The structure of a chromosome

DEFINITION OF CHROMOSOME:

- **German biologist Walter Flemming in the early 1880s revealed** that during cell division the nuclear material organize themselves into visible thread like structures which were named as chromosomes which stains deep with basic dyes.

- **Chrome** is coloured and **soma** is body, hence they mean "**colored bodies**" and can be defined as higher order organized arrangement of DNA and proteins. It contains many genes or the hereditary units, regulatory elements and other nucleotide sequences.

- **Chromosomes** also contain DNA-bound proteins, which serve in packaging the DNA and control its functions.
- **Chromosomes** vary both in number and structure among organisms and the number of chromosomes is characteristic of every species.

- Benden and Bovery in 1887 reported that the number of chromosomes in each species is constant. W.S. Sutton and T. Boveri in 1902 suggested that chromosomes are the physical structures which acted as messengers of heredity.

- **Chromosomes** are tightly coiled DNA around basic histone proteins, which help in the tight packing of DNA.
- During interphase, the DNA is not tightly coiled into chromosomes, but exists as chromatin.

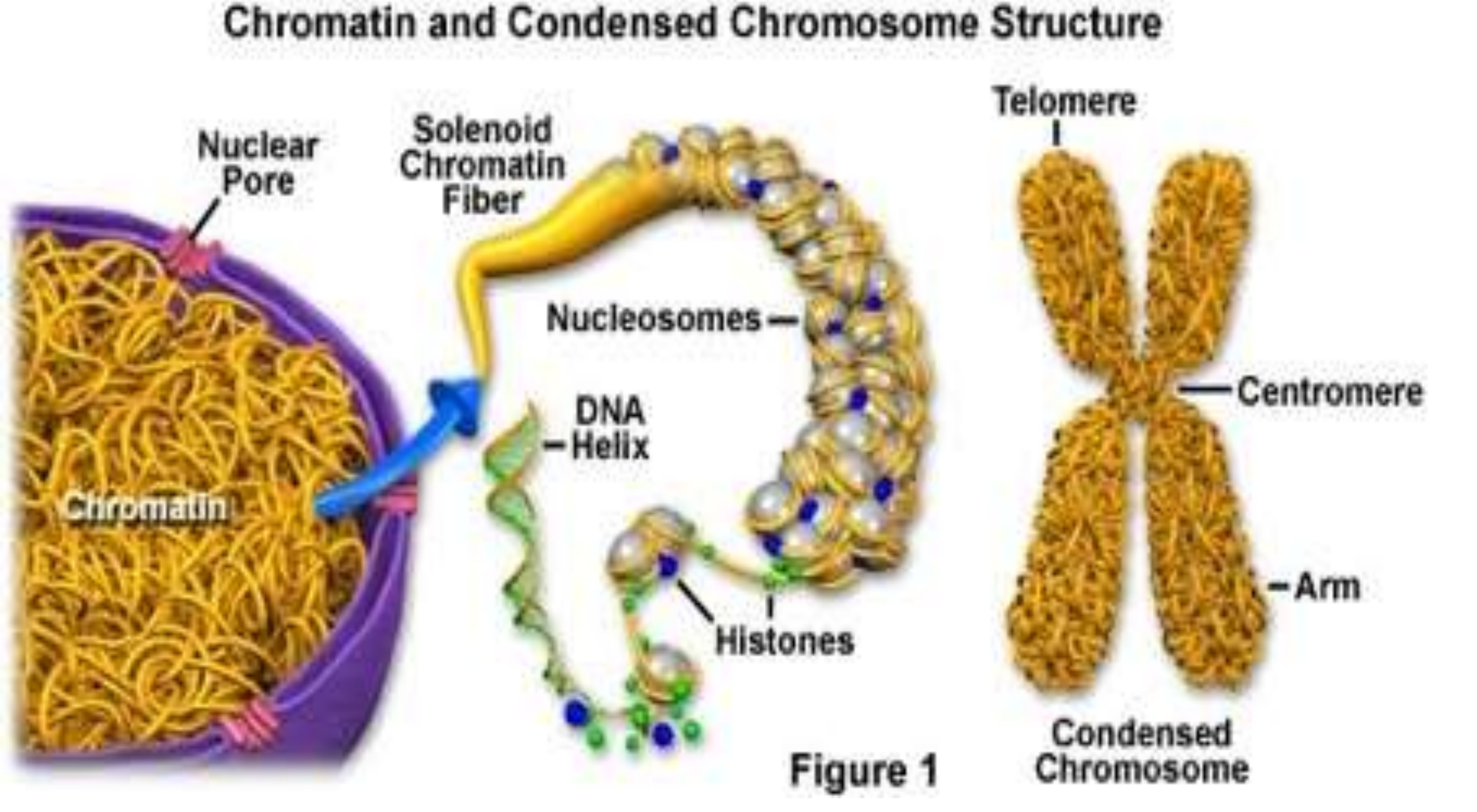
CHEMICAL STRUCTURE

Chemically the chromosomes are made of proteins and nucleic acids.

PROTEINS It is mainly Protamines, Histones and smaller amount of acidic proteins.

NUCLEIC ACIDS It is de-oxy ribose Nucleic Acids (DNA). Genes are nothing but the segments of DNA.

- In eukaryotes to fit the entire length of DNA in the nucleus it **undergoes condensation** and the degree to which DNA is condensed is expressed as its **packing ratio** which is the **length of DNA divided** by the **length into which it is packaged into chromatin** along with proteins.


Chromatin and Condensed Chromosome Structure
Nuclear Pore
Solenoid Chromatin Fiber
Telomere
Nucleosomes
Centromere
DNA Helix
Chromatin
Histones
Arm
Condensed Chromosome
Figure 1

Morphology:

- **Size:** The size of chromosome is normally measured at mitotic metaphase and may be as short as 0.25µm in fungi and birds to as long as 30 µm in some plants such as Trillium.
- However, most mitotic chromosome falls in the range of 3µm in Drosophila to 5µm in man and 8-12µm in maize.
- The monocots contain large sized chromosomes as compared to dicots. Organisms with less number of chromosomes contain comparatively large sized chromosomes. The chromosomes in set vary in size.

- **Shape:**
- The shape of the chromosome changes from phase to phase in the continuous process of cell growth and cell division.
- During the resting/interphase stage of the cell, the chromosomes occur in the form of thin, coiled, elastic and contractile, thread like stainable structures, the chromatin threads. In the metaphase and the anaphase, the chromosome becomes thick and filamentous.

- Each chromosome contains a clear zone, known as **centromere** or kinetochore, along their length.
- The centromere divides the chromosome into two parts and each part is called **chromosome arm.**

- The position of centromere varies from chromosome to chromosome providing it a different shape. They could be **telocentric** (centromere on the proximal end of the chromosome), **acrocentric** (centromere at one end giving it a very short and another long arm), **submetacentric** (J or L shaped chromosome with the centromere near the centre), **metacentric** (v shaped with centromere at the centre).

Structure of Chromosome:

- A chromosome at mitotic metaphase consists of two symmetrical structures called **chromatids.**
- Each chromatid contains a single DNA molecule and both chromatids are attached to each other by **centromere** and become separated at the beginning of anaphase.
- **The chromomeres** are bead like accumulations of chromatin material that are sometimes visible along interphase chromosomes.

- **The chromomere** bearing chromatin has an appearance of a necklace in which several beads occur on a string.
- **Chromomeres** are regions of tightly folded DNA and become especially prominent in polytene chromosomes.

- **Centromere** in a chromosome contain specific DNA sequences with special proteins bound to them, forming a disc shaped structure, called **kinetochore.**
- In electron microscope the kinetochore appears as a plate or cup like disc, 0.20-0.25 nm, in diameter situated upon the primary constriction **or centromere.**
- The chromosomes of most organisms contain only one centromere and are known **as monocentric chromosomes.**

Centromeres:

Centromeres are those condensed regions within the chromosome that are responsible for the accurate segregation of the replicated chromosome during mitosis and meiosis.

When chromosomes are stained they typically show a dark-stained region that is the centromere. The actual location where the attachments of spindle fibres occur is called the **kinetochore** and is composed of both DNA and protein.

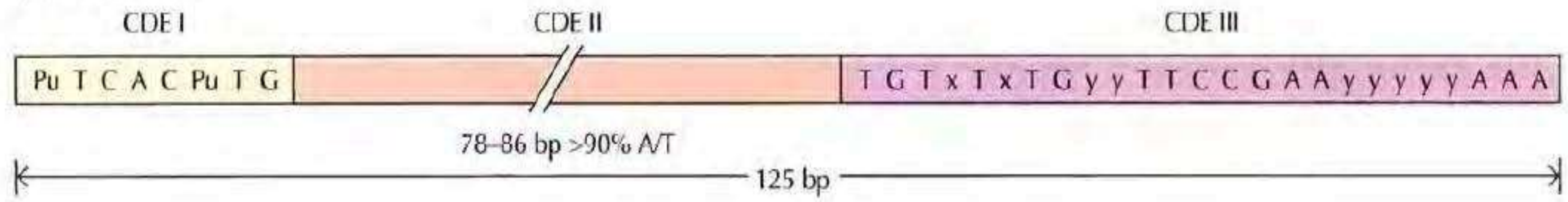
The DNA sequence within these regions is called ***CEN* DNA**. Because *CEN* DNA can be moved from one chromosome to another and still provide the chromosome with the ability to segregate, these sequences must not provide any other function.

Typically CEN DNA is about 120 base pairs long and consists of several sub-domains, CDE-I, CDE-II and CDE-III .

Mutations in the first two sub-domains have no effect upon segregation, but a point mutation in the CDE-III sub-domain completely eliminates the ability of the centromere to function during chromosome segregation.

Therefore CDE-III must be actively involved in the binding of the spindle fibers to the centromere.

The protein component of the kinetochore is only now being characterized. A complex of three proteins called Cbf- III binds to normal CDE-III regions but cannot bind to a CDE-III region with a point mutation that prevents mitotic segregation. Furthermore, mutants of the genes encoding the Cbf-III proteins also eliminates the ability for chromosomes to segregate during mitosis. Additional analyses of the DNA and protein components of the centromere are necessary to fully understand the mechanics of chromosome segregation.



- Some species have diffused centromeres, with microtubules attached along the length of the chromosomes and are termed **holocentric chromosomes.** Chromosomes of *Ascaris megalocephala* are examples of **diffused centromeric chromosomes.**

Figure 10-11a The Biology of Cancer (© Garland Science 2007)

Telomere

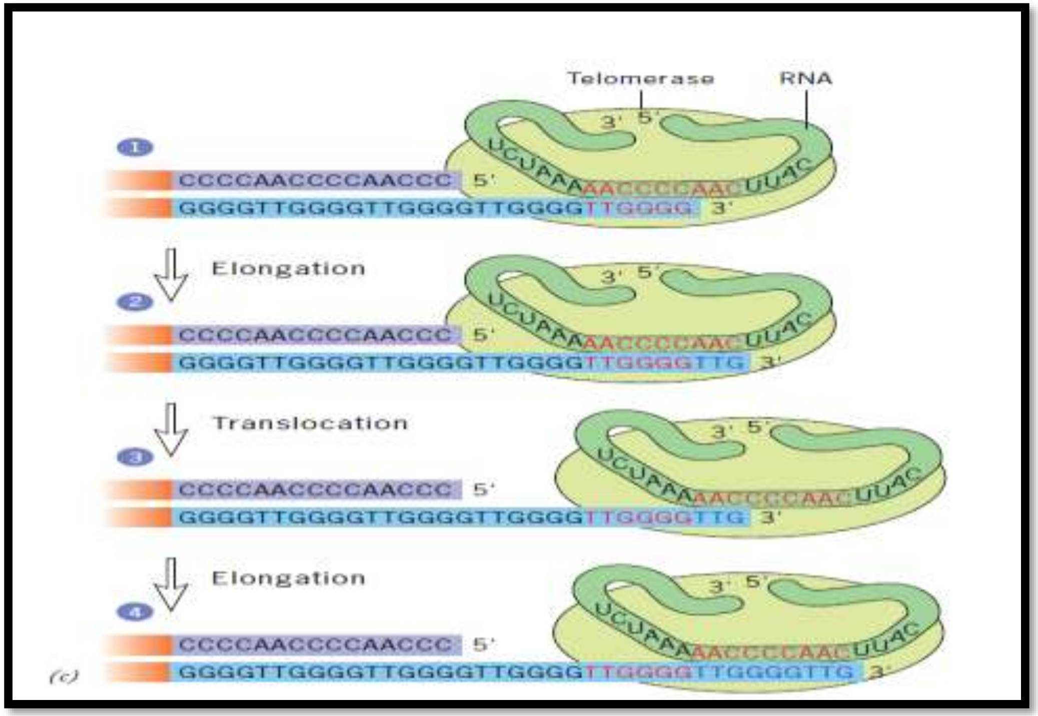
Telomeres are "caps" at the end of the chromosome formed by **repetitive DNA sequences that:**

- Prevent fusions of chromosomes with each others
- Stabilize chromosomes structures

- Certain bacteria possess telomeres in their linear genetic material which are of two types; one of the types **is called a hairpin telomere**. As its name implies, the telomeres bend around from the end of one DNA strand to the end of the complimentary strand. The other type of telomere is known as **an invertron telomere.** This type acts to allow an overlap between the ends of the complimentary DNA strands.
-

Telomere replication:

- Telomere replication is an important aspect in DNA replication. The primary difficulty with telomeres is the replication of the lagging strand.
- Because DNA synthesis requires a RNA template (that provides the free 3'-OH group) to prime DNA replication, and this template is eventually degraded, a short single-stranded region would be left at the end of the chromosome.
- This region would be susceptible to enzymes that degrade single-stranded DNA. The result would be that the length of the chromosome would be shortened after each division. This is known as the end replication problem which is not observed. The action of the telomerase enzymes ensure that the ends of the lagging strands are replicated correctly.



- Telomerase replication. Telomerase contains an RNA primer that is complementary to the end of the G-rich strand, which extends past the C-rich strand. The telomerase RNA binds to the protruding end of the G-rich strand in step 1 and then serves as a template for the addition of nucleotides onto the 3’ terminus of the strand in step 2. After a segment of DNA is synthesized, the telomerase RNA slides to the new end of the strand being elongated in step 3 and serves as the template for the incorporation of additional nucleotides in step 4. The gap in the complementary strand is filled by the replication enzymes polymerase α-primase. This figure has been adapted from Cell and Molecular Biology Concepts and Experiments by Karp,
- 2010.

- Telomerase activity is retained in germ cells and zygote and somatic cells after few cell division cycles do not show such activities because otherwise they would divide indefinitely and lead to cancer. Thus telomeres shrink causing chromosome shortening to a critical point when the cell ceases to grow and divide. An inherited disease called the Werner’s syndrome that causes patients to age much more rapidly than normal is characterized by abnormal telomere maintenance.

- Besides the primary constrictions or **centromeres,** chromosomes also posses secondary constriction at any point of the chromosome and are constant in their position and extent.

- **These constrictions are** helpful in identifying particular chromosomes in a set.
- Chromosomes also contain nucleolar organizers which are **certain secondary constrictions** that contain the genes coding for 5.8S, 18S and 28S ribosomal RNA and induce the formation of nucleoli.

- Sometimes the chromosomes **bear round, elongated or knob like appendages** known as **satellites.**
- The satellite remains connected with the rest of the chromosomes by a thin chromatin filament.

Chromosome structure

short arm **= p**

Centomere

long arm = **q**

Telomere

- **Each chromosome has a p and q arm; p** (petit) is the short arm and **q** (next letter in the alphabet) is the long arm.
- Some of the chromosomes like 13, 14, and 15 **have very small p arms**. When a karyotype is made, the q arm is always put on the bottom and the p on the top. The arms are separated by a region known as the centromere which is a pinched area of the chromosome.

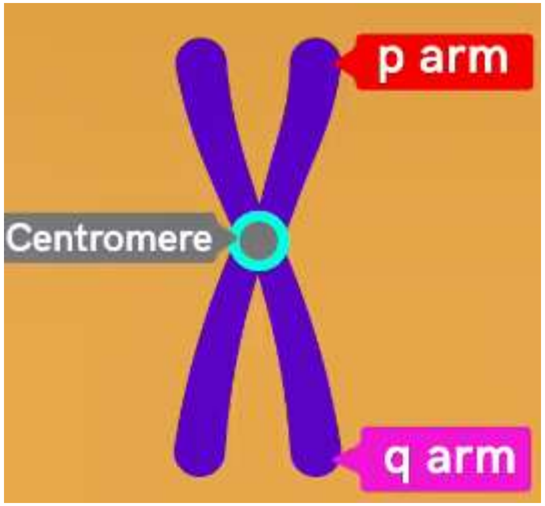
Internal structure of chromosome:

Chromosomes in eukaryotes are composed of chromatin fiber. Chromatin fiber is made of nucleosomes (histone octamers with part of a DNA strand attached to and wrapped around it). Chromatin fibers are packaged by proteins into a condensed structure called chromatin. Chromatin contains the vast majority of DNA and a small amount inherited maternally, can be found in the mitochondria. Chromatin is present in most cells, with a few exceptions, for example, red blood cells.

Chromatin allows the very long DNA molecules to fit into the cell nucleus. Chromosomes may exist as either duplicated or unduplicated. Unduplicated chromosomes are single double helixes, whereas duplicated chromosomes contain two identical copies (called chromatids or sister chromatids) joined by a centromere

External structure:

Each chromosome has a constriction point called the centromere, which divides the chromosome into two sections, or “arms.” The short arm of the chromosome is labeled the “p arm.” The long arm of the chromosome is labeled the “q arm.” The location of the centromere on each chromosome gives the chromosome its characteristic shape, and can be used to help describe the location of specific genes.



❖ Chromosomes in prokaryotes and eukaryotes

prokaryotic chromosome	Eukaryotic chromosome
The typical chromosome formation is absent	The genetic material is organised as distinct structural entities
Only single chromosome per cell	Always two to many chromosomes per cell
Is comparatively shorter	Larger than that of prokaryotes
Contains a covalently closed circular DNA	Contains linear DNA with 2 ends
Chromosomes codes for few proteins	Codes for a large number of proteins
Free in the centre of the cell and not covered by the nucleus	Are always enclosed in the nucleus
Stay in direct contact with the cytoplasm	Separated from the cytoplasm by the nuclear membrane
Sometimes associated with the mesosomes of the plasma membrane	Cannot be associated with the plasma membrane
DNA is not associated with histone proteins	DNA is associated with histone proteins

Nucleosomes are not formed	Association of DNA with histone produces nucleosomes
Contains a single origin of replication	Contains many origins of replications
The negative charge is nullified by Mg ions	The negative charge is nullified by histone protein
Centromere, kinetochore, chromosomal arms are not formed	Centromere, kinetochore, chromosomal arms are formed

Chromatin:

Chemical composition of chromatin

Chromatin consists of DNA, RNA and protein. The protein of chromatin could be of two types: histones and non histones.

DNA: DNA is the most important chemical component of chromatin, since it plays central role of controlling heredity and is most conveniently measured in picograms. In addition to describing the genome of an organism by its number of chromosomes, it is also described by the amount of DNA in a haploid cell.

Histones:

Histones are basic proteins as they are enriched with basic proteins arginine and lysine. At physiological pH they are cationic and can interact with anionic nucleic acids.

They form a highly condensed structure. The histones are of five types called **H1, H2A H2B, H3, and H4-which** are very similar among different species of eukaryotes and have been highly conserved during evolution.

H1 is the least conserved among all and is also loosely bound with DNA.

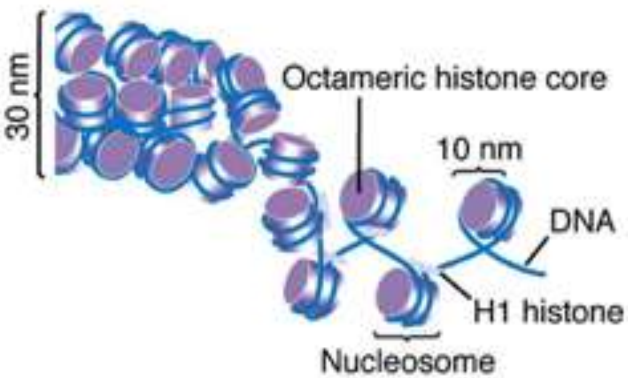
H1 histone is absent in *Sacharomyces cerevisiae*.

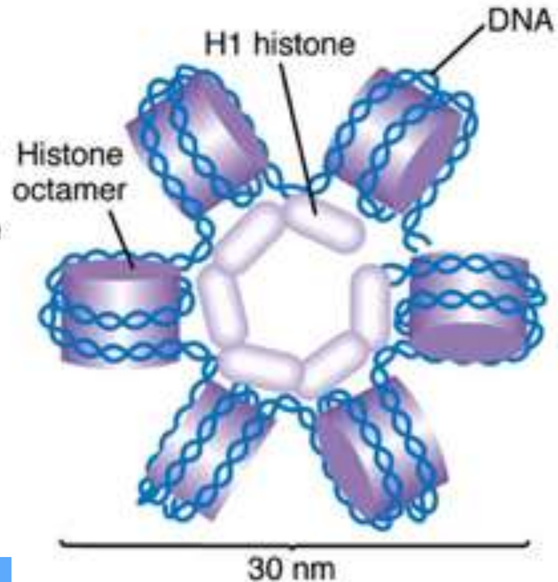
Non-histones:

In addition to histones the chromatin comprise of many different types of non-histone proteins, which are involved in a range of activities, including DNA replication and gene expression. They display more diversity or are not conserved. They may also differ between different tissues of same organism.

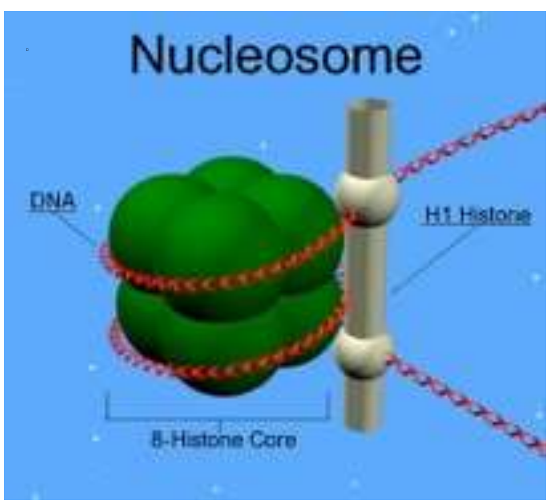
Roger Kornberg in 1974 described the basic structural unit of chromatin which is called the nucleosome.

HISTONE PROTEINS -- NUCLEOSOME





HISTONES: Positive charged proteins that wrap DNA up



NUCLEOSOME

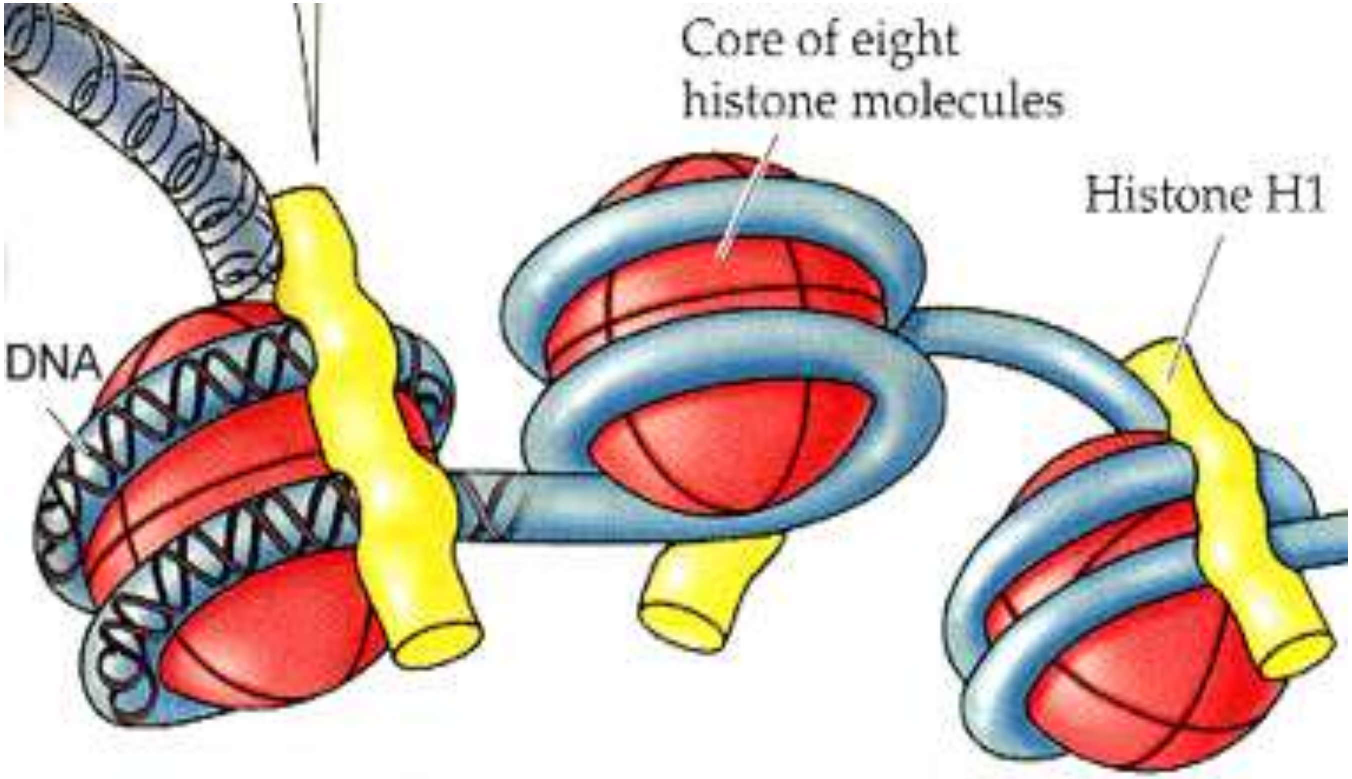
DNA--Histone complex formed by eight histone molecules

2x H3--H4

2x H2A--H2B

Kept together by H1 histone

Nucleosomes have two turns of DNA



The length of DNA per nucleosome varies for individual tissues (154--260bp)

Euchromatin: The lightly-stained regions in chromosome when stained with basic dyes are called **euchromatin** and contain single-copy of genetically-active DNA.

The extent of chromatin condensation varies during the life cycle of the cell and plays an important role in regulating gene expression. In the interphase of cell cycle the chromatin are decondensed and known as **euchromatin** leading to gene transcription and DNA replication.

Heterochromatin:

The word heterochromatin was coined by Emil Heitz based on cytological observations. They are highly condensed and ordered areas in nucleosomal arrays.

About 10% of interphase chromatin is called **heterochromatin** and is in a very highly condensed state that resembles the chromatin of cells undergoing mitosis . They contain a high density of repetitive DNA found at centromeres and telomeres form heterochromatin.

Heterochromatin are of two types, the **constitutive and facultative heterochromatin.** The regions that remain condensed throughout the cell cycle are called **constitutive heterochromatin** whereas the regions where heterochromatin condensation state can change are known as **facultative.**

Constitutive heterochromatin is found in the region that flanks the telomeres and centromere of each chromosome and in the distal arm of the Y chromosome in mammals.

Constitutive heterochromatin possesses very few genes and they also lead to transcriptional inactivation of nearby genes. This phenomenon of gene silencing is known as "position effect". Constitutive heterochromatin also inhibits genetic recombination between homologous repetitive sequences circumventing DNA duplications and deletion.

Whereas facultative heterochromatin is chromatin that has been specifically inactivated during certain phases of an organism's life or in certain types of differentiated cells.

FUNCTION OF CHROMOSOMES

- [I]- The chromosomes are capable of self-duplication. During duplication process the DNA strands unwind. As unwinding starts, each template of DNA forms its complementary strand in double-helix nature. The conversion of the old DNA molecule into two new molecules, helps in duplicating the chromosomes.

Function of chromosomes (continued)...

- [II]- They help in expression of different characters in an organism by synthesizing proteins in cells. A definite protein is accumulated to produce a definite character.

Questions