FREE NOTES · NCERT + NEET LEVEL

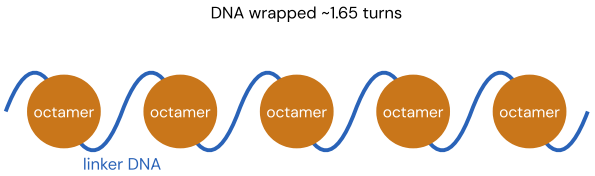
Molecular Basis of Inheritance

DNA structure and packaging, search for genetic material, RNA world, replication, transcription, genetic code, translation, regulation (lac operon), Human Genome Project and DNA fingerprinting.

01 DNA structure and packaging
02 Search for genetic material
03 Replication
04 Transcription
05 Genetic code and translation
06 Regulation, HGP, DNA fingerprinting
07 Extra + tricks
08 Important Q&A
09 Common mistakes
10 Practice (NEET style)
11 Quick revision

01 DNA structure and packaging

- Polynucleotide: nitrogenous base + pentose (deoxyribose) + phosphate. N-glycosidic bond (base–sugar), phosphoester (sugar–phosphate), 3′–5′ phosphodiester (between nucleotides). 5′ phosphate end and 3′ OH end.
- Lengths: φ×174 phage 5386 nucleotides; λ phage 48,502 bp; *E. coli* 4.6×10^6 bp; human haploid 3.3×10^9 bp.
- Watson–Crick (1953) double helix, based on X-ray data of **Wilkins and Franklin**; **Chargaff's rule**: A = T, G = C (purines = pyrimidines). Right-handed, antiparallel; 3.4 nm pitch, 10 bp per turn, 0.34 nm between bp. Total human DNA length ≈ 2.2 m.
- Prokaryotes: negatively charged DNA held with positive proteins in nucleoid. Eukaryotes: **histones** (positively charged; rich in lysine and arginine) form octamer; **nucleosome** = ~200 bp. Euchromatin (loosely packed, active), heterochromatin (dense, inactive). Non-histone chromosomal (NHC) proteins needed for higher packaging.



Nucleosome: ~200 bp DNA around histone octamer (beads-on-string)

Nucleosomes: beads-on-string

02 Search for genetic material

Experiment	Finding
Griffith (1928), *Streptococcus pneumoniae*	S strain (capsule, virulent) heat-killed + live R strain ⇒ mice died; R transformed to S by a "transforming principle"
Avery, MacLeod, McCarty (1933–44)	Transforming principle is DNA (DNase destroyed it; protease and RNase did not)
Hershey & Chase (1952)	Bacteriophage with ^{32}P (DNA) and ^{35}S (protein): only ^{32}P entered bacteria ⇒ **DNA is genetic material**

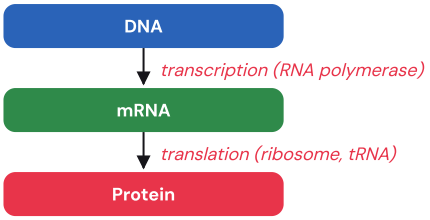
- Criteria for genetic material: replication, chemical and structural stability, scope for slow changes (mutation), expression as Mendelian characters.
- DNA more stable than RNA (2′-OH in RNA makes it reactive; thymine instead of uracil adds stability). **RNA was the first genetic material** (RNA world): it can act as catalyst (ribozymes); DNA evolved from RNA for stability.

03 Replication

- **Semi-conservative**: each new DNA has one old and one new strand. Proved by **Meselson and Stahl** (1958) using ^{15}N (heavy) and ^{14}N in *E. coli*; CsCl density gradient centrifugation: after 1 generation hybrid; after 2 generations equal hybrid and light. Taylor showed it in *Vicia faba* with radioactive thymidine.
- Enzyme: **DNA-dependent DNA polymerase**; polymerises only 5′→3′; very fast (*E. coli*: 4.6×10^6 bp in ~18 min, ~2000 bp/s) and accurate. Energy from deoxynucleoside triphosphates.
- Starts at **origin of replication**; replication fork. **Leading strand** continuous; **lagging strand** discontinuous (Okazaki fragments) joined by **DNA ligase**.
- Eukaryotes: replication in S phase.

04 Transcription

- Copying DNA to RNA; only one strand used. **Template strand** (3′→5′); **coding strand** (5′→3′, same sequence as RNA except T for U; does not code).
- Transcription unit: **promoter** (upstream, towards 5′ of coding strand), structural gene, **terminator** (downstream).
- Bacteria: one RNA polymerase; σ (sigma) factor for initiation, ρ (rho) factor for termination. Transcription and translation can be coupled (no nuclear membrane).
- Eukaryotes: RNA pol I (rRNA 28S, 18S, 5.8S), II (hnRNA = precursor of mRNA), III (tRNA, 5S rRNA, snRNA). Processing: **splicing** (introns removed, exons joined), **capping** (methyl guanosine triphosphate at 5′), **tailing** (poly-A, 200–300 adenylates at 3′).



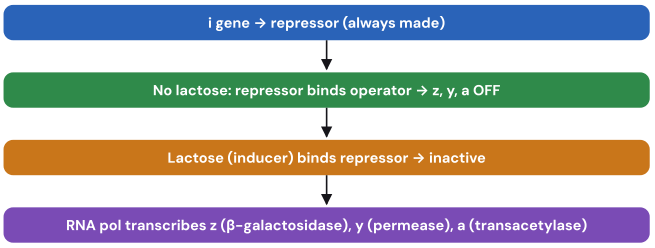
Central dogma (Crick)

05 Genetic code and translation

- George Gamow: triplet code ($4^3 = 64$ codons). Nirenberg, Khorana (synthesis of RNA with defined sequences), Severo Ochoa (polynucleotide phosphorylase) helped decipher.
- Features: triplet; 61 code amino acids, 3 stop codons (UAA, UAG, UGA); one codon = one amino acid (unambiguous, specific); **degenerate** (some amino acids have several codons); read contiguously (no punctuation); nearly **universal**; **AUG** = start codon and codes methionine.
- **tRNA** (adapter molecule, clover-leaf; actual 3D inverted L): anticodon loop, amino acid acceptor end. **Charging** (aminoacylation) uses ATP.
- Translation on ribosome (large and small subunits; 23S rRNA in bacteria is a ribozyme that forms peptide bonds). mRNA has **UTRs** at 5′ and 3′ ends. Initiation at AUG, elongation, termination by release factor at stop codon.

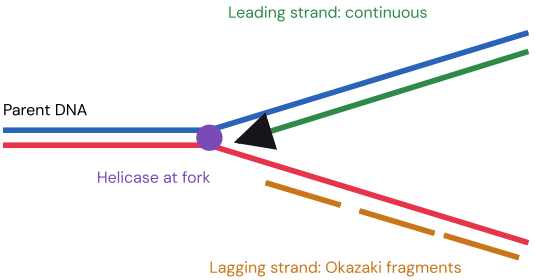
06 Regulation, HGP, DNA fingerprinting

- **Lac operon** (Jacob and Monod): i (regulator), p, o, structural genes z, y, a. Lactose is the inducer. Regulation is mainly at transcription initiation; this is **negative regulation**.
- **Human Genome Project** (1990, completed 2003; ~13 years, ~US$ 3 billion). Approaches: Expressed Sequence Tags (ESTs) and sequence annotation; BAC/YAC vectors; automated sequencers (Sanger).
- Findings: 3164.7 million bp; average gene 3000 bases (largest: dystrophin 2.4 million bases); ~30,000 genes; 99.9% bases same in all people; function of over 50% genes unknown; <2% codes proteins; repeated sequences; ~1.4 million SNPs. Chromosome 1 most genes (2968), Y fewest (231).
- **DNA fingerprinting** (Alec Jeffreys): uses **VNTRs** (satellite DNA, repetitive; polymorphism). Steps: isolate DNA, digest with restriction enzymes, electrophoresis, Southern blotting, hybridise with VNTR probe, autoradiography. Used in forensics, paternity disputes, population diversity.



Lac operon: induction by lactose

07 Extra + tricks



Replication fork

Enzyme / protein	Role in replication
Helicase	Unwinds DNA (breaks H-bonds)
Topoisomerase (gyrase in bacteria)	Relieves supercoiling ahead of fork
SSB proteins	Keep strands apart
Primase	Makes RNA primer
DNA polymerase III (bacteria)	Main synthesis 5′→3′
DNA polymerase I	Removes primer, fills gaps
DNA ligase	Joins Okazaki fragments

- Bacteria: **polycistronic** mRNA (one mRNA, many genes); eukaryotes: **monocistronic**.
- **Nirenberg and Matthaei**: poly-U RNA made poly-phenylalanine ⇒ UUU codes Phe (first codon cracked).
- Reverse transcription (RNA → DNA) in retroviruses: exception to central dogma.

08 Important Q&A

Q1. If a DNA has 20% adenine, find % of other bases.

A = T = 20%; G + C = 60% ⇒ G = C = 30%.

Q2. Write the mRNA for coding strand 5′-ATGCATGC-3′.

5′-AUGCAUGC-3′ (same as coding strand with U for T).

Q3. Why did Hershey and Chase use ^{32}P and ^{35}S?

DNA has phosphorus but no sulphur; protein has sulphur but no phosphorus; so labels distinguish them.

09 Common mistakes

- Saying the template strand has same sequence as mRNA (coding strand does).
- Calling the code ambiguous (it is unambiguous but degenerate).
- Saying DNA polymerase works 3′→5′ (it adds in 5′→3′).
- Thinking introns are present in mature mRNA.

10 Practice (NEET style)

1. Who proved semi-conservative replication?
2. Inducer of lac operon?
3. Start codon?
4. Enzyme joining Okazaki fragments?
5. Basis of DNA fingerprinting?

ANSWERS

1) Meselson and Stahl · 2) Lactose · 3) AUG · 4) DNA ligase · 5) VNTRs

11 Quick revision: 5 minutes before the exam

DNA

- A=T, G≡C (Chargaff)
- 0.34 nm, 10 bp/turn
- Nucleosome 200 bp

EXPERIMENTS

- Griffith transformation
- Avery: DNA
- Hershey–Chase ^{32}P
- Meselson–Stahl ^{15}N

EXPRESSION

- Splicing, capping, tailing
- 64 codons, 3 stop
- AUG start

REGULATION/HGP

- Lac: z, y, a; lactose inducer
- ~30,000 genes, 99.9% same
- VNTR fingerprinting

Have a doubt? Ask the AI Doubt Solver at padhaiadda.netlify.app, or take the mock test on this chapter.