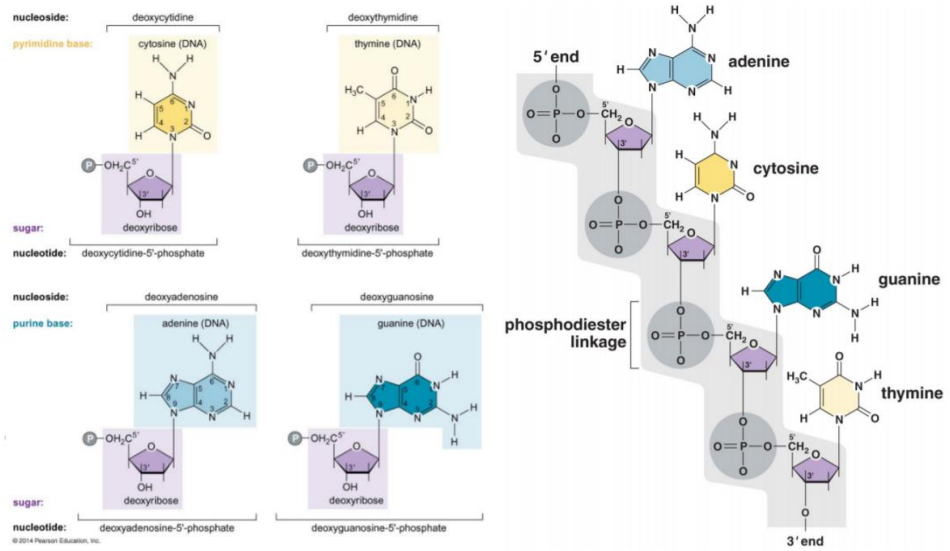
Lecture 1 – Compact Chromosome

Structure of DNA

DNA is a polymer made up of nucleotides: sugar, phosphate, base and are joined together by phosphodiester bonds. DNA is double stranded and nucleotides join together via hydrogen bonds to form base pairs.

- Purines have 2 rings and pairs with pyrimidine with 1 ring; adenine pairs with thymine and cytosine pairs with guanine. These base pairs are complementary and are 'Watson and Crick base pairs'.



DNA have directionality, characterised by 5' and 3' ends (used to distinguish different carbon numbers). The 5' end has a phosphate and 3' end has a hydroxyl. The two strands are anti-parallel (3'-5' and 5' to 3')

Compaction of DNA

Prokaryote: E.coli has one long DNA molecule that is 1.3mmin length, but bacteria only 1um in diameter (the DNA is 1000 times larger than the size of the cell they need to fit in), need to compact into the cell.

- In E.coli, DNA is organised into 50-100 domains/loops, each is independently supercoiled. RNA and protein contribute to folded structure (folded genome)

Eukaryote: Human cell has $6x10^9$ bp of DNA and each base pair has a thickness of 3.4A and the total length of DNA is 2m. Typical human nucleus had diameter 10-15um, need to fit all the DNA molecules into a small molecule.

- In eukaryotes, DNA packaging begins with formation of **nucleosome**, DNA wound around small proteins of **histone**, they have lots of lysine and arginine residues, making them very positively charged at PH7 → binds to negatively charged backbone of DNA.

Nucleosomes

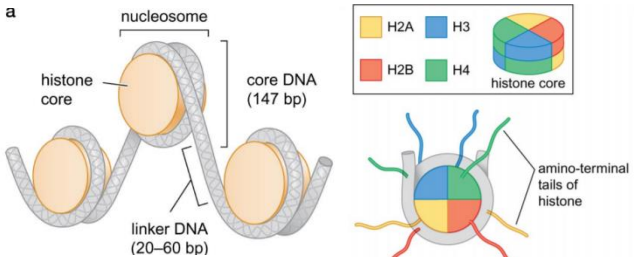
DNA in **eukaryotic** cells is packaged into nucleosomes. Each nucleosome is composed of **8 histone** proteins and DNA is wrapped around them.

- DNA between each nucleosome (the part that is not wrapped around histone) is the **linker DNA** (string in the beads on a string)
- After assembling into nucleosomes, DNA is compacted approximately **6 fold** but it needs to be further compacted
- DNA that is bound with histone is called **core DNA**, wound 1.65 times around the histone octamer.
- The length of DNA wrapped around histone (core DNA) is **constant 147bp** in all eukaryotic cells but length of linker DNA is variable; **20-60bp**.
- Regions of DNA not packaged into nucleosome are engaged in gene expression, replication or recombination.

Histones

Eukaryotic cells have five types of histones: H1, H2A, H2B, H3 and H4. Histone H2A, H2B, H3 and H4 are **core histones**

- Two copies (dimers) of each of H2A, H2B, H3 and H4 form the **protein core** (octamer). Histone H1 is not part of core, it binds to linker DNA and is the **linker histone**.
- Four core histones are present in equal amounts, H1 is half as abundant (only one molecule of H1 can associate with one nucleosome)
- Histone octamer (core) + DNA = nucleosome



Histone fold domain found in every core histone, it mediates assembly of histone only regions (without DNA, histones fold into intermediate forms in solution)

- Domains mediate formation of 'head to tail' **heterodimers** of pairs of histones.
- H3 and H4 histones form heterodimers first, and then form **tetramer** with two molecules of H3 and H4.
- H2A and H2B form heterodimers only, and do not form tetramers.