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).

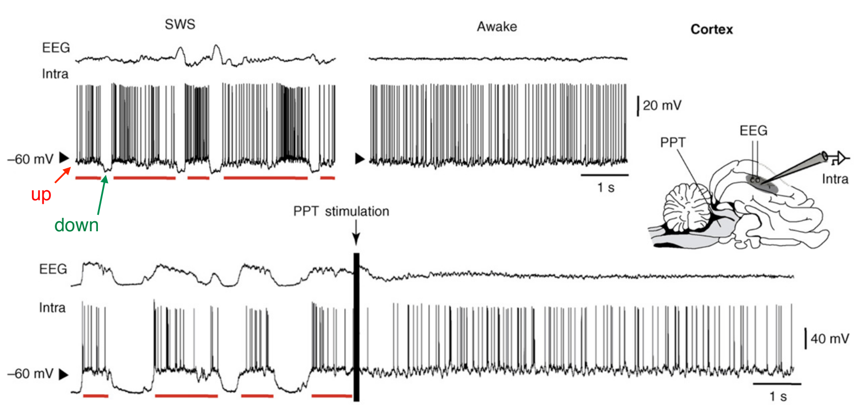
Castro-Alamancos et al. The Neuroscientist 15:625 (2009).

For a recent paper about the functional role of bursting in stimulus representation, see

Lesica and Stanley Journal of Neuroscience 24:10731 (2004).

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. When awake, the brain seems to be permanently in the up state.

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

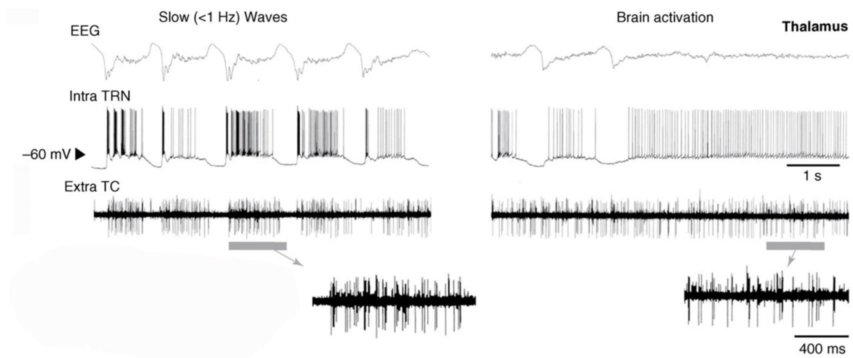


The bottom traces show transition from a slow-wave pattern of up and down states to an activated pattern by stimulating in the pedunculopontine tegmentum (PPT), part of the reticular activating system. This is in a cat anesthetized with ketamine/xylazine.

Destexhe et al. 2007

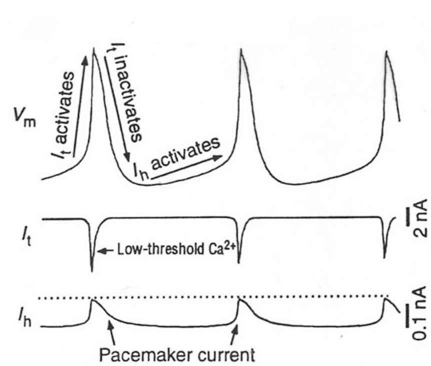
Similar behavior in thalamic neurons. Both intracellular and extracellular recordings are shown (from 4 different neurons). In the example at right, a spontaneous transition to an activated state is seen.

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.

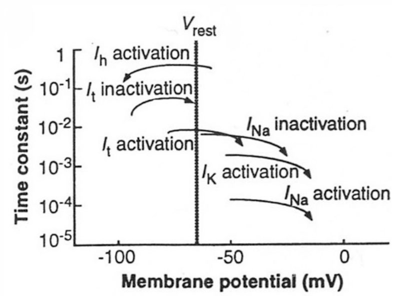


Destexhe et al. 2007

T-Ca and H-channels control the state transitions

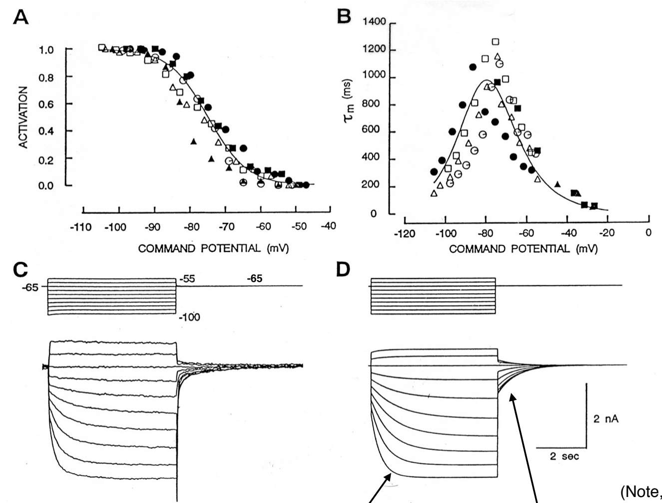


Activation ranges of major channels present in these cells



Steriade et al. 1993

Voltage clamp determination of H-channel properties



(Note, $h_\infty(-65) \approx 0$)

$$h(t) = h_\infty(-65) + \left[h_\infty(V_{Cl}) - h_\infty(-65)\right](1 - e^{-t/\tau_h(V_{Cl})})$$

$$h(t) \approx h_\infty(V_{Cl}) e^{-t/\tau_h(-65)}$$

$$I_H = \overline{g}_H h(V - E_H), \quad \text{so tail current is } I_H = (const) h_\infty(V_{Cl}) e^{-t/\tau_H(-65)}$$

Huguenard and McCormick, 1993

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

T-type calcium current:

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

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

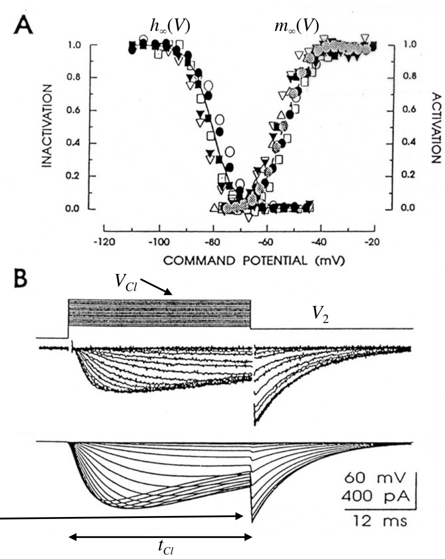
1. h is slower than m
2. voltage ranges of gating differ

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

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

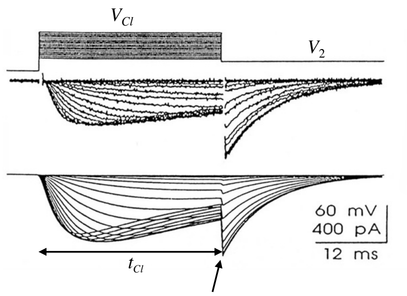
(assume that this doesn't vary much with V_{Cl} or with time during the tail, for *short* V_{Cl} clamps)

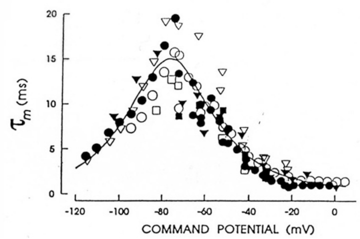
Choose V_2 s.t. $m_\infty(V_2) = 0$



Huguenard and McCormick, 1993

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





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

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:

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

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

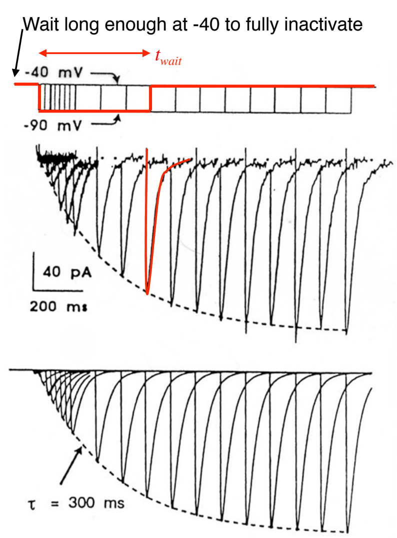
Huguenard and McCormick, 1993

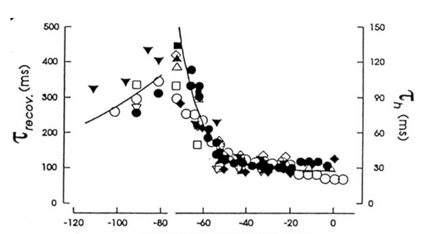
Voltage-clamp determination of T-Channel $\tau_h(V)$

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}):

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





Huguenard and McCormick, 1993

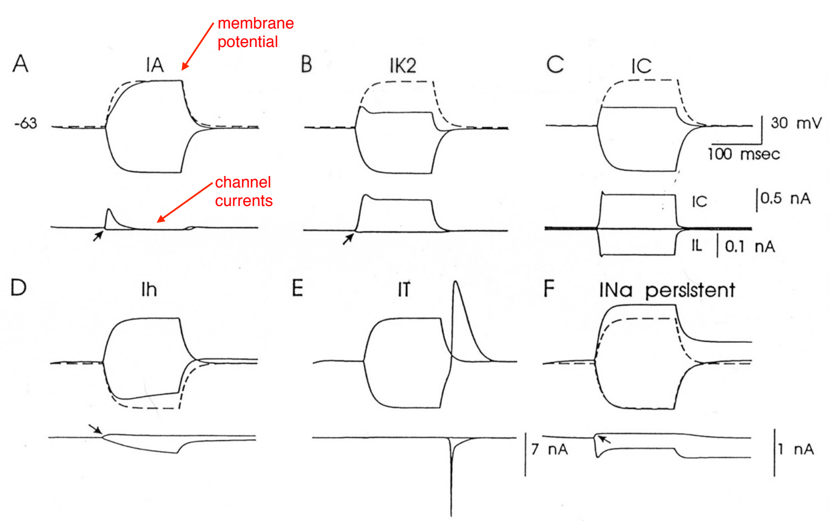
Channels in the model. Note the wide range of conductances.

I_{Na}	m^3h	12 mS	+45 mV	
I_K	$m(V,Ca^{++})$	1 mS	-105 mV	← K(Ca) gating coupled to the L-type Ca^{++} channel only
I_A (2)	m^4h	0.8 mS	-105 mV	← These K^+ channels contain multiple components, with different HH models
I_{K2} (2)	$mh + m^4h$	0.8 mS	-105 mV	←
I_H	h	9 nS	-43 mV	
I_{NaP}	m	7 nS	+45 mV	
I_{Kleak}	1	15 nS	-105 mV	
I_{Naleak}	1	6 nS	+45 mV	

I_{CaT}	m^2h	40×10^{-6} cm^3/s *
I_{CaL}	m^2	80×10^{-6} cm^3/s * ← $m_\infty(V,Ca) = \dfrac{250\,Ca\,e^{V/24}}{250\,Ca\,e^{V/24} + 0.1\,e - V/24}$

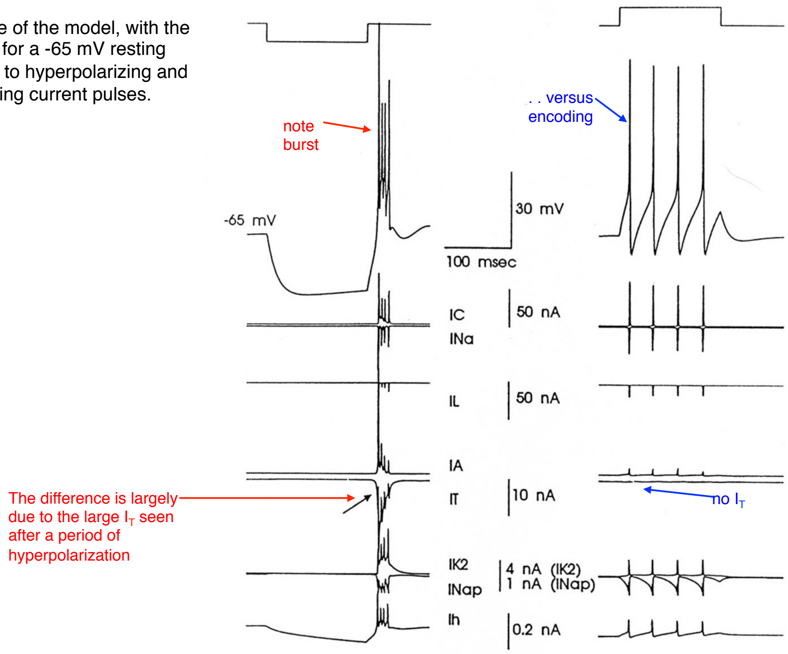
* Note the permeabilities given above translate into very large equivalent conductances (≈600 and 1200 mS) for the Ca^{++} channels.

Voltage responses to current pulses for a membrane containing capacitance, leak conductances and one or two other channels.



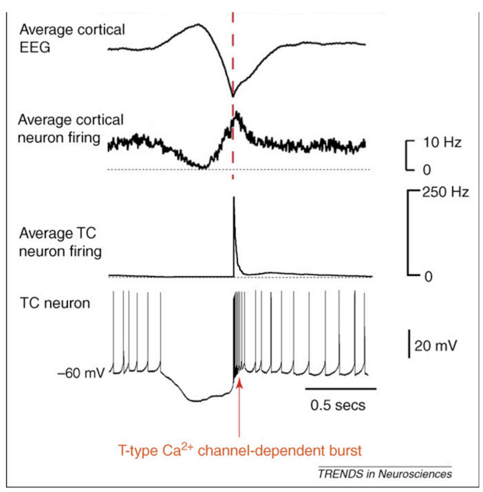
McCormick and Huguenard, 1993

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



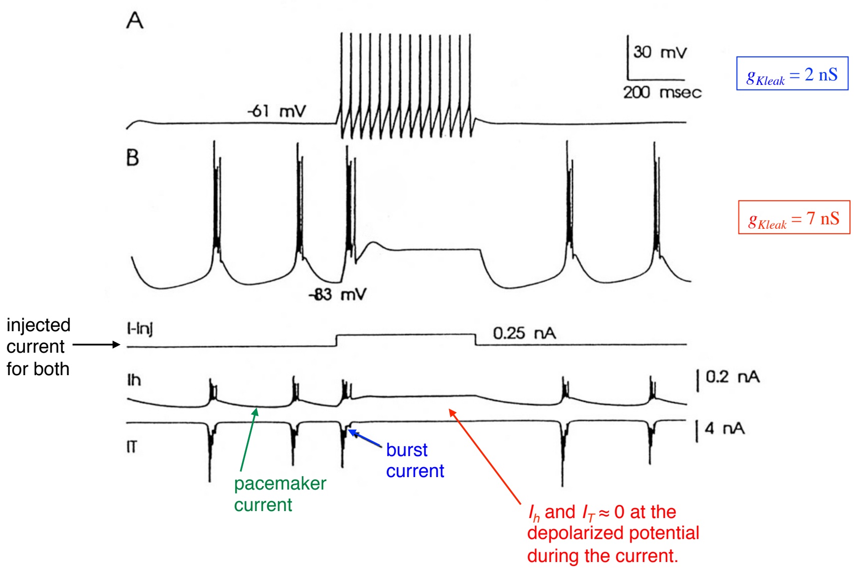
McCormick and Huguenard, 1993

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



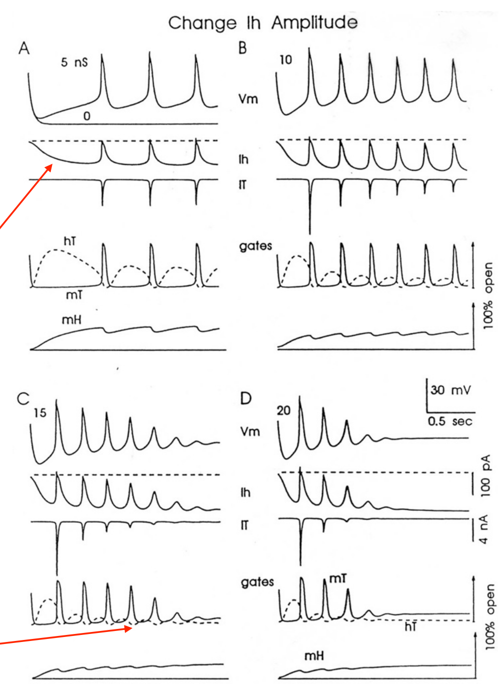
I_h provides the current that depolarizes the cell during bursting limit cycles.

At g_h=0, there is no bursting. As g_h increases, bursts appear and their frequency rises. Results at right are for a model with no Na currents (TTX applied)

inward h current, to depolarize the cell

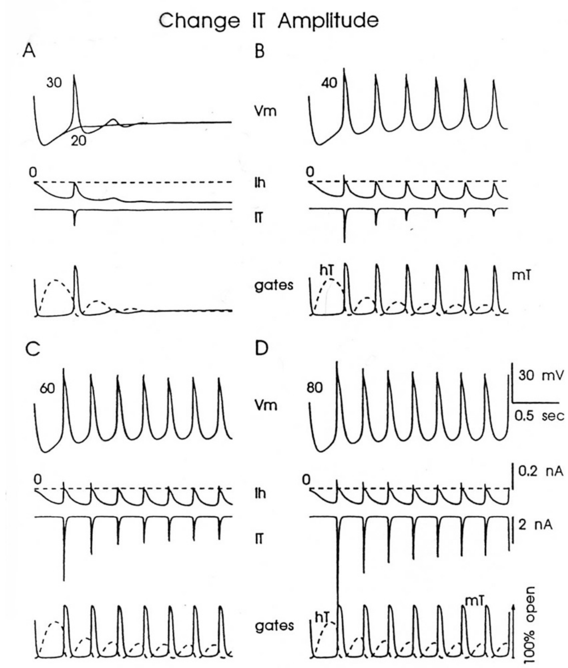
At high enough g_h bursting is transient because of depolarization block (h_T->0)

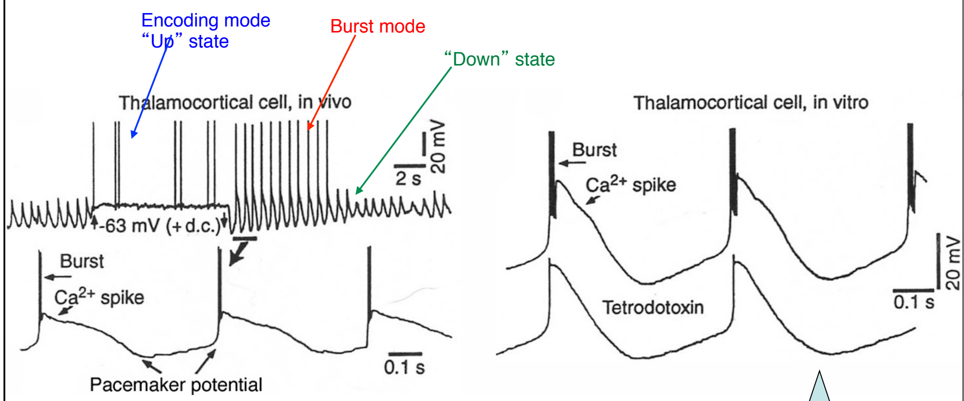
note



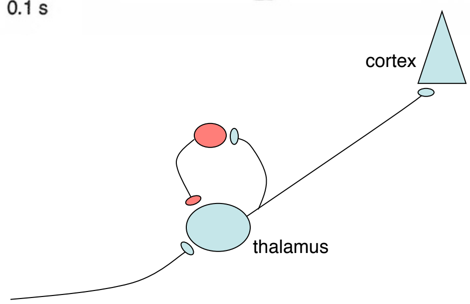
The T-type Ca^{++} current is necessary to the bursting limit cycle.

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



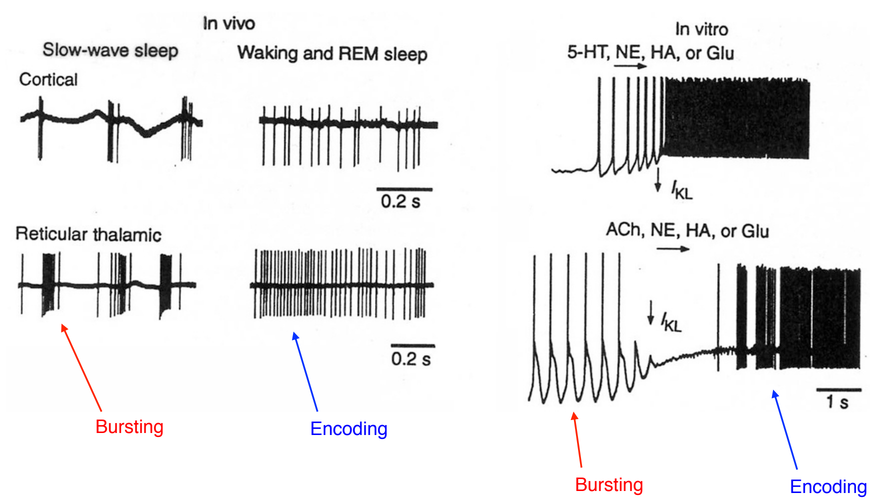


Steriade et al. 1993



Switch in firing mode due to *waking and sleep*

Switch in firing mode due to *neuromodulation*



Steriade et al. 1993