FEEDBACK INHIBITION CAN ENHANCE SPONTANEOUS NEURONAL FIRING

RAMANA DODLA[1] & JOHN RINZEL[1,2]

[1]Center for Neural Science, New York University, New York, NY 10003

[2]Courant Institute of Mathematical Sciences, New York University, New York, NY 10012

CNS 2005

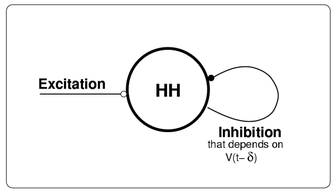
ABSTRACT

Inhibitory interneurons in neocortex, while damping some behaviors, can also facilitate activity, e.g., helping to sharpen transients and synchronize gamma oscillations. We propose that feedback from fast inhibition can also enhance the spontaneous firing of such cells. Here we study an idealized feedback model. We drive the Hodgkin-Huxley conductance-based model by external Poisson alpha-function excitatory synaptic input. Its output spikes lead (1 for 1) to recurrent inhibitory synaptic inputs (delayed in time by δ). We find that the recurrent inhibition can enhance the neuron's firing rate if τ_{in} is fast enough; the dependence of this enhancement on δ is weak.

The spontaneous firing without inhibition is due to temporal summation of subthreshold inputs. The feedback inhibition may reduce the spike threshold of the membrane briefly (e.g., by transiently reducing g_h), and thereby facilitates the next subthreshold excitatory event to evoke a new spike. This mechanism is distinct from classical postinhibitory rebound, and occurs in the current model for a wide range of δ values and for short decay times of inhibition. This may have interesting ramifications in understanding the role of transient inhibition in neocortex.

MODEL

1. We consider a single compartment model with an external excitatory input and a feedback/recurrent inhibition. The model is depicted below:



2. The membrane potential evolves according to the classical Hodgkin-Huxley model equations at T=22 °C [Hodgkin and Huxley 1952].
The voltage evolves according to:

$$C_m dV/dt = -g_{Na} m^3 h\,(V-E_{Na}) - g_K n^4 (V-E_K) - g_L (V-E_L) - I_{syn}(t)$$

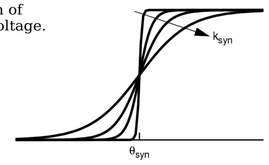
where $I_{syn}(t) = g_{in}(t)(V-E_{exc}) + G_{inh}\, s\,(V-E_{inh})$

3. The excitatory conductance is an alpha function input with peak amplitude G_{in} and time constant τ_{in}; it is delivered at intervals specified by a homogeneous Poisson process with rate λ.

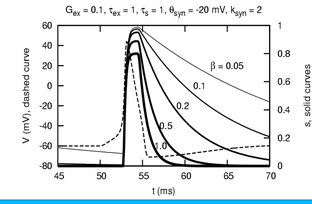
4. The feedback inhibition variable s is obtained by an evolution equation that evolves according to [Wang and Rinzel, 1992]:

$$\tau_s\, ds/dt = \alpha[V(t-\delta)]\,(1-s) - \beta\, s$$

The function α(V) is given by: $\alpha(V) = 4/(1+e^{-(V-\theta_{syn})/k_{syn}})$, and is shown below as a function of static voltage.



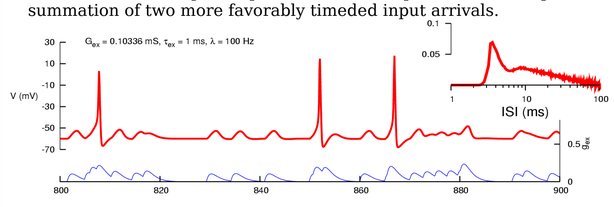
5. The feedback/recurrent inhibition is generated whenever the membrane evokes a spike.
The following plot illustrates the shape of s as a function of β for δ=0. Inhibition is delayed with increasing δ.



RESULTS

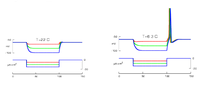
1. Response to a Poisson train of alpha function excitatory input:

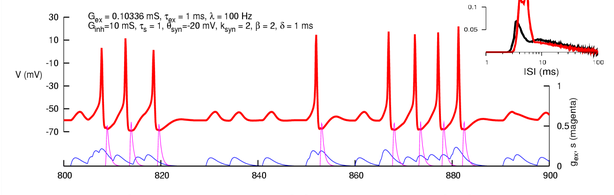
Each input arrival is subthreshold in magnitude, and is 80% of the threshold level. Output response consists of spikes due to temporal summation of two more favorably timeded input arrivals.



2. Response to a Poisson excitatory input with recurrent inhibition:

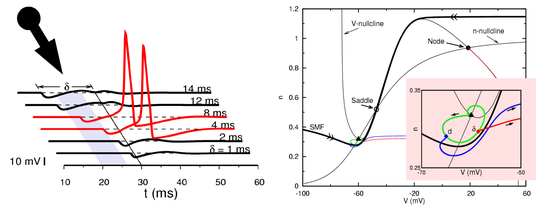
Note that at T=22 °C, the HH model does not elicit classical rebound spike(s) by release after maintained inhibition (see plots on the right), neither it elicits such spikes for brief inhibition.





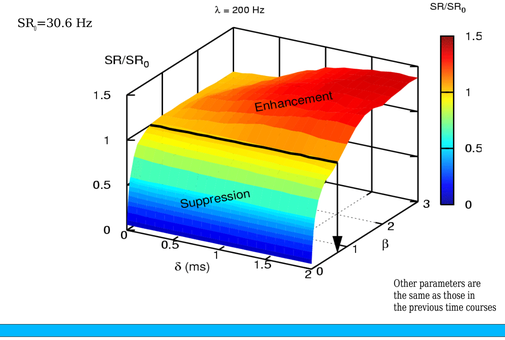
For every spike, a 1:1 recurrent inhibition is generated. This inhibition with some probability falls in a favorable time window ahead of the subsequent randomly-arriving EPSG and thereby facilitate spike generation (see the next box). Such additional spikes from well-timed i-e pairings [Dodla et al., 2005] lead to an enhancement of firing rate.

Mechanism of enhancement due to inhibition:



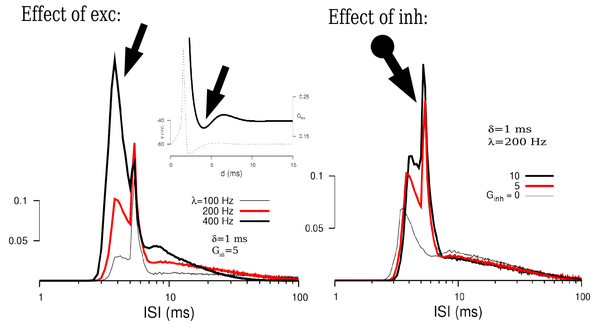
A subthreshold excitation if preceded by well timed inhibition (falling in grayed region) evokes a spike [3]. The phase plane portrait (right) shows enhancement mechanism for a reduced 2-D model of the HH equations.

3. Enhancement occurring for fast inhibition:



Other parameters are the same as those in the previous time courses

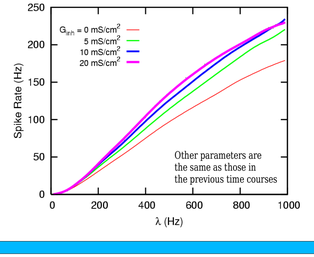
4. ISI density can have multimodal distribution:



The first of the ISI peaks (left plot) is due to damped oscillatory threshold following a spike. The second peak is caused by the PIF effect (right plot).

5. Firing rate vs. input rate for varying G_{inh}:

As input rate increases, the probability of subthreshold input pairs falling in a favorable window increases, thereby leading to increase in firing rate. Recurrent inhibition enhances this firing rate for a range of input rates.



CONCLUSIONS

1. We have shown that appropriately delayed brief inhibition can act like a positive feedback, and can enhance the output response of a model neuron through PIF mechanism.

2. The enhancement occurs due to a subthreshold excitatory input that falls (with favorable timing) in the wake of an inhibitory (feedback) transient after a preceding spike.

3. Enhancement occurs for faster time constants of the recurrent inhibition.

4. The ISI density distribution can be multimodal. The first ISI peak reflects oscillatory threshold following a spike, and the second ISI peak is due to the spikes caused by enhancement.

REFERENCES

[1] A. L. Hodgkin and A. F. Huxley. *J. Physiol.* 117:500-544, 1952.

[2] X.-J. Wang and J. Rinzel. *Neural Computation.* 4:84-97, 1992.

[3] R. Dodla, G. Svirskis, and J. Rinzel, *submitted*, 2005.

[4] X.-J. Wang and G. Buzsaki, *J. Neurosci.* 16:6402-6413, 1996.

[5] R. D. Traub, M. A. Whittington, I. M. Stanford, and J. G. R. Jefferys, *Nature.* 383: 621-624, 1996.