River Valley High School
2025 JC1 H2 Biology

Lecture Topic 9: Organisation of Genomes - Eukaryotes

Name: _____ ( ) Class: 25J____ Date: _____

References

Title	Authors
Biology (9th Edition)	Campbell and Reece
Biology: An Australian Focus (3rd Edition)	Knox, Ladiges, Evans and Saint
Molecular Cell Biology (6th Edition)	Lodish, Berk, Kaiser, Krieger, Scott, Bretscher, Ploegh and Matsudaira
Molecular Biology of the Cell (5th Edition)	Alberts, Johnson, Lewis, Raff, Roberts and Walter
Principles of Genetics (3rd Edition)	Snustad and Simmons

H2 Biology Syllabus 9477 (2025)

Candidates should be able to use the knowledge gained in the following section(s) in new situations or to solve related problems.

Related Topics	Content
Control of Gene Expression - Eukaryotes	Control of eukaryotic gene expression
Organisation of Genomes - Prokaryotes	Prokaryotic genome

Learning Outcomes

2B. Organisation of Genomes

a. Describe the structure and organisation of viral, prokaryotic and eukaryotic genomes (including DNA/RNA, single-/double-stranded, number of nucleotides, packing of DNA, linearity/circularity and presence/absence of introns).

e. Describe the structure and function of non-coding DNA in eukaryotes (i.e. portions that do not encode protein or RNA, including introns, centromeres, telomeres, promoters, enhancers and silencers) (knowledge of transposons, satellite DNA, pseudo-genes and duplication of segments is not required).

Lecture Outline

I. Structure and Organisation of Eukaryotic Chromosomes

- A. Relating Structure of Eukaryotic Chromosomes to Cell Cycle
- B. Packing of DNA in Eukaryotic Chromosomes
- C. Organisation of DNA in Eukaryotic Chromosomes
  - i. Coding and Non-coding DNA
  - ii. Relating Structure of Centromere to its Role
  - iii. Relating Structure of Telomere to its Role
- D. Comparing the Structure/Organisation of Prokaryotic & Eukaryotic Chromosomes

Websites

URL	Description
https://www.dnalc.org/resources/3d/08-how-dna-is-packaged-advanced.html	packing of DNA in eukaryotic chromosome.
https://highered.mheducation.com/sites/9834092339/student_view0/chapter14/telomerase_function.html	description of telomerase action. *Note: you would need to use a laptop/desktop and download a chrome extension (e.g. “Flash Player for Chrome”) to view the tutorial.

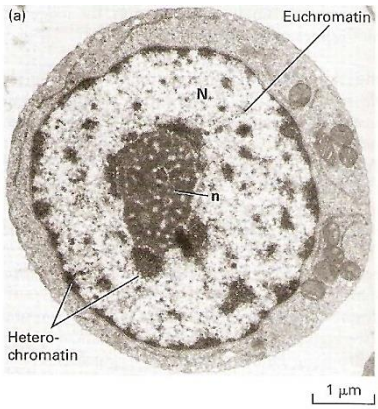
I. STRUCTURE AND ORGANISATION OF EUKARYOTIC CHROMOSOMES

The genomes of most eukaryotes are larger and more complex than those of prokaryotes. In this chapter, we shall consider the characteristics of eukaryotic genome[1] (in particular, the eukaryotic nuclear genome), i.e. the features of genes and the other DNA sequences that comprise the genome, and how these DNA is structured and organised by proteins within the cell.

Since the bulk of the eukaryotic genome is packed into chromosomes found in the nucleus[2], let's revisit key concepts related to the structure of eukaryotic chromosomes.

A. Relating Structure of Eukaryotic Chromosomes to Cell Cycle

1. The structure of eukaryotic chromosomes varies greatly during the cell cycle.

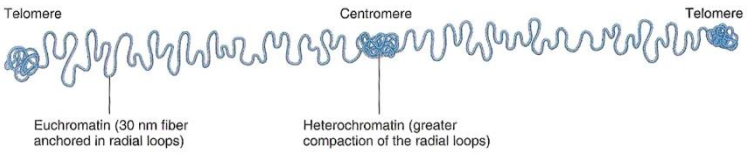


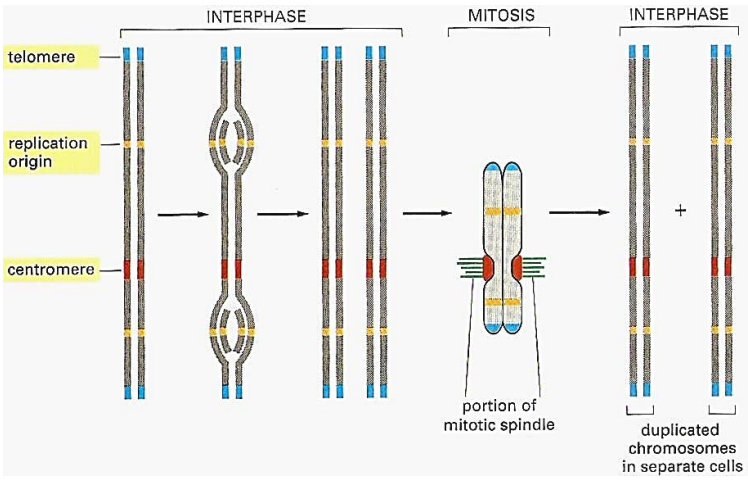
For non-dividing cells:

Each "chromosome" comprises one DNA double helix, which exists as decondensed chromatin so that genes are accessible to the transcriptional machinery.

From the electron micrograph,

- Euchromatin is decondensed and is thus transcriptionally active.
- Heterochromatin does not fully decondensed following cell division and is thus transcriptionally inactive.





For dividing cells:

During that part of interphase **before S phase**, each "chromosome" comprises one DNA double helix, which exists as decondensed chromatin.

After S phase (i.e. semi-conservative DNA replication), each chromosome comprises two DNA double helices, which exists as

- decondensed chromatin after S phase of interphase and before prophase; and
- two identical sister chromatids (i.e. condensed form) during nuclear division (i.e. from prophase to telophase).

[1] Definition of genome: the genetic material of an organism or virus, i.e. the complete complement of an organism's or virus's genes along with its non-coding nucleic acid sequence.
[2] Recall that chloroplasts and mitochondria contain their own genome, which are not stably inherited.

2. Eukaryotic chromosomes are characteristically **linear structures** that contain a centromere, which is responsible for attaching chromosomes to the kinetochore microtubules during cell division.

3. Consider mitotic metaphase chromosomes, which are large enough to be seen under a light microscope.

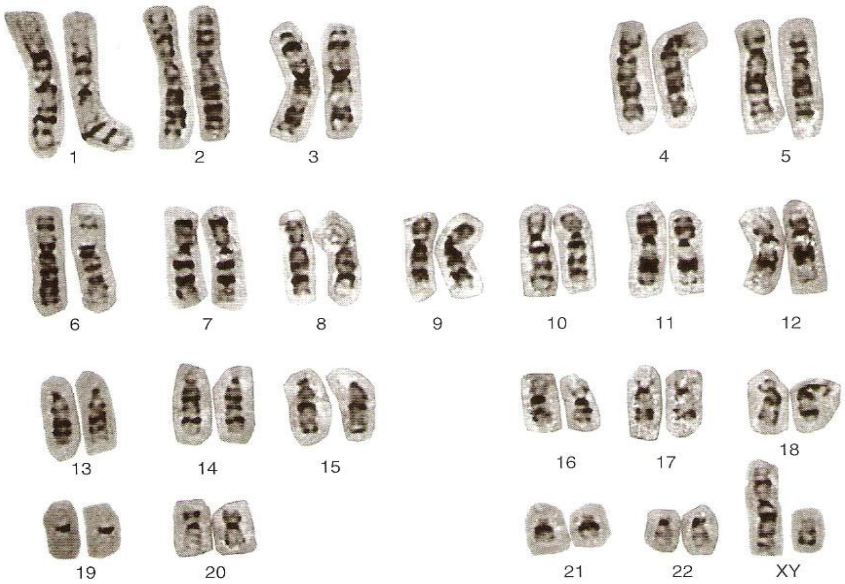


Figure 35–6. A human karyotype (of a man with a normal 46,XY constitution), in which the metaphase chromosomes have been stained by the Giemsa method and aligned according to the Paris Convention. (Courtesy of H Lawce and F Conte.)

Using the above example of the **human male karyotype**, we see that

i. the human genome is packaged into 23 pairs of chromosomes.

ii. the karyotype above shows a diploid genome. i.e. two sets of 23 chromosomes.

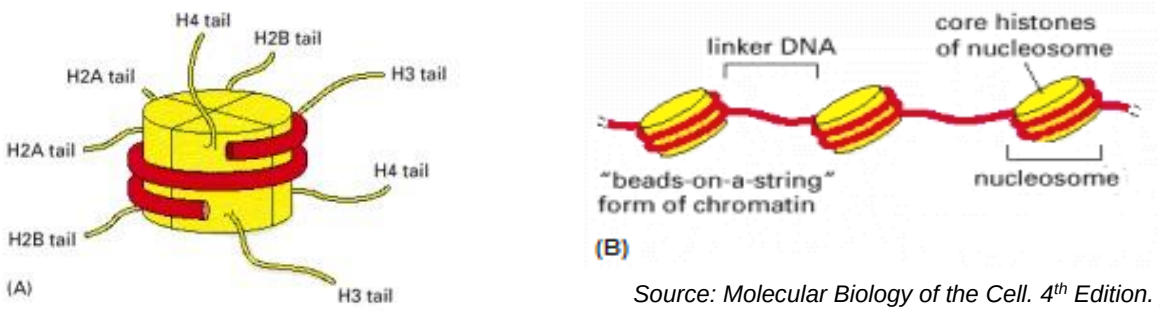
iii. the haploid genome (i.e. one set of 23 chromosomes) consists of 3 x 10^9 base-pairs (bp) – this stretch of DNA is approx. 1000 mm long from end to end.
   - this metre of DNA is subdivided amongst 23 chromosomes of variable size and shape, with each chromosome containing 15 to 85 mm of DNA.

iv. each chromosome has two sister chromatids, indicating that it is taking part in cell division.

B. Packing of DNA in Eukaryotic Chromosomes

First level of condensation:

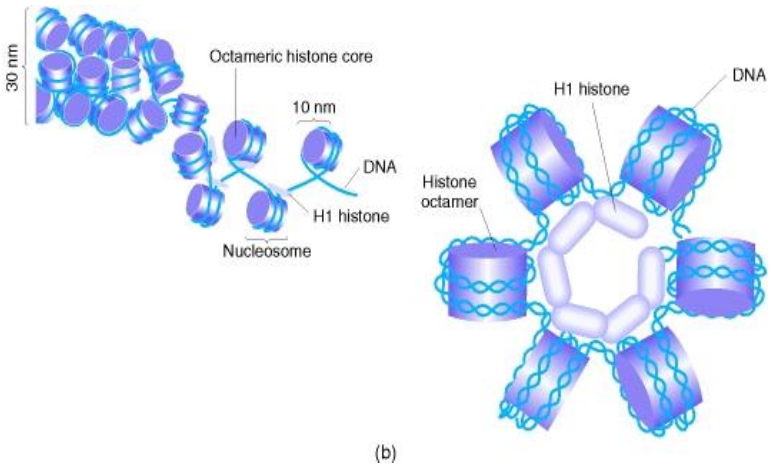
1. DNA is packed into nucleosomes to produce the 10-nm interphase chromatin fibre a.k.a. nucleosome fibre ("beads on a string").
2. A nucleosome consists of DNA wound twice around a protein core composed of an octamer of 4 histone molecules, two each of histones H2A, H2B, H3 and H4.
   - Histones are small proteins (M_r = 11 000) with a high concentration of basic residues, e.g. lysine and arginine (positively-charged R groups), which interact with the negatively-charged sugar-phosphate backbone of DNA.
   - Histones assemble in groups of eight (i.e. an octamer) to form a core upon which DNA is bound.
   - dsDNA, which is 146 bp in length, is coiled 1 ¾ turns around the histone core, forming a nucleosome core. This gives the chromatin a 'beads-on-a-string' look.
   - The 10-nm chromatin fibre consists of the nucleosomes and the linker DNA. Such chromatin resembles beads on a string. Each "bead" is a nucleosome, the "string" between the beads is called linker DNA.
3. In the cell cycle, the histones leave the DNA only briefly during DNA replication and gene expression, processes that require access to the DNA by the cell's molecular machinery.

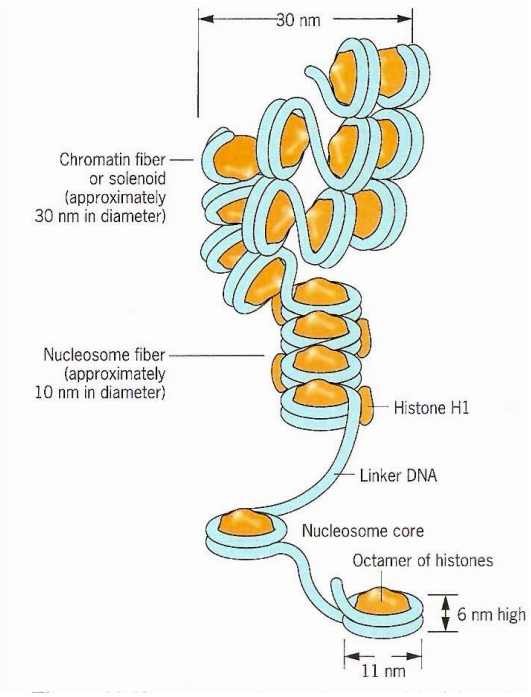


Source: Molecular Biology of the Cell. 4th Edition. pp 20

Second level of condensation:

1. DNA is further folded or coiled to produce the 30-nm chromatin fibre, a.k.a. **solenoid**.
2. Histone H1 and linker DNA is involved in this coiling of the 10-nm nucleosome fibre to produce the 30-nm chromatin fibre.



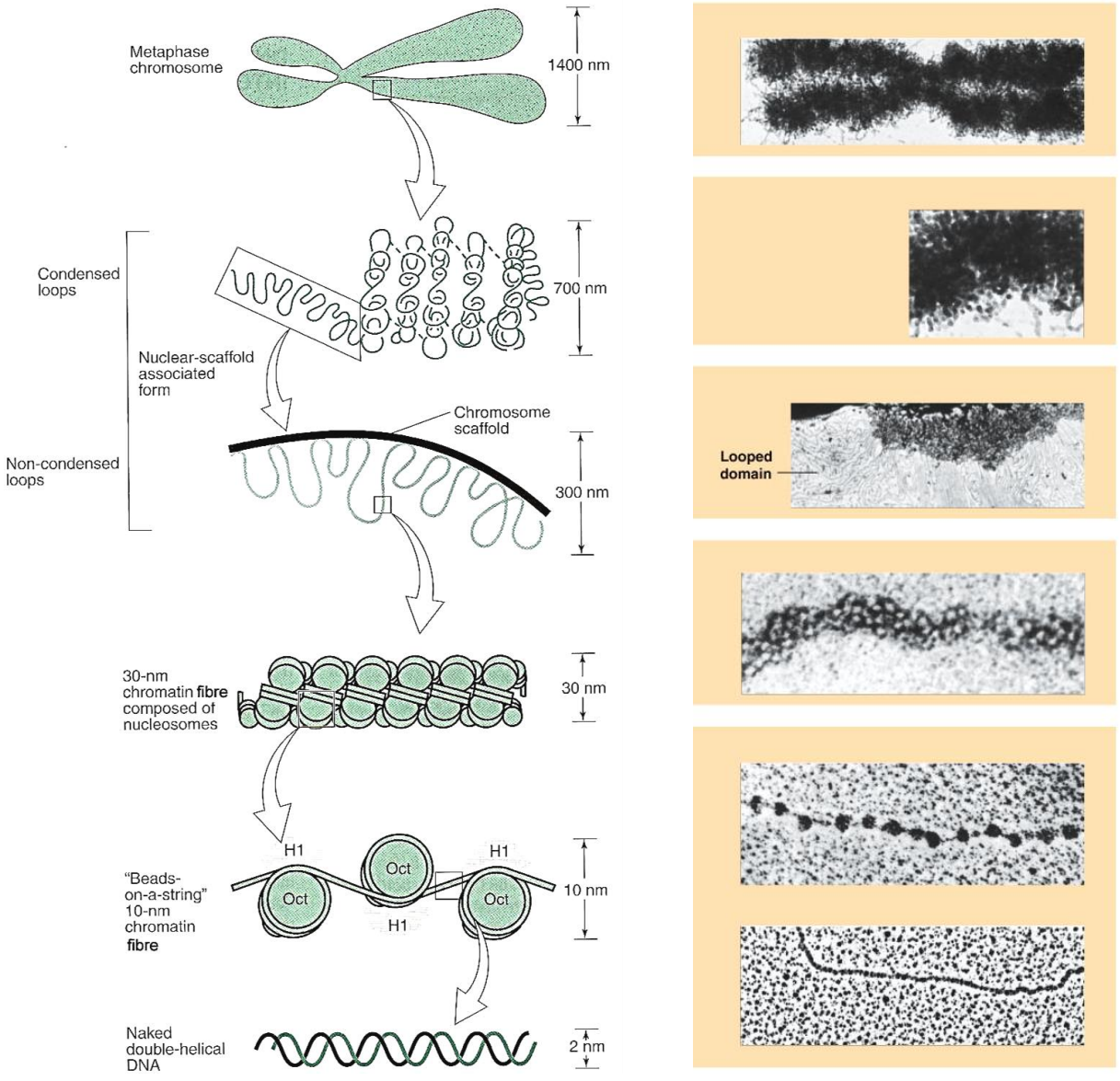


Third level of condensation:

1. Finally, non-histone chromosomal proteins form a scaffold that is involved in condensing the 30-nm chromatin fibre into loops called **looped domains**, forming the 300-nm fibre.
2. In mitotic and meiotic chromosomes, the looped domains themselves coil and fold, further compacting all the chromatin to produce the characteristic metaphase chromosome. The width of one chromatid is 700 nm.
3. Particular genes always end up located at the same places in mitotic and meiotic chromosomes, indicating that the packing steps are highly specific and precise.

Role of condensation:

1. To organise and pack the giant DNA molecules into a more compact structure.
2. Significance of packing into chromatin:
   - To fit within the cell's nucleus.
   - To prevent the long DNA molecules from getting tangled.
3. Significance of packing into chromosome during cell division:
   - To facilitate their segregation into daughter nuclei.
   - DNA molecules of different chromosomes will NOT be entangled and as a consequence, break during separation at anaphase.



C. Organisation of DNA in Eukaryotic Chromosomes

In eukaryotic genomes, only 3% of the DNA sequences are coding regions that code for proteins or RNA. The remaining 97% are non-coding regions.

i. Coding and Non-coding DNA

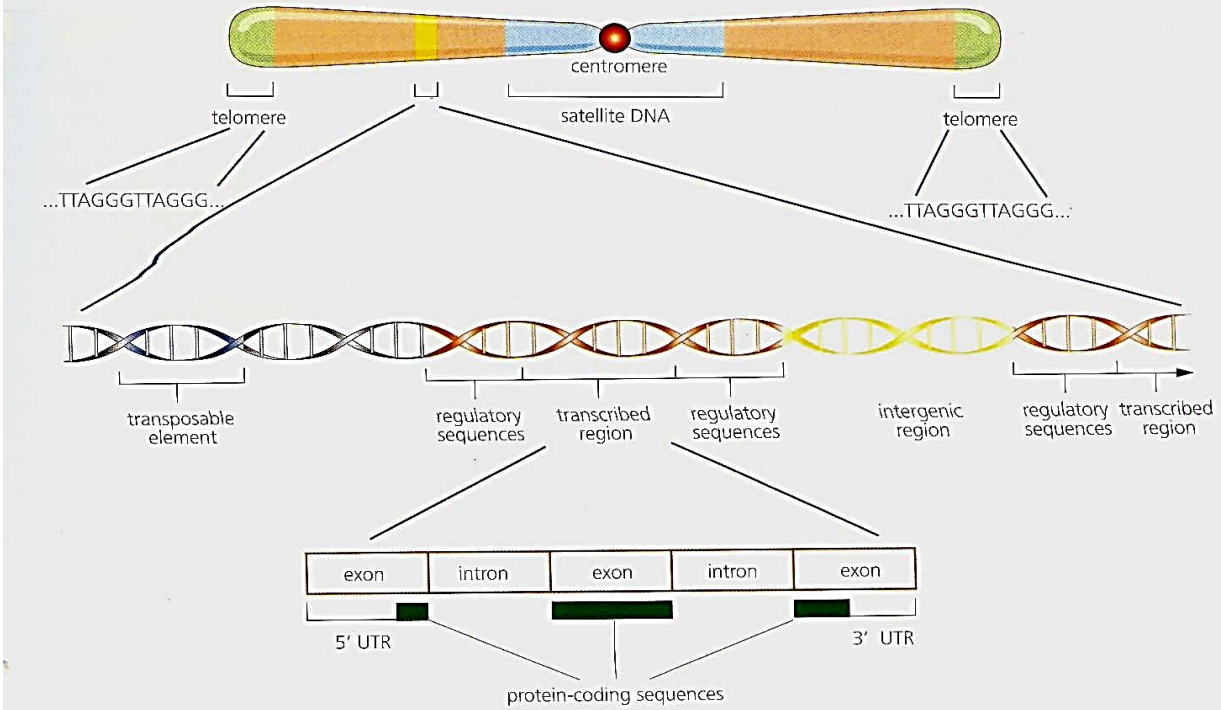


Fig. 12.4 A diagrammatic summary of some of the types of sequences found in a human chromosome. The diagrammatic representation of DNA is not to scale with respect to the sequence types indicated.

Coding Sequences

1. Those DNA sequences that carry information correspond to specific genes. e.g. protein-coding genes and RNA-coding genes[3].
2. Heavily used gene products are encoded by multiple copies of genes. In eukaryotes, heavily used gene products (e.g. histones, rRNAs, snRNAs) are encoded by multiple copies of genes arranged in repeats, either
   i. interspersed (i.e. copies of a sequence are separated by other sequences); or
   ii. in tandem (i.e. copies of a sequence appear one after another, in a head-to-tail fashion, over a long stretch of DNA).
3. In eukaryotes, coding sequences[4] of a protein-coding gene are frequently interrupted by introns, which are non-coding sequences that are interspersed in the genomic coding DNA. The introns are removed from the mRNA product by splicing prior to translation.

[3] Recall: Although most genes are transcribed into mRNAs that encode proteins, some DNA sequences are transcribed into RNAs that do not encode proteins, e.g. tRNA, rRNA, snRNA.
[4] Coding sequence of a protein-coding gene refers to the DNA sequence (i.e. codon sequence) that is ultimately translated into a functional polypeptide.

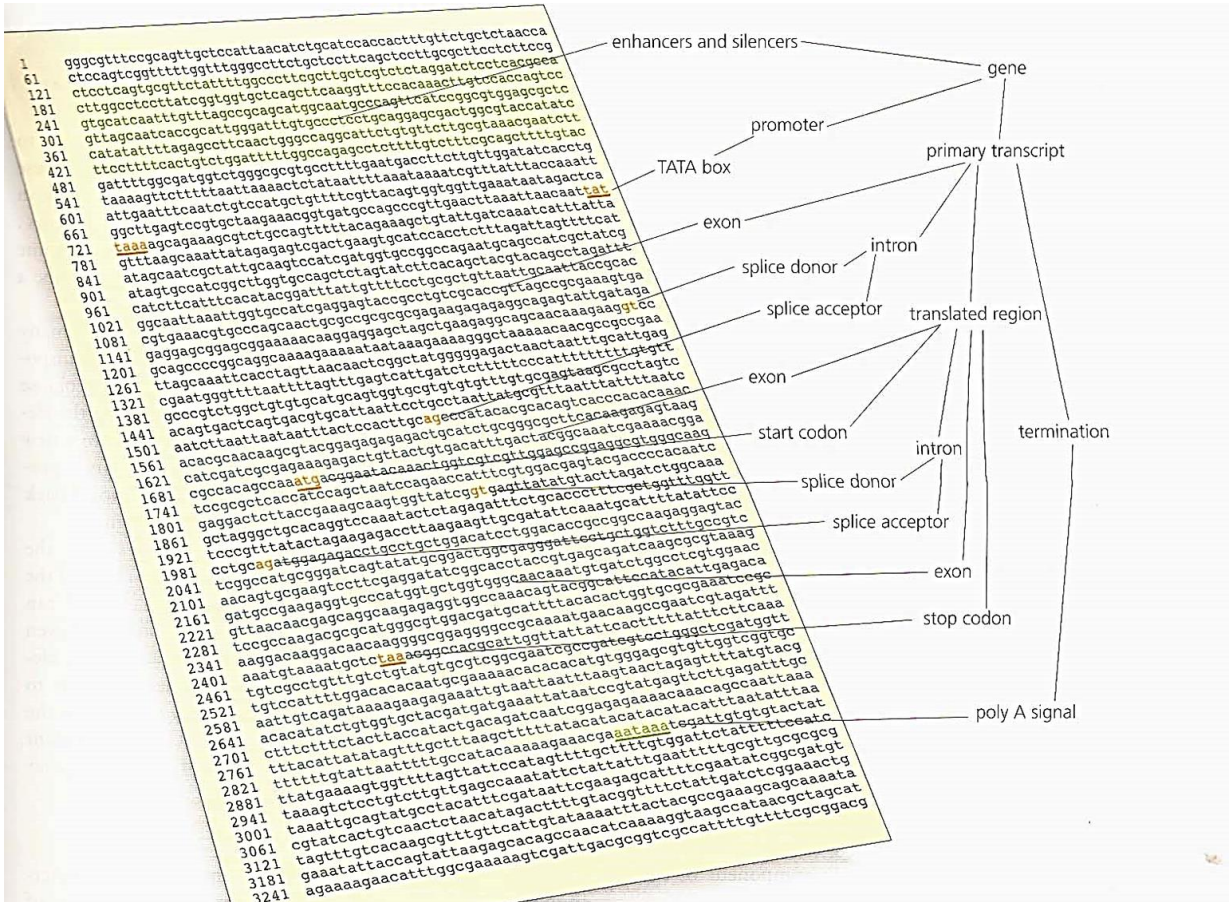
Non-Coding Sequences

1. The amount of non-coding sequences in genomes varies between different species but typically constitutes a high proportion of the total genome sequence.

2. The 3×10^9 bp of the human haploid genome, for example, contains sufficient DNA to code for nearly 1.5×10^6 average-sized genes. However, studies suggest that have less than 1×10^5 proteins!

   i. As little as 2 % of mammalian DNA codes for proteins. Part of the remaining DNA codes for:

   - introns
   - 5' & 3' untranslated regions (UTRs)
   - promoters
   - enhancer and silencer sequences
   - replication origin and termination
   - centromeres and telomeres



Types of sequences found in human genome

ii. Much of the non-coding DNA appears to be composed of **repeated sequences**. Briefly, the repeated sequences are broadly classified as:

a) **Tandemly repetitive DNA**

- which are DNA sequences in which multiple copies are arranged next to each other as in the following example:

  …GTTACGTTACGTTACGTTACGTTACGTTAC……

- can be grouped into three subclasses:
  - Satellite DNA have a core sequence of 5 to 171 bp that is tandemly repeated with total lengths between 100 kb to several Mb;
  - Minisatellites (a.k.a. Variable Number of Tandem Repeats, VNTRs) have a core sequence of about 20 bp with total lengths between 100 and 20000 bp; and
  - Microsatellites (a.k.a. Short Tandem Repeats, STRs) have a core sequence of 2 to 4 bp that is tandemly repeated from 10 to 20 times.
- they are transcriptionally inactive and may play a structural role in the chromosome,
- examples: centromeres and telomeres

b) **Moderately repetitive DNA**,

- the repeated units are not next to each other; instead, they are scattered about the genome.
- examples: promoters, enhancers and origins of replication.

ii. Relating Structure of Centromere to its Role

1. Eukaryotic chromosomes possess identical duplicated sister chromatids connected at a centromere, the relative position of which is characteristic for a given chromosome.
2. Structure:

   The centromere is a repetitive DNA sequence. It is an A-T rich region ranging in size from 10^2 (in brewer's yeast) to 10^6 (in mammals) base-pairs.
3. Function:

   The centromere binds several proteins (forming a complex) with high affinity. This complex, called the kinetochore, provides the anchor for the spindle fibres. The centromere is thus an essential structure for chromosome segregation during cell division.

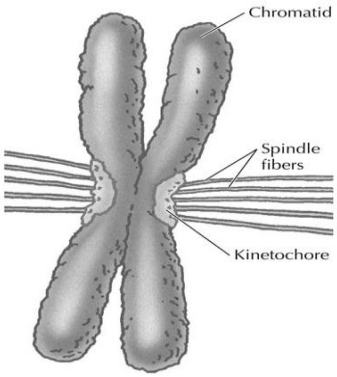
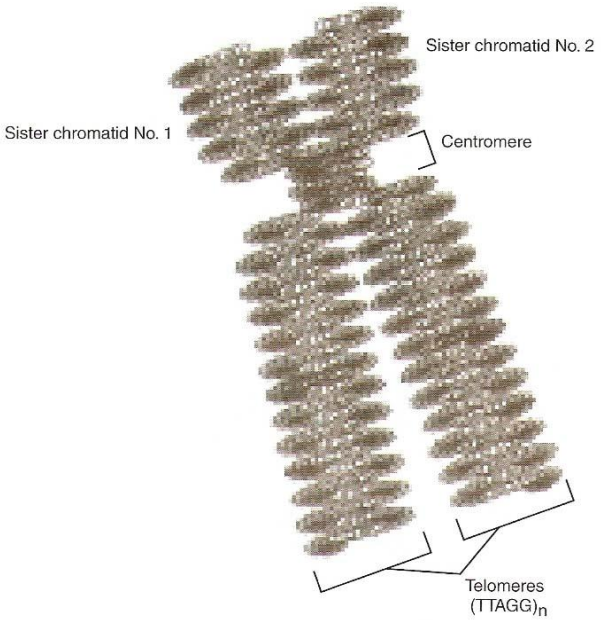


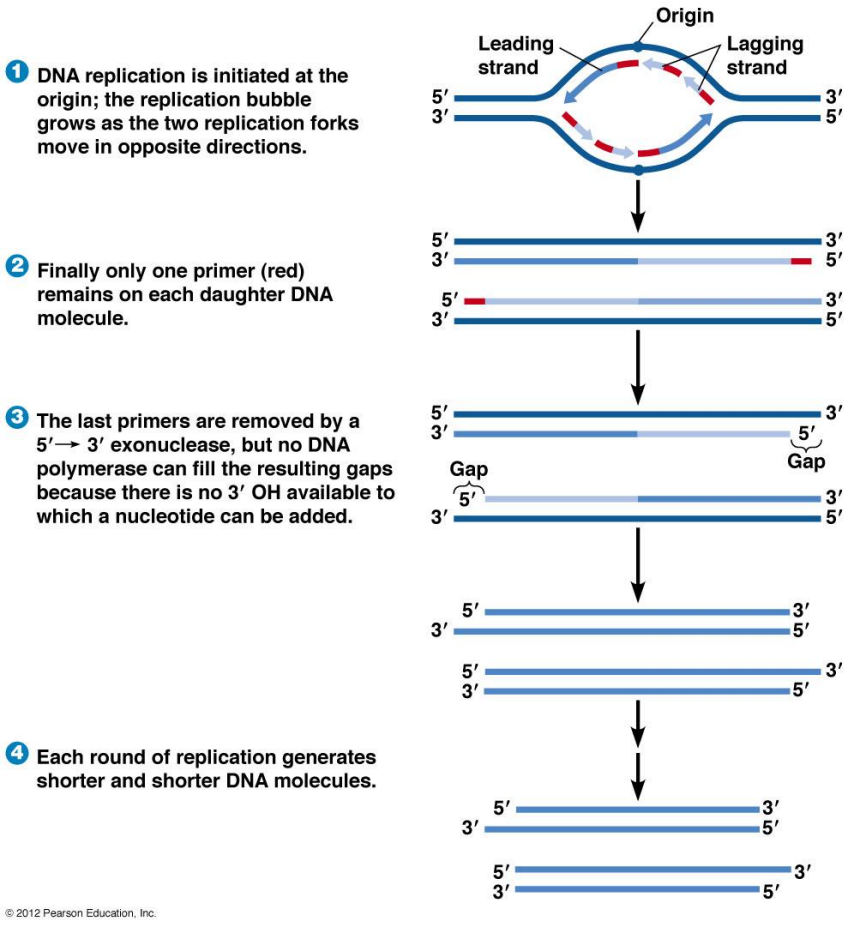
Figure 35–5. The two sister chromatids of human chromosome 12. The location of the A+T-rich centromeric region connecting sister chromatids is indicated, as are two of the four telomeres residing at the very ends of the chromatids that are attached one to the other at the centromere.



iii. Relating Structure of Telomere to its Role

1. The ends of each chromosome contain structures called **telomeres**.
2. Structure:

   Telomeric sequences are repetitive DNA sequences. They are typically short, repeated TG-rich sequences, e.g. TTAGGG in vertebrates. There can be over 2000 of these repeats, generating a telomeric region of 10 to 15 kb in length
3. Function:
   i. To prevent fusion of the ends of the chromosomes with other DNA molecules;
   ii. To prevent exonucleases from degrading the ends of the linear DNA molecules;
   iii. To prevent the loss of genetic information by acting as a disposable buffer;
   iv. To facilitate replication of the ends of the linear DNA molecules without loss of the termini;
   v. To prevent cell cycle arrest / cell death, i.e. specific proteins associated with telomeric DNA prevent the staggered ends of the daughter DNA molecule from activating the cells system for monitoring DNA damage.
4. **Telomere shortening** has been associated with ageing and malignant transformation. Research has shown that telomeres are important for the functional stability of linear chromosomes. Why so?
   i. Since DNA polymerases
      (i) assemble DNA only in the 5' to 3' direction and
      (ii) need a primer, they cannot complete DNA replication to the 5' ends of both daughter DNA strands.
   ii. After the removal of the primer, there is nothing from which the DNA polymerase can extend! DNA polymerase cannot fill the gap because there is no 3' –OH group present as a starting point.
   iii. After many rounds of cell division and hence replication, chromosomes would become progressively shorter because of the gap left after removal of the primer at the 5' end of the lagging strand.



Source: Biology. 6th Edition. pp300.

5. Role of telomerase:
   i. In some cells, such as germ cells, stem cells, the above problem is overcome by the presence of the telomere, a terminal sequence consisting of repeated DNA sequences.
   ii. These repeats are added on to the ends of chromosomes by a special enzyme termed **telomerase**.
6. Structure of telomerase:
   i. Telomerase consists of two components: telomerase reverse transcriptase (TERT) and an RNA template.
   ii. The RNA template is complementary to the telomere repeat sequences and serve as a template for the reverse transcriptase to elongate telomeric DNA.
   iii. Telomerase is absent in most normal human somatic cells but present in germ cells, stem cells, and cancer cells.

BOX 9.4 Telomerases and cellular ageing

Telomerases are required to overcome the inability of DNA polymerases to synthesise the very 5′ end of a chromosome. Curiously, although the germ cells of mammals contain telomerase, the somatic cells do not. The consequence is a progressive shortening of telomere sequences as the somatic cells proceed through cellular divisions. In cultured cells, the shortening eventually results in the loss of essential sequences that were adjacent to the telomeric repeats, causing the cells to die after a certain number of cell divisions. The shortening of telomeres from somatic cells during replication may contribute to the ageing process. It was recently shown that if telomerase expression can be induced in cultured mammalian cells, the cells no longer die as they normally would but continue to proliferate indefinitely. The telomerase has 'immortalised' these cells.

The recent cloning of the sheep, Dolly, from a somatic cell raised a lot of interest and controversy. As the somatic cell from which Dolly was generated should have had shortened telomeres, Dolly might be expected to have shorter telomeres than normal sheep at the same age. A recent study showed that, indeed, Dolly's telomeres were shorter than normal.

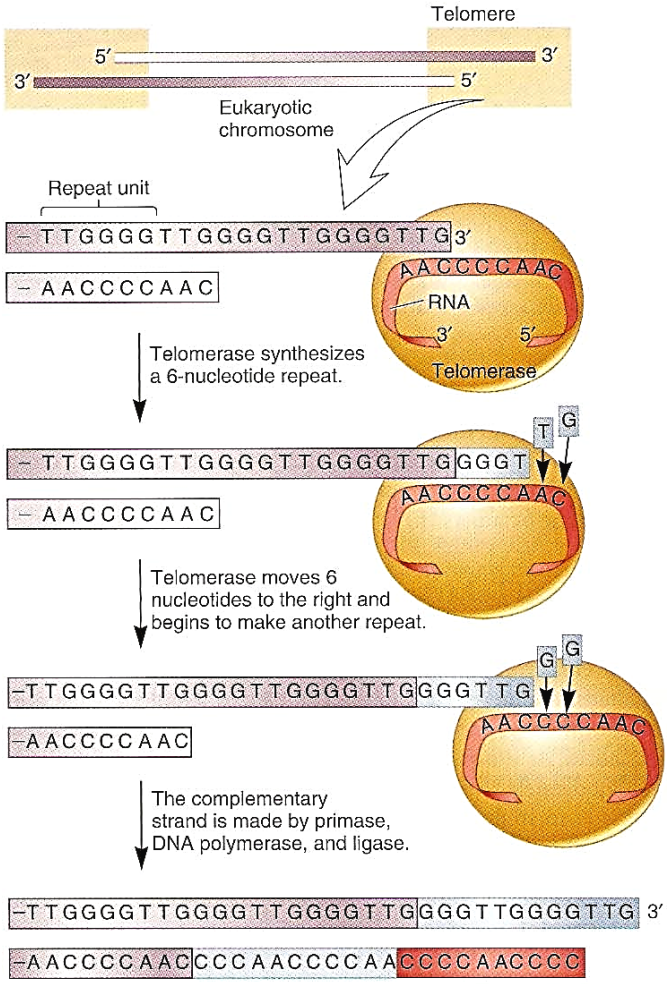
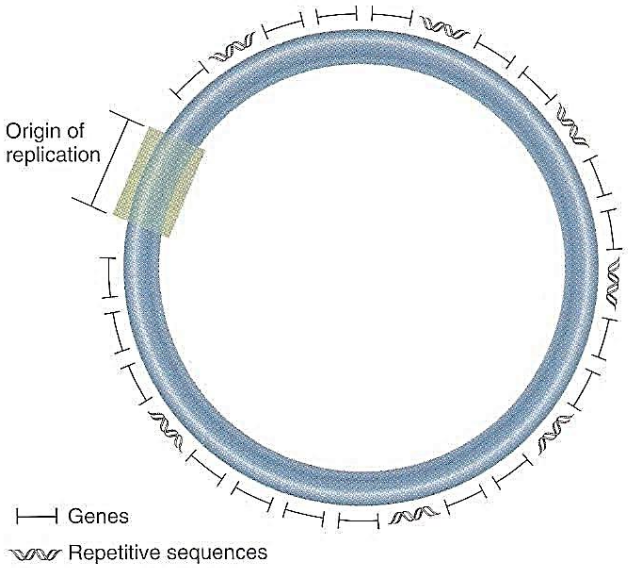


FIGURE 11.25 The enzymatic action of telomerase. A short, three nucleotide segment of RNA within telomerase causes it to bind to the 3′ overhang. The adjacent part of the RNA is used as a template to make a short, six-nucleotide repeat of DNA. After the repeat is made, telomerase moves six nucleotides to the right and then synthesizes another repeat. This process is repeated many times to lengthen the *top* strand shown in this figure. The *bottom* strand would be made by DNA polymerase, using an RNA primer at the end of the chromosome that would be complementary to the telomeric repeat sequence in the top strand.

Source: Biology: An Australian Focus. 3rd Edition. pp. 216

D. Comparing the Structure/Organisation of Prokaryotic & Eukaryotic Chromosomes

Prokaryotic Chromosome:

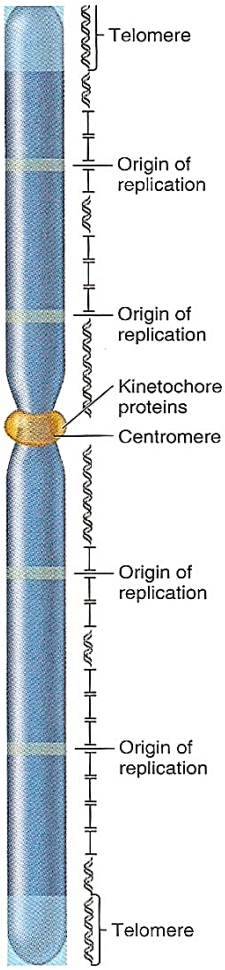


Key features:

- Most, but not all, bacterial species contain circular chromosomal DNA.
- A typical chromosome is a few million base pairs in length.
- Most bacterial species contain a single type of chromosome, but it may be present in multiple copies.
- Several thousand different genes are interspersed throughout the chromosome.
- One origin of replication is required to initiate DNA replication.
- Short repetitive sequences may be interspersed throughout the chromosome.

FIGURE 10.4 **Organization of sequences in bacterial chromosomal DNA.**
Source: Genetics: Analysis and Principles. 2nd Edition. pp. 256

Eukaryotic Chromosome:



Key features:

- Eukaryotic chromosomes are usually linear.
- A typical chromosome is tens of millions to hundreds of millions of base pairs in length.
- Eukaryotic chromosomes occur in sets. Many species are diploid, which means that somatic cells contain 2 sets of chromosomes
- Genes are interspersed throughout the chromosome. A typical chromosome contains between a few hundred and severa thousand different genes.
- Each chromosome contains many origins of replication that are interspersed about every 100,000 base pairs.
- Each chromosome contains a centromere that forms a recognition site for the kinetochore proteins.
- Telomeres contain specialized sequences located at both ends of the linear chromosome.
- Repetitive sequences are commonly found near centromeric and telomeric regions, but they may also be interspersed throughout the chromosome.

FIGURE 10.11 **Organization of DNA sequences within eukaryotic chromosomes.**