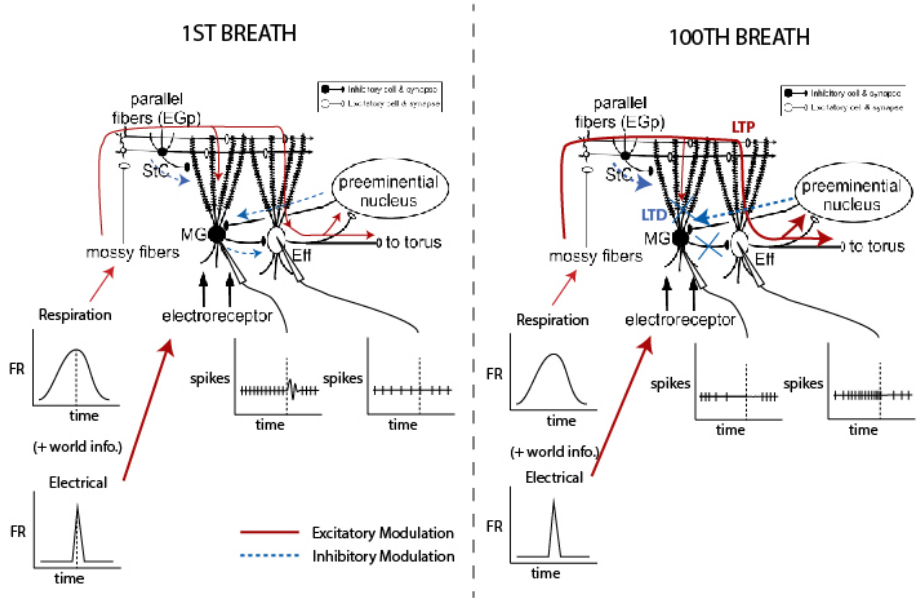
1. Before learning, the MG cells are being modulated at some basal firing rate by excitatory input from parallel fibers and inhibitory input from the StC and preeminental nucleus (PN). Upon receiving an excitatory pulse from the electroreceptor at a particular phase of respiration, this inhibition is temporarily overridden, allowing a broad spike to occur. After many pairings of respiration stimuli and electroreceptor responses, LTD in the parallel fiber synapse onto the MG cell mediated by repeated electroreceptor input will suppress MG output over time. Additionally, LTP occurring at the unmodulated synapses of parallel fibers and the efferent neuron make the output signal more difficult to inhibit by MG firing.



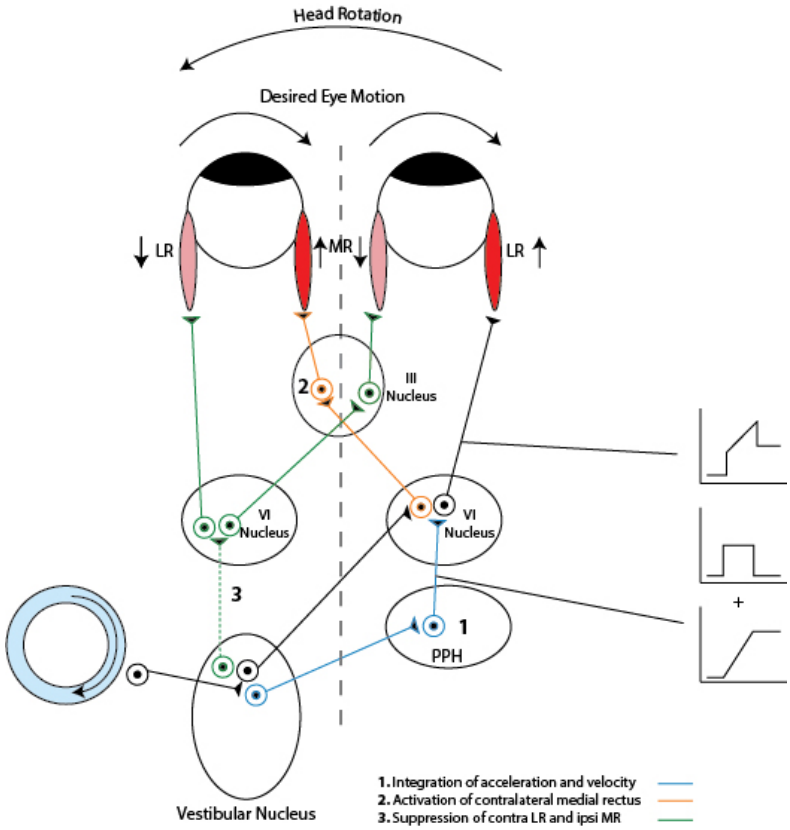
2. The error signal in this circuit is created by the preeminential nucleus (PN), as it receives the motor output from the efferent neuron and has inhibitory control over the MG cells. An unexpected signal to the PN will likely drive strong inhibition onto the MG cells, preventing a broad spike and thus plasticity from occurring in response to that stimuli.
    a. The error computation is being performed in the preeminential nucleus.
    b. This differs from the cerebellar circuit, where the error signal (puff) is carried by the climbing fibers from the inferior olive. In this circuit, the electroreceptors do carry the cause of the error signal (electroreceptor activation), but cannot generate the error signal itself, as they do not receive any motor output for comparison to the input. Instead, the PN responds to an incorrect motor action and will directly inhibit the Purkinje-like MG cells to ensure that the previous response is not linked to the sensory input through plasticity and thus prevent learning of the incorrect response.

The ability to discriminate distances on the order of dorsal root ganglion (DRG) receptive fields (RFs) could be described by a hierarchical model of converging inputs at multiple steps in the somatosensory pathway, much akin to the visual system. This type of model would predict that RFs in the primary somatosensory cortex (S1) are thus tuned to more complex patterns of mechanical stimuli that are encoded across several adjacent DRG RF responses. In the example below, two DRG neurons may be tuned to pressure at their adjacent RFs. Assuming their RF properties are maintained in the thalamus, these two thalamic cells both synapse onto the same cell in area 3. This combined input would cause the area 3 cell be sensitive to two adjacent points within its receptive field (which would encompass the RFs of both DRG neurons). Despite its larger receptive field, this area 3 cell is tuned to more complex features, which allows it to be sensitive to patterns of stimulation that occur within the resolution of DRG RFs.

This model could initially be tested by simply characterising RF properties across different levels of the somatosensory system by recording from these neurons during presentation of tactile stimuli in their receptive fields. This model would predict that the tuning properties of DRGs and thalamic neurons would be relatively simple, where they have a preference for pressure at a specific location (probably with a center-surround structure, as indicated in the figure above). However, we would predict that the neurons in area 3 would be tuned to more complex features. In this simple example, we would predict that these neurons would be tuned to particular distances between two pressure points. We could further extend this model, assuming that hierarchical convergence continues into higher areas and predict that higher level cells are responsive to even more complex stimuli (textures or specific patterns of pressure). However, the example proposed here only takes one tactile modality into account (static pressure). It is easy to imagine that this simple model could generate many different kinds of higher-order RFs through conjunctions of input from other somatosensory modalities (ie. you might find cells sensitive only to pressure and pain, moving patterns of pressure, pain and temperature, etc.).

Chris Angeloni - **Question 3**

1) Because of the physics of fluid kinetics, hair cells, via the vestibular nucleus, can only provide acceleration information to the rest of the circuit. However, to maintain eye movement velocity when the head is no longer accelerating, it is necessary to have velocity information in addition to acceleration information. To achieve this, it is necessary to add a neural integrator to this circuit, which integrates the acceleration signal provided by the vestibular neuron to obtain velocity information. With acceleration and velocity information provided in parallel pathways, it is now possible to sum the velocity and acceleration signals to get a motor signal that will accelerate eye muscle contraction, maintain contraction velocity relative to head rotation velocity after it stops accelerating, and then decelerate to a new stable position when the head stops rotating.



2) The proposed arc only includes innervation of the lateral rectus contralateral to the vestibular input, but it would also be necessary to provide the same movement signal to the medial rectus ipsilateral to the vestibular nucleus in order to ensure fixation of both eyes. Without the same motor commands going to both of these muscles, only one eye will maintain fixation, while the other will remain unmoving, drifting with head rotation. This problem is solved through the decussation of the medial longitudinal fasciculus from the abducens nucleus to the oculomotor nucleus on the opposite side (ipsi to the vestibular input). From the oculomotor nucleus, the same motor command can be sent to the medial rectus of the other eye, allowing both eyes to move in concert.
3) While the previous addition to this circuit allows both eyes to move by contracting muscles on the sides of the eye opposite to the direction of rotation, antagonistic pairing is needed to relax the muscles on the other side of the eye, to prevent the opposing muscles from “pulling against each other,” preventing eye movement. This could be achieved by transmitting inhibitory signals to the muscles contralateral to the contracting muscles via an interneuron. The vestibular afferent could synapse onto an interneuron which then provides inhibitory input to the abducens nucleus, causing the lateral rectus opposite the contracting medial rectus to relax. Through the same pathway mentioned previously, the same input would travel to the contralateral oculomotor nucleus via the MLF to relax the medial rectus contralateral to the contracting lateral rectus of that eye.

a. These results can be reconciled with the interpretation that the direct and indirect pathways are not purely facilitating or suppressing a specific movement, but rather, are allowing for selection from a repertoire of movements. That is, the direct pathway activates the appropriate action routine, while the indirect pathway is also activated to suppress inappropriate action routines.
b. After silencing caudate neurons that preferentially respond to reward I would expect saccade latency to become more erratic, and to not be modulated by the presence of a reward in a given condition. This is because these neurons are likely tracking the reward location and are essential in facilitating motor movements or attentional resources to the rewarded location. When these caudate neurons are silenced, the direct pathway becomes inactive (that is, the information flow from the thalamus to the cortex will be inhibited) while the indirect pathway will allow more thalamocortical feedback. Thus, the reward information in the system is lost, action selection by the direct pathway is inhibited, and suppression of inappropriate actions by the indirect pathway is inhibited. This will result in erratic eye movements with variable latency, that show no selectivity towards rewarded conditions due to a lack of reward-modulated action selection mediated by caudate inhibition.
c. In this hypothetical experiment, using the “future1” and “future2” techniques to specifically silence and activate reward-mediated caudate neurons would predictably alter decision-making in the 2AFC motion direction task. Specifically, I would predict that activating reward sensitive neurons would create a bias in the perceptual decision, causing the monkey be more likely to respond in the direction of rewarded motion (eg. if rightward motion is rewarded, the monkey will be much more likely to respond right when caudate is activated). If these same neurons are inactivated, I predict that the monkey would be unable to do the task, and show a decreased response rate. This particular pattern of results would suggest that we are stimulating/suppressing the direct pathway, which would cause overselection of the correct perceptual decision during stimulation. During suppression, neurons in the direct pathway are being suppressed and thus cannot signal the appropriate perceptual decision. Because the indirect pathway is still intact in this interpretation, inappropriate actions are still being suppressed naturally, while correct actions are being suppressed experimentally, resulting in no response at all.

    Alternatively, we might observe a different pattern of results. It is possible that the monkey shows the same reward bias when these caudate neurons are stimulated using “future2” but shows noisy and incorrect responses when they are deactivated using “future1.” These results may suggest that we are modulating the indirect pathway. In the first case, stimulation of the indirect pathway is suppressing incorrect direction estimates, which allows for optimal selection of the correct, rewarded response, thus creating a response bias towards the reward (which may even exceed normal rewarded response biases). During inactivation, however, the indirect pathway is unable to suppress incorrect decisions, causing the monkey to erratically respond to the motion stimuli at chance. Depending on whether the neurons being manipulated are in the direct or indirect pathway, we can expect diverging results.