Inhibition: Effects of Timing, Time Scales and Gap Junctions

I. Auditory brain stem neurons and subthreshold integ'n.

- Fast, precise (feed forward) inhibition shapes ITD tuning.
- Facilitating effects of brief inhibition: PIF, PIR etc.

w/ Svirskis, Dodla, Sanes, Kotak

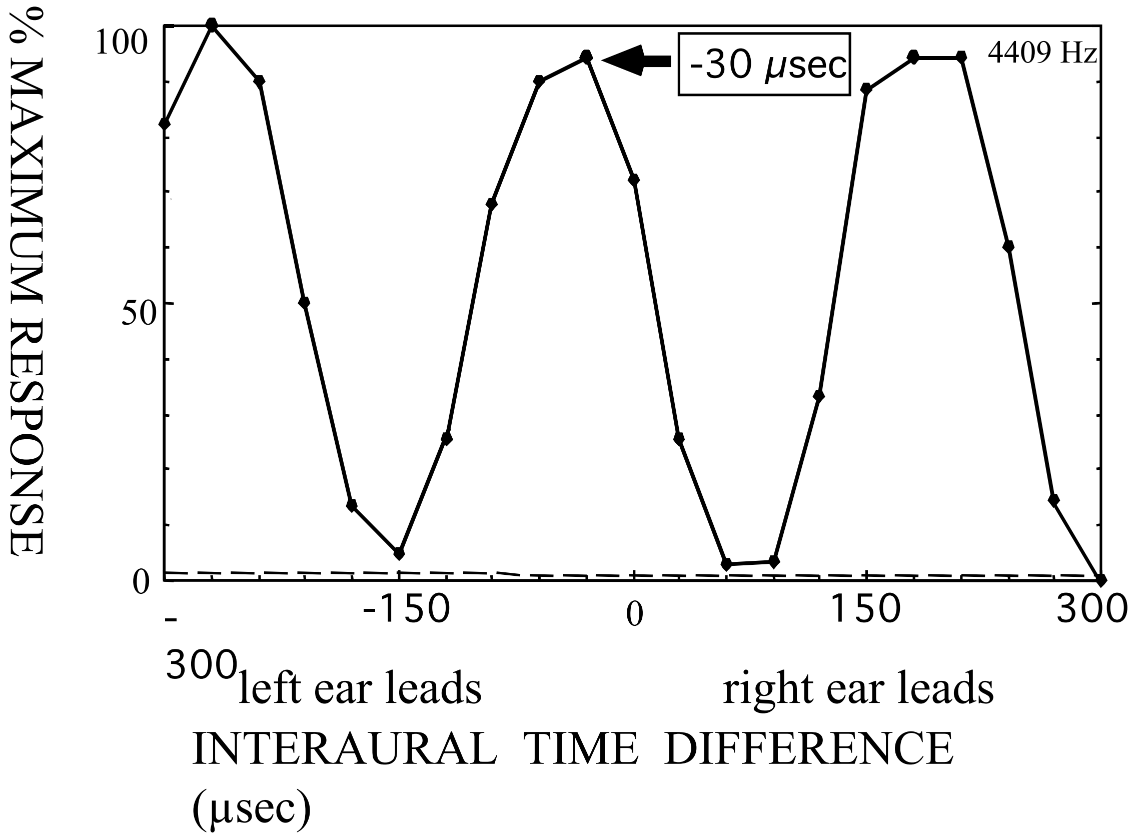
II. Synchonization/locking with inhibition

- Sync'ing between coupled cells, w/ slow decay inhib'n.
- Gap junctions and inhib'n in neocortex slices; weak coupling. w/ Lewis
- Very fast inhibition; gap junctions can stabilize anti-phase then in-phase.

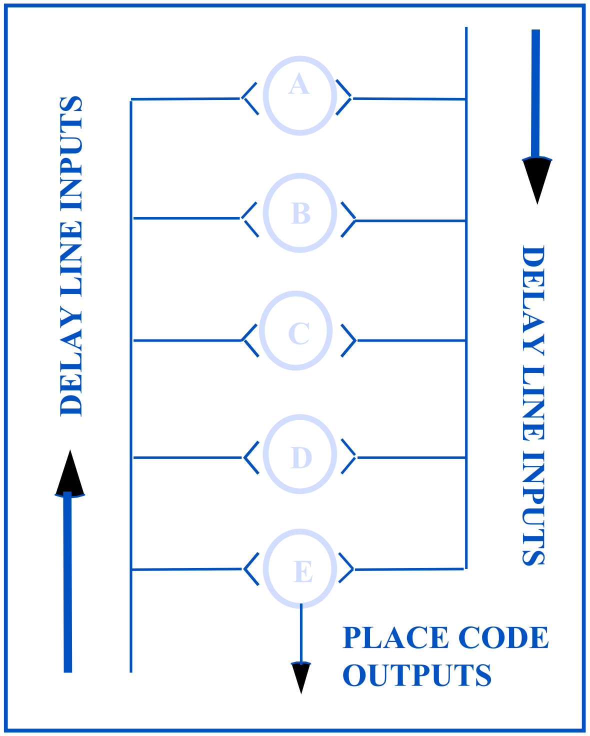
w/ Bem, Terman

Auditory brain stem neurons and subthreshold integration.

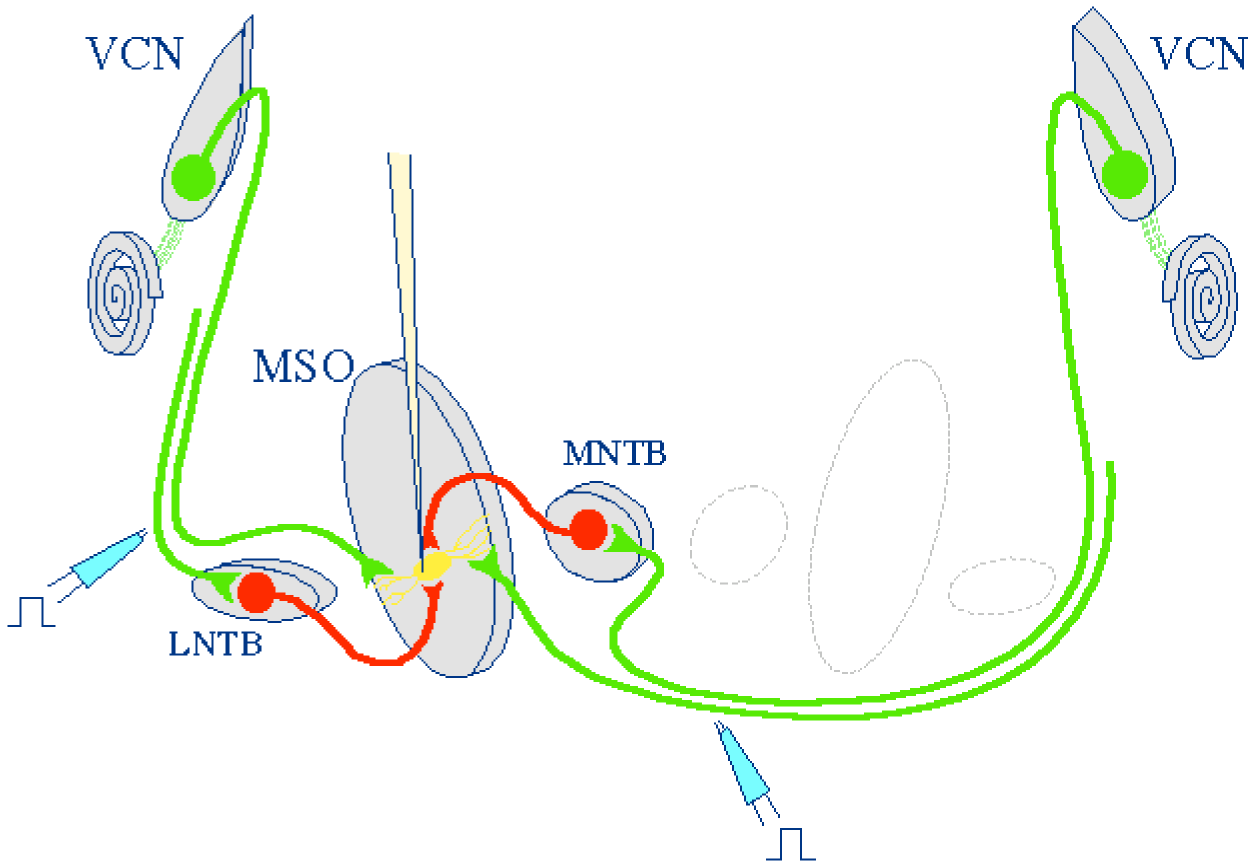
In vivo data from the barn owl shows NL neurons encode ITD



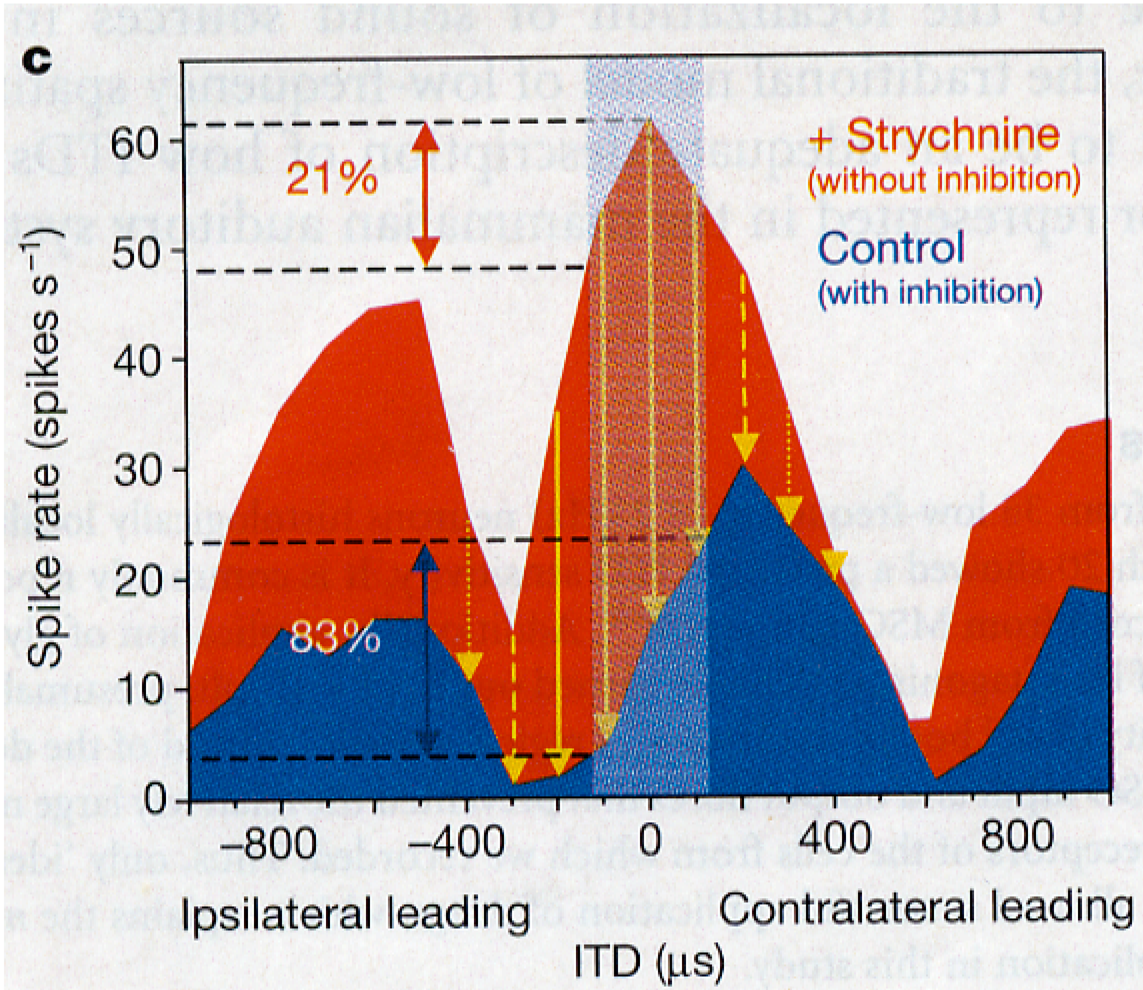
ITD sensitivity arises from a **coincidence detection** mechanism, as in the Jeffress model



Schematic of circuit for low frequency coincidence detection in mammals. (D Sanes w/ focus on gerbil.)



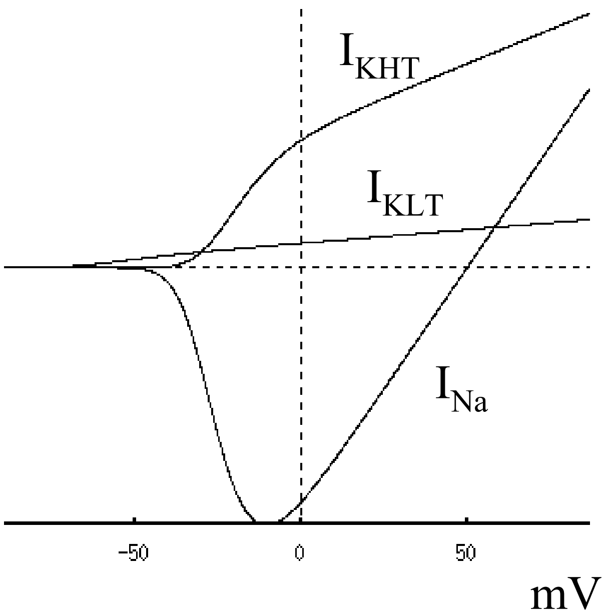
Tuning for Interaural Time Difference (ITD), shaped by transient inhibition



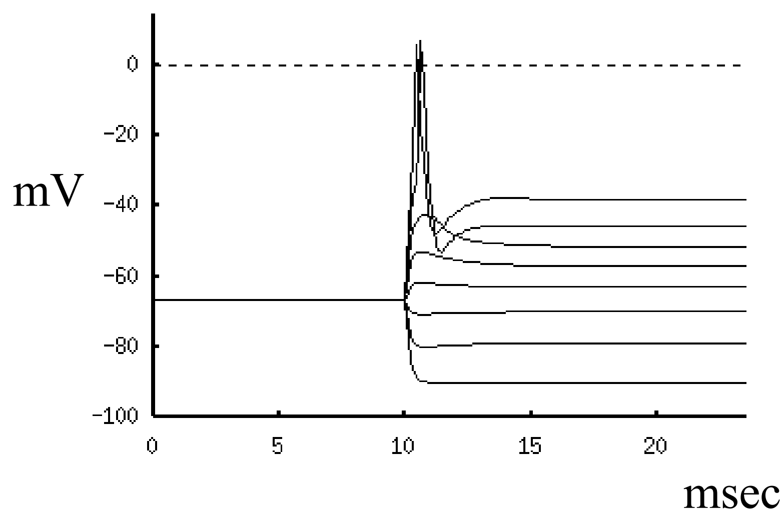
Brand et al, 2002

HH-type model with currents: I_{NA} I_{KHT} and subthreshold I_{KLT} (Rathouz & Trussell, '98)

J Neurosci, 2002

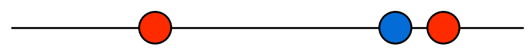


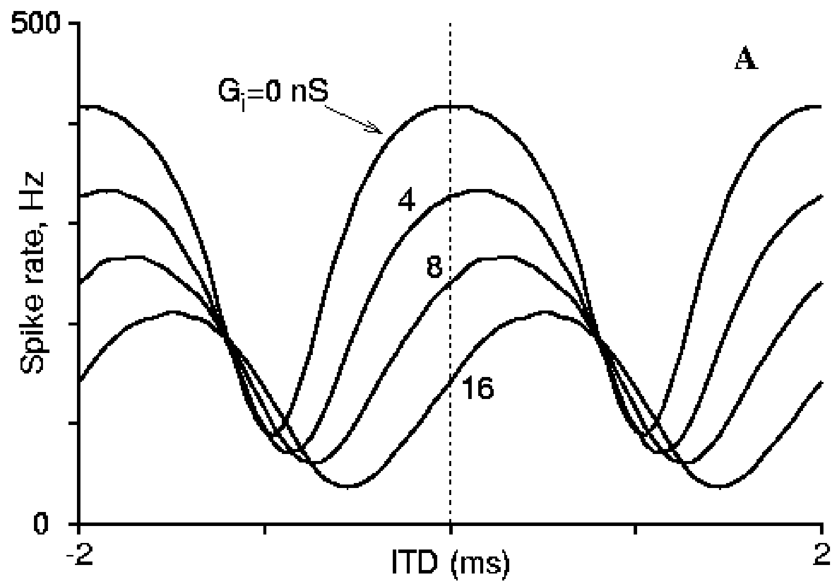
Phasic firing properties



Subthreshold negative feedback: eg, I_{KLT}
improves: SNR, phase-locking, CD, narrows integration time window (rev corr'ln)

Effect of brief and precise timed inhibition on tuning for the HH-like model.





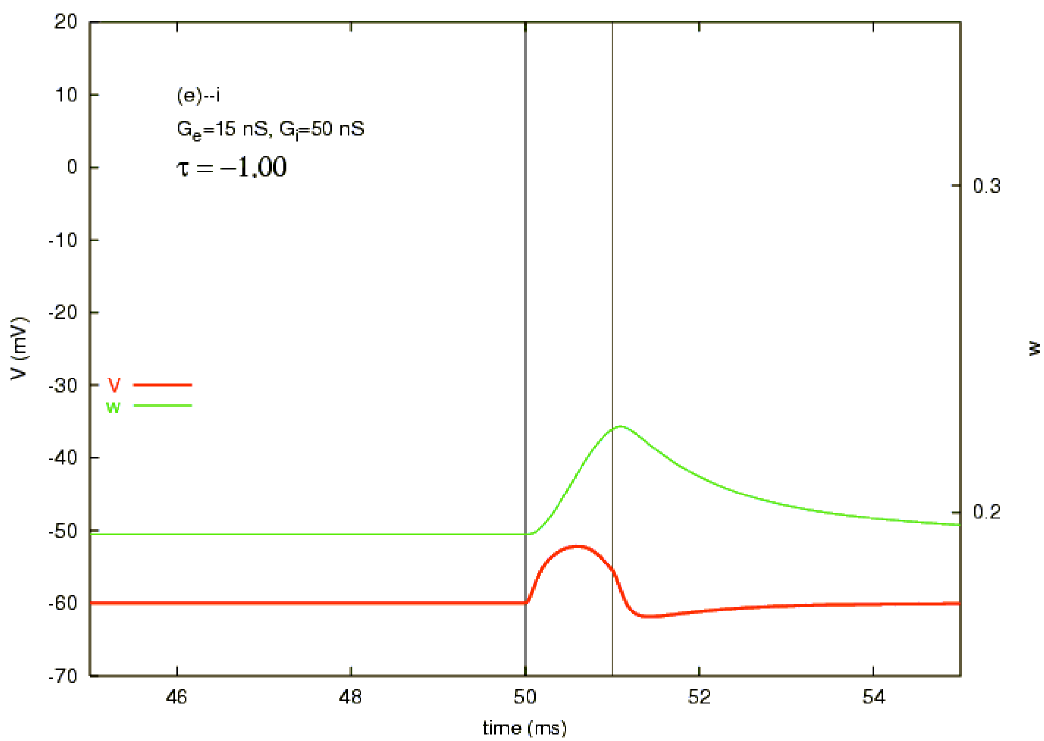
ipsi leading   contra leading

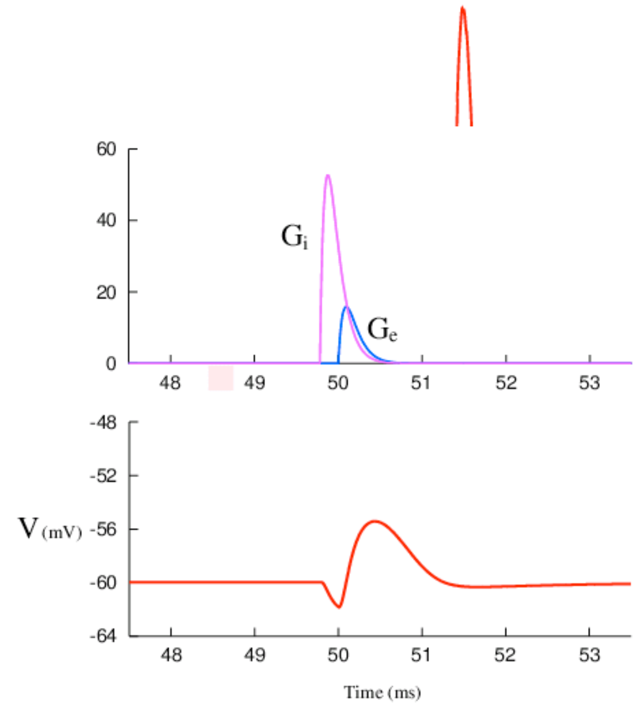
Svirskis,Dodla,Rinzel
Biological Cybernetics, 2003

Input: periodically modulated Poisson; 500 Hz;
delay (ITD) between ipsi & contra

Temporal summation of excitation and inhibition

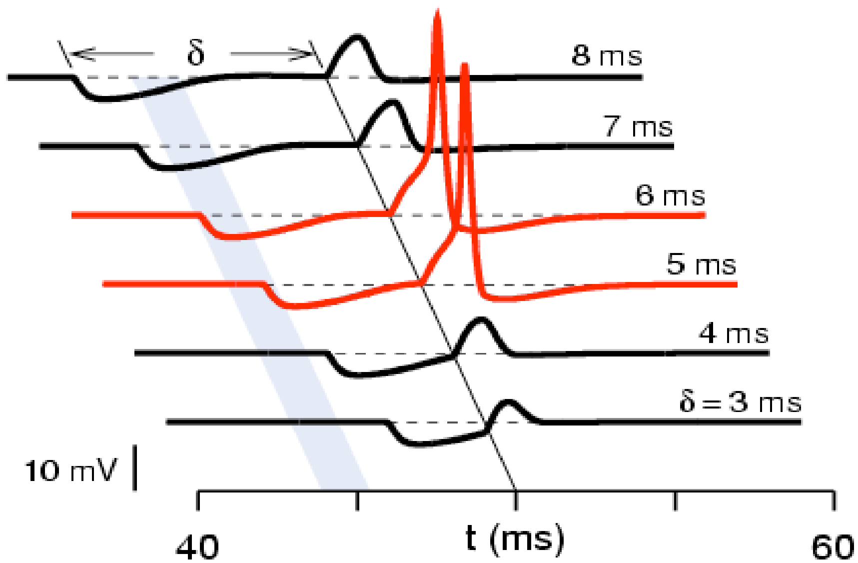
Subthreshold nonlinearities:
ipsp can enhance epsp,
and lead to spiking



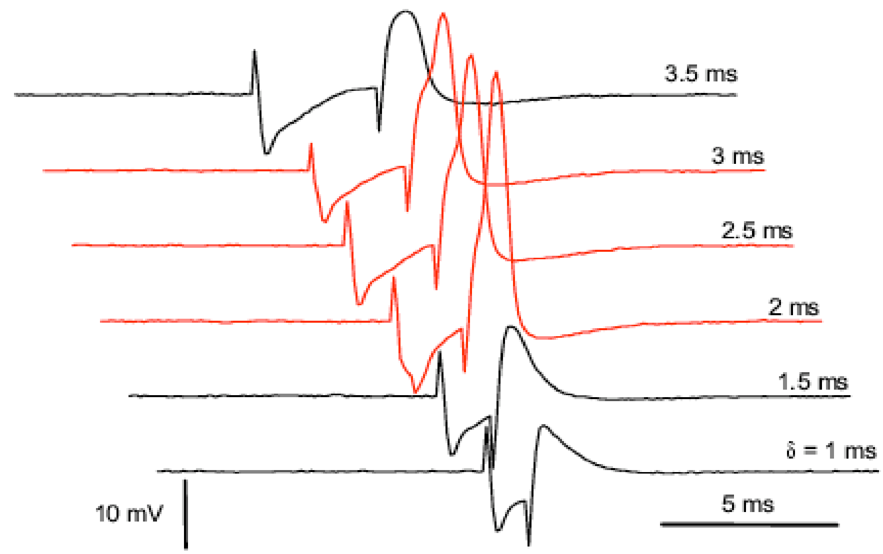


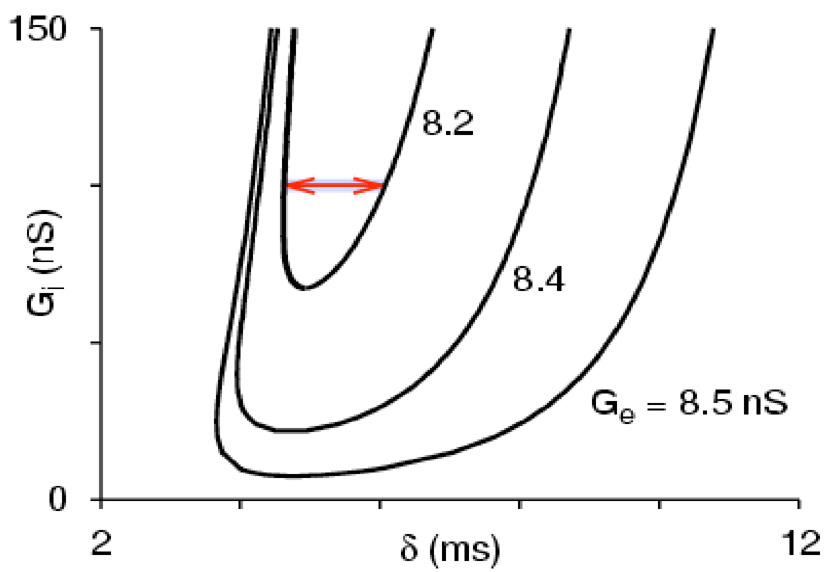
Model of "coincidence-detecting" cell in auditory brain stem.
Has a subthreshold K^+ current I_{KLT} .

Theory

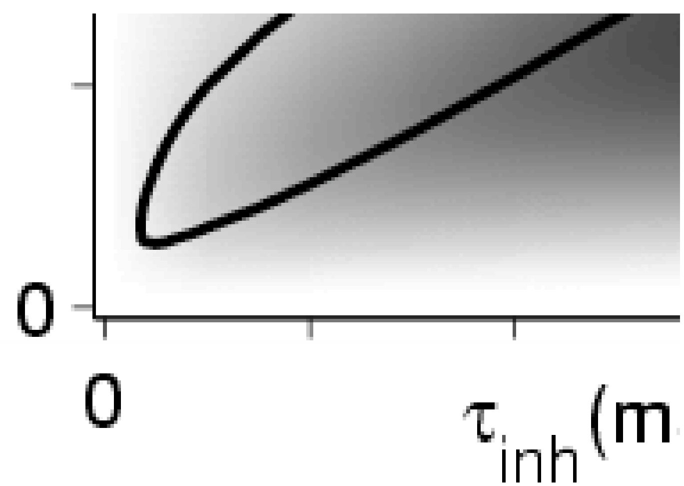


Experiment (Gerbil MSO, slice)

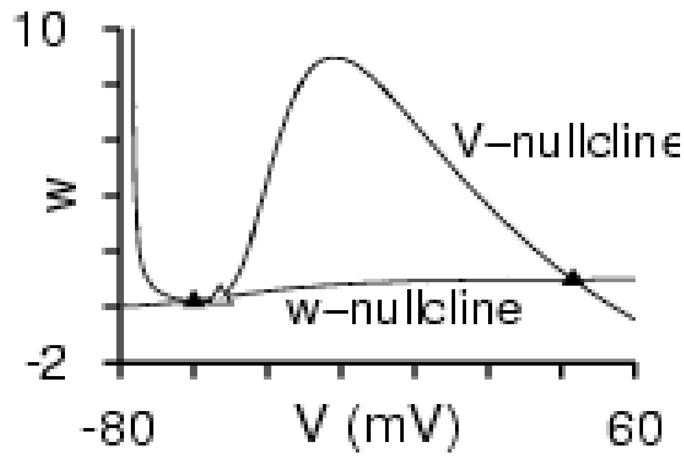


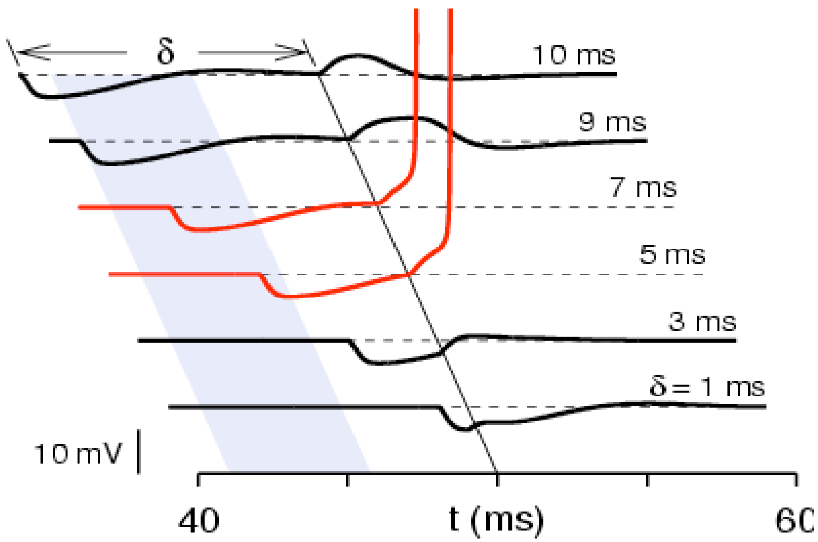


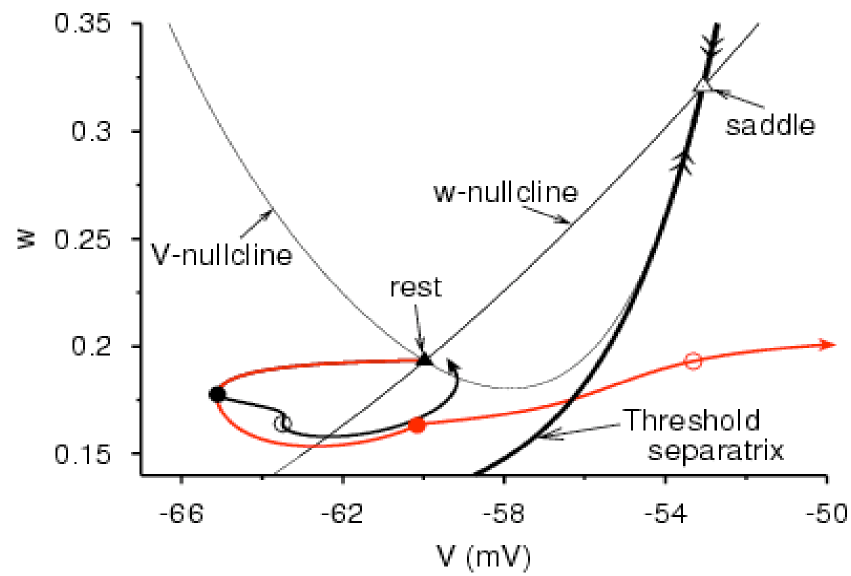
Brief inhib'n: 0.1< □$_{inh}$ < 1.0 msec



Reduced 2-variable model:
V-w (activ'n of I_{KLT}) ;
$m=m_\infty(V)$; h,n frozen



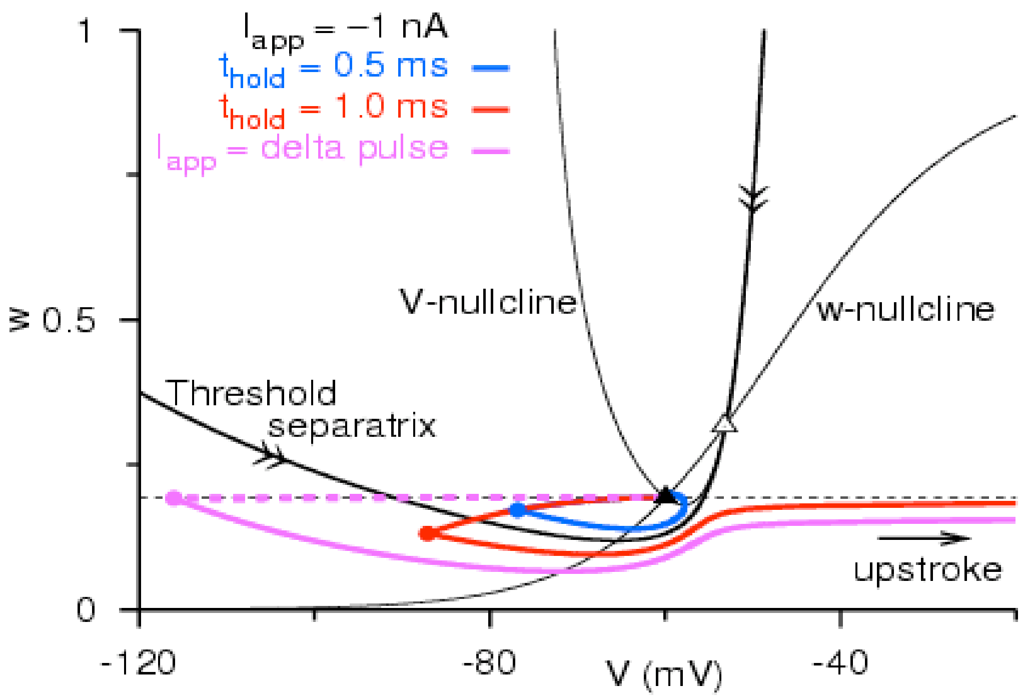


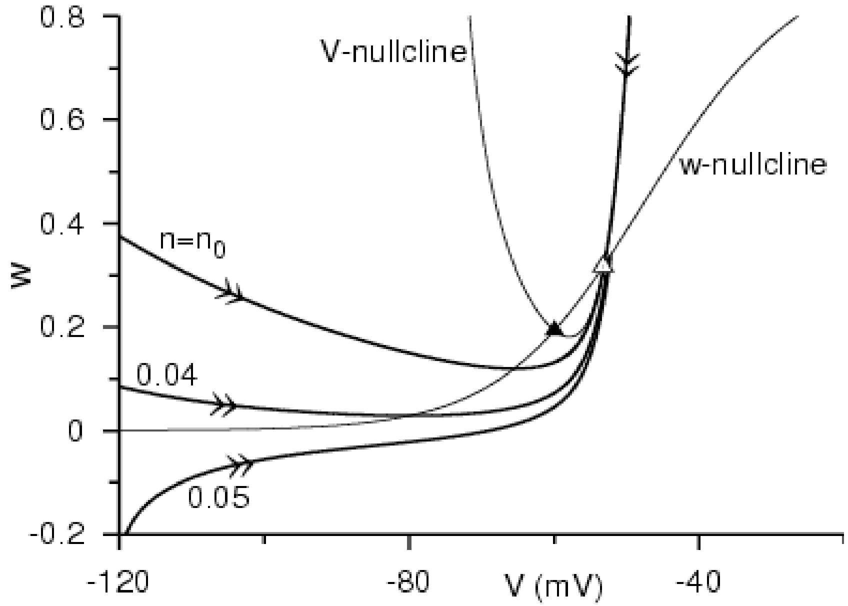


PIR: I_{app} <0; duration t_{hold}

Threshold separatrix must cross w-nullcline (and then w=w rest) ➔ 2 thresholds for _-pulse of Iapp.

FitzHugh ('70s) for HH, w/o geometry.



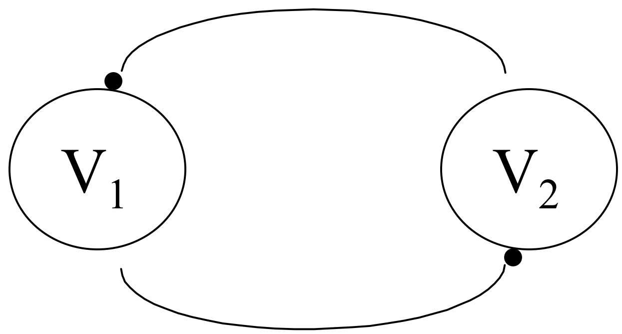


Synchonization/locking with inhibition.

- Time scales
- Gap junctions

Effect of Synaptic Kinetics on Temporal Patterning in an Inhibitory Network

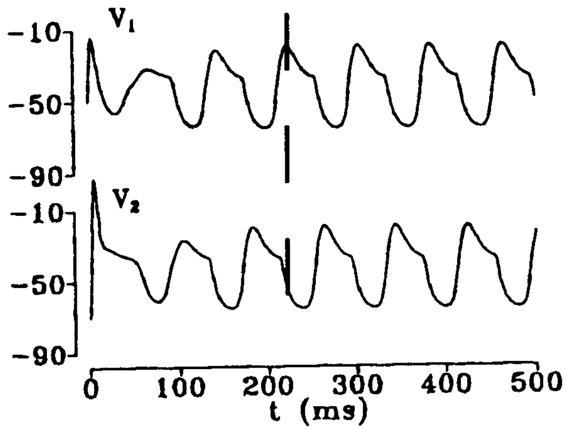
Two mutually inhibitory cells with PIR



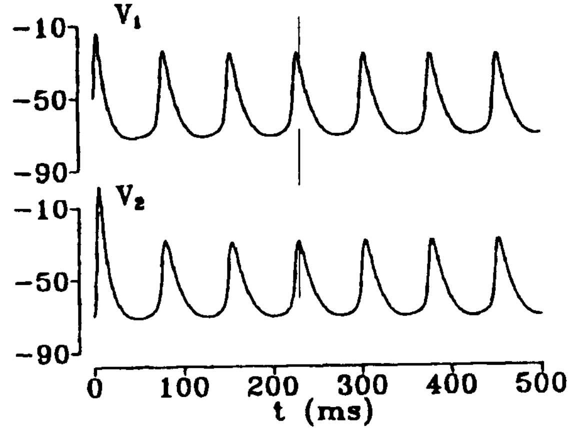
Minimal model for
thalamic relay cells
burst mode
($I_{Ca\text{-}T}$ and I_{leak})

Wang and Rinzel '92

Fast synapses

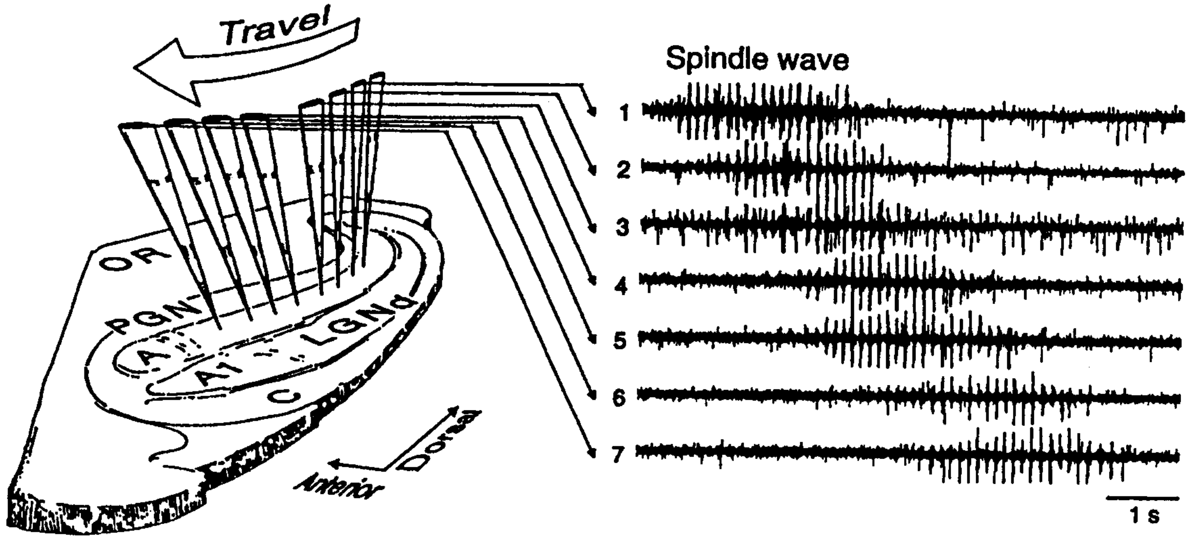


Slow synapses

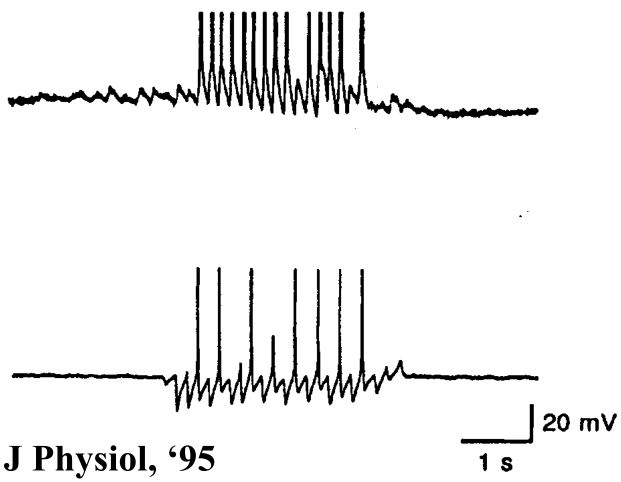


“Spindle Waves” in “Sleeping” Thalamic Slice

McCormick Lab



Kim, et al J Neurophys, '95



Thalamic Reticular Nucleus (PGN), inhibitory cells.

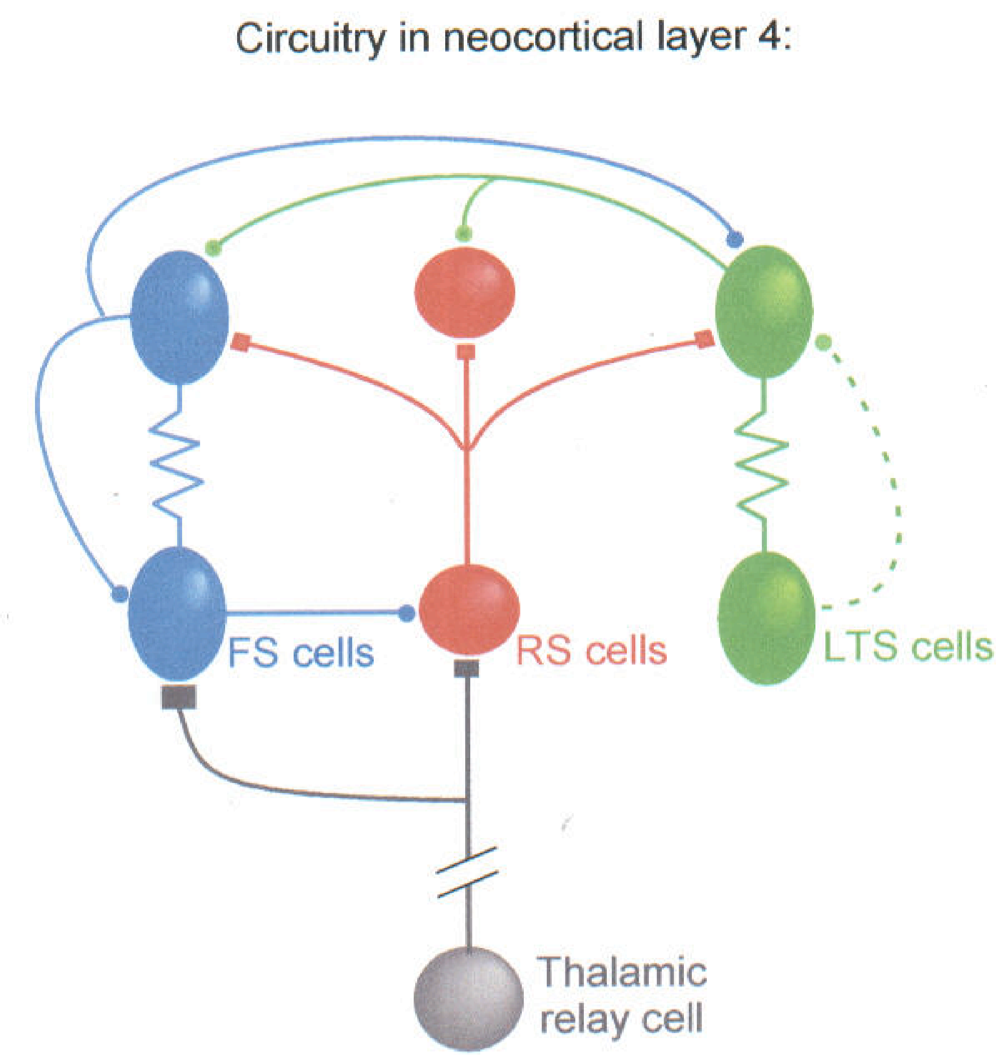
Thalamic Lateral Geniculate Nucleus, excitatory (relay) cells.

Bal, et al, J Physiol, ‘95

Synaptic blocking expts

Inhibitory subcircuits in CNS can have gap junctions.

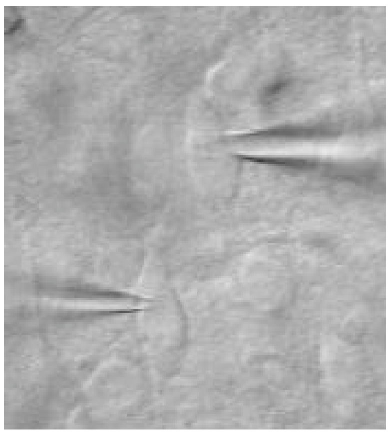
Connors lab and others (Nature, 1999)

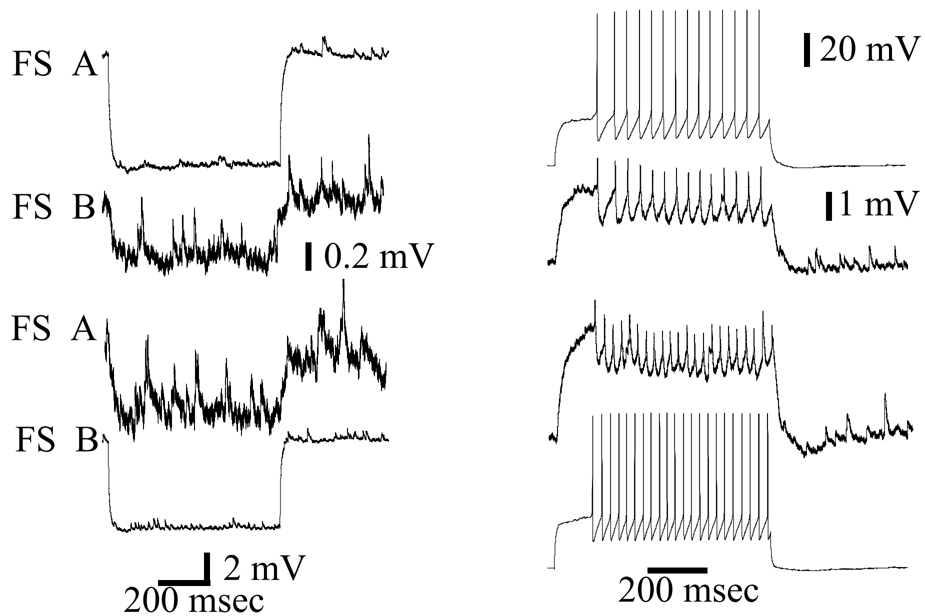


We focus on network (cell-pairs) of Fast Spiking cells. Coupling is weak.

Electrical coupling between Neocortical Interneurons

Dual recordings from pairs of FS cells in layers III - VI of rat barrel cortex



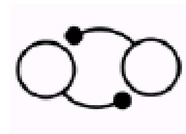


Mancilla, Lewis, Pinto, Rinzel, Connors, 2004

Combined effects of gap junctions and inhibition

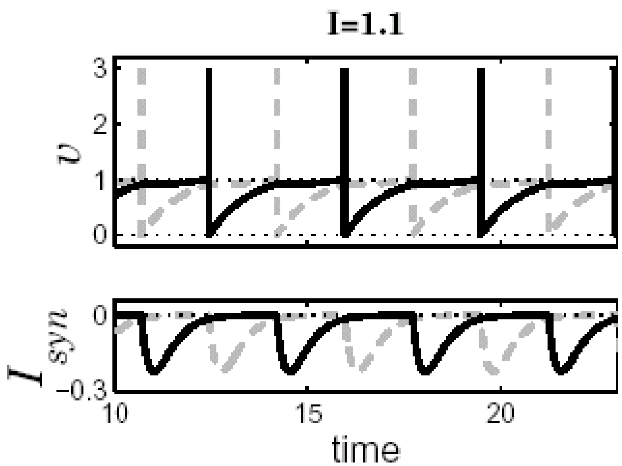
Integrate and fire model neurons - weak coupling

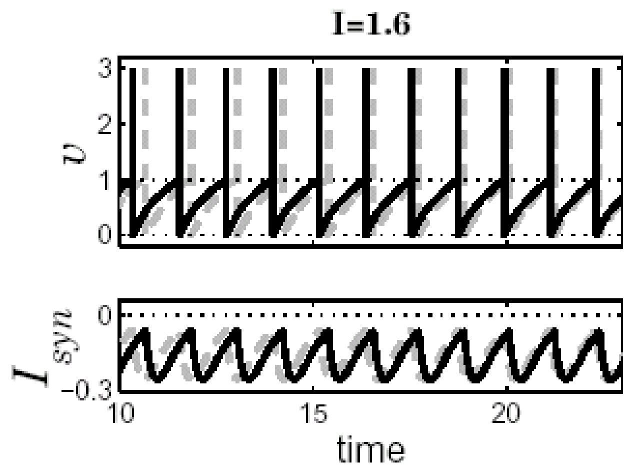
Lewis & Rinzel, 2003

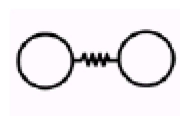


Relatively fast synapses

Synapses slow, compared to fast cells

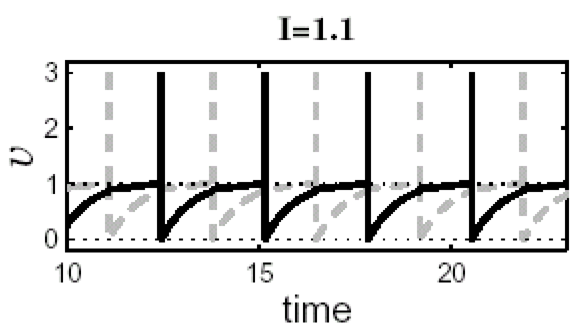


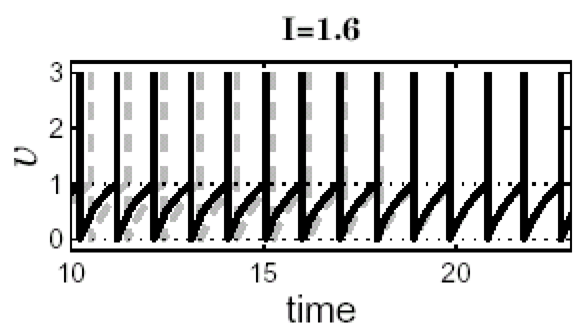




Slow cells

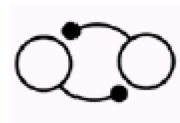
Fast cells, gap jns synchronize

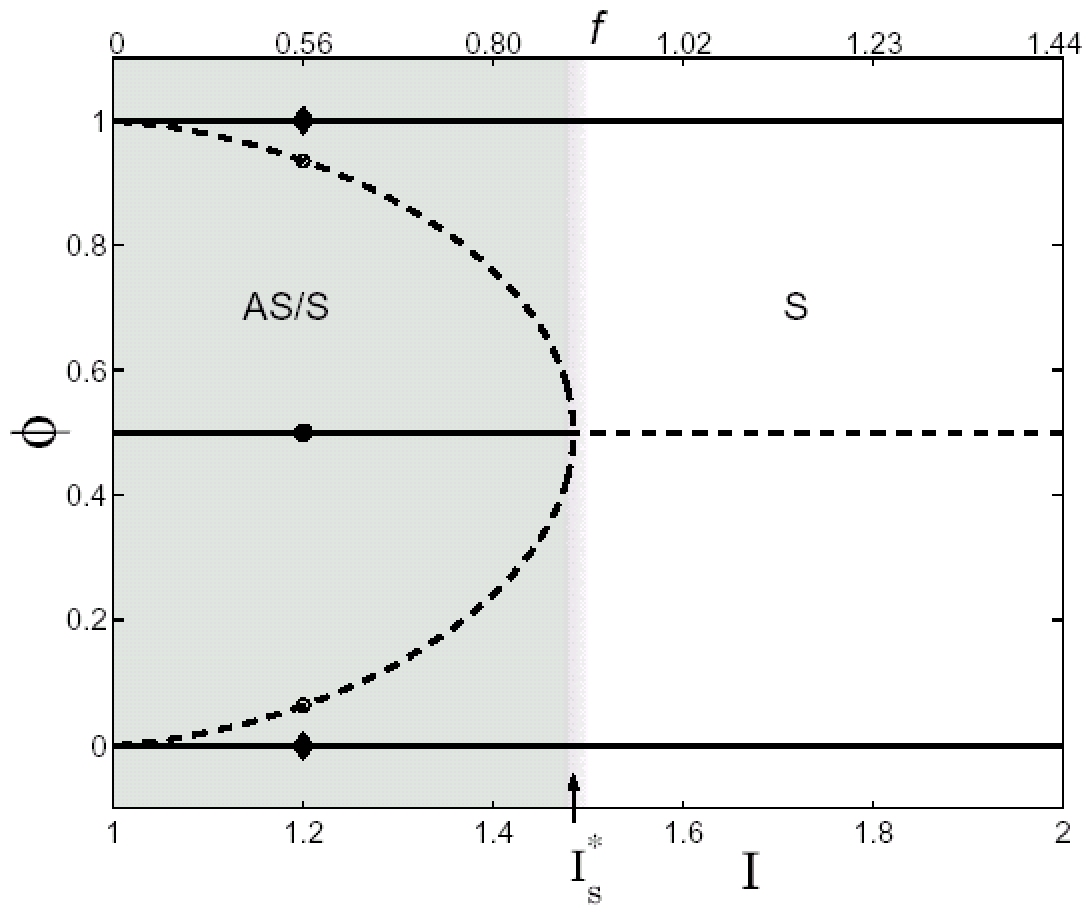




Synchrony or anti-synchrony if cells fast/slow relative to synapses

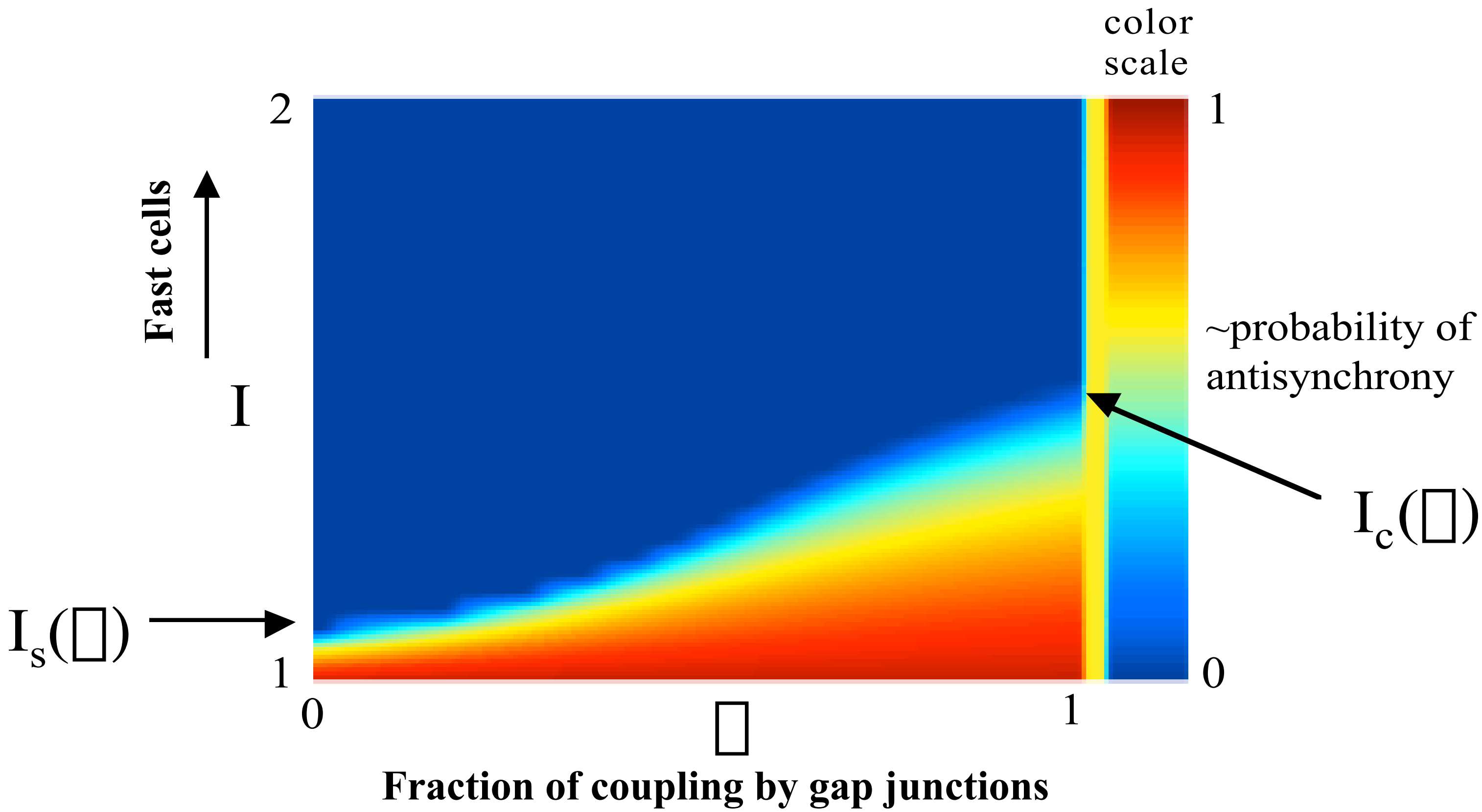
Lewis & Rinzel, 2003
van Vreeswijk, et al, 1994



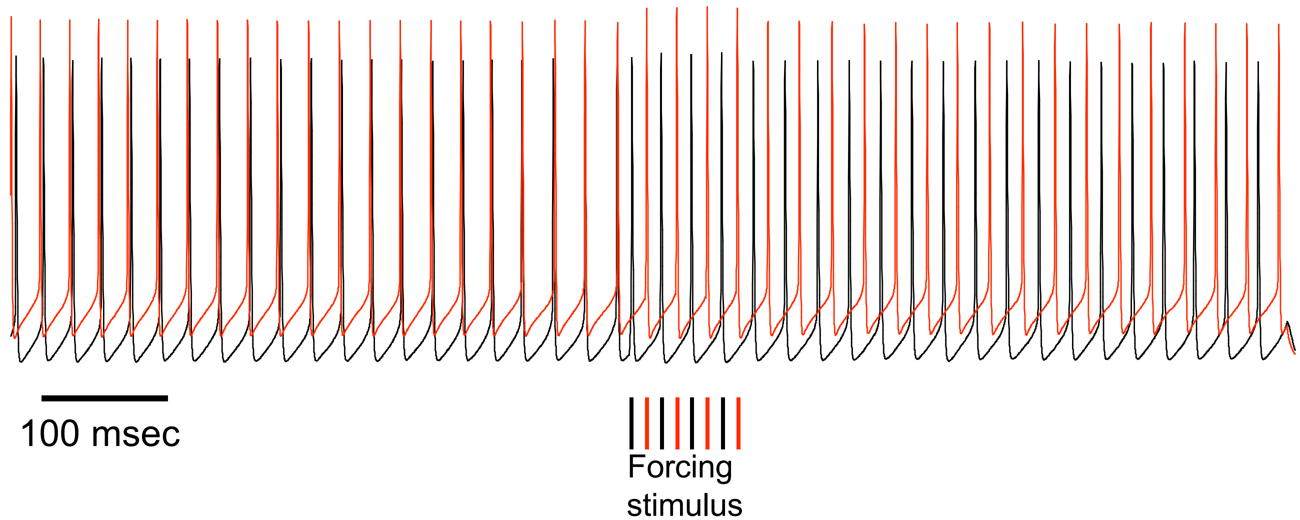


Combined effects of inhibition, gap junctions, and cell frequency.

Lewis & Rinzel, 2003



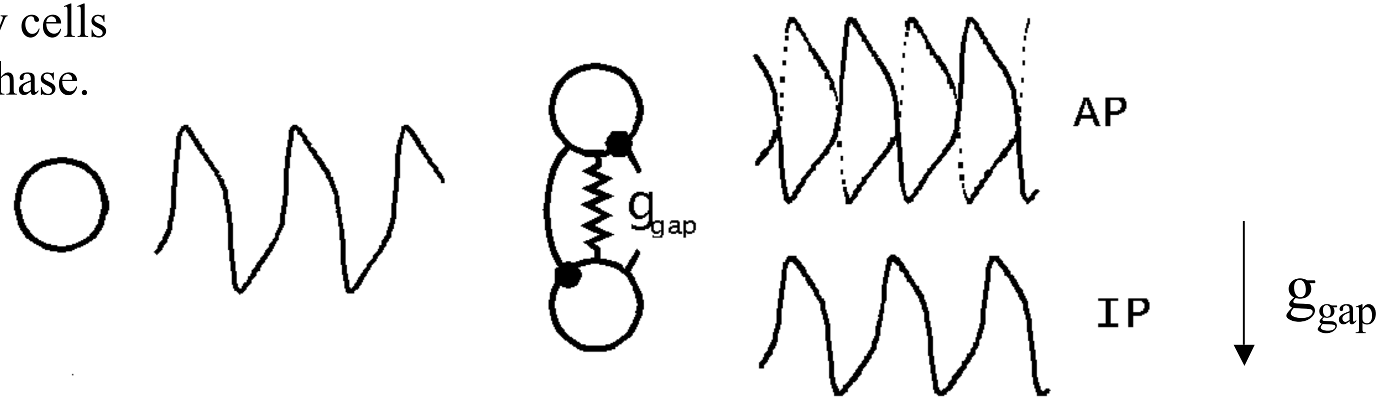
Weak Electrical Coupling Alone - Protocol: DC current steps were used to bring cell pairs to a common firing frequency. Pairs were then forced into anti-phase using 4 or 8 brief suprathreshold current pulses. FS cells in layers III - VI of rat barrel cortex.



Mancilla, Lewis, Pinto, Rinzel, Connors, 2004

Half-Center *Seduction*

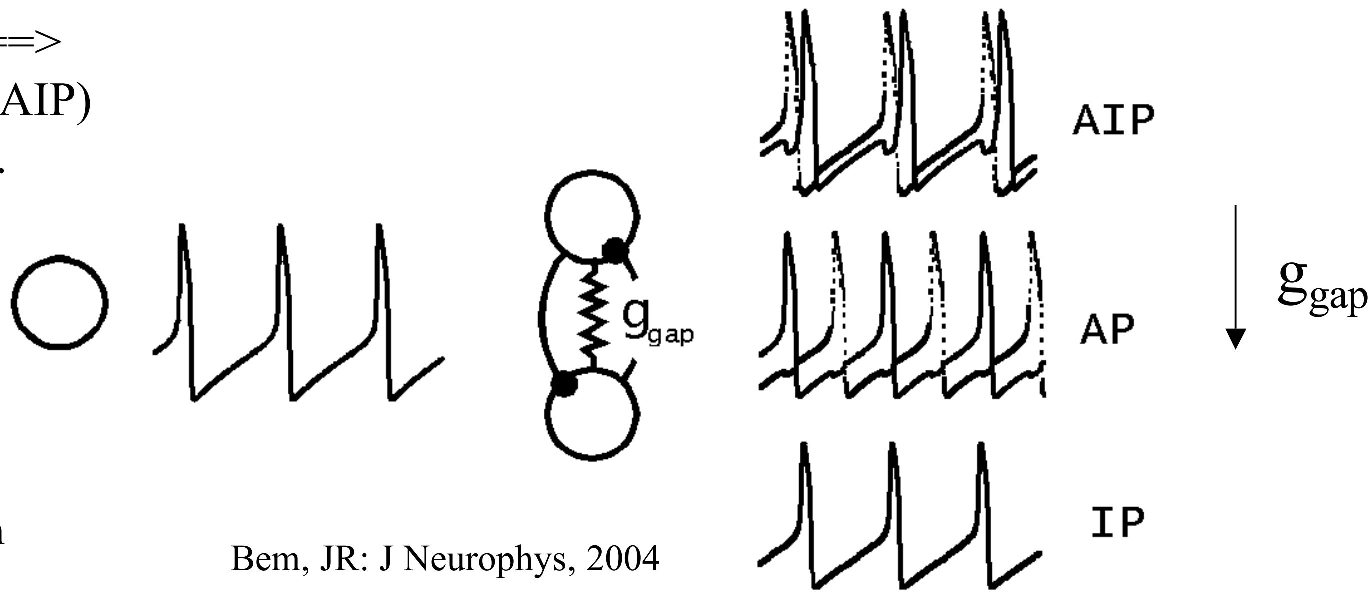
Mutually inhibitory cells
oscillate in anti-phase.



CPGs: Slow wave as burst envelope.
50% duty cycle, instantaneous synapses

FHN-like models;
instantaneous g_{syn}

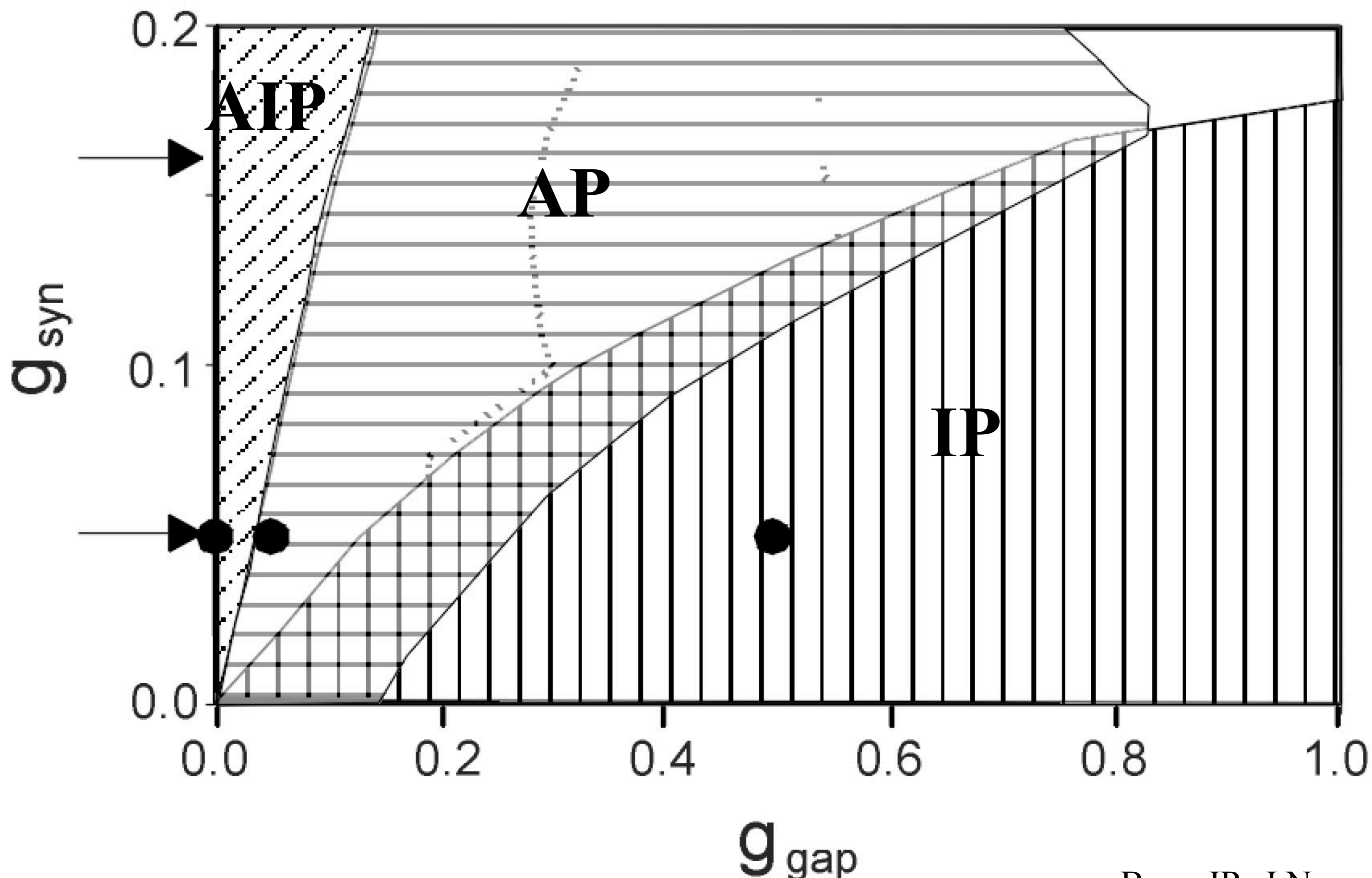
Short duty cycle ==>
Almost in-phase (AIP)
w/o gap junctions.



w/ T Bem, D Terman

Bem, JR: J Neurophys, 2004

Response diagram for duty cycle =0.16



Bem, JR: J Neurophys, 2004

Inhibition and Exciting Consequences

Classical:

- gain control
- timed opposition of excitation
- network rhythmogenesis: recurrent excitation + slower inhibition
- ***half-center oscillator*** CPG: mutual inhibition => anti-phase

Updated:

- shaping of **dynamic** tuning properties
- timed enhancement of excitation

- purely inhibitory network, synchronized; slow _$_{inh}$
- working w/ gap junctions in CNS circuits; LIF models
- very fast inhib'n (relax'n spikers) – almost IP, then w/ modest gap jns AP, bistable w/ IP.