ENHANCEMENT OF NEURONAL RESPONSE DUE TO FAST INHIBITION

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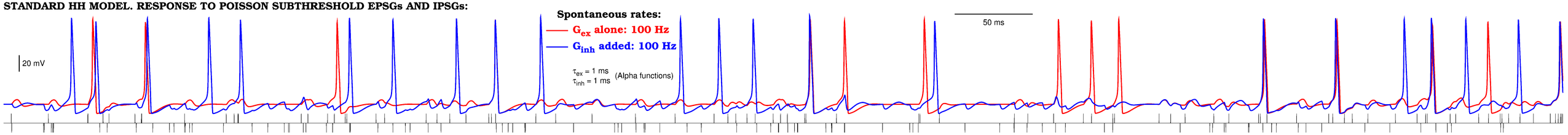
STANDARD HH MODEL. RESPONSE TO POISSON SUBTHRESHOLD EPSGs AND IPSGs:



INTRODUCTION:

Inhibitory synapses are usually believed to contribute to a suppression of neuronal response. For the Hodgkin-Huxley model with subthreshold EPSGs timed at Poisson intervals, we show that brief (Poisson) IPSGs that are faster than the time constant of the membrane and the combined negative feedback of the cell can enhance spike rate. This enhancement is due to: (1) subthreshold EPSGs preceded by well timed IPSGs resulting in postinhibitory facilitation (PIF), and (2) two or more subthreshold IPSGs summing up to result in postinhibitory rebound (PIR). This enhancement may have important implications in both single cell behavior as well as network dynamics.

MODEL:

Classical Hodgkin-Huxley equations with a synaptic current:

$I_{syn} = I_{exc}(t) + I_{inh}(t) = g_e(t)\,(V-E_{exc}) + g_i(t)(V-E_{inh})$
(E_{exc}=10 mV, E_{inh}=-70 mV)

Synapses are modeled with alpha functions with time constants: τ_{ex} (for EPSGs) and τ_{inh} (for IPSGs) each arriving at intervals specified by random Poisson spike trains with rate λ.

CONCLUSIONS:

1. Inhibitory synapses can help enhance the neuronal response if they are faster than the effective membrane time constant and that of the dominant negative feedback near rest.

2. Enhancement in the spike rate occurs due to postinhibitory facilitation (PIF) and postinhibitory rebound (PIR). For both these processes, individual EPSGs and IPSGs are subthreshold.

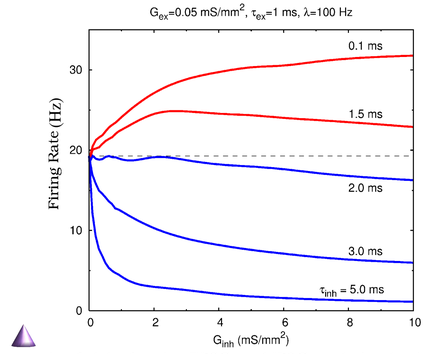
3. For the HH model, the effective membrane time constant gives a good approximation for the critical τ_{inh}.

4. A two dimensional reduced *(V,n)* model explains the enhancement in terms of the trajectory crossing a threshold separatrix.

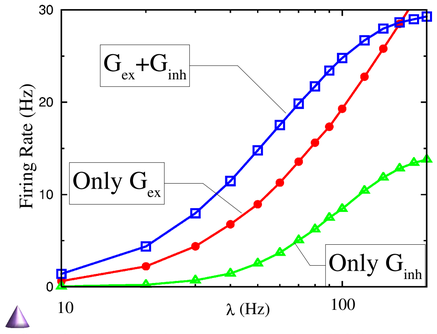
REFERENCES:

[1] A. L. Hodgkin and A. F. Huxley, *J. Physiol.* **117** (1952) 500-544.
[2] R. FitzHugh, *Biophys. J.* **16** (1976) 209-226.

INDUCED ENHANCEMENT:

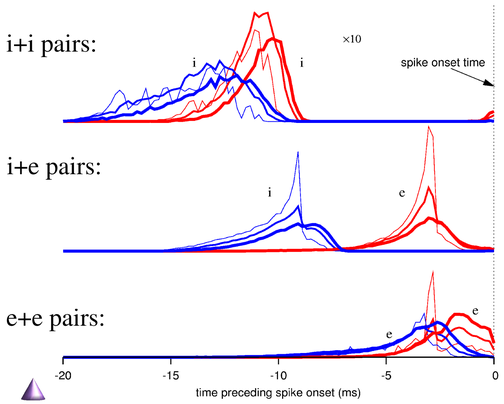


A train of alpha-function EPSGs and IPSGs each timed at independent Poisson intervals with a rate of 100 Hz is applied to a resting HH membrane. For slow IPSGs (τ_{inh} = 2, 3, 5 ms), the firing rate decreases as the strength of inhibition (G_{inh}) increases, as expected. In contrast for faster τ_{inh} (1.5, 0.1 ms) the firing rate exceeds that with G_{inh}= 0, and increases as G_{inh} increases for some lower range.

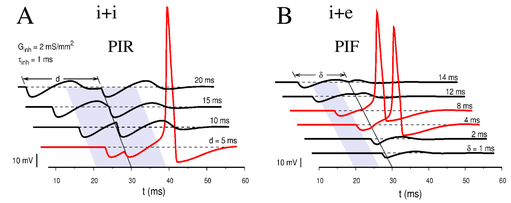


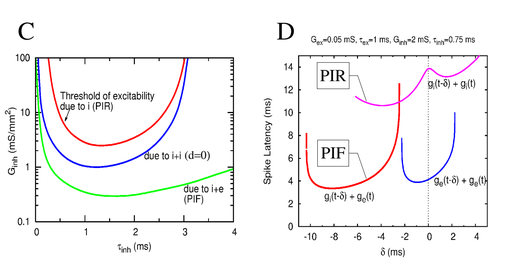
A finite firing rate results due to independent EPSGs and IPSGs. The combined input enhances the firing for spontaneous rates below, say, 100 Hz. (Same parameters as before). We have analytic approximations that predict the firing rate behavior at low input rates. For combined inputs with λ>200 Hz, say, inhibition prevails over the enhancing EPSG and IPSG pairings and the firing rate decreases.

MECHANISMS OF ENHANCEMENT:



The relative occurrence of pairs of excitatory and inhibitory inputs that led to a successful spike reveal that i+e combination is the dominant factor. G_{ex}=0.05, τ_{ex}=1ms, G_{inh}=1, τ_{inh}=1ms. Thick, thin, and thinner curves are respectively for λ = 100 Hz, 50 Hz, and 10 Hz.



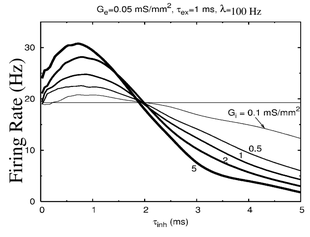


The two main mechanisms involved in the enhancement caused by inhibition are postinhibitory rebound (PIR) (**Fig. A**) and postinhibitory facilitation (PIF) (**Fig. B**). Here isolated pairs of inputs, as opposed to a train of inputs, are used for illustration.

Fig. C shows the parameter regime where PIR occurs for a single inhibitory input **(red).** Also shown, regimes where PIF and PIR occur respectively, for pairing the IPSG with a succeeding subthreshold EPSG **(green)** or with another IPSG **(blue)** of the same strength.

Fig. D shows how close (δ) the individual inputs in each pair should be for evoking a spike in PIR and PIF as well as pairings of two EPSGs by themselves. (Spike latency is the time elapsed from the nearest EPSG/IPSG to the spike upstroke.)

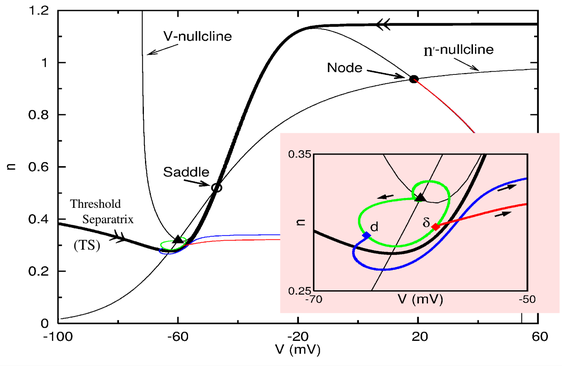
NEED τ_{inh} BRIEF ENOUGH:



Enhancement occurs when τ_{inh} is faster than the combined influence of the effective membrane time constant and the negative feedback, primarily *n*. (See the reduced model)

For the HH model near rest, the effective membrane time constant ($\tau_{m\text{-}eff}$) and τ_n are comparable (1 - 2 ms). This sets the approximate location for the curve-crossings at around 2 ms. For PIF, τ_{inh} should be smaller.

PHASEPLANE EXPLANATION OF ENHANCEMENT:



A 2D reduced HH model with $m=m_\infty(V)$ and $h=h_{rest}$(constant) gives a phase-plane view of the two main mechanisms, PIF and PIR.

Green trajectory is the response to single IPSG.

For PIF: EPSG carries trajectory (red) across right branch of TS.

For PIR: Second IPSG carries trajectory (blue) across left branch.

The U-shape of TS implies that HH model has two thresholds for brief current pulses; one for depolarization and one for hyperpolarization.