MN25 Lecture 4 ⊖ Reduced Models provide geometrical insight into neuronal response to stimulation.

⊖ Reductions must be handled carefully; Bifurcation diagrams may really differ.

⊖ Additional currents modulating the subthreshold dynamics

⊖ <u>Approach</u>: phase plane analysis of switched systems.

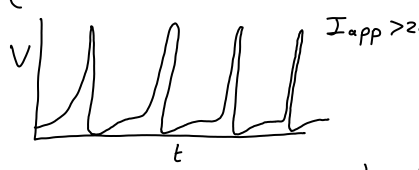
Recall

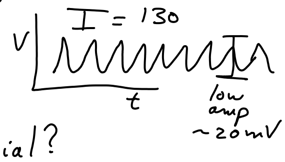
Week 1: Hodgkin-Huxley 4D model →

$$\begin{cases} CV' = -I_{Na} - I_K - I_L + I_{app} \\ X' = \alpha_X(V)X + \beta_X(V)(1-X), \quad X = m,h,n \end{cases}$$

Week 2: Phase planes

Week 3: Codim 1 bifurcations.





Q: What is an action potential?
Reaching a threshold is somewhat too arbitrary.
Mathematically, an oscillation is well defined.

Q: 4D is difficult, let's reduce to a planar model.

<u>Approach ①</u>: Note that $\tau_m(V) = \frac{1}{\alpha+\beta}$ is small, order 0.1–0.5 ms, so just as fast as the potential V.

So set $m = m_\infty(V)$ Reduction by 1 variable.

The figure suggests $n = b_0 - rh \Rightarrow$ This reduces it to a 2D system.

Set $b_0 = 0.8$ $\quad r = 0.9$ bad choice

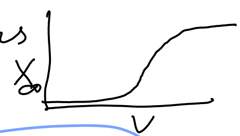
$r = 1.0$ good choice.

We observe that for $r = 1.0$ we have a qualitatively similar bifurcation diagram (sufficiently) as for the original HH model.

<u>Approach ②</u> How could we even compare variables that have different units?

Equivalent Potentials to convert m, h, n to V_m, V_h, V_n

Observation $X_\infty(V) = \frac{\alpha}{\alpha+\beta}$ are monotone functions



So we can invert this function but we will do this only implicitly.

$$X(t) = X_\infty(V_X(t)) \xRightarrow{d/dt} X' = \frac{dX_\infty}{dV_X}\frac{dV_X}{dt} = \frac{X_\infty(V) - X}{\tau_X(V)}$$

equivalent potential for $X = m, h, n$

So we have $\frac{dV_X}{dt} = \frac{X_\infty(V) - X_\infty(V_X)}{\tau_X(V)} \Big/ \left(\frac{dX_\infty(V_X)}{dV_X}\right)$

From the timeseries we see V_m follows V closely and V_n & V_h evolve at the same timescale.

We obtain a 2D model by setting $V_m \to V$, $V_n \to V_h$

Continuing with a zoo of currents. (So sorry we're not closer to artis today.)

§4.1 on conductance-based models

Most neuron models have one mechanism/current responsible for the shape of the action potential

Na^+ in HH // Ca^{2+} for ML.

$$I_{ion} = \bar{g}\, m^p h^q I_{drive}(V, ions)$$

$$I_{cfe} = P_{max}\, zF\xi \left(\frac{C_{in} - C_{out}\, e^{-\xi}}{1 - e^{-\xi}} \right) \simeq \tilde{g}(V - E_{rev})$$

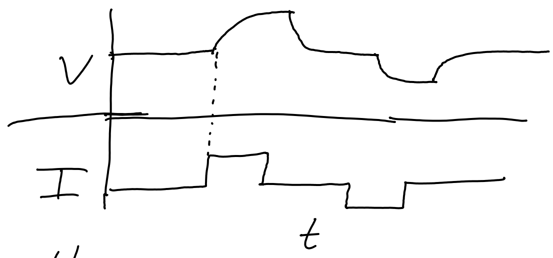
if ion concentration almost constant.

§4.2 T-type Calcium Current

Model without active Na^+, K^+ (Consider them blocked) Is ok as that mostly shapes the spike.

$$\begin{cases} C V' = I_{app} - g_L(V - E_L) - I_T \\ \dfrac{dh}{dt} = (h_\infty(V) - h)/\tau(V) \longleftarrow \text{slow inactivation.} \end{cases}$$

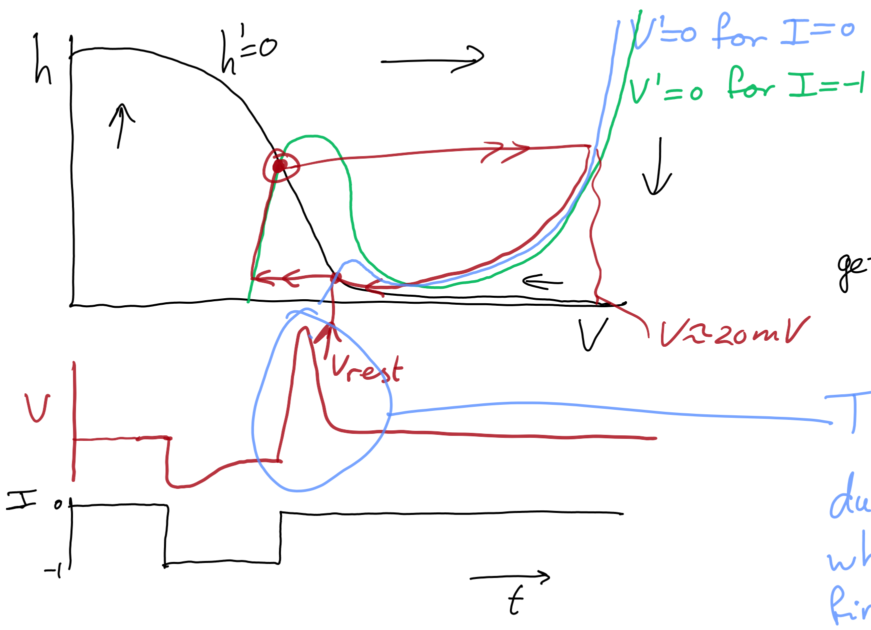
$$I_T = m_\infty^2 h\, I_{cfe}(V, Ca_o, Ca_i)$$



① Relay mode near $V_{Rest} \simeq -60\,mV$

passive response to I_{app}

② For larger inhibitory input, the model has a rebound mode.



means get above the hill.

This is a rebound spike.

due to activation of I_T which is only if you first hyperpolarize sufficiently long.

§4.5 Sag Current (Resilience)

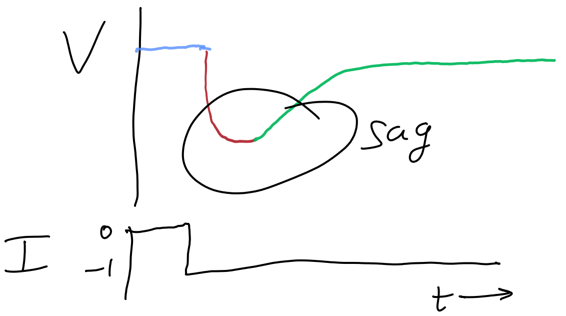
activates upon hyperpolarized.

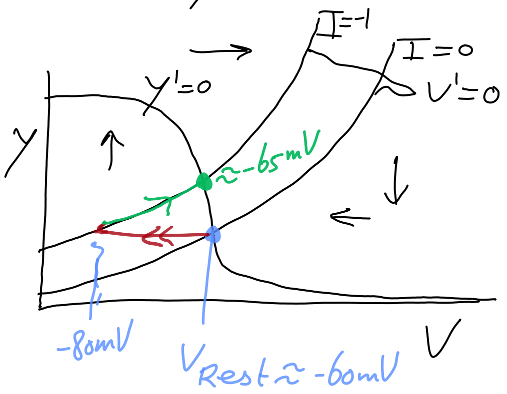
$E_h \simeq -43\,mV$
mix of Na^+ & K^+

$$CV' = I(t) - g_L(V-E_L) - g_h y(V-E_h)$$

$$y' = (y_\infty(t) - y)/\tau_y(V) \leftarrow \text{again slow.}$$

$\rightarrow \tau_y$ is large.



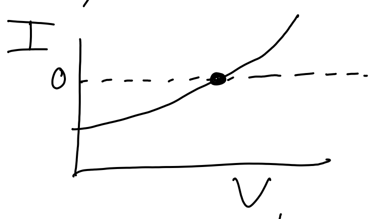


§4.4.3 Potassium (K) Inward Rectifier

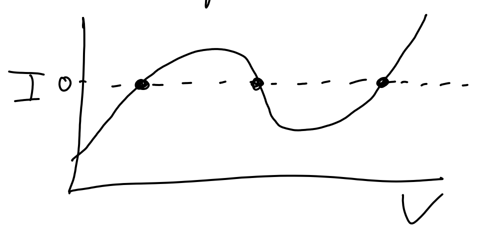
During Patch-clamp, experimentalist fix I_{app} to hold the potential at some value.

$$CV' = -I_{ion}(V) + I_{app} = 0$$

They can measure the IV-curve of a neuron. (s.t. $V'=0$)



monotone



a model for non-monotone IV curves

$$CV' = I - g_L(V-E_L) - g_{Kir}\,h_\infty(V)(V-E_K)$$

I_{Kir} provides additional repolarization. (more negative)

Set $V'=0 \implies I = g_L(V-E_L) + g_{Kir}\,h_\infty(V)(V-E_K)$

$$\frac{dI}{dV} = \underbrace{g_L + g_{Kir}h_\infty}_{\text{positive}} + \underbrace{g_{Kir}\,h'_\infty(V-E_K)}_{h'<0,\text{ could be dominant.}}$$

§4.4.2 M-current Slow potassium current

gate M increases whenever there is a spike.

$$\begin{cases} CV' = -I_{ion} + I_{app} - g_M M(V-E_K) \\ M' = (M_\infty - M)/\tau_M \end{cases}$$

Increases whenever there is a spike. Making it harder to generate the next.