Mutual Inhibition Increases Adaptation Rate in an Electrosensory System [1]

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Abstract

In the electrosensory system of mormyrid electric fish, responses of central neurons to sensory stimuli adapt to eliminate predictable sensory patterns. This adaptation has been shown to rely on synaptic plasticity. However, the rules of synaptic plasticity alone underestimate the experimentally observed rate of adaptation. In this simulation study, mutual inhibition between pairs of central neurons is shown to increase the adaptation rate into the realistic range. The simulations are based on *in vitro* experimental studies to provide the relevant anatomy, physiology, and rules of synaptic plasticity. The results are compared with rates of adaptation derived from *in vivo* experiments.

Key words: Electrosensory; Adaptation; Synaptic plasticity; Mutual inhibition

1 Introduction

This study tests the effect of mutual inhibition on the system level adaptation rate of central neurons in response to changing sensory stimuli. Mutual (reciprocal) inhibition is common in many sensory systems and has been implicated in enhancing spatial contrasts, but its effects on the adaptation rate of sensory neuronal responses has not been previously studied.

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The electrosensory system of mormyrid electric fish [3] provides a good context to study the effects of mutual inhibition on adaptation rates because mechanisms of adaptation have been well characterized [2]. In this system, afferents from electroreceptors project to the electrosensory lateral line lobe (ELL). Medium ganglion (MG) cells in the ELL (Fig. 1A) respond to electrosensory stimuli and have been shown to adapt to changes in predictable sensory stimuli [1]. The responses of MG cells adapt to cancel predictable electrosensory patterns so that sensitivity to novel external stimuli is enhanced.

The predictable electrosensory patterns studied here are the responses of MG cells to the fish's own electric organ discharge (EOD). Corollary discharge signals associated with the motor command that drives the EOD project to the ELL as parallel fibers that terminate on apical dendrites of MG cells. Adaptation of MG cells to changes in EOD-evoked electrosensory patterns result from changes in the synaptic effects of corollary discharge conveying parallel fibers. The change in parallel fiber response cancels the change in sensory response. This synaptic plasticity has been shown to depend on the time difference between the arrival of the presynaptic spike and the occurrence of a postsynaptic dendritic spike (Fig. 1B). This learning rule determines the rate of adaptation unless network properties play a role [9].

There are two types of MG cells that respond oppositely to sensory stimuli. MG_1 cells are hyperpolarized by increased primary afferent activity, and MG_2 cells are depolarized. Anatomical studies suggest [7] that these two types of MG cells are coupled synaptically. Since MG cells are GABAergic [8], coupled pairs of MG cells would be mutually inhibitory. This study shows that this mutual inhibition can increase the rate of adaptation.

2 The Model

The rate of adaptation in the ELL was simulated using a computer model of two MG cells. The MG cells were represented by single-compartment spike response models [4] where the membrane potential was the sum of their inputs. When the membrane potential plus noise crosses a threshold, a spike is generated. The MG cells generate two types of spikes: a narrow spike that is probably axonal and a broad spike that is probably dendritic. The broad spikes have the higher threshold and are the postsynaptic event that is involved in associative synaptic plasticity.

Sensory inputs to the model MG cells were designed to mimic afferent signals following electric organ discharge. The corollary discharge signal was delivered to the MG cells in a delayed series of excitatory postsynaptic potentials (epsps) representing parallel fiber synaptic input. Stellate cell inputs were modeled as

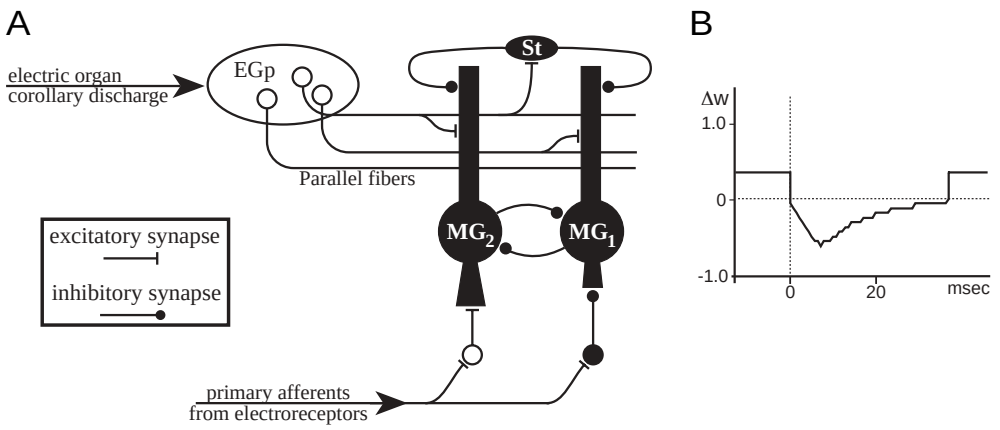

Fig. 1. *Local circuitry of the electrosensory lateral line lobe (ELL).* (A) The electric organ corollary discharge signals enter the ELL through the eminentia granularis posterior (EGp) that contains granule cells giving rise to parallel fibers. The granule cells respond to the correlated discharge at various delays providing the parallel fibers with a series of delayed spikes corollated with each electric organ discharge. Parallel fibers synapse onto medium ganglion cells (MG_1 and MG_2) and inhibitory stellate cells (St). The stellate cells also synapse onto the MG cells. Primary afferent fibers from electrosensory receptors enter the ELL and transmit their information through interneurons, some of which relay the temporal pattern to MG_2 cells, and others that invert the temporal pattern by inhibiting the MG_1 cells. (B) The learning rule of synaptic plasticity for the synapse from the parallel fibers onto the MG cells based on experiments *in vitro* [2]. If a dendritic spike in a MG cell follows the arrival of a parallel fiber spike within 40 msec, then the synapse is depressed proportionally to the excitatory postsynaptic potential; otherwise the synapse is enhanced.

a delayed series of inhibitory postsynaptic potentials (ipsps). Postsynaptic responses were weighted waveforms derived from *in vitro* recordings [5].

Synaptic plasticity was represented by synaptic weight changes and was dependent on the timing of broad spikes. The excitatory weights were depressed proportionally to epsp waveform if a broad spike occured within the range of the epsp, otherwise the weights were increased (Fig. 1B). The rates of synaptic change were set by data for plasticity at excitatory synapses [6].

The axonal spike output was used to inhibit the opposing MG cell. An ipsp was added to the membrane potential of the MG_1 cell for each spike generated by the MG_2 cell. Simultaneously, each axonal spike of the MG_1 cell added an ipsp to the membrane potential of the MG_2 cell.

Each simulation began with the parallel fiber synaptic weights distributed randomly about their midrange. A sensory image was introduced during the first of a series of EODs. The system was allowed to adapt by synaptic plasticity until the sensory image was cancelled by the parallel fiber inputs.

The system level adaptation was measured by the deviation of the mem-

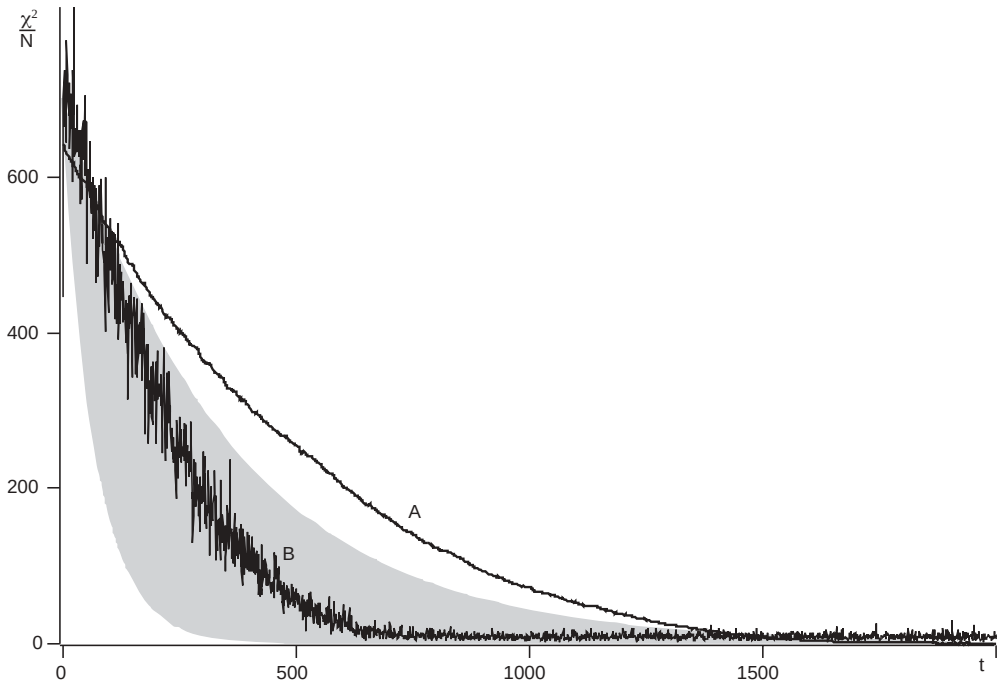

Fig. 2. *Progress of system level adaptation.* The deviation of the average membrane potential from a constant during each cycle as quantified by the mean squared contingency, $\chi^2(t)/N$. At t=0, a simulated electrosensory pattern is introduced. As t progresses, the response to the sensory pattern fades due to synaptic plasticity of parallel fiber synapses onto MG cells. The grey region identifies the range of system level adaptation rates that are based on *in vivo* studies [1]. (A) Trace generated by a simulation without mutual inhibition. (B) Trace generated with mutual inhibition. The noise in trace B is due to the irregular timing of axonal spikes by the opposing MG cell.

brane potential from a constant during each electric organ discharge cycle. Let $V(x_n, t)$ be the noiseless membrane potential at time-step x_n ($n = 1,\ldots$N=150) during the electric organ discharge cycle t. The average of $V(x_n, t)$ over the cycle length is $< V(t) >= (1/N)\sum_{n=1}^{N} V(x_n, t)$. The deviation of $V(x_n, t)$ from a constant was measured with by the mean square contingency,

$$\frac{\chi^2(t)}{N} = \frac{1}{N}\sum_{n=1}^{N}\frac{(V(x_n,t) - < V(t) >)^2}{< V(t) >}, \qquad (1)$$

Adaptation by synaptic plasticity reduces the value of this quantity. A low value implies that the predictable electrosensory signal is virtually eliminated and the system is highly sensitive to novel external stimuli.

3 Results

The graph in Fig. 2 quantifies the time course of adaptation of a simulated MG cell's response to the electric organ discharge. The grey region of the graph shows the range of system level adaptation rates that are consistent with experiments *in vivo* [1]. The realistic region was constructed by finding the best exponential fit ($a + b\exp(-t/\tau)$) for adaptation data in [1]. The realistic adaptation rate is bounded by $\tau = 71$ cycles and $\tau = 357$ cycles.

Trace A gives the result when the excitatory parallel fiber synapses were plastic, but there were no inhibitory connections between the two MG cells ($\tau = 556$ cycles). In this case, the rate of adaptation to the electric organ discharge was outside the acceptable range. Trace B shows the effect of mutual inhibition ($\tau = 213$ cycles). This condition brings the adaptation rate into the range of realistic values.

4 Conclusion

This model predicts that mutual inhibition increases adaptation rates of MG cells in the ELL. The simulations presented here suggest that adaptation of the electrosensory system of mormyrid electric fish relies on more than plasticity at excitatory synapses to provide adaptive mechanisms. The study demonstrates another useful function for mutual inhibition in sensory systems in addition to increasing edge sensitivity through contrast enhancement.

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