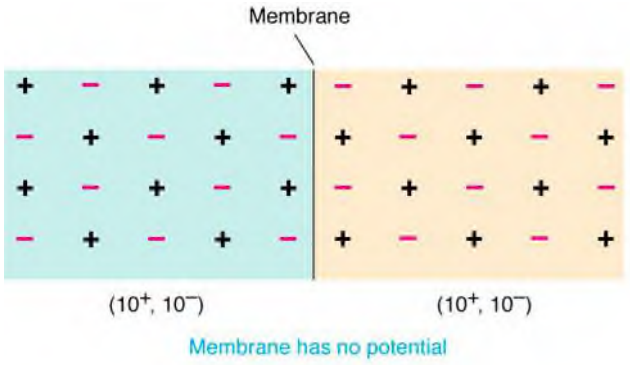
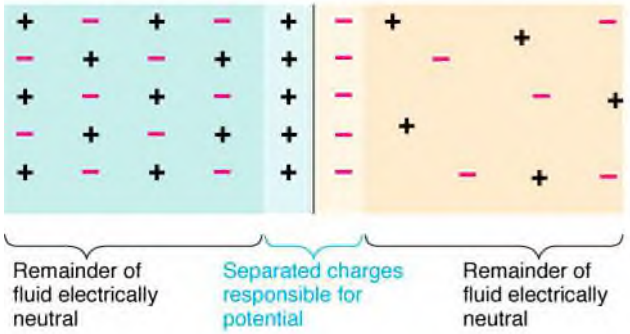
ECE 370
Introduction to Biomedical Engineering

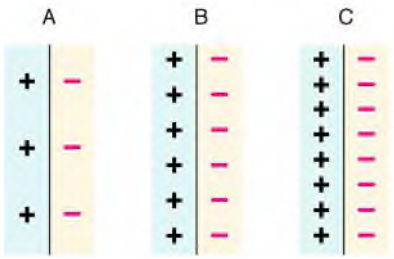
Bioelectricity

Membrane Potential

- **Opposite charges attract and similar repel**
- **Membrane potential → opposite charges across the membrane**
  - Equal number of + and – on each side → electrically neutral
  - Charges separated (more + on one side, more – on other) → electrical potential
  - Measured in V
    - More charge → ↑ V
- **Note:**
  - Only a very small number of charges is involved → majority of ECF and ICF is still neutral

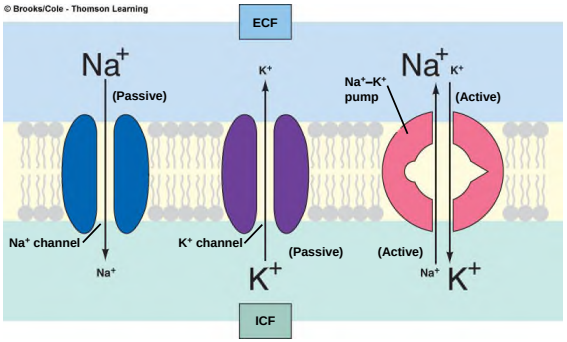






Membrane Potential

- **All cells are electrically polarized**
- **Ions flow through leakage channels**
  - Concentration gradient vs. Electrical Gradient
  - Tend to go to their equilibrium potential (Nerst equation)
    - Na+ ~ +30 mV
    - K+ ~ -90mV
- **Resting membrane potential**
  - Total potential at steady state → combination of all ions (~70 mV)
    - A- trapped only in cells
    - Na+ and K+ not at equilibrium → can diffuse through leakage channels (K+>Na+)
    - Concentration of Na+ and K+ maintained by Na+-K+-pump (most critical role) → requires continuous expenditure of energy



ION	Concentration (millmoles/liter)		Relative Permeability
	Extracellular	Intracellular	
Na^+	150	15	1
K^+	5	150	50-75
A^-	0	65	0

$$E = \frac{RT}{zF} \ln \frac{C_o}{C_i}$$ Nerst Equation

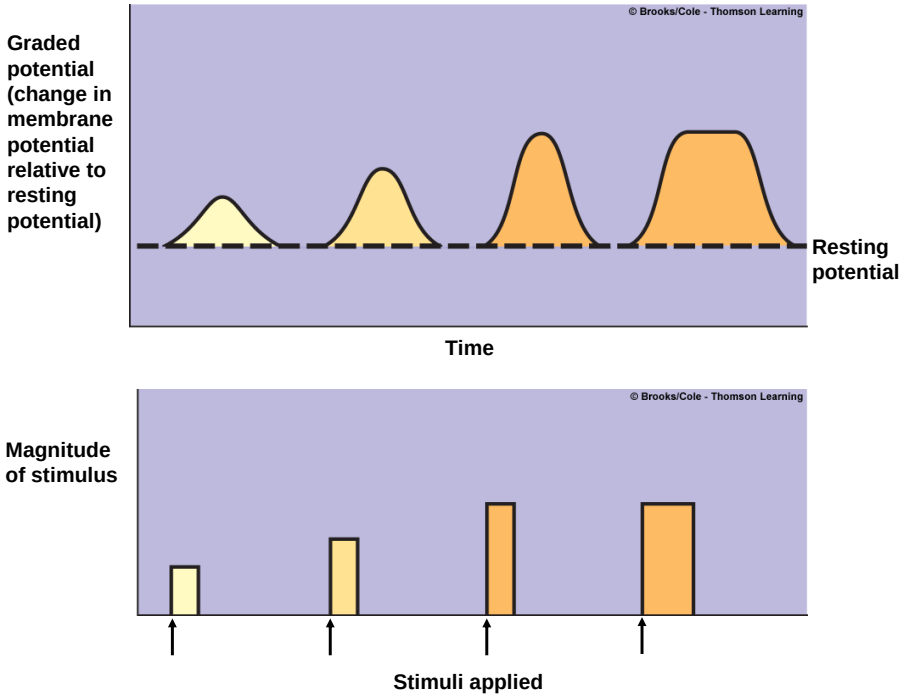
$$E = \frac{RT}{F} \ln \frac{\sum P_{C^+}[C^+]_o + \sum P_{A^-}[A^-]_i}{\sum P_{C^+}[C^+]_i + \sum P_{A^-}[A^-]_o}$$

GHK (Goldman-Hodgkin-Katz) eq.
(for monovanent molecules)

R: gas constant = 8.314472 (Volts Coulomb)/(Kelvin mol)
F: Faraday constant = 96 485.3383 (Coulomb)/(mol)
z: Valance
T: Absolute temperature = 273.16 + ^oC (Kelvin)

Graded Potentials

- **Local changes in membrane potential**
  - Confined to a small area
  - Remaining cell is still at resting potential
  - Triggered by specific events
    - E.g. sensory stimuli, pacemaker potentials, etc
  - Gated channels (usually Na+) open
  - Magnitude and duration proportional to triggering event

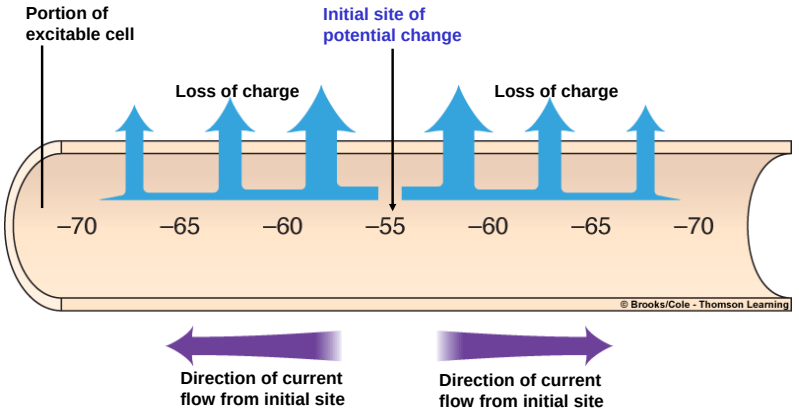


Graded Potentials

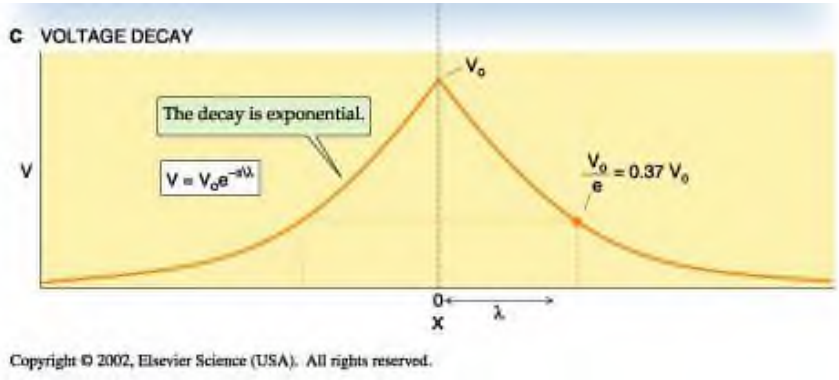
- **Graded potentials die out over short distances**
  - Loss of charge
  - Magnitude decreases as it moves away from the point of origin
  - Completely disappear with a few mm

$$V = V_0 e^{-\frac{x}{\lambda}} \qquad \lambda = \sqrt{\frac{r_m}{r_i}}$$

  - r_i inversly proportional to cross-sectional area
    - ↑ diameter → ↓r_i
  - ↑ r_m → better flow along the axis due to decrease loss of ions through the membrane

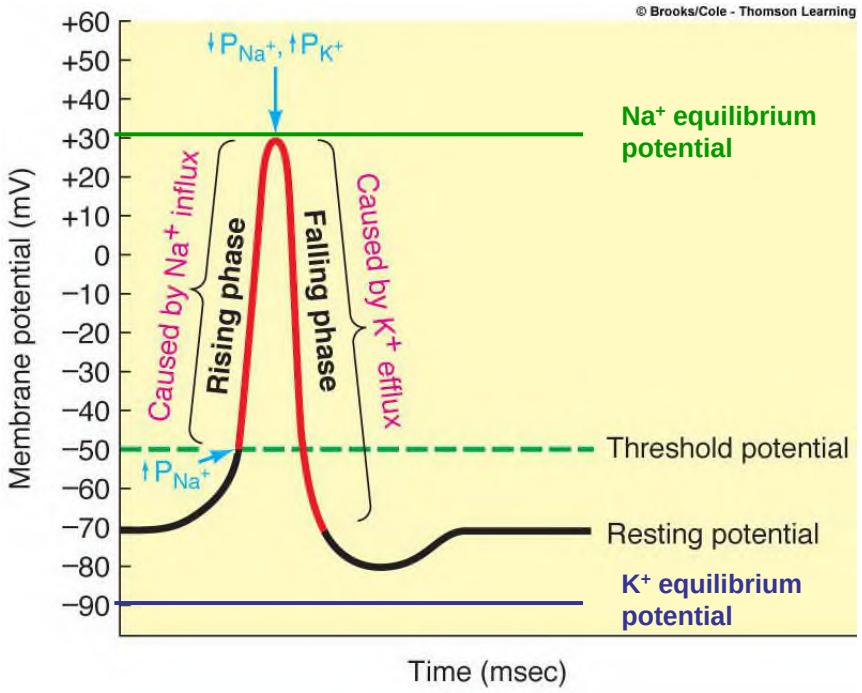


* Numbers refer to the local potential in mV at various points along the membrane.



Action Potentials

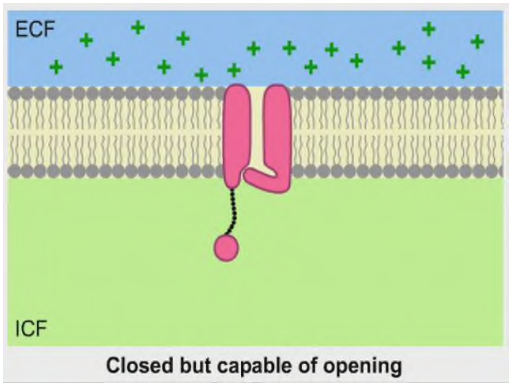
- **Large (~100 mV) changes in the membrane potential**
  - Can be initiated by graded potentials
  - Unlike graded potentials action potentials propagate
  - Transmit information
- **Changes during an action potential**
  - Gradual depolarization to threshold potential (-50 to -55 mV)
    - If not reached no action potential will occur
  - Rapid depolarization (+30 mV)
    - Opening of voltage gated Na+ channels
  - Rapid repolarization leading to hyperpolarization (-80 mV)
    - Inactivation of Na+ channels, opening of voltage gated K+ channels
  - Resting potential restored (-70 mV)
    - All voltage gated channels closed
- **Constant duration and amplitude for given cell type (“all-or-none”)**
  - E.g. Nerves → 1 msec



Action Potentials

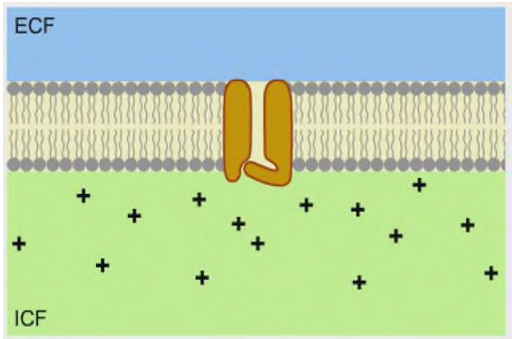
- **AP are a result of changes in ion permeability**
  - Voltage-gated channels
    - Proteins which change conformation depending on potential
    - Allow passage of ions
    - Voltage-gated Na+ channels
      - Activation (immediate) and inactivation gates (delayed)
    - Voltage-gated K+ channels
      - Activation gate (delayed)

Voltage-gated Na^+ channels



Closed but capable of opening

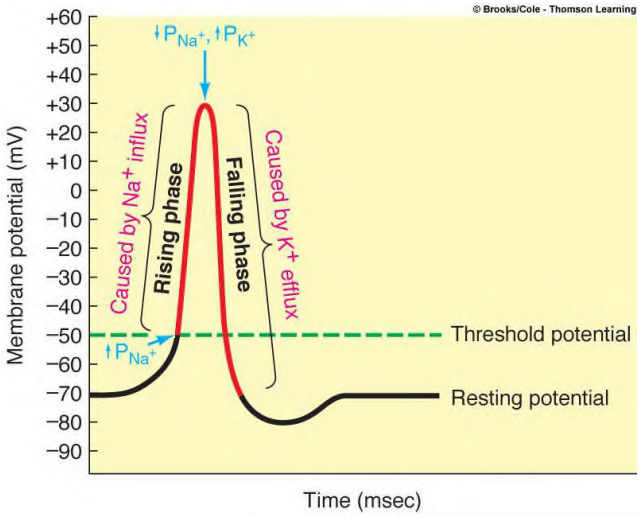
Voltage-gated K^+ channels

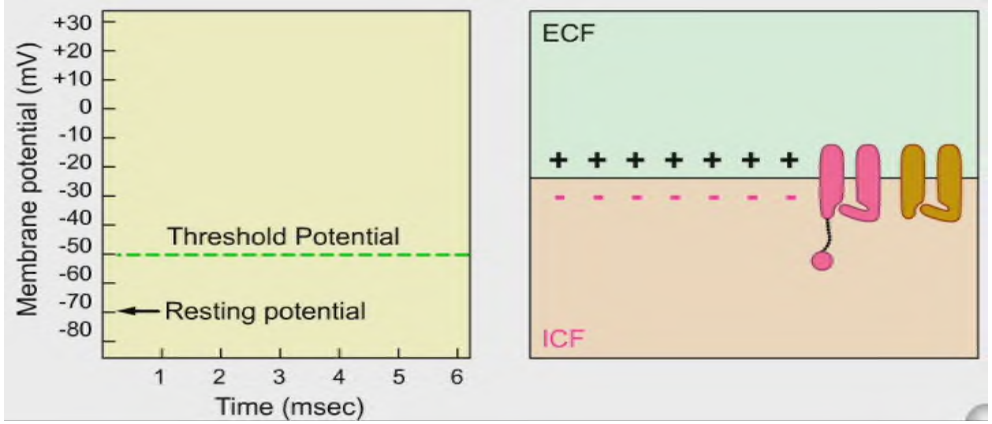


Closed

Action Potentials

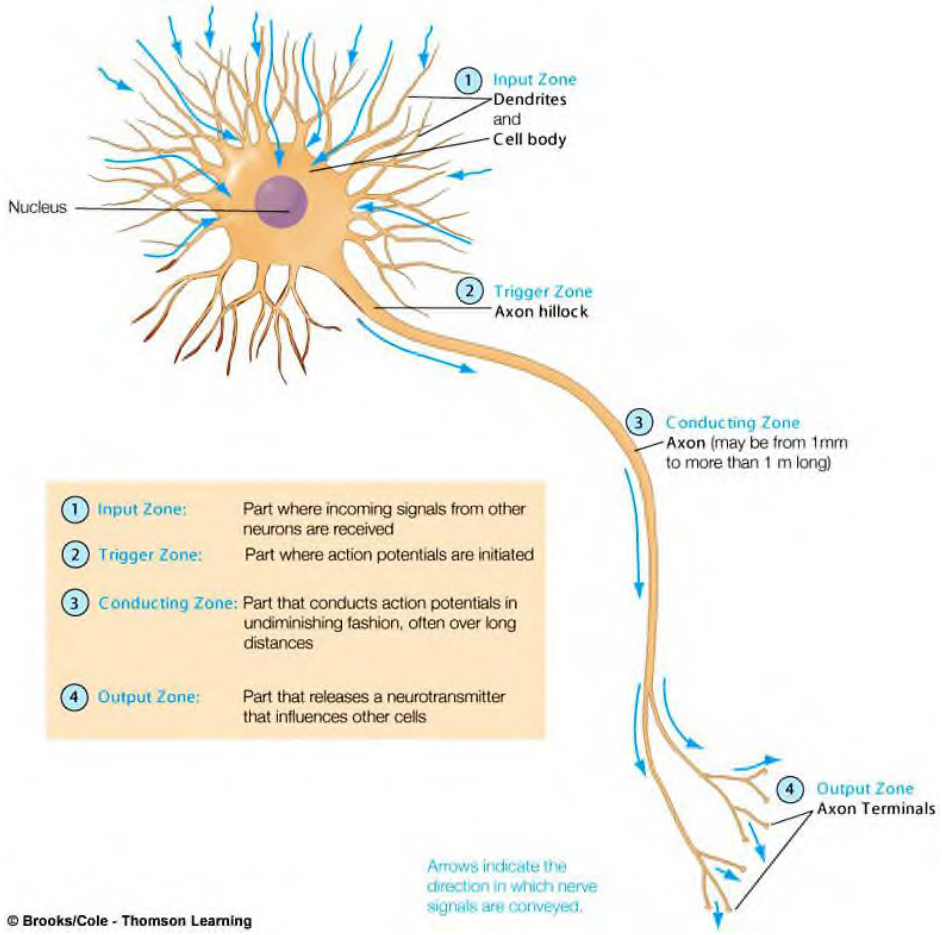
Time	Event	Potential
0 msec	Resting state All channels are closed Graded potential arrives Begins depolarization	**- 70 mV**
2 msec	Threshold reached Activation gates of Na+ channels open Activation gates of K+ channels begin to open slowly Inactivation gates of Na+ channels begin to close slowly	**- 50 mV**
2.5 msec	Peak potential reached Inactivation gates of Na+ channels are now closed Activation gates of K+ channels are now open	**30 mV**
3.75 msec	Hyperpolarized state Activation gates of K+ channels close	**- 80 mV**
5 msec	Resting state Na+-K+-pump restores resting potential Na+ channels are reset to close but active	**-70 mV**





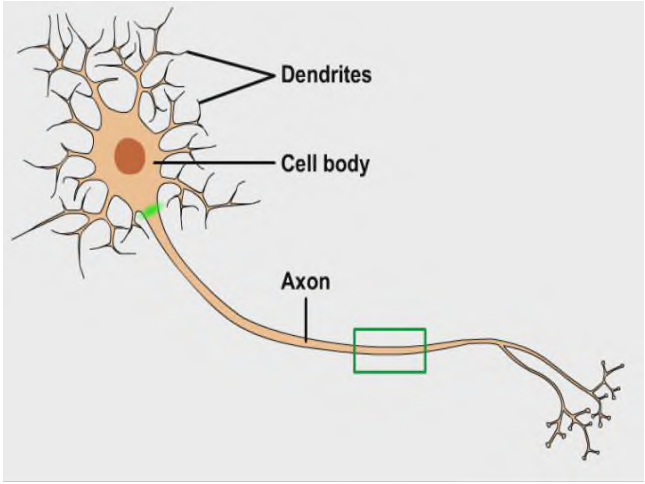
Action Potentials

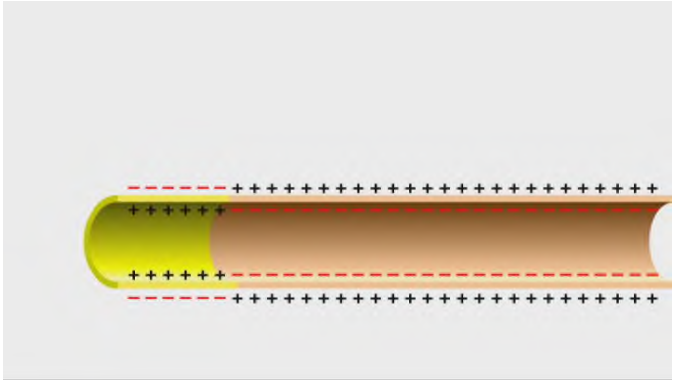
- **Neuron structure**
  - Input Zone
    - Dendrites (up to 400 000)
    - Cell Body
    - Have receptors which receive chemical signals
  - Conduction zone
    - Axon or nerve fiber (axon hillock to axon terminals) <1 mm to >1m
  - Output zone
    - Axon terminal
- **Input**
  - Graded Potentials
  - Generated in the dendrites as a response to chemical signals
  - Can trigger action potentials in the axon



Action Potentials

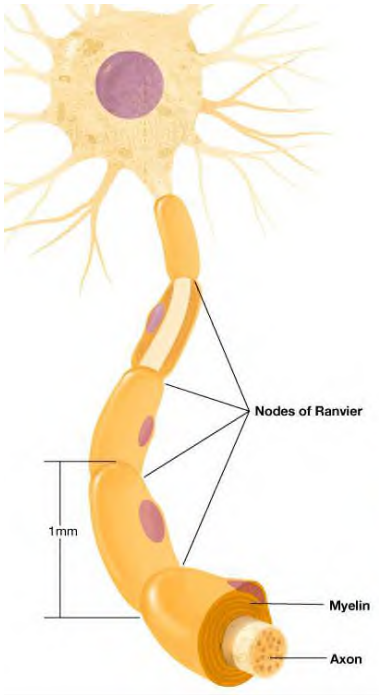
- **AP Propagation**
  - APs initiated at the axon hilloc
    - More voltage-gated channels → lower threshold
  - Once initiated the AP travels the entire axon
    - Contiguous conduction
    - Saltatory conduction
  - Contiguous conduction
    - Flow of ions → depolarization of adjacent area to threshold
    - As AP is initiated in adjacent area, the original AP is ending with repolarization
    - The AP itself does not travel, it is regenerated at successive locations (like “wave” in a stadium)

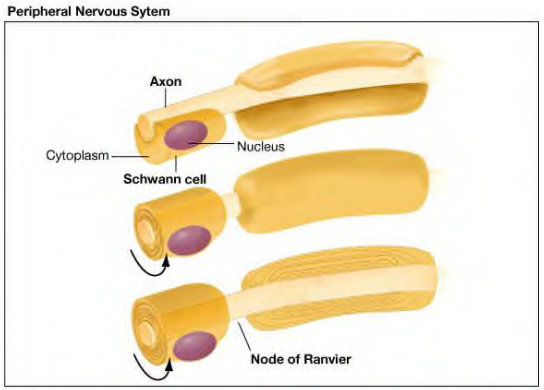


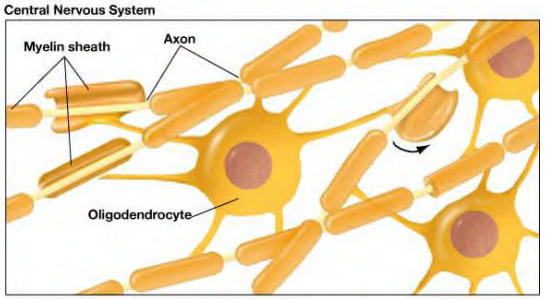


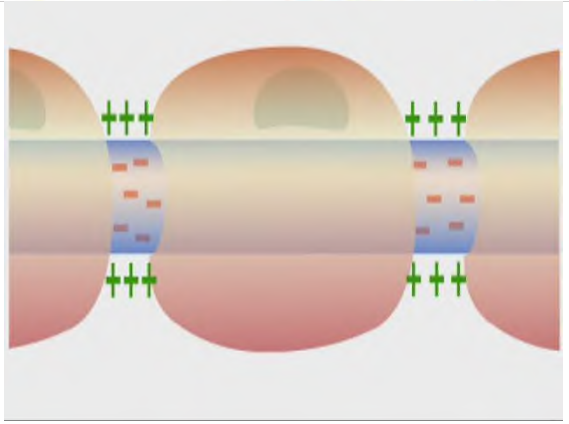
Action Potentials

- **Saltatory Propagation**
  - Some neurons are myelinated
    - Covered with myelin (lipid barrier)
    - No ion movement across myelinated areas
  - Nodes of Ranvier
    - Areas between myelin sheaths
    - Ions can flow → APs can form
  - APs "jump" from node to node → information travels 50x faster, less work by pumps to maintain ion balance
  - Loss of myelin can cause serious problems
    - E.g. multiple sclerosis



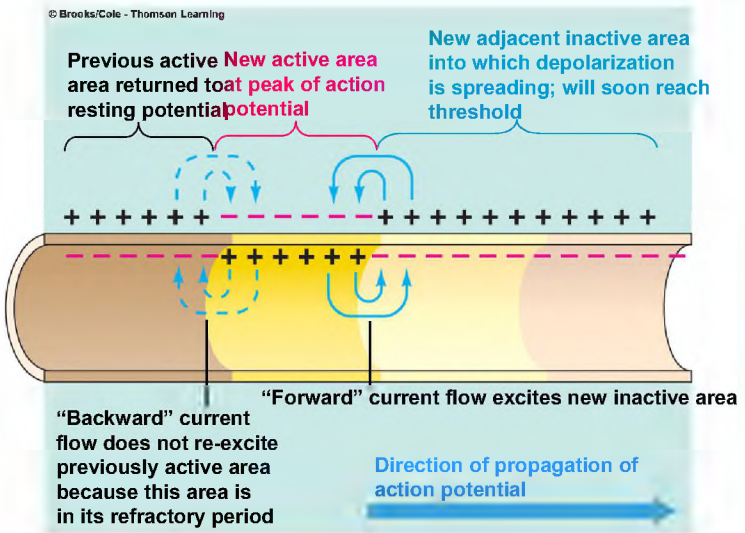


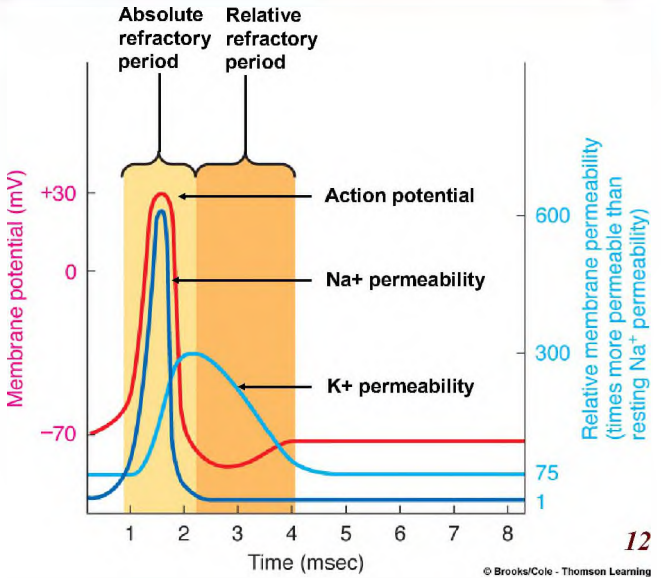




Action Potentials

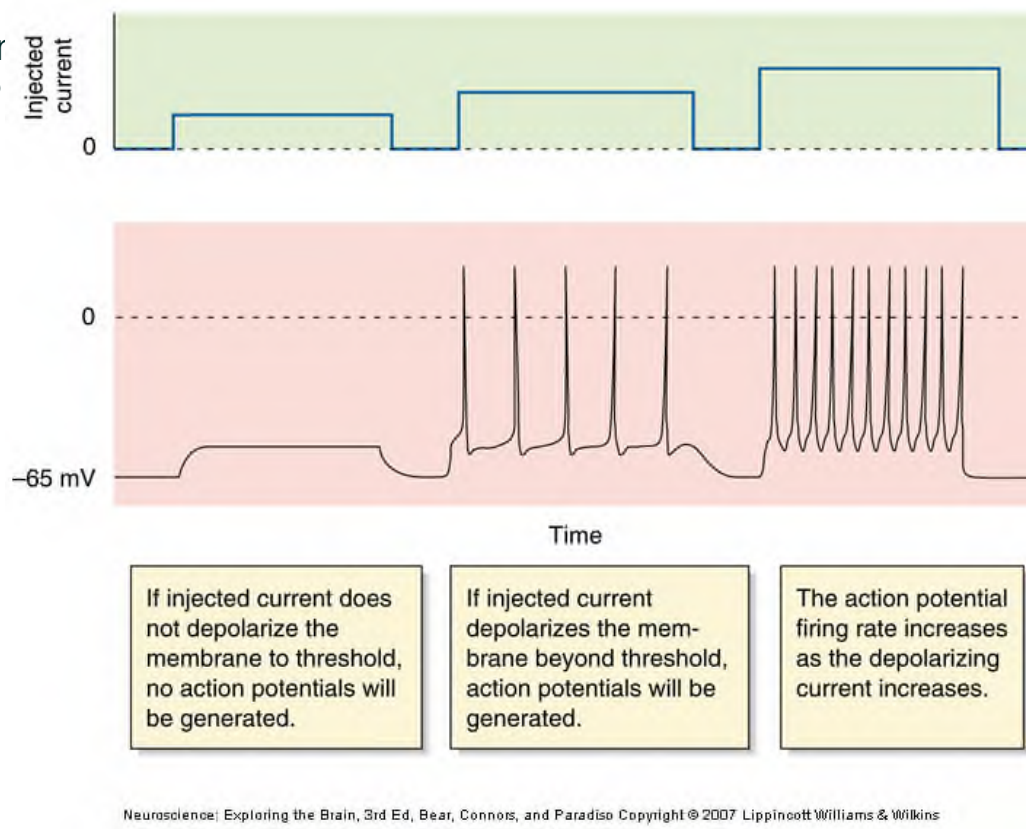
- **Refractory Period**
  - APs do not travel backwards
    - Local currents do not regenerate an AP in the previously-active-now-inactive area
  - Certain time must pass before a second AP can be triggered → ***refractory period***
  - Absolute refractory period
    - During an AP
    - No APs can be triggered
  - Relative refractory period
    - Na^+ channels are mostly inactive
    - K^+ channels are slow to close
    - After an AP → second AP can be triggered only be exceedingly strong signals
  - Refractory period sets an upper limit to the frequency of APs →~2.5 KHz





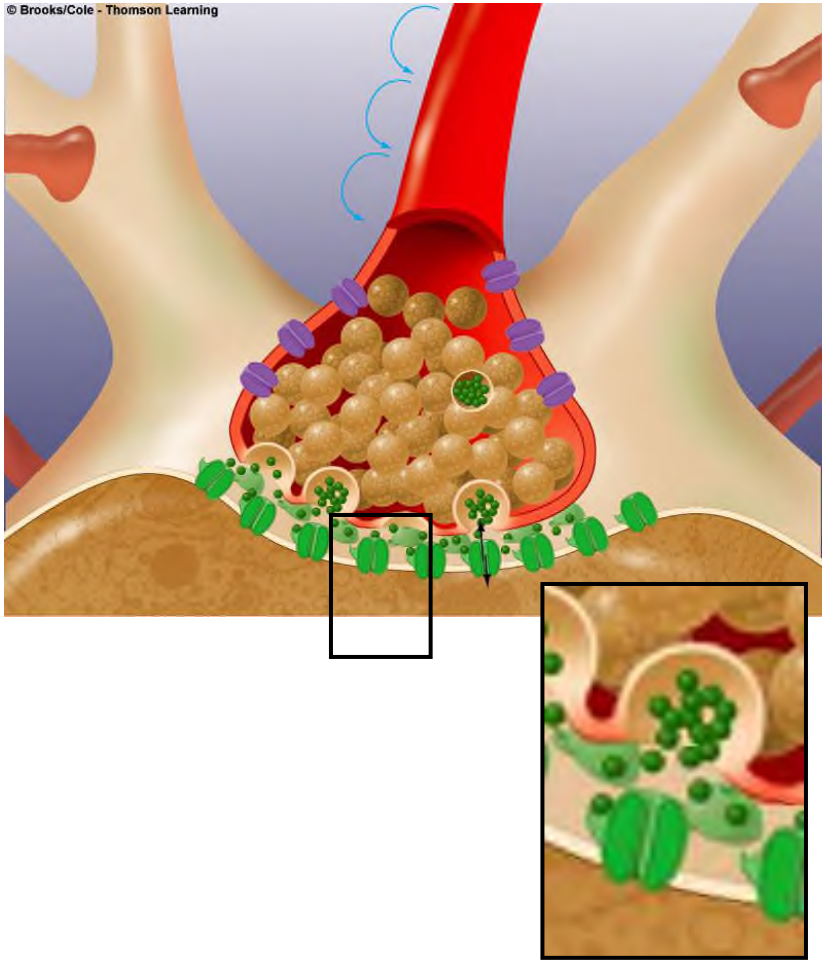
Action Potentials

- **Characteristics of APs**
  - How does strength vary?
    - Always the same! → All-or-None Law
    - Does not decrease during propagation
  - How are stronger stimuli recognized?
    - Faster generation of APs → ↑Frequency
    - More neurons fire simultaneously
  - What determines the speed of APs?
    - Myelination
    - Neuron diameter (↑ diameter →↓ Resistance to local current → ↑ Speed)
    - Large myelinated fibers: 120 m/sec (432 km/hr) → urgent information
    - Small unmyelinated fiber: 0.7 m/sec (2.5 km/hr) → slow-acting processes
    - Without myelin the diameter would have to be huge! (50 x larger)



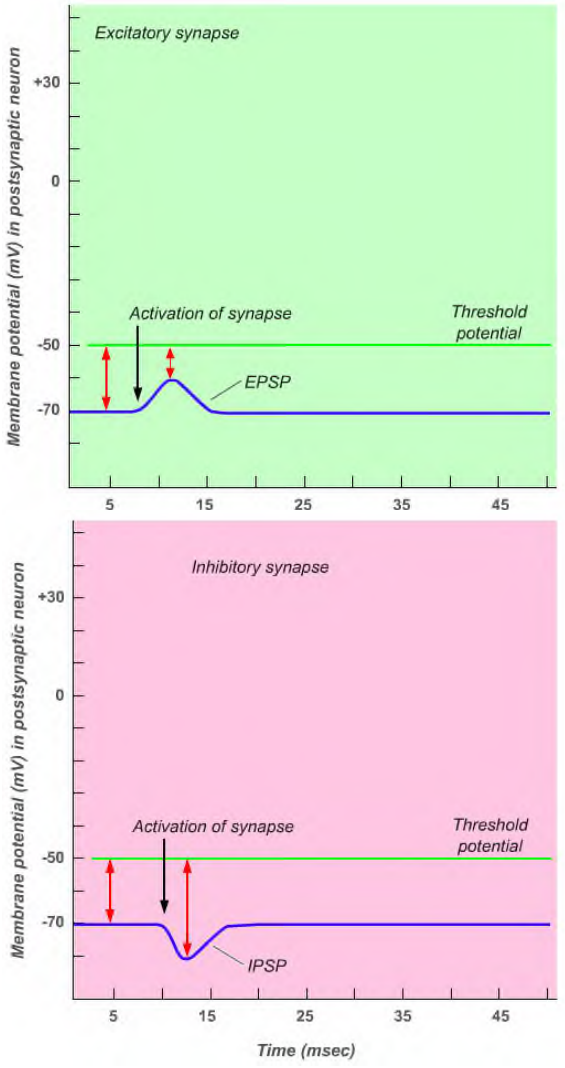
Synapses and Integration

- **Synaptic Signaling**
  - AP reaches the synaptic knob
  - Voltage-gated Ca2+ channels open
  - Ca2+ flows into the synapse from the ECF
  - Ca2+ induces exocytosis of vesicles and release of neurotransmitter
  - Neurotransmitter diffuses across the synaptic cleft to the post-synaptic neuron and binds to specific receptors
  - Binding triggers opening of ion channels
    - Cause permeability changes of different ions
    - Can be
      - excitatory (cations) → depolarization, or
      - inhibitory synapses (anions) → hyperpolarization



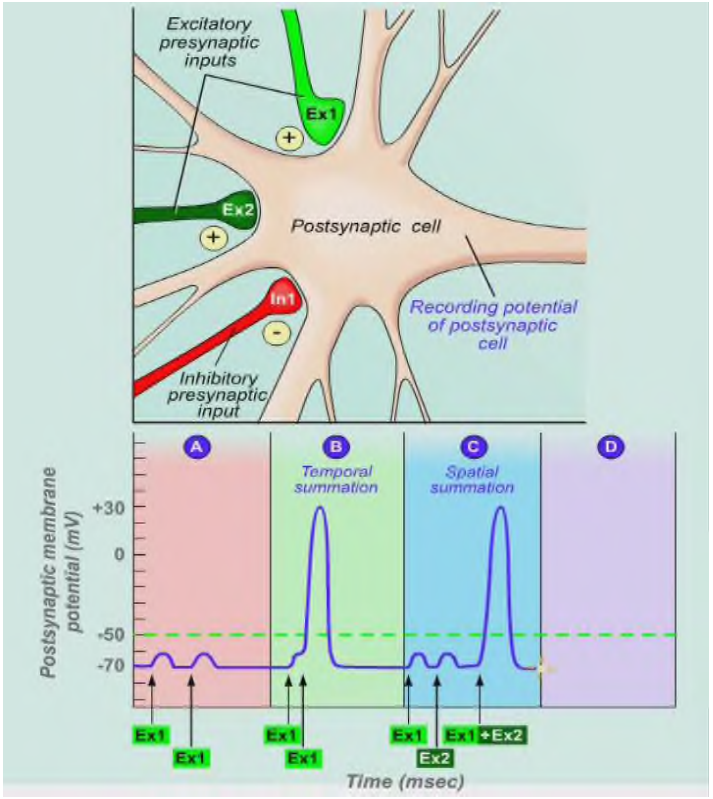
Synapses and Integration

- **Excitatory Synapses**
  - Open non-specific cation channels
  - More Na+ flows into the cell than K+ flows out
  - Net result → Excitatory Postsynaptic Potential (a small depolarization)
- **Inhibitory Synapses**
  - Different neurotransmitters
  - Open either K+ or Cl- channels
  - K+ efflux or Cl- influx → Inhibitory Postsynaptic Potential (a small hyperpolarization)
- **Usually one EPSP is not enough to trigger an AP**
  - Membrane is now more excitable
- **Synaptic Delay**
  - 0.5 to 1 msec
  - Travel through more synapses → ↑Total reaction time



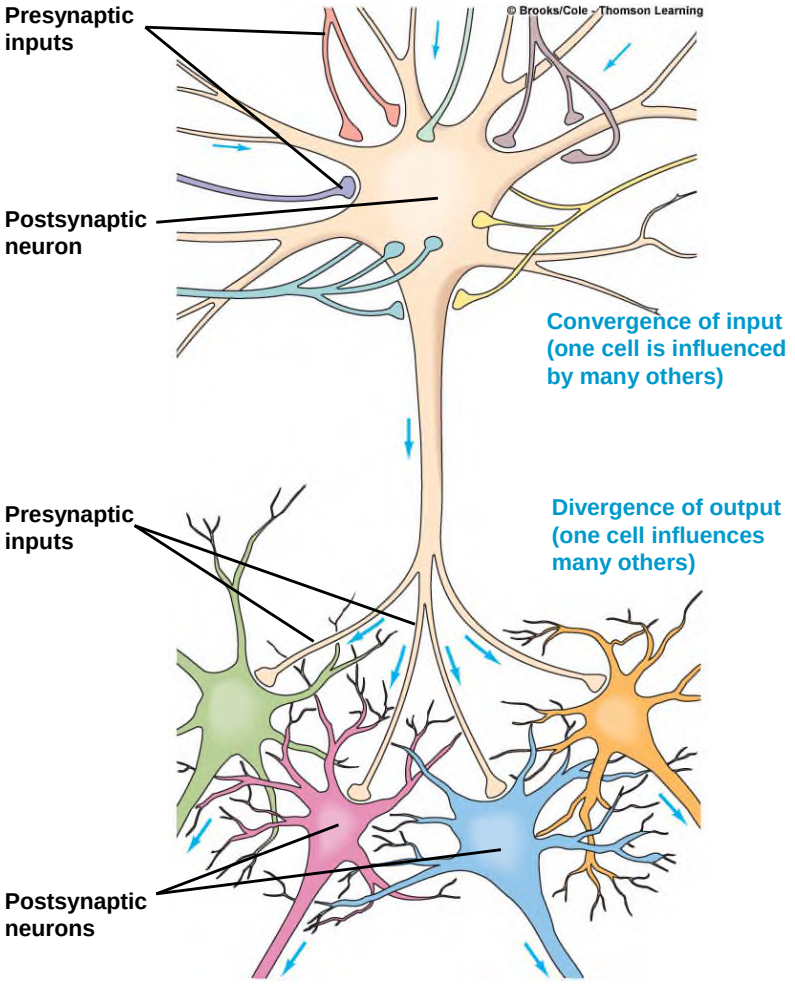
Synapses and Integration

- **Grand Postsynaptic Potential (GPSP)**
  - Summation of EPSPs and IPSPs (graded potentials)
  - About 50 EPSPs are required to initiate AP
  - Temporal Summation
    - EPSPs occurring very close in time can be summed
    - E.g. repeated firing of pre-synaptic neuron because of a persistent input
  - Spatial Summation
    - EPSPs from different but adjacent synapses can be summed
  - Concurrent EPSPs and IPSPs
    - Cancel each other (more or less) depending on amplitude and location



Synapses and Integration

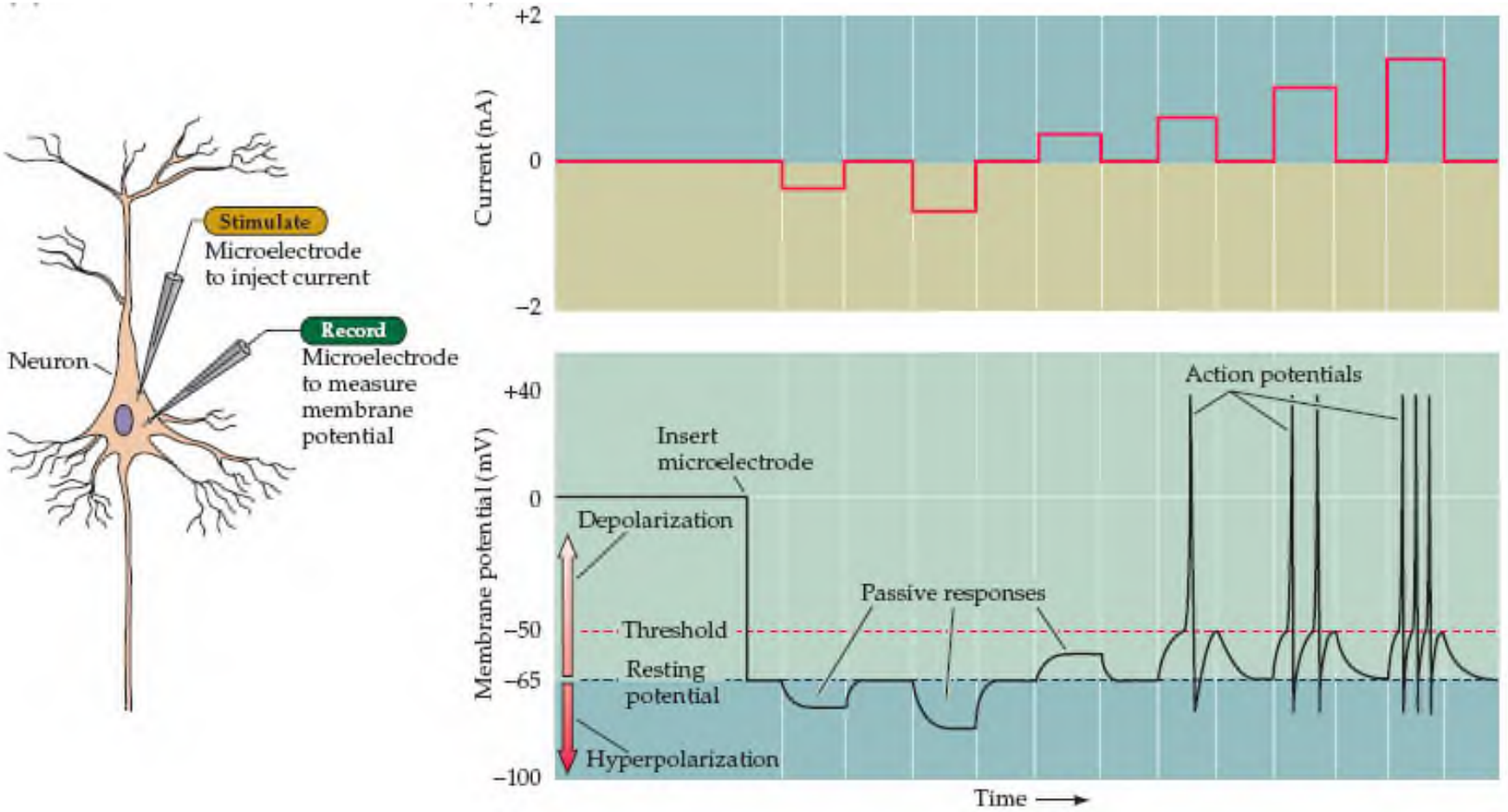
- **Post-synaptic Integration**
  - APs are initiated depending on a combination of inputs
  - Neuron is a complex computational device
    - Synapses = inputs
    - Dendrites = processors
    - Axons/APs = output
  - Signaling and frequency of APs is a result of integration of information from different sources
  - Information not significant enough is not passed at all
  - Neurons are linked into complex networks (10^{11} neurons and 10^{14} synapses in the brain alone!)
    - Converging
    - Diverging
    - Massively parallel processing



Arrows indicate direction in which information is being conveyed.

Bioelectricity of a Single Neuron

- **Response to Current Injection**



Hodgin & Huxley

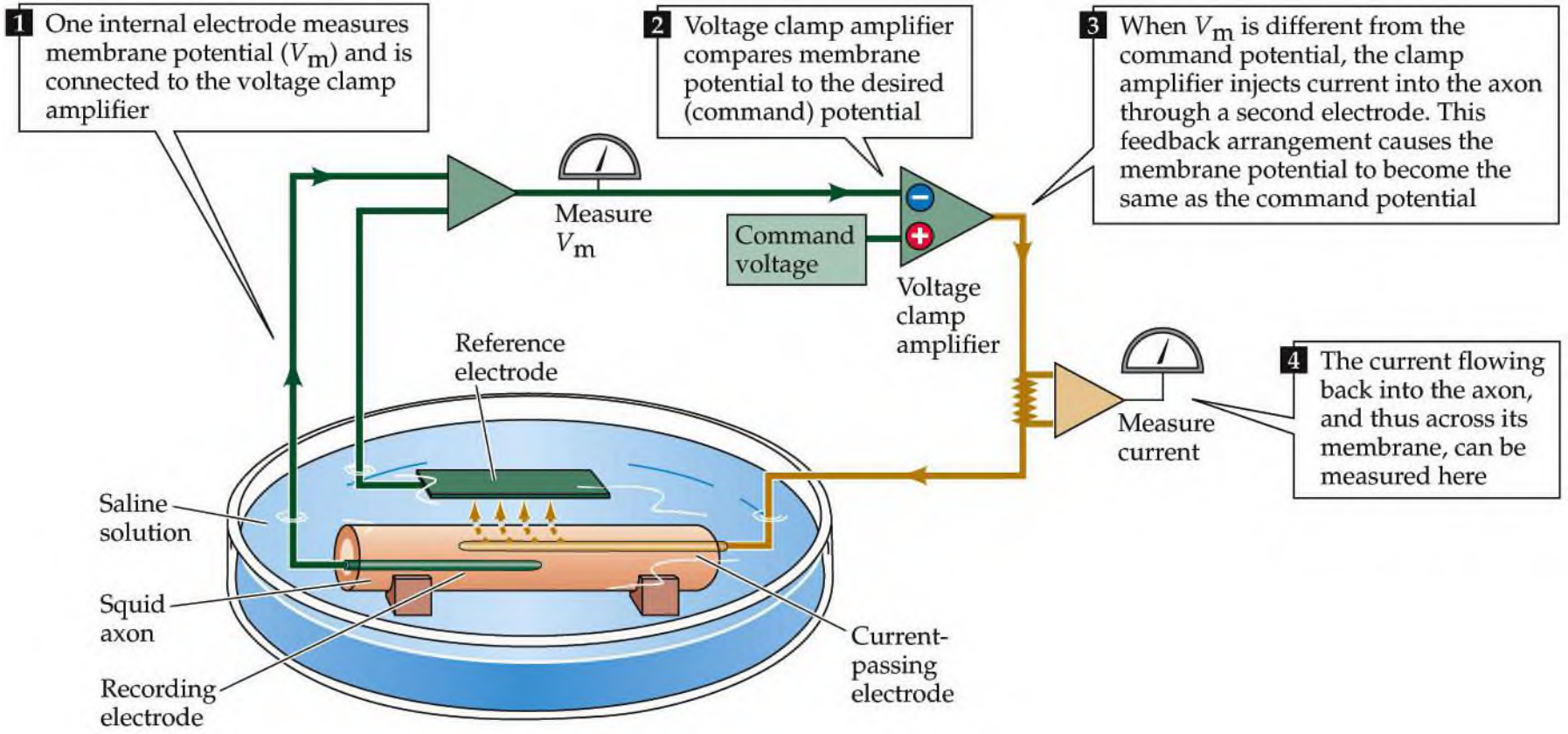
- **Sir Alan Lloyd Hodgkin and Sir Andrew Huxley**
  - Described the model in 1952 to explain the ionic mechanisms underlying the initiation and propagation of action potentials in the giant axon of squid.
- **The model was proposed long before the channel mechanisms were known clearly.**
  - Amazing!
- **This work was recognized by the Nobel prize.**

Hodgkin

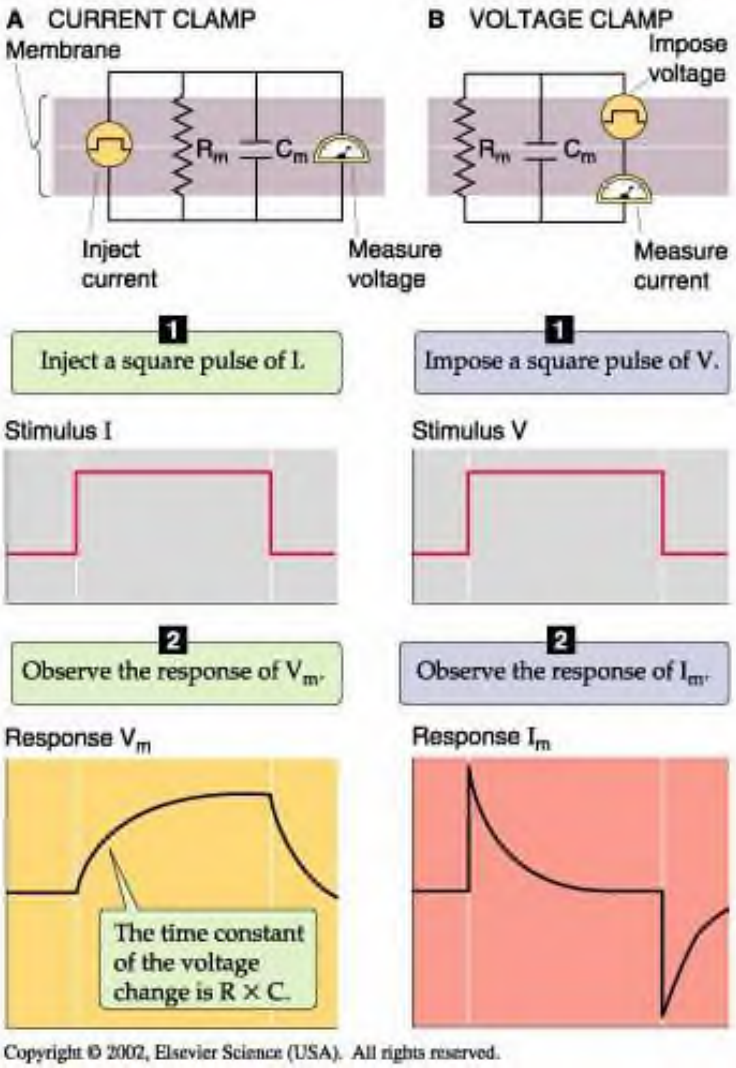
Huxley

The Voltage Clamp Method

- **Electronic feedback circuitry to fix membrane potential & measure the required current (or vice versa for current clamp)**



Passive membrane properties



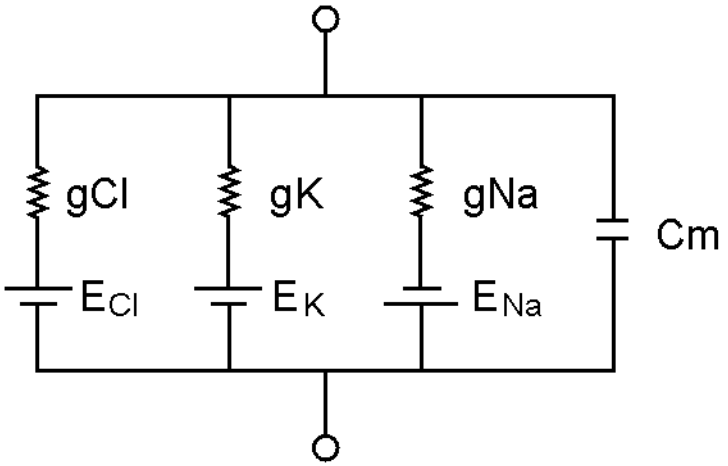
- **Under voltage clamp, the passive response includes:**
  - capacitive current, which flows only at the step onset and offset
  - resistive current (through leak channels), also given by Ohm's law (I = V/R)
- **Under current clamp, the passive response to current injection is a function of the RC characteristics of the membrane**
  - V = IR (Ohm's law) gives the steady state voltage
  - t = RC (gives the kinetics)

Equivalent electrical circuit model

- **Unequal distribution of ions and differential resting conductances of those ions**
  - Use the Nernst equation
  - Combine with Ohm's law
  - An equivalent circuit model to predict a stable resting membrane potential
    - -75 mV seen in many cells
- **This is a steady state and not an equilibrium**
  - K+ and Na+ are **not** at their equilibrium potentials
  - There is a continuous flux of those ions at the resting membrane potential

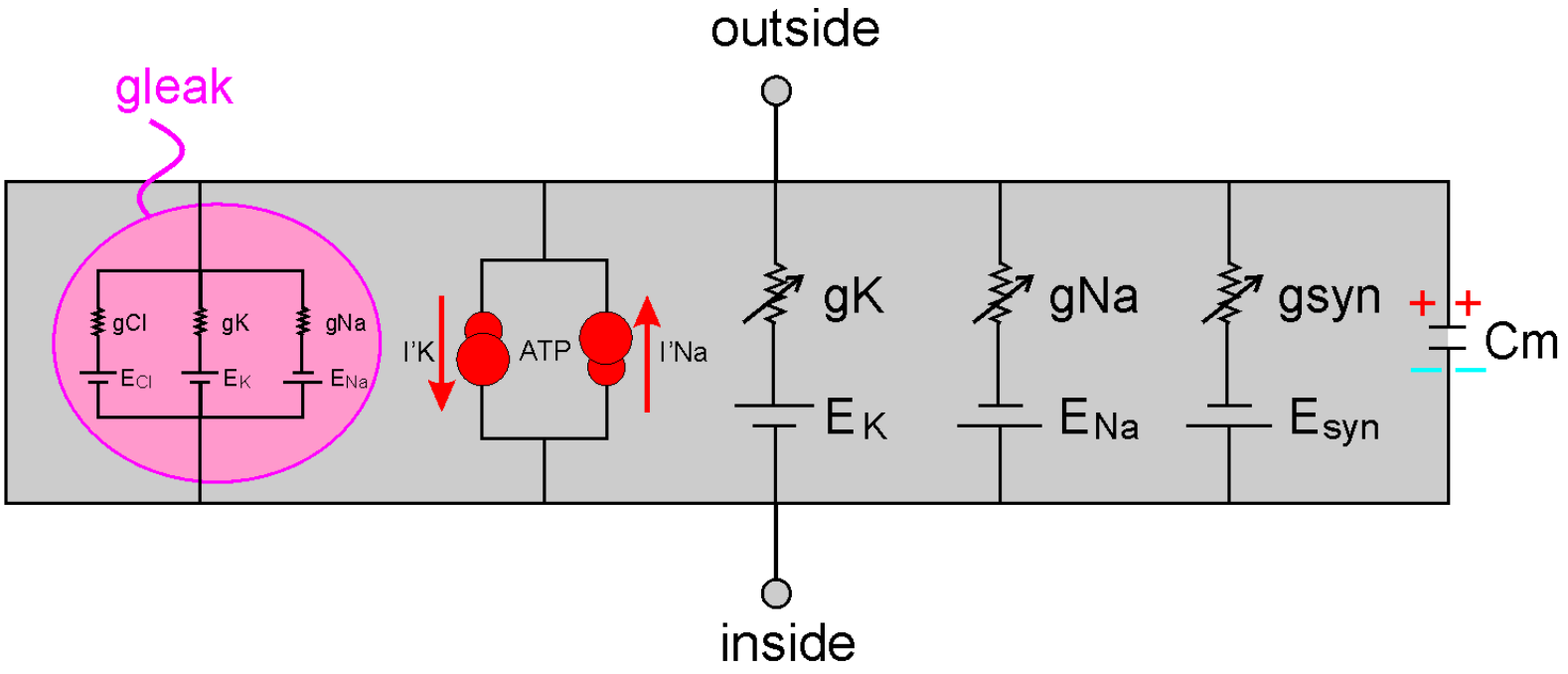
Resting Membrane Potential

$$E_m = \frac{(g_k E_k) + (g_{Na} E_{Na}) + (g_{Cl} E_{Cl})}{g_K + g_{Na} + g_{Cl}}$$



Equivalent electrical circuit model

- **More complete model**
  - Provide energy-dependent pump to counter the steady flux of ions
  - Add voltage-gated K+ and Na+ channels for electrical signaling
  - Add ligand-gated (e.g. synaptic conductances)
  - Obviously, much greater complexity could be imagined



Na+ and K+ conductance in the AP

- **Hodgkin & Huxley used their empirical measures to model Na+ and K+ currents:**

$$I_{Na} = m^3 h \bar{G}_{Na} (V_m - E_{Na}) \qquad I_K = n^4 \bar{G}_K (V_m - E_K)$$

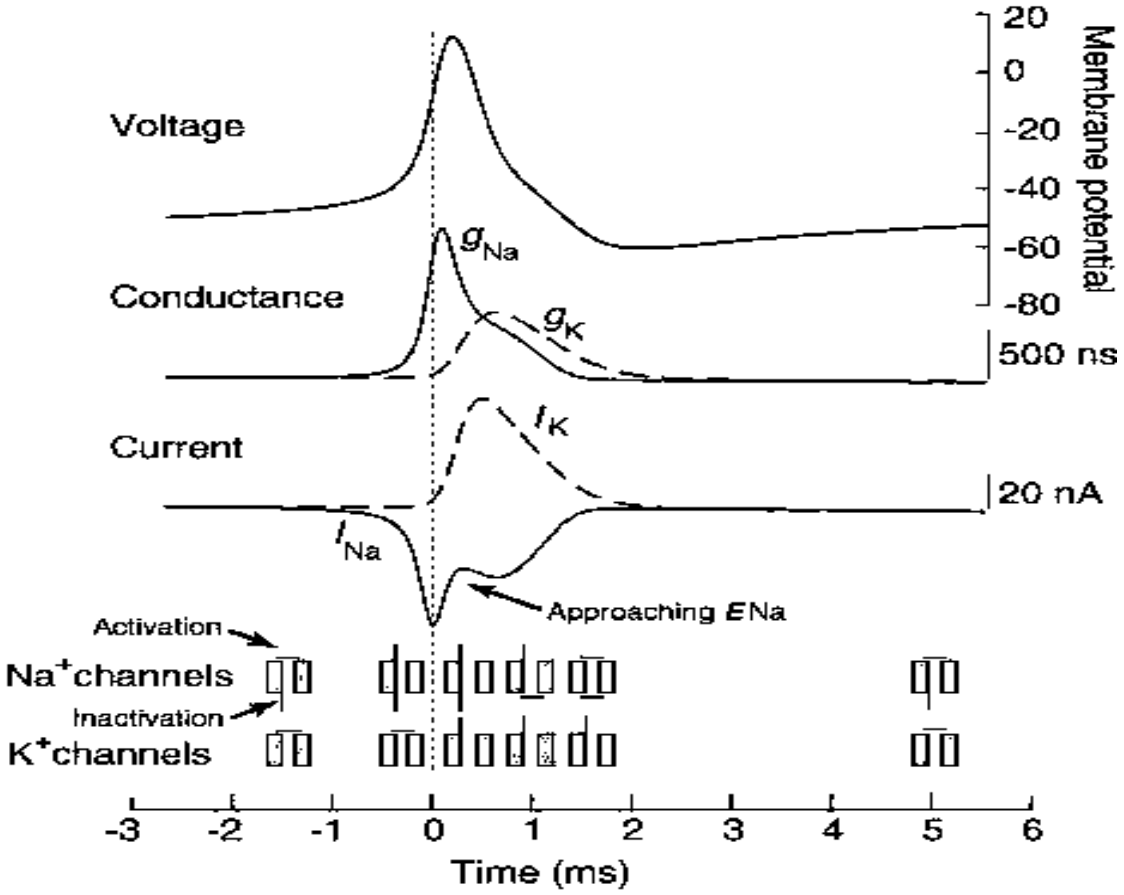
- **they developed an equation that predicts membrane potential based on the sum of capacitive and ionic currents:**

$$I_m = C_m (dV_m/dt) + \bar{G}_K n^4 (V_m - E_K) + \bar{G}_{Na} m^3 h (V_m - E_{Na}) + \bar{G}_L (V_m - E_L)$$

  - The n^4 term provides the pronounced delay in K+ current activation
  - The m^3 term is the Na+ current activation
    - The smaller exponent on the m term allows for faster Na+ current activation
  - The h term is the Na+ current inactivation

Na^+ and K^+ conductance in the AP

$$I_m = C_m\,(dV_m/dt) + \bar{G}_K\,n^4\,(V_m - E_K) + \bar{G}_{Na}\,m^3h\,(V_m - E_{Na}) + \bar{G}_L\,(V_m - E_L)$$



Very Little K^+ Flux Needed to Reach Equilibrium

Question: How much K^+ flows for the potential to reach equilibrium?

Answer: $q = CV = (C/A) \times A \times V$

$$\#\ K^+ \text{ ions} = q/q_e = (1\ \mu F/cm^2) \times 4\pi(10\ \mu m)^2 \times 58\ mV / 1.6 \times 10^{-19}\ C$$
$$= 4.6 \times 10^6 \text{ ions}$$

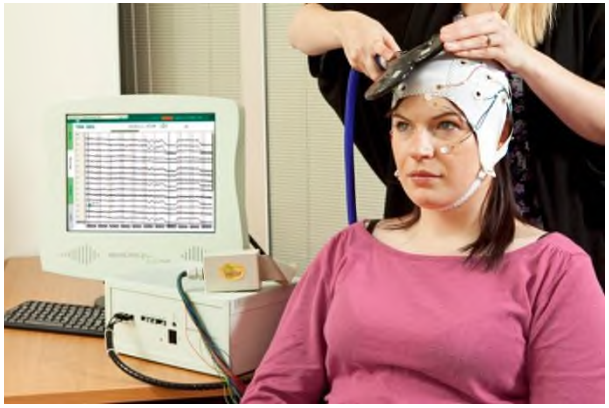
$$\text{Tot. } K^+ \text{ ions} = [K^+] \times N \times 4/3\pi(10\ \mu m)^3$$
$$= 3 \times 10^{11} \text{ ions}$$

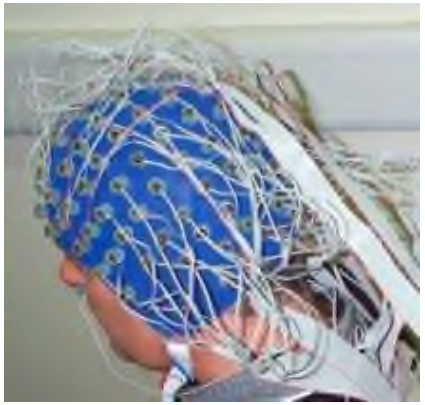
Implication:

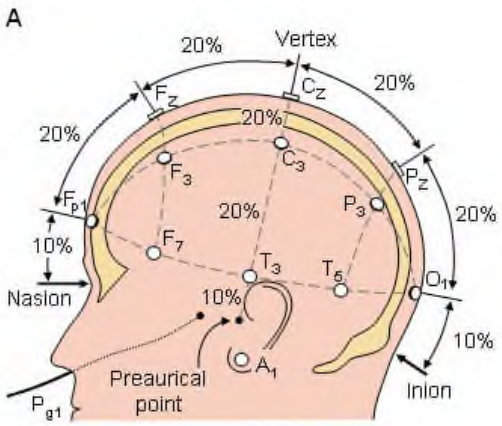
1. Need to move only a minute fraction of the ions to change V
2. Huge amount of energy stored in the ionic gradient (like a battery)

Electroencephalogram (EEG)

- **Bioelectricity of the brain**
  - Measures the brain's electric activity from the scalp
  - Measured signal results from the activity of millions of neurons
- **Measurement System**
  - 10-20 Lead system is most widely clinically accepted
  - Allow localization of diagnostic features in the vicinity of the electrode
  - Often a readily available wire or rubber mesh is used
  - Brain research utilizes even 256 or 512 channel EEG hats

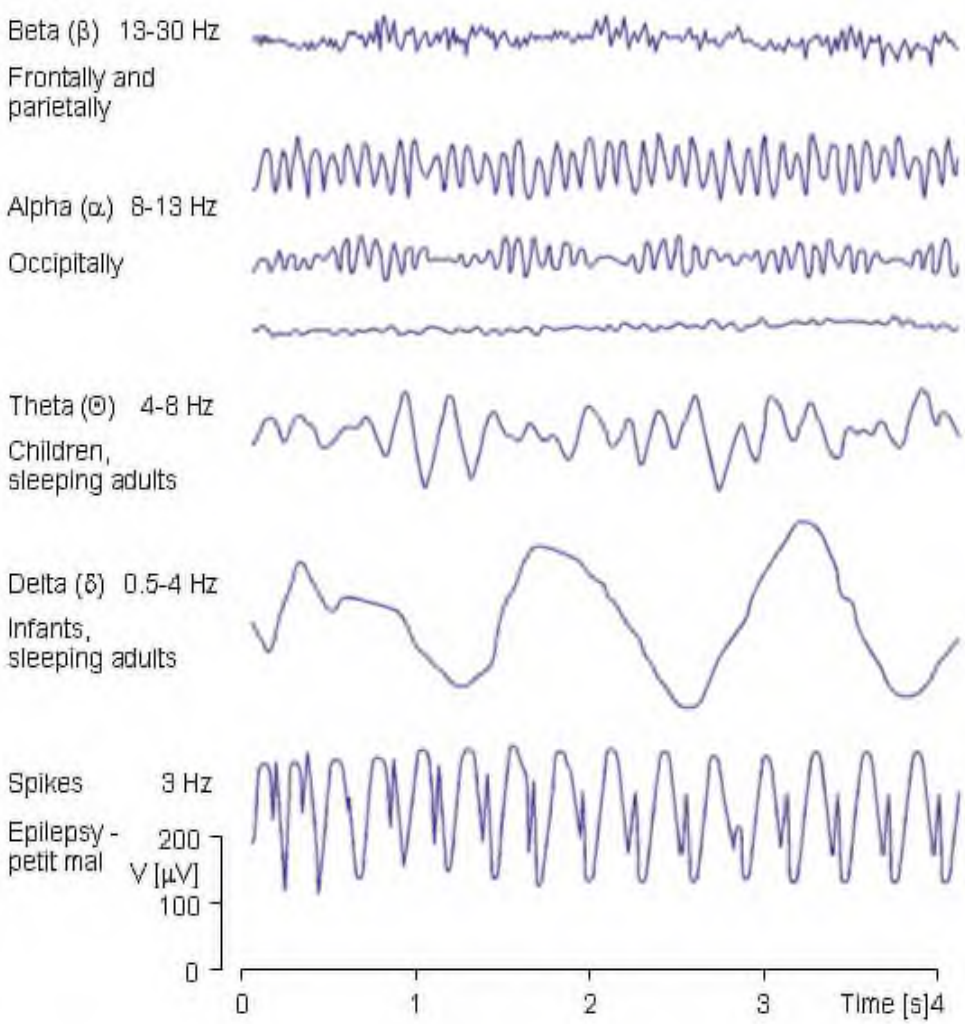






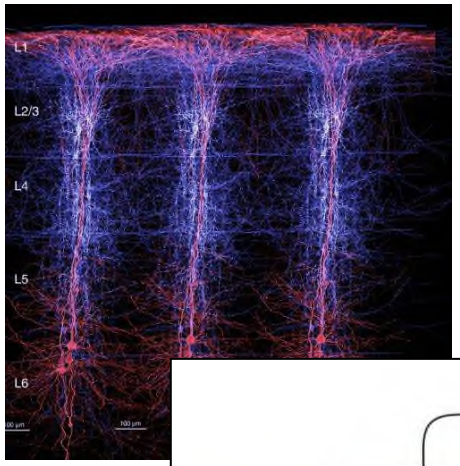
Electroencephalogram (EEG)

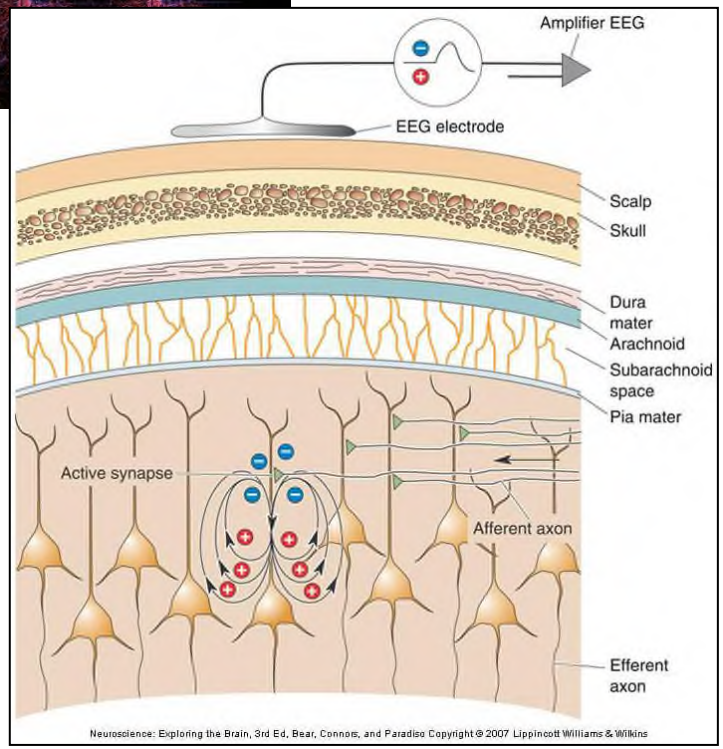
- **Waveforms**
  - Several characteristic patterns
  - Amplitude: 0.001-0.01 mV
  - Bandwidth: 0.5-30 Hz
- **Typical applications:**
  - Diagnostics (Epilepsy, Oncology, ..)
  - Cognitive Sciences
  - Sleep Analysis
  - Human Computer Interfaces (BCIs)
  - Pharmacology
  - Intensive Care, Monitoring



Electroencephalogram (EEG)

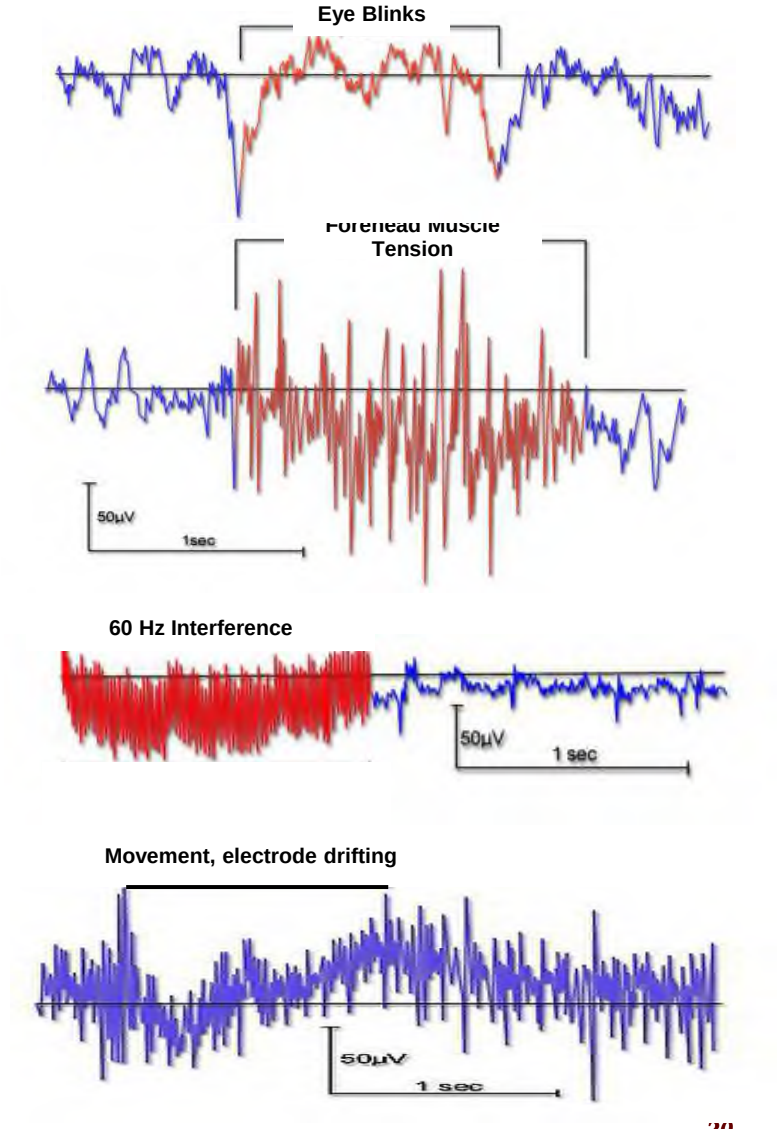
- **Signal origin**
  - The EEG measures
    - not action potentials
    - not summation of action potentials
    - but summation of graded Post Synaptic Potentials (PSPs)
      - Create detectable dipoles
  - EEG represents mainly the postsynaptic potentials of pyramidal neurons close to the recording electrode.
    - Spatially aligned and perpendicular to the cortical surface.
    - The electrical activity from deeper generators gets dispersed and attenuated by volume conduction effects.
    - Can not solve the “inverse problem”





Electroencephalogram (EEG)

- **Noise and Artifacts:**
  - Thermal RF noise
  - Blink artifacts, muscle tension, and similar
  - 50/60 Hz power lines
  - Electrode movement and drifting

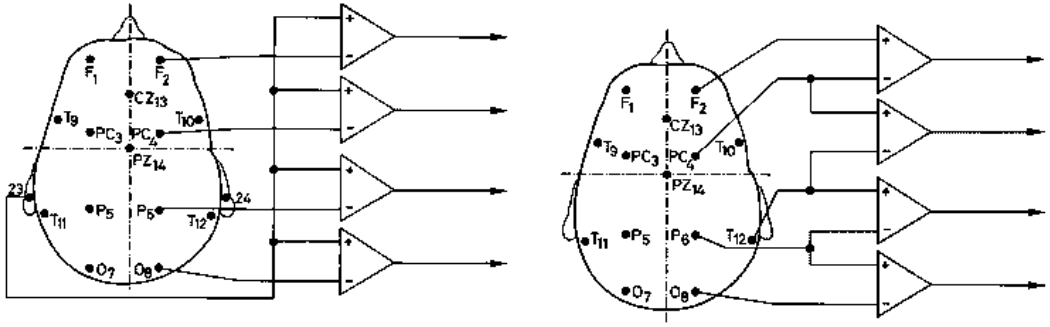


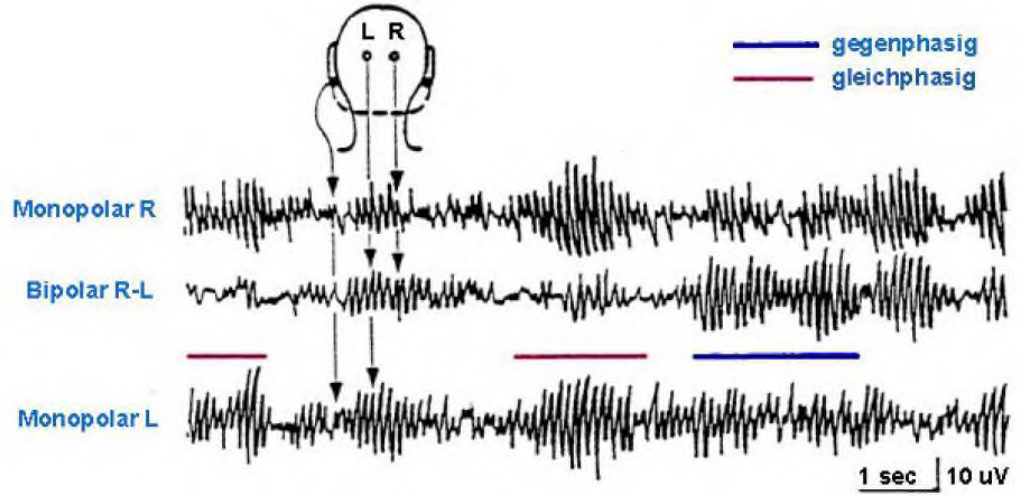
Electroencephalogram (EEG)

- **EEG is a difference in potential between two electrodes**
  - If one electrode is “silent”, it is called “monopolar” recording. The reference sites: ear lobe, mastoid, nose.
    - used in research, because it enables the researcher to localize the event of interest
  - If two electrodes are “active”, it is called “bipolar” recording
    - reduces shared artifacts

Unipolar measurement (indifferential right ear electrode)

Bipolar measurement



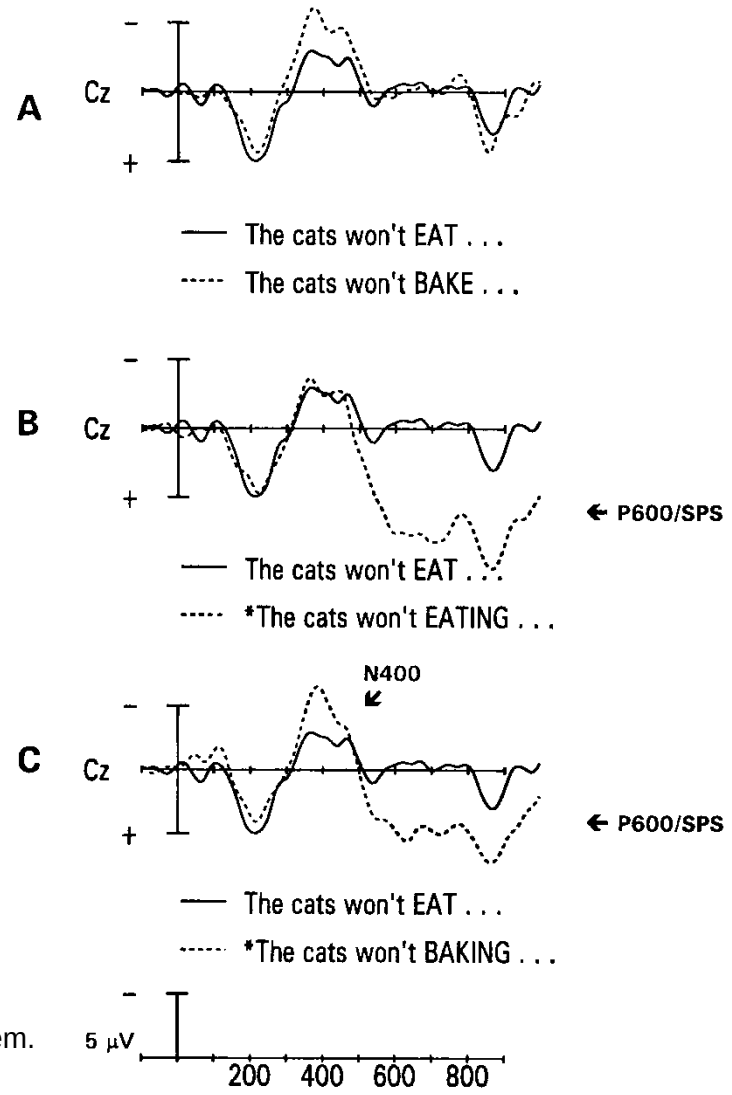


Electroencephalogram (EEG)

- **High-quality biopotential measurements require**
  - Good amplifier design
  - Use of good electrodes and their proper placement on the patient
  - Good laboratory and clinical practices
- **Electrodes should be chosen according to the application**
- **Basic electrode structure includes:**
  - The body and casing
  - Electrode made of high-conductivity material
  - Wire connector
  - Cavity or similar for electrolytic gel
  - Adhesive rim
- **The complexity of electrode design often neglected**

Electroencephalogram (EEG)

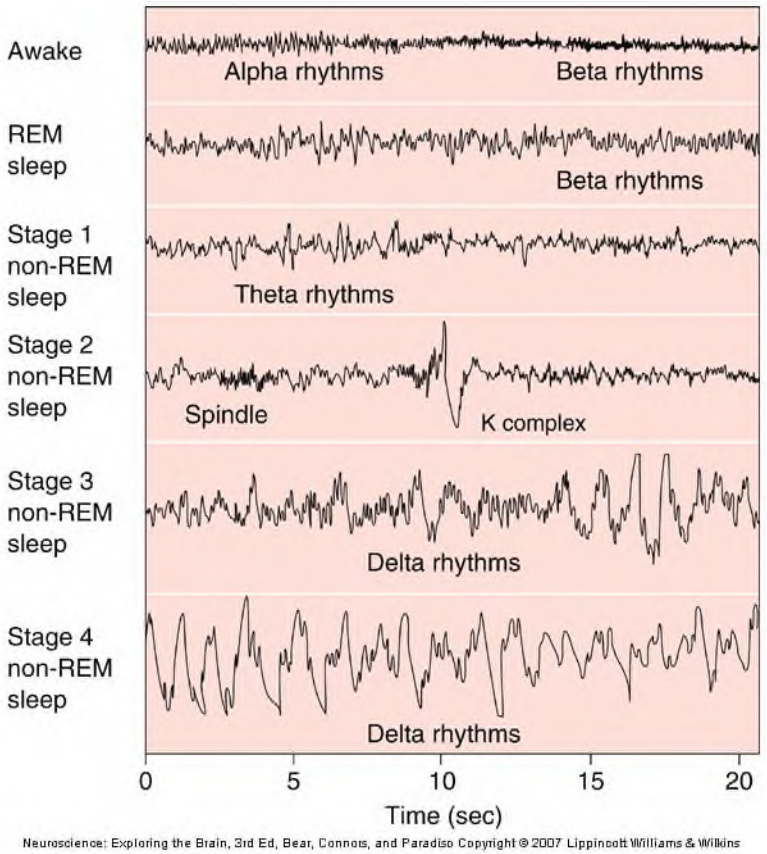
- **Event-related potentials**
  - EEG averaging technique used to study the electrical activity time-locked to an event.
    - Averaging of trials following a stimulus
  - Stimulus
    - Optical, auditory, etc
  - Advantages
    - Noise reduction
      - The noise decreases by the squareroot of the number of trials
  - Disadvantages
    - Needs a considerable amount of trials
      - Far field potentials require up to 1000 measurements
  - Comprises a mixture of different brain rhythms, depending on the filters applied.
  - Only about 20% of the evoked activity is shown
  - Assumption: no habituation occurs (participants don‘t get used to stimulation)



Example of Auditory Evoked Potentials:
Correct (Baseline): The cats won't eat the food Mary gives them.
Semantic mismatch: The cats won't bake the food Mary gives them.
Syntactic mismatch: The cats won't eating the food Mary gives them.
Semantic and syntactic mismatch: The cats won't baking the food Mary gives them.

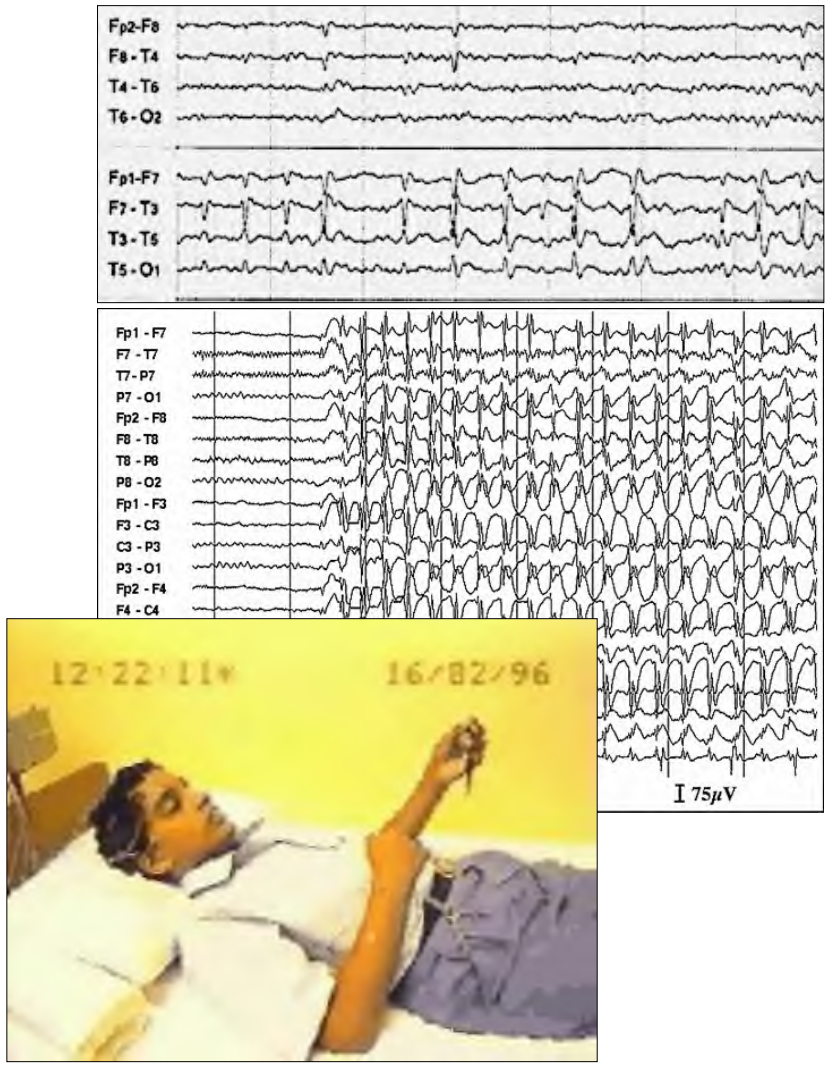
Electroencephalogram (EEG)

- **The EEG can diagnose sleep disorders and anomalies**
- **Sleep**
  - An active process
  - Sleep deprivation = devastating
    - Body requires REM sleep
  - One-third of lives in sleep state
  - 5 stages (90-110 minutes)
  - Stage 1: Light Sleep
    - Reduction of muscle activity
    - Myoclonus
    - Θ waves
  - Stage 2:
    - Eye movement stops
    - θ, κ, spindles
  - Stage 3&4: Deep Sleep, non REM
    - No muscle activity
    - Hard to wake up → disorientations
    - Nightmares, sleep walking, bedwetting.
  - Stage 5: REM
    - Paralysis
    - Rapid eye movement
    - Increased BP, erection, dreaming
    - Affected by caffeine



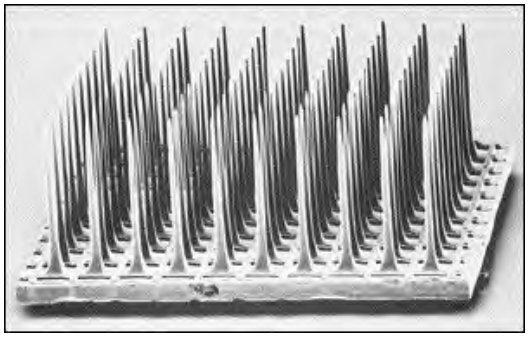
Electroencephalogram (EEG)

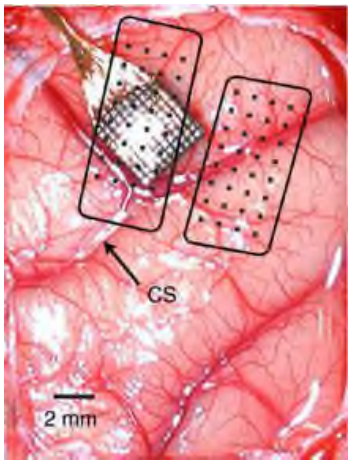
- **Epilepsy**
  - Repeated seizures
  - Causes: Tumour, trauma, infection, vascular disease, many cases unknown
  - Types:
    - Generalized: Entire cerebral cortex, complete behaviour disruption, consciousness loss
    - Partial: Circumscribed cortex area, abnormal sensation or aura
    - Absence: Less than 30 sec of generalized, 3 Hz EEG waves
- **EEG of Epilepsy**
  - Between seizures
    - Rarely any spikes
  - During a seizure
    - Characteristic, large, rhythmic, waves
  - Diagnostic of epilepsy when a seizure is observed
    - 24 hr or overnight monitoring

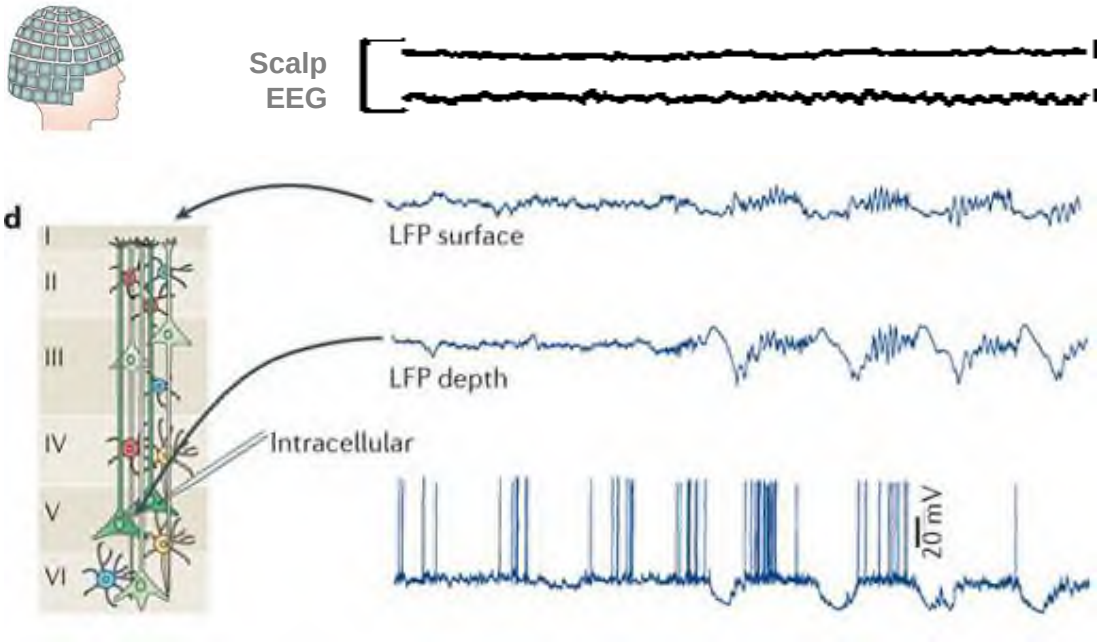


Intracortical EEG

- **Measure the activity of the grey matter directly**
  - Platinum electrodes inserted into the brain below the scalp
- **Disadvantages**
  - Invasive!
- **Advantages**
  - Much more sensitive
  - Less artifacts
  - Can detect signals which do not appear in standard EEG
- **Uses**
  - Monitoring of critically ill patients
  - BCI's

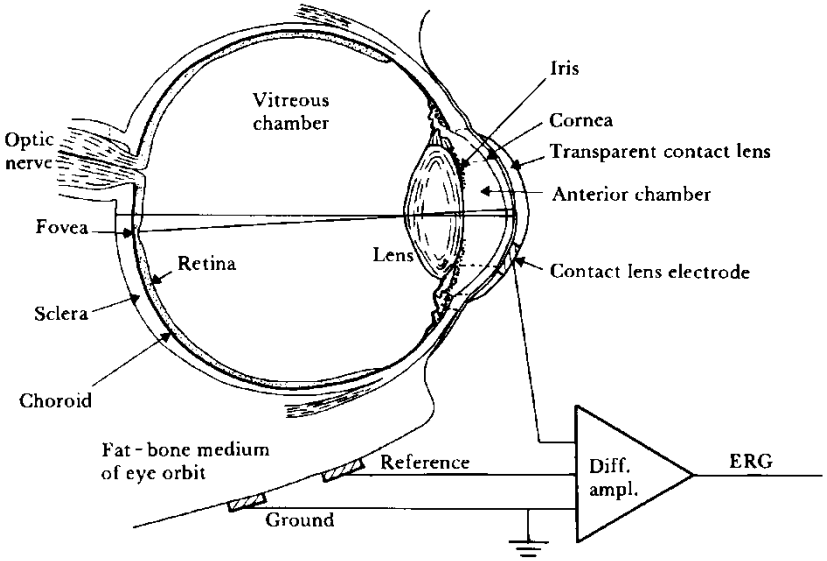






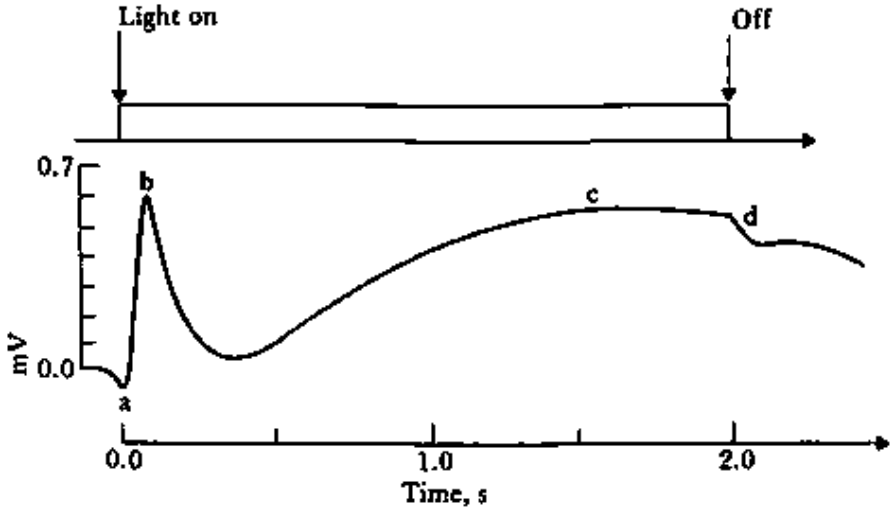
Electroretinogram (ERG)

- **A recording of the temporal sequence of changes in potential in the retina when stimulated with a brief flash of light.**
- **Electrodes**
  - A transparent contact lens contains one electrode
  - The reference electrode can be placed on the right temple



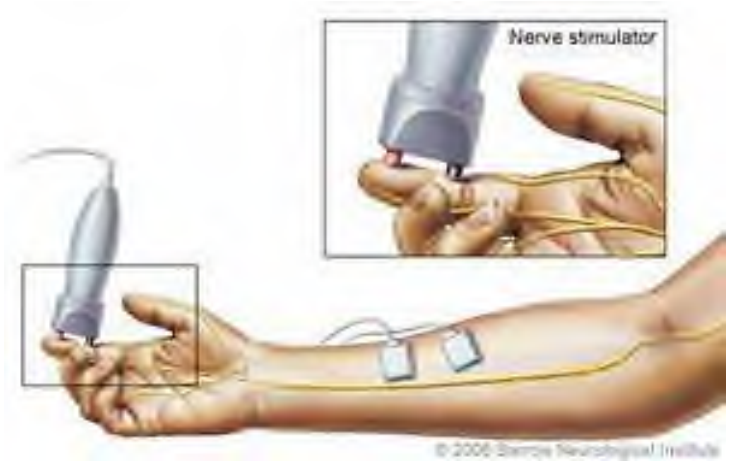
Electroretinogram (ERG)

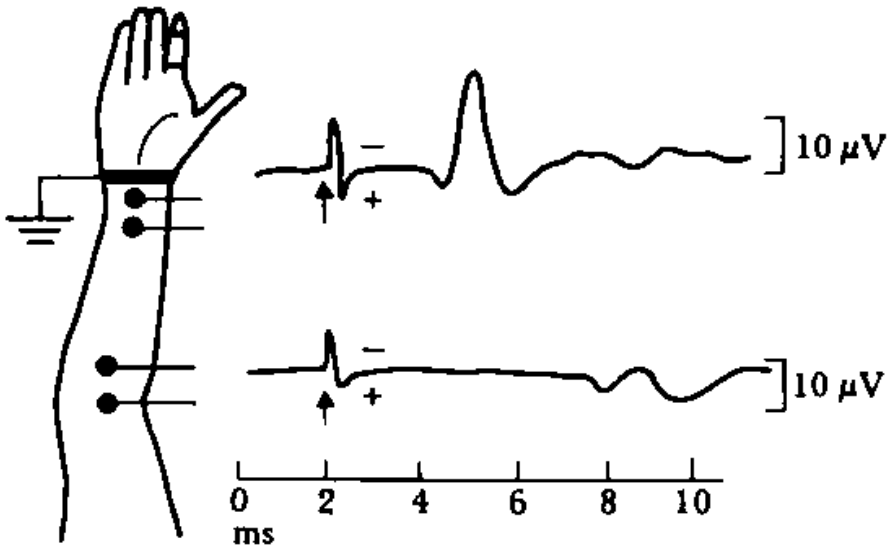
- **a-wave ("late receptor potential“)**
  - Reflects the general physiological health of the photoreceptors in the outer retina
- **b-wave**
  - Reflects the health of the inner layers of the retina
- **Two other waveforms**
  - Sometimes recorded in the clinic
  - c-wave
    - originating in the pigment epithelium
  - d-wave
    - indicating activity of the bipolar cells



Nerve Conduction Studies

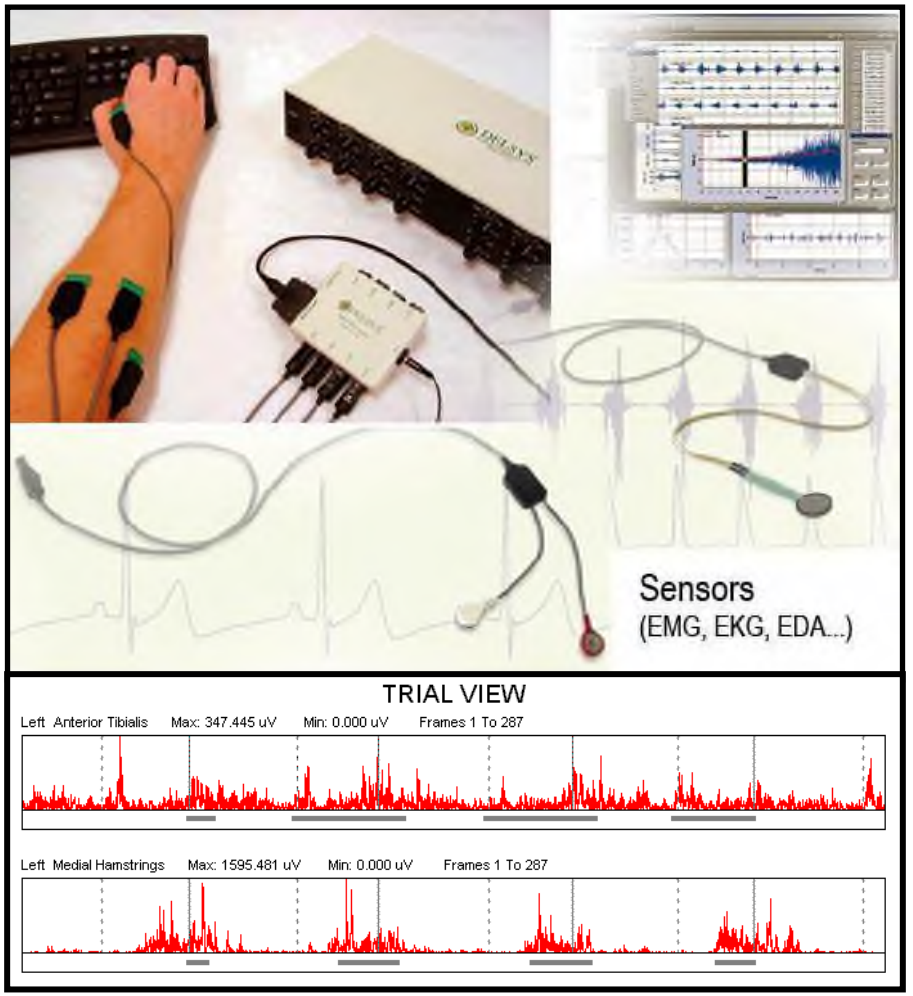
- **Extracellular field response from the sensory nerves of peripheral nerves**
  - Excite at one or more point and measure potentials distally
  - For each stimulation site measure latency, amplitude, duration, and area.
  - A motor conduction velocity can be calculated.
- **Detect loss of axons (as in a typical axonal neuropathy), conduction block from demyelination, etc.**





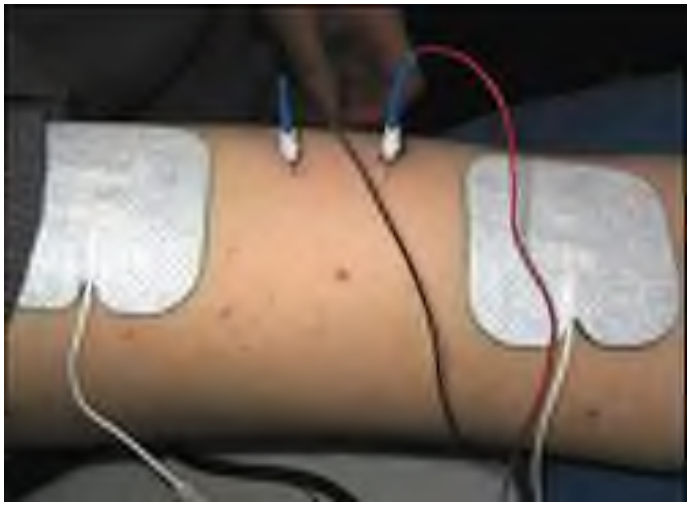
Electromyogram (EMG)

- **Muscle is an excitable tissue**
  - More to come later
- **Electromyogram (EMG) is a technique for evaluating and recording the activation signal of muscles.**
  - Detects the electrical potential generated by muscle cells when these cells contract and relax.
- **Electrical Characteristics**
  - Measured EMG potentials range between < 50 μV up to 20 to 30 mV, depending on the muscle under observation.
  - Typical repetition rate of muscle unit firing is about 7-20 Hz.



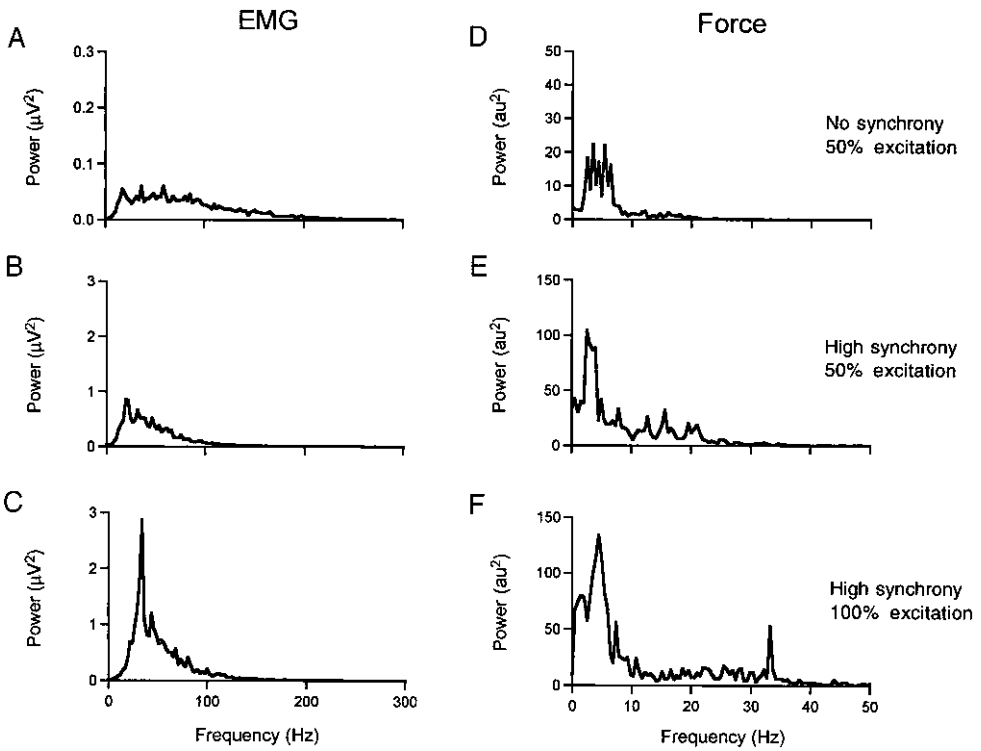
Electromyogram (EMG)

- **Electrical potential difference measured between two points → bipolar electrode configuration used**
- **Bipolar Electrode Types**
  - Intramuscular
    - Fine Wire
    - Needle
  - Extramuscular (Surface)
    - Most common, less invasive
    - Silver-silver chloride electrodes
- **Electrode Placement**
  - Overlying the muscle of interest in the direction of predominant fiber direction
  - Subject is GROUNDED by placing an electrode in an inactive region of body



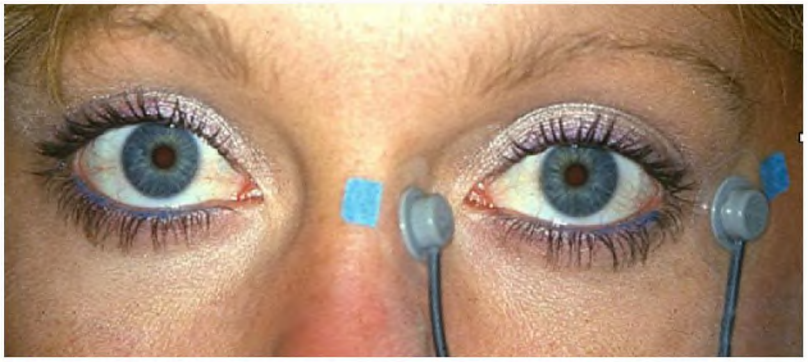
Electromyogram (EMG)

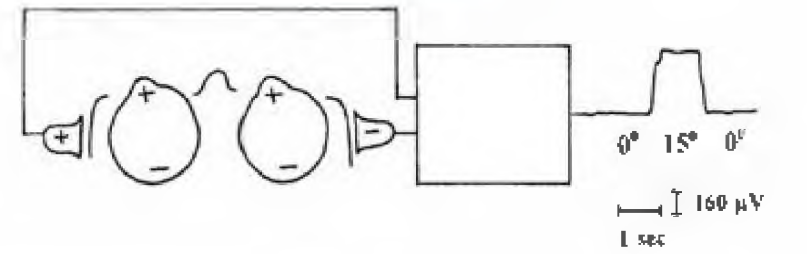
- **What can be learned from an EMG?**
  - Time course of muscle contraction
  - Contraction force
  - Coordination of several muscles in a movement sequence
    - These parameters are DERIVED from the amplitude, frequency, and change of these over time of the EMG signal
- **Applications**
  - Rehabilitation
  - Functional analysis
  - Active Prosthetics
  - Biomechanics, Sports medicine



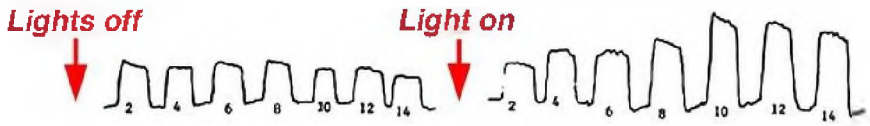
Electro-Oculogram (EOG)

- **Recording of the eye movement.**
  - Two electrodes to the left and the right of the eye or above and below the eye
  - Measure the potential between the two electrode
  - Determine the horizontal or vertical movement of the eye
  - The potential is zero when the gaze is straight ahead.
- **Applications**
  - Diagnostics
  - Functional analysis
  - Sleep and dream research
  - Evaluating reading ability and visual fatigue



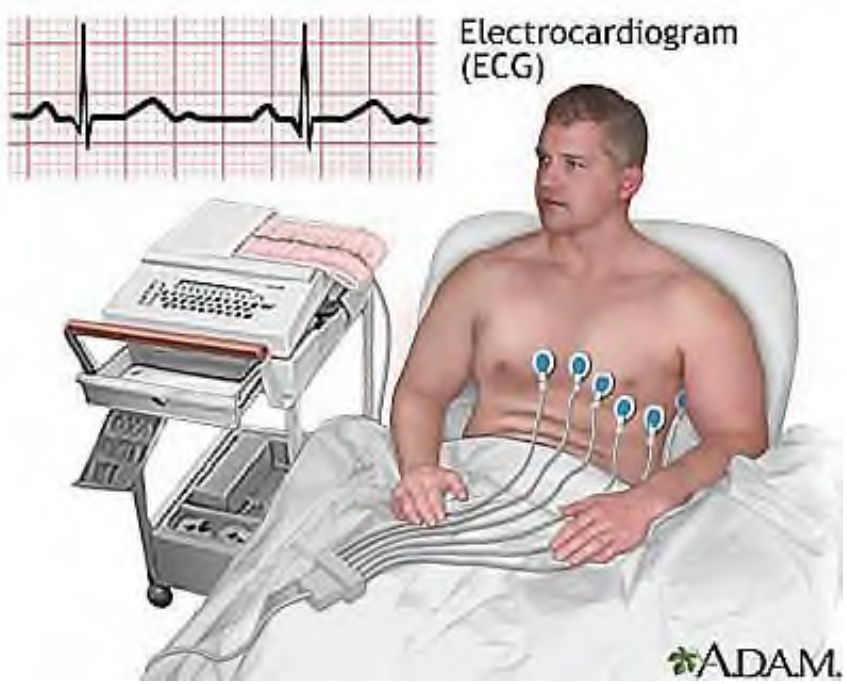


EOG recording of a normal person



Electrocardiogram (ECG)

- After we learn more about the heart



Summary bioelectric signals

	Frequency	Amplitude (mV)
ECG	0,2 – 300	0,1 - 3
EEG	DC – 100	0,005 - 0,2
EEG (cortical)	10 – 100	0,015 - 0,3
EMG	10 – 1000	0,1 - 5
EMG (needle)	10 – 10000	0,05 - 5
EOG	0 – 30	0,1 - 2
Intracell.	0 – 10000	50 - 130