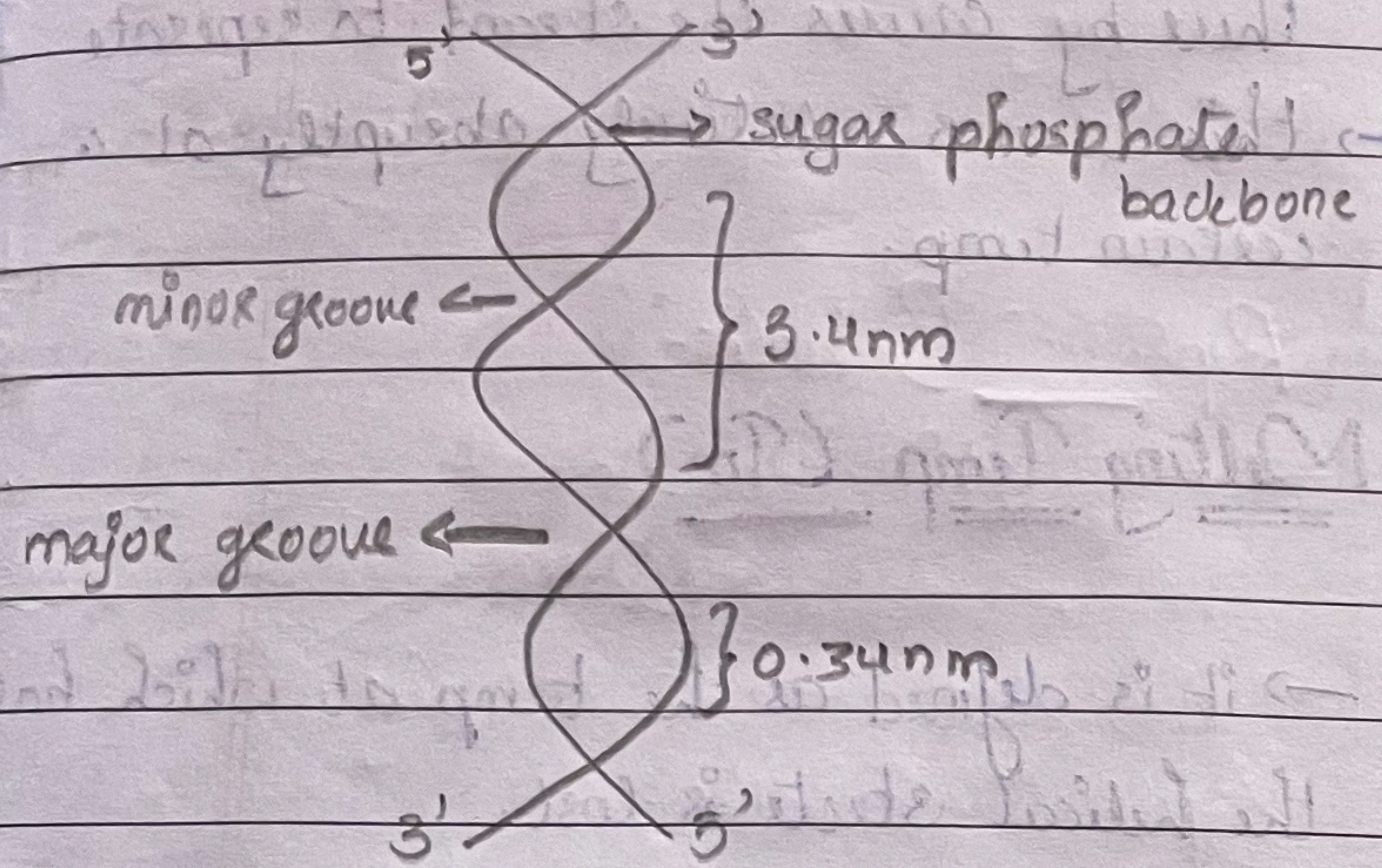
Structure of DNA

→ DNA consists of 2 molecules that are arranged into a ladder-like struct called a Double-Helix

→ a molecule of DNA is made up of millions of tiny subunits called nucleotides.

→ it is a double stranded polynucleotide.

→ each nucleotide consists of N_2 base, pentose sugar, phosphate grp.



→ Watson-Crick model of double helical struct of DNA (1953)

→ adjacent bases are seperated by 0.34nm.

→ the diameter or width of the helix is 2nm.

Nucleotide

→ each base will only bond with one other specific base.

Adenine (A) } forms a base pair
Thymine (T)

Cytosine (C) } forms a base pair
Guanine (G)

→ bcs of this complementary base pairing, the order of the bases in one strand determines the order of the bases in the other strand.

A = T

C ≡ G

→ Edwin Chargaff elicited the base pairing rule of DNA - A with T & G with C.

→ number of purines = number of pyramidines

→ DNA is composed of 4 deoxyribonucleotides of A, G, C & T

Salient Features of Watson & Crick Model

→ right handed double helix

→ base pairing rule; A to T, G to C by H bonds.

→ anti || 5' → 3'
3' → 5'

→ 10 bp forms one spiral.

→ spiral has a pitch of 3.4nm

→ double helical struct forms alternating major & minor grooves.

Types of DNA - A DNA, B DNA, Z DNA, mt DNA

→ DNA is structurally dynamic & can assume a variety of forms.
→ the model proposed by Watson & Crick is called B-DNA
→ when DNA becomes partially dehydrated, it assumes A-form.
→ A DNA is bulkier than B DNA & has 11 bp per turn.

Z DNA

→ left handed, longer, thinner than B DNA
→ has 12 bp per turn
→ phospho diester bond of Z DNA form zig zag hence the name.
→ human DNA may contain Z DNA at regions rich in G C bp.

mt DNA (specific for mitochondria)

→ similar to prokaryotic DNA.
→ has 16,500 nucleotides
→ unique genetic code
→ codes for protein synthesis in mitochondria

→ Clinical significance:-
- mutat^{n} of mt DNA leads to
  a) mitochondrial myopathies - disrupted skeletal muscle fibres - loss of normal f^{n}
  b) Lebers hereditary optic neuropathy - blindness (LHON) in adults, optic nerve degenerat^{n}
  c) OXPHOS diseases - oxidative phosphoryl^{n} diseases - mitochondrial encephalopathy, lactic acidosis & stroke like episodes (MELAS).

Melting of DNA / Denaturat^{n} of DNA

→ double stranded DNA may be denatured & seperated by heat.
→ heating disrupts the H-bonds b/w bp thus by causes the strand to seperate
→ this occurs relatively abruptly at a certain temp.

Melting Temp (Tm)

→ it is defined as the temp at which half the helical structr is lost.
→ strands may also be seperated by adding acid or alkali to ionise the nucleotide bases and disrupt base pairing.
→ stacked bases in nucleic acids absorbs less UV light than unstacked bases - an effect called hypochromism.

Hyperchromicity of Denaturat^{n}

→ single stranded DNA absorb light more effectively than double helical DNA.
→ absorbance ↑es when double helix is melted into a single strand (hyperchromicity of denaturat^{n}).

Factors af...
→ nature of ... temp than...
→ chemicals- ... So used...
→ inside th... use chem... disrupt...

Annealin...
→ at le... re-ass...
→ abilit... the lab... hybrid...

Higher...
→ DN... boun... cal...
→ hi... ...
→ 5...

Factors affecting Denaturat^n

- → nature of bp - GC bp melt at a higher temp than AT bp.
- → Chemicals - formamide disrupts H-bonding. So used in DNA hybridizat^n studies.
- → inside the cells proteins called helicases use chemical energy (from ATP) to disrupt the structs.

Annealing of Denatured DNA

- → at lower temp, the melted strands are re-associated - which is called annealing.
- → ability to melt & re anneal reversibly in the lab provide powerful tool for DNA hybridization studies.

Higher Organisat^n of DNA

- → DNA in eukaryotic chromosome is tightly bound to a grp of small basic proteins called histones.
- → histones constitute half the mass of eukaryotic chromosome.
- → 5 major histones :-
  - H_1 ⟶ loosely attached to DNA
  - H_2A, H_2B ⟶ lysine rich } core histones
  - H_3, H_4 ⟶ arginine rich }
- → histone octomer - 2 copies each of H_2A, H_2B, H_3, H_4
- → in higher organisms, DNA is organised inside the nucleus.
- → double stranded DNA is wound twice over histones, it is called nucleosomes which condenses DNA & stabilizes it.
- → such long stretch of DNA in associat^n with histones form chromatin.
- → these chromatin condenses to form chromosome
- → DNA wraps twice around histone octomer to form one nucleosome.
- → all histones are present in equimolar conc except H_1.
- → histones are synthesized in the cytoplasm, then migrate to the nucleus.
- → After synthesis, undergo several covalent modificat^{ns}.

Covalent Modifications of Histone

- → phosphorylation of Serine & Threonine of H_1 - helps in condensat^n of chromatin to chromosomes.
- → phosphorylat^n of H_2B - associated with DNA replicat^n.
- → acetylat^n of serine & lysine - ↑es transcriptional activity of chromatin.

Super Coiling of DNA

- → an imp prop of DNA structs is supercoiling
- → during replicat^n, super coiling is removed by enzymes called topoisomerases.