DNA Packaging

Reger Kornberg in 1974 reported that chromosome is made up of DNA and protein. The organization of DNA is much more complex in eukaryotes.

Each chromosome contains a single DNA molecule, extending from one end of the chromosome to the other end. DNA molecule is coiled and folded many times and associated with various proteins, forming a "**chromatin**" which contains roughly equal amounts of DNA and proteins. The chromosomal proteins are divided into **Histone** proteins and **Non-Histone** proteins.

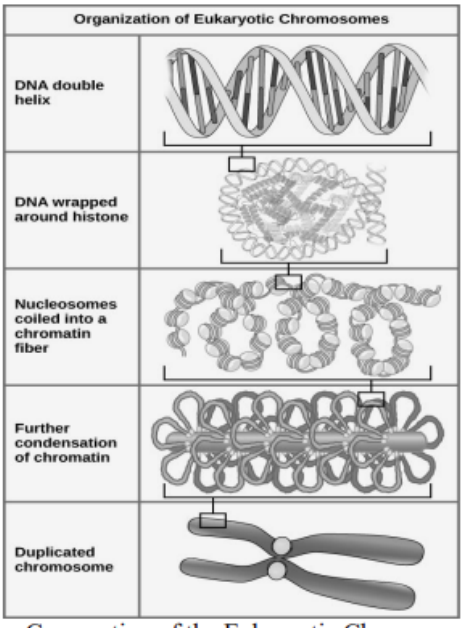


Fig: Compaction of the Eukaryotic Chromosome

Histones are the proteins that facilitate the DNA packaging into chromatin fibres. Histone proteins are positively charged and have many arginine and lysine amino acids that bind to the negatively charged DNA. Histones are of two types:

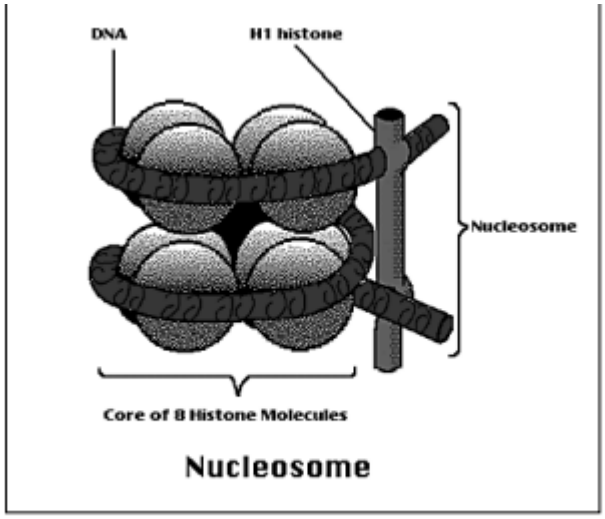
- Core Histones
- Linker Histones

H2A, H2B, H3 and H4 are the core histones. Two H3, H4 dimers and two H2A, H2B dimers form an octamer. Linker histones lock the DNA in place onto the nucleosome and can be removed for transcription. Histones can be modified to change the amount of packaging a DNA does. The addition of methyl group increases the hydrophobicity of histones. This results in tight DNA packaging. Acetylation and phosphorylation make the DNA more negatively charged and loosens the DNA packaging.

Non-histones are heterogeneous groups of structural and regulatory proteins with many functions found in the structure of chromatin and they present in a little amount, Non-histone proteins have many different functions because they contain : Structural proteins enter in the structure of some definite parts of DNA♣ molecule and play the main role in the spatial organization of DNA within the nucleus as they are responsible for shortening DNA about 100,000 times by forming the packed chromatin.

Regulatory proteins determine whether the DNA code will be used in making♣ RNA, proteins and enzymes or not.

Packaging of DNA: At the first level of packaging the DNA double helix is packaged into so-called nucleosomes: sets of about 200 base pairs of the DNA are wound round a nucleus of eight proteins, the histones. Due to their amino acid composition the histone proteins are positively charged, but they can be modified by enzymes, so that their total charges changes. Thus, a certain class of enzymes – histone acetyl transferases – cause acetyl moieties to be attached, thereby neutralizing the intrinsic charge of the histones. Another class of enzymes – histone deacetylases – can remove these acetyl moieties again and thereby restore the positive intrinsic charge of the histones. Since the components of the DNA – the nucleotides – are negatively charged, the charge state of the histones assumed to have considerable influence on the packaging density of the DNA in the chromatin.



DNA can be further packaged by forming coils of nucleosomes, called chromatin fibers. These fibers are condensed into chromosomes during mitosis, or the process of cell division. However, packaging of chromatin into chromosomes that we are most familiar with occurs only during a few stages of mitosis. Most of the time, DNA is loosely packaged. A DNA molecule in this form is about seven times shorter than the double helix without the histones, and the beads are about 10 nm in diameter, in contrast with the 2-nm diameter of a DNA double helix. The next level of compaction occurs as the nucleosomes and the linker DNA between them are coiled into a 30-nm chromatin fiber. This coiling further shortens the chromosome so that it is now about 50 times shorter than the extended form. In the third level of packing, a variety of fibrous proteins is used to pack the chromatin. These fibrous proteins also ensure that each chromosome in a non-dividing cell occupies a particular area of the nucleus that does not overlap with that of any other chromosome

DNA replicates in the S phase of interphase. After replication, the chromosomes are composed of two linked sister chromatids. When fully compact, the pairs of identically packed chromosomes are bound to each other by cohesion proteins. The connection between the sister chromatids is closest in a region called the centromere. The conjoined sister chromatids, with a diameter of about 1 µm, are visible under a light microscope. The centromeric region is highly condensed and thus will appear as a constricted area. Regions that are necessary for making proteins and are important for the cell are

loosely packed and called euchromatin. By having a loose packing of DNA in Paper –V, Cytology B.Sc. Part III euchromatin, proteins involved in transcription can easily get in and make RNA. On the other hand, some regions of DNA which are called heterochromatin and are tightly packed through DNA as well as through good ol' histone methylation.

Why is DNA Packaging required?

The length of the DNA is around 3 meters that need to be accommodated within the nucleus which is only a few micrometres in diameter. In order to fit in the DNA molecules into the nucleus, it needs to be packed into an extremely compressed and compact structure called chromatin. During the initial stages of DNA packaging, the DNA is reduced to an 11 nm fiber that denotes approximately 5-6 folds of compaction. This is achieved through a nucleosome order of packaging.

There are three orders of DNA packaging

1. The first order DNA packaging – Nucleosome.
2. The second order DNA packaging – Solenoid fibre
. 3. The third order DNA packaging – Scaffold loop Chromatids Chromosome.