In the previous lecture we learned how Mormyrid electric fish produce an 'electromotor' command and then receive an electrosensory response after a delay. The motor output and the sensory response are time-locked to each other. The fish builds an expectation of the sensory response so that it can remove it from the rest of the sensory inflow, not by inhibitory blanking, but by forming a negative image of the expected input.

Meek, Grant and Bell. The Journal of Experimental Biology 202, 1291–1300 (1999)

**Principal Cell Plasticity**

<table>
<thead>
<tr>
<th>EOD command</th>
<th>C alone, pre</th>
<th>C+S, initial</th>
<th>C-alone, post</th>
</tr>
</thead>
<tbody>
<tr>
<td>(6 min of C-S pairing)</td>
<td></td>
<td></td>
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</tbody>
</table>

This is an example of a modifiable difference copy.

In the previous lecture we also looked at a case of negative image formation in an electric fish from South America, where there is no corollary discharge for the EOD command.

**Bastian: Sensory Consequence of Movement of Tail**

Experimental paradigm:
1) Tail movement controlled by motor.
2) Electric discharge continues and stimulates electroreceptors.
3) Electrode near skin monitors the EOD amplitude.

**Electroosensory Feedback From Tail Bending is Cancelled in ELL**

The cancellation is modifiable over time.
If tail is not bent during artificial Amplitude modulation, there is no effect.

The same experiment was done with *Eigenmannia*, but this time without the benefit of proprioceptive input (no tail bending).

Pairing of electrosensory stimulation with ventilation movements in Skate also produces a negative image of expected sensory input.

In principal cells of the mormyrid ELL, pairing a EOD command discharge with an intracellular stimulus can result in formation of negative image (only under strong stimulation).

The Basic Architecture
Sensory input arrives from below and stimulates pyramidal cell to fire. Predictive input comes from above through parallel fibers. Synaptic modification changes strength of predictive input as a consequence of simultaneous action.

**Theory to Explain Negative Image**

Recording Plasticity in Slice Preparation

Recording intracellularly from an ELL cell from mormyromast region of mormyrid ELL. Stimulate parallel fibers with two sets of electrodes in molecular layer of ELL.

**Spike timing dependent plasticity** is anti-hebbian. If the broad spike occurs after the EPSP, the synaptic weight is decreased. If the broad spike occurs before the EPSP, it strengthens. This sculpts a negative image of the expected input.

Defining Spike-Timing-Dependent Plasticity (A) A presynaptic cell connected to a postsynaptic cell repeatedly spiking just before the latter is in part causing it to spike, while the opposite order is acausal. (B) In typical STDP, causal activity results in long-term potentiation (LTP), while acausal activity elicits long-term depression (LTD; Markram et al., 1997b; Bi and Poo, 1998; Zhang et al., 1998). At some cortical synapses, the temporal window for LTD (dashed gray line) is extended (Feldman, 2000; Sjöström et al., 2001). These temporal windows are often dose-spike dependent, with LTD being absent at low-frequency (gray continuous line, Markram et al., 1997; Sjöström et al., 2001), and presynaptic bursting relaxing the LTD timing requirements to hundreds of milliseconds (Debanne et al., 1994; Sjöström et al., 2003).
Donald Hebb
"Let us assume that the persistence or repetition of a reverberatory activity (or ‘trace’) tends to induce lasting cellular changes that add to its stability. . . When an axon of cell A is near enough to excite a cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A’s efficiency, as one of the cells firing B, is increased." (Hebb, 1949).

Henry Markram1,*, Wulfram Gerstner1 and Per Jesper Sjöström2,3 Frontiers in Synaptic Neuroscience. August 2011

Methods (continued)
Identification of Mossy Fibers in Egp.
1) Previous studies by Bell (1991) recorded from cells in Egp with similar properties and found no synaptic activity, spikes arising directly from baseline.
2) Several fills with biocytin (3 from proprioceptive input, 2 with EODc input)
3) No neurons responded to both EODc and proprioception.
4) Pairing of EODc synaptic activity and narrow spike activity by averaging responses before and after EODc, narrow spikes removed.

The main players in cerebellar function are:
Granule cells: which receive input from mossy fibers, and send their outputs to Purkinje cells via parallel fibers
Purkinje cells: the ‘Principal Cell’ of the Cerebellum
Climbing fibers: bring ‘error signals’ from the inferior olive to ONE Purkinje cell.
Rationale


"Influential theories of cerebellar function have postulated that highly selective or sparse coding in Granule Cells allows Purkinje cells to acquire selective responses through associative synaptic plasticity. Granule Cells that selectively encode specific combinations of sensory and/or motor signals could allow Purkinje-like cells to generate more specific negative images."

"Nothing is yet known about how such signals are recoded in GCs or about the significance of GC input representations for the generation of negative images."

Overall theme for cerebellar function. A direct pathway from input to output (i.e. the vestibular system to the eye muscles in the case of the VOR) is accompanied by an "indirect pathway" through the cerebellum - vestibular collateral (mossy fiber) to granule cell to parallel fiber to Purkinje cell. Parallel fibers excite Purkinje cells on synaptic spines. When there is an error in the VOR, information about image slip on the retina comes from the inferior. This is a strong depolarization which causes a dendritic spike in the Purkinje cell, and this causes synaptic weights from parallel fibers to depress, weakening the inhibitory input on the vestibular neurons, thereby adjusting the gain of the eye reflex.

Cerebellum and “cerebellar-like” structures

Most vertebrates possess both a cerebellum and other brain structures with cerebellum-like architectures.

1) A MOLECULAR LAYER with many parallel fibers + dendrites of Purkinje-like cells.
2) A LARGE NUMBER OF GRANULE CELLS which carry information from many central structures about the state of the animal: sensory information from a large number of senses, corollary discharges from motor centers (predictive of sensory input to the principle cells).
3) PRINCIPAL CELLS with SPINES. Parallel fibers terminate on spines of principal cells, or on the smooth dendrites of inhibitory stellate cells.

Cerebellum-like structures operate as adaptive sensory filters that predict sensory inputs into the deep cerebellar nuclei, thus providing a continuous prediction of parallel fiber inputs in the molecular layer.
The cerebellar-like structure is defined by the molecular layer, the principal cell, and the numerous inputs from granule cells via parallel fibers.

The Basic Architecture


Figure 1: Schematic drawing showing major features of cerebellar-like memory structures. Inhibitory inhibitory cells of the molecular layer are shown in black. Blue upward arrows indicate afferent input from the primary sensory cortex to the molecular layer. Green downward arrows indicate the efferent output from the granule cells to the molecular layer. Orange downward arrows indicate the efferent output from the Purkinje cells to the molecular layer. Red downward arrows indicate the efferent output from the granule cells to the molecular layer. Yellow downward arrows indicate the efferent output from the granule cells to the molecular layer.
Anatomy

Injection of biotinylated dextran into molecular layer of ELL labels: MG cells (GABAergic cells in ELL) granule cells which project via parallel fibers to MG cell dendrites.

Many Mossy Fibers provide proprioceptive sensory information from tail.

(most common type of unit)

responds to tail bend, not EODc.

Spike rate unchanged by EODc.

Firing rate is 20-150 Hz.

Has a best tail angle.

Spike rate encodes tail angle shown for 3 units that prefer contralateral bend, 3 that prefer ipsilateral bend.

Some proprioceptor units respond to schnauzenorgan displacement, trunk displacement or fin.

Some mossy fibers respond to EOD command

Putative MossyFiber cell responding to EODc.

No spontaneous activity.

Response precedes EODc.

3 units showing differing latencies of responses.

Stereotyped rasters.

Summed histograms of spikes per command from 30 such units.

Active for up to 400 msec after EODc.

Other Examples of Removing Expected Inputs

- Adaptation of receptors or neurons to maintained stimuli removes responses to constant stimulus.

- Lateral inhibition: remove expected mean levels over space.*

Both methods use simple non-plastic cellular changes (self inhibition, intra-cellular inhibition).

