Introduction to Radiobiology
Lesson 2

Master of Advanced Studies in Medical Physics
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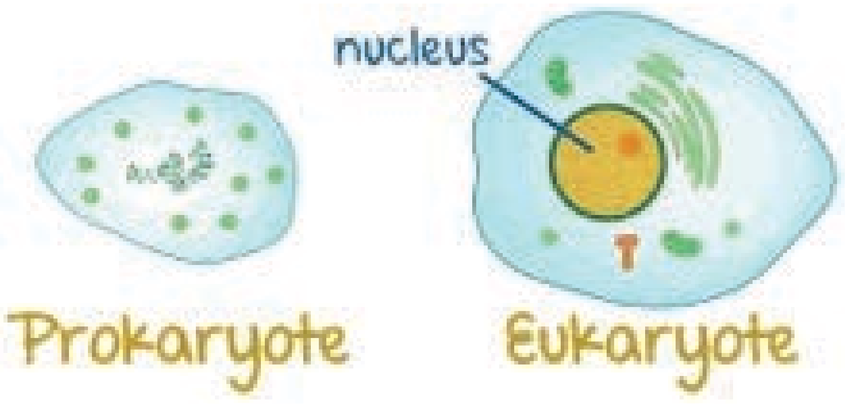
Edoardo Milotti
Physics Dept. – University of Trieste

The common structure of the living



Cells in each Kingdom are either:

•**Prokaryotes**: cells lack a nucleus and are usually very simple organisms.
Archaebacteria and Eubacteria are Prokaryotes.

•**Eukaryotes**: cells have a nucleus. ***Protists, Fungi, Plants and Animals are Eukaryotes.***

EUKARYOTIC CELLS	PROKARYOTIC CELLS
The cells of "complex" organisms, including all plants and animals	"Simple" organisms, including bacteria and blue-green algae
Contain a nucleus and many other organelles, each surrounded by a membrane (the nucleus and mitochondrion have two membranes)	Lack a nucleus and other membrane-encased organelles
Can specialize for certain functions, such as absorbing nutrients from food or transmitting nerve impulses; groups of cells can form large, multicellular organs and organisms	Usually exist as single, virtually identical cells
Most animal cells are 10–30 micrometers across, and most plant cells are 10–100 micrometers across	Most are 1–10 micrometers across

Kingdom	Description	Examples
Archaebacteria	*Prokaryote*, one-celled, live in harsh places on Earth	Thermophiles, Halophiles, Methanogens
Eubacteria	*Prokaryote*, common bacteria, found everywhere, one-celled	E.coli, staphylococcus
Protista	*Eukaryote*, some one-celled, some multi-celled, diverse	Euglena, Paramecium, Slime Mold
Fungi	*Eukaryote*, multi-celled, heterotrophic	Mushrooms, Morels
Plantae	*Eukaryote*, multi-celled, autotrophic	Angiosperms (flowers), gymnosperms, mosses, ferns
Animalia	*Eukaryote*, multi-celled, heterotrophic	Worms, sponges, insects, amphibians, birds, mammals

Radiation affects all cells and organisms, but in different ways …

LD_{50} = dose that kills 50% of the population
LD_{100} = dose that kills 100% of the population

Lethal radiation doses (Gray)

Organism	Lethal dose	LD_{50}	LD_{100}	Class/Kingdom
Dog		3.5 ($LD_{50/30\ days}$)[14]		Mammals
Human	4–10[15]	4.5[16]	10[17]	Mammals
Rat		7.5		Mammals
Mouse	4.5–12	8.6–9		Mammals
Rabbit		8 ($LD_{50/30\ days}$)[14]		Mammals
Tortoise		15 ($LD_{50/30\ days}$)[14]		Reptile
Goldfish		20 ($LD_{50/30\ days}$)[14]		Fish
Escherichia coli	60		60	Bacteria
German cockroach		64[15]		Insects
Shellfish		200 ($LD_{50/30\ days}$)[14]		-
Common fruit fly	640[15]			Insects
*C. elegans**		160-200 [18]	≫ 500-800[19][20]	Nematode
Amoeba		1,000 ($LD_{50/30\ days}$)[14]		-
Habrobracon hebetor	1,800[8][9]			Insects
Milnesium tardigradum	5,000[12]			Eutardigrade
Deinococcus radiodurans	15,000[15]			Bacteria
Thermococcus gammatolerans	30,000[15]			Archaea

from https://en.wikipedia.org/wiki/Radioresistance

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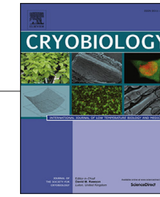

Recovery and reproduction of an Antarctic tardigrade retrieved from a moss sample frozen for over 30 years

Megumu Tsujimoto [a, *], Satoshi Imura [a, b], Hiroshi Kanda [a]

[a] National Institute of Polar Research (NIPR), 10-3 Midori-cho, Tachikawa-shi, Tokyo 190-8518, Japan
[b] SOKENDAI (The Graduate University for Advanced Studies), Tokyo, Japan

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ABSTRACT

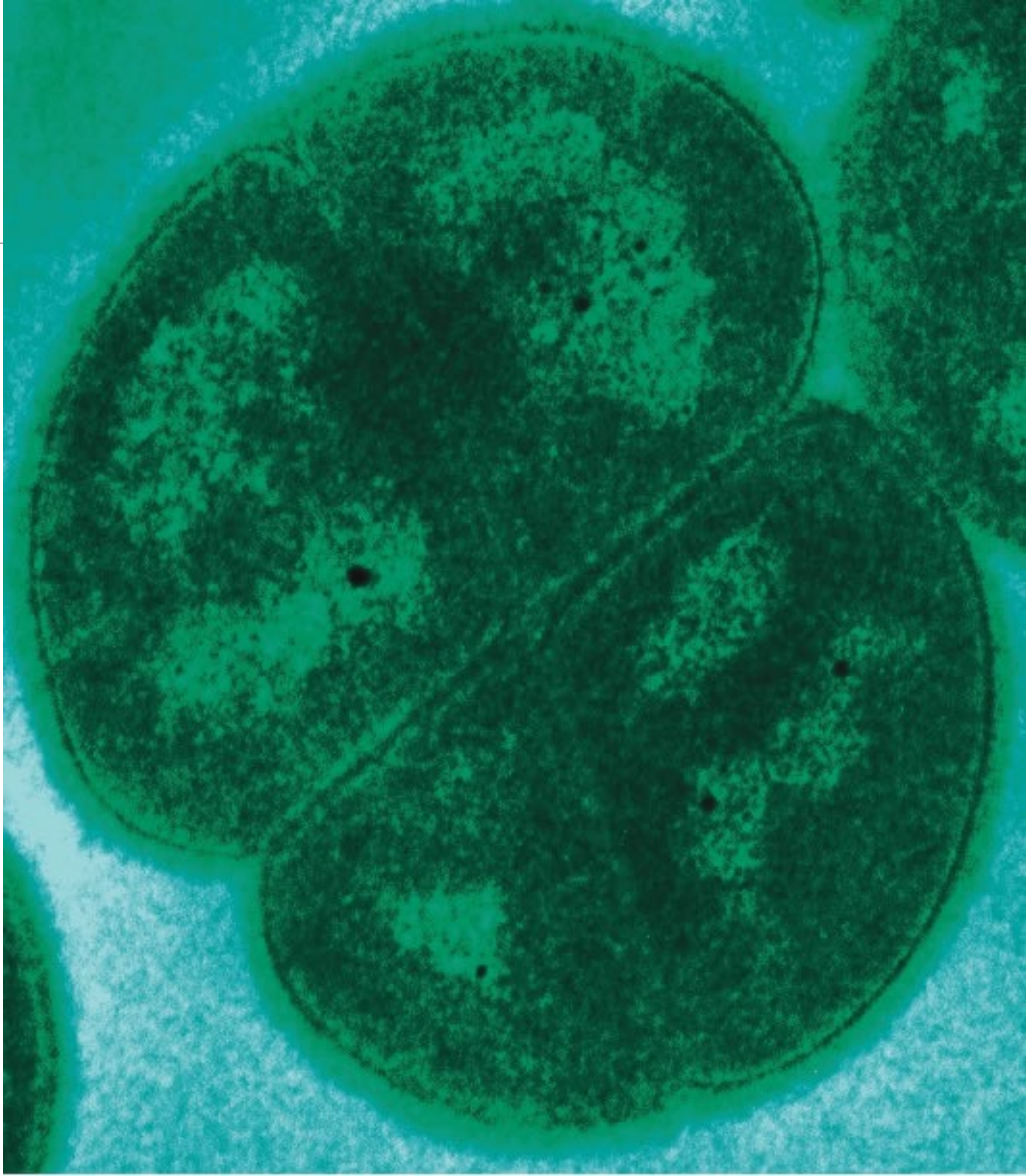
Long-term survival has been one of the most studied of the extraordinary physiological characteristics of cryptobiosis in micrometazoans such as nematodes, tardigrades and rotifers. In the available studies of long-term survival of micrometazoans, instances of survival have been the primary observation, and recovery conditions of animals or subsequent reproduction are generally not reported. We therefore documented recovery conditions and reproduction immediately following revival of tardigrades retrieved from a frozen moss sample collected in Antarctica in 1983 and stored at −20 °C for 30.5 years. We recorded recovery of two individuals and development of a separate egg of the Antarctic tardigrade, *Acutuncus antarcticus*, providing the longest records of survival for tardigrades as animals or eggs. One of the two resuscitated individuals and the hatchling successfully reproduced repeatedly after their recovery from long-term cryptobiosis. This considerable extension of the known length of long-term survival of tardigrades recorded in our study is interpreted as being associated with the minimum oxidative damage likely to have resulted from storage under stable frozen conditions. The long recovery times of the revived tardigrades observed is suggestive of the requirement for repair of damage accrued over 30 years of cryptobiosis. Further more detailed studies will improve understanding of mechanisms and conditions underlying the long-term survival of cryptobiotic organisms.

Antarctic tardigrades revived beyond 30 years freezing

Deinococcus radiodurans

is an extremophilic bacterium, one of the most radiation-resistant organisms known.

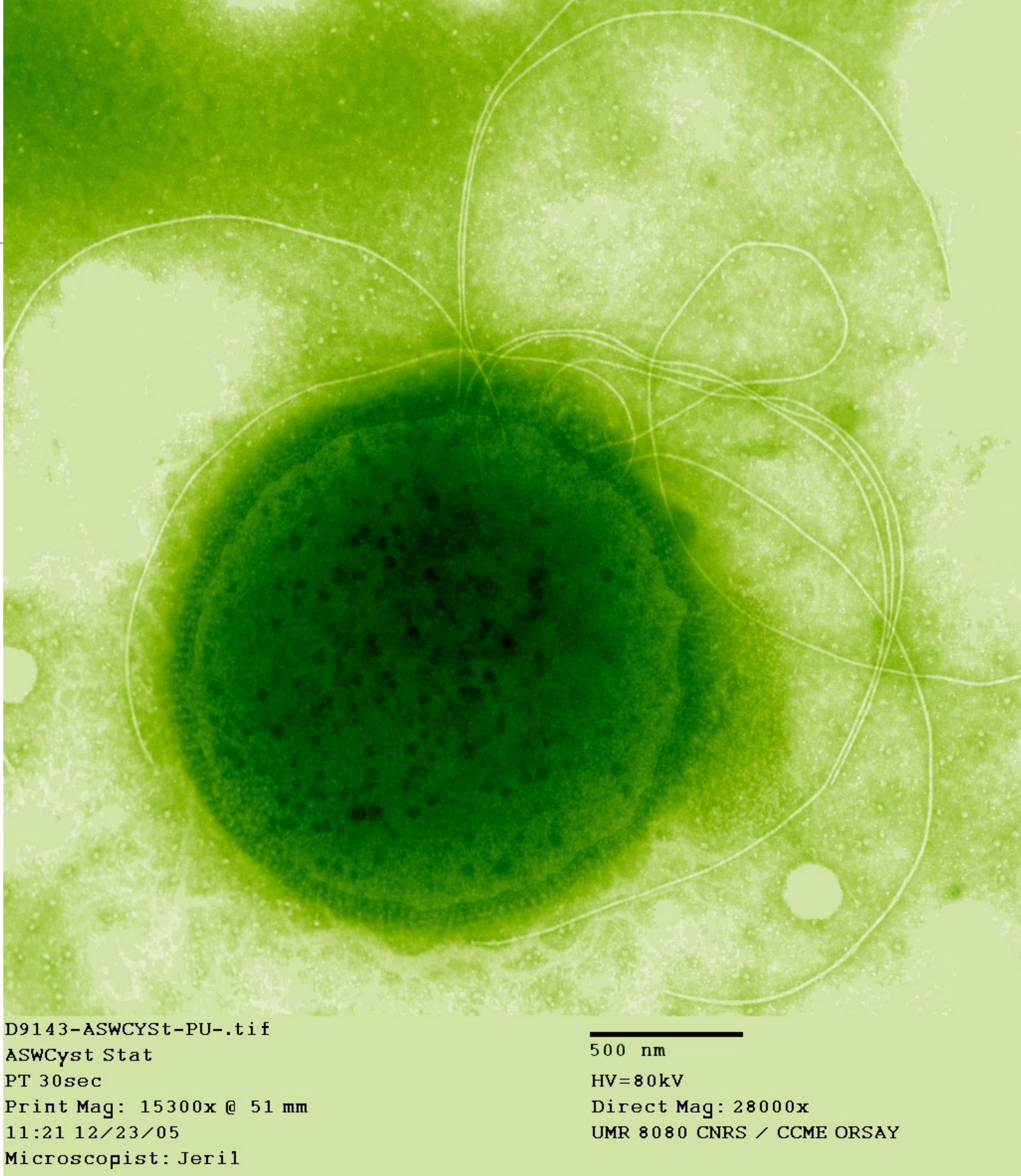
It can survive cold, dehydration, vacuum, and acid, and is therefore known as a polyextremophile and has also been listed as the world's toughest bacterium in The Guinness Book Of World Records.



Thermococcus gammatolerans

is an archaea extremophile and the most radiation-resistant organism known to exist.

Discovered in 2003 in a submarine hydrothermal vent in the Guaymas Basin about 2,000 meters deep off the coast of California, Thermococcus gammatolerans thrives in temperatures between 55–95 °C with an optimum development at approximately 88 °C.



While the action of radiation is the same, cells counter damage in different ways

It is now essential to learn about the basic biology of cells, how radiation damages the structures that make up cells, and how damage is managed by different cells.

Basic definitions

- A group of cells that together perform one or more functions is referred to as ***tissue***.
- A group of tissues that together perform one or more functions is called an ***organ***.
- A group of organs that perform one or more functions is an ***organism***.

Human cells are either somatic cells or germ cells.

Germ cells are either a sperm or an egg, all other human cells are called somatic cells.

Cells propagate through division:

- *Division of somatic cells is called **mitosis** and results in two genetically identical daughter cells.*
- *Division of germ cells is called **meiosis** and involves two fissions of the nucleus giving rise to four sex cells, each possessing half the number of chromosomes of the original germ cell.*

- *When a somatic cell divides, two cells are produced, each carrying a chromosome complement identical to that of the original cell.*
- *New cells themselves may undergo further division, and the process continues producing a large number of progeny.*

Somatic cells are further classified as:

- ***Stem cells***, which are undifferentiated cells that can differentiate into specialized cells and can divide (through mitosis) to produce more stem cells. In mammals, there are two broad types of stem cells: embryonic stem cells, and adult stem cells, which are found in various tissues.
- ***Progenitor cells***, which are cells that, like a stem cell, have a tendency to differentiate into a specific type of cell, but is already more specific than a stem cell and is pushed to differentiate into its "target" cell. The most important difference between stem cells and progenitor cells is that stem cells can replicate indefinitely, whereas progenitor cells can divide only a limited number of times.

In adult organisms, stem cells and progenitor cells act as a repair system for the body, replenishing adult tissues. In a developing embryo, stem cells can differentiate into all the specialized cells—ectoderm, endoderm and mesoderm (see induced pluripotent stem cells)—but also maintain the normal turnover of regenerative organs, such as blood, skin, or intestinal tissues.

- ***Transit cells***, which are cells in movement to another population.
- ***Mature cells***, which are fully differentiated and do not exhibit mitotic activity.

From the point of view of tissues:

Classification of tissues based on cellular components

- ***Epithelial tissue:*** formed by cells that line cavities and surfaces of blood vessels and organs
- ***Muscle tissue:*** cells that give muscles the ability to contract
- ***Connective tissue:*** cells that support, connect or separate different types of tissues and organs
- ***Nerve tissue:*** cells that make up the nervous system

Classification based on tissue function

- ***Stroma***, that part of tissue or organ that has connective or structural role (all the parts without specific functions of an organs like connective tissue, blood vessels, nerves, etc.)
- ***Parenchyma***, the functional part of the tissue or organ.

A few important examples of parenchyme

Brain
The brain parenchyma refers to the functional tissue in the brain that is made up of the two types of brain cell, neurons and glial cells.

Lungs
Lung parenchyma is the substance of the lung outside of the circulatory system that is involved with gas exchange and includes the pulmonary alveoli and respiratory bronchioles.

Liver
The liver parenchyma is the functional tissue of the organ made up of around 80% of the liver volume as hepatocytes. The other main type of liver cells are non-parenchymal.

Tumors
The tumor parenchyma, of a solid tumour, is one of the two distinct compartments in a solid tumour. The parenchyma is made up of neoplastic cells. The other compartment is the stroma induced by the neoplastic cells, needed for nutritional support and waste removal.

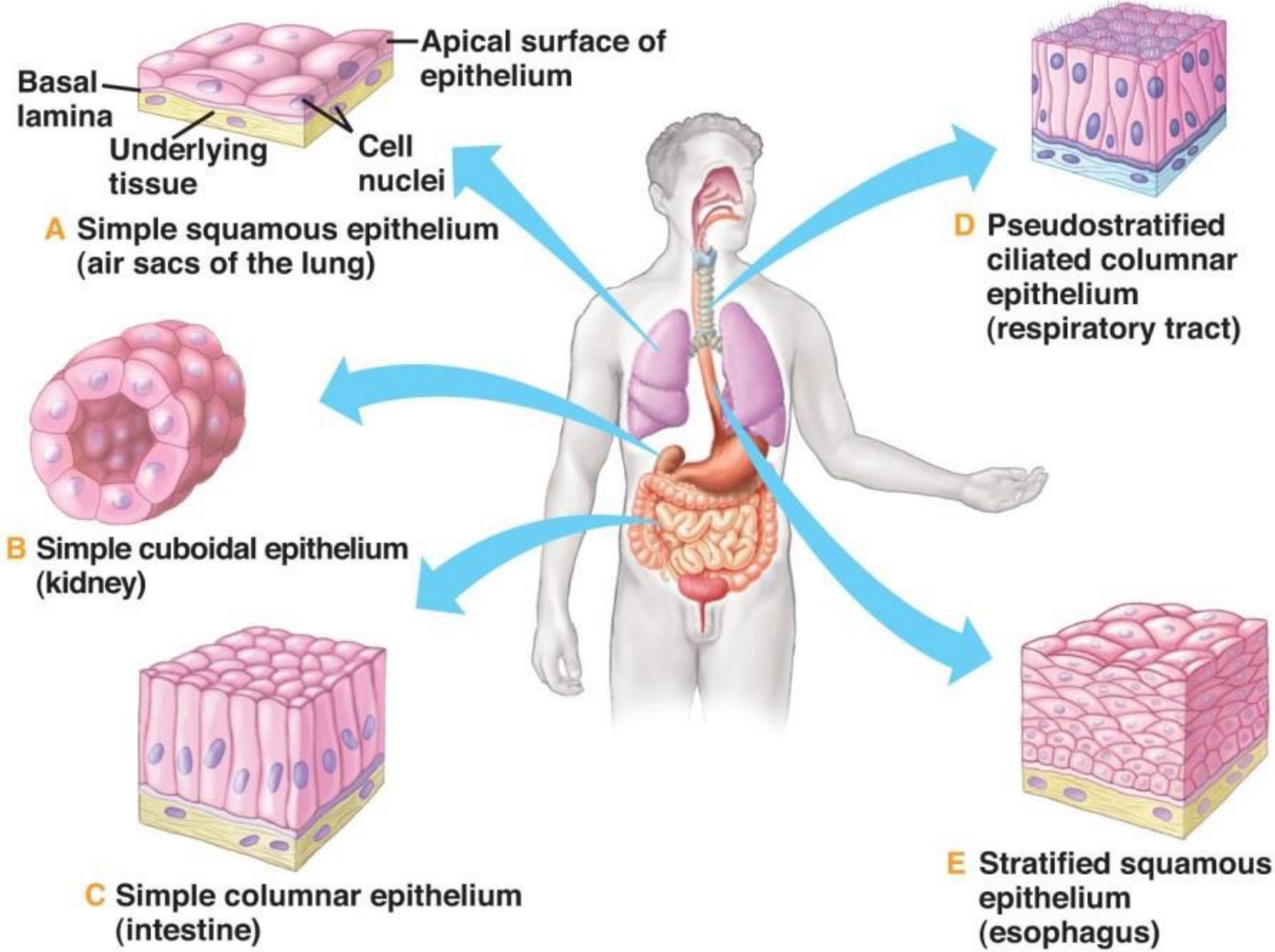
Other important key words:

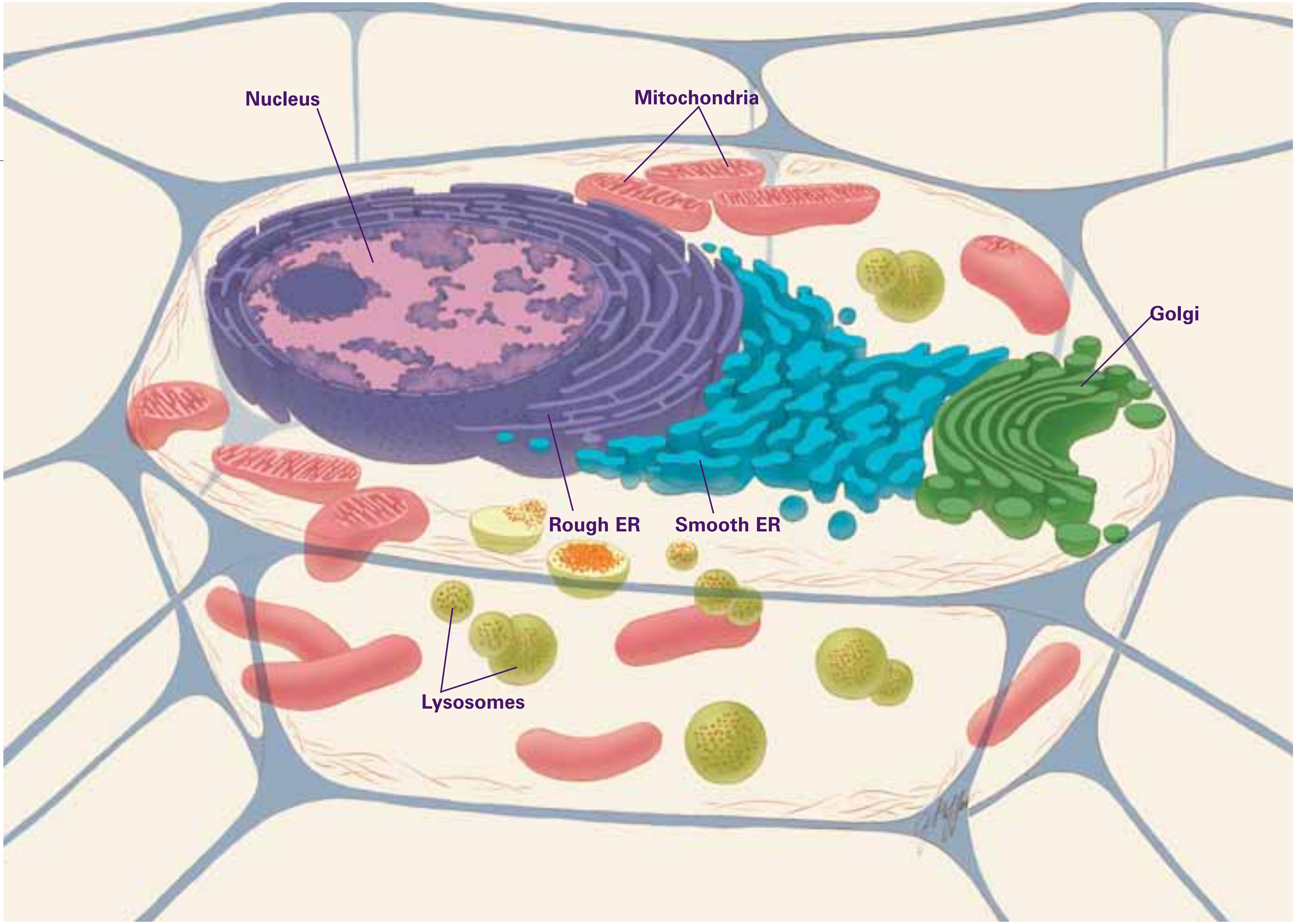
- ***Mesenchymal cells***, cells that lack polarity and are surrounded by a large extracellular matrix.
- ***Hematopoietic cells, or hemocytoblasts***, cells that give rise to all other blood cells

- ***Sarcoma***, is a cancer that arises from transformed cells of mesenchymal origin. Thus, malignant tumors made of cancellous bone, cartilage, fat, muscle, vascular, or hematopoietic tissues are, by definition, considered sarcomas.
- ***Carcinoma***, is a malignant tumor originating from epithelial cells.
- ***Blastoma***, is a tumor, more common in children, caused by malignancies in precursor cells (blast cells or simply blasts). Blasts are unipotent cells (cells that have lost most or all of the stem cell multipotency)

Human sarcomas are quite rare. Common malignancies, such as breast, colon, and lung cancer, are almost always carcinoma.

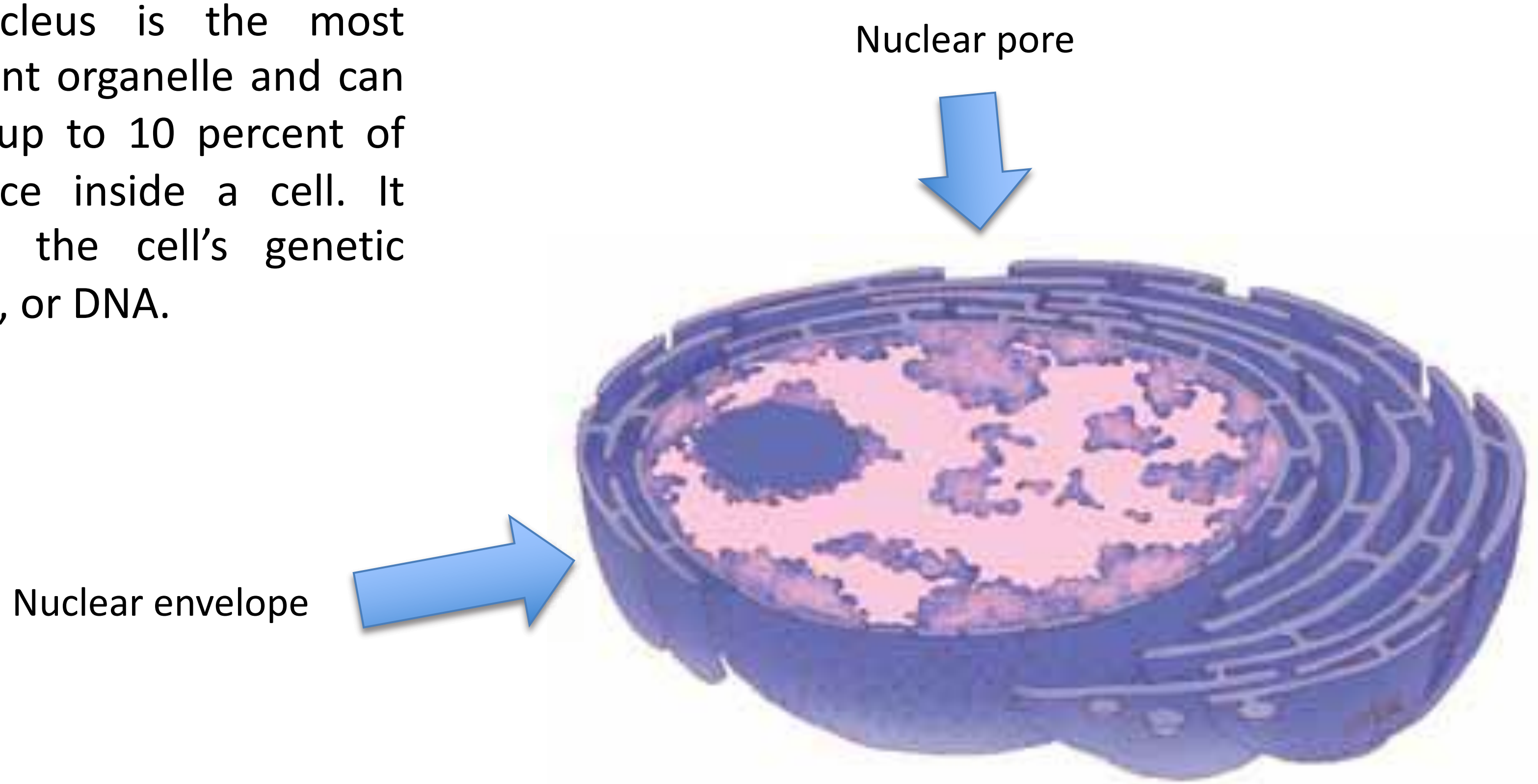
Each specific type of cells makes up different tissues throughout the organism (example, epithelial cells)




Nucleus
Mitochondria
Golgi
Rough ER
Smooth ER
Lysosomes

The Nucleus

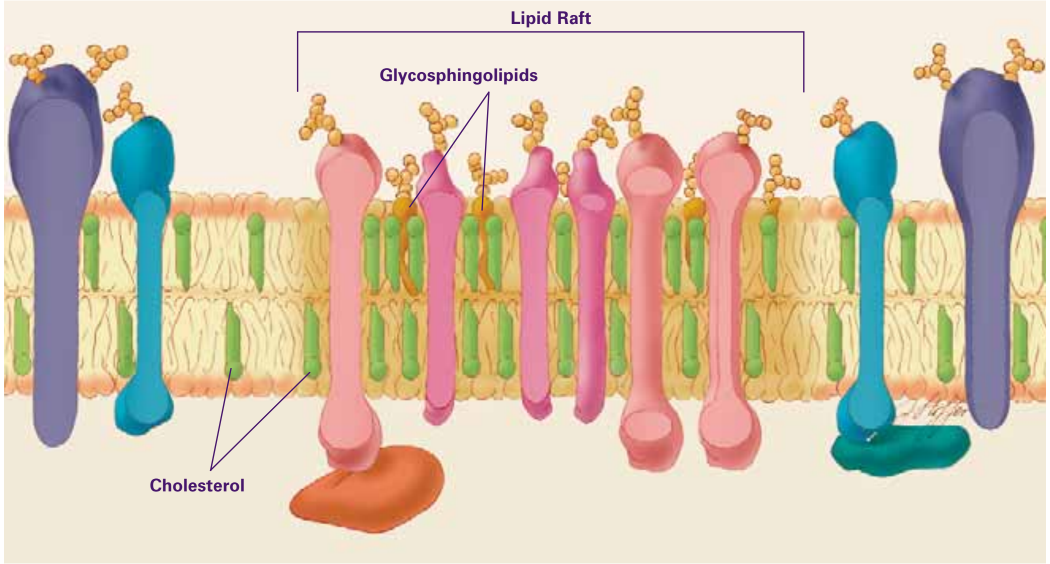
The nucleus is the most prominent organelle and can occupy up to 10 percent of the space inside a cell. It contains the cell's genetic material, or DNA.



The Cell Membrane

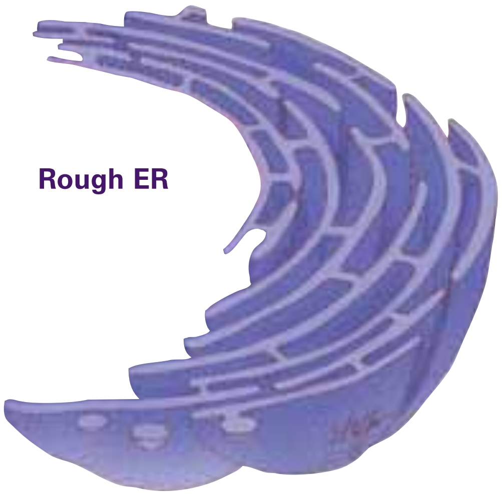
Every cell is contained within a membrane punctuated with special gates, channels, and pumps.

The cell's outer membrane is made up of a mix of proteins and lipids (fats). Lipids give membranes their flexibility. Proteins transmit chemical messages into the cell, and they also monitor and maintain the cell's chemical environment.



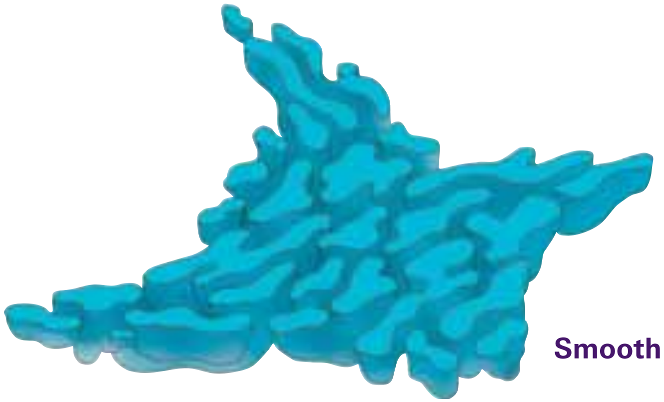
Endoplasmic Reticulum

Close to the nucleus, there are several interconnected sacs. This network of sacs, the **endoplasmic reticulum** (ER), often makes up more than 10 percent of a cell's total volume.



The **rough ER** is covered with **ribosomes**, which are sophisticated molecular machines made up of more than 70 proteins and 4 strands of **RNA**, a chemical relative of DNA. Ribosomes have a critical job: assembling all the cell's proteins.

The smooth ER has a different shape and function. A labyrinth of branched tubules, the smooth ER specializes in synthesizing lipids and also contains enzymes that break down harmful substances.



The Golgi Complex

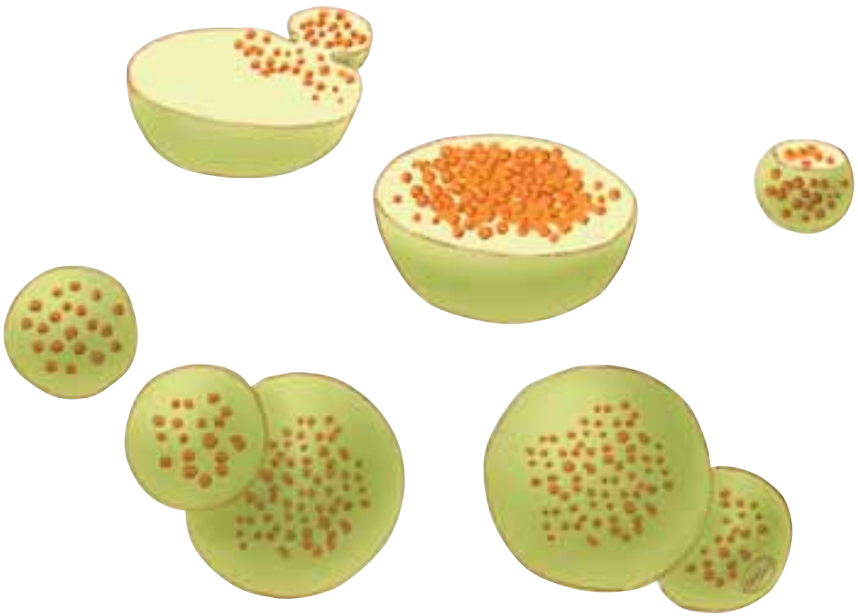
The **Golgi** complex, also called the Golgi apparatus or, simply, the Golgi, receives newly made proteins and lipids from the ER, puts the finishing touches on them, addresses them, and sends them to their final destinations.

One of the places these molecules can end up is in **lysosomes**.

Lysosomes

Lysosomes are organelles with powerful enzymes and acids decompose anything that ends up inside into their component parts, almost all of which the cell recycles as nutrients or building blocks.

Lysosomes also act as cellular garbage trucks, hauling away unusable waste and dumping it outside the cell. From there, the body has various ways of getting rid of it.

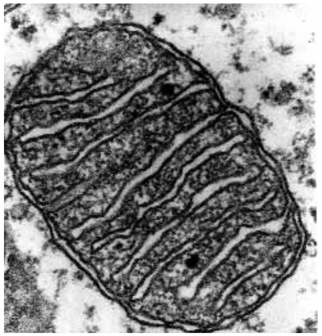


Mitochondria

The main energy source in your body is a small molecule called **ATP**, for adenosine triphosphate. ATP is made in organelles called **mitochondria** tha convert energy from your food into ATP.

Mitochondria are encased in an outer membrane. But they also have an inner membrane which is four or five times larger than the outer membrane. So, to fit inside the organelle, it doubles over in many places, extending long, fingerlike folds into the center of the organelle. These folds increase the surface area available to the cell machinery that makes ATP. In other words, they increase the ATP-production capacity of mitochondria.

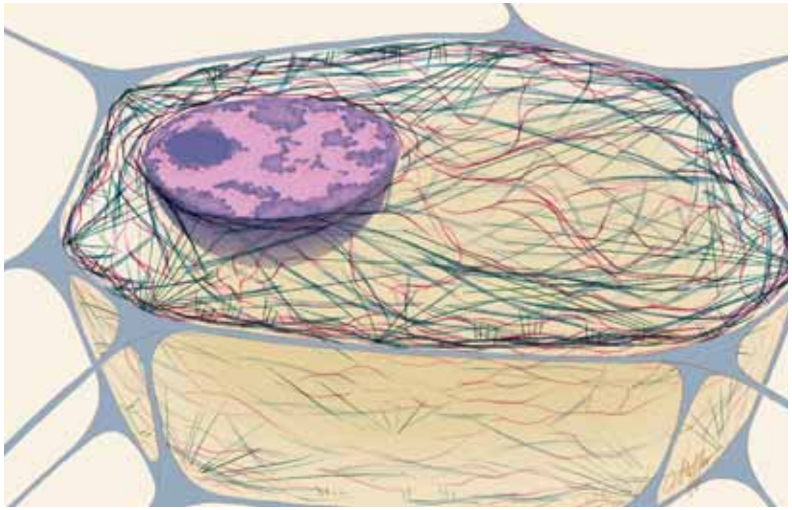
The space inside mitochondria is filled with enzymes, DNA, special mitochondrial ribosomes, and other molecules necessary to turn on mitochondrial genes.



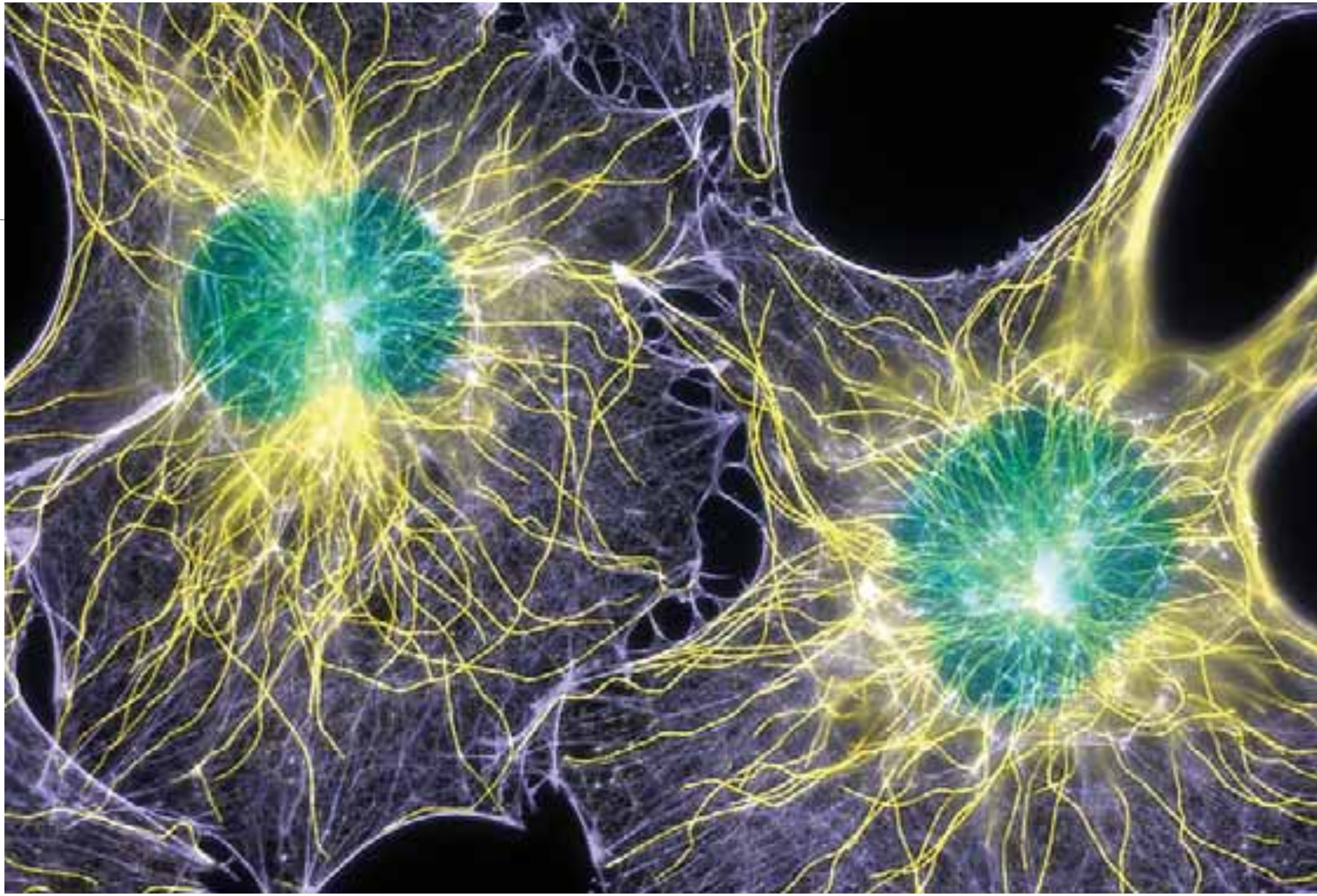
Cytoskeleton

The **cytoskeleton** is the cell's skeleton. Like the bony skeletons that give us stability, the cytoskeleton gives cells shape, strength, and the ability to move.

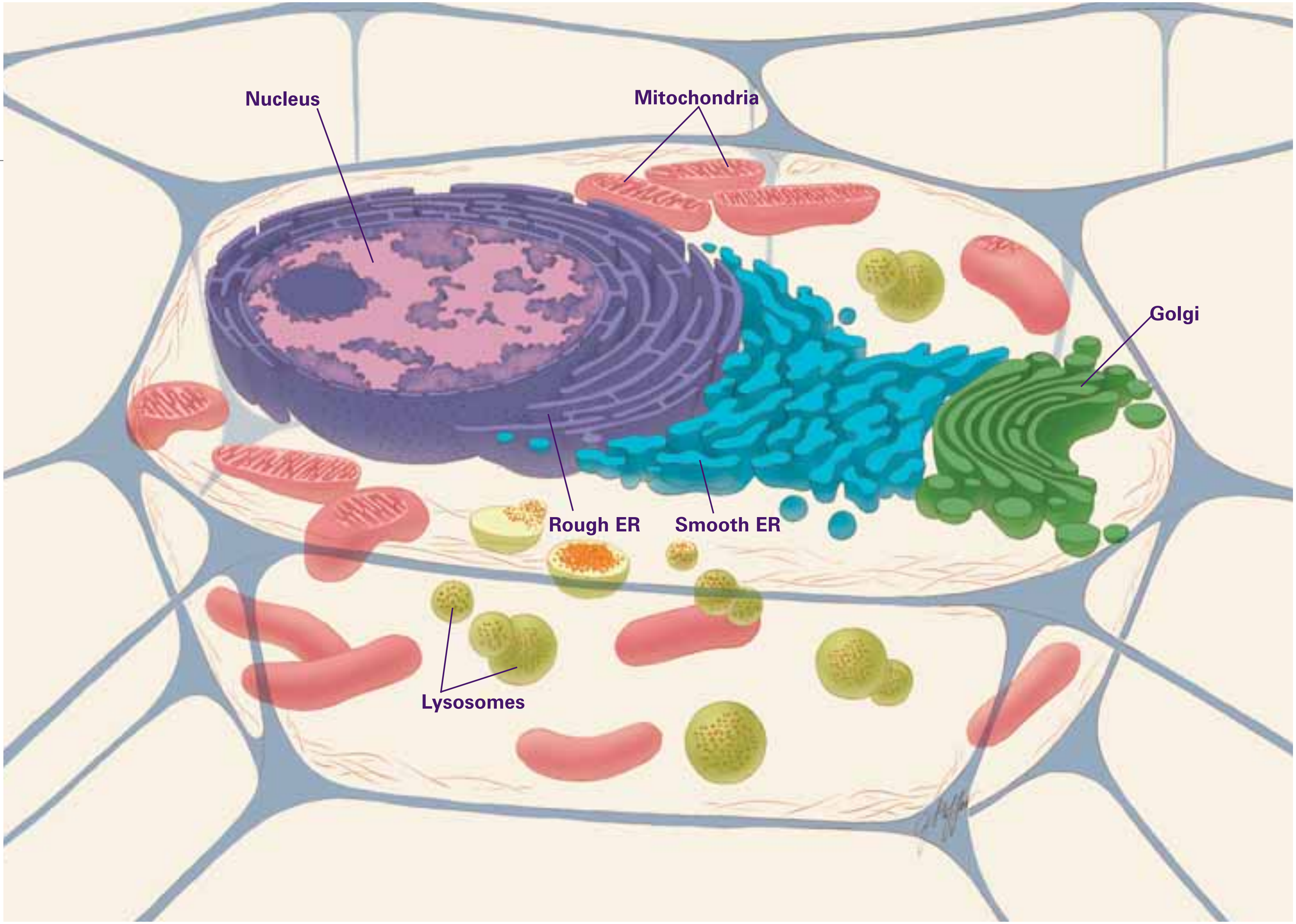
The cytoskeleton is made up of three types of fibers that constantly shrink and grow to meet the needs of the cell: **microtubules**, **intermediate filaments**, and **actin filaments**. Each type of fiber looks, feels, and functions differently.



The three fibers of the cytoskeleton — microtubules in blue, intermediate filaments in red, and actin in green—play countless roles in the cell.



In these cells, actin filaments appear light purple, microtubules yellow, and nuclei greenish blue.
This image, which has been digitally colored, won first place in the 2003 Nikon Small World Competition.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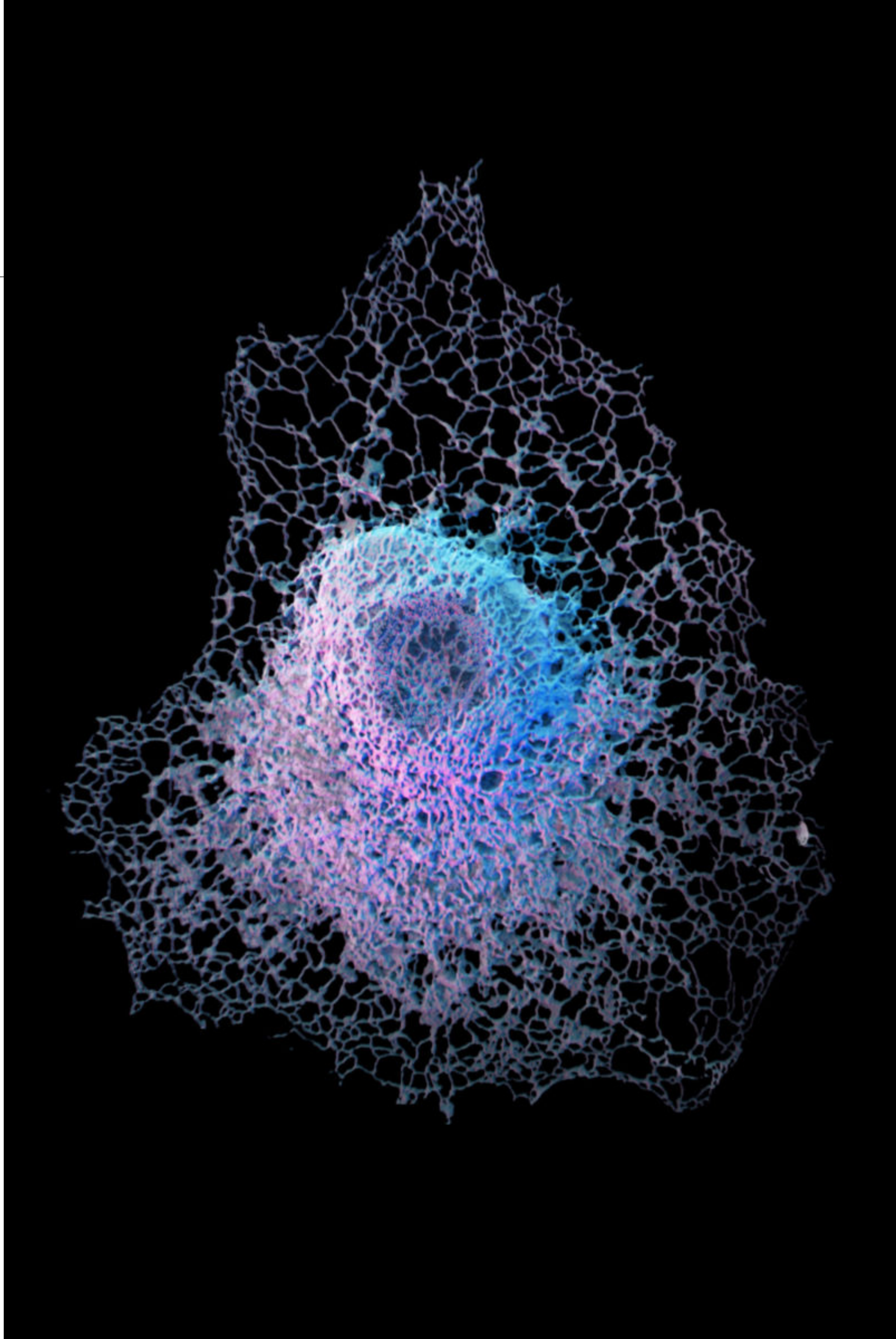
https://www.nikonsmallworld.com



3D rendering of the endoplasmic reticulum in a tissue culture cell

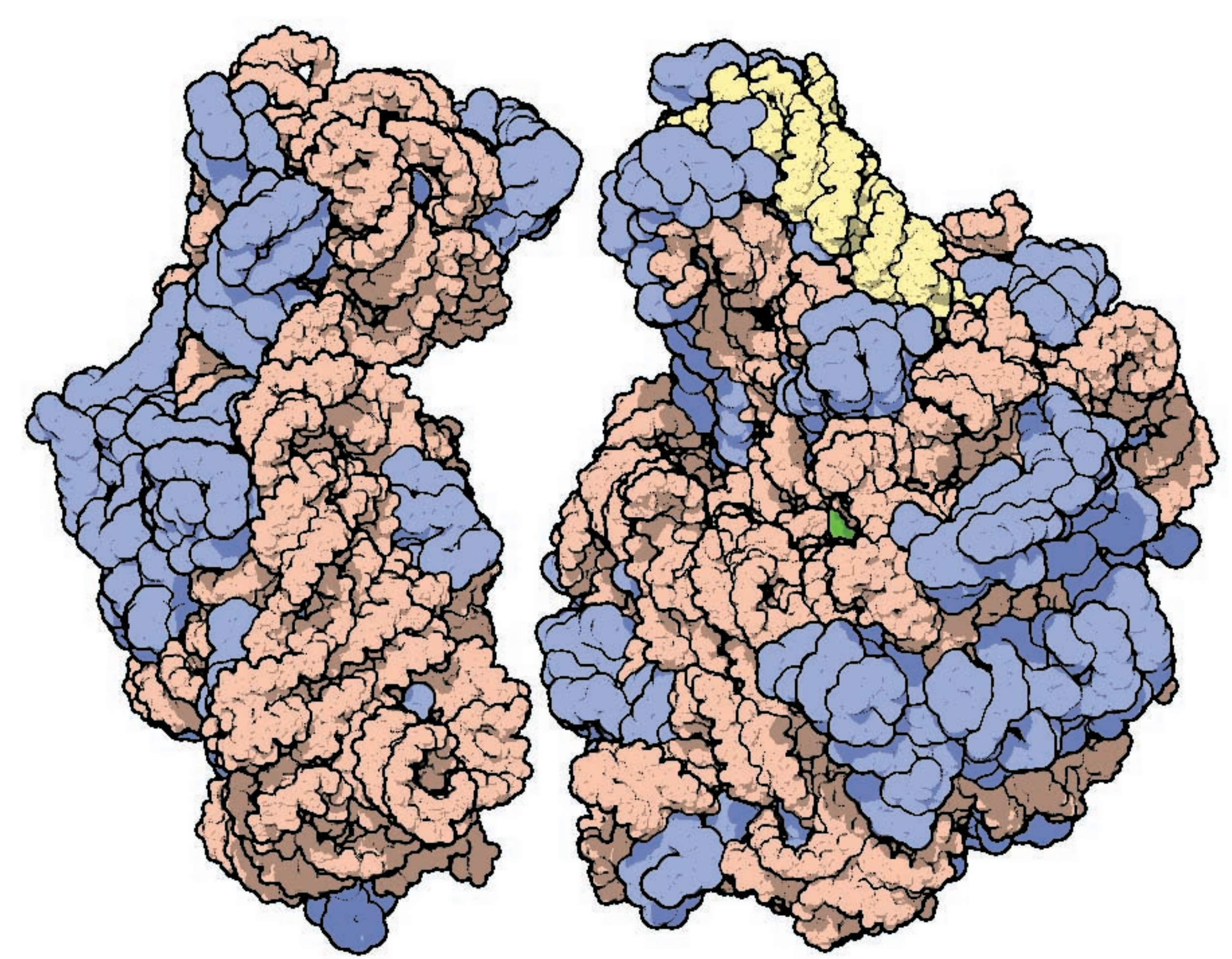
(Andrew Moore, Nikon Small World 2022 Photomicrography Competition)

https://www.nikonsmallworld.com/galleries/2022-photomicrography-competition/3d-rendering-of-the-endoplasmic-reticulum-in-a-tissue-culture-cell

	ACTUAL SIZE (AVERAGE)	PERCEIVED SIZE WHEN MAGNIFIED 3 MILLION TIMES
Cell diameter	30 micrometers*	300 feet
Nucleus diameter	5 micrometers	50 feet
Mitochondrion length	Typically 1–2 micrometers but can be up to 7 micrometers long	18 feet
Lysosome diameter	50–3,000 **nanometers***	5 inches to 30 feet
Ribosome diameter	20–30 nanometers	2–3 inches
Microtubule width	25 nanometers	3 inches
Intermediate filament width	10 nanometers	1.2 inches
Actin filament width	5–9 nanometers	0.5–1 inch

Length scales in the microscopic world of cells (1)

- 0.1 nm (nanometer) diameter of a hydrogen atom
- 0.8 nm Amino Acid
- 2 nm Diameter of a DNA helix
- 4 nm Globular Protein
- 6 nm microfilaments
- 7 nm thickness cell membranes
- **20 nm Ribosome**
- 25 nm Microtubule
- **30 nm Small virus (Picornaviruses)**
- **30 nm Rhinoviruses**
- 50 nm Nuclear pore
- 100 nm HIV
- 120 nm Large virus (Orthomyxoviruses, includes influenza virus)
- 150-250 nm Very large virus (Rhabdoviruses, Paramyxoviruses)
- 150-250 nm small bacteria such as Mycoplasma

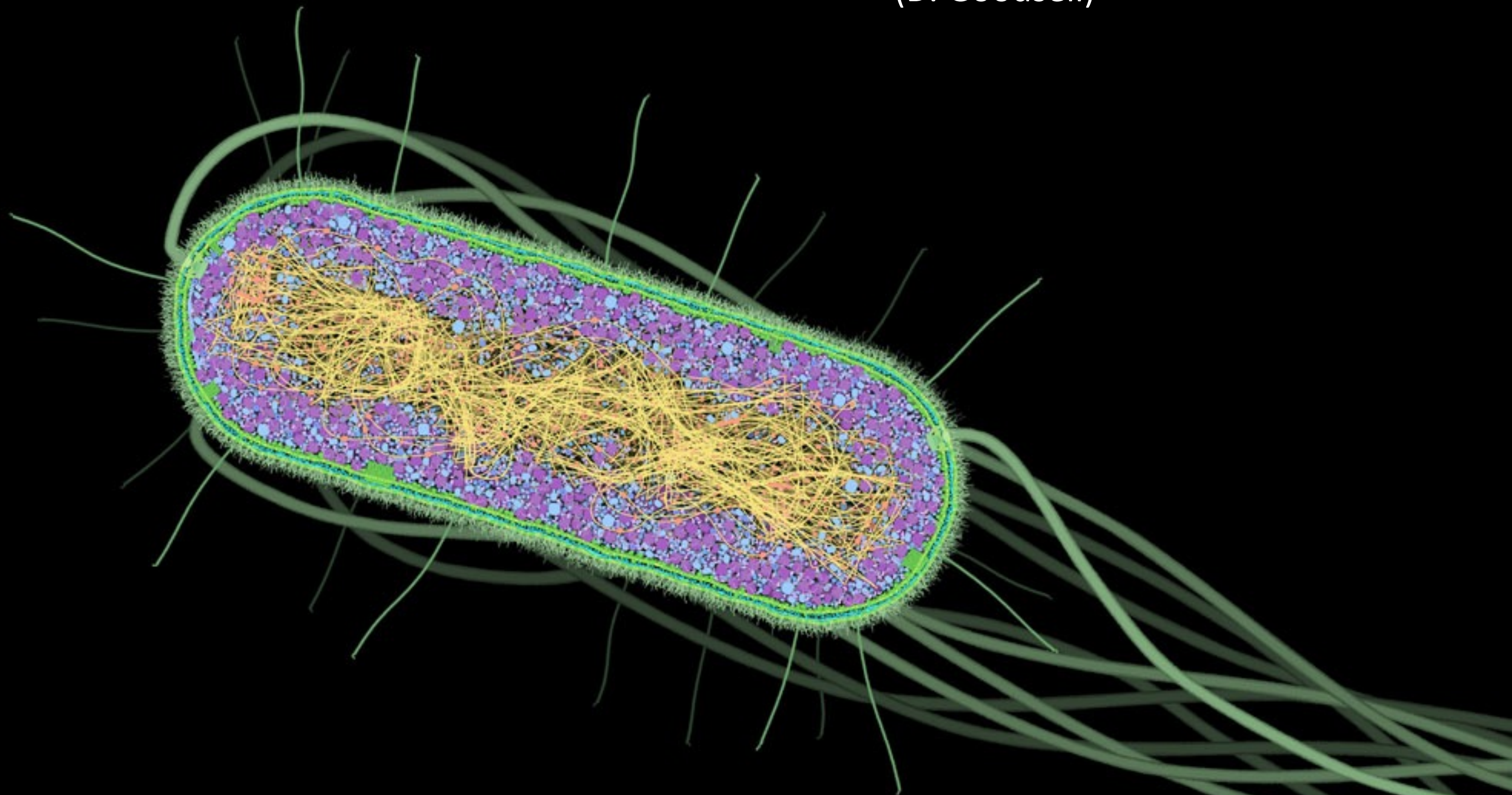


SARS-Cov-19, about 120 nm diameter

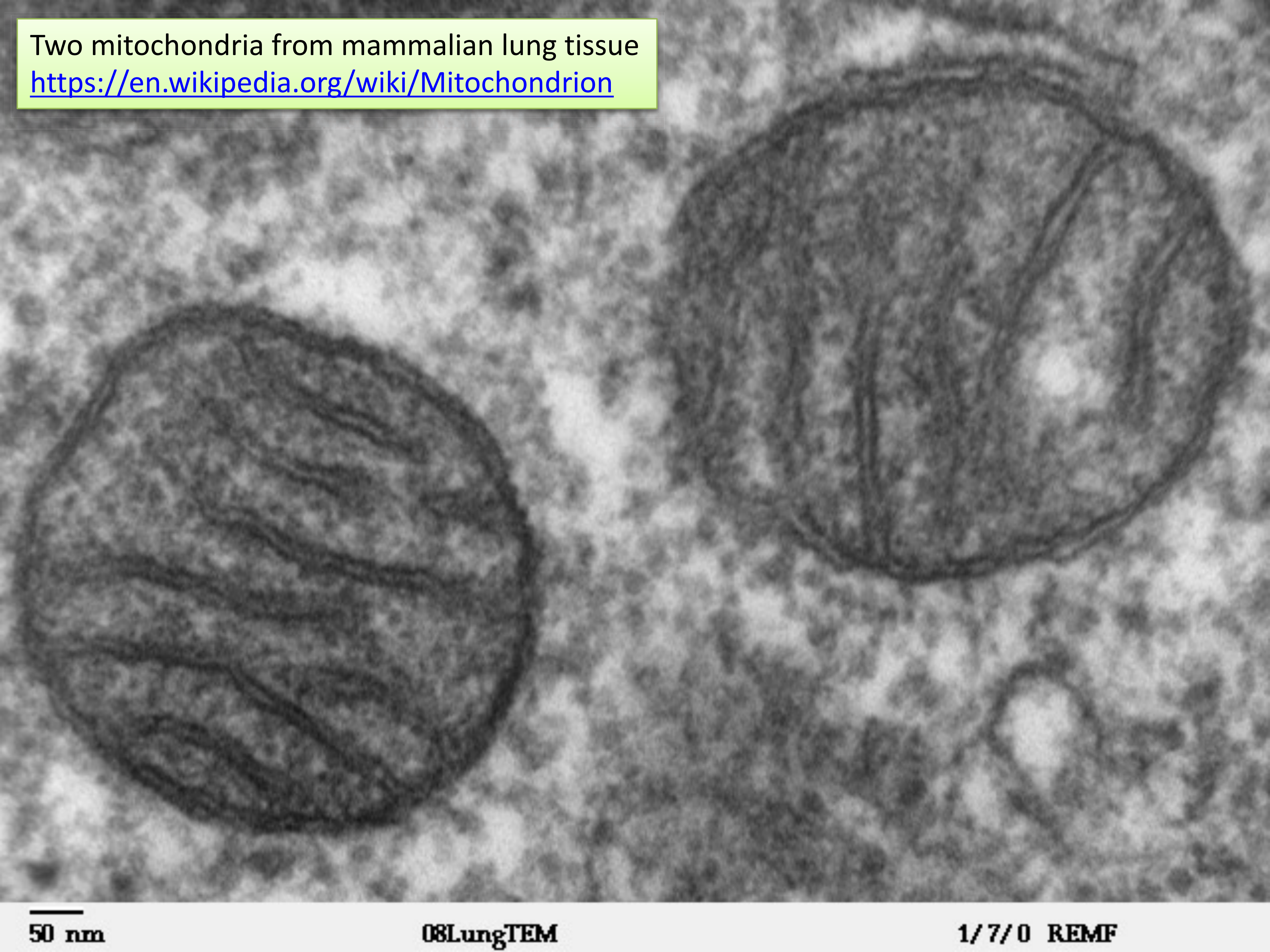
The 5th generation of Intel Core processors contains about 1.3 billion transistors, which measure 14 nm – smaller than most viruses. However, viruses are considerably more complex than a single transistor.

Length scales in the microscopic world of cells (2)

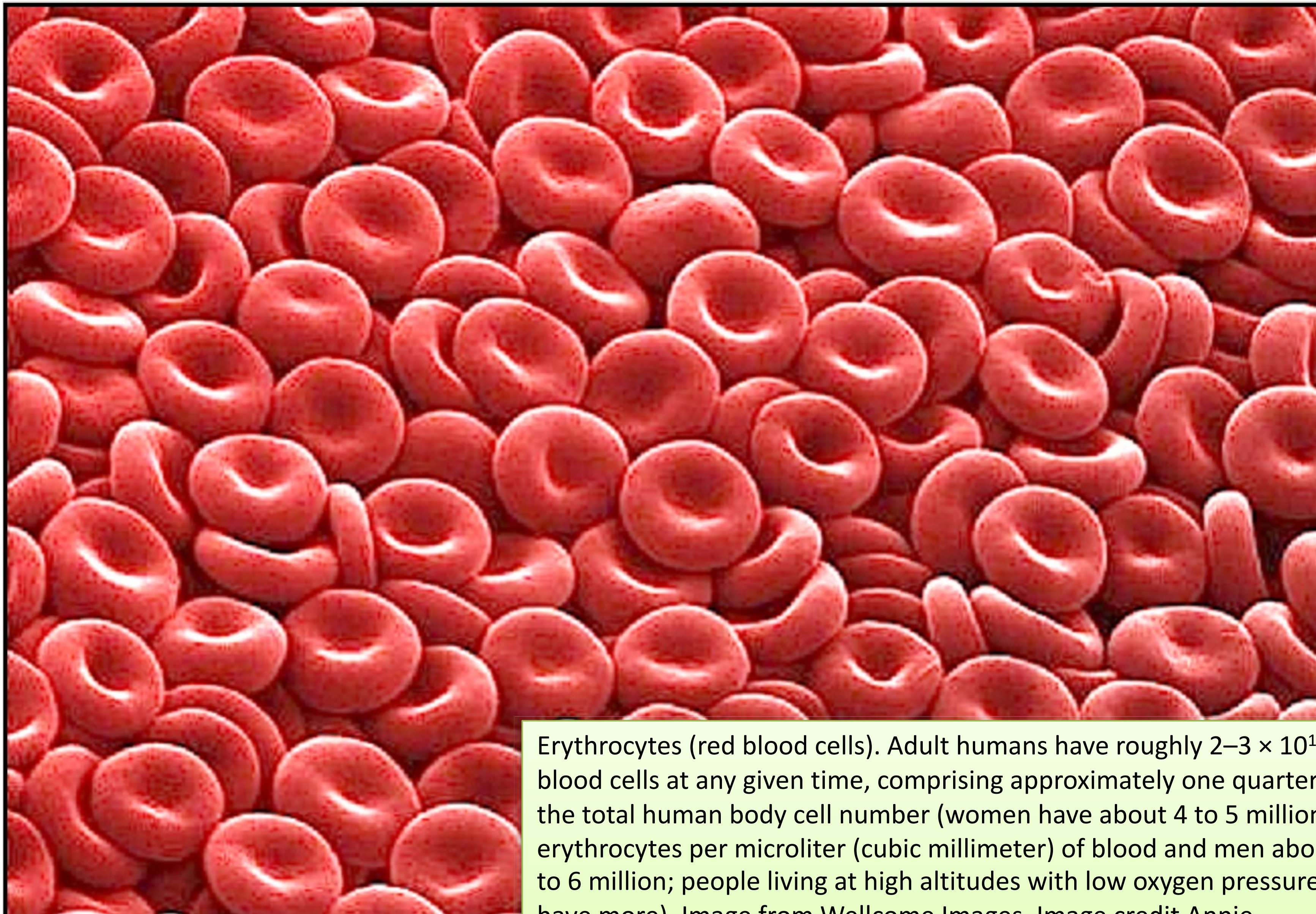
- 200 nm Centriole
- 200 nm (200 to 500 nm) Lysosomes
- 200 nm (200 to 500 nm) Peroxisomes
- **800 nm giant virus Mimivirus**
- (1 - 10 μm) the general sizes for Prokaryotes
- 1 μm Diameter of human nerve cell
- **2 μm E.coli - a bacterium**
- **3 μm Mitochondrion**
- 5 μm length of chloroplast
- 6 μm (3 - 10 micrometers) the Nucleus
- **9 μm Human red blood cell**



A pictorial representation of E. coli
(D. Goodsell)



Two mitochondria from mammalian lung tissue
https://en.wikipedia.org/wiki/Mitochondrion



Erythrocytes (red blood cells). Adult humans have roughly 2–3 × 10^{13} red blood cells at any given time, comprising approximately one quarter of the total human body cell number (women have about 4 to 5 million erythrocytes per microliter (cubic millimeter) of blood and men about 5 to 6 million; people living at high altitudes with low oxygen pressure have more). Image from Wellcome Images. Image credit Annie Cavanagh.

(http://www.anatomybox.com/tag/erythrocytes/)

Exercise: how many cells in the human body?

Known facts:

- diameter of one human cell, about 20 μm
- density of cells ≈ density of water

Exercise: how many cells in the human body?

Known facts:

- diameter of one human cell, about 20 µm
- density of cells ≈ density of water

Volume of one cell: $$\frac{4\pi}{3}R^3 \approx 4 \times 10^{-15}\mathrm{m}^3$$

Mass of one cell: $$\approx 4 \times 10^{-15}\mathrm{m}^3 \times 10^3\mathrm{kg/m}^3 = 4 \times 10^{-12}\mathrm{kg}$$

Number of cells in a 60 kg individual: $$\boxed{\frac{60\mathrm{kg}}{4 \times 10^{-12}\mathrm{kg}} = 1.5 \times 10^{13}}$$

Length scales in the microscopic world of cells (3)

- 10 µm
- (10 - 30 µm) Most Eukaryotic animal cells
- (10 - 100 µm) Most Eukaryotic plant cells
- 90 µm small Amoeba
- 100 µm Human Egg (oocyte)
- up to 160 µm Megakaryocyte
- up to 500 µm giant bacterium Thiomargarita
- up to 800 µm large Amoeba
- 1 mm (1 millimeter, 1/10th cm)
- 1 mm Diameter of the squid giant nerve cell
- **up to 40mm Diameter of giant amoeba Gromia Sphaerica**
- 120 mm Diameter of an ostrich egg (a dinosaur egg was much larger)
- 2 meters Total length of DNA in a human cell
- 3 meters Length of a nerve cell of giraffe's neck

(adapted from http://en.wikibooks.org/wiki/Cell_Biology/Introduction/Cell_size)

Exercise: how many meters of DNA in the human body?

Exercise: how many meters of DNA in the human body?

$$2\mathrm{m} \times \left(1.5 \times 10^{13}\right) = 3 \times 10^{13}\mathrm{m}$$
$$\approx 200 \text{ A.U.}$$

One Astronomical Unit is the average Earth-Sun distance: $1 \text{ A.U.} \approx 1.5 \times 10^{11}\mathrm{m}$

Gromia sphaerica is a large spherical amoeba, a single-celled organism classed among the protists and is the largest in the genus Gromia.

It was discovered in 2000, along the Oman margin of the Arabian sea, at depths from 1,163 to 1,194 meters. Specimens range from 4.7 to 38 millimeters in diameter.

https://en.wikipedia.org/wiki/Gromia_sphaerica

Dividing HeLa cells. Coloured scanning electron micrograph (SEM) of HeLa cells undergoing cytokinesis (cell division). Cytokinesis occurs after nuclear division (mitosis), which produces two daughter nuclei. The two daughter cells are still connected by a midbody, a transient structure formed from microtubules. HeLa cells are a continuously cultured cell line of human cancer cells, which are immortal and so thrive in the laboratory. They are widely used in biological and medical research. **These cells have a diameter of about 15 µm**.

From: http://www.sciencephoto.com/media/137829/view#

Cell replication exercise