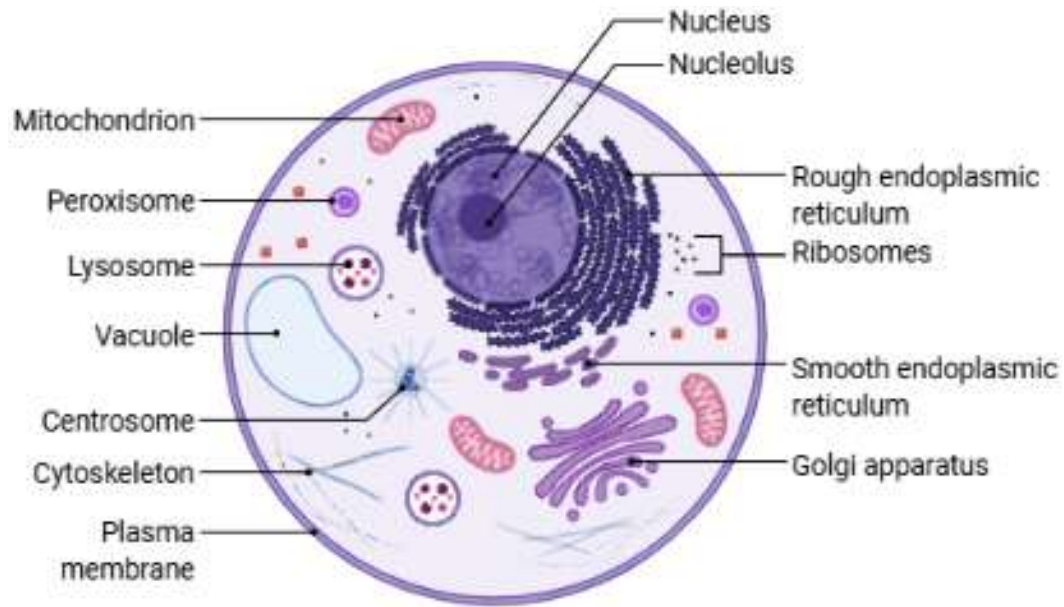
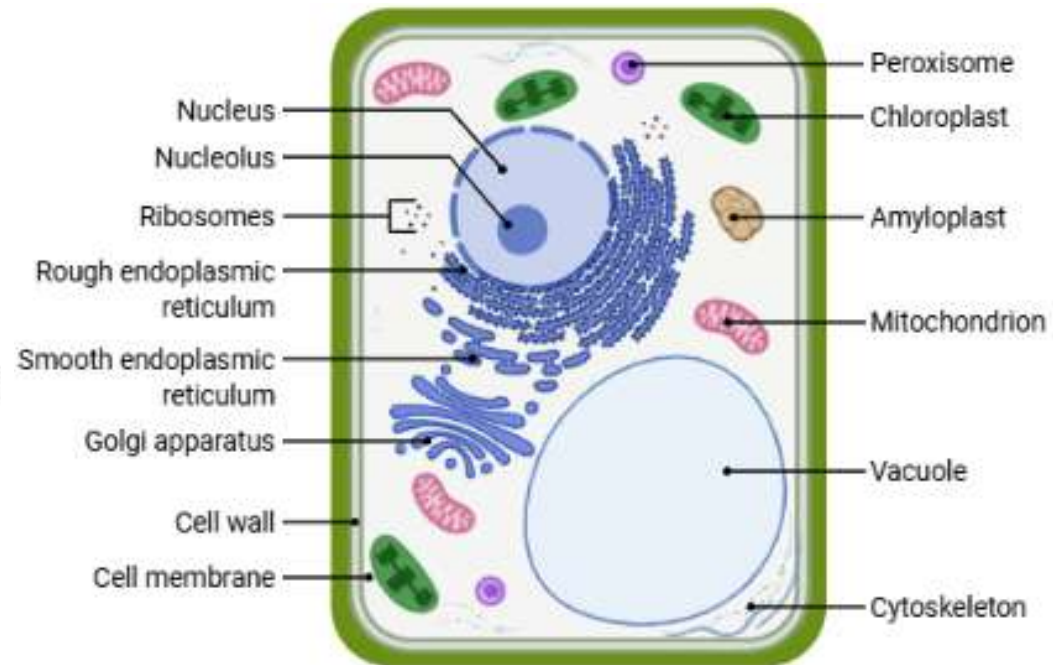


Eukaryotic vs Prokaryotic cells

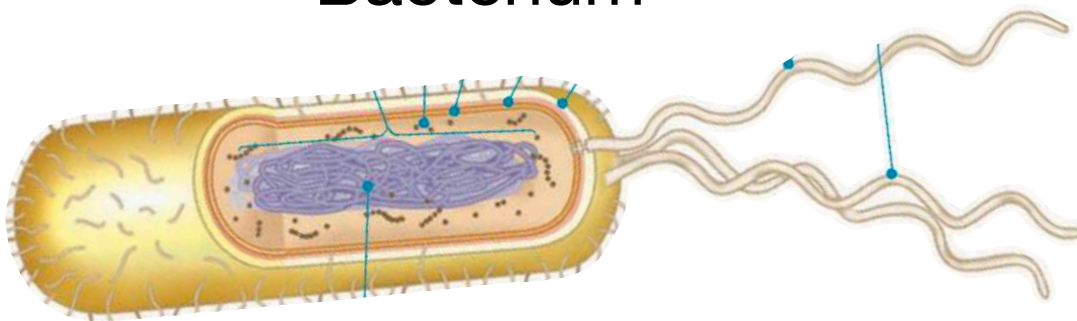
Animal cell



Plant cell



Bacterium



No compartments, but there are “territories” where material accumulates: e.g. nucleoid - DNA accumulates here

Same machinery converts information in DNA to RNA and proteins

Same plasma membrane structure and function

Eukaryotic and Prokaryotic cells

Cells and organisms made up of cells look different, but have the same basic organization

Apartments look different, but have the same basic organization



Bacteria



Archaea



Plants



Fungi



Molluscs



Flatworms



Sharks



Fish



Turtles



Birds



Mammals

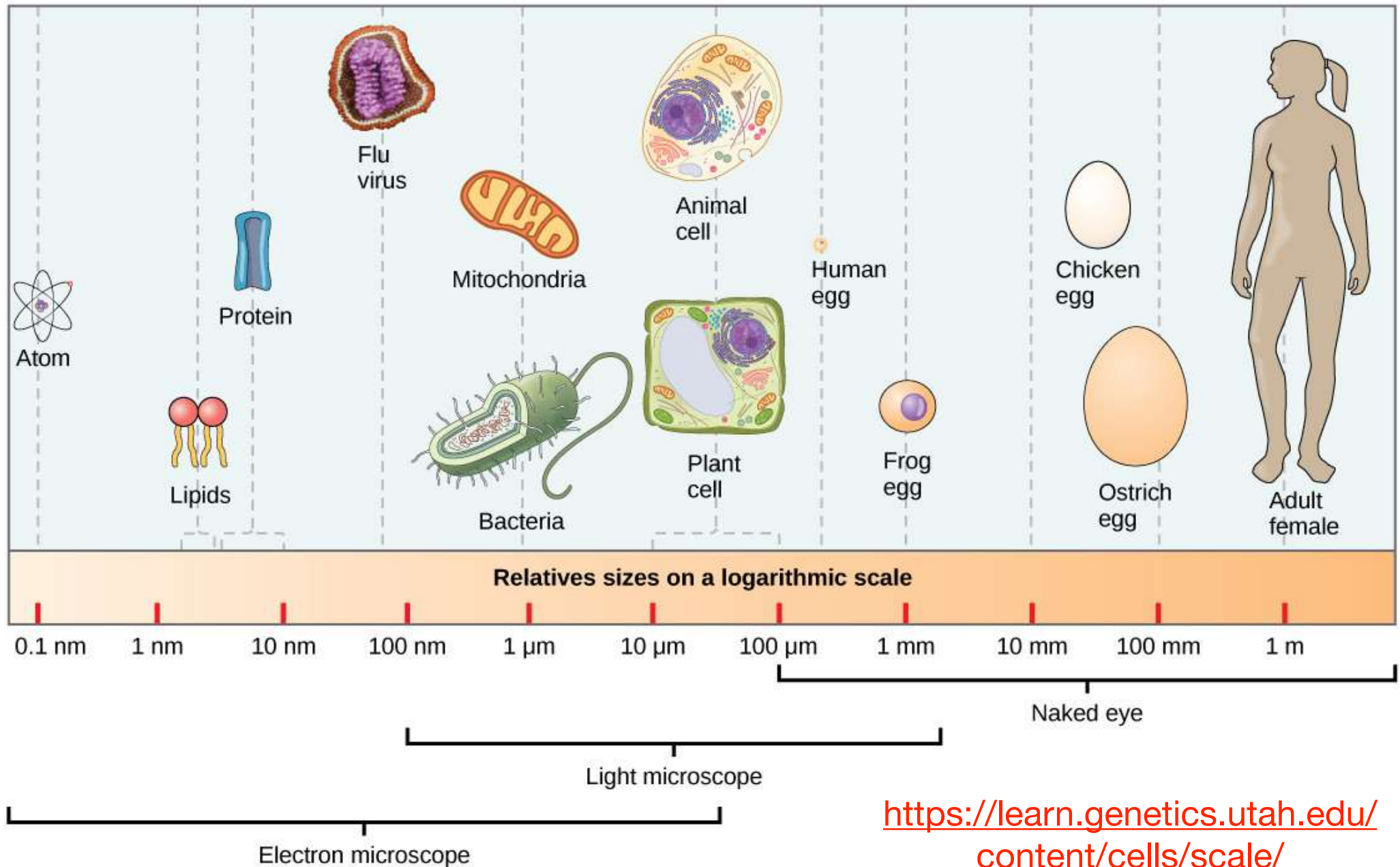


Primates



An apartment

Cells span a wide range of length scales



<https://learn.genetics.utah.edu/content/cells/scale/>

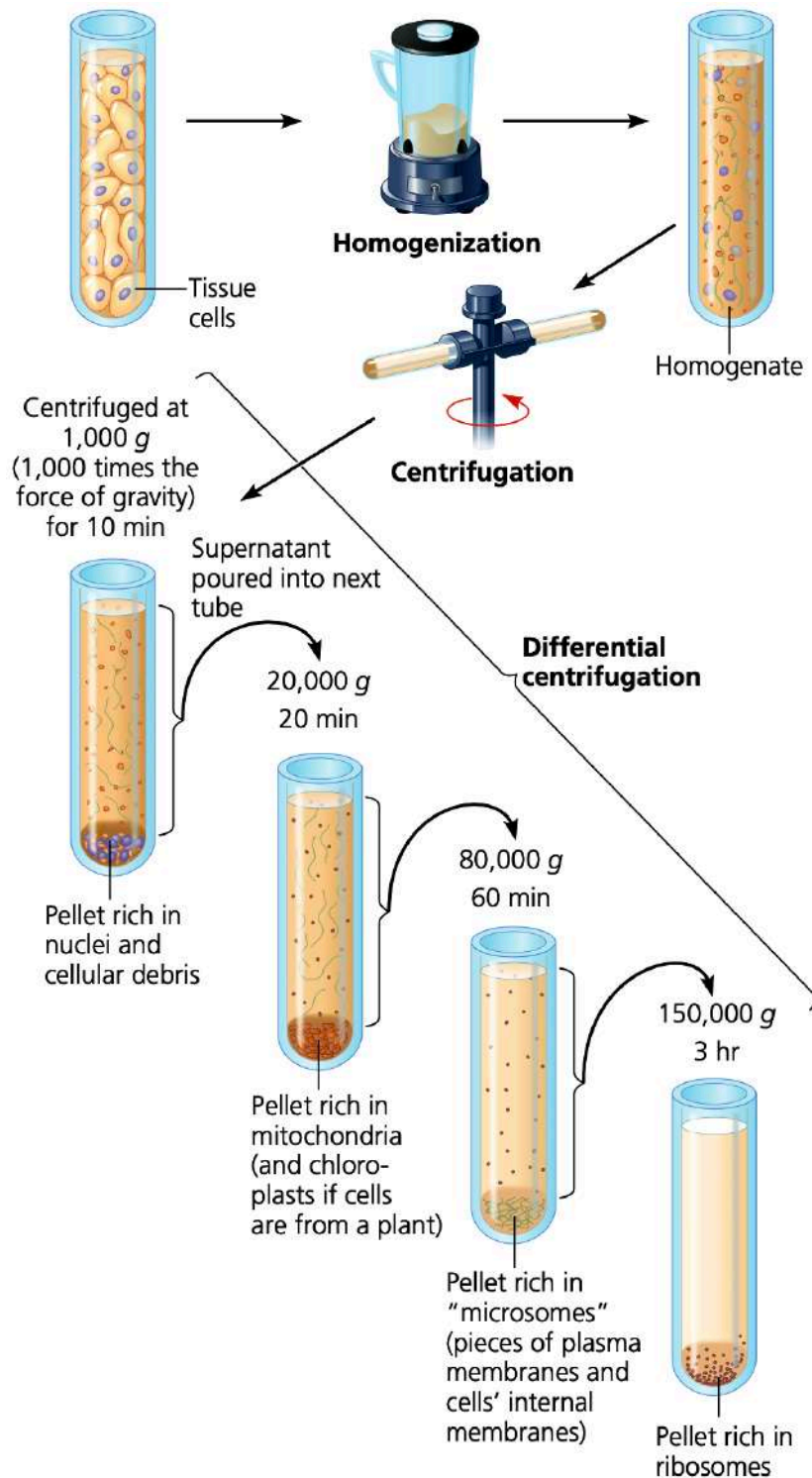
The Cell Theory

- All organisms are made up of one or more cells
 - All the life functions of an organism occur within cells
 - All cells come from preexisting cells
 - The cell has hereditary information (DNA) that is passed on from cell to cell
-
- Was developed based on observations under microscopes of plant and animal cells by several scientists
-
- Proposed first by the botanist, Matthias Schleiden, in 1838, and then by the zoologist, Theodor Schwann, in 1839

How does one study cells and their organization?

1. Which cell to study?
2. Which cell in which animals to study?
3. What are the tools or equipment required?

1. Which cell to study? - those we can easily obtain or work with under controlled conditions
2. Which cell in which animals to study? - those cells and animals we can grow or keep in the laboratory - model systems or organisms
3. What are the tools or equipment required? - need microscopes and other ways to study microscopic structures



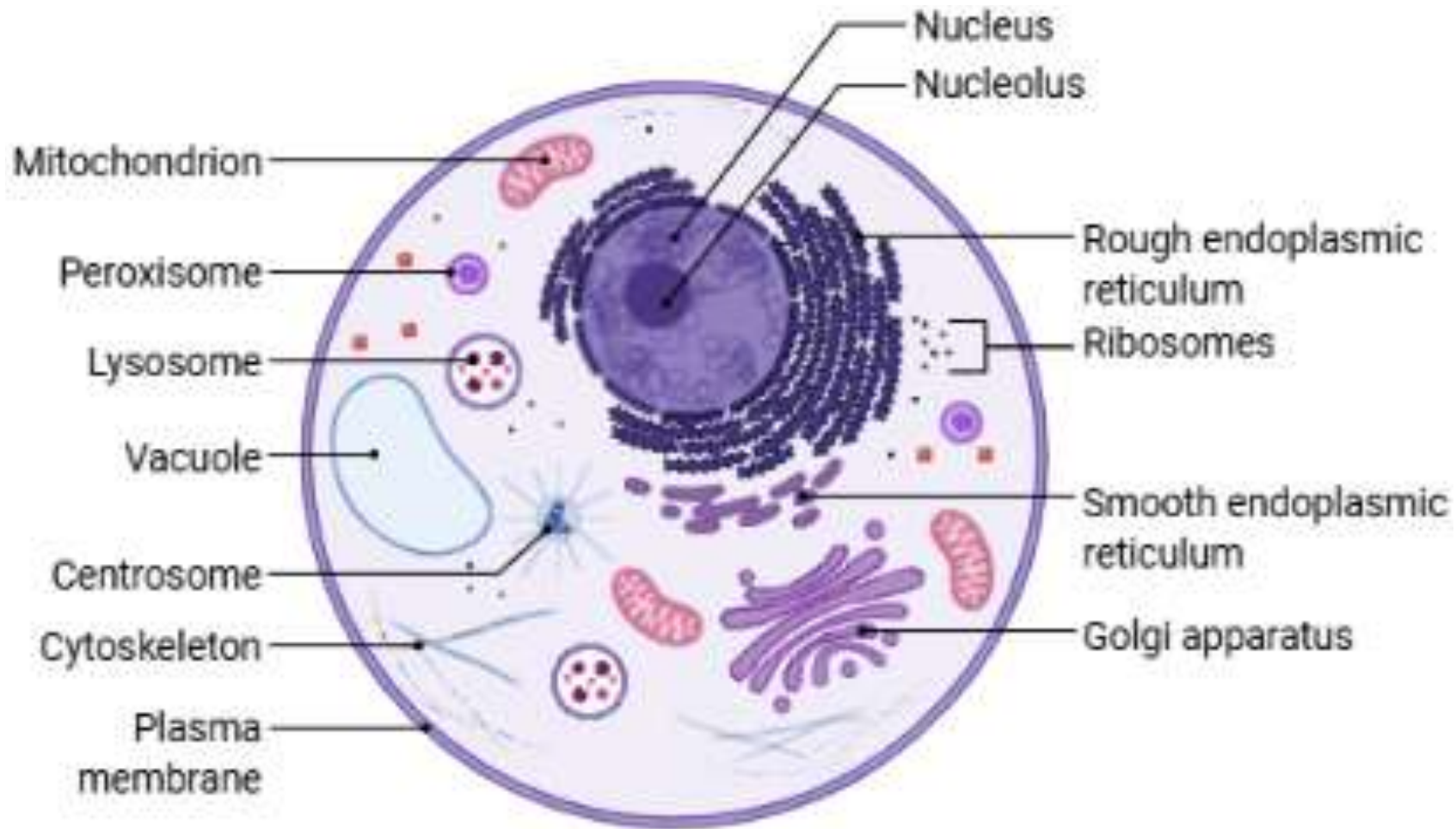
Studying cells by biochemical fractionation

- Cell fractionation is used to isolate (fractionate) cell components **based on size and density**
- Cells are homogenized to break them up
- The resulting mixture (homogenate) is centrifuged
- The supernatant (liquid) is poured into another tube and centrifuged at a higher speed for a longer period
- Process is repeated several times
- This “differential centrifugation” results in a series of pellets, each containing different cell components

To understand how something works, break it up and study its individual components

Plus in Lecture 1: Microscopy

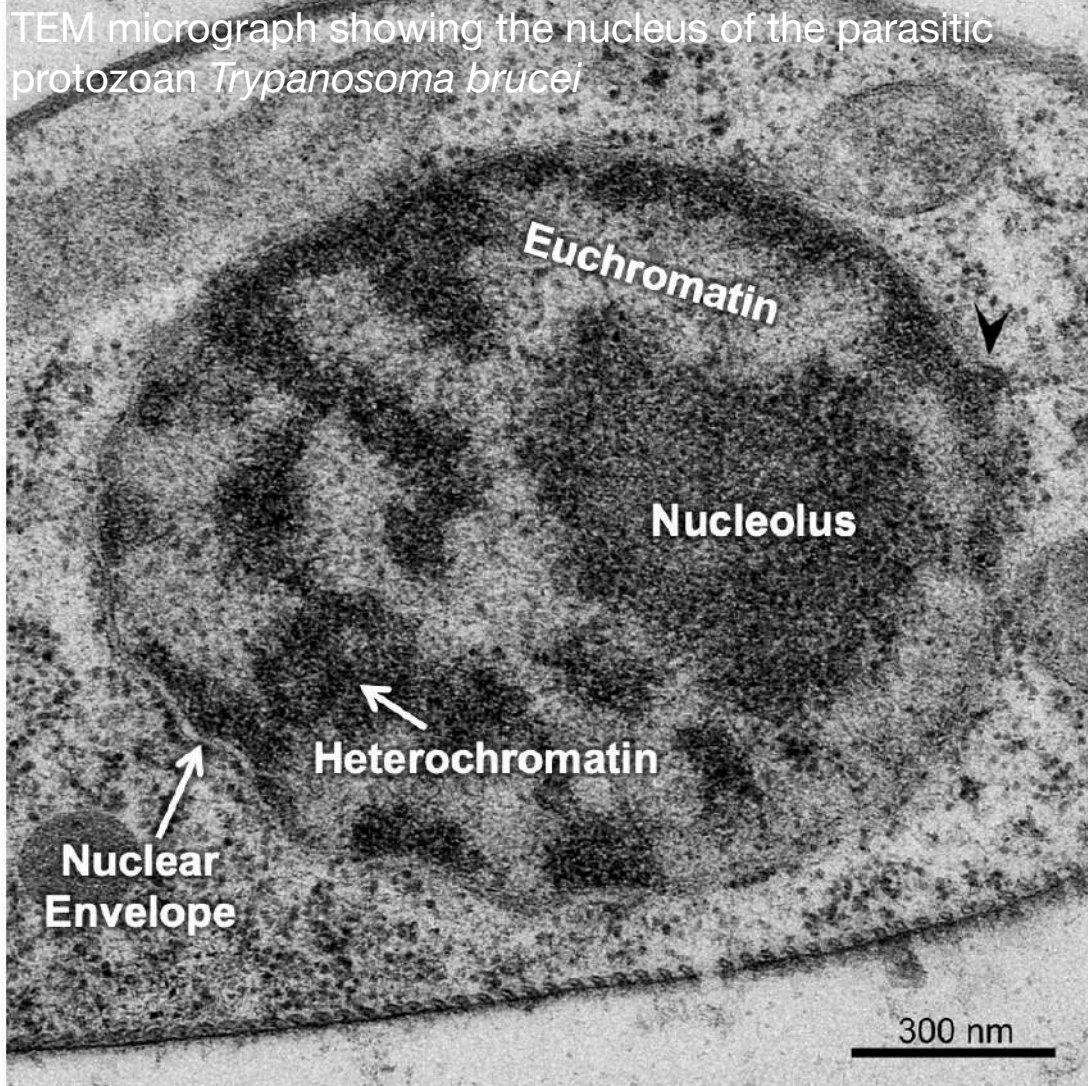
In a differential centrifugation process cellular constituents separate on the basis of size and density



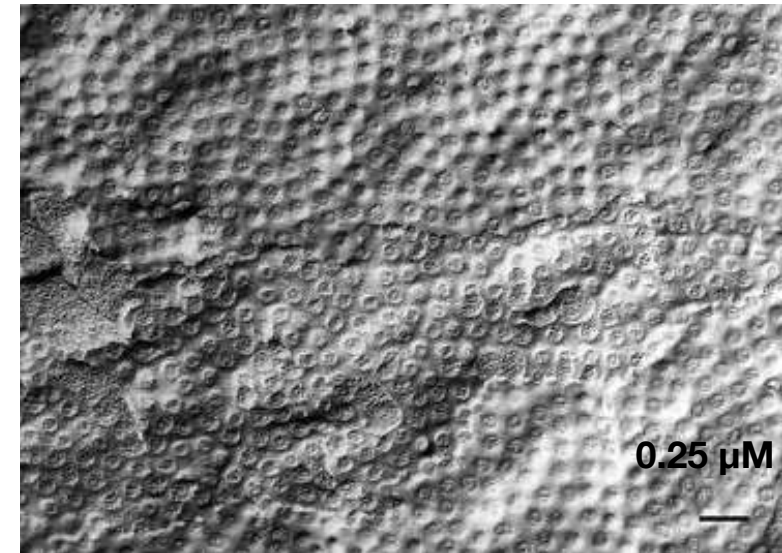
The technique is applied in innovative ways for biomedical research and health



Cellular organelles: Nucleus



Membrane bound compartment in eukaryotes which houses the genetic material (DNA)



Surface of the nuclear envelope has nuclear pores - allows entry and exit

- Euchromatin and Heterochromatin are two physical states in which DNA exists in the nucleus
- Nucleolus is a region inside the nucleus where ribosomes are made

Cellular organelles: Nucleus

Human DNA in one cell ~ 2 meters (~6.5 ft long)

Human cell nucleus ~ 10 micro M

The DNA is 6-7 orders of magnitude bigger than the nucleus

To fit inside the nucleus the DNA strands must be “packed”

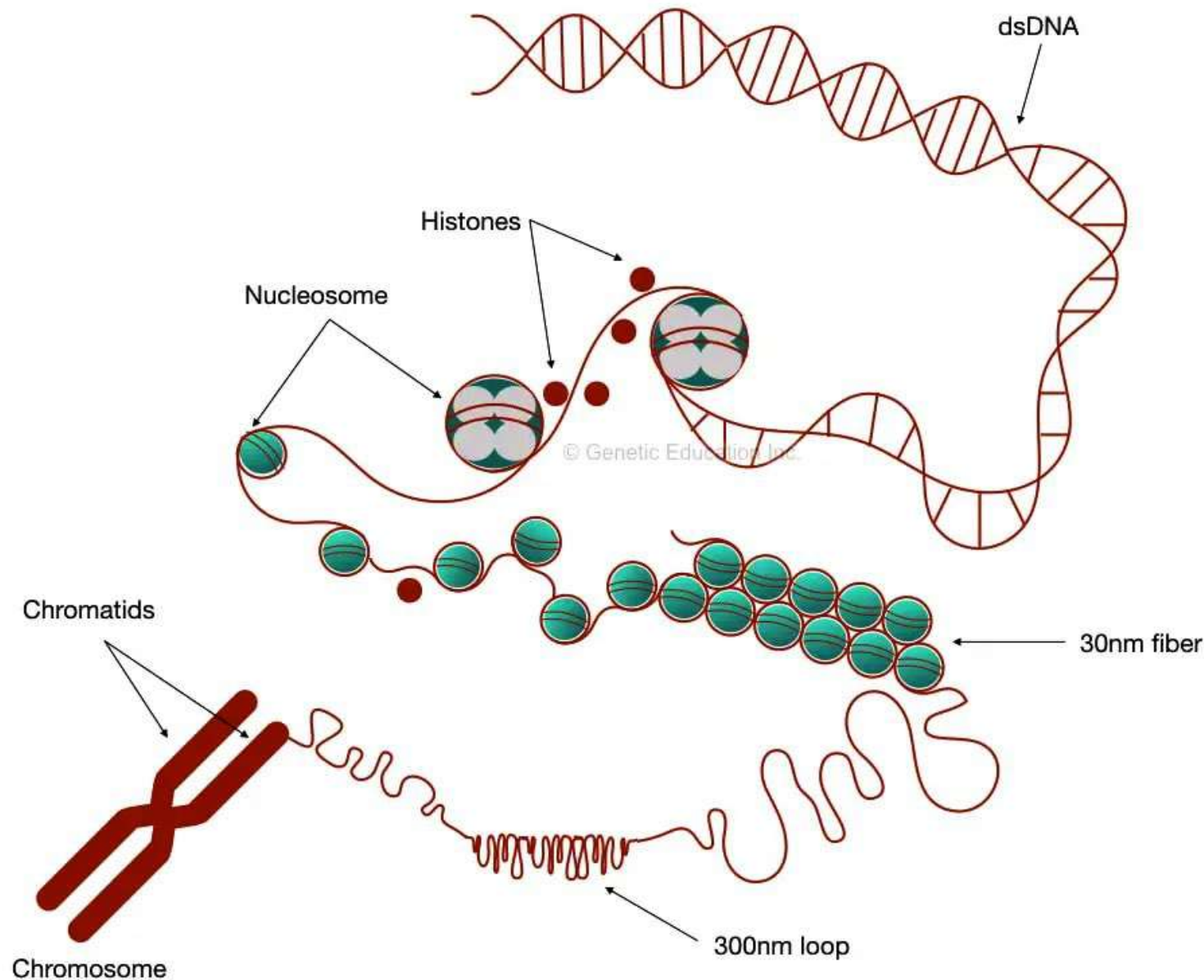


Disorganized or badly packed stuff occupies more space

- DNA inside the nucleus is not randomly pooled
- DNA is looped around an octamer of proteins known as histones
- Allows organized packing of long strands into a small compartment

Cellular organelles: Nucleus

DNA packaging has several layers. The basic unit is a nucleosome



Cellular organelles: Nucleus

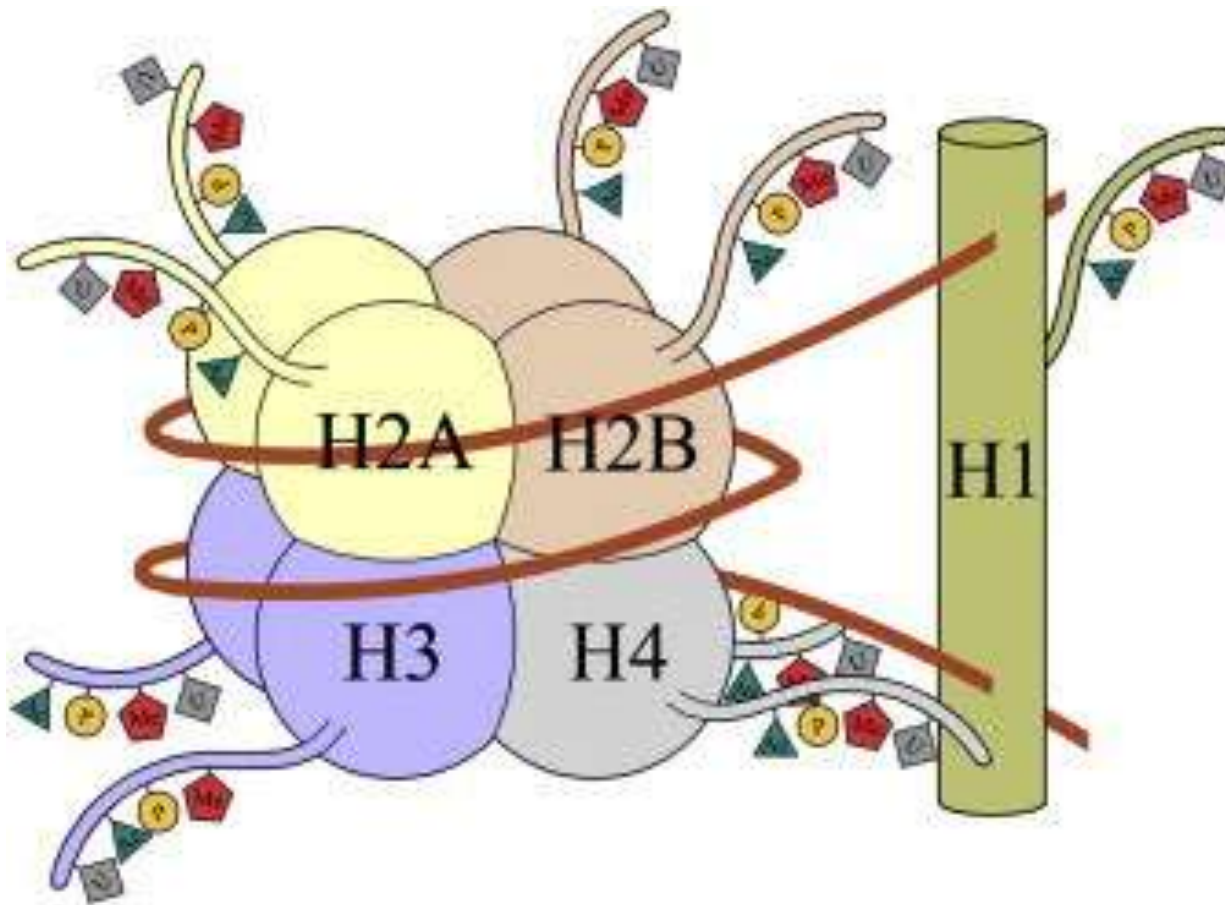
DNA packaging has several layers. The basic unit is a nucleosome



<https://www.youtube.com/watch?v=gbSIBhFwQ4s>

Cellular organelles: Nucleus

Nucleosome: octamer of 4 types of histone proteins with a strand of DNA wrapped around it



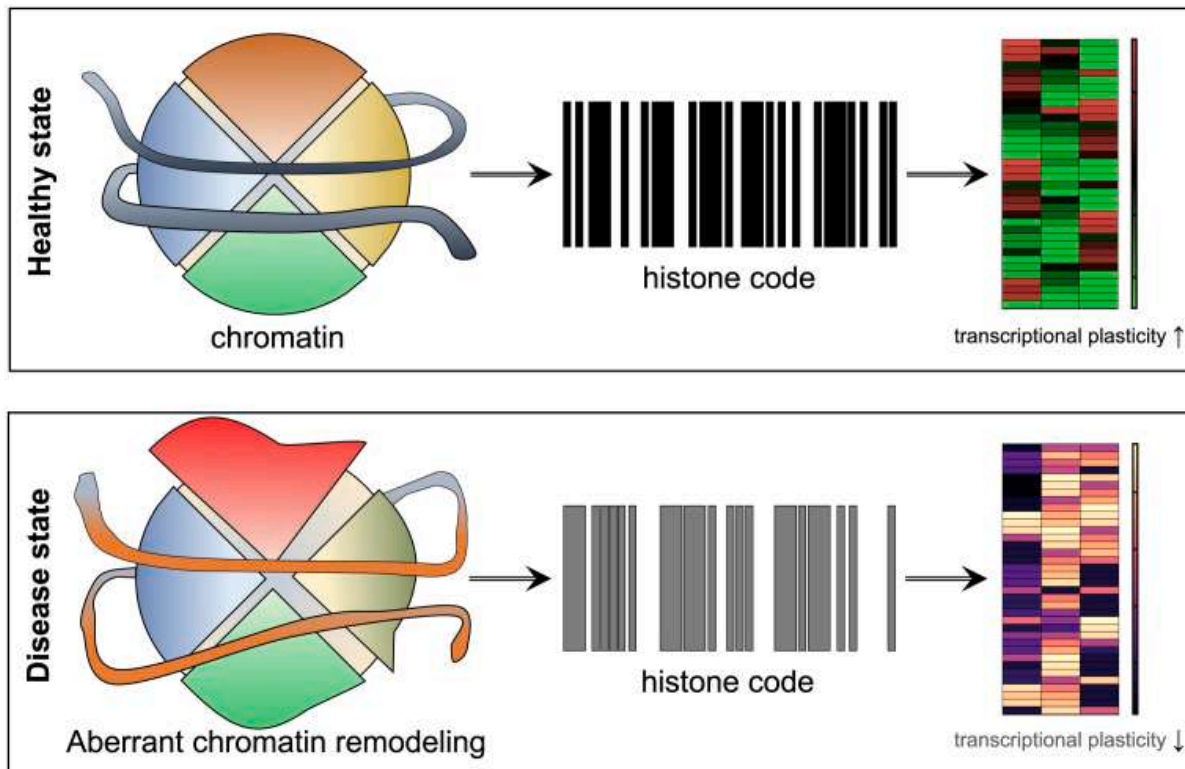
- Histone proteins have a “head” and “tail”
- “Tail” can be modified with chemical marks - acetylation, methylation, phosphorylation etc
- DNA strand can also be chemically modified
- The modifications decide how “tight” or “loose” the DNA strand is wrapped around the nucleosome
- This makes the DNA accessible or not accessible for certain functions

The multiple tails and multiple modifications allow for the emergence of a “histone code” for every segment of DNA

Cellular organelles: Nucleus

The “histone code” is a hypothesis which states that transcription of a segment of DNA depends on the chemical modifications of the histone proteins, especially the histone tails

In many diseases the “histone code” is found to be altered. The idea is that if this code is altered, DNA transcription from that segment of DNA can increase or decrease causing abnormal gene regulation

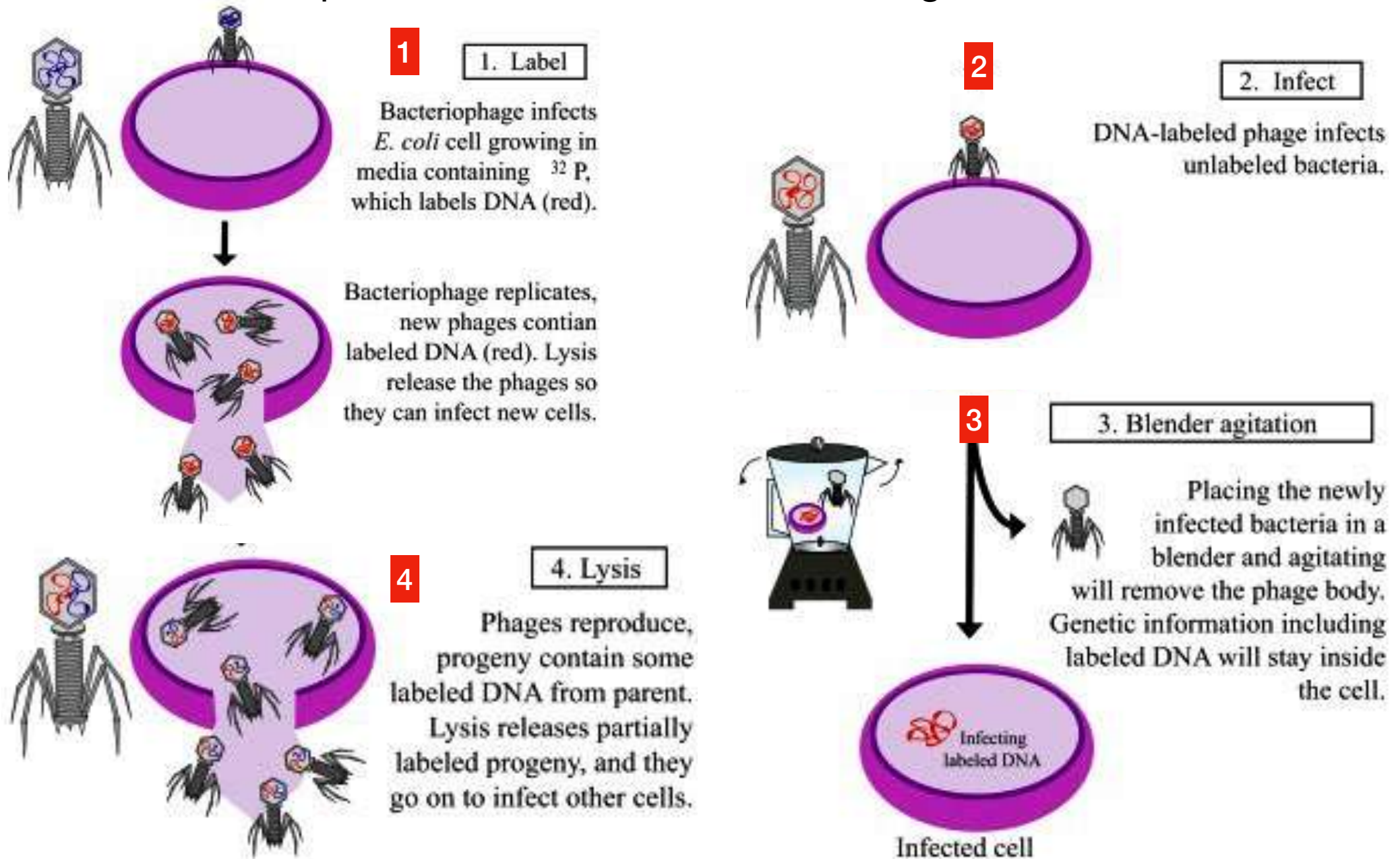


Examples where the histone code is found to be altered:

- Autoimmune diseases
- Neurodegenerative diseases
- Dementia
- Sepsis
- Cancers

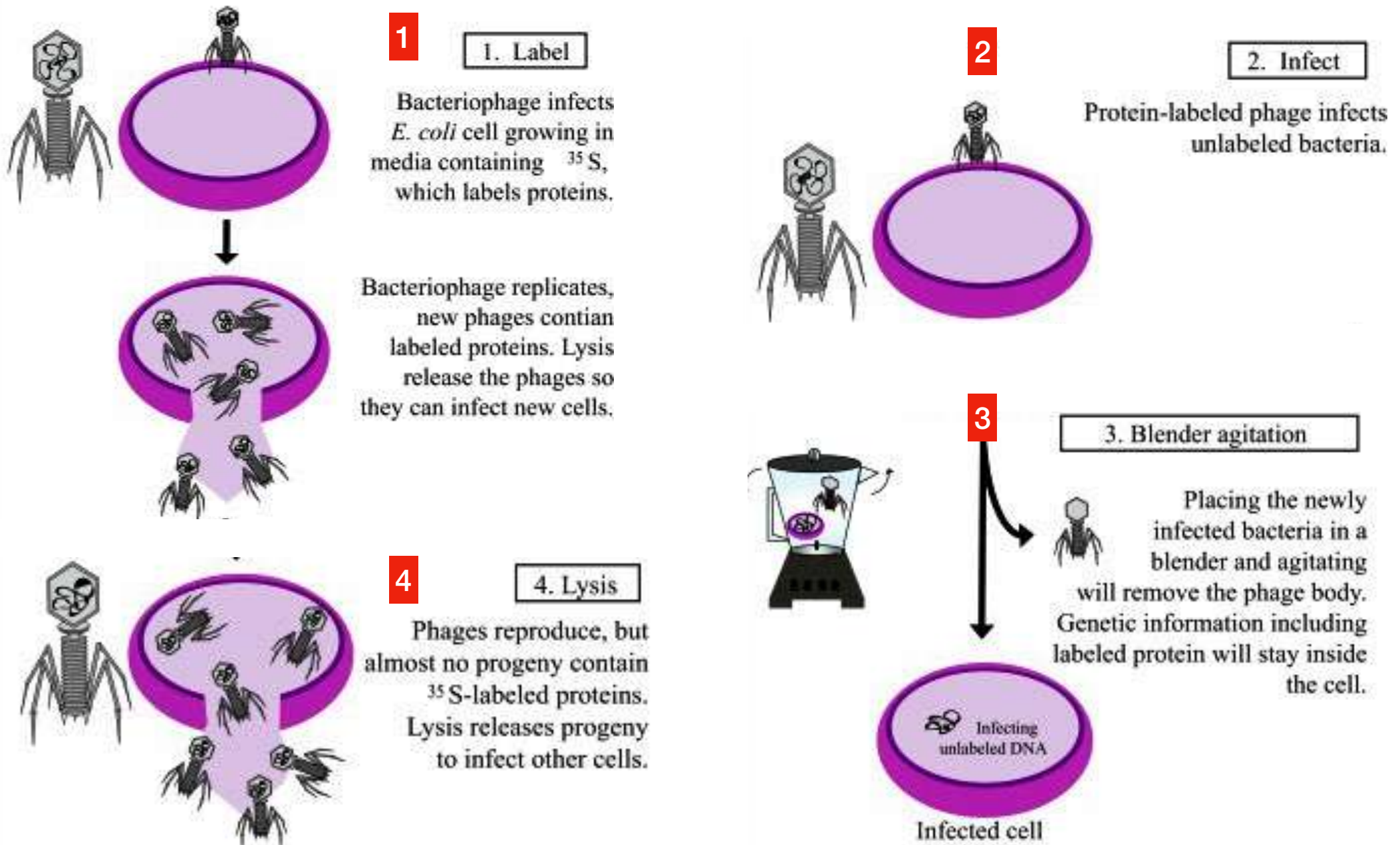
Cellular organelles: Nucleus

How was it proven that **DNA is the carrier** of genetic information?



Cellular organelles: Nucleus

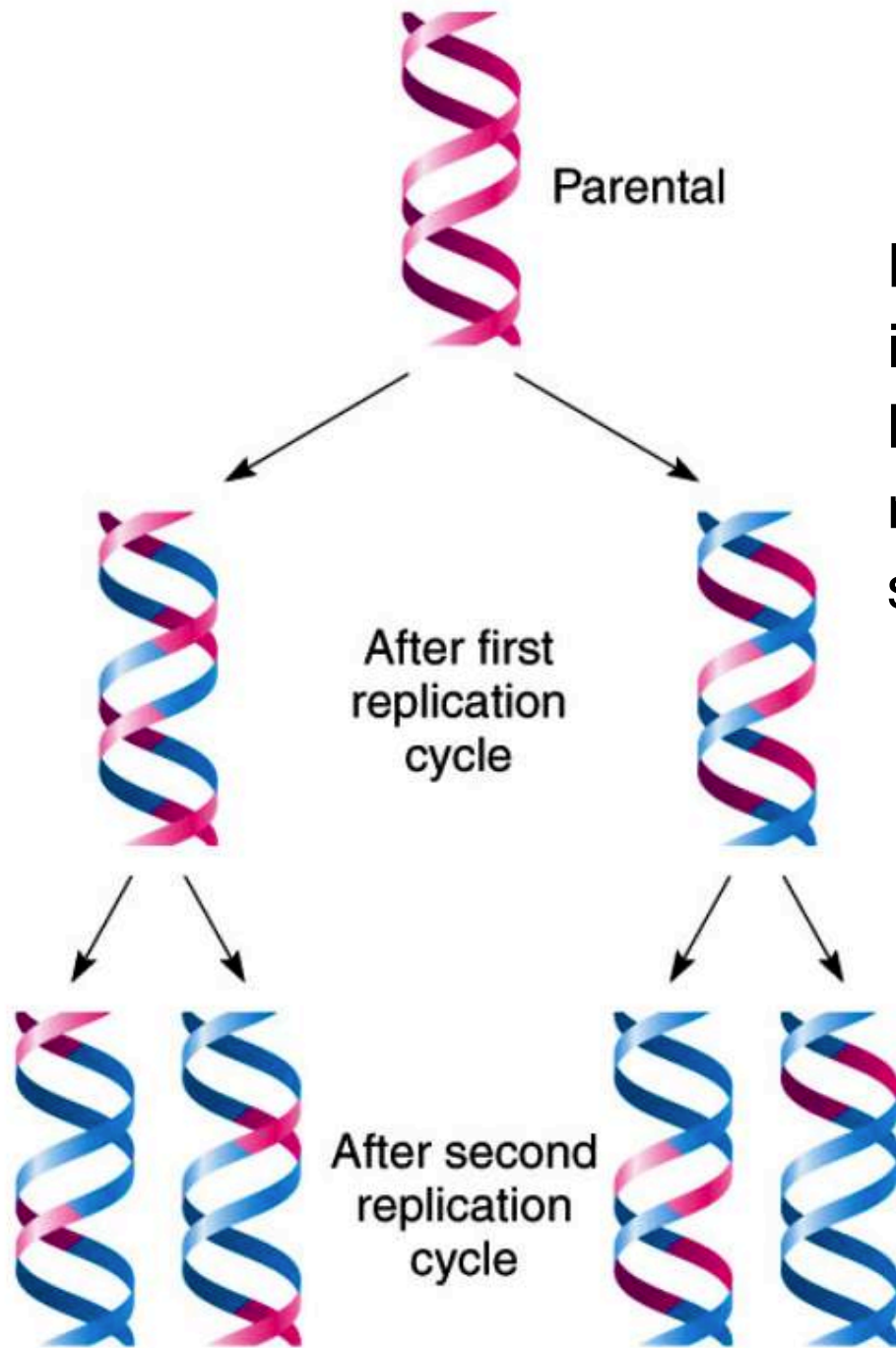
How was it proven that **PROTEINS are not** the carrier of genetic information?



Cellular organelles: Nucleus - DNA replication

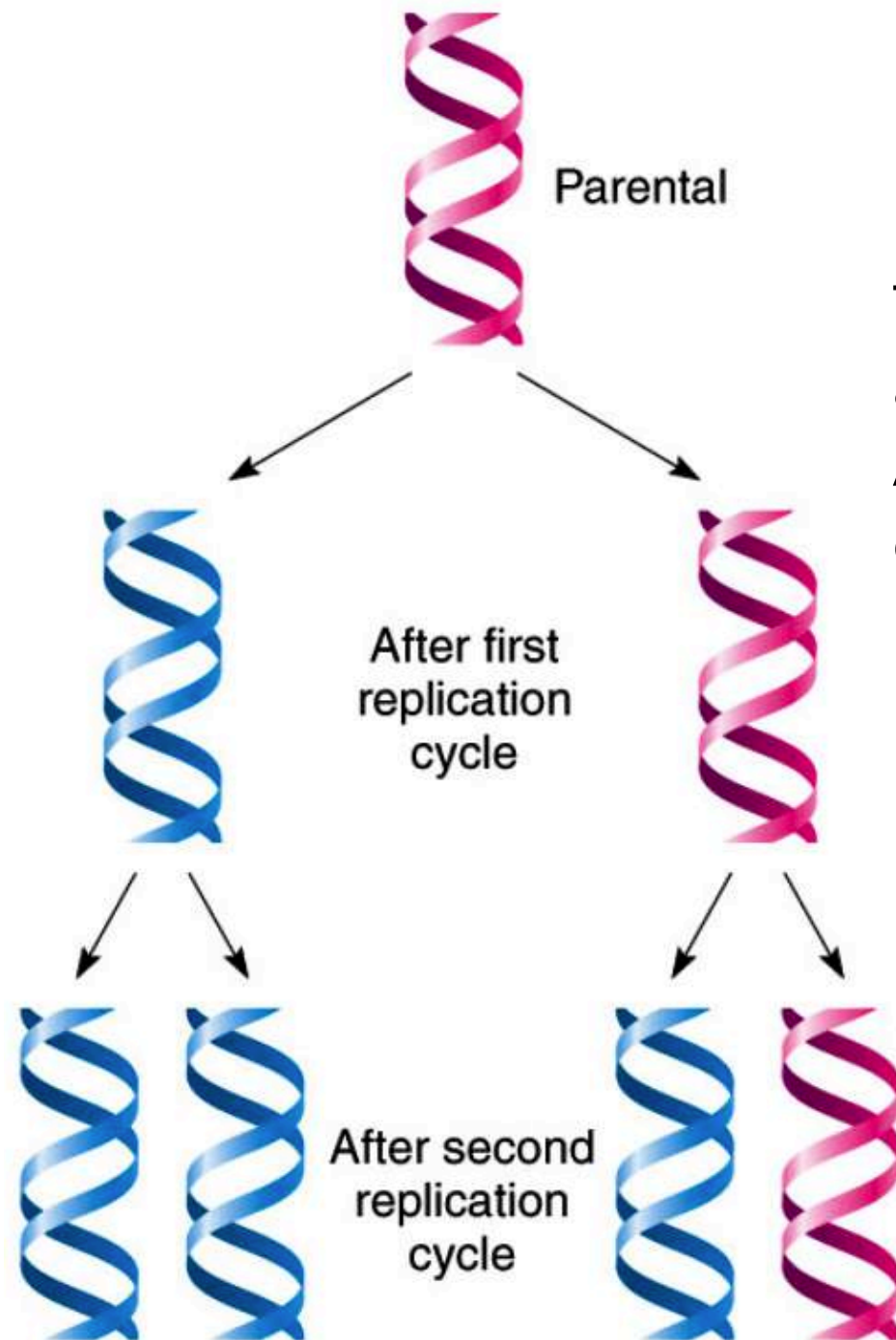
Dispersive model of DNA replication

DNA material in the two parental strands is distributed more or less randomly between two daughter molecules, new molecules have patches of parental strand and new strands



INCORRECT

Cellular organelles: Nucleus - DNA replication



Conservative model of DNA replication

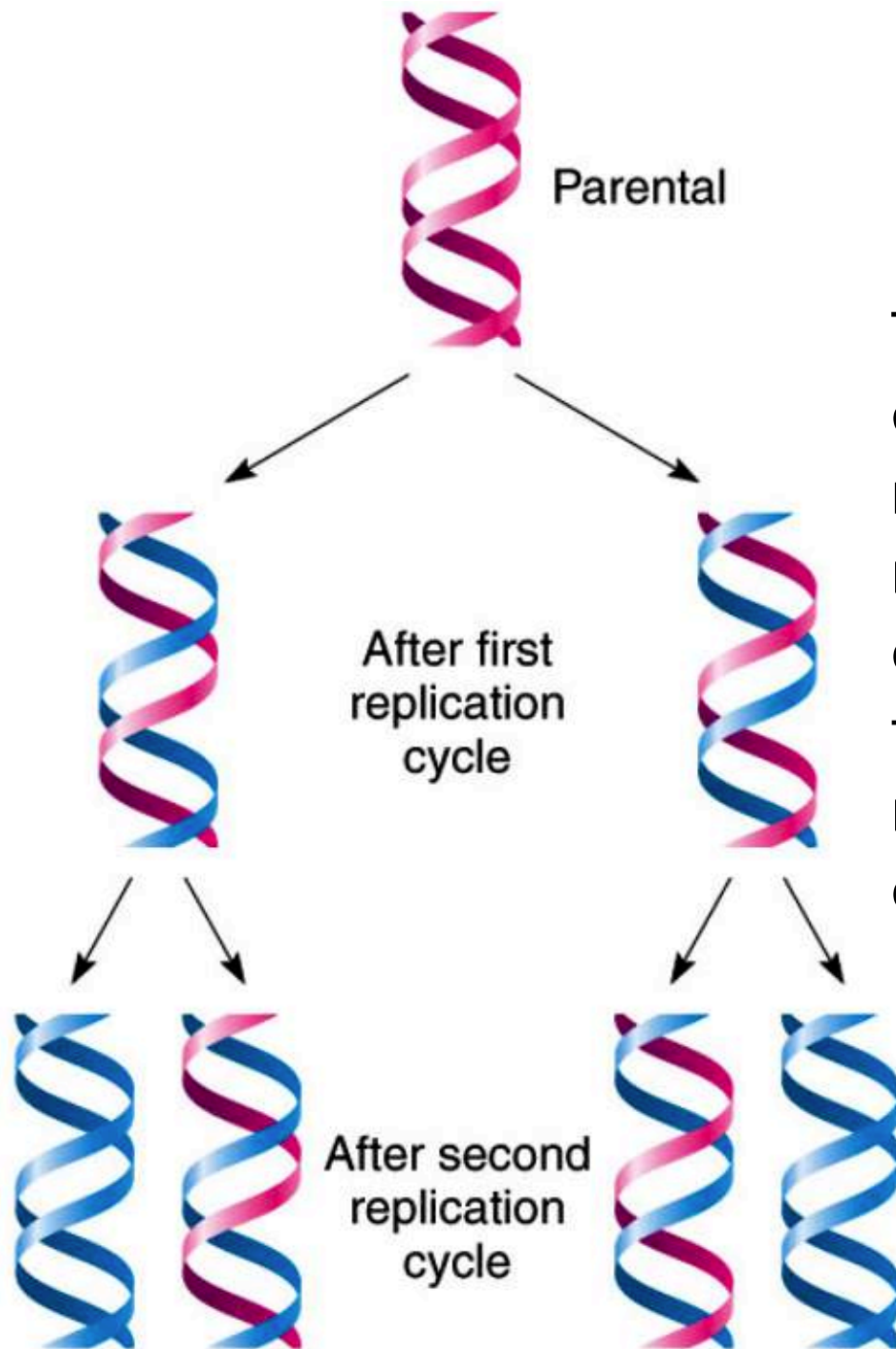
The parental molecule directs synthesis of an entirely new double-stranded molecule. After replication, one molecule is conserved as two old strands and the new molecule has two new strands.

INCORRECT

Cellular organelles: Nucleus - DNA replication

Semi-Conservative model of DNA replication

The two parental strands separate and each makes a copy of itself. After one round of replication, the two daughter molecules each comprises one old and one new strand. After two rounds, two of the DNA molecules consist only of new material, while the other two contain one old and one new strand.



CORRECT

Start ^{15}N -containing
mediumContinue growing
first generation
in ^{14}N medium**Replication
cycle 1**

Continue growing

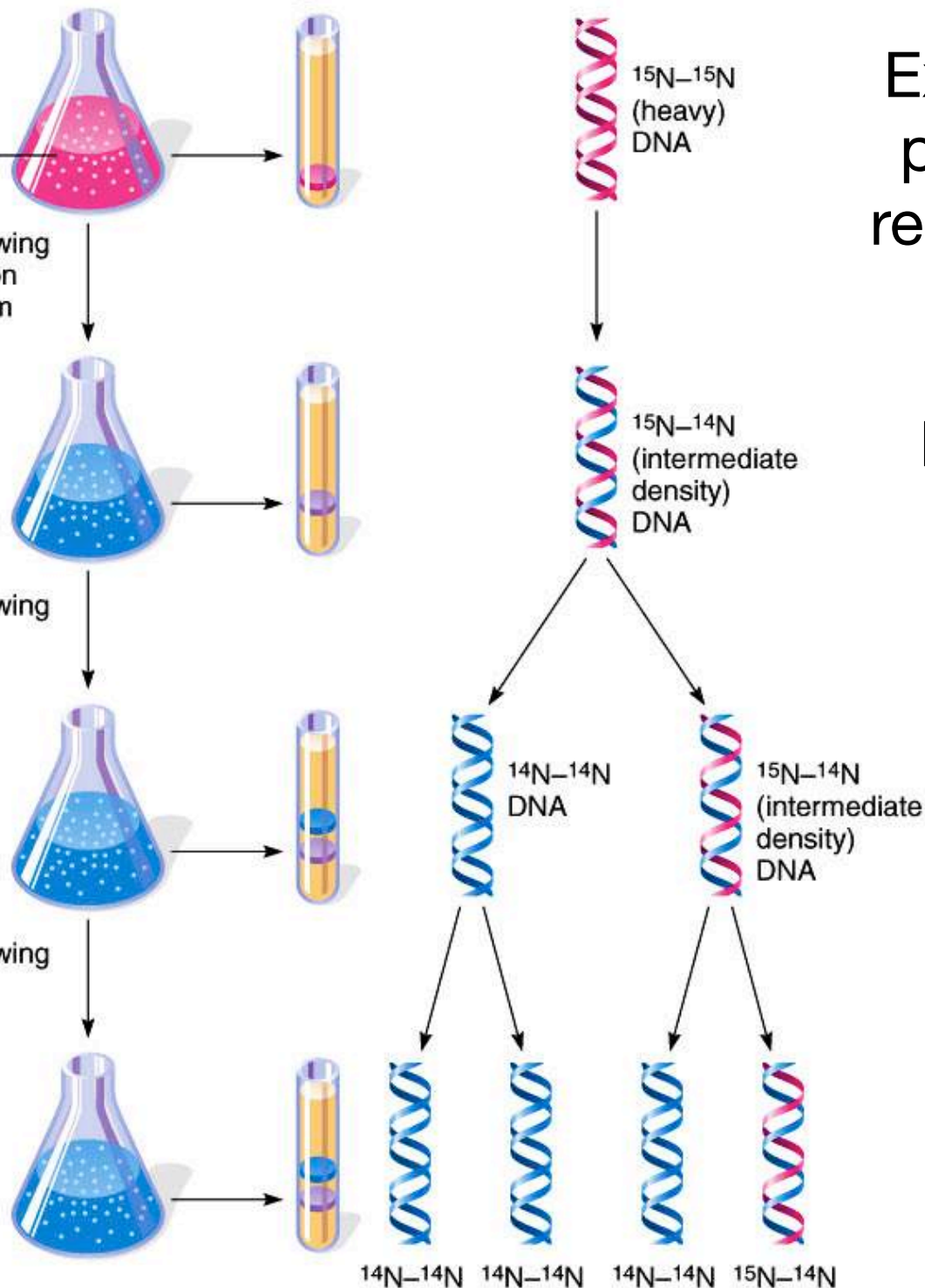
**Replication
cycle 2**

Continue growing

**Replication
cycle 3** ^{15}N - ^{15}N
(heavy)
DNA ^{15}N - ^{14}N
(intermediate
density)
DNA ^{14}N - ^{14}N
DNA ^{15}N - ^{14}N
(intermediate
density)
DNA ^{14}N - ^{14}N ^{14}N - ^{14}N ^{14}N - ^{14}N ^{15}N - ^{14}N

Experiment which
proved that DNA
replication is semi-
conservative

Meselson Stahl
experiment

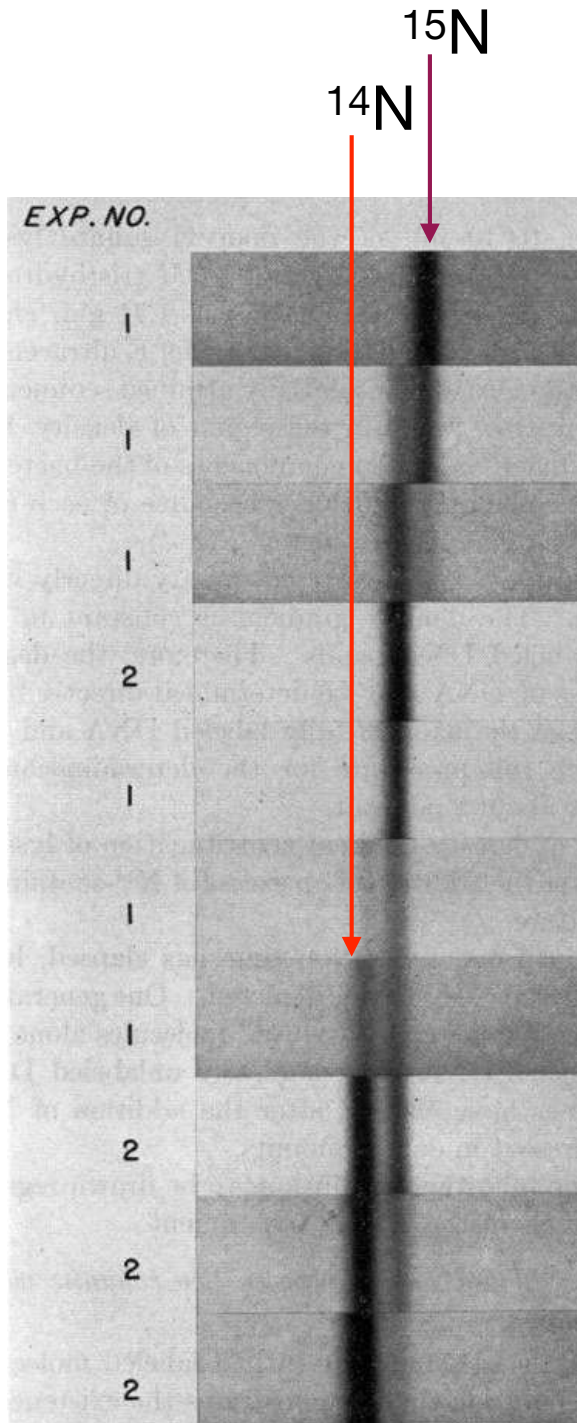


Meselson Stahl experiment

- *E. coli* was grown for many generations in $^{15}\text{NH}_4\text{Cl}$ medium to label the DNA with the heavy isotope ^{15}N
- The medium was diluted 10-fold with $^{14}\text{NH}_4\text{Cl}$ as exponential growth continued
- Samples were taken from the growing bacterial culture at various times to analyze the distribution of DNA densities in a CsCl gradient
- ^{15}N and ^{14}N isotopes have different densities
- They will “settle” in a gradient of CsCl at different positions

<https://www.jove.com/v/1352/dna-extraction-from-022-m-sterivex-filters-cesium-chloride-density>

Meselson Stahl experiment



- If the semi-conservative model is correct, then as the bacteria divides (DNA replicates), the original ^{15}N label (seen as a band on the CsCl gradient) should get diluted (the band becomes less intense as cells divide)
- Additionally, the ^{14}N label (seen as a band on the CsCl gradient) should get enhanced (the band becomes more intense as cells divide)
- Eventually there will be no strand made of only ^{15}N
- There will always be some hybrid ^{15}N - ^{14}N strands. This amount is constant as it depends on the original number of ^{15}N strands
- The comparative intensity of the ^{15}N - ^{14}N band will be less than that of the ^{14}N strands