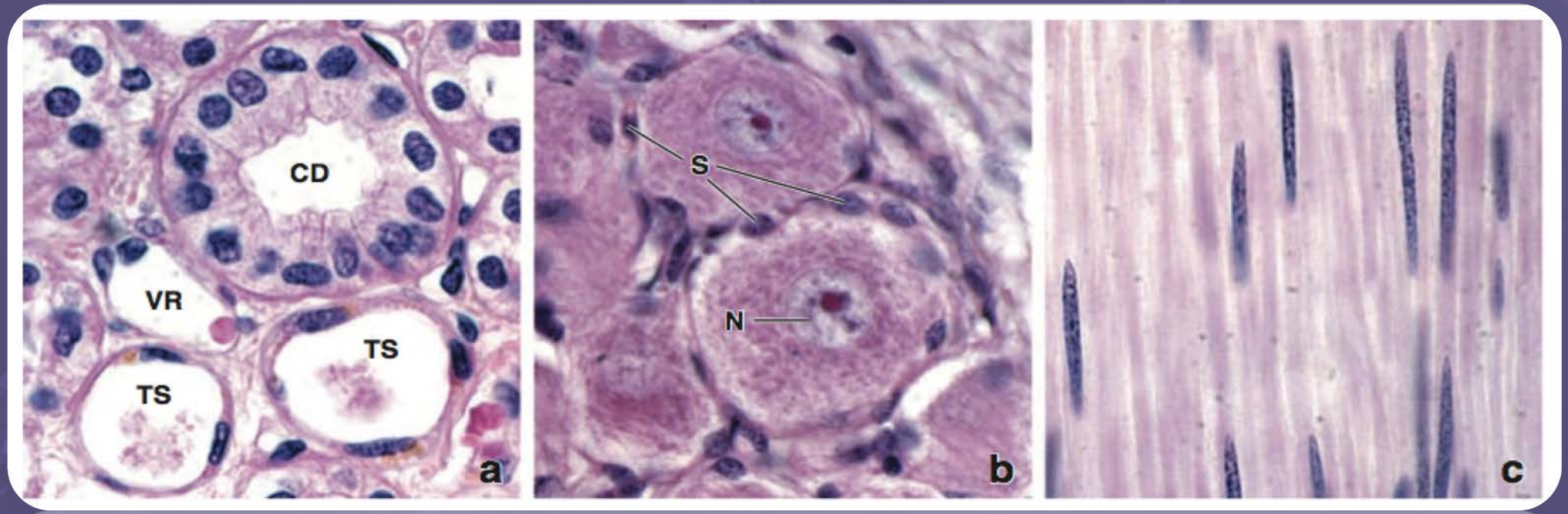
Cell nucleus
Genes-the flow of genetic information

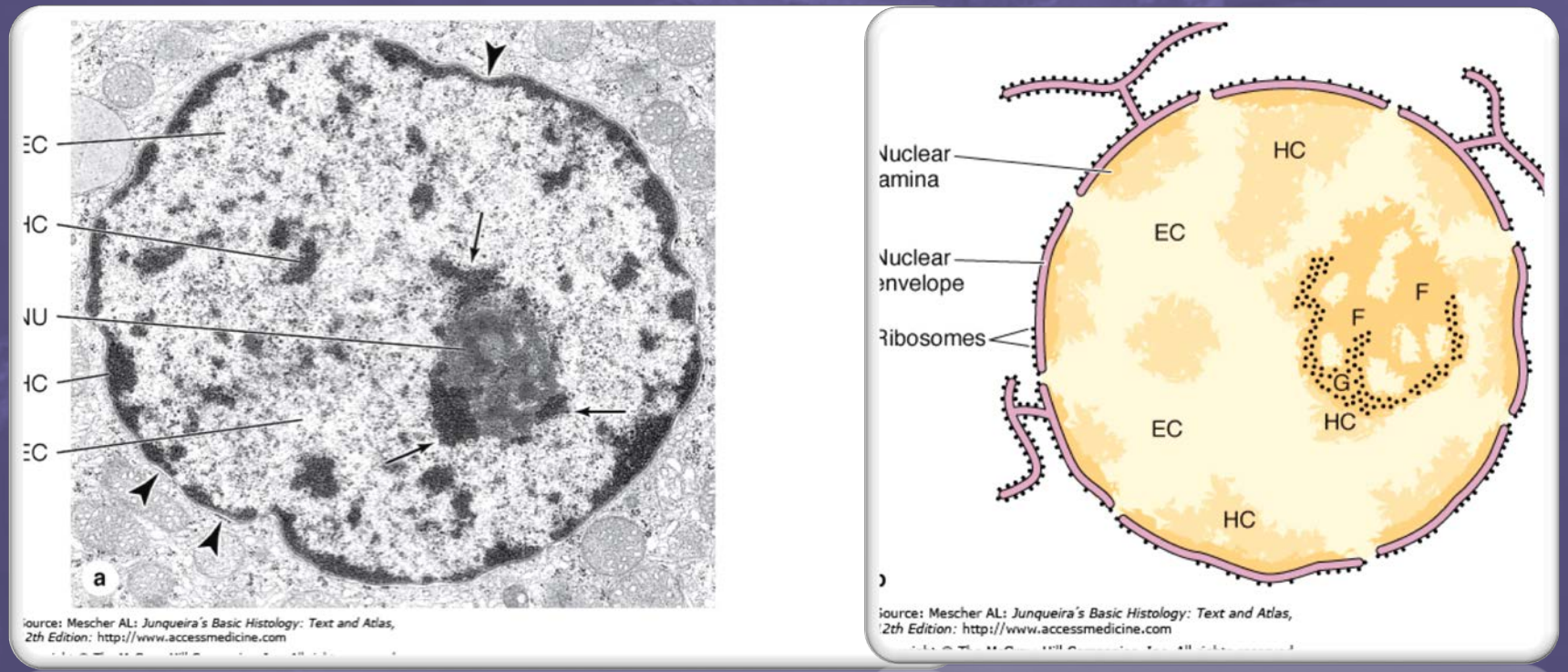
The nucleus is a membrane-limited compartment that contains the genome (genetic information) in eukaryotic cells.

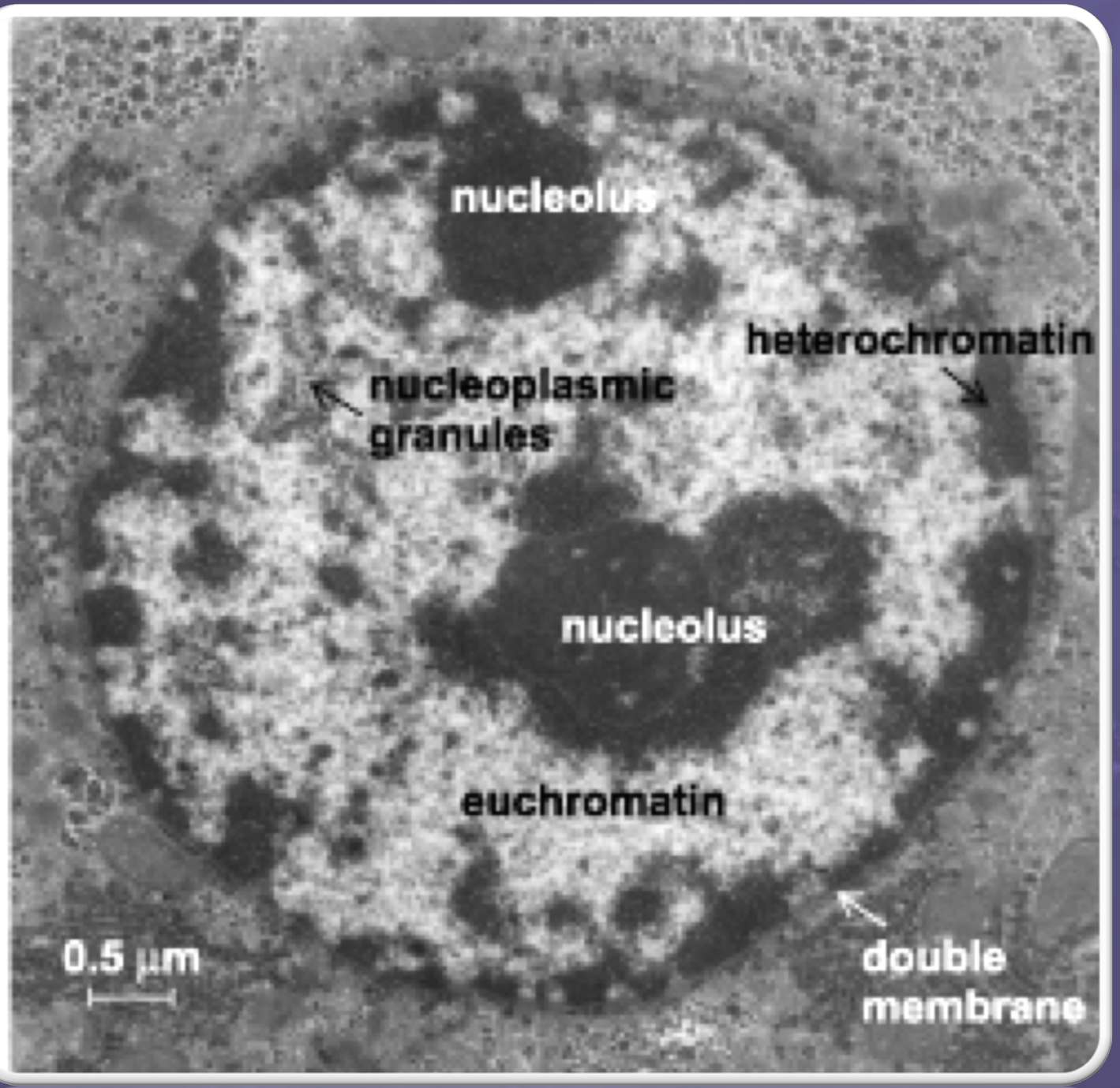
- directs protein synthesis via rRNA, mRNA, tRNA, noncoding RNAs
- Size - 3,5-20 um
- 99% of cell genome
- Mono poli bi cariocyte



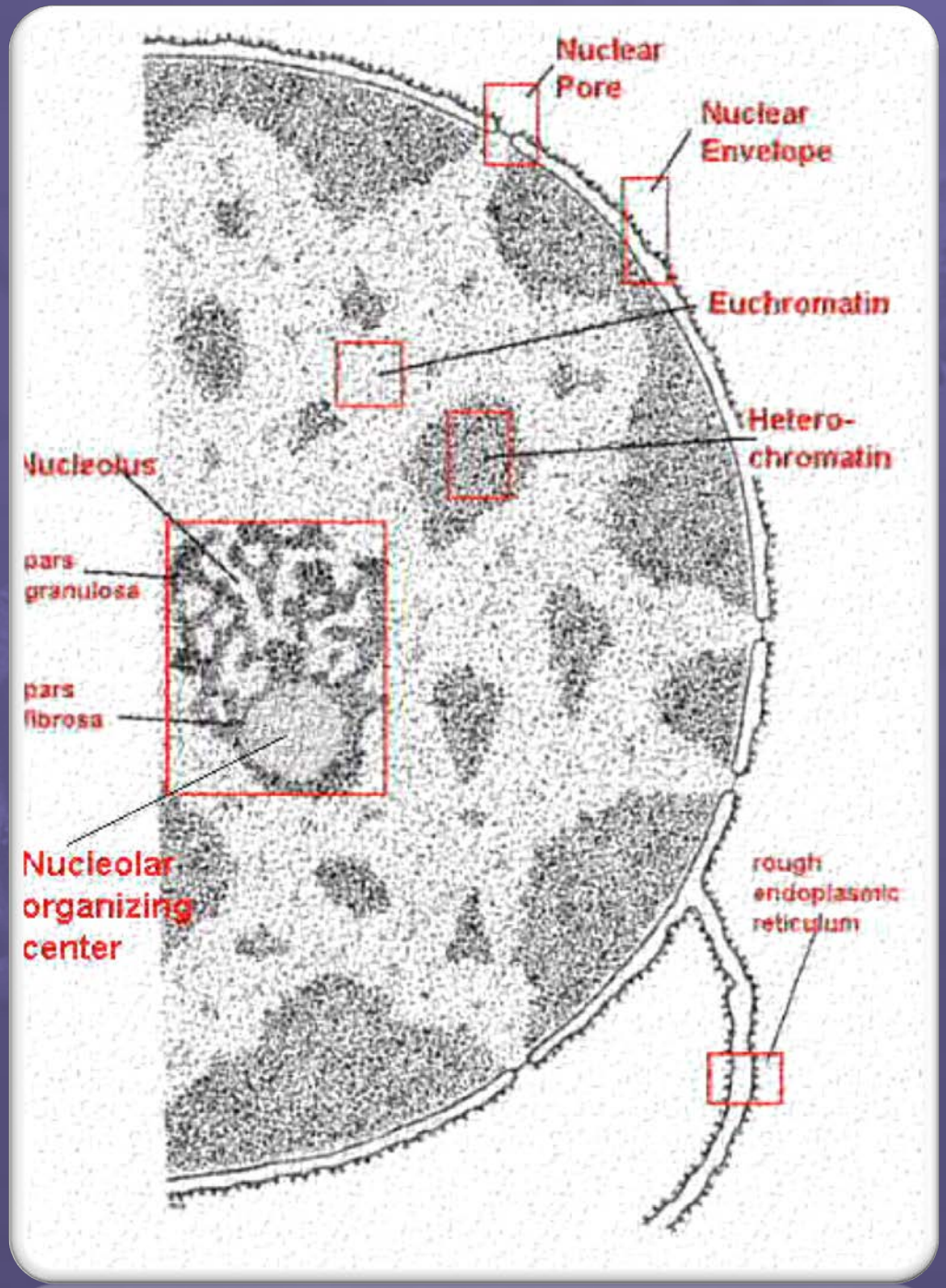
Structural components of the nucleus.

- Chromatin - organized as euchromatin or heterochromatin, contains DNA associated with nuclear proteins
- Nucleolus, where ribosomal RNA (rRNA) is synthesized and ribosomal subunits are assembled
- Nucleoplasm – matrix containing various macromolecules and nuclear particles
- Nuclear envelope - membrane system that surrounds the nucleus

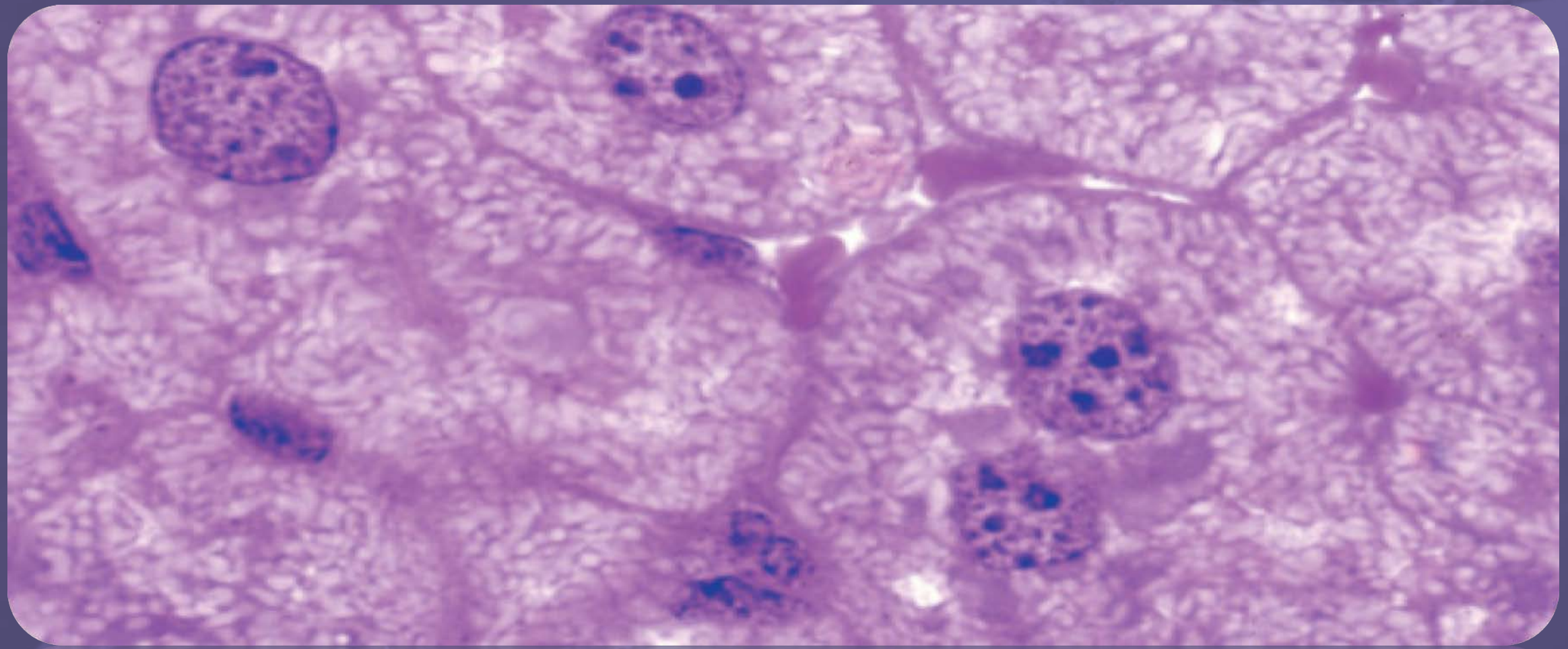


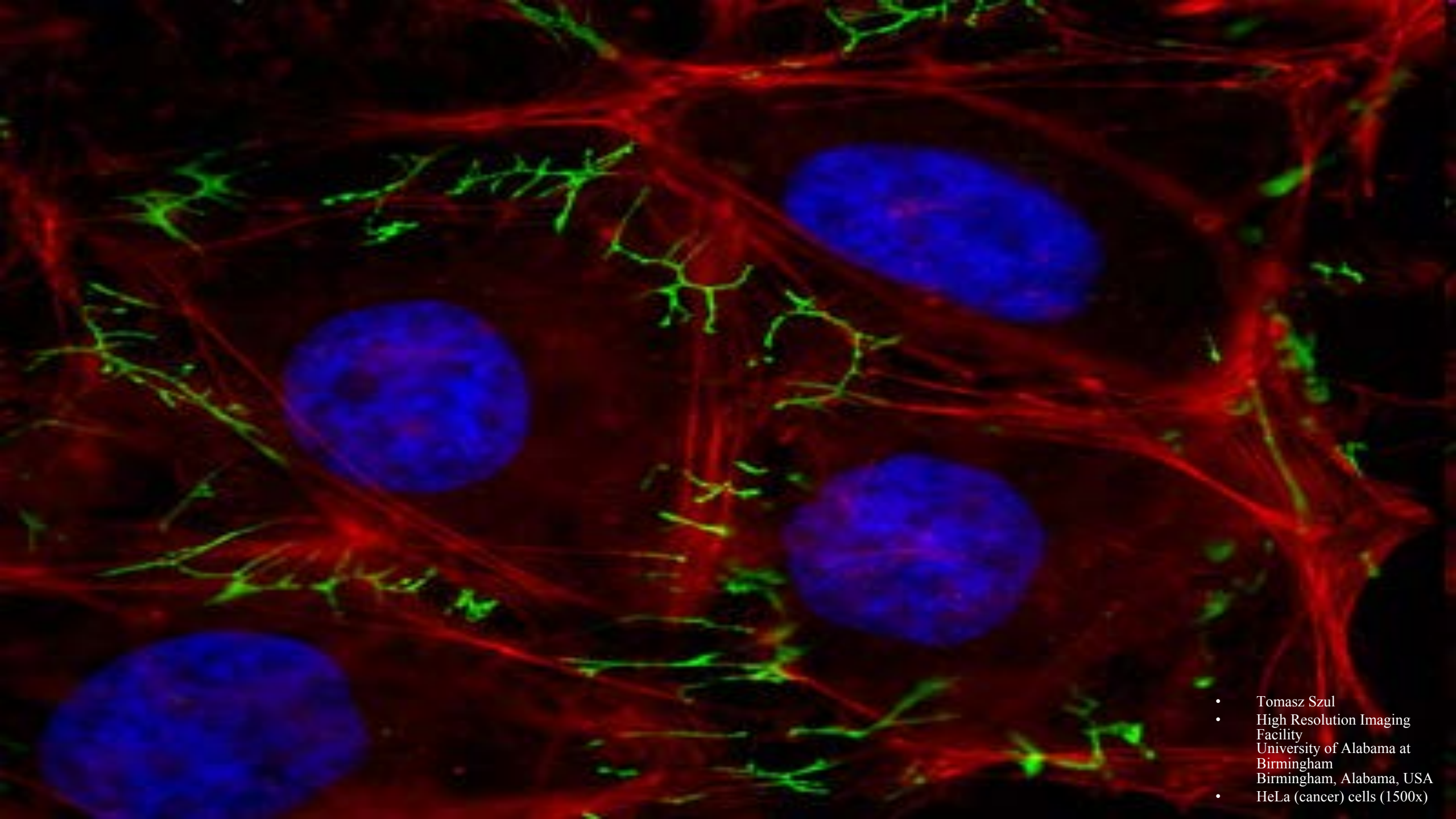


http://www.answers.com/topic/cell-nucleus-1

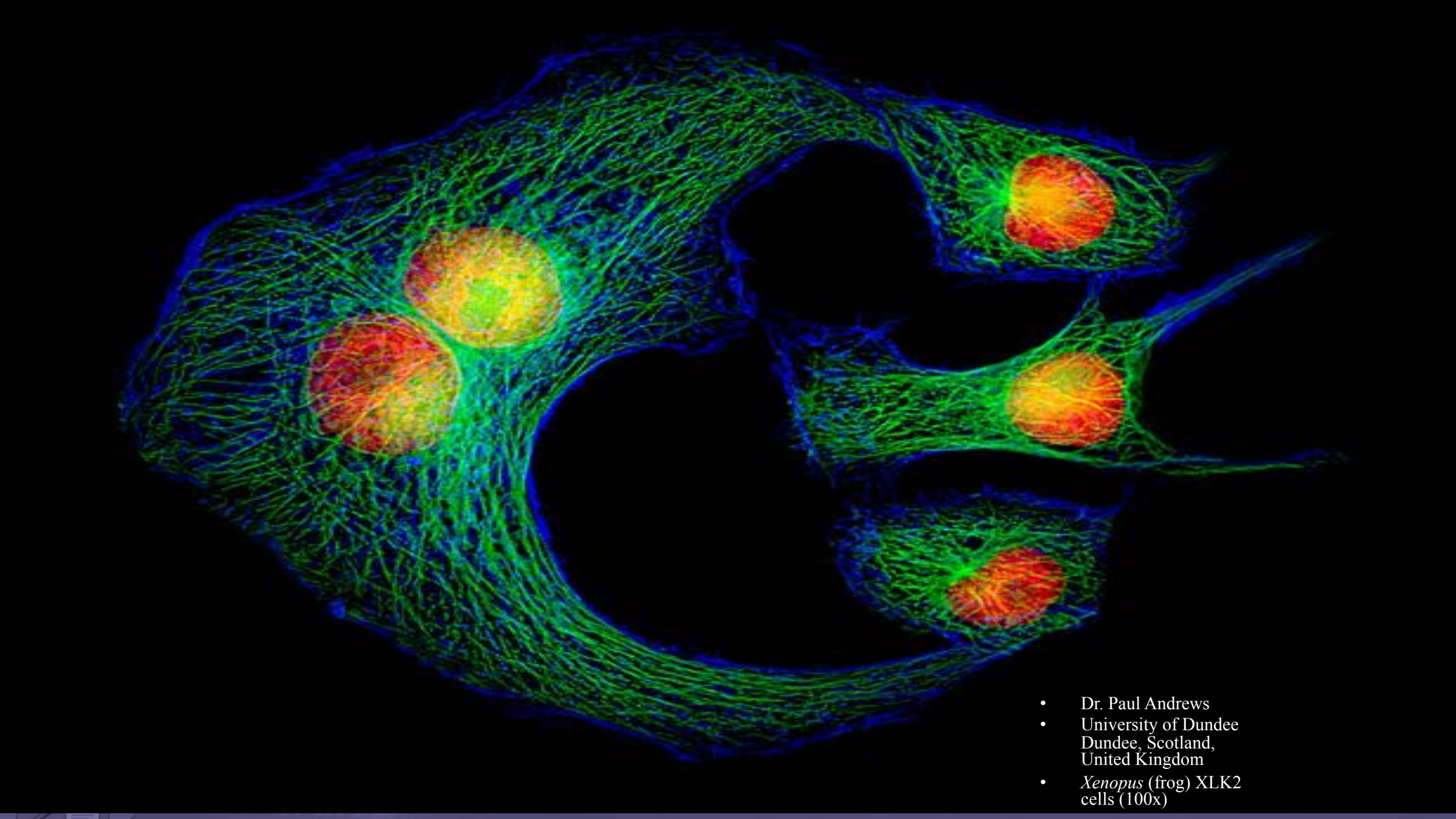

Nuclear Pore
Nuclear Envelope
Euchromatin
Hetero-chromatin
Nucleolus
pars granulosa
pars fibrosa
Nucleolar organizing center
rough endoplasmic reticulum

Nuclei of large, active cells.

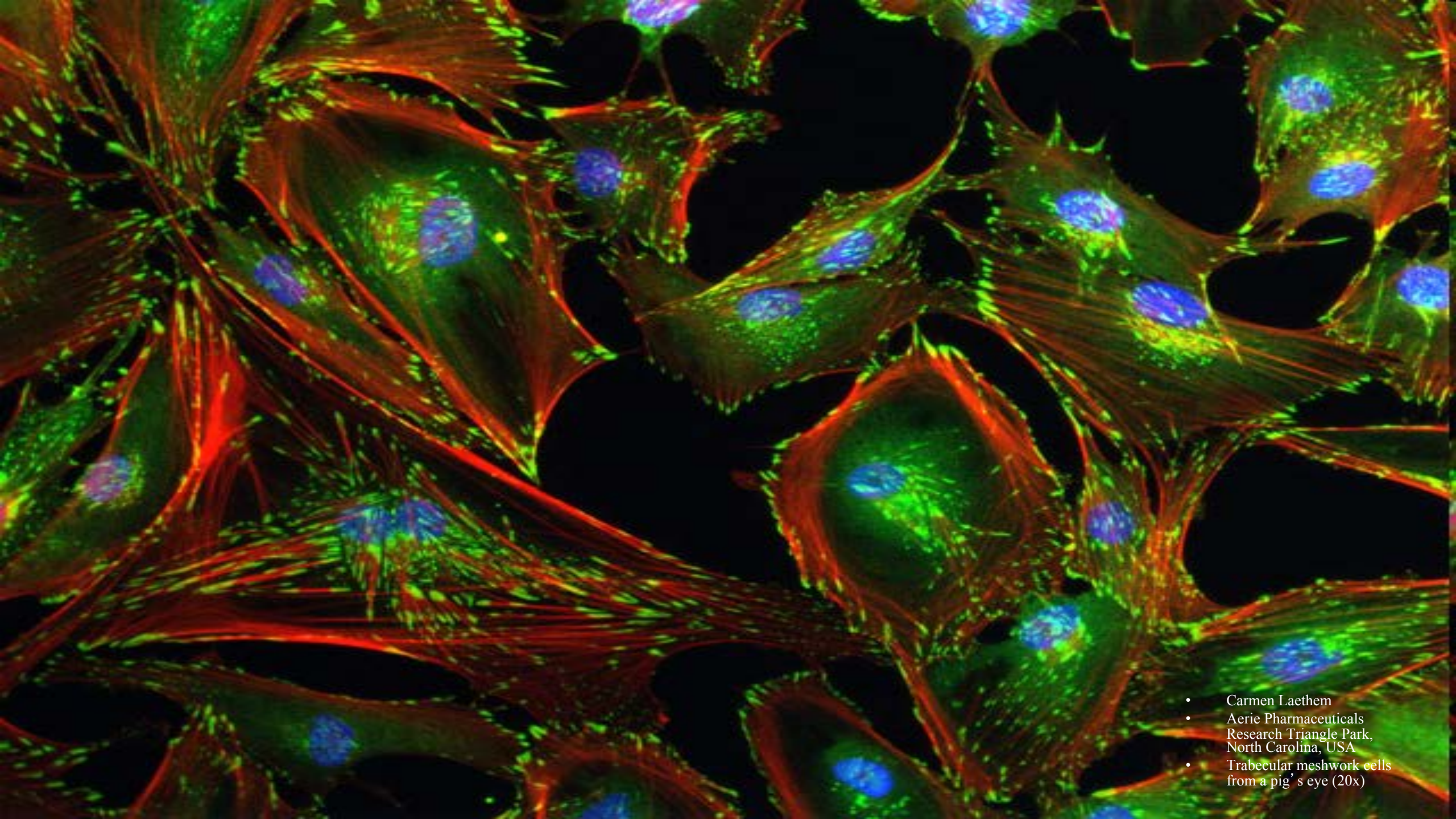




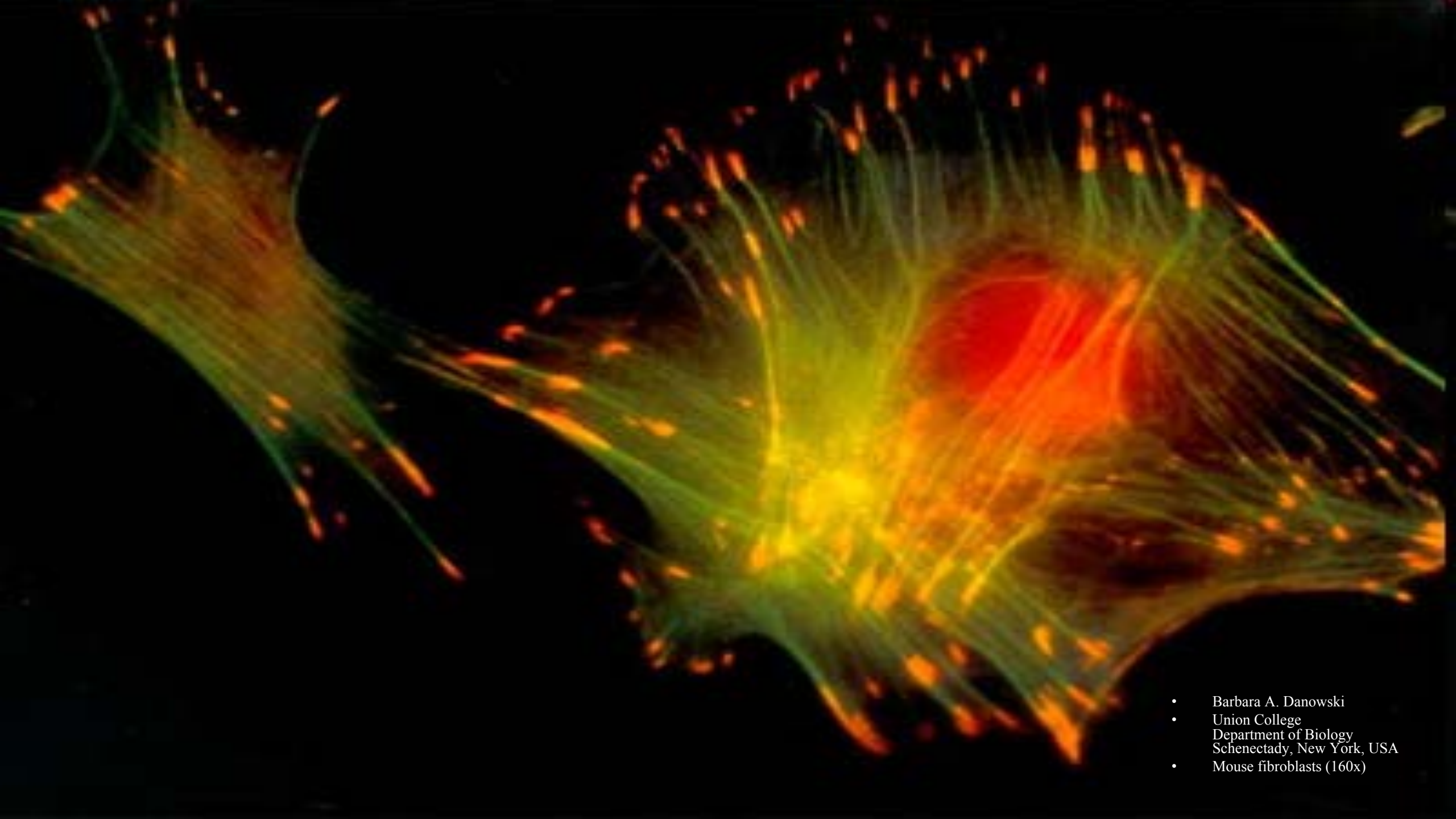
- Tomasz Szul
- High Resolution Imaging Facility
  University of Alabama at Birmingham
  Birmingham, Alabama, USA
- HeLa (cancer) cells (1500x)



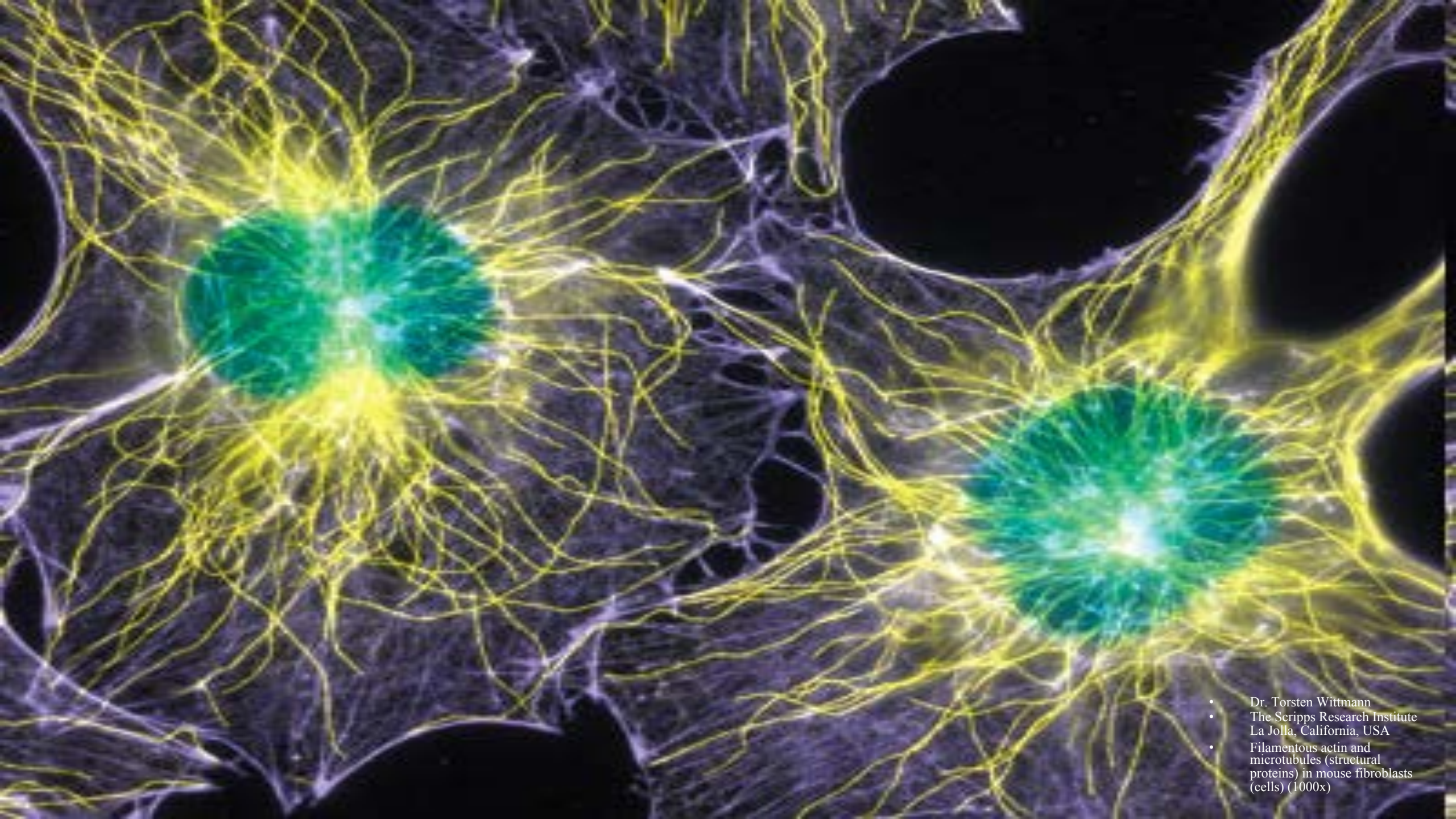
- Dr. Paul Andrews
- University of Dundee
  Dundee, Scotland,
  United Kingdom
- *Xenopus* (frog) XLK2
  cells (100x)



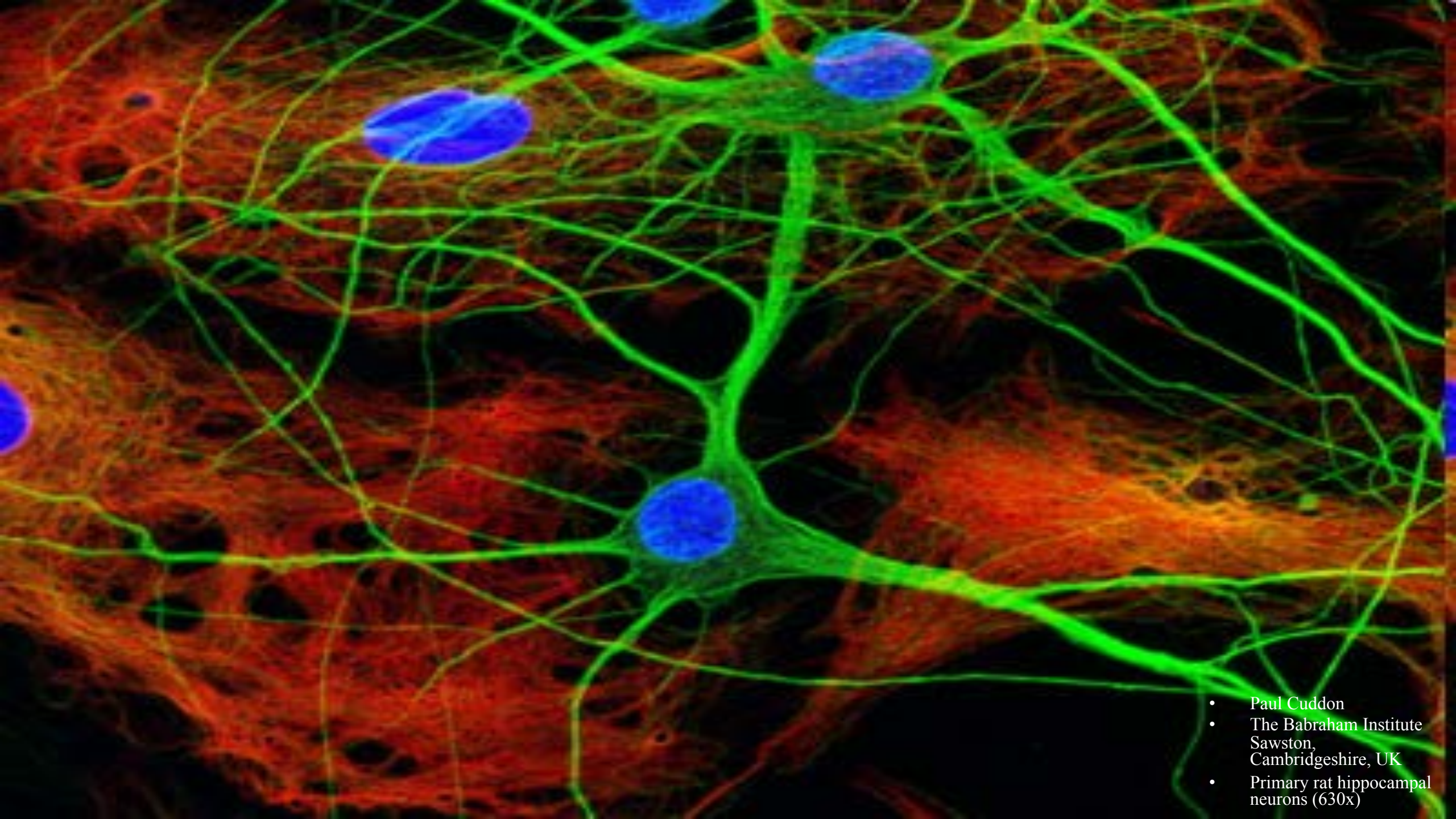
- Carmen Laethem
- Aerie Pharmaceuticals Research Triangle Park, North Carolina, USA
- Trabecular meshwork cells from a pig’s eye (20x)



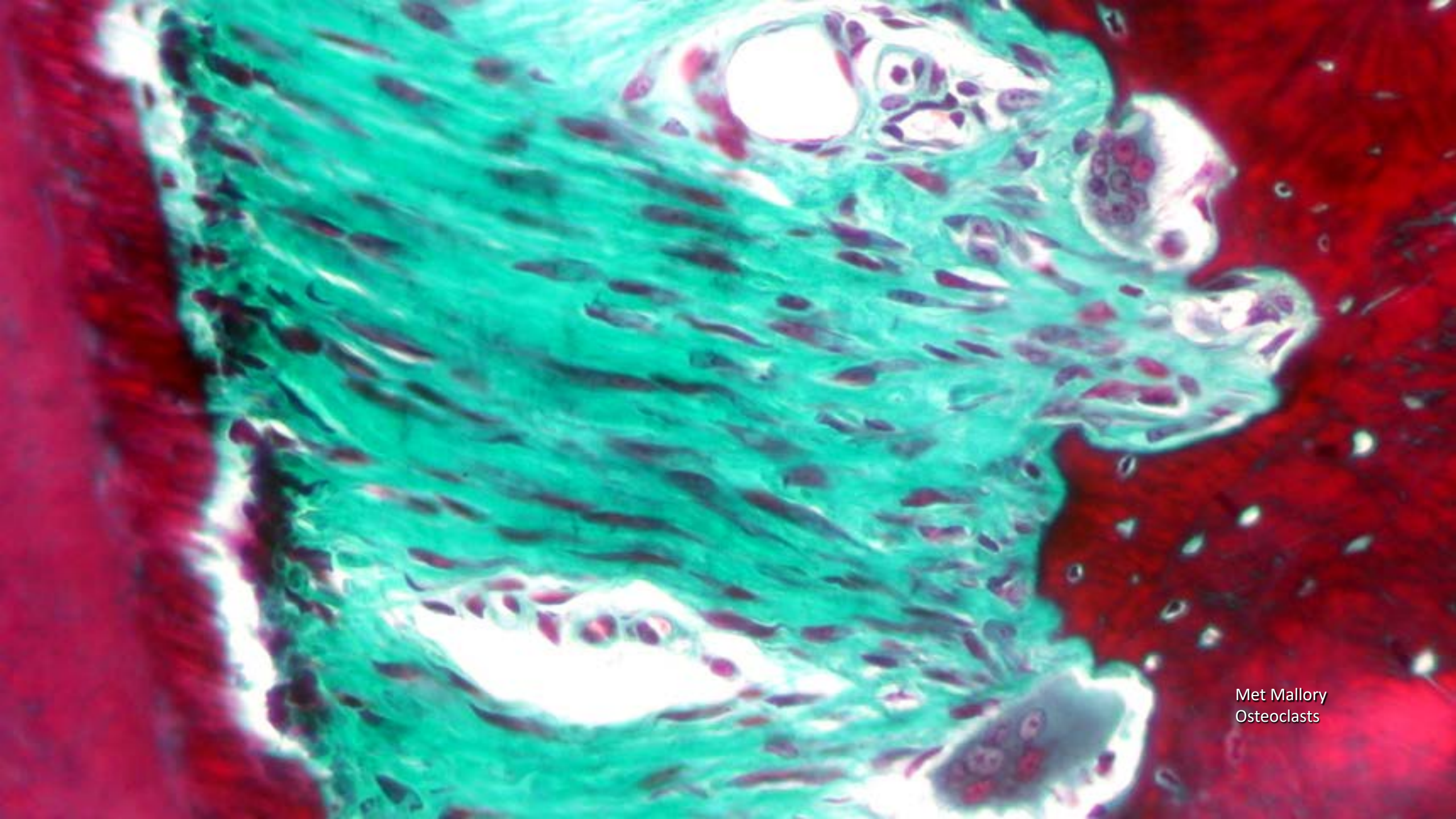
- Barbara A. Danowski
- Union College
  Department of Biology
  Schenectady, New York, USA
- Mouse fibroblasts (160x)



- Dr. Torsten Wittmann
- The Scripps Research Institute
  La Jolla, California, USA
- Filamentous actin and microtubules (structural proteins) in mouse fibroblasts (cells) (1000x)

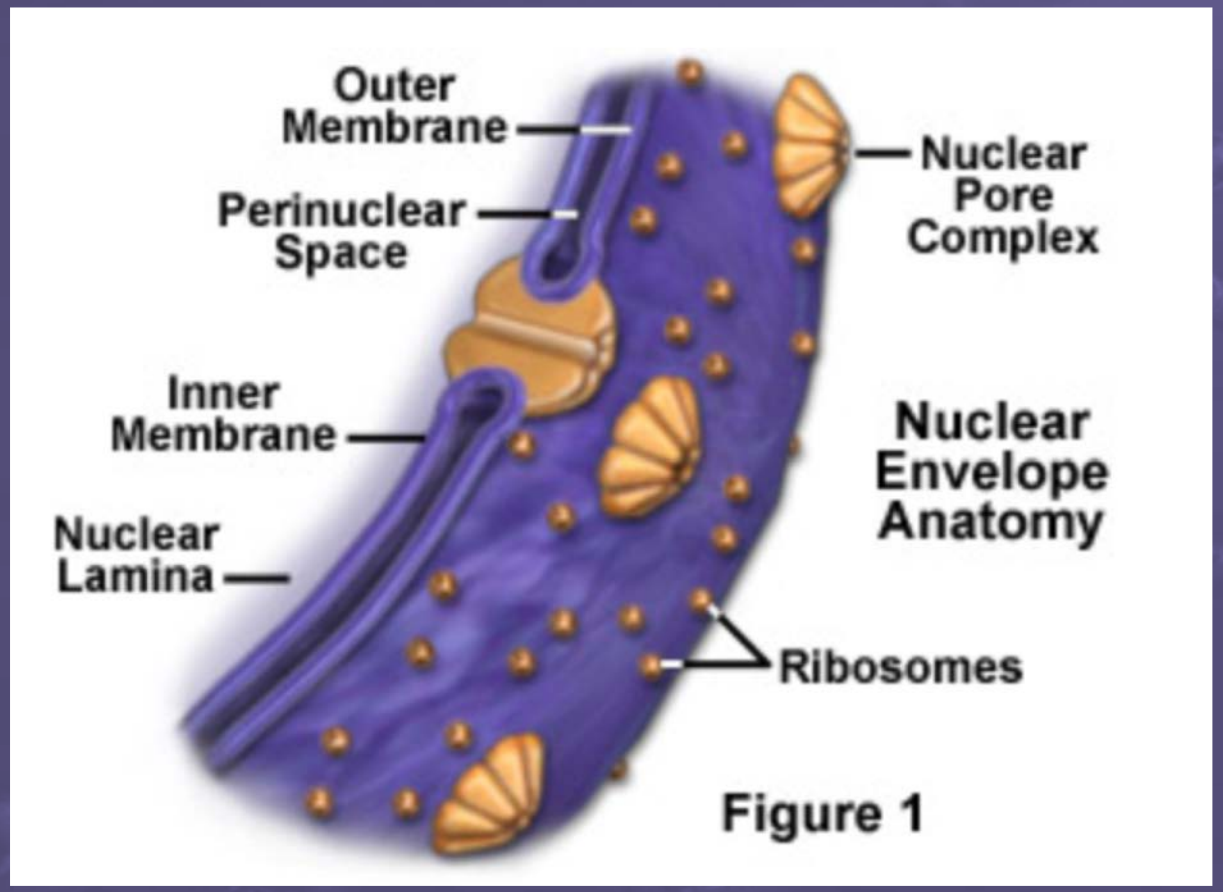


- Paul Cuddon
- The Babraham Institute Sawston, Cambridgeshire, UK
- Primary rat hippocampal neurons (630x)


Met Mallory
Osteoclasts

Nuclear envelope

- composed of **inner** and **outer nuclear membranes with perinuclear cisterna**
- is perforated by **nuclear pores**



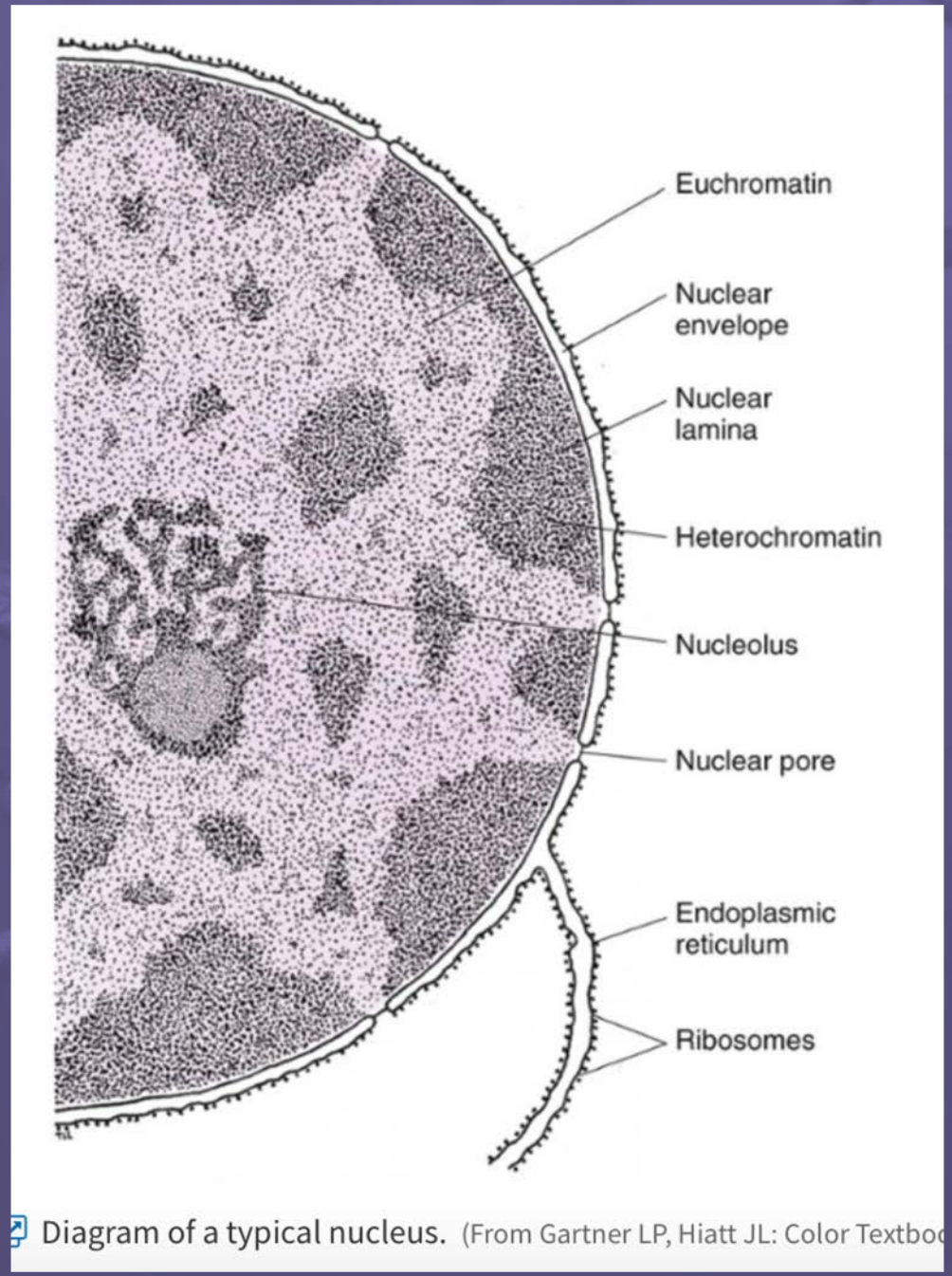
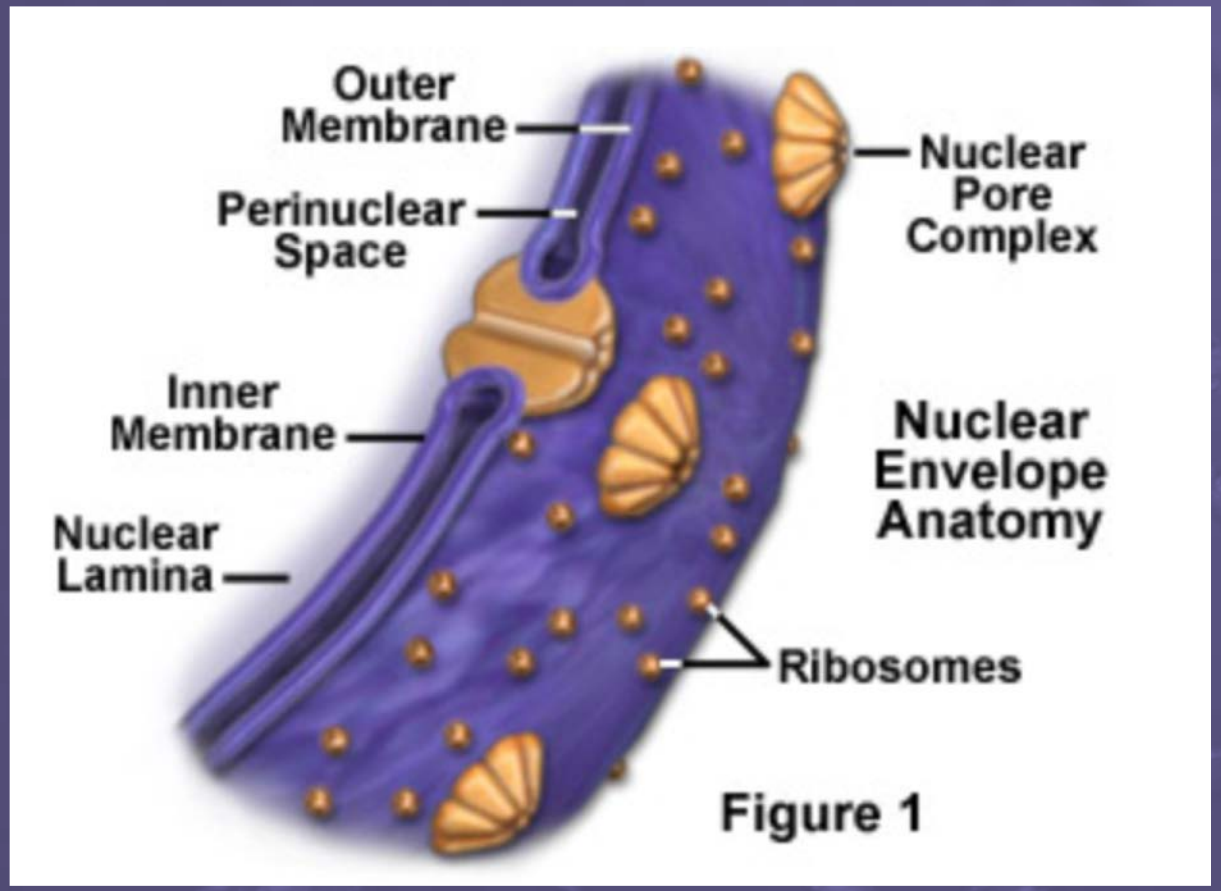


Diagram of a typical nucleus. (From Gartner LP, Hiatt JL: Color Textboo

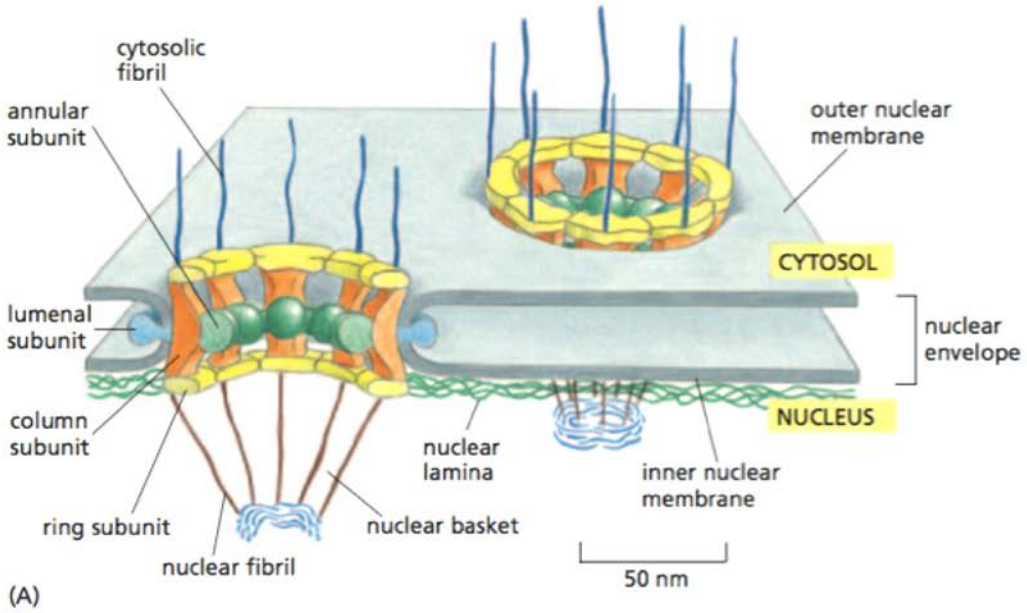
Functions of the nuclear membrane include:

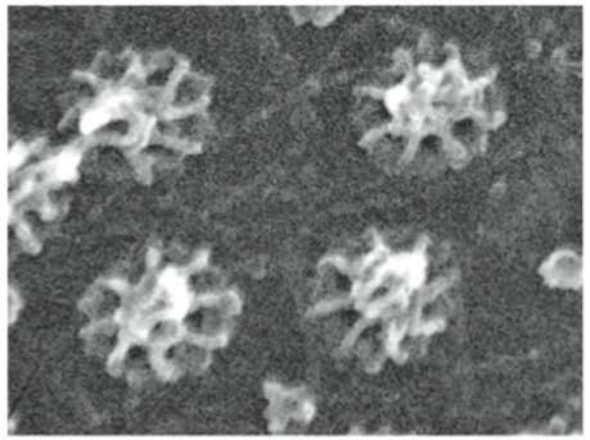


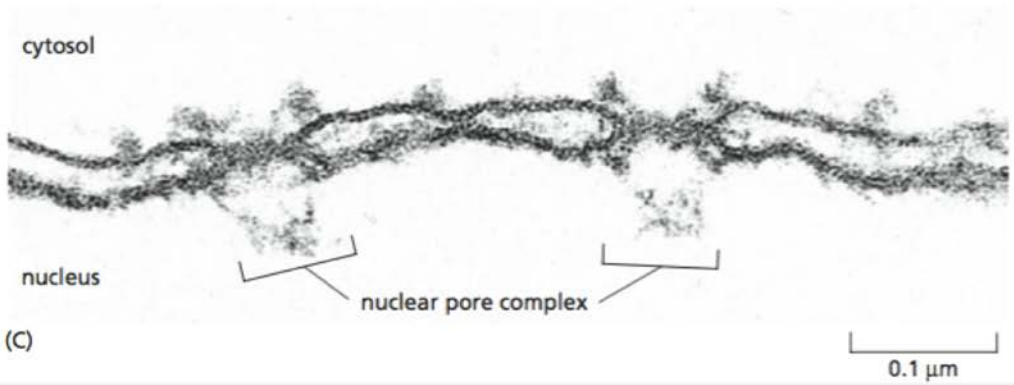
- **Compartmentalizing.** The nuclear membrane is vital in separating the nuclear material from the cellular material. Compartmentalization is vital in eukaryote cells to prevent the free mixture of cellular material with the nuclear material.
- **Shape and stability of the nucleus.** With the help of the lamina inside the nucleus, the double membrane helps keep the nucleus from collapsing and interfering with the functions of the nucleus.
- **Regulation of substances in and out of the nucleus**. Proper function of the nucleus requires the regulation of what proteins and enzymes are allowed in and out of the nucleus. The control of these passages is carried out by the thousands of nuclear pores. Each pore has its own regulatory proteins that only allow specific substances to pass in or out of the nucleus.
- **Communication.** The nuclear membrane and nuclear pores regulate the chemical communication between the nucleus and the rest of the cell. This communication is vital to the overall welfare and function of the cell.

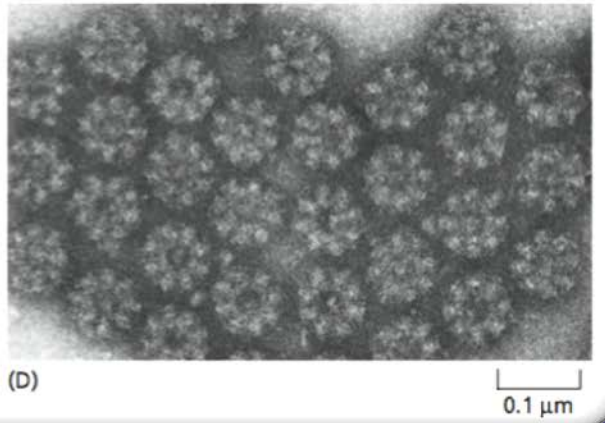
http://creationrevolution.com/2011/02/nuclear-membrane-–-simple-cell-part-17/

nuclear pore complexes









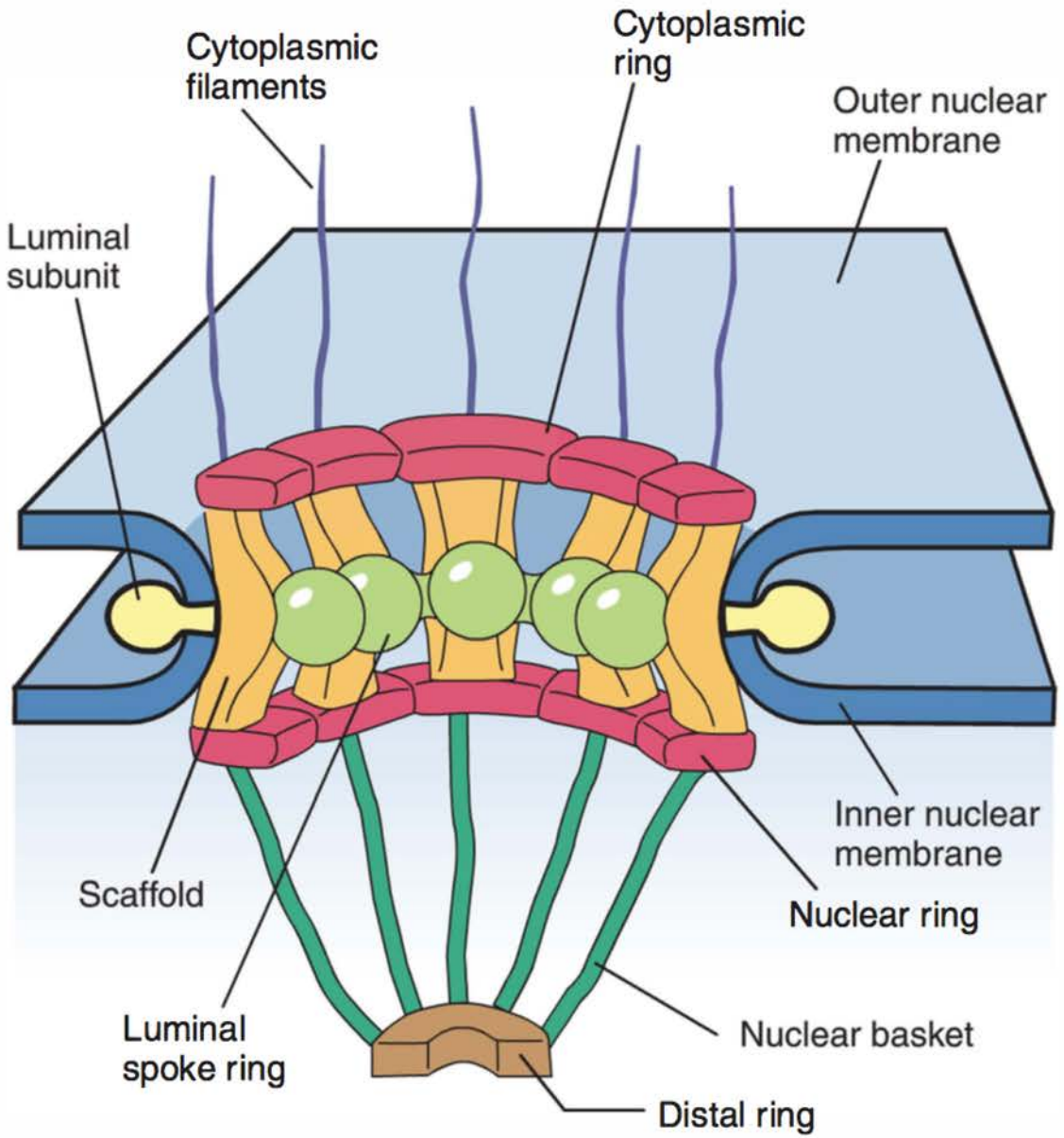
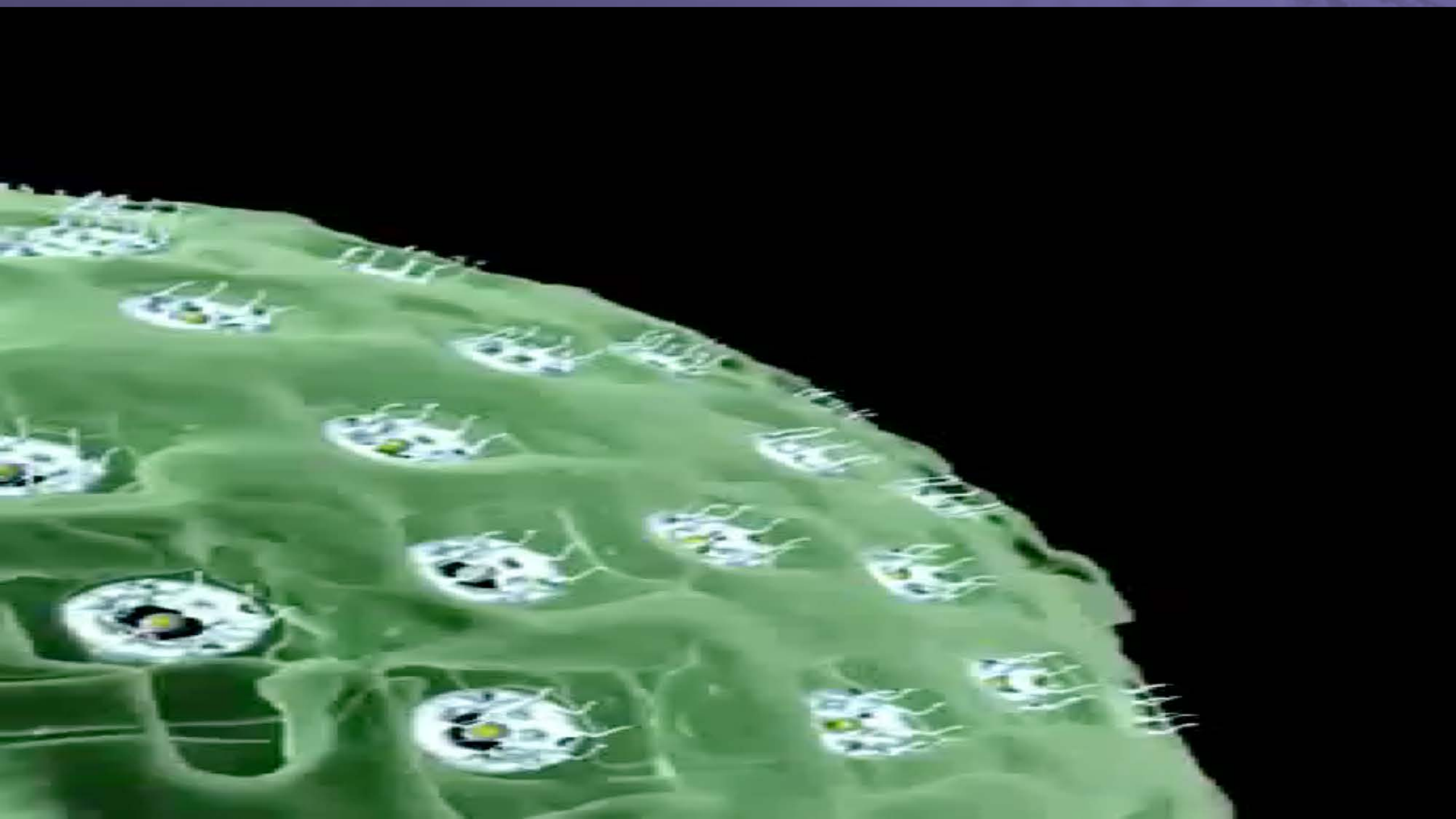
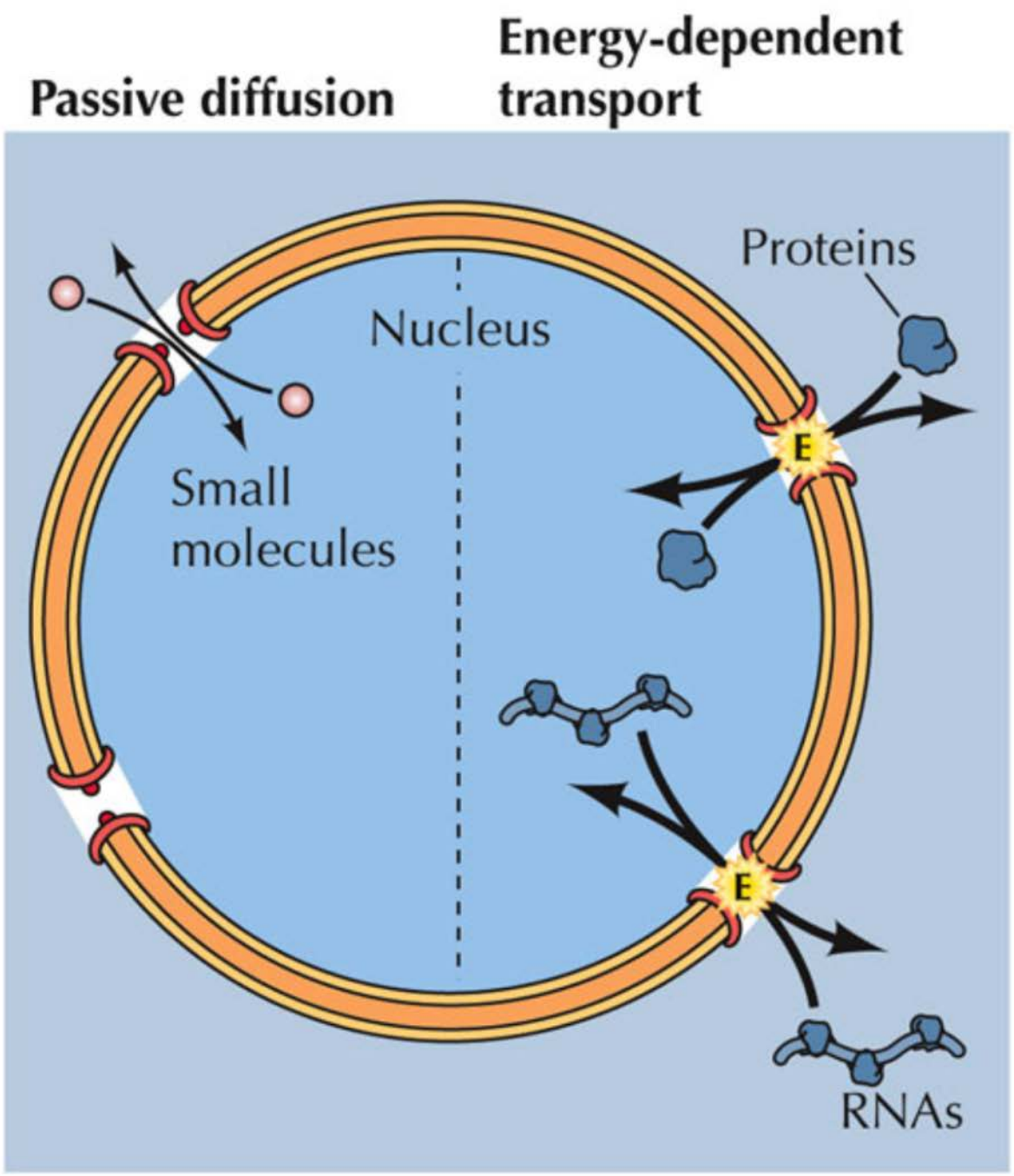
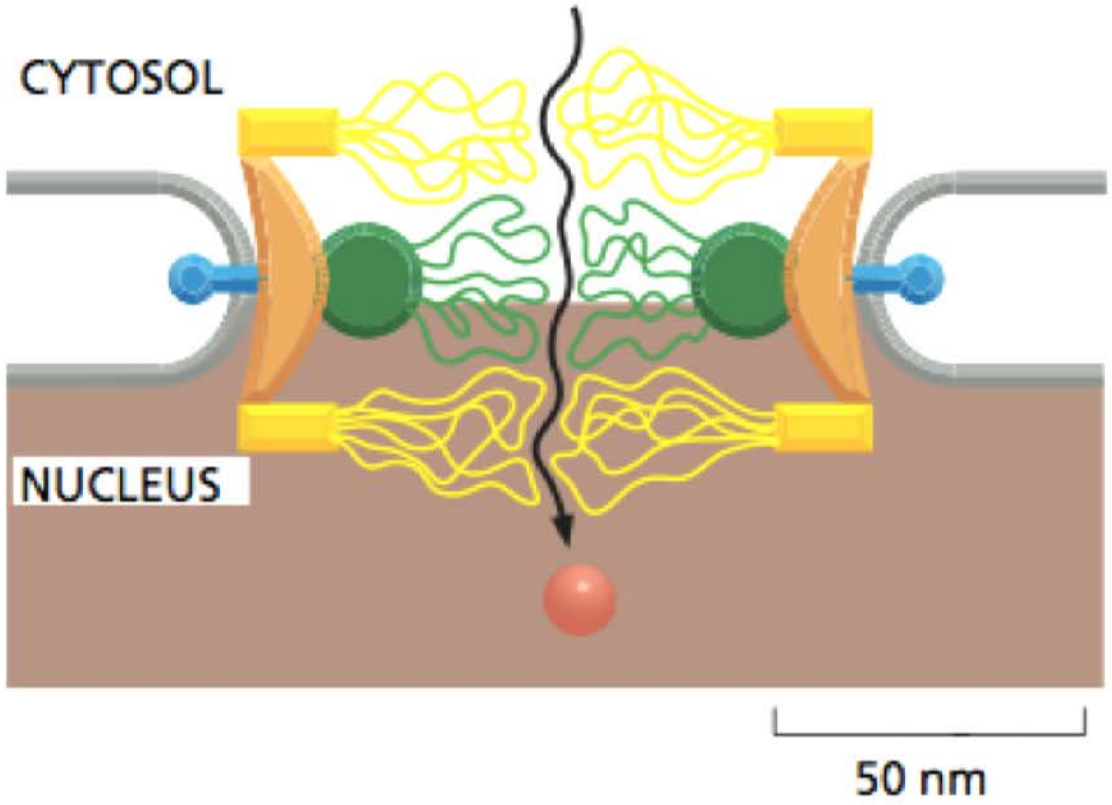


FIGURE 2.2. The nuclear pore complex. (Copyright 1994 from *Molecular Biology of the Cell*, 3rd ed., by Alberts et al. Adapted with permission from Garland Science/Taylor & Francis LLC.)

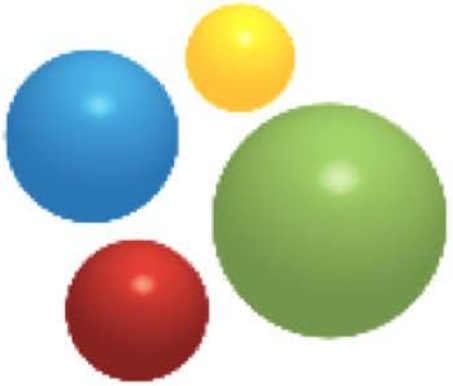




THE CELL, Fourth Edition, Figure 9.6 © 2006 ASM Press and Sinauer Associates, Inc.



size of molecules
that enter nucleus
by free diffusion

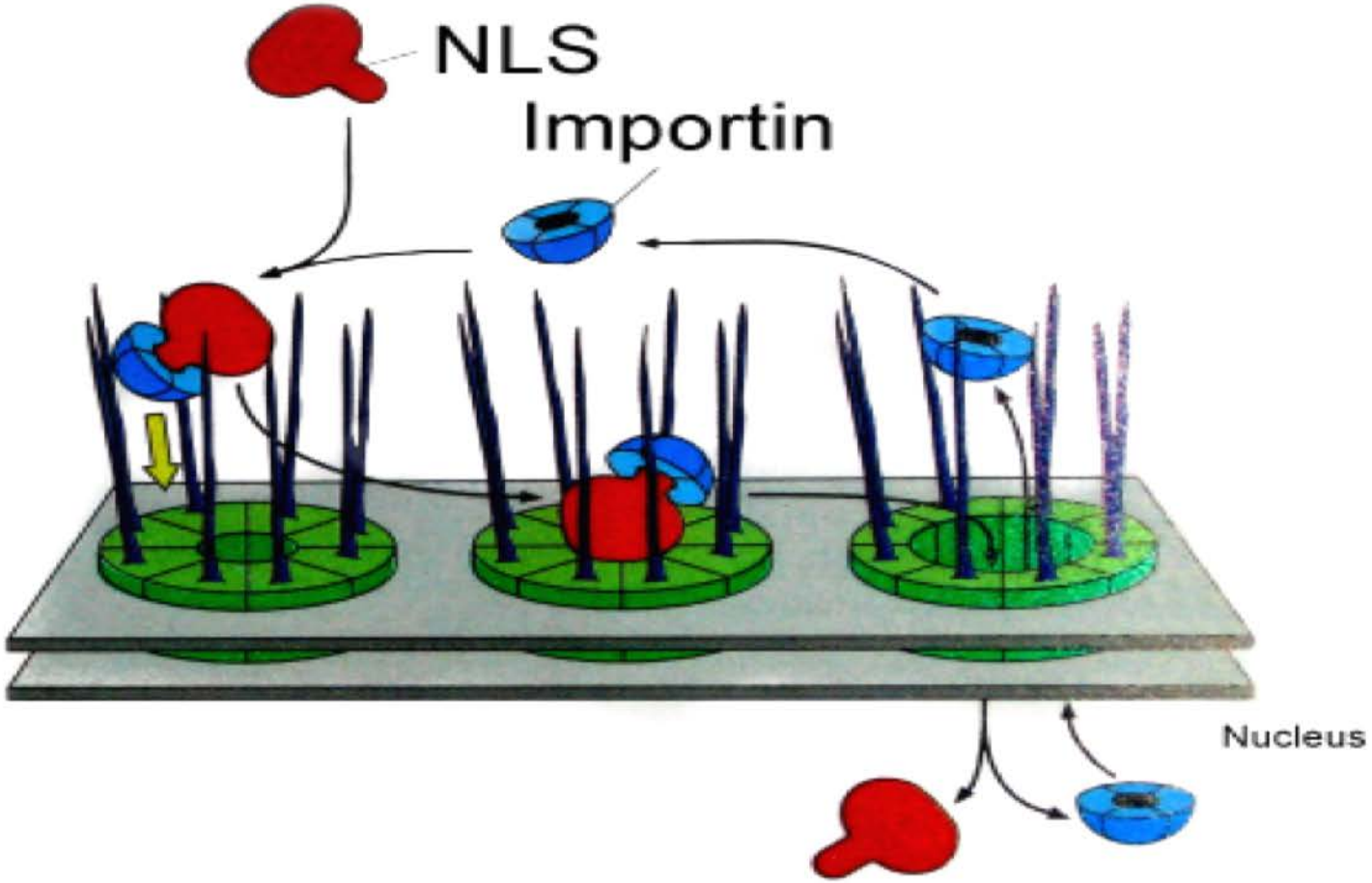


size of macromolecules
that enter nucleus
by active transport

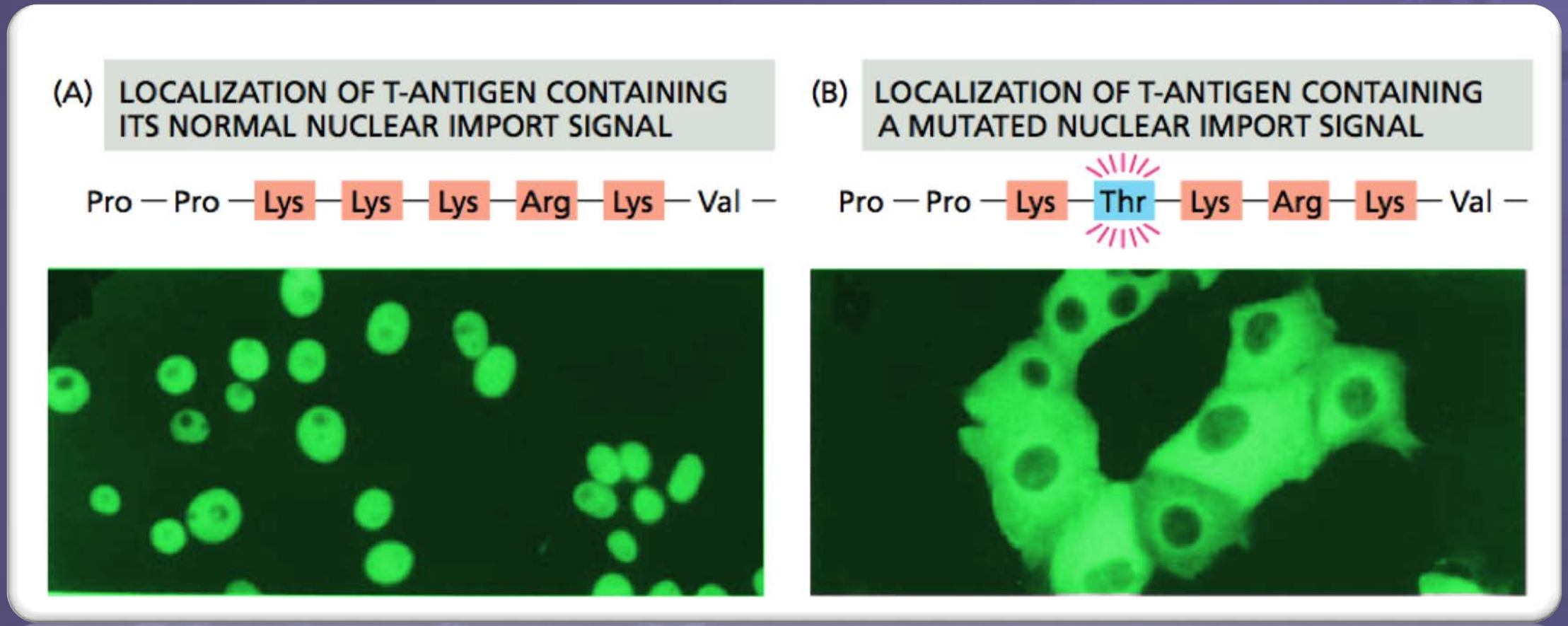
- **A model for the gated diffusion barrier of the NPC.**

An active mammalian cell can synthesize about 20,000 ribosome subunits per minute, and at certain points in the cell cycle, as many as 30,000 histones per minute are required by the nucleus.

receptor-mediated transport



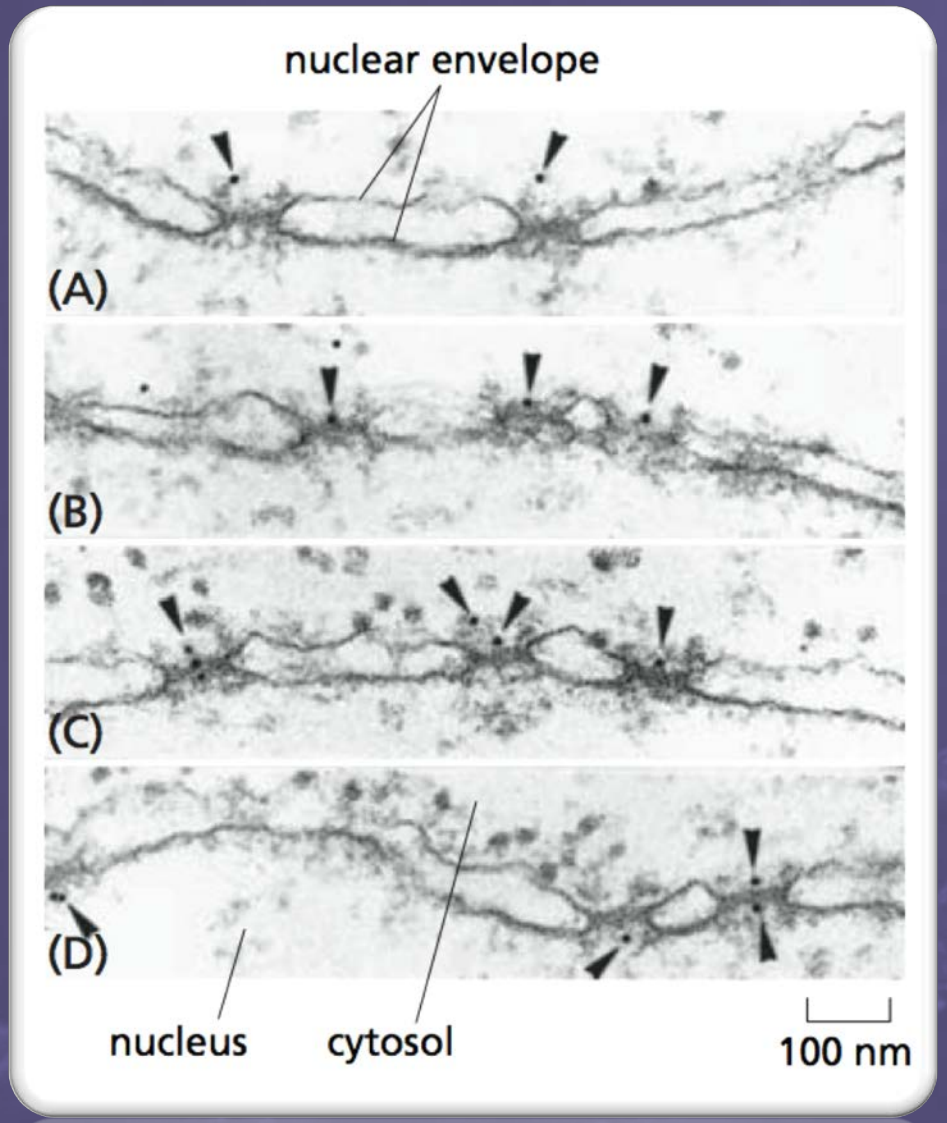
The function of a nuclear localization signal



Immunofluorescence micrographs showing the cell location of SV40 virus T-antigen containing or lacking a short sequence that serves as a nuclear localization signal. (A) The normal T-antigen protein contains the lysine-rich sequence indicated and is imported to its site of action in the nucleus, as indicated by immunofluorescence staining with antibodies against the T-antigen.

(B) T-antigen with an altered nuclear localization signal (a threonine replacing a lysine) remains in the cytosol.

Visualizing active import through NPCs.



- This series of electron micrographs shows colloidal gold spheres *(arrowheads)* coated with peptides containing nuclear localization signals entering the nucleus through NPCs. Gold particles were injected into living cells, which then were fixed and prepared for electron microscopy at various times after injection.

Nuclear lamina

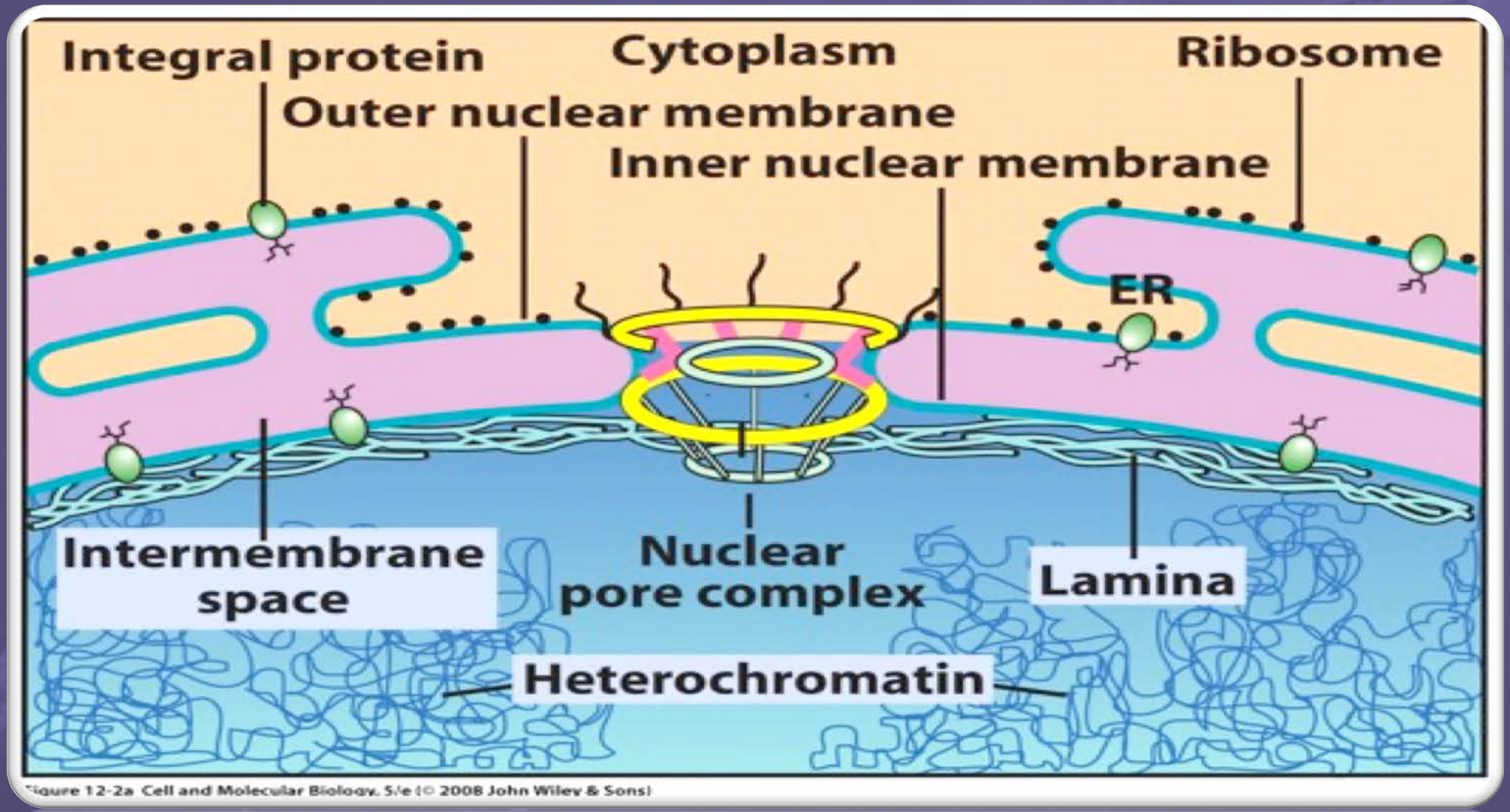
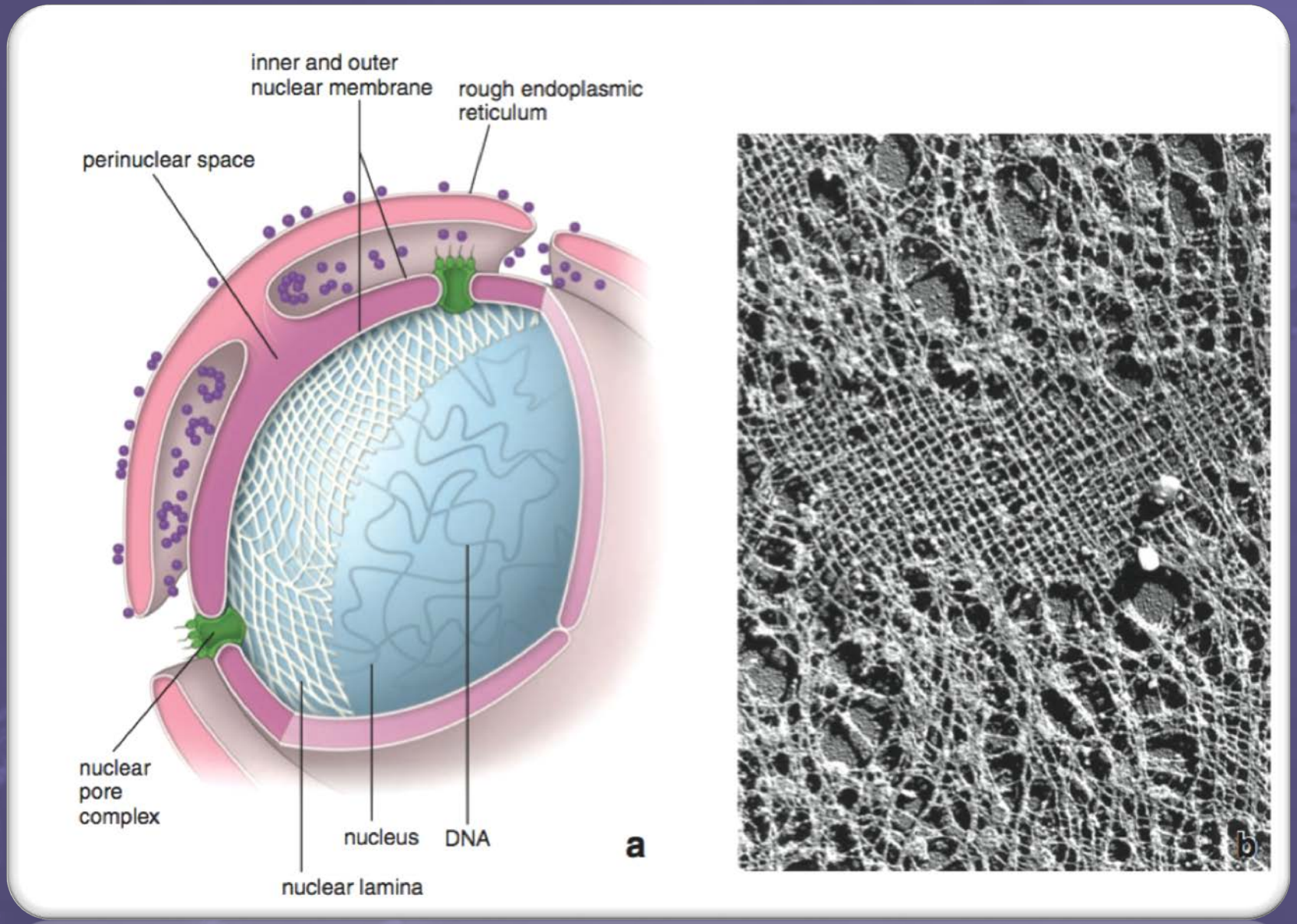
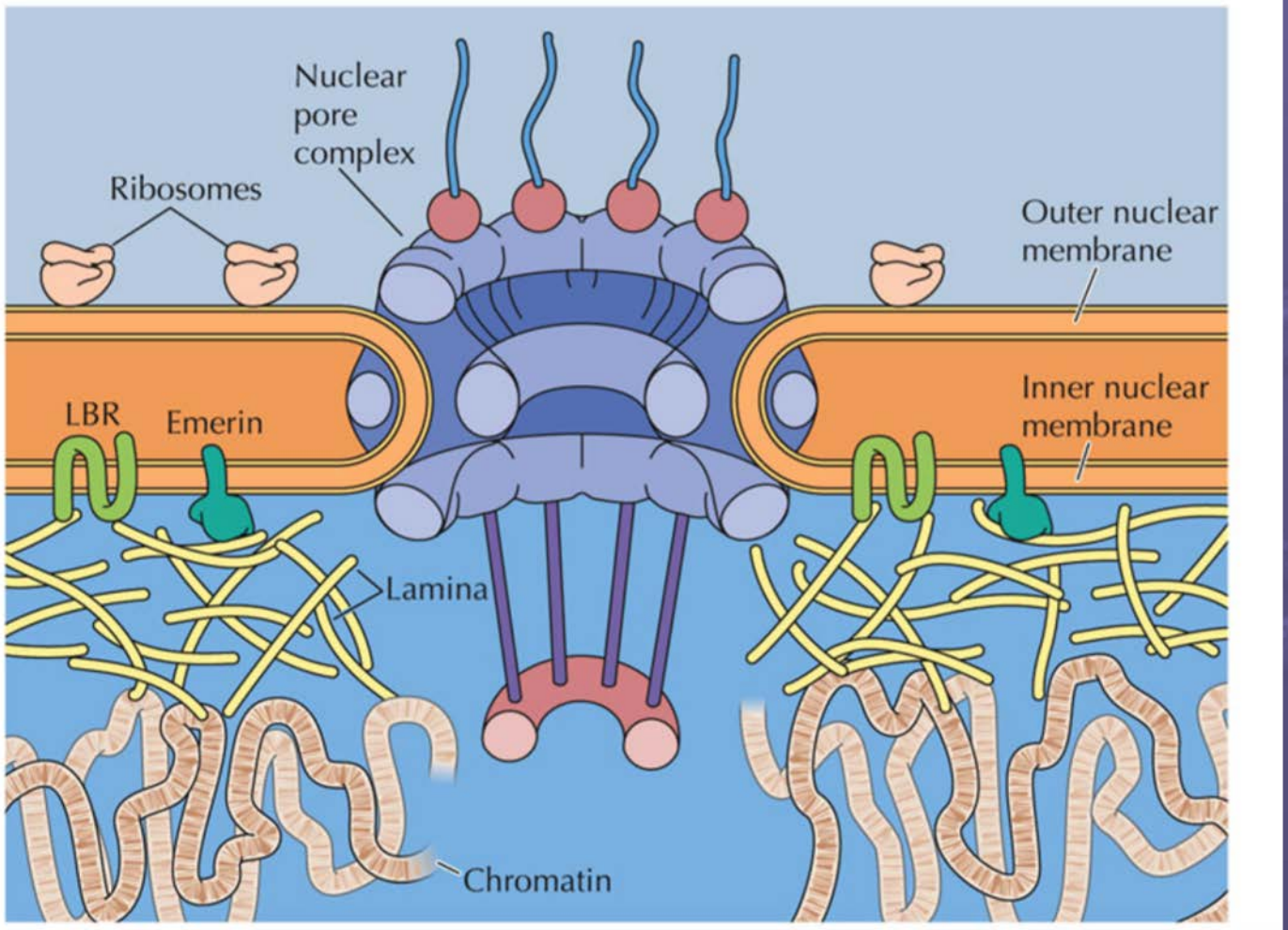


Figure 12-2a Cell and Molecular Biology, 5/e (© 2008 John Wiley & Sons)

The nuclear lamina is a dense (~30 to 100 nm thick) fibrillar network inside the nucleus of a eukaryotic cell. It is composed of intermediate filaments and membrane associated proteins.


inner and outer
nuclear membrane
rough endoplasmic
reticulum
perinuclear space
nuclear
pore
complex
nucleus
DNA
nuclear lamina
a
b

Nuclear lamina - function

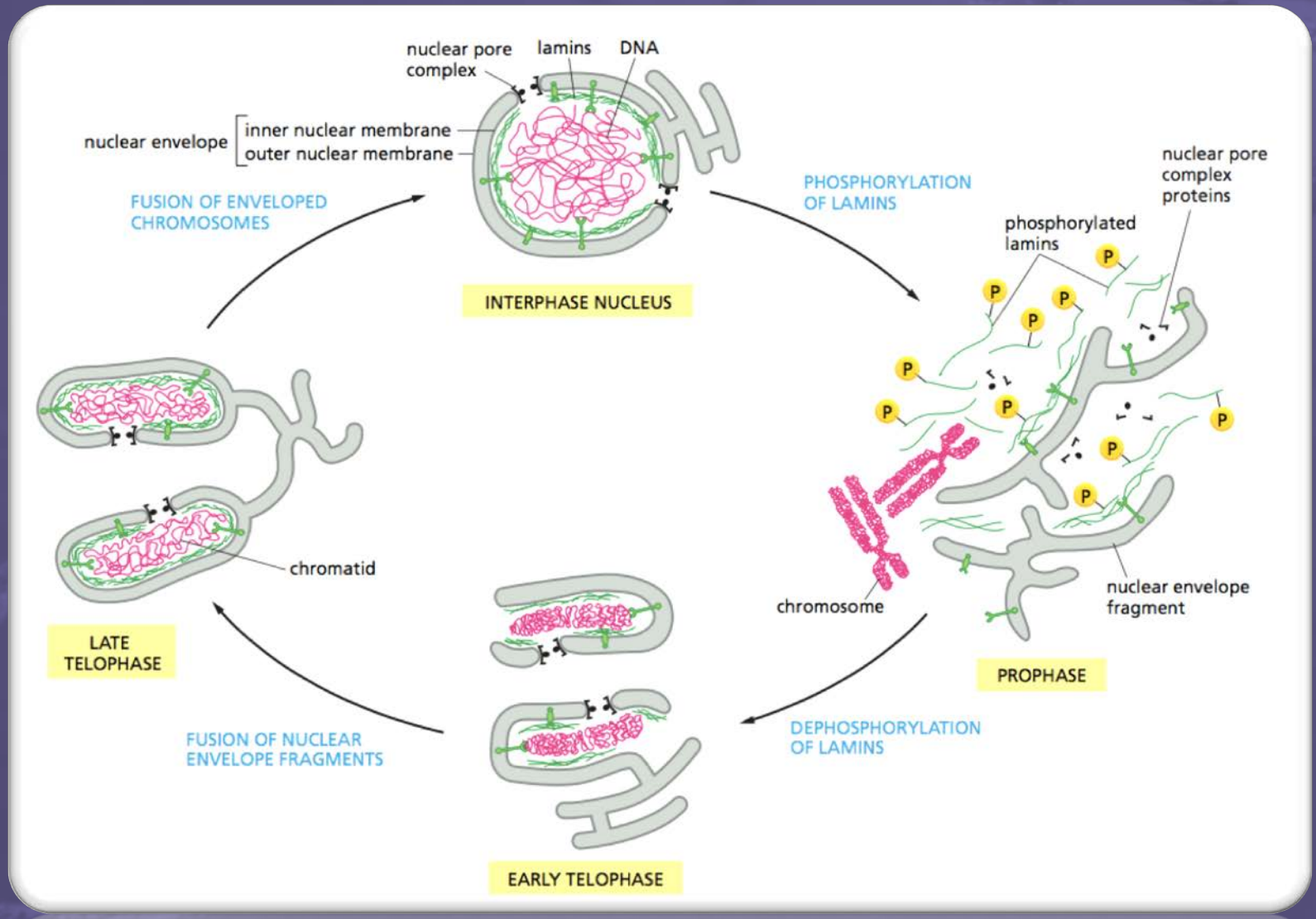


THE CELL, Fourth Edition, Figure 9.5 © 2006 ASM Press and Sinauer Associates, Inc.

- contains binding sites for chromatin, helping to organize chromatin in the nucleus
- determinants of nuclear size, shape, mechanical integrity, and positioning of nuclear pores
- play important roles in DNA replication, transcription

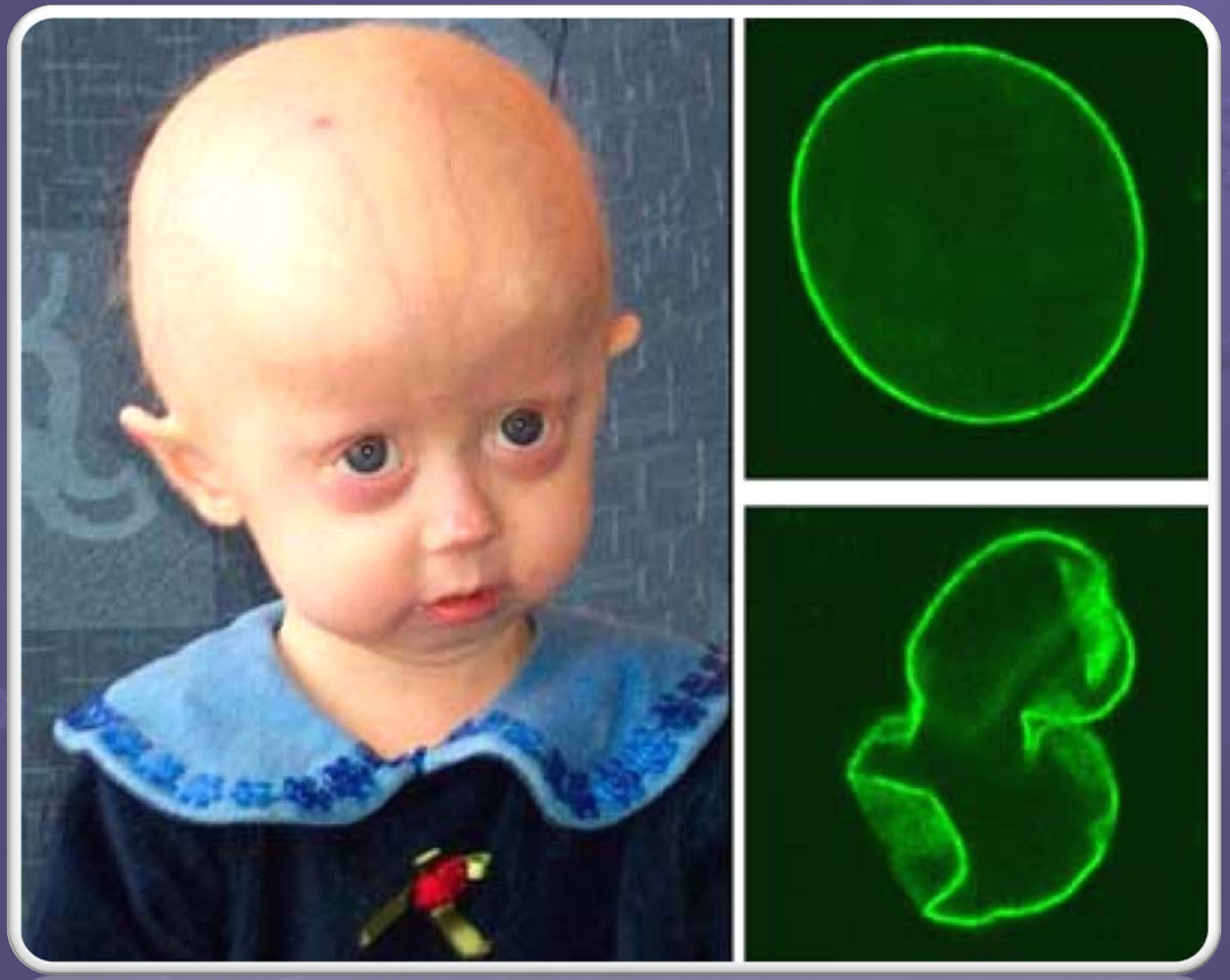
Nuclear lamina - function

Nulcear lamina plays role in disassembly of the nucleus in mitosis and the reassembly of the nucleus in daughter cells



- X-linked Emery-Dreifuss muscular Dystrophy
  - Results form mutations in the nuclear envelope protein, emerin.
- Non-Sex Linked Emery Dreifuss Muscular Dystrophy
  - Results from mutations in the LMNA gene which is a single gene that encodes lamin A and C.
- Hutchinson-Guilford Progeria Disease
  - Results from a 150 bp deletion within the lamin A gene.

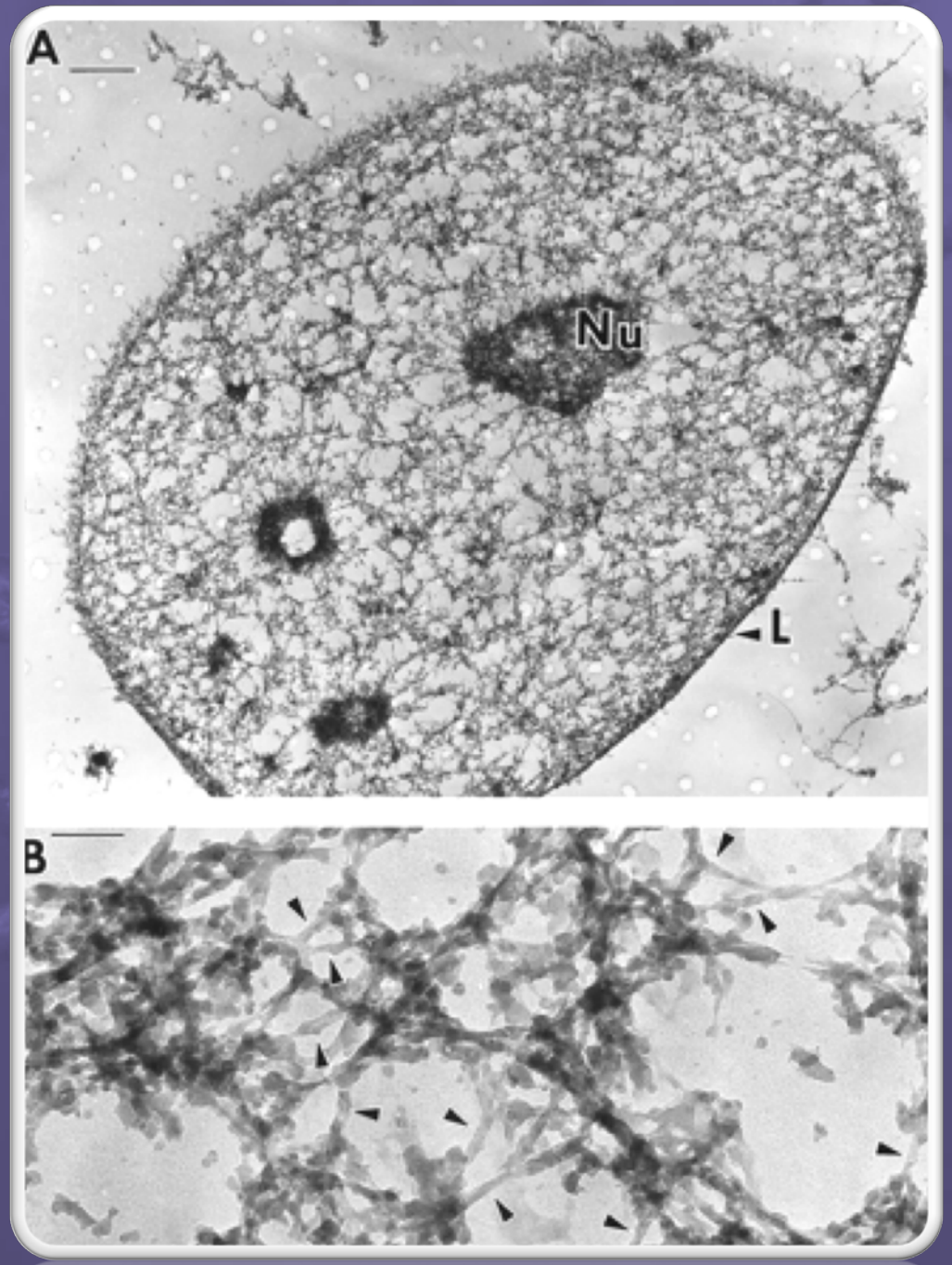
Hutchinson-Gilford Progeria Syndrome



http://www.eurasnet.info/clinicians/alternative-splicing-and-disease/list-of-diseases/hgps

nuclear matrix or “nuclear-scaffold”

- nuclear matrix is the network of fibres found throughout the inside of a cell nucleus and is somewhat analogous to the cell cytoskeleton
- responsible for maintaining 3d structure of chromatin
- 98% compose of protein



http://www.pnas.org/content/94/9/4446.full

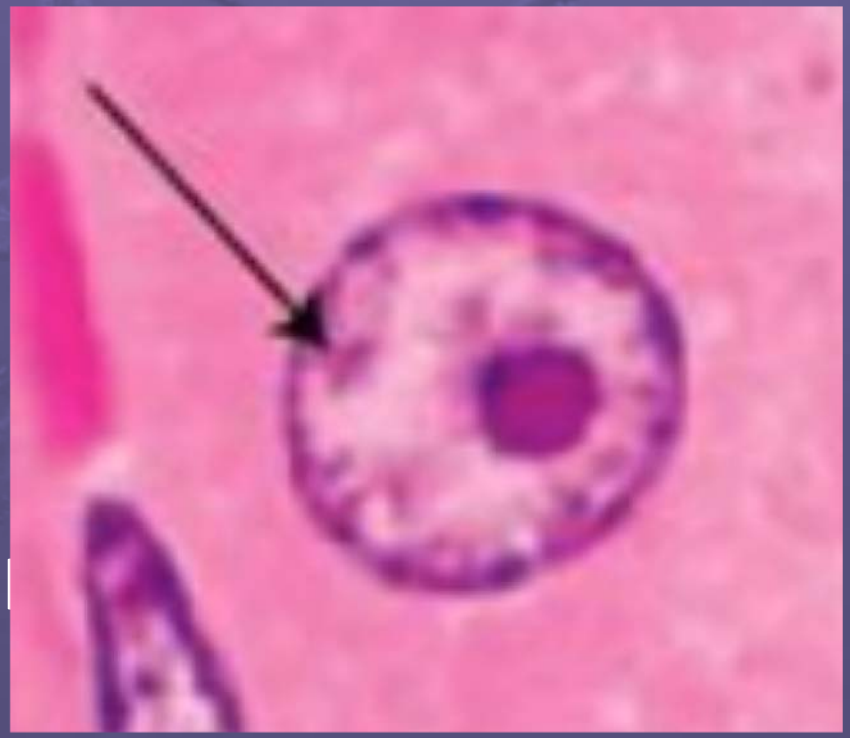
Chromatin

- **complex of DNA and proteins - consists of DNA double helix complexed with histones and nonhistone proteins.**
- Function
  - folding of the DNA strand
  - protecting the DNA from physical damage
  - controlling transcriptional activity of DNA
  - controlling the precise duplication of DNA in preparation for cell division
  - facilitating the repair of DNA

- two forms of chromatin are found in the nucleus: a condensed form called *heterochromatin* and a dispersed form called *euchromatin*.

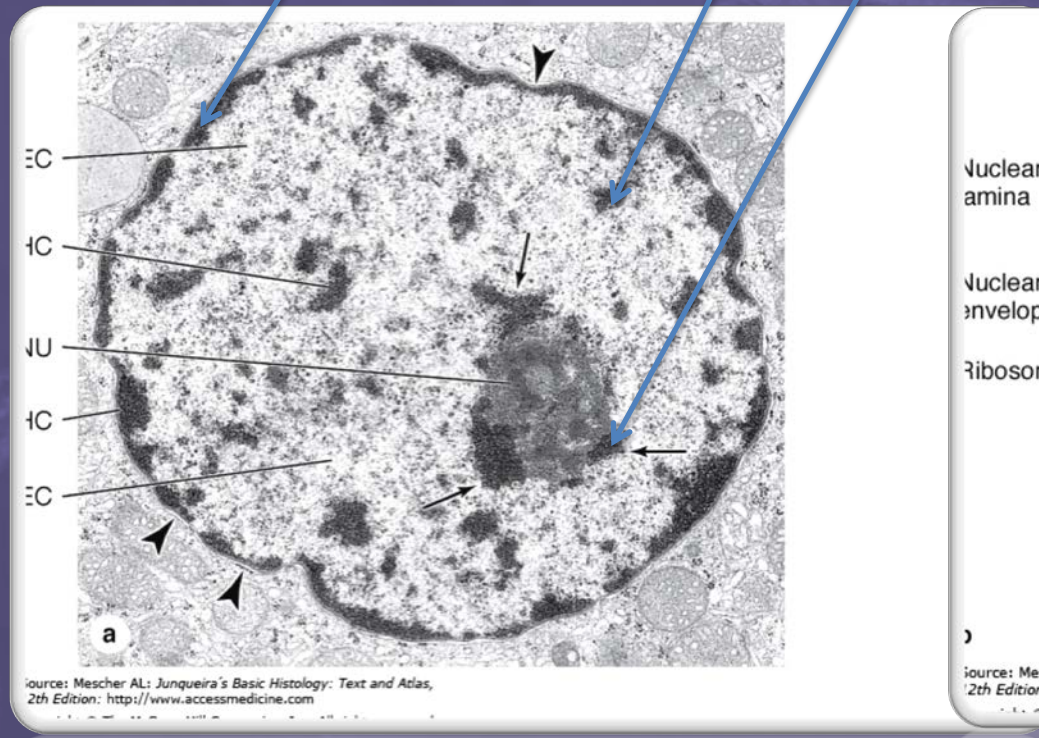
Heterochromatin:

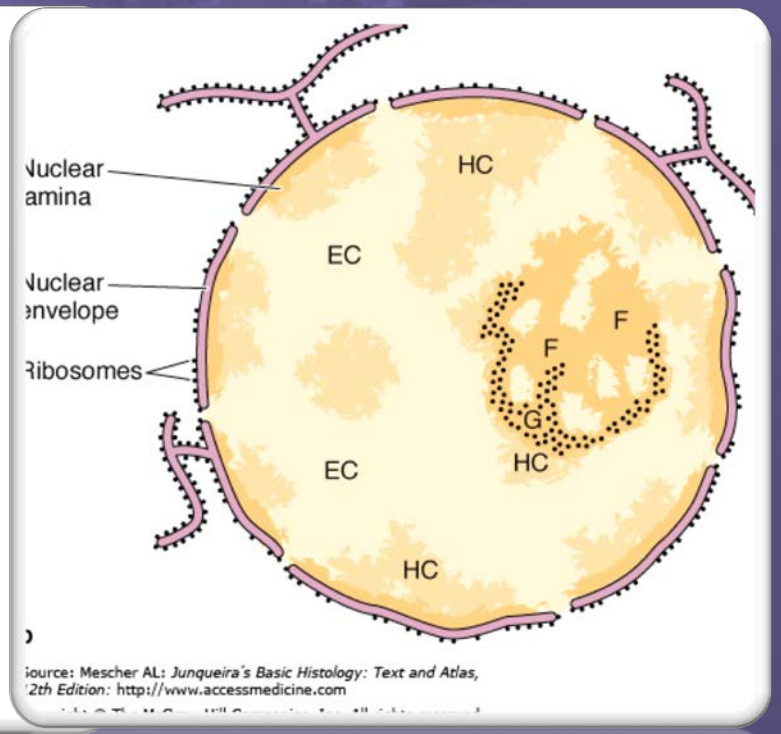
- condensed, not transcribed,
- It is formed from euchromatin that is folded into 30-nm-thick fibers.
- On light microscope as basophilic clumps
- Functions:
  - maintaining the integrity of chromosomal centromeres and telomeres
  - during meiosos, play role in interchromosomal interactions and chromosomal segregation



Heterochromatin is disposed in three locations

- Marginal chromatin is found at the periphery of the nucleus (the structure light microscopists formerly referred to as the nuclear membrane actually consists largely of marginal chromatin).
- Karyosomes are discrete bodies of chromatin irregular in size and shape that are found throughout the nucleus.
- Nucleolar-associated chromatin is chromatin found in association with the nucleolus.





Constitutive heterochromatin

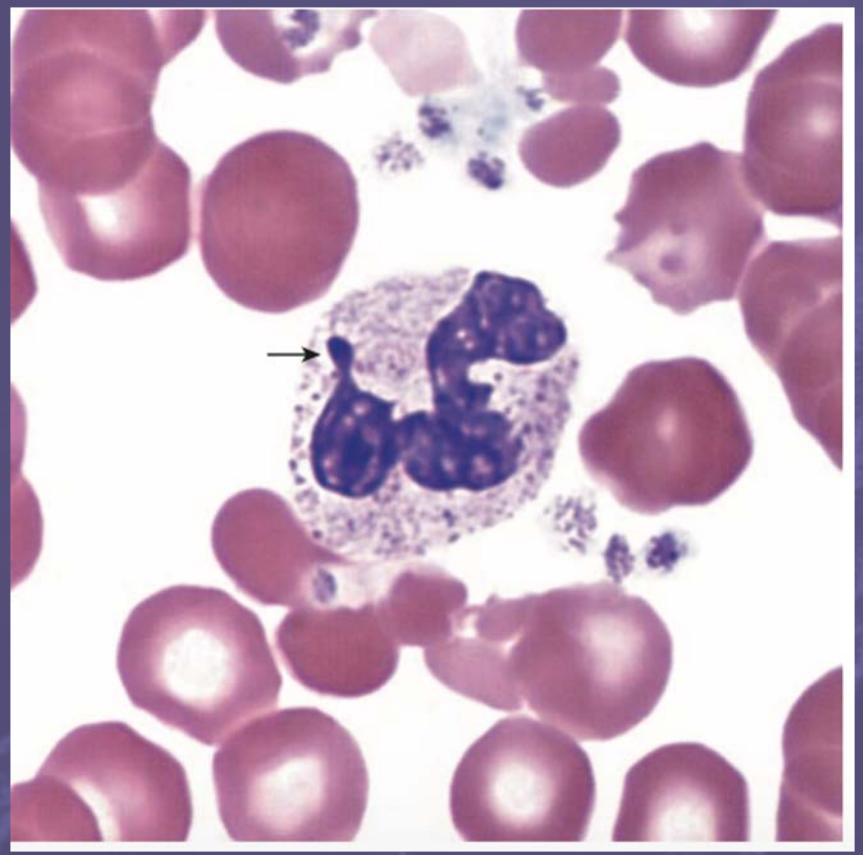
- Constitutive heterochromatin domains are sections of DNA that occur throughout the chromosomes of eukaryotes, but particularly at the **centromeres and telomeres**. They often consist of very highly condensed, repetitive DNA and are largely transcriptionally silent

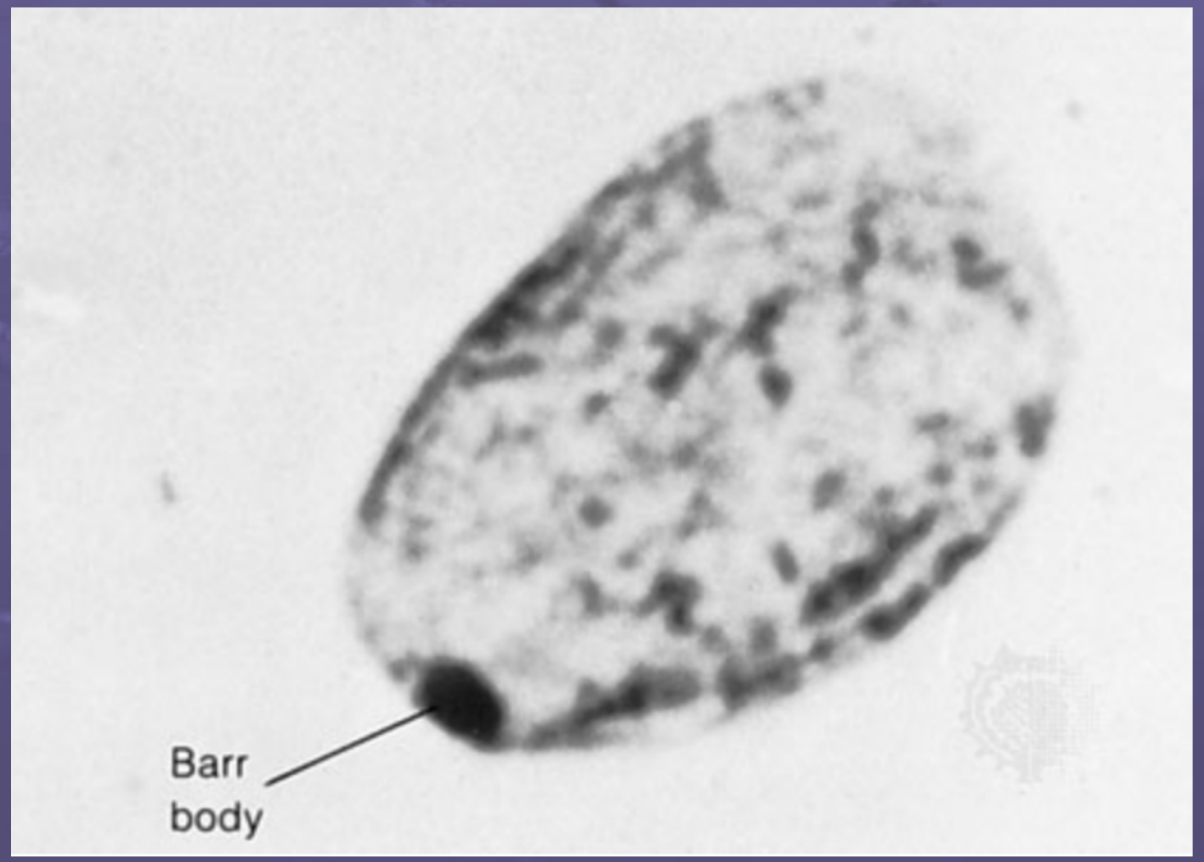
Facultative heterochromatin

- The regions of DNA packaged in facultative heterochromatin will not be consistent between the cell types within a species, and thus a sequence in one cell that is packaged in facultative heterochromatin (and the genes within are poorly expressed) may be packaged in euchromatin in another cell (and the genes within are no longer silenced)

Barr body

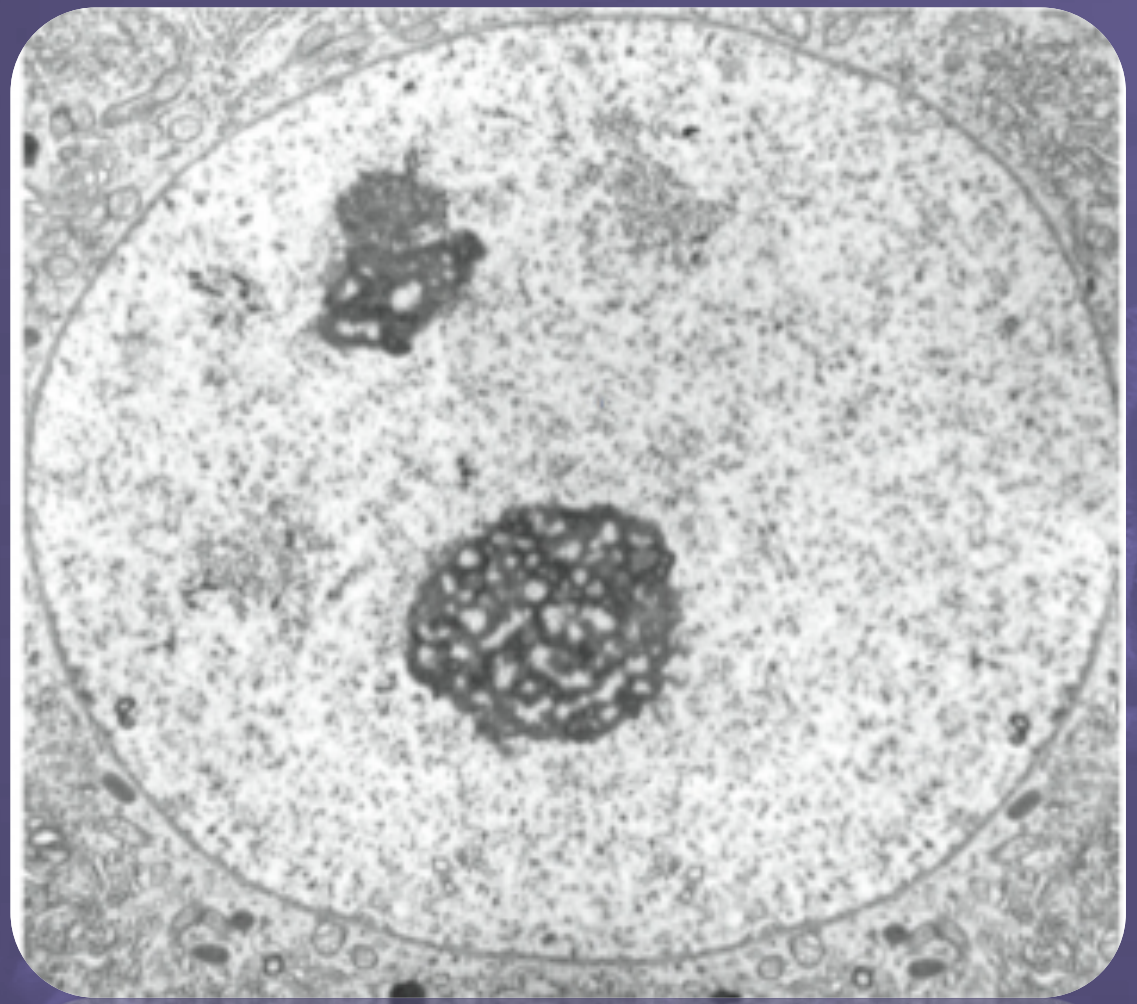
- One of female X chromosome repressed in the interphase nucleus and exist only in the tightly packed heterochromatic form

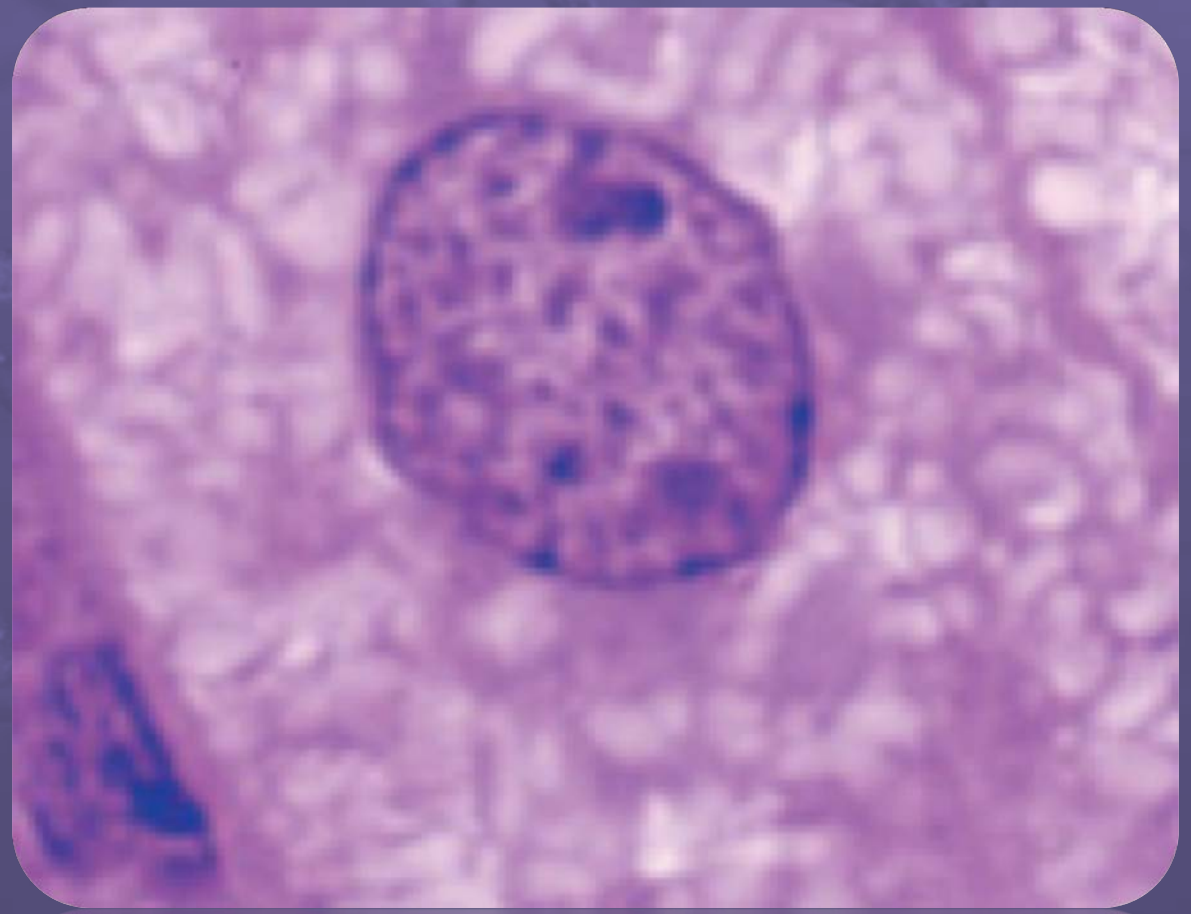




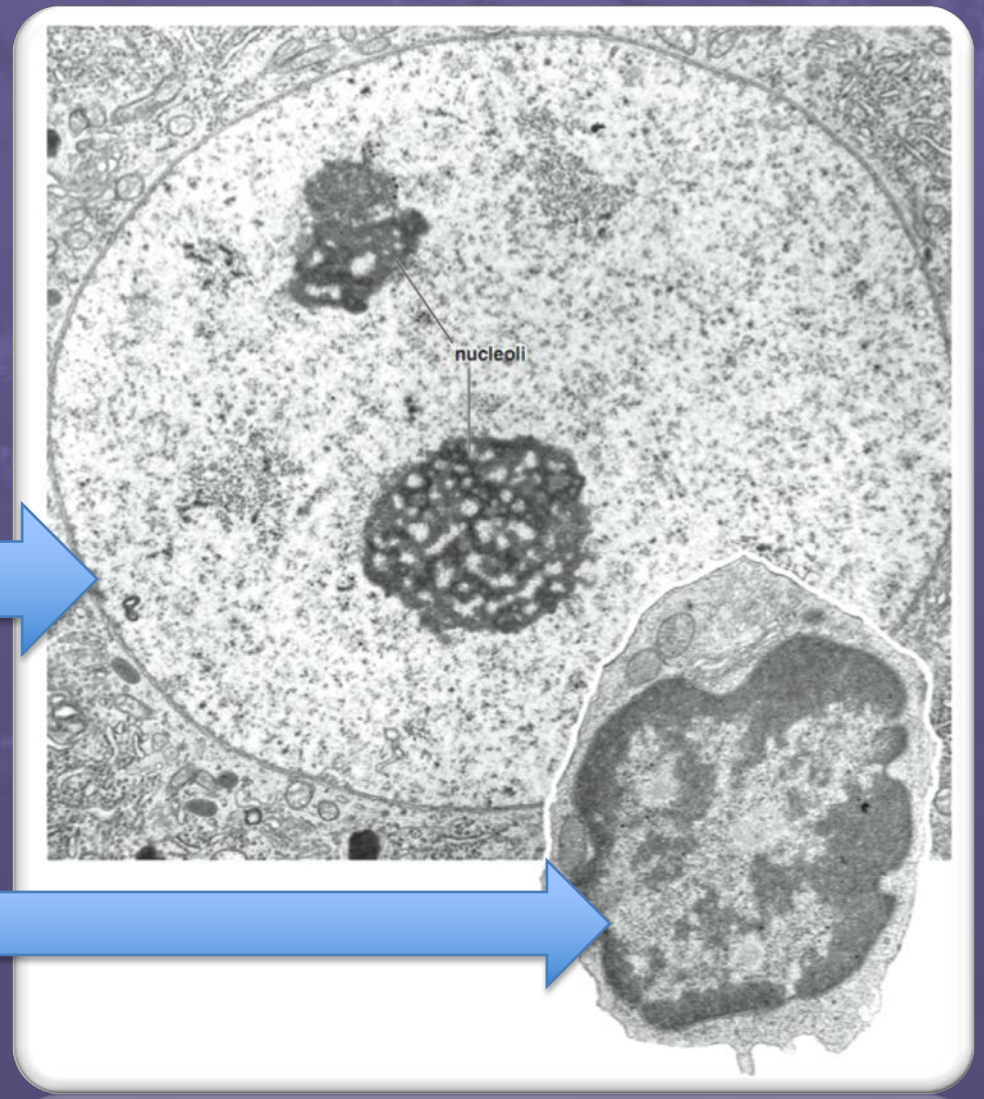
http://media-2.web.britannica.com/eb-media/47/59347-004-CFF810FF.jpg

Euchromatin indicates active chromatin—that is, chromatin that is stretched out so that the genetic information in the DNA can be read and transcribed. It is prominent in metabolically active cells such as neurons and liver cells.



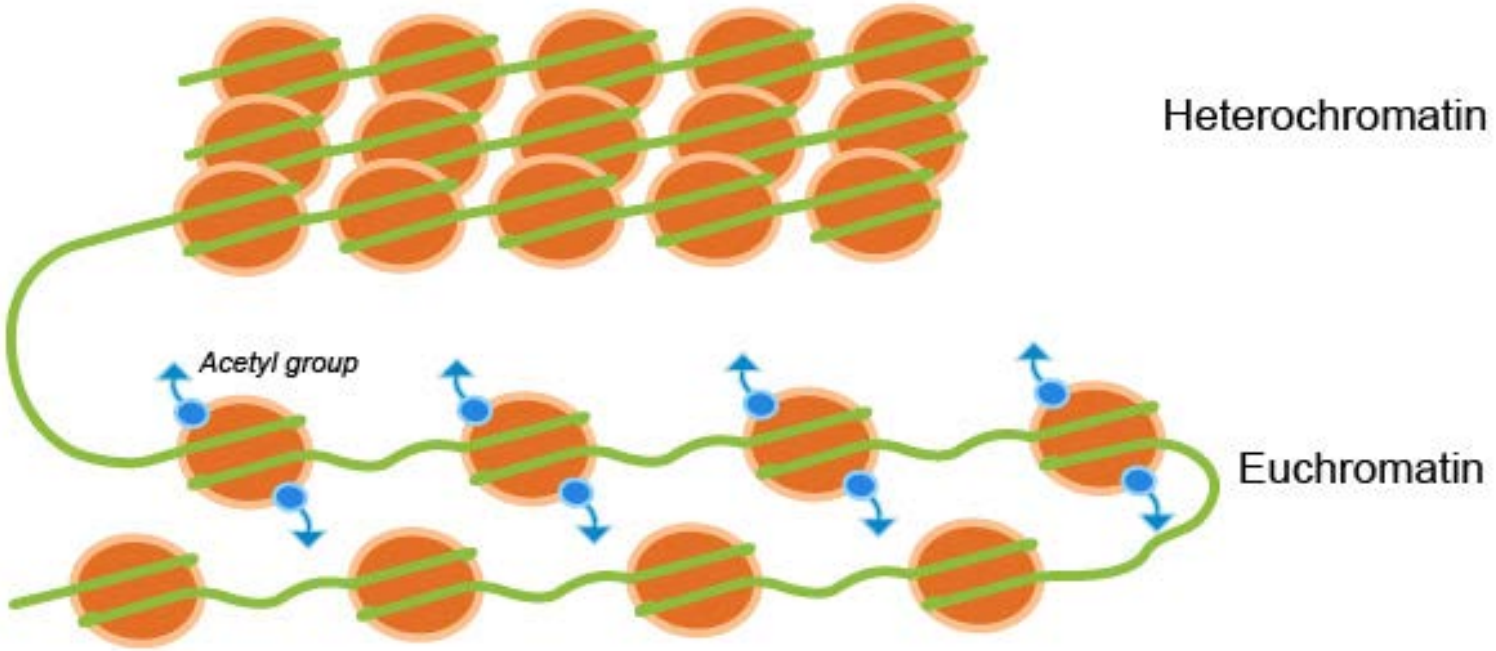


- Heterochromatin predominates in metabolically inactive cells such as small circulating lymphocytes and sperm or in cells that produce one major product such as plasma cells.
- The euchromatin/ heterochromatin ratio is higher in malignant cells than in normal cells.



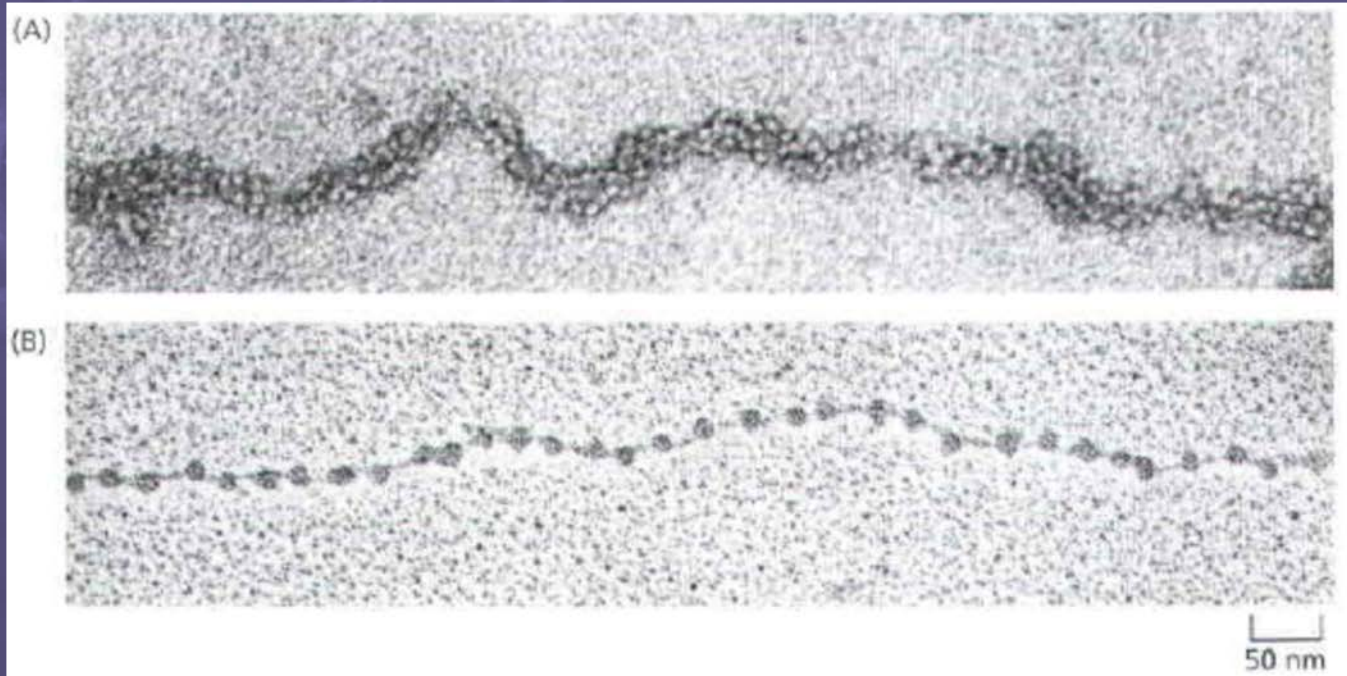
Euchromatin	Heterochromatin
Lightly staining regions	Darkly staining
Less tightly packed chromatin fibers therefore non condensed	Tightly packed chromatin fibers therefore condensed
Not visible – light microscope, undergo regular changes in morphology with cell division	Visible, remain highly condensed in all stages
Genetically active regions	Genetically inactive regions – either they lack genes/ contain genes that are not expressed
Replicates earlier during S phase	Replicates later during S phase
GC rich	AT rich

- https://www.slideshare.net/naveens50/nucleus-morphology-function



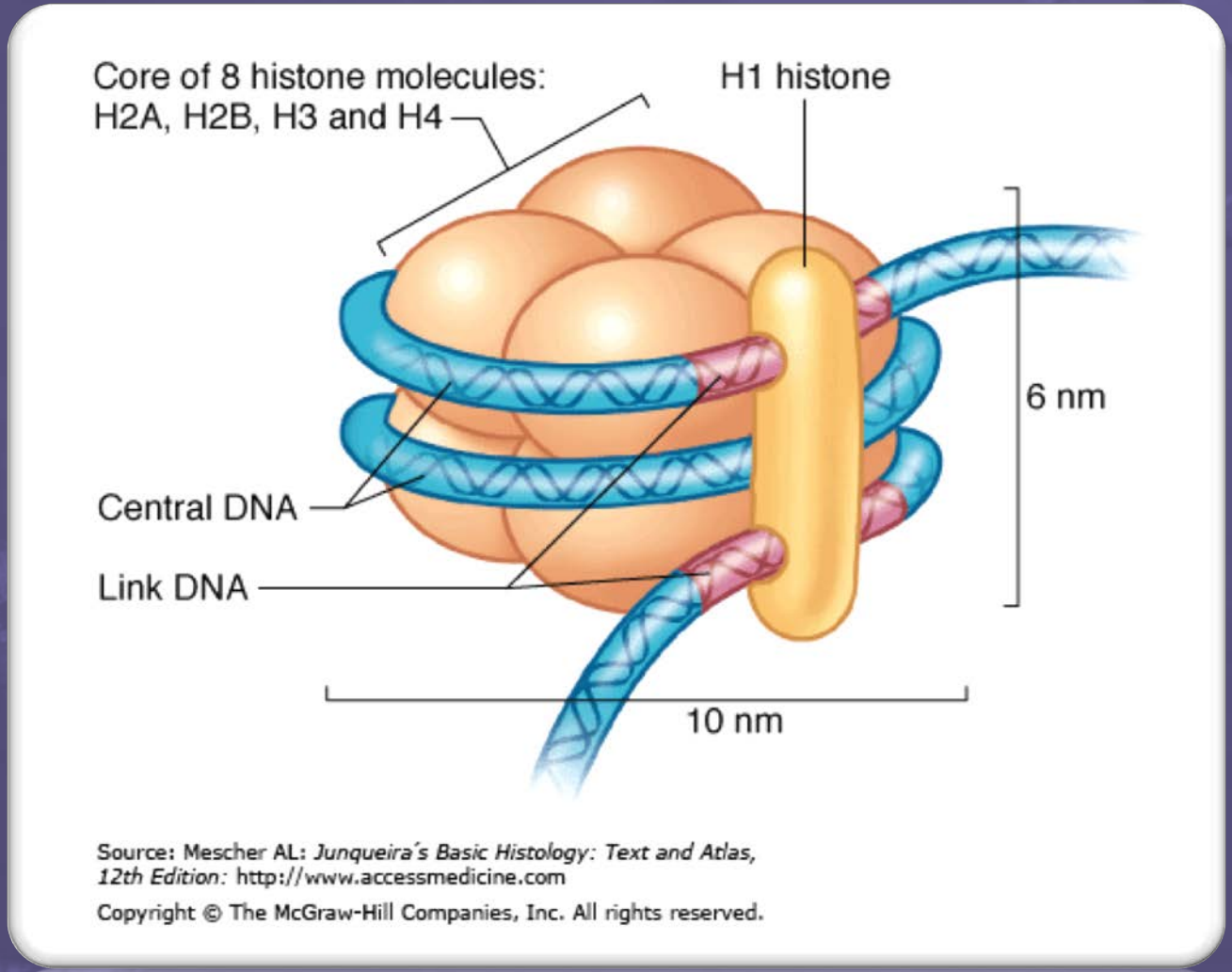
30 nm fiber (solenoid)

Nucleosomes
(beads on a string)



nucleosomes

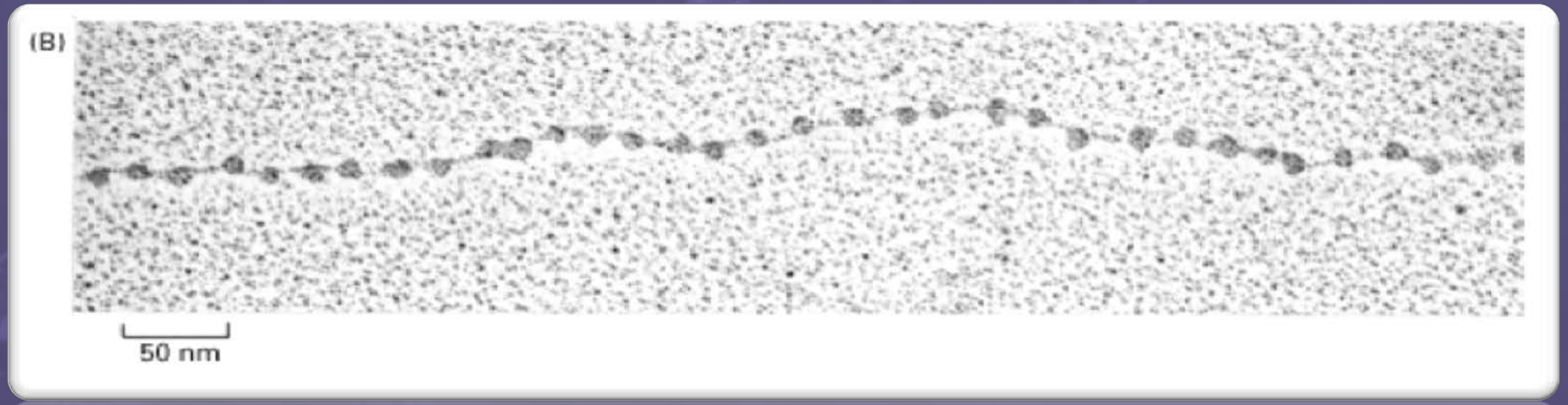
- **The smallest units of chromatin structure are macromolecular complexes of DNA and histones called nucleosomes.**



Source: Mescher AL: *Junqueira's Basic Histology: Text and Atlas, 12th Edition:* http://www.accessmedicine.com

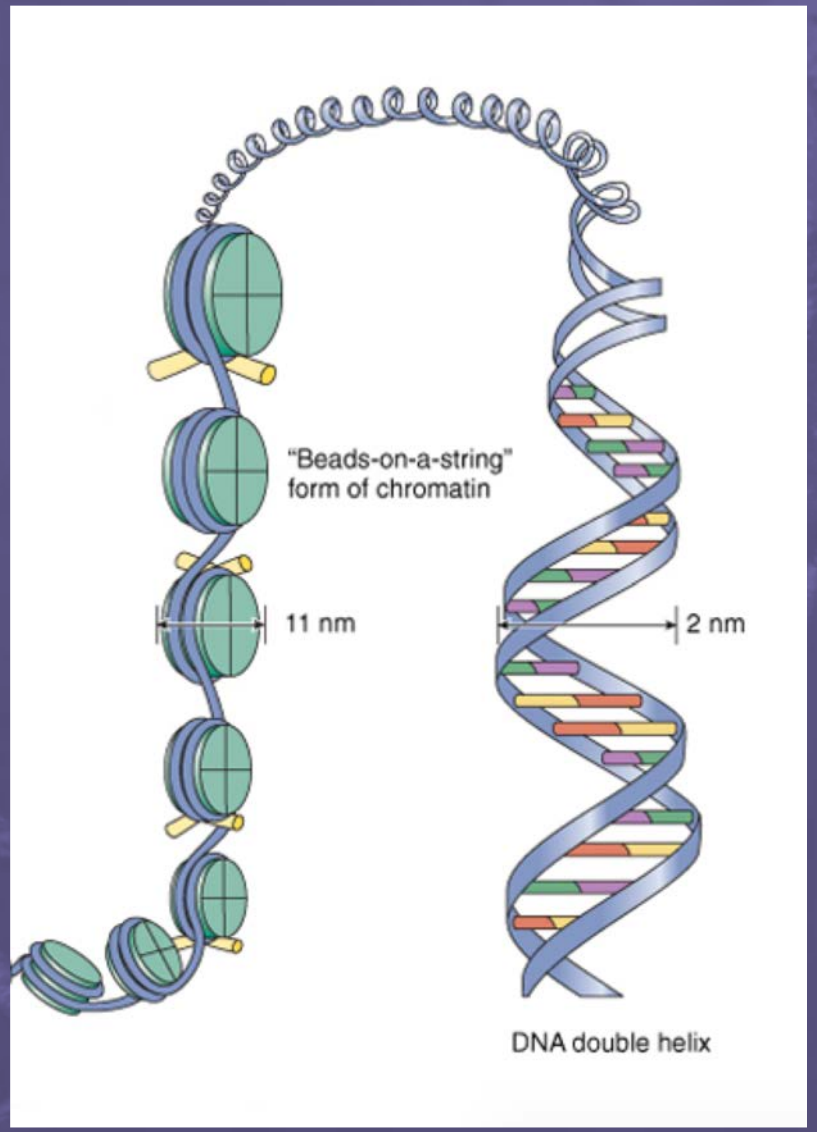
nucleosomes

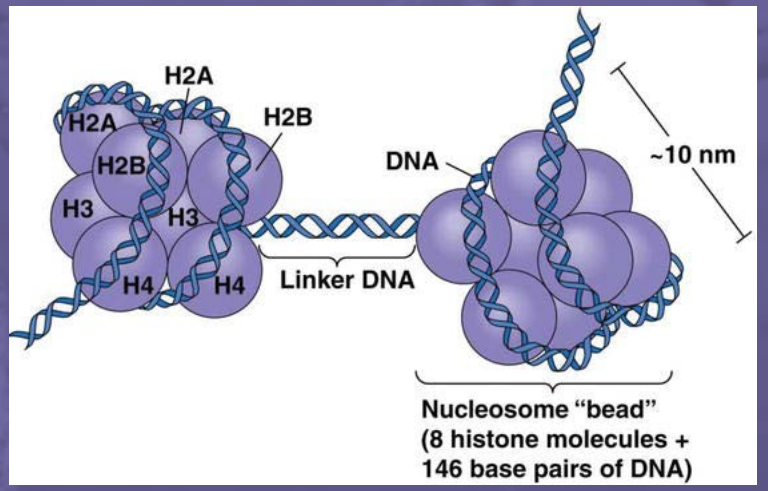
- represent the first level of chromatin folding and are formed by the coiling of the DNA molecule around a protein core
- The core of the nucleosome consists of eight histone molecules (called an octamer).
- Two loops of DNA (approximately 146 nucleotide pairs) are wrapped around the core octomer.
- When chromatin is extracted from the nucleus, the nucleosomal substructure of chromatin is visible in transmission electron microscopy (TEM) and is often described as “beads on a string”

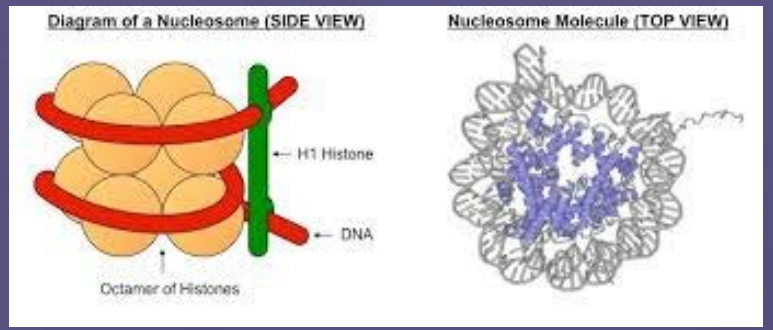


nucleosomes

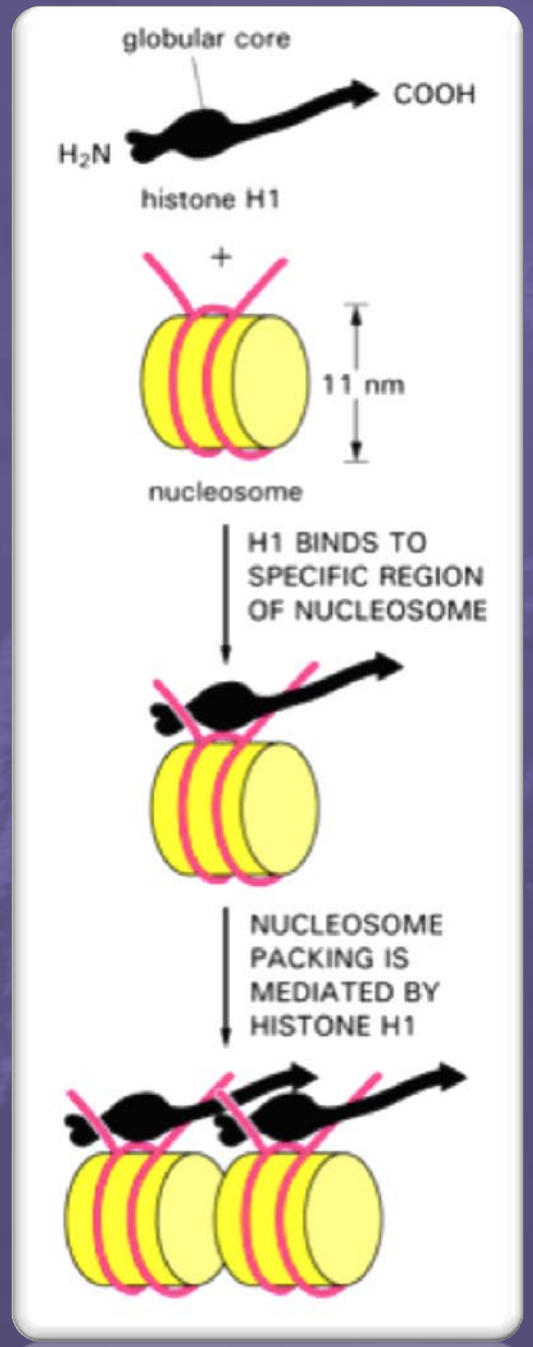
- diameter - 11-nm
- This step shortens the DNA molecule by approximately sevenfold relative to the unfolded DNA molecule.
- The DNA extends between each particle as a 2-nm filament that joins adjacent nucleosomes.





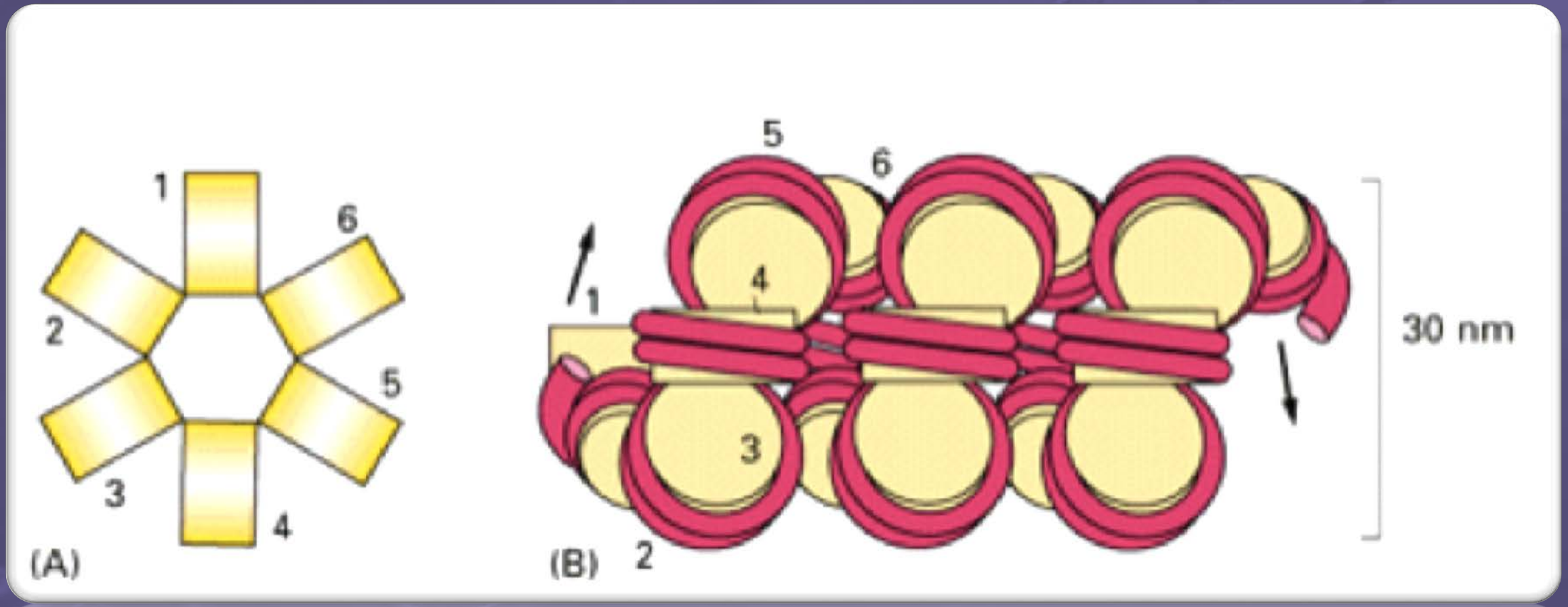


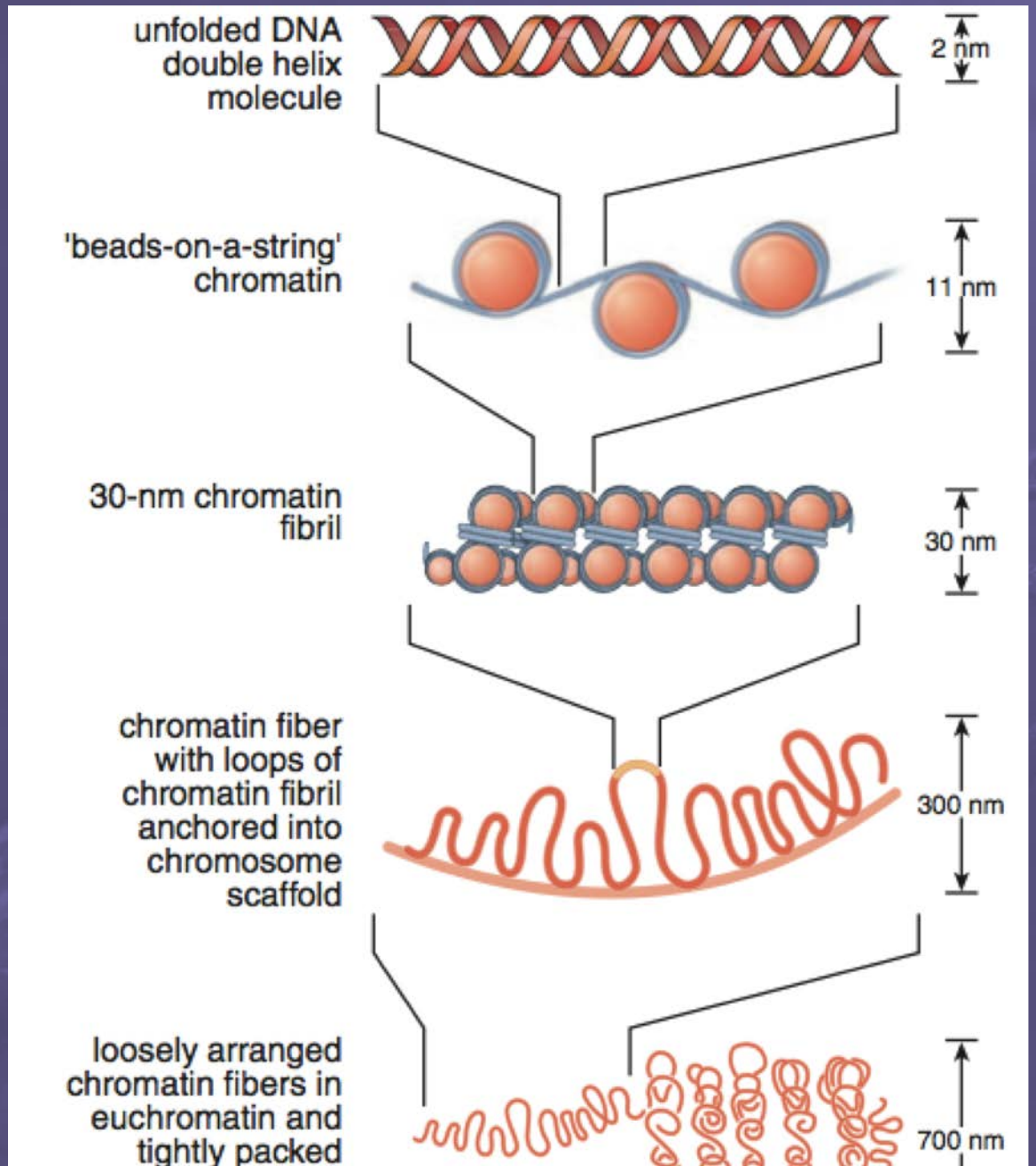
histone H1 is help pack adjacent nucleosomes together



30-nm chromatin fibril

- six nucleosomes form one turn in the coil of the chromatin fibril
- 40-fold shorter than unfolded DNA

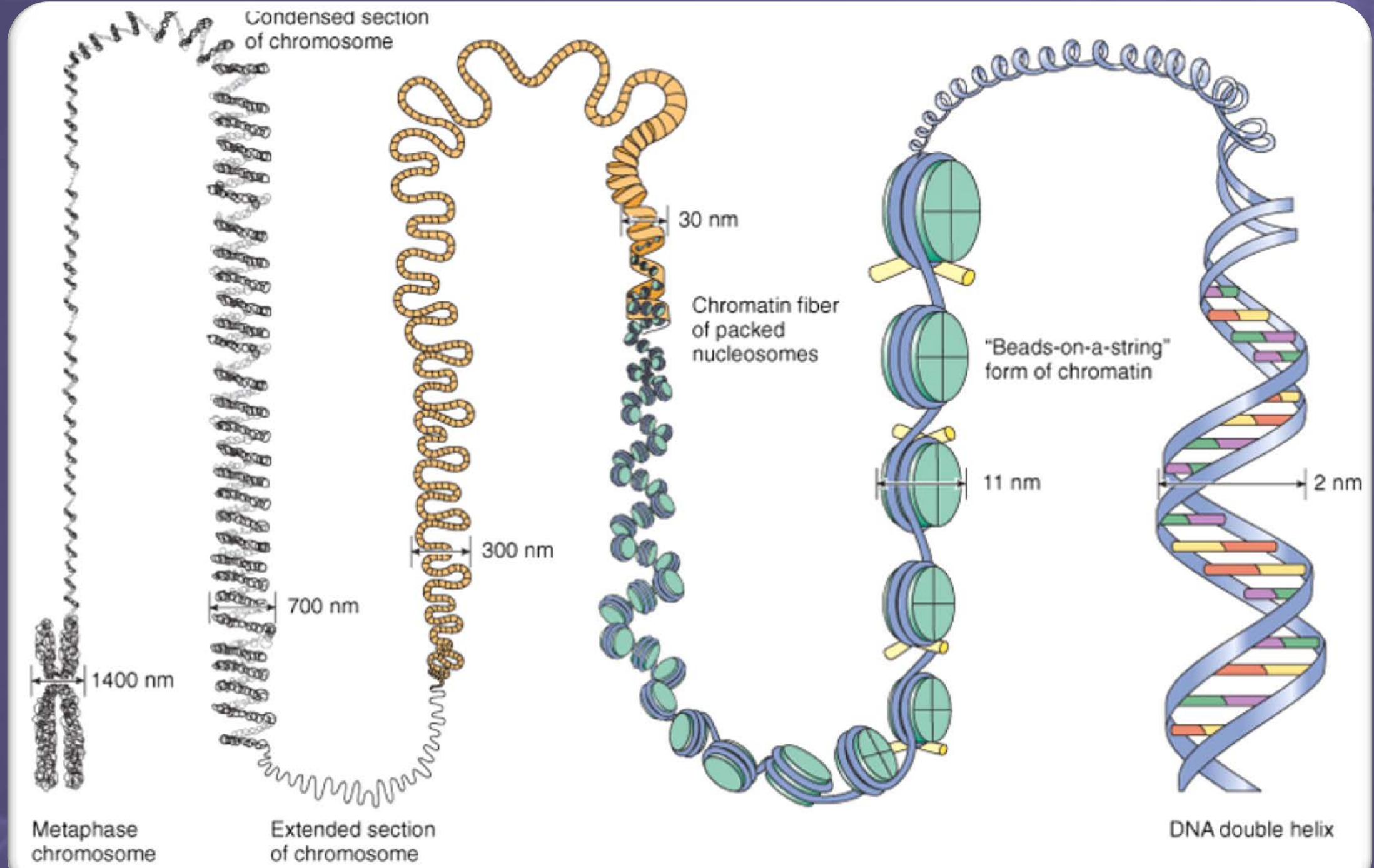




From DNA to chromatin.

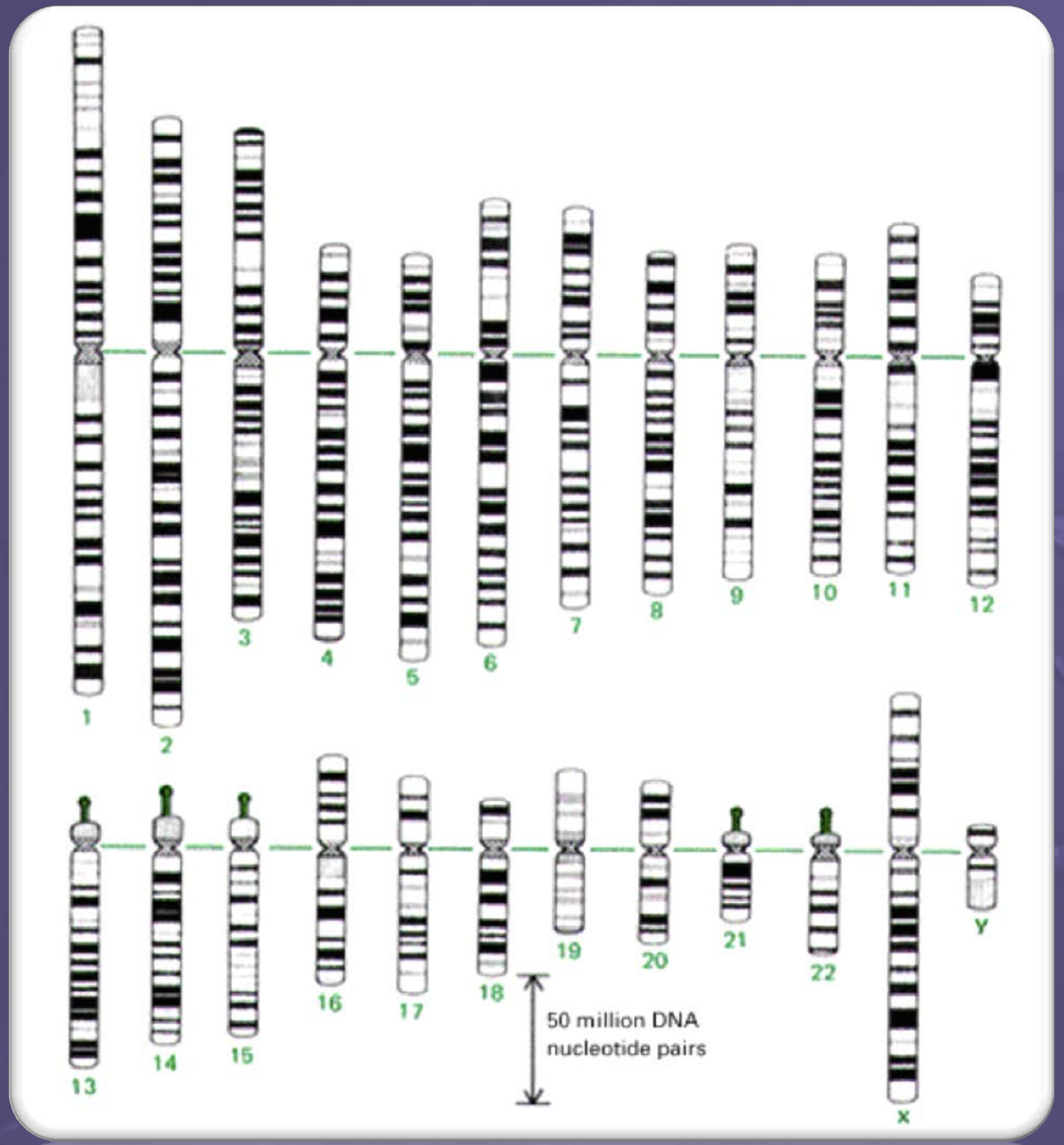
During cell division, chromatin fibers formed from chromatin loop domains attached to a flexible protein scaffold undergo condensation to form chromosomes
Each chromosome is formed by two chromatids that are joined together at a point called the centromere.

1. DNA Wrapping



karyotype

- Karyotype refers to the number and morphology of chromosomes and is characteristic for each species.
- **In a karyotype, chromosome pairs are sorted according to their size, shape, or emitted fluorescent color.**
- In the past, chromosomes were routinely stained with Giemsa stain; however, with the recent development of in situ hybridization techniques, the fluorescent in situ hybridization (FISH) procedure is now more often used to visualize a chromosomal spread.


1
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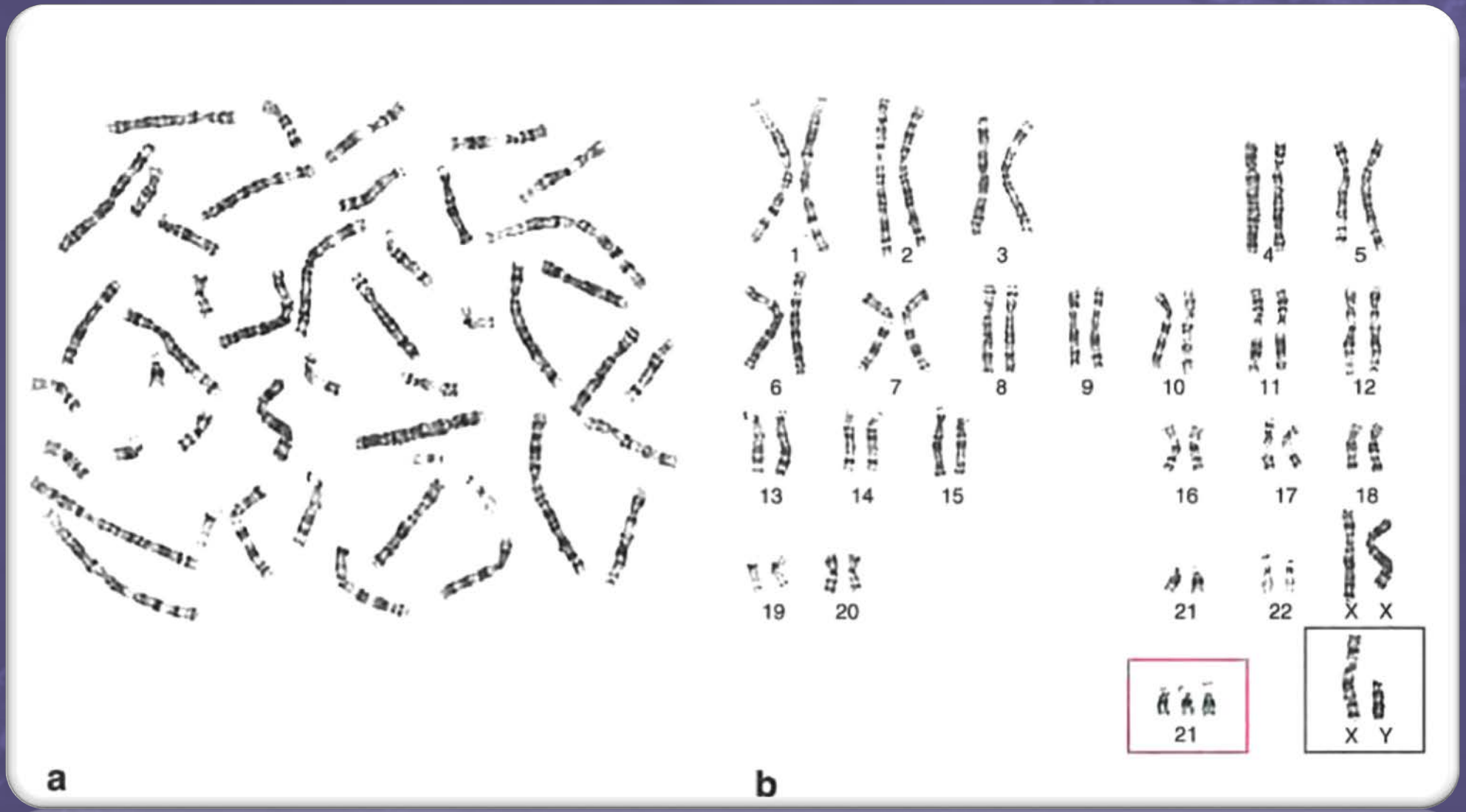
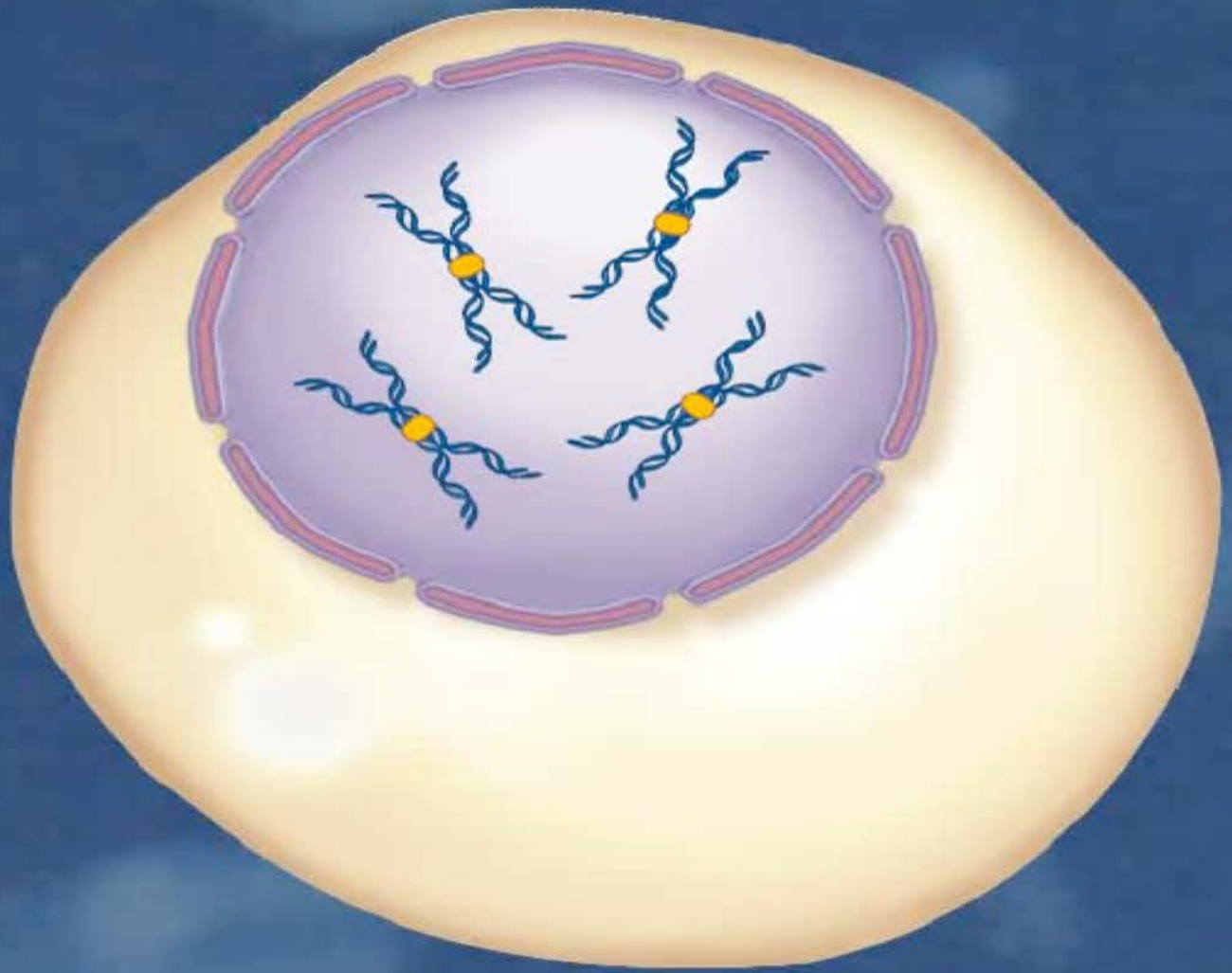
11
12
13
14
15
16
17
18
19
20
21
22
X
Y
50 million DNA
nucleotide pairs

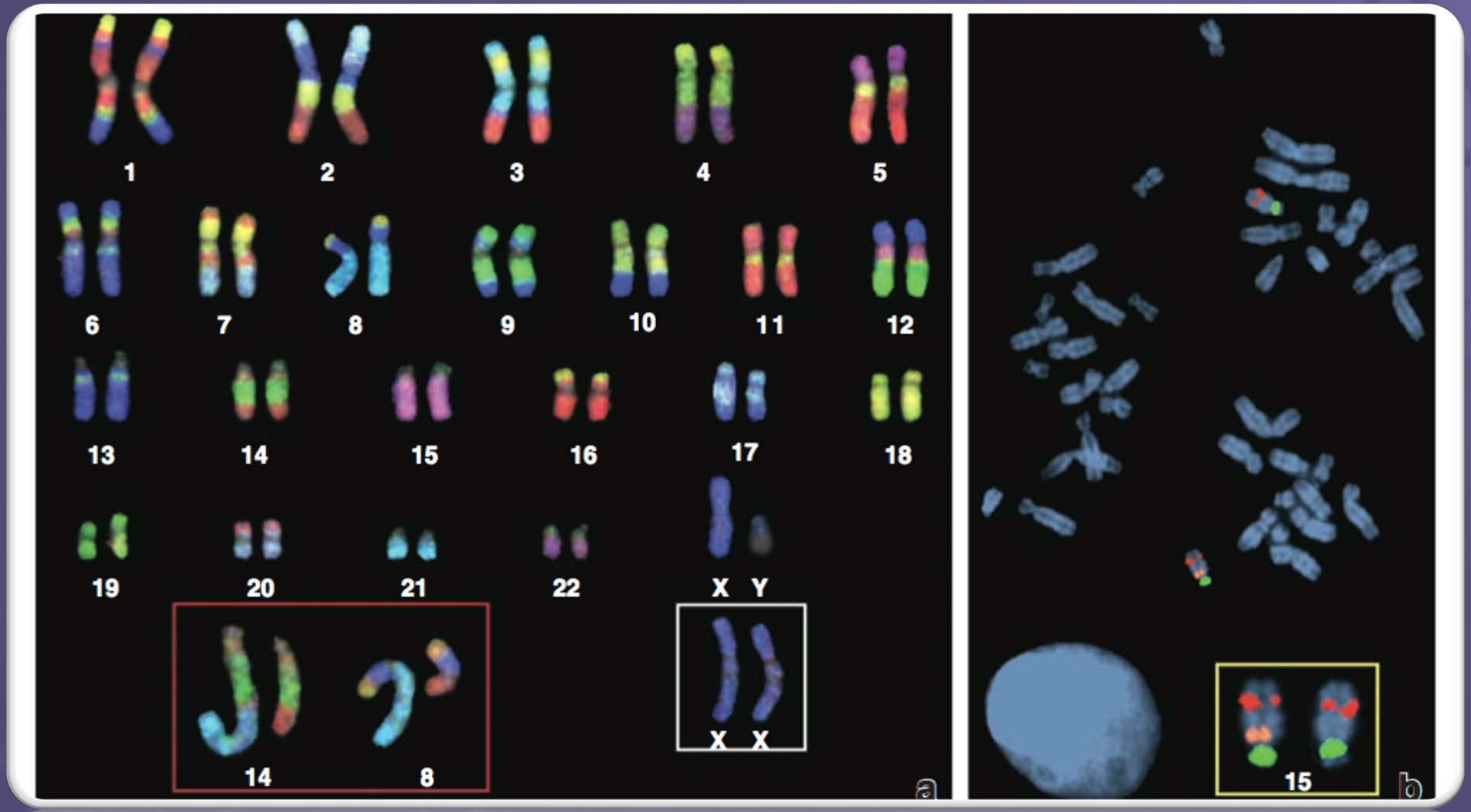
Examination of chromosomes.

a. Metaphase spread.

b. Karyotype of a normal female.



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21
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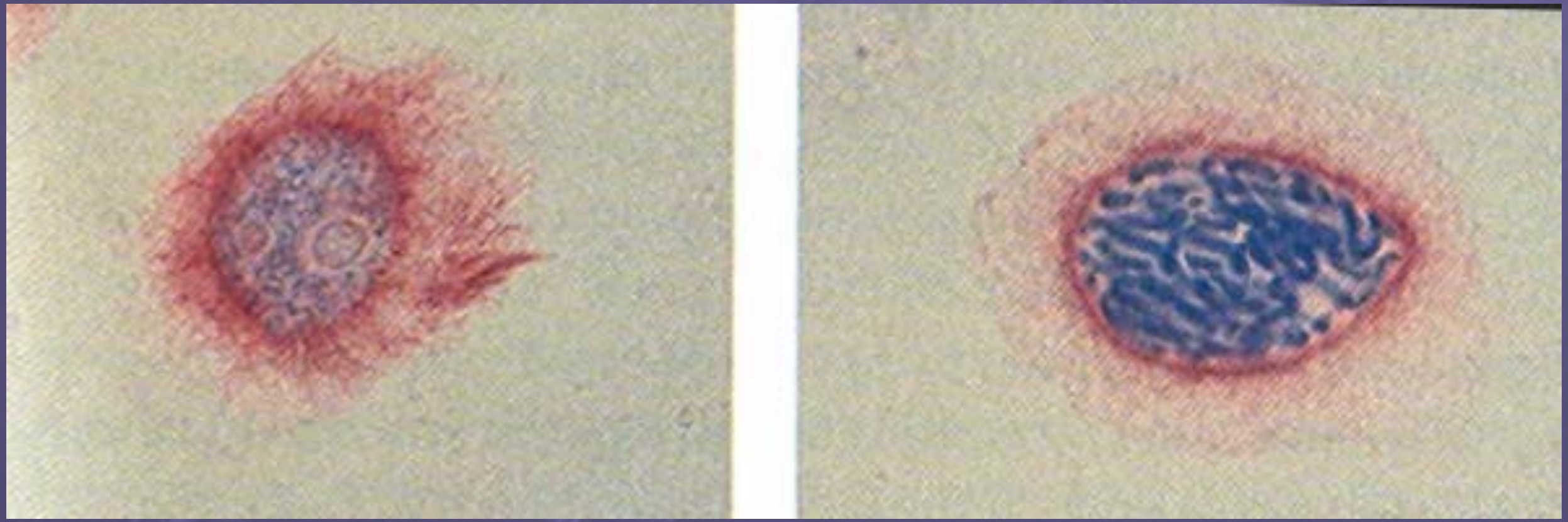
X Y
14
8
X X
a
15
b

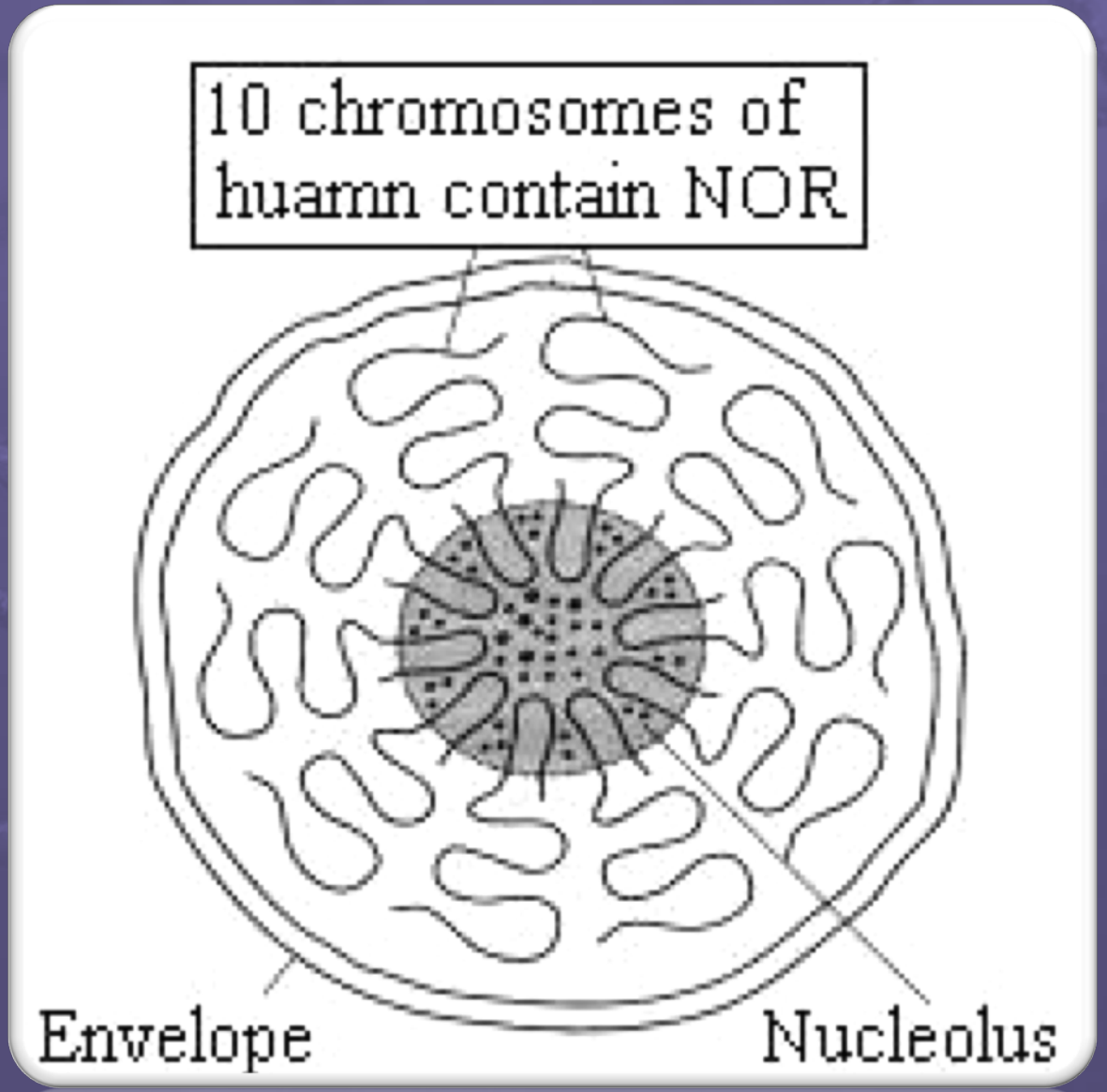
Nucleolus is disassembled during prophase of cell division



nucleolus

The nucleolus has three morphologically distinct regions:

- **nucleolar organizing regions (NOR)** is composed of tandem repeats of rRNA genes, which can be found in several different chromosomes. The human genome, contains more than 200 clustered copies of the rRNA genes on five different pair of chromosomes (13, 14, 15, 21, 22)
- **Fibrillar material** (pars fibrosa) contain ribosomal genes that are actively undergoing transcription and large amounts of rRNA.
- Granular material (pars granulosa) represents the site of initial ribosomal assembly and contains densely packed preribosomal particles.



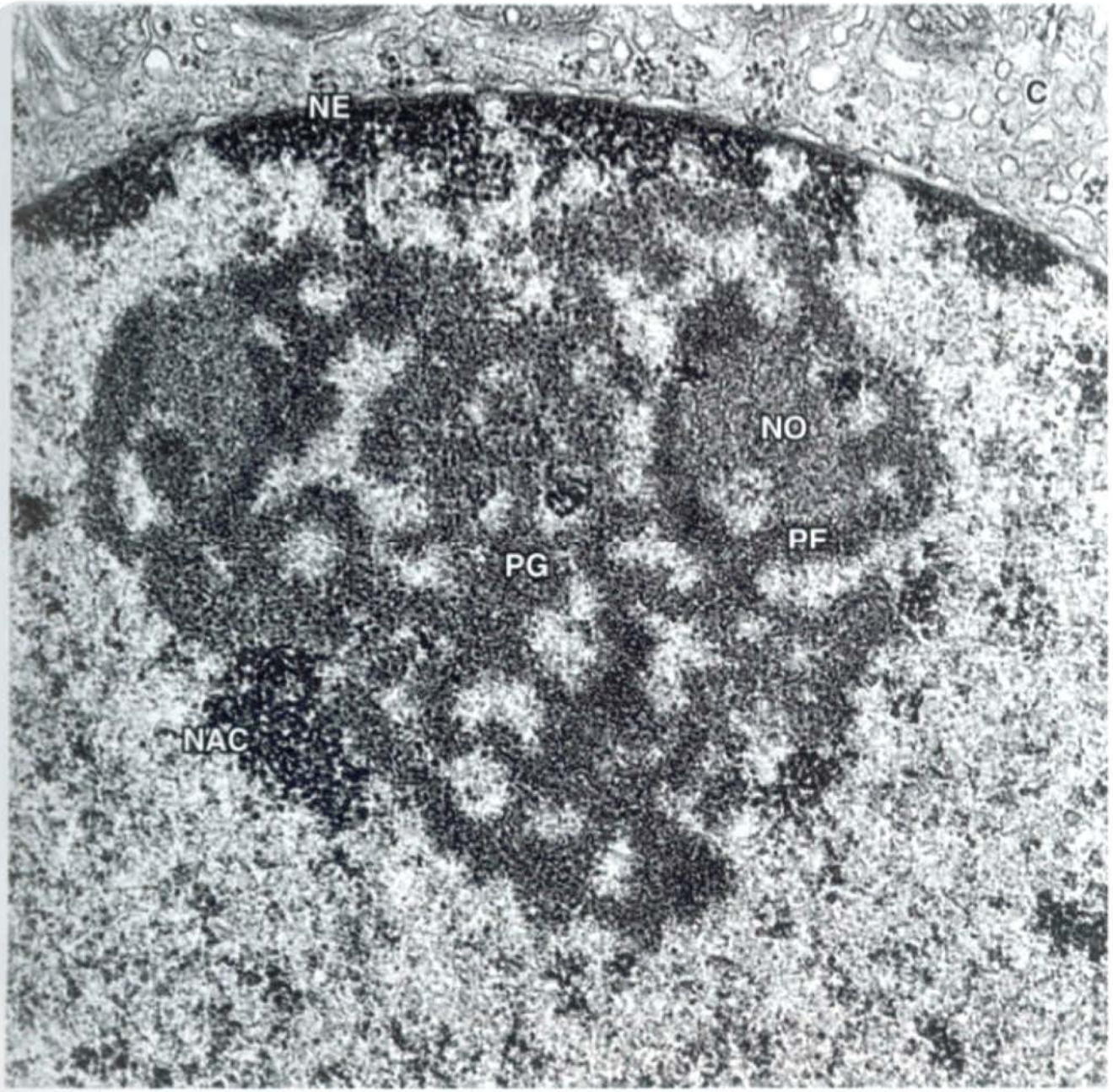
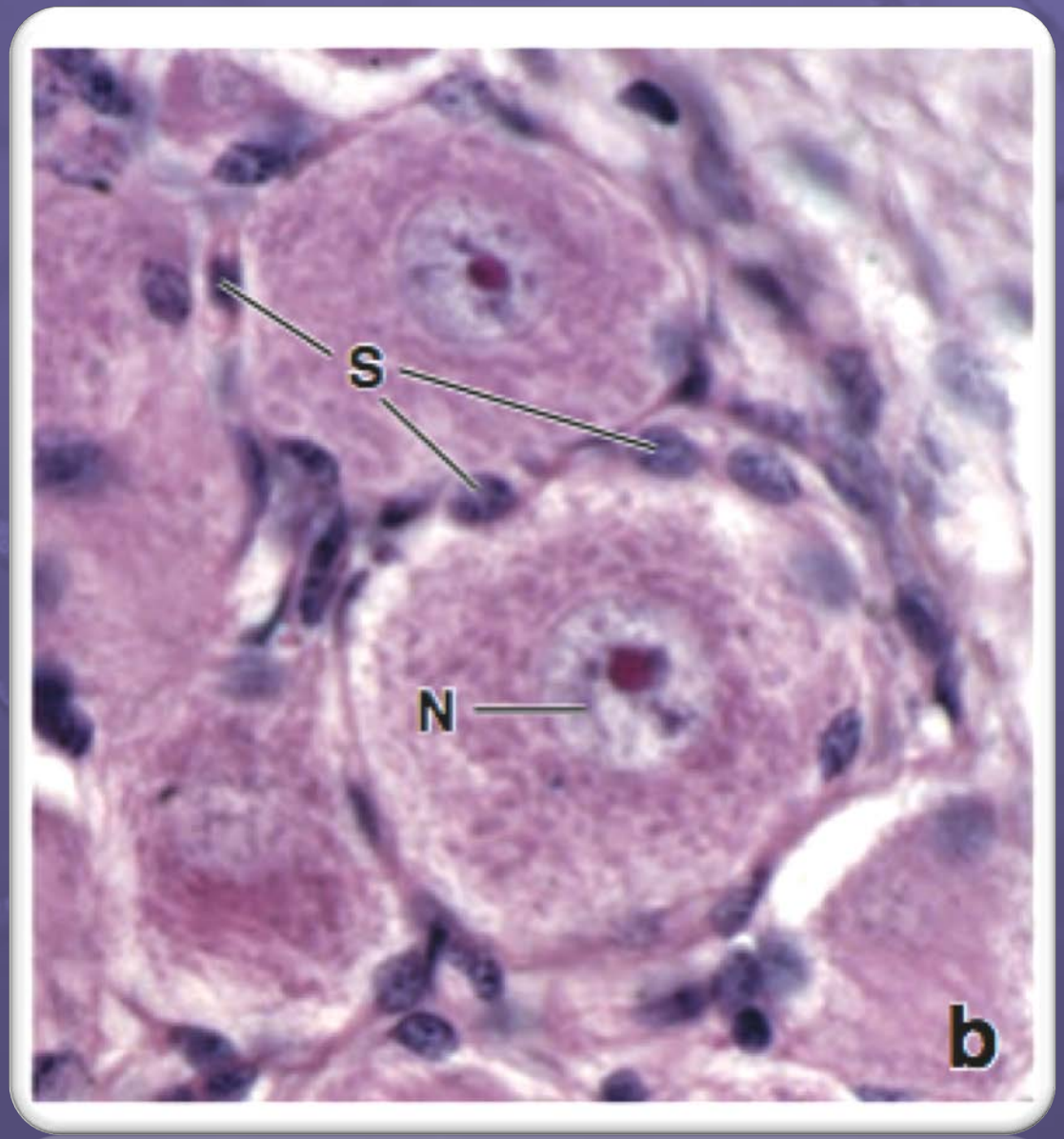


Figure 3–8. Nucleolus in a human adrenocortical cell. The nucleolar organizer DNA (NO), pars fibrosa (PF), pars granulosa (PG), nucleolus-associated chromatin (NAC), nuclear envelope (NE), and cytoplasm (C) are shown.

- **The nucleolus stains intensely with hematoxylin and basic dyes and metachromatically with thionine dyes.**
- The nucleolus varies in size but is particularly well developed in cells active in protein synthesis. Some cells contain more than one nucleolus.

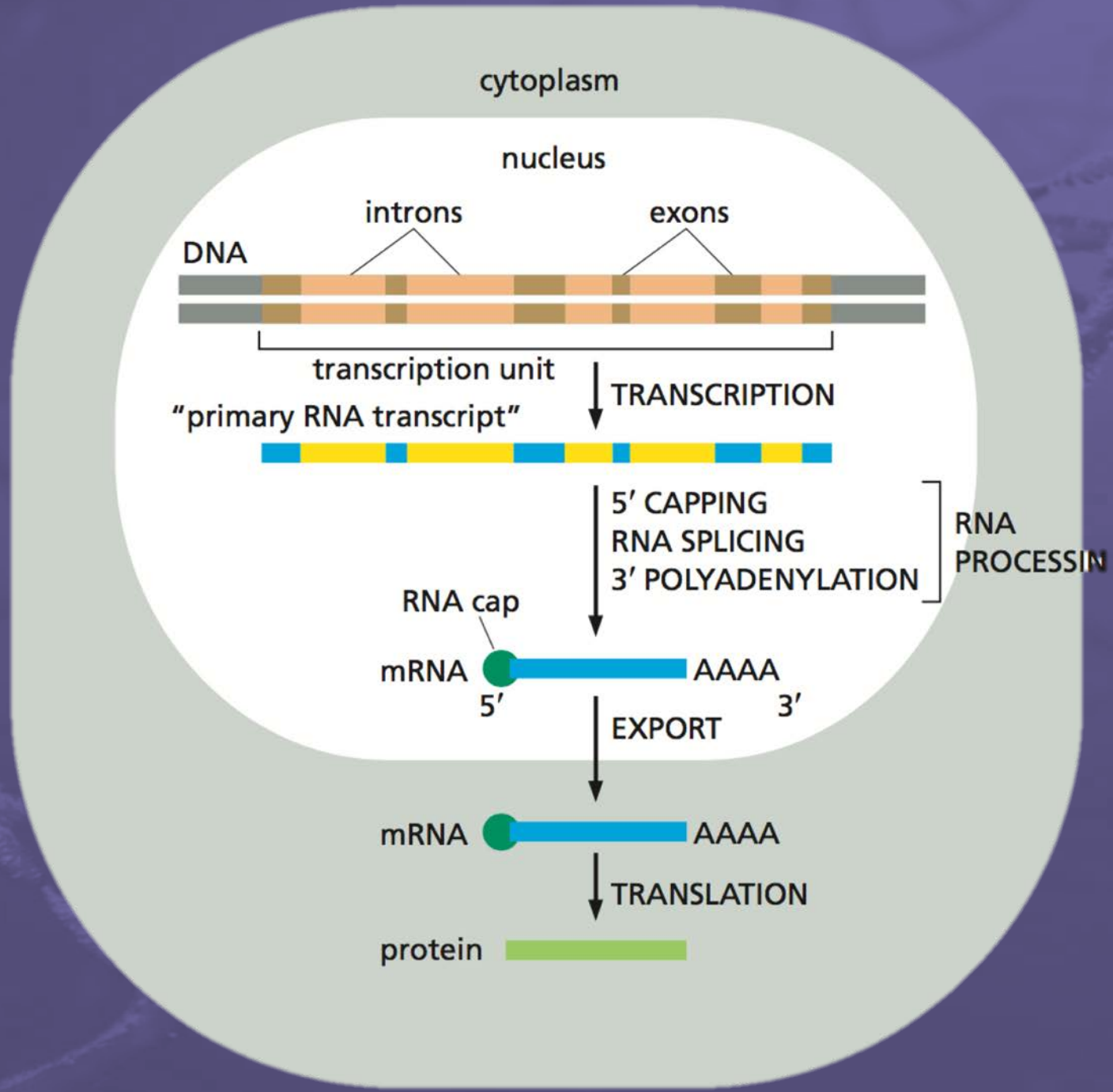


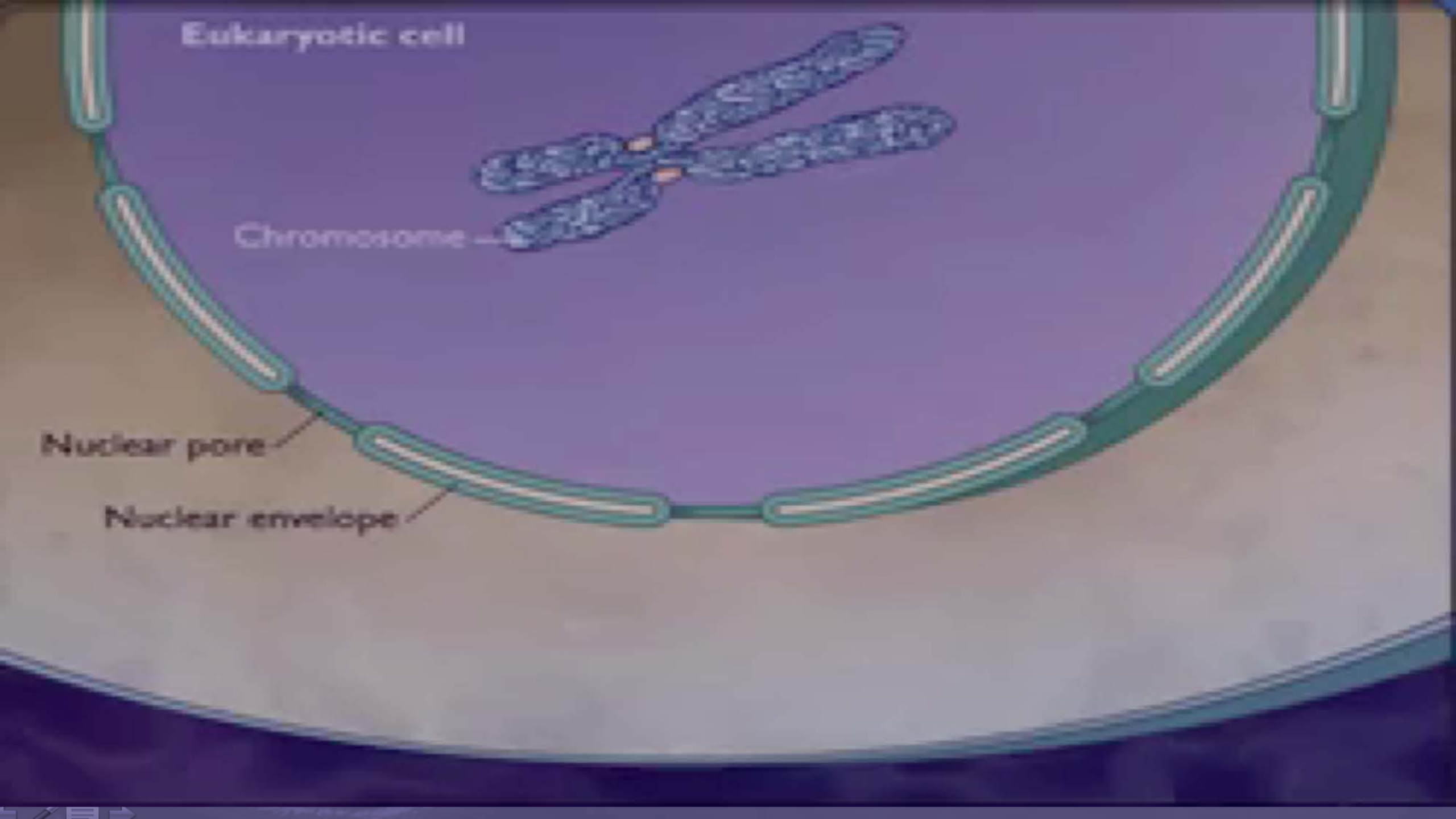
Nucleolus - summary

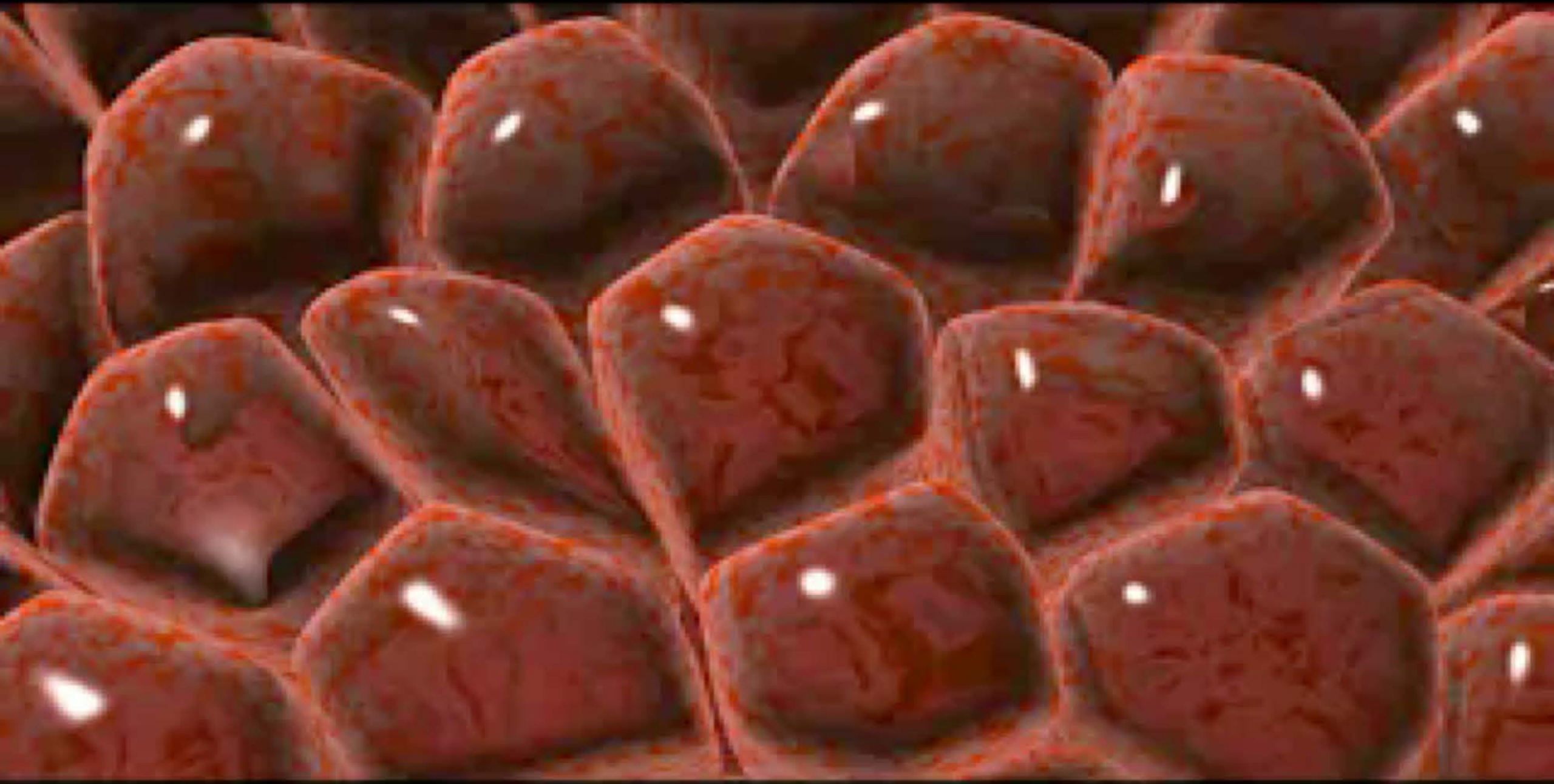
- **The nucleolus is the site of ribosomal RNA (rRNA) synthesis and initial ribosomal assembly.**
- The nucleolus is a nonmembranous region of the nucleus that surrounds transcriptionally active rRNA genes.

Control of Gene Expression

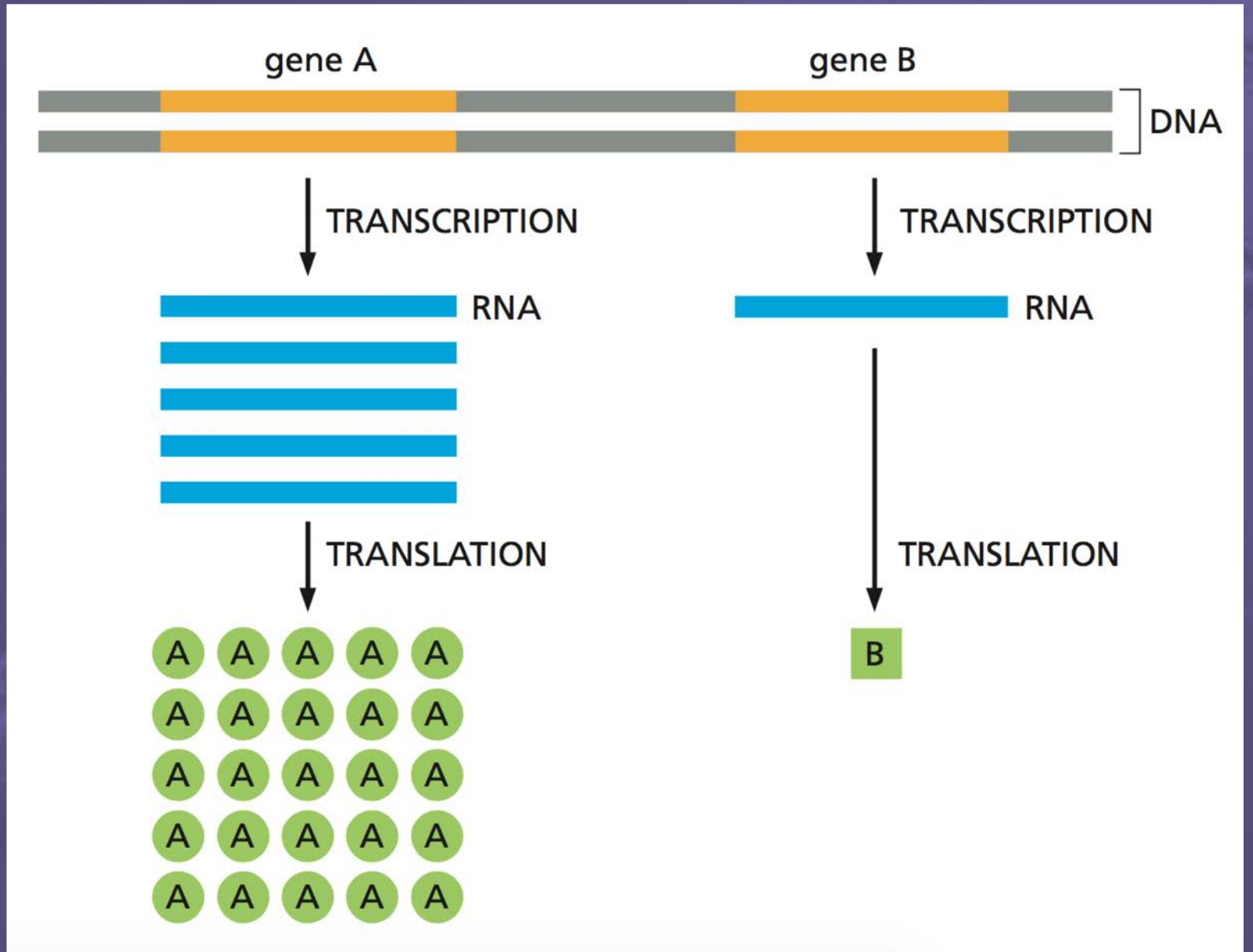
Summary of the steps leading from gene to protein in eucaryotes

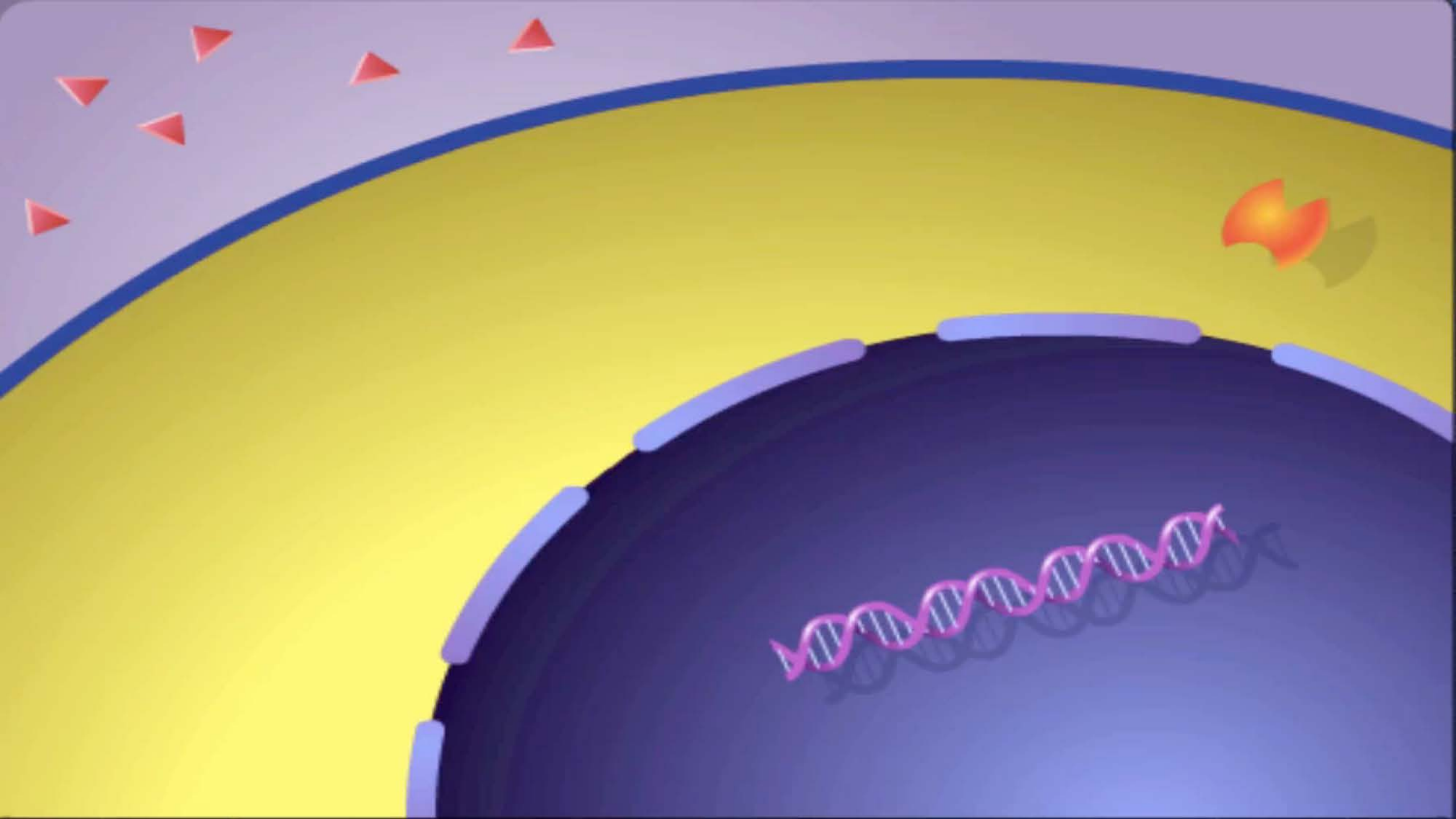



Eukaryotic cell
Chromosome
Nuclear pore
Nuclear envelope

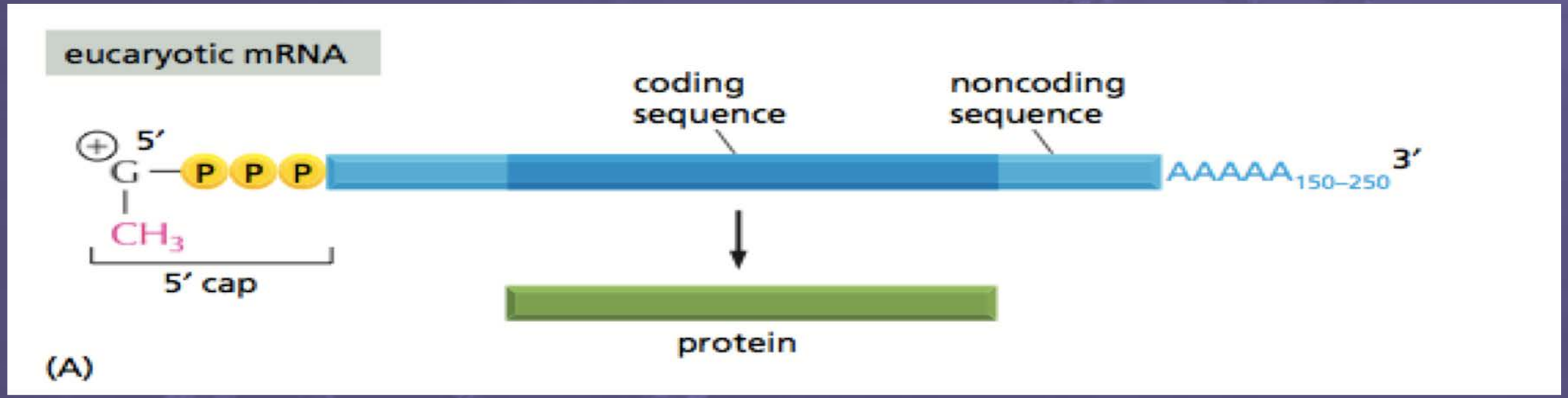


Genes can be expressed with different efficiencies.

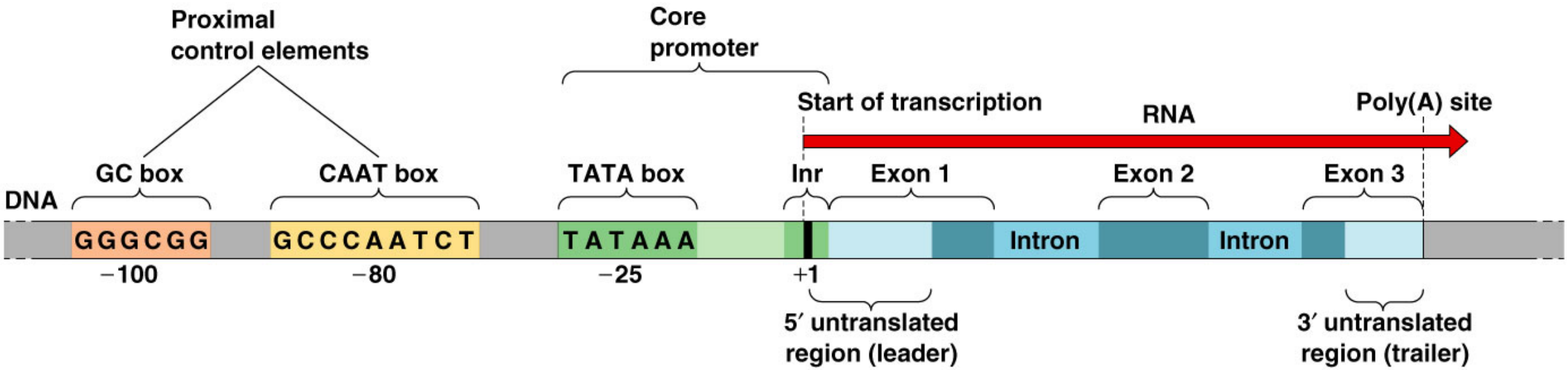




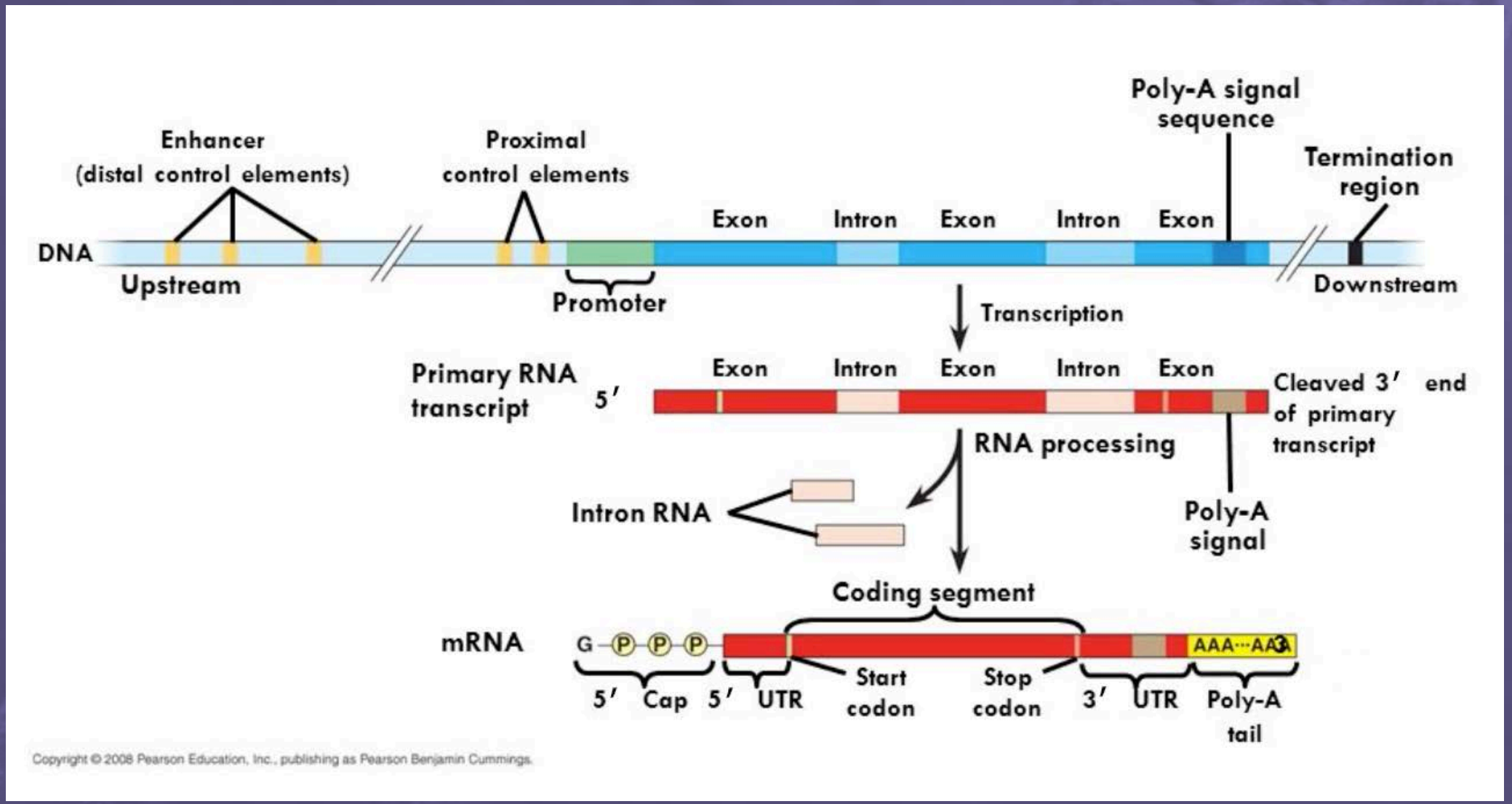
structure of mature eucaryotic mRNA molecules



Structure of eukaryotic Gene



Structure of eukaryotic Gene



- To initiate transcription, RNA polimerase requires the assistance of transcription factors
- **General transcription factors** are essential for transcription of **all** genes

Initiation of transcription of a eukaryotic gene by RNA polymerase II. To begin transcription, RNA polymerase requires several general transcription factors.

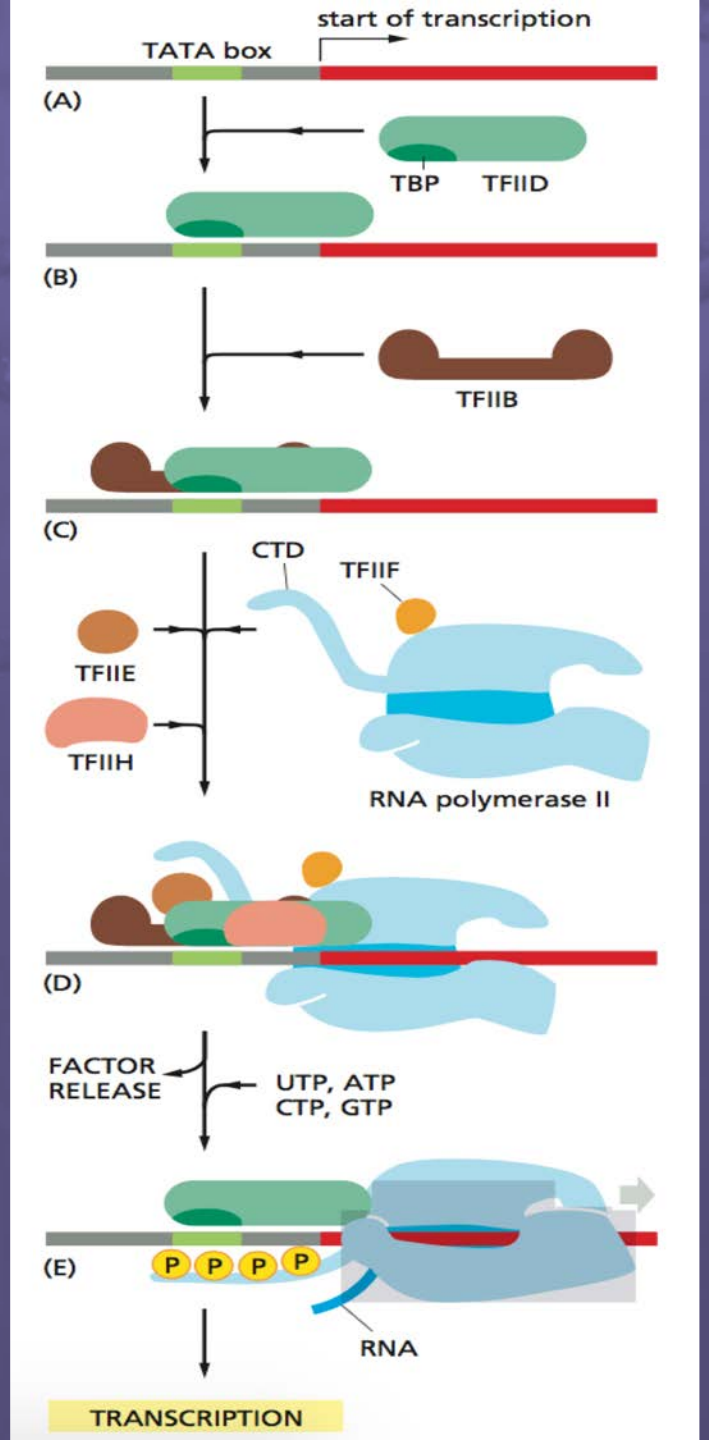
(A) The promoter contains a DNA sequence called the TATA box, which is located 25 nucleotides away from the site at which transcription is initiated.

(B) (B) Through its subunit TBP, TFIID recognizes and binds the TATA box, which then enables the adjacent binding of TFIIB

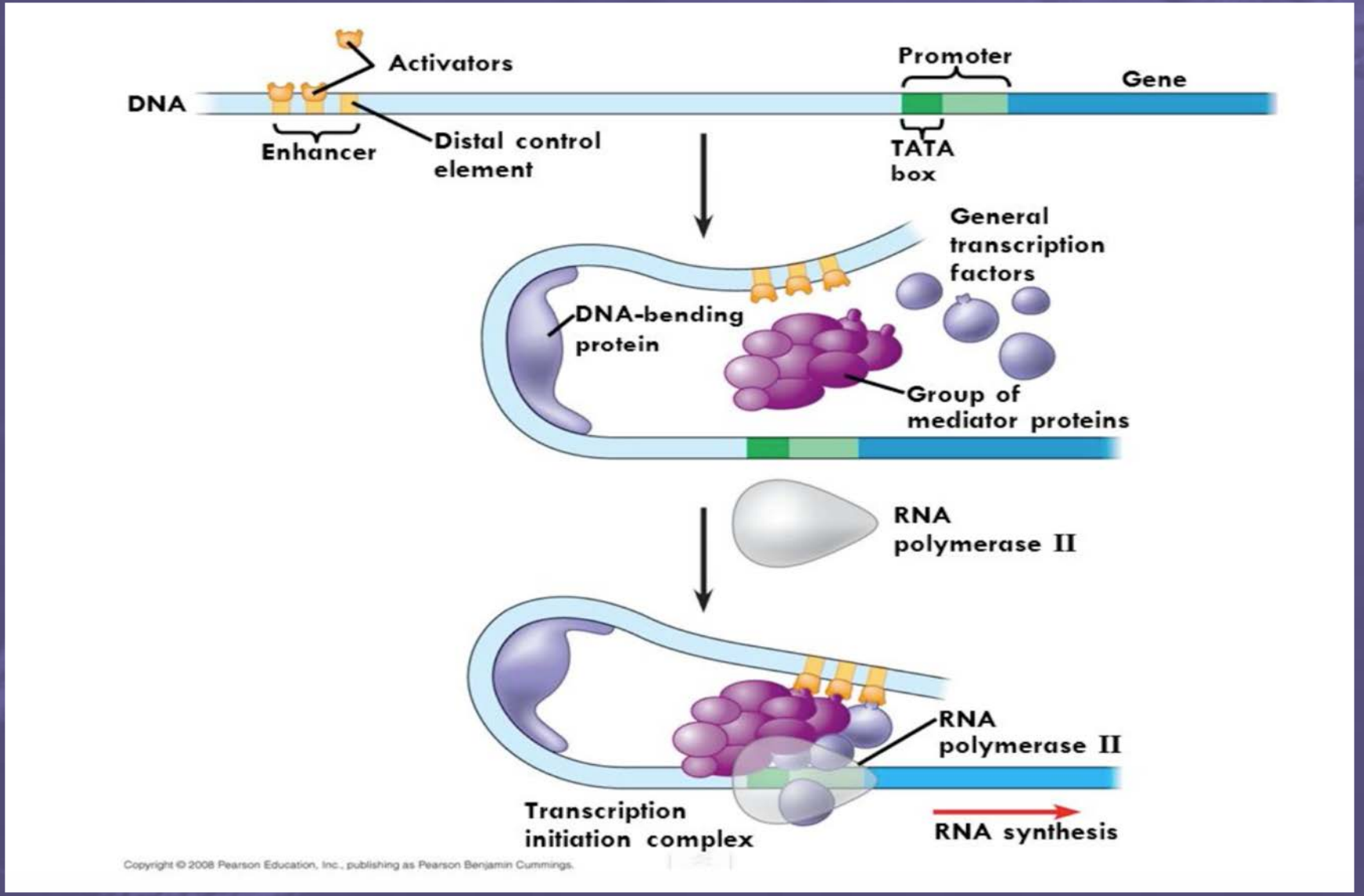
(C) For simplicity the DNA distortion produced by the binding of TFIID is not shown.

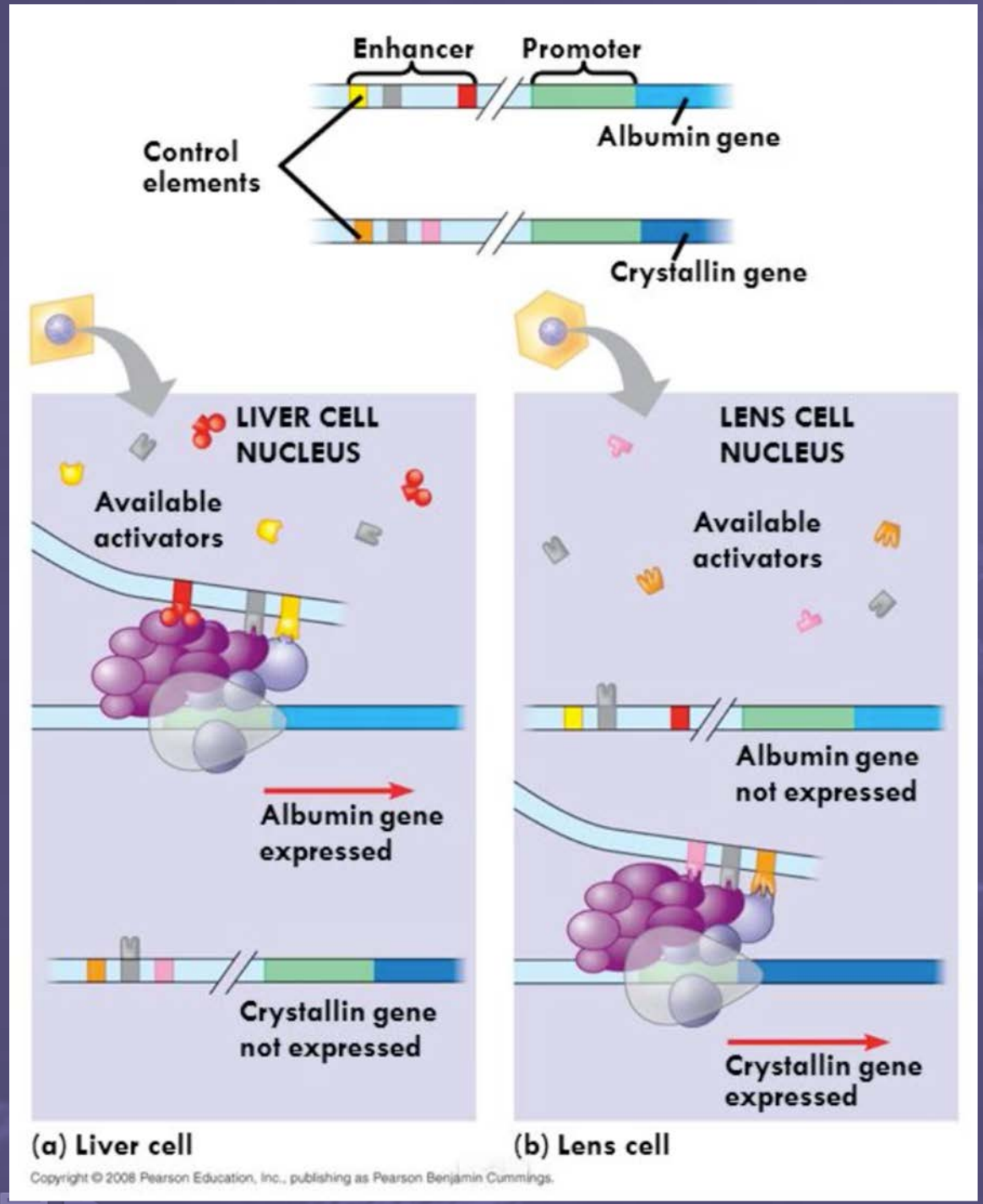
(D) The rest of the general transcription factors, as well as the RNA polymerase itself, assemble at the promoter.

(E) TFIIH then uses energy from ATP hydrolysis to pry apart the DNA double helix at the transcription start point, locally exposing the template strand. TFIIH also phosphorylates RNA polymerase II, changing its conformation so that the polymerase is released from the general factors and can begin the elongation phase of transcription. As shown, the site of phosphorylation is a long C-terminal polypeptide tail, also called the C-terminal domain (CTD), that extends from the polymerase molecule.

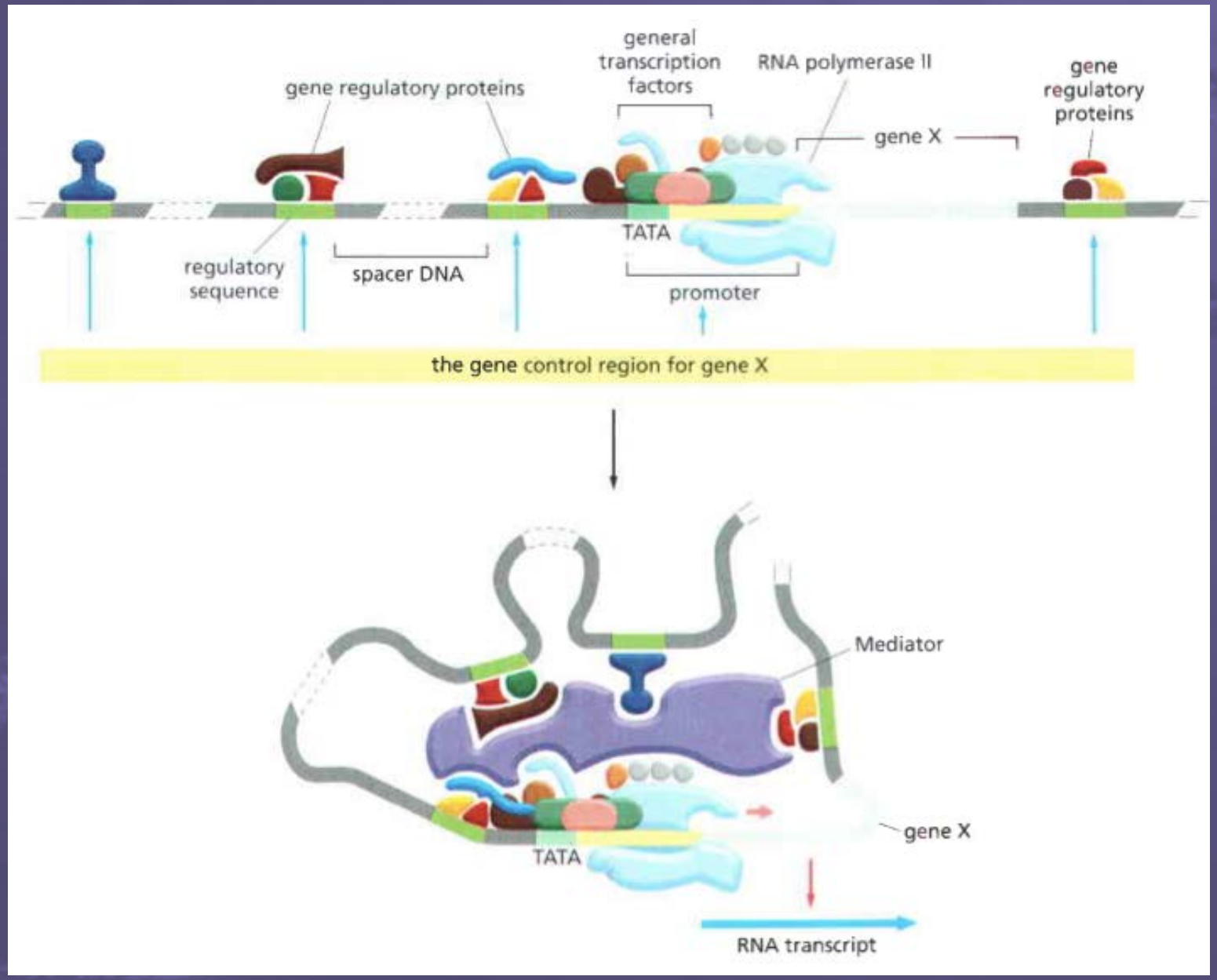


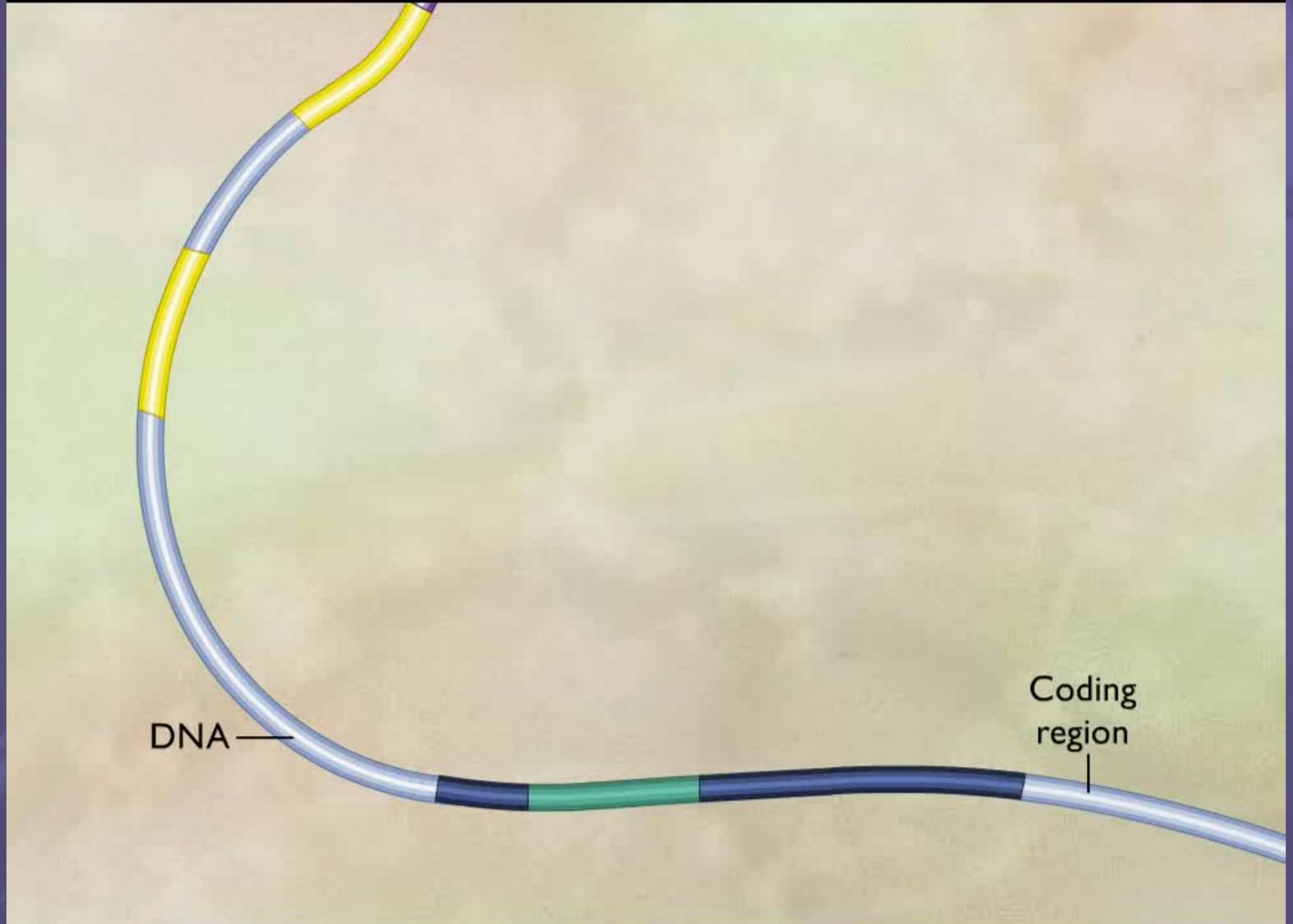
- High levels of transcription of particular genes depends on specific transcription factors
- They may act as activator or repressor of transcription of target genes





The gene control region of a typical eucaryotic gene.




DNA
Coding region

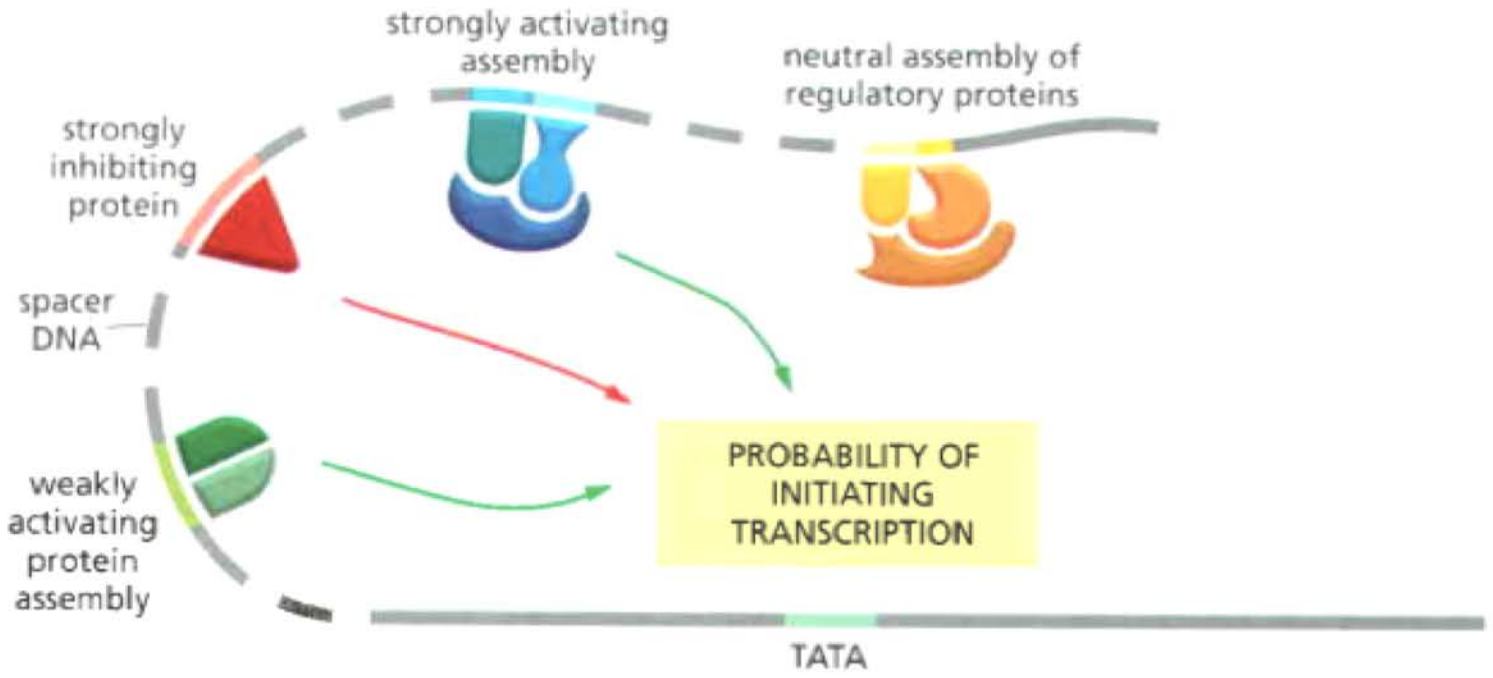
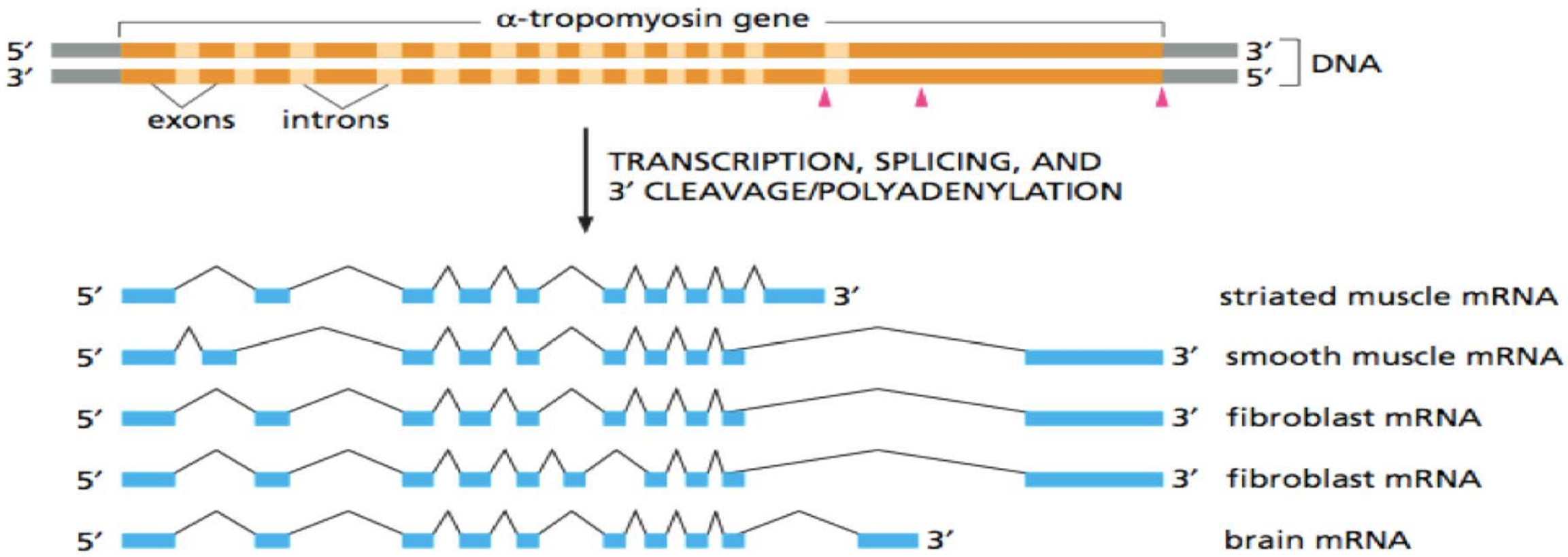
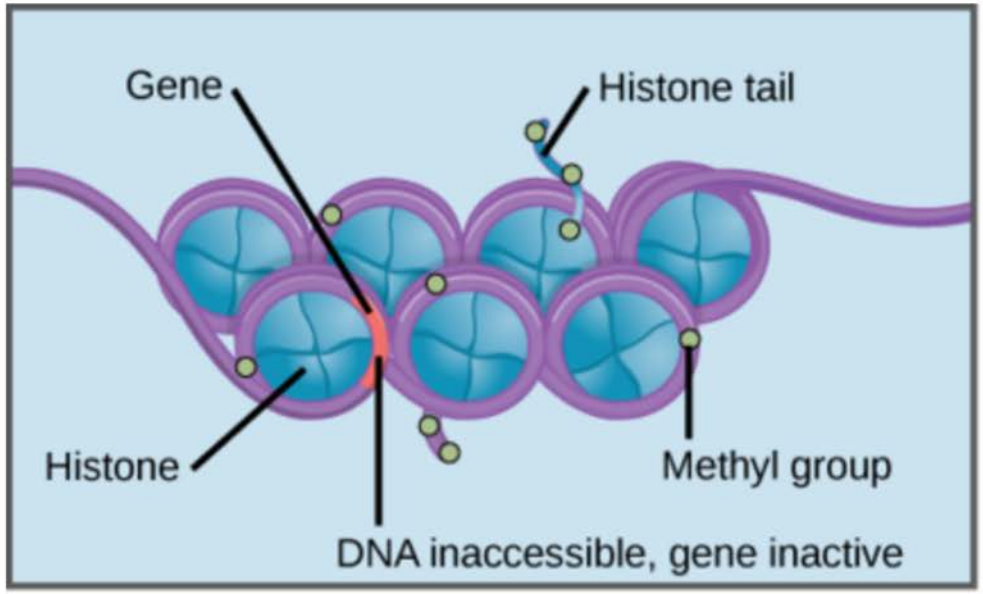


Figure 7–58 The integration of multiple inputs at a promoter. Multiple sets of gene regulatory proteins can work together to influence transcription initiation at a promoter, as they do in the *Eve* stripe 2 module illustrated in Figure 7–56. It is not yet understood in detail how the cell achieves integration of multiple inputs, but it is likely that the final transcriptional activity of the gene results from a competition between activators and repressors that act by the mechanisms summarized in Figures 7–46 and 7–50.

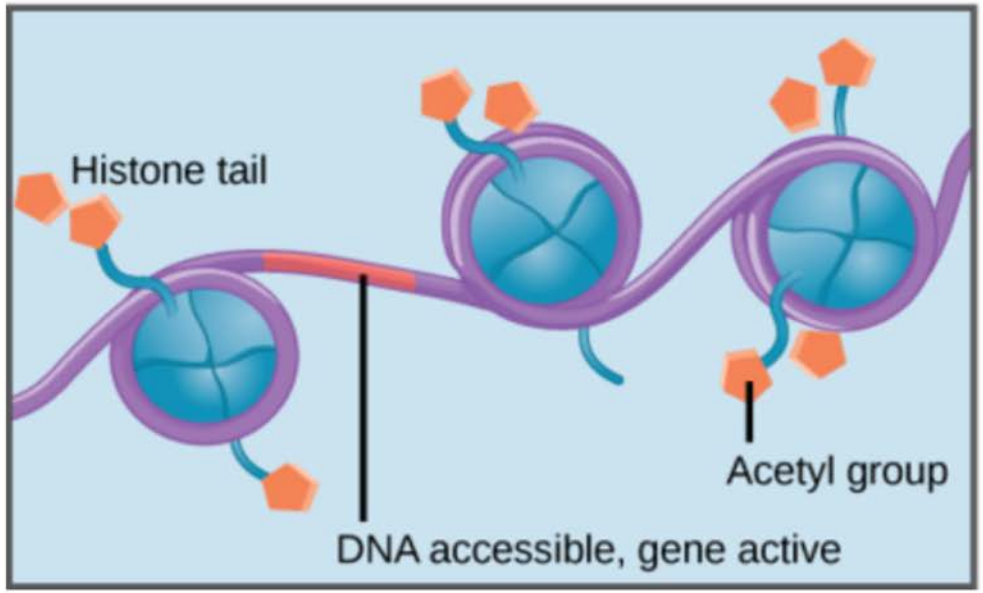
Alternative splicing of the alpha-tropomyosin gene



Epigenetic control of gene expression

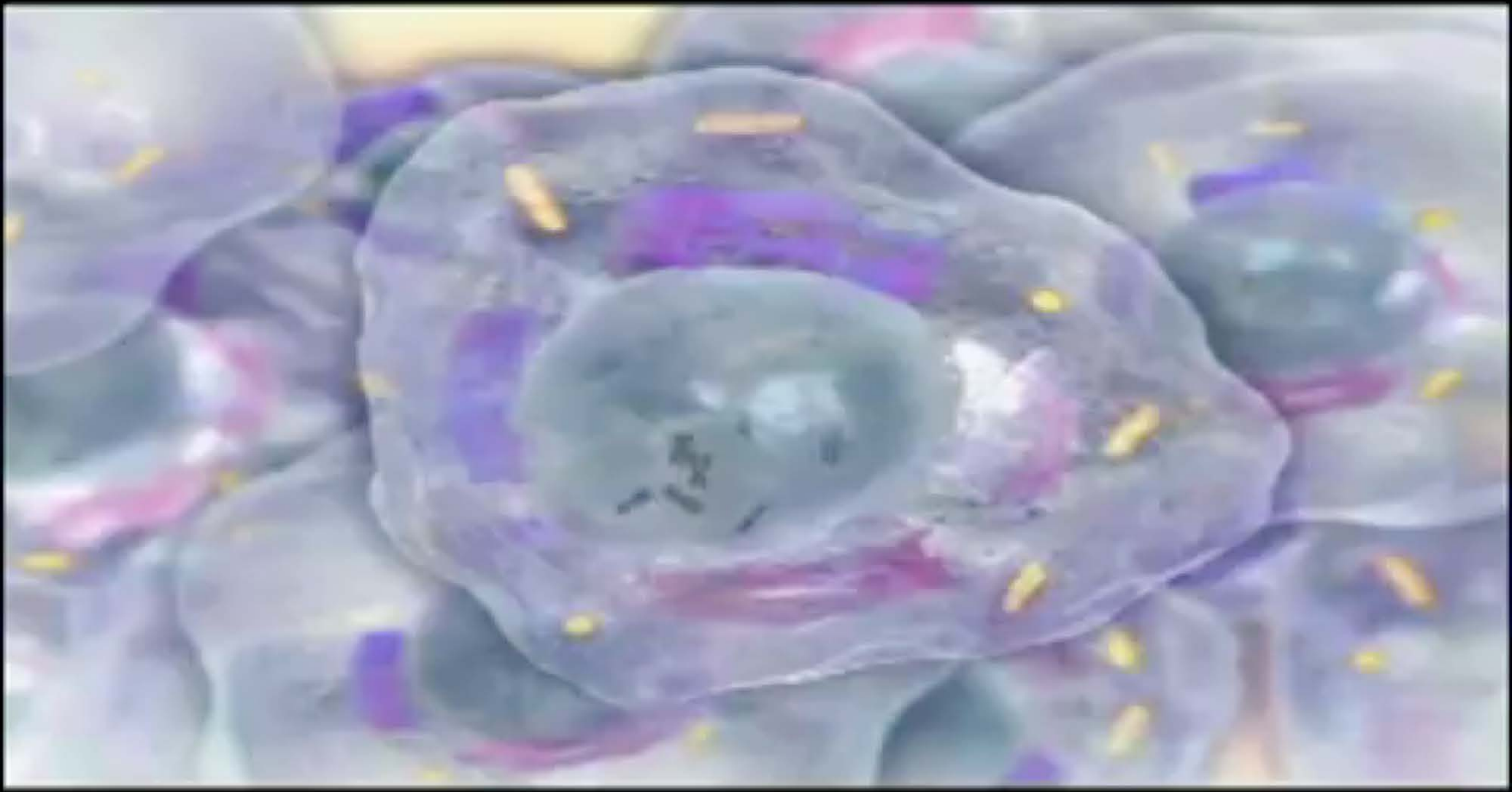


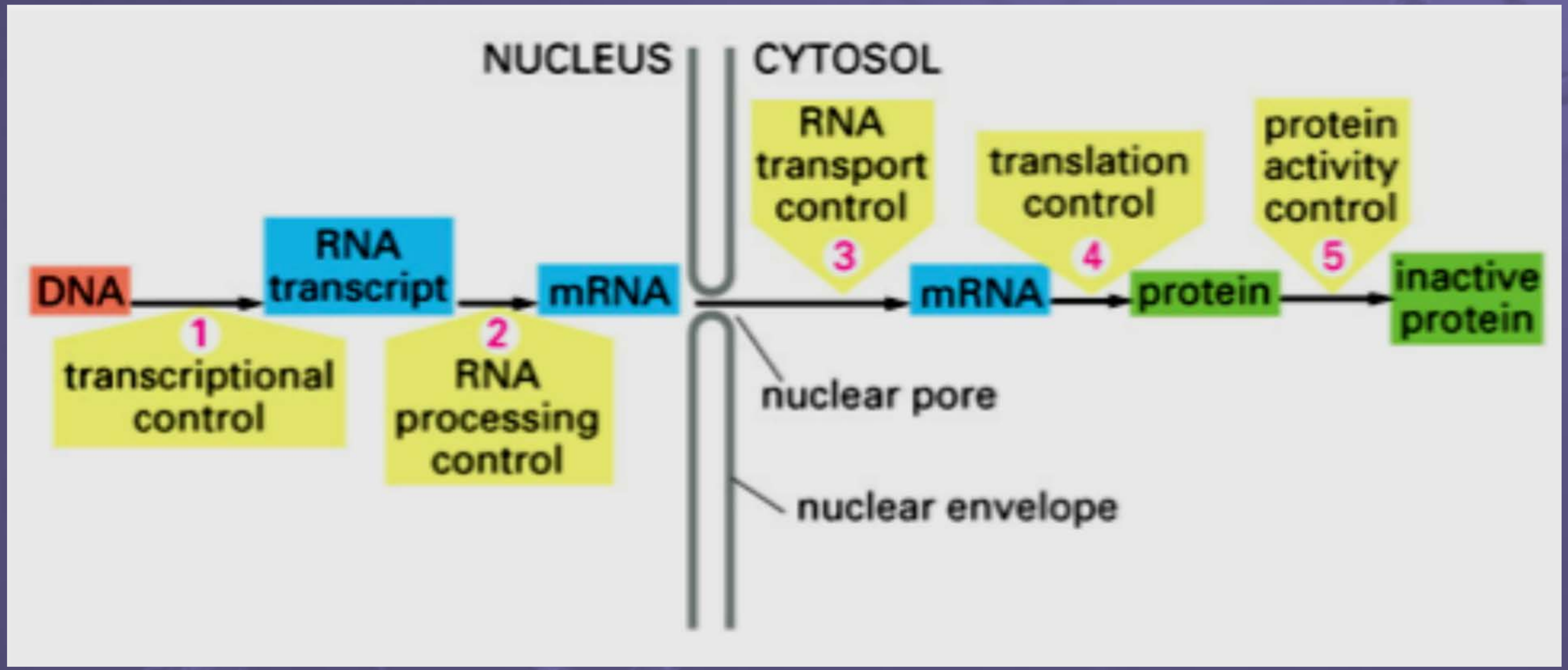
Methylation of DNA and histones causes nucleosomes to pack tightly together. Transcription factors cannot bind the DNA, and genes are not expressed.

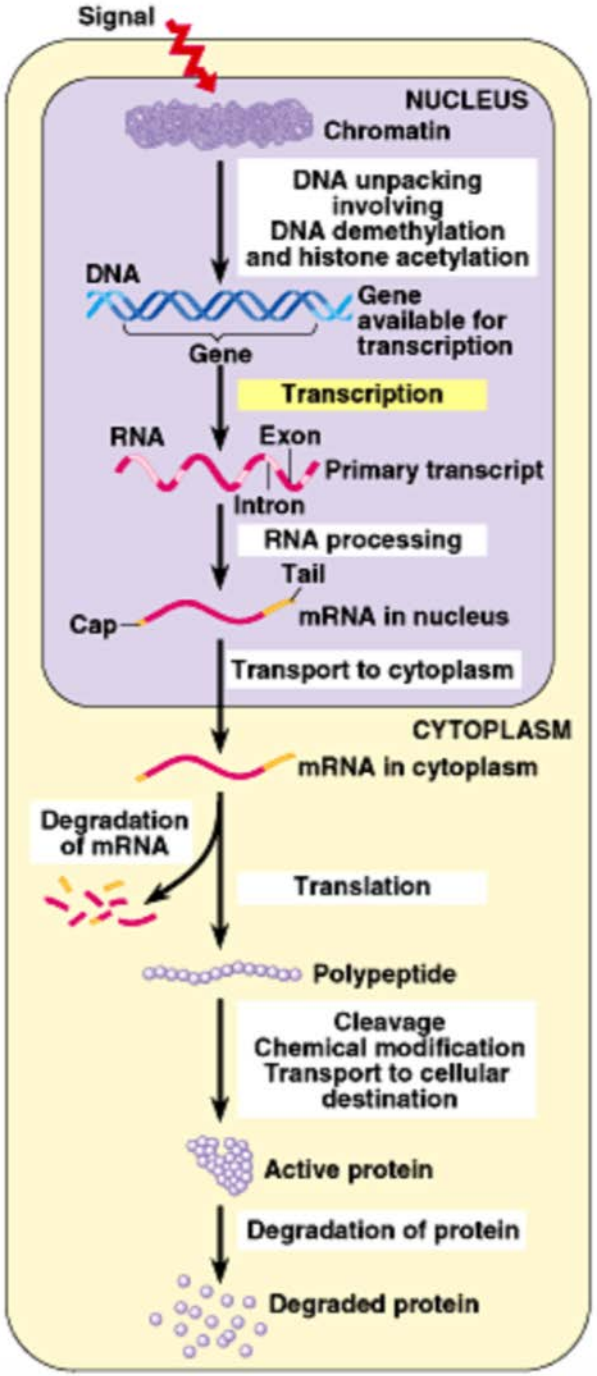


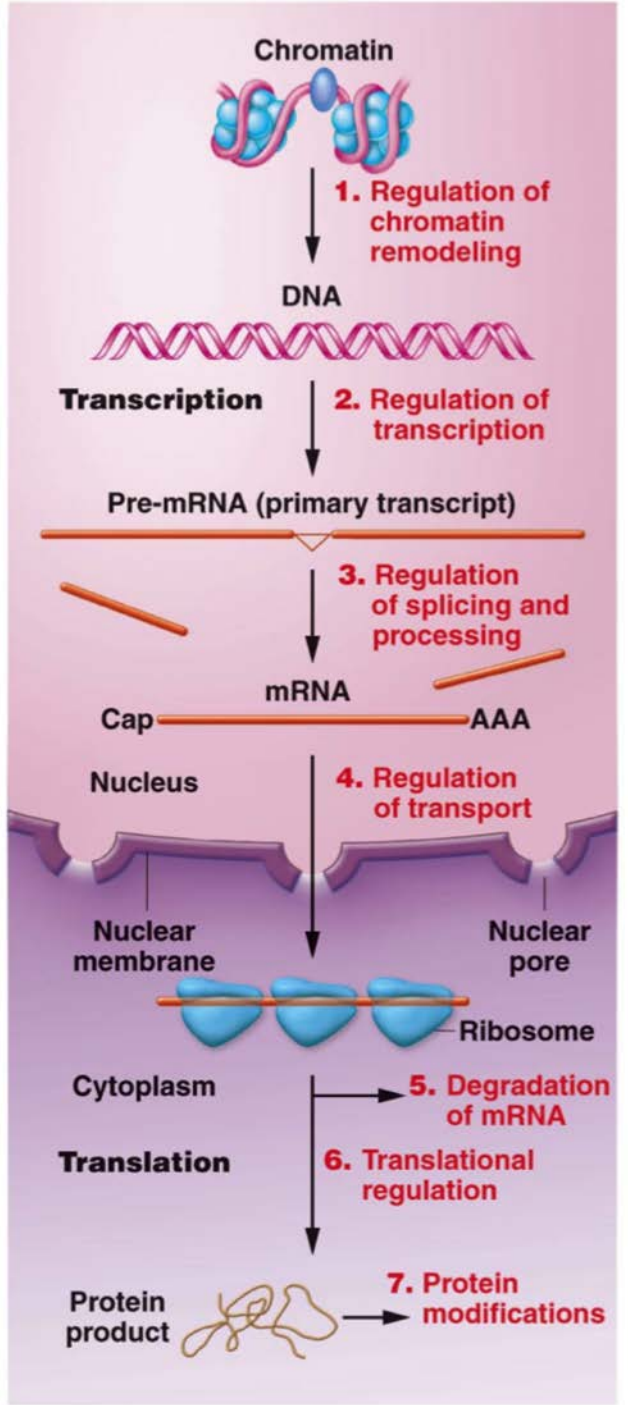
Histone acetylation results in loose packing of nucleosomes. Transcription factors can bind the DNA and genes are expressed.

https://www.boundless.com/biology/textbooks/boundless-biology-textbook/gene-expression-16/eukaryotic-gene-regulation-113/epigenetic-control-regulating-access-to-genes-within-the-chromosome-459-11682/

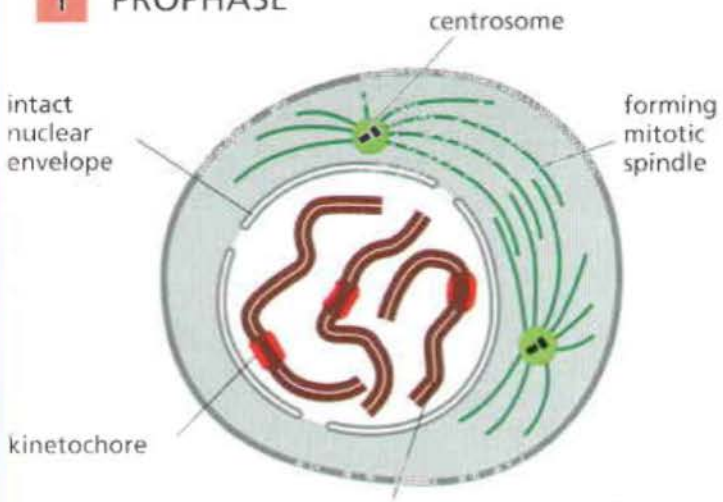



NUCLEUS
CYTOSOL
DNA
1
transcriptional control
RNA transcript
2
RNA processing control
mRNA
RNA transport control
3
mRNA
translation control
4
protein
protein activity control
5
inactive protein
nuclear pore
nuclear envelope



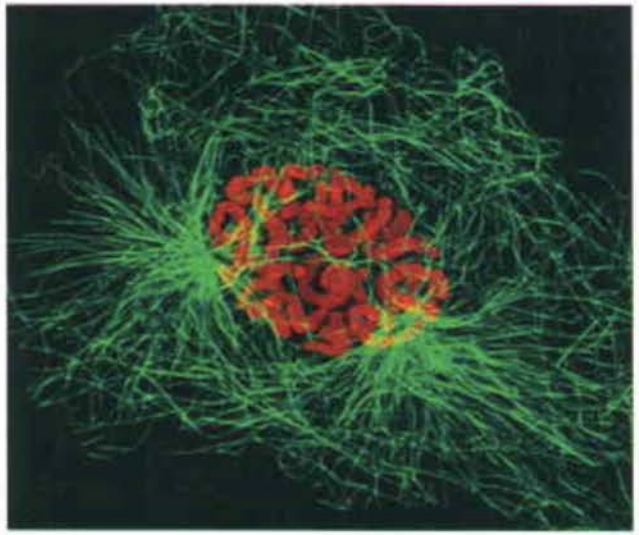


1 PROPHASE

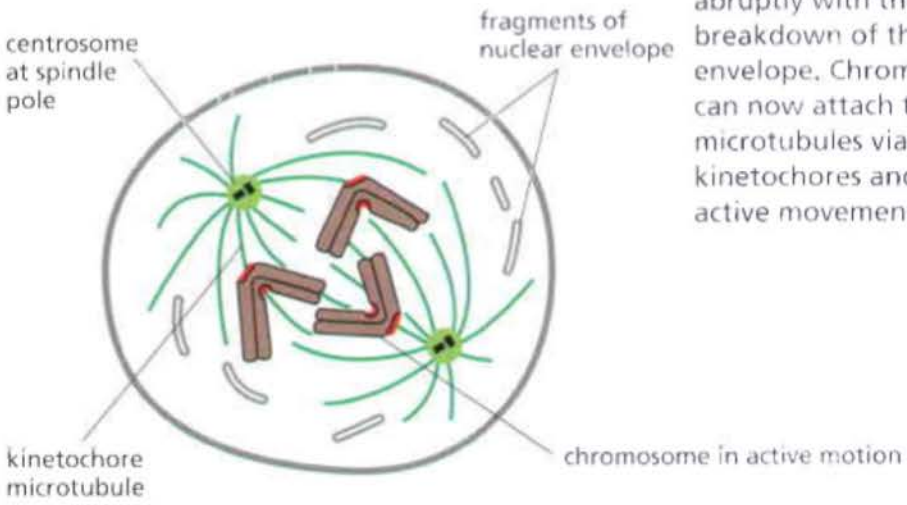


condensing replicated chromosome, consisting of two sister chromatids held together along their length

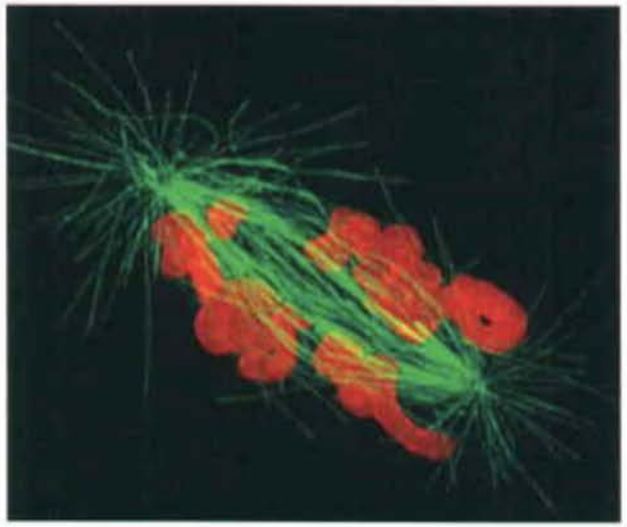
At prophase, the replicated chromosomes, each consisting of two closely associated sister chromatids, condense. Outside the nucleus, the mitotic spindle assembles between the two centrosomes, which have replicated and moved apart. For simplicity, only three chromosomes are shown. In diploid cells, there would be two copies of each chromosome present. In the photomicrograph, chromosomes are stained *orange* and microtubules are *green*.



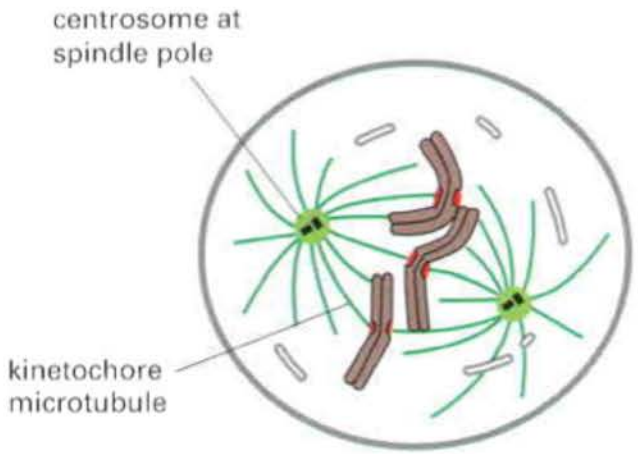
2 PROMETAPHASE



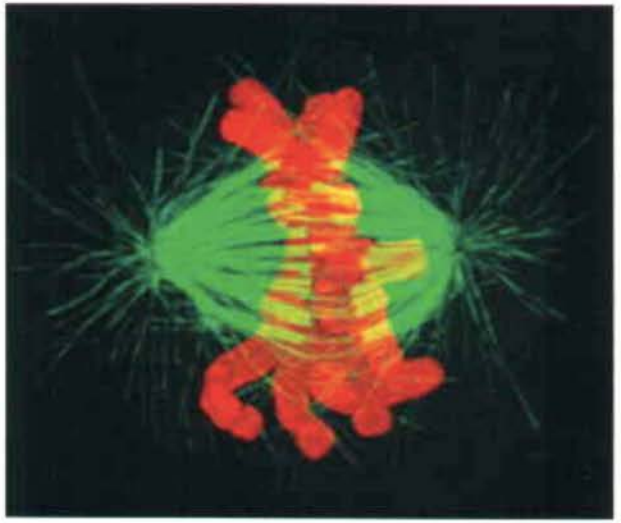
Prometaphase starts abruptly with the breakdown of the nuclear envelope. Chromosomes can now attach to spindle microtubules via their kinetochores and undergo active movement.



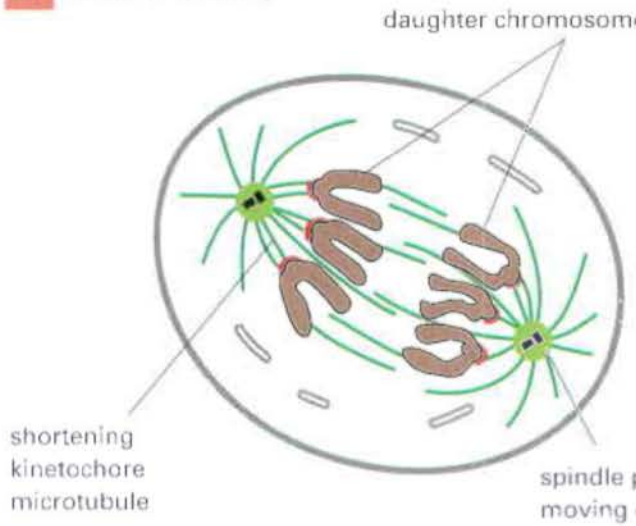
3 METAPHASE



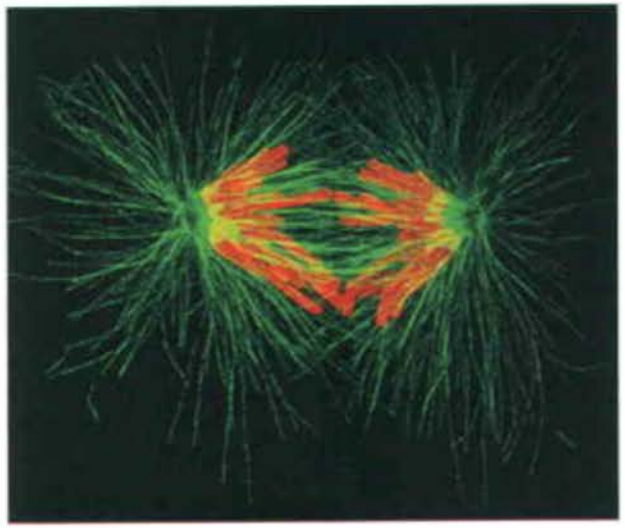
At metaphase, the chromosomes are aligned at the equator of the spindle, midway between the spindle poles. The kinetochore microtubules attach sister chromatids to opposite poles of the spindle.



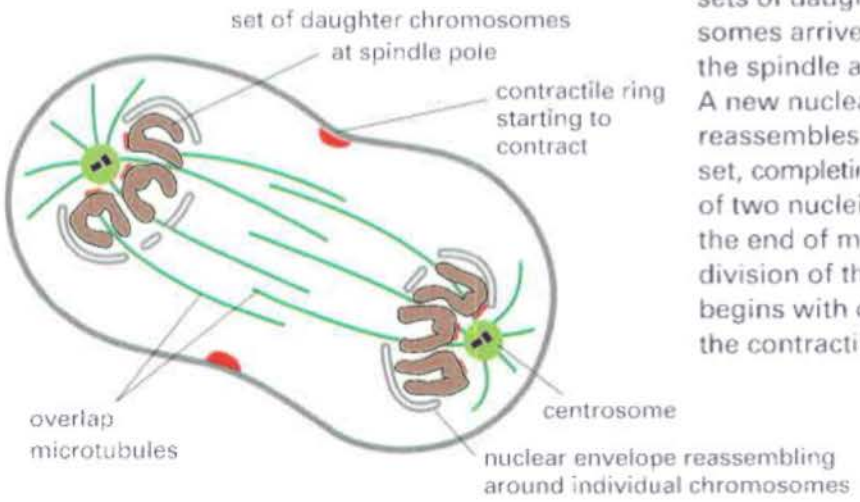
4 ANAPHASE



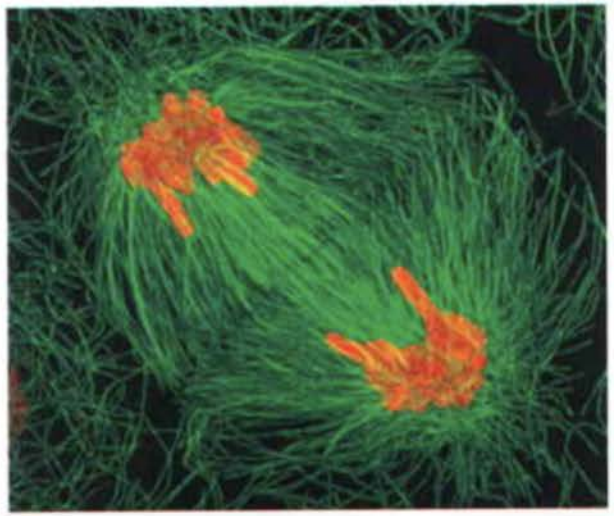
At anaphase, the sister chromatids synchronously separate to form two daughter chromosomes, and each is pulled slowly toward the spindle pole it faces. The kinetochore microtubules get shorter, and the spindle poles also move apart; both processes contribute to chromosome segregation.



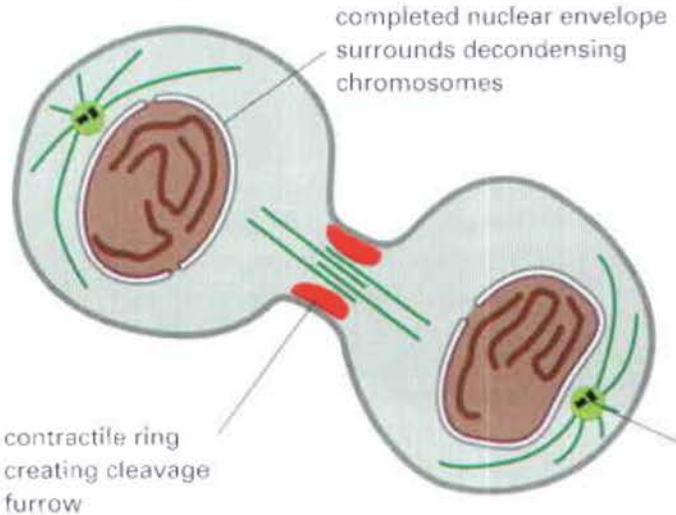
5 TELOPHASE



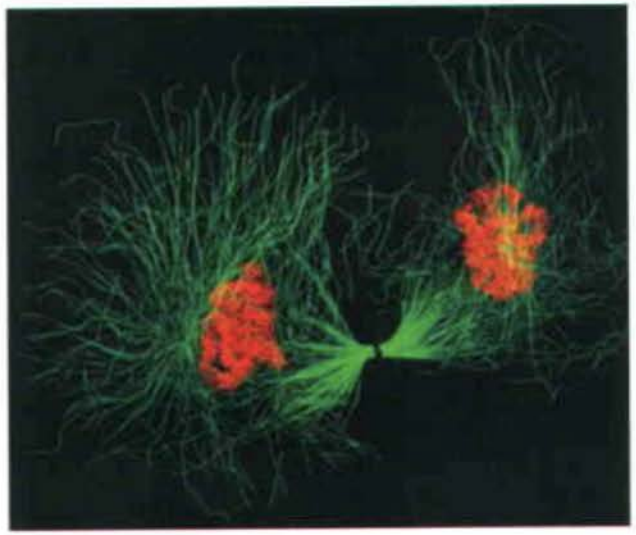
During telophase, the two sets of daughter chromosomes arrive at the poles of the spindle and decondense. A new nuclear envelope reassembles around each set, completing the formation of two nuclei and marking the end of mitosis. The division of the cytoplasm begins with contraction of the contractile ring.



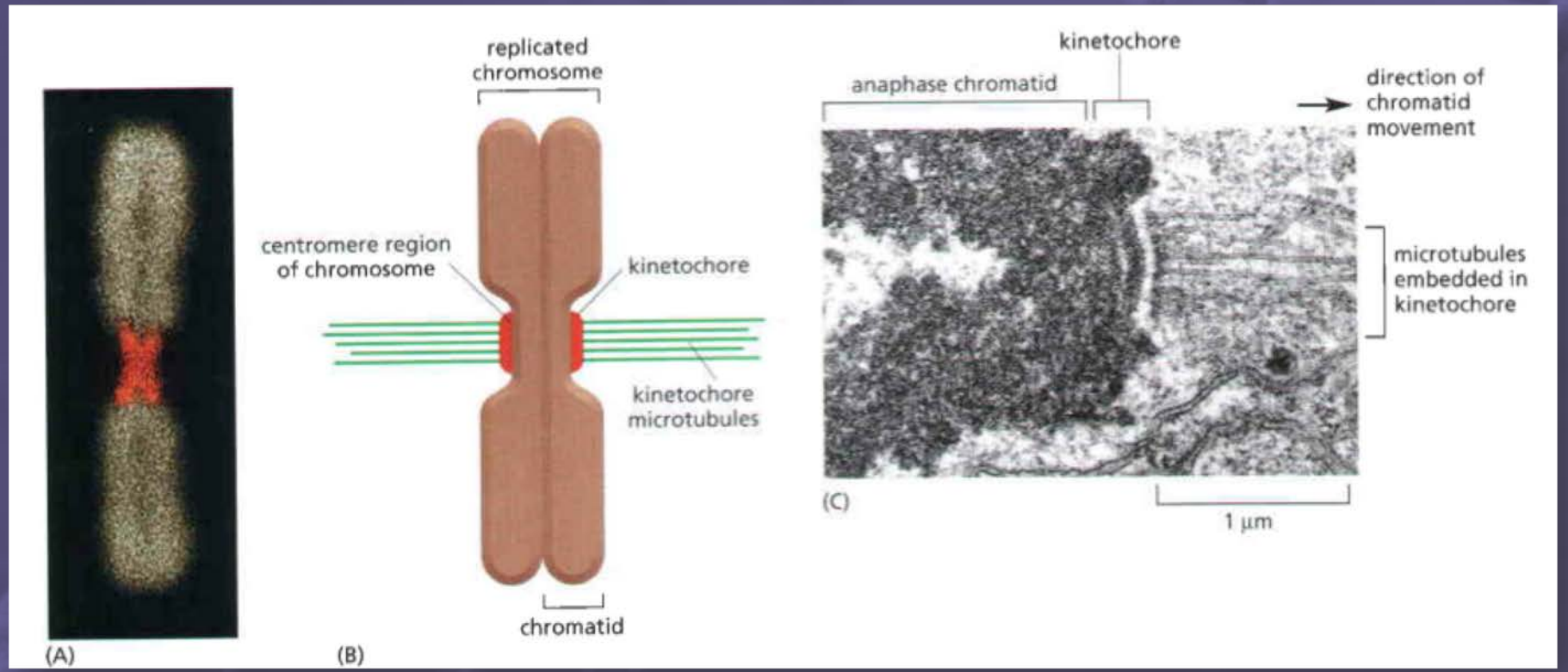
6 CYTOKINESIS

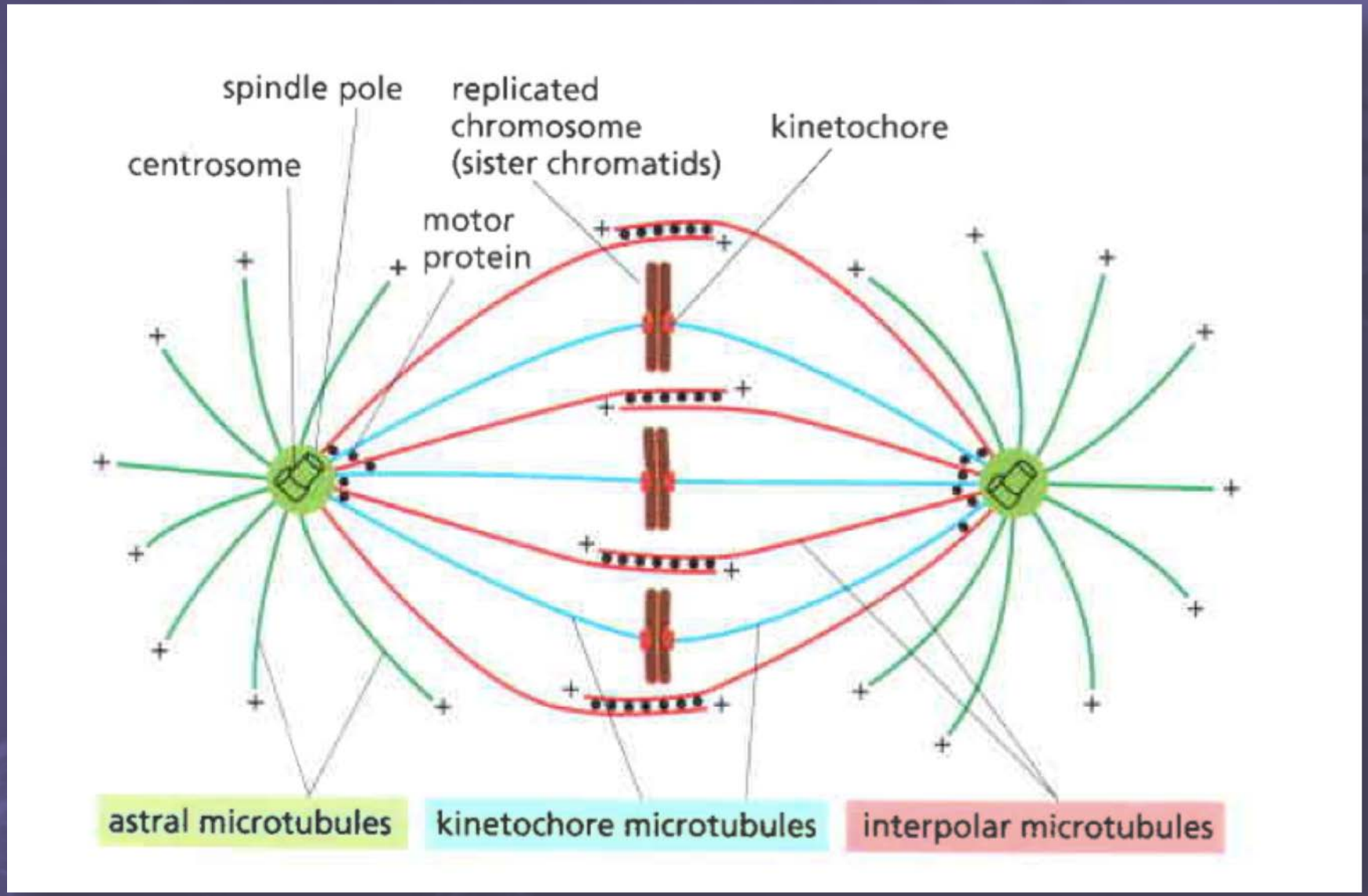


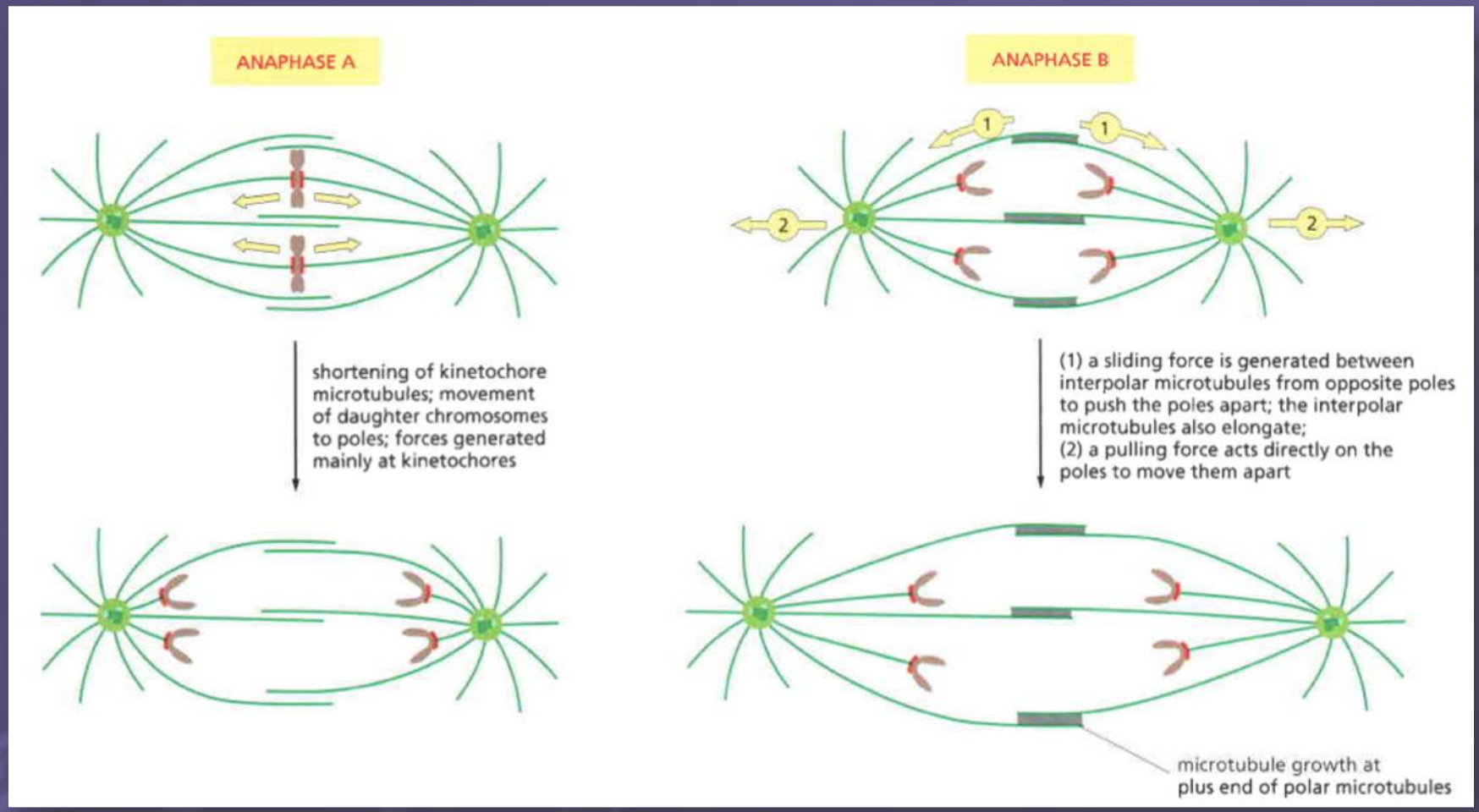
During cytokinesis, the cytoplasm is divided in two by a contractile ring of actin and myosin filaments, which pinches the cell in two to create two daughters, each with one nucleus.



(Micrographs courtesy of Julie Canman and Ted Salmon.)


(A)
replicated chromosome
centromere region of chromosome
kinetochore
kinetochore microtubules
chromatid
(B)
kinetochore
anaphase chromatid
direction of chromatid movement
microtubules embedded in kinetochore
(C)
1 μm


spindle pole
centrosome
replicated
chromosome
(sister chromatids)
kinetochore
motor
protein
astral microtubules
kinetochore microtubules
interpolar microtubules


ANAPHASE A
shortening of kinetochore microtubules; movement of daughter chromosomes to poles; forces generated mainly at kinetochores
ANAPHASE B
1
1
2
2
(1) a sliding force is generated between interpolar microtubules from opposite poles to push the poles apart; the interpolar microtubules also elongate;
(2) a pulling force acts directly on the poles to move them apart
microtubule growth at plus end of polar microtubules

- What is a nucleosome?
- A. the region of the nucleolus with linear RNA
- B. the region of the nucleolus with granular RNA
- C. the region of the nucleolus which contains the nucleolar organizer DNA
- D. the region of the DNA molecule that is wrapped around 4 different types of histone molecules
- E. another name for a heterochromatinized X chromosome

- D. is correct.
- The nucleosome is that part of the DNA which is wrapped around histones giving a beads-on-the-string appearance.

- Which or the following histones is NOT involved in the formation of the nucleosome?
- A. HI
- B. H2A
- C. H2B
- D. H3
- E. H4

- What would the A-T-G-C-C-G-T-A-A nucleotide sequence in one DNA strand become in the newly synthesized complementary strand during DNA replication?
- A. A-T-G-C-C-G-T-A-A
- B. A-U-G-C-C-G-U-A-A
- C. T-A-C-G-G-C-A-T-T
- D. U-A-G-C-C-G-A-U-U

- All of the following are special sequences in nuclear chromosomal DNA EXCEPT.
- A. centromere
- B. kinetochore
- C. telomere
- D. replication initiation site
- E. nucleolar organizer

- B. is correct.
- The kinetochore region of each chromosome is a nucleoprotein area associated with the centromere DNA sequence.

- DNA is permanently inactive in transcription for all cell types in the organism in which of the following?
- A. constitutive heterochromatin
- B. facultative heterochromatin
- C. both constitutive and facultative heterochromatin
- D. euchromatin
- E. neither euchromatin nor heterochromatin

- DNA is active in transcription for any particular kind of cell in which of the following?
- A. constitutive heterochromatin
- B. facultative heterochromatin
- C. both constitutive and facultative heterochromatin
- D. euchromatin
- E. neither euchromatin nor heterochromatin