Memory-based expectations in electrosensory systems
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Adaptive processing of electro-sensory information occurs in the cerebellum-like structures of three distinct groups of fish. Associations within each of these structures result in the generation of negative images of predictable features of the sensory inflow. Addition of these negative images to the actual inflow removes the predictable features, allowing the unpredictable, information-rich sensory signals to stand out. Evidence from all three groups of fish indicates that the negative images are mediated by plasticity at parallel fiber synapses.

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Abbreviations
DON dorsal octaval nucleus
ELL electrosensory lobe
EOD electric organ discharge
epsp excitatory post-synaptic potential
NMDA N-methyl-D-aspartate

Introduction
Removal of expected or predicted sensory input is one of the very general functions of sensory processing. Organisms are interested in what is new, and predictable sensory inputs convey no information. Thus, adaptation of receptors or neurons to maintained stimuli removes expected levels of stimulation over time, and lateral inhibitory networks remove expected mean levels over space. Simple and universal expectations such as these can be removed by non-plastic cellular or network mechanisms, but plasticity and memory-like mechanisms are needed to take full advantage of all the predictability available to an organism. Associations between stimuli of the same modality, between stimuli of different modalities, or between motor commands and their feedback can all be used to predict sensory patterns. But such associations come and go, varying with the individual and the circumstances, and memory-based mechanisms are needed to make use of them.

The generation and subtraction of memory-based expectations has been demonstrated in the electrosensory systems of three different groups of fish, and some of the cellular mechanisms responsible for these expectations have also been identified.

The electrosense and cerebellum-like sensory structures
All animals in the water create electric fields around them, and a surprisingly large number of different groups of fish possess electroreceptors in their skin that are exquisitely sensitive to such fields [1,2••]. Electric fish, not only have electroreceptors for sensing current but also possess electric organs for generating current in the form of electric organ discharges (EODs [3]). Such fish detect nearby objects by distortions in the pattern of self-generated current that flows through their skin. Thus, electric fish can not only sense external voltage sources but can also sense the impedances of nearby objects. The sensing of external voltage sources is known as passive electrolocation, whereas the sensing of impedances by means EODs and electroreceptors is known as active electrolocation. Passive electrolocation is mediated by ampullary electroreceptors, which respond to low frequency electrical signals by modulating their discharge frequency up and down. Active electrolocation is mediated by tiburous electroreceptors which are especially sensitive to the high frequency signals contained in EODs.

Primary afferent fibers from electroreceptors terminate in cerebellum-like sensory structures (Figure 1). Similar structures in non-electroreceptive fish, amphibians and mammals receive input from mechanical lateral line receptors, auditory receptors and vestibular receptors. The primary afferent fibers from all of these receptors terminate in the deep layers of the cerebellum-like structures where they form maps of the sensory surface. Principal cells of these structures have basilar dendrites that are affected directly, or indirectly via interneurons, by the primary afferents. These cells also have apical dendrites in the molecular layer that are affected by parallel fiber input. The parallel fibers arise from granule cells located in an external granule cell mass.

The cerebellum-like structures that receive afferent input from electroreceptors and which will be the focus of this review are the electrosensory lobes (ELL) of teleost electric fish and the dorsal octaval nucleus (DON) of elasmobranchs (sharks and rays). Granule cells giving rise to parallel fibres in the ELL and DON receive signals which include: corollary discharge input coupled to motor commands; proprioceptive cues conveying information about movements of the body or the fins; and electrosensory information that descends from higher stages of the electrosensory systems [5–9]. These signals are referred to as ‘predictive’ in Figure 1 because they are likely to be associated with changes in electrosensory input and can therefore be used to predict such changes.

Subtraction of memory-based expectations of sensory input
The generation and subtraction of memory-based expectations has been observed in the electrosensory systems of electric teleosts of the Mormyridae and Gymnotidae families, and elasmobranch fish [10]. Each of these groups is
believed to have evolved their electrosensory system independently [11].

**The mormyrid ELL**

Memory-based expectations were first observed in electric fish of the family Mormyridae in the region of the ELL that receives afferents from ampullary electroreceptors, and is responsible for passive electrolocation [12,13]. Ampullary afferents respond to the pulsatile EOD with a change in discharge frequency; but such responses could interfere with the sensory function of the ampullary system. Responses of these afferents to the fish’s own EOD vary with water conductivity and the surrounding environment. Thus, cancellation or minimizing of the EOD-induced interference requires an adaptive memory-based mechanism.

The principal cells of the mormyrid ELL are not only affected by afferent input from the periphery but also by a centrally originating corollary discharge signal coupled to the motor command that elicits the EOD. Corollary discharge effects are studied in fish in which the synaptic effect of electromotor neurons on the electric organ has been blocked by the drug curare. The EOD is blocked in these fish but the motor command that normally elicits an EOD continues to be emitted. Artificial electrical stimuli are delivered to the receptive field of the cell at fixed times with regard to the motor command. Responses to the corollary discharge are minimal when no electrosensory stimuli have been given for several minutes but become prominent after pairing the command with an effective sensory stimulus for a few minutes (Figure 2). The responses to corollary discharge alone after pairing are a highly specific negative image of the previously paired response to a sensory stimulus [13]. The negative image is specific to the timing of the sensory response after the motor command (out to about 120 ms), to the polarity of the sensory response (increase or decrease in firing frequency; Figure 2a), and to the amplitude of the sensory response. The negative image is also specific to the spatial distribution of the sensory response across the surface of the ELL, as the negative image is only formed if the sensory stimulus is within the receptive field of a cell and evokes a response. During sensory stimulation, the addition of the negative image of past or predicted sensory input minimizes the central effect of predictable features in concurrent afferent input (compare the effect of command plus stimulus at the beginning and at the end of pairing in Figure 2b).

The responses to corollary discharge alone disappear within a few minutes after turning off the sensory stimulus (Figure 2b). This disappearance is not a passive decay, however, but rather an active rematching of the changed sensory input that now follows the motor command [14]. The negative image can last 30 minutes if rematching is prevented by silencing the EOD motor command during the intervening period.

Adaptive corollary discharge effects are also found in regions of the mormyrid ELL that receive afferent input from tuberous electroreceptors and which are responsible for active electrolocation [15,16]. The subtraction of predicted sensory input in these regions probably enhances sensitivity to small changes in EOD-evoked input.

**The gymnotid ELL**

The gymnotid studies have been done in regions of ELL that are responsible for active electrolocation in species with continuous, near sinusoidal EODs. The electric organs of these species extend from near the head to the tip of the tail. When the tail is bent, the electroreceptors on
Negative images of predicted sensory responses in the ELL of mormyrid fish. Recorded cells were in the ampullary region of the ELL. 

(a) At the left, three histograms show responses to EOD motor command alone before pairing (top), responses to command paired with a brief (1 ms) excitatory sensory stimulus (middle, stimulus indicated by arrow head), and responses to command alone after pairing for 5 minutes (bottom). Right: same cell 6 minutes later when the response to command alone have returned to a baseline level. Same sequence as in (a), except that the pairing was with an inhibitory sensory stimulus. (In ampullary electroreceptors, a simple inversion of the stimulus from a positive to a negative voltage inverts the response.) In both cases, the responses to command alone after pairing are opposite to the effects of the previously paired stimuli. 

(b) Raster display of another cell in the ampullary region showing the effect of pairing the EOD command with a brief sensory stimulus that evoked a pause-burst in cell activity. The EOD command occurred at time 0. The electro sensory stimulus was delivered immediately afterwards, as indicated by the black line. The response to command plus stimulus is reduced after several minutes of pairing and this is as a result of the development of a response to command alone that is a negative image (a burst-pause) of the previously paired sensory response. (Reproduced with permission from [14].)

one side of the body are more strongly affected by the EOD, whereas those on the other side are less strongly affected. These changes in EOD-evoked afferent responses caused by tail movement, however, convey no information about external conductances and would in fact interfere with their perception.

The potentially interfering effect of tail movement is removed by the addition of a negative image of predicted sensory input, as in the ampullary region of the mormyrid ELL. Cells in the ELL of a discharging gymnotid fish were recorded while passively bending the tail ([5,17,18•]. Figure 3a). Initially, tail bend alone had little effect on the cells. An effective electrosensory stimulus was then delivered to the receptive field of the cells at a fixed phase of the tail bend. When the electrosensory stimulus was turned off after several minutes of pairing, tail bend alone now evoked vigorous responses from the cells that were opposite to the effects of the stimulus. As in the mormyrid ELL, this negative image was specific to the timing (phase), polarity, amplitude and spatial location of the previously paired stimulus. Similarly, the disappearance of the negative image after turning off the sensory stimulus is an active rematching of the change in sensory input and not a passive decay [17].

Two different types of predictive signals are used to evoke the negative images in the gymnotid ELL — proprioceptive signals indicating changes in body position, and whole body electrosensory stimuli. The role of proprioceptive signals was demonstrated by repeating the tail bending experiments in a fish in which the electric organ was silenced. The role of whole body electrosensory stimuli was demonstrated by keeping the fish still while delivering an electrosensory stimulus to the whole body that mimicked the voltage changes caused by tail movement. Pairing a local electrosensory stimulus with the whole body electrosensory stimulus at a fixed phase resulted in a negative image of the response to a local electrosensory stimulus that was evoked by the whole body stimulus.

The elasmobranch DON

Studies of adaptive sensory processing in elasmobranchs have been done in the passive electrolocation system of skates [19,20•,21]. Elasmobranch electroreceptors are extremely sensitive to electric fields (thresholds >0.01 μV/cm) and respond strongly to the fields created by the fish’s own ventilation [22], but such responses convey no useful information and could interfere with the passive electrolocation of external voltage sources.

Principal cells of the DON do not respond to the fish’s own ventilation even though the afferent fibers respond strongly [22]. The cancellation of responses to afferent input is largely due, once again, to the addition of a negative image of predicted sensory responses. This was demonstrated by delivering electrosensory stimuli to the receptive fields of DON cells at a fixed phase of the ventilatory rhythm (Figure 3b). Responses to the extra electrosensory stimulus decreased after a few minutes of pairing and were essentially gone after 25 minutes. When the extra stimulus was turned off, ventilation alone evoked strong responses (Figure 3b) which had not been present before the pairing and which were negative images of the paired sensory effects. The negative images were specific to the timing (phase), polarity, amplitude and spatial location of the paired sensory stimuli, as in the other two systems. The elasmobranch system used three distinct types of predictive signals to evoke
the negative images: corollary discharge signals associated with ventilatory motor commands; proprioceptive signals associated with ventilation; and whole-body electrosensory stimulation associated with ventilation [20*].

Disappearance of the negative image within a few minutes after turning off the electrosensory stimulus is again, as in mormyrids and gymnotids, an active rematching of the change in sensory response. This was shown using passive bending of the fin as the predictive stimulus and pairing such bending with a local electrosensory stimulus. The negative image was still present three hours after turning off the electrosensory stimulus, if rematching was prevented by not moving the fin during the intervening three hour period.

**Sites and mechanisms of the plastic change responsible for the negative images**

The negative images of predicted input are due, in large part at least, to plastic changes within the cerebellum-like structures themselves. This was shown by pairing the predictive signals with intracellular current injection rather than with sensory stimuli, reasoning that if the intracellular current affects only the recorded cell and if the pairing results in the generation of a negative image, then changes must have taken place at synapses onto the recorded cell. Depolarizing intracellular current pulses were paired with the EOD corollary discharge in mormyrid fish [23] and with ventilation in elasmobranch fish [20*]. After the pairing, the same predictive signals alone evoked hyperpolarizing responses in both groups of fish. Thus, plastic change appeared to have taken place at synapses between fibers conveying predictive signals and principal cells. Parallel fiber synapses were hypothesized to be the site of plastic change because all of the effective predictive signals are conveyed by parallel fibers and some, such as proprioceptive signals, are conveyed only by parallel fibers. This hypothesis was also suggested by the known plasticity of parallel fiber synapses in the cerebellum itself [24–26].

Plasticity with appropriate characteristics has now been demonstrated at parallel fiber synapses in all three electrosensory structures. Pairing parallel fiber input with postsynaptic depolarization causes a reduction in synaptic efficacy at this synapse [20*,27,28], a form of plasticity referred to as anti-Hebbian [29]. As a result of such plasticity, the association of parallel fiber activity with principal cell activation by electrosensory input will reduce synaptic strength at the paired parallel fiber inputs (relative to other parallel fiber inputs), resulting in a hyperpolarizing response to the predictive signals conveyed by the paired inputs.

The synaptic mechanisms responsible for robust depolarizing responses to predictive signals following pairing with hyperpolarizing sensory responses (Figure 2a, right side) are less clear. Associative synaptic plasticity following pairing with purely hyperpolarizing stimuli is rare [30], and possible mechanisms for such plasticity are obscure. In addition, although pairing parallel fiber input with postsynaptic hyperpolarization yielded an increase in synaptic efficacy in gymnotid and elasmobranch fish, such pairing had no effect in mormyrid fish (C Bell, unpublished data). This difference could reflect the fact that the mormyrid results were obtained in vitro whereas results from the other two groups of fish were obtained in vivo from the whole animal. Postsynaptic spiking is critical for synaptic depression in the mormyrid ELL [31*], but spiking,
although prominent in vivo, is either low or absent in vitro. Thus, the effects of pairing with hyperpolarizing current in gymnotids and elasmobranchs could be due to lack of spikes during current injection and a consequent absence or reversal of synaptic depression. Modeling results in the mormyrid are consistent with such an explanation [32].

Synaptic plasticity has also been demonstrated at a second site in the gymnotid ELL, at synapses made by descending fibers from a higher order electrosensory nucleus [28,33,34]. This plasticity is very similar to that found at parallel fiber synapses in the same fish and could be part of the explanation for negative image formation in response to whole body electrosensory stimuli.

The characteristics and mechanisms of plastic change at parallel fiber synapses have been examined in both the mormyrid and gymnotid ELL. In the mormyrid, synaptic depression was found to require the occurrence of a postsynaptic dendritic spike and to depend on the precise timing of the spike relative to epsp (excitatory post-synaptic potential) onset [27,31•]. Depression developed when the postsynaptic spike occurred within 50 ms of epsp onset, whereas other timing relations yielded potentiation or no effect. The depression required activation of NMDA receptors and changes in postsynaptic calcium. The requirement for NMDA receptor activation explains the timing dependence of the learning rule in that simultaneous occurrence of glutamate binding and postsynaptic depolarization (caused by the dendritic spike) are needed to open the NMDA channel. Potentiation also occurred at parallel fiber synapses in the mormyrid, but this potentiation appeared to be non-associative and to depend on simple repetition of the parallel fiber stimuli at a sufficiently high rate [31•]. The potentiation could reverse the depression and vice versa, with both potentiation and depression appearing to have a presynaptic locus of expression, as indicated by changes in paired pulse facilitation. Synaptic depression in the gymnotid ELL also depended on NMDA receptors (J Bastian, personal communication) and on changes in postsynaptic calcium [35]. In the gymnotid, however, the site of expression appeared to be postsynaptic for the depression and presynaptic for the potentiation [28].

The characteristics of plasticity at parallel fiber synapses are consistent with such plasticity being responsible for the formation of negative images. The associative anti-Hebbian characteristic provides a simple and direct mechanism for the generation of predictive responses that oppose depolarizing electrosensory responses. The ready reversibility of depression by potentiation and vice versa explains the ready reversibility of negative images (Figure 2a), and the narrow timing window within which depression occurs (Figure 4a) explains the temporal precision with which negative images are formed [32].

Modeling studies also support the conclusion that anti-Hebbian plasticity at parallel fiber synapses is responsible for the formation of negative images. The dots show results from in vitro slice experiments in which parallel fiber-evoked epsps were paired with postsynaptic dendritic spikes evoked by intracellular current pulses. Changes in epsp size were measured as a function of the relative timing of the epsp and the spike during pairing. Epsp depression was present only if the postsynaptic spike occurred within ~50 ms following epsp onset. Other timing delays usually yielded potentiation. The thin continuous line drawn through the experimental points shows the idealized form of the learning rule shown in (a). The illustrated simulation shows the effect of command alone before (C), during (C+S), and after (C) pairing with a sensory stimulus that evokes a pause–burst. The effect of command alone after pairing is a negative image (burst–pause) of the response to the paired stimulus. Compare with Figure 2b. (Reproduced with permission from [32].)
for the generation of negative images [32,36]. A variety of different learning rules for parallel fiber plasticity were tested in a model of the mormyrid ELL [32], and the negative images resulting from the use of an idealized form of the experimentally-determined, asymmetric learning rule (thin continuous line in Figure 4a) were significantly more accurate and more stable than the negative images resulting from any other learning rule.

Conclusions

The role of parallel fiber synapses in generating negative images of predicted sensory input is indicated by the predictive signals that they convey, by the presence of appropriate plasticity at these synapses, and by the modeling studies. Thus, the connection between synaptic plasticity at the cellular level and a systems level adaptive function is relatively secure for these cerebellum-like structures, as secure perhaps as in any vertebrate system.

However, much remains to be elucidated about the generation of negative images before the full value of these cerebellum-like structures for understanding adaptive processing is obtained. Future work must determine the following first, the cellular mechanisms of plastic change; second, the mechanism by which pairing with hyperpolarizing sensory stimuli results in depolarizing predictive responses; third, the possible role of plasticity at inhibitory synapses; and fourth, how the adaptive functions are integrated with other known functions of the circuitry such as lateral inhibition [37,38], gating [39,40], gain control [41], and attention-like processes [42]. Behavioral demonstrations of the subtraction of predictable sensory features are also needed. Finally, work on other systems is required to determine whether knowledge of these electrosensory structures can contribute to an understanding of other cerebellum-like structures, such as the dorsal cochlear nucleus or the cerebellum itself [10,43,44].

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References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as: • of special interest **of outstanding interest


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20. Bodznick D, Montgomery J, Carey M: Adaptive mechanisms in the elasmobranch hindbrain. J Exp Biol 1999, 202:1357-1364. This article provides a good summary of both systems-level and cellular-level studies of negative image formation in the DON of elasmobranch fish. The article also shows that in the elasmobranch fish, corollary discharge signals associated with motor commands, proprioceptive signals, and descending electrosensory signals from higher centers can all serve as predictive signals which can elicit negative images of predicted sensory patterns after suitable periods of association.


