Origin of Biopotentials

- Outline
  - bioelectric phenomena at the cellular level
  - volume conductor potential distributions
  - functional organization of the peripheral nervous system
  - other bioelectric sources: heart, retina, brain

- Recordings of bioelectric phenomena
  - electrocardiogram (ECG)
  - electroencephalogram (EEG)
  - electroneurogram (ENG)
  - electromyogram (EMG)
  - electroretinogram (ERG)

- Exercise: Match recordings above to sources below
  - retina, active skeletal muscle, nerve, brain, cardiac muscle

Electrical Activity at Cellular Level

- Source of bioelectric potentials
  - electrochemical activity of a certain class of cells
    - known as *excitable cells*
  - components of nervous, muscular, & glandular tissue
- Electrical states of excitable cells
  - resting state
  - action state
- *You Tube Videos*
  - Action potentials
    - http://www.youtube.com/watch?v=SCasruJT-DU
    - http://www.youtube.com/watch?v=yrsJ9HlnZ5s&feature=related
    - http://www.youtube.com/watch?v=MtJyHp_AZL8&feature=related
  - Muscle action
    - http://www.youtube.com/watch?v=70DyJwwFnkU&feature=related
  - Also: search “how the body works”

Cell Membrane Potentials

- Cell Membrane
  - very thin (7-15 nm) lipid-protein complex
    - transmembrane ion channels (pores) allow flow of ions across the membrane
    - like a leaky capacitor: a thin dielectric material acts as a charge separator
  - impermeable to intracellular protein and other organic anions
  - selectively permeable to sodium (Na^+) potassium (K^+) and chlorine (Cl^-) ions
  - ion concentration difference across membrane creates a diffusion gradient
  - ions flow, creating an electric field that opposes flow, until an equilibrium is established
    - similar to p-n junction, ions flow by diffusion and create a potential difference which inhibits further flow of charged ions

Equilibrium Potential

- Equilibrium transmembrane (resting) potential
  - when net current through the membrane is zero
- Nernst equation
  - assumes K^+ to be the main ionic species involved in the resting state
    - that is, $P_k >> P_{Na}$

$$E_K = \frac{RT}{nF} \ln \frac{[K]_o}{[K]_i} = 0.0615 \log_{10} \frac{[K]_o}{[K]_i} \quad \text{(V)}$$

n is the valence of the K^+
$[K]_i$ and $[K]_o$ are the intracellular and extracellular concentrations of K^+ in moles per liter
R is the universal gas constant
T is absolute temperature in K
F is the Faraday constant

- Goldman–Hodgkin–Katz (GHK) formulation
  - accounts for influence of other ionic species in internal/external media

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

P_M is the *permeability coefficient* of the membrane for a particular ionic species M (K, Na, Cl)

Resting State

- Resting state
  - excitable cells maintain a steady electrical potential difference between the internal and external environments (-50 to -100 mV)
  - membrane is
    - slightly permeable to sodium ions (Na+)
    - freely permeable to potassium and chlorine ions (K+, Cl-)
- Example concentrations of the major ion species
  - from frog skeletal muscle
    - buildup of K inside cell
    - buildup of Na & Cl outside cell

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

(in millimoles per liter)

  - equilibrium potential using GHK formulation

$$E = 0.0581 \log_{10}\left[\frac{P_K(4) + P_{Na}(145) + P_{Cl}(4)}{P_K(155) + P_{Na}(12) + P_{Cl}(120)}\right]$$

$$= 0.0581 \log_{10}\left(\frac{26.9\times10^{-6}}{790.24\times10^{-6}}\right) = -85.3\text{mV}$$

Assuming room temperature (20 °C) and typical values of permeability coefficient for frog skeletal muscle (P_{Na} = 2 ´ 10^{-8} cm/s, P_K = 2 ´ 10^{-6} cm/s, and P_{C1} = 4 ´ 10^{-6} cm/s)

Membrane Ion Flow

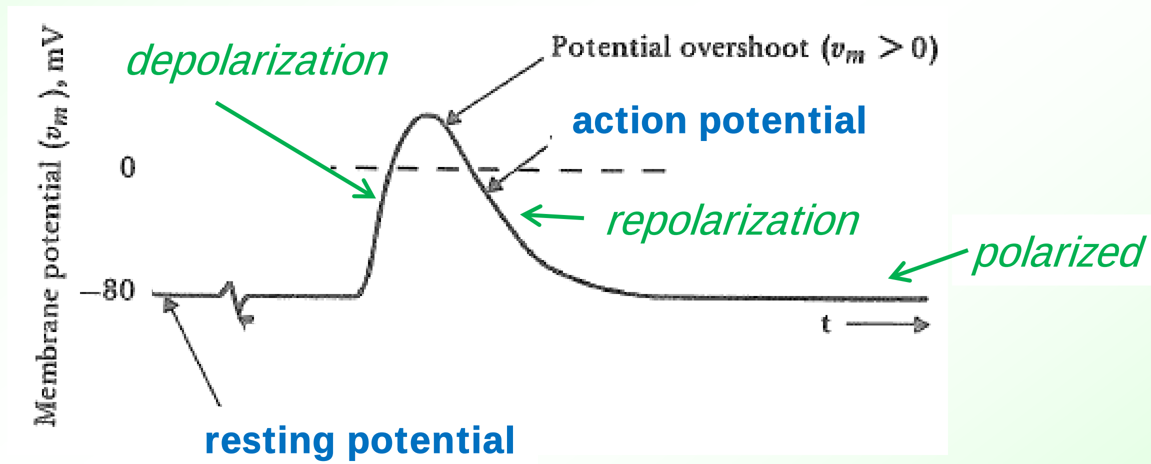
- Maintaining steady state ionic imbalance
  - requires continuous transport of ions against electrochemical gradients
- Active transport mechanism located in the membrane
  - the *sodium–potassium pump*
    - actively transports Na^+ out of cell and K^+ into cell in the ratio $3Na^+ : 2K^+$
    - associated pump current i_{NaK} is a net outward current that tends to increase the negativity of the intracellular potential
    - energy for the pump is provided by a common source of cellular energy, adenosine triphosphate (ATP) produced by mitochondria in the cell
- Factors influencing the flow of ions across the membrane
  - diffusion gradients
  - inwardly directed electric field
  - membrane structure (availability of pores)
  - active transport of ions against an established electrochemical gradient

Cell Membrane Polarization

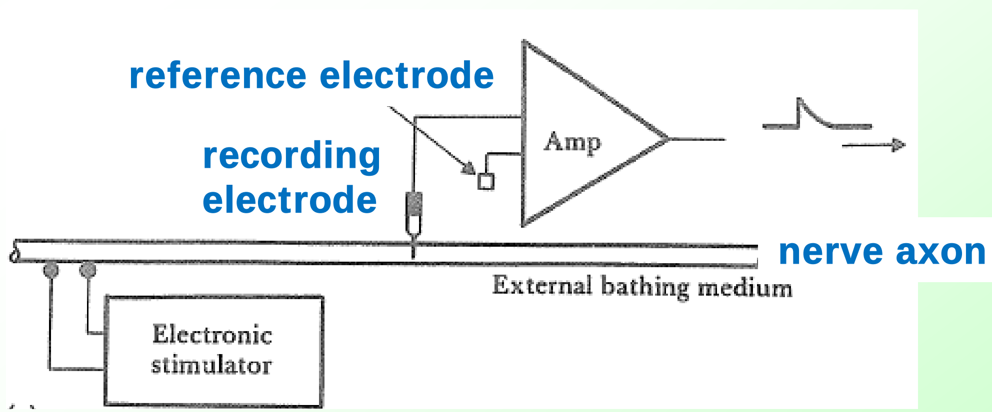
- Three states of cell membrane
  - polarized: the cell membrane is at a steady resting potential
  - depolarized: when the magnitude of membrane potential decreases
  - hyperpolarization: increase in magnitude of membrane potential
- Action potential: brief transient disturbance of membrane potential
  - change in membrane potential due to a stimulus adequate to bring about depolarization sufficient to exceed its threshold potential and thereby elicit an all-or-none action potential
  - change in potential from resting level
    - a certain amount (of potential) for a fixed duration of time
    - for example: a nerve fiber, $\Delta v \approx 120$ mV and the duration is ≈ 1 ms
  - further increases in intensity or duration of stimulus beyond that required for exceeding the threshold level produce only the same result
- Return to resting state
  - repolarization: return to membrane equilibrium after action potential

Electrical Recording from a Nerve Fiber

- Recording of action potential of an invertebrate nerve axon
  - cell membrane potential vs. time
  - resting potential
  - action potential

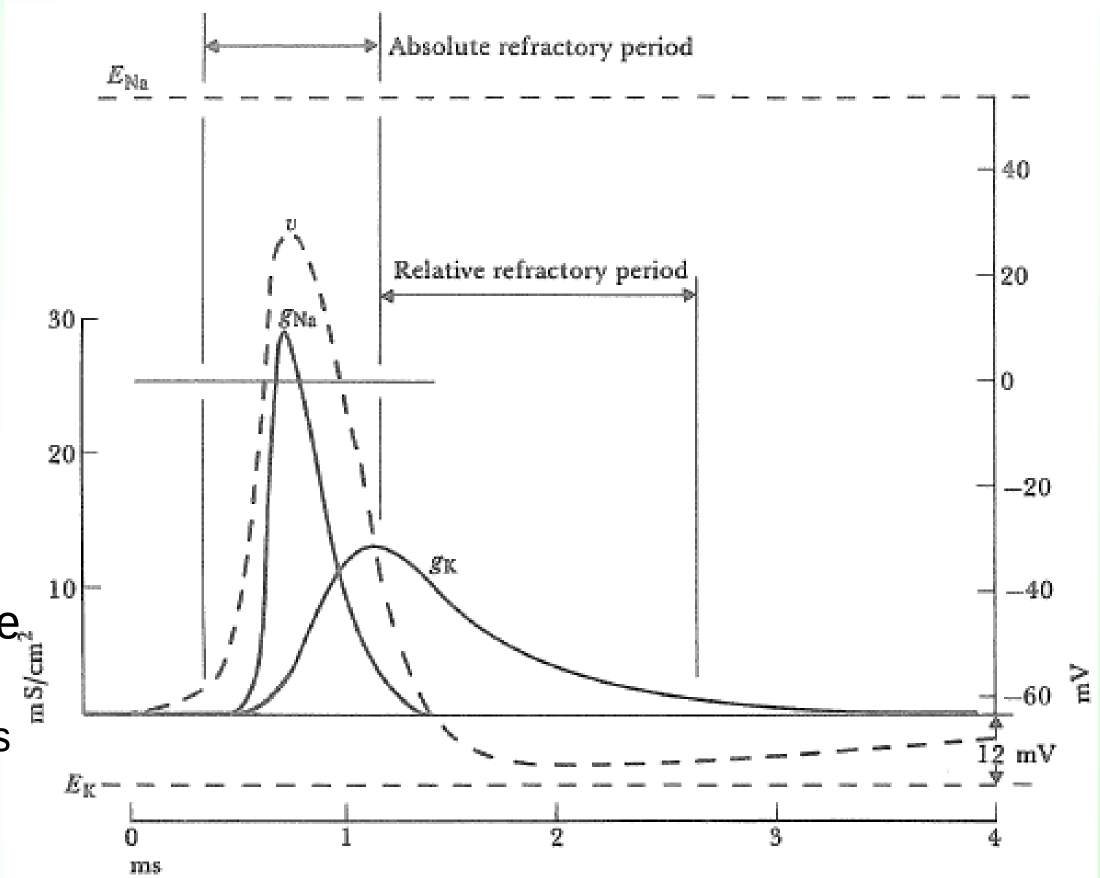


- Recording of cell activity can be made via a penetrating micropipet



Action Potential

- Absolute refractory period
  - membrane cannot respond to any stimulus
    - no matter how intense
- Relative refractory period
  - action potential can be elicited by an intense superthreshold stimulus
- Set upper limit action potential frequency
  - EX: for nerve axon with absolute refractory period of 1 ms
    - max action potential frequency is 1000 impulses/s
  - but, typical neuron firing rate is ~30 Hz

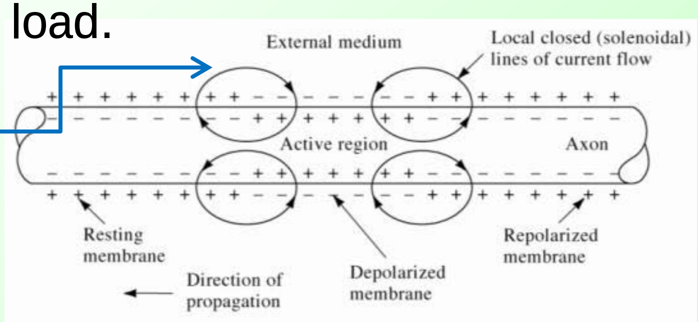


Transmembrane potential (v) and membrane ionic conductance changes for sodium (gNa) and potassium (gK) during the action potential

Volume Conductor Electric Field

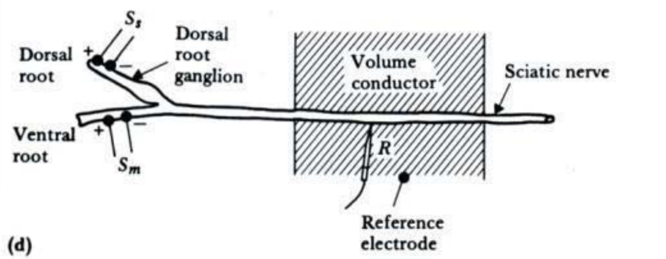
- Most biomedical recordings occur on the surface of the body
- How does microscopic cellular electrical activity conduct to the body's surface for gross, external measurement?
- Volume conductor electric field
  - model for link (mapping) between
    - microscopic electrical activity generated within the bioelectric source
    - macroscopic potential distribution produced at the surface of the body
  - describes flow of action current through the conducting medium
    - conducting medium = infinite (relative to source) volume conductor
  - two components of the model
    - bioelectric source – modeled as a constant current source.
    - conducting medium – modeled as an electrical load.
  - lends to insight into the interpretation of recorded waveforms

local current flow as action potential moves through axon

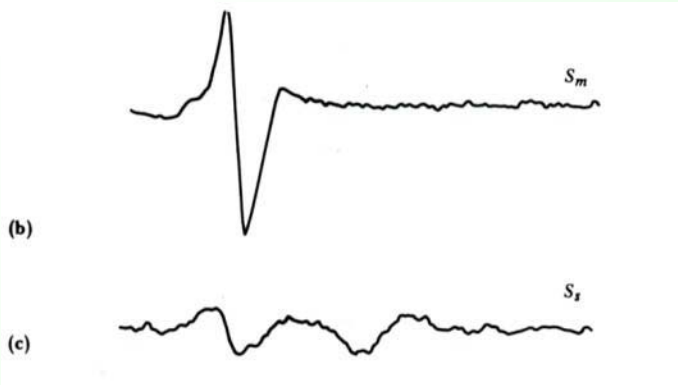


Volume Conductor Experiment

- Experiment
  - Extracellular field potentials (128 responses averaged) recorded at the surface of an active frog sciatic nerve in an extensive volume conductor
  - Stimulate
    - motor nerve only (*Sm*)
    - sensory nerve only (*Ss*)
    - both together (*Sm* + *Ss*)



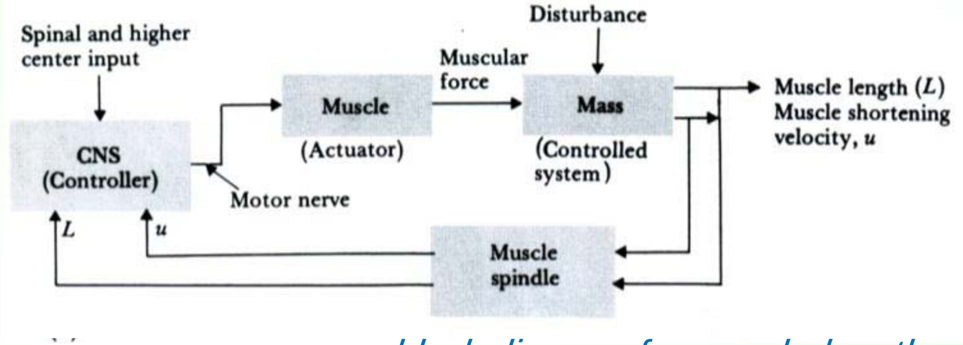
- Results
  - Recorded surface potential
    - (b) only motor nerve excited
    - (c) only sensory nerve excited
    - (a) both motor and sensory excited



- Observations
  - approximate superposition of motor and sensory responses

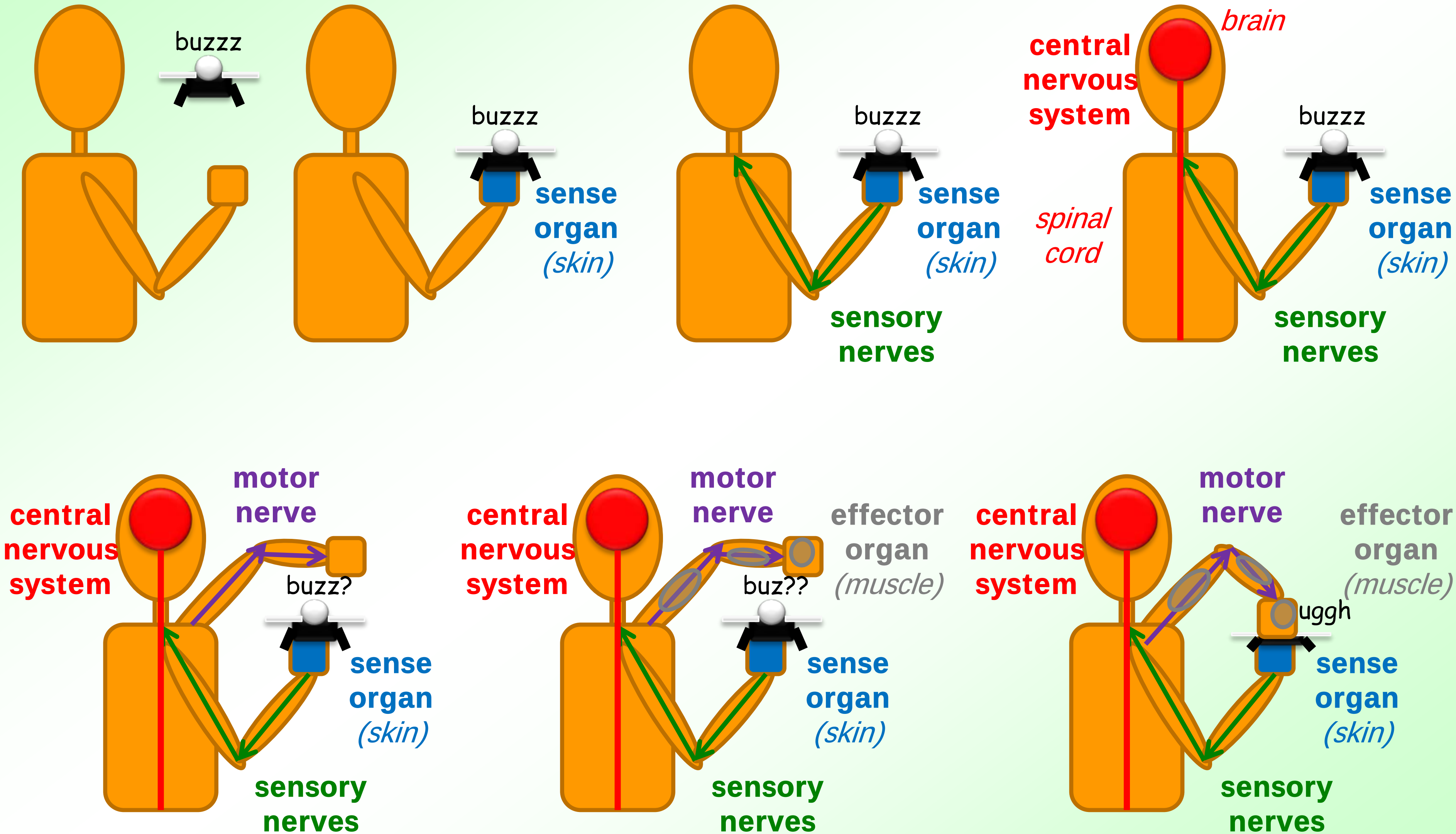
Organization of Peripheral Nervous System

- *Reflex arc*
  - functional organization of spinal nervous system (global feedback sys.)



block diagram for muscle-length control system. note features of a negative-feedback loop

- Reflex arc components
  1. **sense organ**
     - many individual sense receptors that respond to a stimulus such as pressure, temperature, touch, or pain
  2. **sensory nerve**
     - performs the task of transmitting information (encoded in the form of action potential frequency) from a peripheral sense receptor to other cells lying within the central system (brain and spinal cord)
  3. **central nervous system (CNS)**
     - where information is evaluated, and, a "motor" decision is implemented
       - e.g., action potentials are initiated in motor-nerve fibers
  4. **motor nerve**
     - a communication link between the CNS and peripheral muscle
  5. **effector organ (muscle)**
     - respond to the driving stimuli (action potentials) conducted by motor-nerve fibers
     - e.g., skeletal muscle fibers that contract (shorten) when stimulated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spinal
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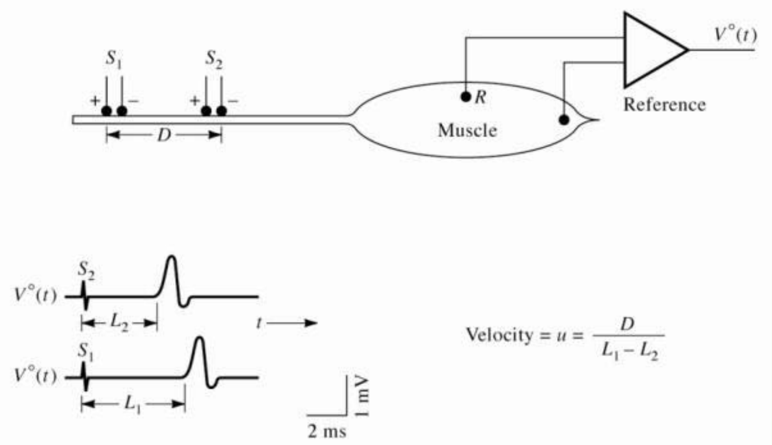
Junctional Transmission

- Communication links in reflex arc
  - intercommunication between neurons (neuro–neuro junctions)
    - called ***synapses***
  - communications between neurons and muscle fibers
    - called ***neuromuscular junctions***
    - occur at small specialized regions of the muscle fiber
      - called *end-plate regions*
  - junctional transmission process is electrochemical in nature
    - e.g., prejunctional fiber involved in the neuromuscular junction releases a neurotransmitter substance *acetylcholine* (ACh), which diffuses across a very small fluid-filled gap region approximately 20 nm in thickness
    - electrochemical transmission process at the junction involves a time delay on the order of 0.5 to 1.0 ms

Electroneurogram (ENG)

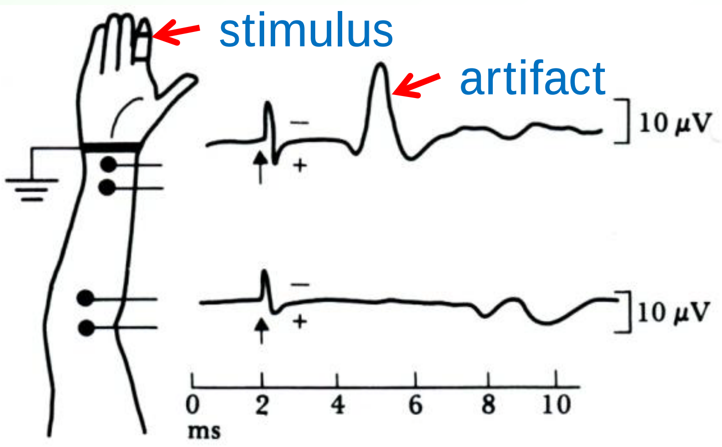
- ENG measures electrical activity of neurons in the central nervous system (brain, spinal cord) or peripheral nervous system (nerves, ganglions)
  - done by placing an electrode in the neural tissue to record neuron action potential or one or a group of neurons
- ENG can measure <u>conduction velocity</u> in a peripheral nerve
  - done by stimulating motor nerve at 2 points a known distance apart and recording difference in arrival time at measurement point
  - conduction velocity can show nerve regenerating following nerve injury



Measurement of neural conduction velocity via measurement of latency of evoked electrical response in muscle. The nerve was stimulated at two different sites a known distance D apart.

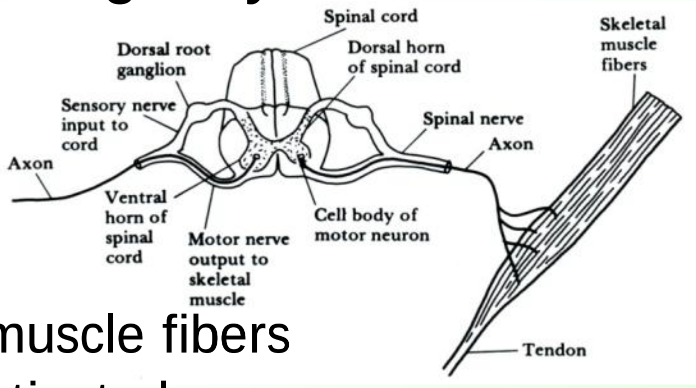
Example ENG Measurement

- Extracellular field responses from sensory nerves
  - Stimulus: ring stimulating electrodes at index or 3rd finger (diff. nerves)
  - Measurand: evoked potential at lower wrist and upper elbow.
  - Artifacts: long stim pulses cause muscle contractions, limb movement
    - undesired signals in addition to desired neural action potentials
  - Instrument: High-gain, high-input impedance differential amp with good CMRR and low noise (<10uV)
  - Observe: potential at the wrist is triphasic and larger magnitude than the delayed potential recorded at the elbow
    - difference is due to the size of the volume conductor at each location and the radial distance of the measurement point from the neural source



Electromyogram (EMG)

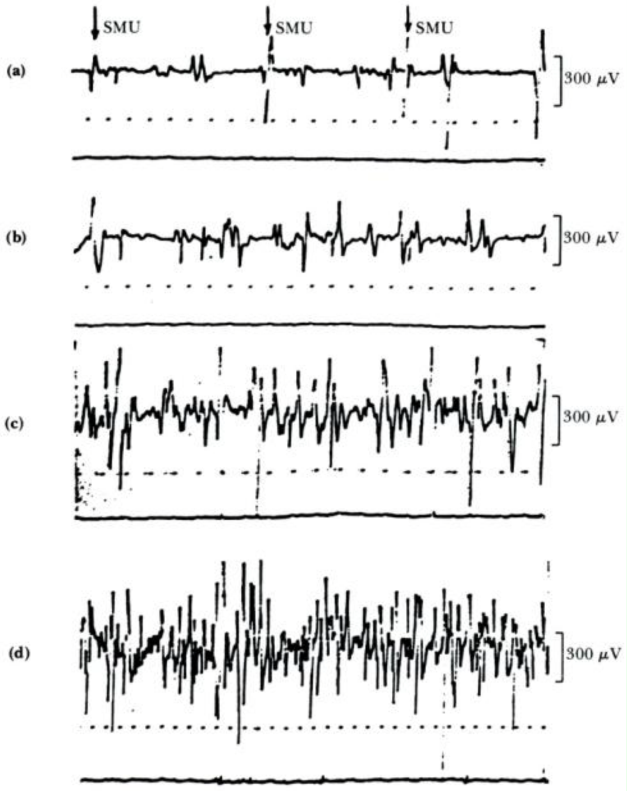
- EMG detects the electrical potential generated by muscle cells activated electrically or neurologically
  - composed of superimposed motor unit action potentials (MUAPs) from several motor units



- Motor unit
  - a single motor nerve fiber and the bundle of muscle fibers
  - smallest unit of skeletal muscle that can be activated
- Single motor unit (SMU) is a bioelectric source located in a volume conductor consisting of all other muscle fibers
- The evoked field potential from the active fibers of an SMU
  - has a triphasic form of brief duration (3 to 15 ms)
  - amplitude of 20 to 2000 mV
  - frequency of discharge varies from 6 to 30 per second

Electromyogram (EMG)

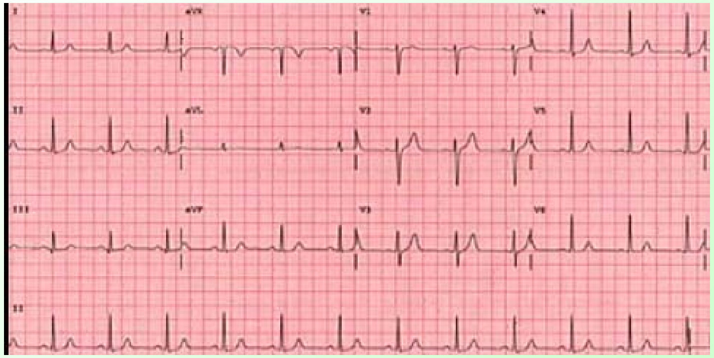
- Surface electrodes for EMG record from multiple SMU
  - the signals are superimposed
  - can be used only with superficial muscles
  - sensitive to electrical activity over wide area
- Insertion electrodes and fine-tipped electrodes can be used to localize the potential recorded from isolated SMU
- Shape of SMU potential
  - can indicate peripheral neuropathy
  - can be modified by disease



Motor unit action potentials from normal muscle during progressively more powerful contractions. In the interference pattern (c), individual units can no longer be clearly distinguished, (d) interference pattern during very strong muscular contraction. Time scale is 10 ms per dot.

The Electrocardiogram (ECG)

- ***Electrocardiogram***: measures potentials on body surface due to neuromuscular activity of the heart
  - ideally, but often see interference from other neuromuscular activities
- Source of ECG signal
  - electrical activation sequence of the heart's ventricle leads to
  - production of closed-line action currents that flow in the thoracic volume conductor leading to
    - considered a purely passive medium containing no electric sources or sinks
  - potentials that can be measured on the outer surface of the medium
- Video examples
  - http://www.youtube.com/watch?v=te_SY3MeWys&feature=related
  - http://www.youtube.com/watch?v=nK0_28q6WoM&feature=related
- Other resources
  - Bioelectromagnitism (http://www.bem.fi/book/index.htm)
    - Ch.6 covers the heart



typical ECG showing multiple electrode potentials

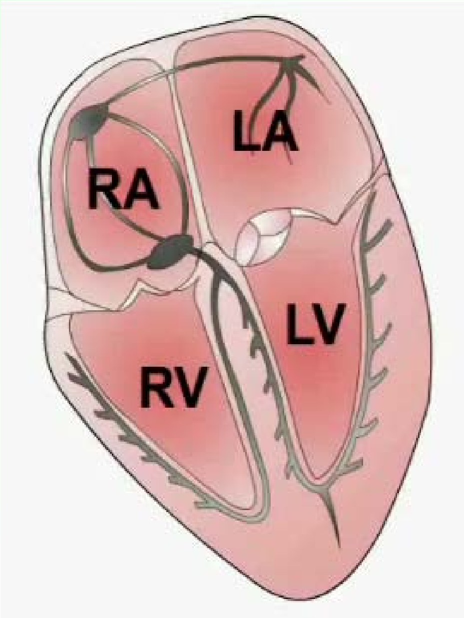
Cardiac Operation & Electrical Activity

- How does the heart work?
  - Best video
    - http://www.youtube.com/watch?v=D3ZDJgFDdk0&feature=related
  - Basic function
    - http://www.youtube.com/watch?v=H04d3rJCLCE&feature=related (0-1:05)
  - Electrical activity
    - http://www.youtube.com/watch?v=H04d3rJCLCE&feature=related (2:45-end)
  - And once again to drive it home...
    - http://www.youtube.com/watch?v=MGxxRyJTmwU

Anatomy of the Heart

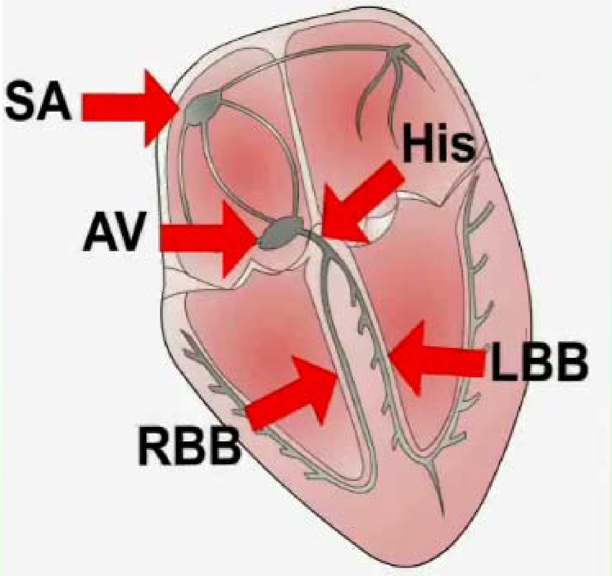
- Chambers
  - Right & Left Atria
    - blood storage chambers
  - Right & Left Ventricles
    - function as a blood pump

- Conducting System
  - Sinoatrial (SA) node
  - Atrioventricular (AV) node
  - Bundle of His
  - Right/Left bundle branches
    - Purkinje fibers



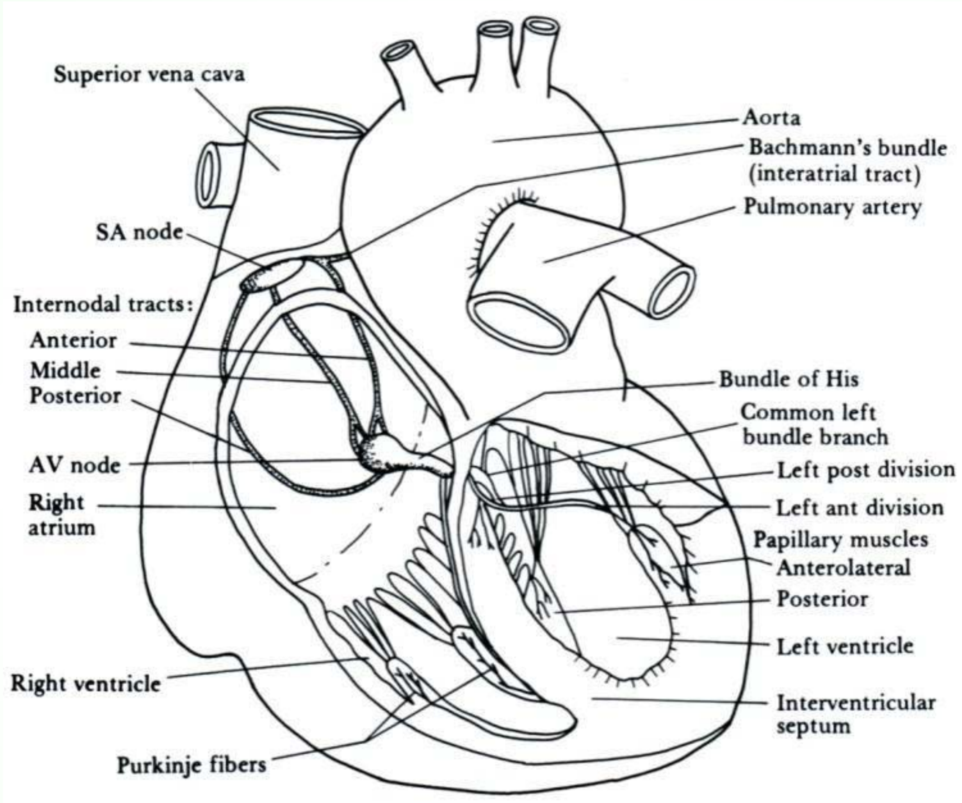
Right?? --- Left??

- Anatomical Connectivity
  - Right: to Lungs
    - re-oxygenate blood
  - Left: to Circulatory system
    - deliver oxygen to the body
- Activity Phases
  - Resting phase
    - ***diastole***
  - Pumping phase
    - ***systole***



The Heart

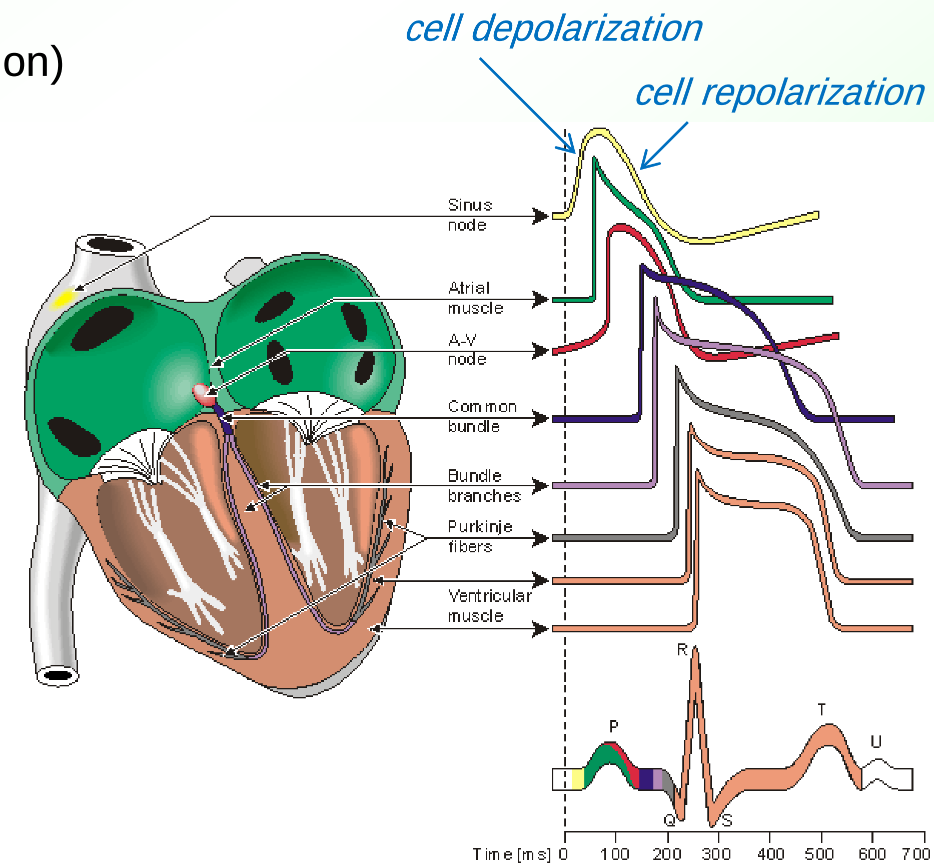
Distribution of specialized conductive tissues in the atria and ventricles, showing the impulse-forming and conduction system of the heart. The rhythmic cardiac impulse originates in pacemaking cells in the sinoatrial (SA) node, located at the junction of the superior vena cava and the right atrium. Note the three specialized pathways (anterior, middle, and posterior internodal tracts) between the SA and atrioventricular (AV) nodes. Bachmann's bundle (interatrial tract) comes off the anterior internodal tract leading to the left atrium. The impulse passes from the SA node in an organized manner through specialized conducting tracts in the atria to activate first the right and then the left atrium. Passage of the impulse is delayed at the AV node before it continues into the bundle of His, the right bundle branch, the common left bundle branch, the anterior and posterior divisions of the left bundle branch, and the Purkinje network. The right bundle branch runs along the right side of the interventricular septum to the apex of the right ventricle before it gives off significant branches. The left common bundle crosses to the left side of the septum and splits into the anterior division (which is thin and long and goes under the aortic valve in the outflow tract to the anterolateral papillary muscle) and the posterior division (which is wide and short and goes to the posterior papillary muscle lying in the inflow tract).



Electrophysiology of the Heart

- Action potential to the heart
  - starts at the SN
  - travels through the heart with delay at each point
  - ECG represents superposition of all signals
    - **P wave** (atrial depolarization)
    - **QRS complex** (ventricular depolarization)
    - **T wave** (ventricular repolarization)

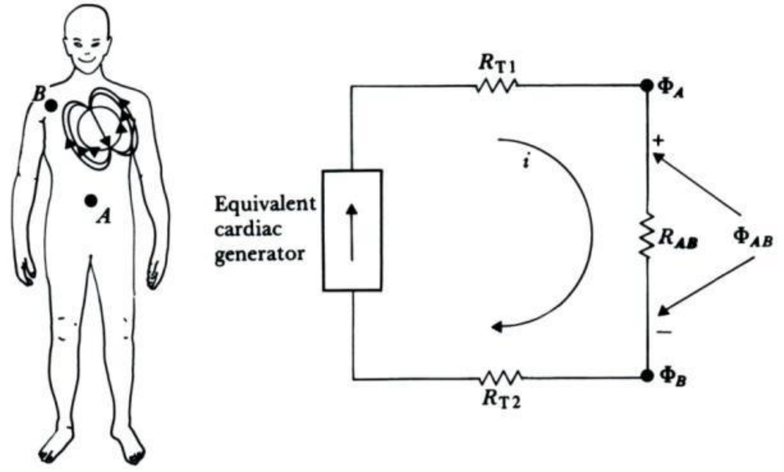
Location in the heart	Event	Time [ms]	ECG-terminology	Conduction velocity [m/s]	Intrinsic frequency [1/min]
SA node	impulse generated	0		0.05	70-80
atrium, Right	depolarization *)	5	P	0.8-1.0	
Left	depolarization	85	P	0.8-1.0	
AV node	arrival of impulse	50	P-Q	0.02-0.05	
	departure of impulse	125	interval		
bundle of His	activated	130		1.0-1.5	
bundle branches	activated	145		1.0-1.5	
Purkinje fibers	activated	150		3.0-3.5	
endocardium					
Septum	depolarization	175		0.3 (axial)	20-40
Left ventricle	depolarization	190		-	
epicardium	depolarization	225	QRS	0.8	
Left ventricle	depolarization	250		(transverse)	
Right ventricle					
epicardium					
Left ventricle	repolarization	400			
Right ventricle	repolarization			0.5	
endocardium			T		
Left ventricle	repolarization	600			



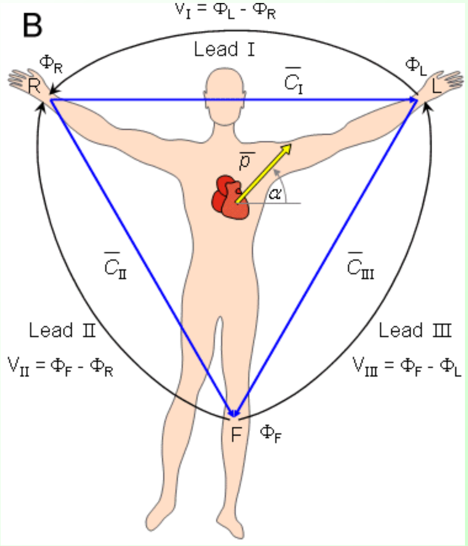
source: Bioelectromagnetism, http://www.bem.fi/book/index.htm

ECG Body Surface Potentials

- Heart dipole
  - heart considered an electrical equivalent generator
  - electrical activity represented by net equivalent current dipole
    - located at the electrical center of the heart



- Einthoven triangle
  - approximation of lead vectors of limb leads
  - determines electrode placement for ECG



Generation of ECG signal in Einthoven limb leads

- source: Bioelectromagnetism, http://www.bem.fi/book/index.htm

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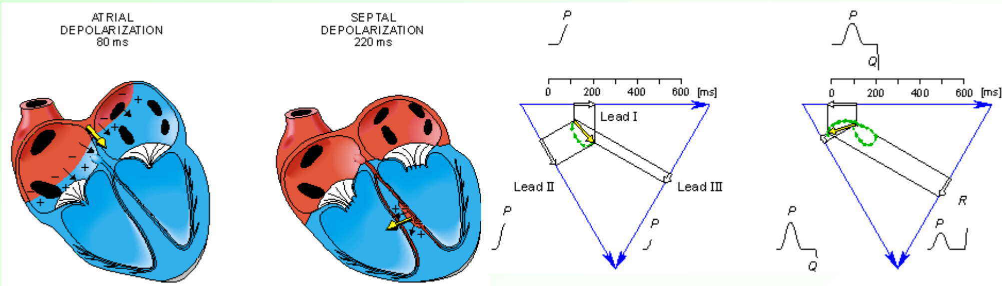
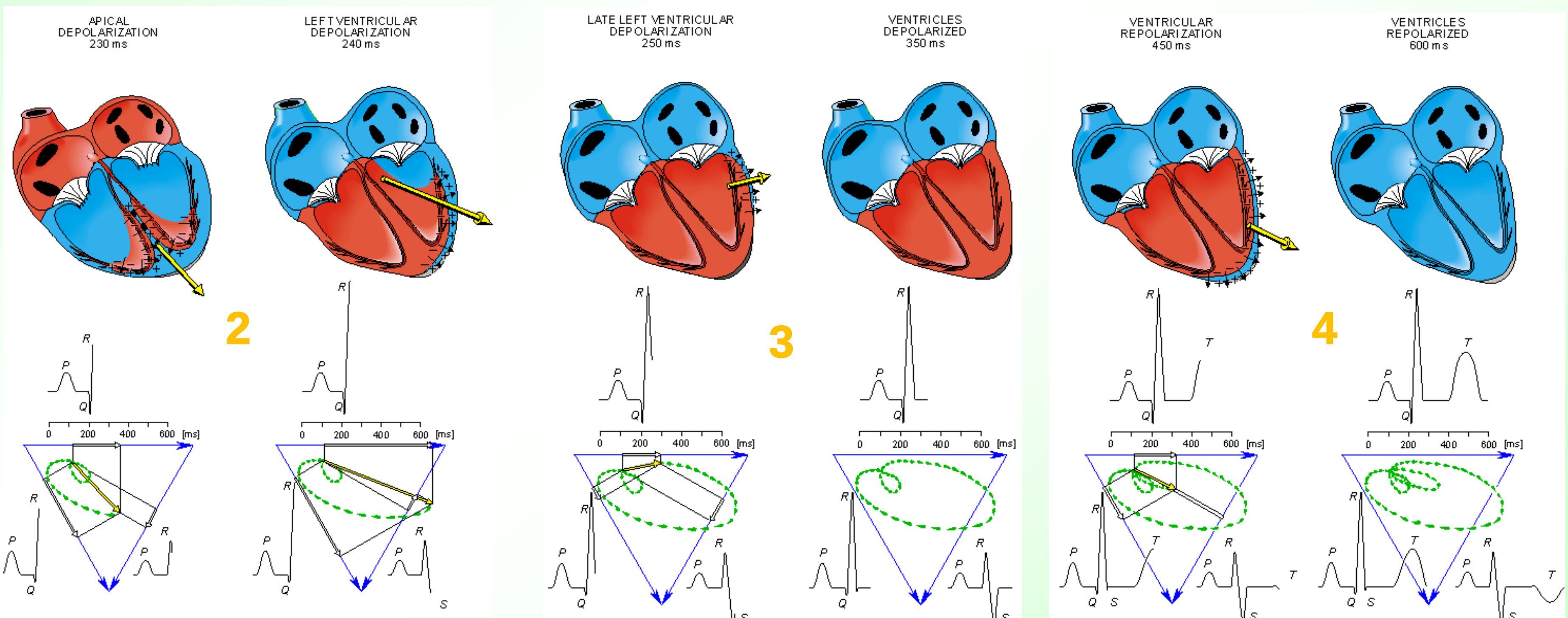
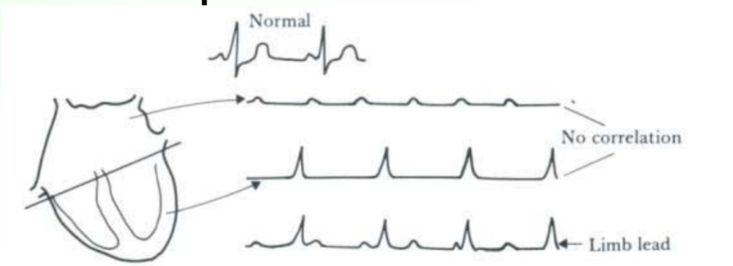


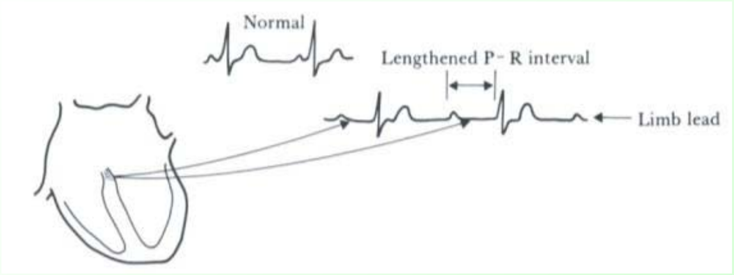


Normal/Abnormal Cardiac Rhythms

- Heart Rate
  - Normal heart rate is 70 beats per minute
    - Bradycardia: slow heart rate (during sleep)
    - Tachycardia: accelerated rate (during emotions)
- Under abnormal conditions
  - any part of the heart become dominant cardiac pacemaker
    - activity of SA node is depressed
    - bundle of His is damaged
    - other sites discharge at a rate faster than the SA node
  - Examples

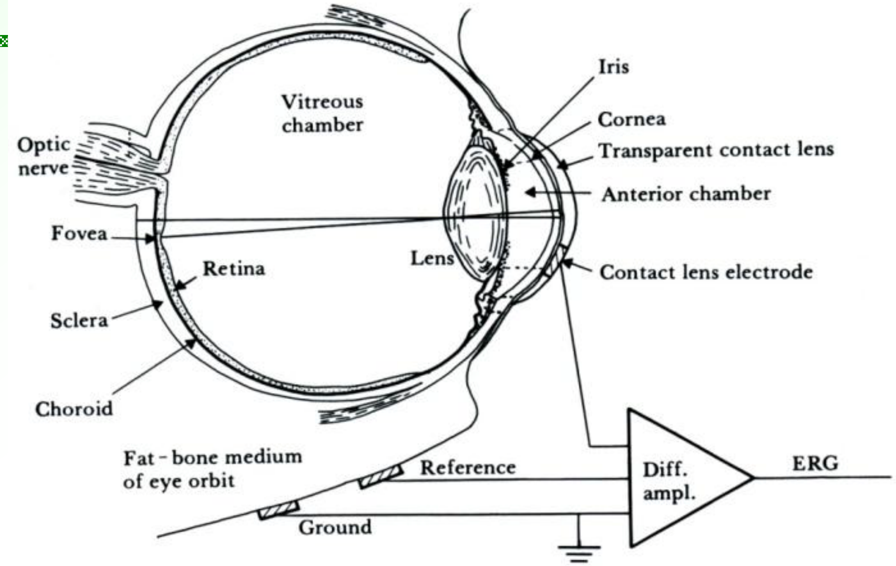


Complete heart block. Cells in the AV node are dead and activity cannot pass from atria to ventricles. Atria and ventricles beat independently, ventricles being driven by an ectopic (other-than-normal) pacemaker



First-degree heart block. AV block wherein the node is diseased (examples include 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.

Anatomy of Vision

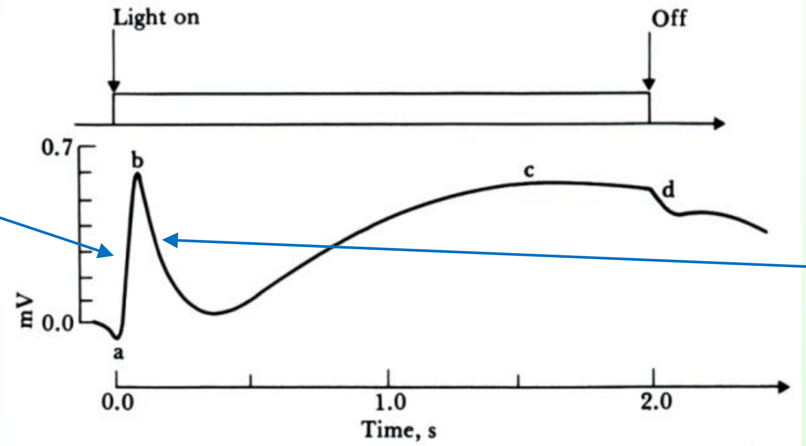


- The normal eye
  - an approximately spherical organ
  - about 24 mm in diameter
- Retina
  - located at the back of the eye
  - is the <u>sensory portion of the eye</u>
- Light-transmitting parts of the eye (in order light hits them)
  - cornea, anterior chamber, lens, vitreous chamber
- Eye pressure maintained by aqueous humor.
- Photoreceptors, bipolar/horizontal, amacrine, ganglion cells.
- rods: respond to dim light, cones: color vision and bright light. Rods consist of photopigment called rhodopsin.

Electroretinogram (ERG)

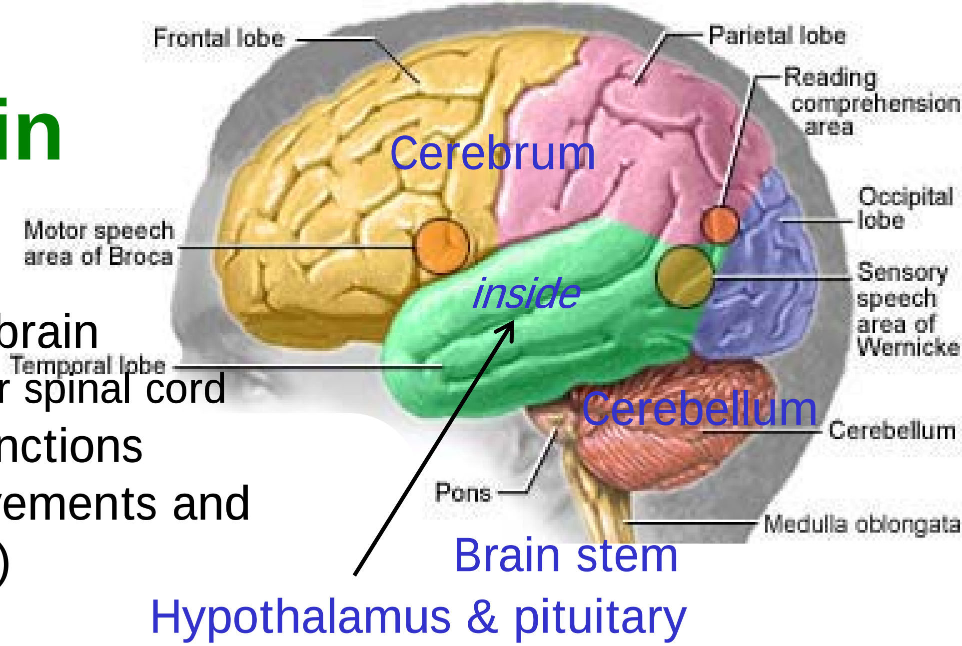
- When retina is stimulated with a brief flash of light
  - characteristic temporal sequence of changes in potential can be recorded between
    - exploring electrode (placed on inner surface of retina or on the cornea)
    - and an indifferent electrode placed elsewhere on the body
- These potential changes are collectively known as the *electroretinogram* (ERG)
  - they are clinically recorded with the aid of an Ag/AgCl electrode embedded in a special contact lens

Early receptor potential (ERP)



Late receptor potential (LRP)

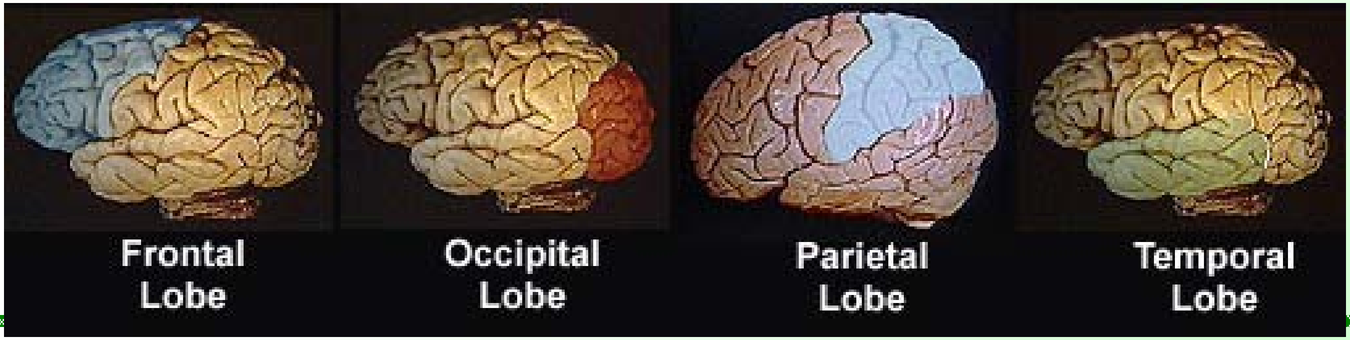
Anatomy of the Brain



- Brain stem
  - consists of the medulla, pons and midbrain
    - medulla = enlarged portion of the upper spinal cord
  - controls the reflexes and automatic functions (heart rate, blood pressure), limb movements and visceral functions (digestion, urination)
- Cerebellum
  - integrates information from the vestibular system that indicates position and movement and uses this information to coordinate limb movements
- Hypothalamus and pituitary gland
  - control visceral functions, body temperature and behavioral responses such as feeding, drinking, sexual response, aggression and pleasure.
- Cerebrum (also called the cerebral cortex or just the cortex)
  - integrates information from all of the sense organs, initiates motor functions, controls emotions and holds memory and thought processes
  - makes up 85% of the brain’s weight
  - functional part of the cerebrum is the cerebral cortex
    - thin layer (1.5 to 4.0 mm in thickness) covering outer surface of cerebrum

Lobes of the Brain

- Frontal lobe
  - Concerned with reasoning, planning, parts of speech and movement (motor cortex), emotions, and problem-solving
- Occipital lobe
  - Concerned with many aspects of vision
- Parietal lobe
  - Concerned with perception of stimuli related to touch, pressure, temperature and pain
- Temporal lobe
  - Concerned with perception and recognition of auditory stimuli (hearing) and memory (hippocampus)

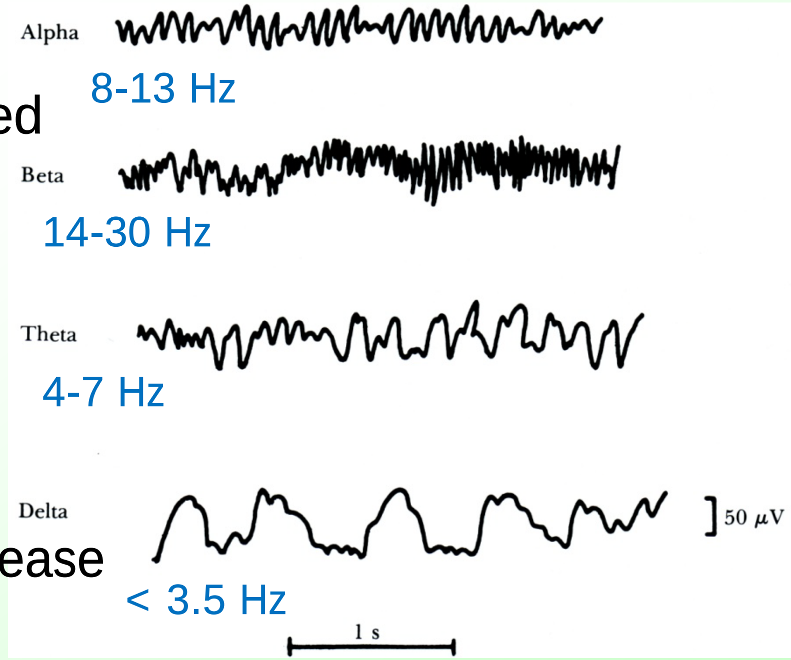


Electroencephalogram (EEG)

- EEG measures potential fluctuations recorded from the brain
- Brain electrical activity recorded with three types of electrodes
  - scalp
    - electrode cap, relatively far from the brain, traditional EEG
  - cortical
    - electrodes are placed on the exposed surface (cortex) of the brain
    - recording is called an *electrocorticogram* (ECoG)
  - depth electrodes
    - thin insulated needle electrodes placed into the neural tissue of the brain
    - often called neural probes
      - surprisingly little damage to the brain tissue using micro-electrode arrays
- Recorded fluctuating potentials represent a superposition of the field potentials produced by a variety of active neuronal current generators within the volume conductor medium
  - although neural probes can record single neuron events

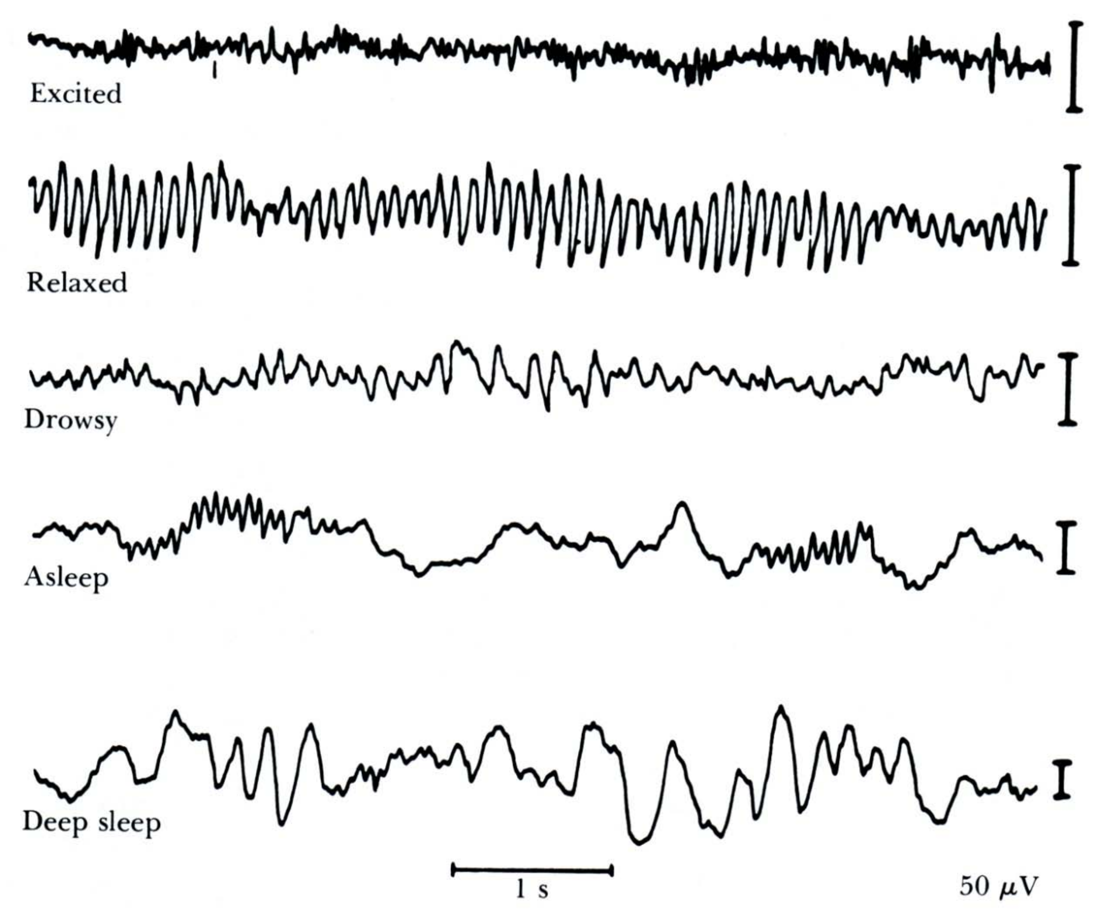
Bioelectric Potentials from the Brain

- Recorded potentials from the brain are called brain waves
  - Entire record is called electroencephalogram (EEG)
- Brain recordings demonstrate continuous oscillating electric activity
  - <u>Intensity</u> and <u>pattern</u> of recording are determined by the overall excitation of the brain
- Alpha waves
  - occur when the subject is awake but rested
- Beta waves
  - occur during intense mental activity
- Theta wave
  - emotional stress, disappointment
- Delta waves
  - occur in deep sleep or in serious brain disease



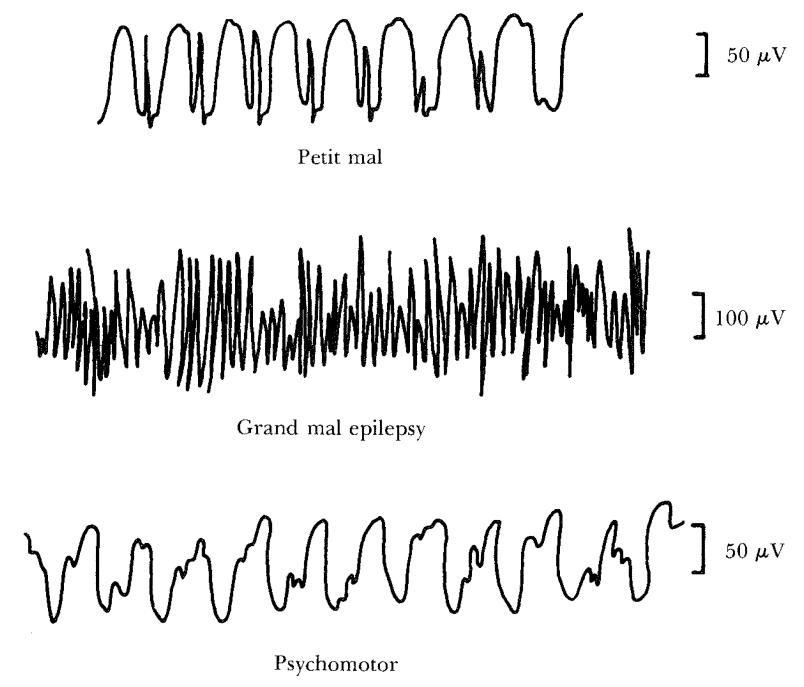
EEG Sleep Patterns

- Changes that occur as a human subject goes to sleep
  - Alpha rhythms dominate when the subject is relaxed



Abnormal EEG Waveforms

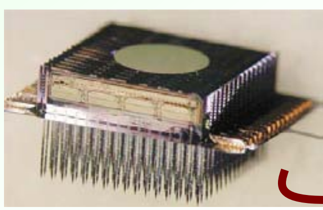
- Clinical EEG is used for diagnosis of different forms of epilepsy
- Epilepsy
  - uncontrolled excessive activity by either a part or all of the central nervous system
  - General epilepsy: involves the entire brain at once
  - Grand mal: person looses consciousness
  - Petit mal: person retains consciousness



- EEG has also been shown to be useful for locating tumors

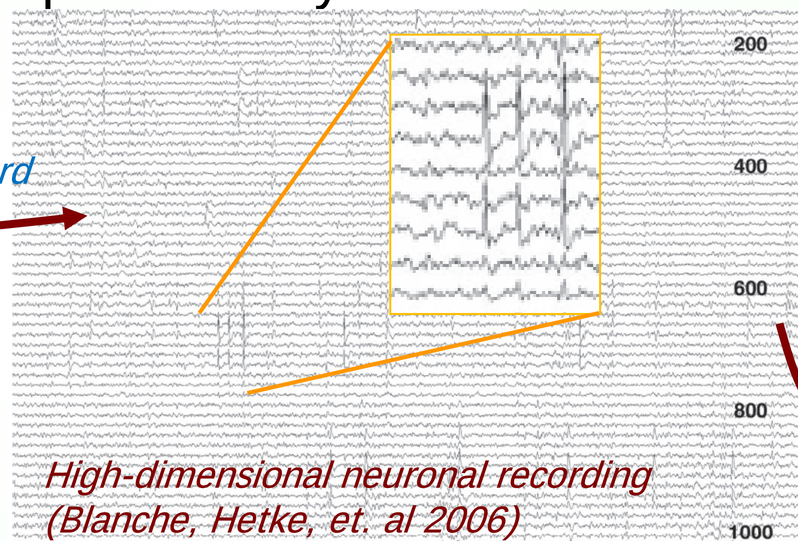
Neural Probes

- Brain is a volume conductor & recordings from scalp represent superposition of many (~millions) of individual neural events
- Neural probes
  - needle-like micro-electrode arrays (MEA) placed into the cerebrum through small openings in the scalp
  - can record individual neural events
  - part of Brain-Machine Interface (subject of later guest lecture)
  - element of neural prosthetic system



1024 Channel (MEA)
(Wise et. al 2005)

Record



High-dimensional neuronal recording
(Blanche, Hetke, et. al 2006)

Control

Prosthetic arm