ZOO 332H1S - **Lecture 1,2**
Jan. 06, 2003
Introductory Neurobiology

C.S.Sherrington with one of his pupils (J.C.Eccles) in the mid 1930's

People

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Required text

- **From Neuron to Brain** - Nicholls, Martin, Wallace and Fuchs (2001), 4th Ed., Sinauer Publishers
  - or:
- ***Neuroscience*** *- Purves et al. (2001), 2nd Edition*
- Are available in the Bookstore
- You'll need it or an equivalent, and lecture notes to do well in this course. . .
- Web page notes contain most of the figures used in lectures (but not all)

Alternate textbooks of interest - NOT required but...

Essentials of Neural Science and Behavior; edited by Kandel, Schwartz and Jessell (1995; Appleton and Lange); if you really like this style of writing/presentation then you may check-out the larger, more complete version of this text by Kandel *et al.* (although it also costs more $$ it is a better investment than Essentials – for the long term)

The Neuron - Levitan and Kaczmarek (1997; 2nd Ed., Oxford)

Content

- Course content is defined by the lectures, text (Nicholls *et al.*), and handouts - tests and exams will be based on this material
- Lectures and tutorials are to
  - Assist you in learning
  - Add explanations & material (some of which may not be in the textbook)
  - Bring in guest speakers
- Guest lecturer material is N.B… and could be on the exam.

The Web

- ZOO332H1S web site is at
  - http://www.zoo.utoronto.ca/zoo332/myweb/homepg.htm

NOTE: If needed, I can put a copy of slides printed from the web pages in RWZL 019.

* Acknowledgement: I am very grateful to Professors Ian Orchard and JJB Smith for their kindness and generosity when I began teaching of this course.

Prerequisite Material

- Neurobiology section of ZOO252Y or equivalent (Intro Physiol textbook)
- Prof. Smith's web site for ZOO252 at
  - http://www.zoo.utoronto.ca/...
  - Chapter 1 & 2 of Nicholls *et al*.

TODAY (Ch.1 NMWF)

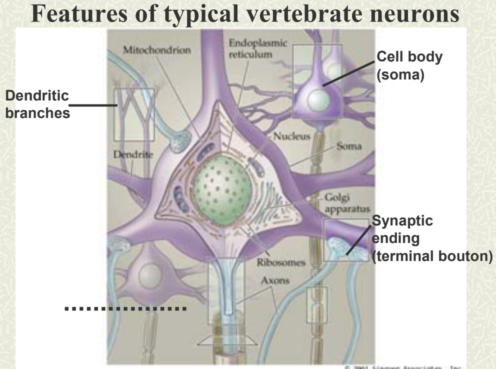
Properties of neurons

- **morphology ("typical" neurons)**
- **connectivity**
- **response/coding**
- **support**

Differentiate: neuron, nerve, axon, nerve bundle, nerve fibre, *etc*.

Electrical Properties of Neurons (begin)

Features of typical vertebrate neurons



Purves *et al.* 2001

Diverse Morphology (part 1)

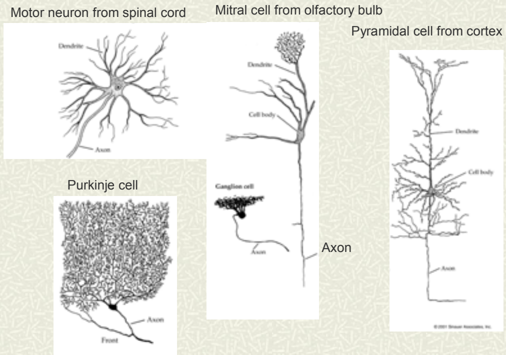


Fig 1.4

Structure and Connections of Cells in the Mammalian Retina

-original scheme proposed by Ramon y Cajal (*ca*. 1909-1911), general path of information flow

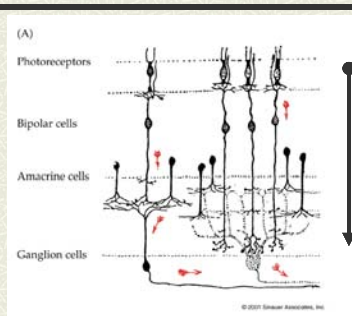


Fig1.2

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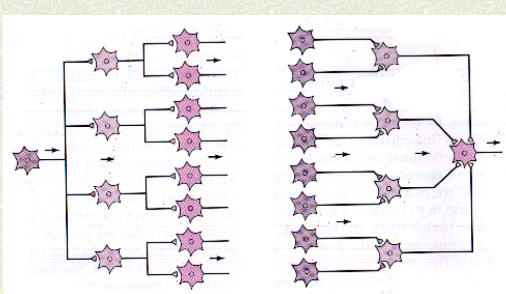
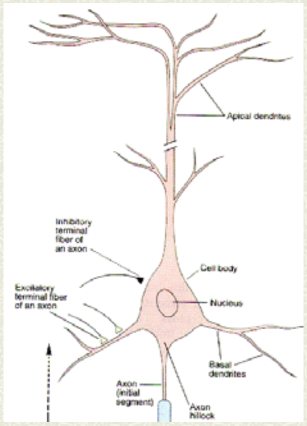
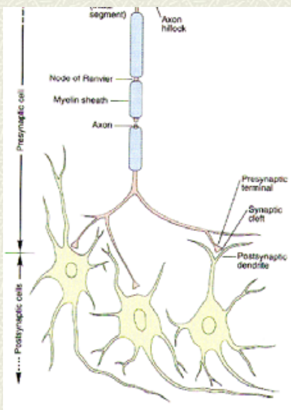
Connectivity of neurons

Divergence . . . . . . and convergence



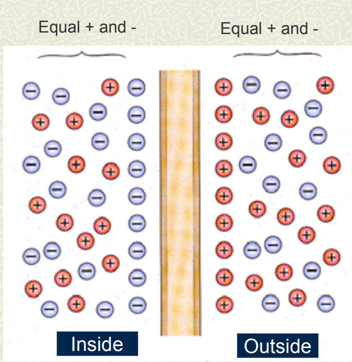
Cont...Features of typical vertebrate neurons





2-1

All cells have a membrane potential V_m



Recording from the Nervous System

Extracellular Recordings

Record from group of cells or single cell (A – cortical neuron)

Diversity of preparations

Advantages and disadvantages

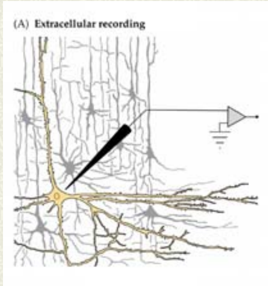


Fig 1.6

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cont…Recording from the Nervous System

Intracellular Recording

Fluid filled, glass capillary microelectrode; high R; tip size

Impale single cell; resting and APs

Patch Clamp Recording

Several configurations (later)

Very high R (giga-ohm seal); tip size

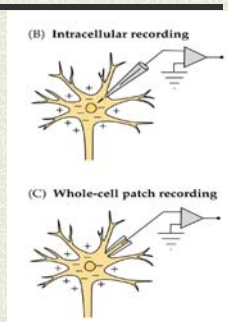

Fig 1.6

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Localized Graded Potentials

- Intracellular recordings made using microelectrodes
- signal from receptor cell, causes membrane potential in bipolar cell to become less negative = depolarization
- size of signal
- passive spread (local potential)
- chemical transmitter

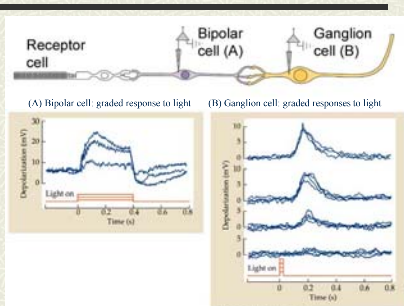

Fig 1.8

Action Potential

- Current injected
- Threshold
- Membrane potential
- AP propagates
- Transmitter release

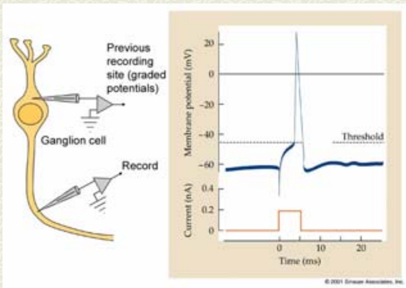

Fig 1.9

Excitation and Inhibition

- Stimulus
- Membrane potential
- Threshold
- APs on EPSP
- Transmitter release
- IPSPs effect on excitability

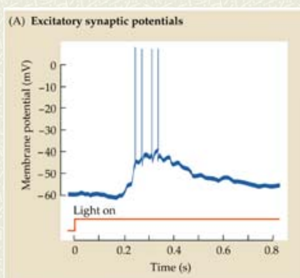

Fig 1.12

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cont…Excitation and Inhibition

- Stimulus
- Membrane potential
- Threshold
- IPSPs effect on excitability
- response dependent upon cell type (receptor(s)), not stimulus

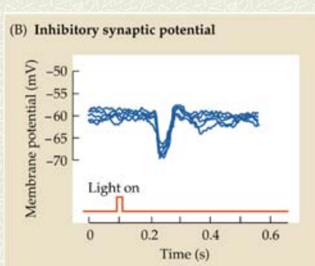

Fig 1.12

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Frequency as a signal of intensity

- Stimulus
- Membrane potential
- Threshold
- EPSP effect on excitability
- Frequency, not amplitude of APs
- Transmitter release

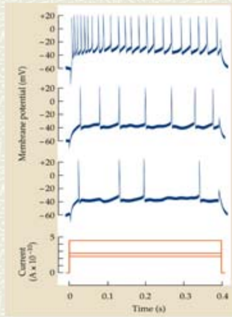

Fig 1.12

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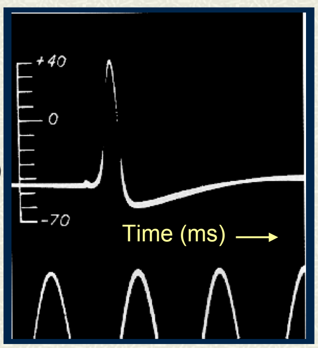
E_m (mV)

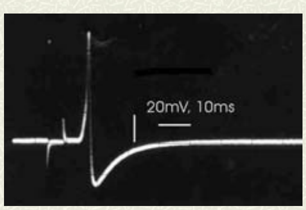


Action potential from squid giant axon (Hodgkin & Huxley, 1939)

Hodgkin (1949) and Huxley (1974)

Action Potential - Cockroach DUM Neuron

- **D**orsal **U**npaired **M**edian neuron
- bars
- RP -45 mV
- AP evoked by stimulus to N5L of T3



- (N5L contains axons which innervate leg muscles; T3 is the 3rd thoracic ganglion of *P. americana* (L.) (more on this later))

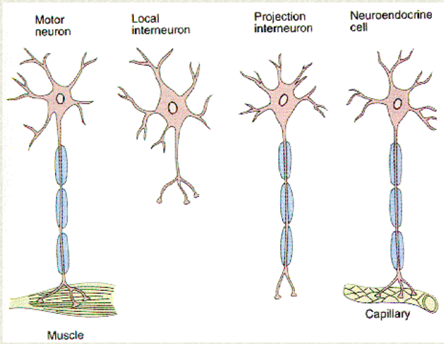
Functional regions of neurons

Input

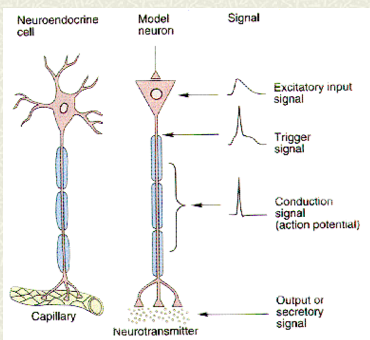
Trigger

Conduction

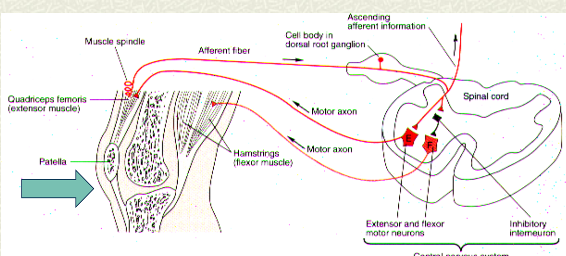
Output



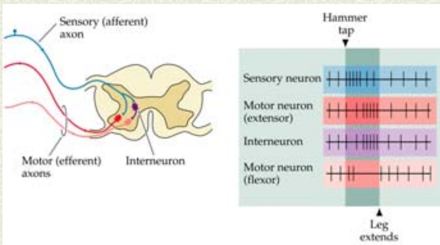
cont…Functional regions and electrical recording



Back to Neurons in action - A "typical" monosynaptic reflex system: the mammalian "knee-jerk"

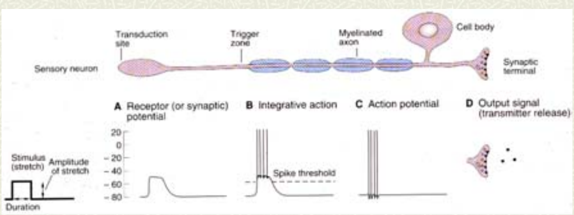


cont…. the mammalian "knee-jerk"



Purves *et al.*, 2001

Action of sensory neurons



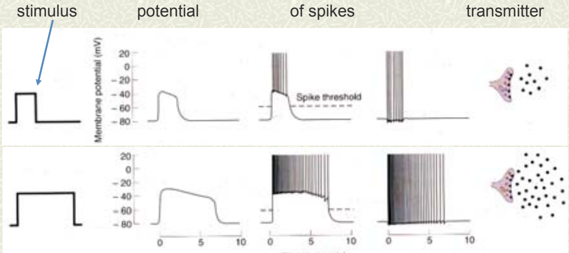
Size and duration of stimulus is represented by different patterns of APs and subsequently by quantity of NT released

Stronger stimulus

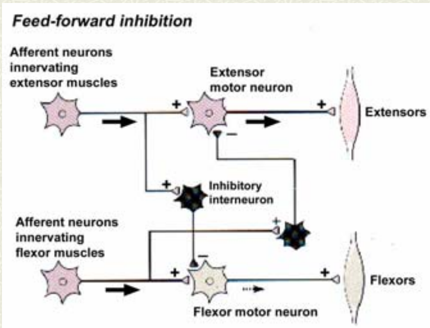
Larger receptor potential

Higher frequency of spikes

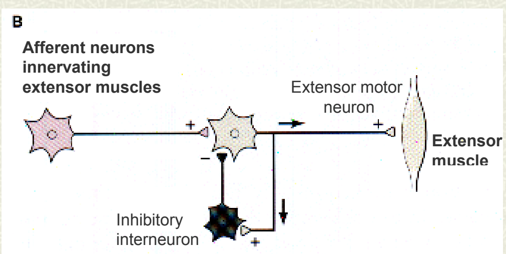
More transmitter



Inhibitory neurons in nerve circuits



Feedback Inhibition (autoregulation)

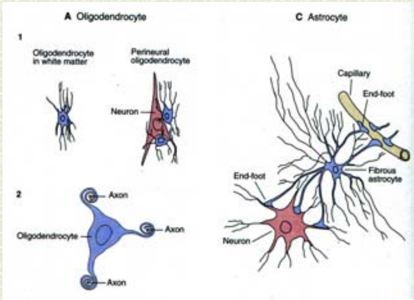


Support System for Neurons - Neuroglial Cells (we will return for more on this later)

- Both CNS and PNS neurons surrounded by ***satellite cells*** - Schwann cells (PNS) and neuroglial cells (CNS)
- CNS neuroglia - oligodendrocytes, astrocytes, radial glia cells
- Oligodendrocytes and Schwann cells form myelin around axons
- Very close apposition of glial and neuronal membranes
- Interesting components of glial cell membrane (dynamic interactions with other glial cells (GJ) and between glial cells and neurons - support, trophic, development, signalling)

Two Main Groups of Vertebrate Glial cells (CNS)

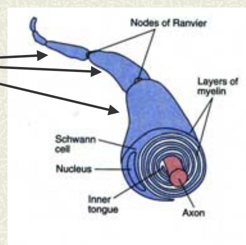
- Not neurons
- Subtypes
- Markers which identify types
- Other types of glial cells



Glial cell of the PNS (Peripheral NS) - Schwann Cells

Single Schwann cells

- analogous to oligodendrocytes
- form myelin around large axons
- around small axons but no myelin



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Lecture 2 - Jan. 2003.

Chapter 7 – NMWF

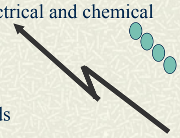
Neurons as Conductors of Electricity

(Cable Properties)

Neural Events

How does information travel around the nervous system?

Signalling in the nervous system – electrical and chemical



- Propagation of APs along axons by spread of electrical current
- Regenerative nature of APs depends on passive spread of current in local circuits ("local circuits of current flow")
- Attenuation of passive currents
- neuron geometry, electrical characteristics, myelination,

cont…Neural Events

- Ions in solution carry current
- By definition current is the movement of positive charge
- Current flow
  - due to the movement of ions (charged particles) across a resistance (the membrane)
  - Passive current flow – electrical
- Change in potential difference (V) across the membrane

Neurons signal electrically:

- receptor potentials
- synaptic potentials
- pacemaker potentials
- action (spike) potentials

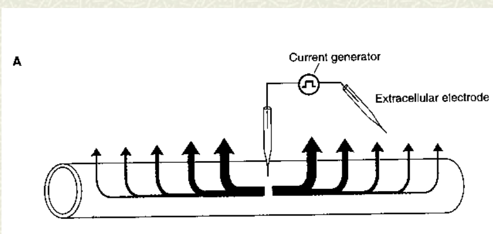
During these events V_m changes

- What determines the size of the change?
- What determines the rate of the change?
- Are these things important?

Cell processes, e.g. axons - Spread of <u>electrotonic</u> potentials

The axon as a conductor (like a copper wire with insulating jacket) – very bad…

<u>BUT</u>, properties of an axon that allow it to conduct electrical signals…



Pathways for Current Flow

- Stimulus, steady injection of current
- Membrane potential
- Threshold
- Current flow – thickness of arrows, related to current density at various positions

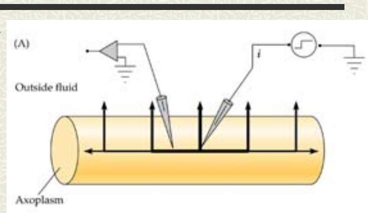


Fig 7.1

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cont…Pathways for Current Flow

- Stimulus, steady injection of current
- **(B)** Membrane potential measured at various points along axon
- decay of voltage (current) is exponential, with length constant given by λ (lambda)
- **(C)** equivalent electrical circuit (very simplified)

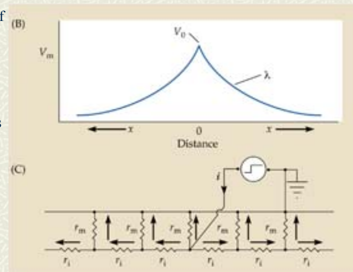

Fig 7.1

Effect of Capacitance on Time Course of Potentials

Rectangular pulse of current (i) delivered

(A) resistance (R) only, V change; time course

(B) Purely Capacitance (C), R8 of change of V proportional to applied current (i)

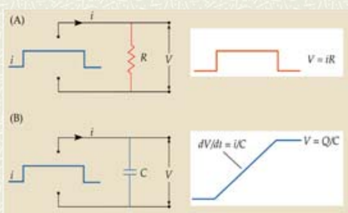

Fig 7.2

cont…Effect of Capacitance on Time Course of Potentials

(C) RC network – current applied to charge capacitance as well as across the R; V rises exponentially to final value determined by time constant,

τ = RC

(D) Electrical model of cable with R and C; note also r_i (internal or axoplasmic R)

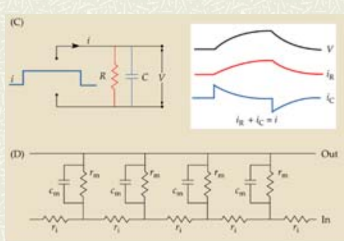

Fig 7.2

Current Flow During an Action Potential

1. Local circuit causes depolarization toward threshold
2. Membrane potential reaches threshold
3. Cascade of Na^+ entry
4. Positive current spread ahead of AP
5. Repolarization of membrane potential
6. Refractory period

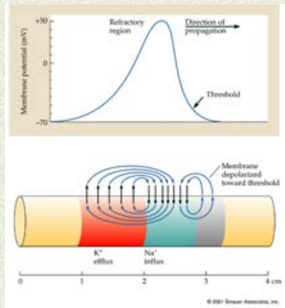

Fig 7.2

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Action Potentials and current flow in myelinated nerves (1)

- (Return to this in more detail later)
- Recall, role of myelination in CNS and PNS
- Structure of myelin
- Conduction velocity
- Consequence of loss of myelin? *Eg*. MS, GBS (more on this in later lectures)

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cont…Action Potentials and current flow in myelinated nerves (2)

Classic experiment of Tasaki (1959) showing current flow mainly through the nodes of Ranvier, little through internodal (myelinated) region

Note chamber #2: in (A) recording from node; in (B) – next slide – recording current flow from internodal region

Note 1st outward current (passive) then strong inward current (Na^+)

ohhh yes….

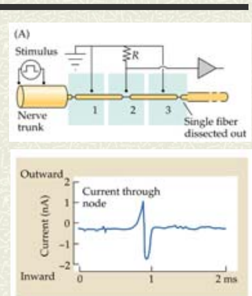

Fig 7.5

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cont…Action Potentials and current flow in myelinated nerves (3)

- When record current from internodal region
- Recall structure of myelin
- Recall cable/passive properties
- Recall saltatory conduction
- Recall threshold

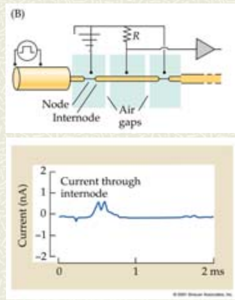
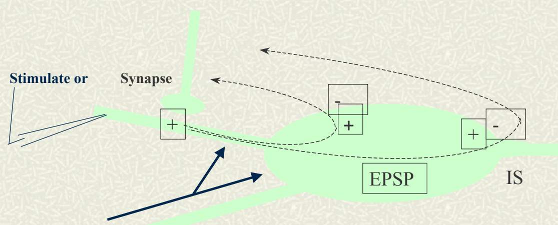


Fig 7.5

Synaptic currents act at a neuron's initial segment (axon hillock)

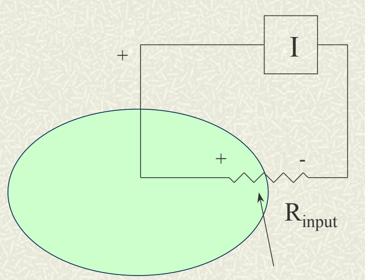


No APs in here (usually, but very much depends upon individual neuron (see pg. 128))

This story has become much more complex.

How effective is the EPSP current at the initial segment?

Cont...Injecting a current



$\Delta V_m = I \times R_{input}$

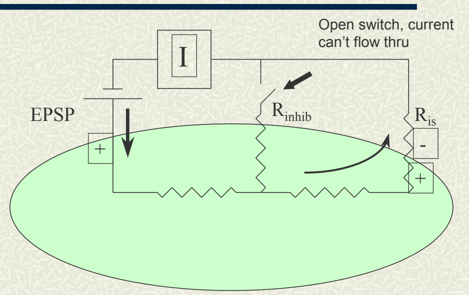
So ΔV_m is proportional to

- amplitude of membrane current I_m
- value of input resistance R_{input}
- R will depend on size of cell:
  - large cells, more membrane, more channels, smaller resistance
  - small cells, higher resistance
- so anything that changes membrane current (*e.g.*, a PSP) will have a larger effect in a smaller cell

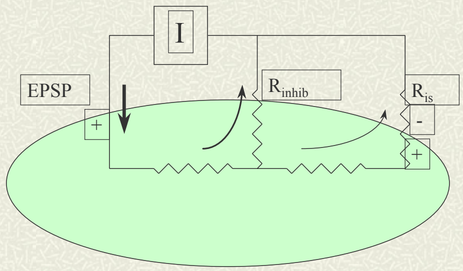
also

- R will depend on number of open channels
- So an inhibitory PSP can "short-circuit" the effect of an EPSP by decreasing R ***(make sure you understand this!) - see next slides***

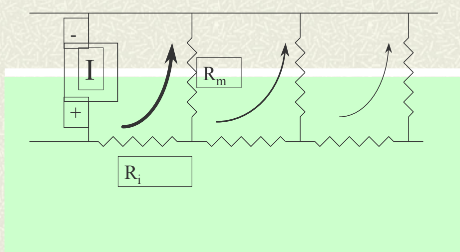
Action of synapses



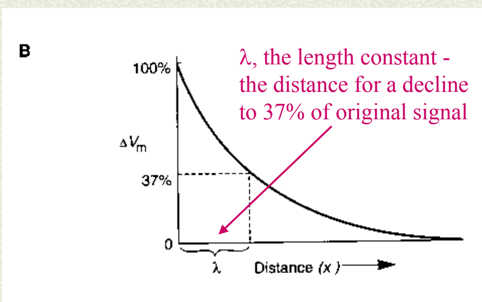
Cont...Action of synapses



cont. Spread of electrotonic potentials



Attenuation with distance



9-5

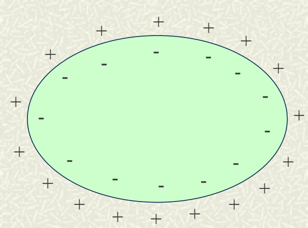
The length constant

- Typically 1 - 2 mm in a myelinated axon, about the same as the distance between Nodes of Ranvier (**not** coincidentally)
- Much smaller in fine dendrites

What about rate of change of potential across the membrane?

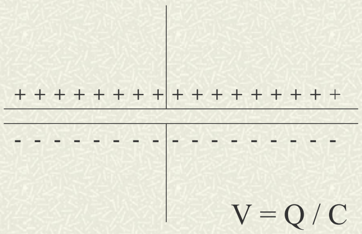
- helps determines how large is a remote PSP
- helps determine conduction velocity
- depends on membrane *capacitance*

Resting cells are -ve inside



This is a *steady state* - no **net** current is flowing

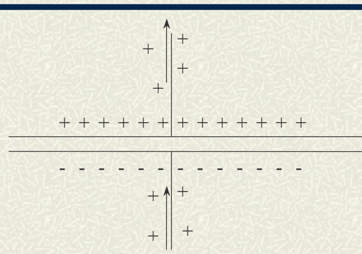
The membrane has capacitance



$$V = Q / C$$

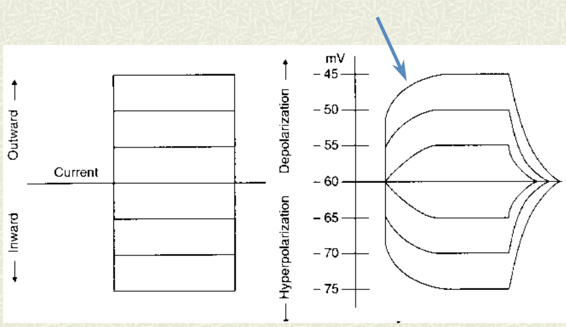
So to *change* V, charge (Q) must be changed

cont...The membrane has capacitance

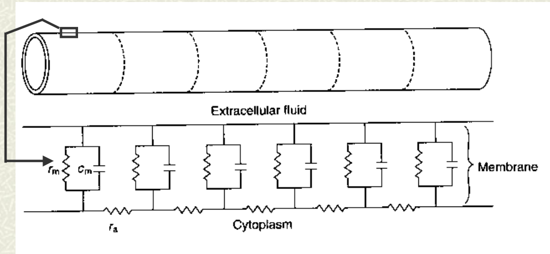


and *rate of change* of V is proportional to rate of movement of charge, i.e., *current*

which explains the delays in ΔV_m

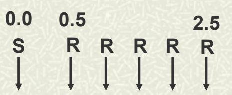


Equivalent resistance circuit

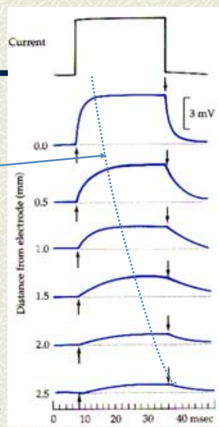


Signals attenuate in space and time

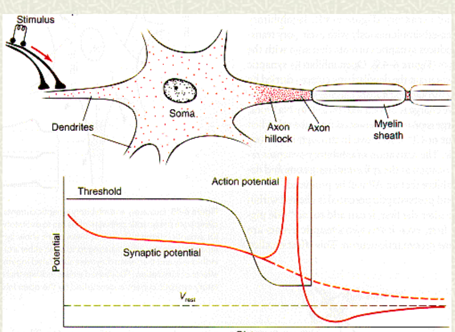
Note delay in reaching maximum voltage change



NMW 5-3



This is important in the spread of synaptic, receptor and action potentials



Next week….

Channels, resting and action potentials