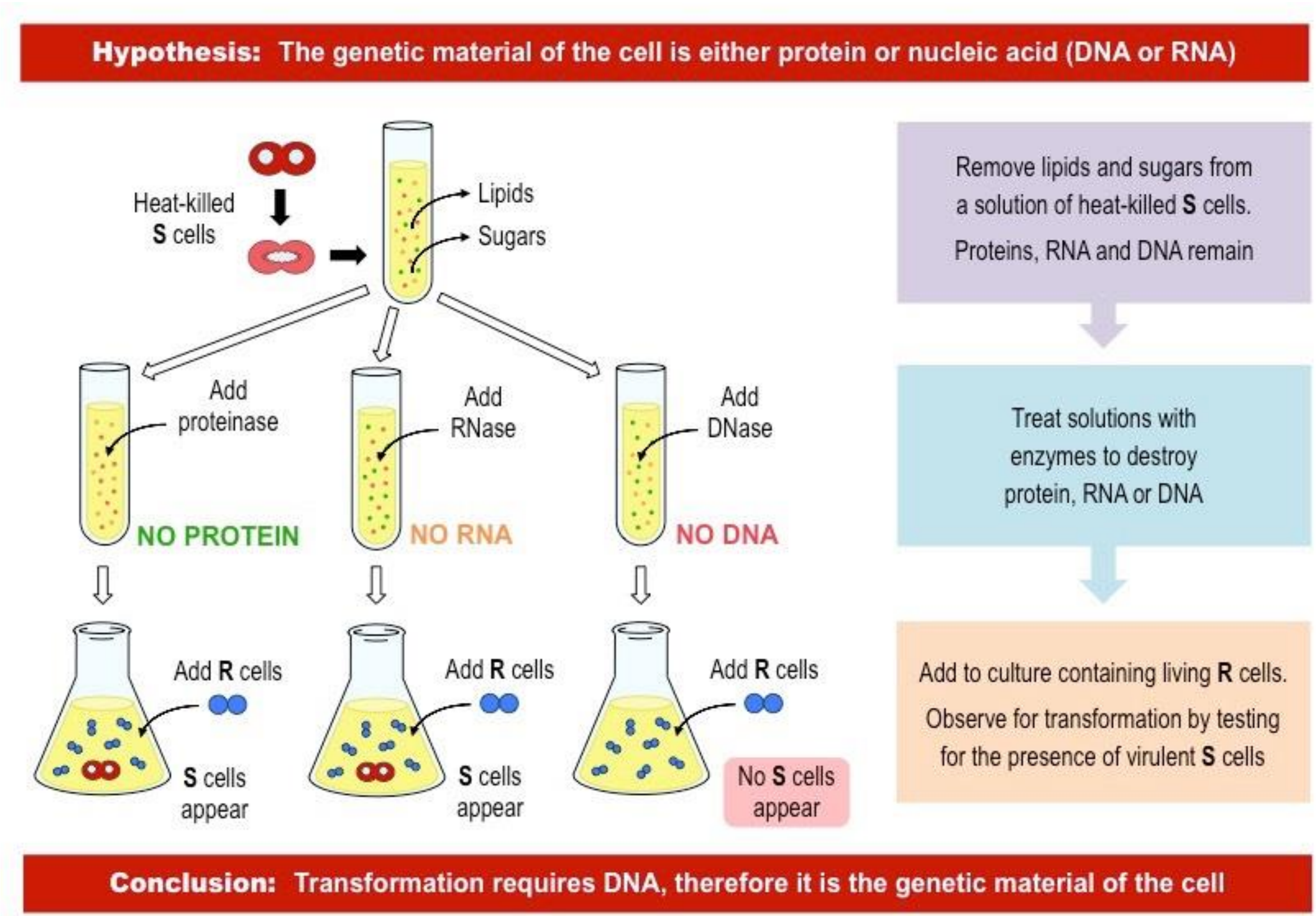


Experiment that Proves DNA is Our Genetic Material

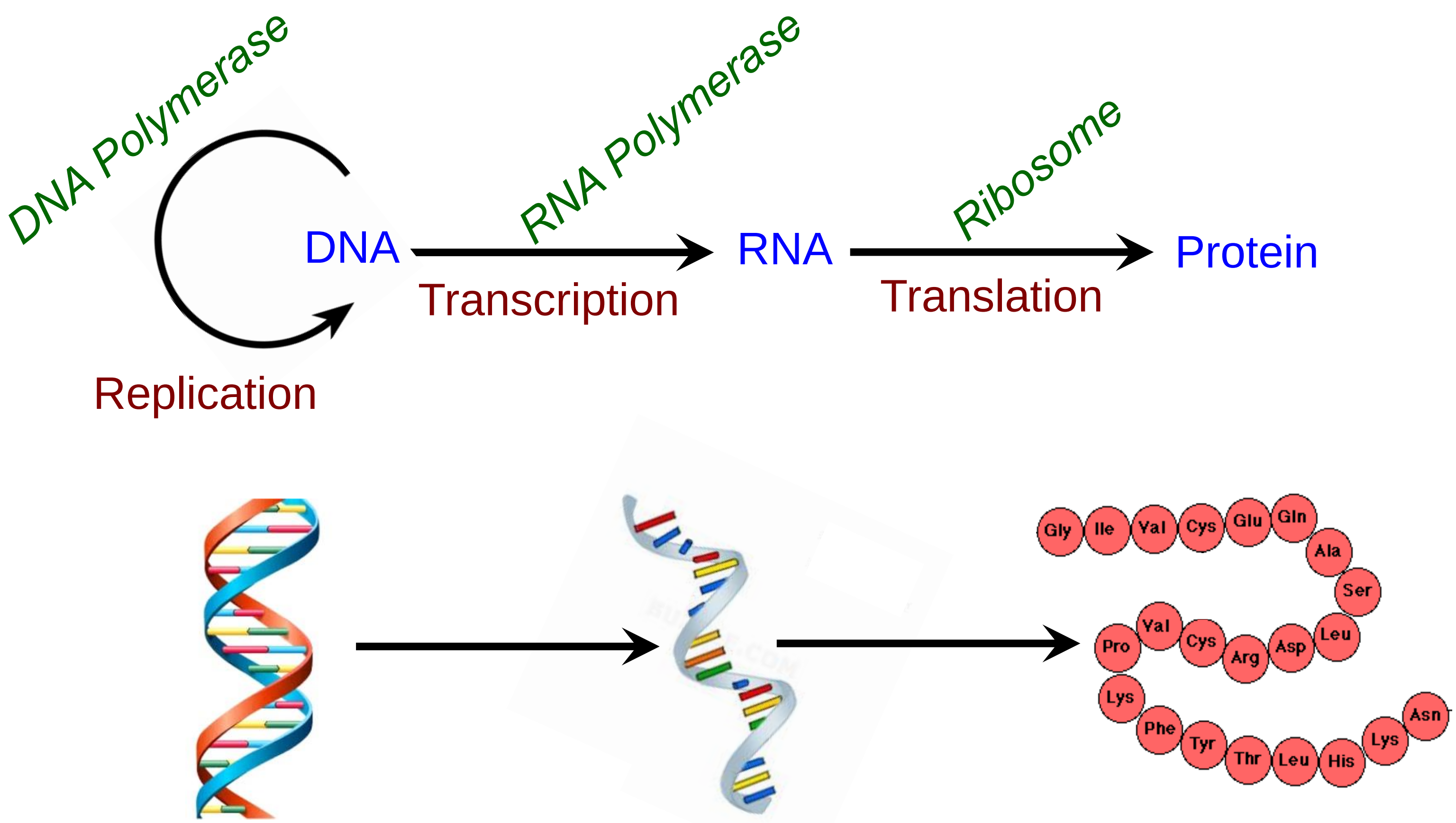


Frederick Griffith’s experiment with bacteria (*Streptococcus pneumoniae*) (1928).

Experiment that Proves DNA is Our Genetic Material



Flow of Genetic Information:
The Central Dogma of Molecular Biology



DNA

Polymer of
nucleotides

RNA

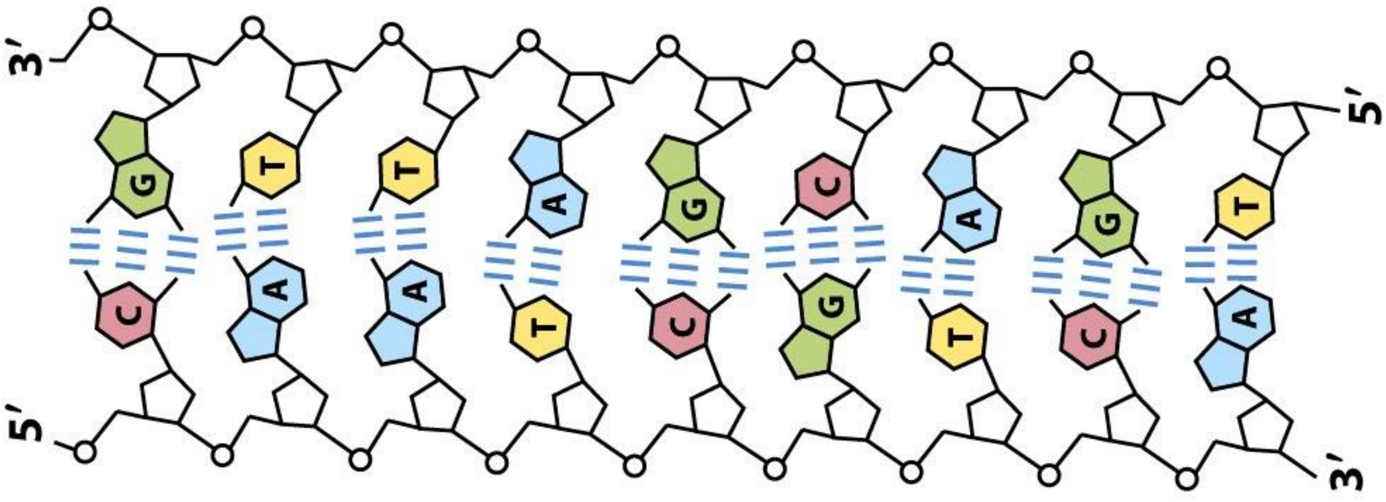
Polymer of
nucleotides

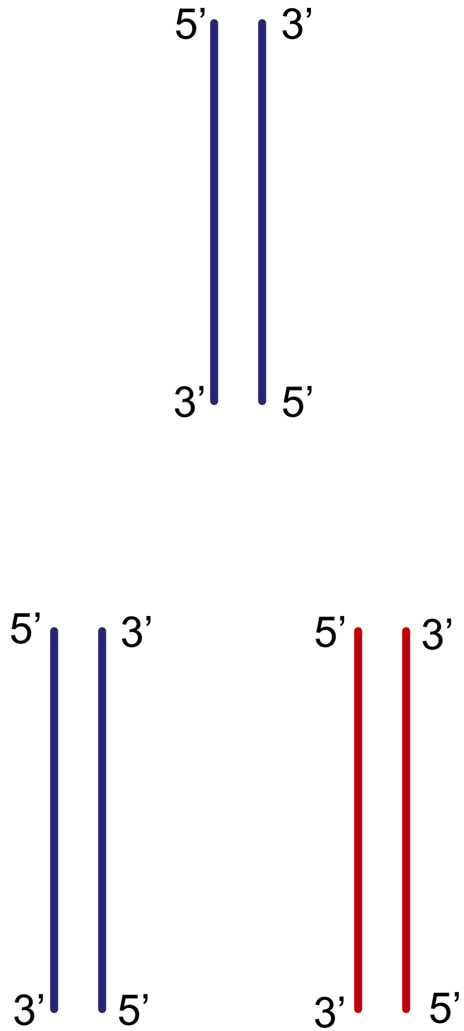
Protein

Polymer of
amino acids

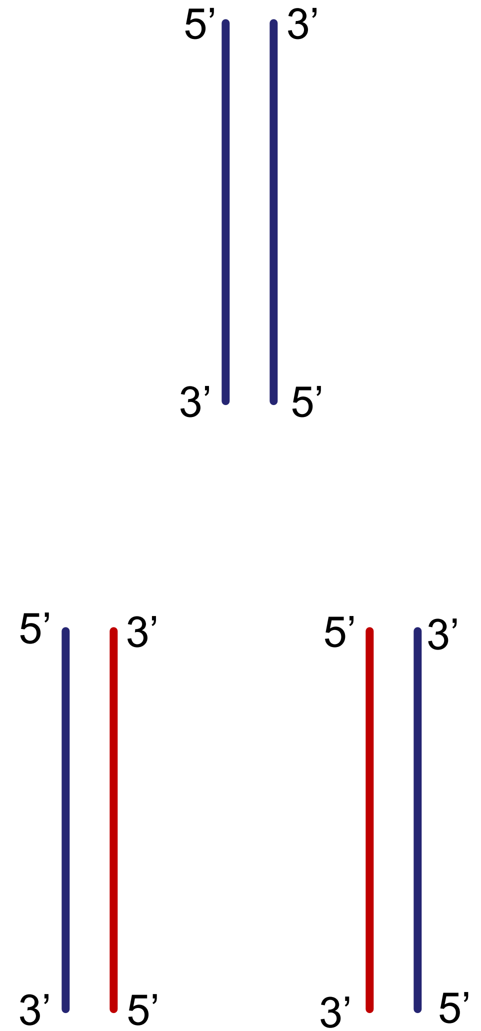
DNA Replication: An Overview

(Copying of the genetic information)



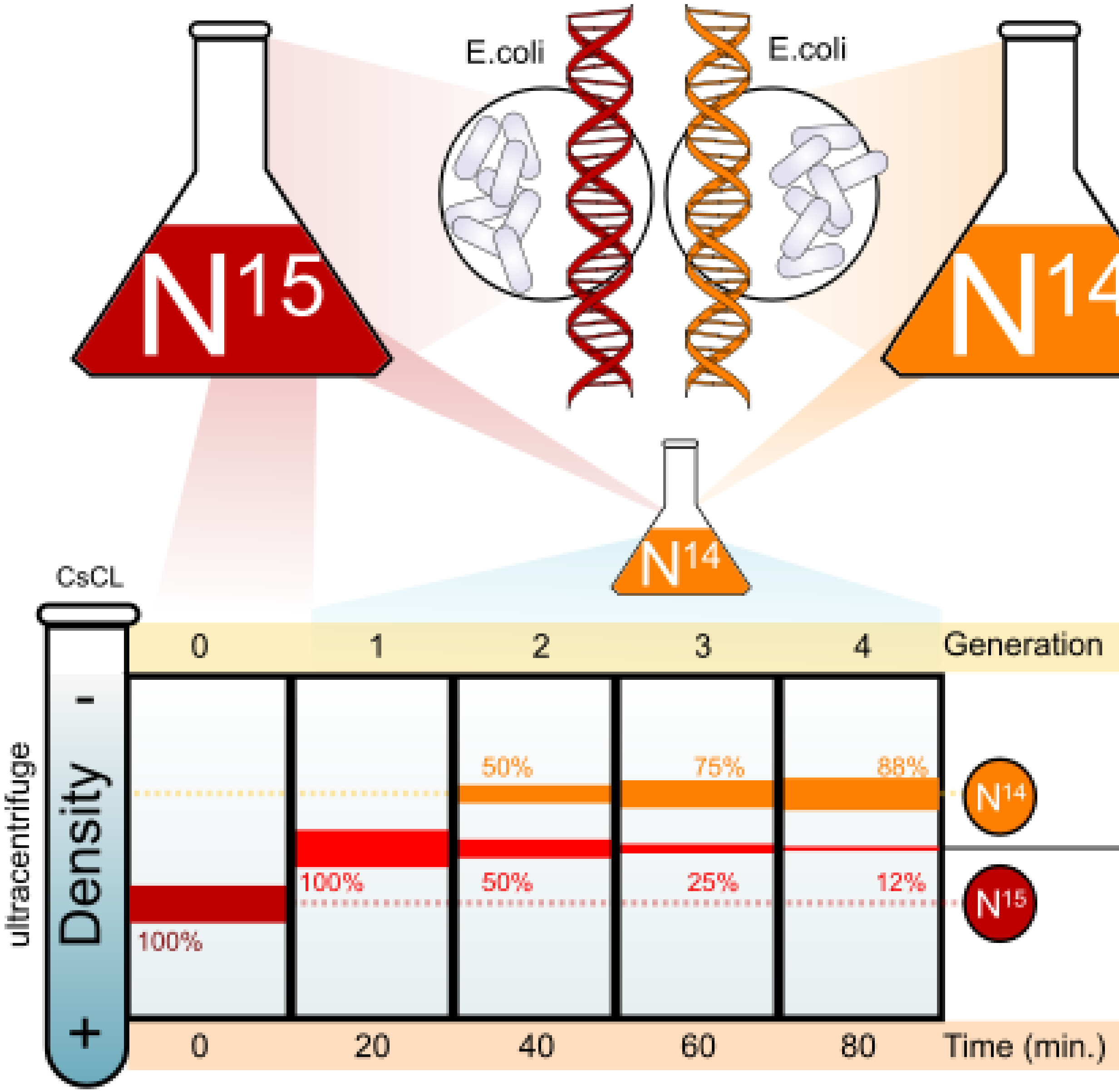


Conservative Replication

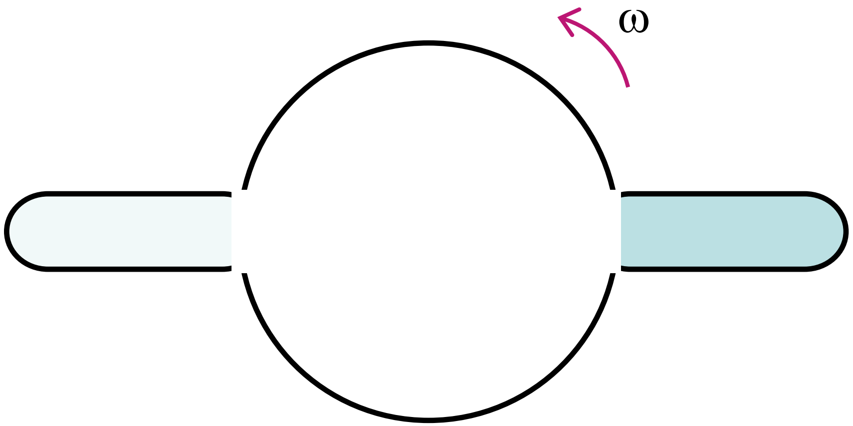


Semi-conservative Replication

The Meselson-Stahl Experiment (1958)

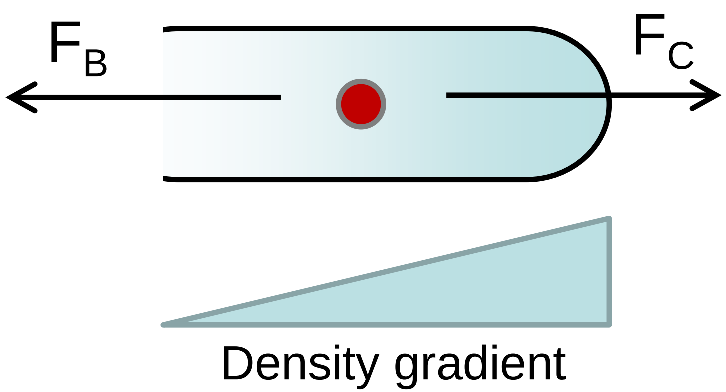


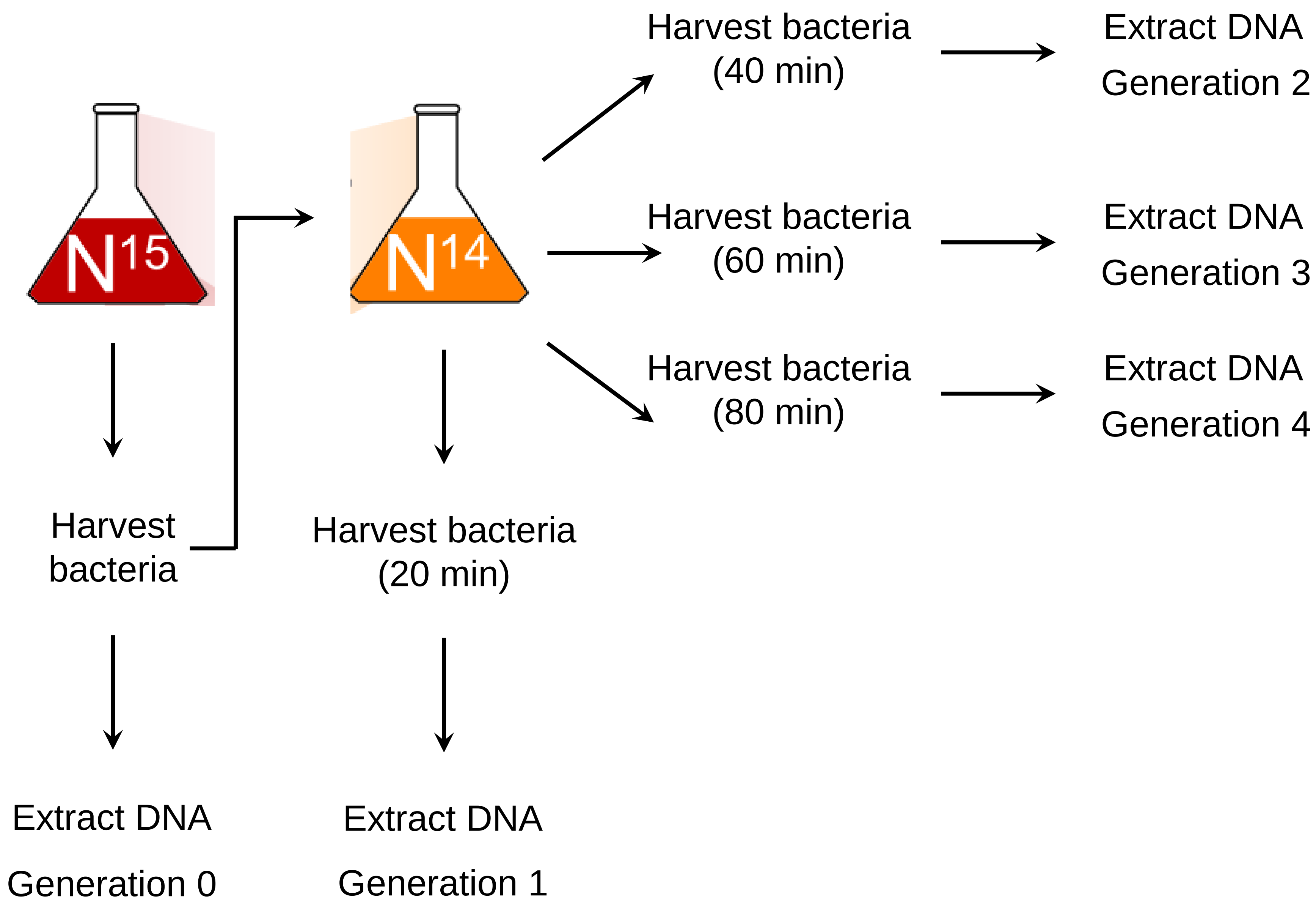
Centrifugation with density gradient



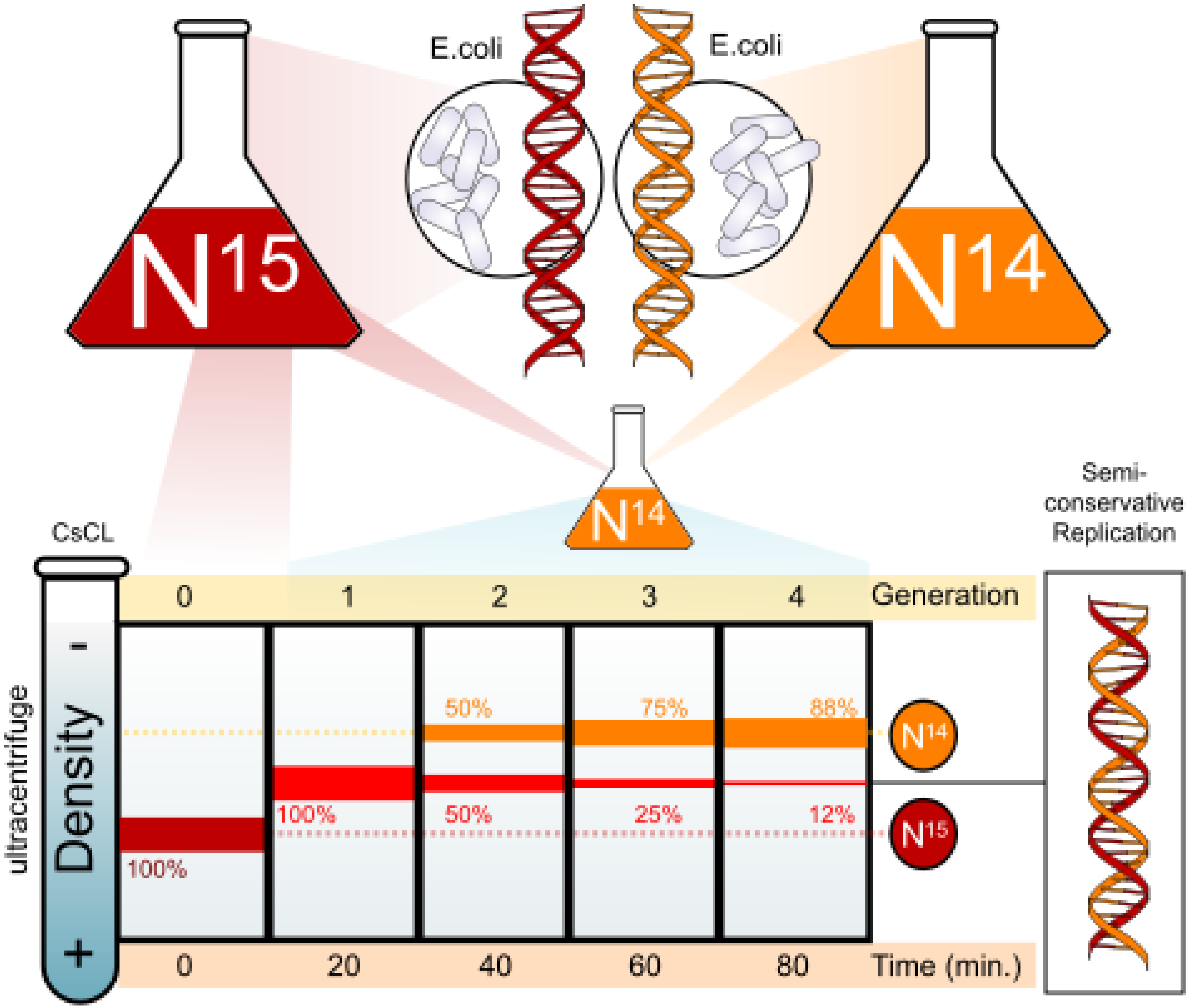
DNA with HIGHER density will move to the RIGHT i.e. BOTTOM of the tube.

DNA with LOWER density will stay at the LEFT i.e. TOP of the tube.

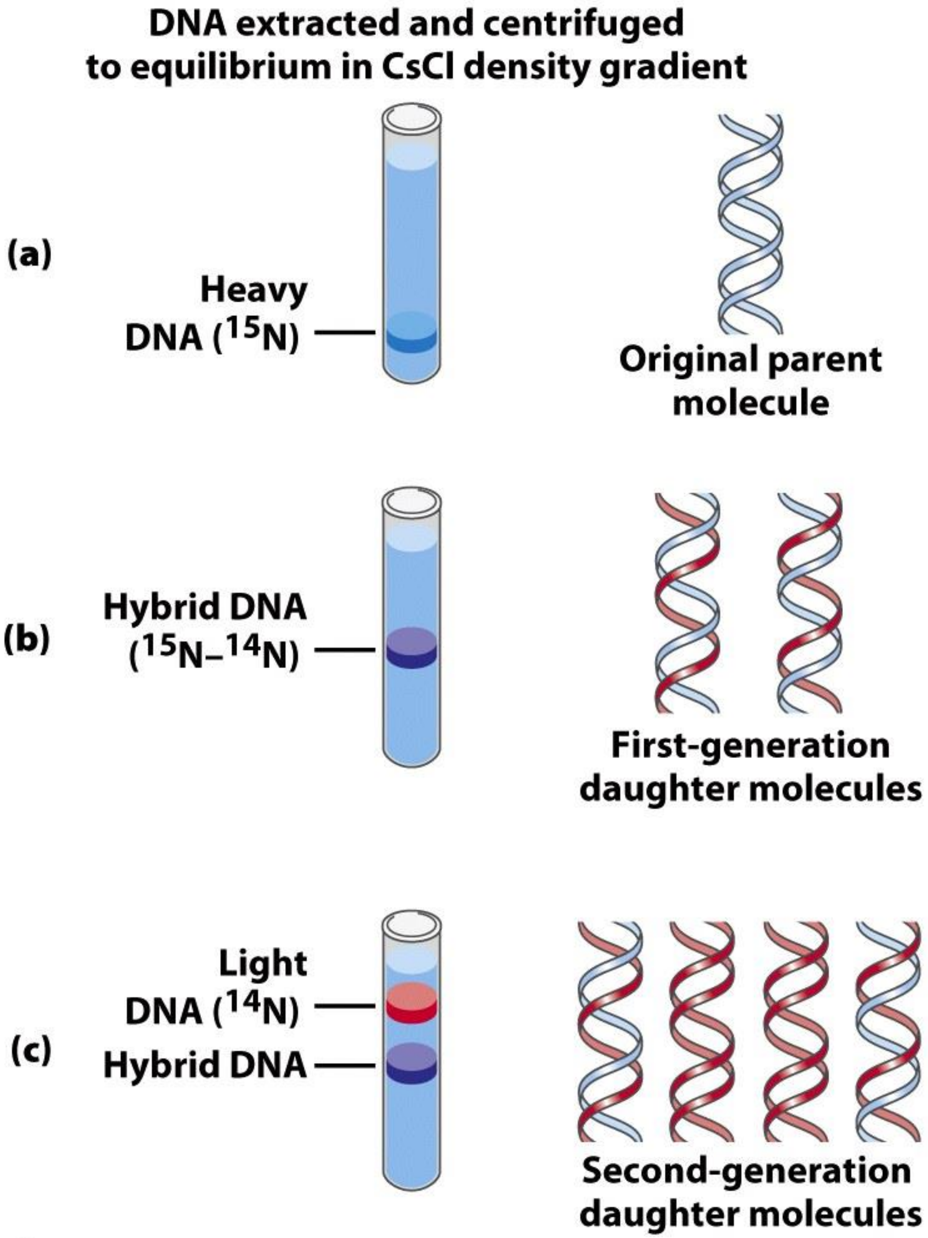



N15
N14
Harvest bacteria
(40 min)
Extract DNA
Generation 2
Harvest bacteria
(60 min)
Extract DNA
Generation 3
Harvest bacteria
(80 min)
Extract DNA
Generation 4
Harvest bacteria
Harvest bacteria
(20 min)
Extract DNA
Generation 0
Extract DNA
Generation 1

The Meselson-Stahl Experiment (1958)



The Meselson-Stahl Experiment Supports Semiconservative Replication

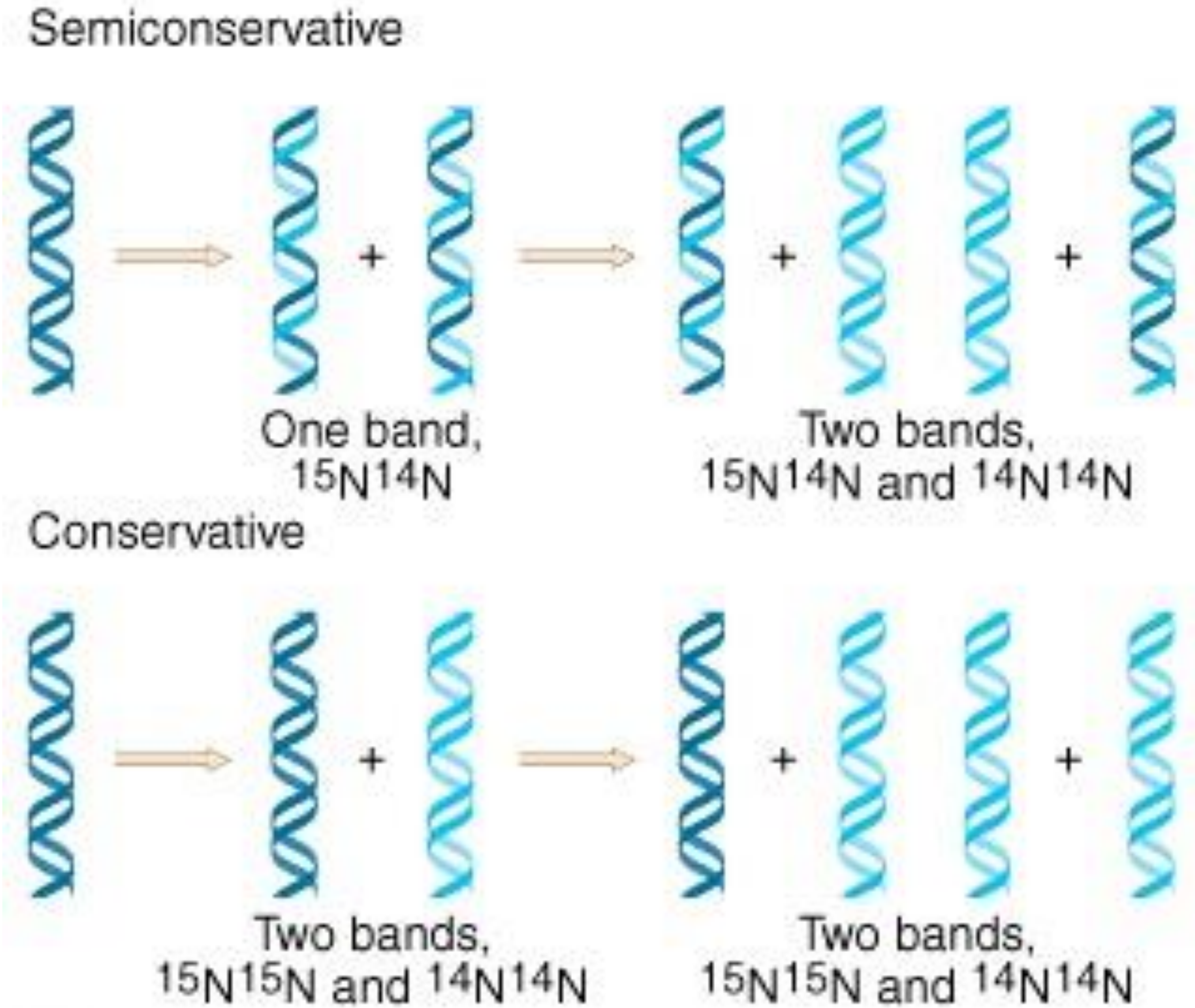


Meselson and Stahl grew a culture of *E.coli* for many generations in a medium that contained ^{15}N as the sole nitrogen source. ($^{15}NH4Cl$).
After many generations, all the *E.coli* cells had ^{15}N incorporated into the purine and pyrimidine bases of their DNA.

Meselson and Stahl took a sample of these bacteria and switched the rest of the bacteria to a medium that contained only ^{14}N (washed them before transferring to remove the medium containing ^{15}N).
They purified the DNA sample collected from the bacteria just before transfer to the ^{14}N containing medium.

Meselson and Stahl collected some of the bacteria after each division and extracted DNA from the bacterial cells (Collected samples of bacteria over the next few cellular generations).
Under the conditions they used, *E.coli* replicates its DNA every 20 minutes. They took samples at an interval of 20 minutes.

After extracting DNA from bacteria they checked for the density of DNA


Semiconservative
+
+
+
One band,
$^{15}N^{14}N$
Two bands,
$^{15}N^{14}N$ and $^{14}N^{14}N$
Conservative
+
+
+
Two bands,
$^{15}N^{15}N$ and $^{14}N^{14}N$
Two bands,
$^{15}N^{15}N$ and $^{14}N^{14}N$