ORGANISATION OF CHROMOSOMES

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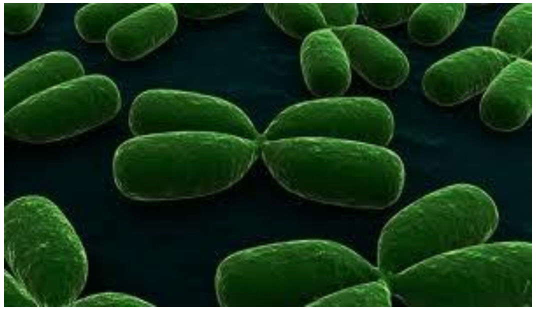
INTRODUCTION



- Chromosomes are the structures that contain the genetic material
  - They are complexes of DNA and proteins
- The genome comprises all the genetic material that an organism possesses
  - In bacteria, it is typically a single circular chromosome
  - In eukaryotes, it refers to one complete set of *nuclear* chromosomes
    - Note: Eukaryotes possess a mitochondrial genome
      Plants also have a chloroplast genome

Cont…

- The main function of the genetic material is to store information required to produce an organism
  - The DNA molecule does that through its base sequence

- DNA sequences are necessary for
  1. Synthesis of RNA and cellular proteins
  2. Proper segregation of chromosomes
  3. Replication of chromosomes
  4. Compaction of chromosomes
     - So they can fit within living cells

VIRAL GENOME

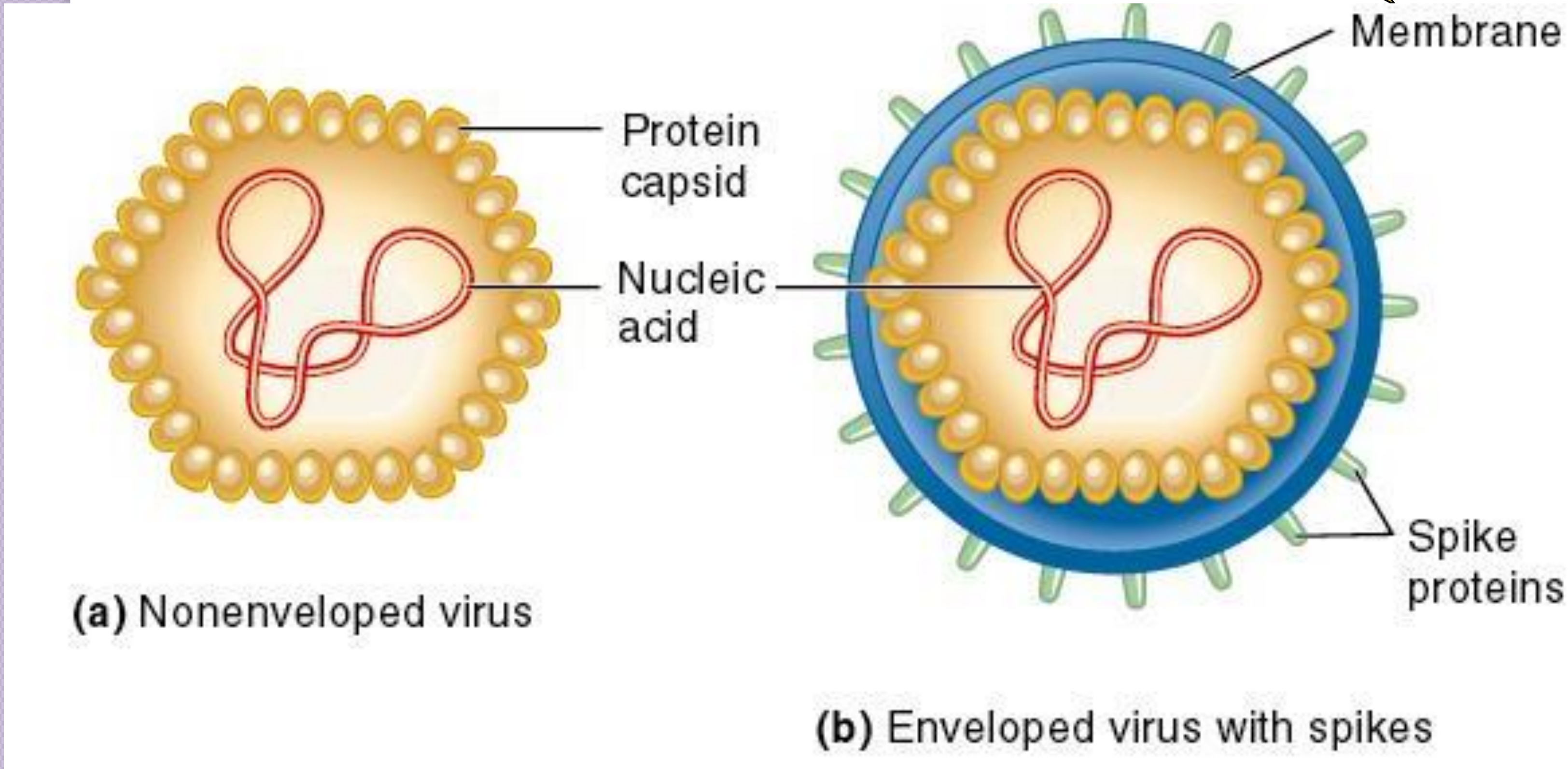
- Viruses are small infectious particles containing nucleic acid surrounded by a capsid of proteins
- For replication, viruses rely on their host cells
  - ie., the cells they infect
- Most viruses exhibit a limited host range
  - They typically infect only specific types of cells of one host species
- A viral genome is a term used as in whole of the genetic material.
  - Also termed the viral chromosome
- The genome can be
  - DNA or RNA
  - Single-stranded or double-stranded
  - Circular or linear

- Viral genomes vary in size from a few thousand to more than a hundred thousand nucleotides

GENERAL STUUCTURE OF VIRUSES

Lipid bilayer

Picked up when virus leaves host cell



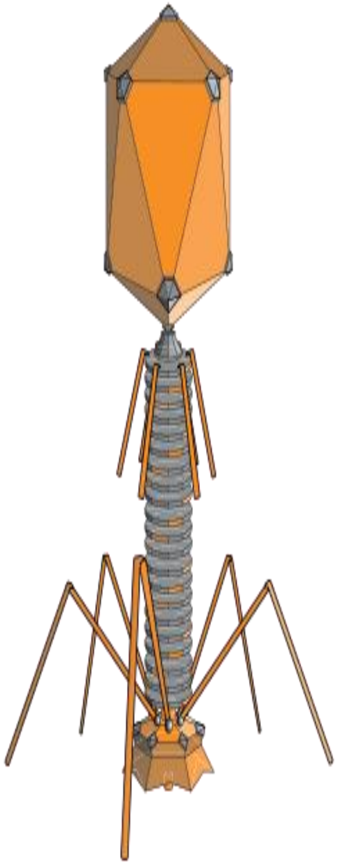
(a) Nonenveloped virus

(b) Enveloped virus with spikes

Cont……

- Bacteriophage is very common virus consists of NA+ ptn which is usually enclosed by 3 types of capsid structure
- Icosahedral
- Filamentous
- Head and tail

Phage	Host	Shape	Genome	Genome size (kb)	No. of genes
MS^2	E.coli	Icosahedral	SS linear RNA	3.6	3
M13	E.coli	Filamentous	SS linear DNA	6.7	10
T_7	E.coli	Head and tail	DS linear DNA	39.9	55+



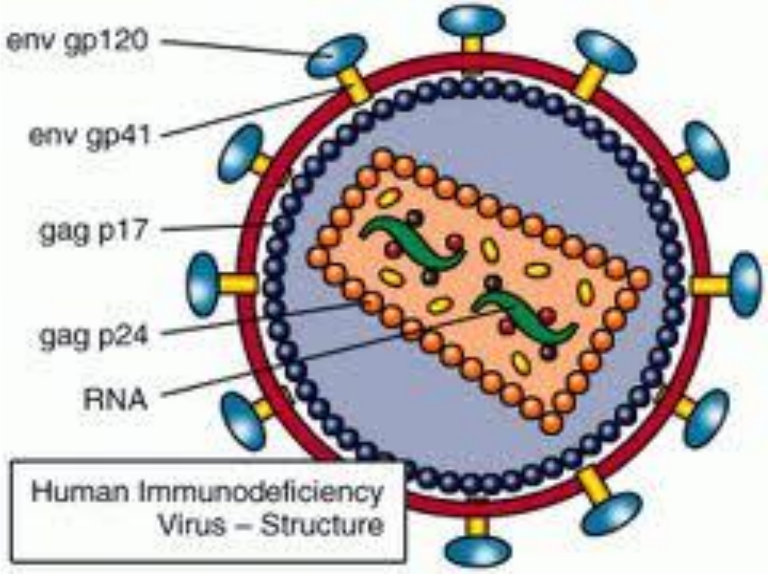
Cont……

- Eukaryotic virus consist of capsid + NA
- Capsid can be of Icosahedral and filamentous.

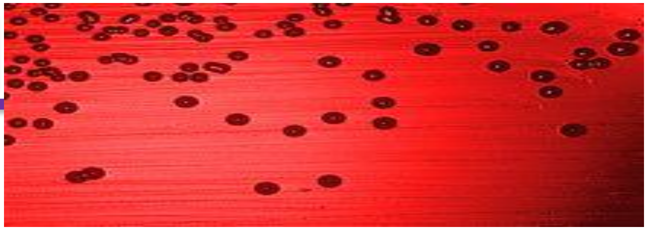
Virus	Host	Types of genome [1]	Size of genome	No. of gene
Parvovirus	Mammals	SS linear DNA	1.6 kb	5
Tobacco mosaic virus	Plant	SS linear RNA	3.2 kb	4

1- From is given which exist in phage protein.

Example – HIV virus



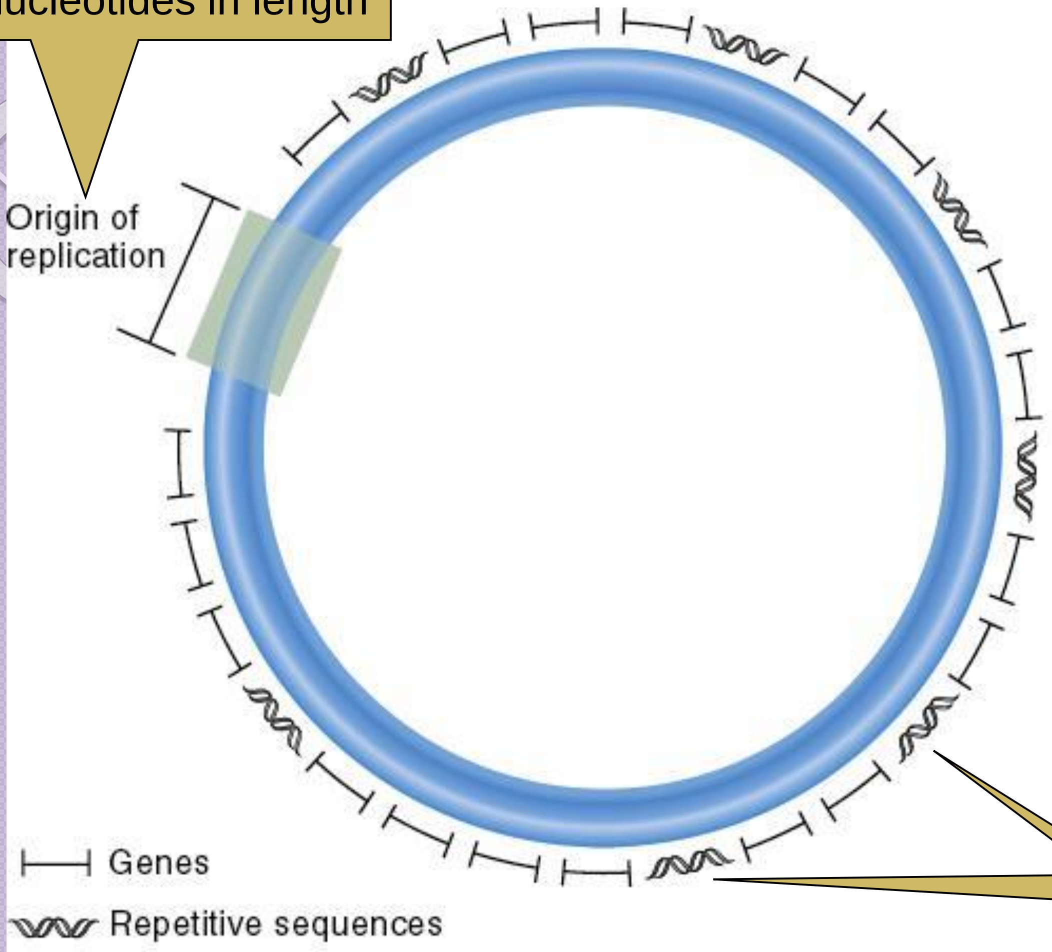
BACTERIAL GENOM



- Bacterial chromosomal DNA is usually a circular molecule that is a few million nucleotides in length.
  - *Escherichia coli* → ~ 4.6 million base pairs
  - *Haemophilus influenzae* → ~ 1.8 million base pairs

- A typical bacterial chromosome contains a few thousand different genes
  - Structural gene sequences (encoding proteins) account for the majority of bacterial DNA
  - The no transcribed DNA between adjacent genes are termed intergenic regions

A few hundred nucleotides in length



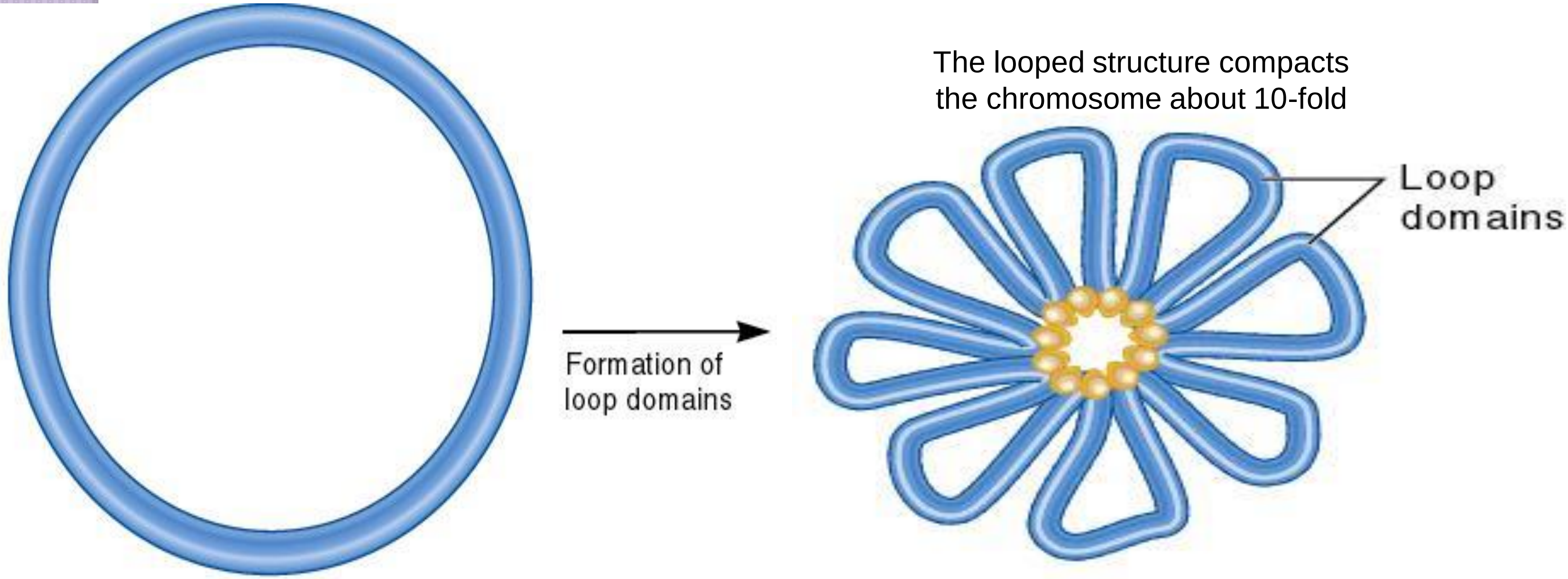
Key features:

- 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.

These play roles in DNA folding, DNA replication, and gene expression

To fit within the bacterial cell, the chromosomal DNA must be compacted about a 1000-fold This involves the formation of loop domains. The number of loops varies according to the size of the bacterial chromosome and the species.

E. coli has 50-100 with 40,000 to 80,000 bp of DNA in each.



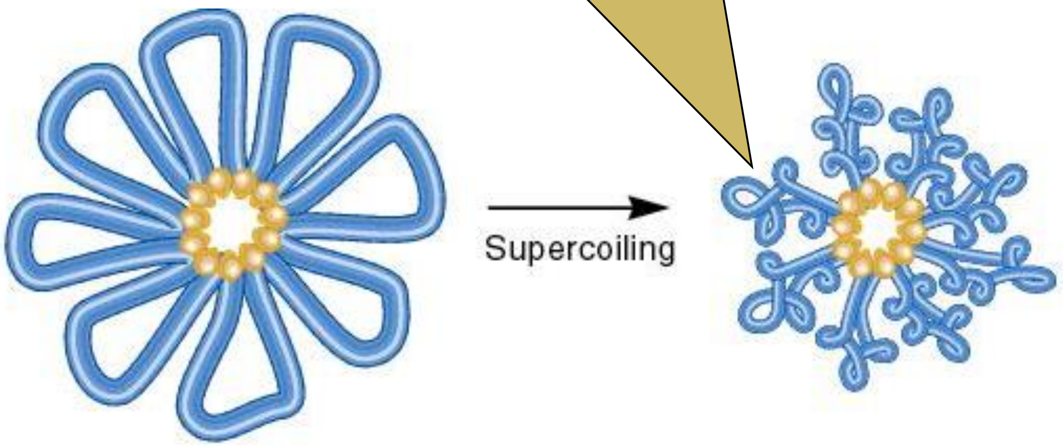
The looped structure compacts the chromosome about 10-fold

(a) Circular chromosomal DNA

(b) Looped chromosomal DNA with associated proteins

- DNA super coiling is a second important way to compact the bacterial chromosome

Supercoiling within loops creates a more compact DNA



(a) Looped chromosomal DNA

(b) Supercoiled and looped DNA

A SCHEMATIC ILLUSTRATION OF DNA SUPER COILING

EUKARYOTIC CHROMOSOMES

- Eukaryotic species contain one or more sets of chromosomes
  - Each set is composed of several different linear chromosomes

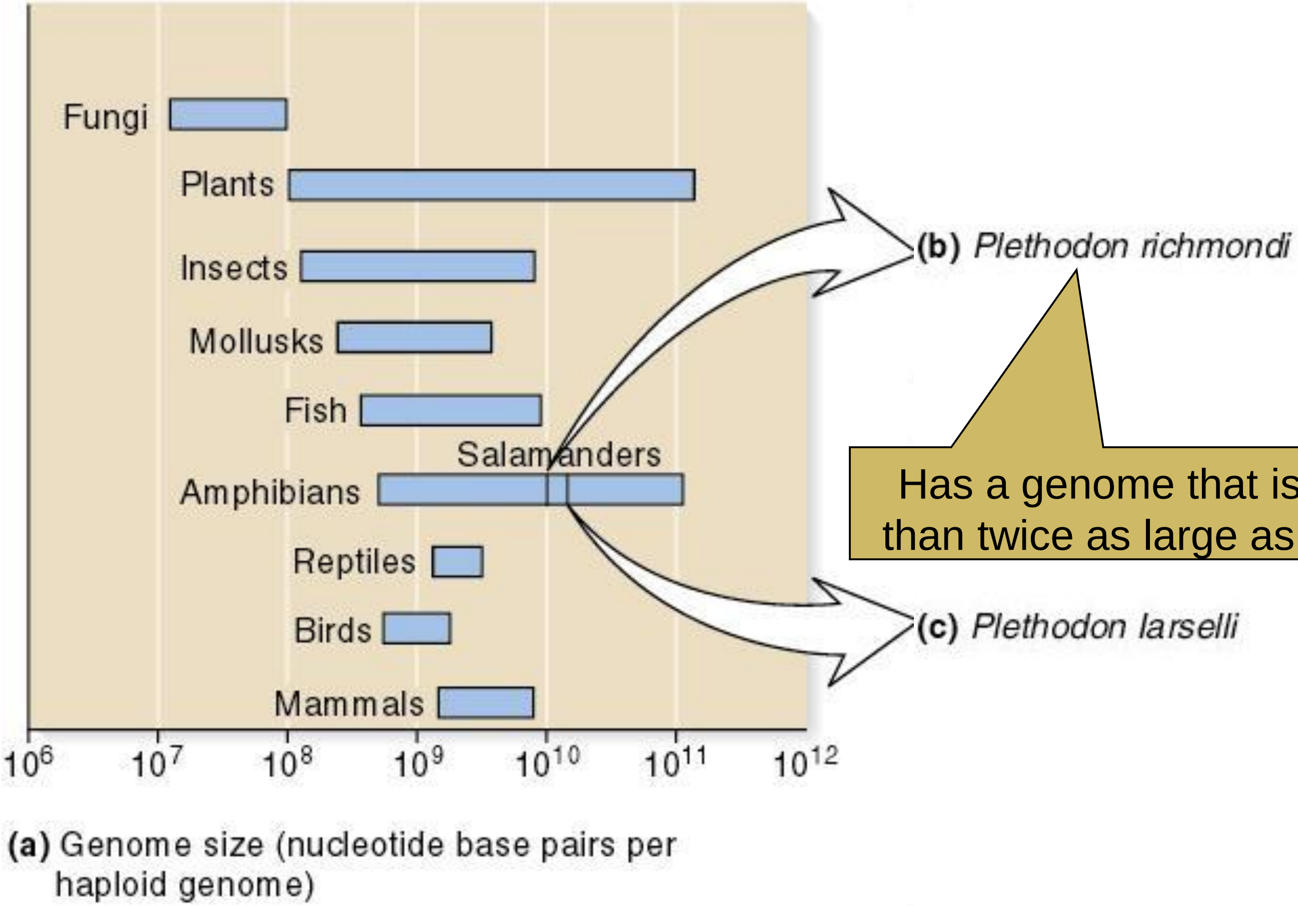
- The total amount of DNA in eukaryotic species is typically greater than that in bacterial cells

- Chromosomes in eukaryotes are located in the nucleus
  - To fit in there, they must be highly compacted
    - This is accomplished by the binding of many proteins
    - The DNA-protein complex is termed

- Eukaryotic genomes vary substantially in size

- In many cases, this variation is not related to complexity of the species
  - For example, there is a two fold difference in the size of the genome in two closely related salamander species.

  - The difference in the size of the genome is not because of extra genes
    - Rather, the accumulation of repetitive DNA sequences
      - These do not encode proteins



Has a genome that is more than twice as large as that of

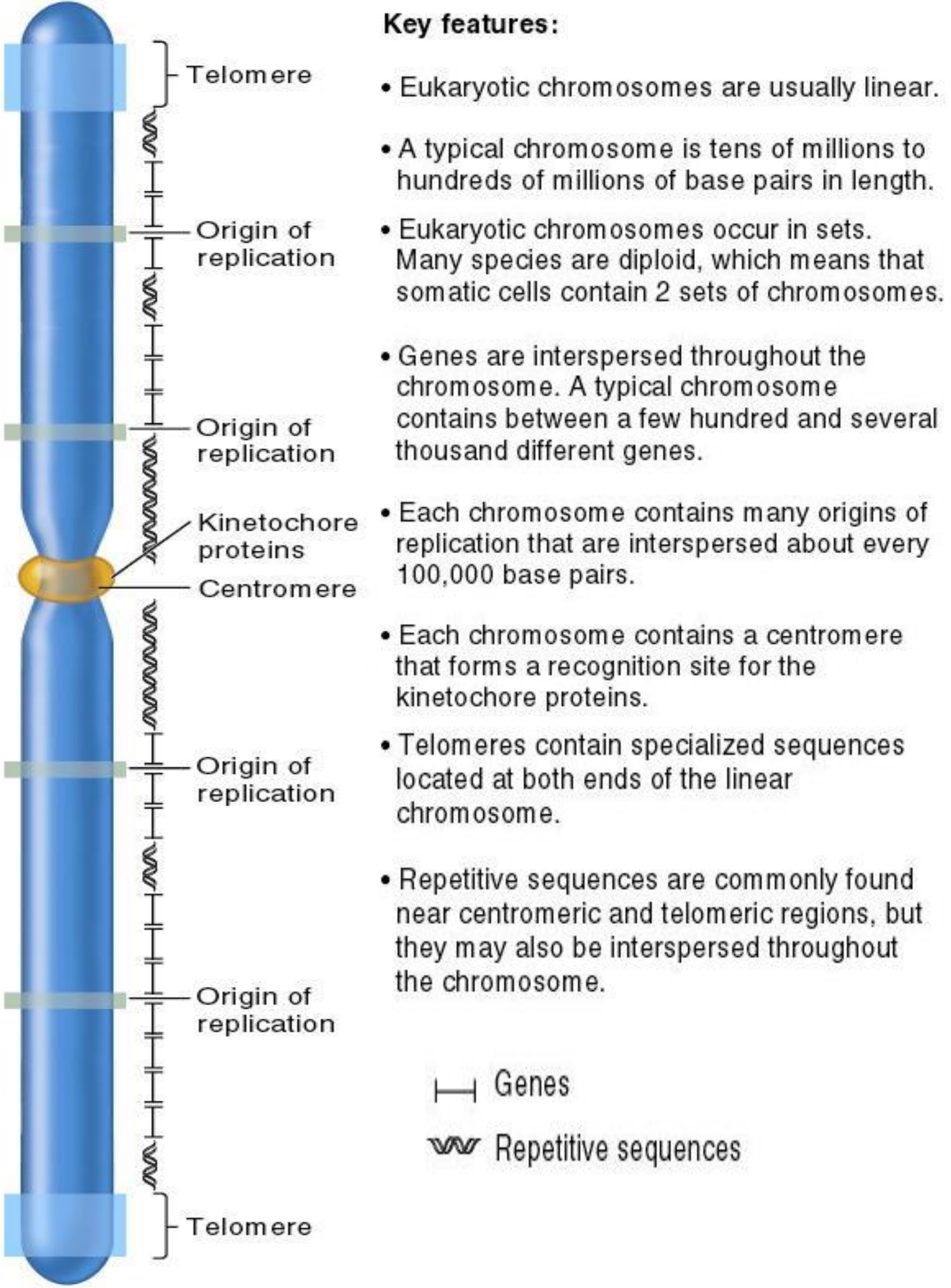
SIZE V/S COMPLEXITY OF THE SPECIES

Organization of Eukaryotic Chromosomes

- A eukaryotic chromosome contains a long, linear DNA molecule

- Three types of DNA sequences are required for chromosomal replication and segregation
    - Origins of replication
    - Centromeres
    - Telomeres

A TYPICAL CHROMATID



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 several 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.

Dude, mitosis starts in five minutes...
I can't believe you're not condensed yet.

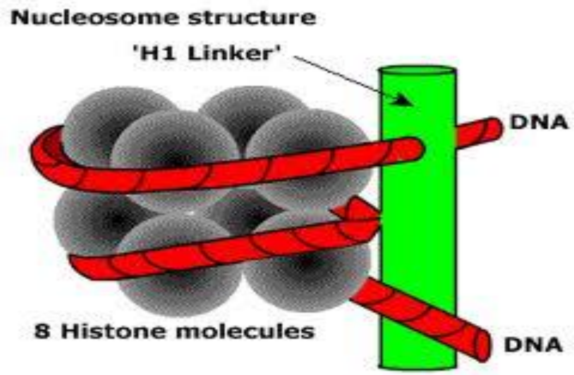
http://www.promega.com/

DNA to chromosomes ????????????

Eukaryotic Chromatin Compaction

- If stretched end to end, a single set of human chromosomes will be over 1 meter long!
  - Yet the cell’s nucleus is only 2 to 4 mm in diameter
    - Therefore, the DNA must be tightly compacted to fit

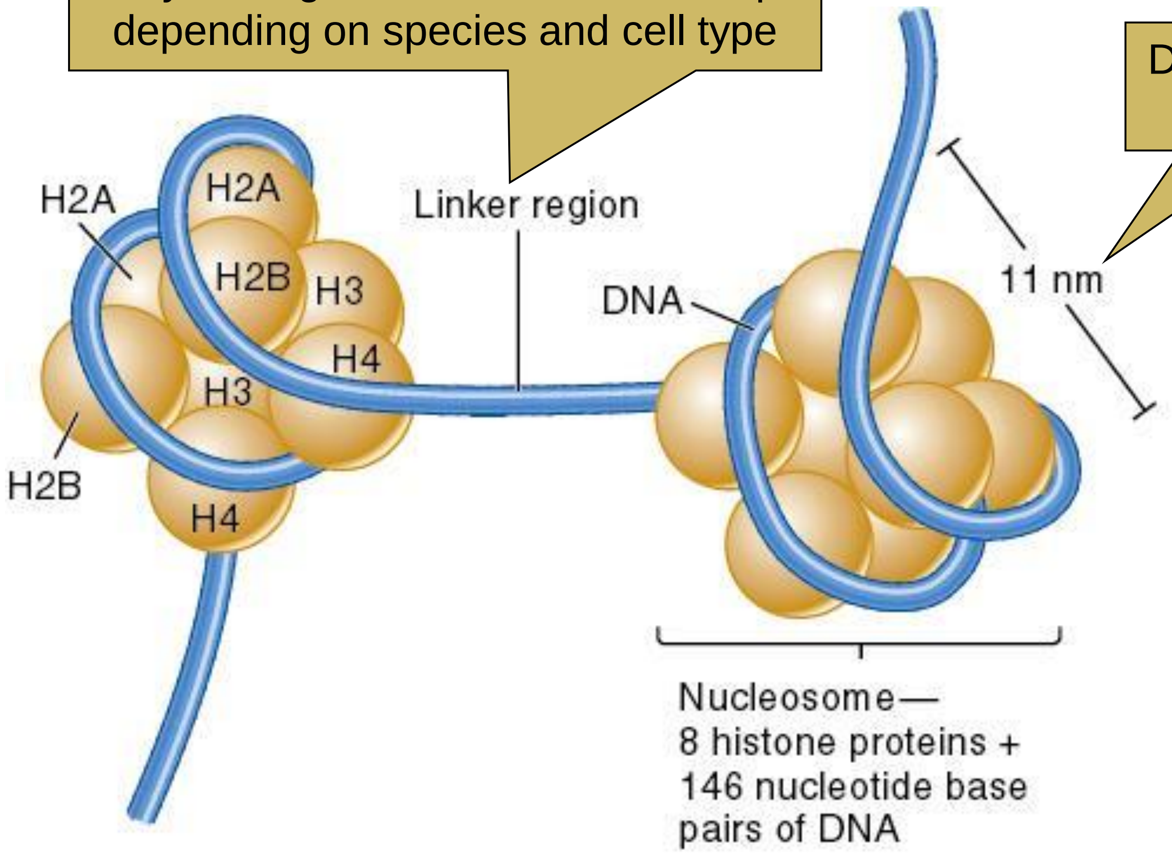
- The compaction of linear DNA in eukaryotic chromosomes involves interactions between DNA and various proteins
  - Proteins bound to DNA are subject to change during the life of the cell
    - These changes affect the degree of chromatin compaction



NUCLEOSOMES

- The repeating structural unit within eukaryotic chromatin is the nucleosome

- It is composed of double-stranded DNA wrapped around an octamer of histone proteins
  - An octamer is composed two copies each of four different histones
  - 146 bp of DNA make 1.65 negative superhelical turns around the octamer



Vary in length between 20 to 100 bp, depending on species and cell type

Diameter of the nucleosome

(a) Nucleosomes showing core histones

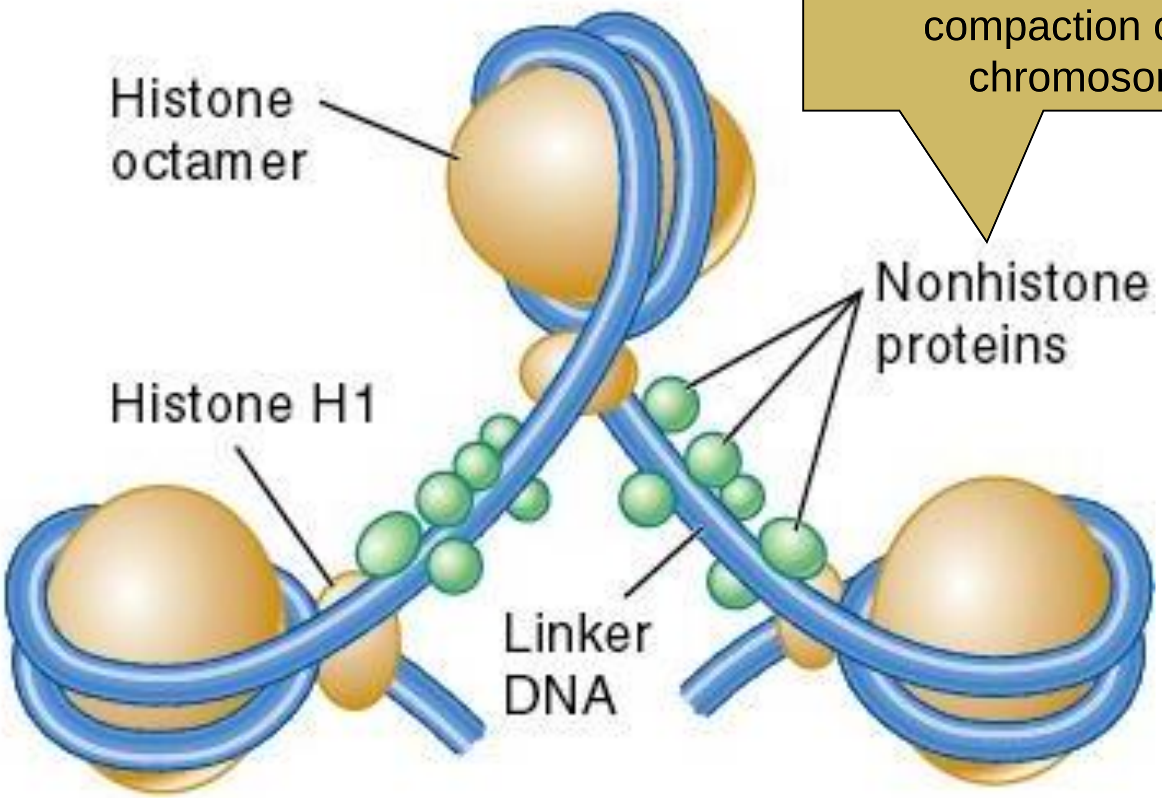
- Overall structure of connected nucleosomes resembles “beads on a string”
  - This structure shortens the DNA length about seven-fold!!!!!!!!!!

- Histone proteins are basic
  - They contain many positively-charged amino acids
    - Lysine and arginine
  - These bind with the phosphates along the DNA backbone

- There are five types of histones
  - H2A, H2B, H3 and H4 are the core histones
    - Two of each make up the octamer

  - H1 is the linker histone
    - Binds to linker DNA
    - Also binds to nucleosomes
      - But not as tightly as are the core histones

Play a role in the organization and compaction of the chromosome



(b) Nucleosomes showing linker histones and nonhistone proteins

Nucleosomes Join to Form a 30 nm Fiber

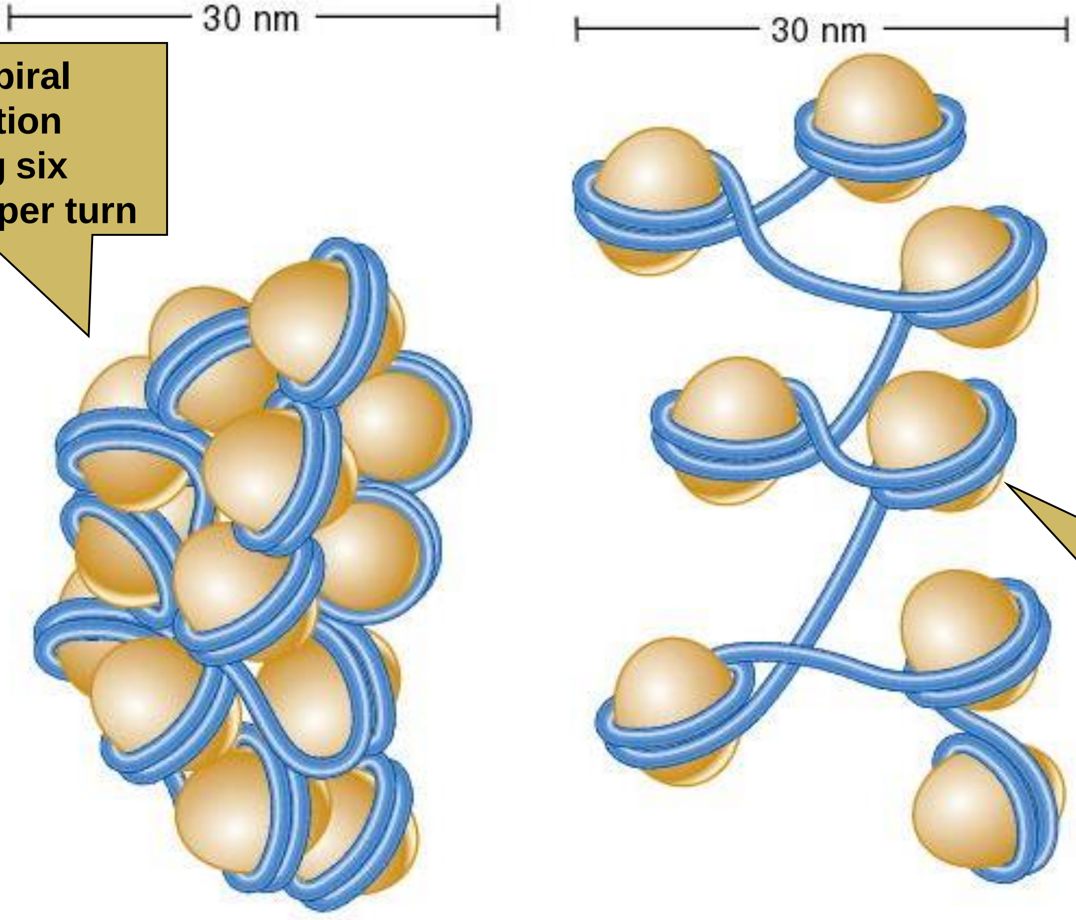
- Nucleosomes associate with each other to form a more compact zig-zag structure fiber of 30 nm. This was reveled by F.Thoma in 1977.

- Histone H1 plays a role in this compaction
  - At moderate salt concentrations, H1 is removed
    - The result is the classic beads-on-a-string morphology
  - At low salt concentrations, H1 remains bound
    - Beads associate together into a more compact morphology

- The 30 nm fiber shortens the total length of DNA another seven-fold!!!!!!!!!!!!!!!!!!!!!!!!!!!

- Its structure of 30 nm fiber has proven difficult to determine
  - The DNA conformation may be substantially altered when extracted from living cells

  - Two models have been proposed
    - Solenoid model
    - Three-dimensional zigzag model



Regular, spiral configuration containing six nucleosomes per turn

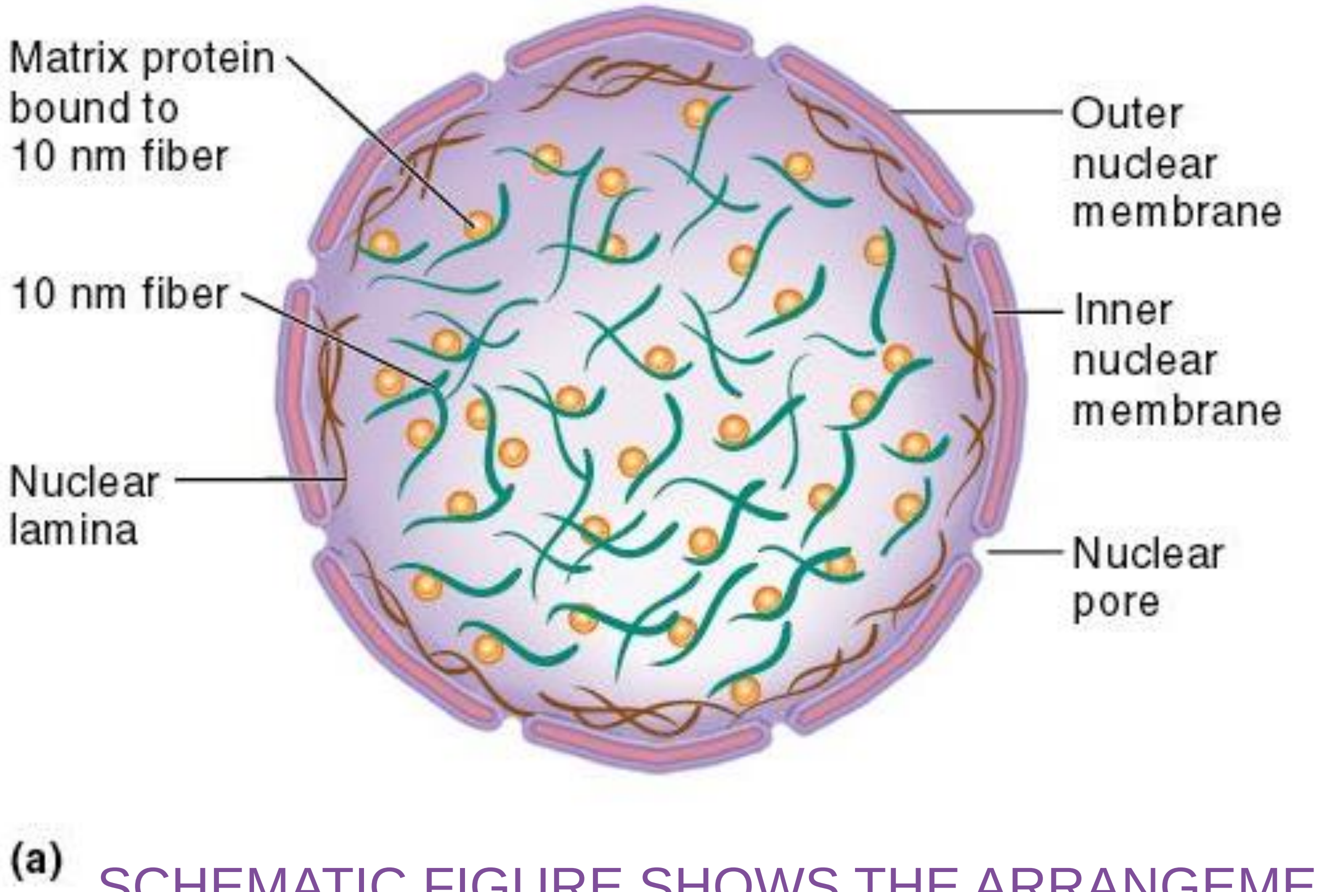
Irregular configuration where nucleosomes have little face-to-face contact

(b) Solenoid model (not correct)

(c) Three-dimensional zigzag model

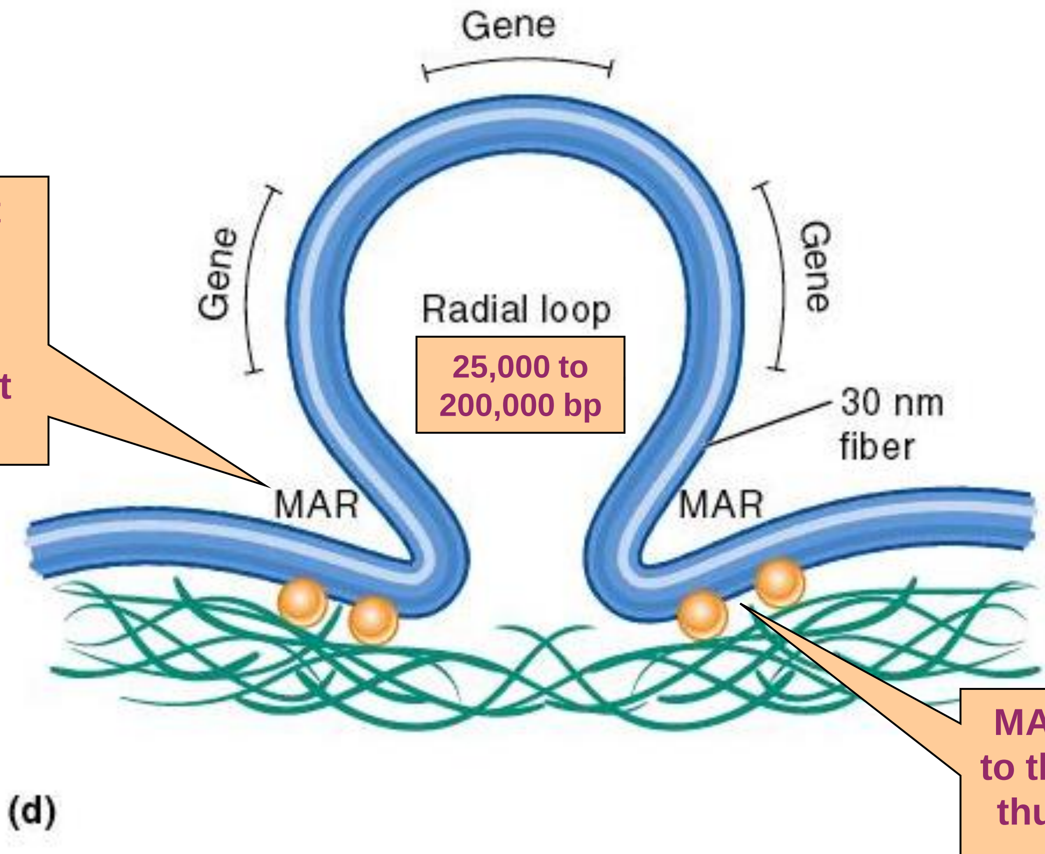
Further Compaction of the Chromosome

- So far the DNA have been shortened the about 50-fold
- A third level of compaction involves interaction between the 30 nm fiber and the nuclear matrix
- The nuclear matrix is composed of two parts
  - Nuclear lamina
  - Internal matrix proteins
    - 10 nm fiber and associated proteins



SCHEMATIC FIGURE SHOWS THE ARRANGEMENT OF THE MATRIX WITHIN THE CELL

- The third mechanism of DNA compaction involves the formation of radial loop domains



Matrix-attachment regions

or

Scaffold-attachment regions (SARs)

25,000 to 200,000 bp

MARs are anchored to the nuclear matrix, thus creating radial loops

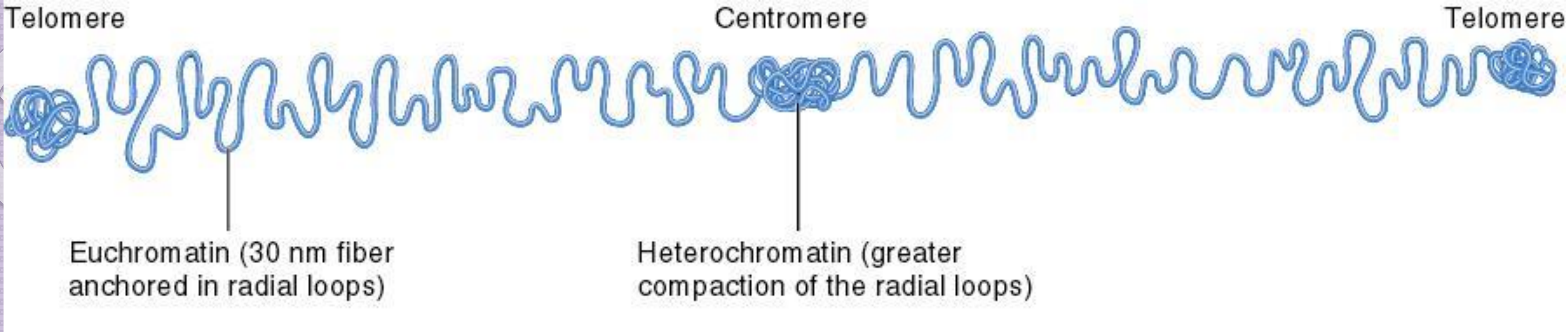
Further Compaction of the Chromosome

- The attachment of radial loops to the nuclear matrix is important in two ways
  - 1. It plays a role in gene regulation
  - 2. It serves to organize the chromosomes within the nucleus
    - Each chromosome in the nucleus is located in a discrete and nonoverlapping chromosome territory

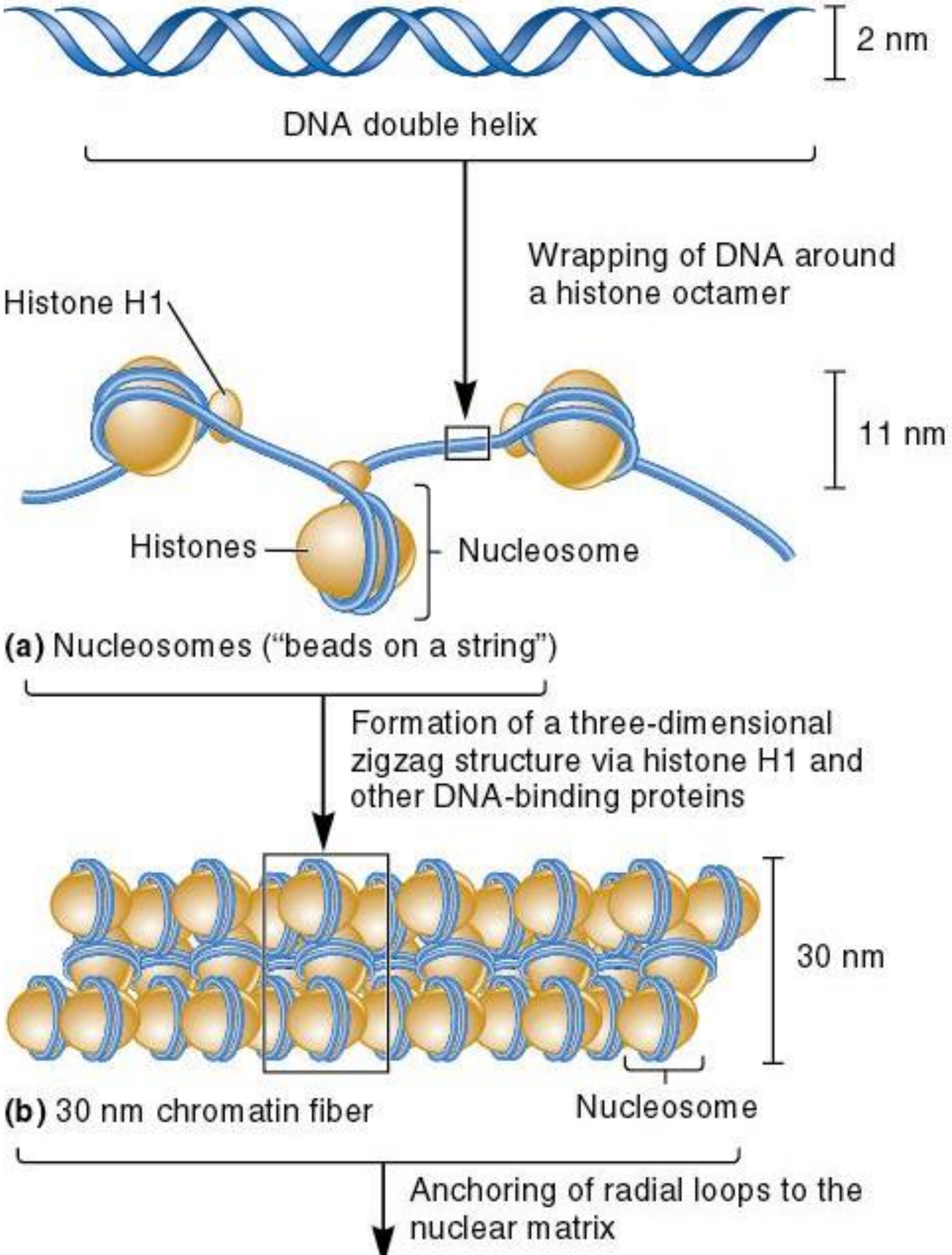
Heterochromatin *vs* Euchromatin

- The compaction level of interphase chromosomes is not completely uniform (German cytologist E. Heitz in 1928)
  - Euchromatin
    - Less condensed regions of chromosomes
    - Transcriptionally active
    - Regions where 30 nm fiber forms radial loop domains

  - Heterochromatin
    - Tightly compacted regions of chromosomes
    - Transcriptionally inactive (in general)
    - Radial loop domains compacted even further



- There are two types of heterochromatin
  - Constitutive heterochromatin
    - Regions that are always heterochromatic
    - Permanently inactive with regard to transcription
  - Facultative heterochromatin
    - Regions that can interconvert between euchromatin and heterochromatin
    - Example: Barr body



2 nm

DNA double helix

Wrapping of DNA around a histone octamer

Histone H1

11 nm

Histones

Nucleosome

(a) Nucleosomes (“beads on a string”)

Formation of a three-dimensional zigzag structure via histone H1 and other DNA-binding proteins

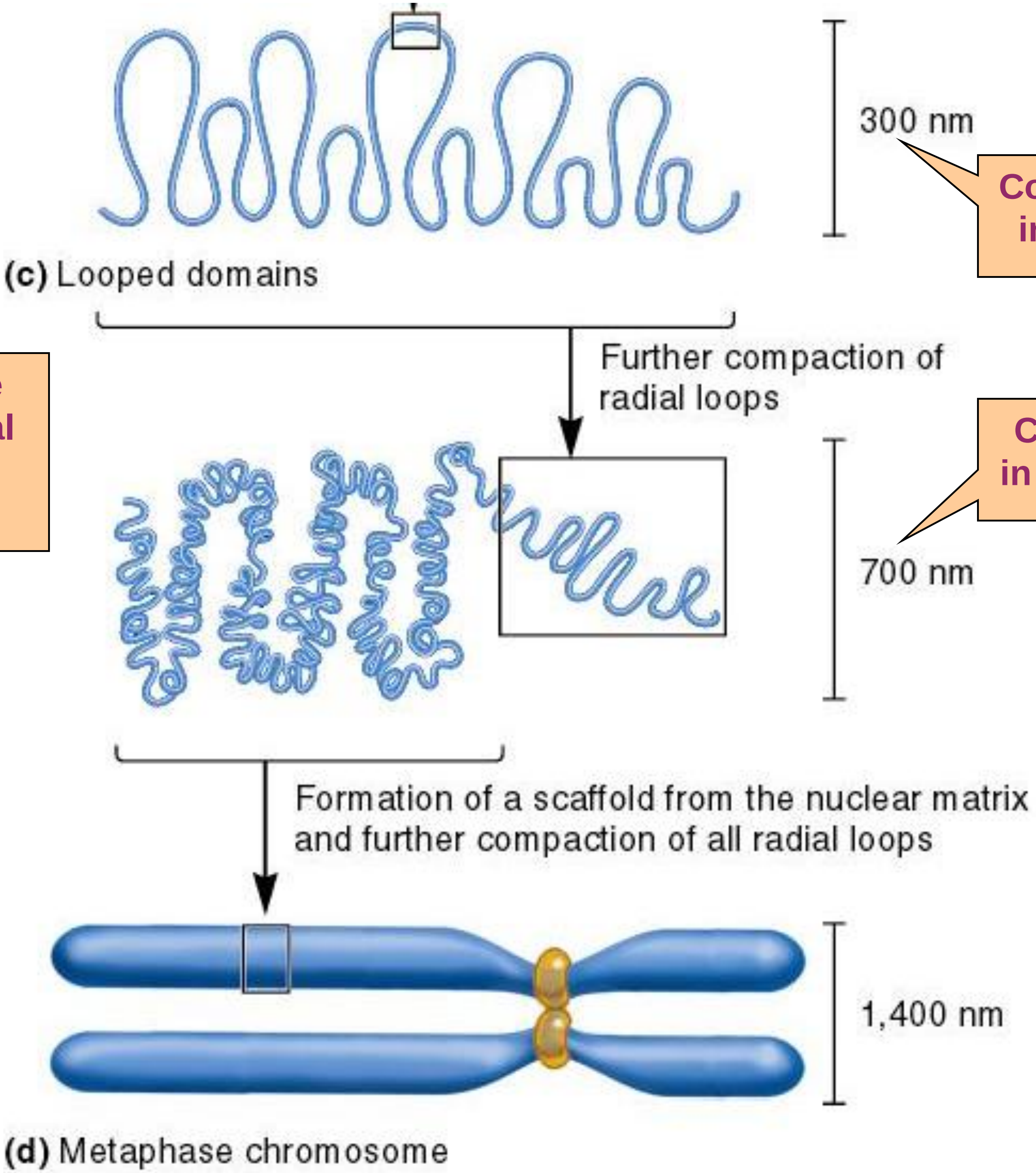
30 nm

Nucleosome

(b) 30 nm chromatin fiber

Anchoring of radial loops to the nuclear matrix

During interphase most chromosomal regions are euchromatic

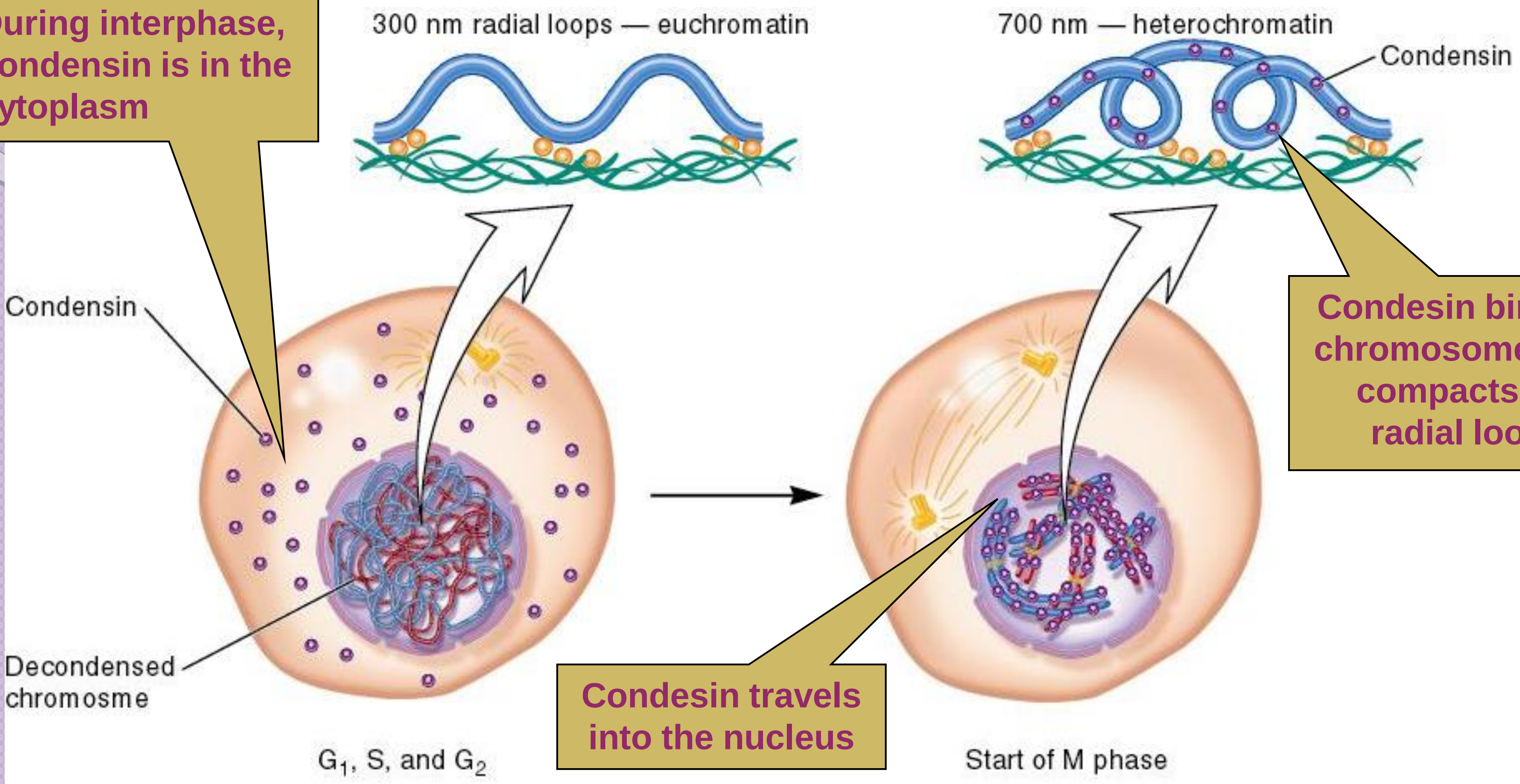


Compaction level in euchromatin

Compaction level in heterochromatin

THE CONDENSATION OF A METAPHASE CHROMOSOME BY CONDENSIN

The number of loops has not changed
However, the diameter of each loop is smaller



During interphase, condensin is in the cytoplasm

Condesin travels into the nucleus

Condesin binds to chromosomes and compacts the radial loops

Metaphase Chromosomes

- As cells enter M phase, the level of compaction changes dramatically
  - By the end of prophase, sister chromatids are entirely heterochromatic
  - Two parallel chromatids have an overall diameter of 1,400 nm

- These highly condensed metaphase chromosomes undergo little gene transcription
- In metaphase chromosomes the radial loops are highly compacted and stay anchored to a scaffold
  - The scaffold is formed from the nuclear matrix

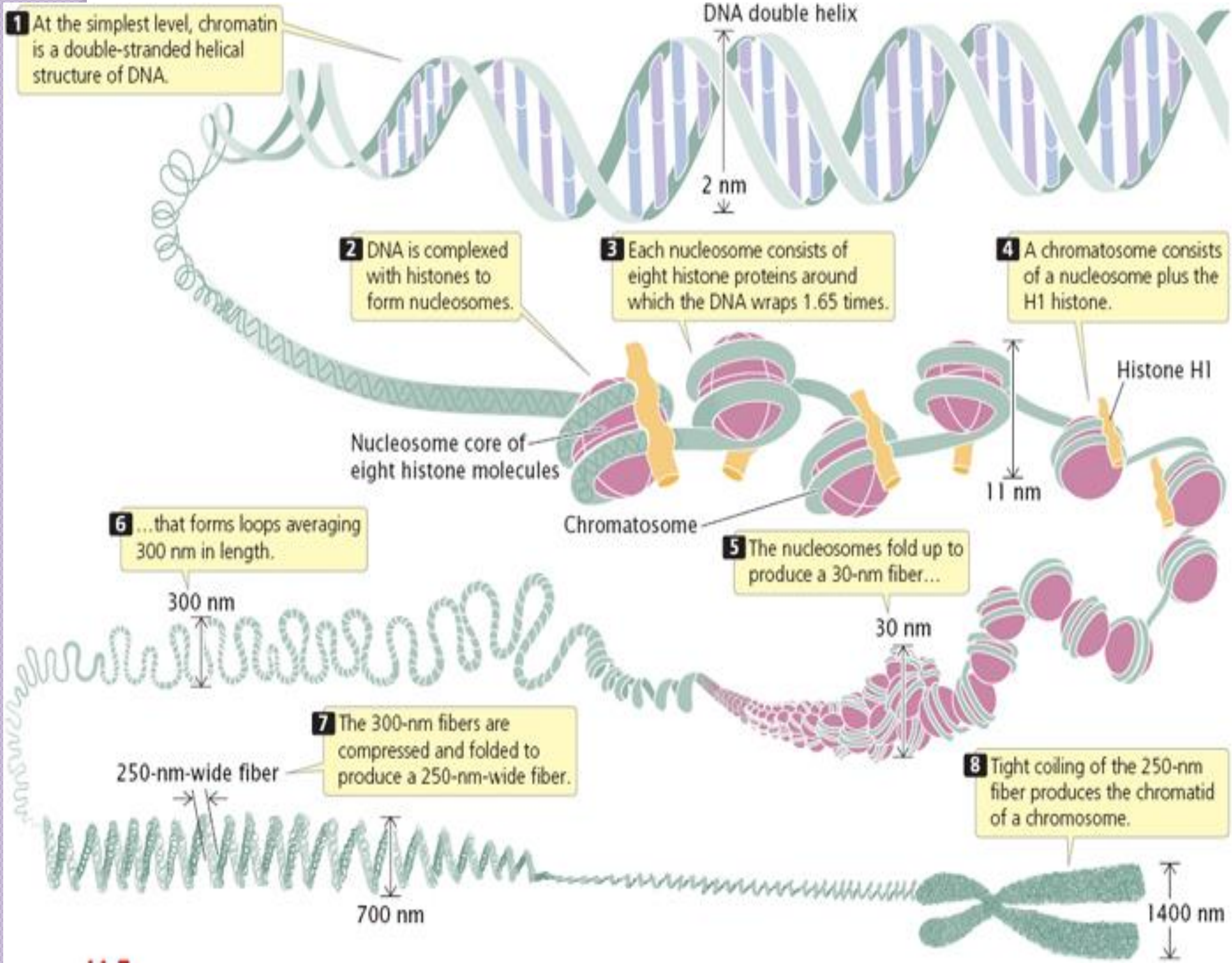
- Histones are needed for the compaction of radial loops

- Two multiprotein complexes help to form and organize metaphase chromosomes

  - Condensin
    - Plays a critical role in chromosome condensation

  - Cohesin
    - Plays a critical role in sister chromatid alignment

- Both contain a category of proteins called **SMC proteins**
  - Acronym = **S**tructural **m**aintenance of **c**hromosomes
  - SMC proteins use energy from ATP and catalyze changes in chromosome structure
  - ❖ lets view the process of chromosomes organizations once again..!!!!!!!!!!!!!!!!!!!



1 At the simplest level, chromatin is a double-stranded helical structure of DNA.

2 DNA is complexed with histones to form nucleosomes.

3 Each nucleosome consists of eight histone proteins around which the DNA wraps 1.65 times.

4 A chromatosome consists of a nucleosome plus the H1 histone.

5 The nucleosomes fold up to produce a 30-nm fiber…

6 …that forms loops averaging 300 nm in length.

7 The 300-nm fibers are compressed and folded to produce a 250-nm-wide fiber.

8 Tight coiling of the 250-nm fiber produces the chromatid of a chromosome.

Excuse me, your mess during DNA remolding….!!!!!!!!!!!!

<u>THANK U FOR UR CO- OPERATION</u>