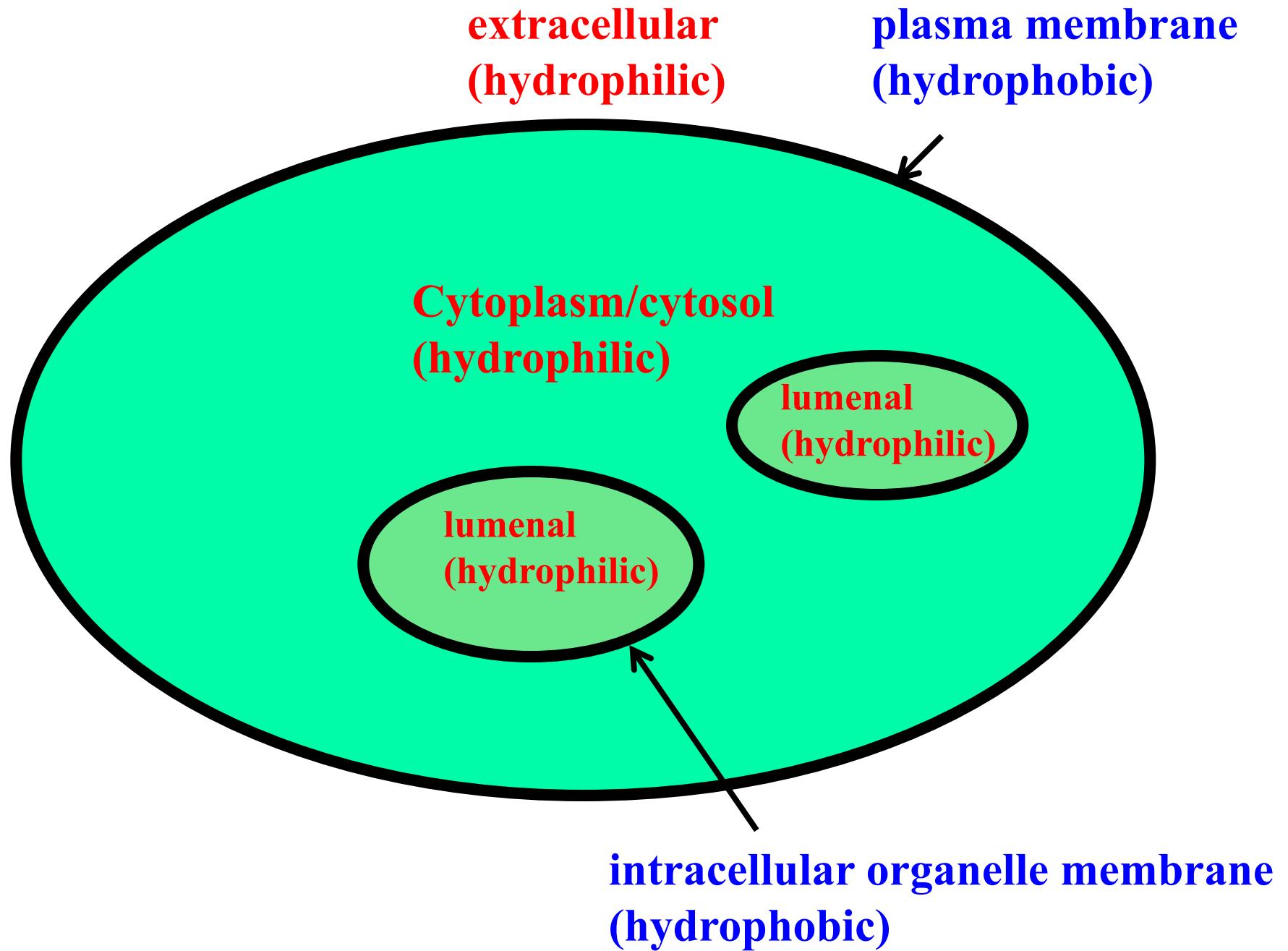


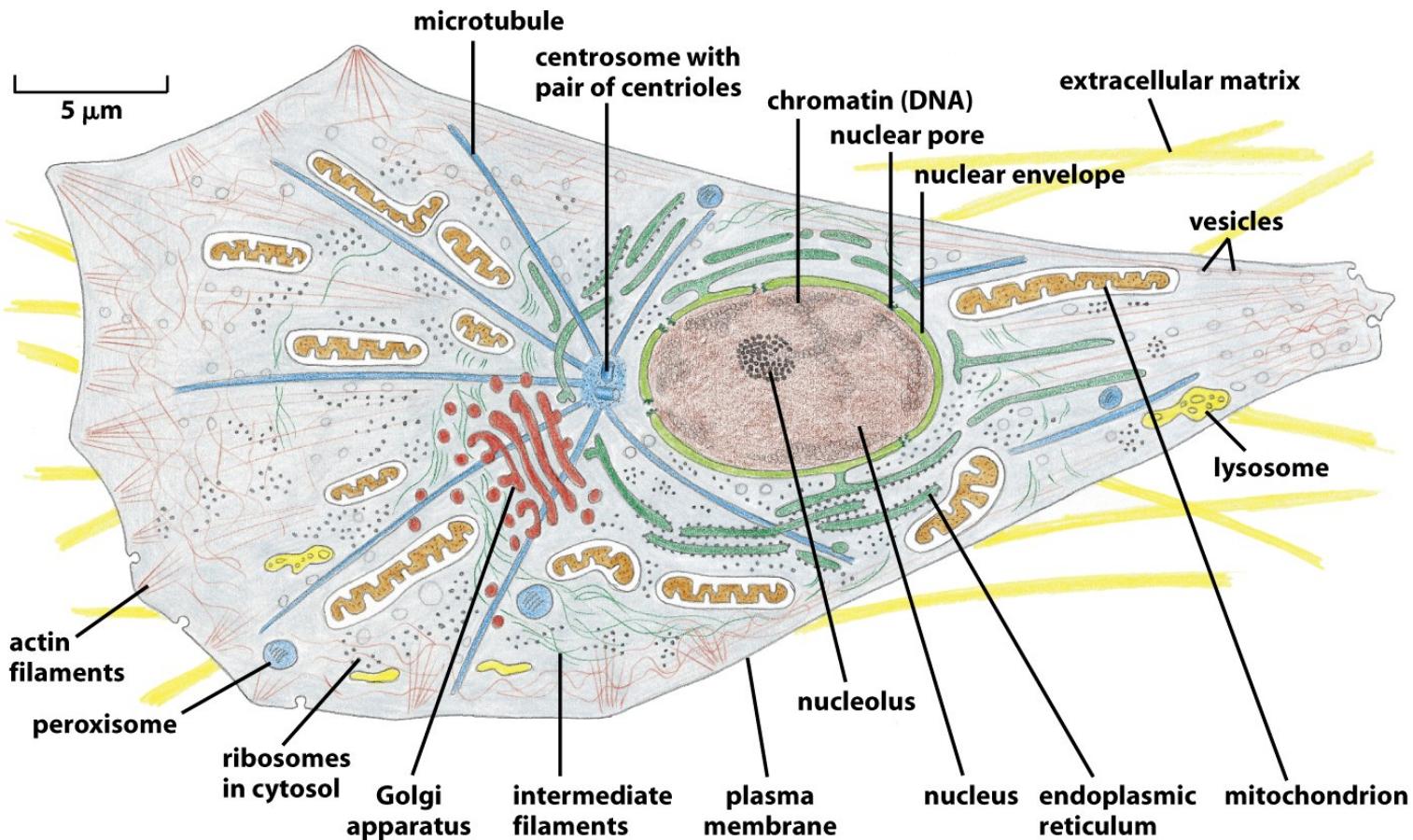
Cell Anatomy: Cells Have Multiple Membranes and Organelles



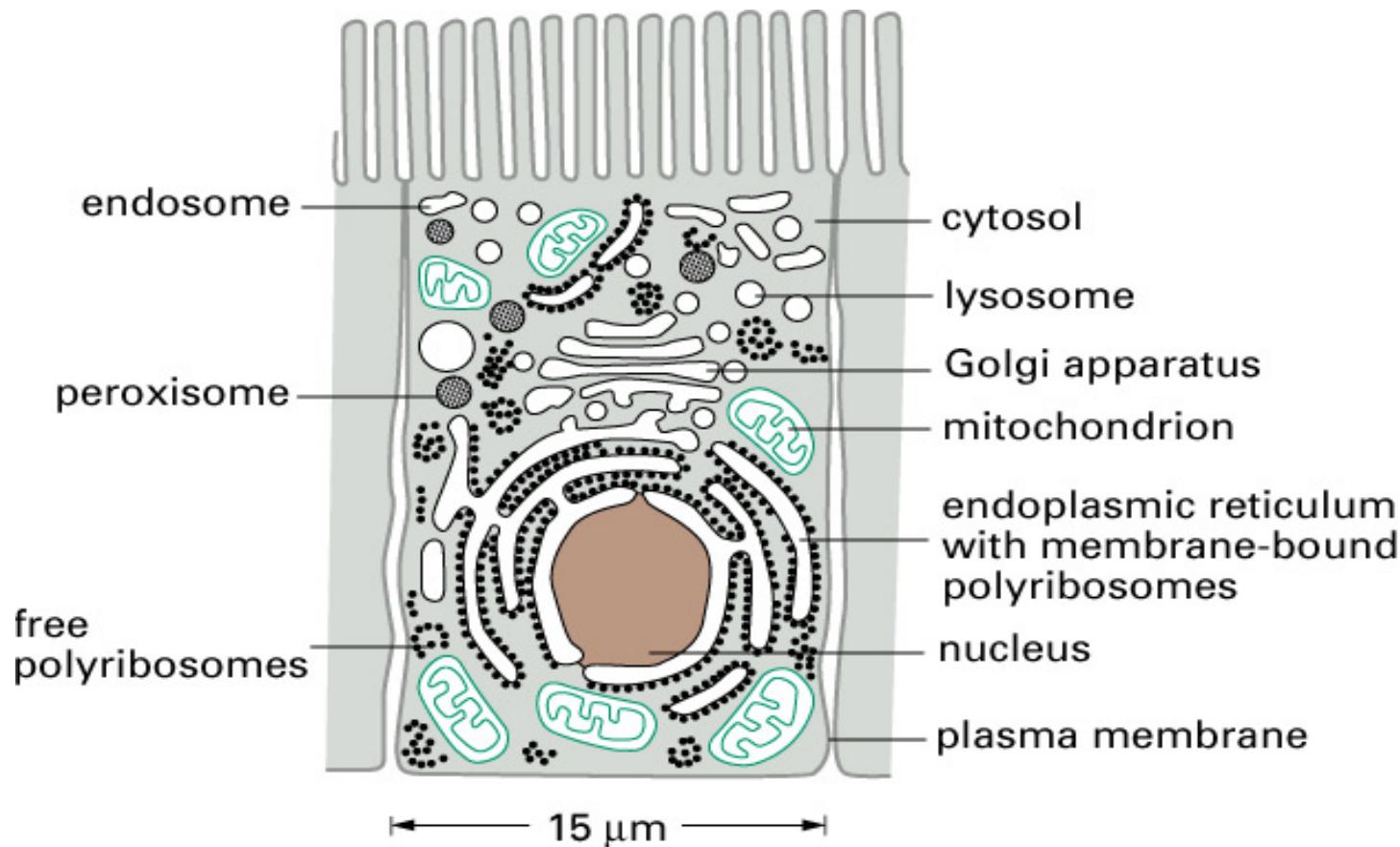
Main Intracellular Organelles or Compartments

- Nucleus:** Contains nuclear genome, DNA and RNA synthesis (has two membranes).
- Peroxisomes:** Oxidizes toxic molecules and fatty acids.
- Mitochondria:** ATP synthesis via oxidative phosphorylation, has its own genome (has two membranes).
- Chloroplasts (plants):** Site of photosynthesis, has its own genome (has two membranes).
- Endoplasmic Reticulum (ER):** Site of lipid and membrane protein synthesis, the secretory pathway, intracellular Ca^{2+} storage for signaling (cytosolic, nuclear, mitochondrial and peroximal proteins are synthesized in the cytosol).
- Golgi:** Receives and modifies membrane proteins & lipids from the ER, then sorts them into endosomes, lysosomes, and the plasma membrane, the secretory pathway. Cycling among compartments occurs.
- Endosomes:** Storage and sorting compartments of internalized plasma membrane proteins and lipids.
- Lysosomes:** Degradation site of cellular organelles and macromolecules, as well as internalized foreign particles.

Various Major Anatomical Features of the Cell

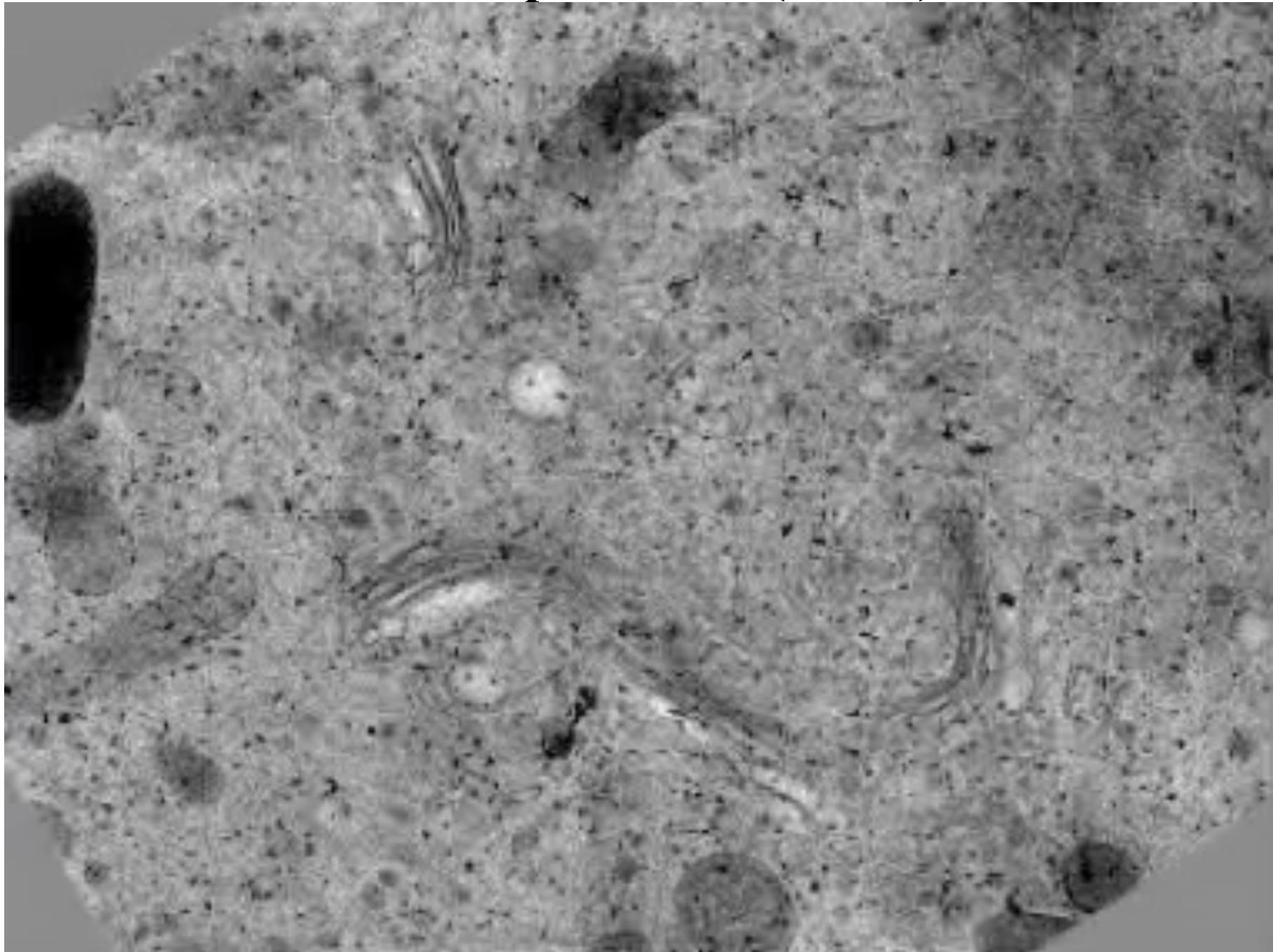


Various Major Anatomical Features of the Cell



Each compartment has unique protein and lipid composition.

Cell Compartments (movie)

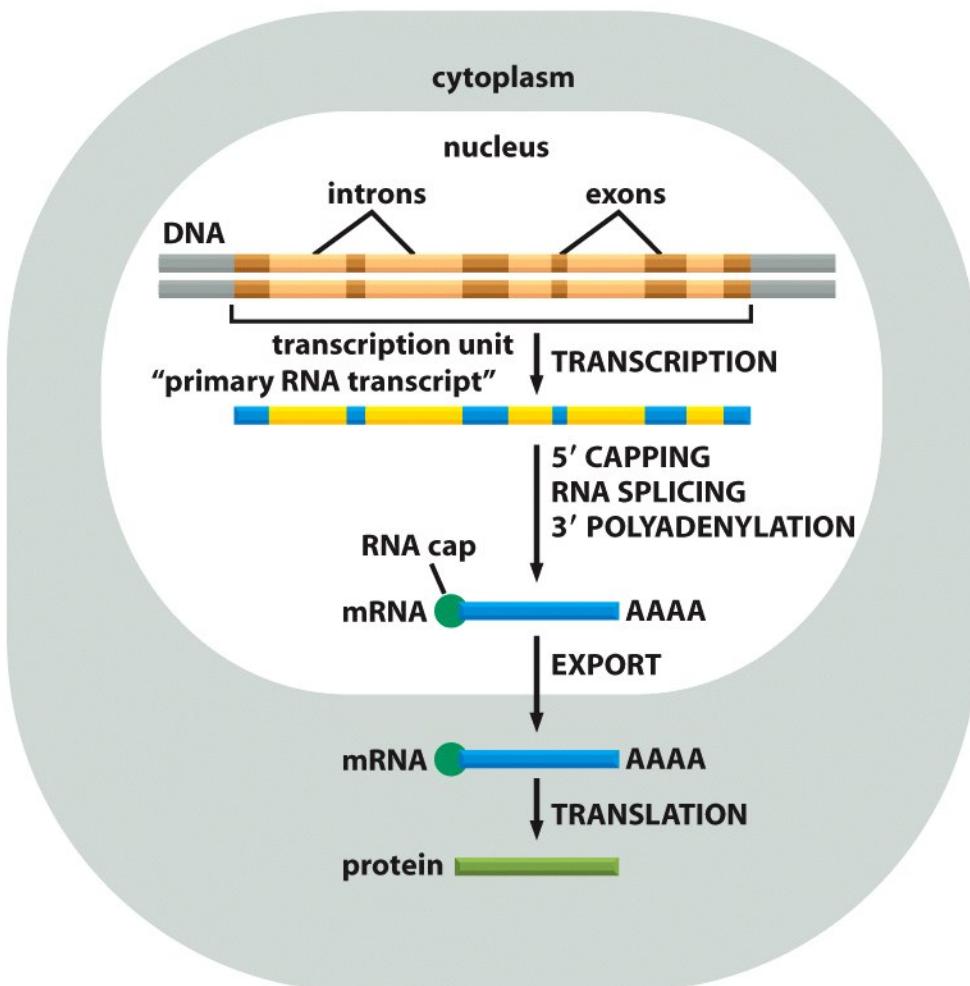


Nucleus

The Eukaryotic Cell Nucleus Contains Almost All Genetic Information

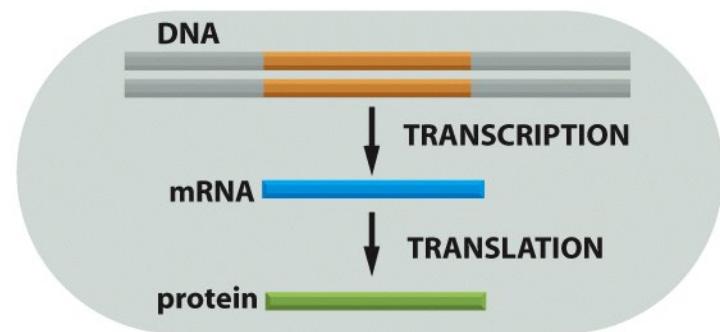
(A)

EUCARYOTES



(B)

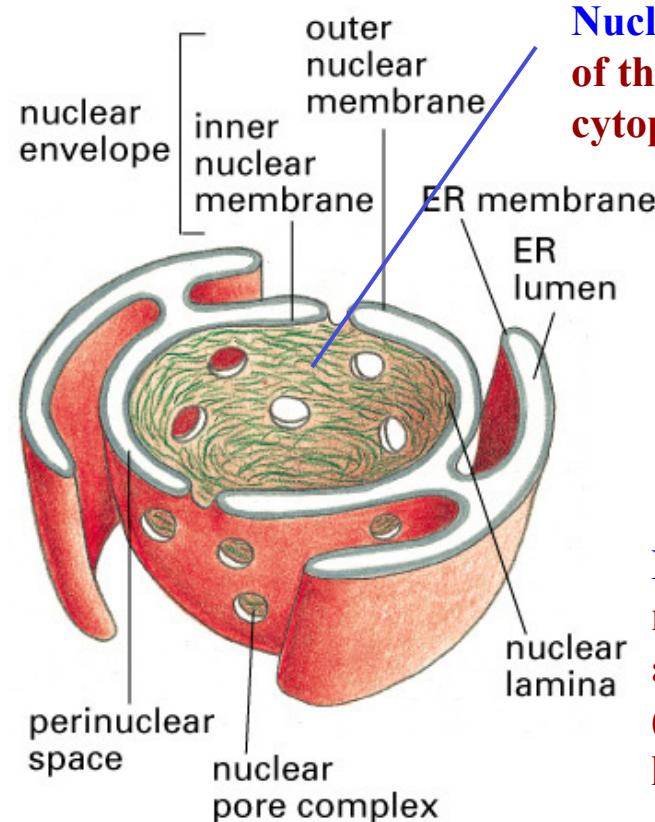
PROKARYOTES



No such structure exists among prokaryotes

Structure of the Nucleus

Nuclear envelope is composed of two (outer and inner) membranes with the outer nuclear membrane connected to the ER membrane.



Nucleoplasm is the liquid equivalent of the nucleus to the “cytosol” of the cytoplasm.

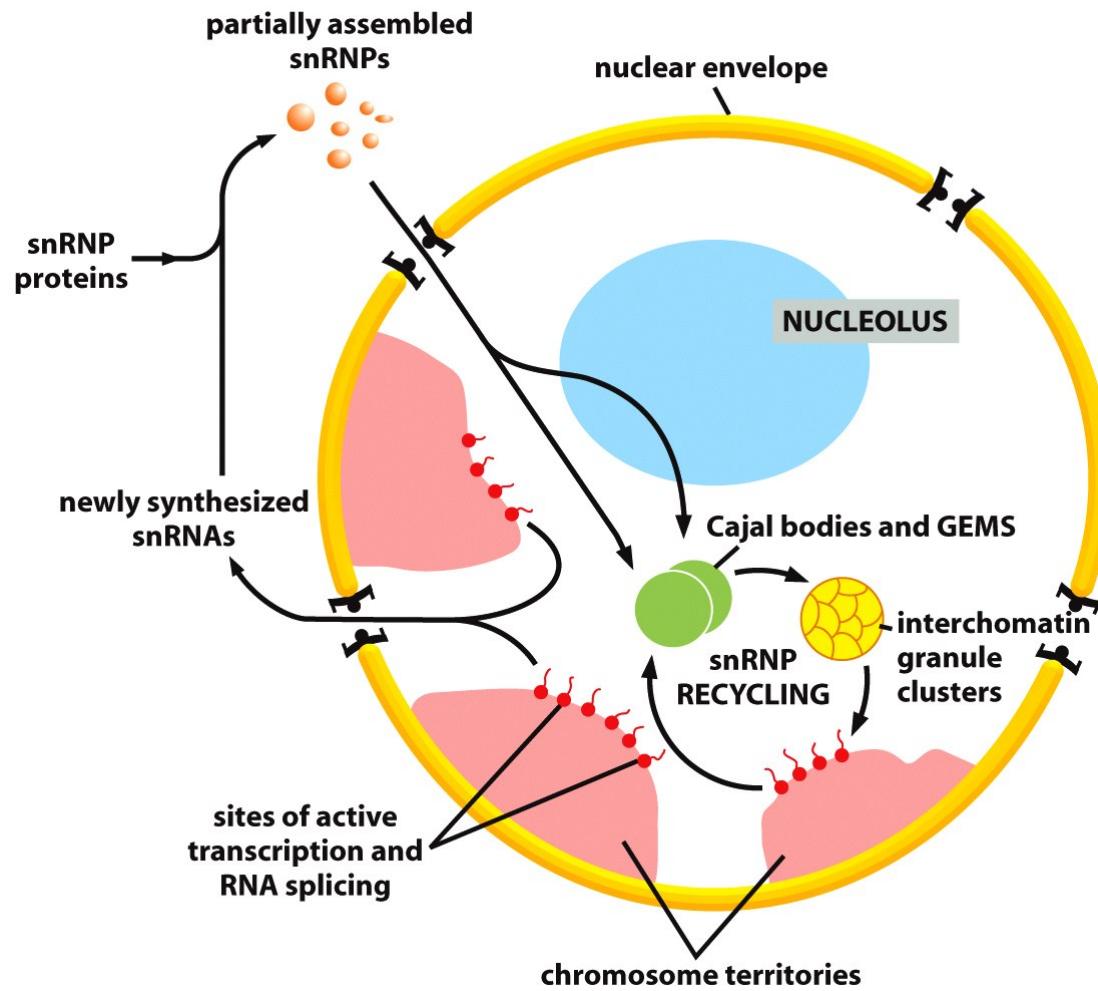
Nucleus (subnuclear structure, not shown) is a compartment where ribosomes are produced.

Perinuclear space is the space between the outer and inner membranes and it is connected to the ER lumen.

Nuclear lamina is a structure near the nucleus inner membrane and it is composed of lamin (a cytoskeletal protein) and lamin-associated proteins.

Nuclear pore complex (NPC) is a large protein complex located at where the outer and inner nuclear membranes meet. It is the gate of the transport between cytosol and nucleus.

The Nucleus Contains a Variety of Subnuclear Structures

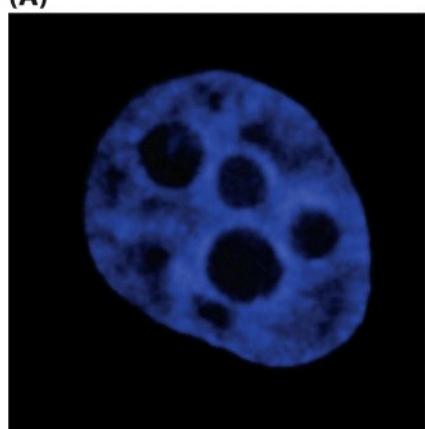
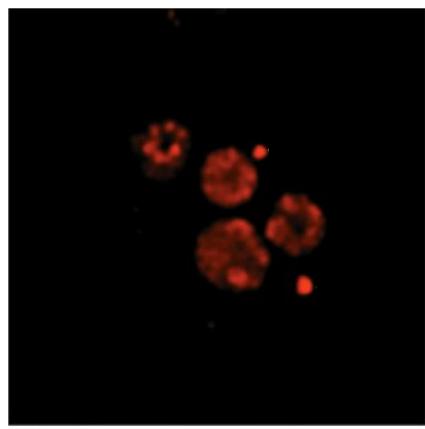


Most of these subnuclear structures are involved in the modulation of gene expression at the level of rRNA or mRNA.

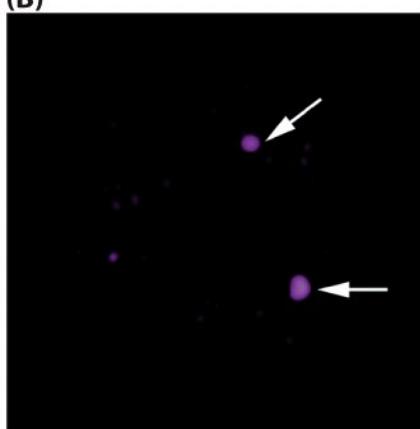
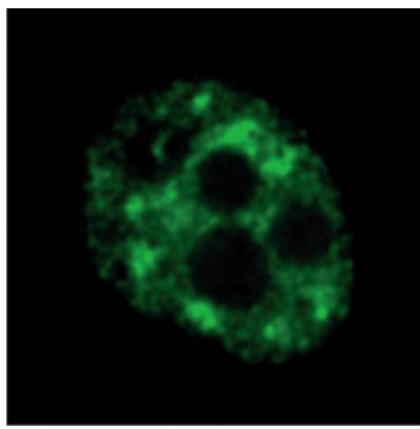
Visualization of Subnuclear Structures

Nucleolus (nucleoli)
& Cajal bodies

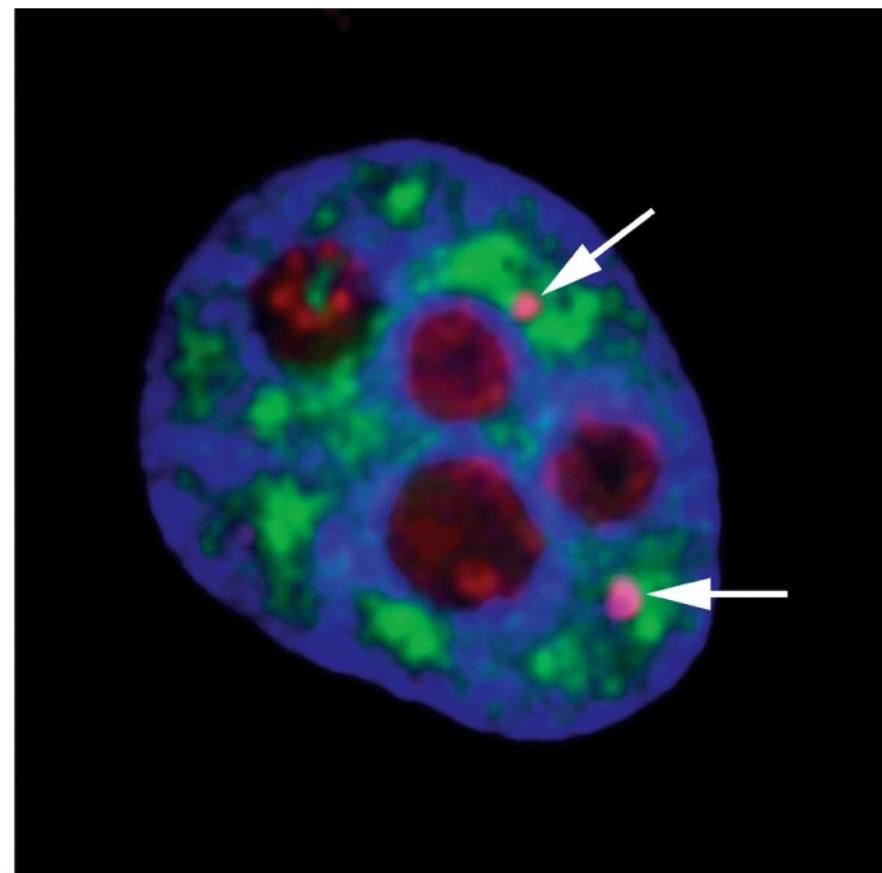
interchromatin
granules



chromatin



Cajal body



5 μm

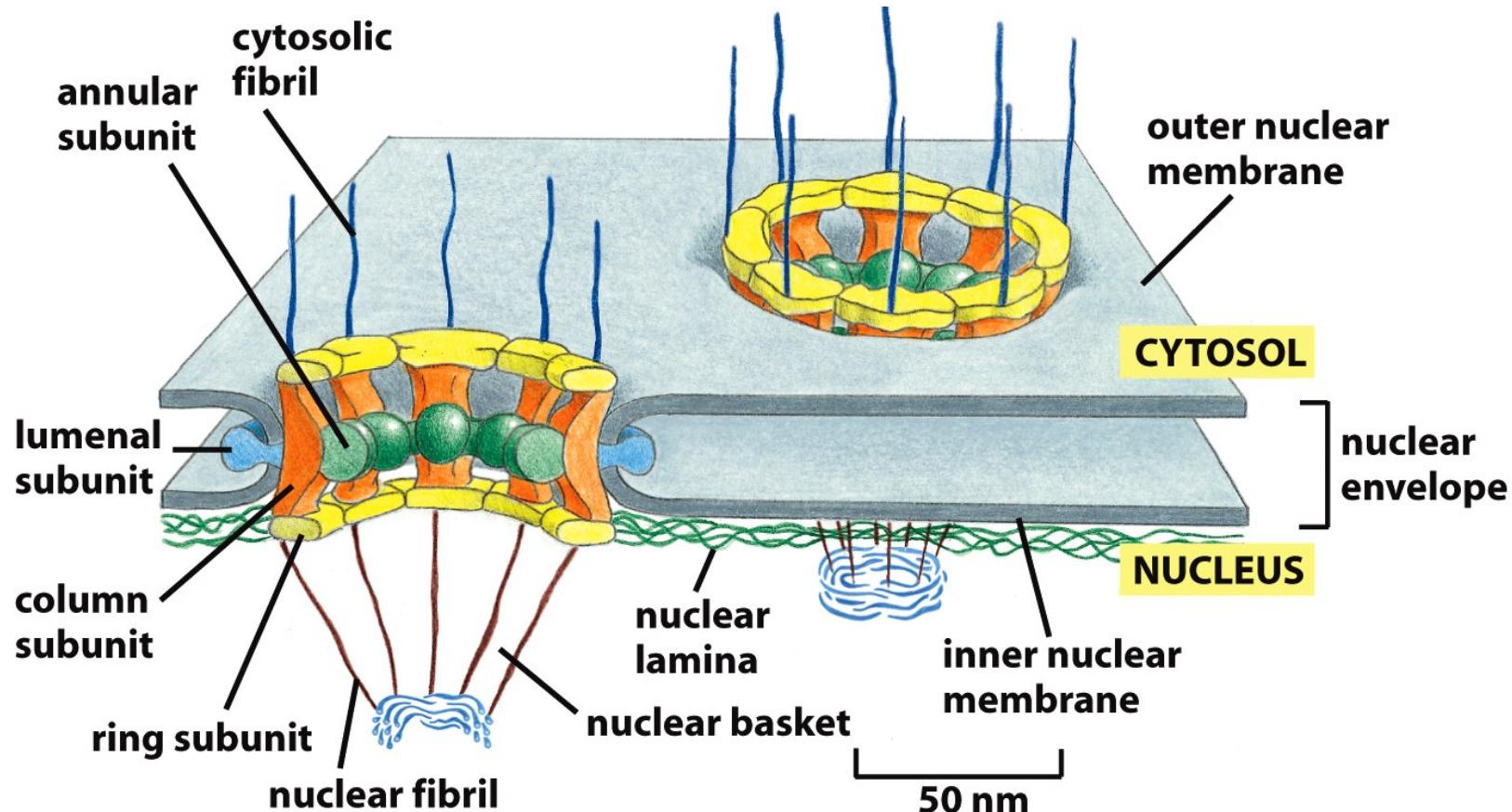
The Biogenesis of Nuclear Proteins

The nucleus acquires its proteins from the cytosol.

**Newly synthesized nuclear proteins enter the nucleus
by the Nuclear Pore Complex (NPC).**

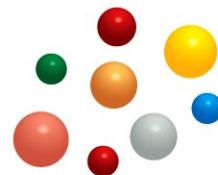
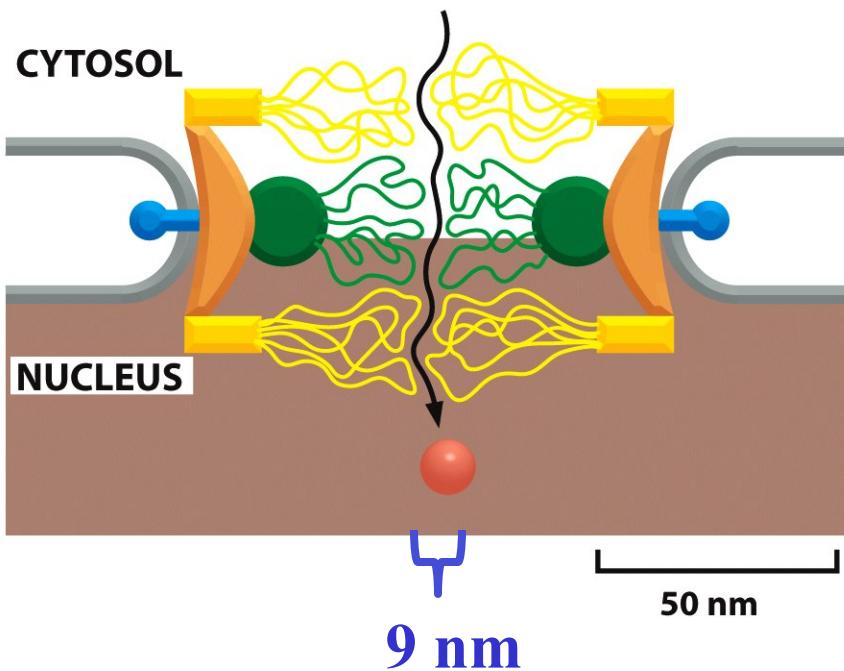
Nuclear Pore Complex (NPC)

Each NPC contains ~100 different proteins



Nucleoporins: a major component of NPC complex (> 50 members found)
lining the central pore of the NPC complex.
They are primary mediators of the cytoplasm-nucleus transport.

Passive Transport of Small Molecules through the NPC



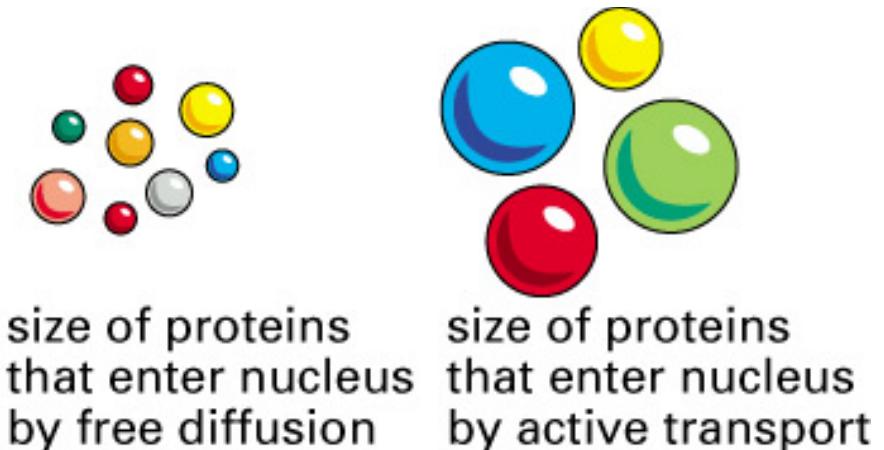
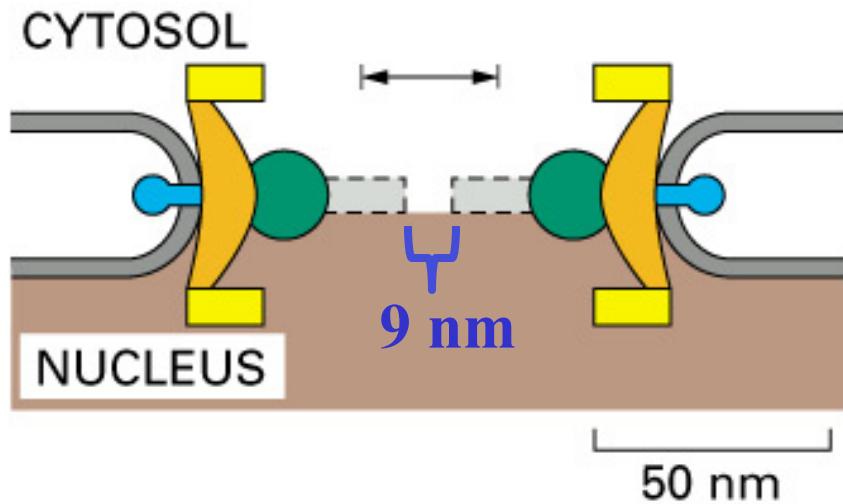
water, ions,
small metabolites,
small proteins (<60 kD)

size of molecules
that enter nucleus
by free diffusion

pore size estimated from
free diffusion experiments

Protein larger than 60 kD can be found in the nucleus. How are these transported?

Transport of a Ribosome by the NPC

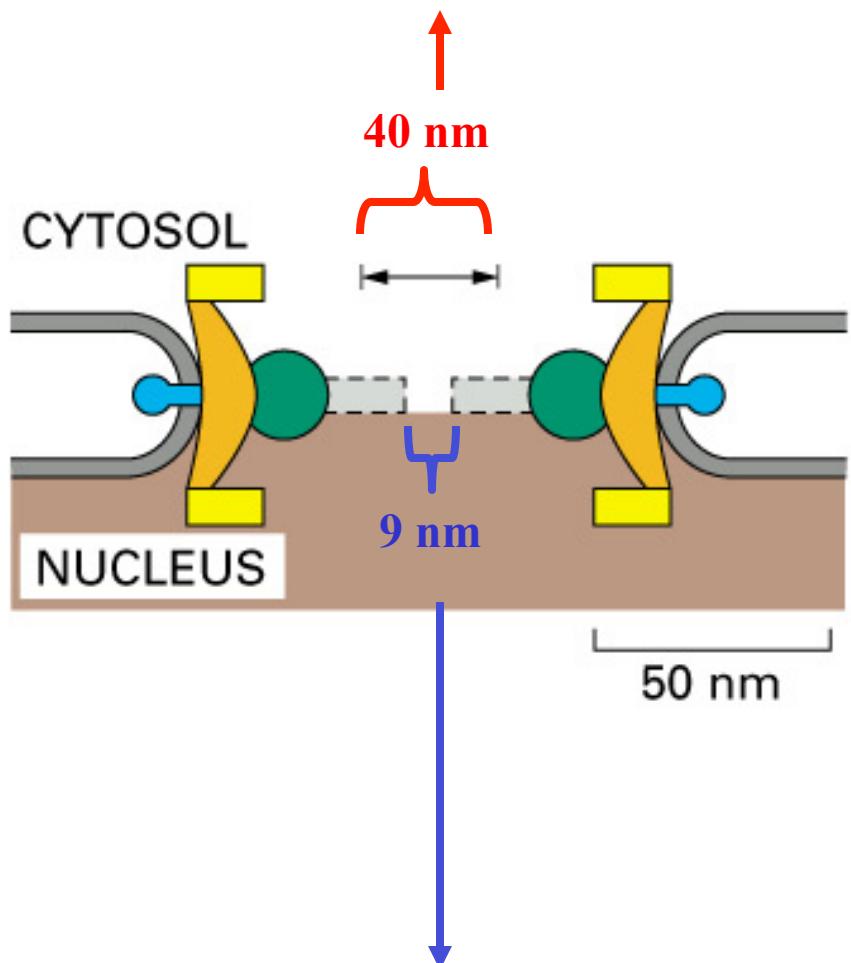


For example, ribosome assembly takes place in the nucleus but the assembled ribosome needs to be in the cytosol to translate mRNA. Thus, a completely assembled ribosome composed of many proteins and RNAs (>20 nm, >1000 kD) must go through the NPC to enter the cytosol.

How does this happen given that the pore size of free diffusion is 9 nm?

Active transport of large molecules through the NPC

during the active transport.

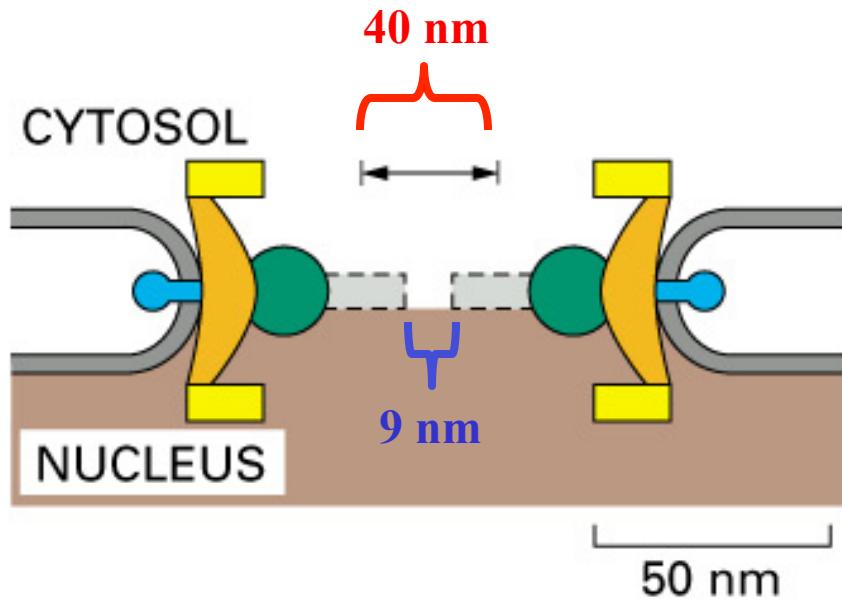


The large pore size of NPC during the active transport can allow the large protein complex such as a ribosome to go through

during the passive transport

Transport Through the Nuclear Pore Complex

Thus NPC functions as a diaphragm with adjustable pore size



water, ions,
small metabolites,
small proteins (<60 kD)



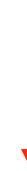
protein or protein
complex (>60 kD)



size of proteins
that enter nucleus
by free diffusion



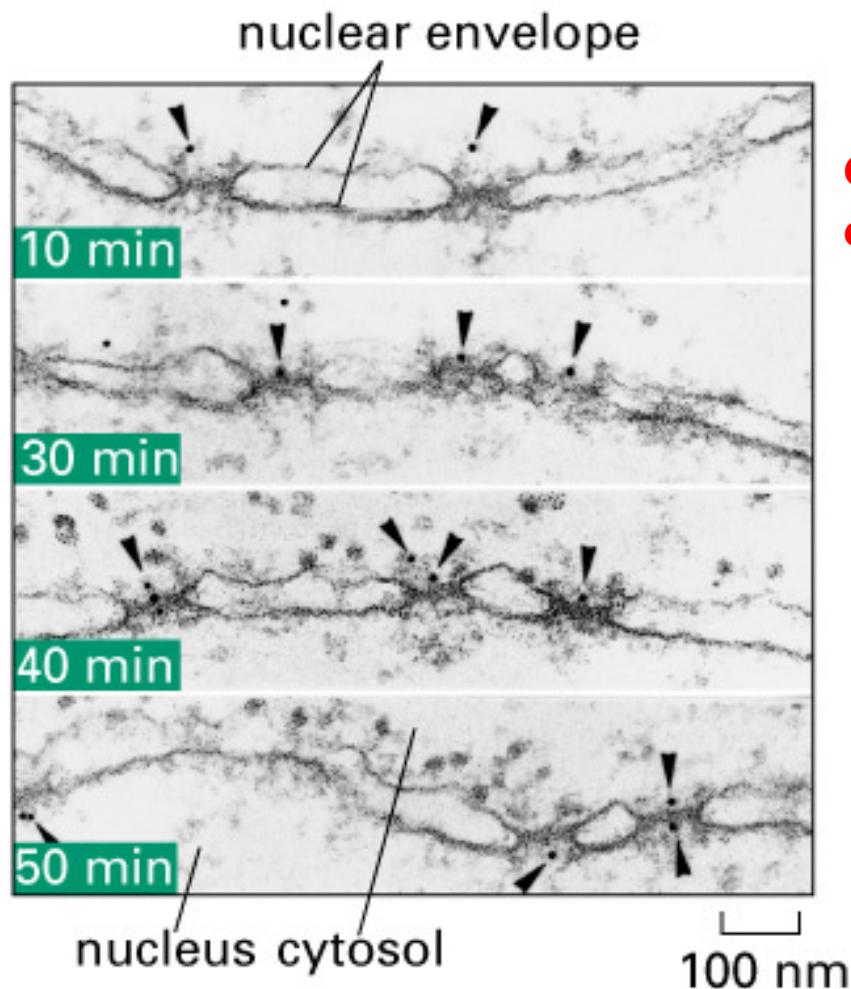
passive diffusion
no energy required



active transport
energy required

Evidence of Active Transport by the Nuclear Pore Complex

Gold particles coated with a peptide containing a nuclear localization signal injected into a cell (gold is electron dense allowing the visualization (arrows) by electron microscopy)



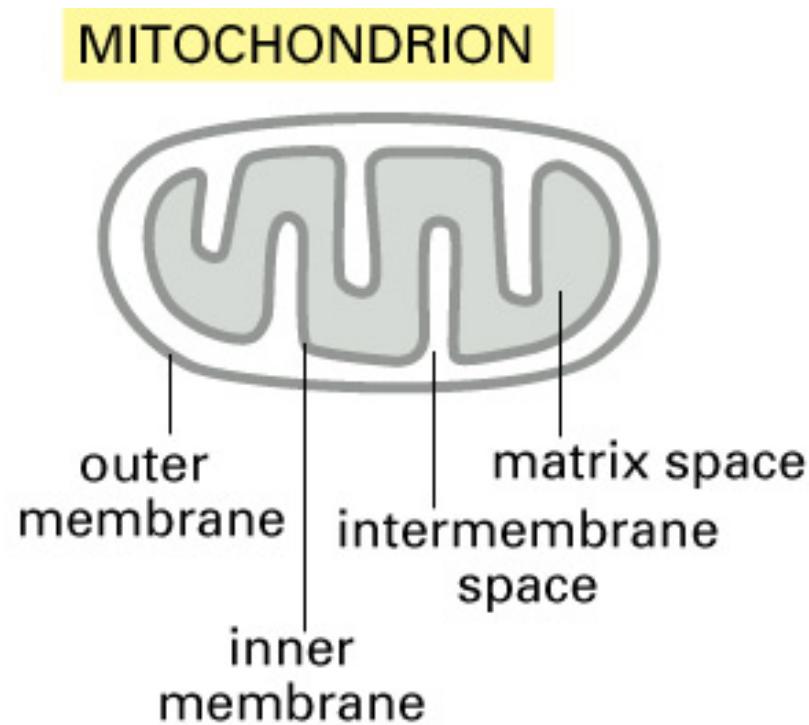
Gold particles first attached to the cytoplasmic side of a NPC

Gold particle then moved into the NPC

Gold particle has appeared in the nucleus

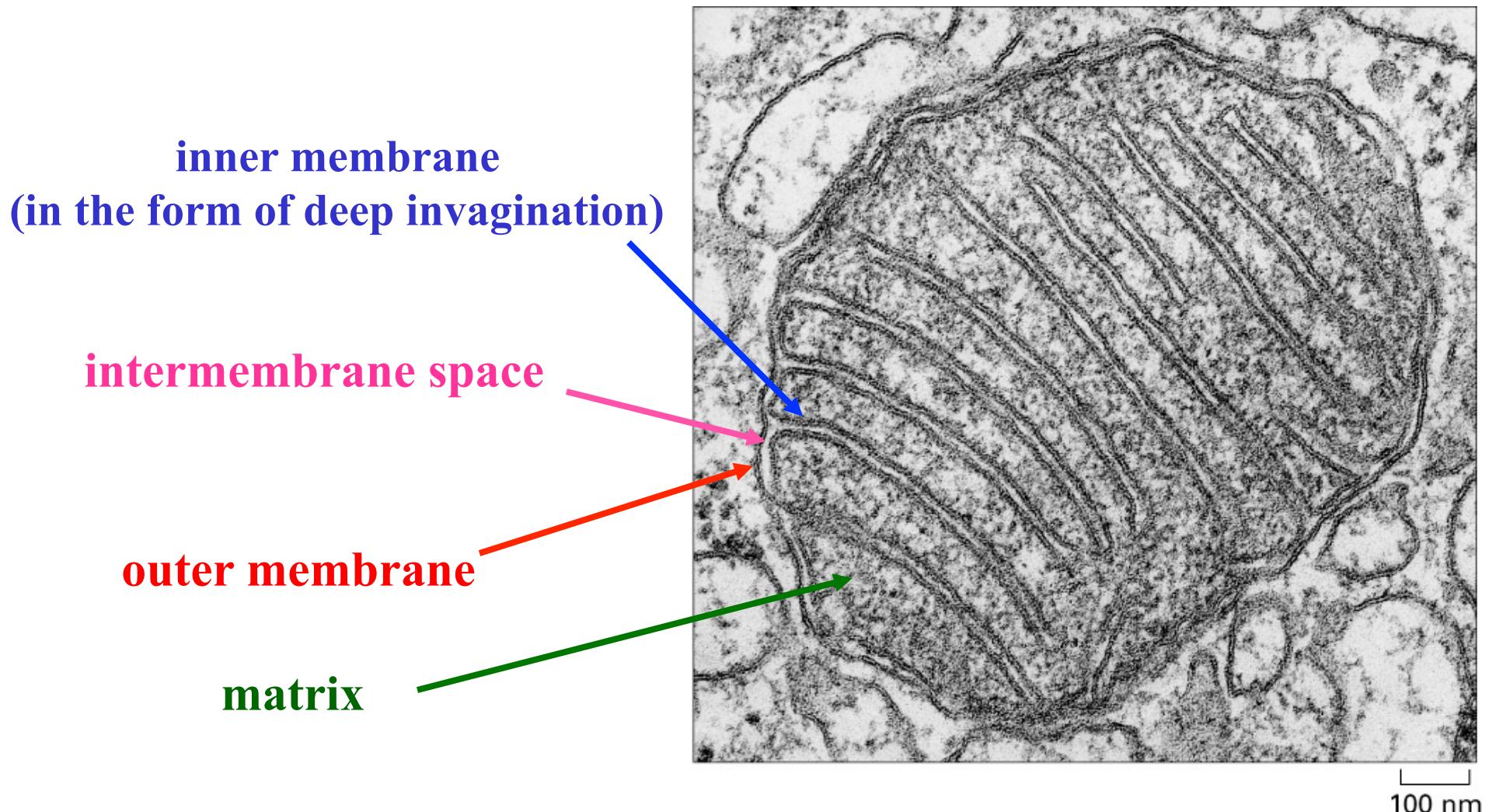
Mitochondria

Basic Anatomy of Mitochondria



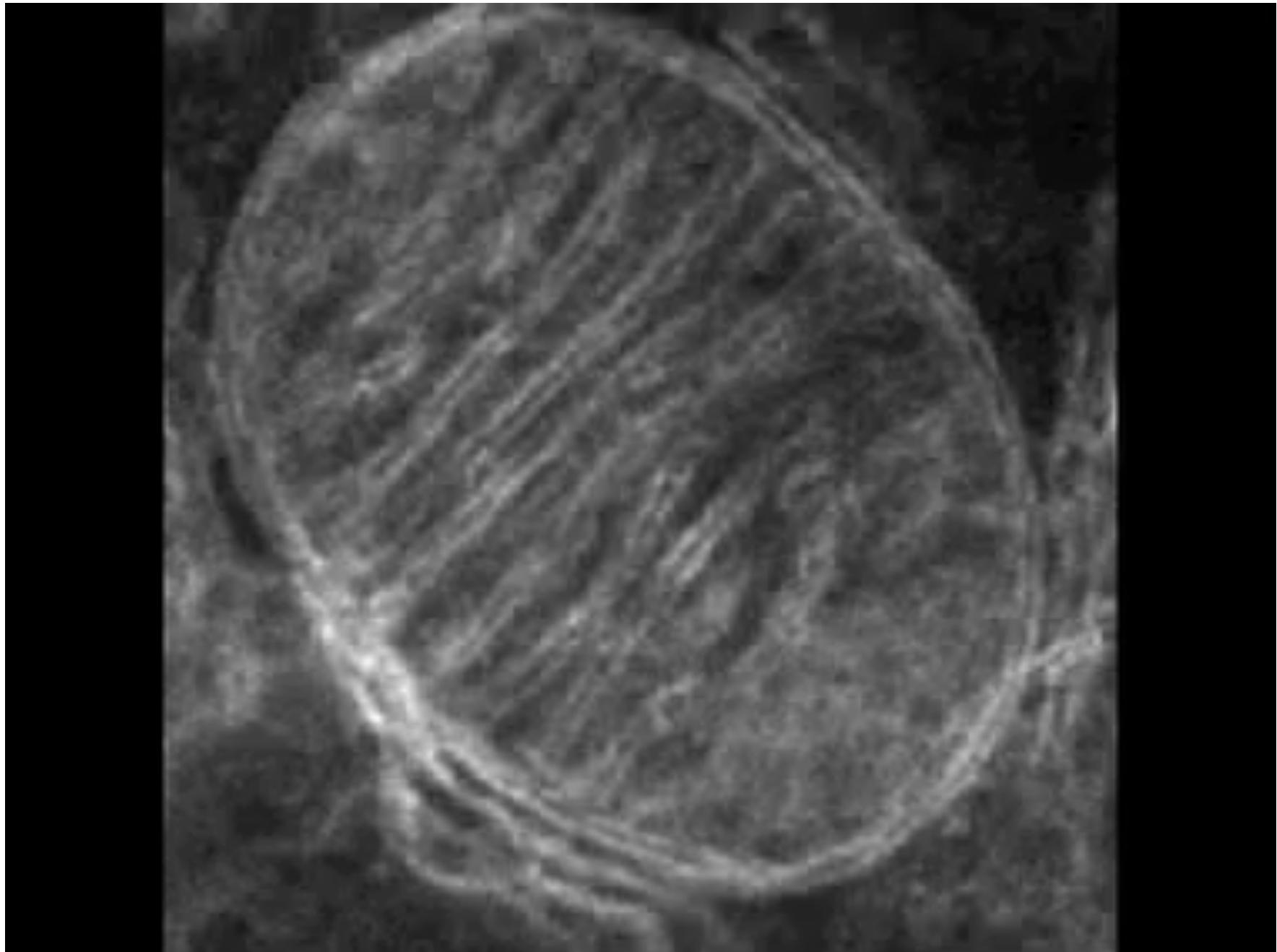
There are contact sites where the outer and inner membranes are in close proximity (not shown here).

Structure of Mitochondria: a closer look



Note the invagination of the inner membrane and the electron-dense materials associated with it – what does this unique structure tell you?
(high surface to volume ratio and protein enriched (~75% protein content))

Mitochondrian (movie)



Function of Mitochondria

(1) Mitochondria are ATP-generating factories required for life.

Oxygen-dependent energy production:

Prokaryotes: plasma membrane

Plants: chloroplasts

Other eukaryotes: mitochondria

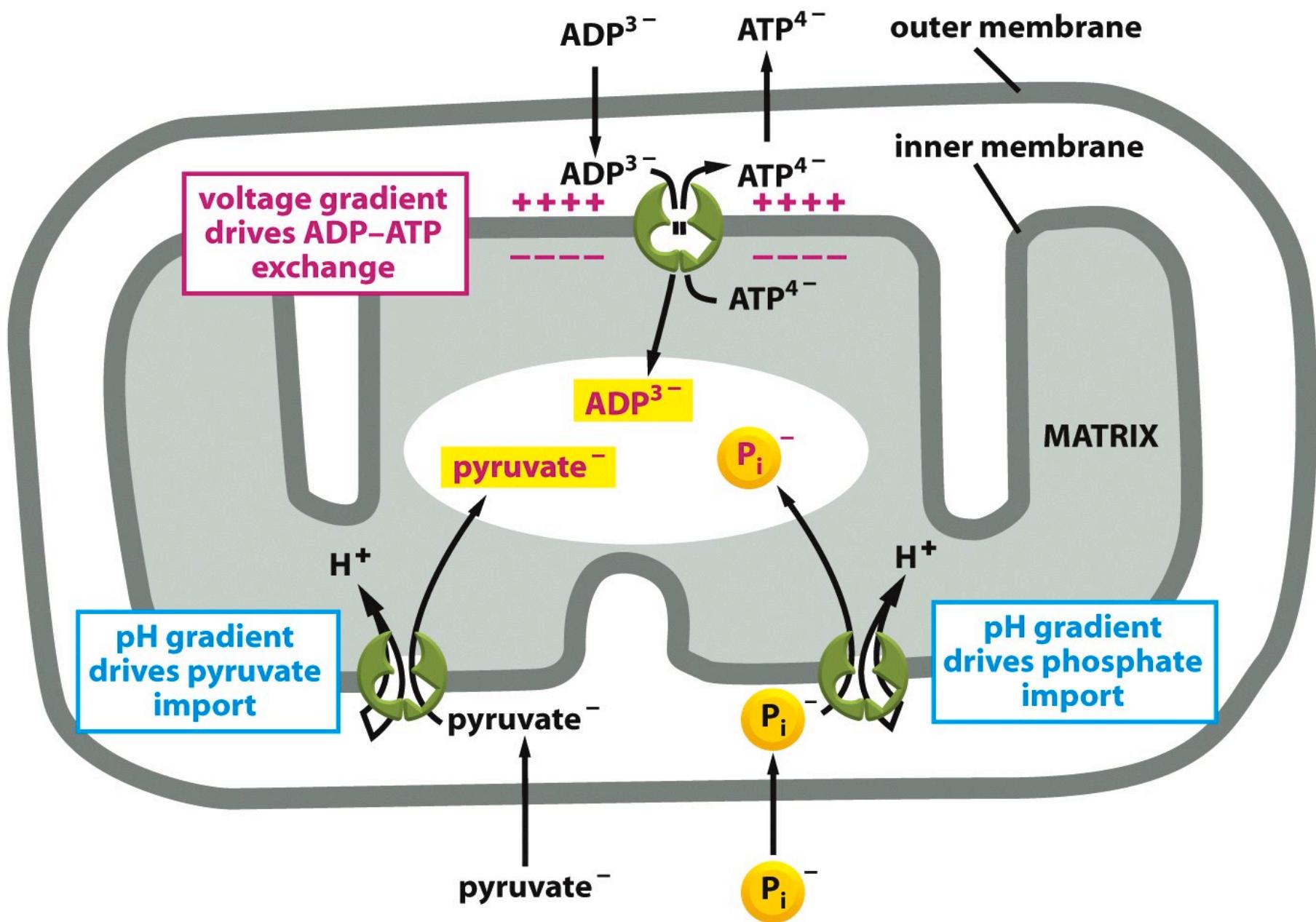
For each glucose metabolized:

2 ATP molecules are generated in the cytosol

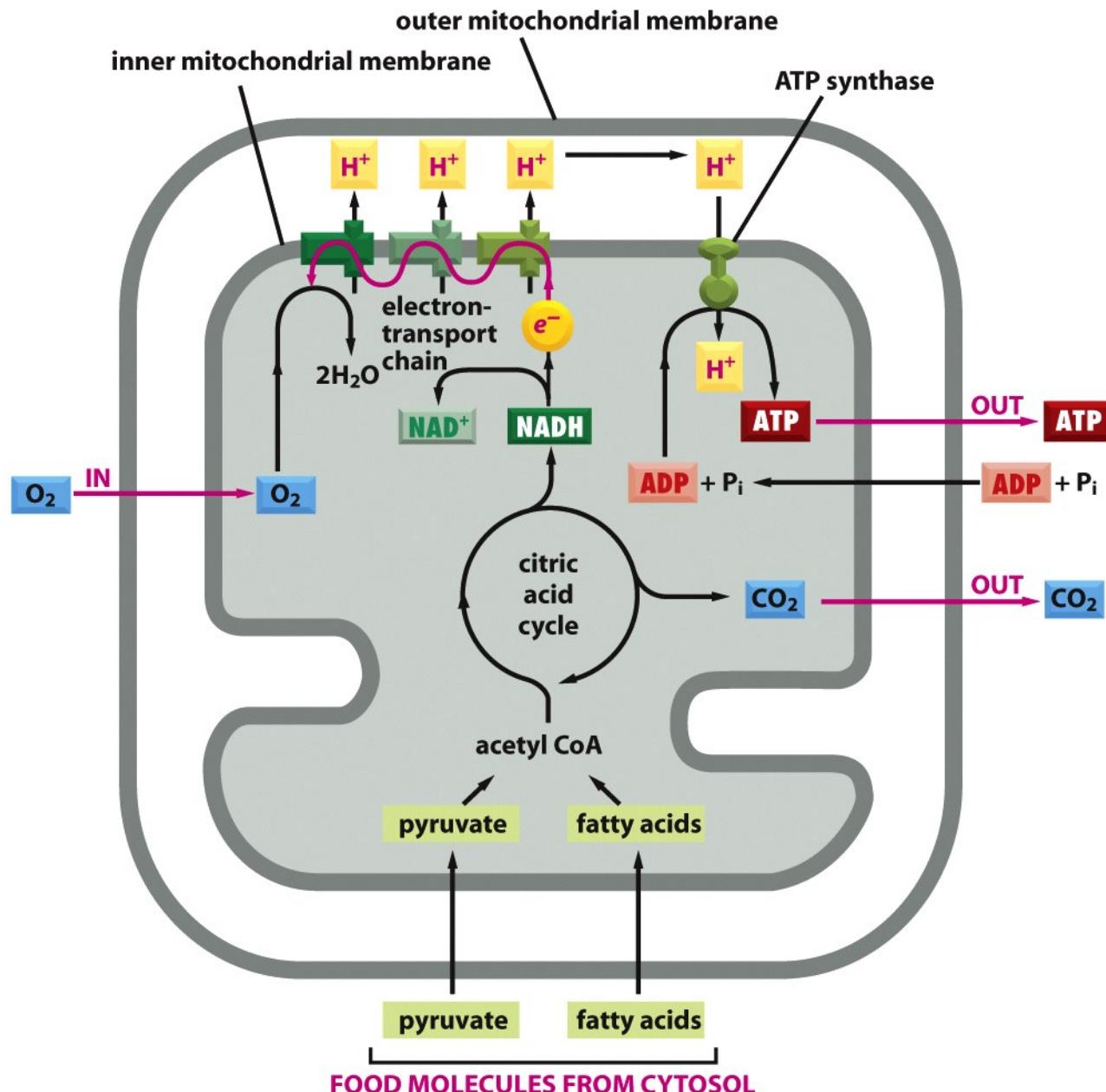
28 ATP molecules are generated in the mitochondria

(2) In addition to producing energy in the form of ATP, mitochondria play a role in signaling that controls cell death (apoptosis), cell division, and other processes.

Active Transport Processes Involved in the Mitochondria

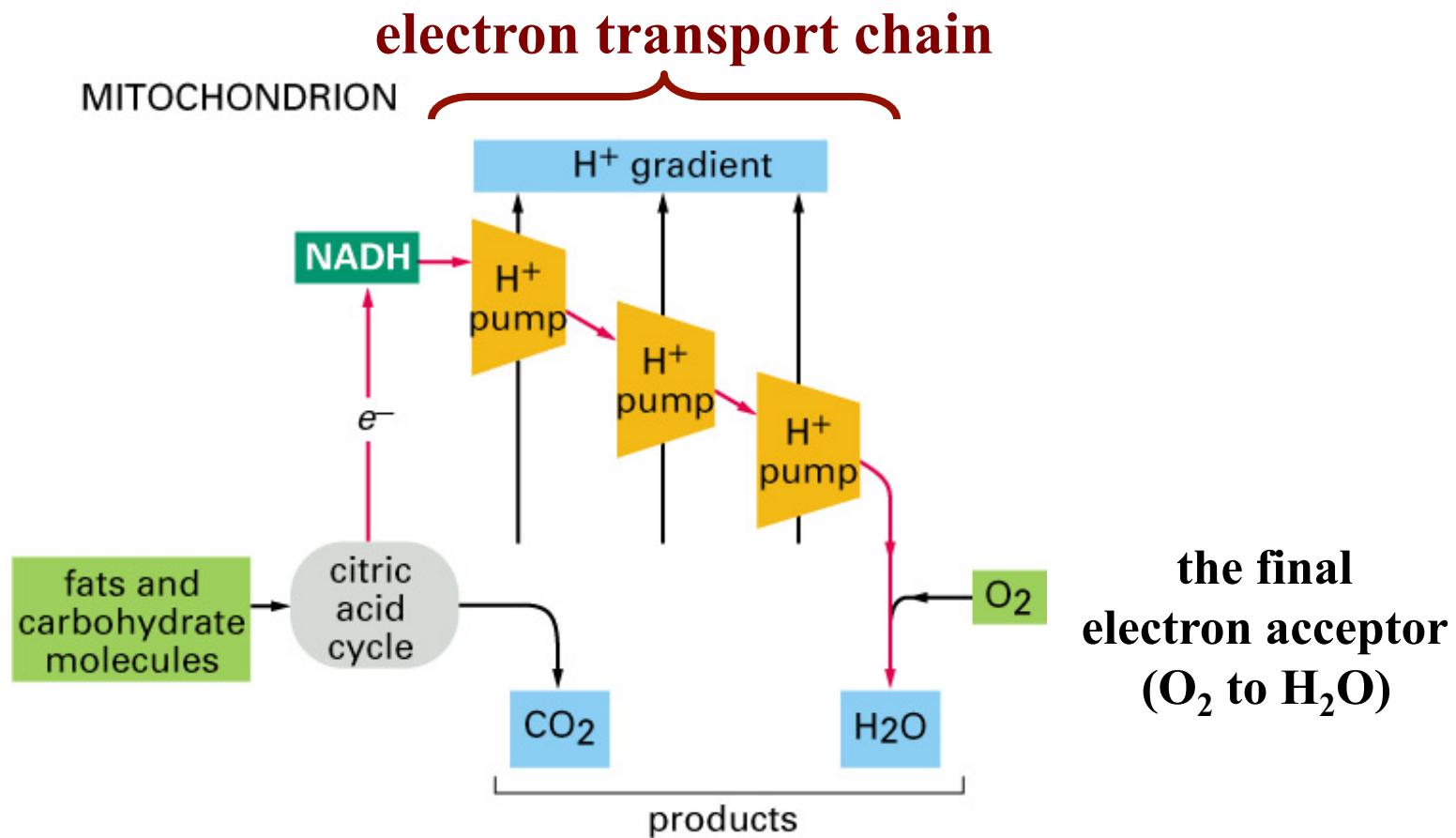


Electron transport chain and ATP synthase generate ATP



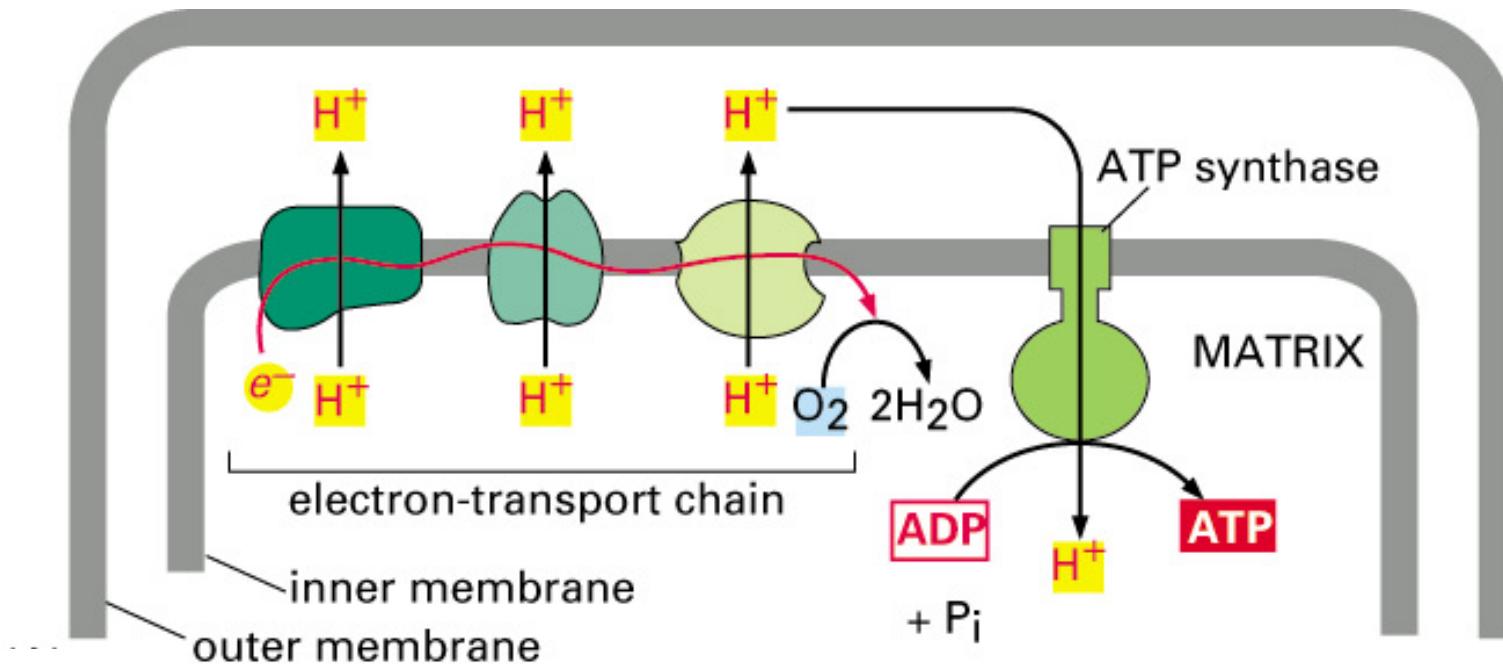
The Electron Transport Chain Couples Electron Transport to the Proton (H^+) Gradient

The electron transport occurs in a series of downhill reactions, called the electron transport chain. Each reaction is coupled to proton transport against the proton concentration which contributes to the formation of a H^+ gradient.



NAPDH is the initial electron donor and O_2 is the terminal electron receiver

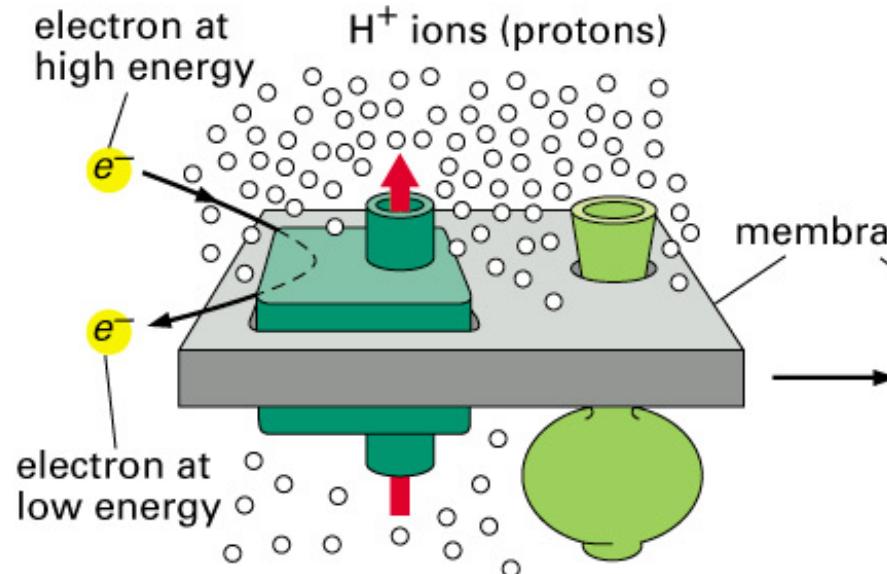
The H⁺ - ATPase Couples the Proton Gradient to ATP Synthesis: General Mechanism of Oxidative Phosphorylation



Electron transport chain components & ATP synthase
are located on the inner mitochondrial membrane.

Similar Mechanisms are Used to Generate ATP in Bacteria, Plants, and Animals

Energy released from downhill electron transport drives uphill proton transport

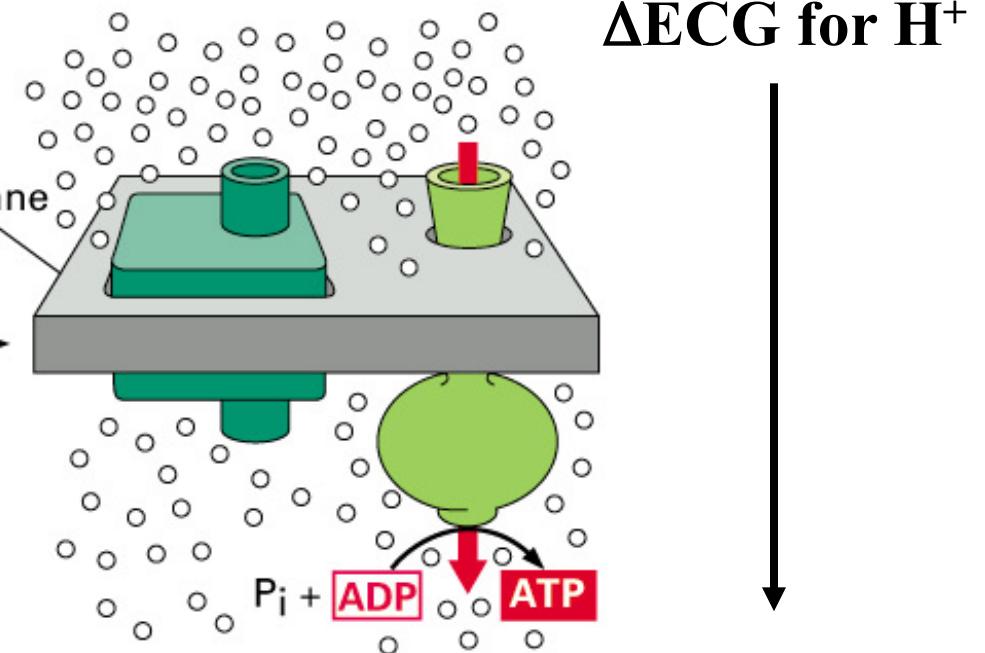


STAGE 1: ELECTRON TRANSPORT DRIVES PUMP THAT PUMPS PROTONS ACROSS MEMBRANE

electron transport coupled H^+ pump

e^- transport

Energy released from downhill proton transport drives ATP synthesis



STAGE 2: PROTON GRADIENT IS HARNESSSED BY ATP SYNTHASE TO MAKE ATP

H^+ -dependent ATP synthase

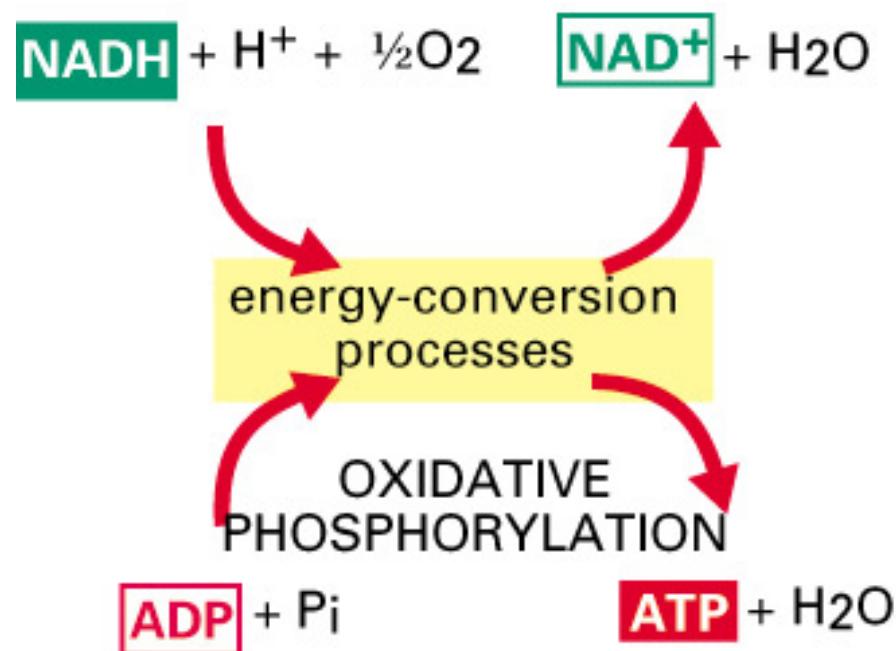
H^+ gradient

ATP

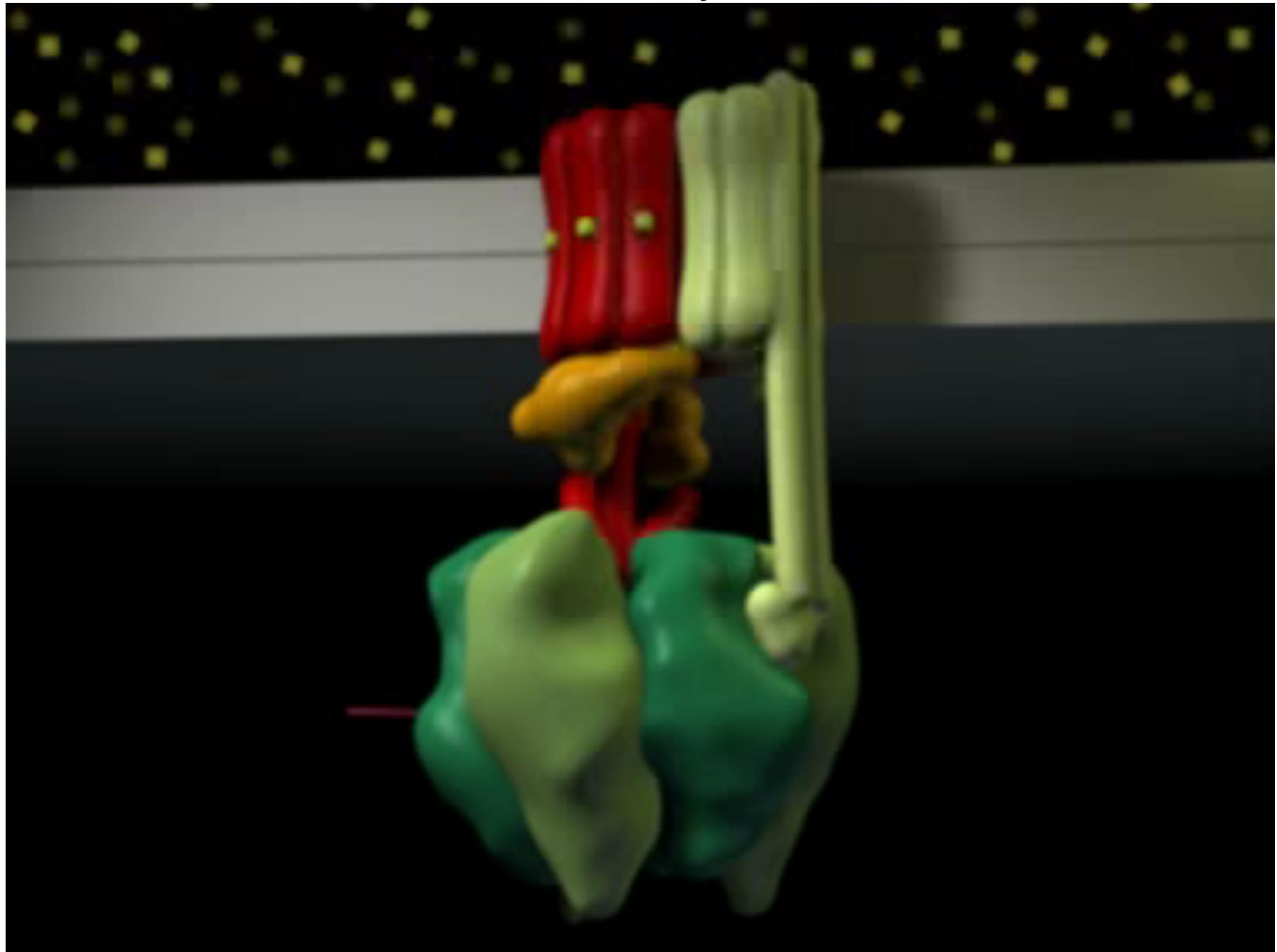
e^- transport \longrightarrow H^+ gradient \longrightarrow ATP

ATP Production by Mitochondria

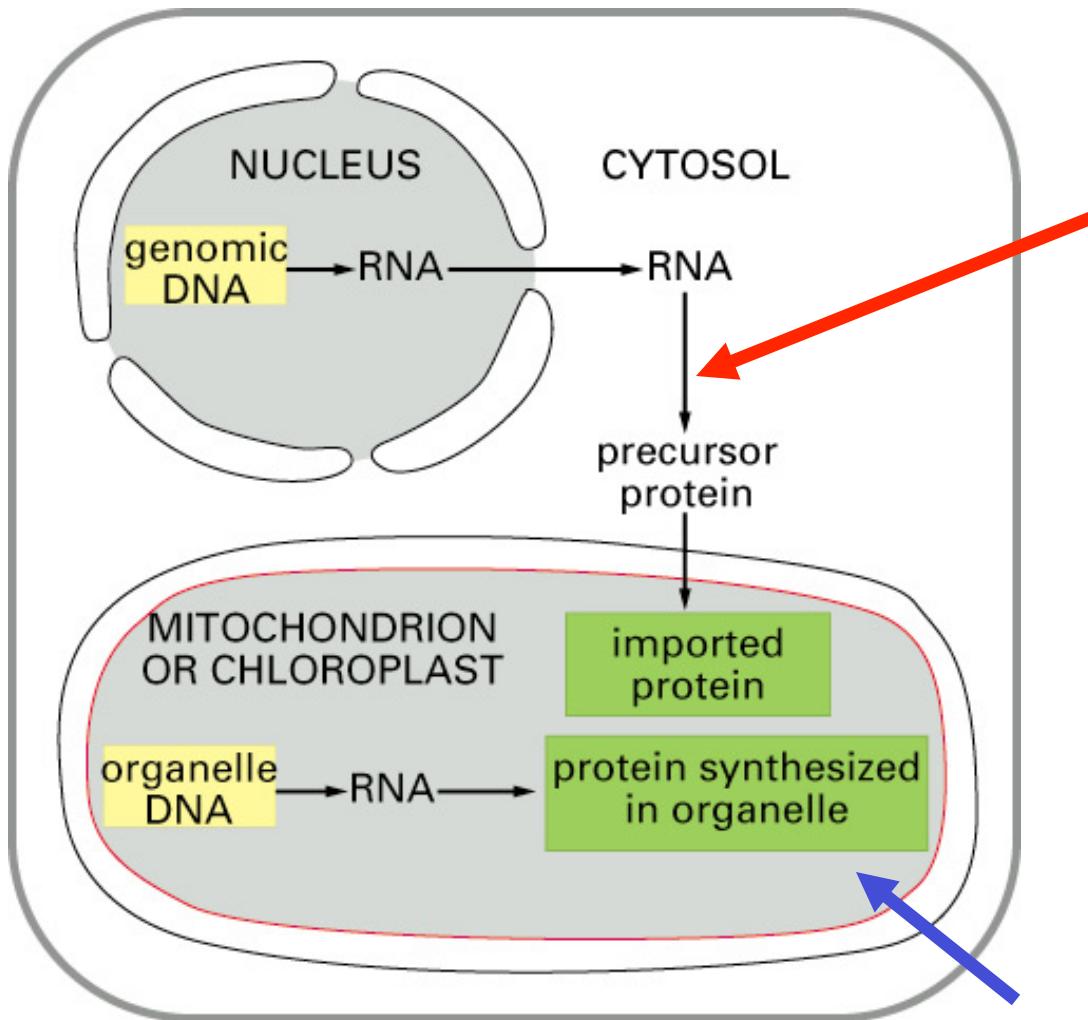
The net reaction is the oxidation of NADH to NAD⁺, the reduction of O₂ to H₂O, and the phosphorylation of ADP to ATP. Therefore it is also called oxidative phosphorylation (oxidative: NADPH to NAD⁺, phosphorylation: ADP to ATP).



Mitochondrial ATP Synthase (movie)



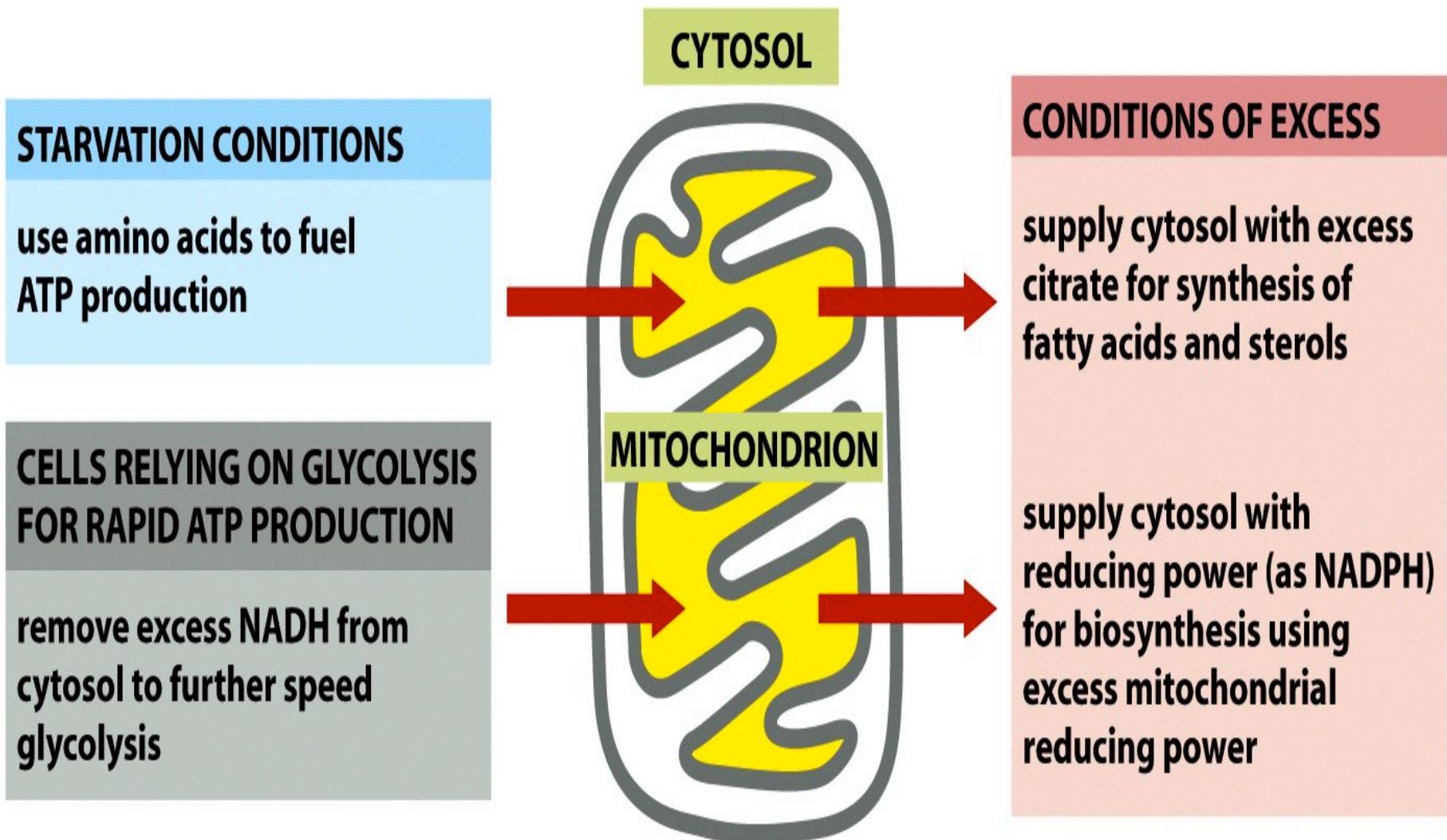
The Biogenesis of Mitochondrial Proteins



The major pathway (99%) cytosol-to-mitochondria transport (occurs at the membrane contact sites).

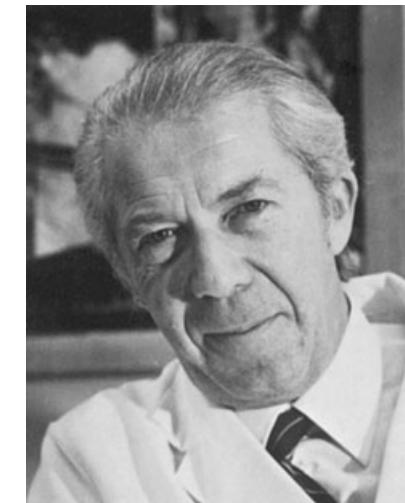
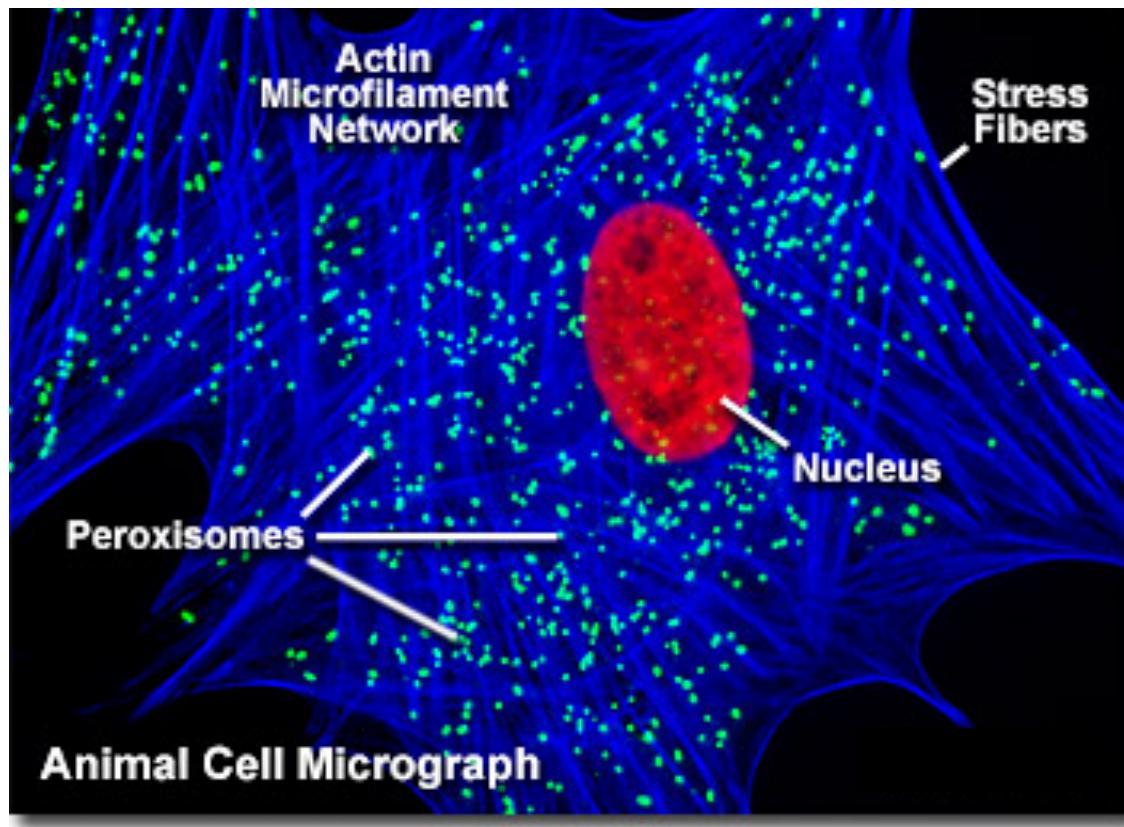
**The minor pathway (1%, 37 genes in human);
30/37 genes are linked to disease.**

Roles of Mitochondria in Cellular Metabolism in Addition to ATP Production



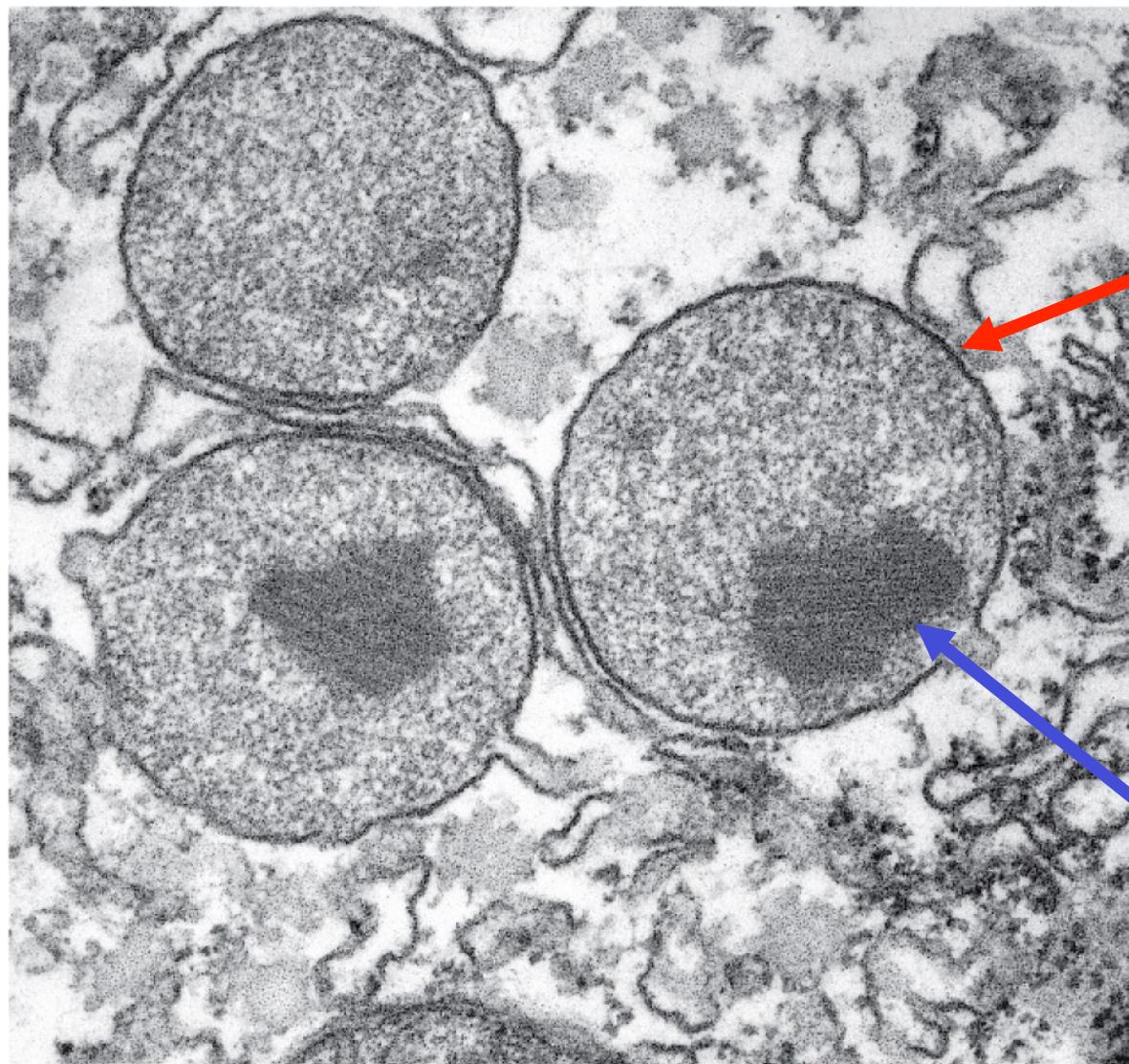
Peroxisomes

Peroxisomes (and Lysosomes) were Discovered by Christian de Duve



1917-present
1974 Nobel prize in
Physiology or Medicine

Basic Anatomy of Peroxisomes



200 nm

one membrane

enzymes involved in
oxidation

Functions of Peroxisomes

(common theme: utilizing O₂ or H₂O₂ for oxidation)

breakdown of fatty acid molecules

(fatty acid molecules → acetyl CoA)

(ADL: adrenoleukodystrophy, a human disease caused by mutations of a gene whose product is required for transport of a fatty acid-oxidation enzyme)

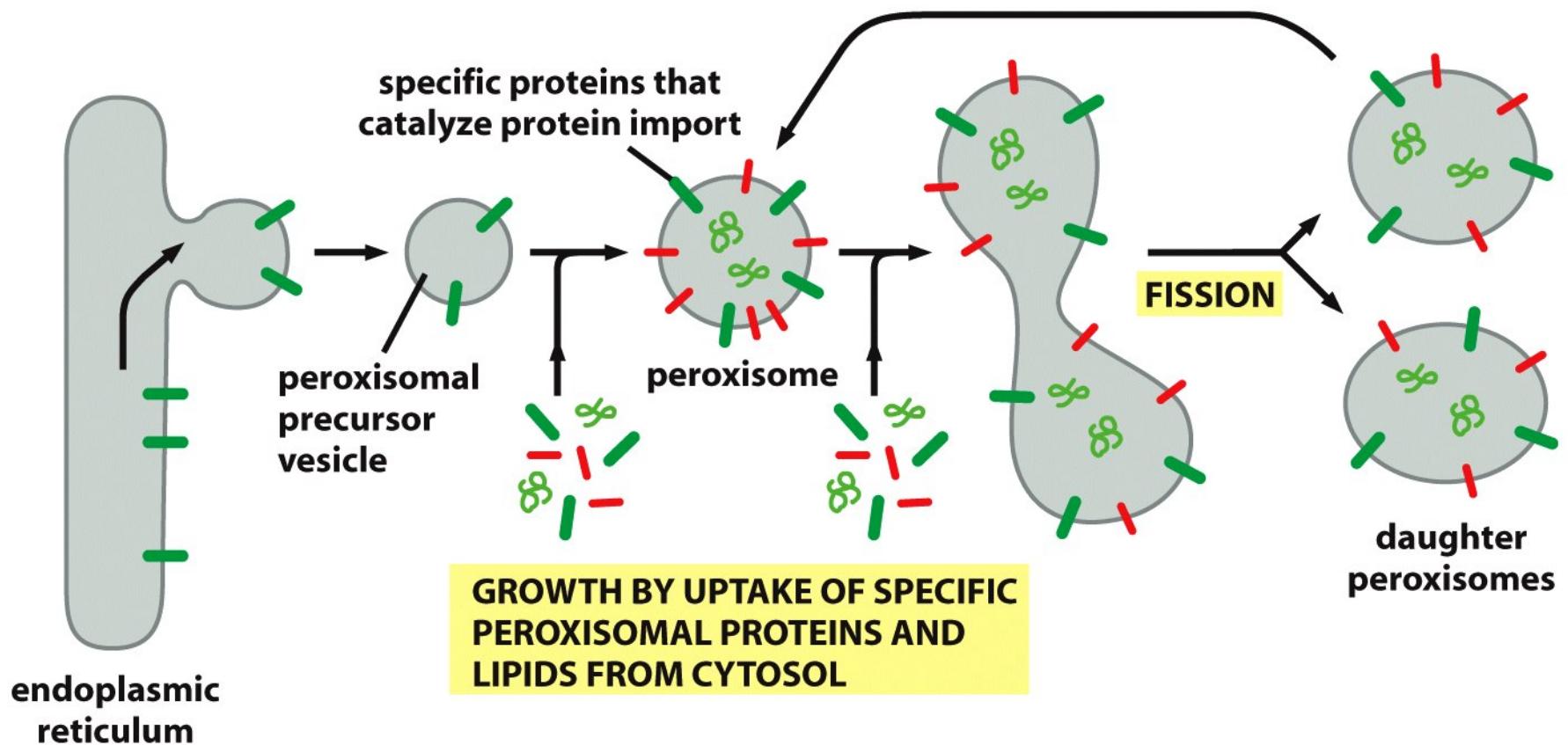
involved in synthesis of plasmalogens

(major phospholipid component in myelin sheath of nerve cells)

detoxification

(ethanol + H₂O₂ → acetaldehyde + 2H₂O)

The Origin of Peroxisomes

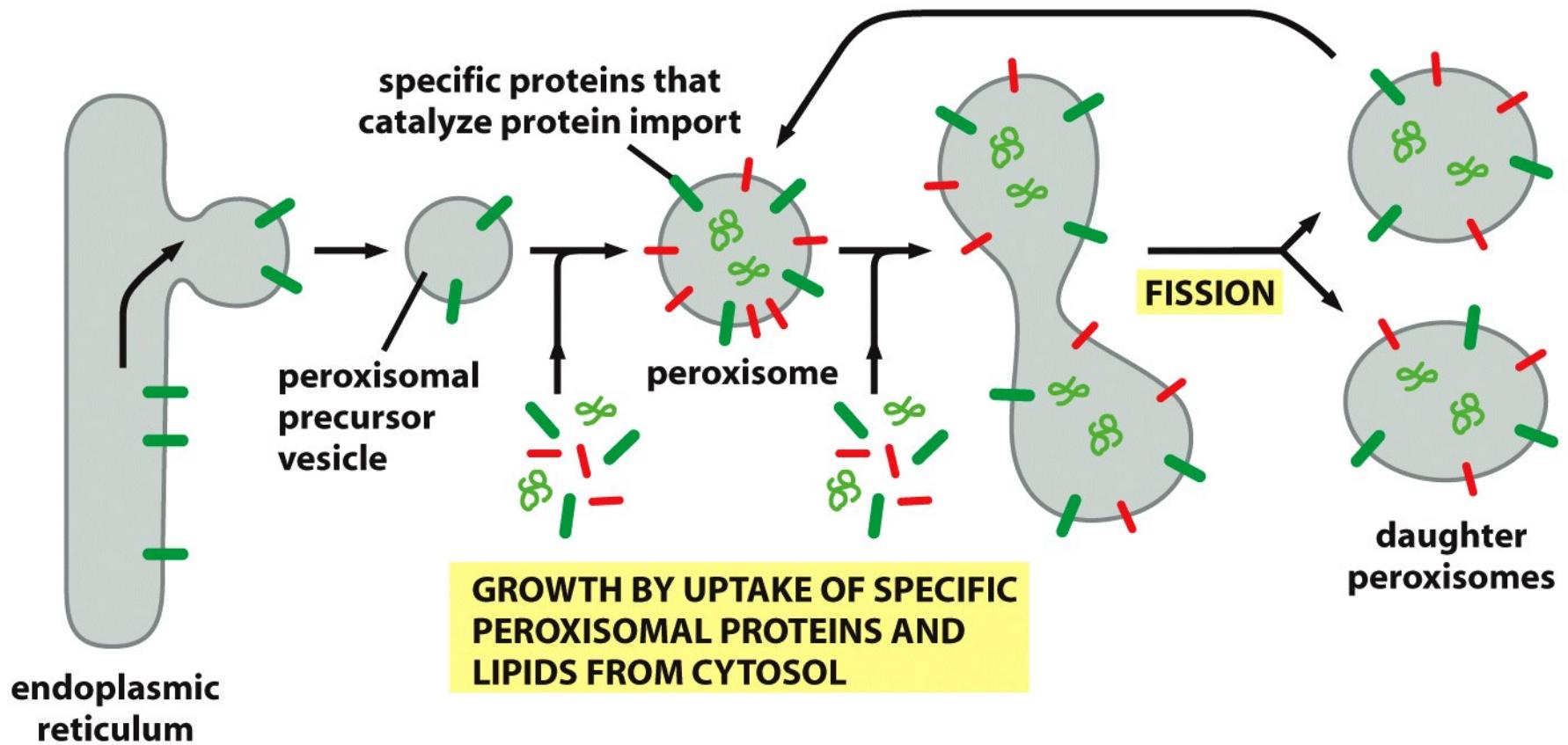


Two different sources of peroxisomal proteins

The cargo selection mechanism at the ER

The cargo import mechanism at the nascent peroxisomes.

Peroxisomes



Empty peroxisomes: Zellweger syndrome.
Mutation in gene encoding Peroxin 2 (Pex2).
Post-natal (after birth) lethality.