Cellular dynamics involved in sound localization

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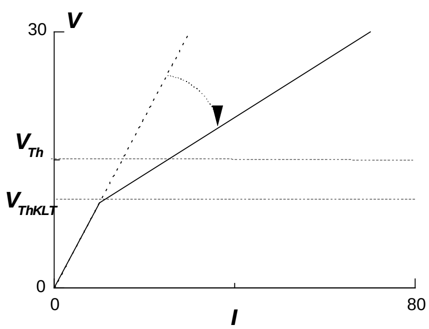
The early stages of binaural processing involve components that appear to be well-designed for precise temporal processing. Neurons that perform coincidence detection for low frequency inputs respond best to rapidly changing inputs. They fire in a phasic manner not tonically and they phase-lock with high vector strength (VS) up to 2 KHz or so. Several features at the biophysical level have been identified, to more or less extent, in the avian nucleus laminaris (NL) and the mammalian medial superior olive (MSO) that distinguish these neurons. They have fast ionic currents and brief time constants; they receive bilateral inputs on segregated bipolar dendrites and the excitatory synaptic currents are generally fast; they have a low-threshold potassium current that renders them phasic. This talk will review some of these features and describe recent modeling and experimental studies that provide additional insights into the nonlinear mechanisms by which enhancement to temporal processing can occur.

It is understandable how a low threshold K+ current (I_{KLT}), once activated by a sustained and strong excitatory input, could raise the threshold for subsequent spike generation – rendering a cell unable to fire repetitively. One can also appreciate how this increased conductance could reduce the effective membrane time constant and the integration time, possibly refining a cell's ability to phase-lock and to detect coincidence of inputs. Here we focus on these issues with idealized computational models and in vitro experiments on gerbil MSO neurons. We direct special attention to the effects of I_{KLT} on transient and not strong inputs. How does I_{KLT} enable a cell to detect transient synchronized inputs in the presence of ongoing noisy spontaneous activity? Our results emphasize as a major factor that determines whether or not I_{KLT} influences spiking the rate of stimulus driven depolarization compared to the activation rate for I_{KLT}, $1/\tau_A$.

Some of our insights can be demonstrated with a very idealized model. For our minimal model we enhance the usual leaky integrate-and-fire model by incorporating a time-dependent rectification that kicks in below firing threshold. This current that mimics the effect of I_{KLT} reduces membrane resistance, after becoming fully activated, by 100% (Fig 1).



$$C\dot{V} = -G_m V - G_{KLT} n(V - V_{ThKLT}) + I(t)$$
$$\dot{n} = \frac{n_\infty(V) - n}{\tau_{KLT}}$$

Figure 1. The steady state current voltage relation is piecewise linear. The rectified component activates above $V=V_{ThKLT}$ with a time constant TK. The model neuron fires when V reaches V_{Th} and then an outward current, I_{KAHP}, is turned on (not shown) which decays with time constant of 5 msec. The resting membrane time constant is 2 msec. In this reduced model the activation gating function $n_\infty(V)$ is steep, a step function of V.

This model behaves phasically over a substantial range of input current steps (I) that without I_{KLT} would lead to tonic firing. In this range it fires just a single spike after the I onset.

We imagine that the model neuron receives convergent spontaneous input from noisy and uncorrelated input lines, random small EPSCs at high rate. Its spontaneous firing rate for balanced excitatory and inhibitory inputs is on the order of 10 Hz. A single large (but subthreshold) EPSC is presented, representing a transient highly coincident set of inputs. In order to characterize the model neuron's responsiveness or detection ability for a transient input we compute the PSTH or probability of firing (per unit time) associated with this EPSC in this noisy background. As one expects (Fig 2A) the peak in firing probability is somewhat reduced by the presence of I_{KLT}. However the distribution's tail is more significantly affected – it is greatly reduced, evidencing that I_{KLT} has diminished the spontaneous firing rate of the cell. An important consequence is that the signal to noise ratio (taken as the ratio of firing probabilities for signal and for the spontaneous inputs) has dramatically increased. Summed spontaneous inputs that randomly cause the cell to fire in the absence of I_{KLT} are no longer in some instances adequate for evoking a spike. That is, when temporal summation for some spontaneous inputs occurs over time scales comparable to TK the spontaneous firing rate will drop. On the other hand the cell's responsiveness to the synchronous EPSC is changed only slightly because the rate of depolarization occurs faster than the activation of I_{KLT} . This reduction in the temporal window for integration is also seen by a reverse correlation analysis of the input that causes the cell to fire (Fig 2B).

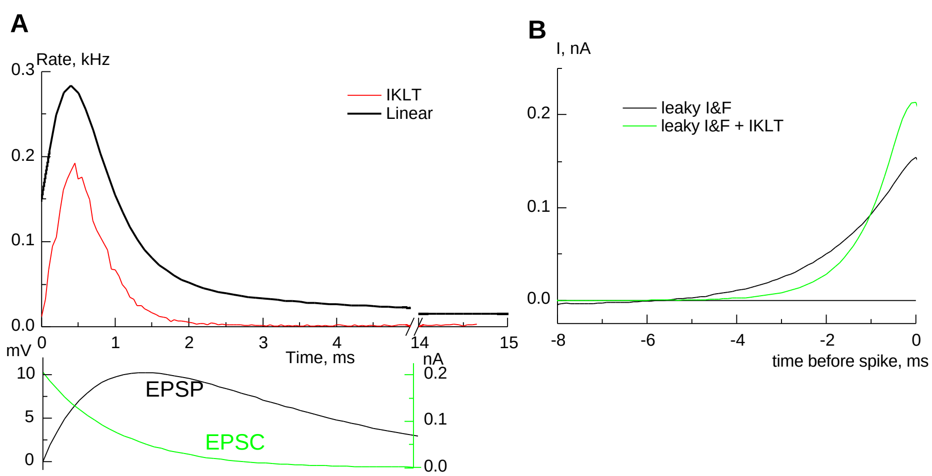


Figure 2. A. Post stimulus time histogram for single EPSC (lower panel in A) with and without I_{KLT} in leaky integrate-and-fire model. B. Spike triggered average of input current (reverse correlation).

The enhanced precision of spike timing is also revealed by an increase in VS for periodic inputs that involve summation of weakly synchronized small inputs. Here we are thinking of detecting a signal that represents temporal organization, i.e., low frequency (< 1 KHz) modulation, in the presence of the noisy spontaneous background. Just as for strong inputs that are phase-locked with high precision to the carrier signal, vector strength declines as signal frequency increases (Fig 3). Our simulations show that this VS decline is reduced with I_{KLT} present. This figure also shows that similar results to

these (and those of Fig 2) have also been obtained with an HH-like conductance-based model that incorporates the quantitative description of I_{KLT}, based on Trussell's voltage clamp results in MN neurons.

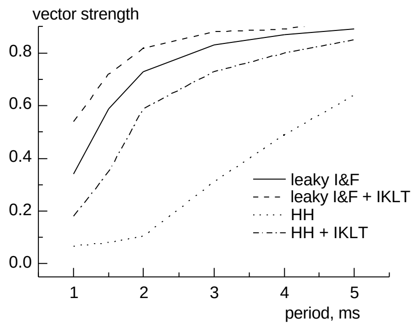


Figure 3. Vector strength versus period for periodically modulated Poisson EPSC trains. Results shown with and without I_{KLT} for leaky integrate-and-fire and for conductance based model.

Our in vitro experiments in gerbil MSO neurons are confirming the presence of a DTX-sensitive low threshold IK. This current underlies rectification in the subthreshold I-V relation and DTX has been used to convert a phasic cell to tonic mode. Our preliminary results on the responsiveness to transient inputs are consistent with Fig 2. Our program will continue to explore ways of understanding how the cellular biophysics enables these cells to detect signals in a noisy and transient environment.