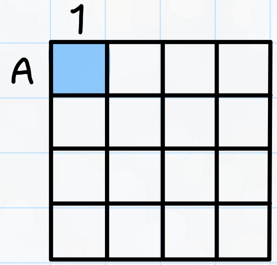
A1.2 Nucleic Acids

Guiding Questions
How does the structure of nucleic acids allow hereditary information to be stored?
How does the structure of DNA facilitate accurate replication?

Linking Questions
What makes RNA more likely to have been the first genetic material, rather than DNA?
How can polymerization result in emergent properties?



Theme: Unity and Diversity

Level of Organization: Molecules

Written and drawn by:

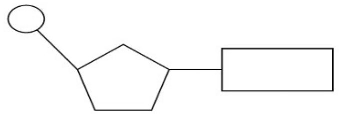
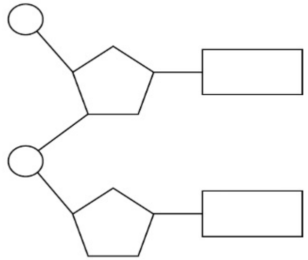
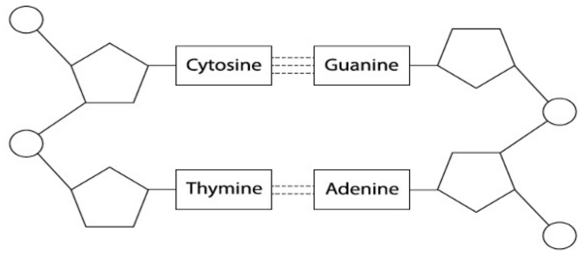
Peter Marier

NOTEWORTHY SCIENCE

MARIER

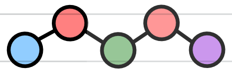
https://www.interaliamag.org/articles/david-goodsell-molecular-landscapes/

SL Learning Outcomes

A1.2.1	DNA as the genetic material of all living organisms	Some viruses use RNA as their genetic material but viruses are not considered to be living.
A1.2.2	Components of a nucleotide	In diagrams of nucleotides use circles, pentagons and rectangles to represent relative positions of phosphates, pentose sugars and bases. 
A1.2.3	Sugar–phosphate bonding and the sugar–phosphate "backbone" of DNA and RNA	Sugar–phosphate bonding makes a continuous chain of covalently bonded atoms in each strand of DNA or RNA nucleotides, which forms a strong "backbone" in the molecule. 
A1.2.4	Bases in each nucleic acid that form the basis of a code	Students should know the names of the nitrogenous bases.
A1.2.5	RNA as a polymer formed by condensation of nucleotide monomers	Students should be able to draw and recognize diagrams of the structure of single nucleotides and RNA polymers.
A1.2.6	DNA as a double helix made of two antiparallel strands of nucleotides with two strands linked by hydrogen bonding between complementary base pairs	In diagrams of DNA structure, students should draw the two strands antiparallel, but are not required to draw the helical shape. Students should show adenine (A) paired with thymine (T), and guanine (G) paired with cytosine (C). Students are not required to memorize the relative lengths of the purine and pyrimidine bases, or the numbers of hydrogen bonds. 
A1.2.7	Differences between DNA and RNA	Include the number of strands present, the types of nitrogenous bases and the type of pentose sugar. Students should be able to sketch the difference between ribose and deoxyribose. Students should be familiar with examples of nucleic acids.
A1.2.8	Role of complementary base pairing in allowing genetic information to be replicated and expressed	Students should understand that complementarity is based on hydrogen bonding.
A1.2.9	Diversity of possible DNA base sequences and the limitless capacity of DNA for storing information	Explain that diversity by any length of DNA molecule and any base sequence is possible. Emphasize the enormous capacity of DNA for storing data with great economy.
A1.2.10	Conservation of the genetic code across all life forms as evidence of universal common ancestry	Students are not required to memorize any specific examples.

HL Learning Outcomes

A1.2.11	Directionality of RNA and DNA	Include 5' to 3' linkages in the sugar–phosphate backbone and their significance for replication, transcription and translation.
A1.2.12	Purine-to-pyrimidine bonding as a component of DNA helix stability	Adenine–thymine (A–T) and cytosine–guanine (C–G) pairs have equal length, so the DNA helix has the same three-dimensional structure, regardless of the base sequence.
A1.2.13	Structure of a nucleosome	Limit to a DNA molecule wrapped around a core of eight histone proteins held together by an additional histone protein attached to linker DNA. **Application of skills:** Students are required to use molecular visualization software to study the association between the proteins and DNA within a nucleosome.
A1.2.14	Evidence from the Hershey–Chase experiment for DNA as the genetic material	Students should understand how the results of the experiment support the conclusion that DNA is the genetic material. **NOS:** Students should appreciate that technological developments can open up new possibilities for experiments. When radioisotopes were made available to scientists as research tools, the Hershey–Chase experiment became possible.
A1.2.15	Chargaff's data on the relative amounts of pyrimidine and purine bases across diverse life forms	**NOS:** Students should understand how the "problem of induction" is addressed by the "certainty of falsification". In this case, Chargaff's data falsified the tetranucleotide hypothesis that there was a repeating sequence of the four bases in DNA.

DNA is a macromolecule, which is a polymer , made from many repeating monomers

↳ Specifically, DNA (Deoxyribonucleic acid) is a polynucleic acid made from many nucleotides

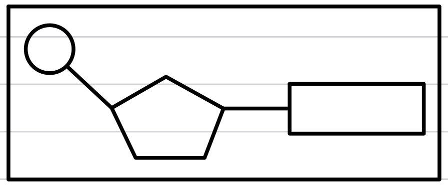
Nucleotide

↳ the building blocks of nucleic acids

↳ composed of Carbon, Oxygen, Hydrogen, Nitrogen, Phosphorus

↳ made up of 3 parts:

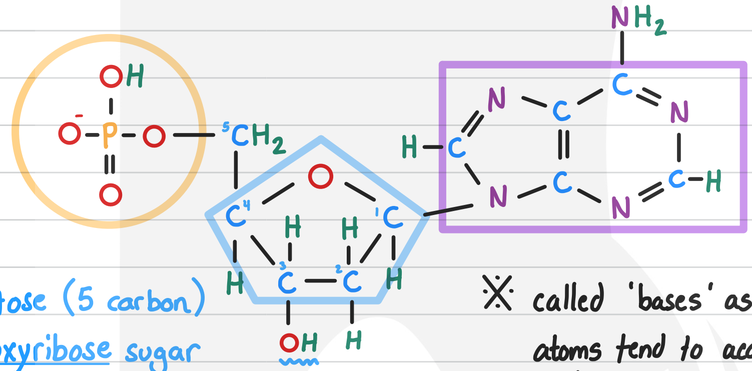
How to draw:



1 phosphate group

2 pentose (5 carbon) deoxyribose sugar

3 nitrogenous base → 4 different types

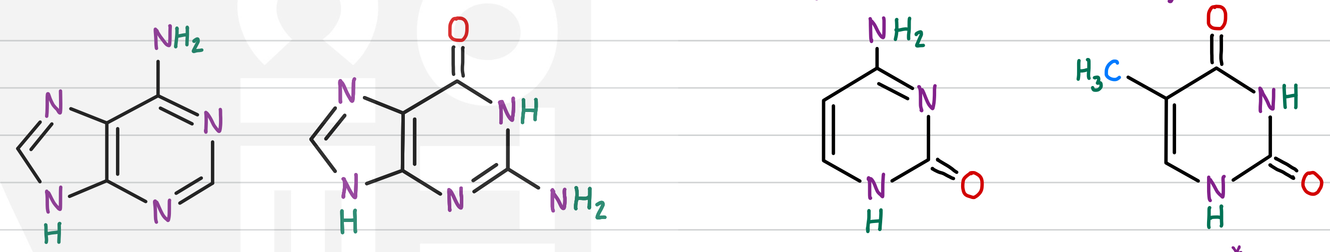


※ called 'bases' as nitrogen atoms tend to accept protons (H^+) in solutions

Purines: 2-ringed structure nitrogenous base

Pyrimidines: 1-ringed structure nitrogenous base

Adenine (A) Guanine (G) Cytosine (C) Thymine (T)*

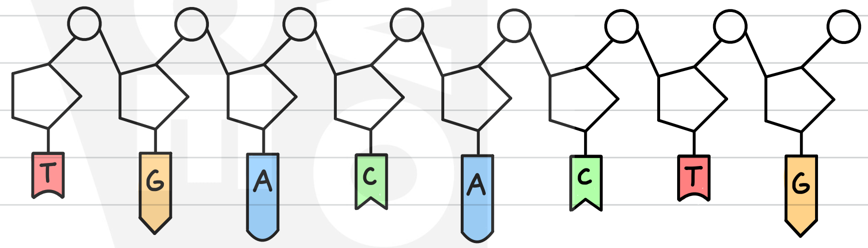


* only DNA not RNA

↳ Every DNA molecule will be composed of nucleotides containing phosphate and deoxyribose but the nitrogenous base attached can differ

↳ the sequence of the nitrogenous bases makes up the genetic code and is how genetic information is stored (instructions for proteins)

protein synthesis D1.2

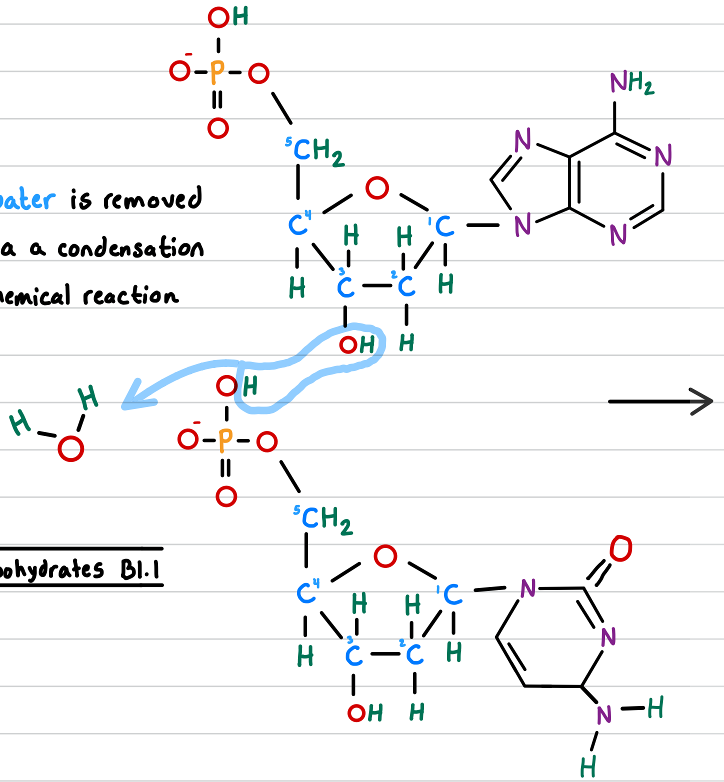


i.e. TGACACTG

Sugar-Phosphate 'backbone'

↳ the phosphate group of one nucleotide bonds covalently to the deoxyribose of the other, forming a phosphodiester bond and a strong backbone to the DNA molecule

↳ water is removed via a condensation chemical reaction

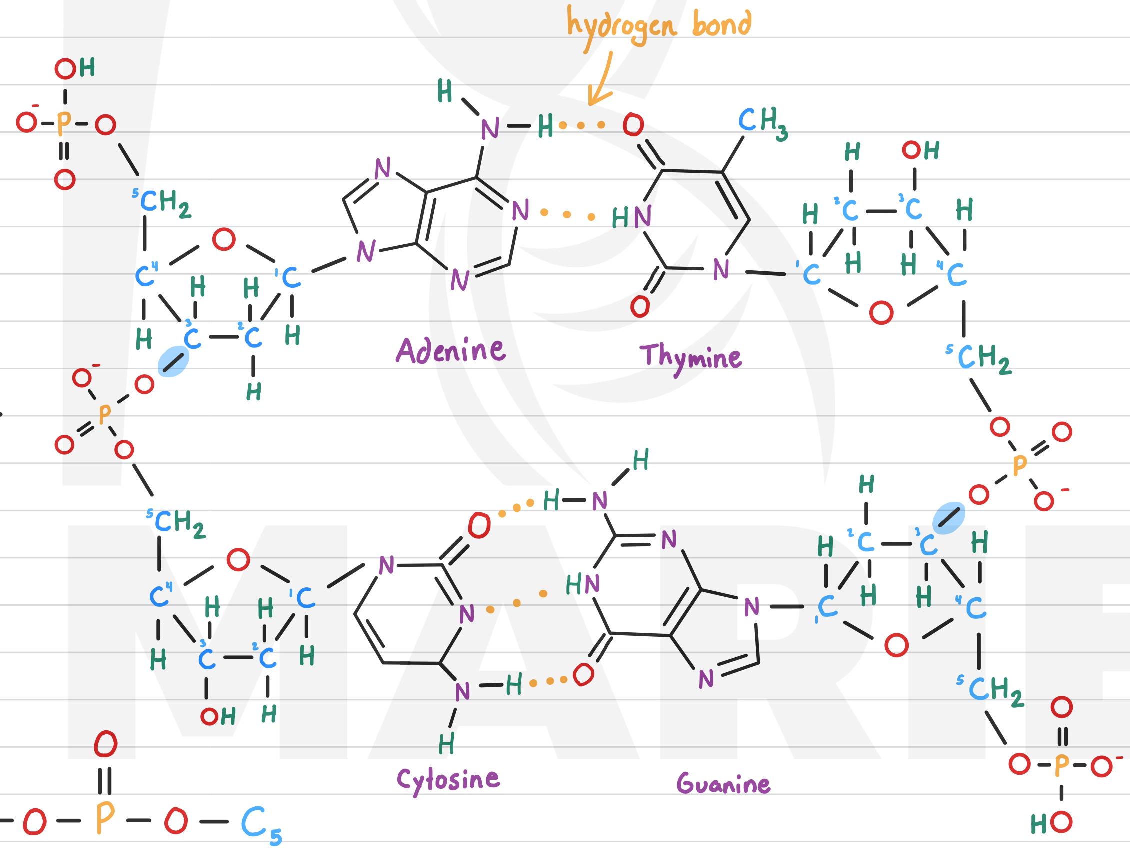


carbohydrates B1.1

※ phosphodiester: $C_3 - O - \overset{O}{\overset{\|}{P}} - O - C_5$

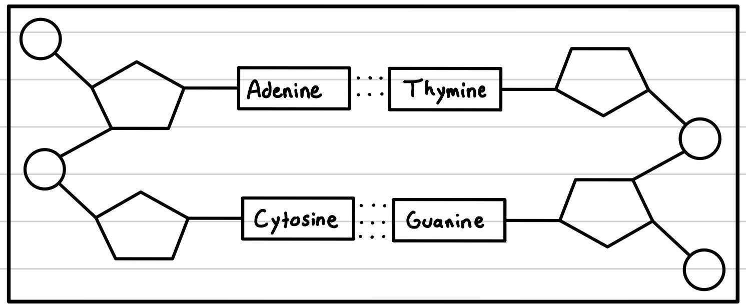
DNA antiparallel double helix

hydrogen bond



How to draw:

↳ DNA is a double-standed polymer, linked together by hydrogen bonds

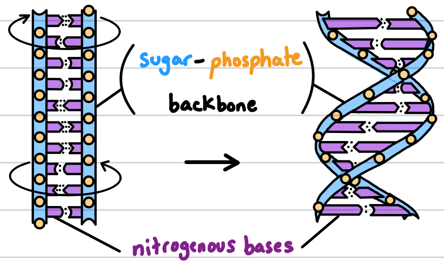


↳ Nitrogenous bases pair in a very specific fashion - Complementary base pairing:

- Adenine only forms hydrogen bonds with Thymine (A:::T)
- Cytosine only forms hydrogen bonds with Guanine (C:::G)

↳ The two strands of DNA are parallel to each other but they run in opposite directions thus they are antiparallel

↳ DNA's structure is like a twisted ladder where each side twists into a helix around the other



※ if not antiparallel, H-bonds won't form

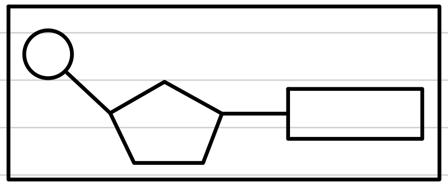
Like DNA, RNA is a polymer (polynucleotide) made of nucleotides

↳ However, as its name Ribonucleic acid suggests, its composition is slightly different

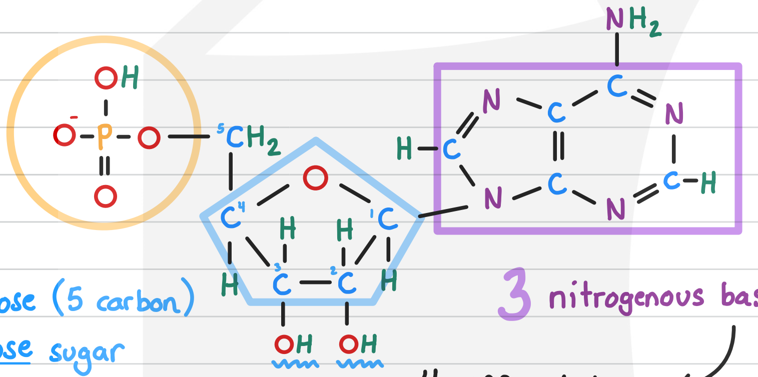
Nucleotide

↳ composed of Carbon, Oxygen, Hydrogen, Nitrogen, Phosphorus
↳ made up of 3 parts:

How to draw:



1 phosphate group

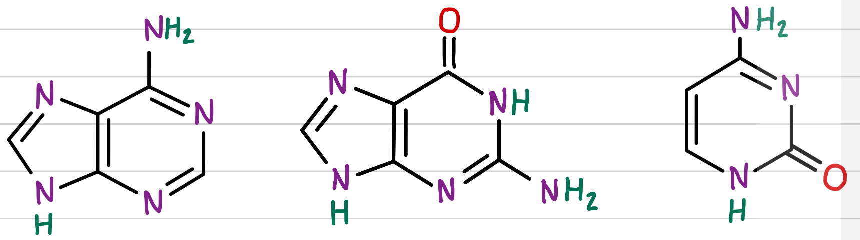


2 pentose (5 carbon) ribose sugar

3 nitrogenous base

4 different types

Adenine (A) Guanine (G) Cytosine (C) Uracil (U)*

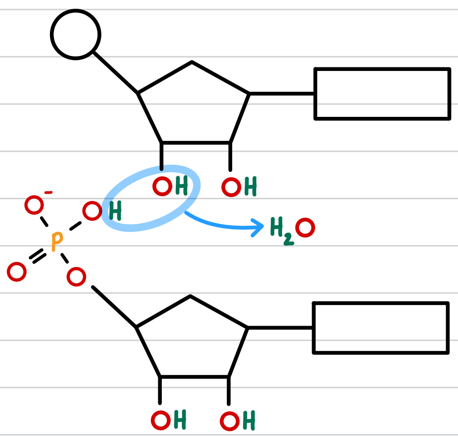


*only found in RNA
complementary to Adenine

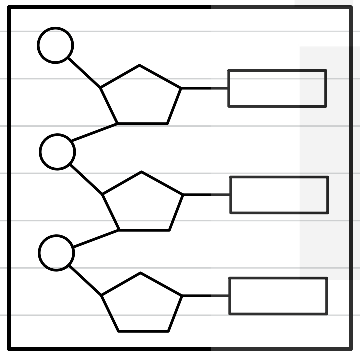
↳ Like DNA, the sequence of RNA nitrogenous bases code for information, although typically temporarily

Sugar-Phosphate 'backbone'

↳ RNA forms a 'backbone' made by phosphodiester covalent bonds between the phosphate and ribose sugar formed via condensation reactions, which release water



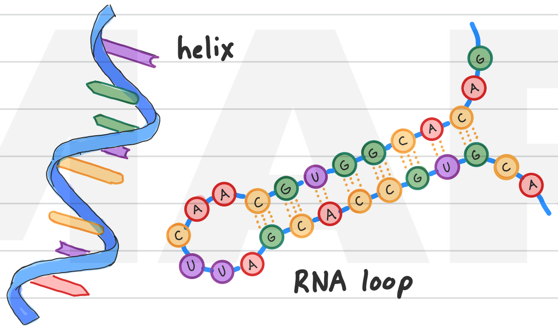
How to draw:



RNA structure

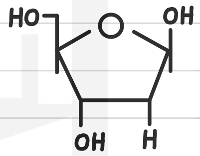
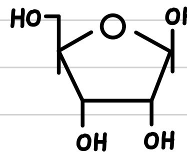
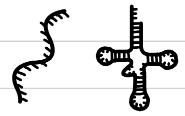
↳ RNA is a single-stranded polymer

↳ while typically exists as a helix, it can also form loops and bond complementarily via Hydrogen bonds



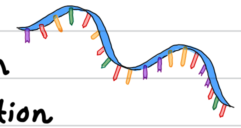
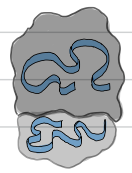
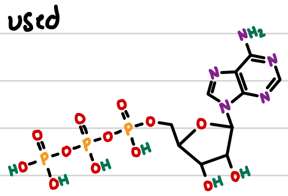
helix

RNA loop

	DNA	RNA
Similarities	nucleic acids composed of nucleotides nucleotides comprise of a phosphate group nucleotides comprise of the nitrogenous bases Adenine, Cytosine and Guanine backbones are joined with phosphodiester bonds nitrogenous bases form hydrogen bonds via complementary base pairing	
differences	typically composed of two strands (double-stranded)	typically composed of one strand (single-stranded)
	nucleotide composed of deoxyribose sugar 	nucleotide composed of ribose sugar 
	nucleotide composed of nitrogenous base thymine T	nucleotide composed of nitrogenous base uracil U
	Shaped into a double helix 	variety of shapes 
	longer polymer (millions of nucleotides)	shorter polymer (hundreds to thousands of nucleotides)

Examples of nucleic acids

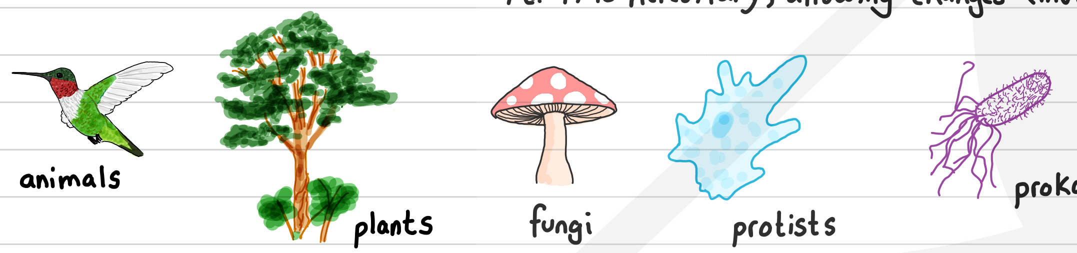
protein synthesis D1.2

- **DNA** used as long-term hereditary storage for all living organisms
genetic information is stored as genes where it can be transcribed and translated into proteins 
- **Messenger RNA (mRNA)** synthesized complementarily from a DNA gene during transcription
carries information necessary to make a protein during translation 
- **Transfer RNA (tRNA)** special DNA codes for tRNA. tRNA binds to specific amino acids and carries them to the ribosome and mRNA for translation 
- **Ribosomal RNA (rRNA)** special DNA codes for tRNA. rRNA is a main component of ribosomes. Helps bind mRNA, tRNA and catalyses bonds in translation 
- **Adenosine triphosphate (ATP)** Single nucleotide nucleic acid. The primary molecule used by systems to store, transfer and use chemical energy
The purpose of cellular respiration is to convert chemical energy within food into ATP 

cell respiration C1.2

A1.2.1—DNA as the genetic material of all living organisms. A1.2.8—Role of complementary base pairing in allowing genetic information to be replicated and expressed. A1.2.9—Diversity of possible DNA base sequences and the limitless capacity of DNA for storing information. A1.2.10—Conservation of the genetic code across all life forms as evidence of universal common ancestry.

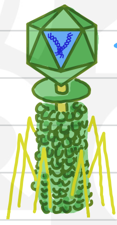
All living organisms use DNA as genetic material: information in the form of genes that can be passed from parent to offspring i.e. it is hereditary, allowing changes (mutations) to be transmitted



↳ In eukaryotes, DNA is found within the nucleus of cells, whereas in prokaryotes within cytoplasm

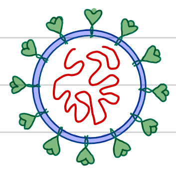
cell structure A2.2

↳ Some viruses use DNA and others use RNA as genetic material



ex: bacteriophage

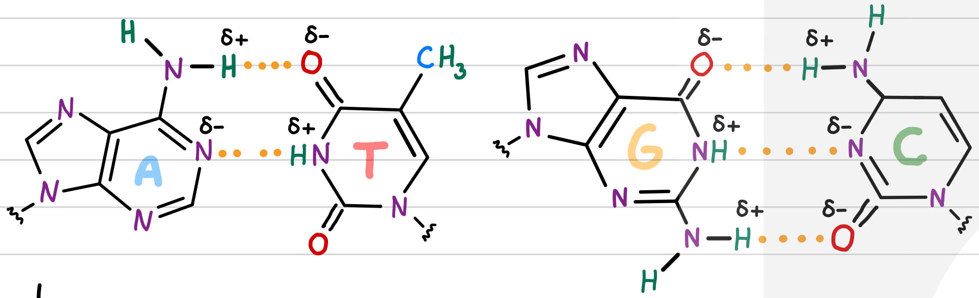
viruses A2.3



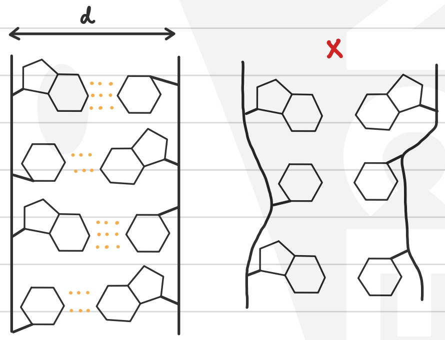
ex: SARS-CoV-2
ex: HIV

※ Viruses are not considered 'alive' and 'living organisms' as they require a host for most processes of life such as reproduction and metabolism

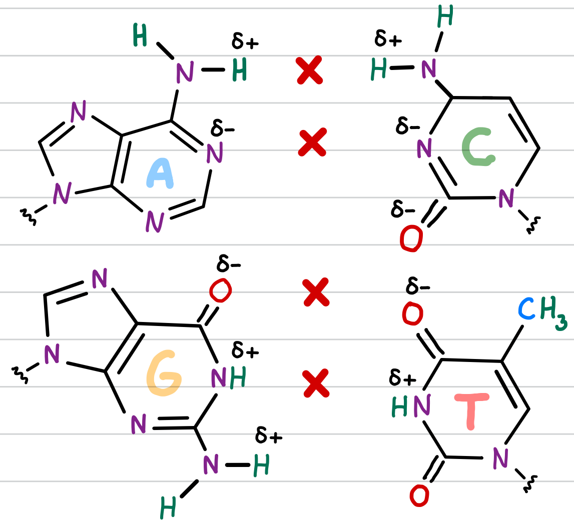
As mentioned previously, nitrogenous bases form very specific pairings – complementary base pairing where hydrogen bonds form between them



• Purines (double rings) always bind with pyrimidines (single rings) as it maintains a stable, constant diameter for a DNA double helix



• If nitrogenous bases had any other pairing (ex: A and C or G and T) hydrogen bonds wouldn't form as partial charges would repel and not attract



↳ Due to the orientation of the partial charges, A:::T and G:::C

↳ Due to complementary base pairing, the sequence of DNA on one strand determines the other. ex:

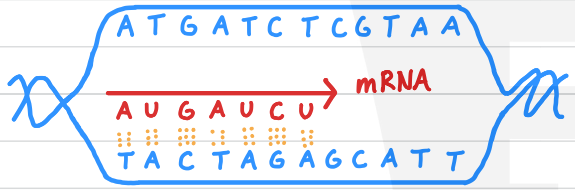
?
ATTCCGCAT → TAAGGCGTA
ATTCCGCAT

↳ This property is used in many crucial biological processes.

1 DNA replication – each strand acts as a template to build a new copy

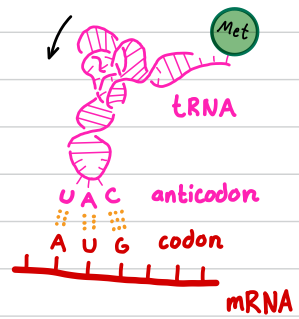
DNA replication D1.1

2 Transcription – one DNA strand acts as a template to make a complementary mRNA strand



3 Translation – mRNA codons match up with tRNA anticodons complementarily to ensure the correct amino acid is brought and correct protein synthesized

protein synthesis D1.2



※ gene expression = protein synthesis, i.e. transcription and translation

Although DNA has only 4 bases the order in which they combine is limitless

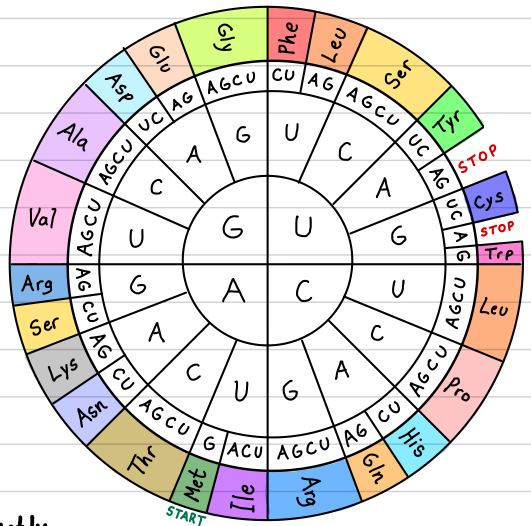
↳ with 'n' bases, there is 4^n possible sequences ex: just 10 bases $4^{10} = 1{,}048{,}576$ possibilities!

↳ DNA can be any length (that can fit into a cell), adding to its potential diversity
ex. in humans the longest DNA molecule is ~260 million base pairs!

↳ DNA has a diameter of just 2 nm, thus huge amounts can be stored in small volumes
ex: human DNA unwound is 2m long (3.2 gigabases) which fits in a nucleus ~10 μm in diameter!

※ compared with modern information storage DNA is economical both in terms space and material used

DNA's information is stored as genes in triplet codes called codons which code for amino acids in protein synthesis
↳ as there are 4 bases, there is 4^3 or 64 different codons →

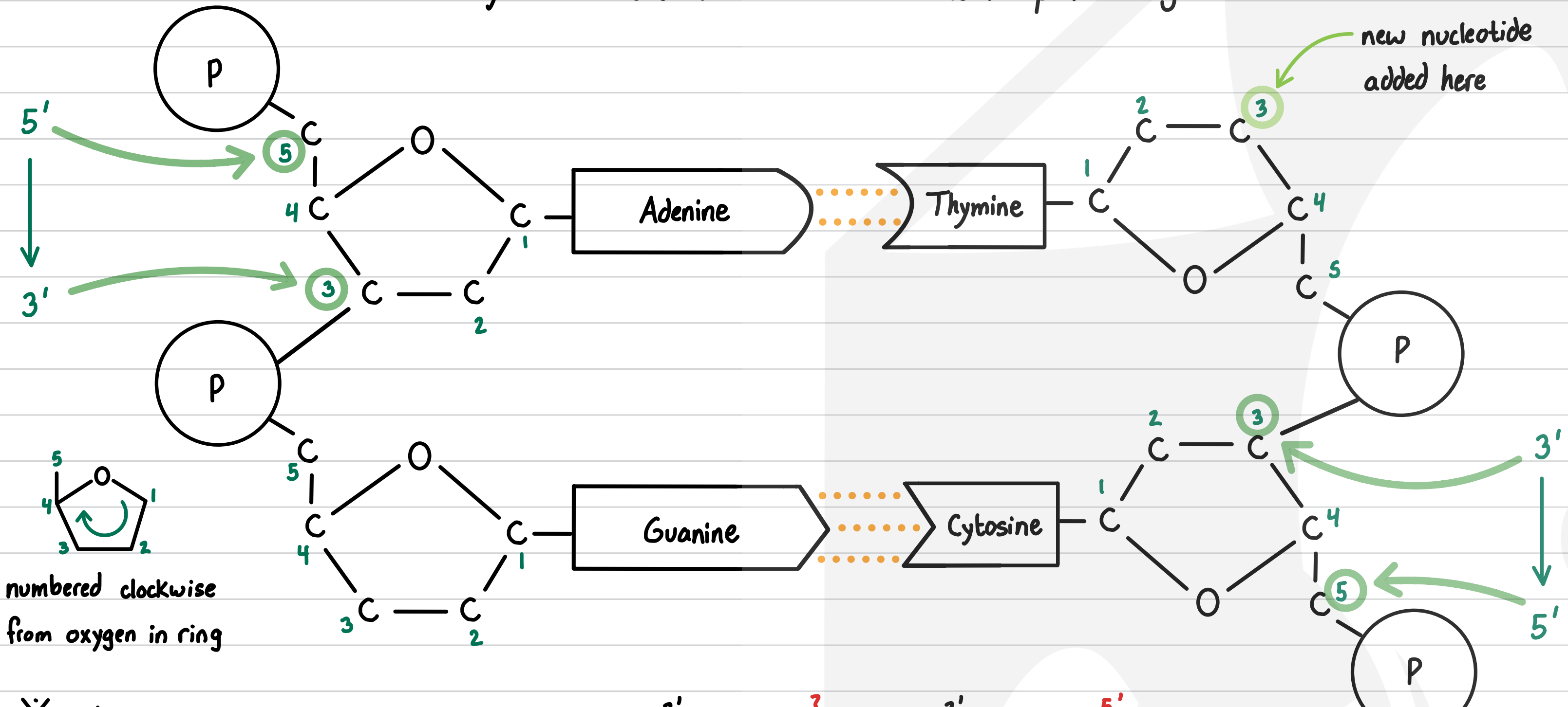


↳ same code is used by all living organisms, from bacteria to whales ∴ it is universal
ex: AGC codes for Ser in all organisms, thus the code is conserved

↳ this supports the idea that all life arose from a common ancestor where this code originally started and has largely remained unchanged throughout evolution

※ this is far more probable than the same exact code evolving separately many times independently

A more specific manner to describe the 'direction' of DNA and RNA strands are by the orientation of the carbons in the pentose sugar



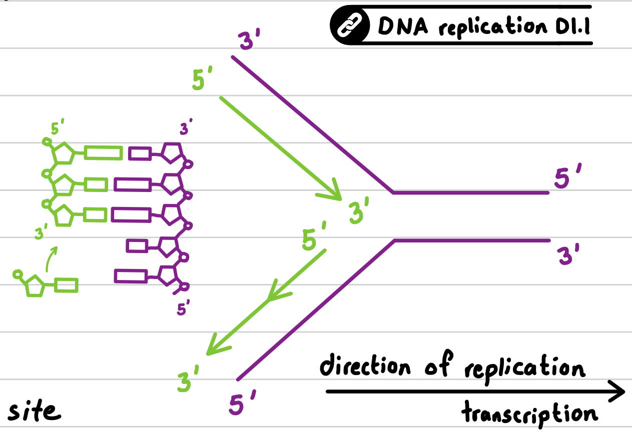
※ You can extrapolate the ends in DNA only given one

ex: 3'______? → 3'______5'
?______? 5'______3'

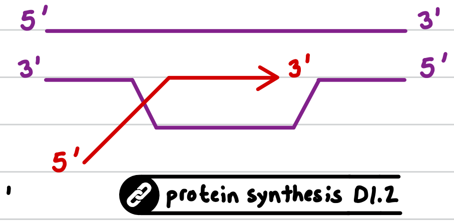
The directionality of DNA and RNA impacts biological processes:

1 DNA replication - DNA nucleotides are always added to the 3' end of the growing polynucleotide. The 5' phosphate of the free nucleotide forms a phosphodiester bond with the deoxyribose at the 3' carbon ∴ replication occurs 5' to 3'

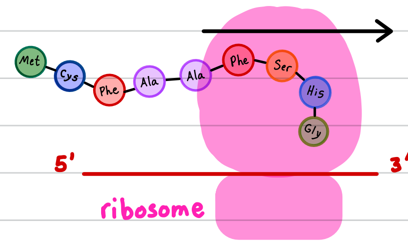
↳ This is because the nucleotides must face the correct direction to fit into the enzyme's active site



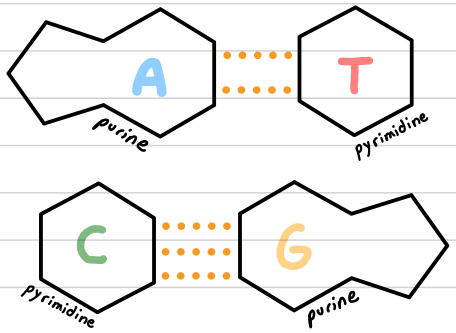
2 Transcription - RNA nucleotides are added to the 3' end of the growing mRNA polynucleotide. 5' phosphate of the free nucleotide forms a phosphodiester bond with the ribose at the 3' carbon ∴ transcription occurs 5' to 3'



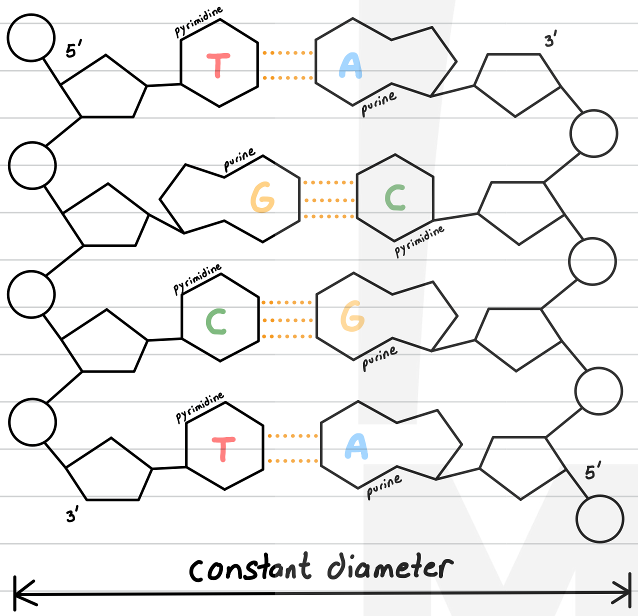
3 Translation - mRNA carries sequence information for synthesizing a polypeptide (protein) as codons which determine the order amino acids are joined by ribozymes. The ribosome moves along mRNA towards the 3' end. ∴ translation occurs 5' to 3'

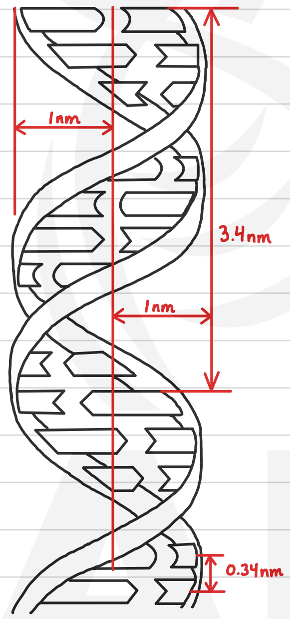


As mentioned previously, each nitrogenous base pair is composed of 1 purine (2 rings) and 1 pyrimidine (1 ring)



Due to complementary base pairing, no matter what the nitrogenous base sequence, the DNA molecule will have 3 rings across - 1 purine and 1 pyrimidine, maintaining a stable, regular double helix shape

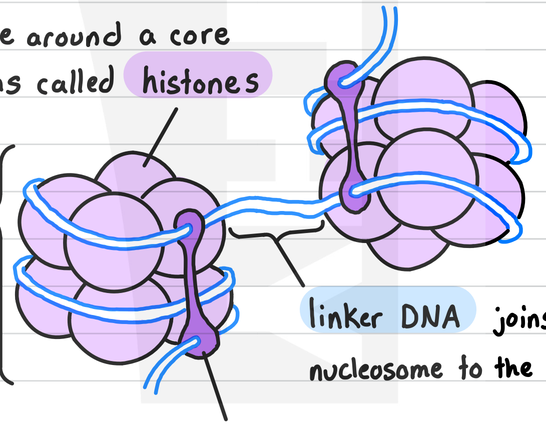




The total length of DNA in a single human cell is ~2m which is contained in a ~10μm nucleus - how?

↳ DNA is wrapped twice around a core composed of 8 proteins called histones

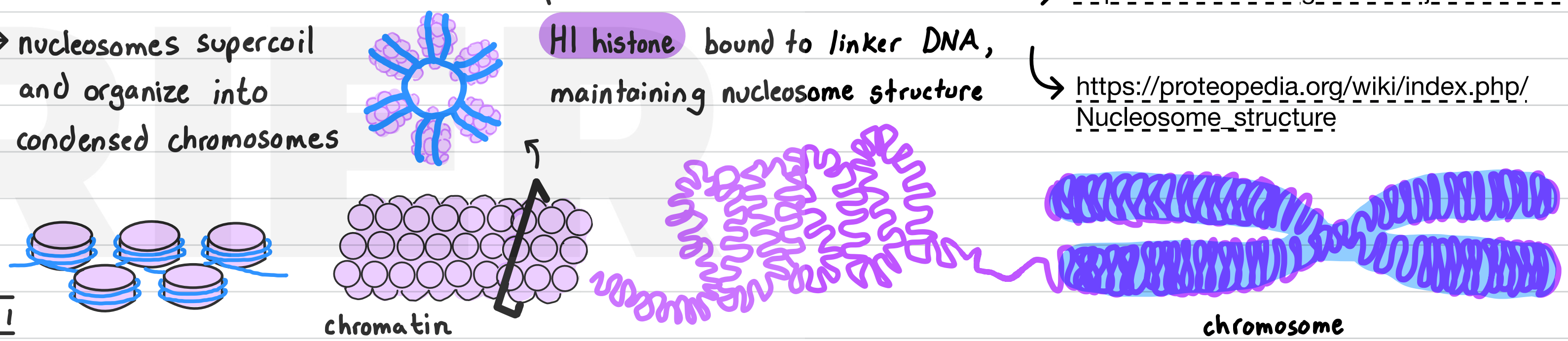
nucleosome is a structural unit comprising DNA wrapped around an octamer of histones



linker DNA joins one nucleosome to the other

↳ nucleosomes supercoil and organize into condensed chromosomes

H1 histone bound to linker DNA, maintaining nucleosome structure



cell + nuclear division D2.1

Application of Skills

Explore nucleosome structure using molecular visualization software at the following websites:

↳ http://earth.callutheran.edu/Academic_Programs/Departments/BioDev/omm/jsmol/nucleosome/nucleosome.html

↳ https://www.rcsb.org/structure/2CV5

↳ https://www.rcsb.org/3d-view/jsmol/1aoi/1

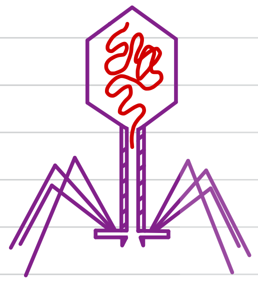
↳ https://proteopedia.org/wiki/index.php/Nucleosome_structure

- Since the late 1800s, it was known that chromosomes played a role in heredity but as they are roughly 50% proteins and 50% nucleic acids, it was unclear which chemical was responsible
- Proteins were a strong contender to be the hereditary genetic material of living organisms due to their increased capacity for variety and complexity: DNA composed of only 4 types of nitrogenous bases whereas proteins are comprised of 20 types of amino acids thus it would allow more complexity

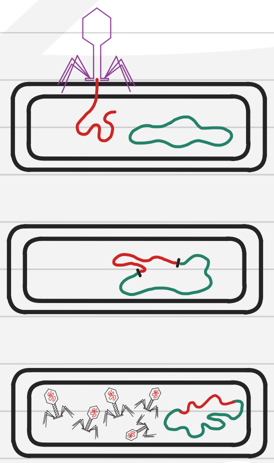
How did we determine DNA and not protein is the genetic material? $\boxed{\text{Hershey-Chase experiment}}$

Background information

- The experiment uses the bacteriophage T2 virus which infect E. coli bacteria
- Bacteriophage is composed of a protein coat (capsid) which holds DNA
- It was unclear whether the virus parasitizes host using DNA or protein



viruses A2.3



① Bacteriophage injects genetic material into bacterium

② Viral genetic material incorporated into that of the host - hijacking it

③ Hijacked bacterium creates new viruses which burst out and spread

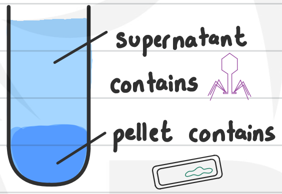
- Radioisotopes are unstable isotopes of elements which release energy in order to become more stable in the form of radiation or particles (radioactive decay), which can be detected by apparatus such as a Geiger counter
  ↳ NOS: radioactive labelling as a technique became available post WW II and this technique now allowed scientists to trace chemicals in biological systems, allowing the following experiment to occur

Methodology

① Two different bacteriophages were produced:
↳ one with radioactive phosphorus (^{32}P) which was incorporated into the DNA (and not protein as P is found in nucleic acids but not amino acids) ∴ labelling DNA
↳ one with radioactive sulfur (^{35}S) which was incorporated into the protein coat (and not DNA as S is found in some amino acids but not nucleic acids) ∴ labelling protein

② Each set of labelled viruses were cultured with E. coli bacteria and allowed to infect the cells

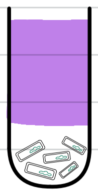
③ Culture was put in blender to dislodge viruses and centrifuged to separate components by density



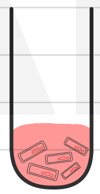
④ Supernatant and pellet analyzed for radioactivity: radioisotope found in pellet suggests genetic material as this is what was injected into bacteria by virus

Results

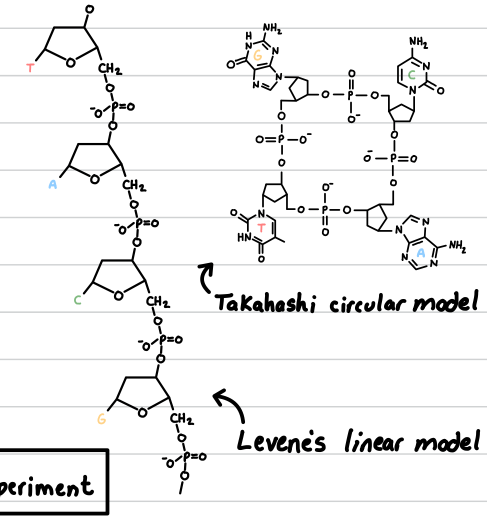
↳ ^{35}S largely present in supernatant not in pellet
∴ viral protein did not enter bacterial cells
∴ protein is not genetic material



↳ ^{32}P largely present in pellet
∴ viral DNA entered bacterial cells
∴ DNA is likely genetic material



- Levene was a major contributor to our understanding of DNA: he established the prescence of the phosphate-sugar backbone, deoxyribose as the sugar and coined the term 'nucleotide'
- However, he incorrectly hypothesized that DNA was composed of 4 repeating nucleotides (tetranucleotide) in equal base proportions
  ↳ As a tetranucleotide is not adequately variable, Levene hypothesized DNA could not be the genetic material but rather proteins

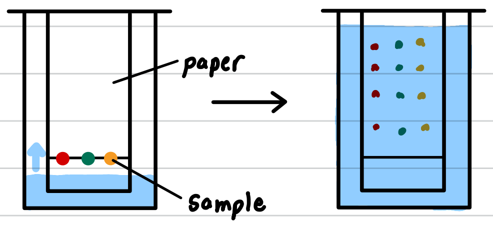


How did we determine complementary base pairing in DNA? $\boxed{\text{Chargaff's experiment}}$

Methodology

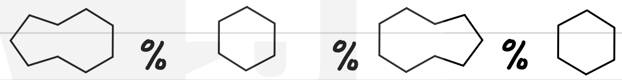
photosynthesis C1.3

- In order to test if DNA was a tetranucleotide, samples of DNA from a range of species were analyzed to determine their nucleotide composition
  ↳ Paper chromatography was used to separate different DNA samples into their respective nitrogenous bases
  ↳ UV spectrophotometry was then used to quantify the relative amounts of each base present



solvent travels up via capillary action, separating molecules based on chemical properties

Results



DNA source	Adenine %	Thymine %	Guanine %	Cytosine %
human	29.3	30.0	20.7	20.0
octopus	33.2	31.6	17.6	17.6
yeast	31.3	32.9	18.7	17.1
maize	26.8	27.2	22.8	23.2
wheat	27.3	27.1	22.7	22.8
E. coli	24.7	23.6	26.0	25.7

Adenine : Thymine ~1:1; Guanine : Cytosine ~1:1

↳ across all DNA sources, the proportion of A and T were ~ equal, as were G and C
↳ proportion of purines (A, G) were ~equal to pyrimidines (T, C)

※ relative quantities varied across species

↳ if tetranucleotides were the structure, proportion of all bases would be equal, i.e. 1:1:1:1 ∴ hypothesis falsified

NOS: in science, knowledge claims are built using inductive reasoning, i.e.
observations ⟶ detect patterns ⟶ form generalizations ⟶ make conclusions about unobserved

↳ Problem: inductive reasoning cannot give certainty as there is no way to be sure generalization is always true
∴ inductive generalizations are tentative, as new evidence can show them to be incorrect

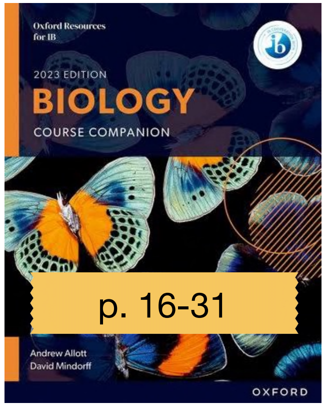
↳ Solution: falsification allows for certainty as we can show what is not true through counter-examples
※ nothing is 'proven' in science - evidence either supports or falsifies hypotheses

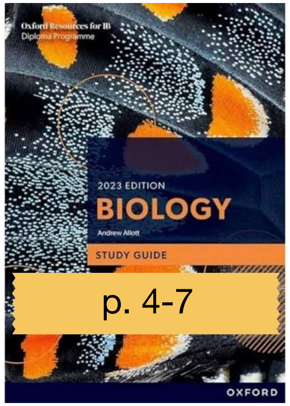
Resource Links

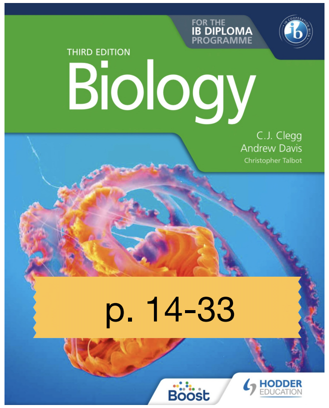
each resource is hyperlinked

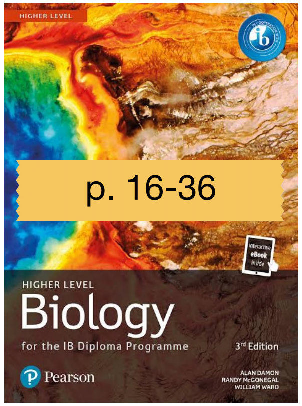
NOTEWORTHY SCIENCE
MARIER

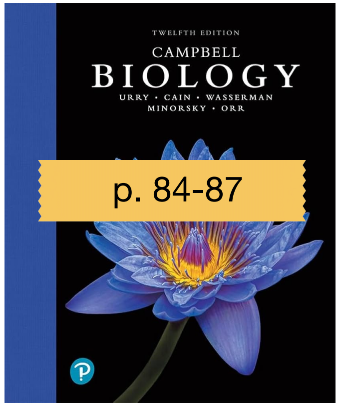
Textbooks











Simulators / Interactives

DNA HOME

DNA timeline

DNA LEARNING CENTER

Chargaff experiment

LabXchange

DNA structure

The Fundamentals of Biochemistry: Interactive Tutorials

Watson-Crick Base Pairs

Created by Dr. David Fahrney. Edited by Ben Robinson.

Base pairs

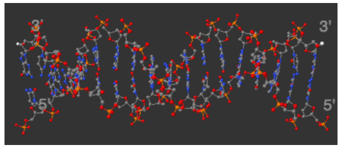
Articles

Fry, M. (2016). Dissolution of hypotheses in biochemistry: three case studies. History & Philosophy of the Life Sciences, 38(4). https://doi.org/10.1007/s40656-016-0118-x

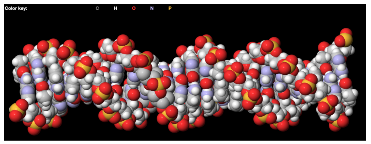
Hershey, A. D., & Chase, M. (1952). INDEPENDENT FUNCTIONS OF VIRAL PROTEIN AND NUCLEIC ACID IN GROWTH OF BACTERIOPHAGE. The Journal of General Physiology, 36(1), 39–56. https://doi.org/10.1085/jgp.36.1.39

Simply Psychology. (2023, July 31). Karl Popper: Theory of Falsification. https://www.simplypsychology.org/karl-popper.html#:~:text=The%20Falsification%20Principle%2C%20proposed%20by,by%20observing%20a%20black%20swan.

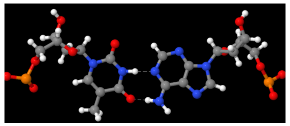
3D models



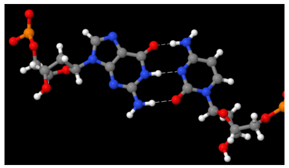
DNA



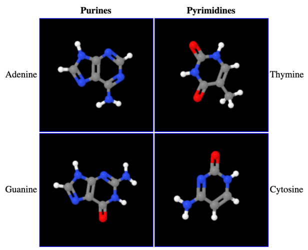
DNA



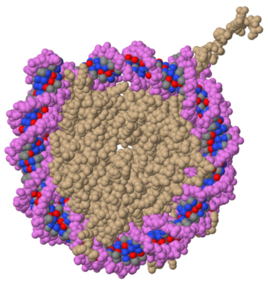
A-T pair



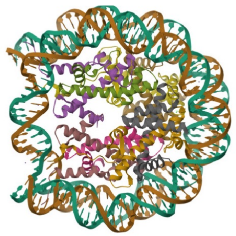
C-G pair



DNA bases



Nucleosome



Crystal structure of human nucleosome core particle

COMPLEX BETWEEN NUCLEOSOME CORE PARTICLE (H3,H4,H2A,H2B) AND 146 BP LONG DNA FRAGMENT