9.09J/7.29J - Cellular Neurobiology, Spring 2005
Massachusetts Institute of Technology
Department of Brain and Cognitive Sciences
Department of Biology
Instructors: Professors William Quinn and Troy Littleton

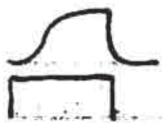
2/23/04

K^+ channels - 4 voltage sensor gates in series ($\frac{1}{12}$ probability of one gate being open)

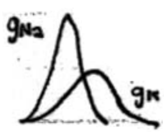
Na^+ channels - 4 voltage sensor gates also; 3 to open during depolarization, one swings closed slowly

- cytoplasmic loops w/ positive charge swing into Na^+ channel to inactivate it

what causes K^+ channels to inactivate? repolarization



- turn off voltage clamp, see if changes in voltage well modeled by H+H model (it is)
  - reasonable correspondance of shape, w/ threshold bifurcation, overshoot, undershoot, etc, also refractory period (absolute + relative)
    - ↳ larger depolarization can give action potential
- w/ math, can use H+H model to simulate propagated action potential as well (need accurate velocity of propagation: too fast will blow up high, too slow will blow up low)
  - velocity, when found (21 m/s in theory, 19 m/s in reality), is constrained in model



repolarization: (and hyperpolarization)
- increased potassium conductance
- inactivation of sodium channels
  - ↳ closed + ineligible for reopening (once closed, will stay closed as long as cell stays depolarized, b/c of charge repulsion)
  - most of refractory period caused by Na^+ channel inactivation (no increase in g_{Na} w/ depolarization)

Quinn's law: if you have mole of electron, you're in trouble
no uncompensated charges in nature
10^{-14} mols of Na^+ going in, K^+ going out: very small amount, make big electrical changes

H+H model: batteries + conductances, kinetic model (rises + falls in conductance), all true
- what's different is that H+H didn't know there were channels + that channel opening/closing all-or-

none, changes in voltage change probability of channel opening

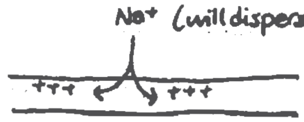
- channel opening + closing somewhat random; more likely to be open at start of depolarization
- summation of channels give you (as shown by patch clamp)

- blocking channels w/ drugs still gives you residual currents (gating currents) w/ voltage change
  - can see electrical changes due to charge movement
  - what gates see isn't voltage but electrical field strength
    - distance across membrane 100 Å : electrical field strength of kV/cm; higher from -20 to
      - 150 or so, start to break down membrane

- not just 2 kinds of conductance channels (except in squid axon)
  - inward current not carried just by Na^+, also by Ca^{2+} (at presynaptic terminal)
  - many kinds of K^+ channels: regulate excitability of cell (20-50 kinds, 10-30 in given cell)
  - Na^+ and Ca^{2+} channels almost same

    some K^+ channels inactivate (don't know why), some regulated by 2° messengers, Ca^{2+}, etc. (don't need to know in detail)

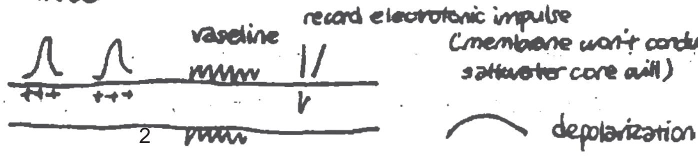
- recording from dendrite gives synaptic potentials, decrease w/ distance, different magnitudes (unlike action potential, which is propagated undiminished, constant magnitude)
  - cylindrical membrane like axon, but inexcitable (ohmic): see how depolarization affects different patches
    - first, look at axon (excitable, w/ voltage-gated Na^+ channels)



Na^+ (will disperse, spread out by charge repulsion: will depolarize ahead, maybe enough to get above threshold, depolarize, reiterate down axon)

- makes discrete steps out of something continuous

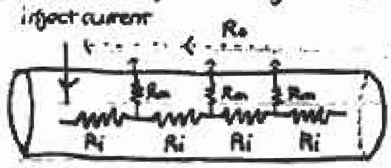
- to test this theory of propagation, put vaseline on patch of membrane, will stop AP propagation, record from ahead



(membrane won't conduct, but saltwater core will)

- electrotonic conduction contributes to threshold (can get to threshold w/ subthreshold current)
  - AP propagated this way, w/ electrotonic conduction to threshold

- take Na^+ channels out, look at just electrical properties of current spread

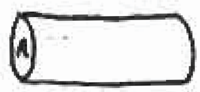


one dimension of voltage variation → (simplified from dendritic bush)

equivalent to ladder circuit

- every unit length like every other unit length in terms of electrical properties

R_o is negligible (so small in proportion to R_i) b/c surface area outside cell larger than surface area inside: huge wide resistor, more conductive paths)

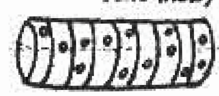


$R = \frac{l}{A}\rho$ ← resistivity of salt water

each unit will have same resistance (R_i)

- membrane is leaky insulator, low resistance

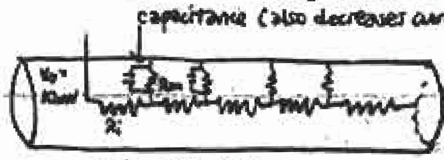
(channels)



each section has leakage current (R_m)

- how does current leak out, voltage drop, from site of injection? (everything ohmic so far, no capacitance)

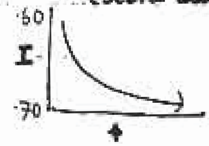
capacitance (also decreases current spread, decreases λ: also leakage path) also spreads things out in time — important for looking at synaptic I spread in dendrites



100% I, 90% I, 81% I (0.9×0.9)
(100nA) (90nA)

- current leaks out proportionately
  - each leakage path will be same
- current across membrane also proportionate (scales down fractionally)

exponential decrease: if 50%, goes down like ½ life (if steps small enough, looks continuous)



$V_m = I_m R_m$ ← negative b/c disappears completely eventually w/ distance

$V_m(x) = V_0 e^{-x/\lambda}$ ↳ length constant

- eg water in hose, constant leakage: more at first holes, less at holes further down electric fields linear; can add

- V_0 = displacement from resting

---

how does geometry affect λ?

- the better the conduction, the longer the impulse can travel
- the better the insulation, the longer the impulse travels
- λ = time it takes for impulse to decay to 1/e
  - smaller R_i = longer λ
  - larger R_m = longer λ

λ increases as R_i ~~increa~~ decreases

λ increases as R_m increases

2° order differential equation, so $\lambda = \sqrt{\frac{R_m}{R_i}}$

- can be resistance to return path (R_o)
  - in which case $\lambda = \sqrt{\frac{R_m}{R_i + R_o}}$

this is leaky circuit, like leaky cable: exponential decrease w/ space constant
- this works perfectly well for nonexcitable membranes (dendritic processes)

- for axon, increasing λ increases propagation velocity (current can spread farther ahead)
  (velocity directly proportional to λ in linear fashion)
  - w/ squid, membranes & salt water increase length constant $\lambda = \sqrt{\frac{R_m}{R_i}}$
    axons thicker, lowers R_m (double area of membrane, twice as many channels)

    <u>but</u>, lowers R_i by factor of 4, not 2 (b/c of πr^2)

    gives fast escape reflex (giant axons common for invertebrate escape reflexes)
  - people, instead, increase R_m w/ myelination (except at nodes of Ranvier)

7.29J / 9.09J Cellular Neurobiology
Spring 2012