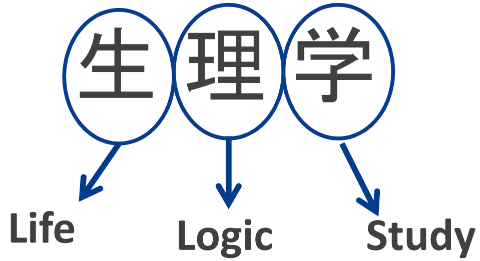
School of Medical Sciences

Physiology 1A

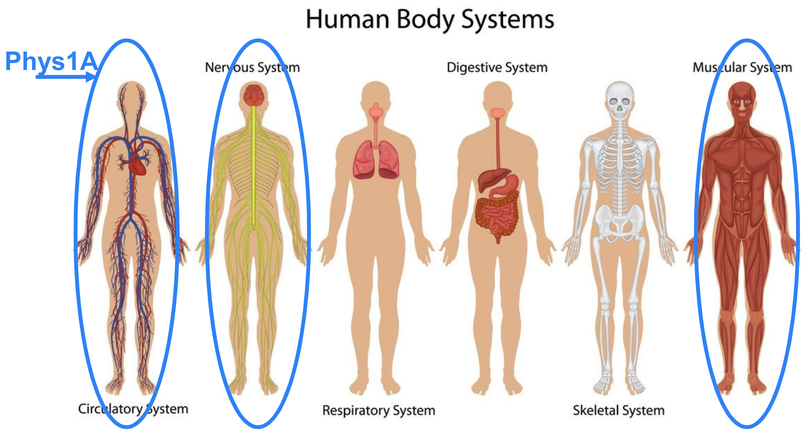
Cell Physiology

Andrew Moorhouse;
a.moorhouse@unsw.edu.au; 9385 2575

Physiology – The study of body function



Physiology – The study of body function



Note, also other systems, (e.g. endocrine, reproductive) and alternate names (e.g., digestive = gastrointestinal, circulatory = cardiovascular)

http://www.reflexologystudio.org/uploads/2/8/3/6/2836815/1052239_orig.jpg

Cell Physiology:

- Cells are the fundamental units in each of the body systems and organs
- Common principles about cell functions = the logical starting point for the study of Physiology
- Examples of what *single* cells do (& how this contributes to body function)?

a) ……..
b) ……..
c) ……..

Cell Physiology:

e.g. 1. Cells in the Ear “Hearing”

See the link at the lab page of Physiologist, Professor Johnathon Ashmore’ who 1st did this experiment:
https://www.ucl.ac.uk/ear/research/ashmorelab

Cell Physiology:

e.g. 1. Cells in the Ear “Hearing”

Single cells in the hearing organ of the ear (the cochlear) that detect and respond to sound waves

Sound waves (converted to fluid movements in the ear) cause the voltage of these cochlear hair cells to change

In special outer hair cells, the voltage change also causes the cells to move/contract, which allows for an amplification of the sound transduction

The video was obtained by plugging the Walkman/tape player output into the input of the pipette electrode (shown attached to the cell)

See the link at the lab page of Physiologist, Professor Johnathon Ashmore’ who 1st did this experiment:
https://www.ucl.ac.uk/ear/research/ashmorelab

Cell Physiology:

e.g. 2. Cells in the Brain signaling “Wake-Up”

See the link at the lab page of physiologist, Professor Davis McCormick at Yale whose lab’ did this experiment:
https://medicine.yale.edu/lab/mccormick/

Cell Physiology:

e.g. 2. Cells in the Brain signaling “Wake-Up”

The movie shows a live recording of action potentials from a single nerve cell in a brain area called the thalamus (this was an in vitro experiment in a brain slice)

The nerve is firing action potentials, and initially this is at a slow rhythmic frequency but when the nerve is stimulated (by “depolarization”) the firing pattern changes to a burst firing mode

This is similar to what happens when we wake up. So this change in firing pattern signals to our cortex to “Wake Up”

(experiment conducted by Physiologist Professor David McCormick at Yale

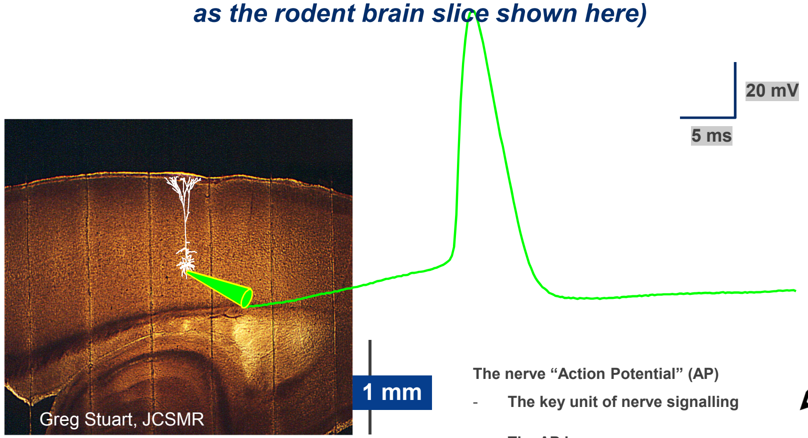
See the link at the lab page of physiologist, Professor Davis McCormick at Yale whose lab’ did this experiment:
https://medicine.yale.edu/lab/mccormick/

biology image library
www.biologyimagelibrary.com
© David McCormick
Credit: David McCormick

Cell Physiology:

e.g. 2. Cells in the Brain firing APs

(APs can also be measured using in vitro brain preparations, such as the rodent brain slice shown here)

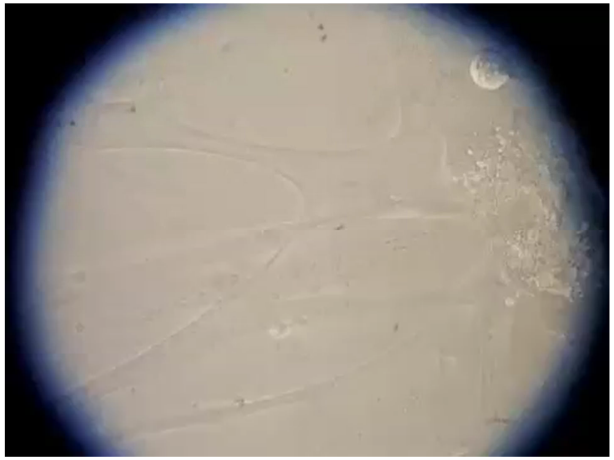


The nerve "Action Potential" (AP)

- The key unit of nerve signalling
- The AP is……

Cell Physiology:

e.g. 3. Muscle cells contracting



Electrical Pulse Stimulation of Cultured Human Skeletal Muscle Cells as an In Vitro Model of Exercise
Nataša Nikolić et al PLOS One, March 22, 2012; DOI: 10.1371/journal.pone.0033203

Cell Physiology:

e.g. 3. Muscle cells contracting

The movie shows a video of cultured muscle cells spontaneously contracting.

The Physiologists who did this experiment were interested in the mechanisms by which exercise can increase muscle strength. They tried to mimic this in vitro

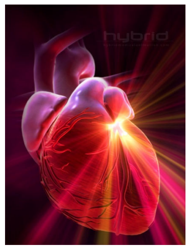
Note the cells are quite different when in culture / in vitro compared to when in our bodies, but they still mediate their basic function of contracting.

Electrical Pulse Stimulation of Cultured Human Skeletal Muscle Cells as an In Vitro Model of Exercise
Nataša Nikolić et al PLOS One, March 22, 2012; DOI: 10.1371/journal.pone.0033203

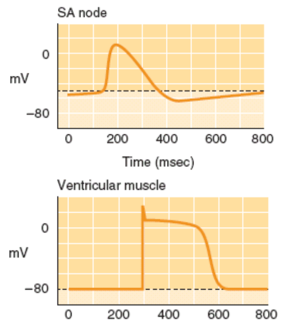
Cell Physiology:

e.g. 3. Muscle cells contracting

Muscle contraction is important for movement (skeletal muscles), for processing food, controlling blood flow or secreting substances from glands (smooth muscle), and for heart beat (cardiac muscle)



Action potentials in different cardiac muscle cells

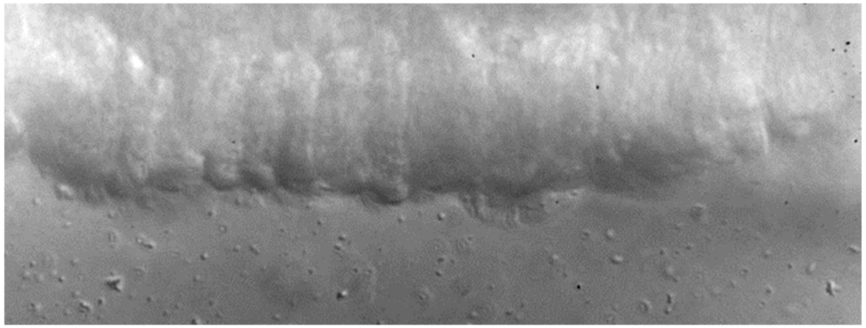


Jeff Johnston hybrid animations

Boron & Boulpaep, 2003

Cell Physiology:

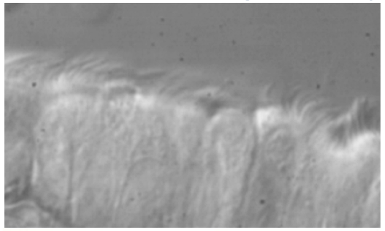
e.g. 4. Airway epithelial cells

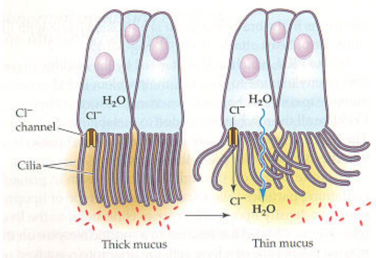


Francis and Lo, Ex vivo Method for High Resolution Imaging of Cilia Motility in Rodent Airway Epithelia J Vis Exp. 2013; (78): 50343.

Cell Physiology:

e.g. 4. Airway epithelial cells





- The movie shows airway epithelial cells with their hair like protrusions called cilia.
- These cilia, along with the secreted mucus, help to move particles along the airways. This enables you to swallow or cough up the many bacteria and pollutants in the air.
- Airway epithelial cells need to secrete mucus and water to enable the phlegm to move along the airways. This is driven by osmotic, chemical and electrical gradients across the epithelial.
- If your epithelial cells cant secrete the water and salts effectively, you can get thick mucus (left panel) & die from respiratory infections (eg cystic fibrosis)

Upper image: Am J Physiol Lung Cell Mol Physiol 296: L1067-L1075, 2009; doi:10.1152/ajplung.00001.2009 Initiation and maturation of cilia-generated flow in newborn and postnatal mouse airway. Lower image: Purves et al., 2004

Cell Physiology:

3 examples of cell function:

1. **Cochlear outer hair cells moving (detect and amplify sound)**
2. **Thalamic neuron changing to tonic firing (signal wake-up)**
3. **Cultured skeletal muscle cell contracting (movement)**
4. **Airway epithelial cells secreting fluids (to keep airways clear)**

What was a common physiological element to their cell function?

"Excitable Cells":

- *Cells with **a potential difference** (or voltage) across their cell membrane*
- *Cells that use electrical and/or chemical signaling*
- *Cells that **move molecules across their membranes** using electrical and chemical forces (described later)*
- *E.g.s, nerve cells, muscle cells, epithelial cells*
- *The basic processes of all the major physiological systems*

“Excitable Cells” / Cell Physiology

Learning activities:

- 6 lectures, 3 Online tutorials, 1 face-face prac, 1 online prac

Responsibilities:

Please attend class promptly and be quiet in class. In exchange I will:

- clarify lecture and overall Learning Objectives

- provide sample exam Qs and reading lists

- be available for queries by appointment

Chs 1, 2, 4, 5, 7 & 8 of Stanfield’s Principles of Human Physiology

Learning Aims – lecture 1

- To describe very generally two examples of a single cell function
- To be able to define what is meant by excitable cells and give some examples
- To appreciate single cells use chemical and electrical signaling
- To schematically draw a cell membrane and to identify the functional components of a typical membrane phospholipid and give an example
- To know the terms polar and non-polar and how it relates to membranes and ions
- To relate the basic components of an electrical circuit to a potential difference across the cell membrane
- ***Reading: Ch 1 of Stanfield, Ch 2.2.-2.4 (inclusive)***

Ch 1 p1-12, Ch 2, p 29-42 of Stanfield’s Principles of Human Physiology

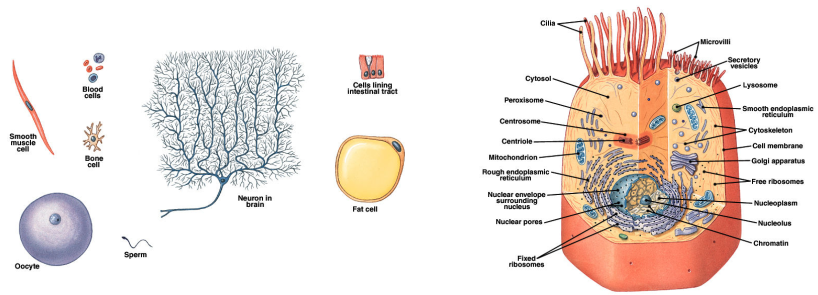
“Excitable Cells”:

- *Cell function involves moving things (e.g., water, ions) across their cell membranes to mediate electrical and chemical signaling. Hence important questions are:*
  - *How do substances move across the membrane?* Weds
  - *What are the properties of the cell membrane?* now
  - *Review basic physics and chemistry about solutions and membranes, and about electricity.*

Cells Physiology: The basic functional unit

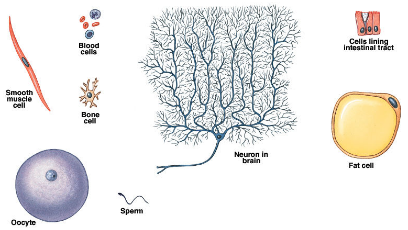
Single cells come in different sizes and shapes with different functions related to the body system they belong to. However there are common structural and functional features. They all move substances across their membrane and maintain different transmembrane electrical and ionic gradients

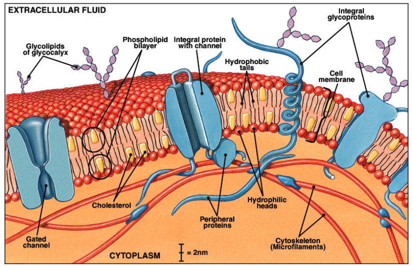
http://www.cellsalive.com/cells/cell_model.htm



Cells: The basic functional unit

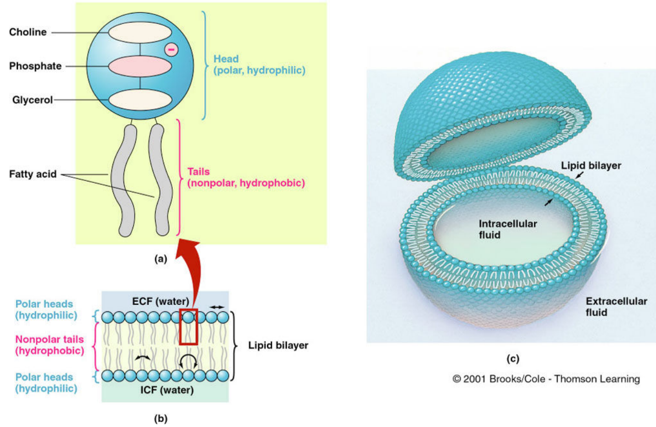
- http://www.cellsalive.com/cells/cell_model.htm





The *cell membrane* is a critical component for excitable cells. It separates the external and internal solutions

Cell membranes composed of lipid bilayers with integral membrane proteins



The hydrophobic interior of the lipid bilayer makes the membrane impermeant to solutes, hence separating external and internal solutions

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A closer look at the structure of a typical membrane lipid (e.g., phosphatidylcholine)

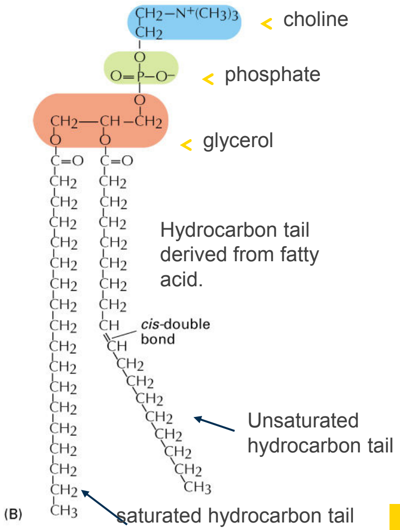

Figure 10–2 part 2 of 3. Molecular Biology of the Cell, 4th Edition.

Phospholipids

- Phosphatidylcholine
- Phosphatidylethanolamine
- Phosphatidylserine
- Phosphatidylinositol

Sphingolipids

Glycolipids

Cholesterol

- (No polar headgroup)

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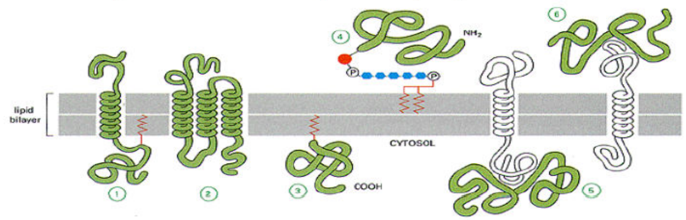
Membrane Proteins

- Integral membrane proteins (1-2) spanning the lipid bilayer
- Lipid anchored membrane proteins (3-4)
- Peripheral membrane protein (5-6)



A major component of biological membranes (3-4/100 nm2, millions/cell) and include mostly transporters, receptors, adhesion molecules

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Internal and External solutions

- *Total body water = 42 litres.*
- *Intracellular solution, inside cells = 28 L*
  - *(High in proteins and potassium)*
  - *(typically negative charge at membrane)*

Extracellular solution, outside cells = 14 L

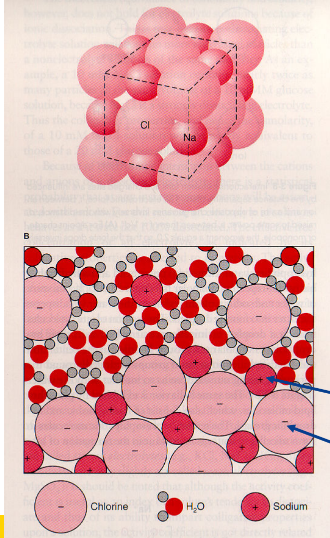
- *= plasma (3L)*
- *= interstitial fluid (outside cells) = 11 L*
- *= high in sodium, low in protein*
- *(positive charge at membrane)*

TABLE 4.1 Millimolar Concentrations of Selected Solutes in Intracellular Fluid (ICF)* and Extracellular Fluid (ECF)

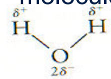
Solute	ICF (mM)	ECF (mM)
K^+	140.0	4.0
Na^+	15.0	145.0
Mg^{2+}	0.8	1.5
Ca^{2+}	<0.001 †	1.8
Cl^-	4.0	115.0
HCO_3^-	10.0	25.0
P_i	40.0	2.0
Amino acids	8.0	2.0
Glucose	1.0	5.6
ATP	4.0	0.0
Protein	4.0	0.2

mM = millimolar
*Intracellular fluid composition varies for different cell types.
†Refers to calcium ions free in the cytosol. A significant quantity of intracellular calcium is sequestered in membrane-bound organelles and/or bound to proteins.

Ions in solution



Partial charges (dipoles) on a water molecule



Ions in solution are surrounded and stabilized by water molecules (hydrated)

water loving: hydrophilic / polar

water hating: hydrophobic / non-polar

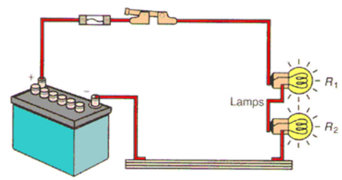
cation (positive; Na^+, K^+, H^+, Ca^{2+})

anion (negative; Cl^-, HCO_3^-, SO_4^{2-})

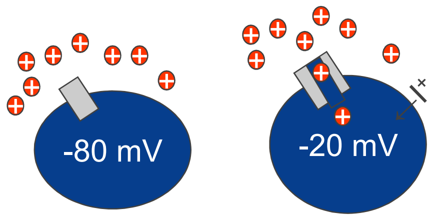
Biological electricity

- In the adjacent electrical circuits, the battery provides the driving force, the circuit is complete when the switch is closed, the current is carried by electrons flowing in a conductor (wire) and the current flows through a resistor (light bulbs) to cause some response

$e^- \rightarrow (\leftarrow I^+)$



- In excitable cells, the electrochemical potential provides the driving force, the switch is an ion channel and the current is carried by ions (a cation in adjacent figure) to results in a response (depolarization).



Cell at rest

Activated cell

Review of Electricity

- *Charge* (Q or q) is a fundamental property of matter; either positive or negative; like charges repel & opposites attract. Measured in Coulombs (C). The charge on a single electron (or monovalent ion) is 1.6 * 10^{-19}C (the elementary charge).
An electric field emanates from any charged point or surface.

- to separate charge requires work. Once separated they possess potential energy. *Voltage* (V) is the electrical potential difference between charges (1V = 1joule/C)

- *Current* (I) is the flow of charge. Measured in amperes, A (1A = 1C/s)

- *Resistance* is a measure of how easily charge can move under a given potential difference. R=V/I (Ohm's Law). *Conductance* (g) = 1/R.

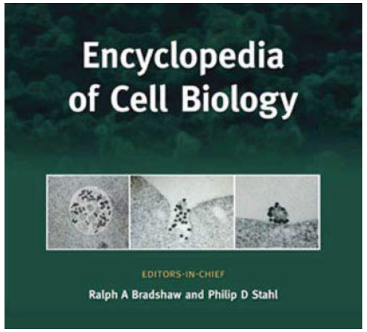
- *Capacitance* (C) is the ability to store separated charge. Two conductors separated by an insulator. C is the charge separated divided by the potential difference thus produced (C=Q/V). Accompanies the electrical potential across cells.
The units is farads (1F = C/V). Stores charge when voltage changes.

Reading Lists and Lecture Objectives on Moodle

A key resource:

Membrane Potential: Concepts

AJ Moorhouse, UNSW Australia, Sydney, NSW, Australia



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Excitable Cell Physiology – The study of body function

Ussain Bolt: world's fastest man

- **Why do my muscles get tired?**
  - *(muscle cell physiology)*
- **How can I get more sprinting energy?**
  - *(insulin secretion, glucose uptake,)*
- **Will supplement X reach my muscles?**
  - *(Stomach uptake, muscle cell physiology)*
- **How can I co-ordinate my running?**
  - *(nerve physiology, muscle control)*
- **Why am I so fast?**
  - *(nerve physiology, muscle control)*
- **Will increasing my heart make me faster?**
  - (Cardiovascular physiology)

http://hubpages.com/sports/10-amazing-feats-achieved-by-human-beings

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