

Temporal and Directional Properties of Barrel Cortical Neurons

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Neurodynamics Course Project, Winter 2008

Abstract

In this project, we use recent findings from electrophysiological recordings and a previous model of the cellular properties of barrel cortical neurons to explore their implications on the dynamic properties of directional tuning in barrel cortex. We find that directional tuning is influenced by the frequency and speed of whisker directions, even in the low frequency range of natural whisking. We also explore the effects of deflecting multiple whiskers under different thalamic and barrel interconnectivity paradigms. Finally, we use the model to propose how recent experimental manipulations of cortical blood flow may influence tuning in the model.

1. Introduction

Rodents such as rats and mice depend on their vibrissae (whiskers) to gain information about their surroundings. Rodents typically whisk at 5-15 Hz during exploratory whisking, and can whisk up to 25 Hz during so called “foveal” whisking [1]. The vibrissa system is an ideal model system for understanding the properties of active sensory processing in the mammalian neocortex, as inputs from each vibrissa are mapped in spatially distinct units in the thalamus and cortex. These units consist of “barrel” shaped fields, where each collection of cells in a barrel corresponds to inputs from one “primary” whisker. The primary whisker drives the cells in its corresponding barreloid (thalamus) and barrel (somatosensory cortex) most strongly, but deflections of other “secondary” whiskers can also modulate the responses in a barrel. In addition to the neatly organized cortical maps of vibrissa space, cells within a barrel are known to be directionally tuned, and it has recently been shown that there are directional tuning maps within single barrels [2]. In these maps, cells with similar preferred directions are found near each other in the barrel. In the present analysis, we explore the proposed mechanisms underlying this directional tuning, and examine the parameters that may modulate directional tuning of barrel cortical neurons. In particular, we examine how tuning may depend on the frequency and speed of whisker deflections, and how simultaneous deflections of multiple whiskers may alter tuning properties. We also briefly explore a novel hypothesis that blood flow may actually directly take part in the neural computations performed in cortex [3,4]. The results of the present analysis, along with previous explorations of similar phenomena [5], suggest that the neural representation of direction is dependent on the context in which stimuli are encountered.

2. Model of Directional Tuning in Barrel Cortex

At least one component of directional tuning in barrel cortex is thought to arise from the amplitude and relative timing of excitatory and inhibitory inputs from thalamus. Recent in vivo electrophysiological recordings have shown that when a whisker is deflected, neurons in layer IV

of rat barrel cortex receive pulses of excitatory and inhibitory conductance, the dynamics of which are dependent on the angle of whisker deflection [6].

When the whisker is deflected along its preferred direction, both conductances are at maximum amplitude. The excitatory pulse occurs approximately 2ms before the inhibitory pulse, causing a brief period of depolarization. As the angle of deflection becomes further from the preferred direction and closer to the null direction, both excitatory and inhibitory conductances decrease, but excitation decreases more than inhibition and arrives later. As a result, the cell is depolarized less and has less time to generate spikes as the direction becomes further from the preferred direction of the cell.

This effect was recently modeled with an integrate and fire model neuron with typical physiological parameters of layer IV barrel cortical neurons [5]. We implemented this model, using the structure and measured numerical values of the excitatory and inhibitory inputs [6, modeled in 5] to explore their various implications for the dynamics of directional tuning properties in barrel cortical neurons. The results of our implementation of the model for single whisker deflections are shown in Fig 1. Here, we defined the preferred direction to be at 0 degrees, and the null direction at 180 degrees. The cell output tuning curve is created by counting the number of spikes evoked by deflections in each direction and dividing by the number of spikes evoked in the preferred direction. Similarly, tuning of the synaptic inputs is computed by integrating the membrane potential without generating spikes, finding the peak value of the membrane potential in the time window following the deflection, and normalizing to the peak membrane potential of the preferred direction.

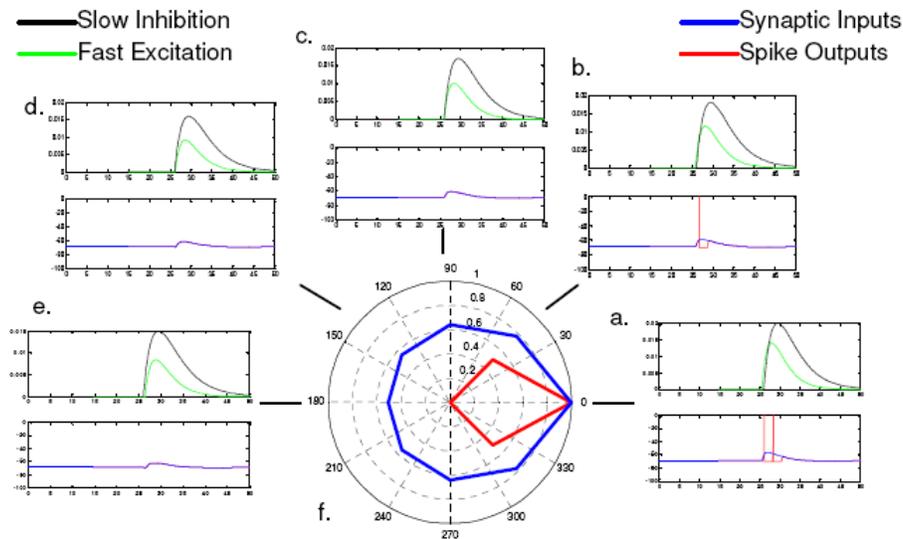


Figure 1. Directionally Tuned Responses to Single Deflections. (a) A barrel neuron tuned to 0 degrees receives fast excitation (green) and slower inhibition (black) following deflections towards 0 degrees. This input results in brief, strong EPSPs (blue) that lead to spikes (red) when the whisker is deflected near 0 degrees. (b-e) Excitation becomes more delayed relative to inhibition at directions away from 0 degrees, leading to fewer spikes. (f) Normalized synaptic and spiking directional tuning profile for this cell.

3. Stimulus Dependence of Directional Tuning Properties

3.1. Frequency Dependence

It has been suggested that the representation of direction in barrel cortex may depend on the nature of the problem the animal is trying to solve. For example, as a rat drags its whiskers across a bumpy surface, it has been shown that the whiskers alternate between being stuck on the bumps and then rapidly released, causing high frequency oscillations [7]. The nature of the deflections may be drastically different from the structure of deflections that occur during exploratory or foveal whisking in the presence of an object, where presumably the whisker contacts an object once per cycle. This raises the possibility that the ability to distinguish direction may be different in the two cases. In Puccini et al., the authors apply a train of directed deflections drawn from a random walk across a diagonally connected grid with Poisson distributed inter-deflection times. They demonstrate that directional tuning is indeed stronger when the deflections occur at a mean rate of 20 Hz than when they occur at a mean rate of 200 Hz.

In our implementation, we applied similar deflection trains with Poisson distributed inter-deflection times, and the direction of each deflection was chosen at random from one of 8 directions (0, 45, 90, 135, 180, 225, 270, 315 degrees; Fig 2).

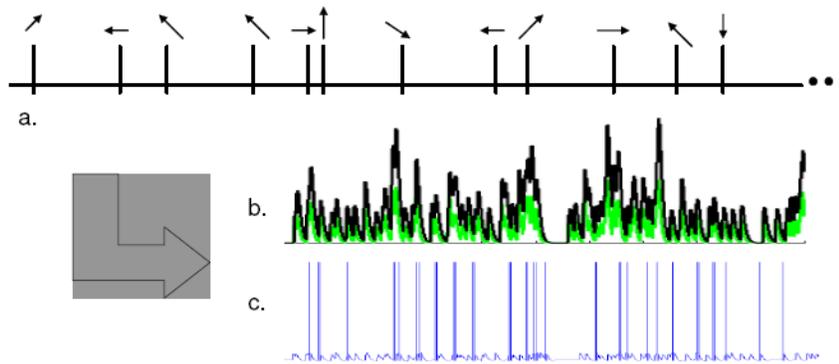


Figure 2. Stimulation Paradigm. (a) Impulse trains of whisker deflections with Poisson distributed interdeflection intervals. Direction of each impulse is selected at random the 8 target directions. (b) This type of stimulation leads to time-varying patterns of excitatory (green) and inhibitory (black) conductances which caused spikes (c) in an integrate and fire model of a layer IV barrel neuron.

Directional tuning was computed by counting the number of spikes in a 30 ms time window following the time of each deflection, and comparing the average number of spikes evoked following each directed deflection. We ran the simulation for 40 seconds, and characterized the magnitude of the directional tuning vector (R , see below) as a metric of the strength of directional tuning. This metric is defined by the vector average of the normalized firing rates ($f.r.$, see below) in the 30 ms windows projected along the direction which evoked them (θ , see below):

$$C = \sum_{i=\text{deflections}} f.r._i \cdot \cos(\theta_i)$$

$$S = \sum_{i=\text{deflections}} f.r._i \cdot \sin(\theta_i)$$

$$R = \sqrt{S^2 + C^2}$$

The variability in the directional tuning magnitude was characterized by resampling with replacement 1000 times from the pairs of firing rates and deflection directions, and then computing the 95% confidence interval for tuning magnitude. The results are shown in Fig 3d.

Our results mimic those of Puccini et al; we observe strong tuning at 20 Hz and weaker tuning at 200 Hz. Unlike Puccini et al, we chose a stimulus that was not necessarily physiologically realizable. This enabled us to not bias our observation of directional tuning at high frequencies. We demonstrate with this model that there is a general tradeoff between directional tuning magnitude and deflection frequency that is consistent across all frequencies from at least 10-250 Hz. This arises from deflections evoking conductance pulses that last several tens of

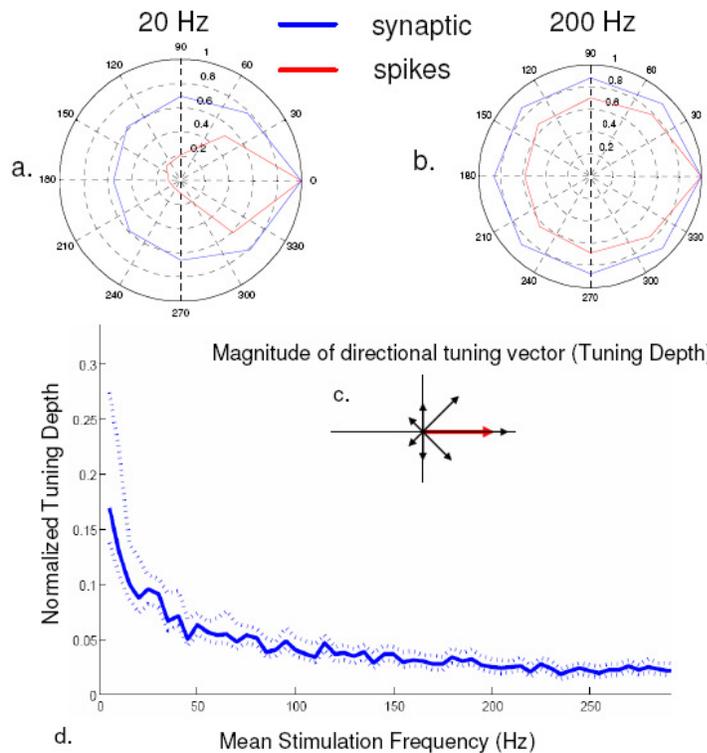


Figure 3. Frequency dependence of directional tuning. (a,b) Typical directional tuning profiles at 20 Hz and 200 Hz. (c) Illustration of definition of tuning depth (d) Dependence of directional tuning magnitude on mean deflection frequency.

milliseconds, and from the membrane effectively low-pass filtering the conductance input before generating spikes. If these pulses occur within a short time period they can summate and drive the cell to threshold even if the most recent deflections are not the preferred direction. Thus, as the rate of information the whisker receives increases, the ability of a single cell to determine the direction of that particular deflection is decreased.

The results of our simulation confirm those of Puccini et al.: that the strength of these conductance-derived directional signals may be context dependent. For example, the direction of

whisker deflections may not be particularly useful or relevant when the animal is attempting to determine the texture of a surface, which is a stimulus likely to drive the whiskers at high frequencies, but may become more relevant if the animal is attempting to determine the shape or position of an object. In addition, we demonstrate that the strength of directional tuning is frequency dependent even in the range of frequencies at which exploratory and foveal whisking occur (5-25 Hz, see Fig 3); in fact, the dependence on frequency is strongest for these low frequencies, suggesting that the animal may be able to shape its neural representation of an object by choosing the frequency with which to whisk. Still, of course, the extent to which the animal uses the information contained in these directional signals even at low frequencies is unknown.

3.2. Deflection Speed Dependence

We also sought to characterize the effect of deflection speed on directional tuning, as the shape of an object or the texture of a surface may affect the temporal pattern of how a whisker is deflected. The previous results assume that a deflection occurs instantaneously, but if the deflection were to happen over a longer period of time, the conductance pulses evoked may also be spread out in time. This would appear to have a similar effect to increasing the frequency of deflections, as it similarly increases the effect of conductance pulses from prior deflections on the number of spikes elicited by the current deflection. Therefore, in our simulation we again used impulse deflection pulse trains in random directions with Poisson distributed deflection times, but the deflection signal was then convolved with a Gaussian smoothing filter. We ran our simulation with different smoothing widths, by varying standard deviation of the Gaussian smoothing window from 0.1ms to 2ms. We characterized the properties of the resulting tuning curves by examining both the tuning depth (as before), and also the tuning width, defined as the (interpolated) angle over which the firing rate is above half its maximum value. The results of our simulation with different smoothing widths are shown in Fig 4, at both 20 Hz and 200 Hz. Fig 4c,d show the shapes of the tuning curves for the most extreme values of the smoothing window width that were tested (0.1 ms and 2ms). In Fig 4f, we show the dependence of the tuning depth parameter on the width of the smoothing window. Indeed, lengthening the time over which a whisker deflection occurs decreases the strength of directional tuning at 20 Hz, but not at 200 Hz. Fig 4g shows the dependence of the tuning width parameter on the smoothing width. Again, at 200 Hz there is broad tuning that is independent of the temporal signature of the whisker deflection. At 20 Hz, though, there was a sharp drop in tuning width as the deflection time increases above ~1ms.

At low frequencies, the decrease in directional tuning strength as the deflections are slowed in time indicates a loss of directional information. However, this loss could be compensated for by the change in the “shape” of the tuning, because the preferred direction becomes more prominent relative to the other directions (decrease in tuning width). Again, we see that another stimulus parameter, deflection speed, can alter the neural representation of direction in barrel cortical neurons. This change in representation could allow an animal to switch its strategy for computing direction as the nature of the input changes. Whether the animal actually uses these potential cues remains to be tested experimentally.

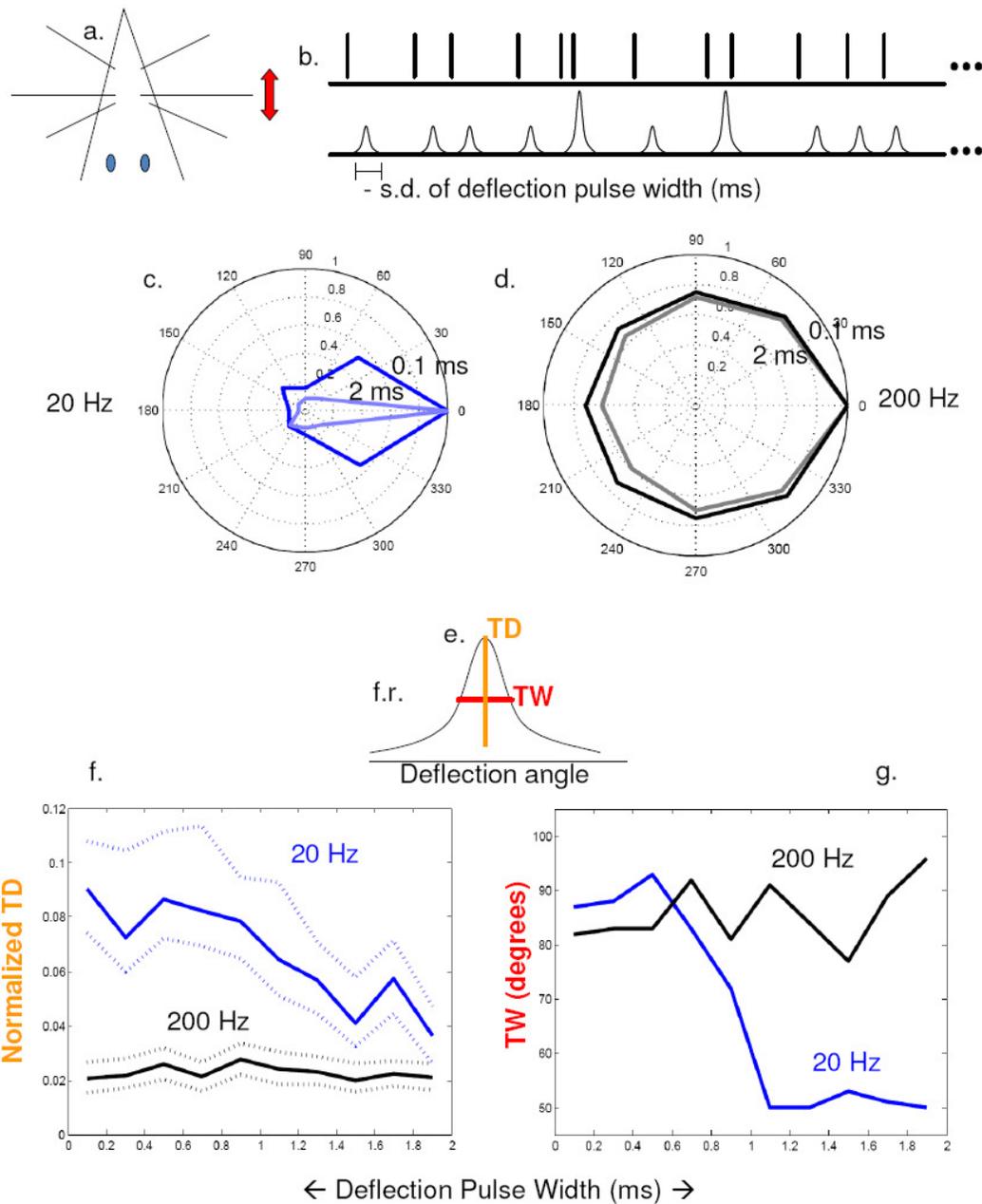


Figure 4. Deflection Speed Dependent Directional Tuning. (a) Illustration of the position of a whisker undergoing a deflection. (b) Example time course of whisker displacements. (c) Tuning profile (of spikes) for fast and slow deflections at a mean frequency of 20 Hz. (d) Same as c, except the mean deflection frequency is 200 Hz. (e) Illustration of the definition tuning width and tuning depth parameters. (f) Tuning depth vs. deflection speed at 20 Hz (blue) and 200 Hz (black). (g) Tuning width vs deflection speed at 20 Hz (blue) and 200 Hz (black).

4. Thalamic and Barrel Connectivity

Although whisker barrels are classically known to respond to one “primary” vibrissa, they can receive input from non-primary vibrissae as well, either directly or indirectly. Here, we define a

vibrissa next to the primary vibrissa as the secondary vibrissa. Input from a secondary vibrissa is delayed by ~ 5 ms relative to input from the primary vibrissa [8]. In other words, if a deflection of the primary vibrissa result in a postsynaptic potential (PSP) 10 ms later, a deflection of the secondary vibrissa will result in a PSP 15 ms later. The magnitude of the PSP is reduced as well. A PSP from the primary vibrissa will be roughly twice the magnitude of the PSP from a secondary vibrissa [8,9]. Our model took this into account by adding a time delay of 5 ms to the PSP evoked by vibrissa stimulation, and halving the peak conductance to account for the reduction of the PSP. In our simulation, both the primary and secondary whiskers were always deflected simultaneously in the same direction.

The exact circuit and synaptic conductances are unclear. Therefore, we modeled the input from secondary whiskers in two ways. We first assumed that the barrel corresponding to the primary whisker receives input only from the secondary whisker barrel neurons tuned to the same direction. In this case, there was an increase in the tuning width of the cell (Fig. 5). This was the result of very slight increases in excitatory input causing the cell to spike when it previously would not.

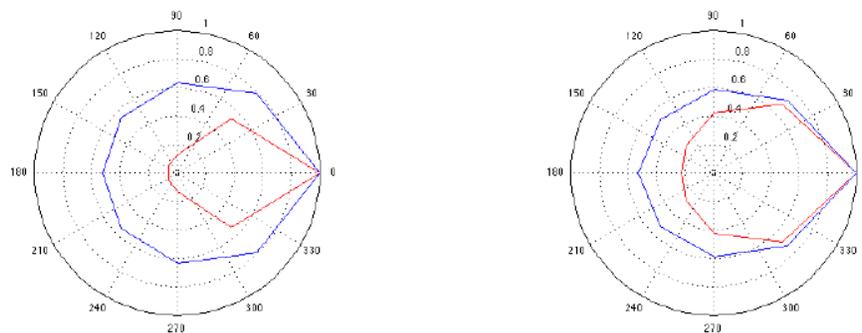


Figure 5. Effect Of Input From Secondary Whisker With One Connection
 Red is the tuning profile with input solely from one whisker, blue is from two whiskers. The stimulus is 20 Hz (*left*) and 200 Hz (*right*). Tuning width increases with secondary input. In this case, the input is of deflections in a single direction.

The thalamic input could also arrive from a series of inputs such that every tuning direction is represented. We used connections tuned to eight steps of 45 degrees in order to represent “every” direction (Fig. 6). To maintain an overall halving of synaptic conductance from these inputs, each input was reduced to one-eighth strength. In this case, tuning was still broader than with single whisker deflections, but much less so than in the previous case. This was due to inhibition increasing everywhere affected by synaptic input. This broadening of tuning in both these cases is perhaps surprising, as there would appear to be more information about direction in when multiple whiskers are deflected. Again, though, broad tuning may better represent direction under some coding schema. It is also possible that if the stimulus is large enough to hit two whiskers then direction might not be as relevant.

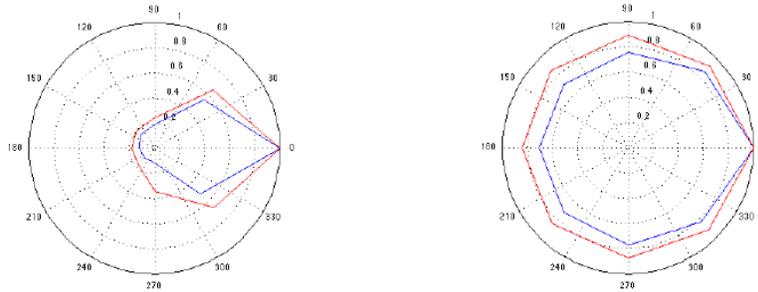


Figure 6. Effect Of Input From Secondary Whisker With Eight Connections
 Blue is the tuning profile with input solely from one whisker, red is from two whiskers. The stimulus is 20 Hz (*left*) and 200 Hz (*right*). Tuning width increases with secondary input but much less so than when there is only one extra thalamic input. In this case, the input is of deflections in every direction.

5. Blood flow

Recent evidence has shown that dilated blood vessels increase the resting potential of a cell [4]. This suggests that blood flow can take part in neural computation. To determine the effect on whisker barrel directional tuning, we ran our model with different resting potentials (Fig. 7). When the resting potential was lower, corresponding to decreased blood flow, there was a marked increase in directional sensitivity. Conversely, when blood flow was increased the directional tuning widened. This suggests that blood flow may indeed have a significant effect on computational properties of a cell.

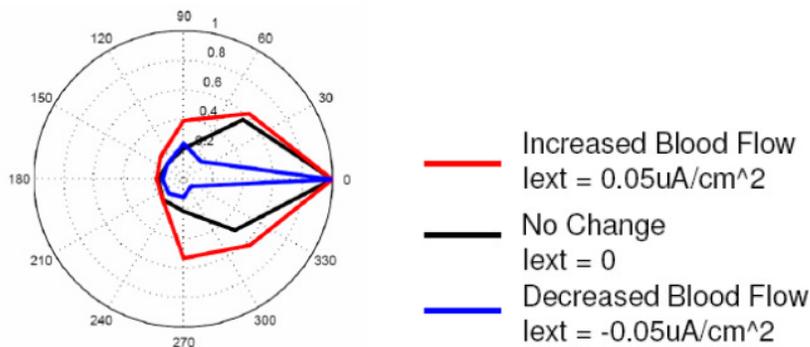


Figure 7. Potential effect of cortical blood flow on directional tuning. The resting potential of the cell was elevated or depressed by injecting a steady state external current, to model the effects of vasodilation (or constriction) in recent experimental findings (see text).

6. Conclusion

The model of Puccini et al. provides a basis for investigation of directional sensitivity in rodent barrel cortex. Using a novel set of stimuli, frequency and deflection speed were found to be determinants of directional sensitivity across many stimulus conditions, highlighting that

“directional tuning” of barrel cortical neurons is meaningless unless we have a notion of the context in which the stimulus is encountered.

We further determined the effects of simultaneous stimulation of primary and non-primary vibrissa. If it is assumed that secondary thalamic inputs to barrel cortex behave in a similarly directional-sensitive way as the primary inputs, the result is a massive decrease in directional selectivity. However, as the number of differentially selective inputs increases, the tuning also increases. This is due to the dynamics of the excitatory and inhibitory inputs.

Finally, we examined whether the effects of increased blood flow substantially change the computation of a directionally selective cell. We showed that, given the recent results from vaso-dilation experiments, blood flow may be able to alter the directional tuning properties of a cell. Perhaps actively regulating blood flow to the barrel field may be able to set an optimal level of tuning for the task at hand.

In this paper we demonstrate that in the rat whisker barrel, both intrinsic and extrinsic features can affect tuning: stimulus context and blood flow. Furthermore, knowing the precise tuning properties of connections (convergence of inputs and barrel inter-connectivity) may help us understand how direction is computed in barrel cortex. However, it remains to be seen how this form of directional selectivity is affected by stimuli in recordings from awake behaving animals, and whether or not directional cues are actually used by the animal. Perhaps rodents change their whisking patterns over time or depending on the type of surface presented to them. Inter- and intra-barrel dynamics can also play potential roles in orientation discrimination. Are there other potential mechanisms underlying directional tuning in barrel cortex? Are there cases where a rodent would *want* a cell to be less directionally tuned? These questions remain open for future work.

7. References

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