

Askesis: Negative Pathway

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1 Overview

The purpose of the negative pathway is to filter out potential movements produced by the positive pathway, leaving only the desired movements as output from the deep nuclear cells. Our theory of the negative pathway is very similar to the perceptron model of Albus, although we modify the input to each perceptron slightly.

1.1 Granular cells encode sets of mossy fibers

Granular cells are the most numerous cells in the human brain; 3/4 of the neurons in the brain are granular cells in the cerebellum. This number suggests that they must embody some sort of combinatorial explosion, which is a feature found in both Marr's and Albus's models.

Each granular cell has synapses with 4-5 mossy fibers, but not all of these synapses are necessarily active. We posit that each granular cell learns a subset of their inputs that co-occur most frequently, and subsequently fire only when all of those inputs are active. We will call this subset the active set of the granular cell.

In the case that all the mossy fibers in the active set arise from muscle spindles, a given granular cell will encode a particular set of muscle lengths, which will in some cases suffice to specify the angular location of some joint, or even several joints. In other cases, it is still a potentially useful feature to feed to the classifier.

We postulate that the granular cell learns the active subset by looking for co-occurrences of its inputs. There are two mechanisms available to the granular cell: it can strengthen or weaken the mossy fiber-granular cell synapse, and it can raise or lower the threshold for the granular cell to fire ("intrinsic plasticity").

In order to be biologically feasible, the strengthening or weakening of the mossy fiber-granular cell synapse should be based solely on information that is locally available. Fortunately, these synapses live inside of glomeruli which also receive input from Golgi cells, so we can use the firing of the Golgi cell when we decide whether to strengthen or weaken the synapse.

As we will discuss below, Golgi cells can be fired either by the firing of several nearby (and thus likely to be related) mossy fibers, or by the firing of

some number of nearby granular cells. Of interest here is the first mechanism; if we know that several nearby mossy fibers have fired, then it is likely that the “true” active set is firing. By “true” active set, we mean the largest set of mossy fibers that fire together more than a certain threshold amount of the time. If a particular mossy fiber is active at the same time as the true active set (as signified by the firing of the Golgi cell), then it is probably a member of the active set, so we should strengthen the synapse between the mossy fiber and the granular cell. If the mossy fiber is not active at the same time, we should weaken the synapse. This can be accomplished by using something like the BCM rule, except that we should use the firing of the Golgi cell in place of the post-synaptic activation.

Let $G_i^{init}(t)$ be the fraction of the time that the i -th granular cell is firing during a small time window ending at time t , so that $G_i^{init}(t) = 1$ when the i -th cell is firing at its maximum rate. We can assume that the timings of the individual mossy fibers are independent and random, i.e., given the rate at which each is firing, and given that the granular cell only fires when all of its active inputs fire, we can assume that the rates simply multiply:

$$G_i^{init}(t) = \prod_{j \in \mathcal{A}_i} M_j(t),$$

where \mathcal{A}_i is the active set of the i -th granular cell.

1.2 Timed non-maximal suppression from the Golgi cells

It will commonly be the case that two granular cells have very similar input patterns. For instance, two granular cells can be excited by the same mossy fiber, or by two different mossy fibers with similar firing patterns. In particular, mossy fibers that ultimately encode firings of muscle spindles will be highly correlated if they encode similar lengths of the same muscle. Since granular cells are triggered by sets of mossy fibers, this means that two granular cells could also wind up being highly correlated.

It is therefore desirable to perform what is called non-maximal suppression. Among a set of granular cells that fire in similar situations, we want to select the granular cell that is firing the most rapidly, and suppress the firing of all the other similar granular cells. A particular granular cell is active only if it is the one under its Golgi cell that is firing most rapidly, which indicates that the state it codes for is the closest to the truth.

Golgi cells have two kinds of dendrites, basal dendrites which receive excitatory input from mossy fibers, and apical dendrites which receive excitatory input from parallel fibers. It has been said that the two sets of dendrites are too far apart for the Golgi cell to perform summation, so we should think of the Golgi cell as firing when either 1) several nearby mossy fibers are firing, or 2) many of its parallel fiber inputs are firing.

The Golgi cell also acts to suppress a granular cell that has been firing for more than a certain amount of time. The granular cell is active only if it has

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only recently started firing. Thus its firing encodes the fact that we have very recently arrived at a very particular state. The recentness is known because the granular cell wasn't firing long enough ago to trigger the Golgi cell to suppress it. The particularity is known because the granular cell is suppressing all granular cells which are too similar to it but which are not firing as quickly.

Let $G_i(t)$ be the percentage of the time that the i -th granular cell was firing for a small window of time ending at time t . (So, $G_i(t) = 1$ would imply that the i -th granular cell is firing at its maximum rate.) Let \mathcal{G}_i be the set of granular cells (excluding the i -th granular cell itself) which receive inhibitory input from the same Golgi cell as the i -th granular cell. We then have

$$G_i^{nms}(t) = \begin{cases} 1 & G_i(t-1) < \theta \text{ and } \forall j \in \mathcal{G}_i, G_j(t) < G_i(t) \\ 0 & \text{otherwise} \end{cases},$$

for some threshold θ .

1.3 Purkinje cells as difference of post-Golgi granular images

The Purkinje cells receive input from the granular cells. These synapses are in the molecular layer, the outermost layer of the cerebellum. Each Purkinje cell receives input from something like 100,000 granular cells.

Each Purkinje cell receives in addition a single input from a “climbing fiber”, which is the output of a neuron in the inferior olive. This input is strong enough to trigger the Purkinje cell to fire. It has been established that the synapse between the output of the granular cell and the input of the Purkinje cell is weakened if the granular cell fires at the same time that the climbing fiber fires; this is called long-term depression. Our theory is that the Purkinje cell firing is meant to suppress some specific output; the long-term depression is desirable because it means that we will henceforth not take the firing of a particular granular cell as a reason to fire the Purkinje cell and suppress an output that we desire to see remain unsuppressed.

We should think of each Purkinje cell as receiving a “picture” or “video” of what is going on from the granular cells. The Purkinje cells are receiving as much information as a 300x300 binary image.

$$P_j(t) = \begin{cases} 1 & \sum_j W_{ij}^{pp}(t) G_i^{nms}(t) > \theta_j \\ 0 & \text{otherwise} \end{cases},$$

where

- $G_i^{nms}(t)$ is the output of the i -th granular cell at time t , after non-maximal suppression has been performed by the Golgi cells.
- $W_{ij}^{pp}(t)$ is the weight of the synapse between the i -th parallel fiber (output of the i -th granular cell) and the j -th Purkinje cell.

- We can probably get away with $\theta_j = \theta$, for some constant θ .

We posit the following learning rule for the synapse weights between the parallel fibers (output of the granular cells) and Purkinje cell inputs:

$$W_{ij}^{pp}(t+1) = \begin{cases} W_{ij}^{pp}(t) - c & IO_j(t) = 1, G_i(t) = 1 \\ W_{ij}^{pp}(t) + d & IO_j(t) = 0, G_i(t) = 1 . \\ W_{ij}^{pp}(t) & G_i(t) = 0 \end{cases}$$

Given this learning rule, we can see that the synapse weights of a single Purkinje cell can be thought of as the sum of all post-Golgi granular images from time steps where the climbing fiber did not fire, minus the sum of all post-Golgi granular images from time steps where the climbing fiber did fire:

$$W_{ij}^{pp}(T) = d \sum_{t=1}^{T-1} (1 - IO_j(t)) G_i^{nms}(t) - c \sum_{t=1}^{T-1} IO_j(t) G_i^{nms}(t)$$

We can think of this in the following way: every time step of training is either anti-firing of the Purkinje cell (if the relevant inferior olive cell fired at that time step) or pro-firing (if the relevant inferior olive cell did not fire). We exclude all time steps when $G_i^{nms}(t)$ was zero. We then allow each time step to vote at this synapse, weighting the votes against firing with weight c and the votes in favor of firing with weight d . We perform this computation at each synapse to get the synapse weight W_{ij}^{pp} , which is then used as the weight with which $G_i^{nms}(t)$ is considered. Thus, the Purkinje cell takes each $G_i^{nms}(t)$ into account with a weight that depends on all previous time steps where that cell was active.

1.4 Basket and stellate cells as anti-Purkinje cells

We have a problem here, which is that the synapses between the parallel fibers and the Purkinje cells are always excitatory, so we can never take a granular cell as evidence that we *don't* want to fire the relevant Purkinje cell. This problem is solved by the basket and stellate cells, which inhibit the Purkinje cells and receive their input from the parallel fibers. Whenever we would wind up with a negative synapse weight between the i -th granular cell and the j -th Purkinje cell in the above formulas, this should be interpreted as a positive weight between the parallel fiber of the i -th granular cell and a basket or stellate cell that inhibits the j -th Purkinje cell.

1.5 Symmetry-breaking mechanism for the Purkinje cells

Each Purkinje cell receives as input, in addition to its input from the parallel fibers, collaterals from several nearby granular cells. This input is weighted more

highly than that at the parallel fiber-Purkinje cell synapse. We posit that these collaterals exist to break the symmetry between Purkinje cells that project to the same deep nuclear cell, so that we can learn multiple different classifiers, each of which is capable of suppressing the deep nuclear cell. Otherwise, adjacent Purkinje cells would receive the same input. (Recall that nearby inferior olive cells tend to be coupled with gap junctions, so that the input from the inferior olive would also be the same for each Purkinje cell.)

2 Predictions

Prediction 2.1. Mossy fiber - granular cell synapse should follow the learning rule given above in Section ??.

Prediction 2.2. The Purkinje cells that a particular basket or stellate cell innervates should suppress the same deep nuclear cell. Or, more weakly, they should suppress deep nuclear cells with similar firing patterns.

Prediction 2.3. Each Golgi cell should inhibit roughly the same set of granular cells which excite it. These granular cells should also be excited by the same set of mossy fibers that excite the Golgi cell.

Prediction 2.4. If you prevent a Golgi cell from firing, the granular cells it outputs to should be correlated in their firing patterns. If you then allow the Golgi cell to fire, the granular cells should become less correlated.

Prediction 2.5. Two mossy fiber inputs to a Golgi cell should be more correlated than two mossy fibers which are the same distance apart but which do not synapse on the same Golgi cell.

Prediction 2.6. Either the inferior olive receives a copy of the signal from every command mossy fiber, or the negative pathway does not suppress state transitions. In the latter case, there should be no active synapses between Purkinje cells and state cells.

Prediction 2.7. Each inferior olive cell should send a collateral to the same deep nuclear cell that its Purkinje cell(s) projects to. If this is not the case, then the two deep nuclear cells (the one receiving the collateral and the one receiving the output of the Purkinje cell) should exhibit similar firing patterns.

3 Thoughts

- Can think of NMS as a kind of explaining away.
- Why are there mossy fiber-Golgi cell synapses?
- Does the Golgi cell help the granular cell learn which pair of inputs to choose?

- Purkinje cells have collaterals that suppress nearby Purkinje cells - this is sufficient for symmetry breaking?
- Purkinje cells have collaterals that have “weak inhibitory synapses” with cortical inhibitory interneurons
- There are some connections between collaterals of granular cells and Purkinje cells that take place in the Purkinje layer. These are stronger synapses than those of the parallel fibers. This is the symmetry breaking mechanism.
- Golgi cells have gap junctions with other Golgi cells, which seem to act to synchronize them.
- B/S cells receive collaterals from Purkinje cells
- (Prediction already known to be true.) The parallel fiber-basket cell synapse should be strengthened by the simultaneous firing of the climbing fiber and the parallel fiber, and weakened by the firing of the parallel fiber alone.