DYNAMIC EFFECTS OF SUBTHRESHOLD CONDUCTANCE GATING (G_{KLT} AND G_{NA}) AND OF INHIBITION ON COINCIDENCE DETECTION IN MSO NEURONS

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ABSTRACT

Distinct biophysical properties including multiple voltage-dependent membrane conductances and well-timed transient inhibition contribute to the temporally precise processing characteristics of auditory neurons. We investigate the underlying mechanisms of coincidence detection through *in vitro* experiments (gerbil MSO) using dynamic clamp stimuli and with computational models of the Hodgkin-Huxley type. We focus particularly on what makes these neurons fire, i.e. on how they integrate subthreshold signals in the presence of a noisy synaptic (excitatory and inhibitory) background, as is typical *in vivo*. Consistent with previous reports, the partial blockade of low threshold potassium currents (I_{KLT}) reduced coincidence detection (as well as reduced phase-locking and signal-to-noise ratio). We used analysis by spike triggered reverse correlation for injected current I_{revcor} to evaluate and interpret our results. Blockade of I_{KLT} slowed the rise of I_{revcor}, indicating a less precise time window for integration. Presumably the faster rise, in control, is required to reach threshold before I_{KLT} is activated. Also, spike generation was associated with a preceding (by a few msec) hyperpolarization ("dip") in I_{revcor}, suggesting a drop in excitatory current or increase in inhibitory current to promote spiking. Multiple factors pointed towards the involvement of a second, novel mechanism. Even in the presence of an I_{KLT} antagonist, the dip in I_{revcor} persisted; cells did not convert to tonic mode, but remained phasic; rebound action potentials were produced after termination of a hyperpolarizing stimulus with 30% larger amplitudes as compared to spikes evoked by depolarization. We suggest that the sodium current (I_{Na}) is substantially inactivated at rest and describe some manipulations of I_{Na} in experiments and in computations to further support this suggestion. Our computer model, including conductances for spike generation and for I_{KLT}, shows decreased coincidence detection when I_{KLT} is reduced or when I_{Na} is increased (compensating for substantial inactivation at rest). We hypothesize that favored (on average) temporal combinations of synaptic inputs transiently reduce the inactivation of I_{Na} and deactivate some of I_{KLT} to create the brief temporal window for coincidence detection of small signals in noise.

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Keywords: auditory processing, coincidence detection, reverse correlation.

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