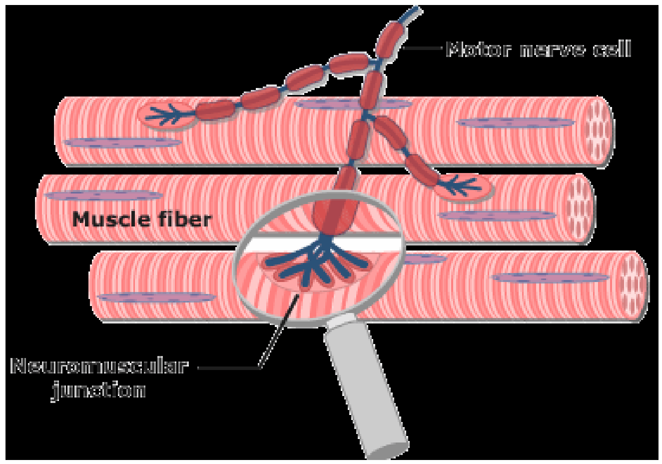
Electrical Stimulation of the Neuromuscular system



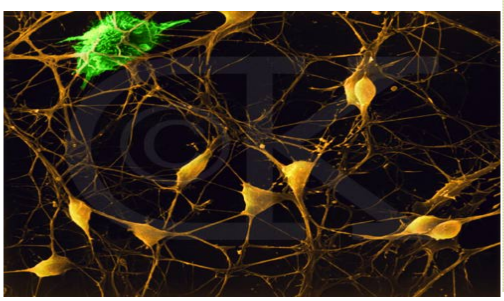
Outline

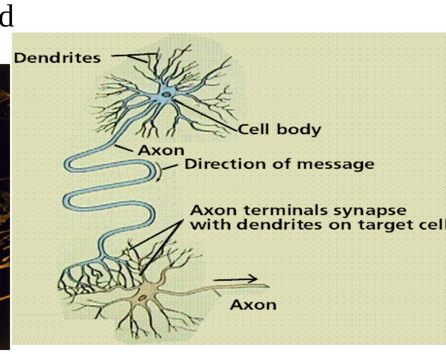
- Introduction
- Neuro-muscular junction, myelin sheet
- Examples of neuromuscular prostheses
  - Upper extremity
  - Lower extremity
  - Bladder stimulation
- Derivatives (∇) and cross, dot products.
- Mathematical formulation of the effect of current stimulation from electrode immersed in conductive media.

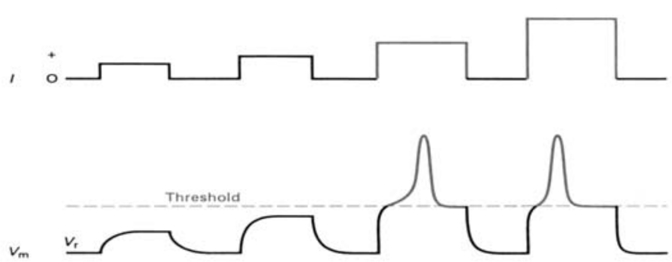
The neuromuscular junction

- http://www.youtube.com/watch?v=ZscXOvDgCmQ (1min)
- http://www.youtube.com/watch?v=YnVY4Waimwg (3min, McGrawHill book)

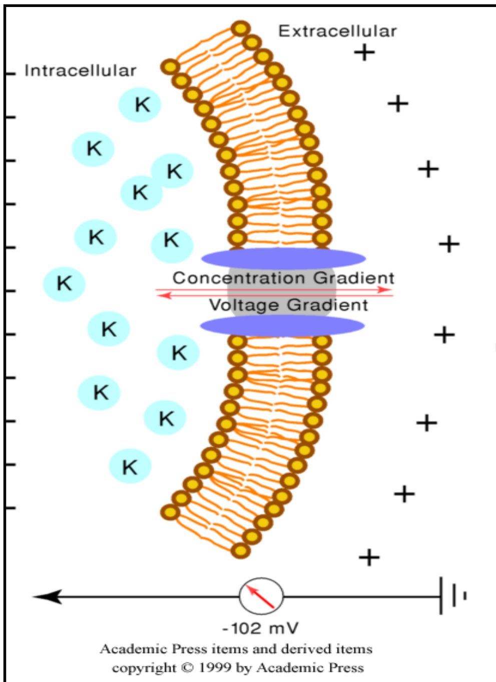
Neurons, revisited

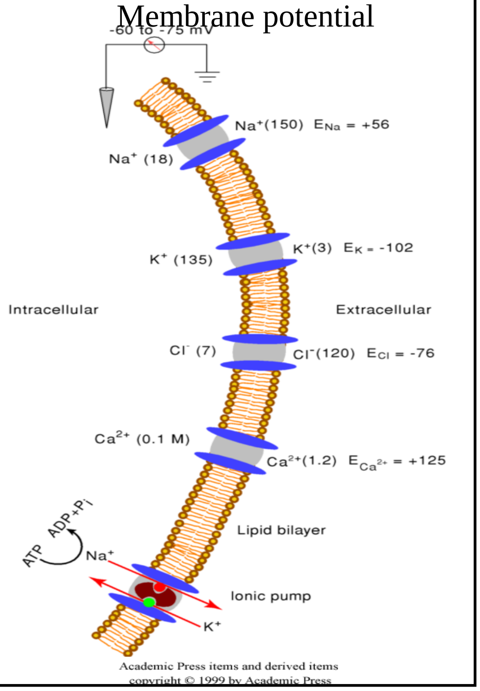




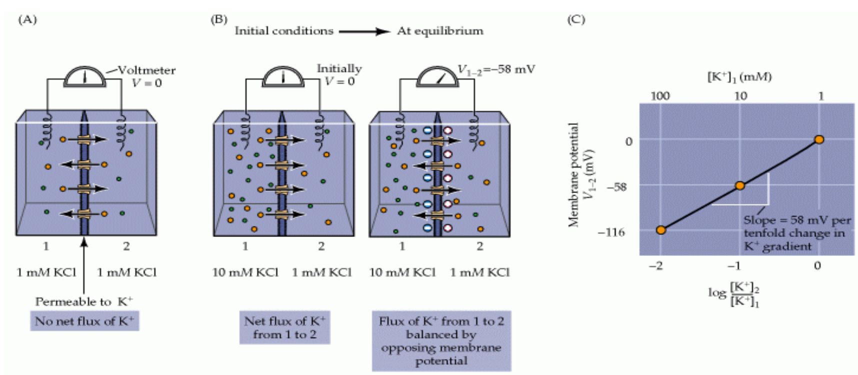


Membrane potential





Membrane potential: how does it come about?

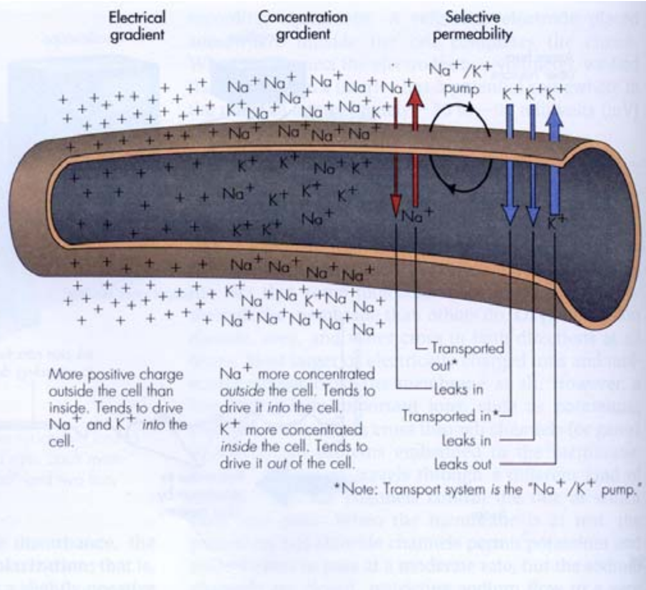


- Charge in each compartment is balanced
  - Outside the cell, sum of anions = sum of cations
    - $[Na^+] + 2[Ca^{++}] + [K^+] = [Cl^-]$
  - Inside the cell, sum of anions = sum of cations
    - $[Na^+] + 2[Ca^{++}] + [K^+] = [Cl^-] + [A^-]$
    - A^- are other anions, which are mostly proteins
    - Anions are impermeant to the membrane

FIGURE **2.15**

Factors controlling sodium and potassium gradients for a membrane at rest

The sodium-potassium pump brings two potassium (K^+) ions into the cell for every three sodium (Na^+) ions it pumps out. As a result of the pump and of the low ability of Na^+ ions to diffuse back through the membrane, sodium ions are much more concentrated outside the cell; the potassium ions are more concentrated inside the cell. Because ions tend to move from an area of greater concentration to an area of lesser concentration, the concentration gradient tends to push Na^+ ions into the cell and K^+ ions out. Because the total positive charge is greater outside the cell than inside, the electrical gradient tends to push both Na^+ and K^+ ions into the cell. For K^+ ions the two gradients almost cancel each other out. For Na^+ ions, both gradients push in the same direction; sodium stays outside the cell only because the sodium channels are closed.

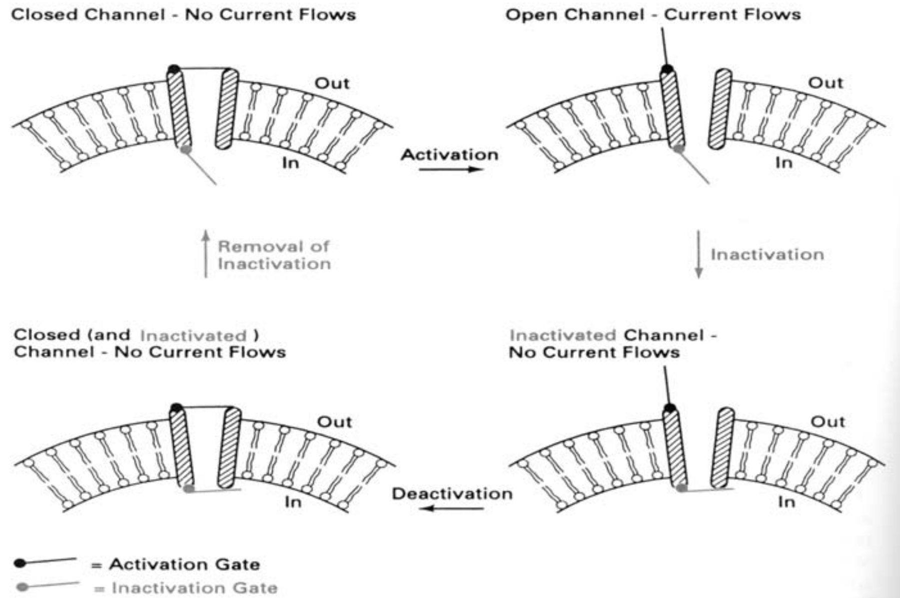


Identifying parts of a stained neuron:

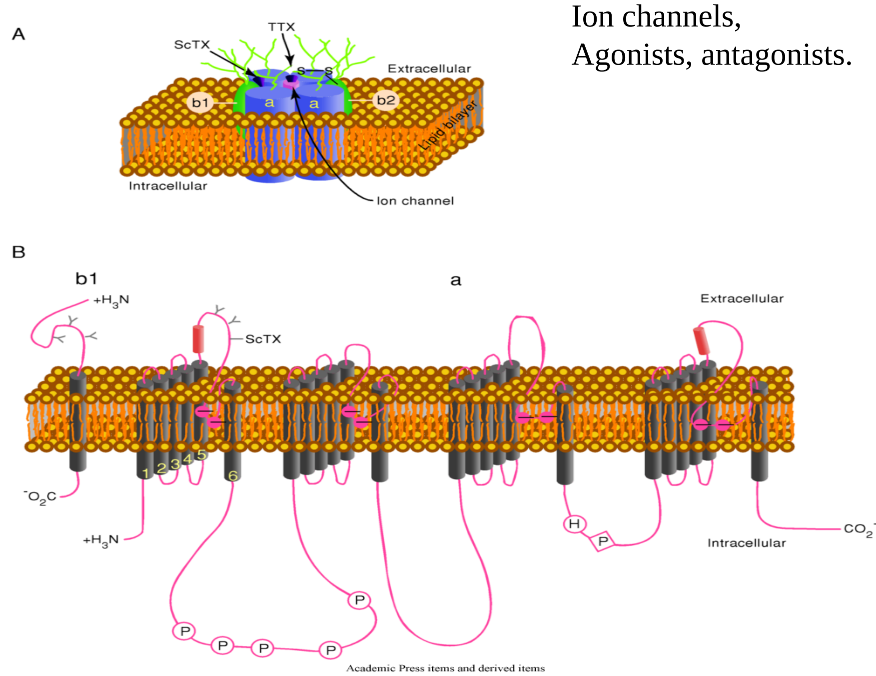
How does a spike happen?

http://www.tvdsb.on.ca/westmin/science/sbioac/homeo/action.htm

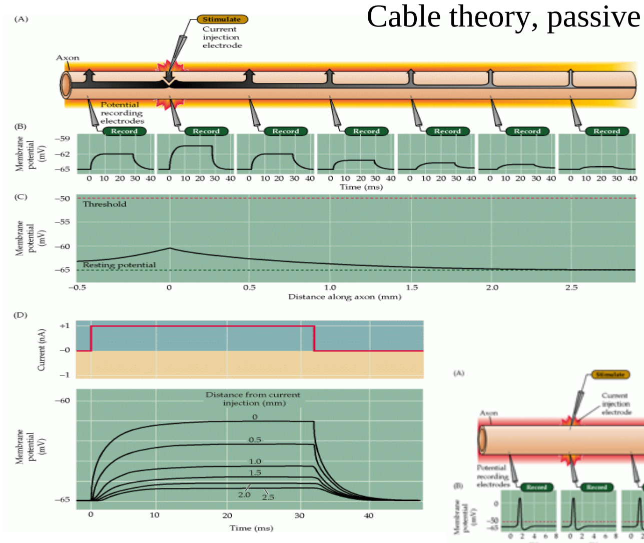
Ion channel states

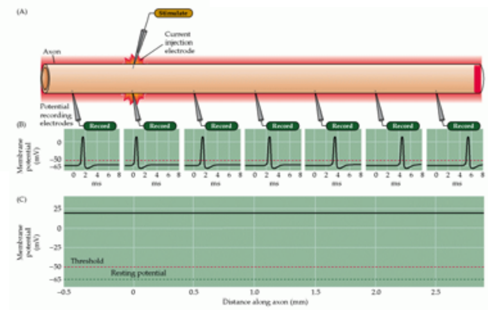


Ion channels, Agonists, antagonists.

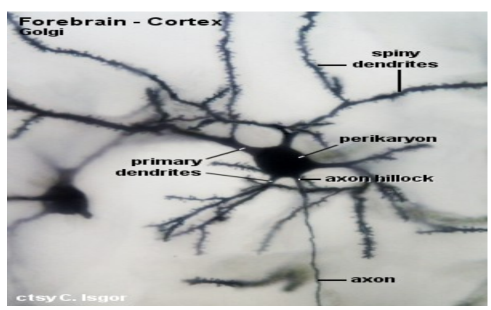


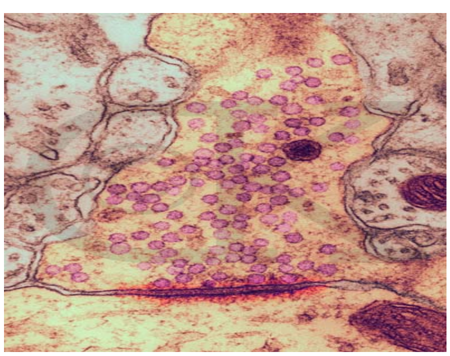
Cable theory, passive conduction.

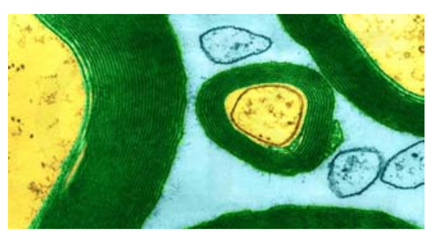




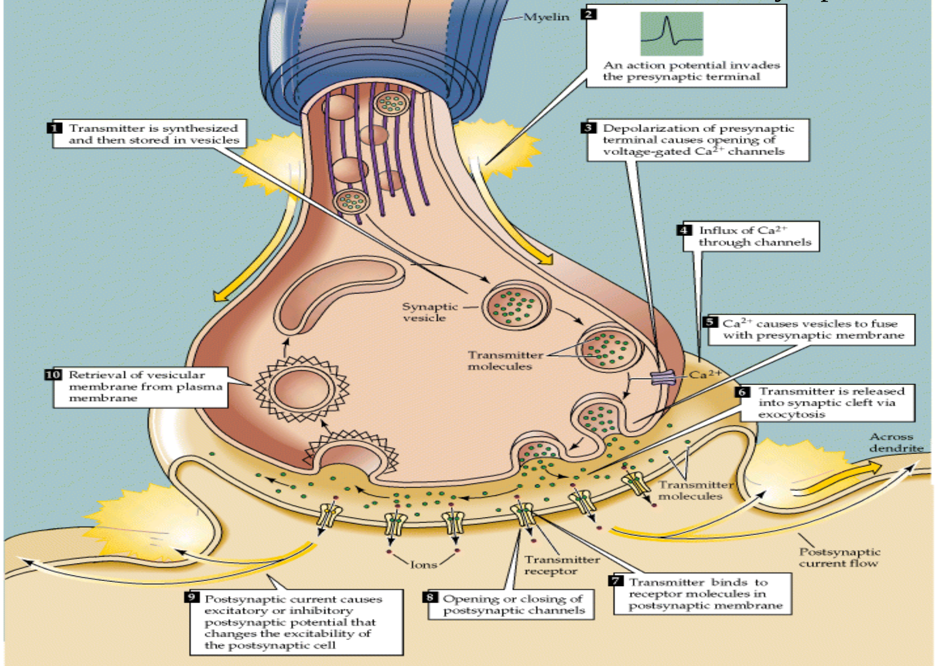
Neurons,
Myelin sheath,
Synapses



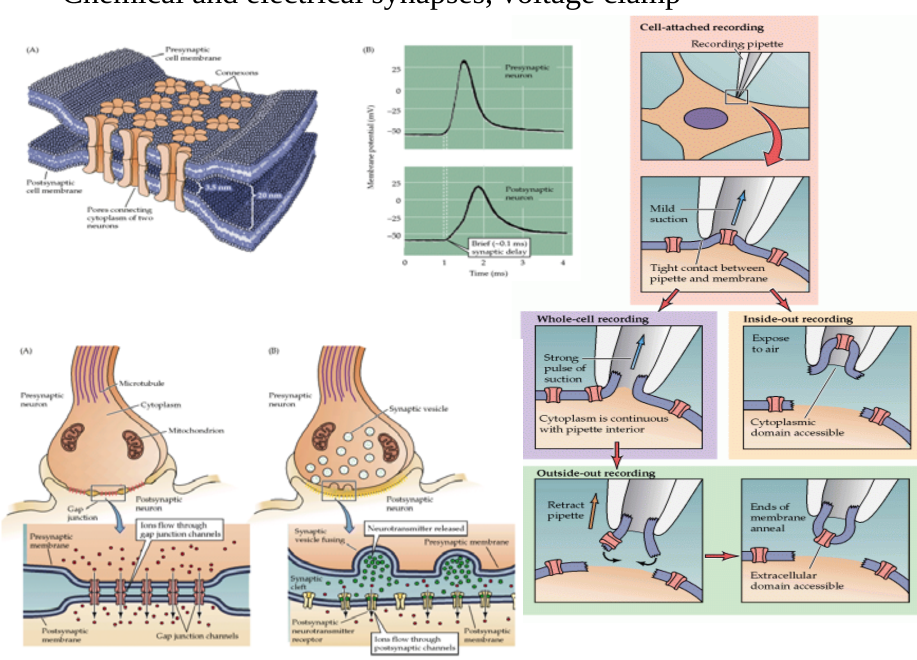




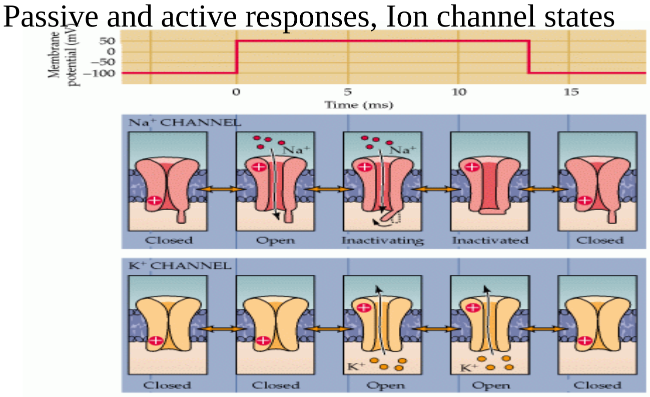
Chemical synapses

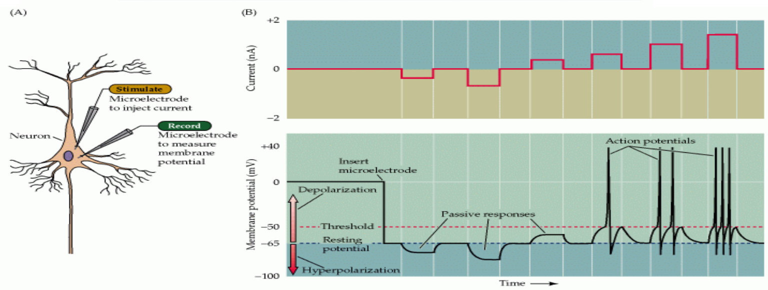


Chemical and electrical synapses, voltage clamp

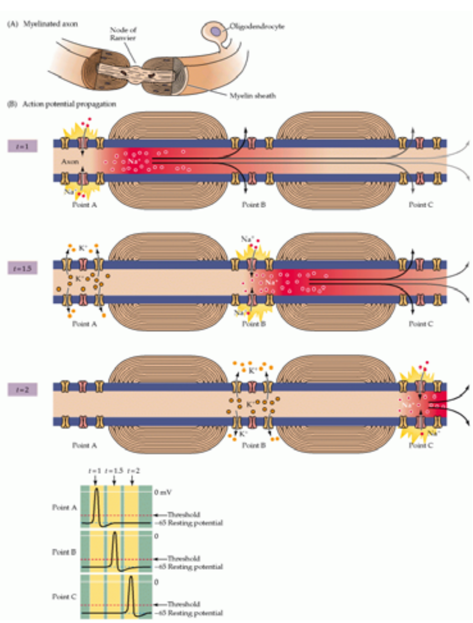


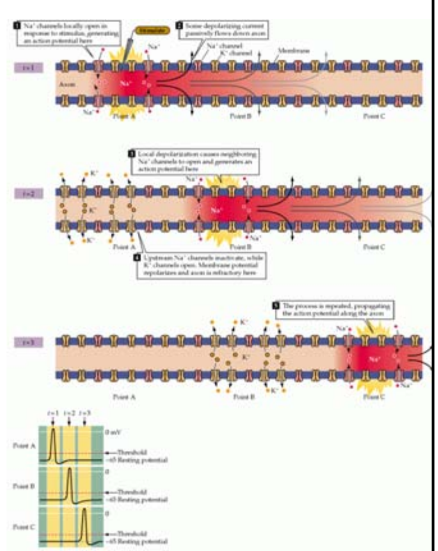
Passive and active responses, Ion channel states



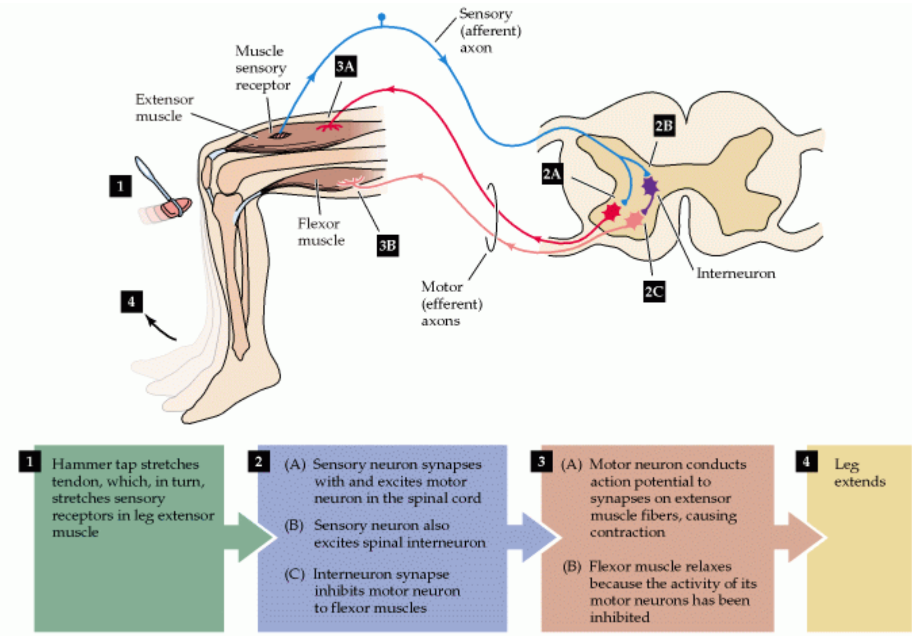


Saltatory conduction

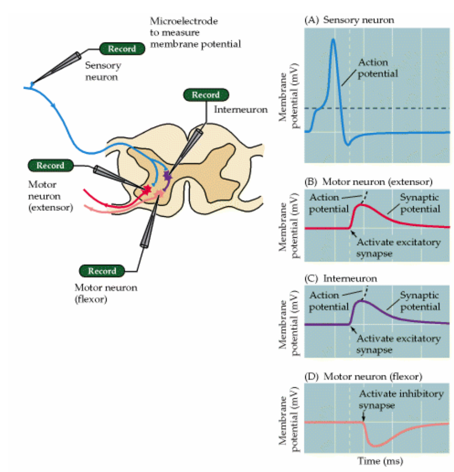




Myotactic reflex



Intracellular responses during the myotactic reflex



Reflex as result of sensory neuron stimulation

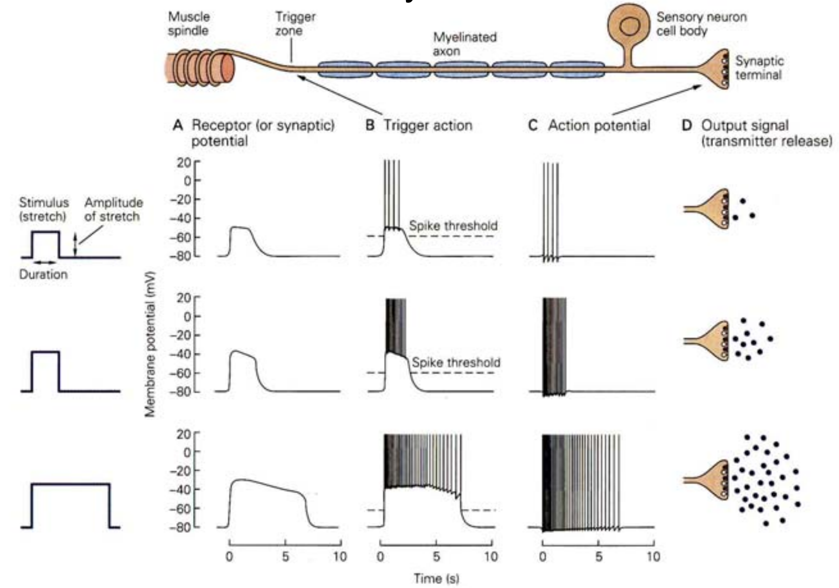


Figure 2-10 A sensory neuron transforms a physical stimulus (in our example, a stretch) into electrical activity in the

their amplitude. The *duration* of the input signal determines number of action potentials. Thus, the graded nature of inpu

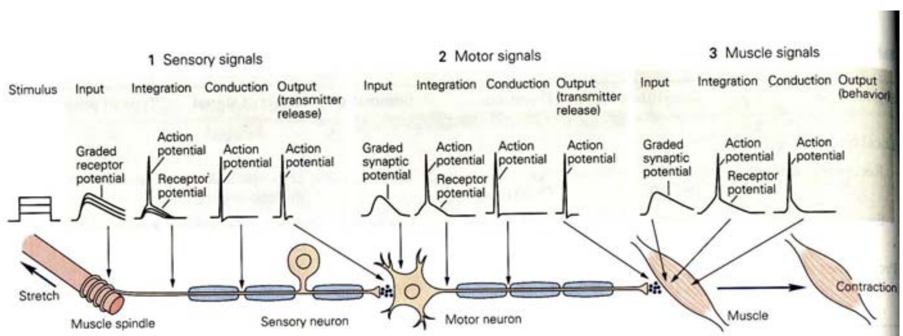


Figure 2-11 The sequence of signals that produces a reflex action.

transmitter diffuses across the synaptic cleft and interacts with receptor molecules on the external membranes of the motor

References – previous 18 slides.

Action potential animation:
http://www.tvdsb.on.ca/westmin/science/sbioac/homeo/action.htm

Books available online:
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Books

Neuroscience book where I took most figures from:
http://www.ncbi.nlm.nih.gov/books/bv.fcgi?call=bv.View..ShowTOC&rid=neurosci.TOC&depth=2

Vertebrate motoneuron

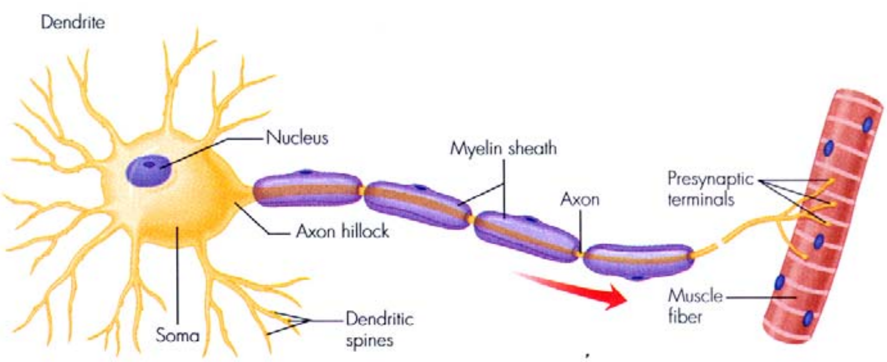


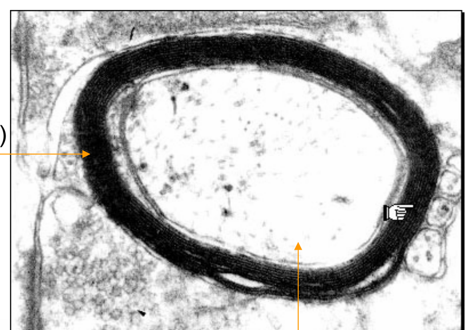
FIGURE **2.4**
The components of a vertebrate motor neuron
The cell body of a motor neuron is located in the spinal cord. The various parts are not drawn to scale; in particular, a real axon is much longer in proportion to the size of the soma.

Myelin

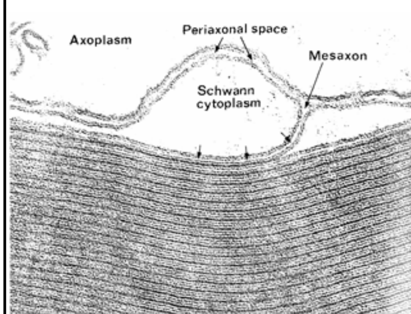
- Tight wrapping of cell membrane around axon
- Cytoplasm of glial cell is gradually squeezed out as cell wraps around
- Result is concentric layers of closely apposed membrane
- Acts as electrical insulator
- Huge increase in speed of action potential transmission

Myelinated axons, nodes of Ranvier

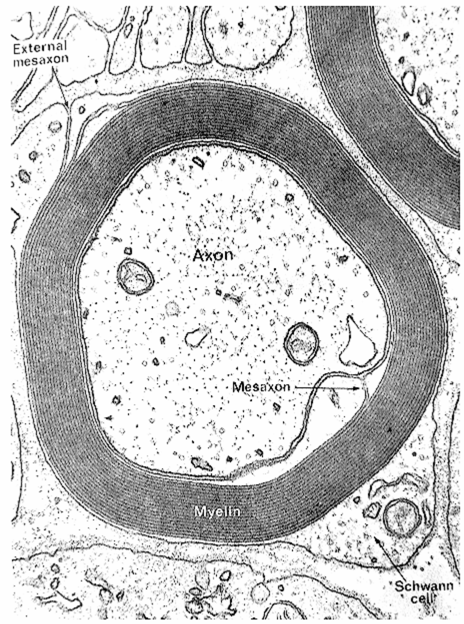
Myelin sheath (transversal section)



Axon (transversal section)



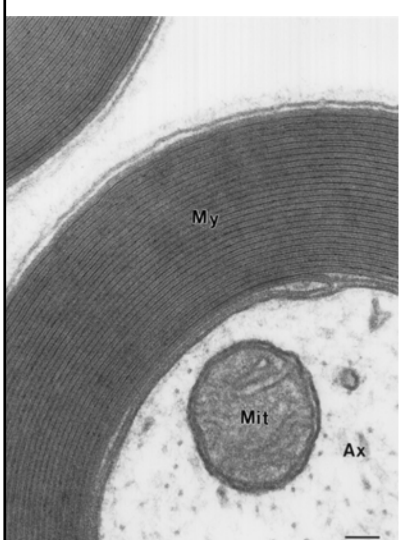
Unmyelinated axons



http://www.udel.edu/Biology/Wags/histopage/empage/en/en.htm

Myelin is produced by glia

- Oligodendrocytes in CNS
- Schwann cells in PNS



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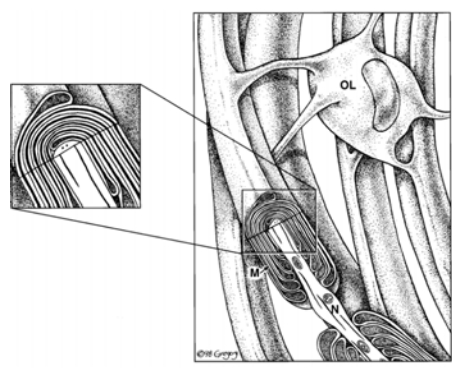

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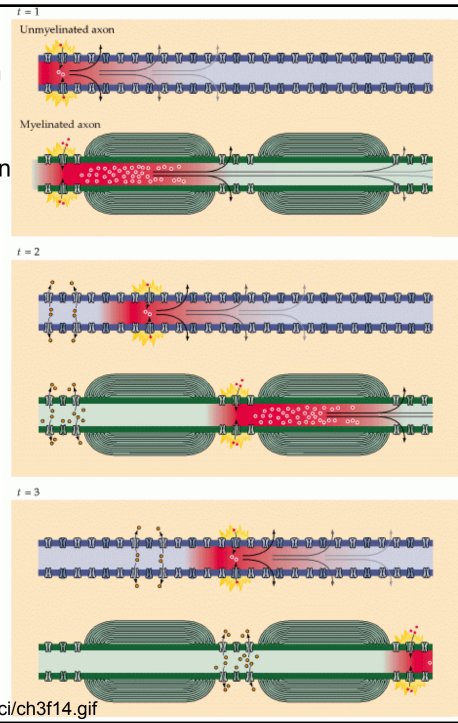
vv.carleton.ca/~neil/neural/neuron-a.html

Nodes of Ranvier

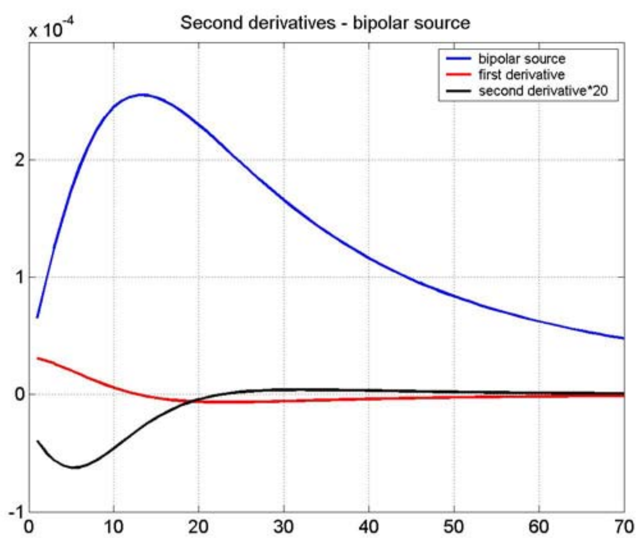
Unmyelinated axon

Myelinated axon



http://www.ncbi.nlm.nih.gov/books/bookres.fcgi/neurosci/ch3f14.gif

Saltatory conduction (Ranvier nodes), and second derivative of the extracellular potential.



Electrode-tissue interface

- Constant current x constant voltage stimulation
- Tissue damage:
  - Passive: presence of foreign object (mechanical)
  - Active: passage of current (electrochemical)

Damage to biological tissue

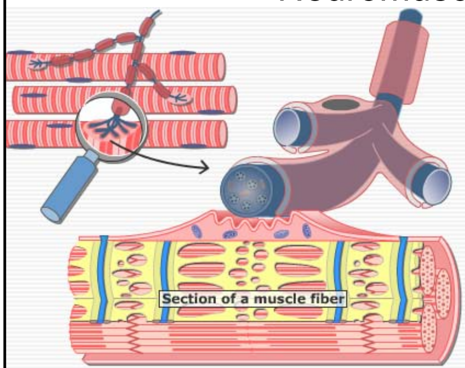
- Passive: vascular or neural
  - How to overcome this?
    - Change electrode size, tip geometry, substrate, anchoring
- Active:
  - primary (reaction products from electrochemistry);
  - secondary (physiological changes associated with neural excitation.

Effect of waveform

- Strength-duration curve (obtained empirically):
  - PW= pulsewidth
  - I_{th}=threshold current
  - I_{rh} = rheobase current, minimum current amplitude if PW→∞.
  - T_{ch} = chronaxie time PW to excite neuron with $2I_{rh}$.
  - $I_{th}= I_{rh}+(I_{th}T_{ch}/PW)$

Anodic vs cathodic stimulation

Neuromuscular junctions



TUTORIAL:

As it approaches the surface of a target muscle fiber, a **motor neuron axon** sheds its **myelin sheath** and splits into a small cluster of fine **terminal branches**.

Each terminal branch sits in a shallow groove in the muscle fiber membrane (sarcolemma) called a **motor end plate** (sole plate). *Please note that many authorities prefer, instead, to use the term motor end plate to refer to the entire neuromuscular junction.*

The tips of the terminal branches, which often expand into **synaptic knobs** (= synaptic bulbs or terminal boutons), contain many mitochondria and **secretory vesicles** filled with acetylcholine (ACh). A non-myelinating **Schwann cell** (teloglia) covers the terminal branches and motor end plates.

A small space known as the **synaptic cleft** exists between the synaptic knob and motor end plate. Acetylcholine molecules, after being released from the synatpic knob, diffuse across this space and bind with receptors on the motor end plate.

Many junction folds occur along the motor end plate. The added surface area provided by these folds increases the amount of membrane available for acetylcholine receptors.

http://www.getbodysmart.com/ap/muscletissue/nervesupply/junction/animation.html

Neuromuscular prostheses

Nervous system injury = impairment of motor functions.

Motor functions: body functions; limb movement.

Objectives of neuroprostheses: restore lost function, increase independence of disabled individuals; reduce economic impact of disability.

Current neuroprostheses use FES (functional electrical stimulation) to activate motoneurons.

Motoneurons: neurons that innervate muscles. Muscles are the actuators (for the desired function).

Current target patients: stroke (750,000/year incidence); SCI (10,000/year incidence, higher prevalence).

Recruitment properties

Magnitude of muscular contraction depends on: (1) electrode type; (2) stimulation waveform shape, time, amplitude; (3)location of electrode relative to motoneuron.

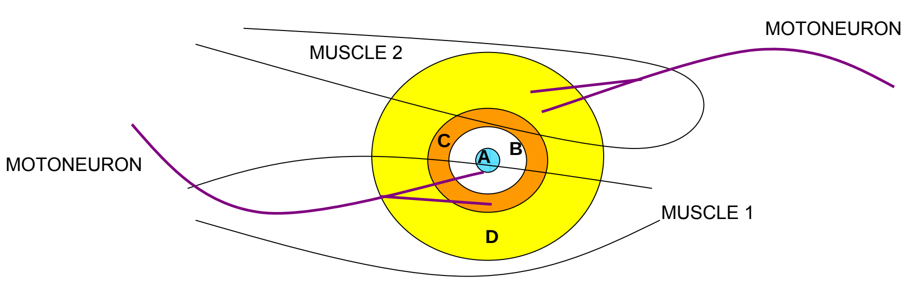
Force modulation can be achieved by: (1) rate modulation (2) recruitment

(1) **rate modulation**: there's summation of muscular contraction if high enough frequency is used, but the muscle is more prone to fatigue. Higher frequency leads to higher (faster) fatigue.

(2) **recruitment**: number of motoneurons stimulated: more neurons means more muscles.

Muscular recruitment through electrical stimulation

A: where the electrode is located. If the stimulus intensity is low, this is the only activated area.
B: (white area) if slightly higher current, only muscle 1 would contract.
C: possibly higher force exerted by both muscles now.
D: everybody is stimulated (both muscles, through activation of both motoneuron.



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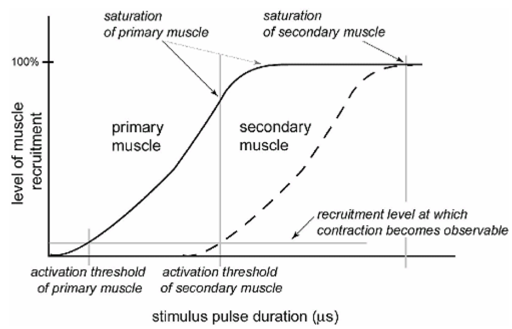
Selectivity of intramuscular stimulating electrodes in the lower limbs

Ronald J. Triolo, PhD; May Q. Liu, MS; Rudi Kobetic, MS; James P. Uhlir, MS



http://www.vard.org/jour/01/38/5/liu-f01.gif

http://www.vard.org/jour/01/38/5/liu385.htm

Recruitment properties

Nonlinearities should be dealt with in the implant: how to measure and deal with fatigue.

There are high gain regions, and plateau regions (why?).

Spillover should also be avoided (they contribute to the nonlinearities)

Muscle stimulation?

- With rare exceptions, neuroprostheses activate paralyzed ***neurons*** at different levels of the nervous system:
  - Spinal cord
  - Spinal roots
  - Peripheral nerves
  - Intramuscular nerve branches

Electrode types

- Surface:
  - Skin has high resistance, and high current needs to be passed before muscle is activated. (Large area is stimulated, unpleasant side effects).
- Implantable:
  - Epimysial (next slide)
  - Intramuscular

IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING, VOL. 44, NO. 10, OCTOBER 1997 921

The Tissue Response to Epimysial Electrodes for Diaphragm Pacing in Dogs

Brian D. Schmit,* *Member, IEEE*, and J. Thomas Mortimer

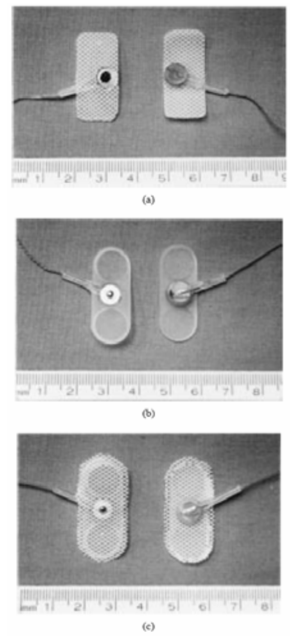


Fig. 1. (a) Electrode Type 1. This electrode is characterized by a stimulating surface placed within a well to reduce high-current densities at the edge of the stimulating surface. A Dacron mesh was molded into the tabs on the sides of the stimulating disk for reinforcement during staple attachment to the muscle. Sixteen Type 1 electrodes were implanted in four dogs. (b) Electrode Type 2. This electrode type has a hemispherical stimulating surface for uniform current density. The tabs are Dacron-free to reduce electrode stiffness. Eighteen Type 2 electrodes were implanted in a total of five dogs. The absence of Dacron reinforcement resulted in staple tearing of the tabs and displacement of the electrodes from the muscle surface in ten samples. (c) Electrode Type 3. This electrode type has a hemispherical stimulating surface for uniform current density. An exposed Dacron mesh was tacked to the electrode on the surface that opposes the muscle. The Dacron was incorporated into the design to reinforce the tabs and to promote tissue ingrowth and mechanical anchoring of the electrode. Ten Type 3 electrodes were implanted in four dogs.

A MULTICENTER STUDY OF AN IMPLANTED NEUROPROSTHESIS FOR RESTORING HAND GRASP IN TETRAPLEGIA

P. Hunter Peckham, PhD*†‡; Michael W. Keith, MD*†‡; Kevin L. Kilgore, PhD*†‡;
Julie H. Grill, MS§; Kathy S. Wuolle, OTR/L, CHT§; Geoffrey B. Thrope§; Peter Gorman, MDxx¶;

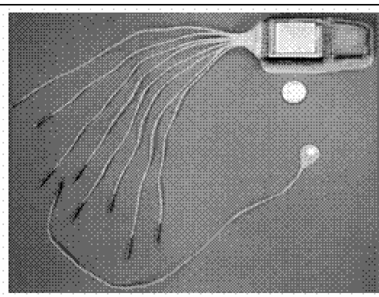


Figure 2. Implanted components of the neuroprosthesis.

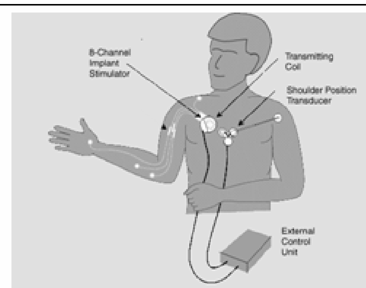


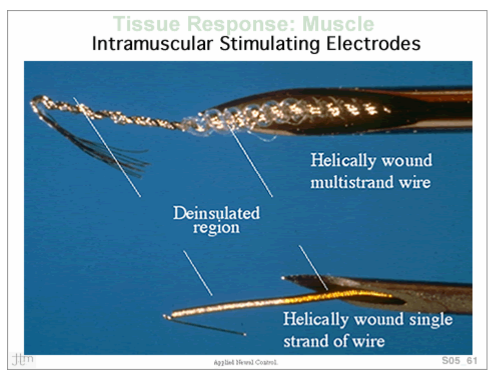
Figure 1. Implanted neuroprosthesis for restoring hand grasp in tetraplegia.

http://www.ifess.org/cdrom_target/ifess01/oral1/peckhamPH.htm

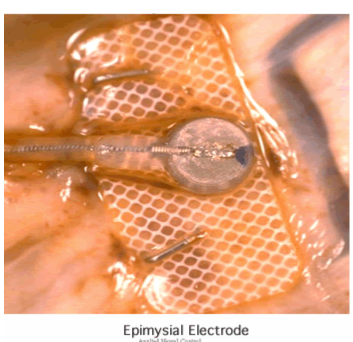
Epimysial versus intramuscular electrodes

- Epimysial and intramuscular are invasive.
- **Epimysial** touches the epimysia (outer sheath of the muscle), near the entry point of the nerve, and is subcutaneously secured.
- **Intramuscular**: inserted through a needle, the needle is retracted, the barbed tips of the “wire” secure it in the muscle.

Photograph of two intramuscular electrodes with helical leads, mounted in hypodermic needles, on with multistranded lead wire (Top) and with single strand wire (Bottom)



http://www.case.edu/groups/ANCL/pages/05/05_61.htm



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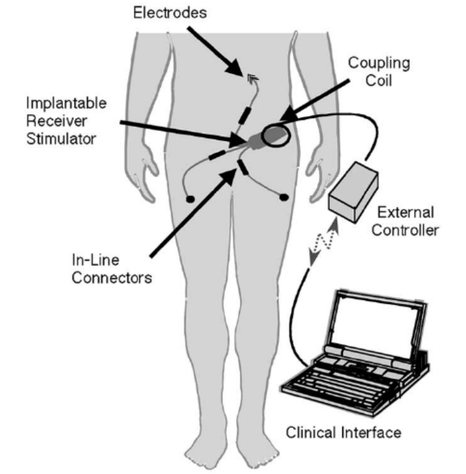


Fig. 2. Schematic of the implanted FNS system for standing. The implantable receiver-stimulator, electrodes and inline connectors are all implanted inside the body. The portable external controller communicates with the implanted system through a coupling coil. The clinical interface enables the clinician to program the external controller using a laptop PC. Six epimysial electrodes are implanted on various lower extremity muscles, and two intramuscular electrodes are implanted in the erector spinae muscles.

Fig. 1. Epimysial electrode used for activation of lower extremity muscles in an implanted FNS system for standing.

Upper extremity applications

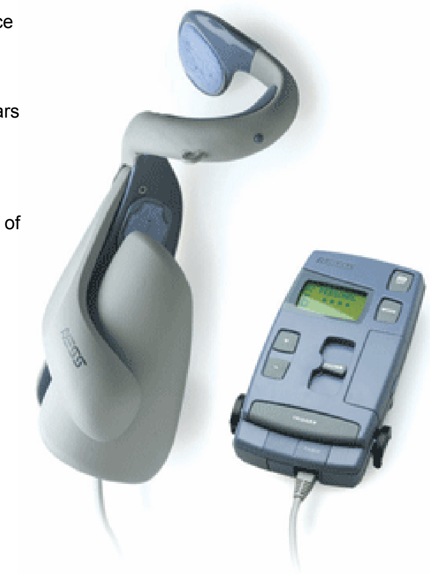
- Restoring hand grasp and release
- Handmaster (Ness, Israel)
- Bionic Glove (Prochazka)
- Freehand system (NeuroControl)

Neuromuscular Electrical Stimulation Systems

http://www.nessltd.com/

The NESS H200 is a non-invasive, portable device for combating and treating the consequences of brain damage.

This personal system is the outcome of many years of development. It is an incorporation and integration of the most effective state of the art upper limb rehabilitation technologies in a single system. It brings the fruits of the latest clinical laboratory research and expertise into the homes of patients for independent use.



The Bionic Glove: An Electrical Stimulator Garment That Provides Controlled Grasp and Hand Opening in Quadriplegia

Arthur Prochazka, PhD, Michel Gauthier, BEng, Marguerite Wieler, BABSc, PT, Zoltan Kenwell, Dipl Eng

Archives of Physical Medicine and Rehabilitation
Volume 78, Issue 6 , June 1997, Pages 608-614

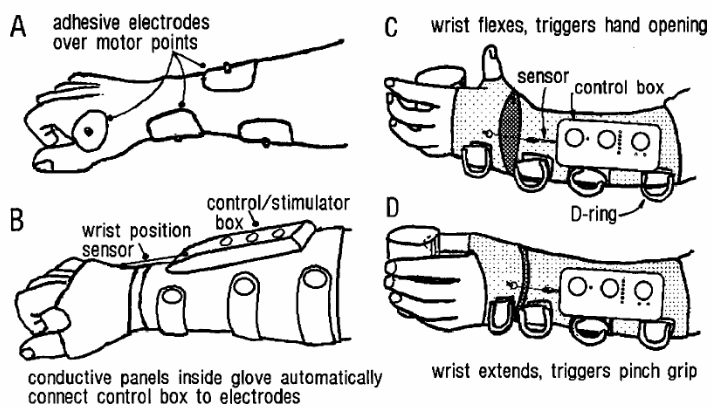
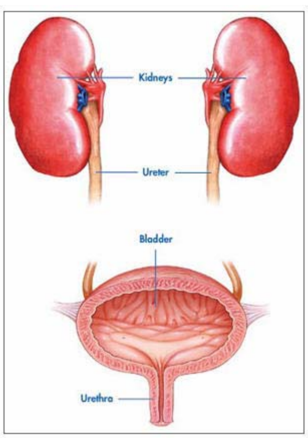
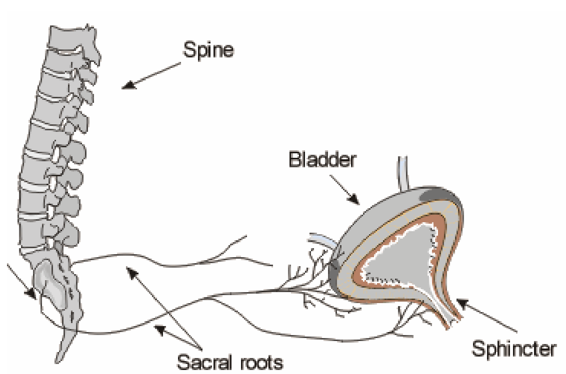


Fig 1. The Bionic Glove. (A) Self-adhesive electrodes are placed over motor points of the muscles to be stimulated. (B) The glove is donned and tightened onto the electrodes, making electrical contact with them (Fig 2). (C) Voluntary flexion of the wrist to a preset trigger angle initiates stimulation of the muscles that open the hand. (D) Extending the wrist to another trigger angle directs stimulation to the muscles that produce grasp.

Urinary Bladder: location and activation





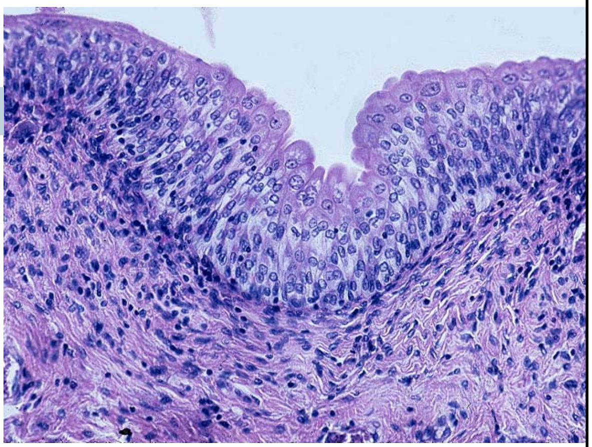
http://www.polystim.polymtl.ca/anglais/urinaire/intrurin.html

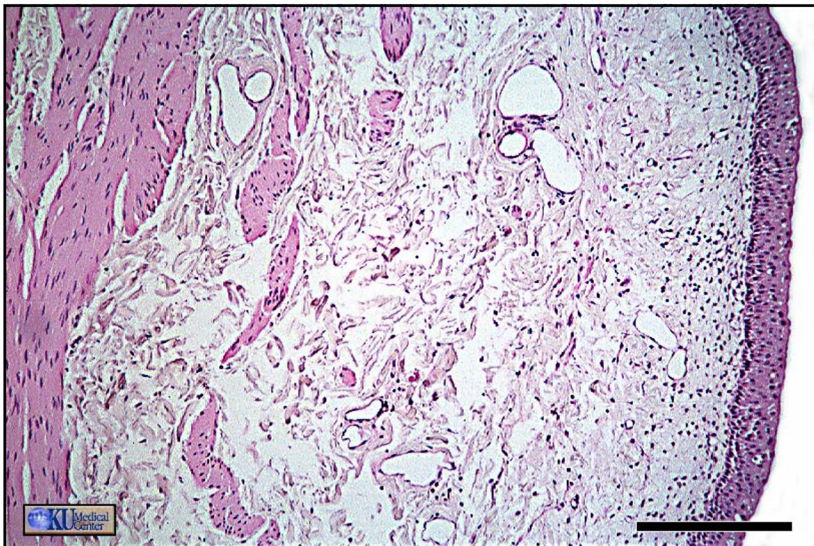
Urinary Bladder: histology

Tutorial Name: Neoplasia
ConceptName: In situ carcinoma
Slide Name: Bladder Transitional Epithelium

Image Description: Transitional epithelium is found only in the conducting passages of the urinary system. Note the columnar surface cells with their large nuclei and prominent nucleoli. These are typical of transitional epithelium.

Structures	Structure Descriptions
lamina propria	In the bladder, this is the rather dense connective tissue layer beneath the epithelium.
transitional epithelium	When the bladder is not distended (as in this slide), the line of swollen cells at the surface is particularly evident.

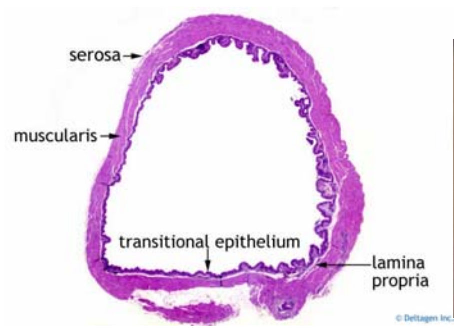


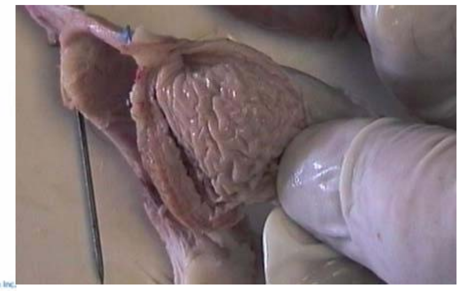


Slide 17 Bladder Wall
The bladder has transitional epithelium and a thick lamina propria to allow for expansion. You will be thankful for this on those long days in lab. Bar = 250 Microns

http://www.kumc.edu/instruction/medicine/anatomy/histoweb/urinary/renal17.htm

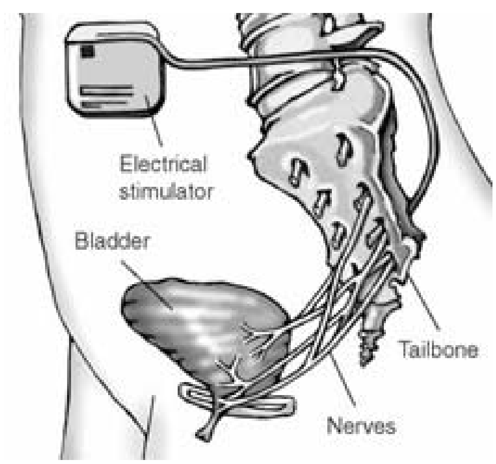
Urinary Bladder: how does it really look?





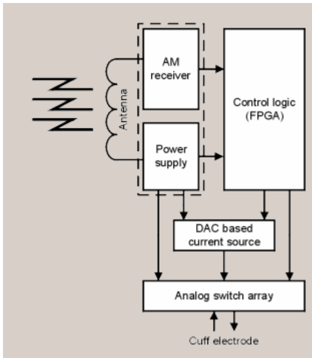
(right) http://www.deltagen.com/target/histologyatlas/atlas_files/genitourinary/urinary_bladder_4x.jpg
(left) http://library.thinkquest.org/15401/images/organs_urinarybladder.jpg

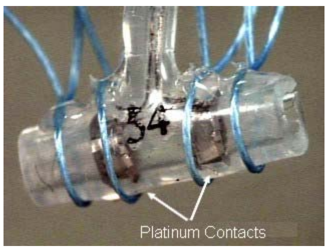
Urinary Bladder Implant. How would you do it?

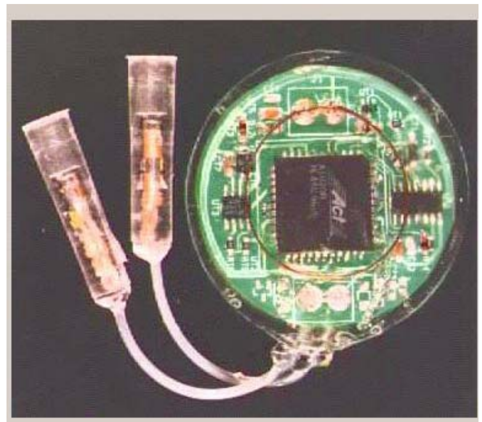


http://kidney.niddk.nih.gov/kudiseases/pubs/nervedisease/images/stimulator.jpg

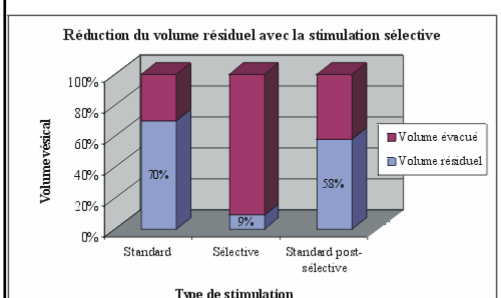
Implantable bladder stimulator

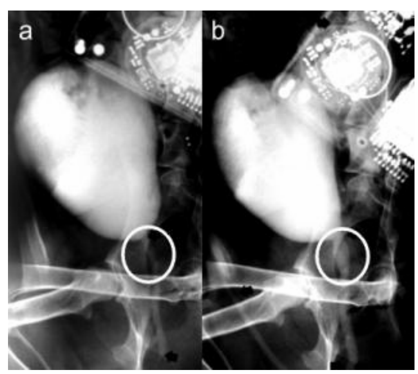






http://www.polystim.polymtl.ca/anglais/urinaire/implant.html

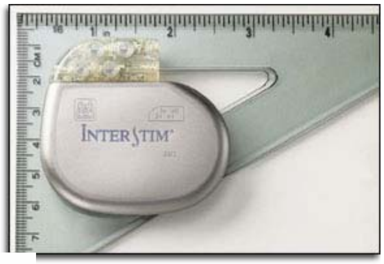


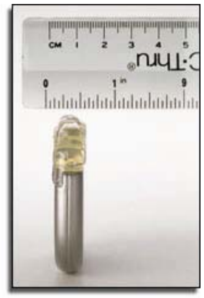


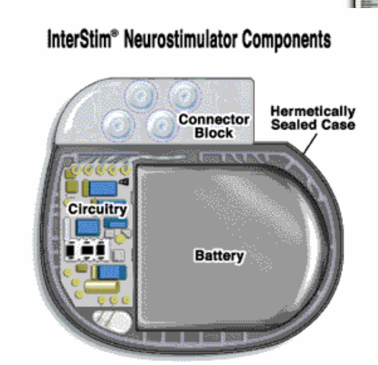
X-rays show the sphincter contracted before stimulation (a) and loosen during stimulation (b). Also, the graph above shows that the stimulation efficiency is enhanced by more than 50% with selective stimulation, leading to an average residual volume of 9%. These results are taken from studies on 8 different subjects.

http://www.polystim.polymtl.ca/anglais/urinaire/implant.html

Medtronic's InterStim™ Bladder Stimulator



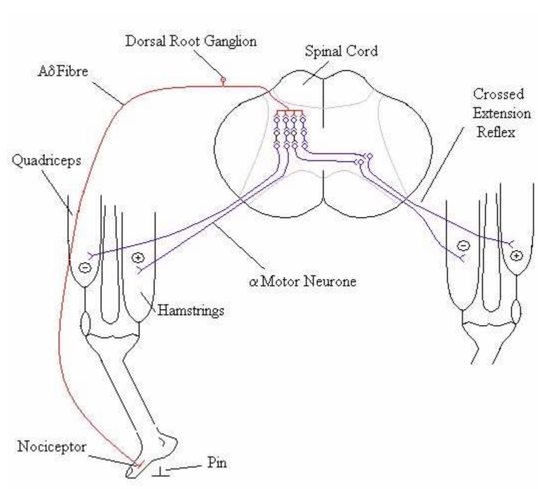




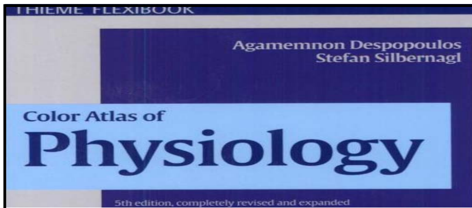
It measures 2.4 inches (6cm) by 2.2 (5.5cm) by 0.4 inches (1cm), with a weight of 1.5 ounces (42 grams)

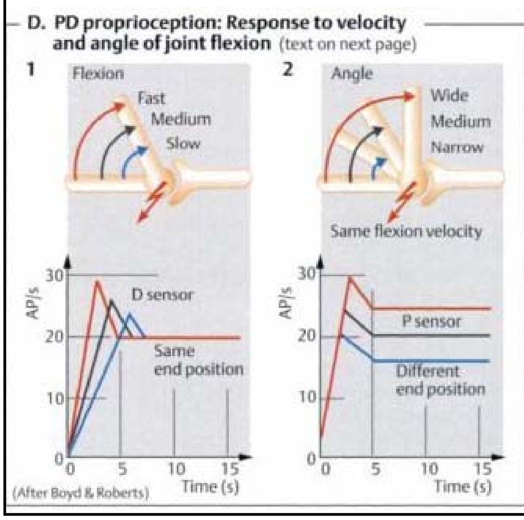
http://www.medtronic.com/servlet/ContentServer?pagename=Medtronic/Website/ConditionArticle&ConditionName=Urgency-Frequency&Article=urinary_art_device

Spinal Reflex – what is it?



http://137.222.110.150/calnet/LMN/LMN.htm





Supraspinal activation (→ **B3**). Voluntary muscle contractions are characterized by *co-activation* of α and γ neurons. The latter adjust the muscle spindles (length sensors) to a certain set-point of length. Any deviations from this set-point due, for example, to unexpected shifting of weight, are compensated for by re-adjusting the α-innervation (*load compensation reflex*). Expected changes in muscle length, especially during complex movements, can also be more precisely controlled by (centrally regulated) γ fiber activity by increasing the preload and stretch sensitivity of the intrafusal muscle fibers (*fusimotor set*).

Hoffmann's reflex can be also used to test the stretch reflex pathway. This can be done by positioning electrodes on the skin over (mixed) muscle nerves and subsequently recording the muscle contraction induced by electrical stimuli of different intensity.

Polysynaptic circuits, also arising from type II afferents complement the stretch reflex. If a stretch reflex (e.g., knee-jerk reflex) occurs in an extensor muscle, the α motoneurons of the antagonistic flexor muscle must be inhibited via *inhibitory Ia interneurons* to achieve efficient extension (→ **D1**).

Deactivation of stretch reflex is achieved by inhibiting muscle contraction as follows: 1) The muscle spindles relax, thereby allowing the deactivation of type Ia fibers; 2) the Golgi tendon organs inhibit the α motoneurons via type Ib interneurons (→ **D2**); 3) the α motoneurons are inhibited by the interneurons (*Renshaw cells*; → **D4**) that they themselves stimulated via axon collaterals (*recurrent inhibition*; → **D3**; p. 321 C1).

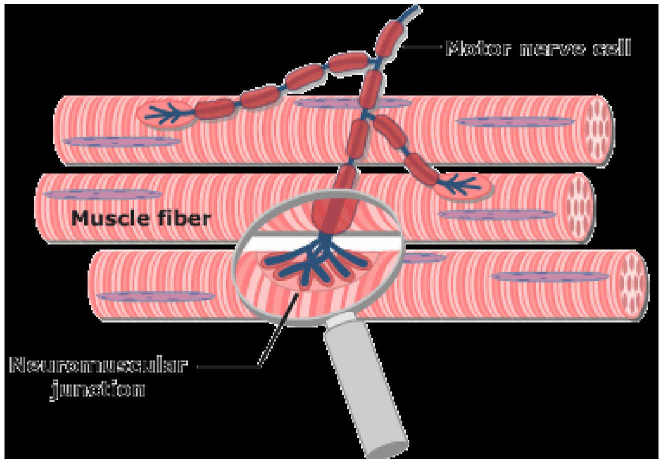
Homework 7

1. Find, in the literature (IEEE, for example) a paper presenting a graph or numbers of FES results, with stimulus intensity versus force (by the muscle). Copy the figure or make one (out of the numbers) and explain (one paragraph is enough) what the implant is for, and what the regions you see are (plateau, high gain, linear, etc).

2. Write me an email with the time and day you can come present your project. It should be a 20min deal. I would like to see all of you on Monday, but if you can't make it, my available days and times are:
   - Monday, Nov 6th, either between 9am and 3pm, or from 5:15 to 7pm.
   - Tuesday Nov 7th, afternoon (12pm to 3:30pm)
   - Wednesday Nov 8th, from 8am to 4pm.

   You should bring a small presentation on your project. Maximum of 10 slides. Be ready to answer questions. This will be the second phase of you project, and you will be graded for it (not as a homework).

Electrical Stimulation of the Neuromuscular system: mathematical derivations and simulations



The “del” operator (nabla, or ∇)

$$\nabla = \mathbf{i}\frac{\partial}{\partial x} + \mathbf{j}\frac{\partial}{\partial y} + \mathbf{k}\frac{\partial}{\partial z}$$

Gradient of p (where p is a scalar field): a vector field!

If we simply multiply a scalar field such as p(x,y,z) by the del operator, the result is a vector field, and the components of the vector at each point are just the partial derivatives of the scalar field at that point, i.e.,

$$\nabla p = \mathbf{i}\frac{\partial p}{\partial x} + \mathbf{j}\frac{\partial p}{\partial y} + \mathbf{k}\frac{\partial p}{\partial z}$$

Now we want to multiply a vector field v by the gradient.

Dot product between vectors a(x,y,z) and b(x,y,z):

____

Cross product between same vectors:

____

1) Dot product between gradient and **v**(x,y,z):
Defined as the DIVERGENCE of **v** (it's a scalar!)

$$\nabla \cdot \mathbf{v} = \frac{\partial v_x}{\partial x} + \frac{\partial v_y}{\partial y} + \frac{\partial v_z}{\partial z}$$

2) Cross product between gradient and **v**(x,y,z):
Defined as the CURL of **v** (it's a vector!)

$$\nabla \times \mathbf{v} = \left(\frac{\partial v_z}{\partial y} - \frac{\partial v_y}{\partial z}\right)\mathbf{i} + \left(\frac{\partial v_x}{\partial z} - \frac{\partial v_z}{\partial x}\right)\mathbf{j} + \left(\frac{\partial v_y}{\partial x} - \frac{\partial v_x}{\partial y}\right)\mathbf{k}$$

Laplacian operator (∇^2): divergence of the gradient. Scalar field!

$$\nabla \cdot \nabla = \frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} + \frac{\partial^2}{\partial z^2}$$

Introduction

- Restoring function is not immediate in paralysis.
  Ex. FreeHand (by NeuroControl™)

- FES (functional electrical stimulation): stimulate the neuromuscular junction, neuron is stimulated first (less charge needed)

- Phrenic nerve stimulation: restore respiration (ventilation)

Quasi-static formulation of Maxwell's equations

Equivalence between dielectric and conductive media: It helps to look in static fields (due to point charges) and relate to fields due to current sources and sinks.

At any point P in the volume conductor, the current flowing could be generated by a source at that point (J_s) or could be the ohmic current generated by a distant source (Plonsey, 1969). Therefore, the current density $\boldsymbol{J}$ at any point is the sum of a source term $\boldsymbol{J}_s$ and an ohmic term $\boldsymbol{J}_\Omega$.

$$\boldsymbol{J} = \boldsymbol{J}_\Omega + \boldsymbol{J}_s = \sigma \boldsymbol{E} + \boldsymbol{J}_s \tag{5.5}$$

Using Eq. (5.1)

$$\nabla \cdot \boldsymbol{J} = \nabla \cdot (\sigma \boldsymbol{E}) + \nabla \cdot \boldsymbol{J}_s = 0 \tag{5.6}$$

Assuming a homogeneous volume conductor, $\nabla \cdot (\sigma \boldsymbol{E}) = \sigma(\nabla \cdot E)$; therefore

$$\nabla \cdot \boldsymbol{E} = -\nabla \cdot \boldsymbol{J}_{s/}\sigma \tag{5.7}$$

Because $\boldsymbol{E} = -\nabla V$

$$\nabla^2 V = \nabla \cdot \boldsymbol{J}_{s/}\sigma = -I_v/\sigma \tag{5.8}$$

where I_v is a volume current in A/m^3 and ∇^2 is the Laplacian operator. The volume current I_v can be calculated from the knowledge of the distribution of sources in the volume conductor. This equation is the equivalent of the Poisson equation derived for dielectrics:

$$\nabla^2 V = -\rho/\varepsilon \tag{5.9}$$

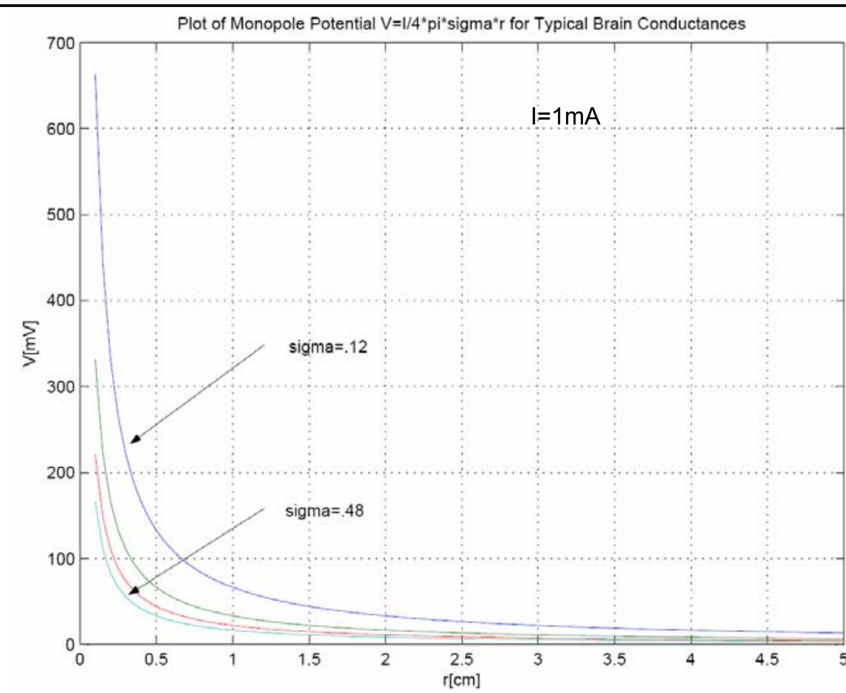
derived for dielectric media. Using the following equivalence,

$$\rho \Leftrightarrow I_v$$
$$\varepsilon \Leftrightarrow \sigma$$

the solution of the Poisson equation for dielectric problems can be applied to the calculation of the current and voltage distribution in volume conductors.

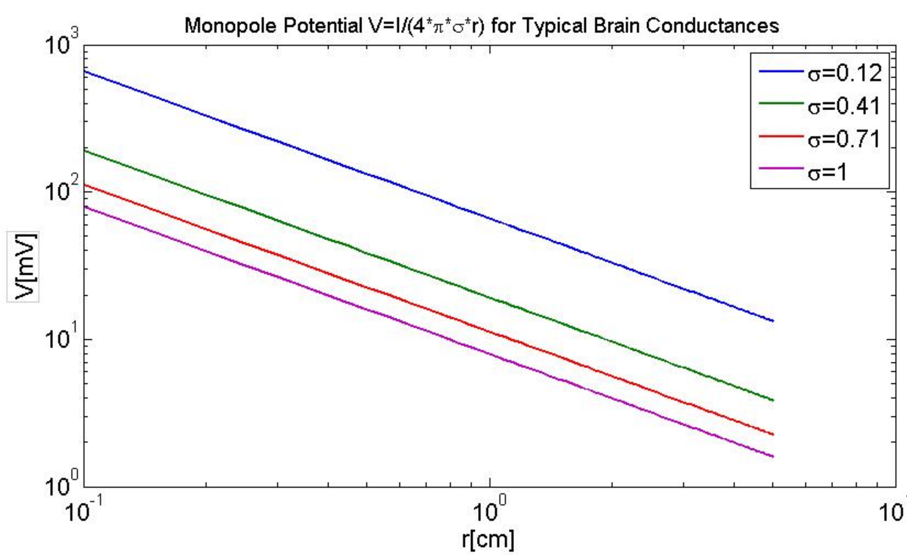
Now let's derive the voltage at a point along the axon of a neuron being stimulated by an electrode with a monopolar current source.

(See notes)

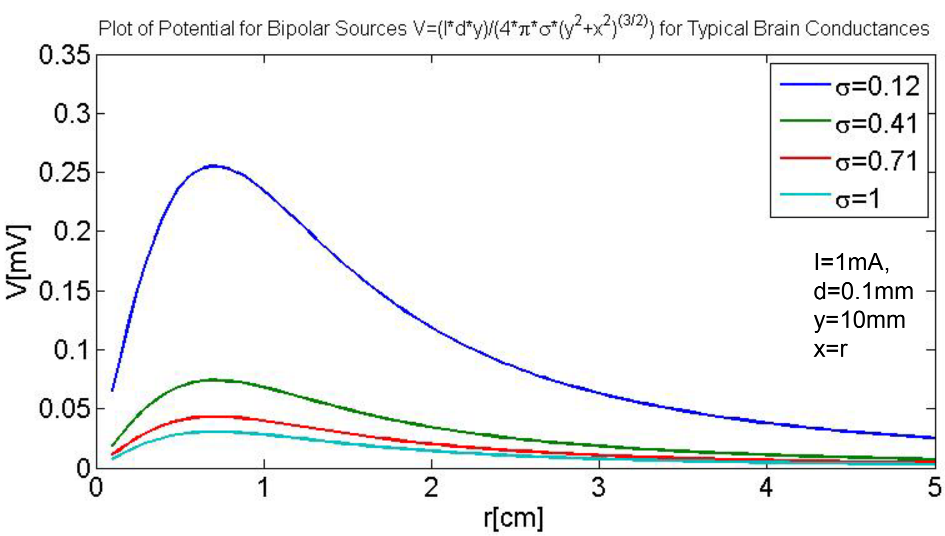


The Matlab code should be either VERY simple, or understandable (if you have never programmed in Matlab in your life).

```
i=1e-3;  % current. Assume I=1mA

sigma=linspace(.12, 1, 4);  % conductivity range

r=linspace(.001, .05, 100);  % axon distance range (in meters)

for k=1:4;
  for j=1:100;
      v(k,j)=i/(4*pi*sigma(k)*r(j));
  end;
end;
plot(r*100,v*1000);
grid
xlabel('r[cm]');
ylabel('V[mV]');
title('Plot of Monopole Potential V=I/4*\pi*\sigma*r for Typical Brain Conductances');
```



Voltage along the axon due to a bipolar source. Current through one electrode has the same amplitude (but opposite sign) as current through the other electrode.



Now plot both sides of an axon – orthodromic and antidromic – for the bipolar stimulation.

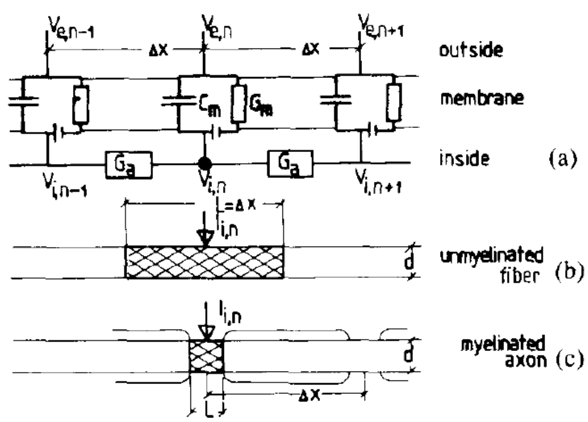


Fig. 1. Electrical network to simulate the currents in an axon. Unmyelinated as well as myelinated fibers are segmented into cylinders of length Δx. Whereas Δx is given by the internodal distance in the myelinated case, Δx depends only on computational accuracy for unmyelinated fibers. Within one segment the membrane is active in the cross-hatched area of length L which is the nodal gap width in (c), and $L = \Delta x$ in case (b). The membrane of every cylinder is simulated by an electric circuit (a) consisting of capacity C_m, an ionic voltage source, and the nonlinear membrane conductance G_m. G_a symbolizes the conductance of axoplasm between two segments. $V_{e,n}$ and $V_{i,n}$ are the external and the internal potential of the nth segment.

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Analysis of Models for Extracellular Fiber Stimulation

FRANK RATTAY

$$f = \frac{\partial^2 V_e}{\partial x^2} = \frac{\rho_e I_{el}}{4\pi}(x^2 + z^2)^{-2.5}(2x^2 - z^2).$$

TABLE I
SYMBOLS AND [UNITS]

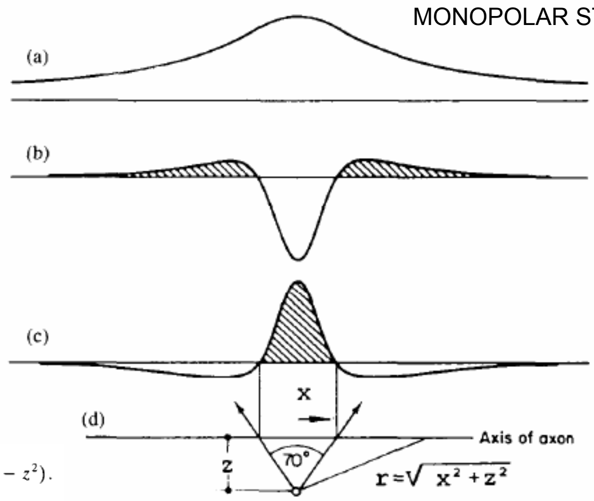
C_m	capacity of membrane	[μF]
c_m	capacity of membrane per cm^2	[μF/cm^2]
G_a	conductance of axoplasm	[mS/cm]
ρ_i	resistivity of axoplasm	[kΩ · cm]
ρ_e	extracellular resistivity	[kΩ · cm]
$V_{i,n}$	internal potential	[mV]
$V_{e,n}$	external potential	[mV]
V_{rest}	internal resting potential	[mV]
V_n	reduced membrane voltage (2)	[mV]
x	length coordinate of the fiber	[cm]
Δx	segmentation length of the fiber	[cm]
L	active length of membrane	[cm]
d	fiber diameter	[cm]
r	distance to electrode	[cm]
z	distance of the electrode to the fiber	[cm]
I_{el}	current of the electrode	[μA]
f	activating function (6)	[mV/cm^2]
x_j, z_j	coordinates of the jth electrode	[cm]
$I_{el,j}$	current of the jth electrode	[μA]
T	temperature	[°]
t	time	[ms]

MONOPOLAR STIM

EXTRACELLULAR **V**
ALONG THE FIBER

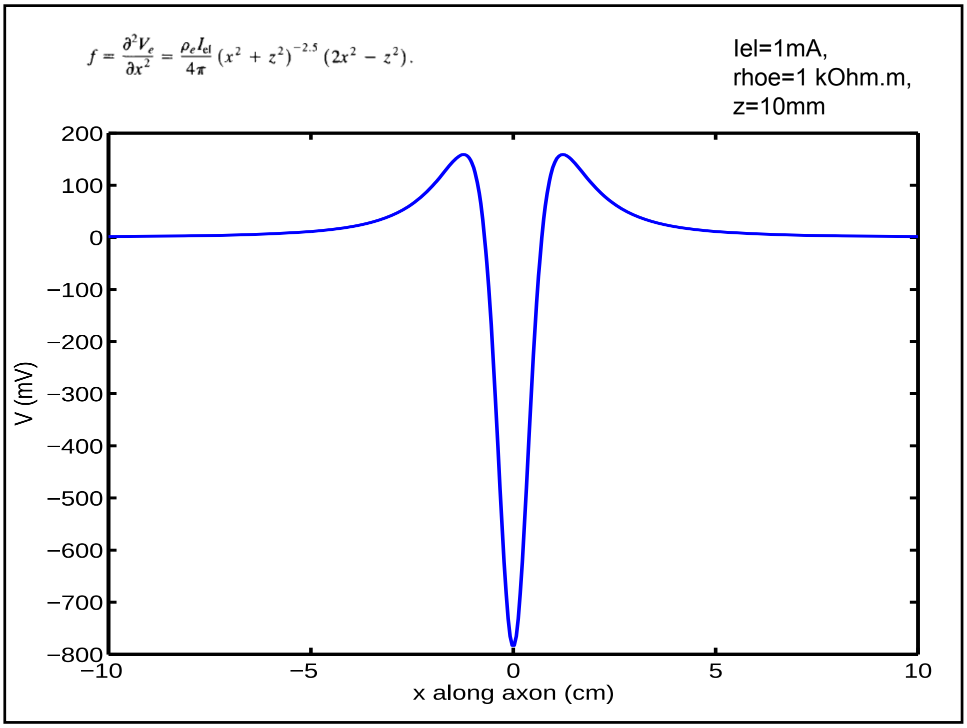
ANODIC STIMULATION

CATHODIC STIMULATION

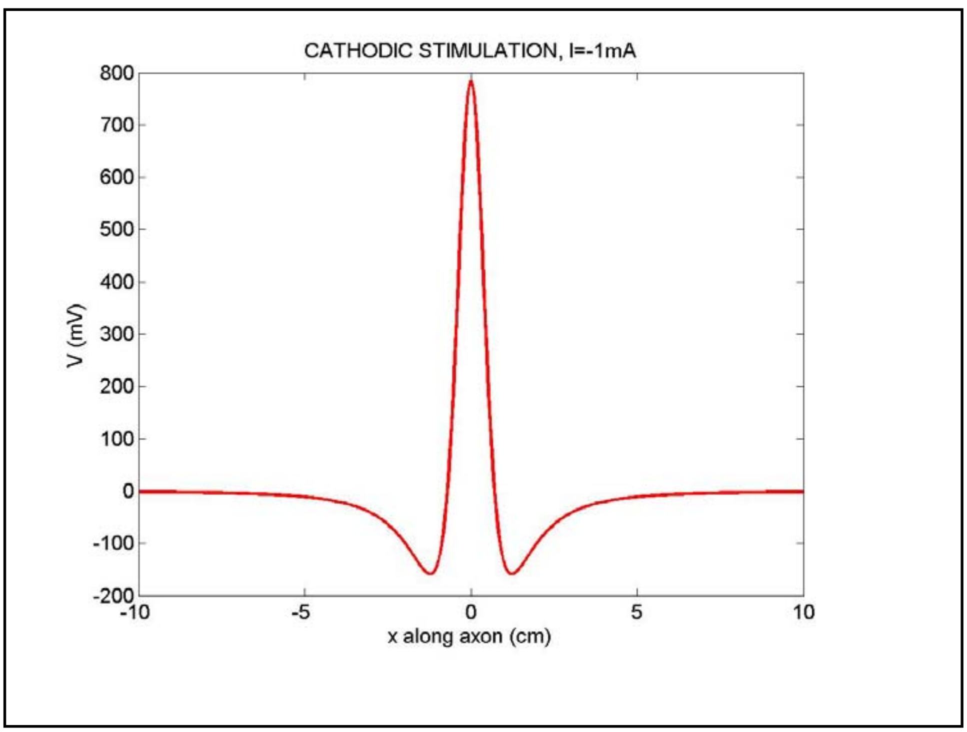


$$f = \frac{\partial^2 V_e}{\partial x^2} = \frac{\rho_e I_{el}}{4\pi}(x^2 + z^2)^{-2.5}(2x^2 - z^2).$$

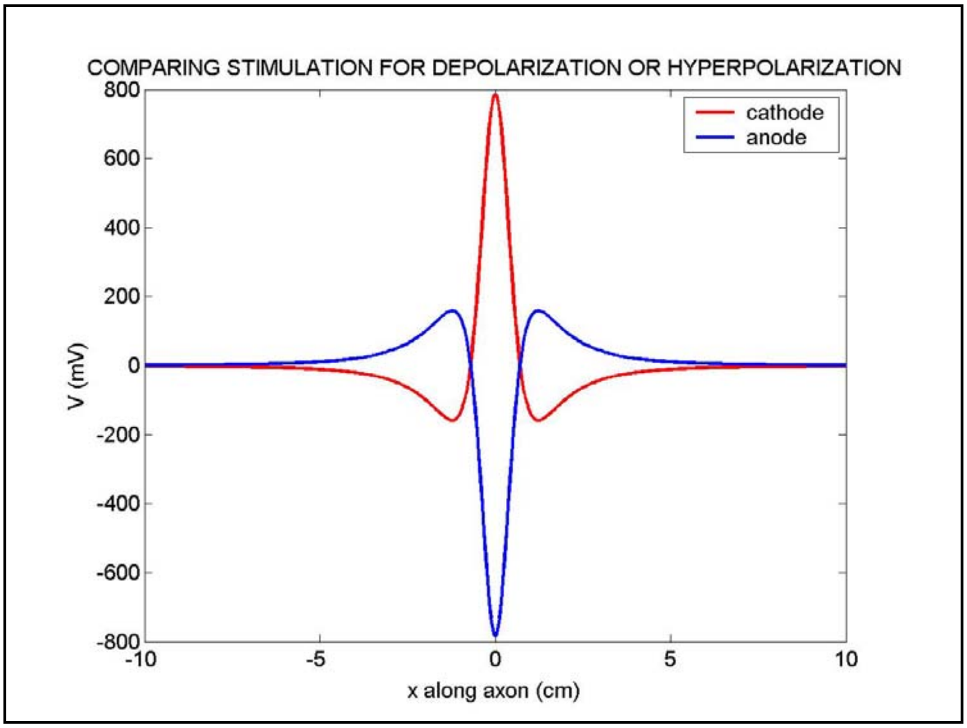
Fig. 2. Stimulation with a monopolar electrode. (a) Change of the extracellular potential along the fiber caused by anodal stimulation. Activating function for anodic (b) and cathodic (c) stimulation. (d) Shows the position of the electrode to get the upper traces. The border between depolarizing and hyperpolarizing regions is given by an angle of 70.5° and this angle does not depend on fiber parameters or the conductance of the extracellular medium [1]. Removing a negative electrode from the axon means to obtain a broader stimulating part; in the case of a myelinated axon more nodes are stimulated.



$f = \frac{\partial^2 V_e}{\partial x^2} = \frac{\rho_e I_{el}}{4\pi}(x^2 + z^2)^{-2.5}(2x^2 - z^2).$
Iel=1mA,
rhoe=1 kOhm.m,
z=10mm
V (mV)
x along axon (cm)



CATHODIC STIMULATION, I=-1mA
V (mV)
x along axon (cm)



COMPARING STIMULATION FOR DEPOLARIZATION OR HYPERPOLARIZATION
cathode
anode
V (mV)
x along axon (cm)
800
600
400
200
0
-200
-400
-600
-800
-10
-5
0
5
10