$K^+$ channels - 4 voltage sensor gates in series (1/2 probability of one gate being open)
$Na^+$ channels - 4 voltage sensor gate 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 channel fit in voltage well modeled by HH model (fit is)
- reasonable correspondence of shape, w/ threshold bifurcation, overshoot, undershoot, etc., also
  refractory period (absolute & relative)
- larger depolarization can give action potential
- w/ math, can use HH 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, w/ of charge repulsion)
- most of refractory period caused by $Na^+$ channel inactivation
  (no increase in time w/ depolarization)

Quinn's law: if you have mole of electron, you're in trouble
no uncompensated charges in nature
$10^{-14}$ mol of $Na^+$ going in, isn't going out... very small amount, make big electrical changes

HH model: batteries + conductances, kinetic model (rises + falls in conductance), all true
- what's different is that HH didn't know there were channels + that channel opening/closing all-or-
- the change 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 \( \sqrt{I} \) \( \sqrt{V} \) (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 Ca²⁺ (at presynaptic terminal)
  - many kinds of K⁺ channels: regulate excitability of cell (20-50 kinds, 10-30 in given cell)
  - Na⁺ and Ca²⁺ channels almost same.
    - some K⁺ channels inactivate (don’t know why), some regulated by 2° messengers, Ca²⁺,
      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 inexutable (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, refute 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

---

vessel

record catecholamine pulse

(record w/membrane won’t conduct, but saline core will)

---

depolarization
- 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.

\[
\text{inject current} \quad \begin{array}{c}
\text{one dimension of voltage variation} \\
\text{(simplified from dendritic bush)}
\end{array}
\]

- Equivalent to ladder circuit.
- Every unit length like every other unit length in terms of electrical properties.
- Surface area outside cell larger than surface area inside:
  - huge wide resistor, more conductive paths.

\[
R = \frac{1}{A} \rho \quad \text{resistivity of salt water}
\]

- Each unit will have same resistance (R\(_i\)).

- Membrane is weakly insulator, low resistance.

- How does current leak out, voltage drop, from site of injection? (Everything ohmic so far, no capacitance, decreases exponentially; also decreases current spread, decreases λ.)

\[
\text{current leaks out proportionately} \quad \text{each leakage path will be same}
\]

- Current across membrane also proportionate.

\[
\text{(scales down fractionally)}
\]

- Exponential decrease: if 50%,
  - goes down like \( \frac{1}{2} \) life
  - Life steps small enough, looks continuous

- e.g. water in base, constant leakage:
  - more at first holes, less at holes
  - Further down

- \( V_m = I_m R_m \) negative in kC disappears completely eventually w/ distance.

\[
V_m(x) = V_0 e^{-x/\lambda}
\]

\( \lambda \) length constant.

3
electric fields linear; can add
- $V_0$: displacement from resting

- how does geometry affect $\lambda$?
- the better the conduction, the longer the impulse can travel
- the better the insulation, the longer the impulse travels
- $\lambda$: time it takes for impulse to decay to $1/e$
  - smaller $R_i$: longer $\lambda$
  - larger $R_m$: longer $\lambda$

$\lambda$ increases as $R_i$ increases; decreases
$\lambda$ increases as $R_m$ increases

2nd 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 membrane (dendritic processes)

- for axon, increasing $\lambda$ increases propagation velocity (current can spread farther ahead)
  (velocity directly proportional to $\lambda$ 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)
  - lasts, lowers $R_i$ by factor of 4, not 2 (blee of $\pi r^2$)
  - gives fast escape reflex (giant axons common for invertebrate escape reflex)
  - people, instead, increase $R_m$ w/ myelination (except at nodes of Ranvier)