CHROMOSOME: STRUCTURE, TYPES AND FUNCTIONS

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Chromosomes (chrom=colour, soma=body) are the rod shaped, dark stained bodies seen during the metaphase stage of mitosis when cells are stained with a suitable basic dye and viewed under a light microscope. Chromosomes were first described by Strasburger (1815), and the term 'chromosome' was first used by Waldeyer in 1888. Chromosomes are composed of thin chromatin threads called chromonemata which undergo coiling and super coiling during prophase so that the chromosomes become progressively thicker and smaller, and become readily observable under light microscope.

Chromosome Number:

The number of the chromosomes is constant for a particular species. Therefore, these are of great importance in the determination of the phylogeny and taxonomy of the species. The number or set of the chromosomes of the gametic cells such as sperms and ova is known as the gametic, reduced or haploid set of chromosomes. The haploid set of the chromosomes is also known as the genome. The somatic or body cells of most organisms contain two haploid set or genomes and are known as the diploid cells. The diploid cells achieve the diploid set of the chromosomes by the union of the haploid male and female gametes in the sexual reproduction. The number of chromosomes in each somatic cell is the same for all members of a given species. The organism with the lowest chromosome number is the nematode, *Ascaris megalocephalus univalens* which has only two chromosomes in the somatic cells (2n = 2). In the radiolarian protozoan *Aulacantha* is found a diploid number of approximately 1600 chromosomes. Among plants, chromosome number varies from 2n = 4 in *Haplopappus gracilis* (Compositae) to 2n=> 1200 in some pteridophytes. Chromosome number of few common animals and plants is given below:

Animals	**Chromosome Number**
1. *Paramecium aurelia*	30 – 40
2. *Hydra vulgaris*	32
3. *Ascaris lumbricoides*	24
4. *Musca domestica*	12
5. *Homo sapiens*	46
Plants	**Chromosome Number**
1. *Mucor* sp.	2
2. *Allium cepa*	16
3. *Aspergillus nidulans*	16

Autosomes and sex chromosomes: In a diploid cell there is two of each kind of chromosome termed as homologous chromosomes, except for the sex chromosomes. For example, in human, there are 23 pairs of homologous chromosomes (i.e., 2n = 46). The human male has 44 non-sex chromosomes, termed autosomes and one pair of heteromorphic or morphologically dissimilar sex chromosomes, i.e., one X chromosome and one Y chromosome. The human female has 44 non-sex chromosomes (autosomes) and one pair of homomorphic (morphologically similar) sex chromosomes designated as XX.

Morphology:

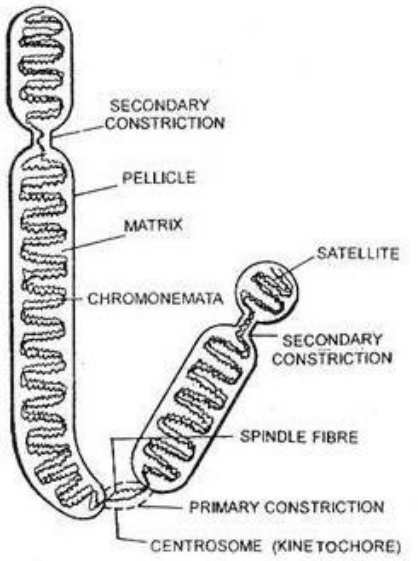
Chromosome morphology changes with the stage of cell division, and mitotic metaphase chromosomes are the most suitable for studies on chromosome morphology. In mitotic metaphase chromosomes, the following structural feature (except chromomere) can be see under light microscope:

(1) Chromatid,
(2) Chromonema,
(3) Chromomeres,
(4) Centromere
(5) Secondary constriction or Nucleolar organizer,
(6) Telomere and
(7) Satellite.

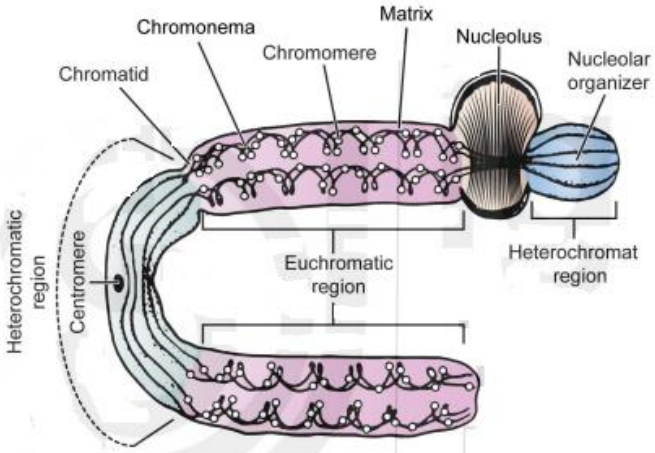
Structure and regions recognized in chromosomes: Structurally, each chromosome is differentiated into three parts: (a) Pellicle, (b) Matrix, (c) Chromonemata.

a) **Pellicle:** It is the outer envelope around the substance of chromosome. It is very thin and is formed of achromatic substances. Certain scientists Darlington (1935) and Ris (1940) have denied its presence.
b) **Matrix:** It is the ground substance of chromosome which contains the chromonemata. It is also formed of nongenic materials.
c) **Chromonema / Chromonemata:** A chromosome appears to consist of spirally coiled thin or filamentous long continuous structure called as chromonema (plural-chromonemata) during early prophase. It is present in the matrix. Chromonemata are the coiled filament in which genes are located and extend along the entire length of the chromosome. It represents chromatids in early stages of condensation. Therefore,

chromatids and chromonema are two names for the same structure i.e. single linear DNA molecule with its associated proteins. Embedded in the matrix of each chromosome are two identical, spirally coiled threads, the chromonemata. The two chromonemata are also tightly coiled together that they appear as single thread of about 800A thickness. Each chromonemata consists of about 8 micro fibrils, each of which is formed of a double helix of DNA.

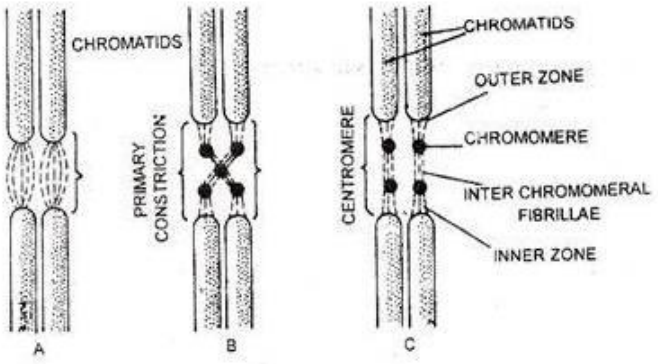


Structure of chromosome at anaphase stage of mitosis.



Detailed graphical representation of different parts of chromosome.

Chromomeres: A Chromomere is also known as an **idiomere.** These are small bead like structures formed by coiling of chromatin threads. Chromomere is able to synthesize greater amounts of nucleoprotein that's why it is of great size than adjacent portions of the chromonema. Chromomeres are observed when chromosomes are highly condensed. The chromomeres are present in the form of small dense masses that can be observed at regular intervals on the chromonemata. These are more distinct in the prophase stage when chromonemata are less coiled and most clearly visible during leptotene and zygotene stages of meiotic prophase. The thin and lightly stained parts between the adjacent chromosomes are termed as inter-chromomeres. The position of chromomeres on chromonemata is constant for a given chromosome. While pairing during zygotene of meiotic prophase the homologous chro- mosomes pair chromomere to chromomere. Chromomeres are regions of tightly folded DNA and are believed to correspond to the units of genetic function in the chromosomes.



Structure of centromere.

Chromatid: At mitotic metaphase each chromosome consists of two symmetrical structures called chromatids. Each chromatid contains a single DNA molecule. Both chromatids are attached to each other only by the centromere and become separated at the beginning of anaphase, when the sister chromatids of a chromosome migrate to the opposite poles.

Centromere: A part of the chromosome is recognised as permanent. It is a small structure in the chromonema and is marked by a constriction. At this point the two chromonemata are joined together. This is known as centromere or kinetochore or primary constriction. Its position is constant for a given type of chromosome and forms a feature of identification. In thin electron microscopic sections, the kinetochore shows a trilaminar structure, i.e., a 10 nm thick dense outer protein aceous layer, a middle layer of low density and a dense inner layer tightly bound to the centromere. The chromosomes are attached to spindle fibres at this region during cell division. The part of the chromosome which lies on either side of the centromere represents arms which may be equal or unequal depending upon the position of centromere.

Depending upon the number of centromeres, the chromosomes may be:

1. Monocentric with one centromere.
2. Dicentric with two centromeres.
3. Polycentric with more than two centromeres.
4. Acentric without centromere. Such chromosomes represent freshly broken segments of chromosomes which do not survive for long.
5. Diffused or non-located with indistinct centromere diffused throughout the length of chromosome.

Telomeres

It is the terminal or tip part of the chromosome. In most eukaryotic organisms, this region contains repetitive nucleotide sequences which protect the ends of chromosome. It also stabilizes

the ends and is extended by special mechanisms that bypass the difficulties of replicating the ends of linear DNA. Its name is derived from the Greek word telos which means "end" and meros meaning, "part". Most of the prokaryotes do not have telomere due to presence of circular chromosome.

Satellites

The terminal segment of a chromosome that is separated from the main body of the chromosome by a secondary constriction is known as Satellite. These are chromosomes that contain secondary constrictions that serve as identifying markers. In humans, chromosome number 13, 14, 15, 21 and 22 are examples of SAT chromosomes. These are acrocentric chromosome, which contain a segment that is separated from the main body of the chromosome by a secondary constriction. The secondary constrictions can be used as markers to identify these particular chromosomes as they are always constant in their positions.

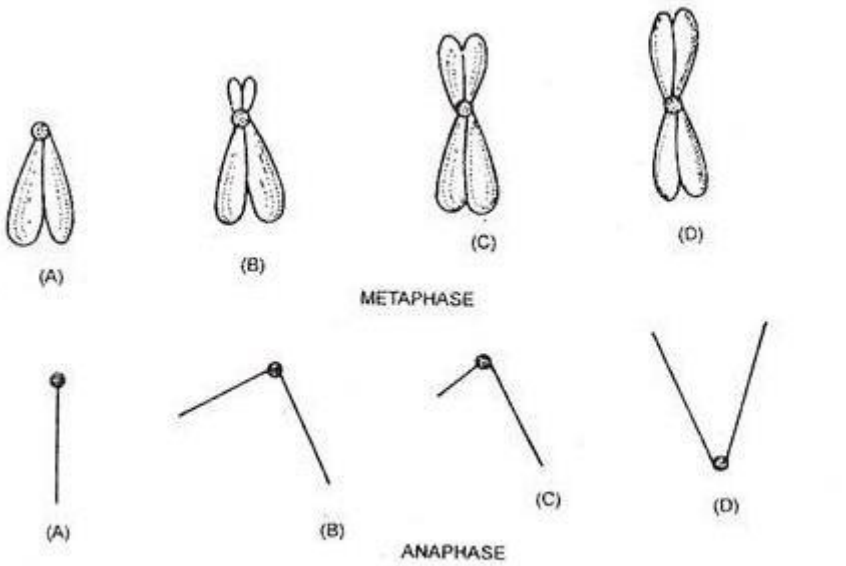
Matrix

Outer membrane of a chromosome is called pellicle, which is formed of achromatic substance. A jelly-like substance encloses this membrane, which is usually called matrix. Chromonemata is present in the matrix.

Depending upon the location of centromere the chromosomes are categorised into:

1. Telocentric are rod-shaped chromosomes with centromere occupying the terminal position, so that the chromosome has just one arm.
2. Acrocentric are also rod-shaped chromosomes with centromere occupying a sub-terminal position. One arm is very long and the other is very short.
3. Submetacentric chromosomes are with centromere slightly away from the mid-point so that the two arms are unequal.
4. Metacentric are V-shaped chromosomes in which centromere lies in the middle of chromosome so that the two arms are almost equal.

Centromere controls the orientation and movement of the chromosomes on the spindle. It is the point where force is exerted when the chromosomes move apart during anaphase.



Metaphase and anaphase configurations of the four classes of chromosomes : (A) Telocentric, (B) Acrocentric, (C) Submetacentric (D) Metacentric.

Secondary Constriction or Nucleolar Organiser: The chromosome besides having the primary constriction or the centromere possesses secondary constriction at any point of the chromosome. Constant in their position and extent, these constrictions are useful in identifying particular chromosomes in a set. Secondary constrictions can be distinguished from primary constriction or centromere, because chromosome bends only at the position of centromere during anaphase. The chromosome region distal to the secondary constriction i.e., the region between the secondary constriction and the nearest telomere is known as satellite. Therefore, chromosomes having secondary constrictions are called satellite chromosomes or sat-chromosomes. The number of sat-chromosomes in the genome varies from one species to the other. Nucleolus is always associated with the secondary constriction of sat-chromosomes. Therefore, secondary constrictions are also called nucleolus organiser region (NOR) and sat-chromosomes are often referred to as nucleolus organiser chromosomes. NOR of each sat-chromosome contains several hundred copies of the gene coding for ribosomal RNA (rRNA).

Telomeres: These are specialized ends of a chromosome which exhibits physiological differentiation and polarity. Each extremity of the chromosome due to its polarity prevents other chromosomal segments to be fused with it. The chromosomal ends are known as the telomeres. If a chromosome breaks, the broken ends can fuse with each other due to lack of telomeres.

Karyotype and Idiogram: A group of plants and animals comprising a species is characterized by a set of chromosomes, which have certain constant features such as chromosome number, size and shape of individual chromosomes. The term karyotype has been given to the group of

characteristics that identifies a particular set of chromosomes. A diagrammatic representation of a karyotype of a species is called idiogram. Generally, in an idiogram, the chromosomes of a haploid set of an organism are ordered in a series of decreasing size.

Uses of Karyotypes:

1. The karyotypes of different groups are sometimes compared and similarities in karyotypes are presumed to present evolutionary relationship.
2. Karyotype also suggests primitive or advanced feature of an organism. A karyotype showing large differences between smallest and largest chromosome of the set and having fewer metacentric chromosomes, is called asymmetric karyotype, which is considered to be a relatively advanced feature when compared with symmetric karyotype which has all metacentric chromosomes of the same size. Flowering plants there is a prominent trend towards asymmetric karyotypes.

Material of the Chromosomes:

The material of the chromosomes is the chromtin. Depending on their staining properties with basic dyes (particularly the Feulgen reagent), the following two types of chromatin may be distinguished in the interphase nucleus.

1. **Euchromatin:** Portions of chromosomes that stain lightly are only partially condensed; this chromatin is termed euchromatin. It represents most of the chromatin that disperse after mitosis has been completed. Euchromatin contains structural genes which replicate and transcribe during G_1 and S phase of interphase. It is considered genetically active chromatin, since it has a role in the phenotype expression of the genes. In euchromatin, DNA is found packed in 3 to 8 nm fibre.
2. **Heterochromatin:** In the dark-staining regions, the chromatin remains in the condensed state and is called heterochromatin. The regions of the chromosome that remains condensed during interphase and early prophase and form the so-called chromocentre. Heterochromatin is characterized by its especially high content of repetitive DNA sequences and contains very few, if any, structural genes. It is late replicating (i.e., it is replicated when the bulk of DNA has already been replicated) and is not transcribed. It is thought that in heterochromatin the DNA is tightly packed in the 30 nm fibre. It is established now that genes in heterochromatic region are inactive. During early and mid-prophase stages, the heterochromatic regions are constituted into three structures namely chromomeres, centromeres and knobs. Chromomeres may not represent true

heterochromatin since they are transcribed. Centromeric regions invariably contain heterochromatin; in salivary glands, these regions of all the chromosomes fuse to form a large heterochromatic mass called chromocentre. Knobs are spherical heterochromatin bodies, usually several times the diameter of the concerned chromosomes, present in certain chromosomes of some species, e.g. Maize; knobs are more clearly observable during pachytene stage in maize. Where present, knobs serve as valuable chromosome markers. Heterochromatin is classified into two groups: (i) Constitutive and (it) Facultative.

(i) Constitutive heterochromatin remains permanently in the heterochromatic state, i.e., it does not revert to euchromatic state, e.g., centromeric regions. It contains short repeated sequences of DNA, called satellite DNA.

(ii) Facultative heterochromatin is essentially euchromatin that has undergone heterochromatinization which may involve a segment of chromosome, a whole chromosome (e.g. one X chromosome of human females and females of other mammals), or one whole haploid set of chromosomes (e.g., in some insects, such as mealy bugs).

Chemical Composition:

Chromatin is composed of DNA, RNA and protein. The protein of chromatin is of two types: the histones and the non-histones. Purified chromatin isolated from interphase nuclei consists of about 30-40% DNA, 50-65% protein and 0.5-10% RNA: but there is a considerable variation due to species and tissues of the same species.

DNA: The amount of DNA present in normal somatic cells of a species is constant for that species; any variation in DNA from this value is strictly correlated with a corresponding variation at the chromosome level. Gametes of a species contain only half of the amount of DNA present in its somatic cells. The amount of DNA present in somatic cells also depends on the phase of cell cycle.

Protein: Proteins associated with chromosomes may be classified into two broad groups: (/) basic proteins or histones and (ii) non-histone proteins. Histones constitute about 80% of the total chromosomal protein; they are present in an almost 1:1 ratio with DNA (weight/weight). Their molecular weight ranges from 10,000-30,000 and they are completely devoid of tryptophan. Histones are a highly heterogenous class of proteins separable in 5 different fractions designated as H_1 H_2a, H_2b, H_3 and H_4. Fraction H_1 is lysin-rich, H_2a and H_2b are slightly lysine rich, while H_3 and H_4 are arginine-rich. These five fractions are present in all cell types of

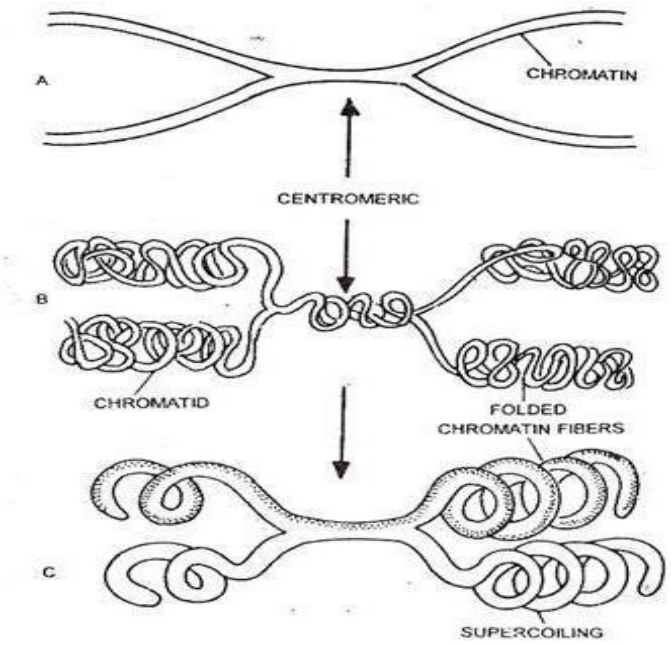
eukaryotes, except in the sperm of some animal species where they are replaced by another class of smaller molecule basic proteins called protamines. Histones play a primary function in chromosome organisation where H_2a, H_2b, H_3 and H_4 are involved in the structural organization of chromatin fibres, while fraction H_1 holds together the folded chromatin fibres of chromosomes. Non-histone proteins make up about 20% of the total chromosome mass, but their amount is variable and there is no definite ratio between the amounts of DNA and non-histones present in chromosomes. There may be 12 to more than 20 different types of non-histone proteins which show variation from one species to the other and even in different tissues of the same organism. This class of proteins includes many important enzymes, such as DNA and RNA polymerases etc.

Ultrastructure of Chromosomes:

Electron microscopic studies have demonstrated that chromosomes have very fine fibrils having a thickness of 2nm-4nm. Since DNA is 2 nm wide, there is possibility that a single fibril corresponds to a single DNA molecule. Several models of chromosome structure have been proposed from time to time based on various types of data on chromosomes.

Folded Fibre Model of Chromosomes:

This model was proposed by Du Praw in 1965 and is widely accepted. According to this model, chromosomes are made up of chromatin fibres of about 230A° diameter. Each chromatin fibre contains only one DNA double helix which is in a coiled state; this DNA coil is coated with histone and non-histone proteins. Thus the 230A° chromatin fibre is produced by coiling of a single DNA double helix, the coils of which are stabilized by proteins and divalent cations (Ca^{++} and Mg^{++}). Each chromatid contains a single long chromatin fibres; the DNA of this fibre replicates during interphase producing two sister chromatin fibres, it remains unreplicated in the centromeric region so that the two sister fibres remain joined in the region. Subsequently, the chromatin fibre undergoes replication in the centromeric region as well so that the sister chromatin fibre are separated in this region also. During cell division the two sister chromatin fibres undergo extensive folding separately in an irregular manner to give rise to two sister chromatids. Folding of the chromatin fibres drastically reduces their length and increases their stainability and thickness. This folded structure normally undergoes supercoiling which further increases the thickness of chromosomes and reduces the length. Most of the available evidence supports this model. Each chromatid contains a single giant DNA molecule. The strongest evidence in the support of the unineme model (single stranded chromatid) is provided by studies on lamp-brush chromosomes.



The folded-fibre model of chromosome organisation. Each chromatin fibre consists of one DNA molecule and has the average diameter of 230A°. This model is widely accepted.

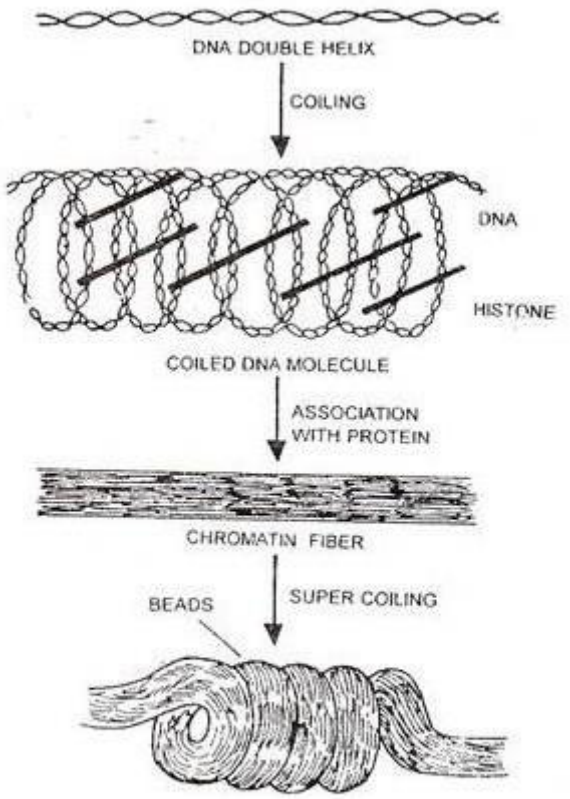
Organization of Chromatin Fibres:

Any model of chromatin fibre structure has to account for (i) packaging of a very long DNA molecule into a unit length of fibre; (ii) production of very thick (230-300A^0) fibres from very thin (20A°) DNA molecules and (iii) the beads-on-a-string ultrastructure of chromatin fibres observed particularly during replication. Two clearly different models of chromatin fibre structure have been proposed:

1. **Coiled DNA Model:** This is the simplest model of chromatin fibre organization and was given by Du Praw. According to this model, the single DNA molecule of a chromatin fibre is coiled in a manner similar to the wire in a spring; the coils being held together by histone bridges produced by binding histone molecules in the large groove of DNA molecules. Such a coiled structure that would be stabilized as a single histone molecule would bind to several coils of DNA. This coiled structure is coated with chromosomal proteins to yield the basic structure of chromatin fibres (type A fibre) which may undergo supercoiling to produce the type B fibre of DuPraw which is akin to the beads seen in electron micrographs of chromatin fibres.
2. **Nucleosome-Solenoid Model:** This model was proposed by Romberg and Thomas (1974) and is the most widely accepted. According to this model, chromatin is composed of a repeating unit called nucleosome. Nucleosomes are the fundamental packing unit particles of the chromatin and give chromatin a “beads-on-a string” appearance in electron micrographs that unfold higher-order packing (Olins and Olins, 1974). One

complete nucleosome consists of a nucleosome core, linker DNA, an average of one molecule of H_1 histone and other associated chromosomal proteins.

Nucleosome Core: It consists of a histone octamer composed of two molecules, each of histones H_2a, H_2b,H_3 and H_4. In addition, a 146 bp long DNA molecule is wound round this histone octamer in 13/4 turns; this segment of DNA is nuclease resistant.



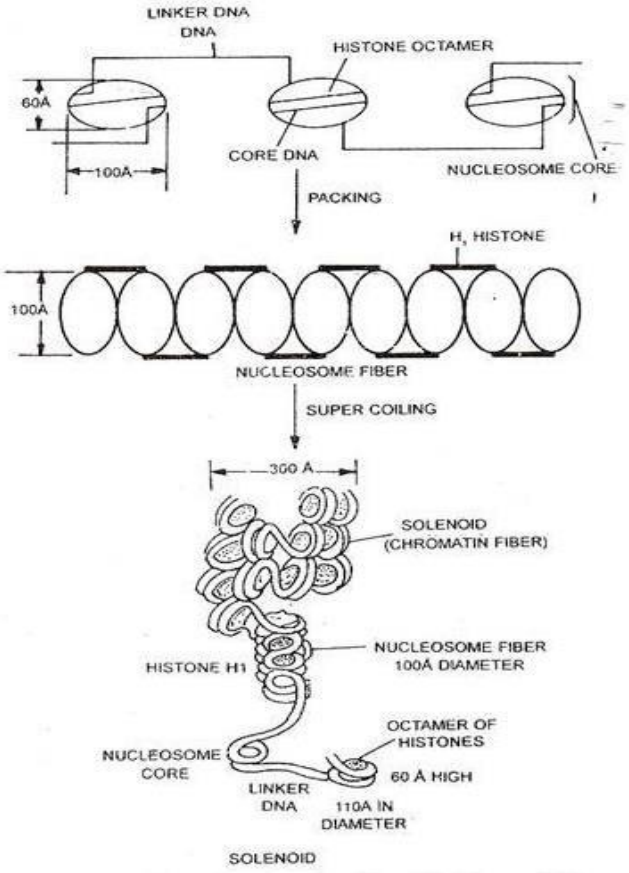
The coiled DNA model of chromatin fibre organisation. This fibre may undergo supercoiling to give rise to the beads seen in chromatin fibres.

Linker DNA: Its size varies from 8bp to 114 bp depending on the species. This DNA forms the string part of the beads-on-a string chromatin fibre, and is nuclease susceptible; and the beads are due to nucleosome cores. Thus, linker DNA joins two neighbouring nucleosomes.

H_1 Histone: Each nucleosome contains, on an average, one molecule of HI histone, although its uniform distribution throughout the length of chromatin fibres is not clearly know. Some studies suggest that the molecules of H1 histone are involved in stabilizing the supercoils of nucleosome chromatin fibres. Other studies suggest that HI is associated on the outside of each nucleosome core, and that one H1 molecule stabilizes about 166 bp long DNA molecule.

Other Chromosomal Proteins: Both linker DNA and nucleosome are associated with other

chromosomal proteins. In native chromatin, the beads are about 110A° in diameter, 60A° high and ellipsoidal in shape. Each bead corresponds to a single nucleosome core. Under some conditions, nucleosomes pack together without any linker DNA, which produces the 100A° thick chromatin fibre called nucleosome fibre which may then supercoil to give rise to the 300A° chromatin fibre called solenoid. The nucleosome model of chromatin fibre structure is consistent with almost all of the evidence accumulated so far.



The nucleosome-solenoid model of chromatin fibre organisation. (The model is widely accepted).

In chromosome structure, histones are positively charged proteins that act as spools, around which negatively charged DNA wraps to form nucleosomes, the basic unit of chromatin packaging. Non-histone proteins (NHPs) are a diverse group of proteins that associate with chromatin and are involved in DNA replication, gene expression regulation, DNA repair, and the higher-order organization of DNA into chromosomes. Together, histones and non-histones compact DNA into the tightly organized structure of a chromosome.

Histone Proteins

- **Role**:

Histones are primarily responsible for the structural packaging and organization of DNA into chromatin.

- **Mechanism**:

  They are positively charged and bind to the negatively charged DNA backbone, forming nucleosomes.

- **Types**:

  The five main types are H1 (or H5), H2A, H2B, H3, and H4.

- **Function**:

  They help protect DNA from damage and allow for the compaction of DNA into higher-order structures within the nucleus.

Non-Histone Proteins (NHPs)

- **Role**:

  NHPs have a wide range of functional roles in a chromosome, including regulation of gene expression, DNA repair, and structural organization beyond the nucleosome level.

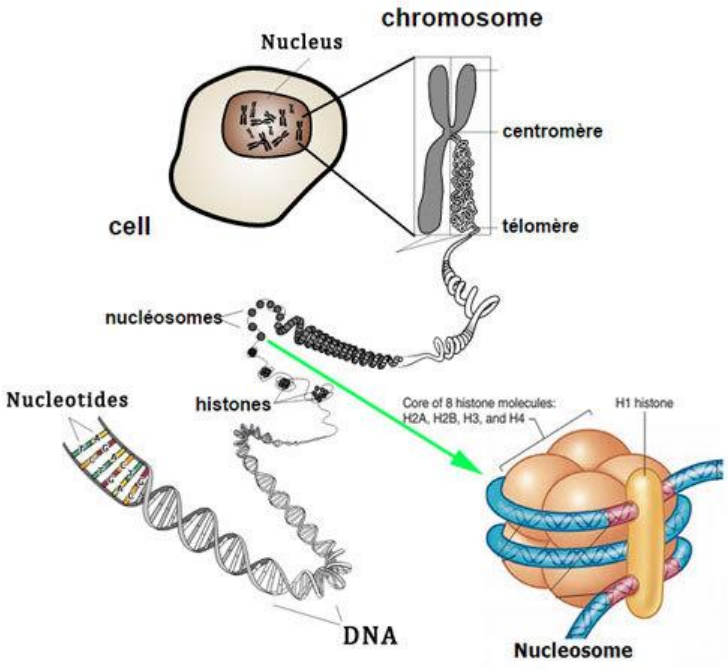
- **Diversity**:

  This is a very diverse group, encompassing scaffold proteins, DNA polymerases, heterochromatin protein 1, and Polycomb proteins, among others.

- **Function**:

  NHPs facilitate processes such as:

- **DNA Replication**: Proteins like DNA polymerase are involved in replicating DNA.
- **Gene Regulation**: Specific NHPs can control the expression of specific genes.
- **Chromatin Remodeling**: Some NHPs, like Polycomb, help remodel chromatin structure.
- **Higher-Order Structure**: Other NHPs contribute to the folding and compression of chromatin fibers into a complete chromosome.



Functions of Chromosomes:

The role of chromosomes in heredity was suggested independently by Sutton and Bover in 1902. This and various other functions of chromosomes may be summarised as under.

1. It is universally accepted that DNA is the genetic material, and that in eukaryotes almost all the DNA is present in chromosomes. Thus, the most important function of chromosomes is to provide the genetic information for various cellular functions essential for growth, survival, development, reproduction, etc., of organisms.
2. Another very important function of chromosomes is to protect the genetic material (DNA) from being damaged during cell division. Chromosomes are coated with histones and other proteins which protect it from both chemical (e.g., enzymes) and physical forces.
3. The properties of chromosomes ensure a precise distribution of DNA (genetic material) to the daughter nuclei during cell division. Centromeres of chromosomes perform an important function in chromosome movements during cell division which is due to the contraction of spindle fibres attached to the centromeric regions of chromosomes.
4. Gene action in eukaryotes is believed to be regulated through histone and non-histone proteins associated with chromosomes.