

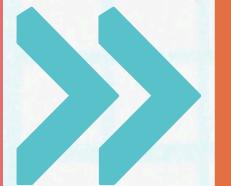
Understanding DNA: Structure, Detection, and Medical Applications

Ken Cho October 2024



Intended Learning Outcomes:

State what DNA is and describe its structure

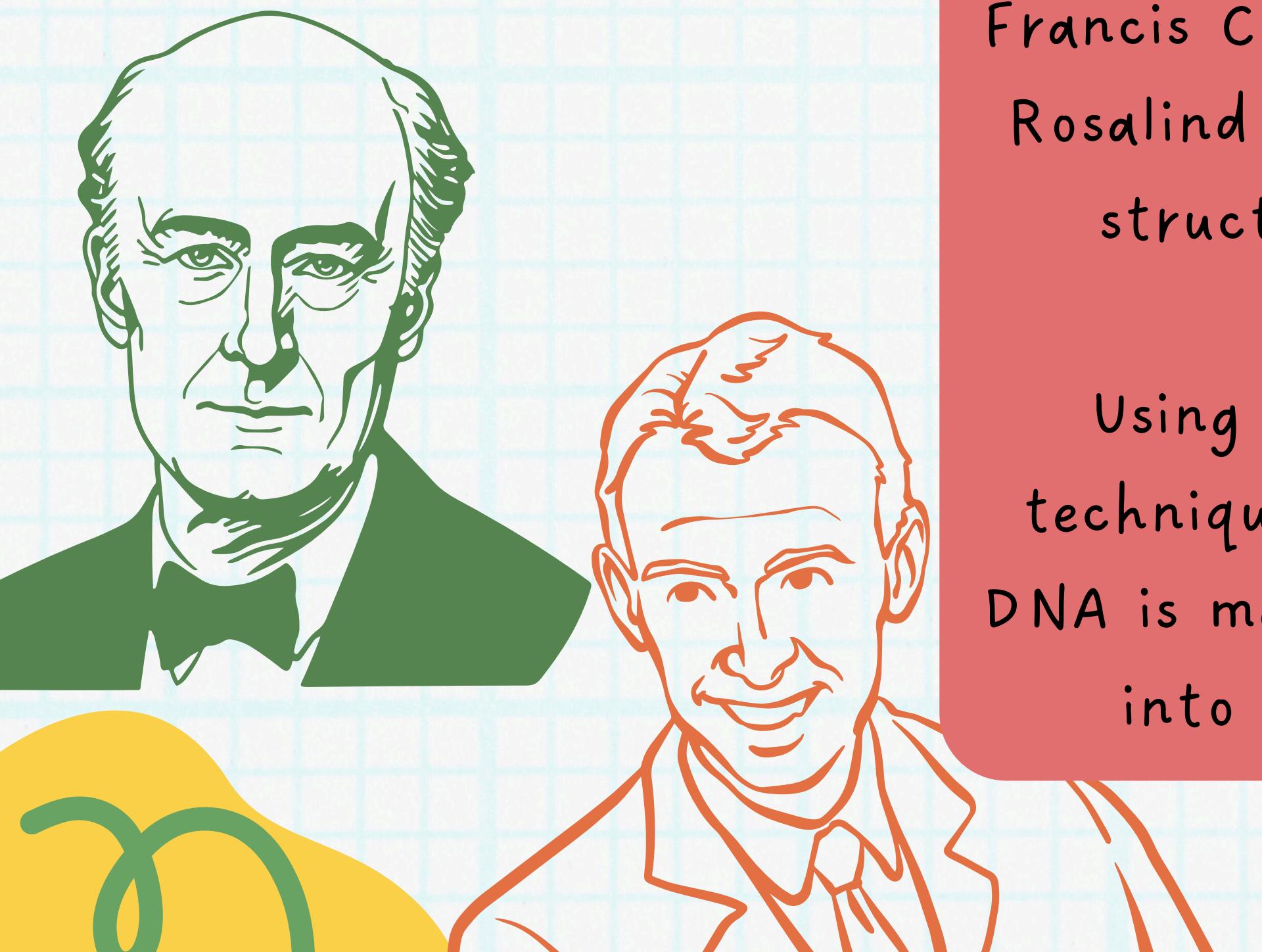


Identify key sequencing methods



Explain how sequencing is used in diagnosing genetic conditions

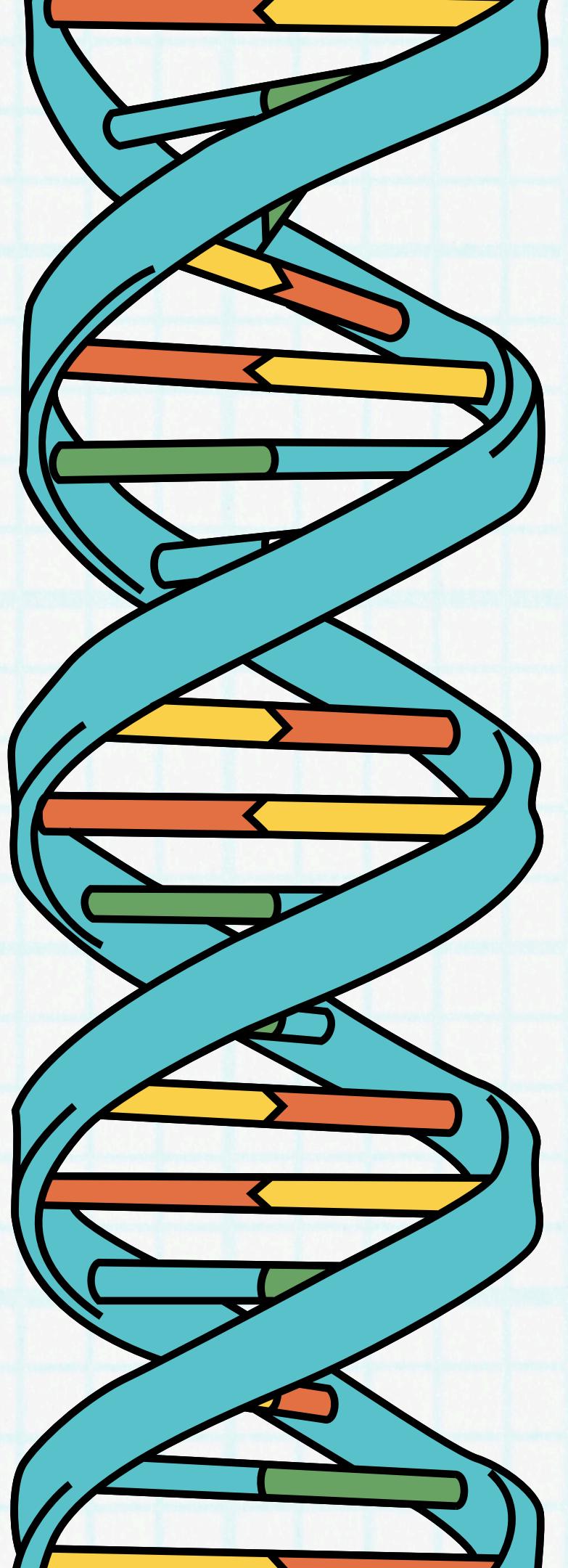
Discovering DNA



Scientists James Watson and Francis Crick built on the work of Rosalind Franklin to discover the structure of DNA in 1953.

Using X-ray crystallography techniques, they discovered that DNA is made of two strands coiled into a double helix shape.





What is a double helix?

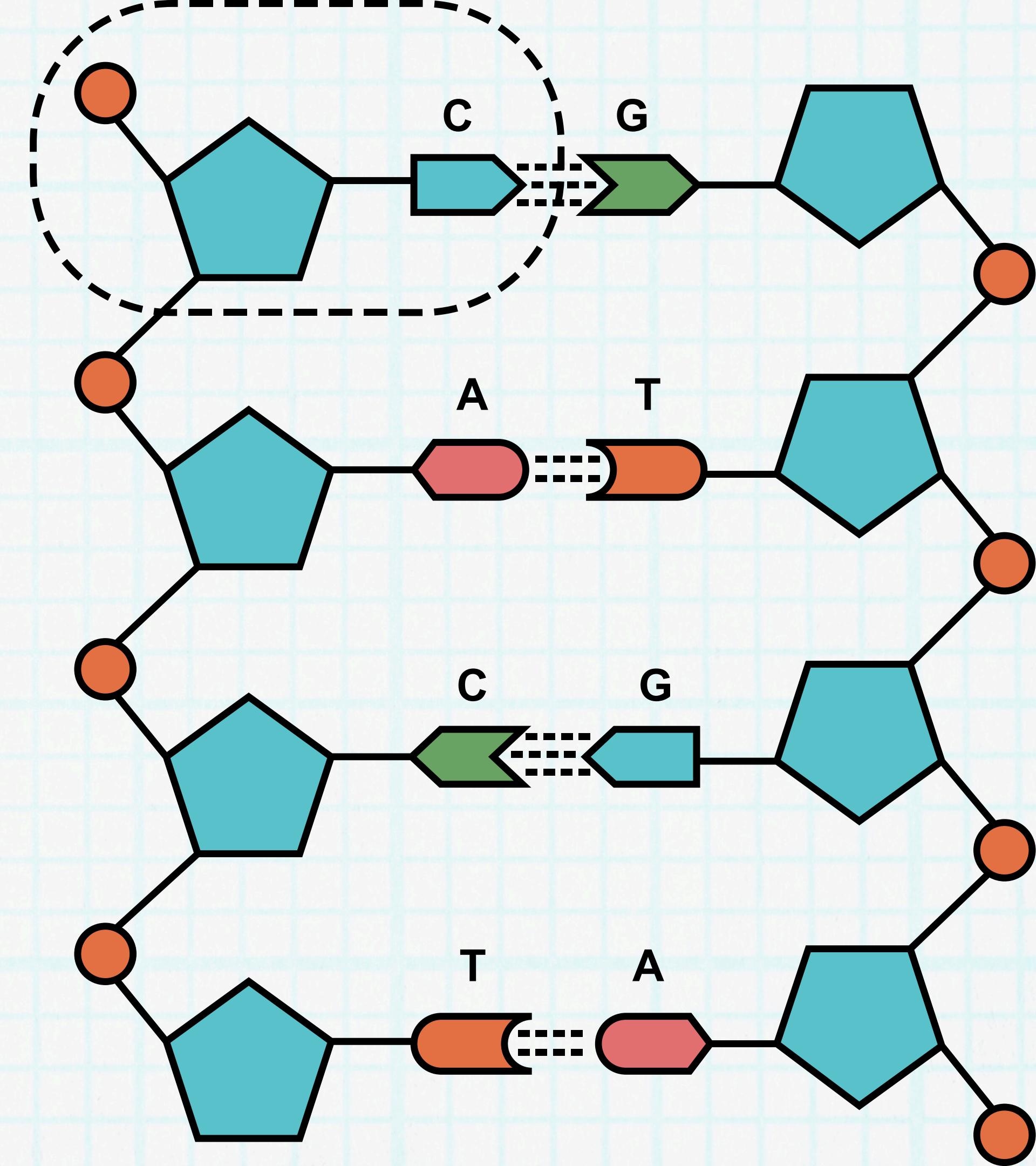
DNA is in a double helix shape.

It consists of two parallel strands of DNA twisted around each other.

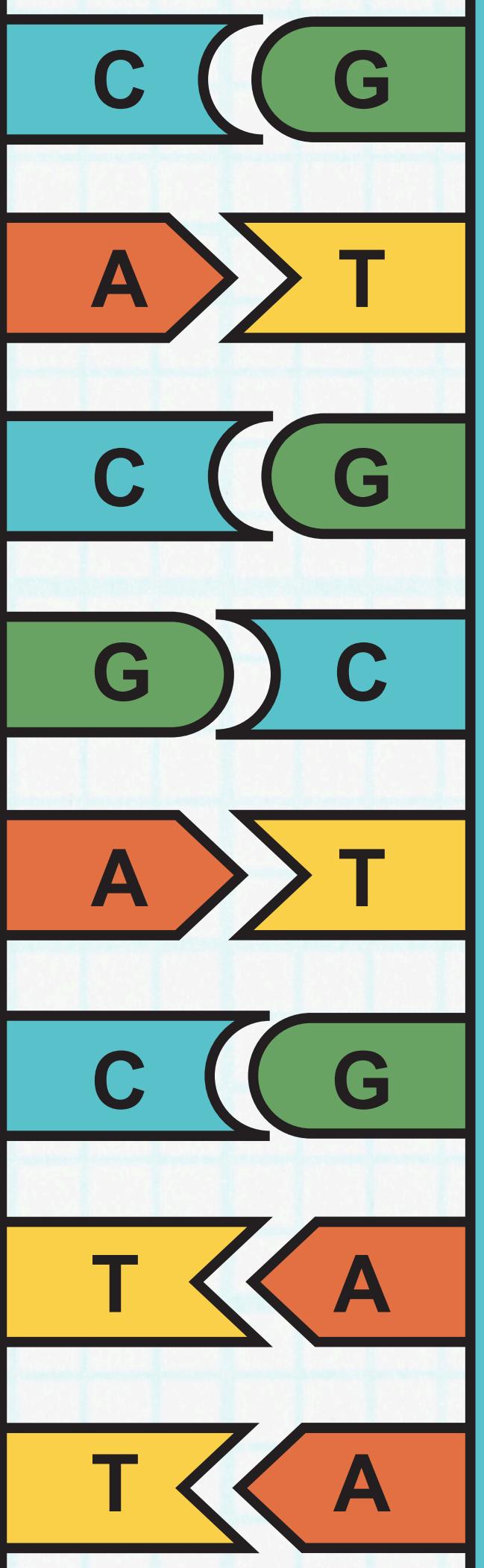
What is a nucleotide?

Nucleotides are the units which DNA is composed of.

Each nucleotide includes a phosphate group, a sugar section and one of the four bases.

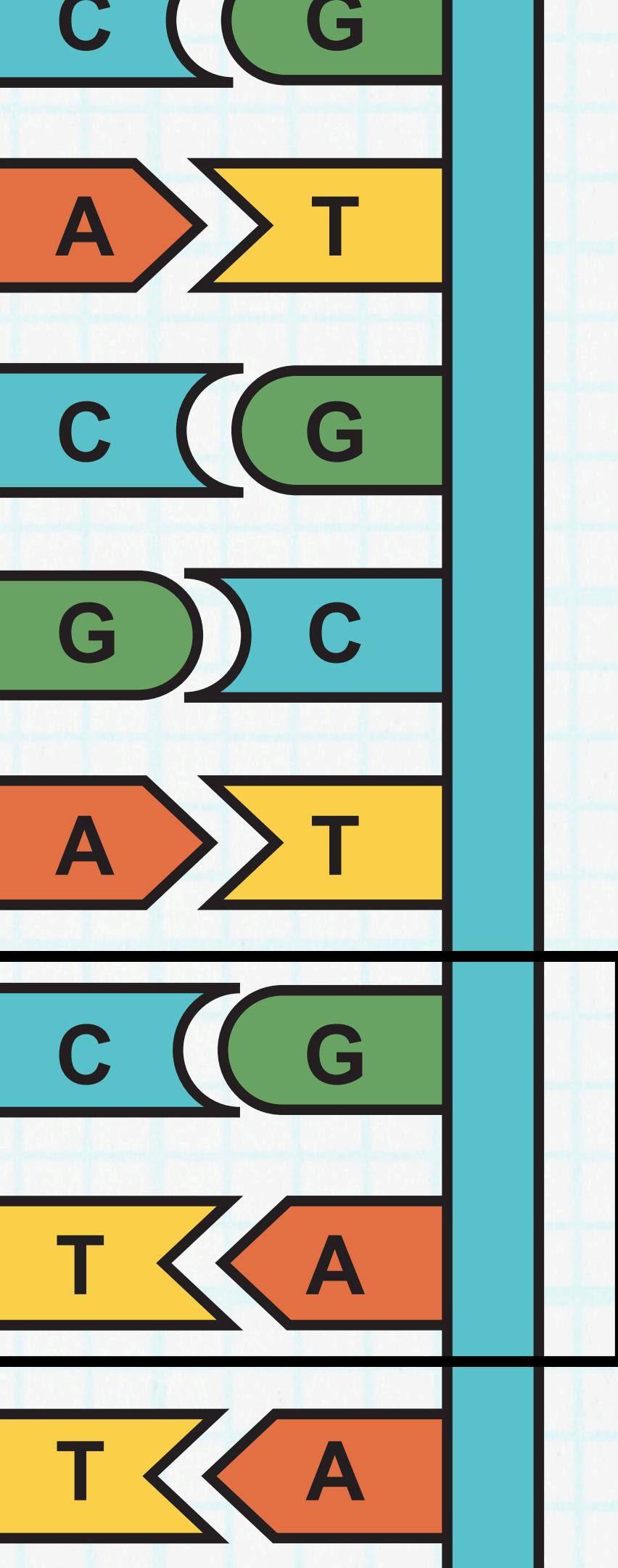
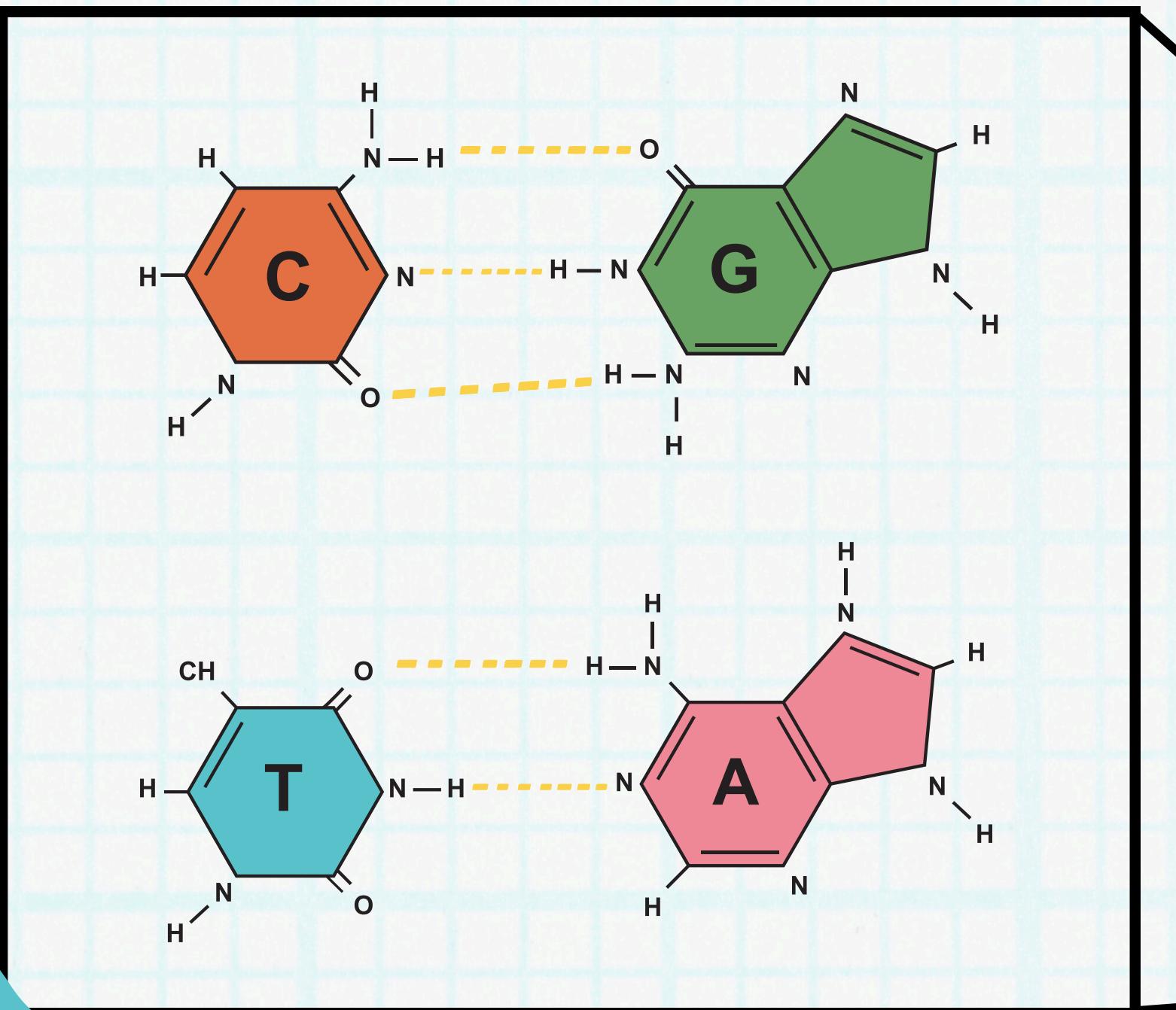


Base pairs



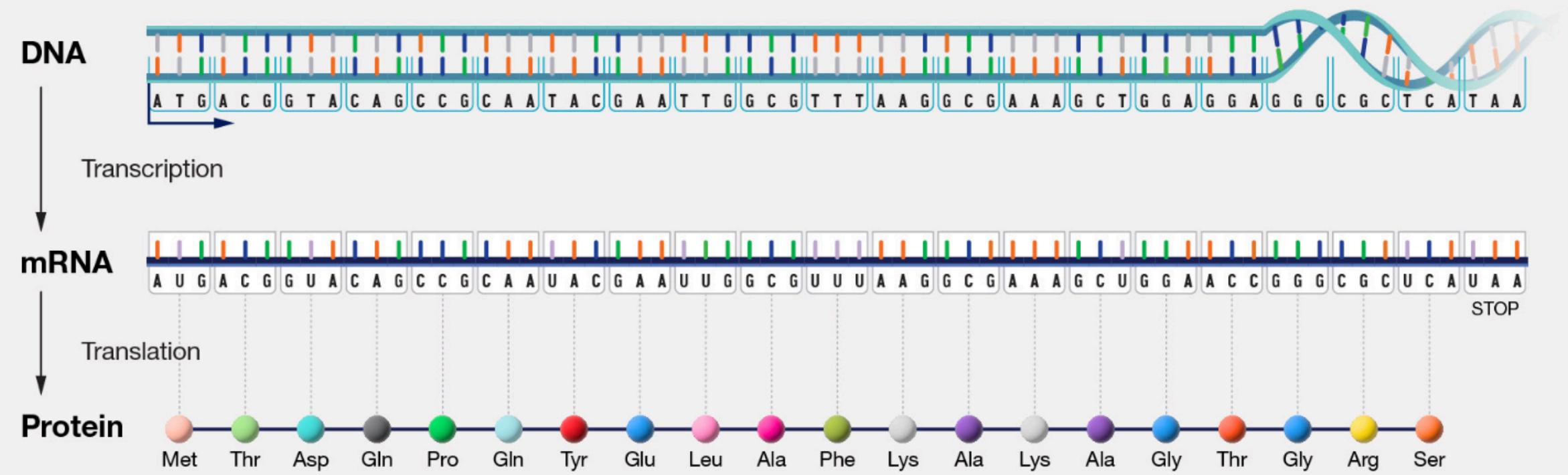
Each nucleotide has a base. There are four different bases in DNA: thymine (T), adenine, (A), guanine (G) and cytosine (C). A and T are a pair. G and C are another pair. The complementary pairs are hydrogen bonded together. This maintains the DNA structure.

A closer look



Central Dogma of Biology

The central dogma (Francis Crick, 1958) of molecular biology is a theory stating that genetic information flows only in one direction, from DNA, to RNA, to protein, or RNA directly to protein.

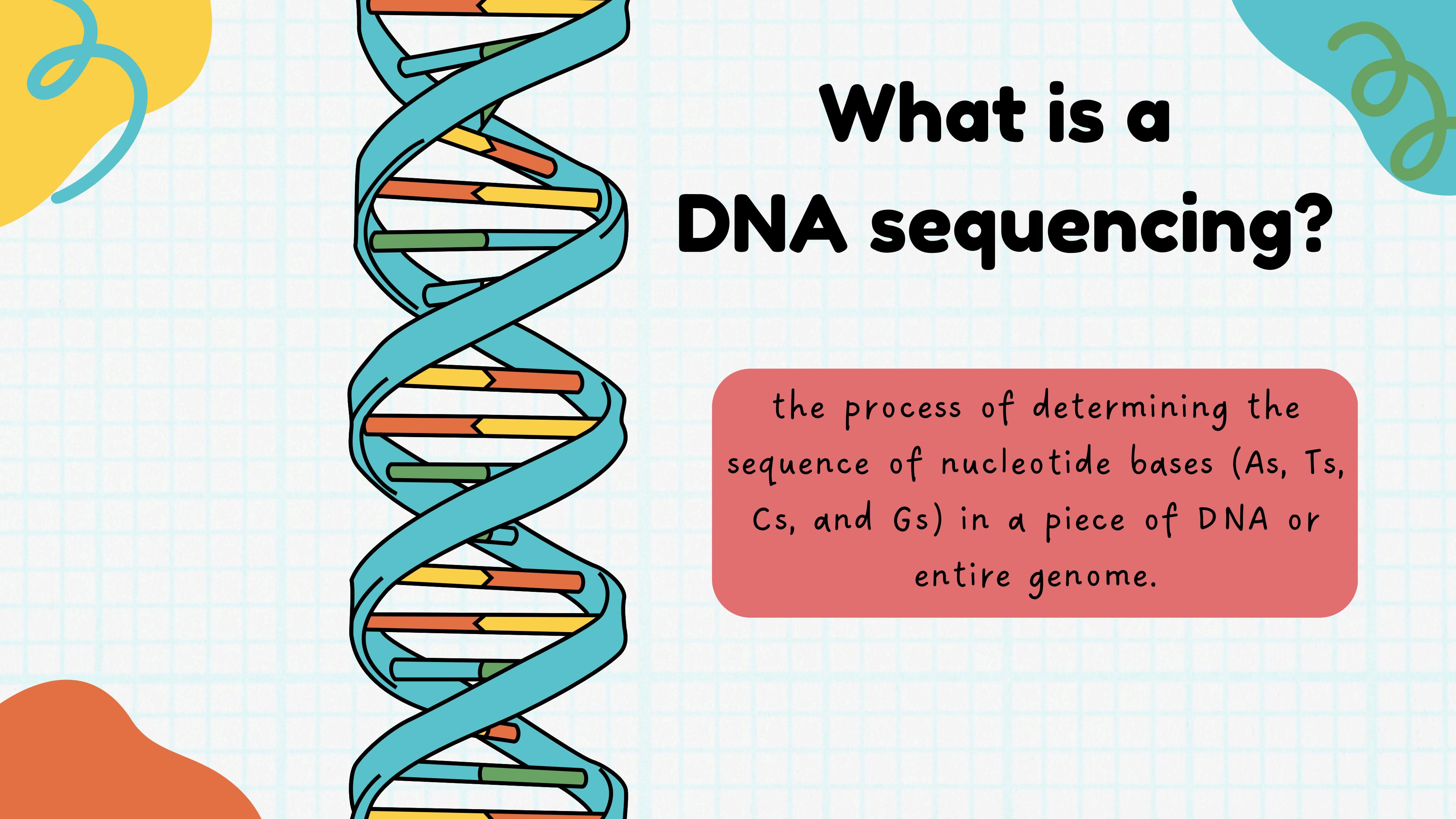


Assessment Task 1:

What is the complimentary sequencing of this following DNA strands?

AGCTTTCA~~T~~TCTGACTGCAACGGGCAATATG

Answer: TCGAAAAGTAAGACTGACGTTGCCGTTATAC

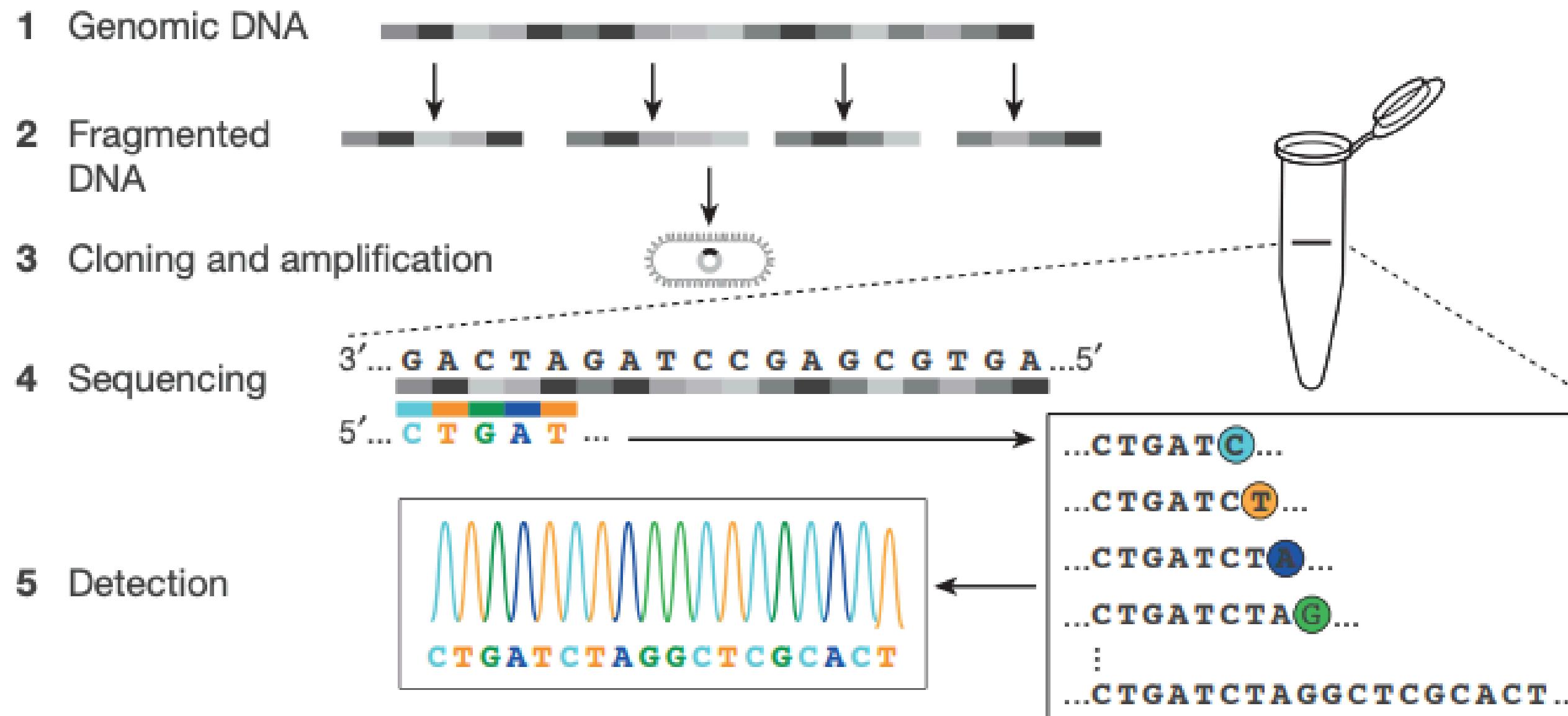


What is a DNA sequencing?

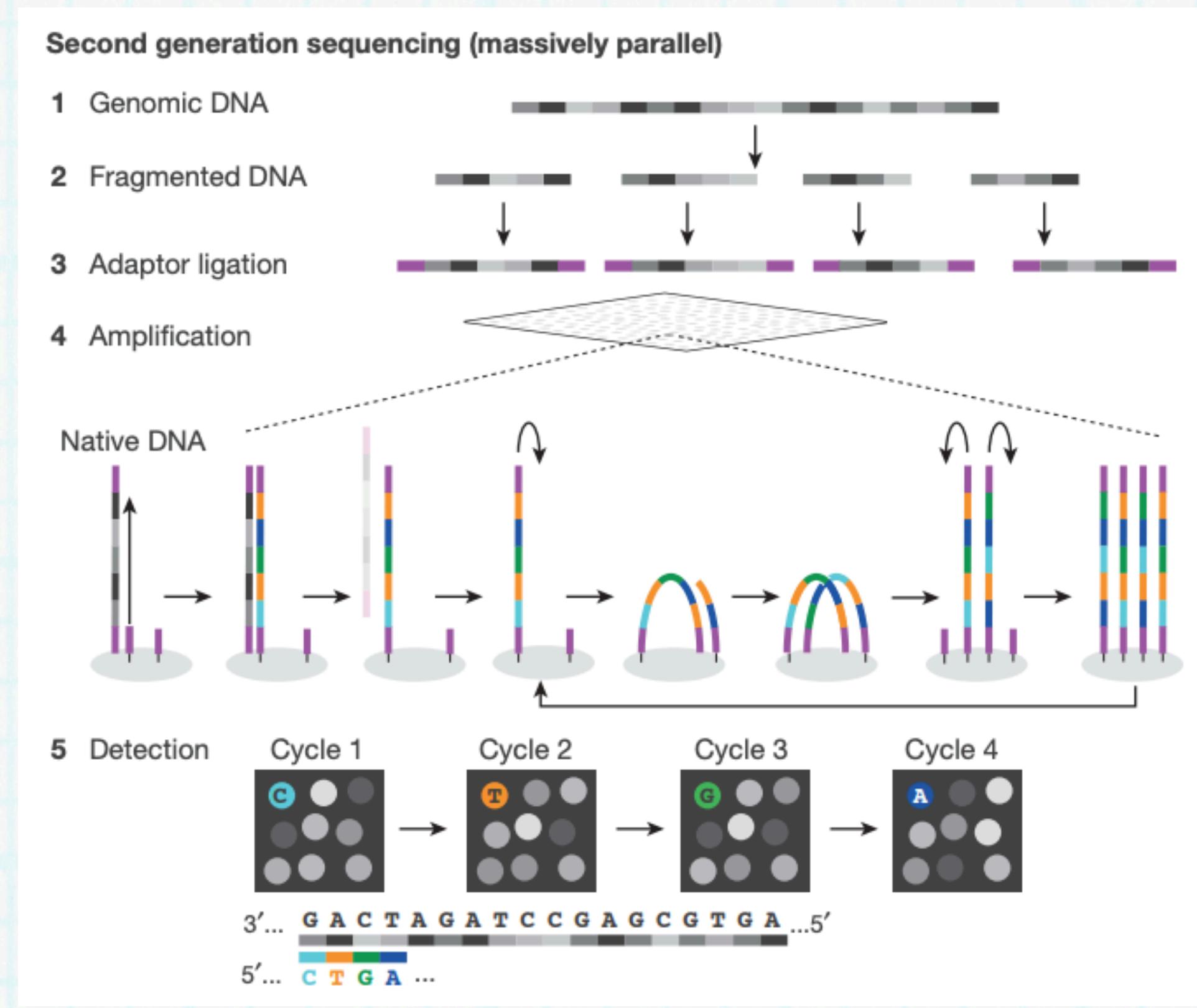
the process of determining the sequence of nucleotide bases (As, Ts, Cs, and Gs) in a piece of DNA or entire genome.

DNA sequencing technologies I

First generation sequencing (Sanger)

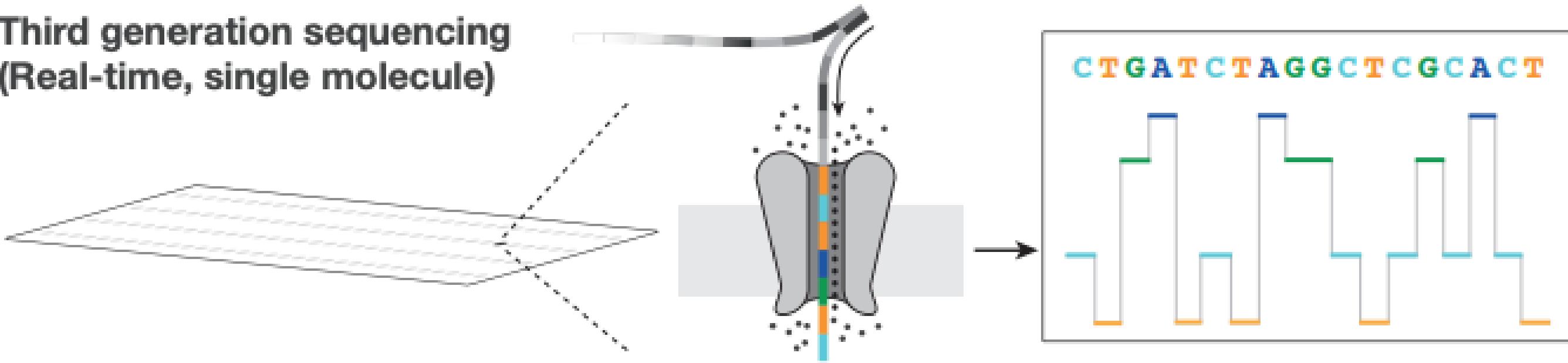


DNA sequencing technologies II



DNA sequencing technologies III

Third generation sequencing
(Real-time, single molecule)



Performance Comparison of different sequencing platform

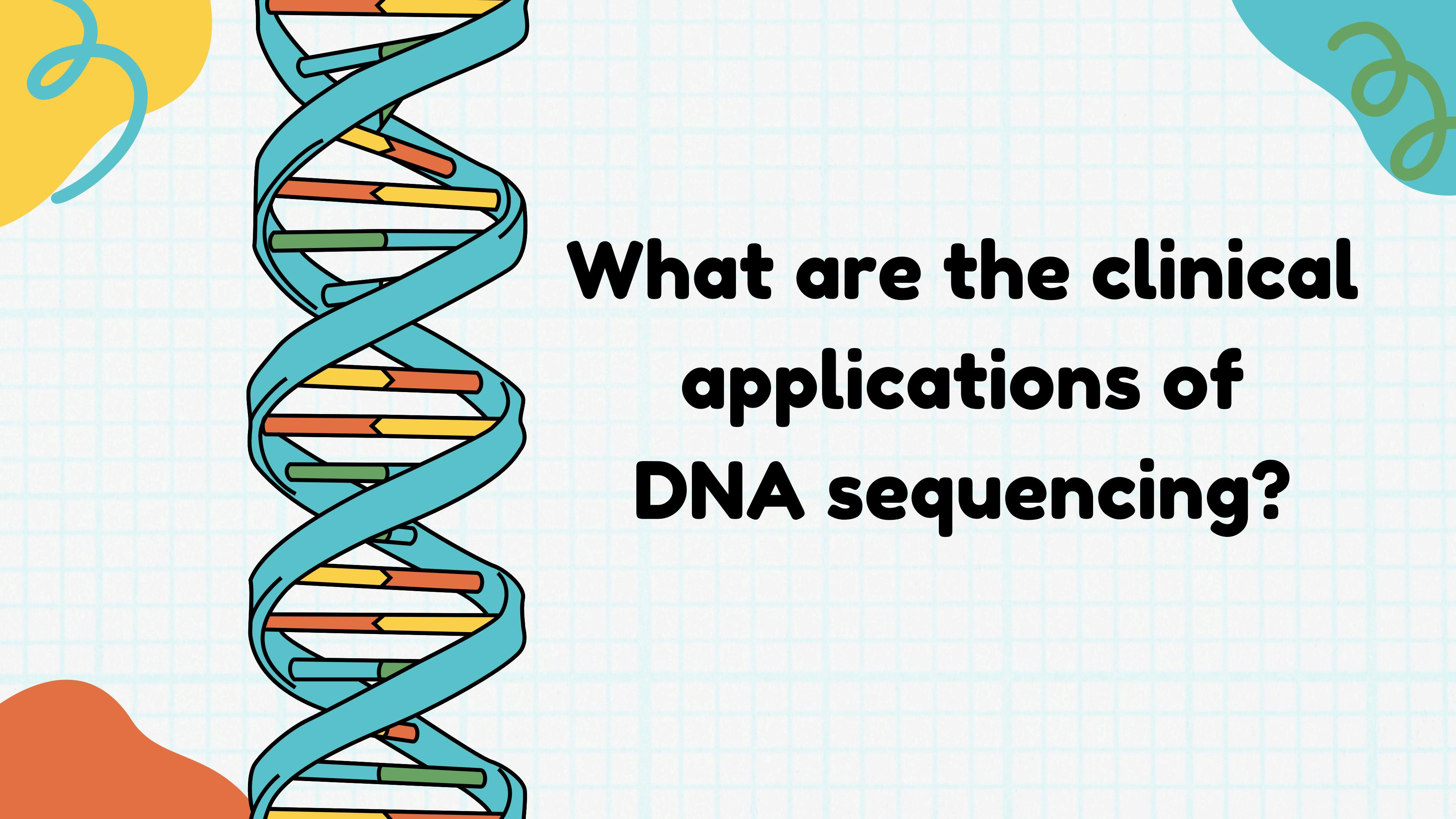
Platform	Generation	Read length	Single pass error rate(%)	No. of reads per run	Time per run	Cost per million bases
Sanger 3730 xl	1st	600-1000bp	0.001	96	0.5-3h	500
Ion Torrent	2nd	200bp	1	8.2×10^7	2-4h	0.1
HiSeq2500(High Output)	2nd	2x125bp	0.1	8×10^9	1-6days	0.03
HiSeq2500(Rapid)	2nd	2x250bp	0.1	1.2×10^9	7-60hrs	0.04
PacBio RSII: P6-C4	3rd	~20kb	13	$3.5-7.5 \times 10^4$	0.5-4hrs	0.40-0.80
PacBio Sequel P6-C4	3rd	~20kb	13	3.7×10^4	0.5-6hrs	0.20-0.40
Nanopore MinION	3rd	~2-5kb	38	$1.1-4.7 \times 10^4$	50hrs	6.44-17.90

Assessment Task 2:

What is one benefit of using third-generation DNA sequencing?

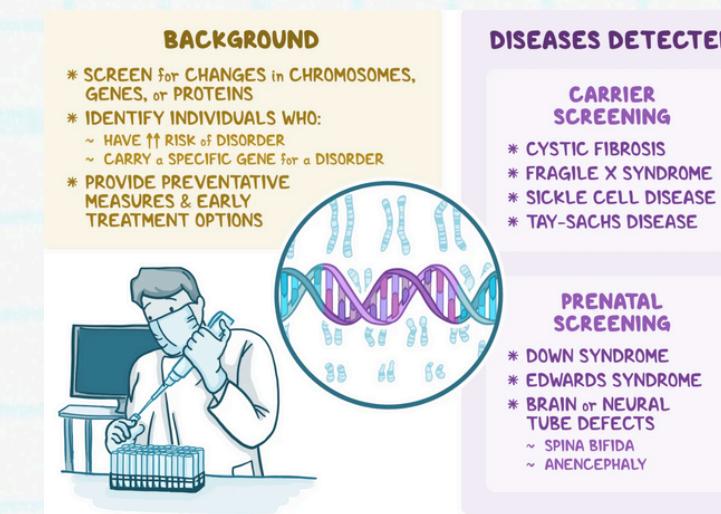
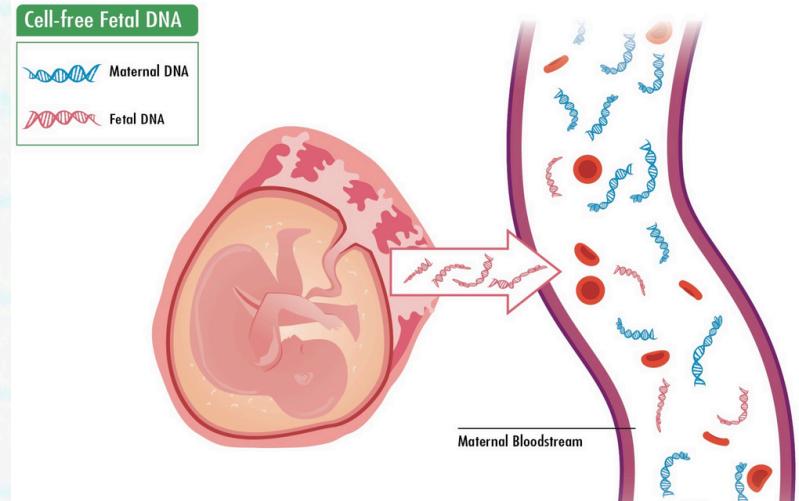
Answer:

One benefit of third-generation DNA sequencing is that it can read longer pieces of DNA in real-time, which helps scientists understand complex genetic information better than shorter reads from earlier methods.



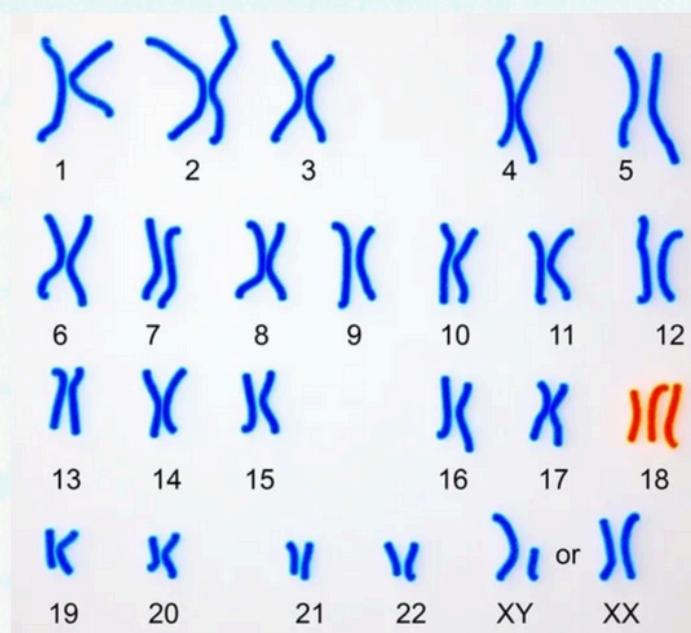
**What are the clinical
applications of
DNA sequencing?**

Non-invasive Prenatal Screening



Trisomy 21 (Down syndrome)

- A flat nose bridge
- A short neck
- Small ears, hands and feet
- Eye diseases



Trisomy 18 (Edward's Syndrome)



- unusually small head
- back of the head is prominent
- ears are malformed and low-set
- mouth and jaw are small (may also have a cleft lip or cleft palate)
- hands are clenched into fists, and the index finger overlaps the other fingers
- Clubfeet (or rocker bottom feet) and toes may be webbed or fused

Cancer diagnosis based on SNP

BRCA Genes

BRCA 1 and **BRCA 2** are genes that inhibit breast, gynecological, and pancreatic tumor growth.



Gene	Nucleotide change	Effect on protein	NCBI SNP	Clinical significance ¹
BRCA1	c.2311T>C	L771L	rs16940	No
	c.3113A>G	E1038G	rs16941	No
	c.4308T>C	S1436S	rs1060915	No
	c.4675+1G>A	INV15+1	rs80358044	Yes
	c.4837A>G	S1613G	rs1799966	No
	c.-41A>G	5'UTL	-	Unknown
BRCA2	c.-26G>A	5'UTL	rs1799943	No
	c.658delGT	V220 (223stop)	rs80359604	Yes
	c.1114A>C	N372H	rs144848	No
	c.3396A>G	K1132K	rs1801406	No
	c.3807T>C	V1269V	rs543304	No
	c.4258G>T	D1420Y	rs28897727	No
	c.4563A>G	L1521L	rs206075	No
	c.5244delC	S1748 (1748stop)	-	Yes
	c.5744C>T	T1915M	rs4987117	minor
	c.7242A>G	S2414S	rs1799955	No
	c.7316delG	G2439 (2468stop)	-	Yes

Cancer Type	SNP Mutation	Location	Targeted Drug Treatment	5-Year Survival Rate with Treatment	5-Year Survival Rate without Treatment
Breast Cancer	rs80357713	BRCA1 gene, chromosome 17	Olaparib (Lynparza)	70%	50%
Colorectal Cancer	rs3802842	MTHFR gene, chromosome 1	Cetuximab (Erbitux)	60%	40%
Ovarian Cancer	rs3814113	BRCA1 gene, chromosome 17	Niraparib (Zejula)	65%	45%
Lung Cancer	rs1051730	EGFR gene, chromosome 7	Erlotinib (Tarceva)	75%	55%
Prostate Cancer	rs1250008	8q24 region	Abiraterone (Zytiga)	80%	60%

Assessment Task 3:

Which genetic defect causes Edward's Syndrome?

Answer:
Trisomy of chromosome 18

Thank you!

Presentation end

