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Model of auditory prediction in the dorsal cochlear nucleus via spike-timing dependent plasticity

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Abstract

This study investigates the learning dynamics of cartwheel cells in the dorsal cochlear nucleus (DCN). Cartwheel cells are excited by parallel fibers that carry information from various sources, such as auditory stimuli, proprioception and recurrent inputs from higher-order auditory processing. Thus, these cells are thought to be involved in multimodal sensory integration. Extracellular in vivo recordings show that mouse DCN cartwheel cells respond well to auditory stimuli. A model of the DCN is presented that predicts how the auditory response of cartwheel cells adapts to predictable patterns of auditory stimuli. In the model, the spike-timing dependent learning rule at the synapse from parallel fibers onto cartwheel cells explains predictive learning in the response of cartwheel cells to auditory stimuli.

Keywords: Temporal processing; Synaptic plasticity; Cochlear nucleus; Complex spikes; Cartwheel cells; Auditory brainstem

1. Introduction

Hearing provides a vital source of information about the environment for animals to avoid capture and seek prey. However, an important challenge for the auditory system is to quickly discern harmless and uninteresting sounds from sounds that could impact the animal's survival. Unexpected and novel sounds could indicate the presence of a predator or prey, and special treatment of these sounds by the auditory system could provide significant advantages for survival. In addition, fast and accurate localization of novel sounds can be critical for survival. Thus, the auditory system would be expected to have developed a filter that cannot only identify novel sounds, but integrate multiple senses to better localize the sounds relative to the animal's position. In order to insure speed in auditory processing of predictive signals, it would be advantageous to begin predictive processing at the initial stages of the auditory system. This predictive processing may occur at the first stage of auditory processing in the brainstem, at the cochlear nucleus (CN).

1.1. Auditory processing in the dorsal cochlear nucleus

The first synapse of the auditory nerve in the central auditory system is in the CN. There are two main divisions of the CN that each receive afferent input: the ventral cochlear nucleus (VCN) and the dorsal cochlear nucleus (DCN). The VCN sends projections to the binaural localization system and parts of the monaural system [15]. The auditory pathway that has been implicated in predictive computations is via the DCN [8]. The DCN is one member of a class of cerebellum-like sensory structures found in fish, amphibia, and mammals [2], and similarities in function are thus expected between the DCN and the entire class of structures such as the electrosensory lateral line lobe in weakly electric fish, the octavolateral nucleus of sharks and rays, and the cerebellum. Because of the similarities, hypotheses about the function of the DCN can be driven by our understanding of the cerebellum and other cerebellum-like structures.

The output neurons of DCN, such as fusiform cells, receive direct primary auditory afferents, but their activity is modulated by inhibitory input from cartwheel cells (Fig. 1A, [4]). Cartwheel cells receive no primary afferents, but are excited by parallel fibers that originate in a granule

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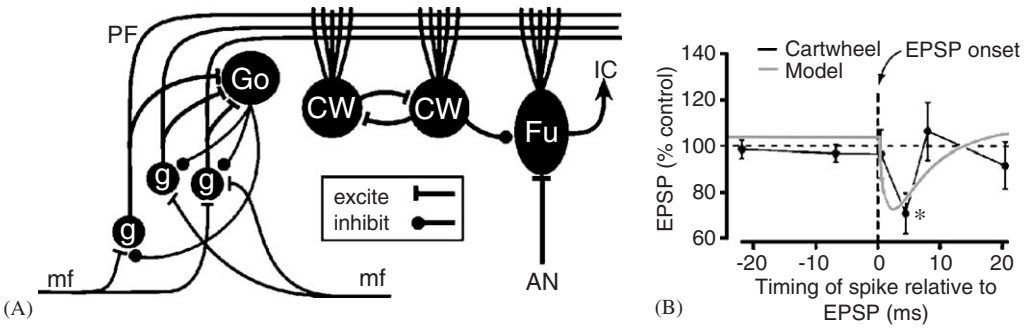

Fig. 1. Local circuitry of the dorsal cochlear nucleus (DCN). (A) Auditory signals enter the DCN through the auditory nerve (AN) and contact fusiform cells (Fu) that project to the inferior colliculus (IC). Mossy fibers (mf) carry signals from various sources and excite granule cells (g) that give rise to parallel fibers (PF). PF synapses excite cartwheel cells (CW) and Fu. STDP at the PF synapse onto CW causes the output to adapt to the temporal pattern of the input signal carried by PF. (B) Data from [12] showing STDP at the PF synapse onto CW. In addition, higher frequency stimulation of PF yields non-associative LTP, thus we add a non-associative shift to the STDP learning rule in our model. The grey trace shows the learning rule used in the DCN model: if a CW spike follows the arrival of a parallel fiber spike within 15 ms, then the synapse is depressed proportionally to the excitatory postsynaptic potential; otherwise the synapse is potentiated.

cell domain that project to the molecular layer of the DCN where the cartwheel cells reside. Other cells types in the granule cell domain include Golgi cells that are excited by granule cells and recurrently inhibit granule cells. One of the inputs to the granule cell domain is in the form of mossy fibers that excite granule cells and possibly Golgi cells. Anti-Hebbian plasticity at the synapses from parallel fibers onto cartwheel cells has been demonstrated in the in vitro slice preparation (Fig. 1B, [12]), and we will show how such plasticity could lead to cancellation of predictable auditory patterns that could be observed in vivo.

1.2. Spike-timing dependent synaptic plasticity (STDP)

The plasticity found at the parallel fiber synapses onto cartwheel cells [3,12] is STDP [1] so that the size and direction of synaptic changes depends on the exact timing between pre- and postsynaptic spikes. Cartwheel cells have two types of spikes: simple spikes and complex spikes, where the latter are dependent on calcium ion currents. The STDP learning rule at the parallel fiber synapse is shown in Fig. 1B [12]: the synapse is depressed only for pairings in which a postsynaptic spike was evoked between 0 and 10 ms after the onset of the parallel fiber postsynaptic potential.

Modeling studies have helped elucidate the function of this learning rule at the systems level [11,14]. Not only do the models generate adaptive responses that cancel predictable sensory patterns, but this particular STDP learning rule measured in vitro appears to be optimal for cancelling sensory images. Two critical component of the model are necessary for cancellation of predictable sensory images. One component is that the parallel fibers deliver spike patterns that are correlated with respect to the sensory stimulation. The correlated patterns provide the necessary temporal structure needed for sensory image cancellation to be sculpted out of the parallel-fiber spikes. The second critical component is a synaptic learning rule that drives the cartwheel cell to a constant output during the correlated input. This second requirement is satisfied by the STDP learning rule shown in Fig. 1B, but any synaptic adaptation mechanism that drives the output neuron's membrane potential to a constant could be used to model similar habituation, as demonstrated mormyrids [11], in elasmobranchs [7] and the cerebellum [6]. Recurrence in the granule cell layer due to Golgi cell inhibition could generate spike patterns correlated with respect to sensory stimuli based on principles of artificial recurrent networks [5]. In the following, we investigate how recurrence in a granule cell domain could generate a dynamical basis of spike patterns in parallel fibers that allows for cancellation of predictable auditory patterns.

2. Model description

To initialize our model of the DCN, we recorded extracellularly from cartwheel cells in the awake mouse during auditory stimuli. The cartwheel cells were identified by the presence of both complex and simple spikes, and their position in the molecular layer of the DCN. The example shown in Fig. 2A was driven by the best frequency of the cell for 200 ms. Cartwheel cells responded with a latency of ≈ 20 ms from the initiation of the auditory stimulus to the first spike. Nearly every auditory stimulation led with a complex spike, followed by mostly simple spikes that outlast the stimulus termination.

To test our hypothesis that recurrent connections in the granule cell domain and the STDP learning rule lead to predictive cancellation of auditory patterns, we conducted numerical studies of the network shown in Fig. 2B. The network consisted of a granule cell domain with synaptic connections to the cartwheel cell. Each model neuron was spiking, but the neurons of the recurrent layer interacted through continuous synapses, synapses that transmitted the spike probability weighted by the recurrent synaptic weight matrix, **W**. The spike probability was calculated from the membrane potential that was the sum of all inputs; $V_i(x_n, t) = \sum_m \varepsilon(x_n - x_m)S_m$, where $S_m = 0, 1$

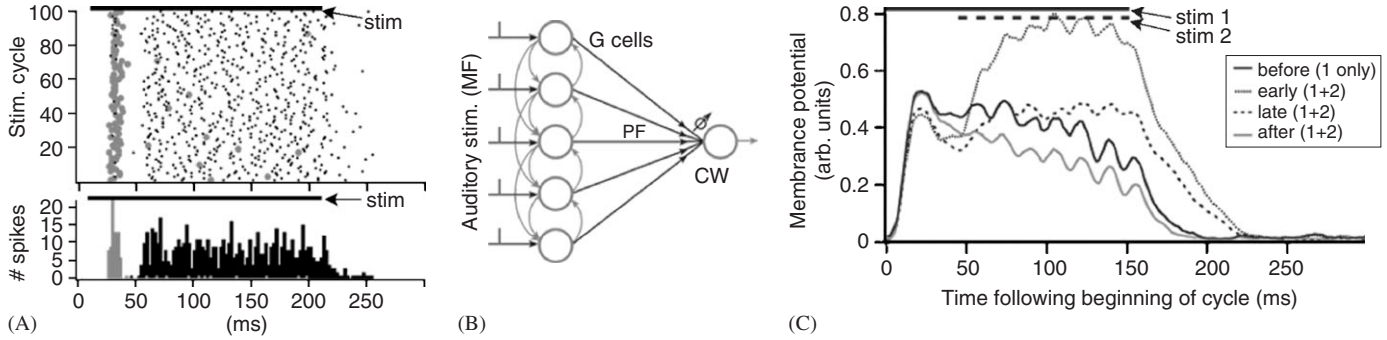

Fig. 2. Adaptation of cartwheel cell predicted by model. (A) Spike responses of cartwheel cell to auditory stimulus (10 kHz, 200 ms, top line) recorded extracellularly in awake mouse. Raster plot (top) shows complex spikes (grey, large dots) initiated with nearly every stimulus onset, and simple spikes (black) outlast stimulus. (B) Recurrent neural network model of DCN with recurrent connections between the 100 granule cells (G). Mossy fiber inputs (MF) auditory stimulus without delay lines. STDP learning rule (Fig. 1) is applied an synapse from parallel fibers (PF) onto cartwheel cell (CW). (C) The membrane potential of simulated cartwheel cell before (solid, black) and after (grey) adaptation by STDP at parallel fiber (PF) synapses to pairing of a second tone (broken, early and late) with the first tone for 75 presentations. Similar results were obtained using integrate-and-fire models that predict a reduction in the response to the initial stimulus following pairing.

reports the presence of a presynaptic spike, $\varepsilon(x_n)$ was the postsynaptic potential waveform, x_n denoted the time within each cycle, and t denoted the cycle. The spike-probability function was defined as $P_i(x_n, t) = (1 + \exp(-\mu(V_i(x_n, t) - \theta)))^{-1}$, where θ is the threshold and μ parametrizes the noise [9,11].

In our simulations, each spiking granule cell was connected to the cartwheel cell by a plastic synapse. The STDP learning rule (Fig. 1B) was applied at each PF synapse onto the cartwheel. The cartwheel cell generated spikes according to its spike-probability function. At the beginning of each cycle, a subset of granule cells received a depolarizing input to represent a postsynaptic potential that initiated the recurrent dynamics. The 100 granule cells were interconnected by weights defined by an orthogonal random weight matrix [13] with eigenvalues <1 [5]. These weights were not varied during adaptation and each synapse contributed to the membrane potential of the postsynaptic granule cell proportionally to the presynaptic spike probability.

3. Results

The fixed point dynamics of the STDP learning rule (Fig. 1B) has been determined previously [10] by expanding the granule cell spike-probability function in the limit of small synaptic strength [9]. The fixed point is the solution of the PF-weights that minimizes the mean squared-difference between the cartwheel cell spike rate and a constant during the stimulus presentation. The learning dynamics implies that the result of pairing two stimuli; (1) a weak auditory stimulus that activates a subset of granule cells and (2) a strong stimulus that activates an independent set of granule cells. The learning dynamics will weaken the weights of stimulus (1) so that after pairing the response to stimulus (1) is reduced during the time-interval when stimulus (2) was presented.

The results of simulations confirmed the analysis. For the period following the initial rise in membrane potential ($x_n > 20$ ms), the membrane potential is flattened for the duration of the stimulation by the STDP learning rule (Fig. 2C). The granule cells exhibit a complicated set of membrane potentials that translate into parallel fiber spikes by the spike-probability function. We have thus shown that the resulting membrane potential of the network shown in Fig. 2B is nearly equivalent to the in vivo result (Fig. 2A).

Our results demonstrate how timing information and STDP are combined to sculpt a negative image of predictable sensory inputs in cartwheel. To predict the effects of adding a second tone to the stimulation, we repeated the simulation, but after the system stabilized to its equilibrium dictated by the learning dynamics, we stimulated a second set of parallel fibers to mimic the introduction of a second tone. The result is shown in Fig. 2C where the second tone first excites the membrane potential, following a latency similar to the first tone, and after 75 pairings of the two tones, the response adapts to a constant response, but slightly extended. When the simulation returns to the condition where only the first tone is presented, then the response is reduced compared to the membrane potential before the pairing took place. We interpret this result to predict that the repeated presentation of a second tone, overlapping with the first tone, will cause the response of cartwheel cells to adapt via STDP so that their response to the first tone alone will be reduced. Thus, cartwheel cells could learn to cancel expected an auditory stimulus that is repeatedly associated with another stimulus.

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