Cellular Organelles

Endoplasmic Reticulum, Golgi Complex, Lysosomes, and Peroxisomes

Learning Objectives:

- Describe the structure, types and functions of endoplasmic reticulum (ER). Describe the role of ER in detoxification process and processing of proteins.
- Compare between rough and smooth ER.

- Describe the structure and function of Golgi complex. Explain how Golgi complex acts as a “Traffic Director” of cellular proteins.
- Describe the structure, activation process, and function of lysosomes.
- Describe the function and origin of peroxisomes.

The Endoplasmic Reticulum (RE):

- The endoplasmic reticulum (ER), "network within the cytoplasm", is an extensive system of interconnected tubes and parallel membranes enclosing fluid filled cavities, or ***cisterns*** *(The membranes interconnect fully, so that the space between them forms a separate fluid-filled compartment from the cytoplasm* ***"the cisternal space").***

- Coiling and twisting through the cytosol, the ***ER is continuous with the outer nuclear membrane and accounts for about half of the cell's membranes.***

- There are two distinct varieties: ***rough ER*** and ***smooth ER.***

The Rough ER:

- ***The external surface of the rough ER is studded with ribosomes***, hence the name ***"rough".***

- Proteins assembled on these ribosomes thread their way into the fluid-filled interior of the ER cisterns . When complete, the newly made proteins are enclosed in vesicles for their journey to the Golgi apparatus where they undergo further processing.

- **The rough ER has several functions:**

  - **Its ribosomes manufacture all proteins secreted from cells**. For this reason, the rough ***ER is particularly abundant and well developed in most secretory cells, antibody-producing plasma cells, and liver cells, which produce most blood proteins.***

  - **It is also the cell's "membrane factory"** where ***integral proteins and phospholipids*** that form part of all cellular membranes are manufactured.

  - **The enzymes needed to catalyze lipid synthesis have their active sites on the external (cystosolic) face of the ER membrane**, ***where the needed substrates are readily available.***

The Smooth ER:

- The smooth ER is continuous with the rough ER and ***consists of tubules arranged in a looping network.*** Most body cells contain relatively little, if any, smooth ER.

- ***Its enzymes (all integral proteins forming part of its membranes) play no role in protein synthesis. Instead, the enzymes catalyze reactions involved with the following tasks:***

  - Metabolize lipids, synthesize cholesterol, and synthesize the lipid components of lipoproteins **(in liver cells).**

  - Synthesize steroid-based hormones such as sex hormones (testosterone-synthesizing cells of **the testes** are full of smooth ER).

  - Absorb, synthesize, and transport fats **(in intestinal cells).**

  - Detoxify drugs, certain pesticides, and cancer-causing chemicals **(in liver and kidneys).**

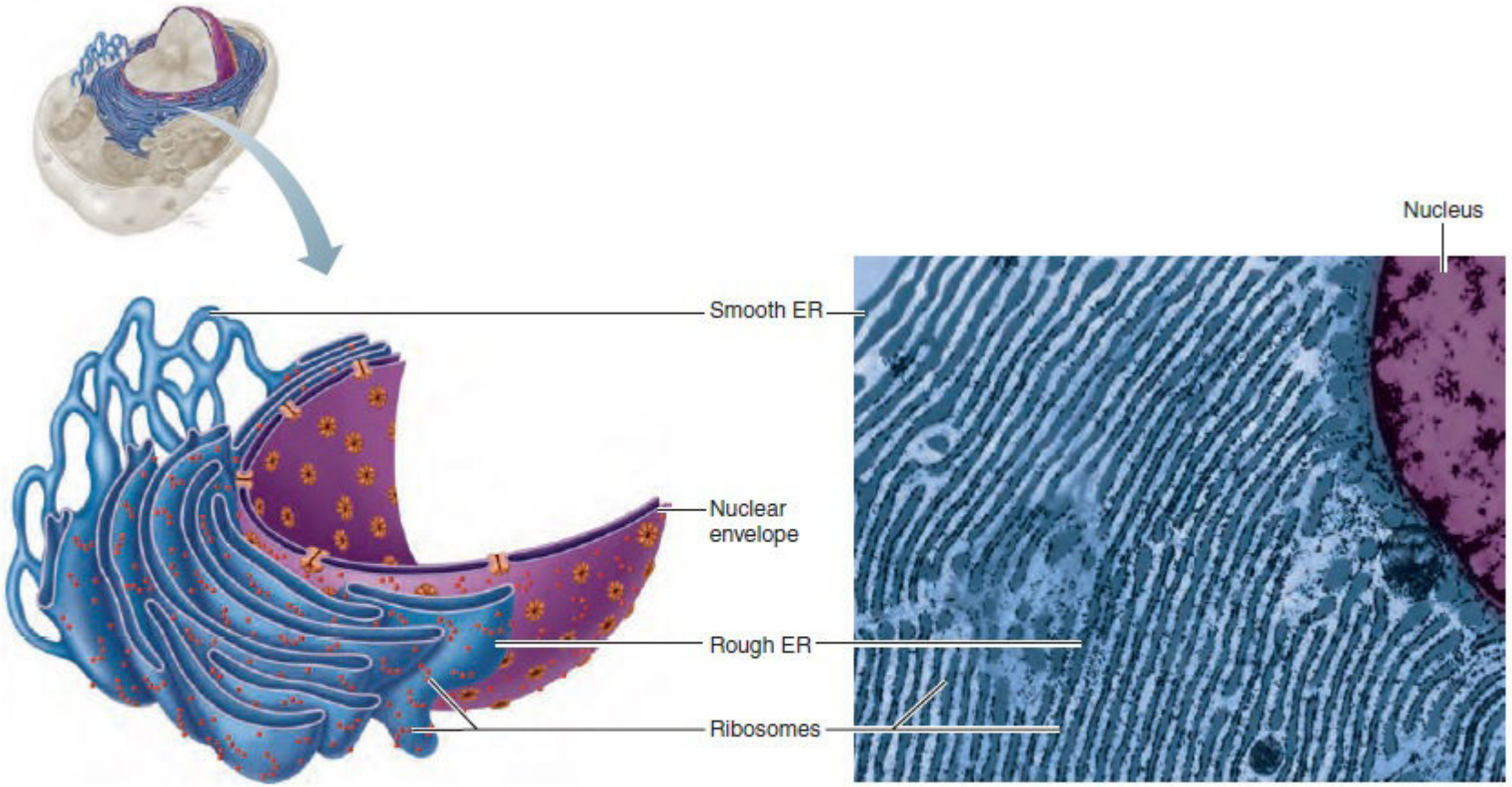
  - Break down stored glycogen to form free glucose **(in liver cells especially).**

The Endoplasmic Reticulum (RE):

ROUGH ER	SMOOTH ER
Has ribosomes attached to outside	No ribosomes
Often consists of flattened saccules	Often more tubular in shape than rough ER
Protein synthesis using ribosomes: Enzymes — Structural proteins Antibodies — Membrane proteins Hormones — Other secretory protein	No protein synthesis
Initial steps of protein glycosylation to make glycoproteins	
Fat synthesis	Fat synthesis
	Liver smooth ER has special functions: - Detoxification of fatty toxins and steroids - Glycogen breakdown

Comparison between Rough & Smooth ER

The Endoplasmic Reticulum (RE):



(a) Diagrammatic view of smooth and rough ER

(b) Electron micrograph of smooth and rough ER (25,000×)

The Endoplasmic Reticulum (RE):

❖ **How does the liver smooth ER detoxify toxic fats and steroids?**

- ➢ **It makes them more water-soluble (polar) so that they can leave the body with the urine.**

❖ **How does it make them water-soluble?** ***This will be studied in detail in the Toxicology course.***

a) It adds hydroxyl groups. (The liver is accustomed to hydroxylation, because hydroxylation of cholesterol is the essential step in synthesizing bile salts). ***Phase-I Reactions.***

b) It causes the fatty material to react with glucuronic acid ***(glucuronidation),*** which is an acid made by carboxylation of glucose. ***Phase-II Reactions.***

❖ **Evidence for this role of the liver smooth ER:**

- ➢ *After barbiturates, liver smooth ER proliferates.*
- ➢ *Cigarette smokers have increased hydroxylation enzymes in the smooth ER.*

The Endoplasmic Reticulum (RE):

❖ **Processing of proteins :**

- After synthesis in the rough ER, protein goes into vacuoles budding off the ER.
- Vacuoles are guided through the cytoplasm, ***by microtubule tracks***.
- Vacuoles go to the Golgi complex for processing & packaging of the proteins in them.
- Complete proteins go into vacuoles budding off the Golgi, and go to their destination, which varies depending on what the proteins were made for.
- Secretory proteins go to the plasma membrane, where exocytosis occurs, and this may contribute to cell growth, by adding to the area of plasma membrane.

Golgi Apparatus/Complex:

- The Golgi apparatus consists of ***stacked and flattened membranous sacs***, ***shaped like hollow dinner plates***, ***associated with swarms of tiny membranous vesicles.***

- *The Golgi apparatus is* ***the principal "traffic director" for cellular proteins***. ***Its major function is to modify, concentrate, and package the proteins and lipids made at the rough ER and destined for export from the cell.***

- **The Golgi's odd shape is a side effect of its job**. A protein complex pulls membranous sacs containing newly synthesized proteins off the Golgi and in the process, ***the membranes are flattened like rubber bands***.

- Transport vesicles that bud off from the rough ER move to and fuse with the membranes at ***the convex cis face***, ***the "receiving" side, of the Golgi apparatus.***

- **Inside the apparatus,** different biochemical processes occur in each saccule, ***so they're like a production line***. **The proteins are modified:** ***Some sugar groups are trimmed while others are added,*** and in some cases***, phosphate groups are added***.

Golgi Apparatus/Complex:

- ***The various proteins are "tagged" for delivery to a specific address***, ***sorted, and packaged*** in at least three types of vesicles that bud from ***the concave trans face,*** or ***"maturing face "*** *(the "shipping" side) of the Golgi stack*:

  - ***Vesicles containing proteins*** destined for export pinch off from the trans face as ***secretory vesicles***, or granules, which migrate to the plasma membrane and ***discharge their contents from the cell by exocytosis***. **This is one pathway:**

    - ***Specialized secretory cells***, such as ***the enzyme-producing cells of the pancreas, have a prominent Golgi apparatus.***

  - The Golgi apparatus ***pinches off other vesicles containing lipids and transmembrane proteins*** destined for the plasma membrane or for other membranous organelles. **This is a second pathway.**

  - The Golgi apparatus also ***packages digestive enzymes into membranous lysosomes that remain in the cell*** .**This is a third pathway.**

Golgi Apparatus/Complex – *Biochemical Functions:*

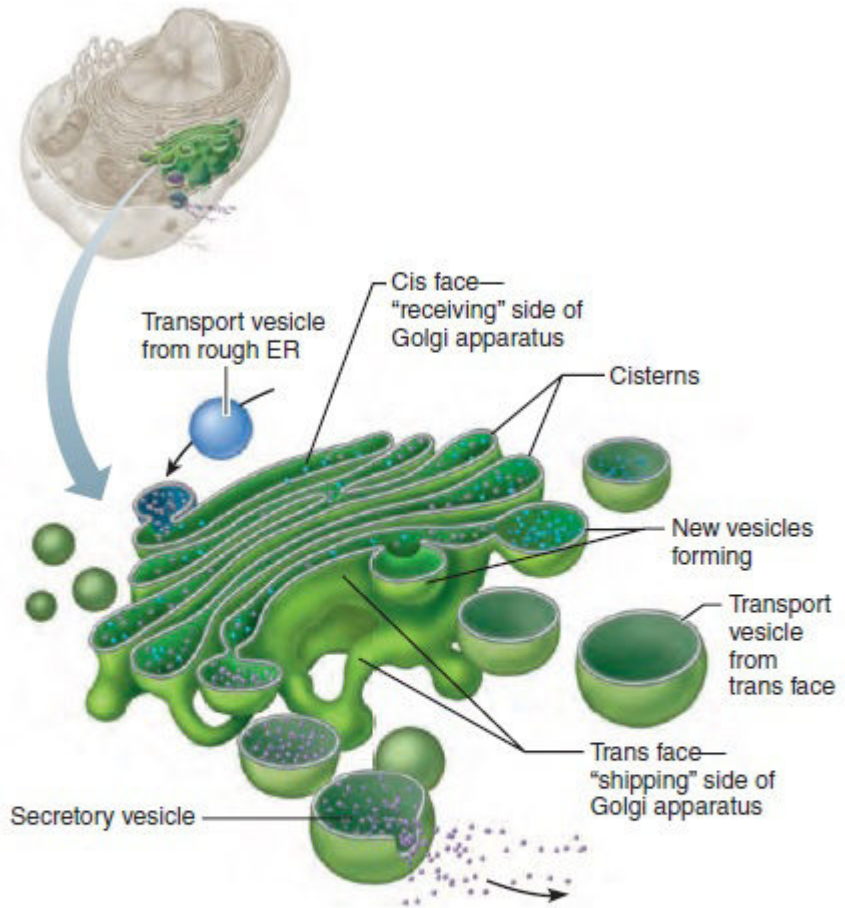
❖ Glycoprotein formation:

- ***Initial steps of glycosylation*** are carried out on the rough ER.
- ***The crude glycoproteins go to the Golgi complex***, where they are pruned down and then other complex sugars are added in specific sequence.
- ***Certain sugars in the crude glycoproteins may act as 'markers", as a communication system*** to "inform" the Golgi complex what is needed in the Golgi processing.

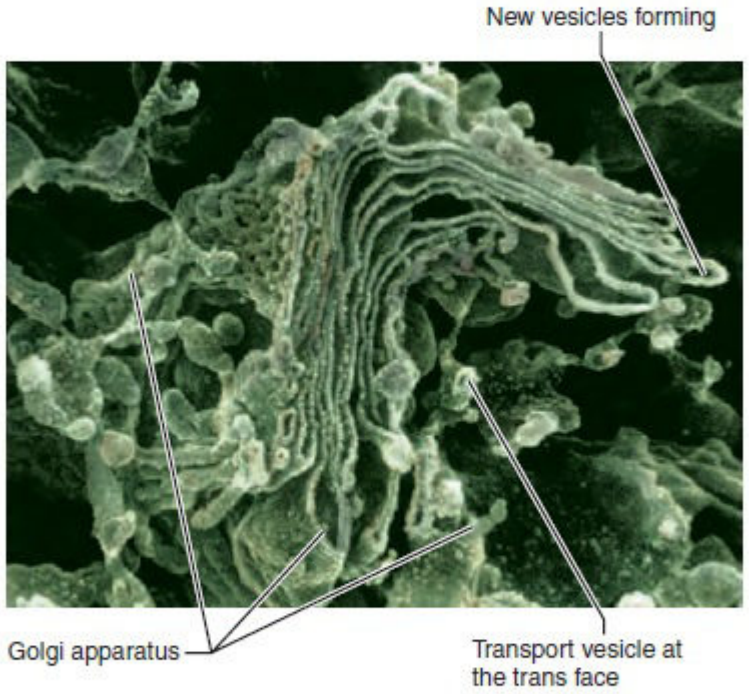
❖ Lysosome formation:

- ***Lysosomal enzymes are made in the rough ER***, as ***inactive "proenzymes".***
- ***They are inactive (for safety reasons) because they are glycosylated*** with a sugar sequence which inhibits their enzyme function.
- ***The sugars may act as "markers "*** enabling the Golgi complex to recognize them.
- ***They emerge from the trans side of the Golgi complex***, as ***"primary lysosomes".*** When swallowing further substances primary lysosomes transform into ***"secondary lysosomes".***

Golgi Apparatus/Complex:

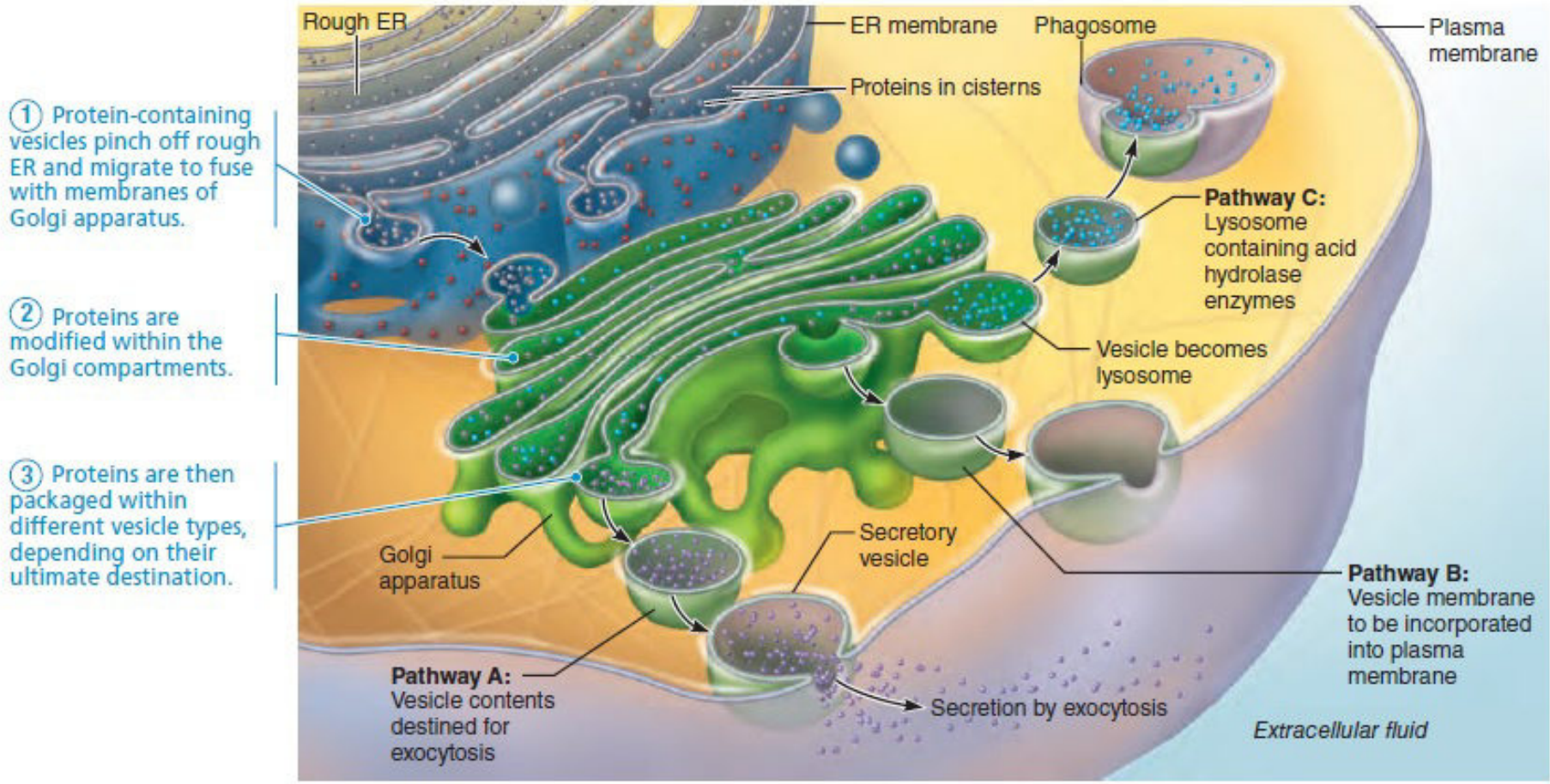


(a) Many vesicles in the process of pinching off from the Golgi apparatus.



(b) Electron micrograph of the Golgi apparatus (90,000×)

Golgi Apparatus/Complex:



The sequence of events from protein synthesis on the rough ER to the final distribution of those proteins. The protein coats on the transport vesicles are not illustrated

Lysosomes:

- Born as ***"endosomes" which contain inactive enzymes***, *lysosomes ("disintegrator bodies") are spherical membranous organelles* ***containing activated digestive enzymes .***

- ***Lysosomes are large and abundant in phagocytes***, the cells that dispose of invading bacteria and cell debris.

- Lysosomal enzymes can digest almost all kinds of biological molecules. ***They work best in acidic conditions and so are called acid hydrolases.***

- The lysosomal membrane is adapted to serve lysosomal functions in two important ways:

  - **First**, ***it contains H^+ (proton) "pumps***," which are ATPases (use energy) that gather hydrogen ions from the surrounding cytosol to maintain the organelle's acidic pH.

  - **Second**, ***it retains the dangerous acid hydrolases*** while permitting the final products of digestion to escape so that they can be used by the cell or excreted. In this way, lysosomes provide sites where digestion can proceed safely within a cell.

Lysosomes - *Activation:*

- Primary lysosomes emerge from the trans Golgi, and lie dormant until activated.
- They are activated by merging with a ***heterophagic or autophagic vacuole.***
- This triggers a proton pump, which acidifies the lysosomal contents.
- *Acidification causes the proenzymes to change to active enzymes*.
- Acidification also turns on the active enzymes, which ***have a pH optimum of about 5.***
- Lysosomal. enzymes include ***proteases, amylases, lipases***, to ***digest all classes of biological materials.***
- After digestion, indigestible material may or may not be expelled by exocytosis.

Lysosomes – *Functions:*

- **Heterophagy:**
  - Cellular nutrition, metabolic functions, such as glycogen breakdown and release.
  - Defense; killing bacterial invaders, or removing foreign particles.
- **Autophagy:** Cleaning up and recycling old worn-out organelles.
- **Autolysis** = cellular suicide (Apoptosis): Removal of unwanted cells and tissues during fetal development (such as the webs between the fingers and toes of a developing fetus).
- **Extracellular digestion** - lysosome releases active enzymes by exocytosis, used by:
  - **Acrosome** on sperm cells which contains enzymes that break down the outer membrane of the ovum.
  - **Osteoclasts** (Breaking down bone to release calcium ions into the blood).

Peroxisomes:

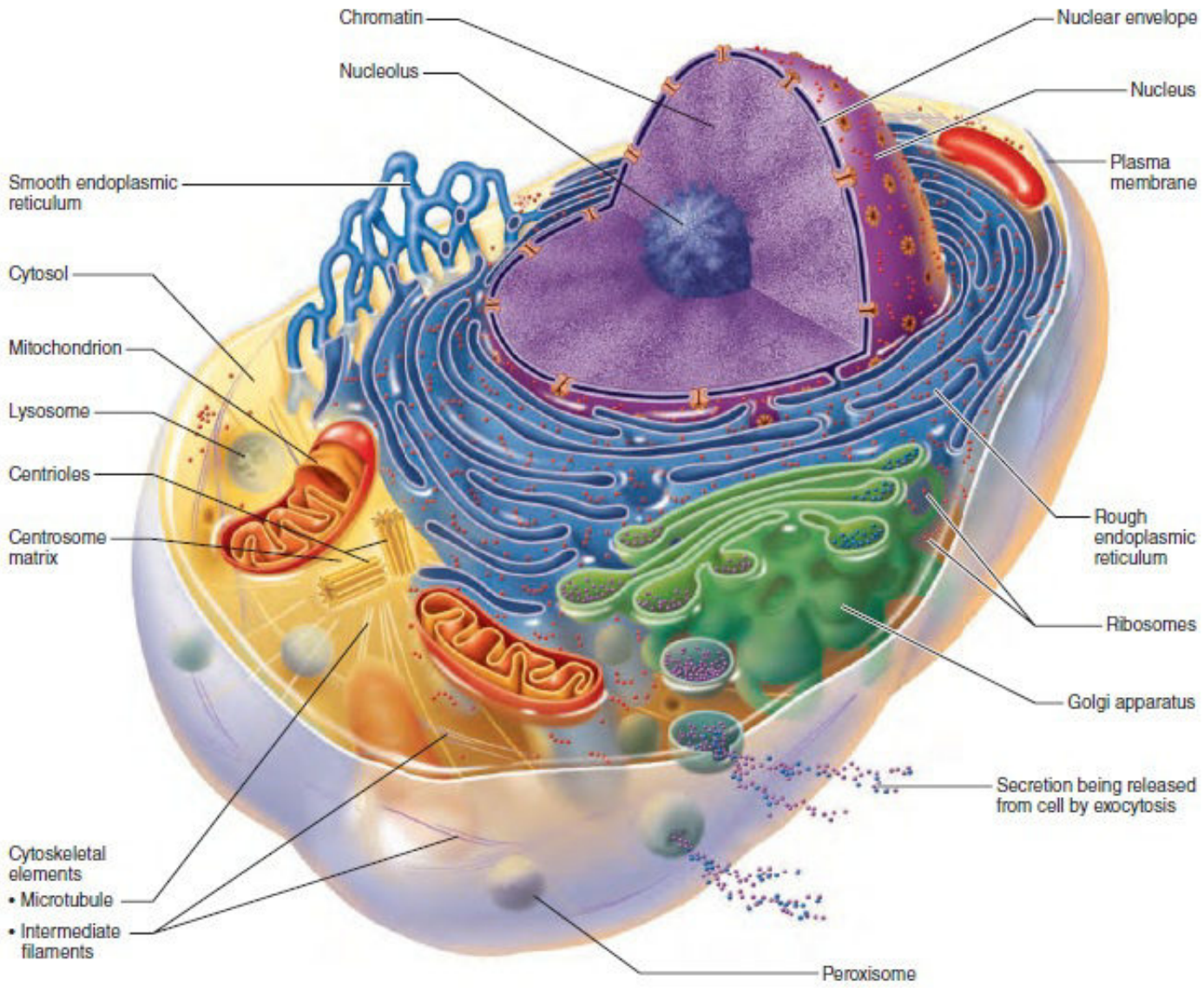
❖ *Peroxisomes are spherical membranous sacs containing a variety of powerful enzymes*, the most important of which are ***oxidases and catalases***. *Oxidases use molecular oxygen (O2) to* ***detoxify harmful substances****, including* ***alcohol and formaldehyde***. ***Their most important function is to neutralize the highly reactive free radicals.***

❖ **Functions:**

- ➢ Neutralization of peroxides, by the enzyme catalase, and others.
- ➢ Production of peroxides to combat bacteria after phagocytosis.
- ➢ Use of peroxides for oxidative detoxification of drugs and fatty acid oxidation. Unusual compounds such as D-amino acids are also detoxified in this way.
- ➢ Regulation of oxygen tension in the cell. Catalase contains heme, enabling it to store oxygen. So that it can supply oxygen when the cell needs it, and it can use up oxygen if oxygen levels rise enough to threaten free radical damage.

❖ **Origin of peroxisomes:**

- ➢ **They are most common in *liver and kidney cells* (active in detoxification).**
- ➢ Peroxisomes look like small lysosomes and for many years it was thought that they were self-replicating organelles formed when existing peroxisomes simply pinch in half. *Recent evidence, however, suggests that most new peroxisomes form by budding off of the endoplasmic reticulum via a special ER machinery that differs from that used for vesicles destined for modification in the Golgi apparatus.*



Structure of the generalized cell. No cell is exactly like this one, but this composite illustrates features common to many human cells. Note that not all of the organelles are drawn to the same scale in this illustration.