

Chromosome Structure

Lec. 10 & 11 | Chromosome Structure

INTRODUCTION

General considerations.

The **Genome** is the genetic complement of an organism. All cells of all individuals of a given species have roughly the same genetic complement. There are some obvious and important exceptions (sometimes referred to as "genomic instability") two lectures worth! Before cells divide, they must therefore duplicate their genetic material (replication; In next lecture) so that each daughter cell also has a full genome. The amount of DNA that encodes genes is often profoundly less than the total genome size, and we will discuss some reasons for this ("**ploidy**", **repetitive DNA**). The genome is stored in DNA, in **Chromosomes**, defined as a single molecule of DNA and its associated proteins. We will discuss several important mechanisms exist to facilitate the stable maintenance of chromosomes in cells (centromere, telomere, chromatin).

Organization of genomes.

A major division in the way in which genomes are organized: prokaryotes (bacteria) vs. eukaryotes (almost everything else).

A. The prokaryotic genome.

Prokaryotic genomes:

- **Small** (10^5 - 10^6 base pairs)
- **Simple**: Genes and proteins in prokaryotes are generally co-linear; the gene is simply the linear, triplet code required to make the protein.
- **Typically one chromosome**, and one copy of that chromosome.
- The Chromosome is often circular.

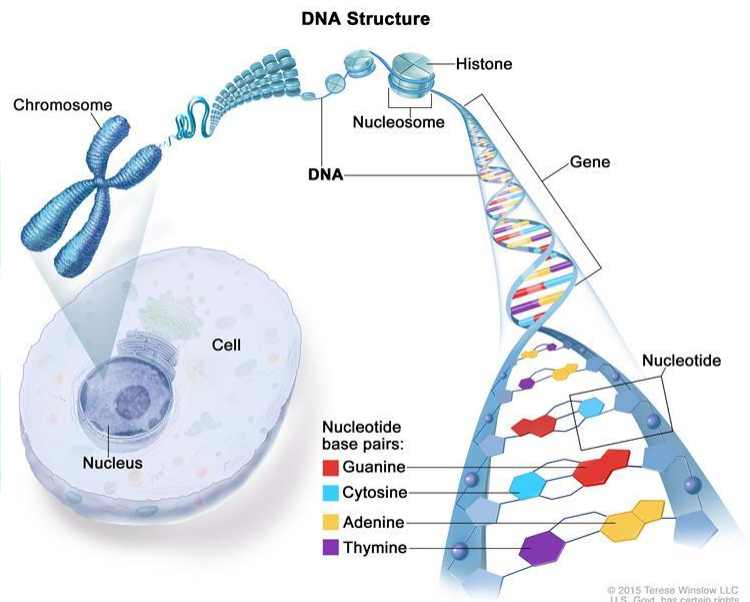
B. The eukaryotic genome.

- **Very large** genomes (10^7 [yeast] to 10^9 [human] base pairs), in the nucleus, large expanses of DNA with no obvious purpose between the genes (intervening sequences) and interrupting the gene (**introns**). Less than 5% of the human genome encodes proteins.
- **Organisms that do sex have a duplicated genome after reproduction**. A single copy of the genome, "**haploid**", is found in sperm and oocytes. After fusion of sperm/oocyte, you have two copies of each chromosome one from the sperm (paternal) and one from the oocyte (maternal). This is termed **diploid**. All cells except **germ** cells (sperm and oocyte) in most sexually reproducing species are diploid.
- Organized into **multiple linear chromosomes** (yeast have 16, humans have 24 different ones (Chromosomes 1 through 22, X, and Y))
- Genome is found in the nucleus, but eukaryotes also have small, circular, prokaryotic-like chromosomes with a different set of genes in organelles (mitochondria, chloroplasts).

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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 and the number of chromosomes is characteristic of every species. Benden and Boveri 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 right Figure. 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.

Eukaryotic chromosomes

The label **eukaryote** is taken from the Greek for '**true nucleus**', and eukaryotes (all organisms except viruses, Eubacteria and Archaea) are defined by the possession of a nucleus and other membrane-bound cell organelles. The nucleus of each cell in our bodies contains approximately 1.8 meters of DNA in total, although each strand is less than one millionth of a centimeters thick. This DNA is tightly packed

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into structures called **chromosomes**, which consist of long chains of DNA and associated proteins. In eukaryotes, DNA molecules are tightly wound around proteins - called **histone proteins** - which provide structural support and play a role in controlling the activities of the genes. A strand 150 to 200 nucleotides long is wrapped twice around a core of eight histone proteins to form a structure called a **nucleosome**. The histone octamer at the center of the nucleosome is formed from two units each of histones H2A, H2B, H3, and H4. The chains of histones are coiled in turn to form a **solenoid**, which is stabilized by the histone H1. Further coiling of the solenoids forms the structure of the chromosome proper.

Each chromosome has a **p arm** and a **q arm**. The p arm (from the French word 'petit', meaning small) is the short arm, and the q arm (the next letter in the alphabet) is the long arm. In their replicated form, each chromosome consists of two **Chromatids**.

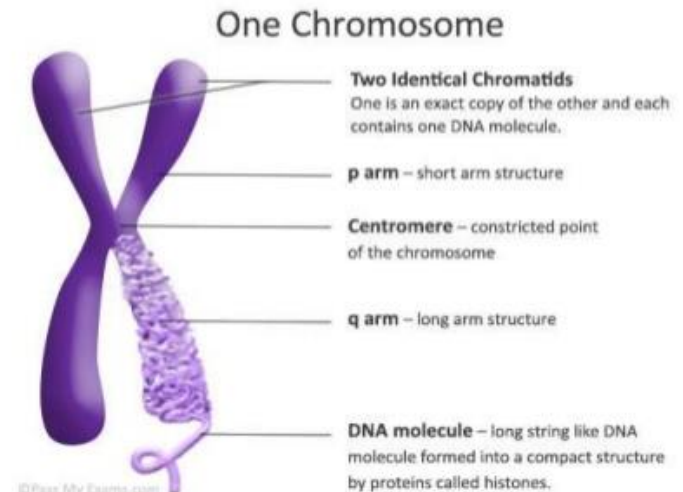
The chromosomes - and the DNA they contain - are copied as part of the cell cycle, and passed to daughter cells through the processes of mitosis and meiosis. Human beings have 46 chromosomes, consisting of 22 pairs of **autosomes** and a pair of **sex chromosomes**: two **X** sex chromosomes for females (**XX**) and an **X** and **Y** sex chromosome for males (**XY**). One member of each pair of chromosomes comes from the mother (through the egg cell); one member of each pair comes from the father (through the sperm cell). A photograph of the chromosomes in a cell is known as a **karyotype**. The autosomes are numbered 1-22 in decreasing size order.

Autosomes and sex chromosomes:

In a diploid cell, there are two of each kind of chromosome (termed homologous 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.

Prokaryotic chromosomes

The **Prokaryotes** (Greek for 'before nucleus' including Eubacteria and Archaea) lack a discrete nucleus, and the chromosomes of prokaryotic cells are not enclosed by a separate membrane.



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Most bacteria contain a single, circular chromosome. (There are exceptions: some bacteria - for example, the genus *Streptomyces* possess linear chromosomes, and *Vibrio cholerae*, the causative agent of cholera, has two circular chromosomes.) The chromosome together with ribosomes and proteins associated with gene expression is located in a region of the cell cytoplasm known as the **Nucleoid**.

The genomes of prokaryotes are compact compared with those of eukaryotes, as they lack introns, and the genes tend to be expressed in groups known as **Operons**. The circular chromosome of the bacterium *Escherichia coli* consists of a DNA molecule approximately 4.6 million nucleotides long.

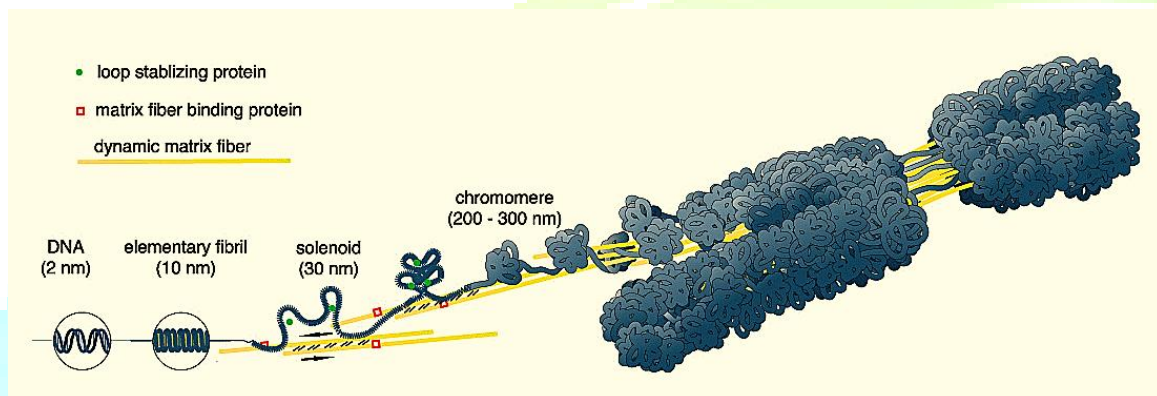
In addition to the main chromosome, bacteria are also characterized by the presence of extra-chromosomal genetic elements called **Plasmids**. These relatively small circular DNA molecules usually contain genes that are not essential to growth or reproduction.

Chromosomes Morphology:

- **Size:** The size of chromosome is normally measured at mitotic metaphase and may be as short as 0.25 μm 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 3 μm in *Drosophila* to 5 μm in man and 8-12 μm 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

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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 μm , 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. Telomere is the chromosomal ends which prevents other chromosomal segments to be fused with it. Besides the primary constrictions or centromeres, chromosomes also possess 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.

Chromatin:

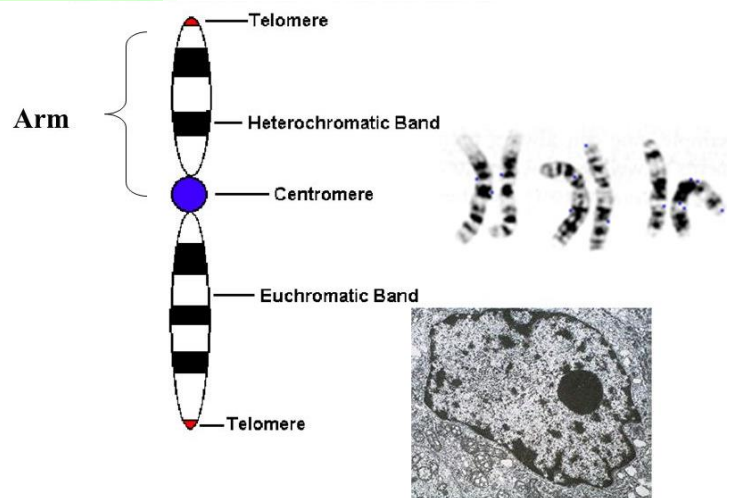
Chemical composition of chromatin

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

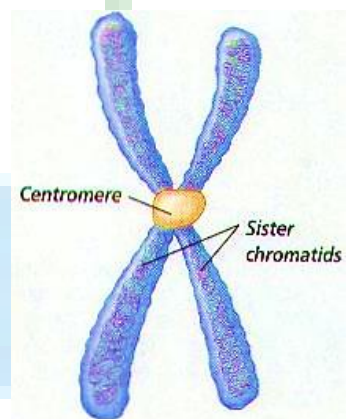
Euchromatin: The lightly-stained regions in chromosome when stained with basic dyes are called euchromatin and contain single-copy of genetically-active DNA. The extent of chromatin condensation varies during the life cycle of the cell and plays an important role in regulating gene expression. In the interphase of cell cycle the chromatin are decondensed and known as euchromatin leading to gene transcription and DNA replication.

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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. Heterochromatin spreads from a specific nucleation site, causing silencing of most of the X chromosome, thereby regulating gene dosage.



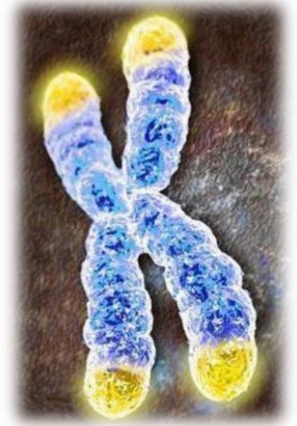
Centromeres: Centromeres are those condensed regions within the chromosome that are responsible for the accurate segregation of the replicated chromosome during mitosis and meiosis. When chromosomes are stained they typically show a dark-stained region that is the centromere. The actual location where 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



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sequences must not provide any other function. Typically CEN DNA is about 120 base pairs long

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.



Types of human chromosomes

There are four types of chromosomes based upon the position of the centromere in humans.

1) Metacentric:

In this type of chromosome the centromere occurs in the centre and all the four chromatids are of equal length.

2) Sub metacentric:

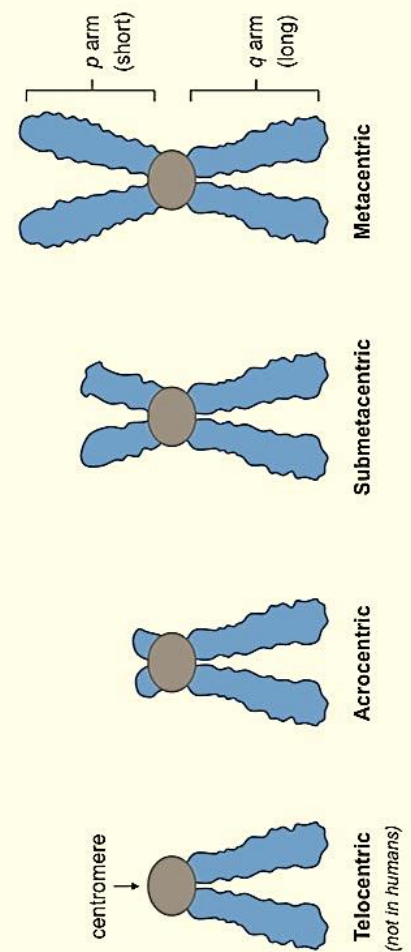
In this type of chromosome the centromere is a little away from the center and therefore chromatids of one side are slightly longer than the other side.

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 Organizer 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.



Human Chromosome Karyotype

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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. 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.

