GENOME STRUCTURE

THE NUCLEOSOME

- IN CELLS, DNA IS ORGANIZED INTO LARGE STRUCTURES – CHROMOSOMES

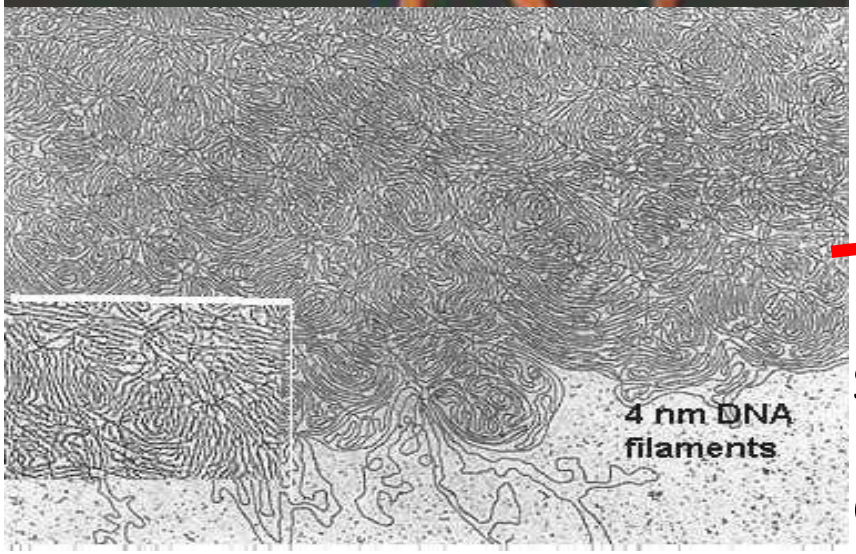
- CHROMOSOMES CAN BE EITHER CIRCULAR OR LINEAR
  - CIRCULAR → Prokaryotes
  - LINEAR → Eucaryotes

- ROUGHLY ONE-HALF OF EACH CHROMOSOME IS COMPRISED OF PROTEIN

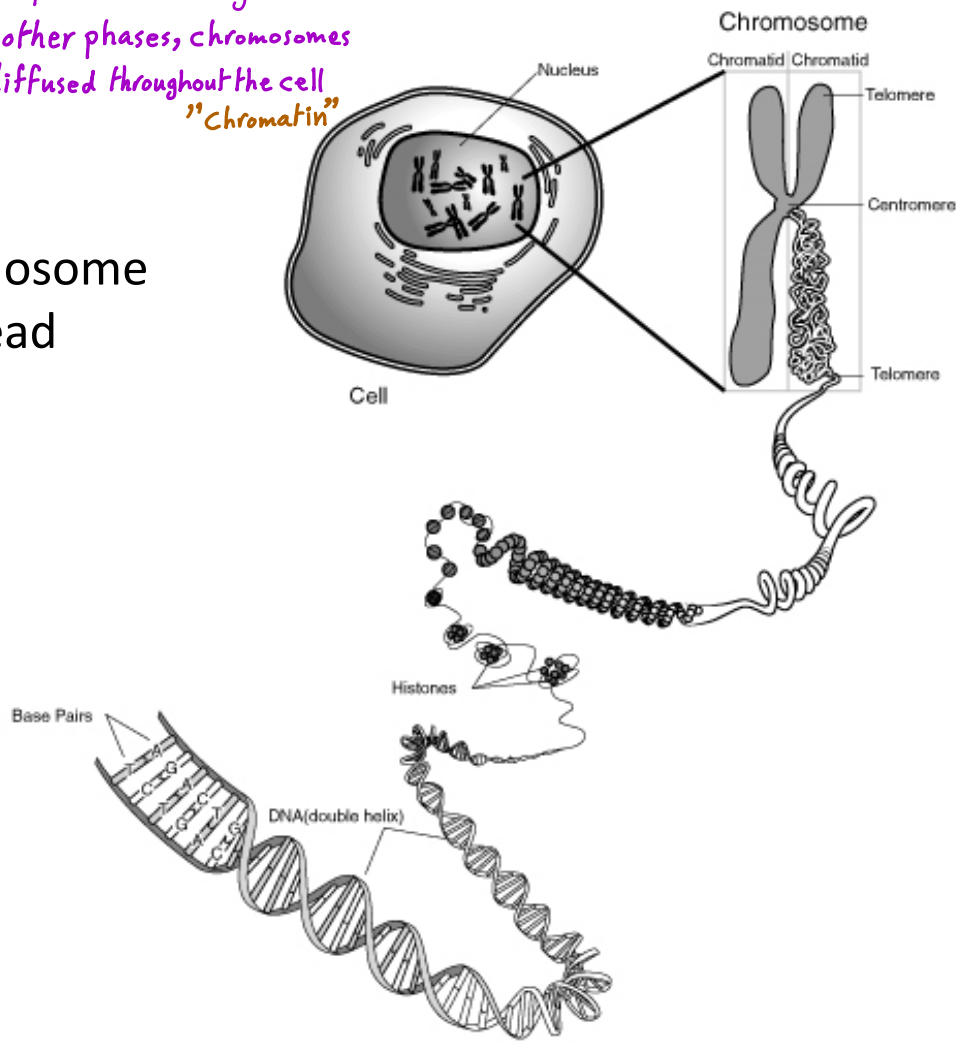
Chromosomes:
Contain lots of DNA!

- Chromosomes appear in this (classic) condensed form only during the Metaphase of cell cycle.
- During other phases, chromosomes will be diffused throughout the cell "Chromatin"

Chromosome Spread



Some of the DNA from one Chromosome



DNA must be highly folded to fit...

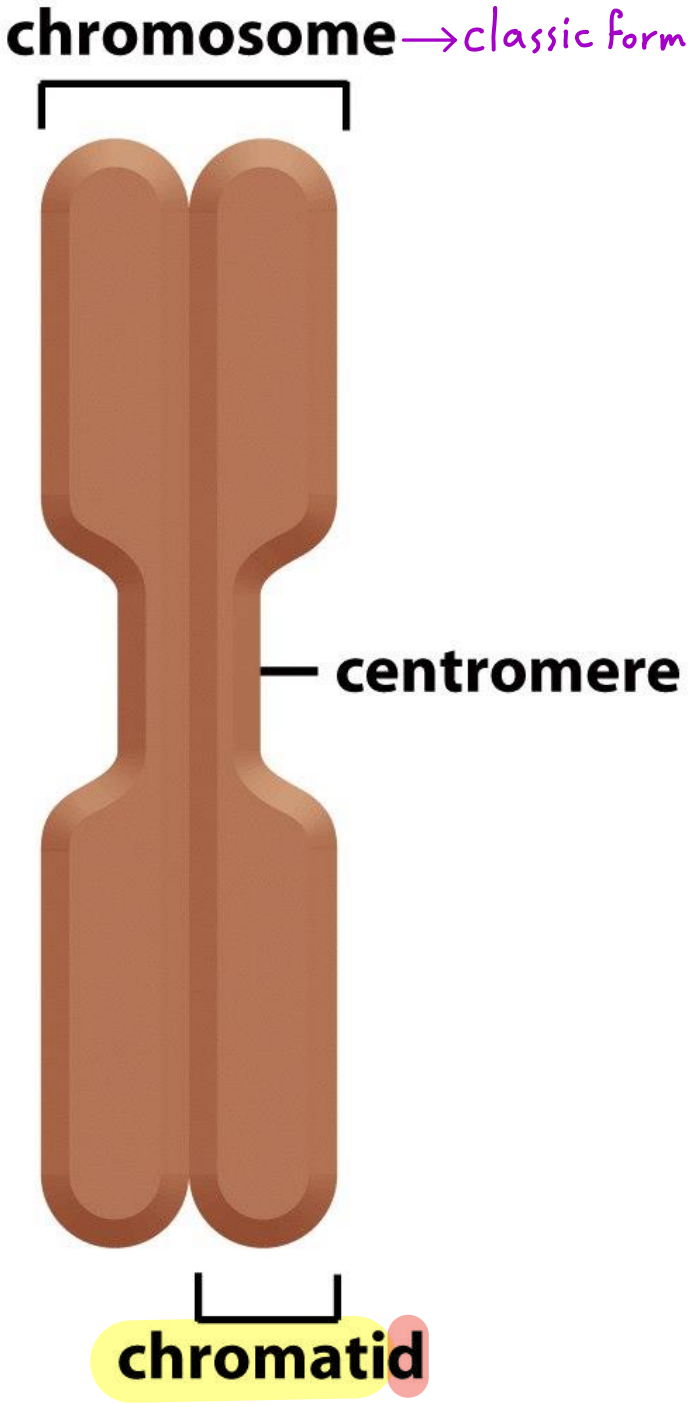
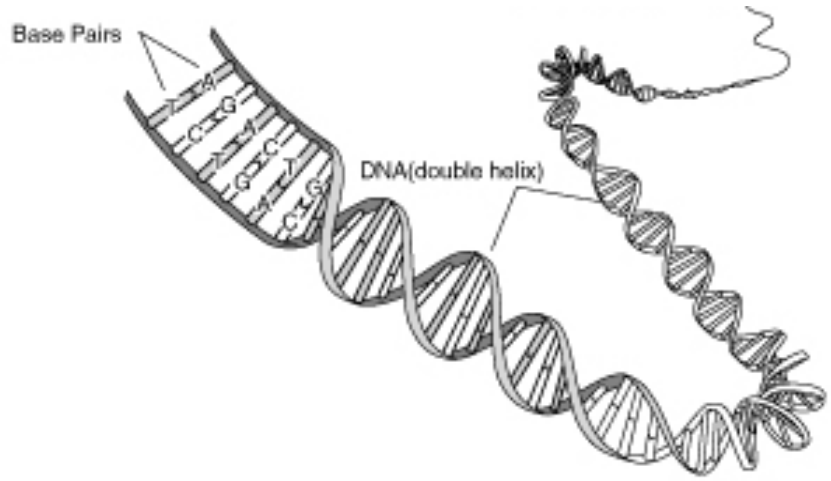


Figure 4-70 *Molecular Biology of the Cell* (© Garland Science 2008)

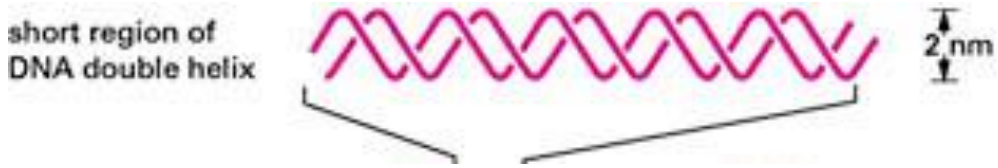
DNA folding

An average human cell measures ~10μm across…. yet contains ~2 meters of DNA!



How to pack it all in???

The DNA double strand is about 2nm across and very long… DNA is highly folded:



- IN SIMPLE ORGANISMS, THE VAST MAJORITY OF DNA IS USED TO ENCODE PROTEIN

* More simple organism = More active genetic material *

- IN CONTRAST, COMPLEX ORGANISMS USE ONLY A SMALL PORTION OF THEIR GENOME TO ENCODE PROTEINS

* Only 3% of Human chromosomes are genes responsiple of RNA/Protein production

* The rest of human chromosomes are

- INCREASED COMPLEXCITY OF REGULATORY ELEMENTS, INTRONS, REGULATORY RNAs

- EXPANSION OF THE NON-CODING REGIONS OF THE THE GENOMES OF MORE COMPLEX ORGANISMS
  * Chromosomes appear exclusivly during metaphase, what's the form of DNA during the rest of cell cycle ??
- THE COMBINATION OF EUKARYOTIC DNA AND ITS ASSOCIATED PROTEINS IS REFERRED TO AS CHROMATIN = diffused form of DNA in nucleas (eukaryotes) or cytoplasm (Prokaryotes)
- NUCLEOSOME – THE FUNDAMENTAL UNIT OF CHROMATIN (Building)

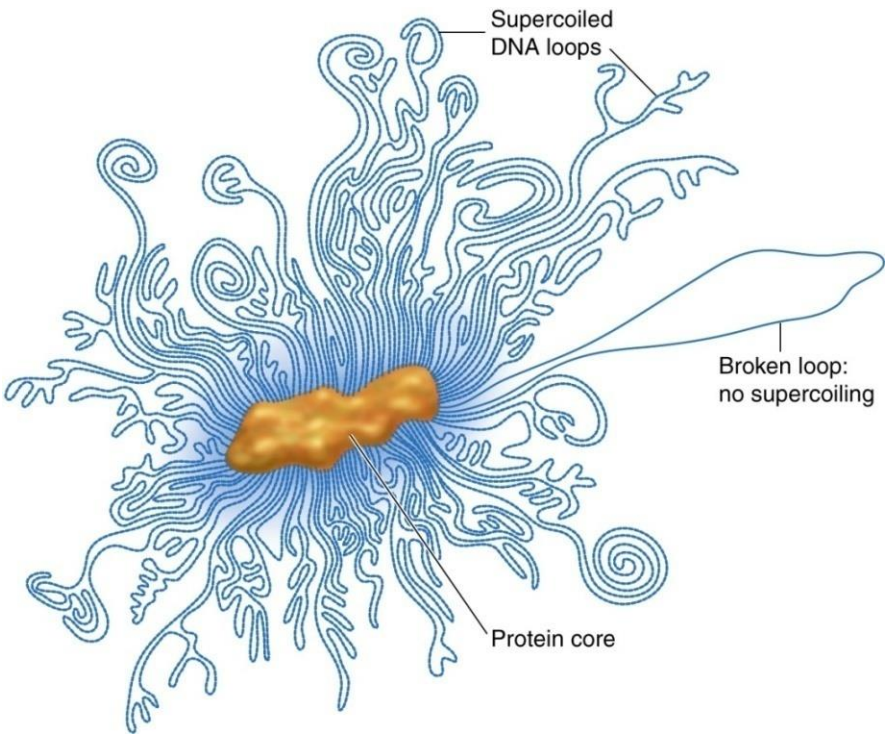


Figure 17.15 The *E. coli* Chromosome Removed from a Cell

- **Chromosomes and Chromatin**
  - DNA is packaged into chromosomes
  - Prokaryotic and eukaryotic chromosomes differ significantly
  - **Prokaryotes**—the *E. coli* chromosome is a circular DNA molecule that is extensively looped and coiled
    - Supercoiled DNA complexed with a protein core

Figure 17.16 Electron Micrograph of Chromatin

- **Eukaryotes** have extraordinarily large genomes when compared to prokaryotes
  - Chromosome number and length can vary by species
  - Each eukaryotic chromosome consists of a single, linear DNA molecule complexed with histone proteins to form **nucleohistone**
    - **Chromatin** is the term used to describe this complex

Figure 17.16 Electron Micrograph of Chromatin

- **Nucleosomes** are formed by the binding of DNA and histone proteins
  - Nucleosomes have a beaded appearance when viewed by electron micrograph

- Histone proteins have five major classes: H1, H2A, H2B, H3, and H4

- A nucleosome is positively coiled DNA wrapped around a histone core (two copies each of H2A, H2B, H3, and H4) 1.65 turns

HISTONES

SMALL BASIC PROTEINS

HISTONES

Q by doctor: if we put histones on electrophoresis, would they move more or less toward the positive side?? less

- BASIC PROTEINS (Lysine and Arginine)

Positivly charged

- Fundamental role in packaging the vast amounts of DNA in higher cells
- Histones are among the most abundant proteins in eukaryotic cells

* collagen is the most abundant Protein in the whole body

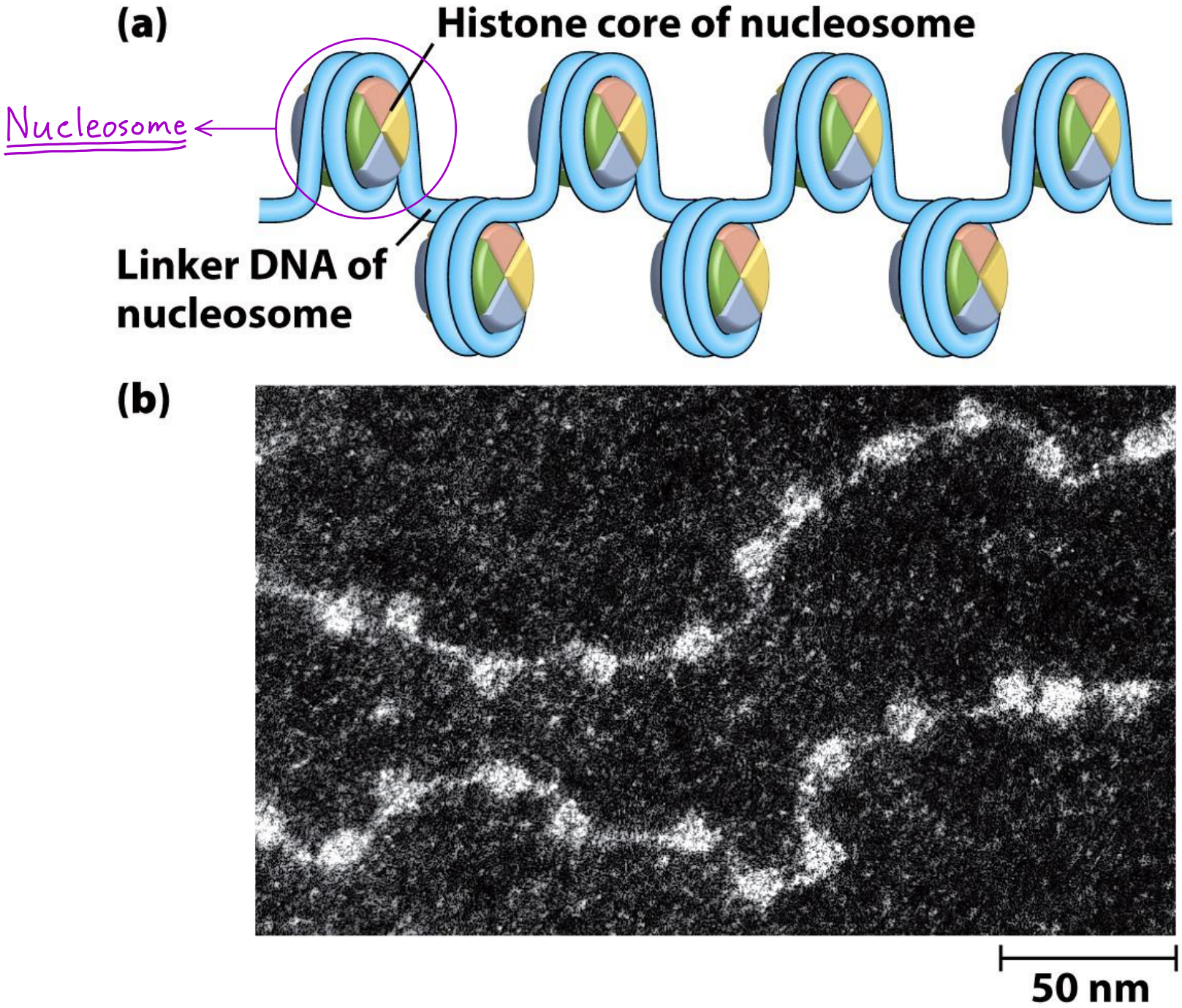
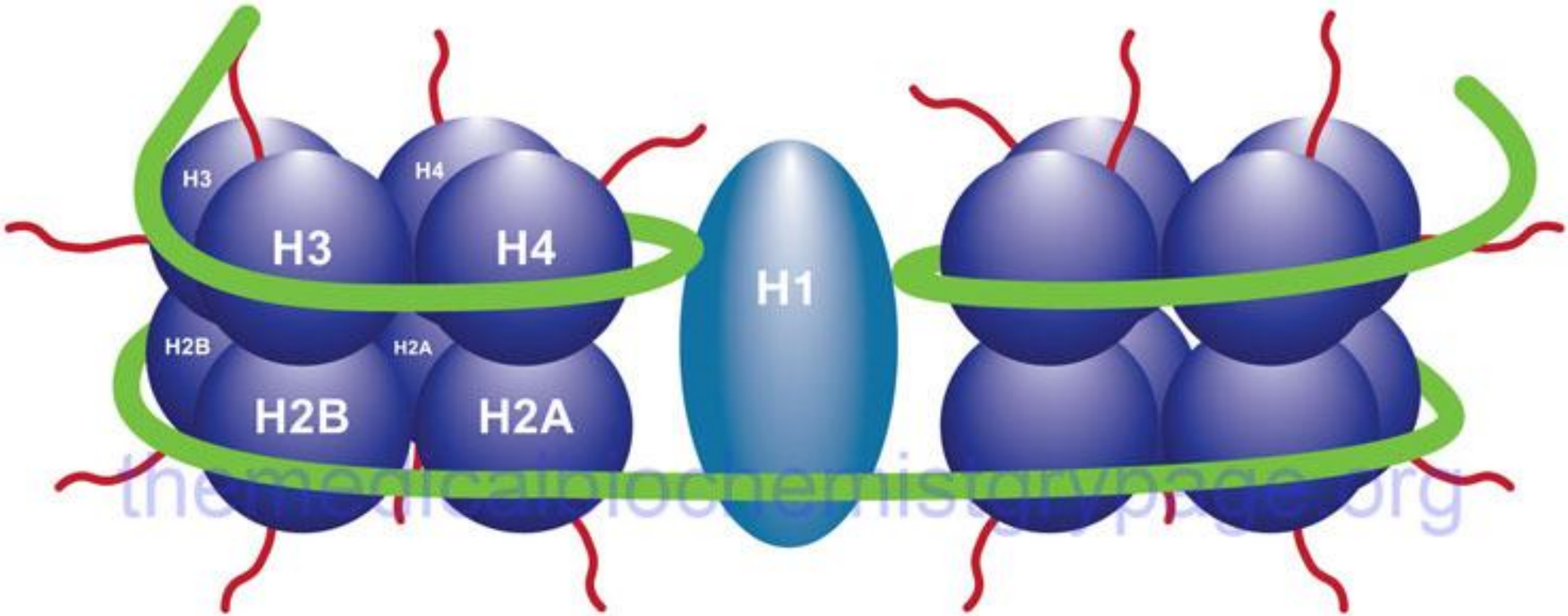


Figure 24-25
Lehninger Principles of Biochemistry, Sixth Edition



Histone tails

Exam Q : which type of histones isn't found in the histone core ?? H1

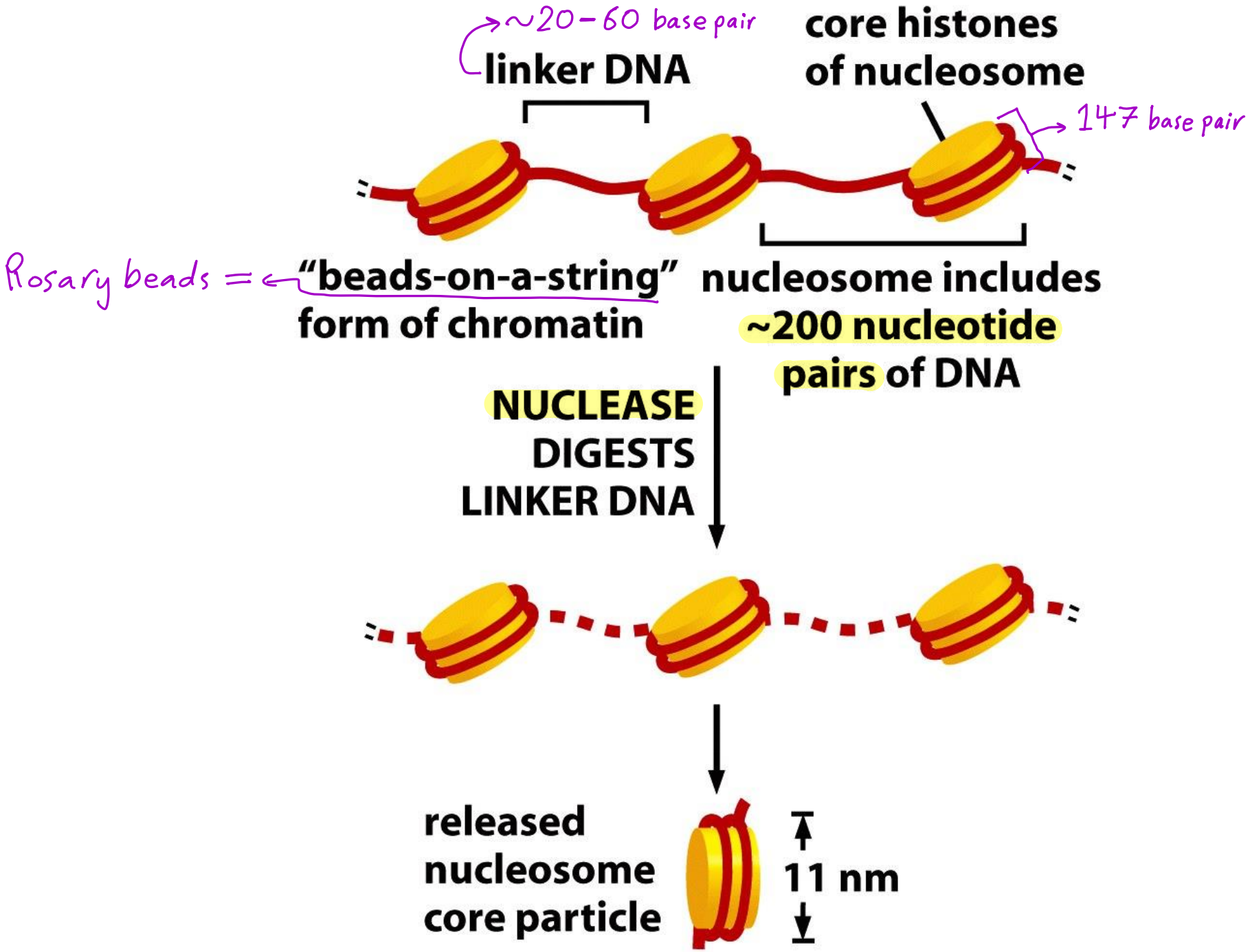


Figure 4-23 (part 1 of 2) *Molecular Biology of the Cell* (© Garland Science 2008)

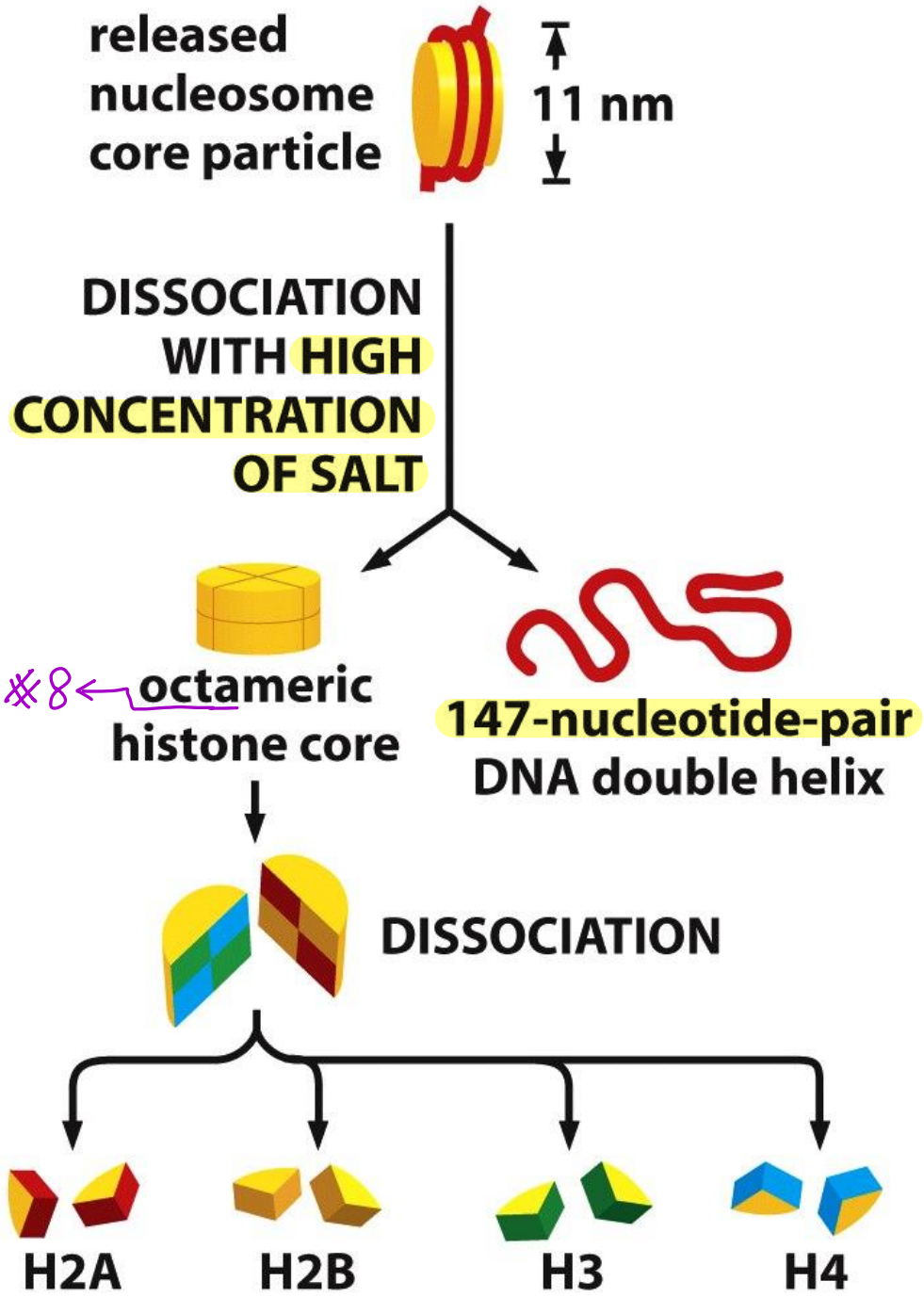


Figure 4-23 (part 2 of 2) *Molecular Biology of the Cell* (© Garland Science 2008)

Chromatin

The thin, active structure of DNA

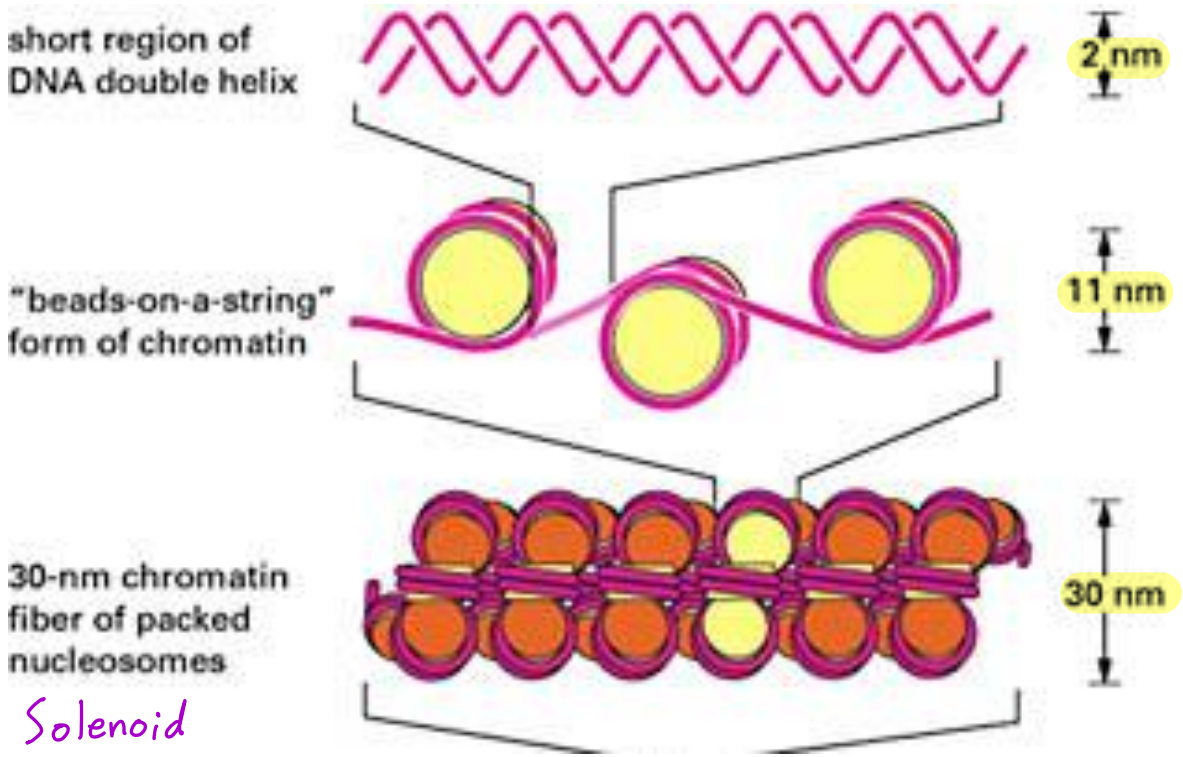
First level of DNA folding

Every 200 nucleotides of DNA wrap around a core of

Histone proteins Giving a “beads on a string” look

Histones are Basic proteins rich in Amino Acids; Lysine & Arginine
-First DNA is wrapped by Histone proteins # 2-4

Addition of Histone protein 1-
Results in a DNA-Histone strand ~30nm wide



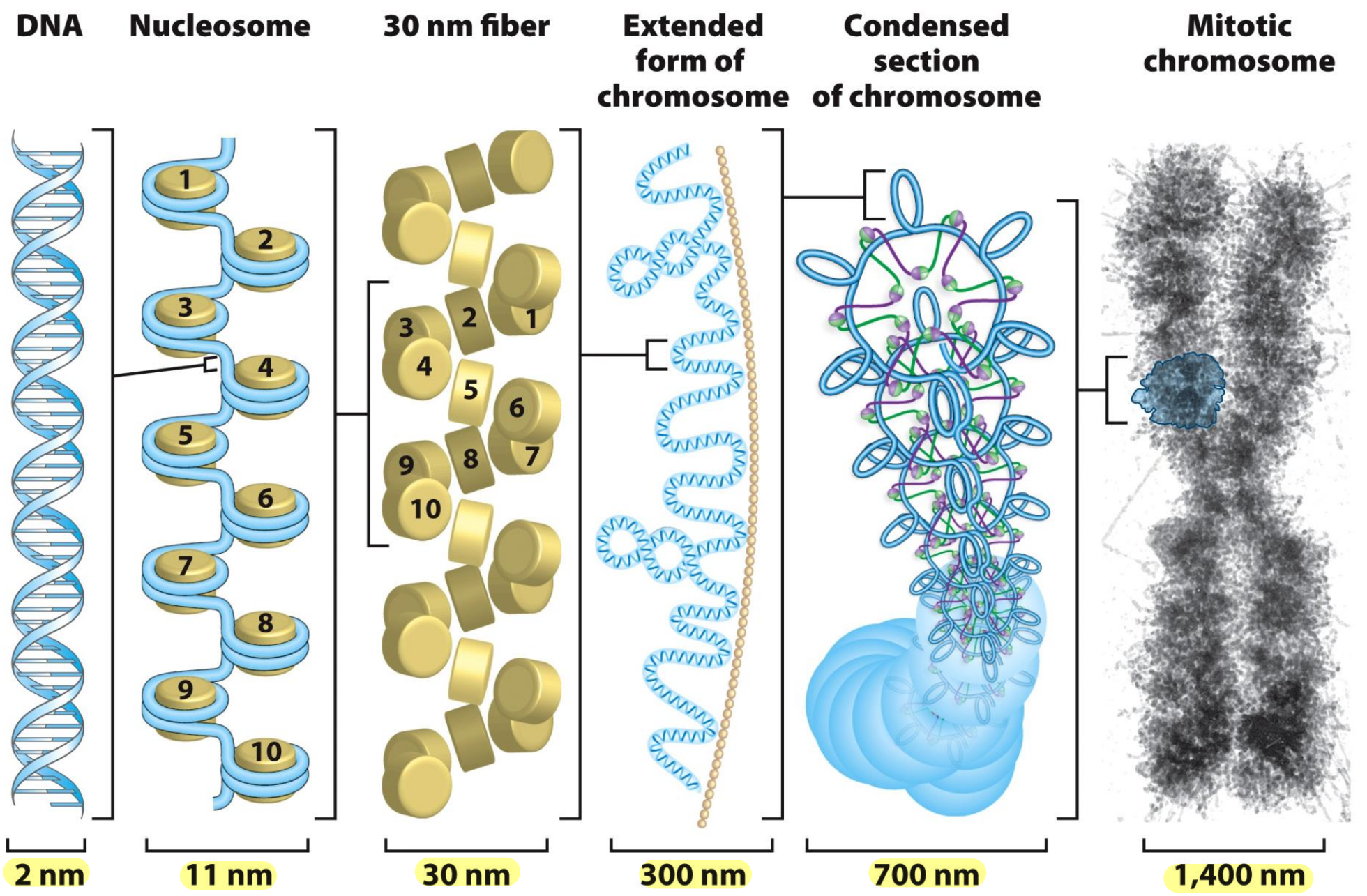


Figure 24-31
Lehninger Principles of Biochemistry, Sixth Edition

- H1 IS NOT PART OF THE NUCLEOSOME CORE PARTICLE
- INSTEAD, IT BINDS TO THE LINKER DNA AND IS THEREFORE CALLED A LINKER HISTONE
- MAJORITY OF EUKARYOTIC DNA IS PACKAGED INTO NUCLEOSOMES
- DNA IS HIGHLY COMPACTED (1000 – 10,000-fold)

- THE DNA MOST TIGHTLY ASSOCIATED WITH THE NCULEOSOME (CORE DNA) IS WOUND ABOUT 1.65 TIMES AROUND THE OUTSIDE OF THE HISTONE OCTAMER

- THE LENGTH OF DNA ASSOCIATED WITH EACH NUCLEOSOME IS APPROX. 147-bp (MICROCOCCAL NUCLEASE)

- THE LENGTH OF THE LINKER DNA BETWEEN NUCLEOSOMES IS 20 – 60 bp

* Is the DNA always present in this condensed compacted form??
No, because it must be relaxed during replication & transcription so the enzymes can attach to it "accessable DNA".

- STRETCHES OF DNA THAT ARE FREE OF NUCLEOSOMES

- REGIONS OF DNA INVOLVED IN GENE EXPRESSION, REPLICATION, OR RECOMBINATION

→ "active regions"

- THESE REGIONS ARE TYPICALLY ASSOCIATED WITH NON-HISTONE PROTEINS THAT ARE EITHER REGULATING OR PARTICIPATING IN THESE EVENTS

HIGHER ORDER CHROMATIN STRUCTURE

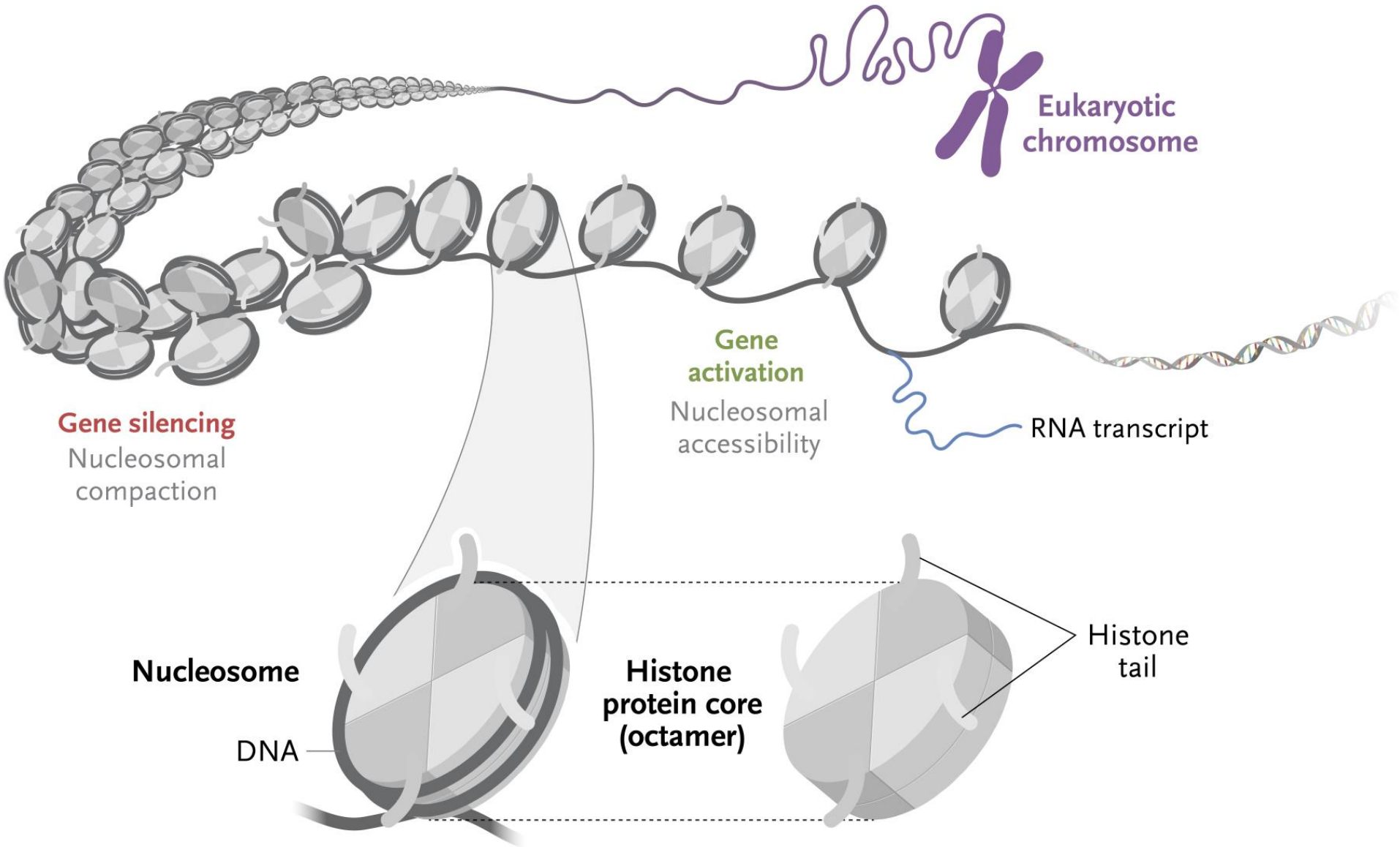
- HETEROCHROMATIN – DENSE STAINING WITH A VARIETY OF DYES, MORE CONDENSED APPEARANCE "Non-accessable"
- SUPPORTS VERY LIMITED GENE EXPRESSION "inactive"
- IS ASSOCIATED WITH PARTICULAR CHROMOSOMAL REGIONS – TELOMERE, CENTROMERE
- IMPORTANT FOR THE FUNCTION OF THESE KEY CHROMSOMAL ELEMENTS

- HETEROCHROMATIC REGIONS ARE COMPOSED OF NUCLEOSOMAL DNA ASSOCIATED INTO HIGHER-ORDER STRUCTURES THAT RESULT IN A BARRIER TO GENE EXPRESSION

- EUCHROMATIN – STAINING POORLY WITH DYES, RELATIVELY OPEN STRUCTURE "accessable"

- SUPPORTS HIGHER LEVELS OF GENE EXPRESSION "active"

* Switching between Euchromatin & Hetrochromatin forms = Proccess of Remodeling → One way of regulating gene expression


Eukaryotic chromosome
Gene silencing
Nucleosomal compaction
Gene activation
Nucleosomal accessibility
RNA transcript
Nucleosome
DNA
Histone protein core (octamer)
Histone tail