Module 2- Chromosome structure and organisation

This module deals with the genetic material of the cell, its structure, with details of the human chromosome and the giant chromosomes.

Module 2 Lecture 1

Genetic material in a cell: All cells have the capability to give rise to new cells and the encoded information in a living cell is passed from one generation to another. The information encoding material is the genetic or hereditary material of the cell.

Prokaryotic genetic material:

The prokaryotic (bacterial) genetic material is usually concentrated in a specific clear region of the cytoplasm called nucleiod. The bacterial chromosome is a single, circular, double stranded DNA molecule mostly attached to the plasma membrane at one point. It does not contain any histone protein. *Escherichia coli* DNA is circular molecule 4.6 million base pairs in length, containing 4288 annotated protein-coding genes (organized into 2584 operons), seven ribosomal RNA (rRNA) operons, and 86 transfer RNA (tRNA) genes. Certain bacteria like the *Borrelia burgdorferi* possess array of linear chromosome like eukaryotes.

Besides the chromosomal DNA many bacteria may also carry extra chromosomal genetic elements in the form of small, circular and closed DNA molecules, called plasmids. They generally remain floated in the cytoplasm and bear different genes based on which they have been studied. Some of the different types of plasmids are F plasmids, R plasmids, virulent plasmids, metabolic plasmids etc. Figure 1 depicts a bacterial chromosome and plasmid.
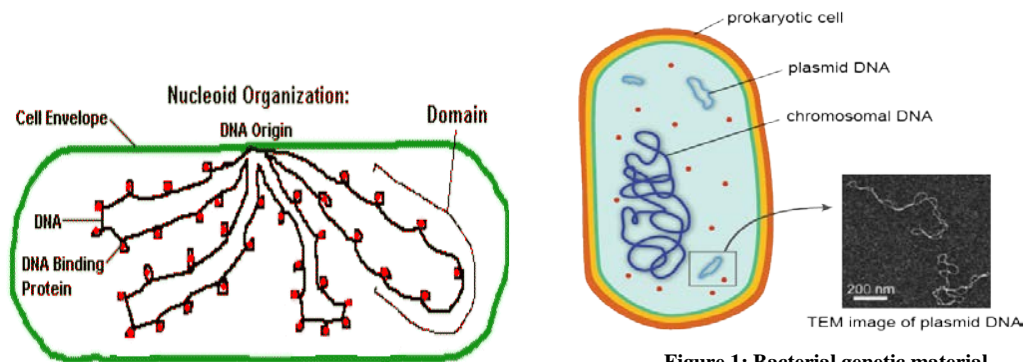

Figure 1: Bacterial genetic material

Virus genetic material:

The chromosomal material of viruses is DNA or RNA which adopts different structures. It is circular when packaged inside the virus particle.

Eukaryotic genetic material:

A Eukaryotic cell has genetic material in the form of genomic DNA enclosed within the nucleus. Genes or the hereditary units are located on the chromosomes which exist as chromatin network in the non dividing cell/interphase. This will be discussed in detail in the coming sections.

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. The term chromosome was coined by W. Waldeyer in 1888. 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 (Table 1) 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. The structure of a chromosome is given in Figure 2. 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.
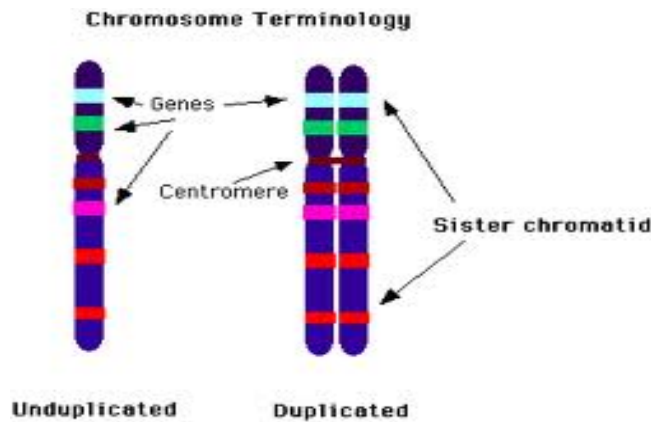
Figure 2: Eukaryotic chromosome

The shortest human chromosome contains 4.6×10^7 bp of DNA. This is equivalent to 14,000 µm of extended DNA. In its most condensed state during mitosis, the chromosome is about 2 µm long. This gives a packing ratio of 7000 (14,000/2). The DNA is packaged stepwise into the higher order chromatin structure and this is known as "hierarchies of chromosomal organization". The level of DNA packaging is schematically represented in Table 2.

Chromosome number:

There are normally two copies of each chromosome present in every somatic cell. The number of unique chromosomes (N) in such a cell is known as its haploid number, and the total number of chromosomes (2N) is its diploid number. The suffix 'ploid' refers to chromosome 'sets'. The haploid set of the chromosome is also known as the genome. Structurally, eukaryotes possess large linear chromosomes unlike prokaryotes which have circular chromosomes. In Eukaryotes other than the nucleus chromosomes are present in mitochondria and chloroplast too. The number of chromosomes in each somatic cell is same for all members of a given species. The organism with lowest number of chromosome is the nematode, *Ascaris megalocephalusunivalens* which has only two chromosomes in the somatic cells (2n=2).

Table 1: Number of chromosomes in different organisms

Organism	No. of chromosomes
Arabidopsis thaliana (diploid)	10
Maize (diploid)	20
Wheat (hexaploid)	42
Common fruit fly (diploid)	8
Earthworm (diploid)	36
Mouse (diploid)	40
Human (diploid)	46
Elephants (diploid)	56
Donkey (diploid)	62
Dog (diploid)	78
Gold Fish (diploid)	100-104
Tobacco(tetraloid)	48
Oat (hexaploid)	42

Autosomes and sex chromosomes:

In a diploid cell, there are two of each kind of chromosome (termed homologus chromosomes) except the sex chromosomes. In humans one of the sex has two of the same kind of sex chromosomes and the other has one of each kind. In humans there are 23 pairs of homologous chromosomes (2n=46). The human female has 44 non sex chromosomes, termed autosomes and one pair of homomorphic sex chromosomes given the designation XX. The human male has 44 autosomes and one pair of heteromorphic sex chromosomes, one X and one Y chromosome.

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. 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. Telomere is the chromosomal ends which prevents other chromosomal segments to be fused with it. 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.

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. This is usually expressed as the amount of DNA per haploid cell (usually expressed as picograms) or the number of kilobases per haploid cell and is called the C value. This is constant for all cells of a species. For diploid cells it is 2C. Extending the C value we reach the C-value paradox. One immediate feature of eukaryotic organisms highlights a specific anomaly that was detected early in molecular research. Even though eukaryotic organisms appear to have 2-10 times as many genes as prokaryotes, they have many orders of magnitude more DNA in the cell. Furthermore, the amount of DNA per genome is correlated not with the presumed evolutionary complexity of a species. This is stated as the C value paradox: the amount of DNA in the haploid cell of an organism is not related to its evolutionary complexity. Lower eukaryotes in general have less DNA, such as nematode
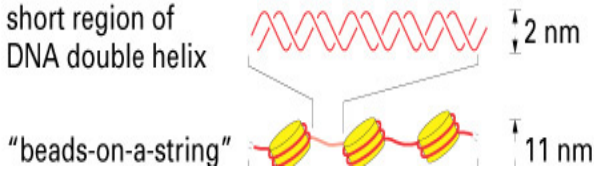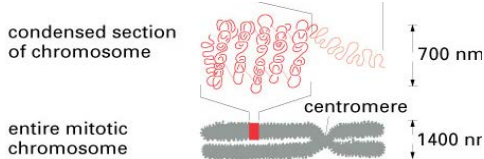
Caenorhabditis elegans which has 20 times more DNA than *E. coli*. Vertebrates have greaer DNA content about 3pg, in general about 700 times more than *E. coli*. Salamander *Amphiuma* has a very high DNA content of about 84pg. Man has about 3pg of DNA per haploid genome.

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. The structural organization of nucleosome to chromosome is explained in Table 2.

**Table 2: The hierarchies of chromosomal organization**

Levels	Summary	Schematic representation
The first level of packing	Winding of DNA around a protein core to produce a "bead-like" structure called a **nucleosome**. This gives a packing ratio of about 6. This structure is invariant in both the euchromatin and heterochromatin of all chromosomes. The protein core is composed of 8 histone proteins, two each of H2A, H2B, H3 and H4. Histone H1 forms the linker between to nucleosomes. 146 bp of DNA is wrapped around each nucleosome.	short region of DNA double helix 2 nm "beads-on-a-string" 11 nm
The second level of packing	Coiling of beads in a helical structure called the **30 nm fiber** that is found in both interphase chromatin and mitotic chromosomes. This structure increases the packing ratio to about 40. This appears to be a solenoid structure with about 6 nucleosomes per turn. This gives a packing ratio of 40, which means that every 1 µm along the axis contains 40 µm of DNA. The stability of this structure requires the presence of the last member of the histone gene family, histone H1. Because experiments that strip H1 from chromatin maintain the nucleosome, but not the 30 nm structure, it was concluded that H1 is important for the stabilization of the 30 nm structure.	30-nm chromatin fiber of packed nucleosomes 30 nm section of chromosome in extended form 300 nm
The final level	The fiber is organized in loops, scaffolds and domains that give a final packing ratio of about 1000 in interphase chromosomes and about 10,000 in mitotic chromosomes. The final level of packaging is characterized by the 700 nm structure seen in the metaphase chromosome. The condensed piece of chromatin has a characteristic scaffolding structure that can be detected in metaphase chromosomes. This appears to be the result of extensive looping of the DNA in the chromosome.	condensed section of chromosome 700 nm centromere entire mitotic chromosome 1400 nm NET RESULT: EACH DNA MOLECULE HAS BEEN PACKAGED INT CHROMOSOME THAT IS 10,000-FOLD SHORTER THAN ITS EXTEI

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. Dosage compensation of X-chromosome or X-chromosome inactivation in mammals is an example of such heterochromatin (Karp 2010). Heterochromatin spreads from a specific nucleation site, causing silencing of most of the X chromosome, thereby regulating gene dosage.

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 (Figure 3). 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.
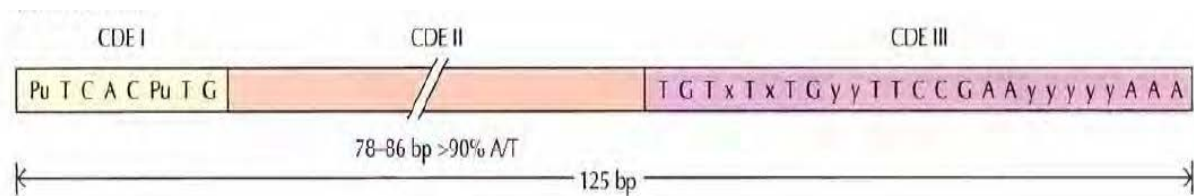

Figure 3: The *S. cerevisiae* centrosome. The *S. cerevisae* centromere (CEN) sequences consist of two short conserved sequences (CDE I and CDE Ill) separated by 78 to 86 base pairs (bp) of ATrich DNA (CDE II). The sequences shown are consensus sequences derived from analysis of the centromere sequences of individual yeast chromosomes. Pu = A or G; x =A or T; y = any base. The figure has been adapted from "The Cell, A Molecular Approach" by Geoffrey M. Cooper, 4th Ed. 2007.

Telomeres: Telomeres are the region of DNA at the end of the linear eukaryotic chromosome that are required for the replication and stability of the chromosome. McClintock recognized their special features when she noticed, that if two chromosomes were broken in a cell, the ends were sticky and end of one could attach to the other and vice versa. However she never observed the attachment of the broken end to the end of an unbroken chromosome suggesting that the end of chromosomes have unique features. Telomere sequences remain conserved throughout vertebrates and they form caps that protect the chromosomes from nucleases and other destabilizing influences; and they prevent the ends of chromosomes from fusing with one another.The telomeric DNA contains direct tandemly repeated sequences of the form $(T/A)_x G_y$ where x is between 1 and 4 and y is greater than 1. Human telomeres contain the sequence TTAGGG repeated from about 500 to 5000 times. 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 was discovered in 1984 by Elizabeth Blackburn and Carol Greider of the University of California, Berkeley. It is a reverse transcriptase that synthesizes DNA using an RNA template. Unlike most reverse transcriptases, the enzyme itself contains the RNA that serves as its template, i.e., telomerase can add new repeat units to the 3' end of the overhanging strand. A well-studied system involves the *Tetrahymena* protozoa organism. The telomeres of this

organism end in the sequence 5'-TTGGGG-3'. The telomerase adds a series of 5'-TTGGGG-3' repeats to the ends of the lagging strand. A hairpin occurs when unusual base pairs between guanine residues in the repeat form. Next the RNA primer is removed, and the 5' end of the lagging strand can be used for DNA synthesis. Ligation occurs between the finished lagging strand and the hairpin. Finally, the hairpin is removed at the 5'-TTGGGG-3' repeat. The replication of telomere has been presented in Figure 4.
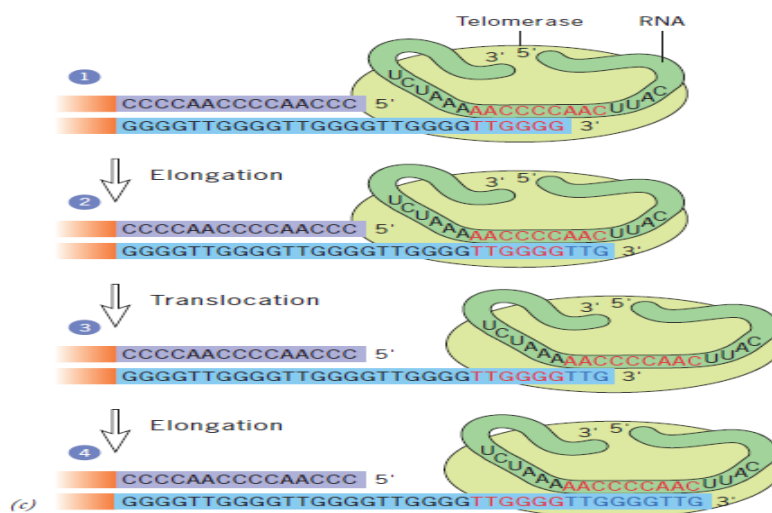
Figure 4: Telomerase replication. Telomerase contains an RNA primer that is complementary to the end of the G-rich strand, which extends past the C-rich strand. The telomerase RNA binds to the protruding end of the G-rich strand in step 1 and then serves as a template for the addition of nucleotides 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.

Module 2 Lecture 2

Human Cromosome: The human genome is 3×10^9 base pairs of DNA and the smallest human chromosome is several times larger than the entire yeast genome; and the extended length of DNA that makes up the human genome is about 1 m long. The human genome is distributed among 24 chromosomes (22 autosomes and the 2 sex chromosomes), each containing between 45 and 280 Mb of DNA **(Figure 1)**. The sex chromosomes are denoted by X and Y and they contain genes which determine the sex of an individual i.e., XX for female and XY for male. The rest are known as autosomes. The haploid human genome contains about 23,000 protein-coding genes, which are far fewer than had been expected before sequencing. In fact, only about 1.5% of the genome codes for proteins, while the rest consists of non-coding genes, regulatory sequences, introns, and noncoding DNA. Chromosomes are stained with A-T (G bands) and G-C (R bands) base pair specific dyes **(Figure 1)**. When they are stained, the mitotic chromosomes have a banded structure that unambiguously identifies each chromosome of a karyotype. Each band contains millions of DNA nucleotide pairs which do not correspond to any functional structure. G-banding is obtained with Giemsa stain yielding a series of lightly and darkly stained bands. The dark regions tend to be heterochromatic and AT rich. The light regions tend to be euchromatic and GC rich. R-banding is the reverse of G-banding where the dark regions are euchromatic and the bright regions are heterochromatic.
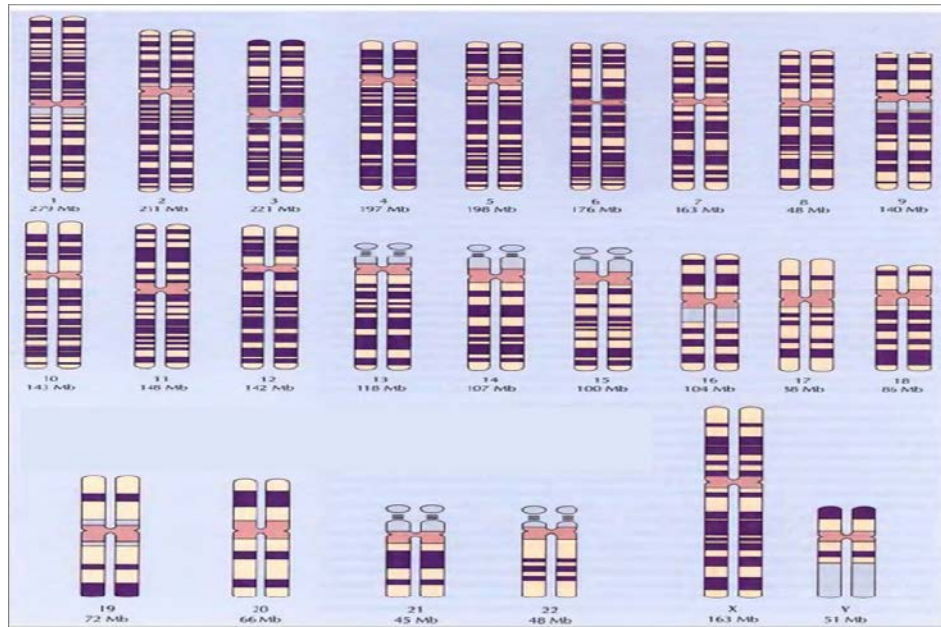
Figure 1: Human metaphase chromosome showing the banding pattern obtained after cytogenetic staining. This figure has been adapted from "The Cell, A Molecular Approach" by Geoffrey M. Cooper, 4th Ed. 2007.

Types of human chromosomes

There are four types of chromosomes based upon the position of the centromere in humans **(Figure 2)**.

1) **Metacentric**: In this type of chromosome the centromere occurs in the centre and all the four chromatids are of equal length.

2) **Submetacentric**: In this type of chromosome the centromere is a little away from the centre and therefore chromatids of one side are slightly longer than the other side.

3) **Acrocentric**: In this type of chromosome the centromere is located closer to one end of chromatid therefore the chromatids on opposite side are very long. A small round structure, attached by a very thin thread is observed on the side of shorter chromatid. The small round structure that is a part of the chromatid is termed as satellite. The thin strands at the satellite region are termed as Nucleolar Organiser Region.

4) **Telocentric**: In this type of chromosome the centromere is placed at one end of the chromatid and hence only one arm. Such telocentric chromosomes are not seen in human cells.
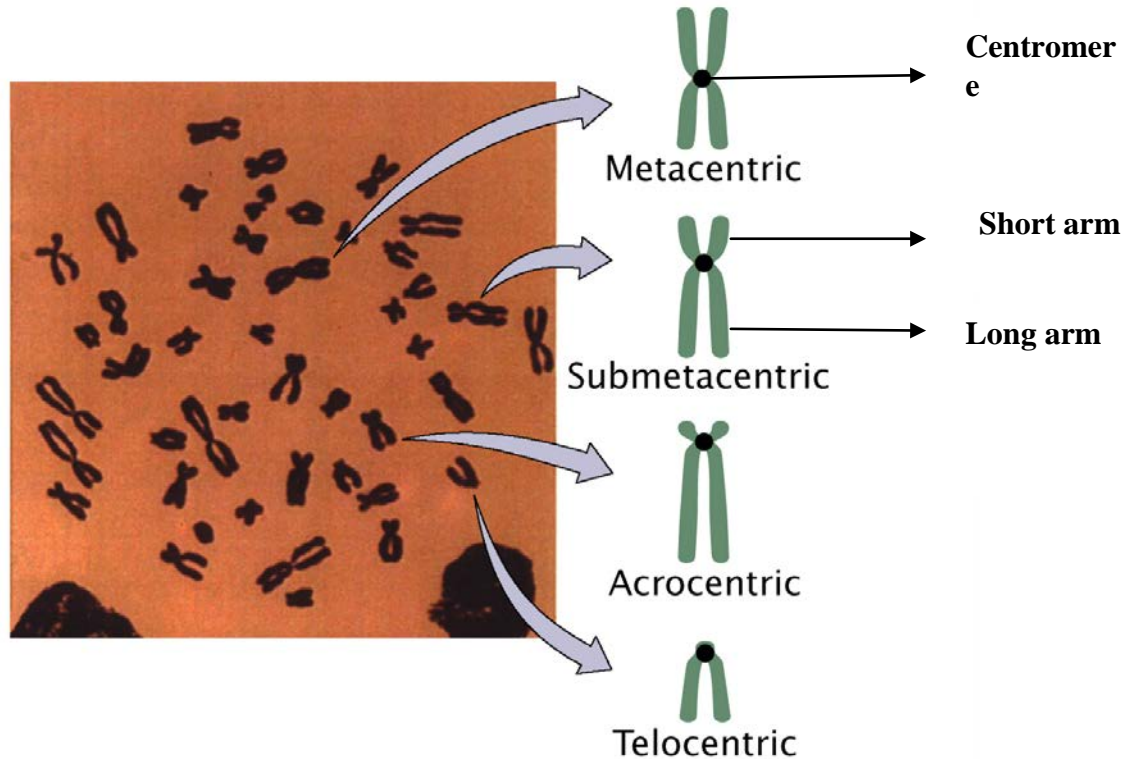

Figure 2: Types of human chromosomes. This figure has been adapted from the "Genetics" by Freeman and company. 2nd Ed, 2005.

Human Chromosome Karyotype

Eukaryotic species have several chromosomes and are detected only during mitosis or meiosis. They are best observed during the metaphase stage of cell division as they are found in the most condensed state. Thus each eukaryotic species is characterized by a **karyotype** which is the numerical description (number and size) of chromosomes in the normal diploid cell. For example, the *Homo sapiens* possess 46 chromosome i,e., 23 pairs **(Figure 3)**. The karyotype is important because genetic research can correlate changes in the karyotype with changes in the phenotype of the individual. For example, Down's syndrome is caused by duplication of the human chromosome number 21. Insertions, deletions and changes in chromosome number can be detected by the skilled cytogeneticist, but correlating these with specific phenotypes is difficult.
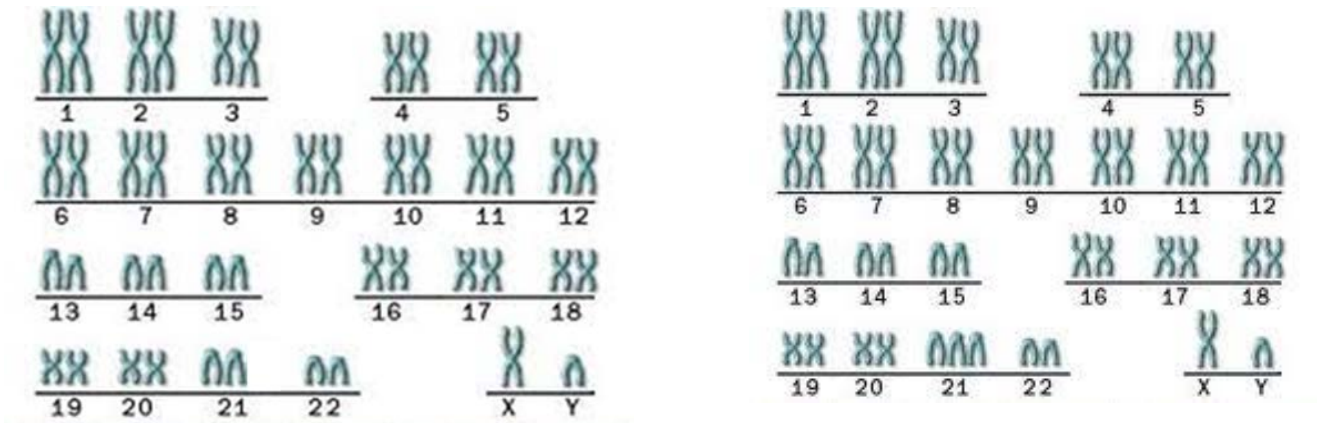
Figure 3: The normal human karyotype (left) and human karyotype in Down's syndrome (Right).

Module 2 Lecture 3

Giant chromosomes:
Some cells at certain particular stage of their life cycle contain large nuclei with giant or large sized chromosomes. Polytene and lampbrush chromosomes are examples of giant chromosomes.

Polytene Chromosome
Giant chromosomes were first time observed by E.G. Balbiani in the year 1881 in nuclei of certain secretory cells (salivary glands) of Chironomas larvae (Diptera). However he could not conclude them to be chromosomes. They were conclusively reported for the first time in insect cells (*Drosophila*) by Theophilus Painter of the University of Texas in the year 1933. Since they were discovered in the salivary glands of insects they were termed as salivary gland chromosomes. The anme polytene chromosome was proposed by Kollar due to the occurrence of many chromonemata (DNA) in them. Cells in the larval salivary gland of *Drosophila,* mosquito *and Chironema* contain chromosomes with high DNA content. However they may also occur in malphigian tubules, rectum, gut, foot pads, fat bodies, ovarian nurse cells etc. Polyteney of giant chromosomes happens by replication of the chromosomal DNA several times without nuclear division (endomitosis) and the resulting daughter chromatids do not separate but remain aligned side by side. During endomitosis the nuclear envelope does not rupture and no spindle formation takes place. The polytene chromosomes are visible during interphase and prophase of mitosis.

They are about 100 times thicker contain 1000 to 2000 chromosomes, than the chromosomes found in most other cells of the organism. When stained and viewed under compound microscope at 40X magnification they display about 5000 bands. In them the chromomere or the more tightly coiled regions alternate with regions where the DNA fibres are folded loosely. A series of dark transverse bands alternates with clear zones of inter bands. Such individual bands can be correlated with particular genes (Figure 1). About 85% of the DNA in polytene chromosomes is in bands and rest 15% is in inter bands. The cross banding pattern of each polytene chromosome is a constant characteristic within a species and helps in chromosome mapping during cytogenetic studies. In *Drosophila melanogaster* there are about 5000 bands and 5000 interbands per genome. These chromosomes are not inert cellular objects but dynamic structures in

which certain regions become "puffed out" due to active DNA transcription at particular stages of development. These chromosome puffs are also termed Balbiani rings. Puffs may apprear and disappear depending on the production of specific proteins which needs to be secreted in large amounts in the larval saliva. Another peculiarity of the polytene chromosomes is that the paternal and maternal chromosomes remain associated side by side and the phenomenon is termed somatic pairing.

Both polyteney and polyploidy have excess DNA per nucleus, but in the later the new chromosomes are separate from each other. A polytene chromosome of *Drosophila* salivary glands has about 100 DNA molecules which are arranged side by side and which arise from 10 rounds of DNA replication ($2^{10}=1024$). *Chironimus* has 16000 DNA molecules in their polytene chromosomes.
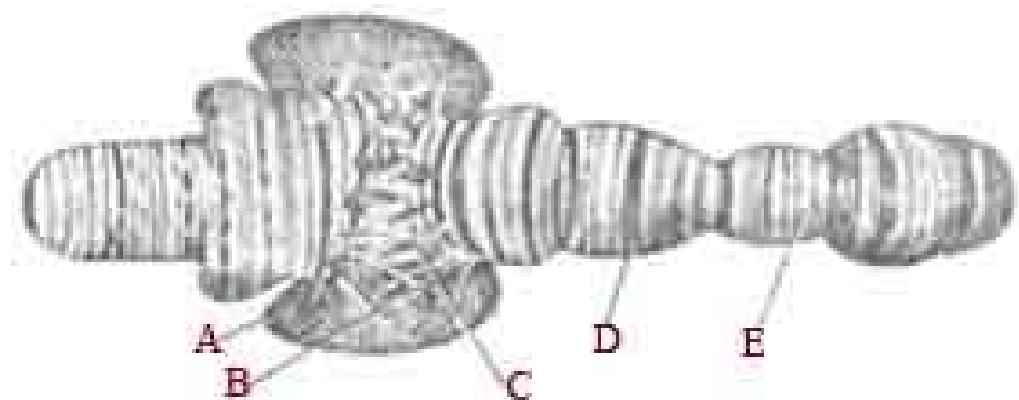

Figure 1: The structure of Drosophilla polytene chromosome. A: mRNA; B-Chromosome puff; C: Chromonemata; D: Dark band; E: Interband. The figure has been adapted from the site http://www.microbiologyprocedure.com/genetics/chromosomes/special-types-of-chromosomes.htm.

Lampbrush chromosome

Lampbrush chromosomes were first observed by Flemming in 1882 in sections of Salamander oocytes and later described by Ruckert in the year 1892. They appeared like brushes used for cleaning lamps, hence the name lampbrush chromosome. They are transitory structures and can be observed during the diplotene stage of prophase I in meiosis in the oocytes of all animal species both vertebrates and invertebrates. They have been described in Sepia (Mollusca), Echinaster (Echinodermata) and in several species of insects, shark, amphibians, reptiles, birds and mammals (humans). Lampbrush chromosomes have also been found in spermatocytes of several species, giant nucleus of Acetabularia and even in plants. Generally they are smaller in invertebrates than vertebrates. They are observed in oocytes because oocytes are high in DNA content.

Lampbrush chromosomes are functional for studying chromosome organization and genome function during meiotic prophase. Additionally lampbrush chromosomes are widely used for construction of detail cytological maps of individual chromosomes.

They are of exceptionally large sizes and present in bivalent form. They are formed due to the active synthesis of mRNA molecules for future use by the egg cells, when no synthesis of mRNA molecule is possible during the mitotic cell division. Lampbrush chromosomes are clearly visible in the light microscope they are organized into a series of chromomeres with large chromatin symmetrical loops extending laterally (**Figure 2**). Each loop appears at a constant position in the chromosome (10,000 loops per chromosome set or haploid set). Each loop has an axis made up of DNA unfolded from the chromosome and is transcriptionally highly active. Wherein several transcription units with polarized RNP-matrix coats the DNA axis of the loop. The majority of the DNA, however, is not in loops but remains highly condensed in the chromomeres on the axis and lacks expression of genes.
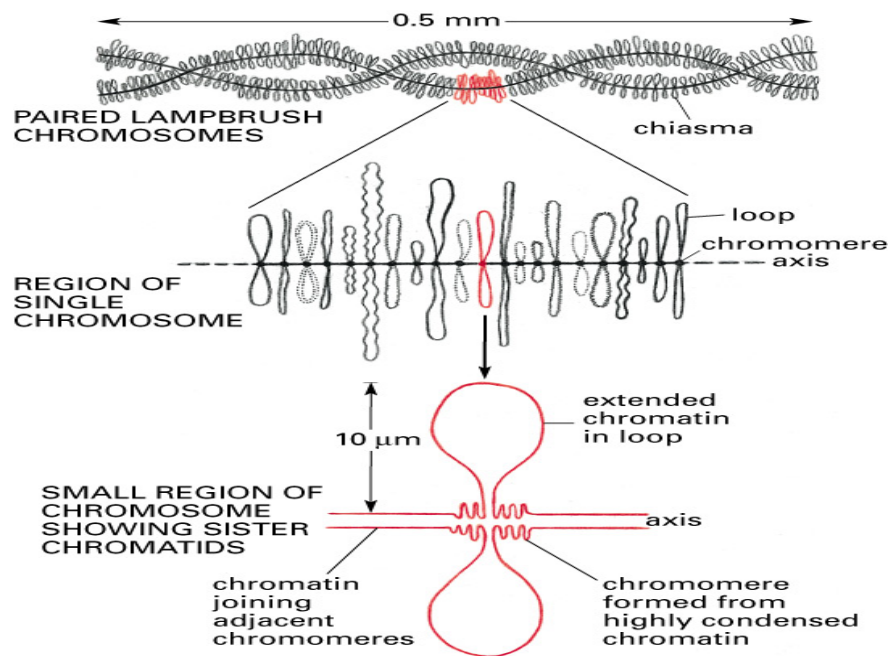

Figure 2: Lampbrush chromosome. This figure has been adapted from the molecular biology of the cell, by Bruce Alberts, 4th Ed. 2008.

The loops perform intense transcription of heterogenous RNA (precursors of mRNA molecules for ribosomal and histone proteins). Thus each lateral loop is covered by an assymetrical matrix of RNA transcripts; thicker at one end of the loop than other. The number of pairs of loops gradually increases during meiosis till it reaches maximum at diplotene. This stage may persist for months or years as oocytes build up supply of mRNA required for further development. As meiosis proceeds further number of loops gradually decrease and loops ultimately disappear due to reabsorption into the chromosome or disintegration.

Certain hypothesis regarding loops are that they may be static or dynamic with new loop material spinning out of one side of a chromosome and returning to a condensed on the other side. This is called spinning out or retraction hypothesis. This hypothesis has been rejected recently through DNA-RNA hybridization studies. The other hypothesis is known as the Master and Slave hypothesis which suggested that each loop pairs and thus chromomere is associated with the activity of many copies of specific genes. There is a master copy at each chromomere and information is transferred to the slave copies which are matched against it to ensure that all are identical. The master copy does not take part in RNA synthesis, but the slave copy is involved in transcription. Large number of duplicate genes ensures higher level of transcription.

Interesting Facts
- If unfolded the DNA in each cell's nucleus would be 2 meters long. Humans have an estimated 100 trillion cells. In other words, if the all the DNA from every cell in a person's body were patched up together they would form a strand of 200 billion kilometers, or more than 1,000 times the distance between Earth and the Sun.

- Genes for the same feature appear in the same locus (place) on each matching pair of chromosomes in every human body cell.

- The 23rd chromosome pair in humans decides what sex you are, and the sex chromosomes are called X and Y.

- In some rare cases people are born with one extra chromosome. Those born with three chromosome 21 have Down's syndrome.

- It takes about 8 hours for one of your cells to completely copy its DNA.

- Human beings share 7% of genes with *E. coli* bacterium, 21% with worms, 90% with mice and 98% with chimpanzees.

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Questions:
1. The products of mitosis are _____.

A. one nucleus containing twice as much DNA as the parent nucleus

B. four genetically identical nuclei

C. four nuclei containing half as much DNA as the parent nucleus

D. two genetically identical nuclei

E. two genetically identical cells

2. Genetically diverse offspring result from _____.

A. binary fission

B. mitosis

C. sexual reproduction

D. cytokinesis

E. cloning

3. How many chromosomes do humans have in their body cells?
A. 48
B. 46
C. 50

4. Which answer is in order from SMALLEST to BIGGEST?

A. gene, chromosome, cell

B. chromosome, gene, cell

C. nucleus, gene, chromosome

5. Sizes of genomes of free-living organisms have been found to range from approximately
A. 2-200 Mbp
B. 0.5-1,000 Mbp
C. 100-2,000,000 Mbp
D. 1,000-1,000,000,000 Mbp
E. 0.5-200,000 Mbp
[1 Mbp = 1 million bp]

6. Most sequences in the human genome belong to

A. Genes

B. Pseudogenes

C. Gene fragments

D. Interspersed repeats

E. Tandem repeats

7. Which of the following genomes is richest in interspersed repeat sequences?

A. *Drosophila* genome

B. Human genome

C. Maize genome

D. *Saccharomyces* genome

E. *E. coli* genome

8. A nucleosome consists of

A. Chromatin and nucleotides

B. Chromatin and histones

C. DNA and chromatin

D. DNA and histones

E. Nucleoids and histone

9. Centromers contain

A. Repeated DNA

B. Chromatids

C. Telomeres

D. Proteins

E. Microtubules

F. Genes

10. Gene density can be high

A. in telomeres

B. anywhere on the chromosomes

C. in centromeres

D. in metaphase chromosomes

E. in anaphase chromosomes

Q11. When can we see chromosomes easily?

Q13. How does dense packing of DNA in chromosome prevent gene expression?

Q14. Illustrate the hierarchy of DNA condensation into chromosomes.

Q15. Differentiate between prokaryotic and eukaryotic genome.

Q16. What are lampbrush and polytene chromosomes and where are they observed?

Q17. What is karyotype? What will happen to human Karyotype in Down Syndrome?

Q18. What is C-value paradox?

Q19. How are telomeres replicated?

Q20. Describe the types of chromosomes.

Q21. What is centromeric DNA?

Q22. What is chromatin? Differentiate between heterochromatin and Euchromatin.

Q23. How polytene chromosomes are formed?

Q24. What will be the result of defective telomere replication?