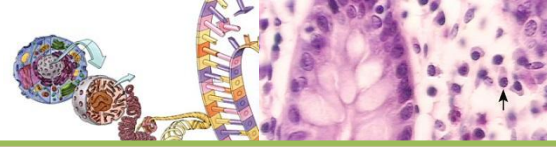
Kusuma School of Biological Sciences

SBL-100

Introductory Biology for Engineers

L-1



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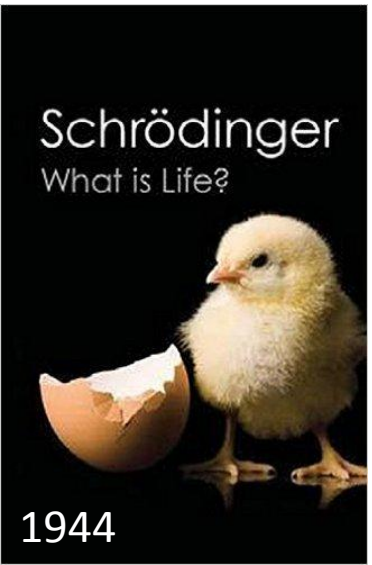
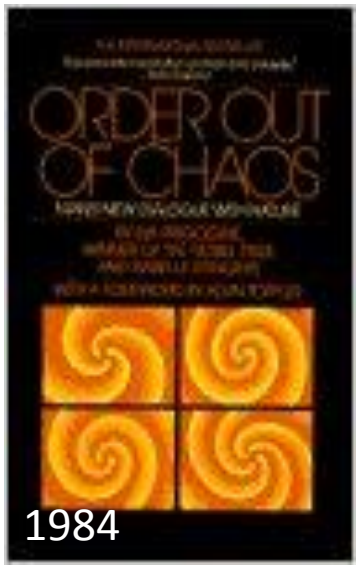
The fundamental laws necessary for the mathematical treatment of a large part of physics and the whole of chemistry are thus completely known, and the difficulty lies only in the fact that application of these laws leads to equations that are too complex to be solved. - **Paul Dirac (1929) - (Physics Nobel 1933)** . What about Biology?

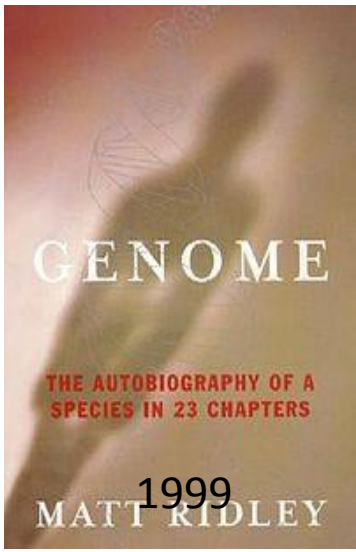
"It is by avoiding the rapid decay into the inert state of 'equilibrium' that an organism appears so enigmatic....What an organism feeds upon is negative entropy." – **Erwin Schrodinegr (1944) - (Physics Nobel 1933) ..**

In a footnote, later, however, Schrödinger explains that by 'negative entropy', he really means *free energy*. In a biological context, the negentropy of a living system is the entropy that it exports to keep its own entropy low.





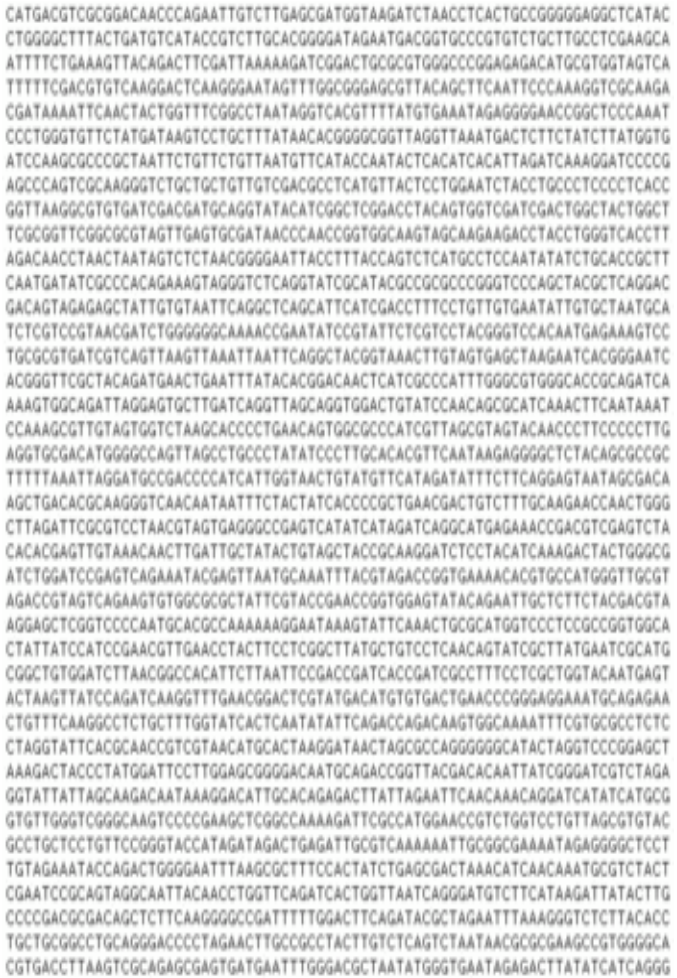
The principle of minimum entropy production says that the steady state of an irreversible process, i.e., the state in which the thermodynamic variables are independent of time, is characterized by a minimum value of the rate of entropy production . **Ilya Prigogine (Chemistry Nobel – 1977)**



"It took about 15 years and $2.7 billion to sequence one person's genomic information back in 2000," It's now possible to sequence a human genome in a single day for ~ $1,000.

Startups:

23andMe is a privately held personal genomics and biotechnology company, founded in 2006 and based in California, USA. The company is named for the 23 pairs of chromosomes in a normal human cell. Its saliva-based direct-to-consumer personal genome test offering estimates of "predisposition for more than 90 traits and conditions ranging from baldness to blindness", was named Invention of the Year by *Time* magazine in 2008.

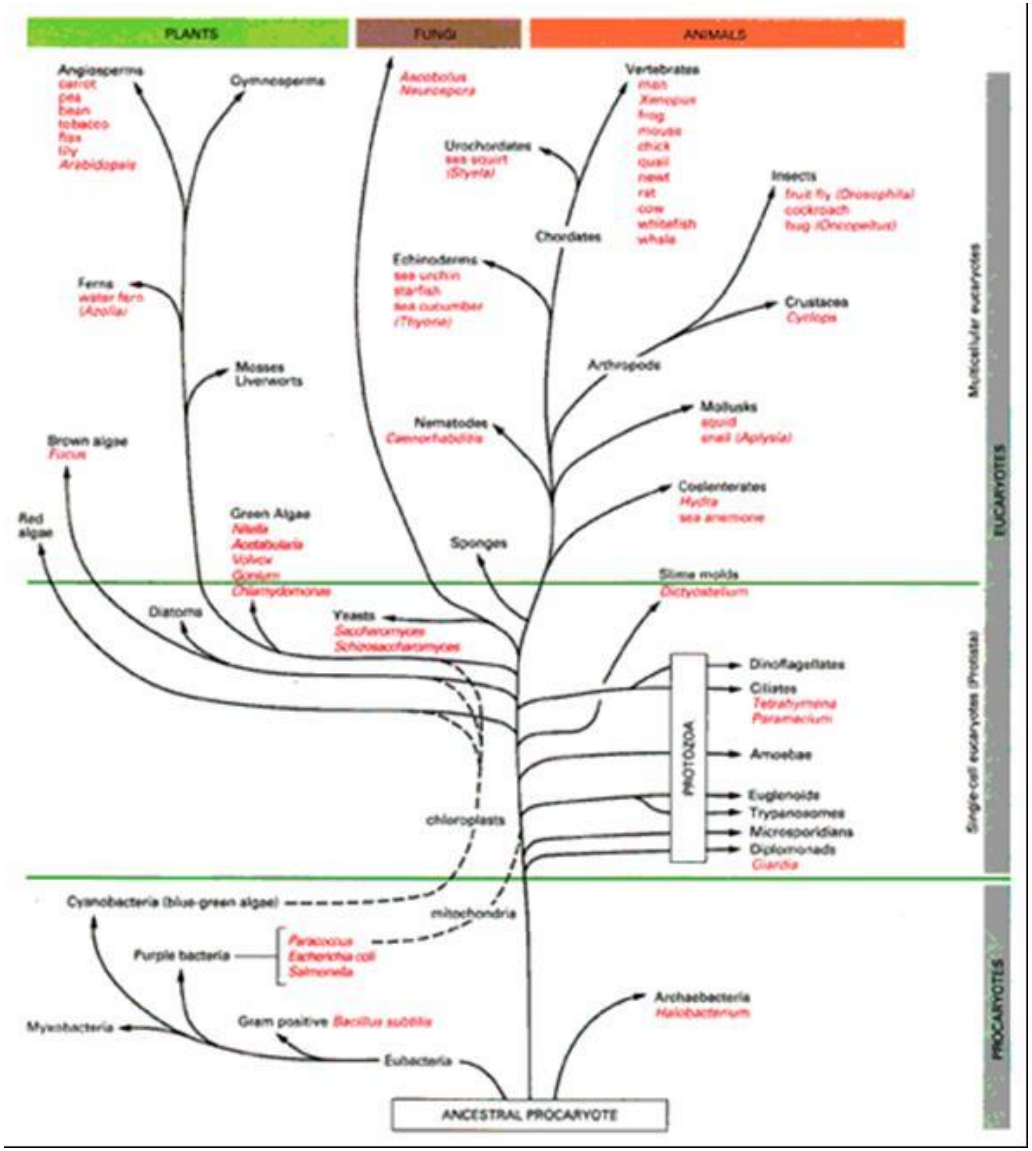


The first viral RNA genome (3.5 KB)(1976)

The first bacterial genome (1.8 MB) (1995)

The first eukaryotic genome (12.1 MB)(1996)

The first human genome (3.3 GB) (2001)

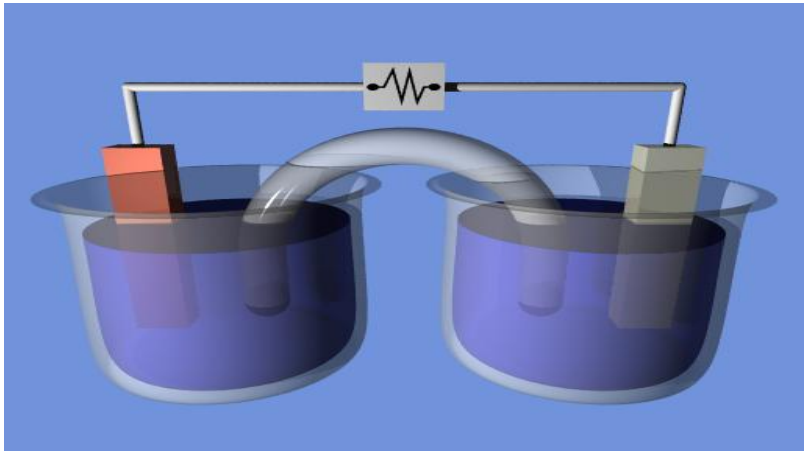


Variations in genome accounts for the diversity. Despite the great diversity in form and function, cells and organisms share a common biochemistry. This commonality has been further proved through the whole genome sequencing namely, the determination of the complete nucleotide sequence of the DNA of an organism in a cell. Mice and humans contain roughly the same number of genes – about 28K protein coding regions. According to Carl Sagan, the difference between humans and chimps is only 160 enzymes.

The tree of life. A possible evolutionary path from a common ancestral cell to the diverse species present in the modern world can be deduced from DNA sequence analysis presenting evolutionary relationships among organisms from the major biological kingdoms. The branches of the evolutionary tree show paths of descent. The length of paths does not indicate the passage of time and the vertical axis shows only major categories of organisms, not evolutionary age. Dotted lines indicate the supposed incorporation of some cell types into others, transferring all of their genes and giving the tree some web-like features. [From: A Alberts, D Bray, J Lewis, M Raff, K Roberts & J D Watson, Molecular Biology of the Cell, p38, Garland, New York (1994)]

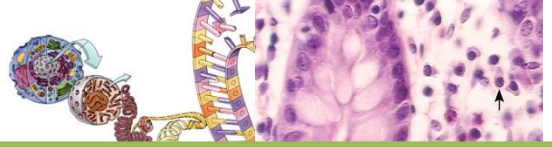
Cell is the basic unit of life!

There are two kinds of cells



Electrical energy to chemical energy → **Voltaic cells**

Chemical energy to electrical energy → **Galvanic cells**



Logic of Living Cells – A Recap

Cell is the smallest entity capable of displaying the attributes associated with the living state: **growth, metabolism, replication and response to external stimuli**. A cell under right conditions can generate the whole organism. Schleiden and Schwann in 1838 proposed that all living organisms are composed of cells.

Adult **human** is made up of about **30 trillion cells** mostly organized into cell collectives called tissues. In contrast, organisms such as bacteria, yeast, amoeba exist as single cells. Size of a human cell is approximately **20 microns .**

It was recognized in 1944 by Avery and coworkers that **DNA is the genetic material** inside the cells which is responsible for the propagation of life.

Unicellular organisms such as bacteria, which lack a nucleus, are referred to as **prokaryotes**. Eukaryotic cells have true nuclei and other organelles such as mitochondria. ***Eukaryotes*** *include life forms ranging from single-celled amoebae to multicellular organisms such as Fungi, Plant and Animal kingdoms including human.*

Eukaryotes are believed to have evolved from prokaryotes over the course of geological time.

A prokaryotic cell

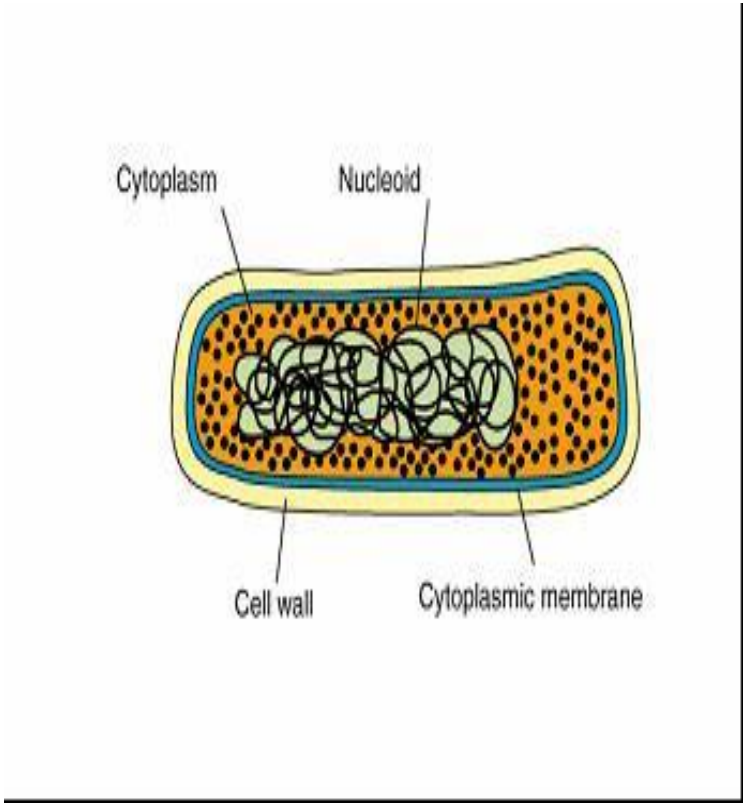
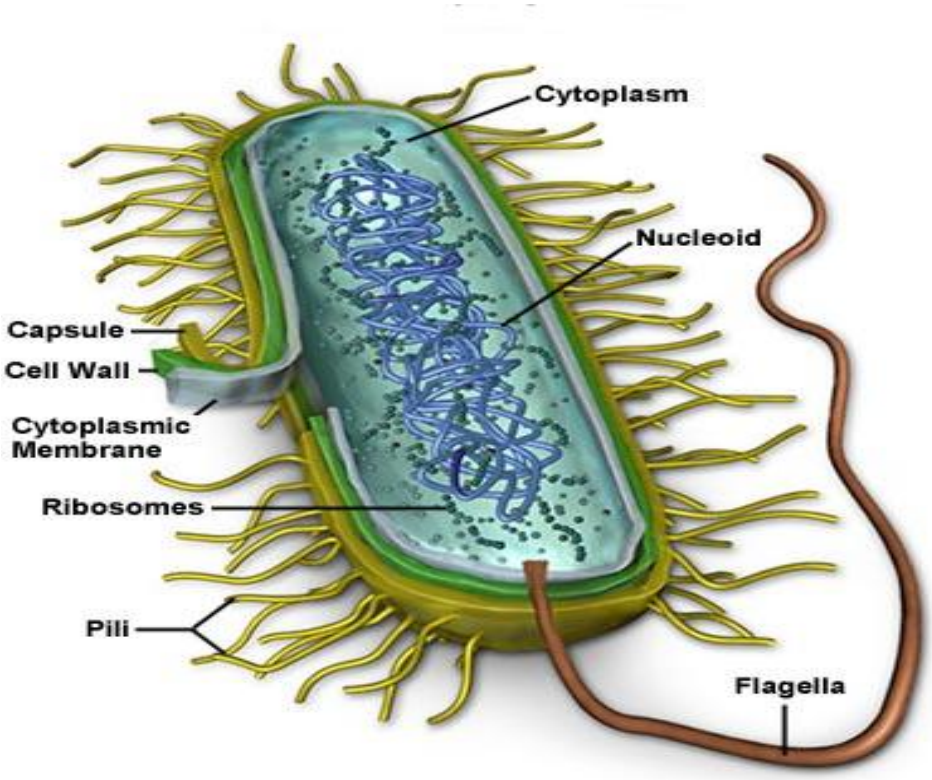


Table : Organelles and their functions in prokaryotes

Structure	Molecular Composition	Function
Cell wall	Peptidoglycan - a rigid framework of polysaccharide cross-linked by peptide chains.	Mechanical support, shape, and protection. Being porous allows small molecules to pass.
Cell membrane	Composed of 45% lipid & 55% protein. The lipids form bilayer.	Highly selective permeability barrier that controls the entry of most substances into the cell.
Nuclear area or Nucleoid	The genetic material is a single tightly coiled DNA molecule 2nm in diameter & over 1mm in length. (Molecular mass of E.coli DNA is $3x10^9$ daltons)	DNA is the blueprint of life, carries the genetic information.
Ribosomes	Bacterial cell comprises ~ 15,000 ribosomes. It consists of 65% RNA & 35% protein	Ribosomes are the sites of protein synthesis.
Storage granules	Granules contain polymers of metabolites such as sugars	When needed as fuel, the polymers are metabolized by energy-yielding pathways
Cytosol	Gelatinous area that is 20% protein by weight	Cytosol is the site for intermediary metabolism by which cells generate energy required for cell growth & function.



A bacterial cell

Bacterial diseases

Bacteria	Disease Caused
Mycobacterium tuberculosis	Tuberculosis
Mycobacterium leprae	Leprosy
Bacillus anthracis	Anthrax
Clostridium tetani	Tetanus
Bordetella pertussis	Whooping Cough
Salmlonella typhi	Typhoid
Helicobacter pylori	Ulcers
Streptococcus pneumoniae	Pneumonia
Cornybacterium diptheria	Diptheria
Vibrio cholera	Cholera
Streptococcus A	Scarlet Fever
Borrelia burgdorferi	Lyme disease

Eukaryotic cells are much larger (5-100 µm) and more advanced in organization (in a structural, evolutionary and functional sense). These not only include the multi-cellular plants, animals and fungi, but also some protozoans and other unicellular organisms like yeasts and algae.

Some differences between prokaryotic and eukaryotic cells.

	Prokaryotic cells	Eukaryotic cells
Size	1-2 µm	5-100 µm
Containment of DNA	Free in the cytoplasm as nucleoid	In nucleus, associated with proteins into multiple chromosomes
Ploidy*	Usually haploid	Always diploid or polyploid
Mechanism of cell replication	Simple division following DNA replication	Mitosis in somatic cells#, meiosis in gametes+
Internal compartmentalization	No	Several different kinds of organelles

* The term ploidy refers to the number of copies of the genetic information carried by each cell.
# Somatic cells are the body cells of organism which are diploid in nature.
+ Gametes (cells that lead to sperm cells & ova or the egg) are haploid in nature and divide by process called meiosis.

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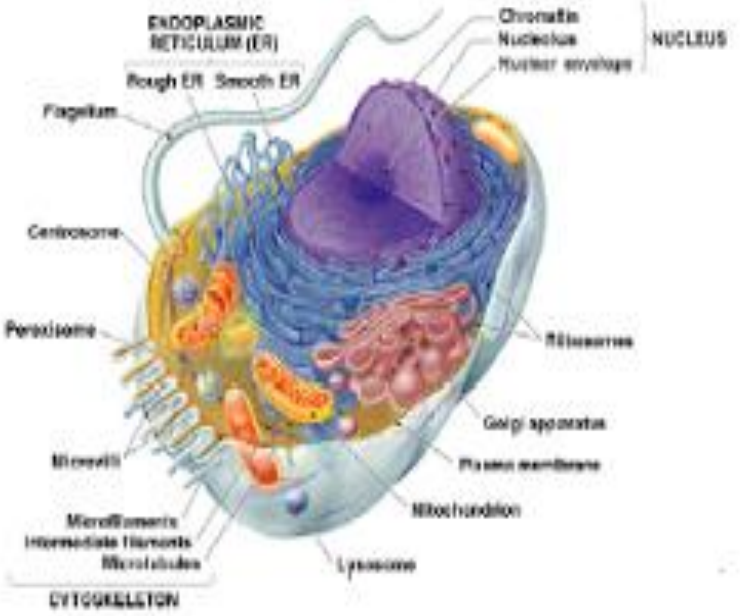
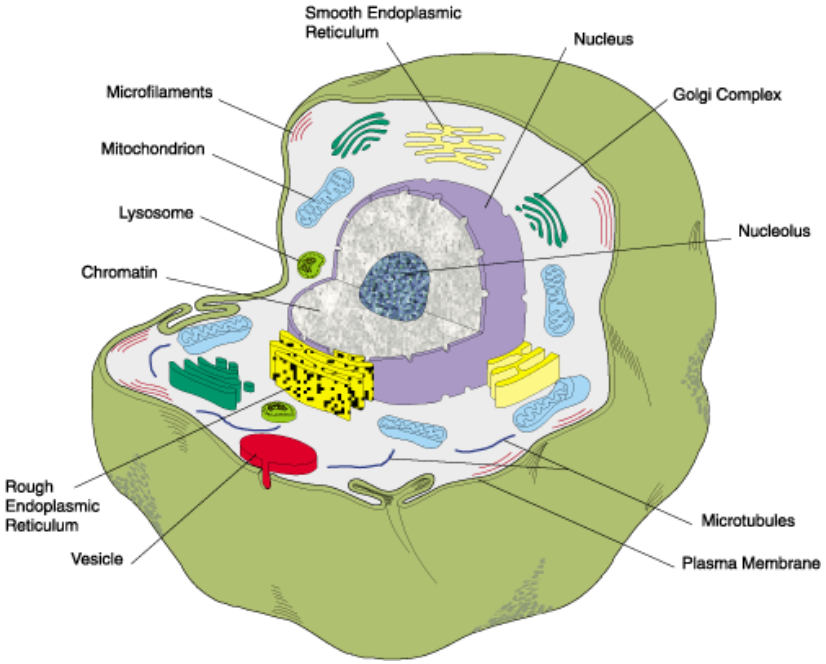
A eukaryotic cell

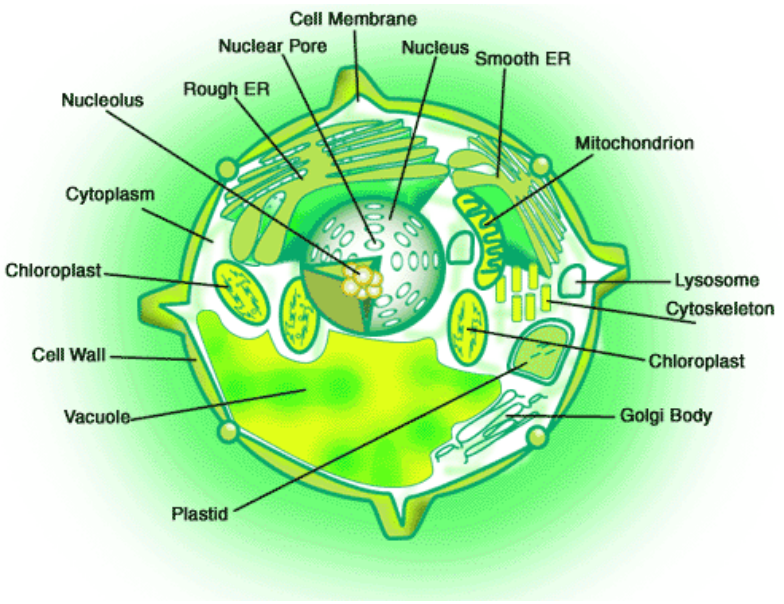


Organelles and their functions in eukaryotes

Structure	Molecular Composition	Function
Cell membrane	Lipids form a bilayer of thickness 7nm in which different proteins are embedded	Selectively permeable outer boundary of the cell. O_2, NO, CO_2, H_2O & some steroid hormones can pass through simple diffusion.
Nucleus	Nucleus is separated from the cytosol by double membrane, the nuclear envelope. DNA is tightly coiled with proteins to form chromatin fibers, the material from which chromosomes are made.	Nucleus is the repository of genetic material organized as chromosomes.
Mitochondria	Mitochondria are organelles surrounded by two membranes. The inner membrane & the interior known as the matrix are sites for energy generation	Mitochondria are the powerhouses of eukaryotic cells where carbohydrates, fats & amino acids are oxidized to CO_2 & H_2O.
Golgi Apparatus	A system of flattened membrane – bounded vesicles stacked into a complex.	Involved in packaging & processing of macromolecules to other cellular compartments
Endoplasmic Reticulum (ER) & Ribosome	Flattened sacs, tubes & sheets of internal membrane lining the cytoplasm of the cell. It is continuous with outer membrane of the nuclear envelope. ER when studded with ribosome forms rough ER. Eukaryotic ribosomes are larger than prokaryotic ribosomes.	Membrane proteins & lipids are synthesized in ER.
Lysosomes	Lysosomes are small vesicles (0.2-0.5 µm) in diameter, bounded by single membrane. They contain hydrolytic enzymes such as proteases, hydrolases & nucleases. Formed by budding of Golgi.	Lysosomes function in intracellular digestion of materials entering the cell. They also function in the controlled degradation of cellular components
Peroxisomes	Peroxisomes are single membrane bound vesicles 0.2-0.5 µm in diameter. They contain a variety of enzymes that use oxygen & generate peroxides. Budding of ER forms peroxisomes.	Peroxisomes oxidize nutrients such as amino acids.
Cytoskeleton	Cytoskeleton is composed of protein filaments which give structure & organization to the cytoplasm	Cytoskeleton determines the shape of the cell & ability to move. It also mediates the internal movements such as migration of organelles.
Chloroplasts	Plant cells contain organelles known as plastids, of which chloroplast is the prominent one.	Chloroplasts are the sites for photosynthesis, the reaction by which light energy is converted to metabolically useful chemical energy in the form of ATP.
Vacuole	Vacuole is the most obvious compartment in the plant cell. It is a very large vesicle enclosed by a single membrane called the tonoplast. They occupy more than 50% of the cell's volume and are usually located at the center of the cell pushing the cytoplasm to the periphery of the cell.	Vacuole functions in the storage, transport of nutrients & cellular waste products.
Cell Wall	Found only in plant cells, the wall is thick, rigid & porous to small molecules	Protection against osmotic or mechanical rupture.

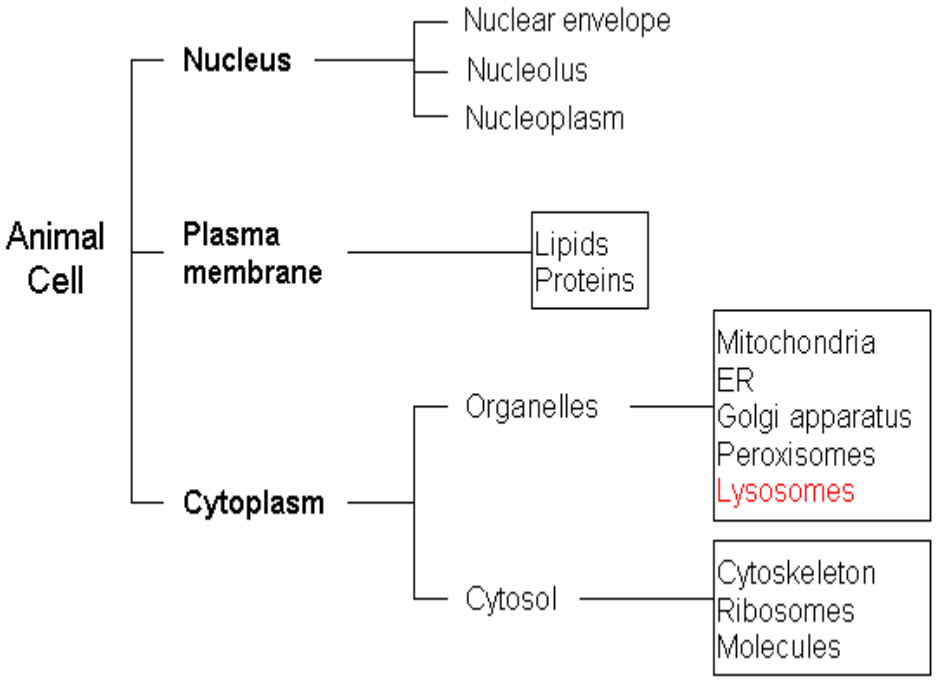


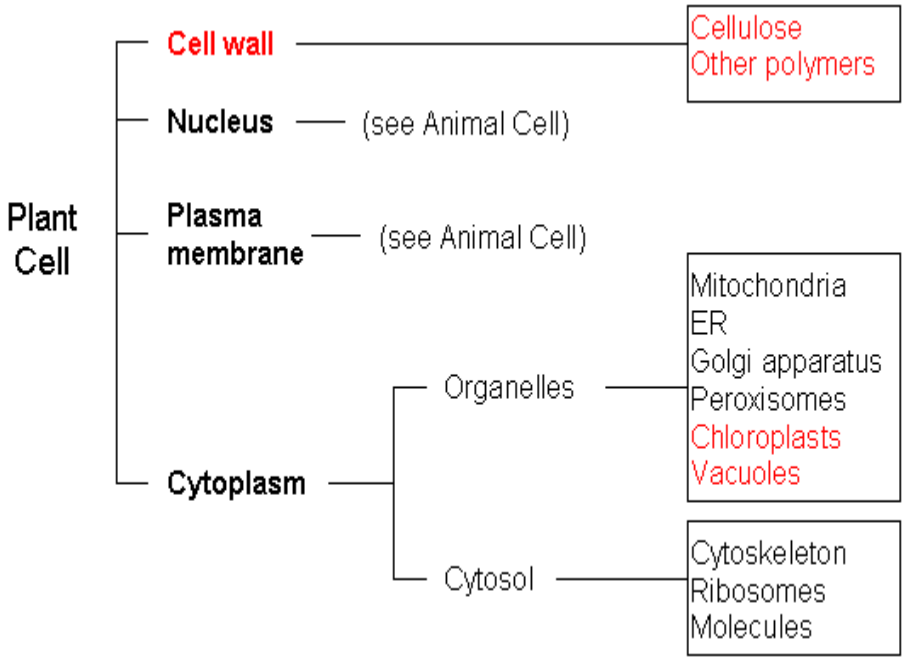
An animal cell. The figure represents a rat liver cell, a typical higher animal cell in which features of animal cells are evident such as nucleus, nucleolus, mitochondria, Golgi bodies, lysosomes and endoplasmic reticulum (ER).

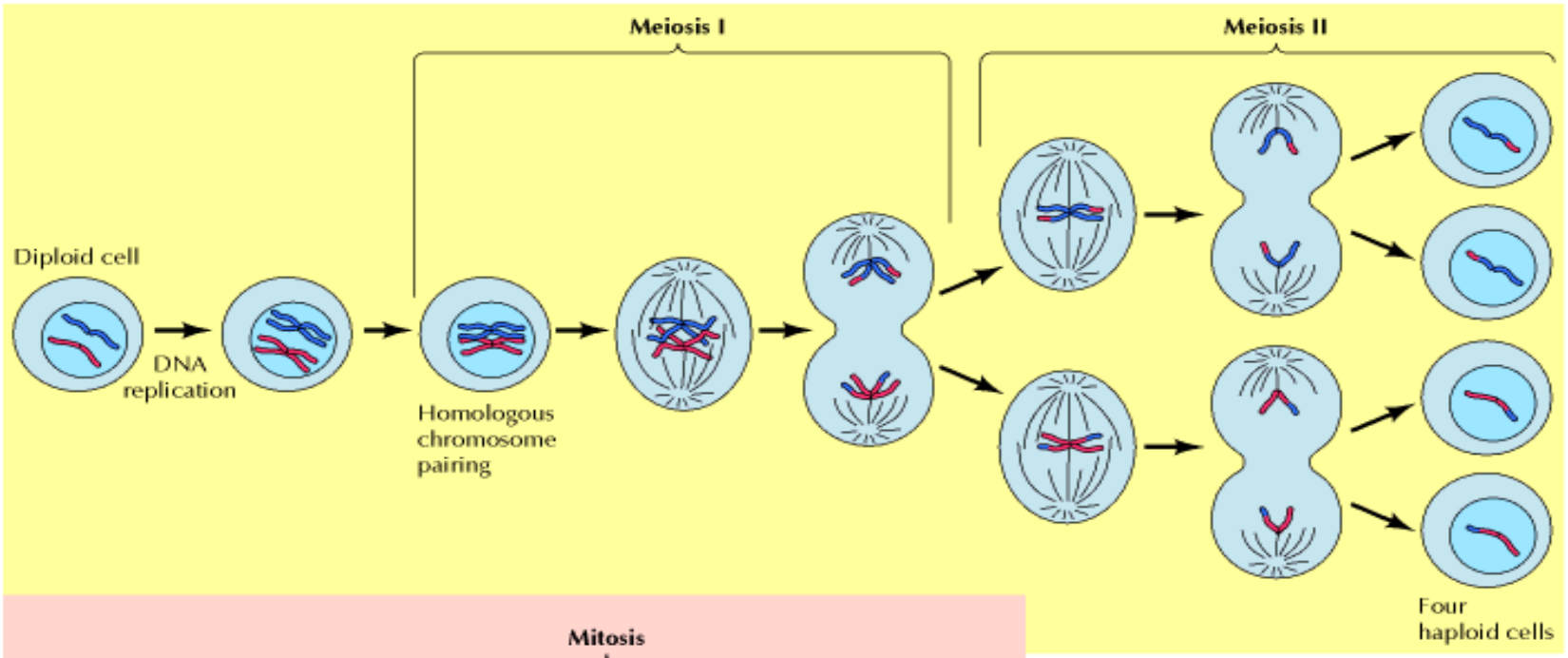


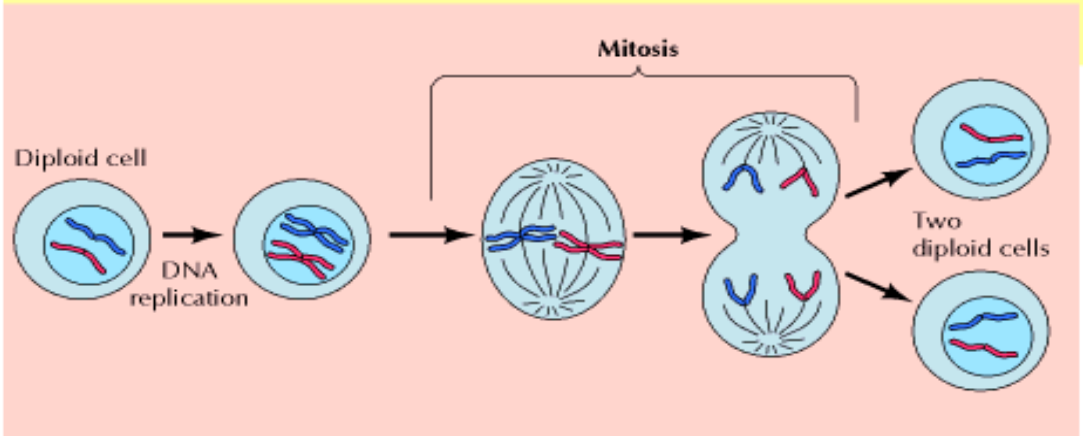
A plant cell (cell in the leaf of a higher plant). Plant cells in addition to plasma membrane have another layer called cell wall, which is made up of cellulose and other polymers where as animal cells have plasma membrane only. The cell wall, membrane, nucleus chloroplasts, mitochondria, vacuole, ER and other organelles that make up a plant cell are featured in the figure.

Differences between animal cell and plant cell



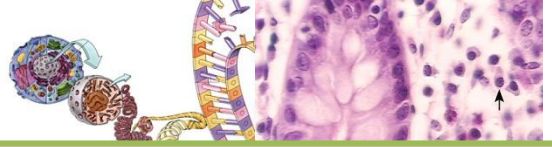






Q. What if there were no meiosis?

Cell division: Stages in meiosis and mitosis



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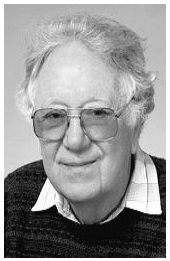
Stem cells are master cells that have the ability to differentiate and ultimately become skin cells, neurons, muscle, blood cells and every other of the 220 cell types that make up the tissues and organs in the body.

The Nobel Prize in Physiology or Medicine 2007

"for their discoveries of principles
for introducing specific gene modifications in mice
by the use of embryonic stem cells"

Mario R. Capecchi
University of Utah
Salt Lake City, UT, USA; Howard Hughes Medical Institute
b. 1937 (in Italy)

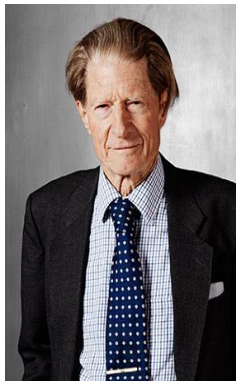
Sir Martin J. Evans
Cardiff University
Cardiff, United Kingdom
b. 1941 (UK)



Oliver Smithies
University of North Carolina at Chapel Hill, Chapel Hill, NC, USA
b. 1925 (in UK)

The Nobel Prize in Physiology or Medicine 2012

for the discovery that mature cells can be reprogrammed to become pluripotent



John B. Gurdon
Gurdon Inst., UK
b. 1933, (UK)

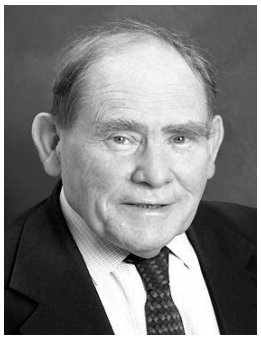
Shinya Yamanaka
U.Strasbourg, France
b. 1941 (Luxembourg)

BJ-L1.13

Apoptosis is a phenomenon of programmed cell death, in which cell nucleus becomes condensed, the cell shrivels and the shrunken corpse is rapidly engulfed and digested by neighboring cells. This is a regular feature of normal animal development. It occurs quickly and leaves no trace.

The Nobel Prize in Physiology or Medicine 2002

"for their discoveries concerning genetic regulation of organ development and programmed cell death"



Sydney Brenner

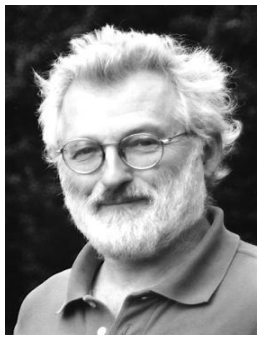
Mol Sci. Instiitute, USA

b. 1927 (South Africa)

H. Robert Horvitz

MIT, USA

b. 1947 (USA)



John E Sulston

Sanger Inst., UK

b. 1942 (UK)

Cells → Tissues

In animals there are four main tissue types:

epithelium – sheets of cells covering surface of animal bodies and line their internal cavities such as lungs and intestines.

connective tissues – blood, bone, cartilage and adipose tissues in which fat is stored. In connective tissue, the spaces between cells are filled by an extracellular matrix consisting of proteoglycans (combination of polysaccharides and proteins).

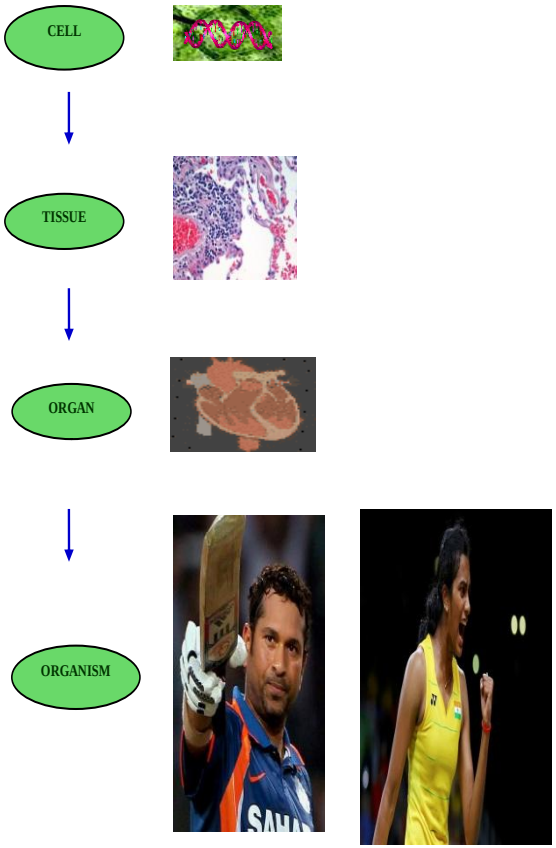
nervous tissue – forms the brain, spinal cord as well the nerves running through the body. Cell types involved are mainly neurons (send and process electrical information via axons) and glial cells (electrical insulation around axons).

muscle tissue – smooth eg. stomach, uterus, blood vessels or striated eg. cardiac and skeletal).

Tissues → Organs → Organ systems

In humans ,there are 10 organ systems.

(1) Skeletal, (2) Muscular; (3) Circulatory; (4) Nervous; (5) Respiratory; (6) Digestive; (7) Excretory; (8) Endocrine; (9) Reproductive; (10) Lymphatic/Immune

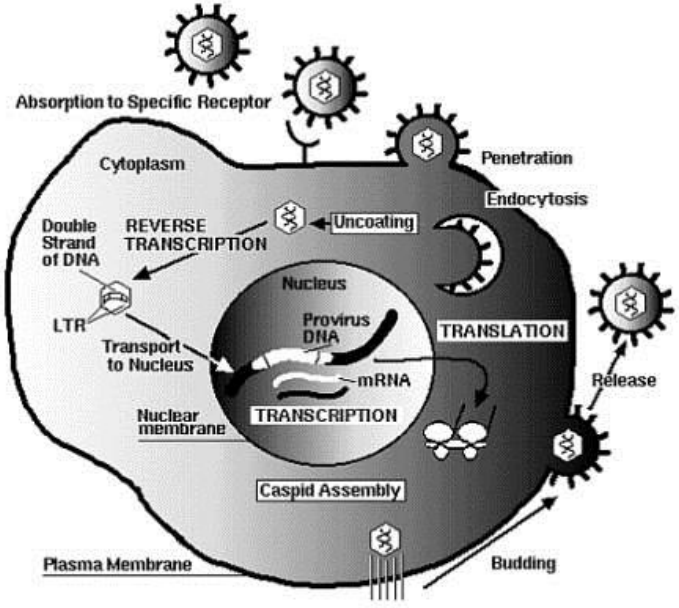


The entire DNA content in a cell is called the **genome**. The entire protein content in a cell is called the **proteome**. **Cellome** is the entire complement of molecules, including genome and proteome within a cell. Tissues are made of collections of cells. Tissue collections make organs. An organism is a collection of several organ systems.

Viruses

Viruses are infectious agents with both living and nonliving characteristics. Some of the living characteristics of viruses are (i) they can reproduce at a faster rate, but only in living host cells and (ii) they can mutate. The nonliving features of viruses are that (i) they are acellular i.e., they contain no cytoplasm or cellular organelles, (ii) they carry out no *metabolism* on their own and must replicate using the host cell's metabolic machinery. In other words, viruses don't grow and divide. Instead, new viral components are synthesized and assembled within the infected host cell. Viruses are supramolecular complexes of nucleic acids, either DNA or RNA enclosed in a protein coat and in some instances, surrounded by a membrane envelope.

Life cycle of a virus



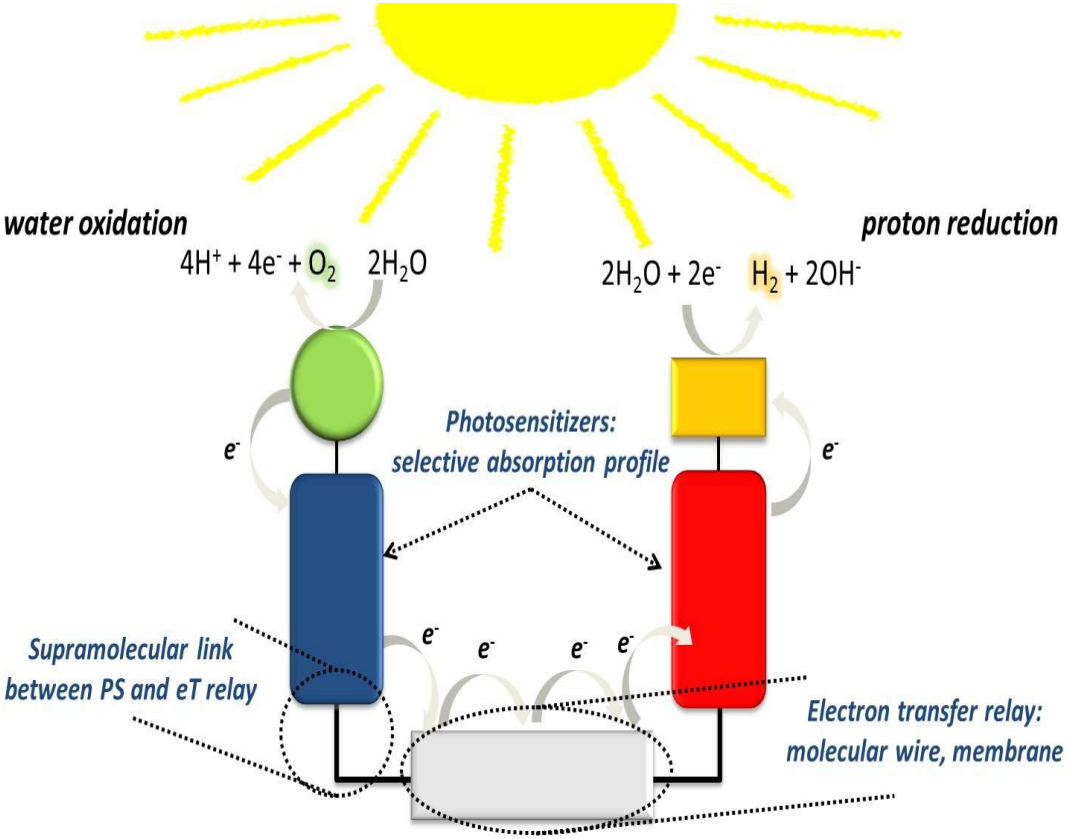
1. Ebola
2. Rabies
3. HIV
4. Smallpox
5. Polio
6. Influenza
7. Dengue
8. Rotavirus
9. .....

Natural Photosynthesis:
Efficiency: 30-40%

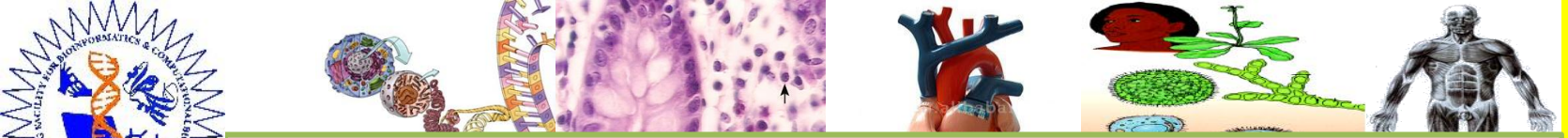
Artificial photosynthesis: (Capture sunlight, split water, produce hydrogen gas etc..)

Solar cells ~ 20% (max) (Not cost effective yet!)

Use catalysts such as Ruthenium+ Manganese; Cobalt+Titanium oxides; nanoparticle coated iron oxides etc..)



Is artificial life possible ?



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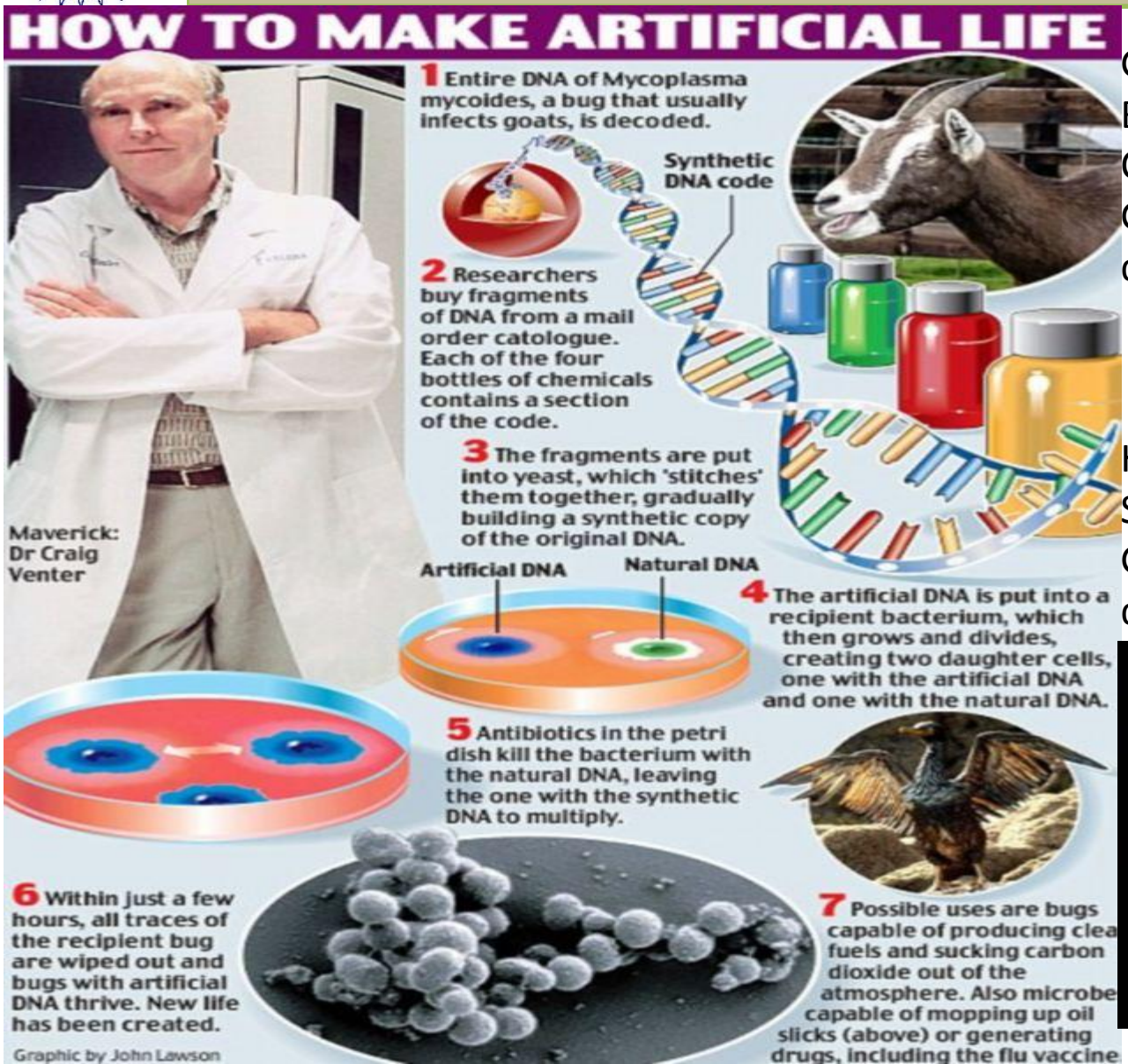


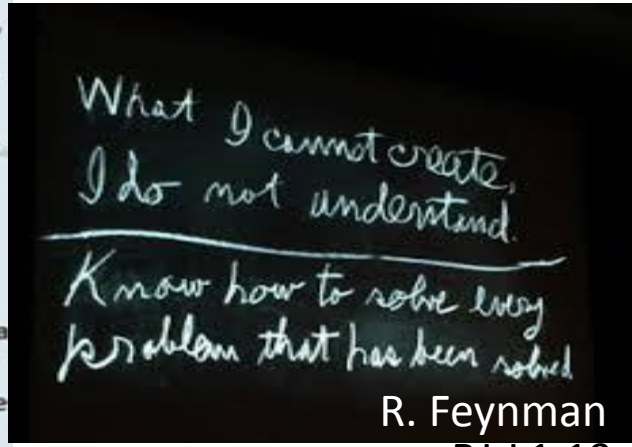
Synthia

Gibson et al., 'Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome', *Science*, May **2010**; doi: 10.1126/science.1190719

Q. Did Venter create a living bacterial cell or a virus?

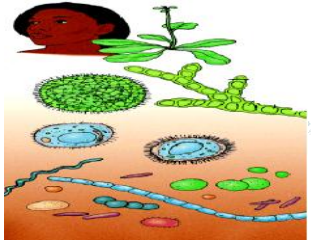
Synthia 3.0

Hutchinson et al., "Design & Synthesis of a Minimal Bacterial Genome", *Science* , Mar **2016**; doi: 10.1126/science.aad6253



R. Feynman



Today's challenge: (Big) Data → Information → Knowledge → Products useful to Society

What is big data in biology?

Vivien Marx, Biology: The big challenges of big data, Nature, 498, 255-260 (2013)

NCBI: http://www.ncbi.nlm.nih.gov/ : Genomic information of more than 70000 organisms

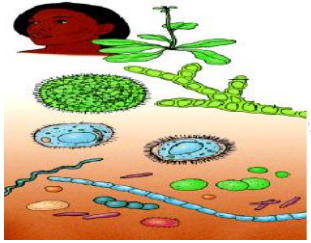
UNIPROT: http://www.uniprot.org/: Protein sequence information with 88 million entries

RCSB: Protein Data Bank: http://www.rcsb.org/: Structural information of 134000 biomolecules

Zinc Database: http://zinc.docking.org/: Over 35 million purchasable compounds

Human genome ~ 3 GB
Genomes + Proteomes + Small molecules ~ hundreds of Petabytes
+ Gene expression data + PPI Networks + ….. ~ Exabytes



Today's challenge: (Big) Data → Information → Knowledge → Products useful to Society

Some key players and what they are doing

Chemical Engineers

Synthetic Genome: Done

Systems Biology, Metabolic networks, drug target identification…

Computer Scientists

Artificial Cell: Done

Artificial Intelligence techniques in genomics, proteomics & drug discovery

Mathematicians

Artificial Liver: Done(?)

Probabilistic methods, Classifiers for sequence, structure analysis & prediction, Optimizers

Electrical Engineers

Artificial Brain ?

Signal recognition in sequences & structures

Biochemical engineers,
Biomedical engineers
Biotechnologists, Biologists

Artificial Human ?

Create synthetic genomic/proteomic constructs, optimize & scale up expressions, understand mechanisms of disease/disorder

Chemists & Physicists

Analyze & interpret genome, proteome & drug discovery at molecular level, simulate processes & synthesize molecules

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Let us use the big data in Biology, generate hypotheses, create new knowledge, make some drugs and get rid of diseases, create some plants and get rid of pollution, solve food and energy shortages……!

← **Quantitative**

Mathematics **Physics** **Chemistry** **Biology**

Empirical →

Let us make Biology more quantitative

Assignment 1 (2020). Formulate a variational theorem for living systems far away from equilibrium!

Assignment 2 (2020). Define an evolutionary potential – a function of time, space and other appropriate variables and set up a differential equation for it! (& Solve it for a few cases with known boundary conditions)!!

Assignment 3 (2020). Dream of all the good things you can do with synthetic life forms and do something about it!!!