MOLECULAR BASIS OF INHERITANCE
THE SEARCH FOR GENETIC MATERIAL

PACKAGING OF DNA

The average distance between the two adjacent base pairs of 0.34 nm (0.34×10^{-9} m or 3.4 Å).
Length of DNA for a human diploid cell is 6.6×10^9 bp $\times 0.34 \times 10^{-9}$ m/bp = 2.2 m.
The length is far greater than the dimension of a typical nucleus (approximately 10^{-6} m).

The number of base pairs in Escherichia coli is 4.6×10^6. The total length is 1.36 mm. The long sized DNA accommodated in small area (about 11.1m in E. coli) only through packing or compaction. DNA is acidic due to presence of large number of phosphate group. Compaction occurs by folding acid attachment of DNA with basic proteins, polyamine in prokaryotes and histone in eukaryotes.

DNA packaging in Prokaryotes : DNA is found in cytoplasm in supercoiled state. The coils are maintained by non histone basic protein like polyamines. This compact structure of DNA is called nucleoid or genophore.

DNA packaging in Eukaryotes : It is carried out with the help of lysine and ariginine rich basic proteins called histone. The unit of compaction is nucleosome. There are five types of histone proteins H_1 H_2A, H_2B. H_3 and H_4. Four of them occur in pairs to produce histone octamer (2 copies of each- H_2A, H_2B, H_3 and H_4, called nubody or core of nucleosome.

Their positively charged ends are directed outside. The negatively charged DNA is wrapped around the positively charged histone octamer to form a structure called nucleosome. A typical nucleosome contains 200 bp of DNA Helix. DNA present between two adjacent nucleosome is called linker DNA. It is attached to H_1 histone protein. Length of linker DNA varies from species to species.
Nucleosome chain gives a beads on string appearance under electron microscope. The nucleosomes furthers coils to form solenoid. It has diameter of 30 nm as found in chromatin. The beads on string structure in chromatin is packaged to form chromatin fibres that are further coiled and condensed at metaphase stage of cell division to form chromosomes. The packaging at higher level requires

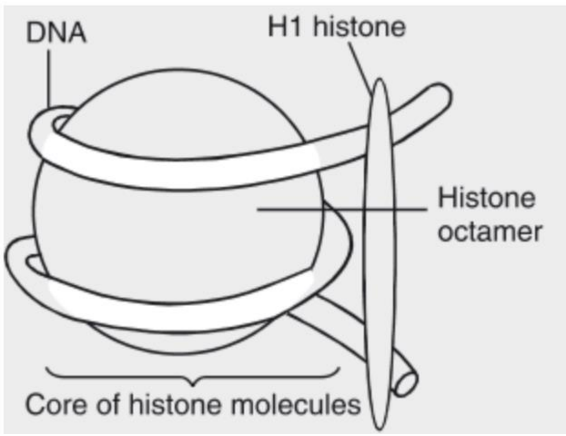
additional set of proteins (acidic) that collectively are referred to as non-histone chromosomal (NHC) proteins.

Non-Histone chromosomal proteins are of three types :

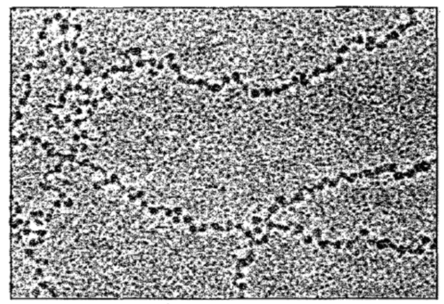
(i) Structural NHC protein

(ii) Functional NHC protein e.g., DNA polymerase, RNA polymerase

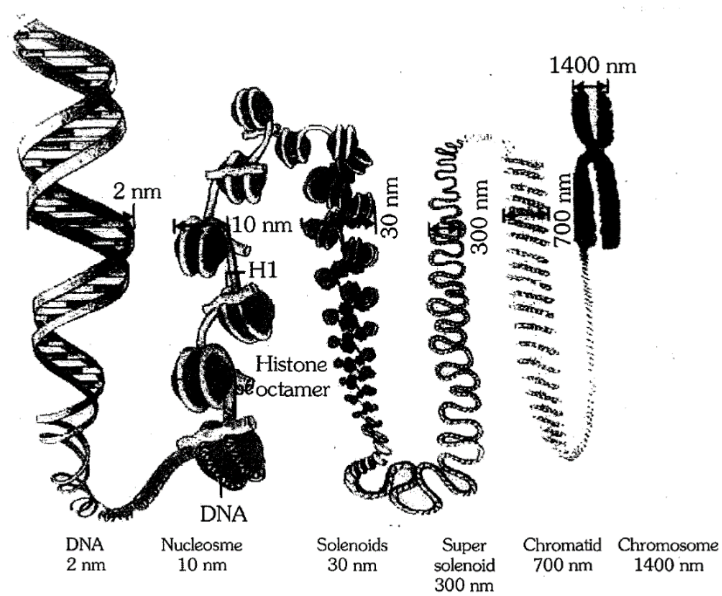
(iii) Regulatory NHC protein



Basic unit of DNA compaction (Nucleosome)



EM picture – ''Beads-on-string



Various steps in the folding and superfilding of basic chromatin components to generate an eukaryotic chromosome

In a typical nucleus, some region of chromatin are loosely packed (and stains light) and are referred to as enchromatin. The chromatin that is more densely packed and stains dark is called as heterochromatin, specifically euchromatin is said to be transcriptionally active and heterochromatin is transcriptionally inactive.

Properties of Genetic Material (DNA versus RNA)

It became an established fact that it is DNA that acts as genetic material. However, it subsequently became clear that in some viruses, RNA is the genetic material (for example, Tobacco Mosaic viruses, QB bacteriophage, etc.).

A molecule that can act as a genetic material must fulfill the following criteria:

(i) It should be able to generate its replica (Replication).
(ii) It should chemically and structurally be stable.
(iii) It should provide the scope for slow changes (mutation) that are required for evolution.
(iv) It should be able to express itself in the form of 'Mendelian Characters'.

If one examines each requirement one by one, because of rule of base pairing and complementarity, both the nucleic acids (DNA and RNA) have the ability to direct their duplications. The other molecules in the living system, such as proteins fail to fulfill first criteria itself. The genetic material should be stable enough not to change with different stages of life cycle, age or with change in physiology of the organism. Stability as one of the properties of genetic material was very evident in Griffith's 'transforming principle' itself that heat, which killed the bacteria, at least did not destroy some of the properties of genetic material. This now can easily be explained in light of the DNA that the two strands being complementary if separated by heating come together, when appropriate conditions are provided. Further, 2 '-OH group present at every nucleotide in RNA is a reactive group and makes RNA labile and easily degradable. RNA is also now known to be catalytic, hence reactive. Therefore, DNA chemically is less reactive and structurally more stable when compared to RNA. Therefore, among the two nucleic acids, the DNA is a better genetic material. In fact, the presence of thymine at the place of uracil also confers additional stability to DNA.

Both DNA and RNA are able to mutate. In fact, RNA being unstable, mutate at a faster rate. Consequently, viruses having RNA genome and having shorter life span mutate and evolve faster.

RNA can directly code for the synthesis of proteins, hence can easily express the characters. DNA, however, is dependent on RNA for synthesis of proteins. The protein synthesising machinery has evolved around RNA. The above discussion indicate that both RNA and DNA can function as genetic material, but DNA being more stable is preferred for storage of genetic information. For the transmission of genetic information, RNA is better.