9.09J/7.29J - Cellular Neurobiology, Spring 2005
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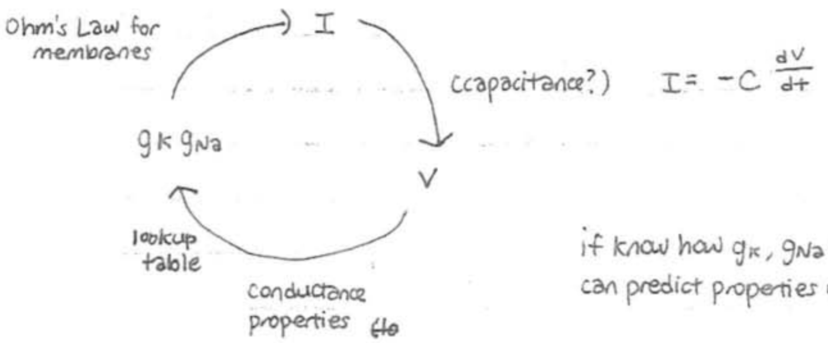
2/18/04

- 2 batteries (Nernst batteries): E_{Na}, E_K (hooked up to two variable conductances)
- correction at high negative potentials due to lots more sodium outside, inward drive

Ohm's Law for Membranes - $I = g_K(V_m - E_K) + g_{Na}(V_m - E_{Na})$

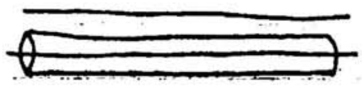
$I = gV$ ↳ voltage important for I_K = difference between V_m and where K^+ wants it to be



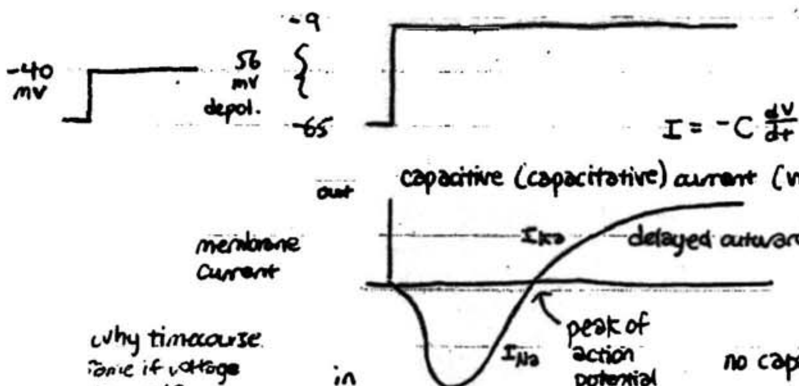
if know how g_K, g_{Na} vary with voltage, can predict properties of excitable membrane

- current is driving force for changing voltage
  voltage changes conductance

- membrane action potential: not propagated, all happens at once



- H+H injected current, got membrane action potential w/ same properties as propagated action potential



provide certain amount of current to discharge membrane capacitance
depolarizing membrane from -65 to -9 will discharge membrane capacitance

capacitive (capacitative) current (very fast, ~40 μs)

delayed outward current (would be hyperpolarizing if no voltage clamp)

no capacitative current after no change in voltage
↳ just electronic properties of membrane, not ionic current

why timecourse same if voltage clamped?

check currents, driving force

$I_{Na} = g_{Na}(V_m - E_{Na})$

↳ +52 mV

inward current when Vm more negative

at $V_m = E_{Na}$, 0 net I_{Na}

more positive Vm than E_{Na}, I_{Na} becomes positive (outward)

↳ reversal potential

Nernst equation says ratio of ion gradient predicts reversal potential

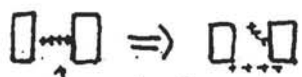
at $V_m = E_{Na}$, no I_{Na}, your I trace is just I_K

- but to do this at other potentials, use drugs (eg TTX to block Na^+ channels)
  (TEA (positive ion, chemical) that clogs up K^+ channels)

- to get conductance from current, divide by voltage $g = \frac{I}{V}$ ← $(V_m - E_{Na})$
  (see figure 8 in handout)

- K^+ conductance rise is exponential
  channels open faster, more channels open at higher depolarizations

no inactivation



gate will give you 1st order rate constant

look up rate constant curve

- 4 charged entities in ~~Na^+~~ K^+? channel

- 4 gates give you correct curve (4^{th} order rxn)
  eg 2 ms after depolarization, ½ gates are open,
  1/16 channels will be open
  (½ × ½ × ½ × ½)
  not exact fit, but almost
  from steepness, know there must be ~6 charges on each gates

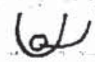
Na^+ channel:  need 3 gates open (although there are 4) : <u>M-gates</u>

doesn't give you inactivation; that comes from <u>h-gate</u> (positively charged, swings slowly closed w/ depolarization, stays closed)

- exponential decay, so only need 1 h-gate

- cytoplasmic loop = h-gate, chewing up cytoplasmic side w/ pronase will give  Na^+ conductance
  - if use Ab, block inactivation
  - restore inactivation by expressing peptide of h-gate region

- theoretical reconstruction of action potential based on H+H's predictions almost identical to real action potential
- bifurcation of V_m at threshold (can go either way)

threshold: no special molecular properties
- just place where $I_K = I_{Na}$ (equilibrium)
  - resting potential same way, no net current, $I_K = I_{Na}$, but is stable equilibrium  forces will restore like marble in hole displace in all different direction
  - however, threshold unstable equilibrium (move a little, see if new forces restore or push further)

     like marble on hill (pushing in one direction accentuates displacement)

  - at resting, $I_{Na} = I_K$, depolarizing a little doesn't change I_{Na} much, just moves V_m a little farther from E_K, get more outward I_K to repolarize $I_K = g_K(V_m - E_K)$
    - hyperpolarizing gives less outward I_K
  - threshold is depolarized enough to make g_{Na} exquisitely sensitive: increase in g_{Na} and I_{Na} w/ each depolarization
    - little more depolarization increases g_{Na}, g_{Na} wins race, I_{Na} wins race, positive feedback

- depolarizing after action potential gives:
  1. absolute refractory period
  2. relative refractory period

  } due to inactivation of Na^+ channels