Timed inhibition affects coincidence detection in an MSO neuron model

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ABSTRACT

Recent experiments (in gerbil, by Brand et al, 2002) call into question the classical Jeffress [1], place-code, model for low frequency sound localization that assumes paired (ipsi and contra) excitatory inputs. However, the interaural time delay (ITD) response curve is strongly influenced by inhibition, shifting its peak into the contra-leading region and out of the physiological range. Meanwhile, the curve's steeply rising ipsi-leading side is positioned near ITD=0; a slope-code is suggested. A computational model (adapted from Rothman et al, 1993) was shown to agree with the experimental results, when the brief inhibition is delivered just in advance of ($\delta = 0.1$ ms) the contra-excitation.

Using this same HH-type model we explore the effect of the timing and strength of brief inhibitory inputs on ITD responses. Some effects can be demonstrated by considering combinations of individual (subthreshold) inputs: EPSG+IPSG or 2 EPSGs+IPSG. For example, as in Brand et al, the ITD tuning shifts towards the contra-leading side if the IPSG is timed to just precede the contra-EPSG. Surprisingly, a single subthreshold EPSG may also elicit a spike if the timing of a brief IPSG falls within a critical but more advanced (say $\delta = 1$ ms) brief time window. This enhancement of the EPSP, a transient form of postinhibitory rebound or exaltation (PIE), depends on the model's low-threshold K+ current. Thus, PIE provides yet another mechanism for responsiveness to precisely timed inputs in the auditory pathway. Correspondingly, PIE also influences the ITD tuning curve for bilateral "tone" inputs (when conductances are modeled by periodically modulated Poisson spike trains); the suppressive effect of inhibition on the rising side (ipsi-leading) is diminished as A increases while the responses are enhanced on the falling side (contra leading) due to PIE.

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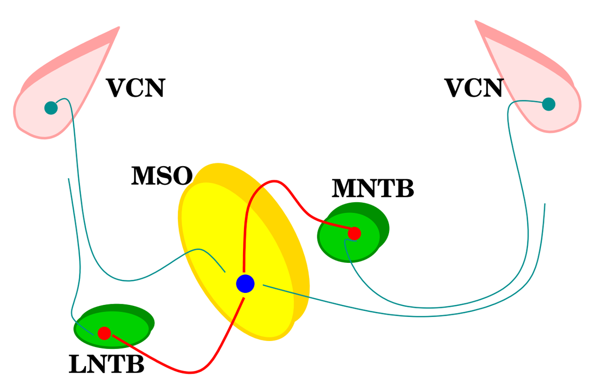
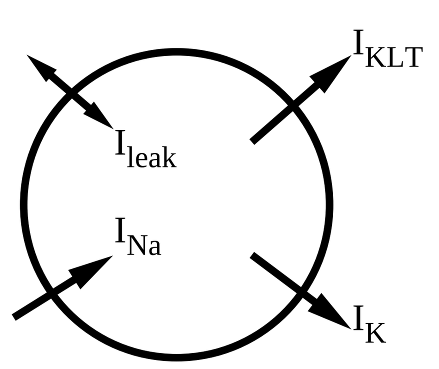
1 Basic model

- The basic model is identical to that of Rothman et al. [2]:

$$C_s \frac{dV}{dt} = -G_{KLT}w(V - E_K) - G_K n(V - E_K) - G_{Na}m^2 h(V - E_{Na}) \\ -G_L(V - E_L) - I_{syn}$$



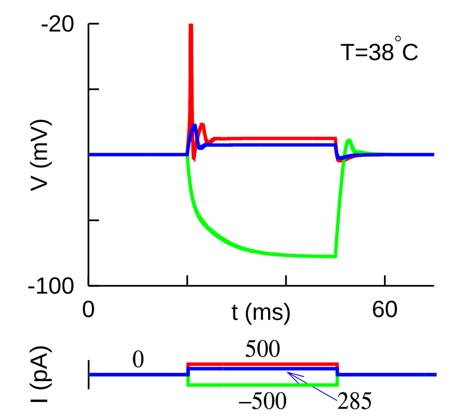
- The synaptic current is the summation of interaural time-delayed contralateral excitation, ipsilateral excitation, and inhibition that leads the contralateral excitation by τ. Contralateral input leads for $ITD > 0$.
- The excitatory and inhibitory synaptic conductances (EPSG and IPSGs) are modeled using an α-function (with a decay time of $0.05ms$) that takes auditory nerve inputs as periodically modulated Poisson spike trains [2].



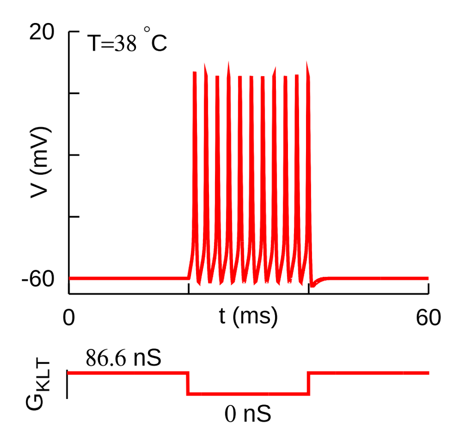
- We first characterize the model in 2.1 and provide a simple mechanism of postinhibitory exaltation (PIE) using single excitatory and inhibitory inputs.
- Then we show in 2.2 coincidence detection (CD) using two EPSGs, and illustrate the effect of inhibition in CD.
- Finally we consider a large number of periodically modulated Poisson spike trains and show that (1) inhibition is more effective on ipsi-leading side for small τ, and (2) with a precise timing, it could enhance the ITD sensitivity on the cotra-leading side due to the PIE effect.

2 Results

2.1 Firing characteristics of the model neuron

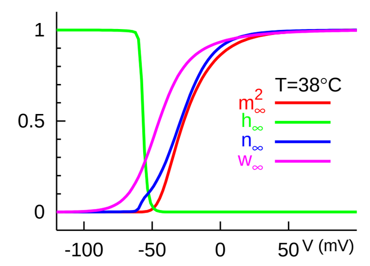


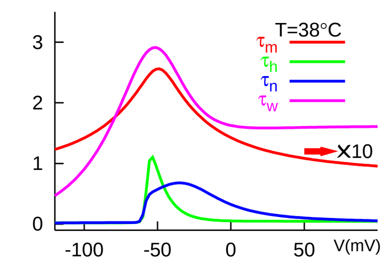
- The model neuron has phasic firing properties.
- Rectification occurs in the subthreshold regime.



- Removing I_{KLT} converts the cell to tonic firing.

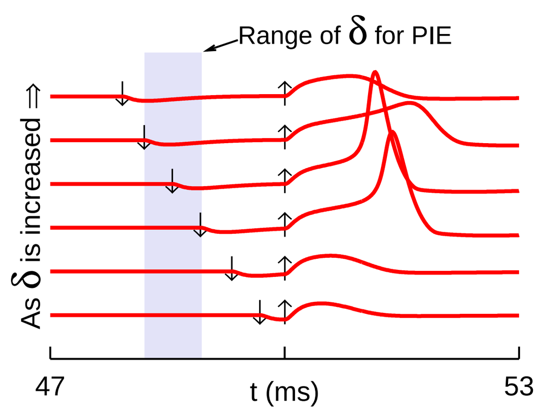
Gating variables and time constants:

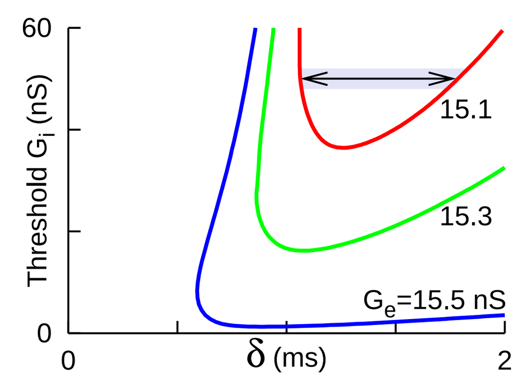




2.2 Postinhibitory Exaltation (PIE) for single EPSG/IPSG

- A subthreshold EPSG ($G_e = 15.1nS$) given at $t = 50$ ms evokes an action potential if a well timed IPSG ($G_i = 50$ nS) leads it (by δ falling in the shaded window).



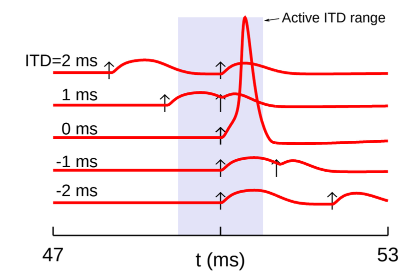


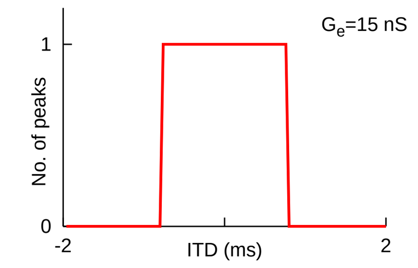
- Such a δ range can be increased or decreased by making a proper choice of G_i for any given value of G_e. The arrows in the shaded region indicate the δ range (as seen above) for $G_i = 50nS$.

2.3 Coincidence detection for 2 EPSGs and an IPSG

CD with two subthreshold EPSGs:

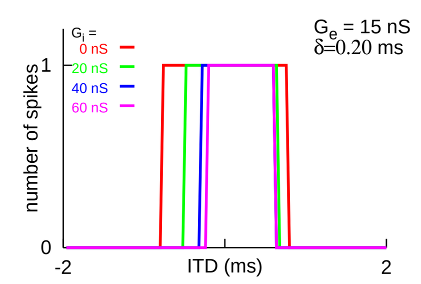
- Two subthreshold EPSGs can act as a coincidence detector by evoking an action potential for a small range of ITD values. The ITD response curve is symmetric.



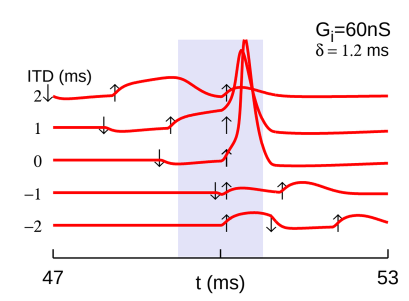


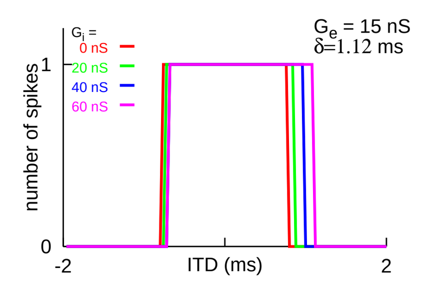
CD with 2 subthreshold EPSGs and an IPSG:

- Inhibition is more effective on the ipsi-leading side than on the contra-leading side for small value of δ as evidenced by Brand et al. [3].



- For longer lead times, however, the PIE effect makes the contra-leading side to have more chance to fire for a range of δ.



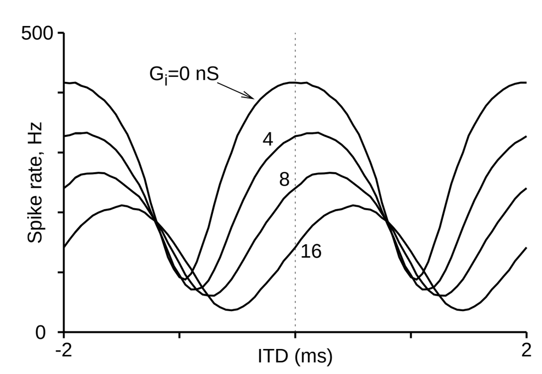


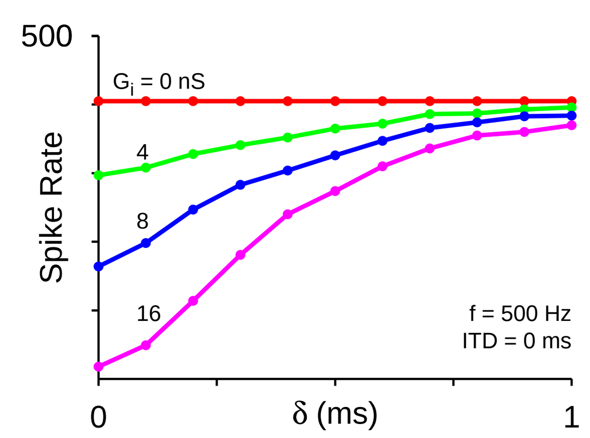
2.4 Coincidence detection with many Poisson inputs

- 25 pairs of (contralateral and ipsilateral) excitatory and 25 inhibitory (time locked to the contralateral) pre-synaptic inputs generated (as described by Rothman et al. [2]) with a 500 Hz modulated Poisson spike train were used in the simulations.

Effect of intensity and timing of inhibition at short δ values:

- For small δ (0.1 ms), the inhibition is more effective on the ipsi-leading side than it is on the contra-leading side as was observed by Brand et al. [3].
($G_e = 3$ nS, $\tau_{ex} = 0.1$ ms, $\tau_{inh} = 0.1$ ms)

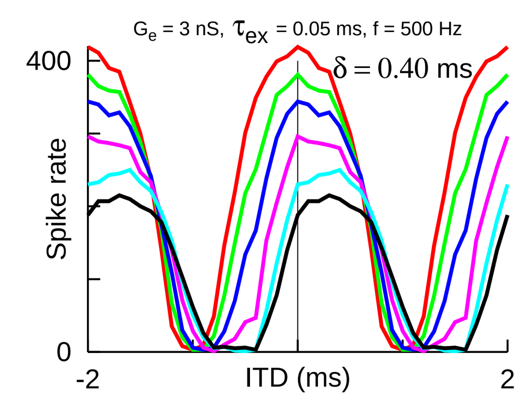


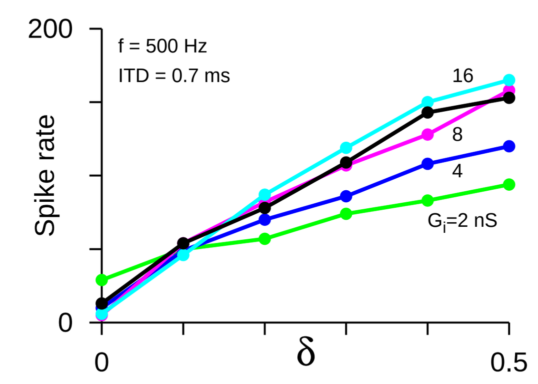


- At fixed δ the firing rate decreases with increasing inhibitory strengths. At longer δ values, such a decrease is small, and generally is at elevated levels.

2.5 Effect of intensity and timing of inhibition at longer δ: The PIE effect

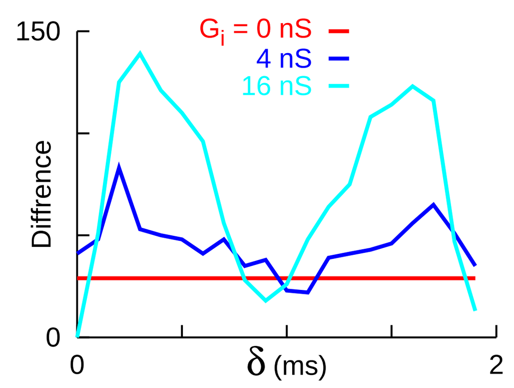
- The contralateral response is enhanced due to the PIE effect for longer δ values.

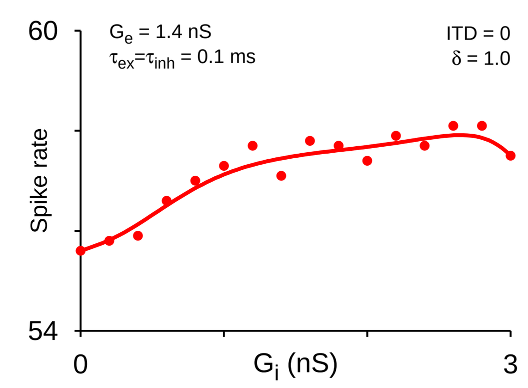




- Such an enhancement occurs beyond a critical value of δ for a range of δ values. This critical value can be tuned by a proper choice of α-function decay rate, and the strength of G_e.

- The difference of maximum and minimum of ITD in a window of width of 0.4 ms around $ITD = 0$. G_i and δ together can help increase the response difference.





- An example of increasing response with inhibition. $G_e = 1.4$ nS, $\tau_{ex} = \tau_{inh} = 0.1$ ms.

3 Conclusions

- Two input model of CD captures the essential features of the effect of inhibition in the MSO coincidence detection.
- The PIE effect is evident both in the 2 input model as well as multi-input Poisson spike train model.
- The steepness (slope) at the zero-coincidence is controlled by δ.

References

[1] L. A. Jeffress. *J. Comp. Physiol. Psychol.*, 41:35–39, 1948.

[2] J. S. Rothman, E. D. Young, and P. B. Manis. Convergence of auditory nerve fibers onto bushy cells in the ventral cochlear nucleus: Implications of a computational model. *J. Neurosci.*, 70:2562–2583, 1993.

[3] Antje Brand, Oliver Behrend, Torsten Marquardt, David McAlpine, and Benedikt Grothe. Precise inhibition is essential for microsecond interaural time difference coding. *Nature*, 417:543–547, 2002.