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Cell and Molecular Biology : What We Know & How We Found Out (Second Edition, Sample Chapter)

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Second Edition
SAMPLE CHAPTER

Cell and Molecular Biology

What We Know & How We Found Out

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Image Adapted From: Microarray

Cell and Molecular Biology

What We Know & How We Found Out

2nd edition (CMB-2e)

SAMPLE CHAPTER

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By

Gerald Bergtrom

To my wife, son and our now extended family whose patience and encouragement made this work possible, to my mentor Herbert Oberlander who gave me the chance and the tools to do science *and*, to my students from whose curiosity I received as much as I gave

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Preface to CMB 2e

Most introductory science courses start with a discussion of scientific method. The 2nd edition of this *interactive Cell & Molecular Biology* electronic textbook, or ***iText*** is no exception. A key feature of **CMB 2e** is still a focus on experimental support for what we know about cell and molecular biology. A sense of how science is practiced and how investigators think about experimental results is essential to understanding the relationship of cell structure and function, not to mention the rest of the world around us. Rather than trying to be a comprehensive reference book, **CMB 2e** selectively details essential methods and experiments that are the basis of our current understanding of the biochemical and molecular basis of cell structure and function. This focus is nowhere more obvious than in the list of ***learning objectives*** and in the Voice-Over PowerPoint ***(VOP)*** presentations provided for each chapter. *Learning objectives* align with chapter content and serve as an aid and guide to learning. They ask students to use new-found knowledge to make connections and demonstrate deeper concept understanding and critical thinking skills. The *VOPs* are freely available on Youtube™ (with optional closed captioning), as are most of the videos linked elsewhere in the *iText*.

There are two versions of **CMB *2e iText*** (all versions of the first edition are still available). The ***Annotated* CMB-2e *iText***, contains many embedded *just-in-time* links to external resources including links to animations of cell process, relevant current research summaries, etc. *Challenge* text boxes raise provocative questions about the iText content, and may be used to provoke class or online discussion (assessed or not!). A **CMB-2e *iText For Instructors*** (available on request) includes these features and adds writing assessments that the author has actually assigned for course credit. These appear in the right margin of the text and are **25 Words or Less** writing assignments that aim to strengthen critical thinking and writing skills. Some of these features are modeled in the **CMB 2e *Sample Chapter***, such as online discussions and low-stakes formative objective quizzes (note that hyperlinks to assessments in the *Sample* and *Instructor* ***iText*** versions require student/instructor login to a course management system and are therefore inactive).

While not comprehensive, this *iText* was written with the goal of creating content that is engaging, free and comparable in quality to very expensive commercial textbooks. To that end, illustrations created especially for the *iText* are supplemented by online open sources (with appropriate attribution). So, whichever CMB 2e version you are use, we encourage instructors to use the interactive features in this *iText* to challenge students. For their part, we encourage students to think about how great experiments were inspired and designed, how alternative experimental results were predicted, how actual data was interpreted, and finally, and what questions the investigators (and we!) might want to ask next. Although the online *iText* is the most efficient way to access links and complete online assignments, students are free to download, read, study, and add your own annotations off-line... or print it out and write in the margins the old fashioned way! Your instructor will undoubtedly provide more detailed instructions for using your ***iText***.

Special Note to Instructors from the Author

All features of the ***Annotated*** version of the CMB 2e *iText* are freely available to you and your students. The ***Complete*** version of the iText is available after filling out a short form identifying you as an instructor. Feel free to add, subtract, modify or embellish any part of any version of the text or interactive content to suit your purposes… and then provide your customized version of the text to your students. Feel free also to ask your students participate in the improvement of the iText… for fun or for credit and then…, share the results your efforts with others!

One final bit of advice: where I provide content updates e.g., in links to very current sources, please be aware (and let the students know) that I refer to the content as new, interesting and not necessarily definitive (i.e., it is subject to confirmation). I hope that you (and perhaps your students!) will enjoy creating and customizing interactive elements in the *iText*. Above all, I hope that your students will achieve a better understanding of how scientists use skills of inductive and inferential logic to ask questions and formulate hypotheses…, and to how they apply concept and method to testing those hypotheses.

Acknowledgements

First and foremost, credit for my efforts has to go to the University of Wisconsin-Milwaukee and the 35-plus years of teaching and research experience that inform the content, concept and purpose of this digital *Open Education Resource* (OER). I want to thank my colleagues in the *Center for Excellence in Teaching and Learning* (CETL) and the Golda Meir Library at UW-M for the opportunity and the critical input that led to what I have defined as an iText (interactive text). Many thanks to Matthew Russell, Megan Haak, Melissa Davey Castillo, Jessica Hutchings, Dylan Barth for help and the inspiration to suggest at least a few ways to model how open course content can be made interactive and engaging. Thanks also to Tim Gritten and Kristen Woodward for putting competent editorial eyes on the *iText*. Finally special thanks to Tim Gritten for walking me through the intricacies of publication of the iText on the UW-M Digital Commons… with uncommon patience!

About the Author

Dr. Bergtrom is Professor (Emeritus) of Biological Sciences and a Learning Technology Consultant (formerly in the Center for Excellence in Teaching and Learning at the University of Wisconsin-Milwaukee. Scientific interests are cell and molecular biology and evolution. Pedagogic interests include blended and online instruction and the use of technology in the service of better teaching and learning. Dedicated to an active learning approach, he has taught face-to-face, blended and so called "flipped" classes, as well as fully online undergraduate and graduate courses in cell and molecular biology. He also developed and co-instructed *Teaching with Technology*, an interdisciplinary course aimed at graduate students that might someday find themselves struggling to teach others. With more than 40 years of experience in teaching and research, he has frequently tested and incorporated pedagogically proven teaching technologies into his courses. In addition to many research publications in cell biology and evolution, he has published on aspects of active blended, online and flipped classroom methods[1-3]. In 2015 Dr. Bergtrom published ***Cell and Molecular Biology*** – *What We Know & How We Found Out*, an *Open Access/Creative Commons* (i.e., no-cost) electronic textbook[4]. The updated second edition (***CMB 2e***) of this textbook was published in 2016[4]. Access to the older editions remain available on the UWM Digital Commons website.

1. Bergtrom, G. (2006) *Clicker Sets as Learning Objects*. Int. J. Knowl. & Learn. Obj. 2:105-110. (http://www.ijello.org/Volume2/v2p105-110Bergtrom.pdf)
2. Bergtrom, G. (2009) *On Offering a Blended Cell Biology Course*. J. Res. Center Ed. Tech. 5(1) (http://www.rcetj.org/?type=art&id=91609&).
3. Bergtrom, G. (2011) *Content vs. Learning: An Old Dichotomy in Science Courses*. J. Asynchr. Learning Networks 15:33-44 (http://jaln_v15n1_bergtrom.pdf)
4. Bergtrom, G. *Cell and Molecular Biology: What We Know & How We Found Out* [*CMB1e*, (2015) and CMB2e (2016), all versions] (http://dc.uwm.edu/biosci_facbooks_bergtrom/)

Table of Contents

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Chapter 1: Cell Tour, Life's Properties and Evolution, Studying Cells

Scientific Method; Cell structure, methods for studying cells (microscopy, cell fractionation, functional analyses); Common ancestry, genetic variation, evolution, species diversity; cell types & the domains of life

http://4.bp.blogspot.com/-qKeCFUJznt0/TxV2D4ume2I/AAAAAAAAcA/lCrSNIpughk/s1600/cd8a4fe01ef3012f2fc800163e41dd5b.gif1109bmp.jpg

I. Introduction

The first two precepts of Cell Theory were enunciated near the middle of the 19th century, after many observations of plant and animal cells revealed common structural features (e.g., a nucleus, a wall or boundary, a common organization of cells into groups to form multicellular structures of plants and animals and even lower life forms). These precepts are (1) Cells are the basic unit of living things; (2) Cells can have an independent existence. The 3rd statement of cell theory had to wait until late in the century, when Louis Pasteur disproved notions of spontaneous generation, and German histologists observed mitosis and meiosis, the underlying events of cell division in eukaryotes: (3) Cells come from pre-existing cells (i.e., they reproduce)

Comment [GKB1]: Explain the statement that *Cells can have an independent existence* in 30 words or less. Put your word count in parenthesis after your response and submit it to the *Life is Good* DropBox by [insert date and time].

We begin this chapter with a reminder of the scientific method, a way of thinking about our world that emerged formally in the 17th century. We then take a tour of the cell, reminding ourselves of basic structures and organelles. After the 'tour', we consider the origin of cells from a common ancestor (the *progenote*) and the subsequent evolution of cellular complexity and the incredible diversity of life forms. Finally, we consider some of the methods we use to study cells. Since cells are small, several techniques of microscopy, cell dissection and functional/biochemical analysis are described to illustrate how we come to understand cell function.

Voice-Over PowerPoint Presentations
Cell Tour Part 1
Cell Tour Part 2
Comments on Life's Properties, Origins and Evolution
Techniques for Studying Cells

Learning Objectives
When you have mastered the information in this chapter and the associated VOPs, you should be able to:

1. compare and contrast *hypotheses* and *theories* and place them and other elements of the scientific enterprise into their place in the cycle of the *scientific method*
2. compare and contrast structures common to and that distinguish *prokaryotes*, *eukaryotes* and *archaea*, and groups within these *domains*
3. articulate the function of different cellular substructures and compare how *prokaryotes* and *eukaryotes* accomplish the same functions, i.e. display the same essential *properties of life*, despite the fact that prokaryotes lack most of the structures
4. outline a procedure to study a specific cell *organelle* or other substructure
5. describe how the different structures (particularly in eukaryotic cells) relate/interact with each other to accomplish specific functions
6. place cellular organelles and other substructures in their evolutionary context, i.e., describe their origins and the selective pressures that led to their *evolution*
7. distinguish between the random nature of *mutation* and *natural selection* in evolution
8. relate archaea to other life forms and engage in informed speculation on their origins in evolution
9. answer the questions “Why does evolution lead to more complex ways of sustaining life when simpler organisms are able to do with less, and are so prolific?” & “Why are *fungi* more like animals than plants?”

II. Scientific Method – The Practice of Science

You can read the link at Scientific Method – The Practice of Science for a full discussion of this topic. For an amusing look at how scientists think, check out Richard Feynman [(1999) *The Pleasure of Finding Things Out: The Best Short Works of Richard Feynman*. New York, Harper Collins]. Here we focus on the essentials of the method and then look at how science is practiced. As you will see, scientific method refers to a standardized protocol for observing, asking questions about and investigating natural phenomena. Simply put, it says look/listen, infer a cause and test your inference. But observance of the method is not strict and is more often honored in the breach than by adherence to protocol! As captured by the Oxford English Dictionary, the essential inviolable commonality of all scientific practice is that it relies on “systematic observation, measurement, and experiment, and the formulation, testing and modification of hypotheses."

In the end, scientific method in the actual practice of science recognizes human biases and prejudices and allows deviations from the protocol. At its best, it provides guidance to the investigator to balance personal bias against the leaps of intuition that successful science requires. As followed by most scientists, the practice of scientific method would indeed be considered a success by almost any measure. Science "as a way of knowing" the world around us constantly tests, confirms, rejects and ultimately reveals new knowledge, integrating that knowledge into our world view.

Here are the key elements of the scientific method, in the usual order:

- Observe natural phenomena (includes reading the science and thoughts of others).
- Propose an explanation based on objectivity and reason, an inference, or hypothesis. An hypothesis is a declarative sentence that sounds like a fact… but isn't! Good hypotheses are testable - turn them into *if/then (predictive)* statements or *yes-or-no* questions.
- Design an experiment to test the hypothesis: results must be measurable evidence for or against the hypothesis.
- Perform the experiment and then observe, measure, collect data, and test for statistical validity (where applicable).
- Repeat the experiment.
- Publish! Integrate your experimental results with earlier hypotheses and prior knowledge. Shared data and experimental methods will be evaluated by other scientists. Well-designed experiments are those that can be repeated and results reproduced, verified and extended.

Beyond these most common parts of the scientific method, most descriptions add two more precepts:

- A *Theory* is a statement well-supported by experimental evidence and widely accepted by the scientific community. One of the most enduring, tested theories is of course the theory of evolution. Even though theories are more generally thought of as 'fact, they are still subject to being tested, and can even be overturned! Even Darwin's notions have been modified over time, but those modifications have only strengthened our understanding that species diversity is the result of natural selection. You can check out some of Darwin's own work [Darwin C. (1859, 1860) *The Origin of Species*] at http://literature.org/authors/darwin-charles/the-origin-of-species/. For more recent commentary on the evolutionary underpinnings of science, check out Dobzhansky T (1973, *Nothing in biology makes sense except in the light of evolution*. Am. Biol. Teach. 35:125-129) and Gould, SJ (2002, *The Structure of Evolutionary Theory*. Boston, Harvard University Press).

- Scientific Laws are even closer to 'fact' than theories! These Laws are thought of as universal and are most common in math and physics. In life sciences, we recognize Mendel's *Law of Segregation* and *Law of Independent Assortment* as much in his honor as for their universal and enduring explanation of genetic inheritance in living things. But we do not call these Laws *facts*. They are always subject to experimental test. Astrophysicists are actively testing universally accepted laws of physics even Mendel's *Law of Independent Assortment* should not be called law (strictly speaking) since it is not true as he stated it (go back and see how chromosomal crossing over was found to violate this law!).

In describing how we do science, the Wikipedia entry suggests that the goal of a scientific inquiry is to obtain knowledge in the form of testable explanations (hypotheses) that can predict the results of future experiments. This allows scientists to gain an understanding of reality, and later use that understanding to intervene in its causal mechanisms (such as to cure disease). The better an hypothesis is at making predictions, the more useful it is, and the more likely it is to be correct.

In the last analysis, think of hypotheses as *educated guesses* and think of Theories and/or Laws as one or more experimentally supported hypothesis that everyone agrees should serve as *guideposts* to help us evaluate new observations and hypotheses.

CHALLENGE: Since "An hypothesis is a declarative sentence that sounds like a fact…", and since both theories and hypotheses are stated as declarative sentences, articulate in your own words the difference between an hypothesis and a theory.

Here is how Wikipedia presents the protocol of the Scientific Method:

The cycle of formulating hypotheses, testing and analyzing the results, and formulating new hypotheses, will resemble the cycle described below:

- *Characterizations: observations, definitions, and measurements of the subject of inquiry*
- *Hypotheses: possible explanations of observations and measurements*
- *Predictions: reasoning by deductive and inferential logic from the hypothesis (note that even widely accepted theories are subject to testing in this way)*
- *Experiments (tests of predictions)*
- *New Characterizations: observations, definitions, and measurements of the subject of inquiry*

A linearized, pragmatic scheme of the five points above is sometimes offered as a guideline for proceeding:

1. *Define a question*
2. *Gather information and resources (observe)*
3. *Form an explanatory hypothesis*
4. *Test the hypothesis by performing an experiment and collecting data in a reproducible manner*
5. *Analyze the data*
6. *Interpret the data and draw conclusions that serve as a starting point for new hypothesis*

…To which we would add the requirement that the work of the scientist be disseminated by publication!

Why did philosophers (not scientists!) come up with systems of deductive and inductive logic so essential to the scientific method? Perhaps because experimental science only became common in the 19th century, when the term *scientist* began to define one who investigated natural phenomena by doing experiments. But long before this, philosophers developed formal rules of logic to try to understand nature, humanity's relationship to nature, and the relationship of humans to each other. The scientific method grew along with increasing empirical observation and experimentation. We recognize these origins when we award the Ph.D. (*Doctor of Philosophy),* our highest academic degree!

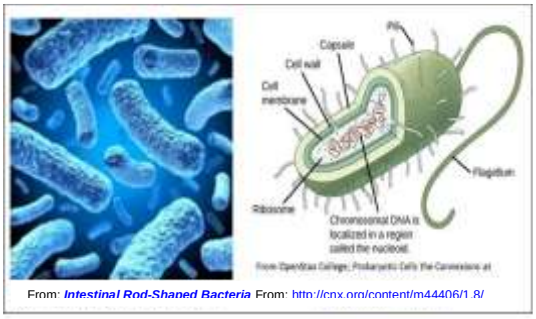
III. Domains of Life

We believe with good reason (as you shall see) that all life on earth evolved from the *progenote*, a cell that existed soon after the origin of life on the planet. *Prokaryotes* lack nuclei (*pro* meaning *before* and *karyon* meaning *kernel*, or *nucleus*). Prokaryotic cells, among the first descendants of the *progenote*, fall into two groups, *archaea* and *eubacteria* (including *bacteria* and *cyanobacteria*, or blue-green algae). Prokaryotes were long defined as a major life grouping, alongside *eukaryotes*. But the recent discovery of *archaea* changed all that! Cells that thrive in inhospitable environments like boiling hot springs or arctic ice were the first to be characterized as *archaea*, but now we know that these unusual organisms inhabit more temperate environments. As of 1990, *eubacteria, archaea* and *eukaryotes* characterize the *three domains of life*. That all living organisms can be shown to belong to one of these three domains has dramatically changing our understanding of evolution.

A. The Prokaryotes (eubacteria = *bacteria* and *cyanobacteria*)

Compared to eukaryotes, prokaryotic cells typically lack a nucleus as well as mitochondria, chloroplasts, internal membranes and other organelles (e.g., endoplasmic reticulum, assorted vesicles and internal membranes). They are typically

unicellular, although a few live colonial lives at least some of the time (e.g., cyanobacteria). Typical rod-shaped bacteria are shown (below left). A schematic diagram of typical bacterial structure is also shown (below right).



From: ***Intestinal Rod-Shaped Bacteria*** From: http://cnx.org/content/m44406/1.8/

1. *Bacterial Reproduction*

Without the compartments afforded by the internal membrane systems common to eukaryotic cells, all intracellular events, from DNA replication to transcription and translation to the biochemistry of life all happen in the cytoplasm of the cell. DNA is a circular double helix that duplicates as the cell grows. While not enclosed in a nucleus, bacterial DNA is concentrated in a region of the cell called the *nucleoid*. Bacteria replicate their DNA throughout the life of the cell, ultimately dividing by *binary fission.* The result is the equal partition of duplicated bacterial *"chromosomes"* into new cells. The bacterial chromosome is essentially naked DNA, unassociated with chromosomal proteins. In contrast, eukaryotic cells divide by mitosis, a time when their DNA is organized into tightly packed chromosomes associated with many different proteins (see below). Just to make life more interesting, we should note that one group of prokaryotes (the *Planctomycetes*) have surrounded their nucleoid DNA with a membrane!

CHALLENGE: How do you imagine these cells would divide their DNA equally between daughter cells during cell division?

2. *Cell Motility and the Possibility of a Cytoskeleton*

Movement of bacteria is typically by *chemotaxis*, a response to environmental chemicals. They can move to or away from nutrients or noxious/toxic substances. Bacteria exhibit one of several modes of motility. For example, many move using

flagella made up largely of the protein *flagellin*. While the cytoplasm of eukaryotic cells is organized by a cytoskeleton of rods and tubes made of *actin* and *tubulin* proteins, prokaryotes were long thought not to contain cytoskeletal analogs (never mind homologs!). However, two bacterial genes were recently discovered and found to encode proteins homologous to eukaryotic actin and tubulin. The *MreB* protein forms a *cortical ring* in bacteria undergoing *binary fission*, similar to the actin cortical ring that pinches dividing eukaryotic cells during *cytokinesis* (the actual division of a single cell into two smaller daughter cells). This is modeled in the cross-section near the middle of a dividing bacterium, drawn below.

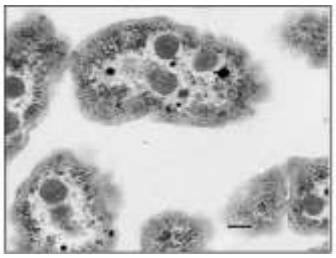

From: https://en.m.wikipedia.org/wiki/File:FtsZ_Filaments.svg

The *FtsZ* gene encodes a homolog of tubulin proteins. Together with flagellin, the MreB and FtsZ proteins may be part of a primitive prokaryotic *cytoskeleton* involved in cell structure and motility.

3. *Some Bacteria have Internal Membranes*

While lacking organelles (the membrane-bound structures in eukaryotic cells), internal membranes that appear to be inward extensions (*invaginations*) of plasma membrane have been known in a few prokaryotes for some time. In some prokaryotic species and groups, these membranes perform capture energy from sunlight (photosynthesis) or from inorganic molecules (*chemolithotrophy*). *Carboxysomes*, membrane bound photosynthetic vesicles in which CO_2 is actually fixed (reduced) in cyanobacteria (shown below).

From: http://en.wikipedia.org/wiki/File:Carboxysomes_EM.jpg



Less elaborate internal membrane systems are found in photosynthetic bacteria.

4. ***Bacterial Ribosomes do the Same Thing as Eukaryotic Ribosomes… and look like them!***

   Ribosomes are the protein synthesizing machines of life. The *ribosomes* of prokaryotes are smaller than those of eukaryotes, but *in vitro* they can be made to translate eukaryotic messenger RNA (mRNA). Underlying this common basic function is the fact that the ribosomal RNAs of all species share base sequence and structural similarities indicating an evolutionary relationship. It was these similarities that revealed the closer relationship of archaea to eukaryotes than prokaryotes.

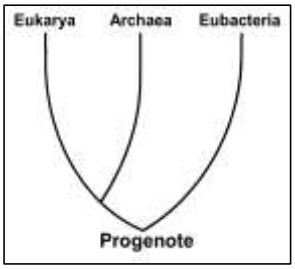
   Clearly, prokaryotes are a diverse group of organisms, occupying almost every wet or dry or hot or cold nook and cranny of our planet. But despite of this diversity, all prokaryotic cells share many structural and functional metabolic properties with each other… and with the archaea and eukaryotes! As we have seen with ribosomes, shared structural and functional properties support the common ancestry of all life. Finally, we not only share common ancestry with prokaryotes, we even share living arrangements with them. Our gut bacteria represent up to 10X more cells than our own! Read more at ***The NIH Human Microbiome Project***. Also check out the following link for ***A Relationship Between Microbiomes, Diet and Disease*.**

B. The Archaebacteria (Archaea)

Allessandro Volta, a physicist for whom the Volt is named, discovered methane producing bacteria (*methanogens*) way back in 1776! He found them living in the extreme environment at the bottom of Lago Maggiore, a lake shared by Italy and Switzerland. These unusual bacteria are *cheomoautotrophs* that get energy from H_2 and CO_2 and generate methane gas in the process. It was not until the 1960s that Thomas Brock (from the University of Wisconsin-Madison) discovered *thermophilic* bacteria living at temperatures approaching 100^{o}C in Yellowstone National Park in Wyoming. The nickname *extremophiles* was soon applied to describe organisms living in any extreme environment. One of the thermophilic bacteria, now called *Thermus aquaticus*, became the source of *Taq* polymerase, the heat-stable DNA polymerase that made the *polymerase chain reaction* (PCR) a household name in labs around the world!

Extremophile and “normal” bacteria both lack nuclei are similar in size and shape(s), which initially suggested that they were closely related to bacteria and were therefore prokaryotes (see the electron micrograph of *Methanosarcina* and *Pyrolobus, below)*. But Carl Woese [Woese CR (2004) *A new biology for a new century*. Microbiol. Mol. Biol. Rev. 68:173-186] compared the sequences of genes for ribosomal RNAs in normal bacteria and an increasing number of extremophiles, including the methanogens. Based on sequence similarities and differences, the extremophiles seemed to form a separate group from the rest of the bacteria as well as from eukaryotes. They were named *archaebacteria*, or *archaea* because these organisms were thought to have evolved even before bacteria.

Woese concluded that *Archaea* were a separate group, or *domain* of life from bacteria and eukaryotes profoundly changing our understanding of phylogenetic relationships. The three domains of life (Archaea, Eubacteria and Eukarya) quickly supplanted the older division of living things into *Five Kingdoms* (*Monera, Protista, Fungi, Plants, and Animals*). Another big surprise from rRNA gene sequence comparisons was that the archaea were more closely related to eukaryotes than bacteria! The evolution of the three domains is illustrated below.

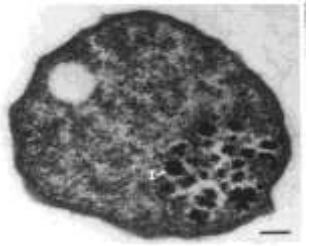


Archaea contain genes and proteins as well as metabolic pathways found in eukaryotes but not in bacteria, speaking to their closer evolutionary relationship to eukaryotes. They also contain genes and proteins as well as metabolic pathways unique to the group, testimony to their domain status.

While some bacteria and eukaryotes can live in extreme environments, the archaea include the most diverse extremophiles:

- Acidophiles: grow at acidic (low) pH.
- Alkaliphiles: grow at high pH.
- Halophiles: require high salt concentrations of salt for growth; *Halobacterium salinarium* is shown below (at the left).

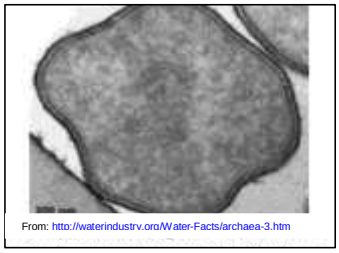
From: Halobacterium



Credit: *James Ferry/Penn State University;*

- Methanogens: produce methane; a cross section of *Methanosarcina acetivorans* is shown, above right. Note the absence of significant internal structure.
- Barophiles: grow best at high hydrostatic pressure.

- Psychrophiles: grow best at temperature 15 °C or lower.
- Xerophiles: growth at very low water activity (i.e., drought conditions).
- Thermophiles/hyperthermophiles: organisms that grow best at 40 °C or higher, or 80°C or higher, respectively. *Pyrolobus fumarii*, shown below, can live at a temperature 113°C.



From: http://waterindustry.org/Water-Facts/archaea-3.htm

- Toxicolerants: grow in the presence of high levels of damaging elements (e.g., pools of benzene, nuclear waste).

Finally, the Archaea are not only extremophiles thriving in unfriendly environments. They include organisms living in more moderate places including soils, oceans and marshes… and even in the human colon. In oceans, they are a major part of plankton. Originally seen as a sideshow among living things, Archaea are particularly abundant in the oceans where they are a major part of plankton, participating in the carbon and nitrogen cycles. In the guts of cows, humans and other mammals, methanogens facilitate digestion, generating methane gas in the process. Cows have even been cited as a major cause of global warming because of their prodigious methane emissions. Methanogenic Archaea are being exploited to create biogas and to treat sewage, while some extremophiles are the source of enzymes that function at high temperatures or in organic solvents. As noted above, some of these have become part of the biotechnology toolbox.

C. The Eukaryotes

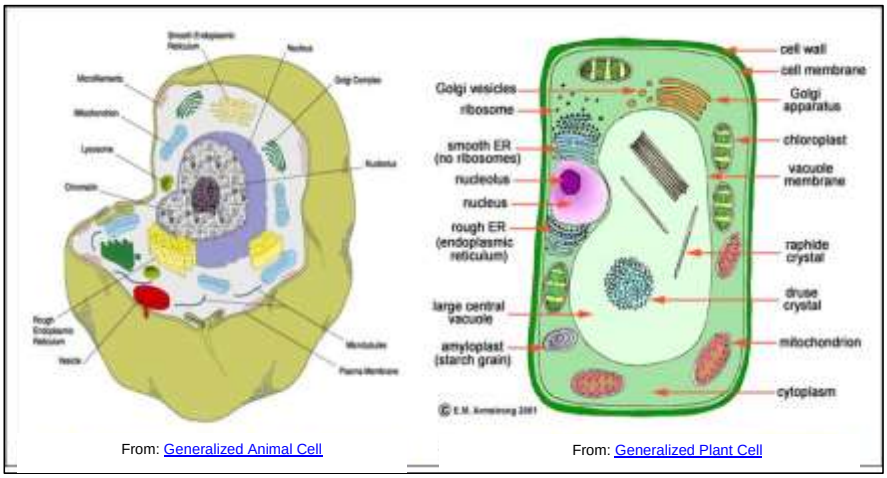
1. Large Compartmentalized Cells

The volume of a typical eukaryotic cell is 1000 times that of a typical bacterial cell. Eukaryotic life would not even have been possible if not for a division of labor of eukaryotic cells among different *organelles* (membrane-bound structures). Imagine a bacterium as a 100 square foot room with one door (the size of a small bedroom,

or a large walk-in closet!). Now imagine a room 1000 times as big. That is, imagine a 100,000 square foot 'room'. Not only would you expect multiple entry and exit doors in the eukaryotic cell membrane, but you would expect lots of interior "rooms" with their own entry ways and exits, to make more efficient use of this large space. The smaller prokaryotic "room" has a much larger *surface area/volume ratio* than a typical eukaryotic "room", enabling necessary environmental chemicals to enter and quickly diffuse throughout the cytoplasm of the bacterial cell. The chemical communication between parts of a small cell is rapid, while communication within eukaryotic cells over a larger expanse of cytoplasm requires the coordinated activities of subcellular components and might be expected to be slower. In fact, eukaryotic cells have lower rates of metabolism, growth and reproduction than do prokaryotic cells. The existence of large cells must therefore have involved an evolution of a *division of labor* supported by *compartmentalization*. Since prokaryotes were the first organisms on the planet, some must have evolved or acquired membrane-bound organelles.

2. *Animal and Plant cell Structure Overview*

Eukaryotic cells and organisms are diverse in form but similar in function, sharing many biochemical features with each other and as we already noted, with prokaryotes. Typical animal and plant cells showing their organelles and other structures are illustrated below (left and right, respectively):



From: Generalized Animal Cell

From: Generalized Plant Cell

Most of the internal structures and organelles of animal cells are also found in plant cells, where they perform the same or similar functions. We begin a consideration of the function of cellular structures and organelles with a brief description of the function of some of these structures and organelles.

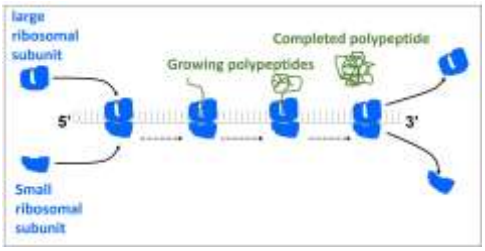
Fungi are actually more closely related to animal than plant cells, and contain some unique cellular structures. While fungal cells contain a wall, it is made of chitin rather than cellulose. Chitin is the same material that makes up the exoskeleton or arthropods (including insects and lobsters!). The organization of fungi and fungal cells is somewhat less defined than animal cells. Structures between cells called *septa* separate fungal hyphae, allowing passage of cytoplasm and even organelles between cells. There are even primitive fungi with few or no septa, in effect creating *coenocytes* that are a single giant cell with multiple nuclei. As for flagella, they are found only in the most primitive group of fungi.

We end this look at the domains of life by noting that, while eukaryotes are a tiny minority of all living species, "their collective worldwide biomass is estimated at about equal to that of prokaryotes" (Wikipedia). On the other hand, our bodies contain 10 times as many microbial cells as human cells! In fact, it is becoming increasingly clear that a human owes as much to its being to its microbiota (see above) as it does to its human cells.

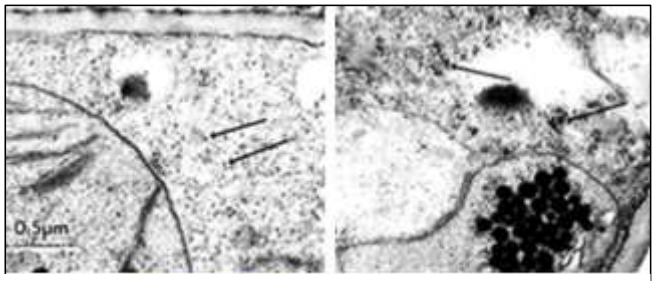
IV. Tour of the Eukaryotic Cell

A. Ribosomes

As noted, these are the protein synthesizing machines in the cell. They are an evolutionarily conserved structure found in all cells, consisting of two subunits, each made up of multiple proteins and one or more molecules of ribosomal RNA (rRNA). Ribosomes bind to messenger RNA (mRNA) molecules and then move along the mRNA, translating 3-base code-words (codons) and using the information to link amino acids into polypeptides. The illustration below shows a 'string' group of ribosomes, called a ***polyribosome*** or ***polysome*** for short.

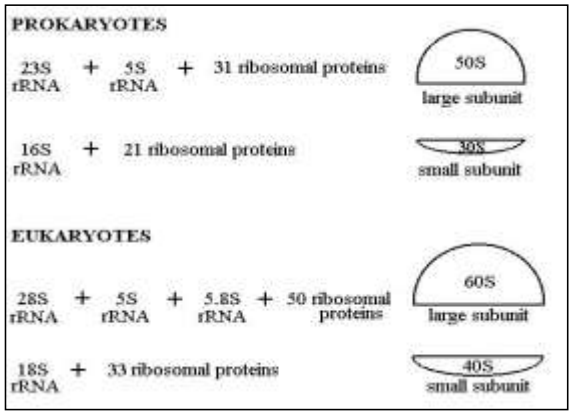


The ribosomes are each moving along the same mRNA simultaneously translating the protein encoded by the mRNA. The granular appearance of cytoplasm in electron micrographs is largely due to the ubiquitous distribution of ribosomal subunits and polysomes in cells. In the electron micrographs of leaf cells from a quiescent and an active dessert plant (*Selaginella lepidophylla*), you can make out randomly distributed ribosomes/ribosomal subunits and polysomes consisting of more organized strings of ribosomes (arrows, below left and right respectively).



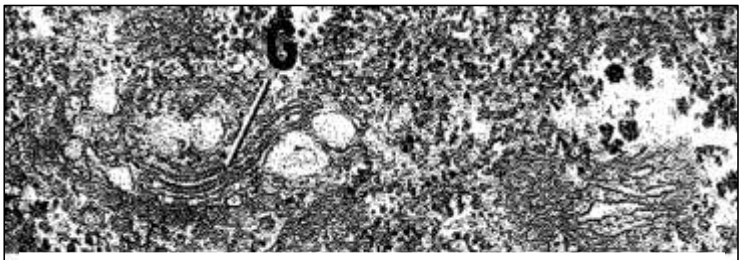
From Bergtrom et al. (1982) J. Ultrastr. Res. 78:269-282

Eukaryotic and prokaryotic ribosomes differ in the number of RNA and proteins in their large and small subunits, and thus in their overall size. When isolated and centrifuged in a sucrose density gradient, they move at a rate based on their size (or more specifically, their *mass*). Their position in the gradient is represented by an "S" value (after *Svedborg*, who first used these gradients to separate particles and macromolecules by mass). The illustration below shows the difference in ribosomal 'size', their protein composition and the number and sizes of their ribosomal RNAs.



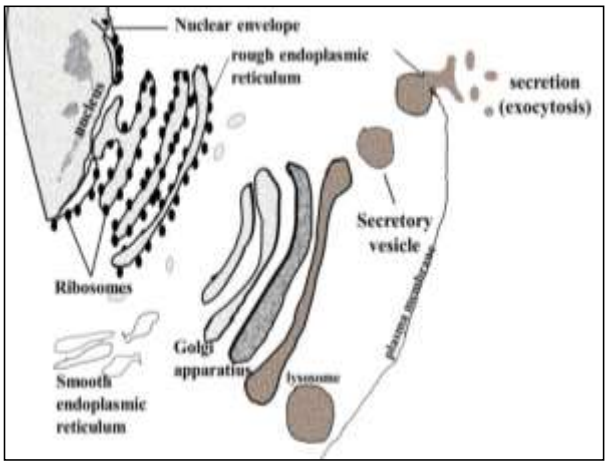
B. Internal membranes and the Endomembrane System

Many of the *vesicles* and *vacuoles* in cells are part of an *endomembrane system*, or are produced by it. The endomembrane system participates in synthesizing and packaging proteins dedicated to specific uses into organelles. Proteins synthesized on the ribosomes of the rough endoplasmic reticulum and the outer nuclear envelope membrane will enter the interior space or lumen, or become part of the RER membrane itself. Proteins incorporated into the RER bud off into *transport vesicles* that then fuse with *Golgi bodies*. See some Golgi bodies (G) in the electron micrograph below.



Adapted from Bergtrom and Robinson (1977) J. Ultrastr. Res. 60:395-405

Packaged proteins move through the endomembrane system where they undergo different maturation steps before becoming biologically active, as illustrated below.



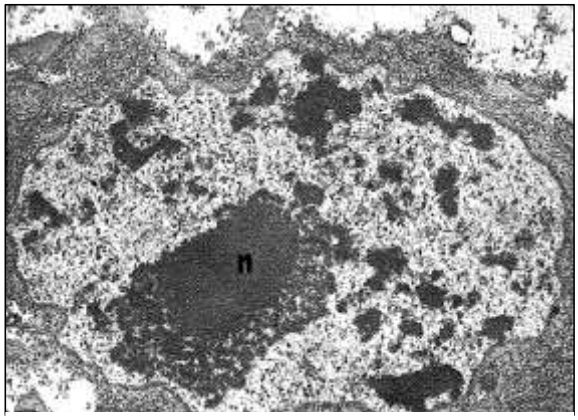
Comment [GKB2]: **Golgi vesicles are part of an intracellular network of membranes called the 'endomembrane system'. Run the animated PowerPoint slide at the following link and answer the questions on the slide at this link: *http://youtu.be/SIM6U0Y6BxQ*. You can spend some time looking up details of endomembrane system function (OK), or answer more simply, using logic to suggest what is going on (Preferred!). Submit your answers to the *Endomembrane Traffic* DropBox no later than [insert date and time].**

Some proteins produced in the endomembrane system are secreted by *exocytosis*. Others end up in organelles like *lysosomes*. Lysosomes contain enzymes that break down the contents of *food vacuoles* that form by endocytosis. *Microbodies* are a class of vesicles smaller than lysosomes, but formed by a similar process. Among them are *peroxisomes* that break down toxic peroxides formed as a by-product of cellular biochemistry.

The *contractile vacuoles* of freshwater protozoa expel excess water that enters cells by *osmosis*; *extrusomes* in some protozoa release chemicals or structures that deter predators or enable prey capture. In higher plants, most of a cell's volume is taken up by a central vacuole, which primarily maintains its osmotic pressure. These and other vesicles include some that do not originate in the endomembrane pathway, but are formed when cells ingest food or other substances by the process of *endocytosis*. Endocytosis occurs when the outer membrane *invaginates* and then pinches off to form a vesicle containing extracellular material.

C. Nucleus

The nucleus is surrounded by a double membrane (commonly referred to as a *nuclear envelope*), with *pores* that allow material to move in and out. As noted, the outer membrane of the nuclear envelope is continuous with the *RER* (rough endoplasmic reticulum), so that the lumen of the RER is continuous with the space between the inner and outer nuclear membranes. The electron micrograph of the nucleus below has a prominent *nucleolus* (labeled n) and is surrounded by RER.



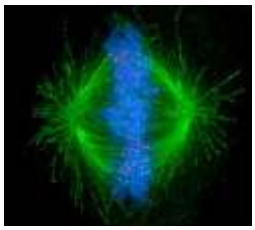
From Bergtrom et al. (1977) J. Ultrastr. Res. 60:395-405

Comment [GKB3]: Check out the VOP clip at this link: http://youtu.be/Bw23E7e0YNk. Then answer the question in the last slide in the clip by completing the sentence "If these structures are nuclei, then..." in 30 words or less. Put your word count in parenthesis after your response. Submit your answers to the *ID Nuclei* DropBox in D2L no later than [insert date and time].

You can almost see the double membrane of the nuclear envelope ion this image. Perhaps you can also make out the ribosomes looking like grains bound to the RER as well as to the outer membrane of the nucleus. The nucleus of eukaryotic cells separates the DNA and its associated protein from the cell cytoplasm, and is where the status of genes (and therefore of the proteins produced in the cell) is regulated. Most of the more familiar RNAs (rRNA, tRNA, mRNA) are transcribed from these genes and processed in the nucleus, and eventually exported to the cytoplasm through *nuclear pores* (not visible in this micrograph). Other RNAs function in the nucleus itself, typically participating in the regulation of gene activity. You may recall that when chromosomes form in the run-up to mitosis or meiosis, the nuclear envelope and nucleus disappear, eventually reappearing in the new daughter cells. These events mark the major difference between cell division in bacteria and eukaryotes.

In both, dividing cells must produce and partition copies of their genetic material equally between the new daughter cells. As already noted, bacteria duplicate and partition their naked DNA chromosomes at the same time during growth and binary fission. Growing eukaryotic cells experience a *cell cycle*, within which duplication of the genetic material (DNA replication) is completed well before cell division. The DNA is associated with proteins as *chromatin* during most of the cell cycle. As the time of cell division approaches, chromatin associates with even more proteins to form *chromosomes*.

Every cell contains pairs of *homologous chromosomes*, both of which must be duplicated. In *mitosis*, the chromosomes are pulled apart by the microtubules of the spindle apparatus (green fluorescence in the micrograph below).

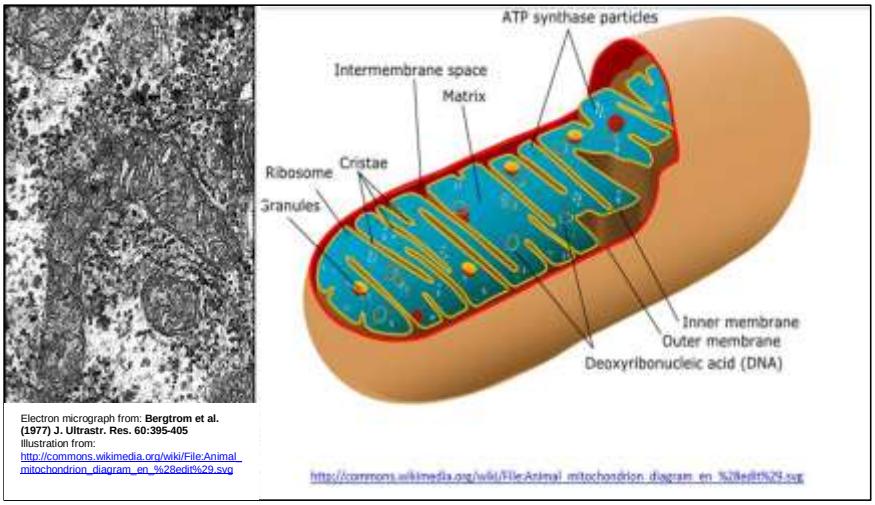


From: http://www.macroevolution.net/spindle-apparatus.html#.UwaL74Vp0eM

Cytokinesis, the division of one cell into two, begins near the end of mitosis. *Sexual reproduction*, a key characteristic of eukaryotes, involves meiosis rather than mitosis. The mechanism of *meiosis*, the division of *germ cells* leading to production of sperm and eggs, is similar to mitosis except that the ultimate daughter cells have just one each of the parental chromosomes, eventually to become the gametes. These aspects of cellular life are discussed in more detail elsewhere.

D. Mitochondria and Plastids

Nearly all eukaryotic cells contain *mitochondria,* seen in the electron micrograph below.



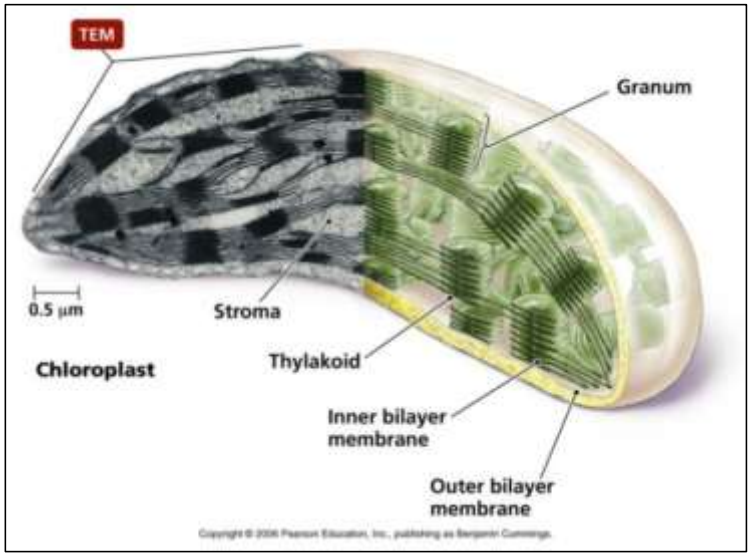
Electron micrograph from: **Bergtrom et al. (1977) J. Ultrastr. Res. 60:395-405**
Illustration from:
http://commons.wikimedia.org/wiki/File:Animal_mitochondrion_diagram_en_%28edit%29.svg

These organelles are surrounded by a double membrane and contain (and replicate) their own DNA, with genes for some mitochondrial proteins. In the illustration above, note that the surface area of the inner membrane is increased by being folded into *cristae*, the site of *cellular respiration* (the oxidation of nutrients in aerobic organisms).

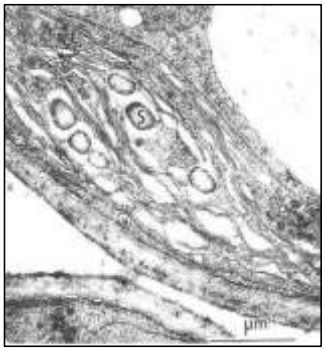
Mitochondria most likely evolved from aerobic bacteria (or protobacteria) engulfed by an early eukaryotic cell that later survived to become *endosymbionts* in the cell cytoplasm. The Endosymbiotic Theory was first proposed by Lynn Margulis [*Sagan, L (1967) On the origin of mitosing cells.* Journal of Theoretical Biology **14** (3): 225–274. (available at: *Margulis L. Endosymbiotic theory*)]. She also proposed an endosymbiotic origin of chloroplasts (see below).

The few protozoa that lack mitochondria have been found to contain mitochondrion-derived organelles, such as *hydrogenosomes* and *mitosomes*; and thus probably lost the mitochondria secondarily. Like mitochondria, the plastids of plants and some algae have their own DNA and evolved from cyanobacteria that were are engulfed by primitive eukaryotic cells. These endosymbionts became chloroplasts and other plastids.

Chloroplasts (illustrated below) and cyanobacteria contain chlorophyll and use a similar photosynthetic mechanism to make glucose.



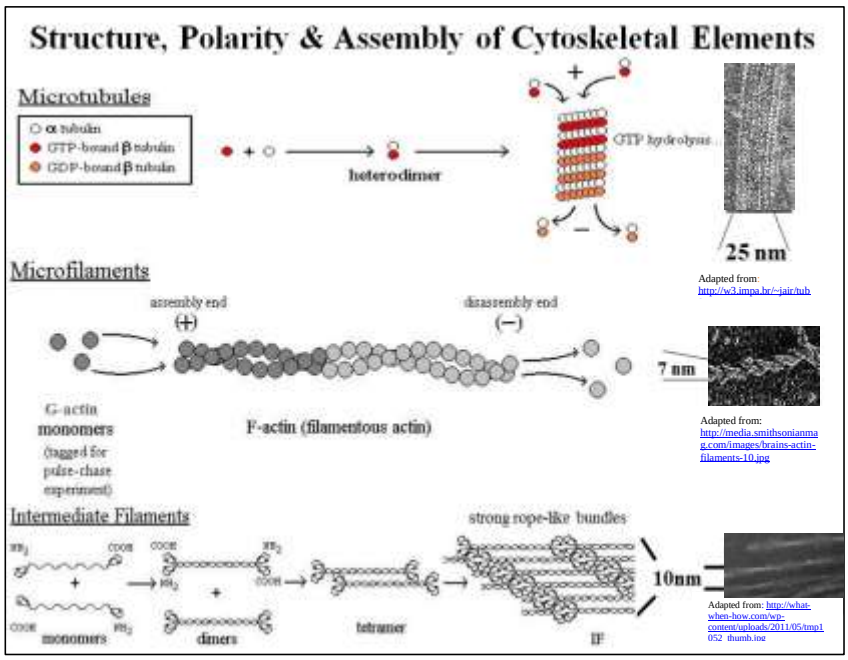
Others plastids develop from chloroplasts to store food; an example is the leucoplast shown below (S is a starch granule). You can see that as a result of starch accumulation, the grana have become dispersed.



From Bergtrom et al., J. Ultrastr. Res. 78:269-282

E. Cytoskeletal structures

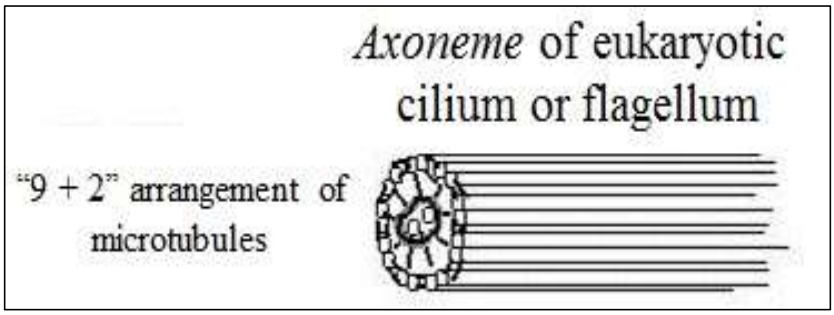
We have come to understand that the cytoplasm of a eukaryotic cell is highly structured, permeated by rods and tubules. The three main components of this cytoskeleton are *microfilaments*, *intermediate filaments* and *microtubules*, with structures illustrated below.



Microfilaments are made up of *actin* monomer proteins. Intermediate filament proteins are related to *keratin*, the same protein found in hair, fingernails, bird feathers, etc. Microtubules are composed of α– and β-*tubulin* proteins. Cytoskeletal rods and tubules not only determine *cell shape*, but also play a role in *cell motility*. This includes the movement of cells from place to place and the movement of structures within cells. We've already noted that a prokaryotic cytoskeleton exists that is in part composed of proteins homologous to actins and tubulins that are expected to play a role in maintaining or changing cell shape. Movement powered by a bacterial flagellum relies on other proteins, notably flagellin (above). Bacterial flagellum structures are actually attached to a molecular motor in the cell membrane that spins a more or less rigid

flagellum to propel the bacterium through a liquid medium. Instead of a molecular motor, eukaryotic *microtubules slide* past one another causing the flagellum to undulate in wave-like motions. The motion of eukaryotic cilia (there is no counterpart structure in prokaryote) is also based on sliding microtubules, in this case causing the cilia to beat rather than undulate. Cilia are involved not only in motility, but in feeding and sensation.

Despite the difference in motion, microtubules in eukaryotic flagella and cilia arise from a basal body (also called a kinetosome or centriole). In the axoneme inside a flagellum or cilium, the microtubules are seen in cross-section to be characteristically arranged as nine doublets surrounding two singlets (see the axoneme below).



Centrioles are often present animal cells, and participate in spindle fiber formation during mitosis. They are also the point from which microtubules radiate thorough the cell to help form and maintain its shape. These structures are themselves comprised of a ring of microtubules. The spindle apparatus in plant cells, which typically lack centrioles, form from an amorphous structure called the *MTOC*, or *MicroTubule Organizing Center*, which serves the same purpose as centrioles in animal cells.

Elsewhere, you will see how microfilaments and microtubules interact with motor (*dynein*, *kinesin*, *myosin*…) and other proteins to generate force that results in the sliding of filaments and tubules to allow cellular movement. You will also see that motor proteins can carry cargo molecules from one place to another in a cell.

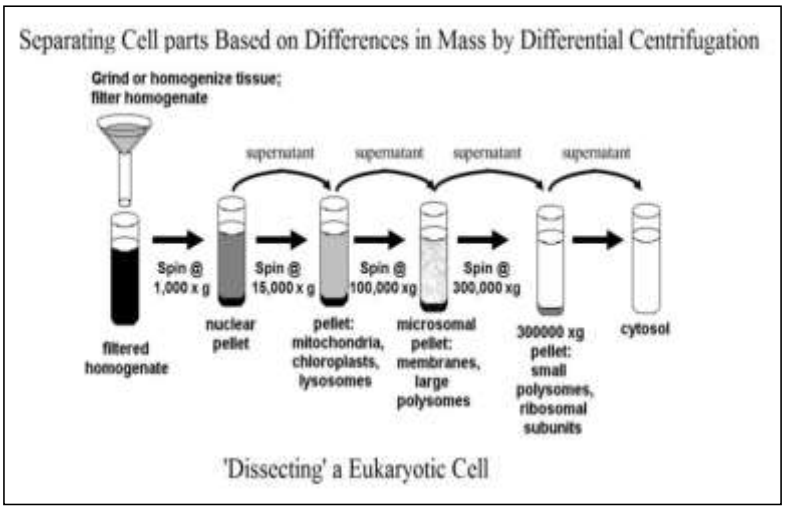
F. Cell wall

We noted that plant (also algal) and fungal cells are surrounded by a rigid cell wall, that creates create a rigid structure outside the cell membrane supporting cell shape. The cell wall also prevents cells from swelling to much when water enters the cell. The major polysaccharides of the plant cell wall are cellulose, hemicellulose, and pectin, while the principal fungal cell wall component is *chitin*.

V. How We Know about Organelle Function

A. Cell Fractionation

We could see and describe cell parts in the light or electron microscope, but we could not definitively know their function until it became possible to release them from cells and separate them from one another. This became possible with the advent of differential centrifugation, a cell fractionation technique that separates sub-cellular structures by differences in their mass. Cell fractionation (illustrated below) and biochemical analysis of the isolated cell fractions were combined to reveal what different organelles do.

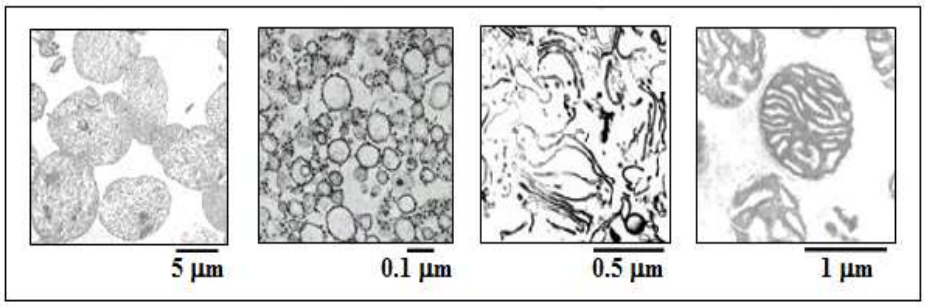


Cell fractionation is a combination of various methods used to separate a cell organelles and components. There are two phases of cell fractionation: homogenization and centrifugation.

1. *Homogenization* is the process of breaking cells open. Cells are broken apart by physical means (such as grinding in a mortar and pestle, tissue grinder or similar device), or treatment with chemicals, enzymes, or sound waves. Some scientists even force the cells through small spaces at high pressure to break them apart.

2. *Centrifugation* is the isolation of the cell organelles based on their different masses. Therefore at the end of this process, a researcher has isolated the mitochondria, the nucleus, the chloroplast, etc.

Scientists use cell fractionation to increase their knowledge of organelle functions. To be able to do so they isolate organelles into pure groups. For example, different cell fractions end up in the bottom of the centrifuge tubes. After re-suspension, the pellet contents can be prepared for electron microscopy. Below are electron micrographs of several such fractions.



From: openi.nlm.nih.gov From: Isolated RER From: Isolated Golgi From: Isolated Mitochondria

The structures can be identified based (at least tentatively) based on the dimensions and appearance of these structures. Can you tell what organelles have been purified in each of these fractions? The functions of sub-cellular structures isolated in this fashion were worked out by investigating their contents and testing them for function. As an example, the structures on the left were found in a low speed centrifugal pellet, implying that they are large structures. They look a bit like nuclei, which are in fact the largest structures in a eukaryotic cell. If you wanted to be sure, what biochemical or functional test might you do to confirm that the structures in the left panel were indeed nuclei? This method has already resulted in our understanding not only of the identity of subcellular structures, but of previously un-noticed functions of many if not all cell organelles.

For a detailed description of the biochemical analysis, review your instructors VOP and/or un-narrated presentation on cell fractionation. This course is devoted to understanding cell structure and function and how prokaryotic and eukaryotic cells (and organisms) use their common biochemical inheritance to meet very different survival strategies. As you progress in the course, you will encounter one of the recurring themes involving the *dissection* of cells. Look for this theme, involving the *isolation* and *analysis of function* of the cell components, and where possible, the re-assembly (*reconstitution*) of cellular structures and systems. Look also for another theme, namely how evolution can account for the biochemical and genetic of life…, *and* its structural diversity.

Comment [GKB4]: Look at the *phase contrast* micro-graph of isolated chloroplasts in this link: http://youtu.be/oZX1H0X7xQY. In 30 words or less, state a working, testable hypothesis consistent with your suspicion that these structures are isolated chloroplasts. Remember that an hypothesis is a declarative sentence, usually stated as an "if..., then..." statement. Put your word count in parenthesis after your response and submit it to the "Chloroplast" D2L DropBox by [insert date and time].

V. Evolution, Speciation and the Diversity of Life

Natural selection was Charles Darwin's theory for how evolution led to the *structural* diversity of species. New species arise when beneficial traits are naturally selected from genetically different individuals in a population, with the concomitant culling of less fit individuals from populations over time. If natural selection acts on individuals, evolution results from the persistence and spread of selected, heritable changes through successive generations in a population. Evolution is reflected as ***an increase in diversity and complexity*** at all levels of biological organization, from species to individual organisms to molecules like DNA and proteins. For an easy read about the evolution of eyes (whose very existence according to creationists could only have formed by intelligent design by a creator), see the article in National Geographic by E. Yong (Feb., 2016, with its beautiful photography by D. Littschwager).

We say that life on earth originated and then evolved from the ***progenote*** some 3.7-4.1 billion years ago. But the progenote may have been only one of many experimental cells formed when conditions on earth were permissive to origins of life. ***Evolution*** began with these first cells; by definition, all cells had all of the properties of life. Therefore, the descendants of "first cells" with their separate origins, would have found different genetic and biochemical solutions to achieving and maintaining life's properties. But all cells and organisms alive today also share the same genetics and biochemistries, suggesting that all life forms other than the progenote never gained a foothold on the planet. At the same time, the descendants of the progenote were evolving, diversifying and generating new species. Since, it is possible that many lineages of its progeny (species) also went extinct…, except for one, which we now call the last Universal Common Ancestor, or LUCA. Repeated speciation, the continual divergence of life forms from this LUCA through natural selection and evolution, is supported by the shared cellular structures, nucleic acid, protein and metabolic chemistries (the 'unity' of life). Since the revolution in molecular biology, shared gene and other DNA sequences have confirmed the shared common ancestry of diverse organisms across all three of life's domains.

These relationships largely confirm what we have learned from the species represented in the fossil record. Morphological, biochemical and genetic traits that are shared across species are defined as *homologous*, and can be used to reconstruct evolutionary histories. The biodiversity that scientists (and environmentalists in particular) try to protect has resulted from millions of years of speciation and extinction. It needs protection from the unwanted evolutionary acceleration from human activities, including blatant extinctions (think passenger pigeon), near extinction (think American bison by the late 1800s), the introduction of invasive aquatic and terrestrial species, and the effects of climate change.

Let's take a closer look at the biochemical and genetic unity among livings things. Albert Kluyver first recognized that cells and organisms vary in form appearance in spite of the essential biochemical unity of all organisms (http://en.wikipedia.org/wiki/Albert Kluyver). We've already considered some of the consequences cells getting larger in evolution when we tried to explain how larger cells divided their labors among smaller intracellular structure (organelles). When eukaryotic cells evolved into multicellular organisms, it became necessary for the different cells to communicate with each other and to respond to environmental cues. Some cells evolved mechanisms to "talk" directly to adjacent cells and others evolved to transmit electrical (neural) signals to other cells and tissues. Still other cells produced hormones to communicate with cells to which they had no physical attachment. As species diversified to live in very different habitats, they also evolved very different nutritional requirements, along with more extensive and elaborate biochemical pathways to digest their nutrients and capture their chemical energy. Nevertheless, Kluyver and many others eventually recognized that despite billions of years of obvious evolution and astonishing diversification, the underlying genetics and biochemistry of living things on this planet is remarkably unchanged. This unity amidst the diversity of life is an apparent paradox of life that we will probe in this course.

A. Genetic Variation, the Basis of Natural Selection

DNA contains the genetic instructions for the structure and function of cells and organisms. When and where a cell or organism's genetic instructions are used (i.e., to make RNA and proteins) is regulated. Genetic variation results from random mutations. Genetic diversity arising from mutations is in turn, the basis of natural selection during evolution.

B. The Genome: an organisms complete genetic instructions

The genome of an organism is the entirety of its genetic material (DNA, or for some viruses, RNA). The genome of a common experimental strain of *E. coli* was sequenced by 1997. For details, see Blattner FR et al. (1997) *The complete genome sequence of Escherichia coli K-12.* Science 277:1452-1474. That of humans was completed by 001, well ahead of the predicted schedule! For more details, see Venter JC (2001) *The sequence of the human genome*. Science 291:1304-1351. Through mutation, genomes exhibit genetic variation, not only between species, but between individuals of the same species.

C. Genomic 'Fossils' Can Confirm Evolutionary relationships.

It has been known for some time that gene and protein sequencing can reveal evolutionary relationships and even familial relationships. Read about an early demonstration of such relationships based on amino acid sequence comparisons

across evolutionary time in Zuckerkandl E and Pauling L. (1965) *Molecules as documents of evolutionary theory.* J. Theor. Biol. 8:357-366. It is now possible to extract DNA from fossil bones and teeth, allowing comparisons of extant, ancient and even extinct species. Thus, DNA has been extracted from the fossil remains of humans, other hominids, and many animals. Sequencing this DNA (see the chapter on DNA Technologies) has revealed our relationship to some of our hominid ancestors and some of these ancient species. The reality though, is that DNA from organisms much older than 10,000 years is typically so damaged or simply absent that relationship building beyond that time is not possible. Now in a clever twist, using what we know of extant gene sequences, investigators recently ***'constructed'*** a genetic phylogeny suggesting the sequences of some of our long-gone progenitors, including bacteria (click here to learn more: http://www.eurekalert.org/pub_releases/2010-12/miot-sd3121510.php). The comparison of these ***'reconstructed'*** ancestral DNA sequences suggests when photosynthetic organisms diversified and when our oxygenic planet became a reality.

D. Origins of Life

Living things were once divided into 5 kingdoms. This classification has been replaced by 3 domains of life. For more detail, check out Woese CR (1998) *The universal ancestor*. Proc. Nat. Acad. Sci. 95:6854-6859. The molecular analyses discussed above lead to the conclusion that all organisms alive today descended from a last universal common ancestor, the ***LUCA***. It is now accepted that there was a time, however brief or long, when the earth was a lifeless (prebiotic) planet. But the question of how life began has been with us since the beginnings or recorded history. We will consider how we approach and suggest answers to questions about the origins of life in a later chapter.

VI. Microscopy Reveals Life's Diversity of Structure and Form

For a gallery of light, fluorescence and transmission and scanning electron micrographs, check out this site (compare these with PowerPoint lecture images): Gallery of Micrographs. The following is a brief description of different microscopic techniques and what they can reveal.

- Light microscopy reveals much of cellular diversity (The Optical Microscope). Check this site through the section on fluorescence microscopy. Click on links to different kinds of light microscopy to see sample micrographs of cell and tissue samples. Also check micrographs and corresponding Drawings of Mitosis section for a reminder of how eukaryotic cells divide.

- A 100 year-old variant of light microscopy, Lattice Light-Sheet Microscopy, was recently updated to allow us to follow subcellular structures and macromolecules moving about in living cells. It was recently applied to follow the movement and sub-cellular cellular location of RNA molecules associated with proteins in structures called RNA granules (check it out at RNA Organization in a New Light).
- Confocal microscopy is a special form of fluorescence microscopy that enables imaging through thick samples and sections. The result is often 3D-like, with much greater depth of focus than other light microscope methods. Click at Gallery of Confocal Microscopy Images to see a variety of confocal micrographs and related images; look mainly at the specimens.
- Transmission electron microscopy (TEM) achieves more power and resolution than any form of light microscopy (Transmission Electron Microscopy). Together with biochemical and molecular biological studies continues to reveal how different cell components work with each other (see cell fractionation, below). The higher voltage in *High Voltage Electron microscopy* is an adaptation that allows TEM through thicker sections than regular (low voltage) TEM. The result is micrographs with greater resolution and contrast.
- Scanning Electron Microscopy (SEM) allows us to examine the surfaces of tissues, small organisms like insects, and even of cells and organelles (Scanning Electron Microscopy; check this web site through *Magnification* for a description of scanning EM, and look at the gallery of SEM images at the end of the entry).
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Some iText & VOP Key words and Terms

Actin	**Eukaryotes**	**Nuclear envelope**
Archaea	**Eukaryotic flagella**	**Nuclear pores**
Bacterial cell walls	**Evolution**	**Nucleoid**
Bacterial Flagella	**Exocytosis**	**nucleolus**
Binary fission	**Extinction**	**Nucleus**
Cell fractionation	**Hypothesis**	**Optical microscopy**
Cell theory	**Inference**	**Plant cell walls**
Chloroplasts	**Intermediate filaments**	**Plasmid**
chromatin	**keratin**	**Progenote**
Chromosomes	**Kingdoms**	**Prokaryotes**
Cilia	**LUCA**	**Properties of life**
Confocal microscopy	**Lysosomes**	**Rough endoplasmic reticulum**
Cytoplasm	**Meiosis**	**Scanning electron microscopy**
Cytoskeleton	**Microbodies**	**Scientific method**
Cytosol	**Microfilaments**	**Secretion vesicles**

Deduction	**Microtubules**	**Smooth endoplasmic reticulum**
Differential centrifugation	**Mitochondria**	**Speciation**
Diversity	**Mitosis**	**Theory**
Domains of life	**Motor proteins**	**Tonoplast**
Dynein	**Mutation**	**Transmission electron microscopy**
Endomembrane system	**Natural selection**	**Tubulins**