# Bil 255 – CMB

## a brief history of CMB

milestones



**Bil 255 - Cell and Molecular Biology...**
**structure, function, & the molecules of cells with**
**Professors Glaser and Mallery - Spring Semesters**

**text (spring 2006): Molecular Cell Biology, 5th Edition**
**by: Lodish et al, Publisher: W.H.Freeman, NY, 2004**

**web resources:**
The Virtual Library of Biochemistry & Cell Biology &
Access Excellence **- a national biology education resource of the National Health Museum & originally sponsored by GENENTECH, Inc.,**
**and for some of the graphics**
= **AE STUDENT RESOURCES***
& Mallery's web links for CMB RESOURCES*.



**Description**:

**The goal of cell biology is to understand the molecular basis of cell function and the fundamental cellular processes ranging from cell division and protein trafficking to signal transduction and cell migration, and to the formation of tissues during development and wound healing. The experimental approaches used in studying cell regulation and function are multidisciplinary and include: biochemical and biophysical approaches and molecular and genetic manipulation of function at both the cellular and organismal levels**

**CMB is the ultimate reductionist philosophy…**
***the methodological approach of 20th century***

**Reductionism is the fundamental research protocol of CMB**
**i.e., "knowing the parts may explain the function of the whole"**



## CMB is rooted in the 2 major theories of Biology

1. **Evolution** - Darwinian Natural Selection
changes in the allele frequency of a population's gene pool
from one generation to another generation… as influenced by a habitat,
which enhances population's reproductive fitness,
& leading to progressively better adaptation via Natural Selection*
principles of morphological change **and** natural selection,
applied repeatedly over millions of cell generations, are basis of evolution
**Voyage of Beagle*** **Snoppy** **Darwin's books & publications**

2. **Cell Theory...**
"All living things are made of cells"...
'small, membrane bounded compartments, filled with
concentrated aqueous solutions of reactive chemicals'
**"All organisms are believed to have descended from a common ancestral cell [LUCA] selected for its better fitness through the processes of evolution, via Natural Selection"**
**Some cell links** **Cell Theory Origins**
**Schleiden (pic)** **&** **Schwann**

Cell Theory  Table 1.1 on page 24 of ECB.

| | | |
|---|---|---|
| 1665 | Robert Hooke publishes *Micrographia* via Royal Society | minute chambers called cells... walls of plant cells (bark) |
| 1680 | Leeuwenhoek publishes *Animacules* | magnifying lens & pond water |
| 1697 | Redi negates Spontaneous Generation | all life arises from per-existing life [??? - controls] |
| 1809 | Jean Baptiste Lamarck | "Living body is a mass of cells" |
| 1824 | Henri Dutrouchet | mild acid dissolves extra-cellular matrix 1st biochem |
| 1833 | Robert Brown | nucleus of orchid cells |
| 1838 | Mathais Schleiden (plants) & Theodor Schwann (animals) | tissues are made of cells = *Cell Theory* - the formal birth of discipline of "Cell Biology" |
| 1858 | Rudolf Virchow | "Every animal appears as sum total of vital units, each of which bears the complete characteristics of life"...suggests cells formed from pre-existing cells |
| 1879 | Walther Flemming | first detailed description of cell division, mitosis & chromosome |
| 1912 | Jacques Loeb | removes sea urchin eggs & chemically induces embryonic development |



## Consequences of Cell Theory

**VITALISM vs. MECHANICALISM**
**living vs. non-living**
**organic vs. non-organic**  Top 10 Properties of Cells*
**Vital Force vs. no vital force**

**Cell Theory replaces Vitalism... the mainstream scientific thought of 17th century,**
Vitalism **was school of scientific thought, that attempts to explain the nature of life as resulting from a vital force, "a soul", peculiar to living organisms and different from all other physical forces found outside living things.**

Mechanists **believed that life is essentially a mechanical process, it can be explained entirely by the workings of laws of physics and chemistry without a 'vital force'.**

"***There are no Laws of Chemistry or Physics unique to the living condition.***"
The cell is the fundamental unit of all life, and though man and mouse have very different anatomical structure, their cells & organelles are the same, thus by studying cells in one organism has direct application to other organisms.



**Cell Types...** (refer to chapter 1)  All Living Organisms are grouped into...
**EUBACTERIA** - true bacteria
**ARCHAEA** - ancient procaryotes  [Collage]
**EUCARYA** - modern eucaryotes

Carl Woese, (interview) compared the nucleotide sequences of small-unit rRNA from many species... rRNA is found in all cells and therefore, if all cells are derived form a common progenitor[NAS-1], their sequence changes over time can indicate divergence (loss of relatedness) through phylogeny
The RNA phylogeny tree produced, by comparing similar & divergent sequences, a tree with 3 distinct branches (Domains) (fig 1.29*)

there are only **2 successful Plans of Cellular Organization**
distinguished primarily by size & type of internal structure (organelles)

**PROKARYOTE** - "before nucleus"
today prokaryotes includes blue green algae & bacteria...
lack membrane bound organelles
genes "naked DNA" - no "chromosomes?"
little to no internal compartmentation figure* + panel1.2 + E.coli*
size range - 0.1 to 10 µm diameter
3 primary forms of shape of prokaryotic cells (fig 1.10*)
(cocci, bacilli, spirochetes)



**EUKARYOTIC [eu -true karyon -nucleus...]** cell plan of multi-cellular organisms
eukarya: include the fungi, algae, protozoa, slime molds, & all plants & animals.

**7 CHARACTERISTIC of EUCARYOTES:** **panel 1-2: animal* & plant* cells**

**nucleus** - single greatest step in evolution of higher animals
genes in "chromosomes" [colored bodies... made of DNA + protein]
contains more DNA (1,000x more) than procaryotes
presence of **organelles-** significant internal compartmentalization of function
*organelle - a subcell part that has a distinct metabolic function*
presence of flexible **cell walls** (allows phagocytosis)
presence of **cytoskeleton** (provides framework to be larger)
usually **larger** - cell volume 10X > than bacteria - size 5.0 to 20 µm diameter
extensive **internal membranes**
**reproduce sexually**

**Essential Concepts or Properties of Cells from Cell Theory…**

**the Cell is the basic unit of Living**

**all living things all cells are derived from other cells...**
**(originally from a single primordial cell [LUCA] some 3 bya**

**all cells extract energy from environment**
**and maintain a homeostasis far from equilibrium**

**all are enclosed by P-lipid bilayer that osmoregulates with environs**

**all use nucleic acids for genetic information**

**all are capable of self-replication**

**all come in 3 domains (archaea, eubacteria, and eukarya)**
**are 2 structural types - prokaryotes & eukaryotes**

**eukaryotes hold subcell parts that catalyze specific functions (organelles)**
notably: **nucleus (DNA-replication blueprint),**
**mitochondria (anaerobic-aerobic oxidation-reduction rx)**
**chloroplast (photosynthesis),**
**ER (protein synthesis),**
**Golgi (polysaccharide trafficing),**
**lysosome (hydrolysis),**
**cytoskeleton (cell shape & framework),**
**cytosol (aqueous reaction vessel of cell).**

refresher on Cell Organelles*



**How Cells Work**... or the **Basic Properties of Cells and thus Life**

cells have an evolutionary origin - via Chemical Evolution toward a LUCA

cells: highly complex mix of biomolecules **(C, O, H, N)** ---> cellular complexity
show structural complexity - review figure 5.22a pg 169 (mcb)
& typical animal & plant cells (fig 5.19 pg 166 - mcb)
cells come in 2 fundamental types - prokaryote & eukaryote (read pgs 2-4)*
cells obey laws of chemistry & physics (the laws of Universe)
cells build and degrade numerous molecules, generally via ATP fig 1.14*
cells metabolize - are capable of 1,000's of reactions (via enzyme pathways
cells acquire and utilize energy -via metabolic pathways:
glycolysis, Krebs, ETC
cells are capable of self regulation
- series of ordered reactions that are self-adjust
cells show division, growth, & differentiation leads to cell Form & Function
cells osmoregulate - control what gets in/out of membranes*



**Basic Properties of Cells and thus Life...**

cells are motile...
cells are involved in numerous mechanical activities assembly, disassembly, movement of organelles, motor proteins
- all via the cytoskeleton fig 1.15*

cells respond to stimuli - via cell surface receptors fig 1.16*

cells grow and divide...
cells can replicate themselves - Mitosis & Meiosis
cells regulate their gene expression (RNA &protein synthesis - fig 1.17*)

cells die - absence of life is a most defining characteristic of living state
appotosis* - programmed cell death due to absence of certain growth signals - fig 1.19*



**Early History of CMB...**

**Between 1860-1900 two new areas of biology evolve…**

1. **Biochemistry - isolation & chemical characterization cell substances**

| | | |
|---|---|---|
| 1828 | Freiderich Wohler | **synthesizes 1st natural biological products.... UREA from urine & oxalic acid from spinach** |
| 1838 | G. Mulder | **isolates fibrous acid precipitate = protein** |
| 1869 | F. Johann Miescher | **isolates an acidic material (nuclein) from from the nuclei of white blood cells and sperm of Rhine river Salmon** |
| 1897 | E. Buchner | **yeast cell extracts convert glucose --> alcohol** |
| 1900's | H. Emil Fischer | **defines peptide bond... 16 of 22 amino acid discovered** |

**Early History of CMB - a 2nd new discipline** NHGRI Timeline Landamrks Pic NHGRI Dynamic History Timeline

**2. Genetics... study of inheritance/characters in plants & animals**

| | | |
|---|---|---|
| 1865 | G. Mendel (Mendel Web) | dominance/recessiveness; dihybrid crosses; true value was his quantitative approach |
| 1900 | Carl CORRENS, Hugo DeVIRES, Ernst TSCHERMAK, | Mendel's work rediscovered by 3 independent geneticists |
| 1902 | Walter SUTTON & Theodor BOVERI | chromosmal theory of inheritance (meiosis matches Mendel) |
| 1902 | Archibold Garrod | - founder of "biochemical genetics" alkaptonuria<br>- 1st idea that gene mutations are defective proteins |
| 1909 | Wilhelm JOHANNSEN | coins term GENE = mendelian unit and concepts of phenotype & genotype |
| 1911 -20's | T.H. Morgan (paper) Alfred Sturtevant Calvin Bridges | Drosophilia.... chromosome linkage, sex chromosomes, mapping, etc. |



**1930 to 1953 - CMB Comes of Age...**

**Period of discovery of chemical nature of gene**
**& a merging of fields of biochemistry & genetics into molecular genetics**

| | |
|---|---|
| 1930 | George Beadle - drosophila eye mutant due to defective enzyme i.e., defective gene = dysfunctional enzyme = mutation |
| 1941 | G.Beadle & E. Tatum - coin concept... "one gene = one enzyme" |
| 1944 | Avery, MacLeod & McCarty - open the era of molecular genetics - **proteases don't alter gene transformation, but DNAses inactivate it, thus DNA is genetic material. 1st use of enzymes to test for active biological products - becomes the vogue experiment of the decade.**<br>Barbara McClintock - jumping genes (transposons) |
| 1952 | Alfred Hershey (biography) & Martha Chase their experiment - use $^{32}P$ & establish DNA as genetic material in viral infection |



**1950-60: Birth of Modern CMB...** ...A Brief History of Biotechnology

Maurice Wilkens [NZ Bio] & Rosalin Franklin - Xray diffraction 3.4mu, 0.34nm, 2.0 nm (Voyager & its golden record)

Erwin Chargaff (pic) - base pairing rules A+G/T+C= 1

Linus Pauling (1951) [osu] - alpha helix-beta sheet – right handed, 3.6 aa/turn (0.54nm)

Watson & Crick (1953) Nature 171: 737-738 & 964-967 (1953).
*"A Structure for deoxyribonucleic acid"* The Discovery of the Structure of DNA
*"General implications of structure of deoxyribonucleic acid"*

Joe Hin Tjo (1955) **defines 46 as the exact number of human chromosomes**

Max Perutz & John Kendrew (1957) - 1st 3D protein structure - myoglobin*

Fred Sanger ('58) - **Nobel** -molecular structure of insulin - made by beta cells of islets of Langerhans; it's a protein of two chains, an alpha chain (21 aa) and a beta chain (with 30), linked by sulfur atoms.
('80) - **Nobel** for helping to determinate of sequence of tRNA



## Bil 255 - Foundations of Cell Molecular Biology

**1980's** and **1990's are the dawn of the modern Cell & Molecular Biology Age** and **is the content of Biology 255**

**my mother (1906) :** auto, airplane, radio, T.V. ... man on the moon
**me (1943) :** heart transplants (who was 1st ?), antibiotics, DNA & transgenic animals, artificial genes & manipulation, cloning, human genome ....

CMB is part of our modern culture - Movies: *Species* *Jurassic Park*

Nobel Prizes in Physiology & Medicine and Chemistry

to repeat.....

**The aim of Modern CMB is to interpret the properties of life & organisms through the structure of their constituent cellular molecules.**

**CMB Asks Fundamental Questions as:**

How did Life originate ?
How does life beget life ?
How does an individual adult (plant or animal) develop from a fertilized seed/egg
What is progression from individual molecules --> to multi-cellular organism?
Ans: The Central Dogma of Molecular Biology: DNA --> RNA --> Protein

**with deciphering of DNA and our understanding of the Central Dogma... some questions have been answered:**

Early origin & evolution of cells must have been due to those cells which used DNA... these cells had a better fit and were selected for...
'Life begets Life' - is now seen at the molecular level, as the faithful replication of DNA...
Development - is the pre-programmed unfurling of an organism's genomic DNA; it's what underlies the growth of all organisms...



**What cells types will we be looking at?** [see pg 24 - 28]*
[a freshman review of Prokaryote, Eukaryote, & Virus]

**Model Organisms*** in Cell & Molecular research include:

*Bacteriophages* - virus infects bacteria; today used as cloning vectors
*Escheriichia coli* - bacteria common to human colon; work horse
*Giardia* - primitive eukaryotic cell, anaerobic protozoan cell with 2 nuclei

other eucaryotic models -
single celled - *Saccharomyces cerevisiae* - yeast [pic]
plants - mustard plants *Arabidopsis thaliana* [pic]
nematode - *Caenorhabditis elegans* - nematode [2002 Nobel]
animals - fruit fly *Drosophilia melangaster*
[Mickey] mouse - *Mus musculus* - common house mouse & its genes

*Single cell culture models*
for genetic & embryonic development model systems...
Hela cells (pic) - (George & Margaret Gey at JHU)
human - fibroblast- connective tissue easily grown in tissue culture
immortal stem cells (Stem Cell Journal)



**So then, what is... CONTEMPORARY CELL & MOLECULAR BIOLOGY**

**CMB is a little bit of this, of that, and some of that, and asks...**
**Is the CELL an independently functioning unit,**
**Is the ORGANISM (plant or animal) and is more than an assembly of individual cells, and includes...**

**Cell Physiology - takes a comparative approach:**
**adaptations to habitats via an evolutionary base...**
**it asks how cells answer universal problems such as: water conservation, cell communication, etc.…**
**Systemic Physiology - organism or organ systems, form & function insect, plant, fish, kidney, etc...physiology**
**Biochemistry - chemical & physical commonality of the mechanisms of cellular reactions**

**Molecular Biology - studies properties of organisms through the structure of its constituent molecules.**



## Reasons to Study CMB

It is a Core Knowledge Area of Biology...
... needed to understand cells as the unit of life
... to learn those properties common to all eukaryotic cells
…a guesstimate :
10 million to 100 million different species of organisms
and each species has many different types of cells
adult human body has some 60 trillion total cells...
the human body has about 200 different kinds of cells,
CMB asks... what do all these cells have in common...
the answer = "their molecules & chemical reactivity"

**WHAT IS CMB ?**
as Erwin Chargaff **(former Chair of Bioc @ Columbia & Heineken Prize winner)** said "CMB is practicing Biochemistry without a license"

**The AIM of modern Cell & Molecular Biology then is to interpret the (questions) properties of organisms through the structure of their constituent molecules.**