THE ORIGIN OF BIOPOTENTIALS

Lecture Notes

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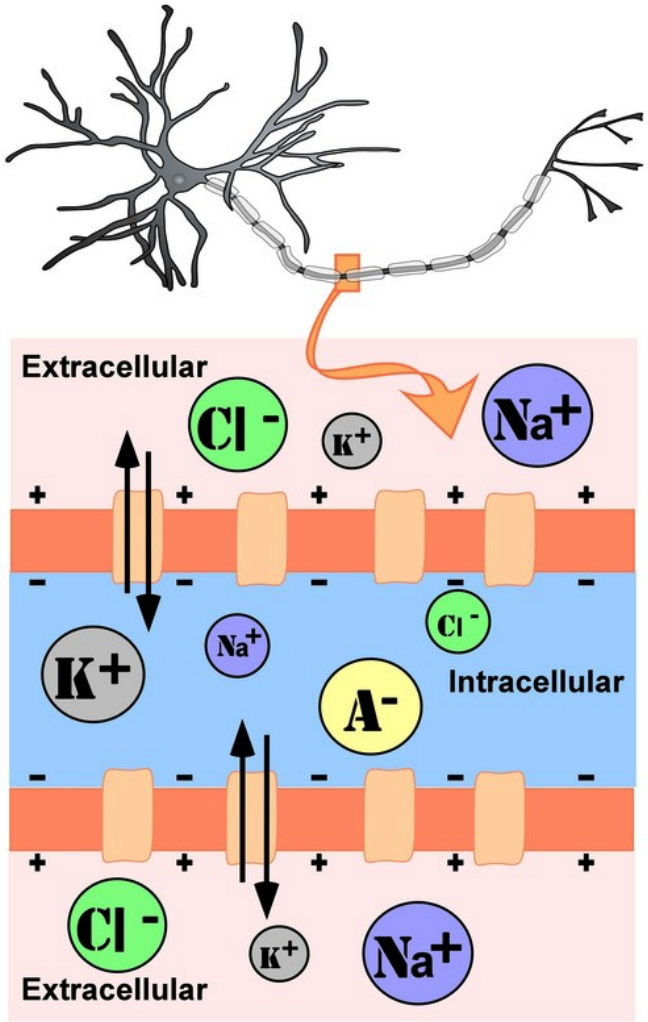
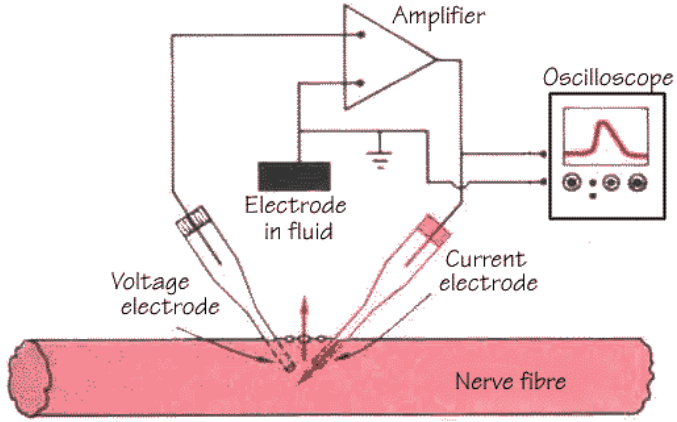
Biopotential : A voltage measured on human body or any other biological system

- ECG : Electrocardiogram (heart)
- EMG : Electromyogram (muscle)
- EEG : Electroencephalogram (brain)

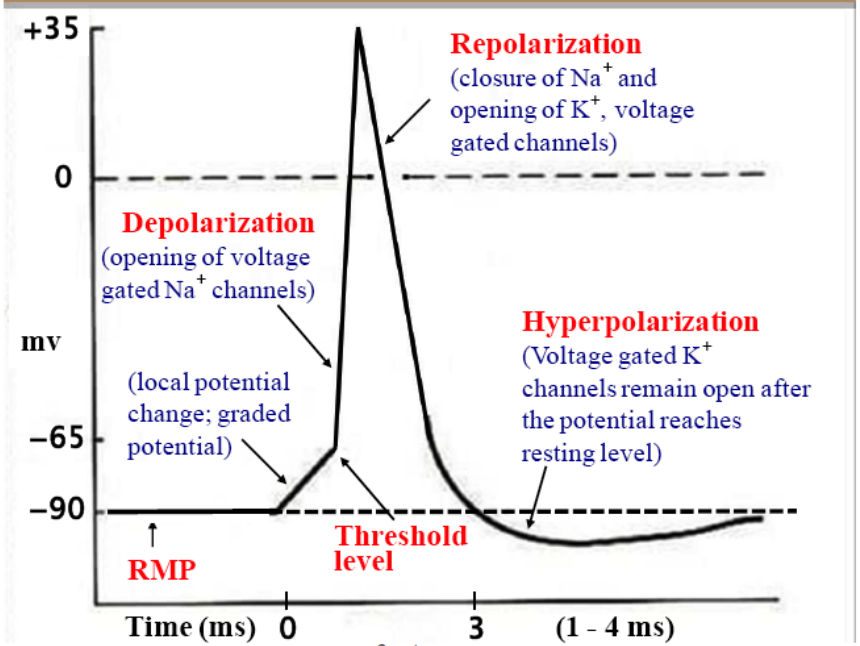
Biopotentials are produced by the combined effect of ion transport in large number of excitable cells.

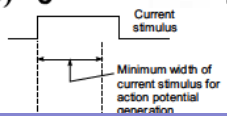
- Muscle contractive tissue
  Cardiac muscle (heart)
  Skeletal muscle (locomotion)
  Smooth muscle (stomach, intestines, blood vessels, lungs ...)
- Sensory or motor nerves in peripheral nervous system
  Somatic $\longrightarrow$ touch & motor control (conscious)
  Autonomic $\longrightarrow$ sensing & control of cardovascular, digestive and other functions (unconscious)
- Neurons in central nervous system
  Brain
  Spinal cord
  Retina
  Coclea



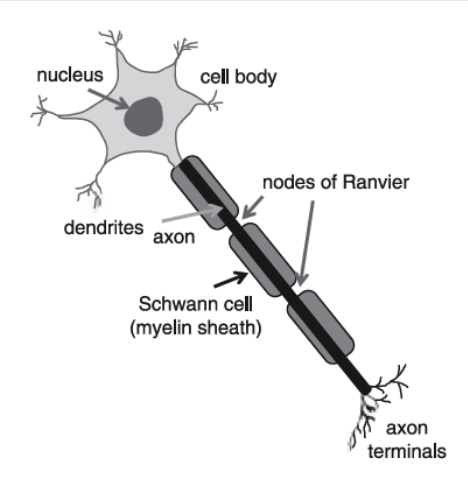


Action potential





Goldman-Hodgkin-Katz Equation



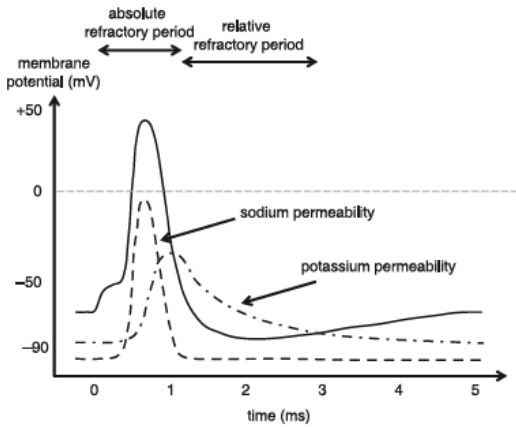
	Intracellular	Extracellular
Na^+	12mM	145mM
K^+	155mM	4mM
Cl^-	4mM	120mM

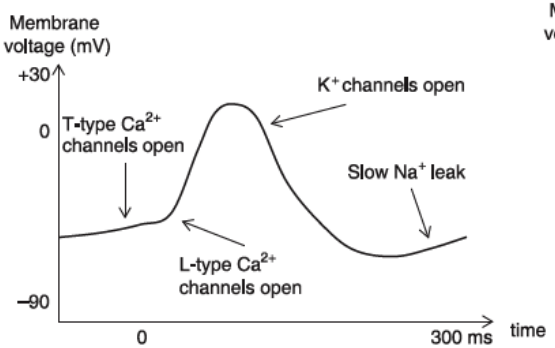
Sodium-Potassium Pump: $3Na^+ \uparrow : 2K^+ \downarrow$

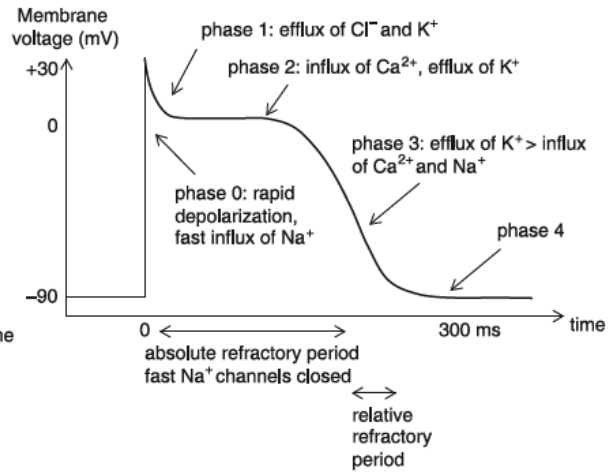
$$E = \frac{RT}{F} \ln \left\{ \frac{P_K[K^+]_o + P_{Na}[Na^+]_o + P_{Cl}[Cl^-]_i}{P_K[K^+]_i + P_{Na}[Na^+]_i + P_{Cl}[Cl^-]_o} \right\}$$

P : Membrane permeability to ionic species
R : Gas constant $= 8.31$ J/(mole K)
F : Faraday's constant $= 96500$ C/mole
T : Absolute temperature in kelvins

All-or-nothing Event







Nerve cell	Cardiac Pacemaker Cell	Cardiac Ventricular cell
Skeletal muscle cell	Sinoatrial Cell	Atrioventricular cell
	Intracellular	Extracellular
Ca^{2+}	10^{-3}mM	2mM

Speed of propagation : 1m/s - 100 m/s

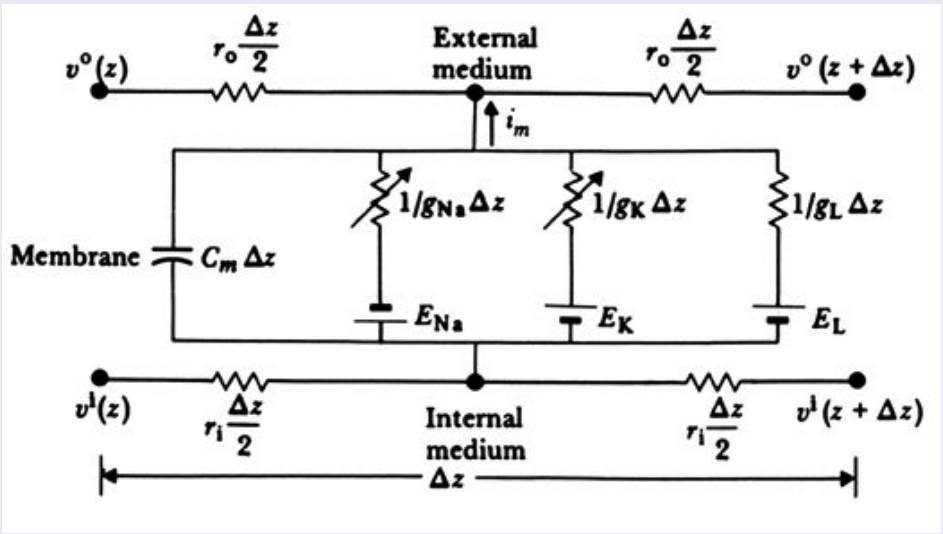
Nerst Equation

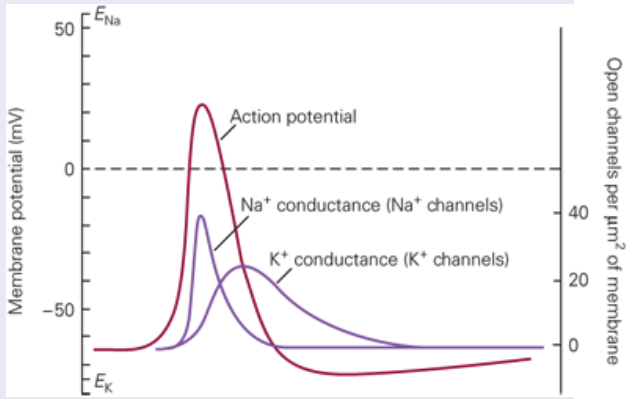
Approximate version of Goldman-Hodgkin-Katz Equation assuming $P_K \gg P_{Na}$,
The equilibrium *transmembrane potential* for K^+ :

$$E_K = \frac{RT}{nF} \ln \frac{[K]_o}{[K]_i}$$

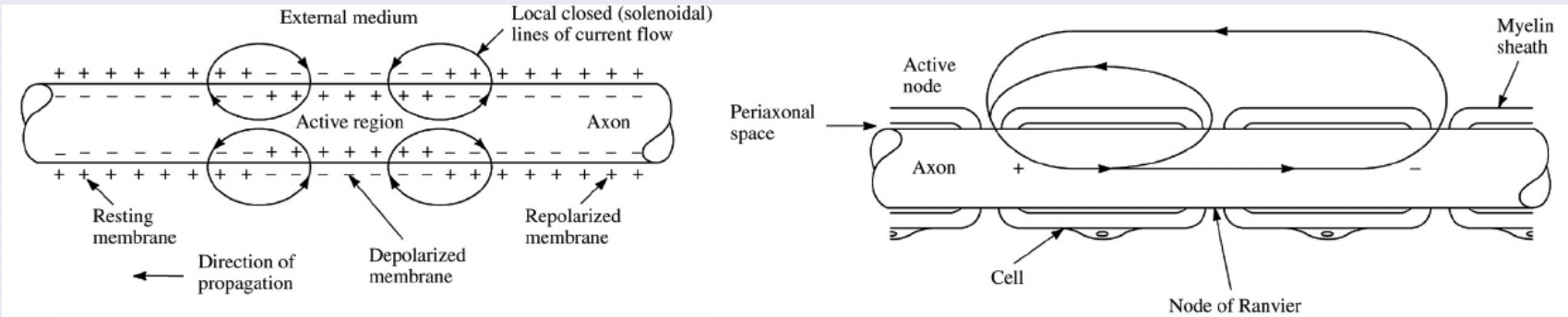
n : valence of K^+

Electrical Model of Unmyelinated Nerve Cell: Hodgkin-Huxley Model





Electrical activity in an excitable neuron



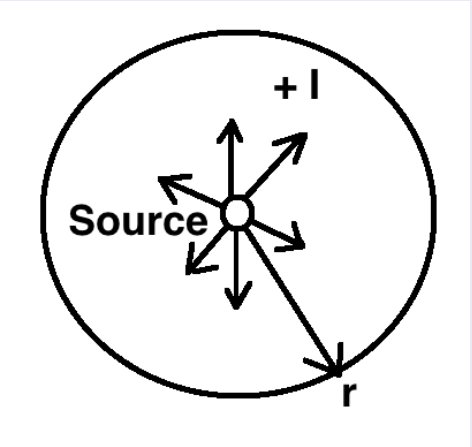
- Solenodial current causes a voltage drop around the axon region causing a more positive voltage towards the direction of propagation.
- In vertebrates, the myelin sheath is interrupted at every 1-2 mm by nodes of Ranvier in the peripheral nerves at the CNS.
- The myelin sheath decreases the capacitance and increases the transverse impedance in the internodal region.
- Source of action potential current flow such as Sodium and Potassium ion channels are localized at the nodes and not uniform over the axon.
- Myelination reduces leakage current, decrease capacitance and improves cable transmission rate by a factor of 20.

Volume Conduction Effect

When a single active cell is immersed in a conducting medium such as body fluid or tissue, two different phenomena occur:

1. The active cell which is a bioelectric source act as a constant current source
2. The active source as a temporal voltage monophasic waveform delivers a solenoidal activation current in the medium over a large range of loading conditions causing a spatial voltage distribution.

This secondary potential due to volume conduction is triphasic, has a greater spatial extent and much smaller in peak to peak which allows us to measure heart, brain or muscle activity on body surface.
Conversely, volume conduction also allows us to measure the safety limits of instrumentation applied to human body.



A source with current density $\vec{J}$ yields a current $\vec{I} = \vec{J} \cdot 4\pi r^2$ where r is the radius of spherical conducting medium.
Electrical field $\vec{E} = \frac{1}{\sigma} J = \frac{I}{4\pi r^2 \sigma}$ and
Electrical potential

$$V(r) - V(\infty) = -\int_{\infty}^{r} \vec{E} \cdot d\vec{r} = \frac{I}{4\pi r \sigma} = V(r).$$

A single cell gives a $100mV$ action potential in $1ms$. The cell diameter is $20\mu m$, and its membrane capacitance is $1\mu F/cm^2$. What is the amplitude of extracellular potential at $10cm$ distance? Assume $\sigma = 0.1\Omega^{-1}m^{-1}$.

Since current goes inside the cell

$C\frac{dV_m}{dt} = -I$

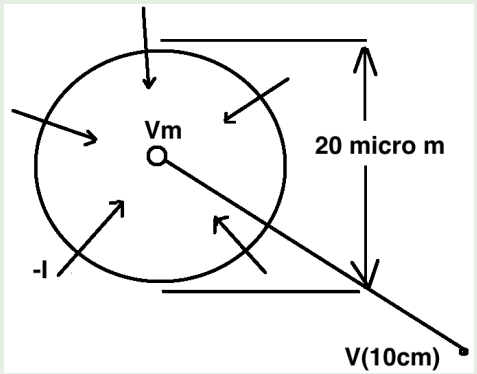
$C = 1\mu F/cm^2 \cdot \pi(20\mu m)^2 = 4\pi pF \approx 12.6pF$

$\frac{dV_m}{dt} \approx \frac{\Delta V_m}{\Delta t} = \frac{100mv}{1ms} = 100V/s$

$\longmapsto I = -1.26nA$

$V(10cm) = \frac{I}{2\pi\sigma 10cm} = -\frac{1.26 \cdot 10^{-9}}{4\pi \cdot 0.1 \frac{1}{\Omega m} \cdot 0.1m}$

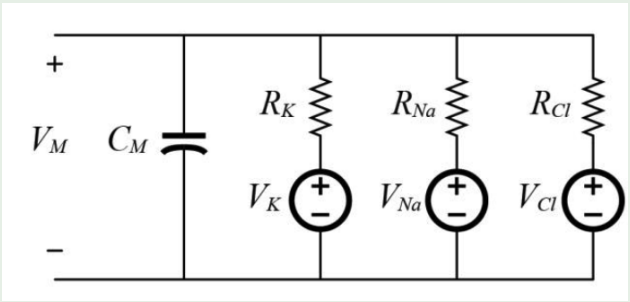
$= -10^{-8}V = -10nV$



Millions of such firing cells are necessary to generate a biopotential.

Self Study Question

Consider the following circuit model for a cell with $R_K = 2.7k\Omega$, $R_{Na} = 30k\Omega$, $R_{Cl} = 3.3k\Omega$.



Ionic species	Intracellular concentration	Extracellular concentration
K^+	397 mM	20 mM
Na^+	50 mM	437 mM
Cl^-	40 mM	556 mM

(a) With the intracellular and extracellular concentrations given in the table above, calculate the Nernst Potential for each of the ionic species: V_K, V_{Na}, and V_{Cl}.

$V_{K^+} = 62mV \ln \frac{[K^+]_o}{[K^+]_i} = 62mV \log \frac{20}{397} = -77mV$

$V_{Na^+} = 62mV \ln \frac{[Na^+]_o}{[Na^+]_i} = 62mV \log \frac{437}{50} = 56mV$

$V_{Cl^-} = -62mV \ln \frac{[Cl^-]_o}{[Cl^-]_i} = 62mV \log \frac{556}{40} = -68mV$

(b) Using the circuit model with Nernst potentials V_K, V_{Na}, and V_{Cl} and the resistances given above, find the membrane potential V_M at steady-state. Hint: At DC steady-state, any capacitance reduces to an open circuit connection.

$g_K = 1/R_K = 1/2.7k\Omega = 3.7 \cdot 10^{-4}S$, $g_{Na} = 1/R_{Na} = 1/30k\Omega = 3.3 \cdot 10^{-5}S$, $g_{Cl} = 1/R_{Cl} = 1/3.3k\Omega = 3.03 \cdot 10^{-4}S$

KCL @ Vm $\longmapsto (V_K - V_M)g_K + (V_{Na} - V_M)g_{Na} + (V_{Cl} - V_M)g_{Cl} = 0$

$V_m = \frac{g_K V_K + g_{Na} V_{Na} + g_{Cl} V_{Cl}}{g_K + g_M + g_{Cl}} = -66mV$

(c) Now find the equilibrium resting potential V_M using the Goldman-Hodgkin-Katz equation. Compare the two values of the membrane potential. Which value is more reasonable for a typical resting potential of a cell? Hint: Membrane conductance (the reciprocal of membrane resistance) for any ion type is directly proportional to membrane permeability for that ion type.

$$V_M = \frac{RT}{F} \ln \left\{ \frac{P_K[K^+]_o + P_{Na}[Na^+]_o + P_{Cl}[Cl^-]_i}{P_K[K^+]_i + P_{Na}[Na^+]_i + P_{Cl}[Cl^-]_o} \right\} = 27 \ln \frac{3.7 \cdot 10^{-4} \cdot 20 + 3.3 \cdot 10^{-5} \cdot 437 + 3.03 \cdot 10^{-4} \cdot 40}{3.7 \cdot 10^{-4} \cdot 397 + 3.3 \cdot 10^{-5} \cdot 50 + 3.03 \cdot 10^{-4} \cdot 556}$$

$V_M = -60.3mV$ which is quite close to Nerst potential.

(d) For a membrane capacitance $C_m = 1\mu F$, find the time constant for the membrane potential V_M of the cell to recover from a transient and settle to its steady-state value.

$$R = 1/(g_K + g_{Na} + g_{Cl}) = 1.42k\Omega$$

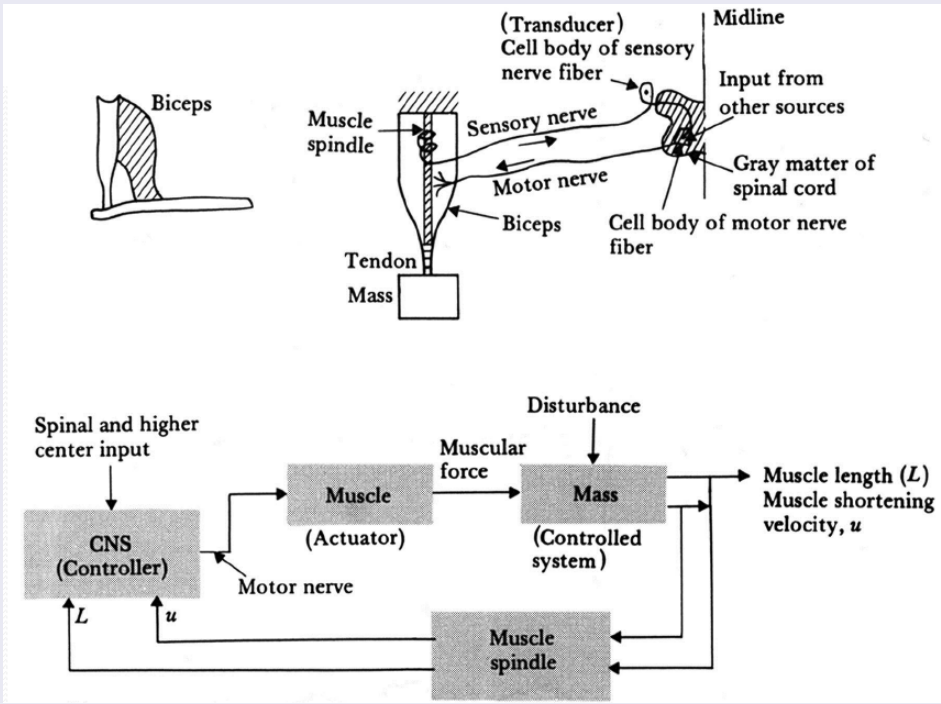
$$\tau = RC = 1.42 \cdot 10^3 \cdot 1 \cdot 10^{-6} = 1.41ms$$

The Reflex Arc: A Negative Feedback System

Components of Reflex Arc
1. A sense organ
2. A sensory nerve
3. CNS
4. A motor nerve
5. The effector organ

- Knee-jerk reflex : Tapping the patellar tendon stretches the specialized lenght receptors called muscle spindles that generate action potential.
- The action potential is carried to CNS and communicates with motoneurons.
- The resulting motor activity brings about contraction of the muscle as a shortening and jerking the knee.

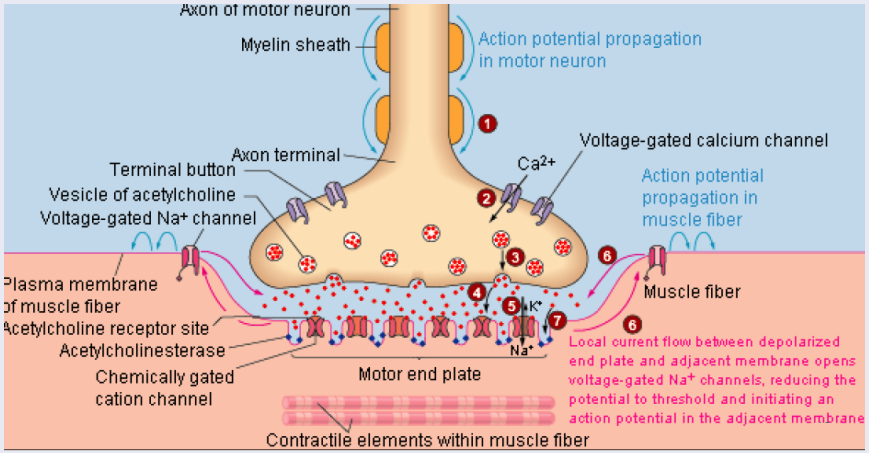
Biceps muscle length control system



Junctional Transmission

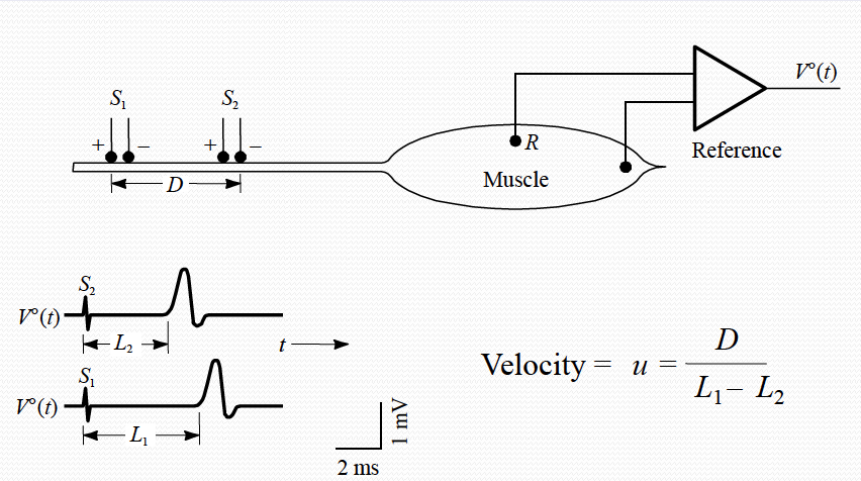
Within the reflex arc there are;

- links between neuron to neuron called synapses,
- links between neurons and muscle fibers called neuromuscular junctions which occur at specialized regions in the fiber called end plate regions.



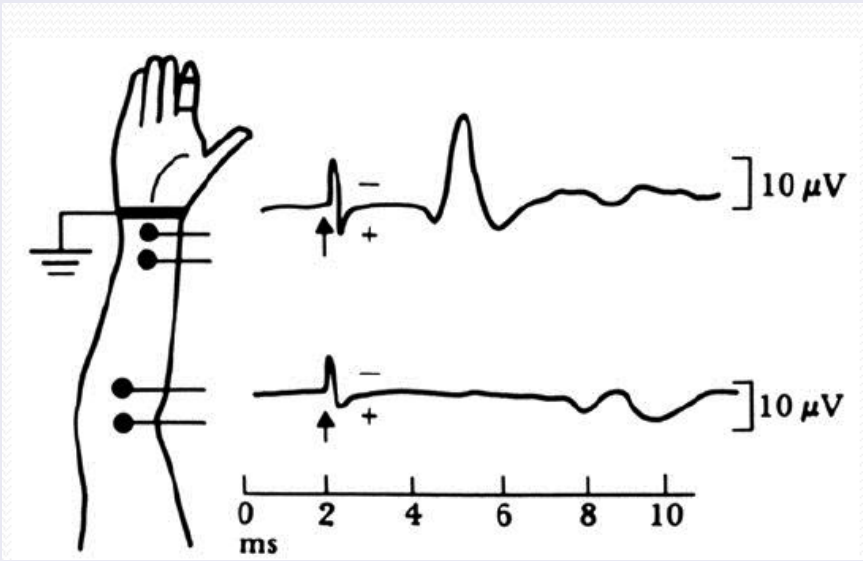
• Neuromuscular junction : 20 nm thickness.
• Junctional transmission is electrochemical.
• Release of Acetylcholine activates an ion channel in postjunctional membrane which generates an action potential.
• Electrochemical transmission : a time delay of 0.5-1 ms,
• Another delay between electrical excitation and mechanical contraction called *excitation-contraction time*.
• At high stimulation rates, mechanical response summates and fuses into a continuous contraction called *tetanus*.

Electroneurogram



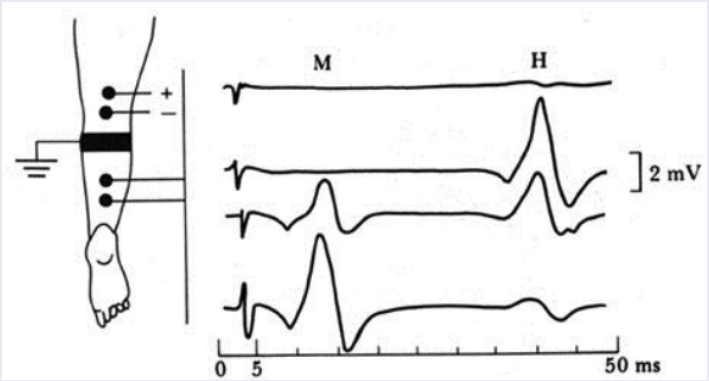
- Measurement of conduction velocity in a peripheral nerve.
- Conduction velocity of the nerve has a clinical value since it slows down in a regenerating nerve after nerve injury.
- The shape of field potentials are also important:
  - If the motor fibers have a uniform conduction velocity, there will be a larger amplitude, shorter duration triphasic response.
  - Slowed down conduction in some motor fibers lead to a decrease in magnitude and broadening of its duration

Field Potentials of Sensory Nerves



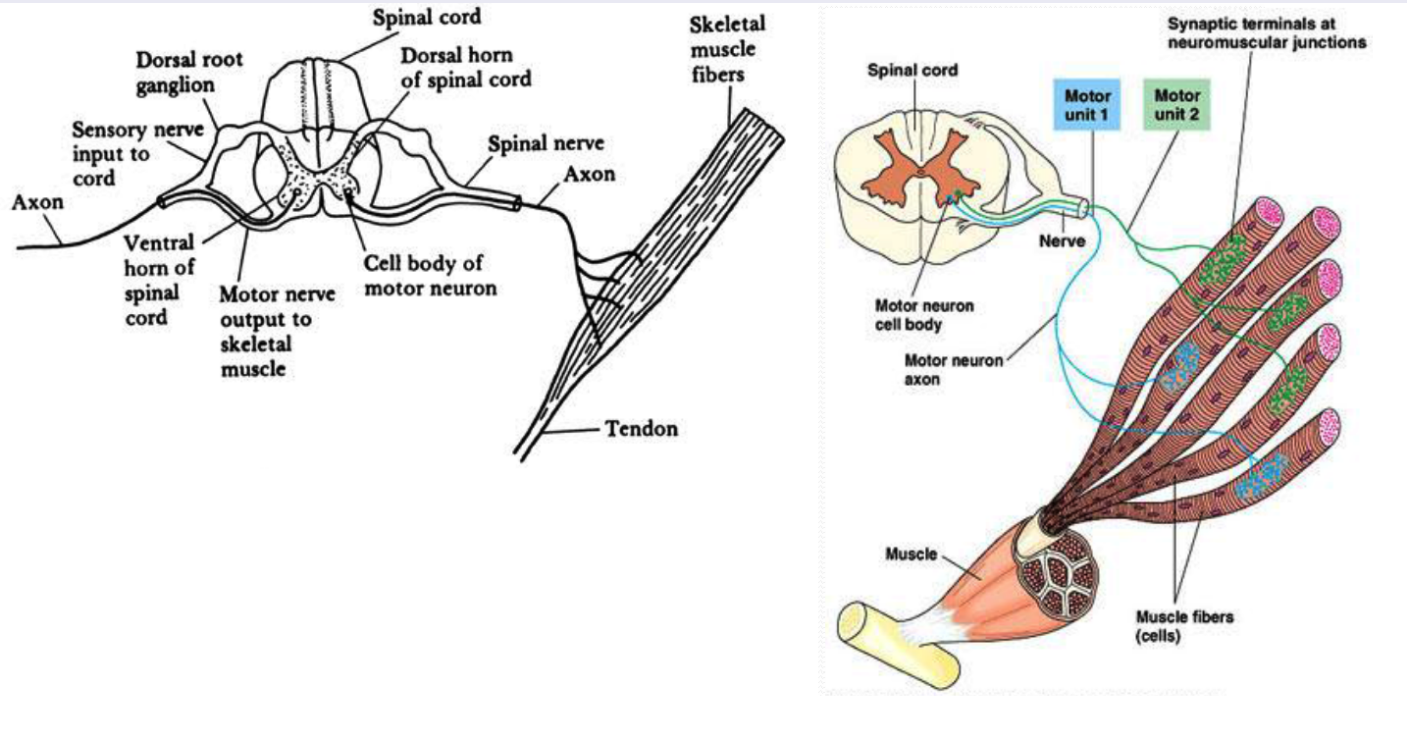
- Median and ulnar nerves of the arm are stimulated from the fingers and measured from distant locations as the upper arm regions.
- 100-300 μs 100V pulses ae applied and the evoked ENG signal is on the order of 10 μV.
- Stimulus unit is isolated from ground to reduce artifacts.
- The amplifier should have low noise, high differential gain, good CMRR and high imput impedance.

Reflexly Evoked Field Potentials



- When a peripheral nerve is stimulated and an evoked potential is recorded in the muscle, sometimes a second potential later than the initial occurs.
- As the stimulus site gets near to the muscle, the latency of the first response decreases whereas the second increases.
- The second response indicates a travel towards the CNS and then a return to the muscle site.
- Its long latency implies that it is a spinal reflex as the electrical homolog of ankle-jerk reflex.
- Low amplitude stimulus triggers only large diameter sensors fibers which cause a discharge in motoneurons in the CNS which in turn produce H response in the gastrocnemius muscle.
- With higher stimuli, smaller motor fibers are triggered producing a short latency muscle response called M wave.
- As the stimuli becomes very strong, the M waves interfere with the production of H wave and inhibit their response since these excited motor fibers are in refractory mode.

Electromyogram (EMG)



- Skeletal muscle is organized functionally on the basis of single motor unit (SMU).
- SMU may contain 10 to 2000 muscle fibers, depending the location of the muscle.
- The volume conduction field potential from the active fibers of an SMU has a triphasic form with 3 to 15 ms duration, 20 to 2000 μV amplitude and 6 to 30 discharges per second.

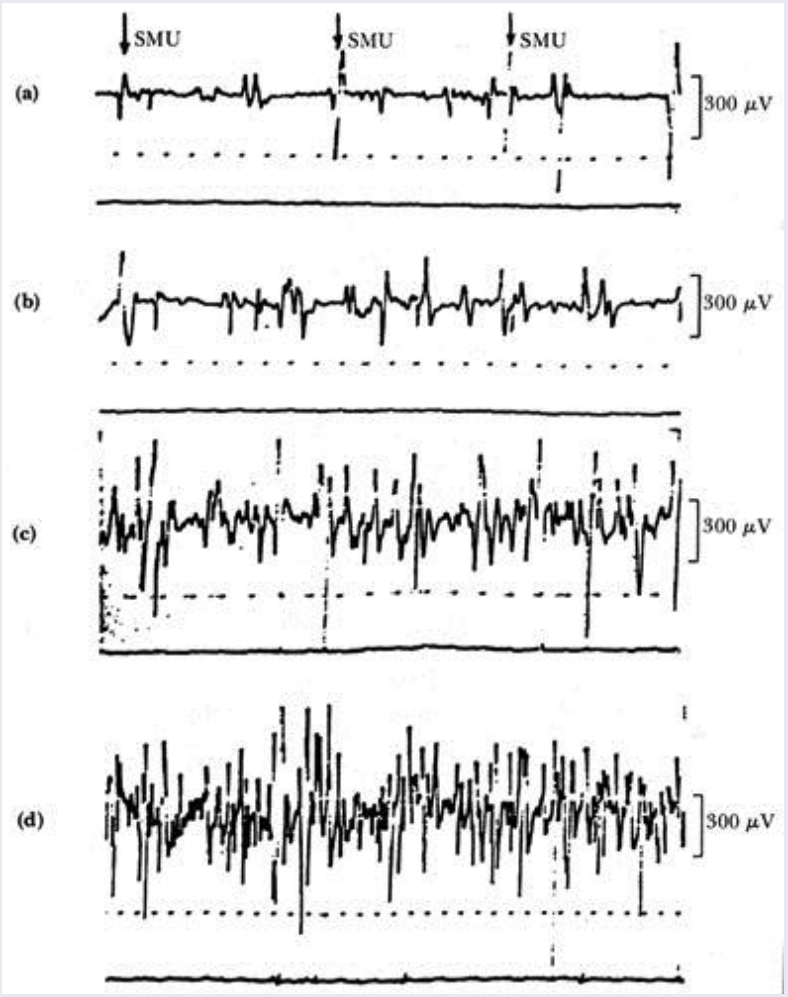
Recording of EMG

• Surface electrodes record field potential of surface muscles and over a wide area.
• Monopolar and bipolar insertion-type needle electrode can be used to record SMU field potentials at different locations.
• The shape of SMU potential is considerably modified by disease such as partial denervation in peripheral neuropathies.
• The needle EMG has a frequency spectrum of 10Hz to 5kHz with an amplitude range of 500μV.
• The surface EMG has a lower frequency range of 10 Hz to 1kHz with an amplitude range of 2mV.

EMG is used in

• the diagnosis of neuromuscular disorders,
• as a measure of relaxation in the application of biofeedback techniques.
• as an index of muscle activity in physiological studies such as gait analysis.

Motor unit action potentials from normal dorsal interosseus muscle



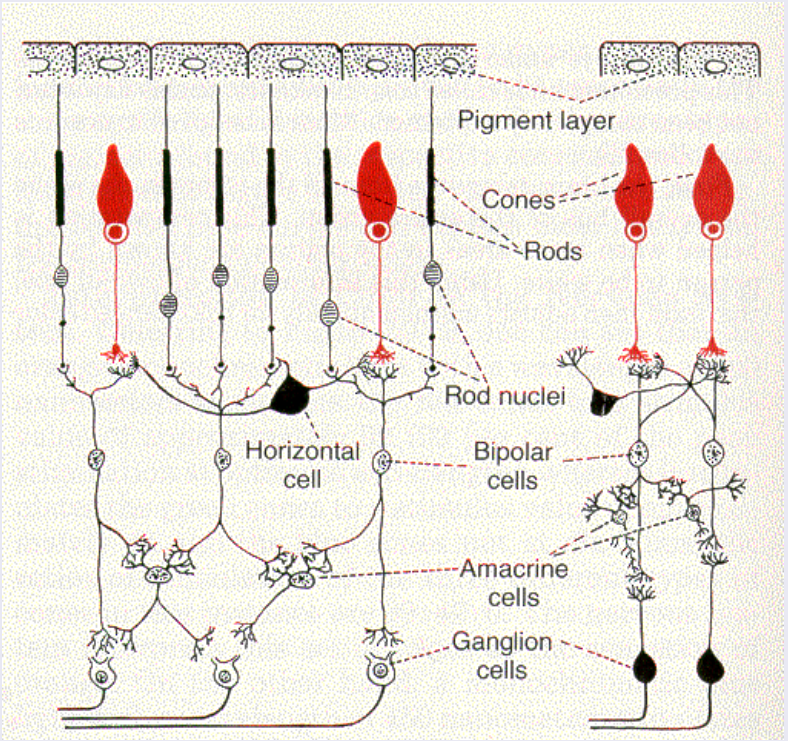
Progressively more powerful contractions.

In the interference pattern, individual units can no longer be clearly distinguished.

Interference pattern during very strong muscular contraction.

Time scale is 10 ms per dot.

Origin of Retinal Potentials



There are more photoreceptors than ganglion cells so there is a convergence pattern.

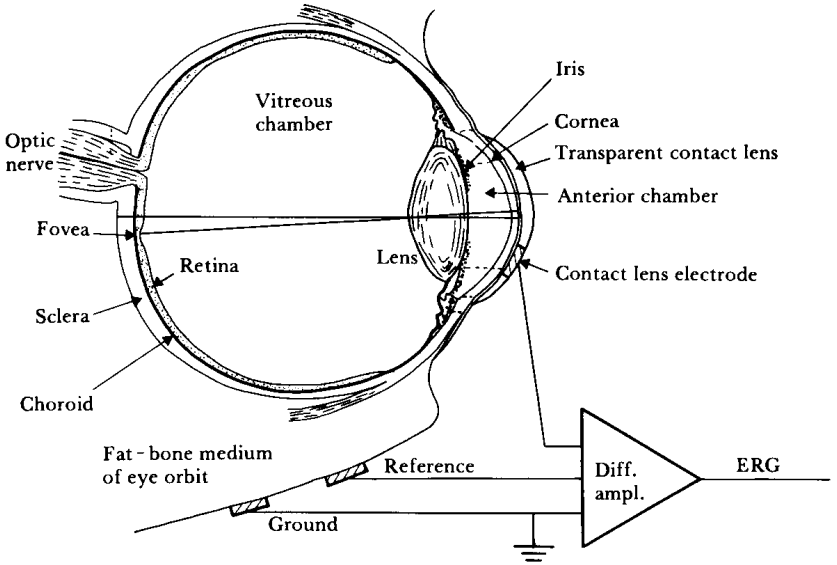
Many photoreceptors terminate into one bipolar cell and many bipolar cells terminate into one ganglion cell.

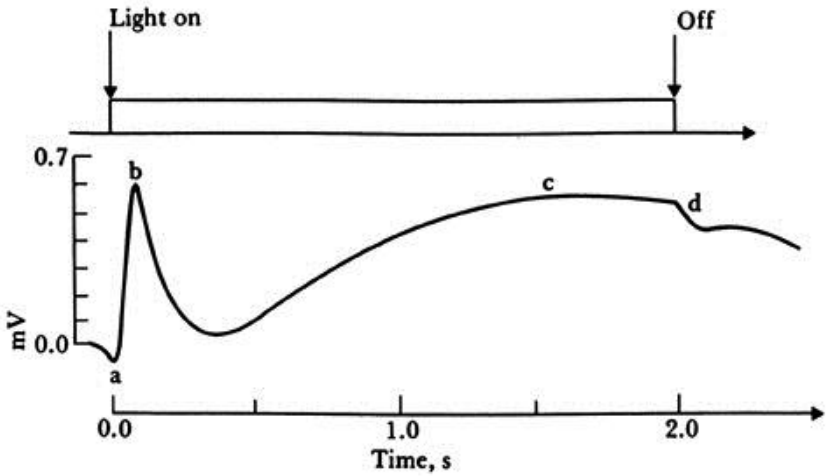
The convergence rate is greater at peripheral parts of the retina than at the fovea.

External layer:region of contact between photoreceptors and bipolar cells.
Internal layer:region of contact between bipolar cells and ganglion cells.
Rod is for dim light vision and uses photopigment called rhodopsin.
Cone is for color vision in brighter light and has either one of red, green or blue photopigments.

Electroretinogram (ERG)

• ERG is a recording of the temporal sequence of changes in potential in the retina when stimulated with a brief flash of light.
• A transparent contact lens containsone electrode and the reference electrode can be placed on the right temple.

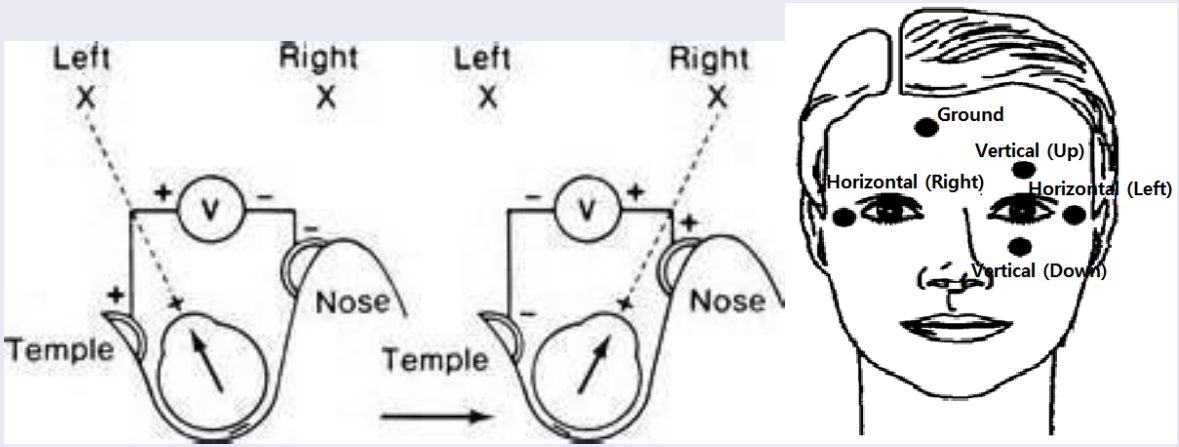




• The a-wave, consists of an early and a late part called *early/late receptor potential* and reflects the output of photoreceptors in the outer retina.
• In contrast, the b-wave reflects the health of the inner layers of the retina.
• c-wave originates in the pigment epithelium.
• d-wave indicates activity of the bipolar cells after stimulus is off.

Electro-oculogram (EOG)

EOG is the recording of the corneal-retinal potential to determine the eye movement.

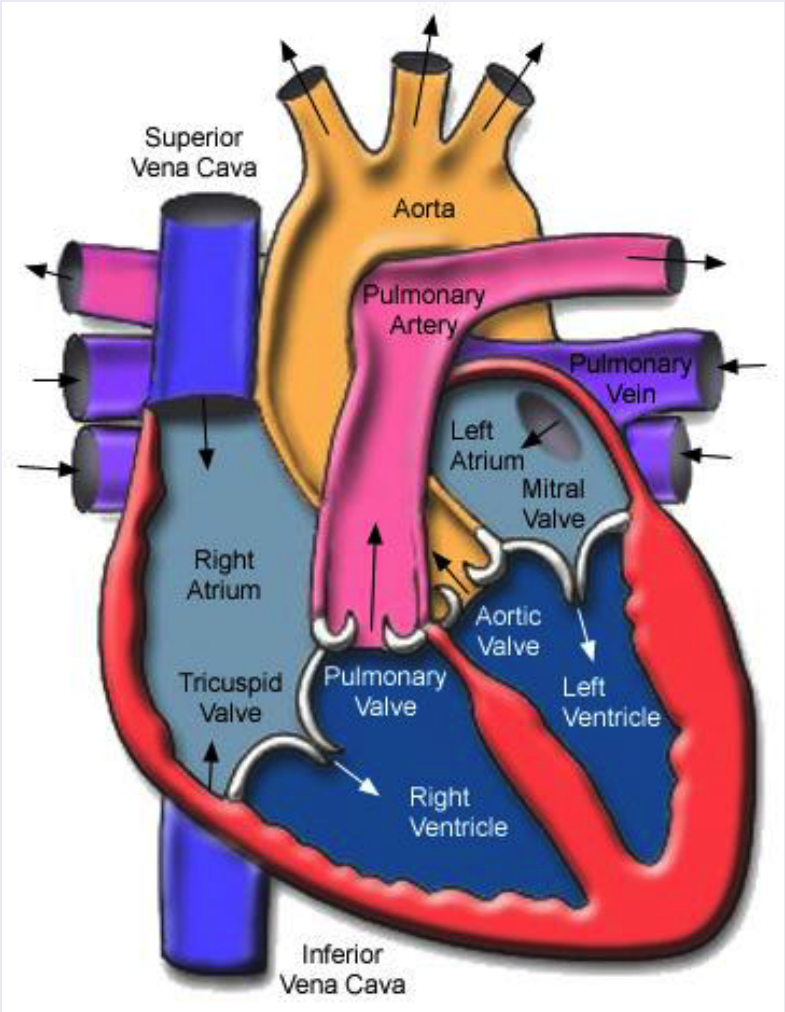


This steady dipole can be measured by placing two electrodes to the left and the right of the eye or above and below to determine the horizontal or vertical movement of the eye.
The potential is zero when the gaze is straight ahead.
The EOG is linearly related to angular displacement up to $\pm 30^o$.
A DC amplifier is required.
Minimum displacement that can be measured is 1^o.

Applications

1. Sleep and dream research.
2. Evaluating reading ability and visual fatigue.

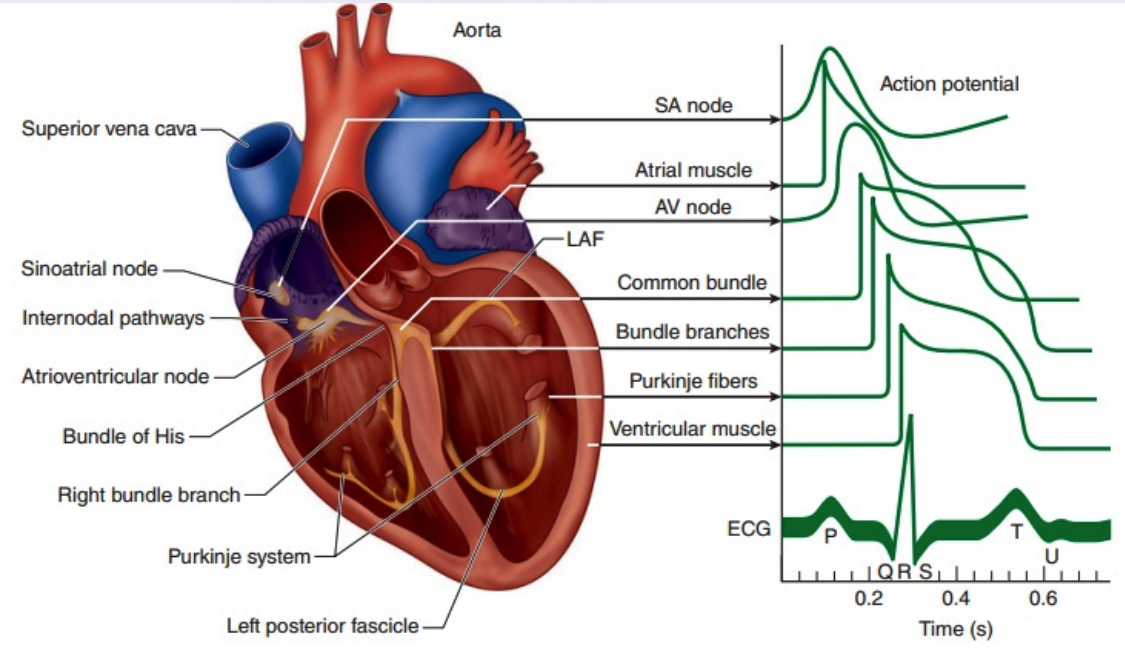
Electrocardiogram (ECG)



Diastole: is the resting or filling phase (atria chamber) of the heart cycle.
Systole: is the contractile or pumping phase (ventricle chamber) of the heart cycle.

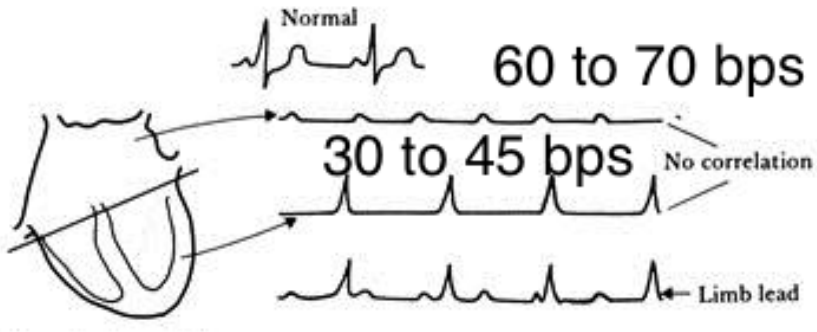
1. Blood (poor with oxygen) flows from the body to the right atrium and then to the right ventricle.
2. The right ventricle pump the blood to the lung.
3. Blood (rich with oxygen) flows from the lung into the left atrium and then to the left ventricle.
4. The left ventricle pump the blood to the rest of the body.

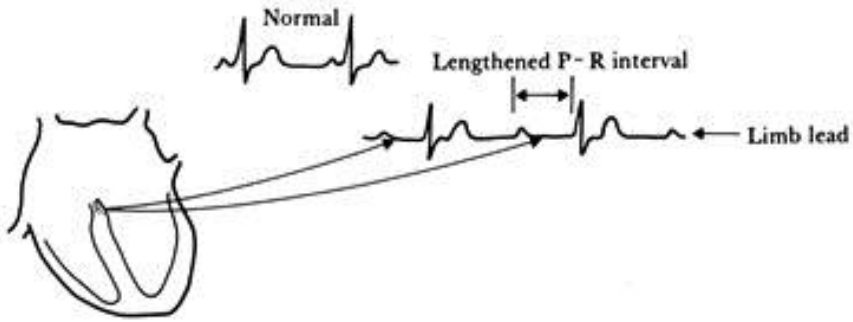
SA node activates first the right and then the left atrium.
AV node delays a signal coming from SA node before distributing it to *Bundle of His*.
Bundle of His and *Purkinie fibers* activate the right and left ventricles



The P-wave shows the heart's upper chambers (atria) contracting.
The QRS complex shows the heart's lower chambers (ventricles) contracting.
The T-wave shows the heart's lower chambers (ventricles) relaxing.
The U-wave believed to be due repolarization of ventricular papillary muscles.
P-R interval is caused by delay in the AV node.
S-T segment is related to the average duration of the plateau regions of the individual ventricular cells.

Heart Block : Dysfunctional *His Bundle*





Complete heart block.

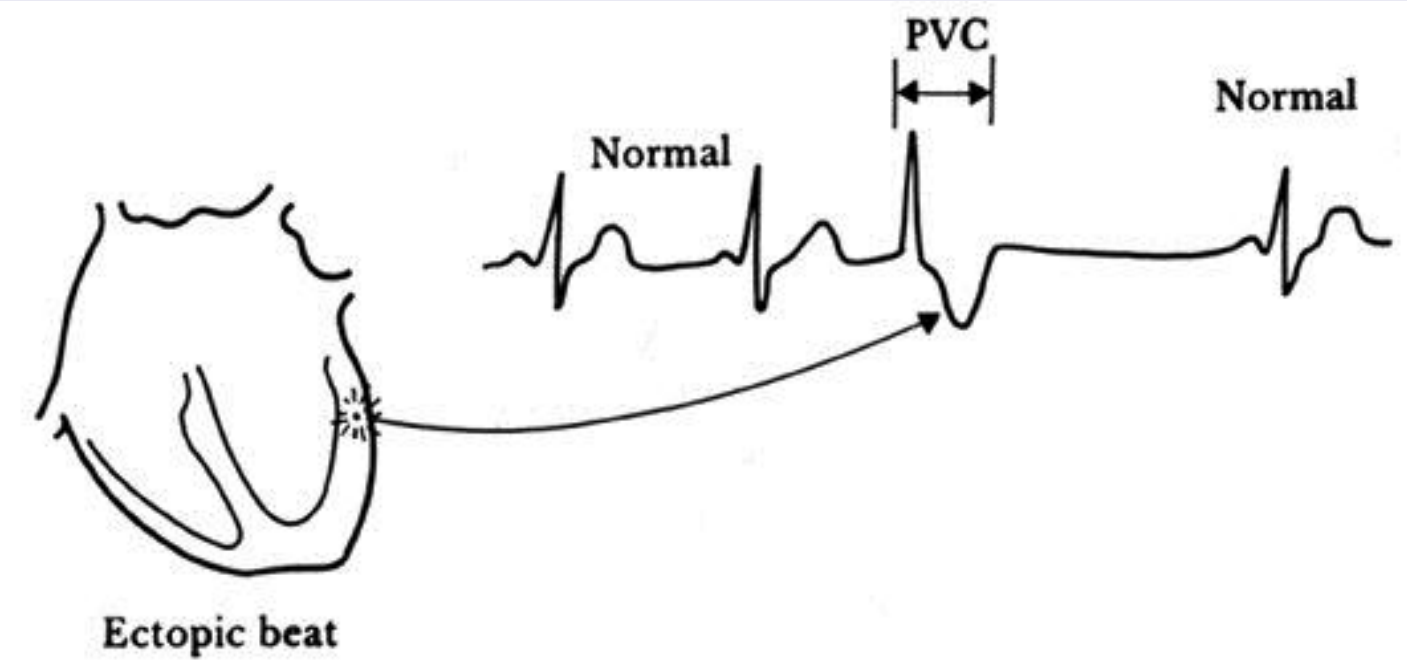
- Cells in the AV node are dead and activity cannot pass from atria to ventricles.
- Atria and ventricles beat independently, ventricles being driven by an ectopic (other-than-normal) pacemaker.

First-degree heart block.

- AV block wherein the node is diseased (like rheumatic heart disease and viral infections of the heart).
- Although each wave from the atria reaches the ventricles, the AV nodal delay is greatly increased.

When one branch of the *bundle of His* is interrupted, then the *QRS* complexes are prolonged while the heart rate is normal.

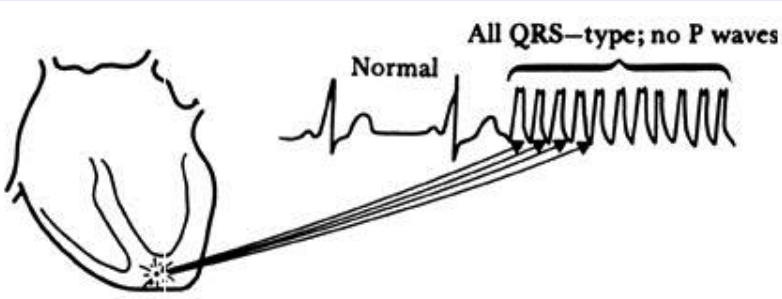
Arrhythmias



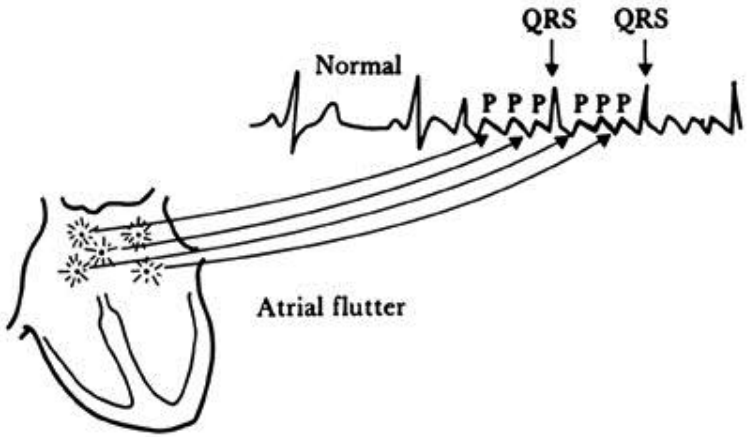
• A portion of the myocardium sometimes becomes irritable and discharge independently.

• An irritable focus, or ectopic pacemaker, within the ventricle or specialized conduction system may discharge, producing an extra beat, or extrasystole, that interrupts the normal rhythm.

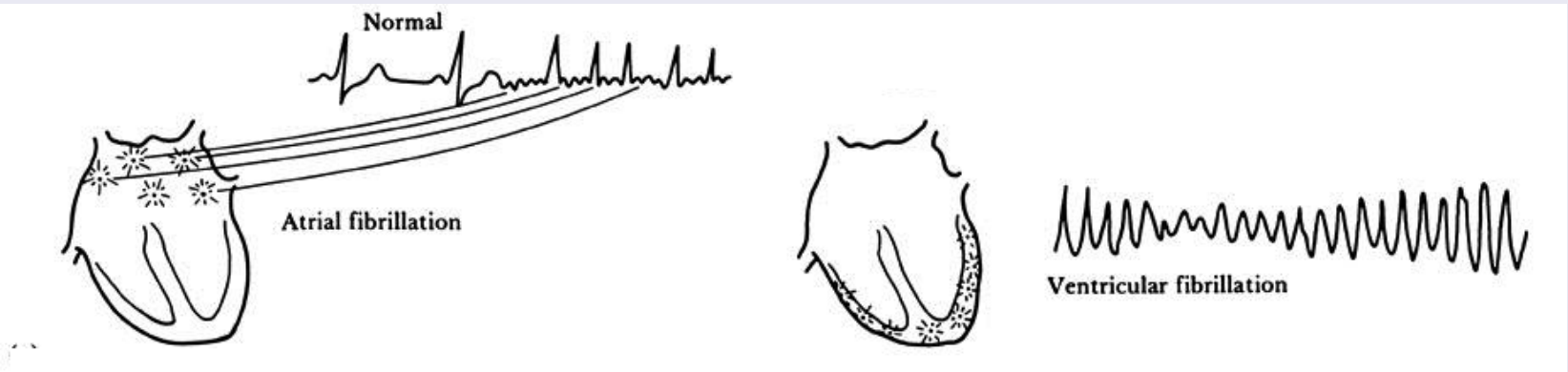
• This extrasystole is also referred to as a premature ventricular contraction (PVC).



Paroxysmal tachycardia
An ectopic focus may repetitively discharge at a rapid regular rate for minutes, hours, or even days.



Atrial flutter
The atria begin a very rapid, perfectly regular "flapping" movement, beating at rates of 200 to 300 beats/min.

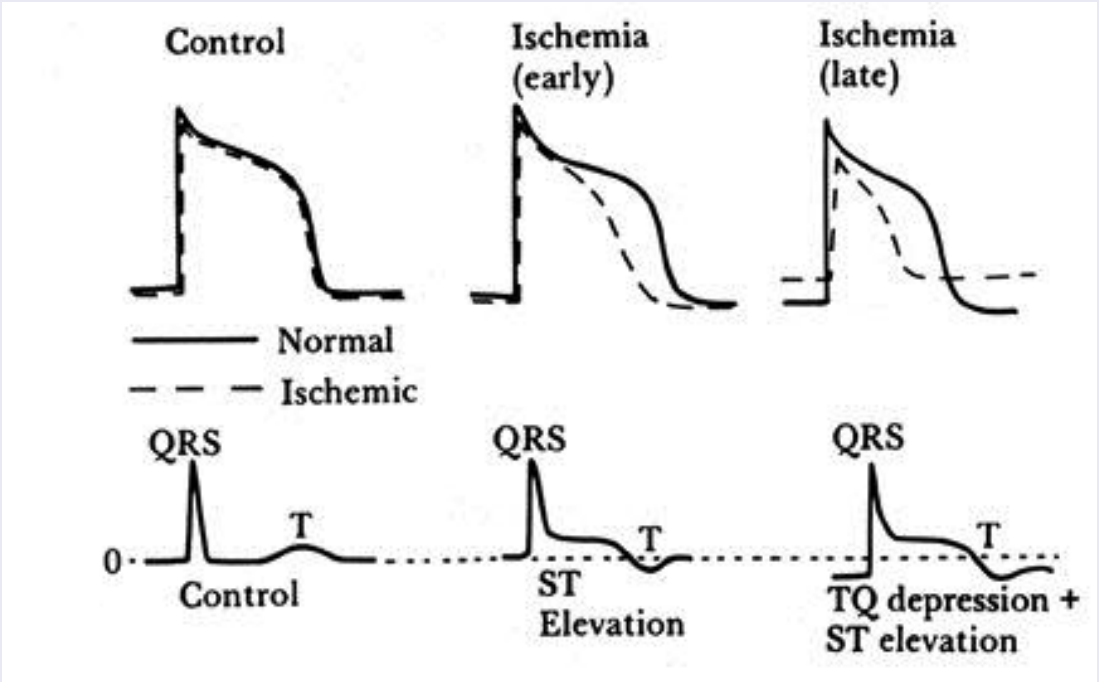


Atrial fibrillation

- The atria stop their regular beat and begin a feeble, uncoordinated twitching.
- Concomitantly, low-amplitude, irregular waves appear in the *ECG*.
- This type of recording can be clearly distinguished from the very regular *ECG* waveform containing atrial flutter.

Ventricular fibrillation

- Mechanically the ventricles twitch in a feeble, uncoordinated fashion with no blood being pumped from the heart.
- The *ECG* is likewise very uncoordinated.

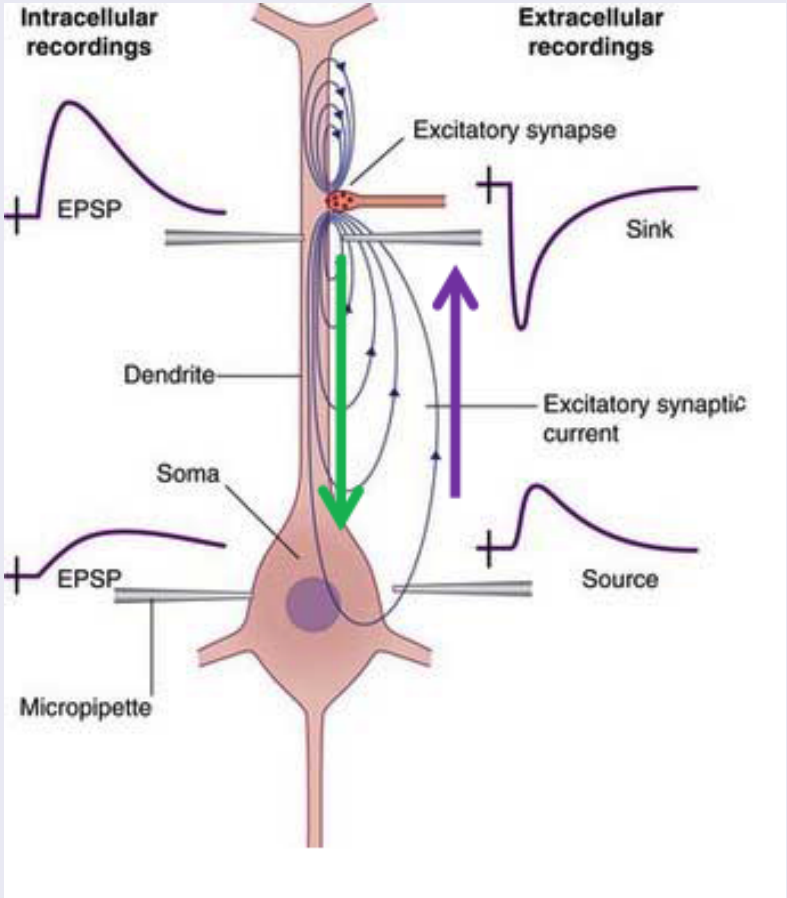


Action potentials recorded from normal (solid lines) and ischemic (dashed lines) myocardium in a dog. Control is before coronary occlusion.

- During the control period prior to coronary occlusion, there is no *ECG S-T* segment shift; after ischemia, there is such a shift.
- There is a loss of K^+ and an uptake of Na^+ within the ischemic cell.
- Ca^+ and H^+ also acumulate within the cell and water shifts inward as well.
- These ionic shifts produce membrane depolarizations and indicate the malfunction of Na^+-K^+ pump.

Origins of Magnetoencephalography/Electroencephalography (M/EEG)

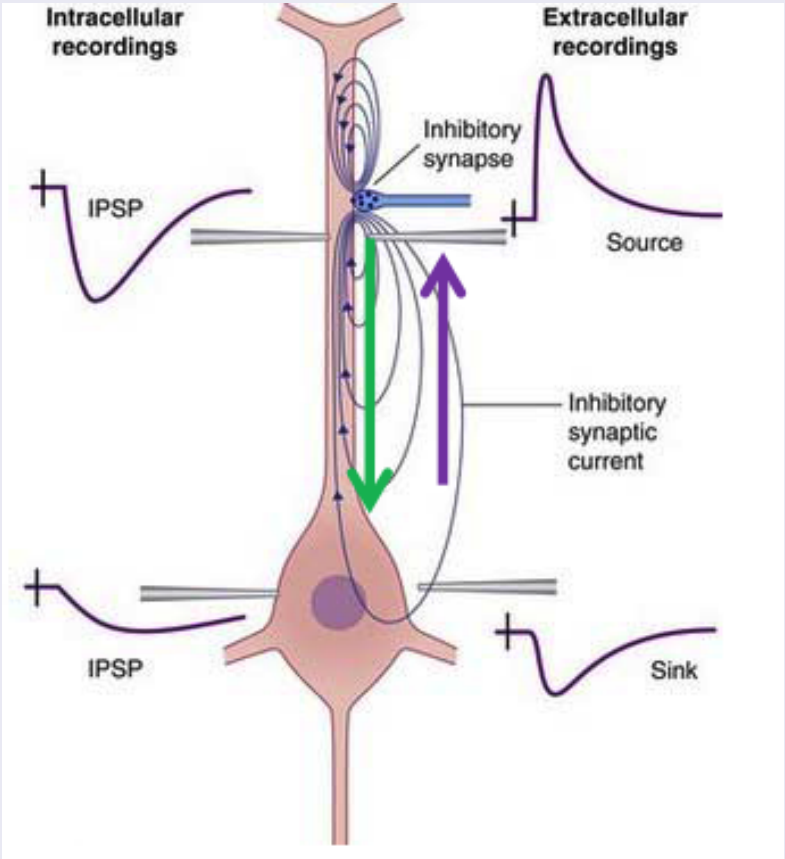
Synaptic input leads to ionic currents across postsynaptic membrane



EPSP

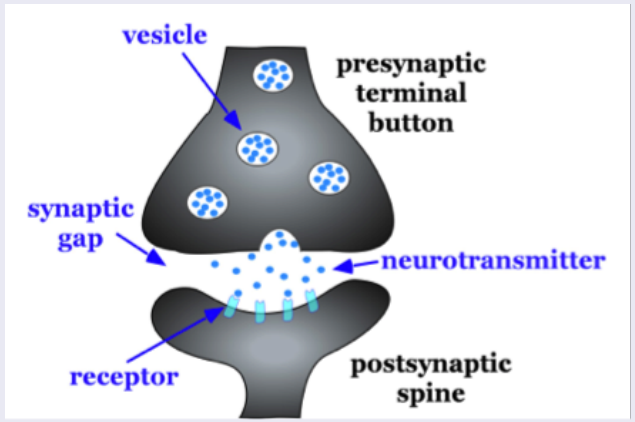
- Influx of positive Na^+ at apical dendrites causes depolarization of the postsynaptic cell.
- Extracellular volume currents complete the loop of ionic flow so that there is no build-up of charge.
- A depolarizing current makes the membrane potential to become more positive and closer to excitation.

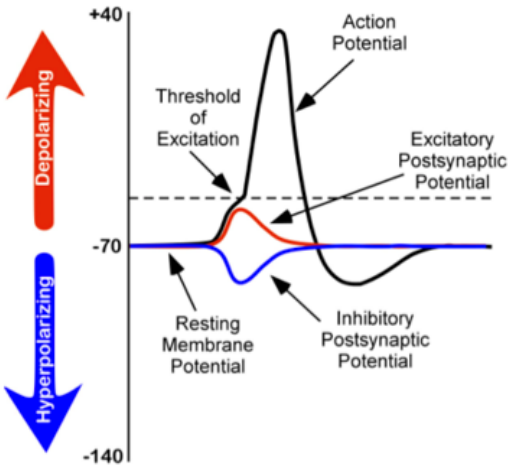
Origins of Magnetoencephalography/Electroencephalography (M/EEG)



IPSP

- Influx of negative Cl^- ions causes hyperpolarization of the postsynaptic cell.
- A hyperpolarizing current makes the membrane potential to become more negative and away from excitation.



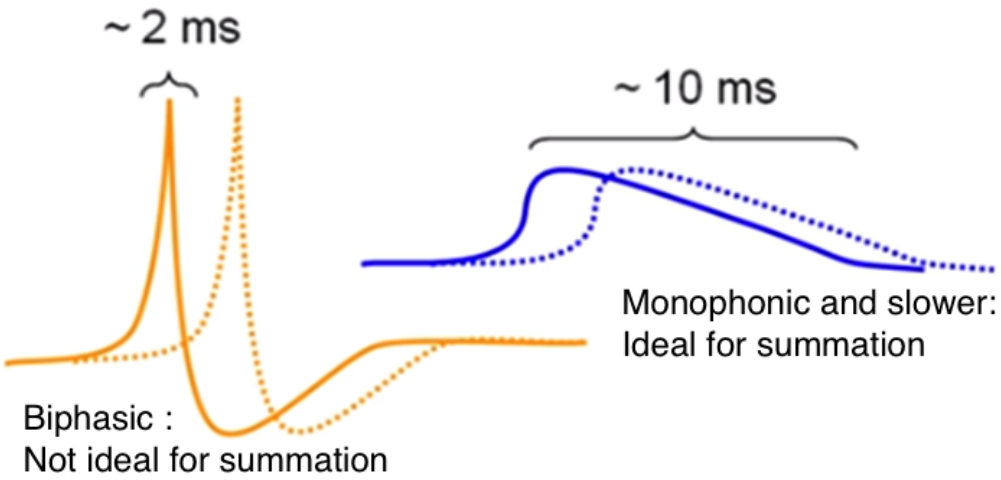


1. **excitatory postsynaptic potentials** (EPSPs): a *depolarizing* current that causes the membrane potential to become more positive and closer to the threshold of excitation; or
2. **inhibitory postsynaptic potentials** (IPSPs): a *hyperpolarizing* current that causes the membrane potential to become more negative and further away from the threshold of excitation.

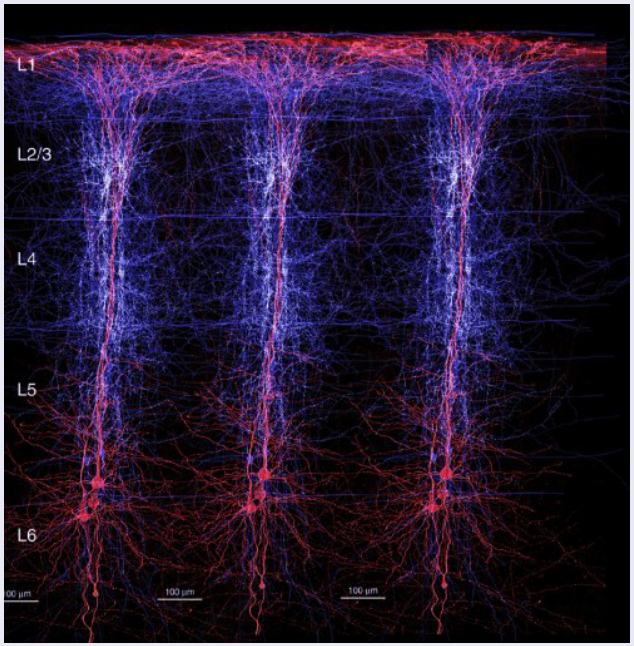
Action Potential:
all-or-nothing potential within a neuron

Release of Neurotransmitter:
chemical signal between neurons

EPSPs and IPSPs:
graded potential within a neuron that can be depolarizing or hyperpolarizing



From Single Neuron to Neural Population

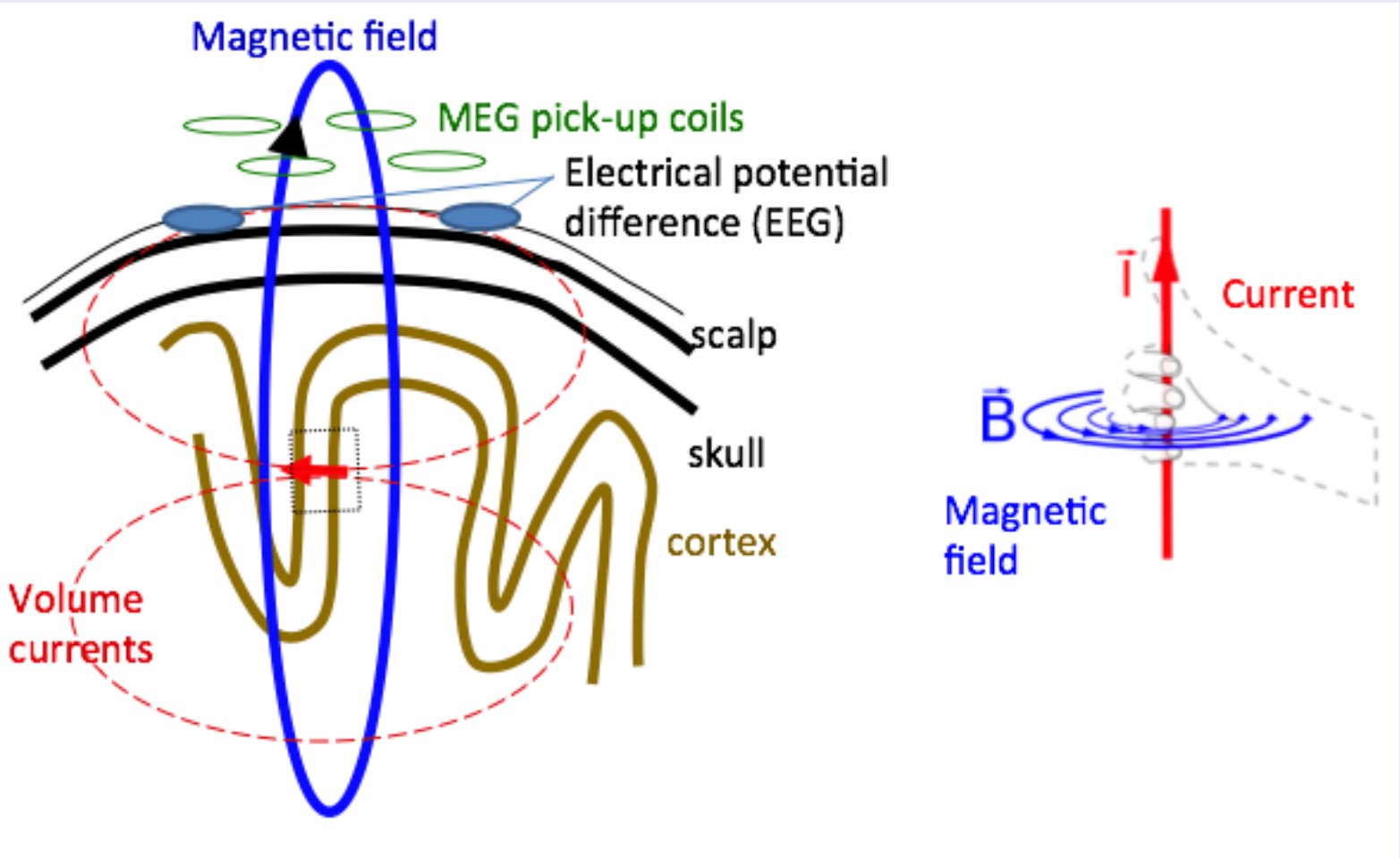


Layer II/II and V pyramidal cells are ideal as current generators because they are:

1. spatially aligned
2. perpendicular to cortical surface
3. recurrently connected
4. receive synchronous inputs

A large number of neurons have to be active simultaneously to generate a measurable MEG/EEG signal.

Primary intracellular currents give rise to volume currents and a magnetic field.



MEG is more sensitive to intracellular currents.
EEG is more sensitive to extracellular currents.

Spontaneous and Evoked Response of MEG/EEG