Foundations - Cells, organelles and cell boundaries

From Cellbiology

Introduction

2012 Lecture Slides:

The 2 major classes of cells are defined by the presence or absence of a nucleus; **Eukaryotic** (with nucleus) and **Prokaryotic** (without nucleus).

Eukaryotes can be further divided into unicellular (only one cell, like prokaryotes) and multicellular (like us) organisms.

A major difference between eukayotes and prokaryotes is the presence of physical compartments (membrane bound) and organelles within the cell. These compartments allow the separation/specialization of processes within the cell. There also exist within each of these physical compartments, functional compartments where specific processes may occur or are restricted.

This lecture is also an introduction to cell compartments and describes the structure of membranes forming these compartments.

About Human Body

Human Cells

- 210+ cell types in body
- total number of estimated cells in the body - $10^{13}$ (American Ten trillion/British Ten billion)

Flora

- bacteria, fungi and archaea
- found on all surfaces exposed to the environment
  - skin and eyes, in the mouth, nose, small intestine
- most bacteria live in the large intestine
- **500 to 1000** species of bacteria live in the human gut
- total number of estimated flora ten times as many bacteria $10^{14}$ (American One hundred trillion/British One hundred billion)

Cell Sizes
- frog or fish egg are the largest individual cells easily visible, approx 1+ mm diameter
- human or sea urchin egg, approx 100 micron (µm) diameter
- typical somatic cell, approx 20 micron diameter
- plant cells are larger, approx 30 x 20 micron
- bacteria are smaller, approx 2 x 1 micron

Cell History

- Robert Hooke (1635-1703) - used early microscopes to view cork tree bark, first to use the term CELL.
- Robert Brown 1825 - identified nuclei in plant cells.
- Theodor Schwann (1810 - 1882) - together with Matthias Schleiden (plants) developed the cell theory in 1839
  - All organisms consist of one or more cells.
  - The cell is the basic unit of structure for all cells.
  - All cells arise only from preexisting cells.

Divisions of Life

Prokaryotic

- bacteria and archaea (single-celled microorganisms previously called archaebacteria)
  - **no cell nucleus** or any other organelles within their cells
  - organisms that can live in extreme habitats Archaea
    (http://www.ucmp.berkeley.edu/archaea/archaea.html)

Eukaryotic

- **cell nucleus**
- plants, animals, fungi, protists

Unicellular and Multicellular

Unicellular

- All prokaryotes and some eukaryotes
  - Yeast + budding, non-budding
  - Protozoa + classified by means of locomotion: flagellates, amoeboids, sporozoans, ciliates
  + often "feed" on bacteria

Multicellular

- Eukaryotes
- Plants and Animals
- Allowed development of specialized cells
- functions and tissues

Prokaryote
Evolutionarily arose first (3.5 billion years ago) Evolution of Cells
- Bacteria are smaller, approx 2 x 1 micron (1x10^-6 m)
- Not all bacteria are dangerous or disease causing
  - The adult human in addition bacteria to the skin surface and lining of the respiratory/digestive tract, also has intestines contains trillions of bacteria made up from hundreds of species and thousands of subspecies)
- Biochemically diverse
- Simple structure, classified by shape (rod-shaped, spherical or spiral-shaped)
- Some prokaryotic cells have also been shown to have a "cytoskeleton", which is different from eukaryotic cells.
- Some bacteria are highly motile Movie - Lyme Spirochete moving back and forth along a platelet. Time-lapse (16x normal) phase-contrast videomicroscopy

(Greek, Karyose = kernel, as in a kernel of grain)

**Prokaryotes Cell Wall**

- Bacterial Shape - Bacterial shapes and cell-surface structures
- Bacterial Membranes - A small section of the double membrane of an E. coli bacterium
  - Bacterial outer membranes - outer membrane contains porins
- Bacterial cell walls - Bacterial cell walls (http://water.me.vccs.edu/courses/ENV108/clipart/cellwall.gif)
  - **Gram-negative** bacteria surrounded by a thin cell wall beneath the outer membrane
  - **Gram-positive** bacteria lack outer membranes and have thick cell walls

(MH - note that some unicellular eukaryotes can also have a cell wall)

- Antibiotics - inhibit either bacterial protein synthesis or bacterial cell wall synthesis Antibiotic targets Gram-positive and Gram-negative bacteria

Bacterial Growth Movie

Molecular Biology of the Cell

Medical Microbiology
- Figure 2-6. Comparison of the thick cell wall of Gram-positive bacteria with the comparatively thin cell wall of Gram-negative bacteria (http://www.ncbi.nlm.nih.gov:80/books/bv.fcgi?db=Books&rid=mmed.figgrp.294)

Prokaryote Mycoplasmas
- smallest self-replicating organisms
- smallest genomes (approx 500 to 1000 genes)
- spherical to filamentous cells
- no cell walls
- surface parasites of the human respiratory and urogenital tracts
  - *Mycoplasma pneumoniae* infect the upper and lower respiratory tract
  - *Mycoplasma genitalium* a prevalent sexually transmitted infection
  - *Mycoplasma hyorhinis* found in patients with AIDS

Prokaryotic and Eukaryotic Cells

The following links describe the major differences between prokaryotic and eukaryotic cells, the way they divide and the way in which antibiotics have their action on prokaryotic cells.

- Molecular Cell Biology Figure 12-6. DNA replication and cell division in a prokaryote (http://www.ncbi.nlm.nih.gov:80/books/bv.fcgi?db=Books&rid=mcb.figgrp.3176)
- Biochemistry Figure 28.15. Transcription and Translation (http://www.ncbi.nlm.nih.gov:80/books/bv.fcgi?db=Books&rid=stryer.figgrp.3980) two processes are closely coupled in prokaryotes, whereas they are spatially and temporally separate in eukaryotes.

Virus

- single compartment, **no membranes**
- not a cell (Latin, *virus* = toxin or poison)
- not alive, infects living cells
- unable to grow or reproduce outside a host cell
- Infect different hosts (animal, plant, and bacterial)
- Classified
  - RNA or DNA viruses
  - double or single stranded

### Virion
- contains the genetic material, DNA or RNA
- within a protective protein coat (capsid)

### Bacteriophage
- A virus that infects bacteria

#### Links:
- NPR - Virus Infection (http://www.youtube.com/watch?v=Rpj0emEGShQ&feature=PlayList&p=49AA6FE8E2B8C71F&index=1)

#### Prion
- no compartments, no membrane
- an infectious prion protein
- not alive
- misfolded normal protein (three-dimensional structure)
- can form aggregates
- Types
  - Creutzfeldt-Jacob disease (CJD) and Kuru a human neural prion disease
  - Bovine spongiform encephalopathy (BSE) in cattle, "mad cow disease"
  - Scrapie in sheep

#### Molecular Biology of the Cell
Figure 6-89. Protein aggregates that cause human disease (http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=mbo4&part=A972&rendertype=figure&id=A1115)

#### Prions Are Infectious Proteins

#### Gene Reviews
Prions
Biological Levels

Cells can be "broken down" into smaller and smaller constituent "parts"

- Whole cell
- Organelles
  - nucleus, mitochondria,
- Components
- Biological polymers
  - chains of molecules
  - consisting of monomer subunits
  - DNA, RNA, Protein, sugars, cellulose
- Organic molecules
  - monomer subunits
  - nucleotides, amino acids, carbohydrate

Eukaryotic Cell Organelles

- Fundamental concept - all cells
  - Specialized exceptions
- Organelle
  - specialized part of a cell that has its own particular function
  - Membrane bound (enclosed)
  - forms "compartments" within the cell

Plasma Membrane Images

The cell membrane (plasma membrane or plasmalemma) encloses or covers all cell types and is 7 nanometers thick (1000 times smaller than the RBC). Begin by some different ways of looking microscopically at membranes.
Compartments

- Physical Compartments
  - membrane bound
  - Nucleus, Cytoplasm, Organelles
  - cell nomenclature based upon presence or absence of these compartments (eukaryotic, prokaryotic)

- Functional Compartments
  - spatial localization
  - targeting
  - activation and inactivation
  - signaling

Major Cellular Compartments

- Nucleus (nuclear) - contains a single organelle compartment
- Cytoplasm (cytoplasmic) - contains many organelle compartments

Organelle Number/Volume

- How many organelles?
- How much space within the cell do they occupy?
- Are all the cells the same?

Take a typical mammalian liver cell....


**Compartments are Dynamic**

Movies showing flexibility of membranes and their changing shape and size.

**Nuclear Compartment**

- Nuclear matrix - consisting of Intermediate filaments (lamins)
- Nucleoli (functional compartment - localised transcription DNA of RNA genes)
- Chromosomes (DNA and associated proteins)

(MH - you will not see chromosomes in interphase nuclei only during mitosis, more in the Nucleus Lecture)

**Cytoplasmic Compartment**

- Cytoplasmic Organelles
  - Membrane bound structures
  - Endoplasmic reticulum, golgi apparatus, mitochondria, lysosomes, peroxisomes, vesicles
- Cytoskeleton
  - 3 filament systems
- Cytoplasmic “structures”
  - Ribosomes
  - DNA -> mRNA -> Protein
  - Proteins
  - Receptors, signaling, metabolism, structural
  - Viruses, bacteria, prions
- Functional compartments
  - occur in nucleus, cytoplasm, in organelles and outside organelles
  - signaling, metabolic reactions, processing genetic information, cytoskeleton dynamics, vesicle dynamics

**Membrane Functions**

Cell membrane (Plasma membrane , plasmalemma) encloses or
Membrane Components

- phospholipids, proteins and cholesterol
- first compartment formed
- prokaryotes (bacteria) just this 1 compartment
- eukaryotic cells many different compartments

Phospholipids

- membranes contain phospholipids, glycolipids, and steroids
- The main lipid components include: phosphatidylcholine (~50%), phosphatidylethanolamine (~10%), phosphatidylserine (~15%), sphingolipids (~10%), cholesterol (~10%), phosphatidylinositol (1%).

Phospholipid Orientation

- A liposome (lipid vesicle) is a small aqueous compartment surrounded by a lipid bilayer.
- A micelle is a small compartment surrounded by a single lipid layer.


Membranes History

(Background only, you do not need to know the details)

- 1890 Charles Overton - selective permeation of membranes, non-polar pass through (lipid soluble), polar refractory
Lipid rafts

- 1905 Irving Langmuir - lipids faced with heads towards water away from organic solvents
- 1925 Gorter and Grendel - monolayer of lipid isolated from rbc
- 1930-40 Danielle-Davson - Proteins coat a bilayer with polar “pores”
- 1960s Robertson - Modification with glycoprotein on one side, therefore asymmetric
- 1972 Singer and Nicholson - proteins “floating” within lipid bilayer like a “liquid” surface
- 1975 Unwin and Henderson - integral membrane proteins, glycoprotein carbohydrate groups on outer surface
- 1997 Simons - cholesterol to form "rafts" that move within the fluid bilayer PMID 9177342

Membrane Proteins

- 20-30% of the genome encodes membrane proteins PMID 9568909
- Proteins can be embedded in the inner phospholipid layer, outer phospholipid layer or span both layers
- Some proteins are folded such that they span the membrane in a series of “loops”

Two major protein transmembrane structures

1. α-helical - ubiquitously distributed
2. β-barrel - outer membranes of Gram-negative bacteria, chloroplasts, and mitochondria

Membrane Protein Functions

- transport channels
- enzyme reactions
- cytoskeleton link
- cell adhesion
- cell identity


Membrane Glycoproteins

- Glycoproteins are proteins which have carbohydrate groups (sugars) attached
- to produce these proteins go through a very specific cellular pathway of organelles (secretory pathway)
- to reach the cell surface where they are either secreted (form part of the extracellular matrix)
- or are embedded in the membrane with the carbohydrate grouped on the outside surface (integral membrane protein)

Membrane Cholesterol

- Small molecule embedded between the phospholipid molecules and regulates lipid mobility (MH - see rafts)
- Cholesterol can be at different concentrations in different regions of plasma membrane
- lateral organization of membranes and free volume distribution
- may control membrane protein activity and "raft" formation
- fine tuning of membrane lipid composition, organization/dynamics, function
- bacterial membranes (except for Mycoplasma and some methylotrophic bacteria) have no sterols, they lack the enzymes required for sterol biosynthesis.

**Links:** MBoC Figure 10-9. Cholesterol in a lipid bilayer (http://www.ncbi.nlm.nih.gov/books/bv.fcgi?highlight=cholesterol&rid=cell.figgrp.2458)

### Bacterial Membranes

**Gram Negative**
- inner membrane is the cell's plasma membrane
- do not retain dark blue dye used in gram staining
- Bacteria with double membranes (Example: Escherichia coli, Salmonella, Shigella.)

**Gram Positive**
- because they do retain blue dye, thicker cell walls
- single membrane comparable to inner (plasma) membrane of gram negative bacteria
- Bacteria with single membranes (Example: staphylo-cocci and streptococci)

(Named after - Hans Christian Gram (1853–1938), a Danish scientist.)

### Membrane Fluidity

- fusion of 2 cells
- FRAP
- membrane domains (polarized cells)
  - epithelia - apical, basal and lateral domains

### Tubular Bridges

(cxtonemes and tunneling nanotubes, TNTs) - New membrane structures identified that can facilitate transfer of cellular signals and components over large distances (hundreds of microns) representing the longest direct connections between cells in vitro and in vivo. File:Bronchial epithelial bridge.mov


### Membrane Specializations

- plasma membrane cytoskeleton
- different directly under membranes
- adhesion complexes
- absorptive and secretory
- synaptic junctions

**Adhesion Specializations**

A series of different types of proteins and cytoskeleton associations forming different classes of adhesion junctions

- Desmosomes (= macula adherens)
- Adherens Junctions (= zonula adherens)
- Septate Junctions
- Tight Junctions
- Gap Junctions

**Membrane Transport**

Three major forms of transport across the membrane

- **Passive** - Simple diffusion
- **Facilitated** - transport proteins
- **Active** - transport proteins for nutrient uptake, secretion, ion balance

**Ion Channels**

- membrane phospholipid impermeable to ions in aqueous solution
- protein channels permit rapid ion flux
  - 1960’s structure and function, ionophores (simple ion channels)
  - 75 + different ion channels, opening/closing, “gating” of ions

**Ion Channel Types**

- 3 rapid + 1 slow gate (gap junction)
  - Voltage-gated - propagation of electrical signals along nerve, muscle
  - Ligand-gated - opened by non-covalent, reversible binding of ligand between nerve cells, nerve-muscle, gland cells
  - Mechanical-gated - regulated by mechanical deformation
  - Gap junction - allow ions to flow between adjacent cells open/close in response to Ca$^{2+}$ and protons

**Some Membrane Issues**

**Cell Apoptosis** - programmed cell death

- membrane "blebbing" encloses cellular component fragments
- do not stimulate inflammatory response, easy removal by macrophages.

**Link:** Time-lapse movie of human HeLa cells undergoing apoptosis
(http://www.nature.com/nrm/journal/v9/n3/extref/nrm2312-s1.mov) | Example of early apoptotic blebbing
Cystic Fibrosis - membrane transport disease

- Chloride channel - protein mutation point mutant, folded improperly, trapped and degraded in ER

Background Textbook References


Search Online Textbooks


Historic Papers

Below are some example historical research finding related to cell membranes from the JCB Archive and other sources.

- **1957** The invention of freeze fracture EM and the determination of membrane structure [Link](http://jcb.rupress.org/cgi/content/full/168/2/174-a) Russell Steere introduces his home-made contraption for freeze fracture electron microscopy (EM), and Daniel Branton uses it to conclude that membranes are bilayers.

- **1971** Spectrin is peripheral [Link](http://www.jcb.org/cgi/doi/10.1083/jcb1701fta1) S. Jonathan Singer, Garth Nicolson, and Vincent Marchesi use red cell ghosts to provide strong evidence for the existence of peripheral membrane proteins.

- **1992** Lipid raft idea is floated [Link](http://jcb.rupress.org/cgi/content/full/172/2/166) Gerrit van Meer and Kai Simons get the first hints of lipid rafts based on lipid sorting experiments.

Links: Sorted JCB Archive -Membranes JCB Archive [Link](http://jcb.rupress.org/misc/fromthearchive.shtml)

"Sometimes you eat the bacteria and sometimes... well, he eats you"


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