

This lecture describes the ion channels present in cortical and thalamic neurons and analyzes how they work together to produce the patterns of spiking activity seen in those cells. The lecture is based on the following:

Huguenard and McCormick J. Neurophysiology 68:1373 (1993)

McCormick and Huguenard J. Neurophysiology 68:1384 (1993)

Steriade et al. Science 262:679 (1993).

Destexhe, Babloyantz, and Sejnowski Bioph. J. 65:1538 (1993).

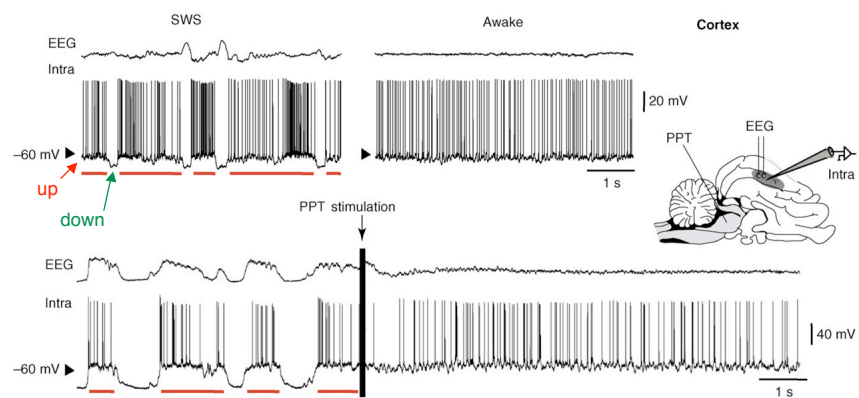
For a discussion of the spiking patterns modeled here, see the following discussions of “Up” and “Down” states

Destexhe et al. Trends in Neurosci. 30:334 (2007).

Castro-Alamancos et al. The Neuroscientist 15:625 (2009).

Neurons in cortex (here) and thalamus (next slide) show two modes of activity, correlated with wake/sleep state. Slow-wave sleep is characterized by switches between up and down states. The awake or activated state seems to be permanently in the up state.

The top traces are intracellular recordings in vivo showing natural sleep and waking states.

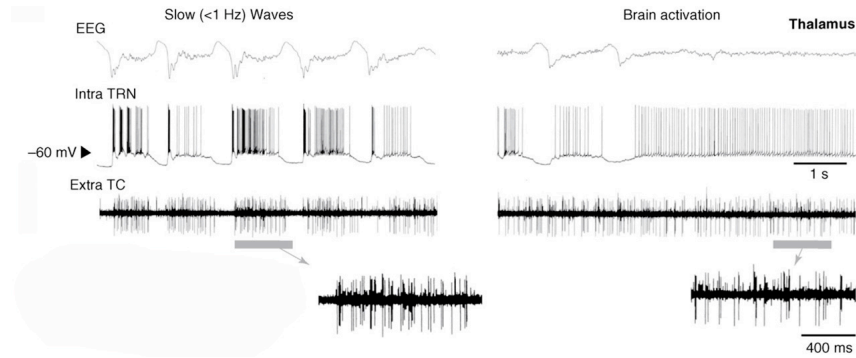


The bottom traces show transition from a slow-wave pattern of up and down states to an activated pattern by stimulating in the pedunculo-pontine tegmentum (PPT), part of the reticular activating system. This is in a cat anesthetized with ketamine/xylazine.

Destexhe et al. 2007

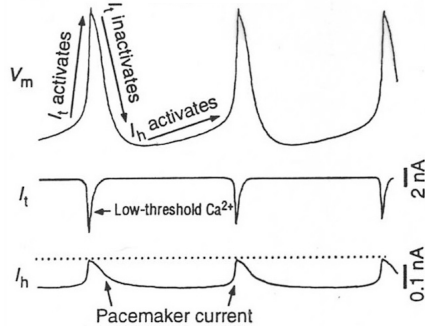
Similar behavior in thalamic neurons. Both intracellular and extracellular recordings are shown (from 4 different neurons). In the example at right, a spontaneous transition to an activated state is seen.

The spiking activity in the up state is quantitatively similar to the activity in the activated state, in terms of rates, interspike intervals, and other features.



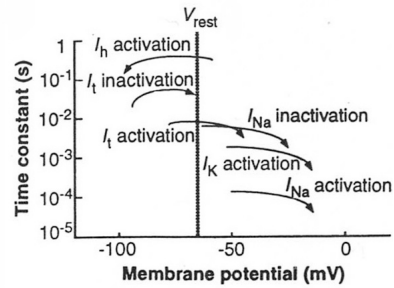
Destexhe et al. 2007

T-Ca and H-channels control bursting

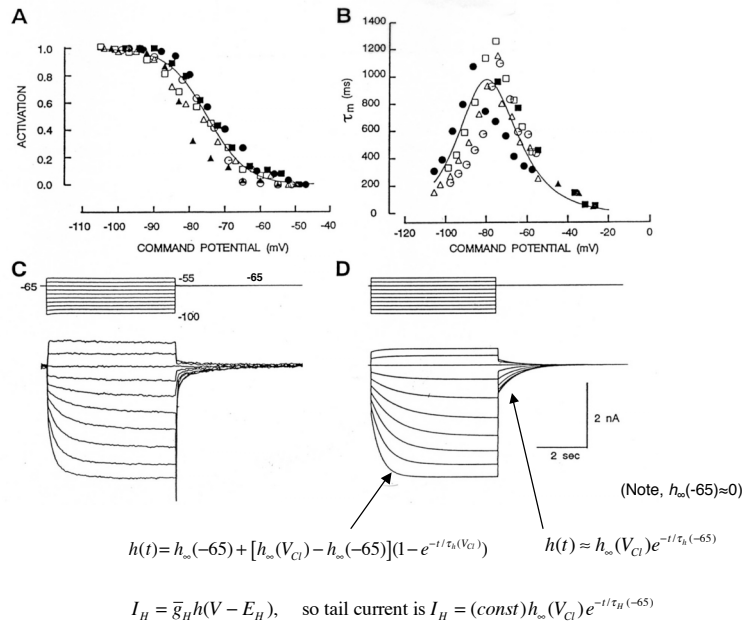


Steriade et al. 1993

Activation ranges of major channels present in these cells



Voltage clamp determination of H-channel properties



Huguenard and McCormick, 1993

Voltage-clamp determination of T-Channel activation properties, $m_{\infty}(V)$

T-type calcium current:

$$I_T = \bar{P}_T m^2 h \frac{(2F)^2}{RT} V \left[\frac{Ca_{in} - Ca_{out} e^{-2FV/RT}}{1 - e^{-2FV/RT}} \right]$$

Problems:

1. Current has both inactivation and activation gates which interact
2. I-V curve is strongly rectifying (modeled by the GHK equation).

Use tail currents at fixed clamp voltage to handle problem 2.

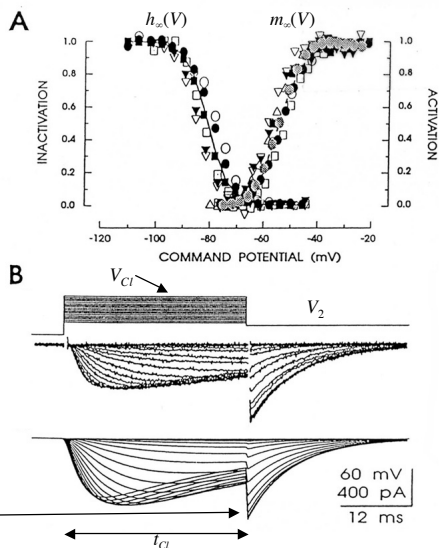
Use approximations to handle problem 1

1. h is slower than m
2. voltage ranges of gating differ

Then to measure $m_{\infty}(V)$, use the tail current

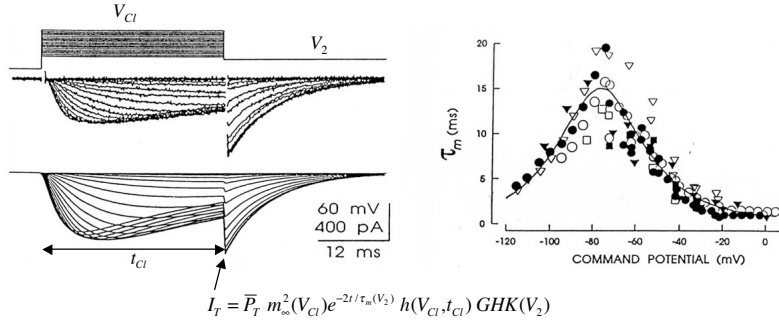
$$I_T = \bar{P}_T m_{\infty}^2(V_{Cl}) e^{-2t/\tau_m(V_2)} h(V_{Cl}, t_{Cl}) GHK(V_2)$$

(assume that this doesn't vary much with V_{Cl} or with time during the tail, for short V_{Cl} clamps)
 Choose V_2 s.t. $m_{\infty}(V_2)=0$



Huguenard and McCormick, 1993

Voltage-clamp determination of T-Channel $\tau_m(V)$ and $h_\infty(V)$



Determine the time constant of activation $\tau_m(V)$ by fixing V_{Cl} and varying V_2

Determine the $h_\infty(V)$ function by making t_{Cl} long enough for h to come to steady state, then the tail current will be:

$$I_T = \bar{P}_T m^2(V_2, t) h_\infty(V_{Cl}) GHK(V_2)$$

and $h_\infty(V)$ can be measured as the amplitudes of the tail currents (correcting for the effects of V_{Cl} on m).

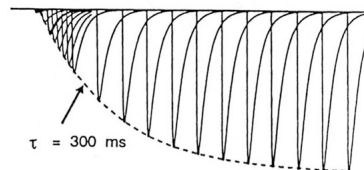
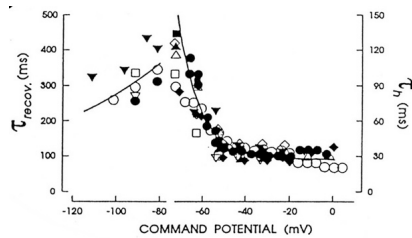
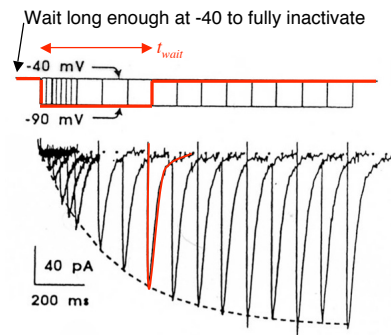
Huguenard and McCormick, 1993

Voltage-clamp determination of T-Channel $\tau_h(V)$

The inactivation gate is fully closed at -40 mV and fully open at -90 mV. With a two-step clamp, measure the rate of opening of the inactivation gate by the increase in amplitude of the currents evoked after various holds at -90 mV.

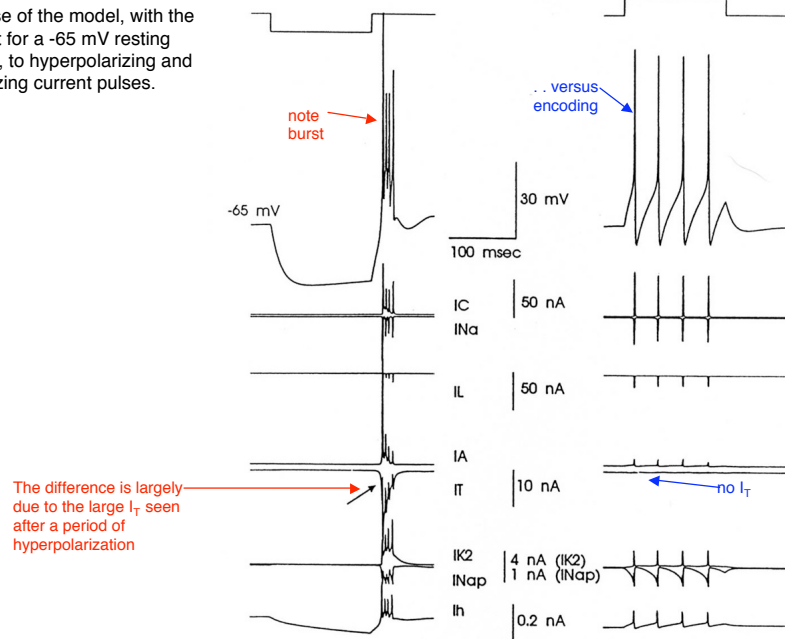
The amplitude of the currents evoked at the end of the wait periods (of duration t_{wait}):

$$I_T = \bar{P}_T m^2(-40, t) h_\infty(-90) [1 - e^{-t_{wait}/\tau_h(-90)}] GHK(-40)$$



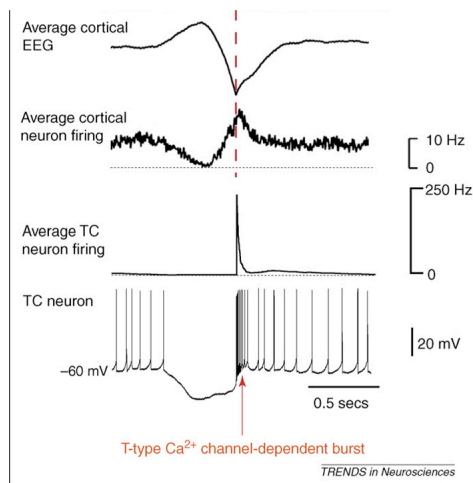
Huguenard and McCormick, 1993

Response of the model, with the leaks set for a -65 mV resting potential, to hyperpolarizing and depolarizing current pulses.



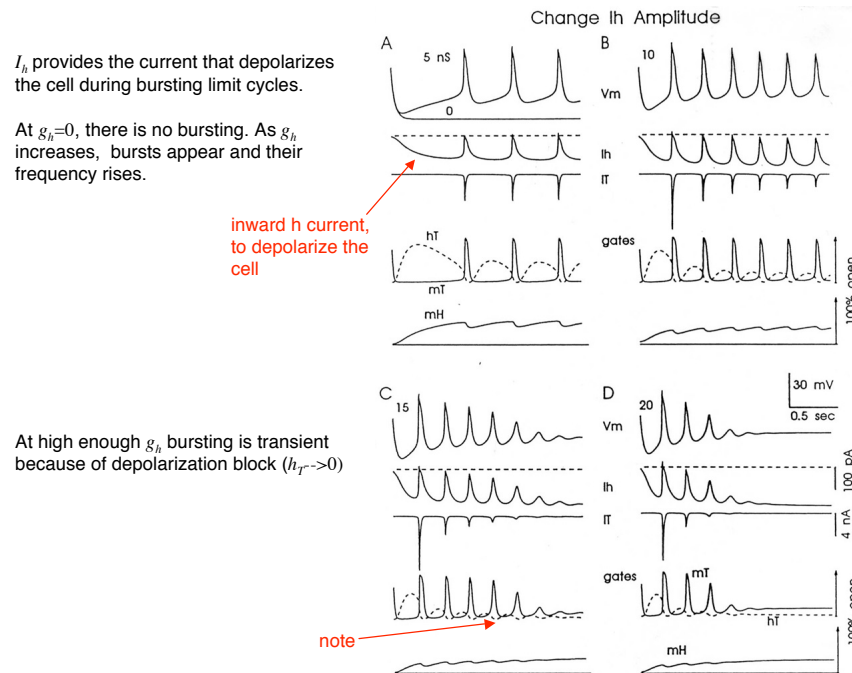
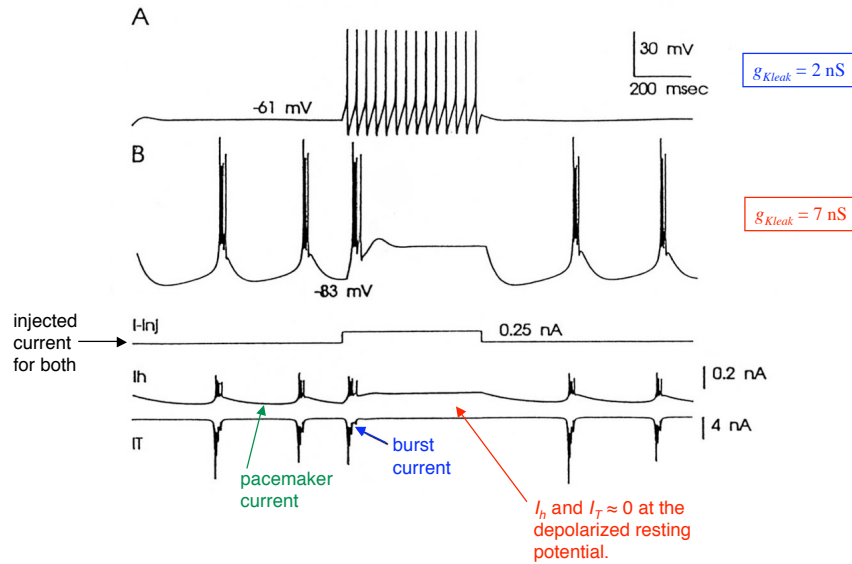
McCormick and Huguenard, 1993

The anode break burst is similar to the burst of spikes that often occurs at the beginning of an up state or at the transition to an activated state.



Destexhe et al. 2007

Modeling neuromodulation: changing g_{Kleak} changes the resting potential and switches the model from encoding to bursting mode



The T-type Ca^{++} current is necessary to the bursting limit cycle.

At P values of 20 or 30, there is no limit cycle. Larger P values give limit cycles, at increasing frequency.

Change IT Amplitude

