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PLASTICITY OF FEEDBACK INPUTS IN THE APTERONOTID ELECTROSENSORY SYSTEM

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Summary

Weakly electric fish generate an electric field surrounding their body by means of an electric organ typically located within the trunk and tail. Electroreceptors scattered over the surface of the body encode the amplitude and timing of the electric organ discharge (EOD), and central components of the electrosensory system analyze the information provided by the electroreceptor afferents. The electrosensory system is used for electrolocation, for the detection and analysis of objects near the fish which distort the EOD and for electrocommunication. Since the electric organ is typically located in the tail, any movement of this structure relative to the rest of the body alters the EOD field, resulting in large changes in receptor afferent activity. The amplitude of these reafferent stimuli can exceed the amplitudes of near-threshold electrolocation signals by several orders of magnitude. This review summarizes recent studies of the South American weakly electric fish *Apteronotus leptorhynchus* aimed at determining how the animals differentiate self-generated or reafferent electrosensory stimuli from those that are more behaviorally relevant. Cells within the earliest stages of central electrosensory processing utilize an adaptive filtering technique which allows the system preferentially to attenuate reafferent as well as other predictable patterns of sensory input without degrading responses to more novel stimuli. Synaptic plasticity within the system underlies the adaptive component of the filter and enables the system to learn to reject new stimulus patterns if these become predictable. A Ca^{2+}-mediated form of postsynaptic depression contributes to this synaptic plasticity. The filter mechanism seen in *A. leptorhynchus* is surprisingly similar to adaptive filters described previously in mormyrid weakly electric fish and in elasmobranchs, suggesting that this mechanism may be a common feature of sensory processing systems.

Key words: synaptic plasticity, long-term depression, post-tetanic potentiation, adaptive filter, electrolocation, apteronotid electrosensory system, *Apteronotus leptorhynchus*.

Introduction

Since the pioneering studies of Lissmann (1958), it has been recognized that the function of electrosensory systems is likely to be very dependent upon changes in the posture of these fish. Since the main electric organ is typically located in the animals' trunk and tail, displacement of these regions relative to the rest of the body changes the amplitude and possibly the spectral characteristics of the signal received by the electroreceptors. Empirical studies have verified that postural changes, similar to those produced by fish actively exploring their environment, result in significant alterations in electric organ discharge (EOD) field amplitude (Bastian, 1974, 1995). These self-generated changes in EOD amplitude can be more than 100 times greater than the threshold changes due to the presence of prey organisms. Hence, these movement-related changes in EOD amplitude might mask weaker electrolocation signals. Alternatively, simulation studies have suggested that the alterations in field geometry due to changes in posture might result in improvements of some aspects of the electric images acquired during electrolocation (Heiligenberg, 1975; Hoshimiya et al., 1980; Rasnow, 1996).

Optimum operation of the electrosensory system would seem to require that some mechanism exist to evaluate the results of self-imposed or reafferent EOD field changes and, as has been suggested previously (Heiligenberg, 1977; Szabo, 1993), proprioceptive signals providing information about the position of the electric organ relative to the rest of the body might be involved. Proprioceptive information can be thought of as providing an indication that a predictable pattern of electrosensory input is to be 'expected' given a certain posture and, as suggested by Bullock (1988), the use of such sensory expectations is probably widespread within sensory processing systems. In the specific case discussed here, a suitable representation of the afferent input expected as a result of changes in posture could be subtracted from the total afferent pattern, thereby improving the detection of novel signals.

This review summarizes recent studies of the effects of changes in posture on the responses of electroreceptors and higher-order cells in the weakly electric fish *Apteronotus leptorhynchus*. The results show that, at least for the simple patterns of postural changes employed thus far, the resulting

reafferent electrosensory stimulus is effectively filtered out in the first processing station in the brain, the electrosensory lateral line lobe (ELL). The mechanism used to remove the reafferent input is very similar to the adaptive filtering mechanisms first discovered by Bell (1981, 1982) and has also recently been shown to be present in the first-order processing centers of elasmobranchs and marine teleosts (Montgomery and Bodznick, 1994; for a review, see Bell et al., 1997).

Contrasting responses of electroreceptors and second-order cells to reafferent electrosensory stimuli

Fig. 1 illustrates *A. leptorhynchus* in an arc-like posture similar to that often seen when these fish actively explore novelties in their environment. The amplitude of the voltage drop across the skin, due to the electric organ discharge (EOD), increases on the side of the body towards which the tip of the tail is moved (ipsilateral to the bend) and decreases contralateral to the bend. The histograms in Fig. 1A,B, summarize the firing of an electroreceptor afferent and ELL efferent (pyramidal cell), respectively, during continuous cyclic tail motion of rather large amplitude (tail motion through an arc of ±45 °). Although the receptor afferent's activity was strongly modulated by this stimulus, the ELL pyramidal cell, which is monosynaptically excited by receptor afferent input, was virtually unresponsive. The envelopes of the EOD amplitude modulations (EOD AMs) due to the imposed tail motion measured at each cell's receptive field are shown in Fig. 1C,D.

Experiments such as that described in Fig. 1 have shown that many ELL pyramidal cells are largely insensitive to suprathreshold EOD modulations if these are linked to changes in the animal's posture. It was also found that repetitive electrosensory stimuli that were electronically generated and not related to changes in the animal's posture could also be filtered out (Bastian, 1995, 1996a).

Pyramidal cells can 'learn' to reject altered patterns of reafferent electrosensory stimuli

The absence of pyramidal cell responses to reafferent stimuli could result if other inputs, perhaps proprioceptive signals, performed a gating function which simply rendered these cells

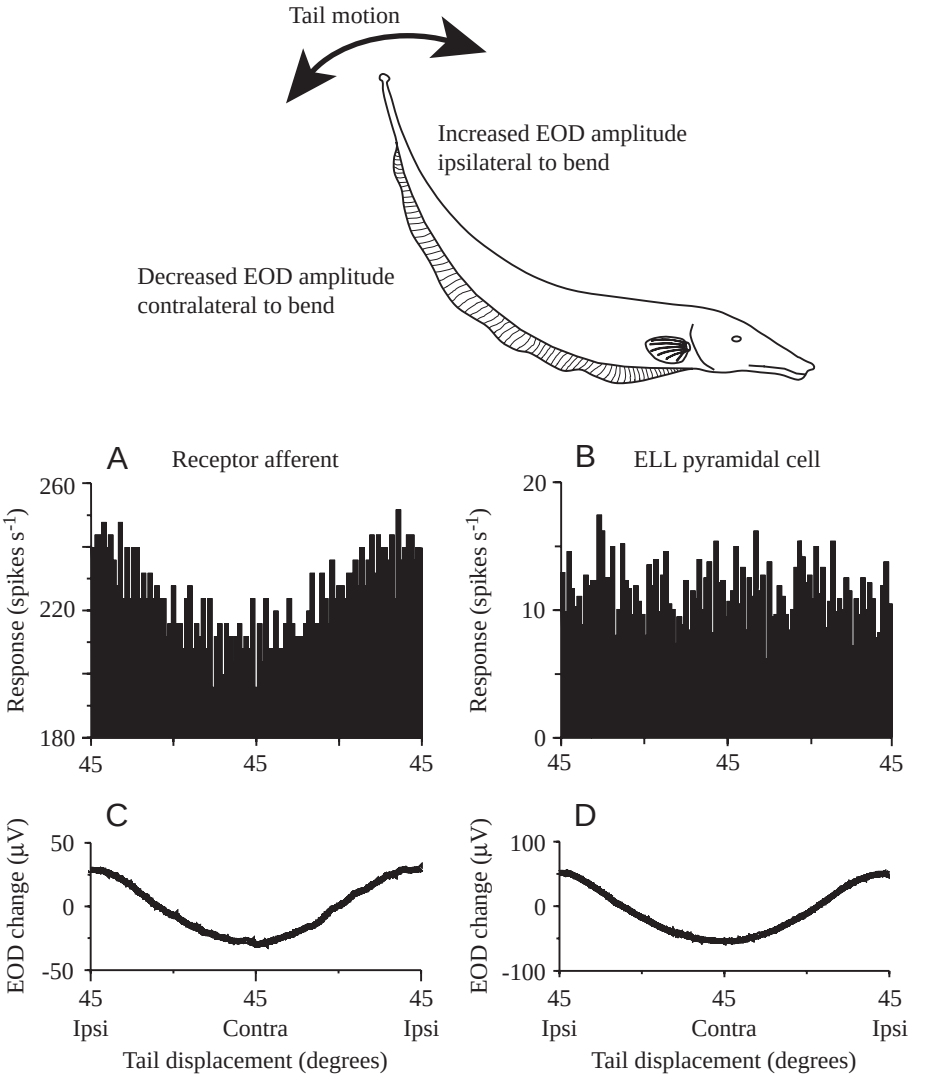


Fig. 1. Diagram illustrating the imposed changes in posture used in experiments assessing the effects of body geometry on electric organ discharge (EOD) amplitude and electrosensory neuron responses. (A) Phase histogram averaging an electroreceptor afferent's responses to five cycles of sinusoidal displacement of the trunk and tail through an arc of ±45 ° at 0.2 Hz. (B) Average responses of a basilar pyramidal cell to 50 cycles of continuous tail movement (±45 °, 0.1 Hz). (C,D) Envelopes of the EOD amplitude modulation, measured within the cell's receptive field, for an electroreceptor afferent (C) and a basilar pyramidal cell (D), resulting from the patterns of tail movement. Contra, contralateral bend; Ipsi, ipsilateral bend; ELL, electrosensory lateral line lobe.

insensitive to electrosensory inputs while posture was changing. An obvious drawback to such a mechanism is that the animals would become 'electrically blind' whenever significant changes in posture occurred. Nevertheless, this idea was tested by applying a 'local' electrosensory stimulus to the receptive field of a pyramidal cell during tail motion and, as shown in Fig. 2, pyramidal cells were capable of responding to a new pattern of input. However, the responses to the local stimulus decayed rapidly with repeated presentations, indicating that the system learned to filter out this new stimulus.

The upper segment of the raster of Fig. 2Bi and the associated period histogram (Fig. 2Ci) show that this pyramidal cell was unresponsive to the EOD AMs resulting from sinusoidal tail movements, although these were well above threshold for driving electroreceptors; the envelope of the EOD modulation recorded at the cell's receptive field is shown in Fig. 2Ai. In the second phase of this experiment, an electronically produced amplitude modulation, phase-locked to the cycle of tail motion, was presented to the fish *via* a local electrode positioned within the pyramidal cell's receptive field. The addition of the local EOD AM resulted in an approximate doubling of the stimulus amplitude (Fig. 2Aii), and the raster display (Fig. 2Bii) shows that the cell initially responded strongly to this new stimulus pattern. However, the responses gradually decayed; after approximately 2 min of continuous stimulus presentation, the responses had nearly disappeared (compare Fig. 2Cii,iii).

That the progressive loss of responsiveness to this new stimulus pattern reflects significant changes in the characteristics of the cell, or of its sources of afferent input, becomes apparent when the local stimulus is removed, restoring the stimulus pattern to its original state. Although the cell was initially unresponsive to the tail-bend stimulus, following removal of the local amplitude modulation, the original stimulus evoked strong responses and, importantly, the time course of this new response was approximately the mirror image of the initial response to the local stimulus (compare Fig. 2Cii,iv). This type of response, first described by Bell (1981) in studies of mormyrid weakly electric fish, is referred to as a 'negative image response'. The negative image response is thought to result from alterations of synaptic inputs which developed during the progressive cancellation of the local stimulus. Neither the cancellation of responses to the local stimulus nor the development of negative image responses occurred when the local stimulus was presented in the absence of tail movement (Bastian, 1996a).

Neural substrates underlying the rejection of reafferent stimuli and the formation of negative image responses

The results of Bell et al. (1993) indicated that the synaptic

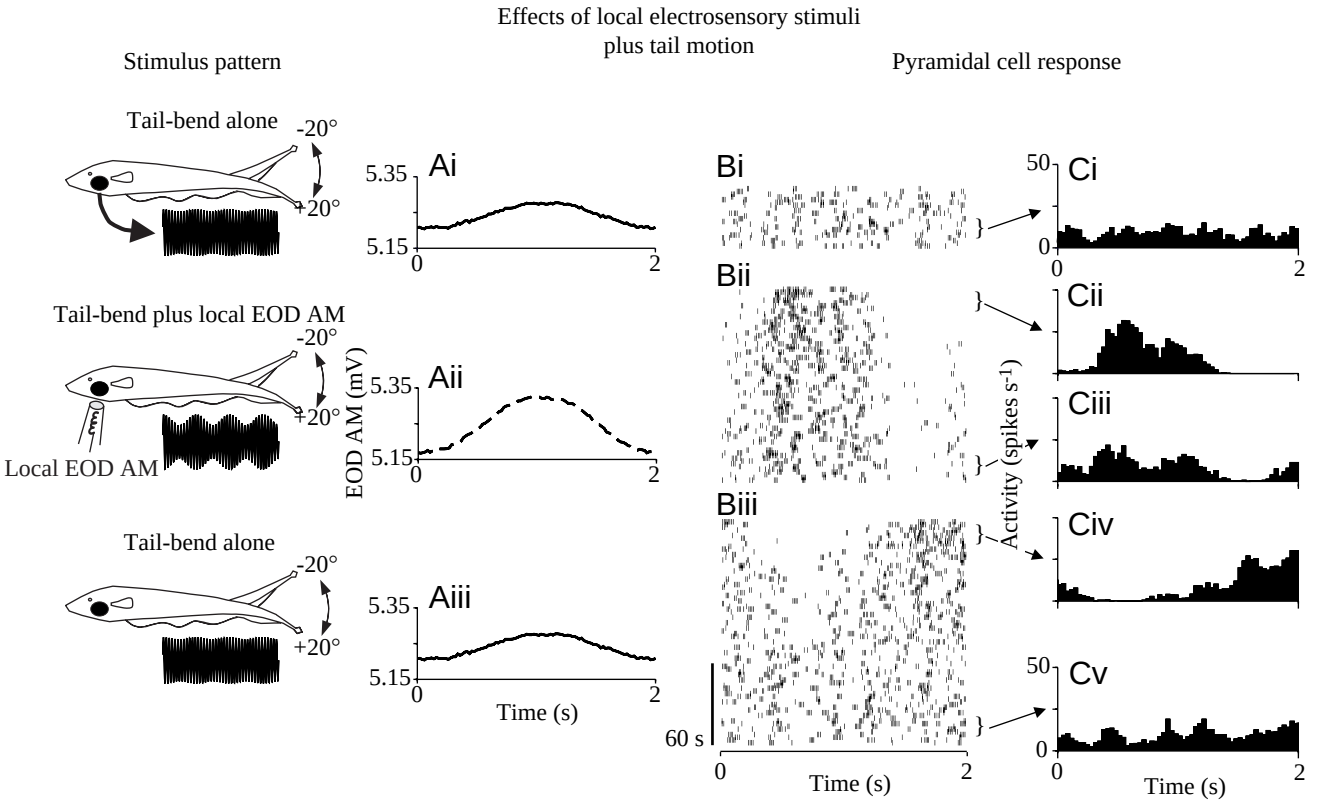


Fig. 2. Stimulus pattern. Envelopes of electric organ discharge amplitude modulations (EOD AMs) measured within the recorded cell's receptive field due to tail displacement (Ai,iii) and tail displacement plus an electronically generated EOD AM (Aii) delivered to the cell's receptive field (shaded region on the outline of the fish). (B,C) Pyramidal cell responses. (B) (i–iii) Raster display of pyramidal cell activity over the time of the tail displacement cycle (0.5 Hz, ±20 °) under the stimulus conditions of Ai–iii. (C) (i–v) Phase histograms of data from 30 consecutive stimulus cycles indicated by the brackets bordering the raster displays.

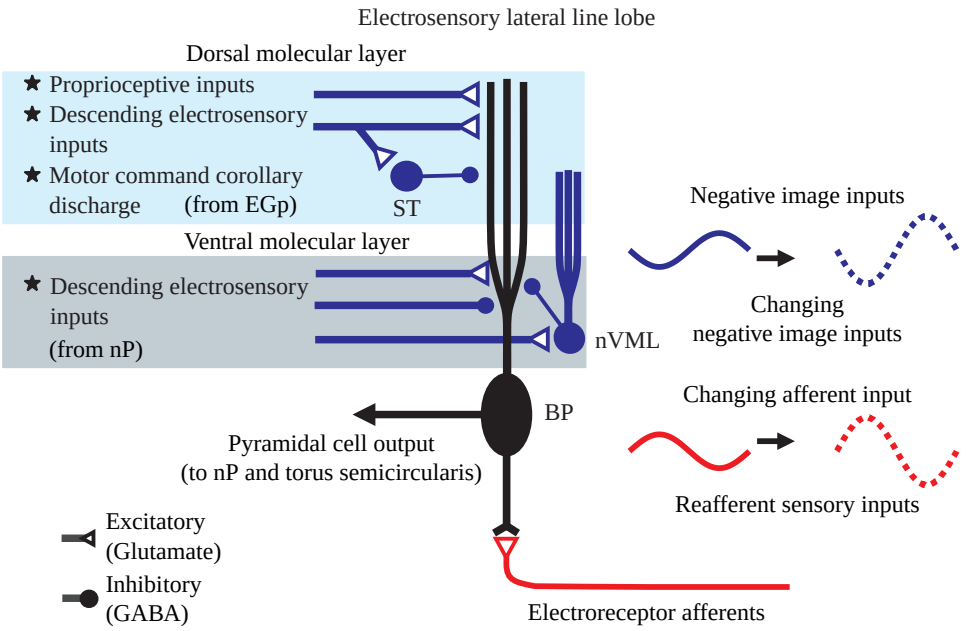


Fig. 3. Simplified diagram of the electrosensory lateral line lobe (ELL) of *Apteronotus leptorhynchus*. BP, basilar pyramidal cell; nVML, ventral molecular layer neuron; ST, molecular layer stellate cell. Waveforms to the right of the diagram illustrate proposed pyramidal cell membrane potential changes (based on the mechanism of 'negative images'; Bell et al., 1993) due to modulations in receptor afferent activity (red) and apical dendritic inputs originating in higher centers (blue). EGp, eminentia granularis posterior; nP, n. praeeminentialis.

inputs responsible for the negative image responses in the mormyrid ELL terminated on the apical dendrites of the pyramidal, or principal, cells and that plasticity at these apical dendritic synapses accounted for the ability of the system to learn to cancel a variety of reafferent stimulus patterns. Similar mechanisms are thought to account for the rejection of predictable sensory inputs by pyramidal cells of gymnotids. Fig. 3 is a highly simplified diagram of an ELL efferent neuron (basilar pyramidal cell, black) along with its receptor afferent inputs and feedback inputs from higher centers (blue) based on the anatomical studies of Maler et al. (1974, 1981, 1982), Maler and Mugnaini (1994) and Sas and Maler (1983, 1987). Changes in the pyramidal cell's membrane potential due to receptor afferent inputs and to synaptic inputs to the apical dendrites are indicated by the lower and upper waveforms next to the cell, respectively. As proposed by Bell et al. (1993), cancellation of a given pattern of receptor afferent input occurs because centrally generated activity provides input to the apical dendrites which results in an opposing pattern of membrane potential change. For example, the initial insensitivity of pyramidal cells to reafferent EOD AMs (Fig. 2Bi,Ci) could result from the cell's receipt of a negative image input which cancels the electroreceptor input (Fig. 3, solid lines). Addition of the local EOD modulation increases the receptor afferent input (lower dashed waveform); initially, this outweighs the negative image input, and the cell responds strongly as shown in Fig. 2Cii. With repeated presentations, however, the negative image is updated to cancel the afferent input more effectively (upper dashed waveform); hence, the cell's responses decay. Upon removal of the local EOD AM, the receptor afferent input returns to its initial state; however, the altered negative image input persists and outweighs the electrosensory input, with the result that the cell temporarily responds in a pattern dictated by these dendritic inputs.

The plasticity involved in updating the negative image inputs to achieve optimal cancellation is described as anti-Hebbian (Bell et al., 1993) and is governed by learning rules proposed by Montgomery and Bodznick (1994). Activity at apical dendritic synapses in conjunction with postsynaptic depolarization (increased receptor afferent input) results in reductions in the synaptic strength of excitatory dendritic inputs and may also potentiate inhibitory inputs. Conversely, postsynaptic hyperpolarization, as occurs with reduced receptor afferent input, results in increases in the net excitation received *via* apical dendrites. Thus, any pattern of pyramidal cell afferent input that repeatedly activates a sufficient population of apical dendritic inputs will be filtered out as the negative image signal is updated.

In gymnotids, dorsal and ventral subdivisions of the ELL molecular layer, the DML and VML, respectively, provide inputs to distal and proximal regions of the pyramidal cell's apical dendrites, respectively, and relay descending electrosensory, proprioceptive and, possibly, corollary discharge information related to motor commands (Maler et al., 1981; Sas and Maler, 1983, 1987; Maler and Mugnaini, 1994). These DML and VML inputs, including that from molecular layer inhibitory interneurons, are thought to provide the signals that give rise to the negative image responses. The remainder of this review focuses on recent experiments that have demonstrated that anti-Hebbian plasticity can be induced at these dendritic synapses as is required to cancel reafferent inputs *via* the negative image mechanism.

Dorsal and ventral molecular layer inputs demonstrate anti-Hebbian plasticity

The projections to the dorsal and ventral molecular layers can be stimulated separately, and stimulation of either pathway

paired with electrosensory stimulation of pyramidal cells was used to test the idea that these molecular layer inputs are plastic. An example of the results from this type of experiment are shown in Fig. 4 for a single pyramidal cell. First, tetanic stimulation was presented alone to either the DML or VML

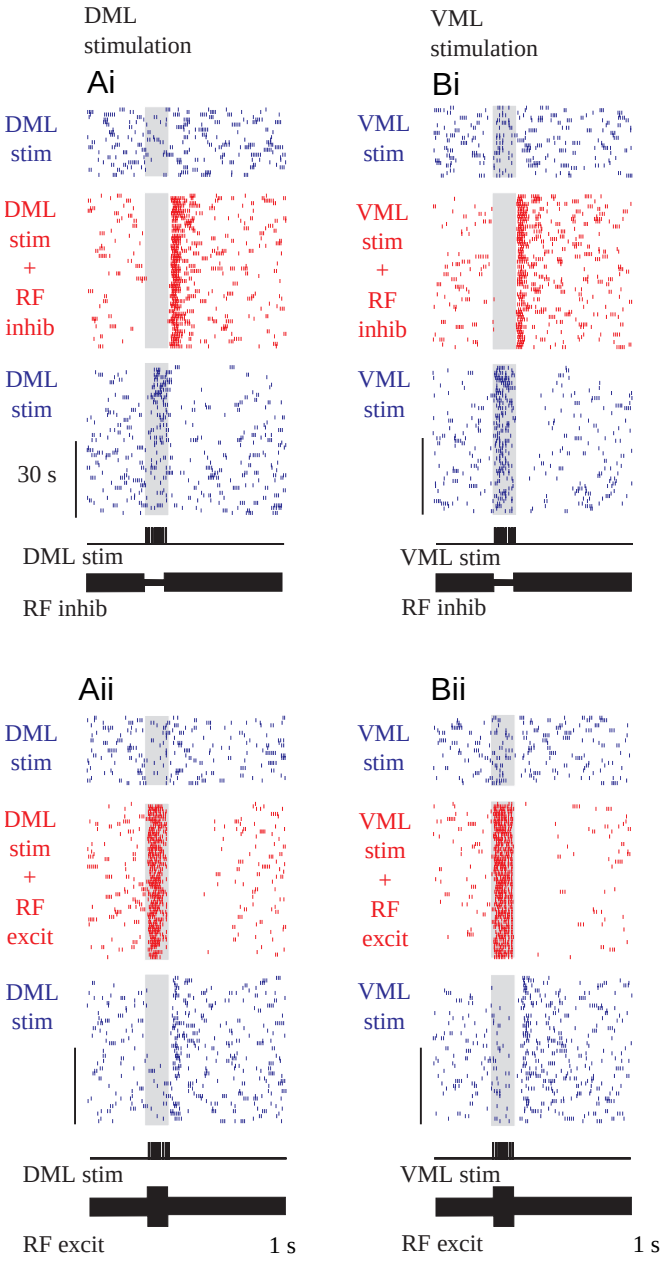


Fig. 4. Responses of a basilar pyramidal cell to tetanic stimulation (stim) of the dorsal molecular layer (DML) or ventral molecular layer (VML) (100 ms train, 15 ms interpulse interval, 1 Hz repetition) before (blue), during (red) and after (blue) pairing the tetanus with excitatory (excit) or inhibitory (inhib) receptive field (RF) stimulation (100 ms stepwise increase or decrease, respectively, of electric organ discharge amplitude applied to the cell's receptive field). The times of stimulus presentation are shaded. (Ai,Bi) Effects of pairing inhibitory electrosensory stimuli with DML and VML tetani, respectively. (Aii,Bii) Effects of pairing excitatory electrosensory stimulation with DML and VML tetani, respectively.

inputs. Stimulus intensity was set to just above threshold for evoking spikes in the pyramidal cell, and tetani were applied at 1 Hz until the responses stabilized. As will be described below, continued tetanic stimulation of either the DML or VML alone results in time-dependent changes in pyramidal cell responses. Responses to 30 replicates of the tetanus are shown in the topmost segments of the raster displays (top blue areas).

In the 'training' phase of this experiment, DML or VML stimulation was paired with stepwise EOD amplitude modulations that either inhibited (RF inhib) or excited (RF excit) the cell (red segments of the rasters of Fig. 4). The inhibitory electrosensory stimuli typically silenced the cell (Fig. 4Ai,Bi) and the excitatory stimuli caused high-frequency spike responses (Fig. 4Aii,Bii). The learning rules proposed by Montgomery and Bodznick (1994) predict that pairing DML or VML stimulation with inhibitory electrosensory stimulation should cause a net increase in the excitation provided by these inputs. The lowest segments of the rasters of Fig. 4Ai,Bi confirm this; following the period of paired stimulation, DML or VML tetani presented alone evoked significantly increased pyramidal cell responses. Spike counts evoked by DML and VML tetani increased by averages of 530 % and 242 % (38 cells), respectively, following this training protocol (Bastian, 1998).

The reciprocal experiment, in which DML or VML stimulation was paired with excitatory electrosensory stimulation (Fig. 4Aii,Bii), did not simply reduce subsequent responses to pathway stimulation towards the cell's spontaneous firing frequency. Instead, as shown by the lowest segments of the rasters, following this treatment, tetani typically evoked inhibition of pyramidal cell firing. This result raises the possibility that both excitatory (EPSP) and inhibitory (IPSP) postsynaptic potential amplitudes are altered following this treatment. Excitatory or inhibitory electrosensory stimuli presented alone caused no changes in DML or VML synaptic efficacy (Bastian, 1998).

Further simplification of the above experiments was achieved with intracellular recordings, which allowed electrosensory stimulation of a cell's receptive field to be replaced by intracellular current injection. Postsynaptic potentials evoked by DML or VML stimulation can then be directly measured, and only the pyramidal cell under study will be hyper- or depolarized. Fig. 5 demonstrates that both DML- and VML-evoked synaptic potentials can be altered by stimulating these pathways in conjunction with postsynaptic changes in membrane potential.

These experiments were conducted in four phases. First, single or twin 'test stimuli' were delivered to either the DML or VML at 1 Hz for 30 s to assess initial EPSP amplitudes. The test stimuli were presented during a weak (approximately 0.3 nA) postsynaptic hyperpolarization to suppress pyramidal cell action potentials in response to the test stimuli. In the second phase of these experiments, a 100 ms burst of stimuli (15 ms interpulse interval) was also applied to the DML or VML. This tetanus typically preceded the test pulses by

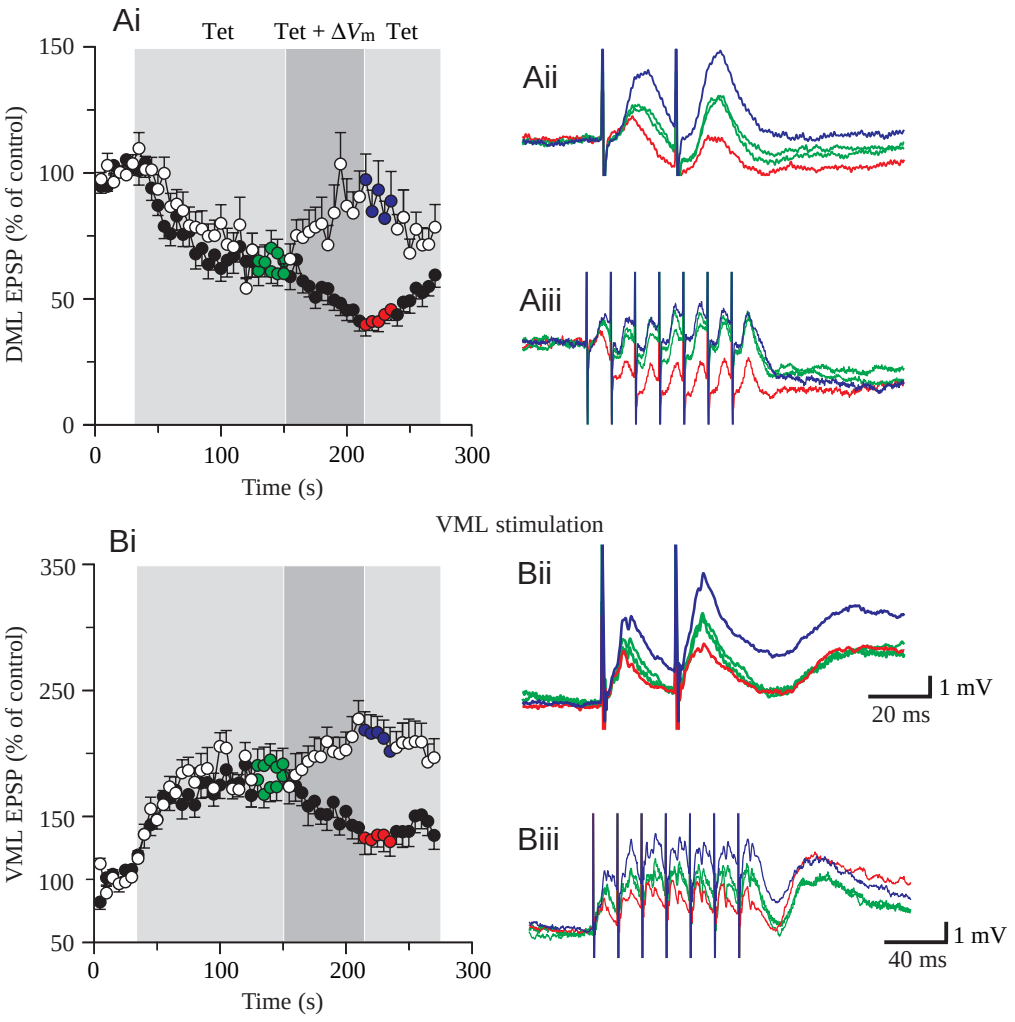


Fig. 5. Summary of changes in dorsal molecular layer (DML)- and ventral molecular layer (VML)-evoked excitatory postsynaptic potentials (EPSPs) (Ai, Bi, respectively) recorded during tetanic stimulation alone (Tet; light shading) and during tetani paired with postsynaptic hyperpolarization or depolarization (Tet+ΔV_m; heavy shading, open and filled circles, respectively). Values are means ± S.E.M.; see Fig. 7 for sample sizes. Examples of EPSPs evoked by paired DML and VML 'test' stimuli and by the tetani are shown in Aii,iii and Bii,iii, respectively. These waveforms are signal averages of 25 consecutive responses immediately prior to presentation of the tetani paired with postsynaptic membrane potential changes (green) immediately after tetani paired with postsynaptic hyperpolarization (blue) and after tetani paired with postsynaptic depolarization (red). Action potential waveforms were removed from the responses to the tetanus; this reduces the amplitude of individual EPSPs and results in the jagged peaks apparent in Fig. 5Biii.

approximately 500 ms, and this treatment had opposite effects on EPSP amplitudes contingent upon which pathway was stimulated. EPSPs evoked by DML test stimuli were depressed when preceded by DML tetani, while VML-evoked EPSPs were potentiated following VML tetani. Average amplitudes of DML and VML test EPSPs are shown in Fig. 5Ai,Bi, respectively. Each point shows EPSP amplitude measured from an average of five consecutive responses, expressed as a percentage of the baseline amplitude, then averaged over the population of cells studied. A comparison of the leftmost lightly shaded regions of Fig. 5Ai,Bi shows the approximately exponential depression and potentiation of DML- and VML-evoked test EPSPs that result from tetanic stimulation of the respective pathways. Test EPSP amplitudes stabilized within approximately 2 min of continuous stimulation in which the 100 ms tetanus followed by the test pulses were repeated at 1 Hz.

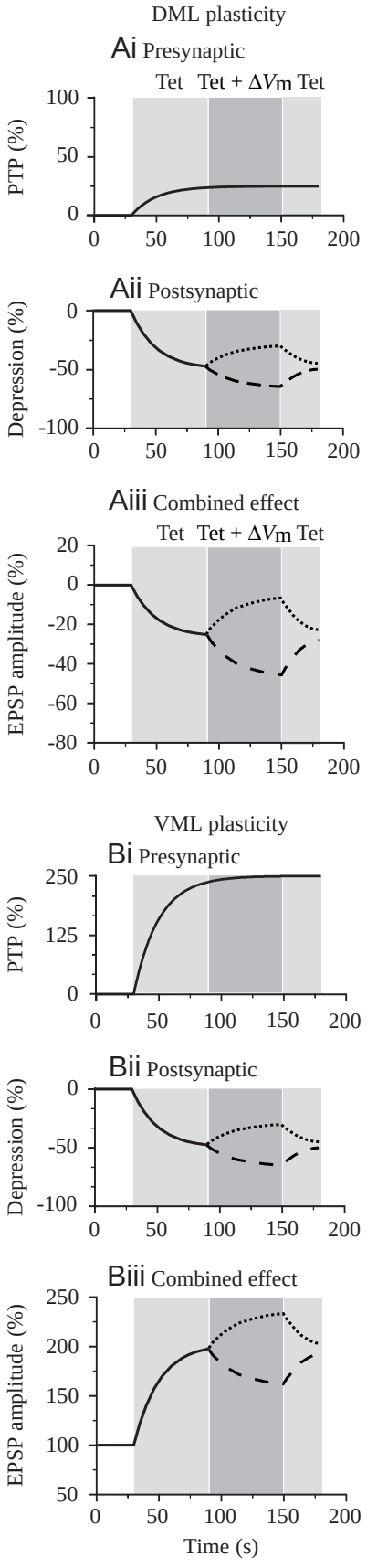
During the third phase of the experiment, the tetanic stimulation was paired with hyper- or depolarization of the pyramidal cell (100 ms, ±0.8 nA). As shown in the heavily shaded regions of Fig. 5Ai,Bi, paired postsynaptic hyperpolarization (open circles) resulted in similar potentiation of both DML- and VML-evoked EPSPs superimposed on the changes due to the tetanus presented alone. Conversely, pairing the DML or VML tetanus with postsynaptic depolarization resulted in depression of the test EPSP amplitudes (filled circles). During the last phase of the experiment, the tetanus was again presented alone, and EPSP amplitudes gradually returned towards their pre-pairing values.

Examples of test EPSPs and responses to the DML and VML tetani recorded before and after pairing with the postsynaptic current injection are shown in Fig. 5Aii,iii,Bii,iii. Each recording is an average of 25 consecutive responses taken either immediately before (green), after the paired tetanus plus hyperpolarization (blue) or after the tetanus paired with depolarization (red). These responses were recorded from a single pyramidal cell and averaged over the times indicated by the same colored circles in Fig. 5Ai and Bi. Responses to the twin test stimuli applied to the DML were clearly potentiated and depressed following tetani paired with hyper- and depolarization (Fig. 5Aii, blue and red, respectively). In addition, following the paired depolarization, a longer-time-course putative IPSP developed (Fig. 5Aii, red). This prolonged hyperpolarization is more apparent in the averaged

responses to the tetanus (Fig. 5Aiii, red), and it is this long-duration hyperpolarization that results in the inhibition of pyramidal cell firing typically seen following either DML tetani paired with excitatory receptive field stimulation (Fig. 4Aii,Bii) or postsynaptic depolarization.

The responses of this cell to VML test stimuli showed similar changes (Fig. 5Bii,iii); however, in this case, no hyperpolarization was seen following tetani paired with postsynaptic depolarization (Fig. 5Bii,iii; red). Other pyramidal cells did show hyperpolarizing responses, similar to those described in Fig. 5Aiii, in response to VML stimulation (Fig. 6 in Bastian, 1996b). Potentiation of VML-evoked EPSPs following tetani paired with postsynaptic hyperpolarization has also been observed in *in vitro* preparations of the gymnotid ELL (Wang and Maler, 1997).

The results of these experiments show that both the DML and VML inputs to pyramidal cell apical dendrites are plastic, and the characteristics of this plasticity are as expected for the generation of negative image inputs. Repetitive patterns of increased receptor afferent input, or pyramidal cell depolarization, result in the depression of concomitantly active excitatory dendritic inputs and, possibly, potentiation of inhibitory inputs. The resulting change in the strength of these dendritic inputs tends to cancel subsequent presentations of the depolarizing stimulus. Decreased receptor afferent input (pyramidal cell hyperpolarization) generates the opposite effect: excitatory dendritic inputs are potentiated, thereby canceling the effects of reduced afferent input.



Pyramidal cell anti-Hebbian plasticity results from the modulation of Ca^{2+}-dependent postsynaptic depression

The changes in EPSP amplitudes resulting from tetanic stimulation of the DML or VML alone, as well as those resulting from tetani paired with changes in the postsynaptic cell's membrane potential, can be explained as a result of the interaction between a presynaptic mechanism such as post-tetanic potentiation (PTP) and a postsynaptic form of depression similar to long-term depression (LTD), which has previously been suggested as a possible mediator of the anti-Hebbian plasticity (Bell et al., 1993). Recent *in vitro* studies (Wang and Maler, 1998) have demonstrated PTP following tetanic stimulation of either the DML or VML, but the mechanism underlying the phenomena associated with each pathway differ. In the case of the VML, PTP was found to be sensitive to presynaptic blockade of the Ca^{2+}/calmodulin-dependent kinase 2 alpha (CaMK2α), but DML PTP was not sensitive to this treatment.

Fig. 6. Diagrammatic illustration of proposed pre- and postsynaptic effects underlying the opposite responses of electrosensory lateral line lobe (ELL) pyramidal cells to tetanic stimulation (Tet) of the dorsal molecular layer (DML) (Ai,ii) and the ventral molecular layer (VML) (Bi,ii) and the similar patterns of anti-Hebbian plasticity evoked by tetani coincident with postsynaptic changes in membrane potential (Tet+ΔV_m) (Aiii,Biii). See text for details. PTP, post-tetanic potentiation.

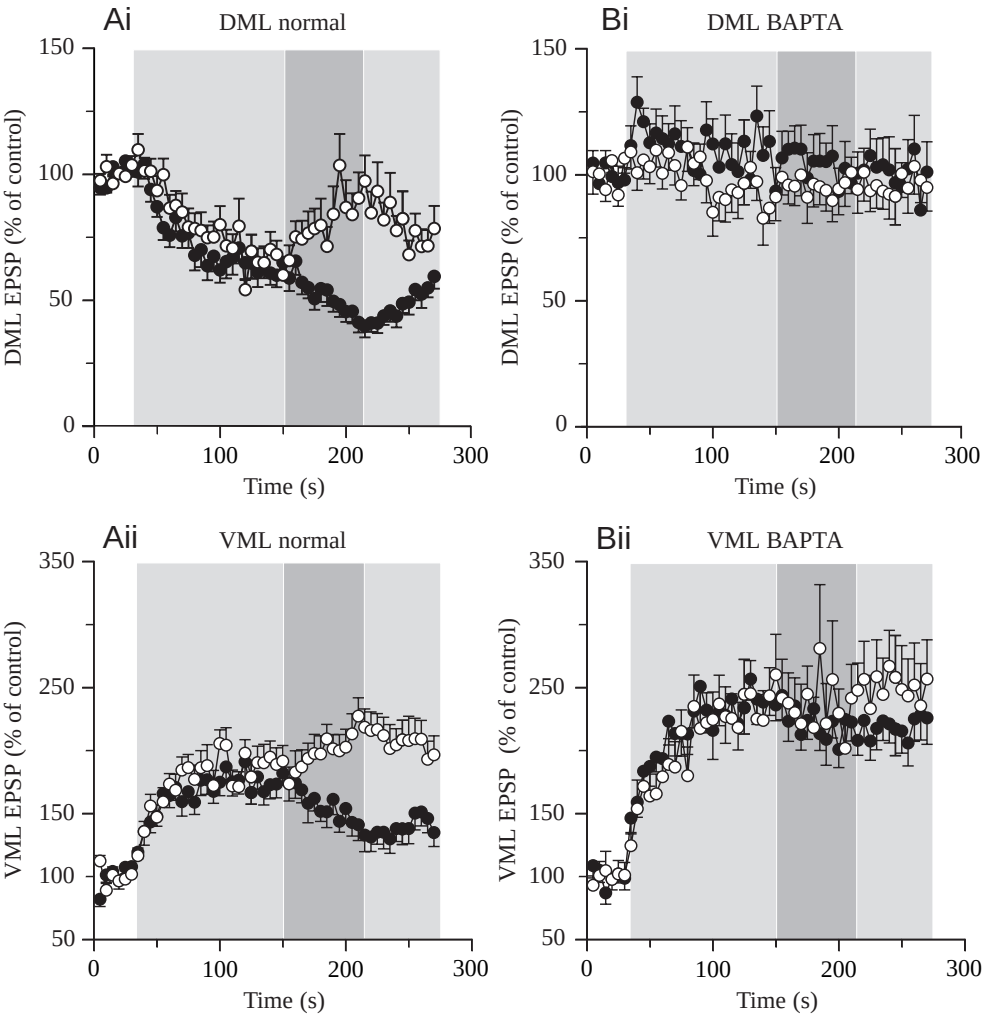


Fig. 7. Comparison of excitatory postsynaptic potential (EPSP) amplitudes evoked in normal pyramidal cells and those loaded with the Ca^{2+} chelator BAPTA. Data from Fig. 5 are reproduced here for comparison with results from BAPTA-treated cells. (Ai,Bi) Dorsal molecular layer (DML)-evoked EPSPs before, during and after tetani paired with postsynaptic hyperpolarization (open circles) and depolarization (filled circles) in normal and BAPTA-treated cells, respectively. In normal cells, pairing hyperpolarization with DML tetani increased average EPSP amplitudes (21 cells) to 129.4±6.6 % of the pre-pairing amplitude. This increase was significant (P<0.001, t-test). EPSP amplitudes were determined from averages of 30 responses immediately preceding and following the paired stimulation. In BAPTA-treated cells, average EPSP amplitudes following the paired hyperpolarization averaged 103.6±7.2 % (N=15, P=0.63). In normal cells, the paired depolarization reduced subsequent EPSP amplitudes to an average of 78.3±5.0 % of pre-pairing values (N=19, P<0.001), but in BAPTA-treated cells following this treatment EPSP amplitudes averaged 101.0±12.0 % (N=15, P=0.95). (Aii,Bii) Ventral molecular layer (VML)-evoked EPSPs recorded under the same conditions. In normal cells, paired hyper- and depolarization changed subsequent EPSP amplitudes to 111.4±2.54 % and 85.4±3.01 % of the pre-pairing values, and both changes were significant (P<0.001, N=25 and N=15, respectively). Following VML tetani plus paired hyperpolarization in BAPTA-loaded cells, EPSP amplitudes averaged 99.3±8.0 % of pre-pairing values (P=0.94, N=11); however, after tetani paired with depolarization, average EPSP amplitude was still reduced to 89.7±3.4 %, P=0.01, N=12). Values are means ± S.E.M.

The proposed pre- and postsynaptic effects and their interactions are depicted in Fig. 6. In the case of the DML, it is proposed that the presynaptic potentiation is inherently weak and is outweighed by the postsynaptic depression. The DML PTP rises to a steady-state level during tetanic stimulation alone (Fig. 6Ai, light shading) and is independent of any postsynaptic manipulations (heavy shading). Fig. 6Aii illustrates the time course of the postsynaptic depression. It also develops in response to the tetanus alone; however, the depression is sensitive to manipulations of the postsynaptic cell's membrane potential. Postsynaptic depolarization enhances the depression (dashed line) while hyperpolarization relieves the depression (dotted line). One possible mechanism underlying this proposed voltage-dependence of the postsynaptic depression is modulation of postsynaptic Ca^{2+} currents. Combining these pre- and postsynaptic effects (Fig. 6Aiii) results in a net depression of DML-evoked EPSPs due to tetanic stimulation alone as well as anti-Hebbian plasticity, as seen in our experiments. The plasticity is, therefore, proposed to arise as a result of modulation of postsynaptic depression.

These same mechanisms can also account for the changes in VML-evoked EPSPs if one assumes that presynaptic PTP at VML synapses is stronger and outweighs the postsynaptic depression. As in the case of the DML, the PTP results from the tetanic stimulation alone and is insensitive to changes in the postsynaptic cell's membrane potential (Fig. 6Bi). The pattern of postsynaptic depression and its voltage-dependence are proposed to be the same as described for the DML inputs (Fig. 6Bii, dashed and dotted lines). Since the presynaptic PTP outweighs the postsynaptic depression, the initial response to the VML tetanus is a net increase in EPSP amplitude, and the anti-Hebbian plasticity resulting from the voltage-dependent modulation of the

postsynaptic depression appears superimposed on this initial potentiation (Fig. 6Biii).

According to this model, the similar patterns of anti-Hebbian plasticity seen at the DML and VML synapses result from a single mechanism, the modulation of postsynaptic depression. The most thoroughly studied form of postsynaptic depression, long-term depression (LTD), occurs in the cerebellum, as well as other structures, and it is well established that a postsynaptic increase in $[Ca^{2+}]$ is one important causal factor (Lev-Ram et al., 1997; Neveu and Zucker, 1996; Bear and Malenka, 1994). The rapid Ca^{2+} chelator 1,2-bis(2-aminophenoxy)ethane-*N*,*N*,*N*′,*N*′-tetraacetic acid (BAPTA) has been used to block different forms of synaptic plasticity, including LTD (Sandkuhler et al., 1997), and this technique was used to buffer postsynaptic changes in $[Ca^{2+}]$ in pyramidal cells.

Intracellular recordings were made from pyramidal cells with microelectrodes filled with 100 mmol l^{-1} BAPTA in 3 mol l^{-1} potassium acetate and, following the establishment of stable recordings, the pyramidal cells were loaded with BAPTA by ionophoresis. The experiments described in Fig. 5 were then repeated with BAPTA-loaded cells. The model proposed in Fig. 6 suggests that, in the case of the DML, blockade of the postsynaptic component should eliminate both the initial depression of EPSP amplitude and the anti-Hebbian plasticity. This prediction was fulfilled: neither the depression due to tetanus nor the changes in EPSP amplitude due to DML tetani paired with hyper- or depolarization were seen (compare Fig. 7Ai,Bi). Instead of EPSP depression, a small transient increase was seen, which may reflect the unmasking of a presynaptic PTP, but this small increase in EPSP amplitude was not statistically significant.

The predicted effects of blocking postsynaptic depression on VML-evoked EPSPs differ. In normal cells, the initial potentiation of VML EPSPs due to tetanic stimulation may be partially masked by the concomitant development of postsynaptic depression. Hence, the potentiation due to tetanus alone should be greater in BAPTA-loaded cells. This was also confirmed: the potentiation of VML-evoked EPSPs was increased from 184 % to 241 % in BAPTA-treated cells (compare Fig. 7Aii,Bii). Elimination of the postsynaptic depression also significantly reduced the anti-Hebbian plasticity of the VML inputs. The EPSP potentiation normally seen following tetani paired with postsynaptic hyperpolarization was eliminated (Fig. 7Aii,Bii, open symbols); however, a smaller but statistically significant EPSP depression following tetani paired with depolarization remained (Fig. 7Aii,Bii, filled symbols).

These experiments provide additional evidence that the anti-Hebbian plasticity associated with the DML and VML inputs to pyramidal cell apical dendrites is a postsynaptically mediated phenomenon and that changes in postsynaptic Ca^{2+} concentration are necessary. Although only changes in EPSP amplitudes have been studied quantitatively thus far, recent *in vivo* studies (Berman and Maler, 1998a,b) raise the possibility that modulation of IPSP amplitudes may also contribute to the EPSP depression described here.

Discussion

The filtering mechanism described for pyramidal cells in the gymnotiform ELL is quite effective in removing reafferent patterns of electrosensory input such as those that appear as a consequence of locomotor activity, and both proprioceptive and descending electrosensory signals contribute to the cancellation. In addition, these cells are able to filter out repetitive, hence predictable, patterns of electrosensory input that are not associated with changes in posture (Bastian, 1995, 1996a). Highly repetitive electrosensory stimuli can arise in social situations when, for example, conspecifics having similar EOD frequencies each sense the beat pattern resulting from their summed discharges. The repetitive amplitude modulations of the beat pattern can disrupt an animal's ability to electrolocate, and the jamming avoidance response is known to reduce the disruptive effects of these amplitude modulations (Heiligenberg, 1991). The ability to filter out these beat-related amplitude modulations centrally *via* the mechanisms described above would further improve the ability to detect novel stimuli in the presence of interfering EODs. Earlier studies comparing the degradation of electrolocation behavior with the receptor afferents' ability to encode electrolocation targets in the presence of jamming signals suggested that such a central filtering mechanism may exist (Bastian, 1987a,b).

The descending dorsal and ventral molecular layer inputs to pyramidal cells may participate in other functions in addition to the attenuation of predictable patterns of afferent input. Earlier studies of the n. praeeminentialis stellate cells, which provide the principal excitatory input to the VML, suggested that these cells might provide positive feedback excitation to augment pyramidal cell responses to behaviorally relevant stimuli such as moving electrolocation targets (Bratton and Bastian, 1990; Maler and Mugnaini, 1993). The reciprocal topography of the ELL pyramidal cell to stellate cell projection (Maler et al., 1982), the strong responses of the stellate cells to moving electrolocation targets and the prominent facilitation that occurs at the stellate cell to pyramidal cell synapses (Berman et al., 1997; Wang and Maler, 1997) support this proposed 'searchlight mechanism'. The anti-Hebbian plasticity demonstrated at this synapse, which would be expected to counteract any positive feedback effects, may limit the duration of this searchlight function. That is, the positive feedback amplification of responses to novel stimuli may be reduced if such stimuli become predictable.

The n. praeeminentialis also contains multipolar cells that provide descending electrosensory input to the ELL dorsal molecular layer *via* the eminentia granularis posterior granule cells. The finding that lesions or local anesthetic blockade of DML inputs enhanced ELL pyramidal cell responses led to the idea that this pathway modulated inhibitory inputs and participated in a gain-control mechanism designed to optimize pyramidal cell responsiveness (Bastian, 1986a,b; Bastian and Bratton, 1990). Subsequent pharmacological studies by Shumway and Maler (1989) demonstrated that blockade of GABAergic transmission within the ELL also disrupted this

gain control function. The anti-Hebbian plasticity present at DML parallel fiber to pyramidal cell synapses might complement a more global gain control function mediated by the dorsal molecular layer, resulting in the optimization of individual pyramidal cell excitability.

The strikingly similar adaptive filtering mechanisms found in the four diverse species studied thus far certainly suggest that this mechanism is likely to be operational in other animals, including more advanced species. Furthermore, the demonstration that predictable stimuli which are not typically reafferent can also be rejected raises speculation that processes similar to adaptive cancellation *via* negative images may be a more general processing strategy operative in a wide variety of sensory systems.

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