Roles of Feedforward and Feedback Inhibition in Controlling Propagating Waves in Visual Cortex

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Abstract

Three populations of inhbitory interneurons in turtle visual cortex that control the generation and propagation of waves of depolarizing activity were studied using a large-scale model of turtle visual cortex. The strength of the inhibitory synapses was altered by changing the value of g_{max} in the synaptic current function specifying $GABA_A$ receptors postsynaptic to supbial, stellate and horizontal cells. Subpial cells control the generation of the waves, but do not have a strong effect on their velocity or duration. Stellate and horizontal cells have little effect on their velocity of the wave, but have a strong influence on their duration.

1. Introduction

The visual cortex of freshwater turtles contains neurons responsive to moving stimuli anywhere in binocular visual space [2], suggesting this cortical area is involved in global motion analysis [8]. Visual stimuli produce waves of activity that originate near the rostral pole of turtle visual cortex and then propagate caudally and medially through the cortex [5, 6]. Comparable waves occur in a large-scale model of turtle visual cortex following simulated activation of geniculate neurons [4]. The spatiotemporal dynamics of these waves appears to contain information about stimuli in visual space in both real and model cortices. One goal of our research is to understand how cellular mechanisms, such as the excitatory and inhibitory mechanisms present in cortical microcircuits, control the generation and propagation of these waves. Turtle visual cortex contains several populations of anatomically distinct inhibitory interneurons [1]. One population, the subpial cells, is embedded in the fascicle formed by afferents from the dorsal lateral geniculate complex as they course through the cortex and is likely involved in feedforward inhibition of pyramidal cells. A second population, the stellate cells, is positioned to receive both geniculate and pyramidal cell inputs and can play a role in both feedforward and feedback inhibition. A third population, the horizontal cells, is dominated by input from pyramidal cells and probably has its principal role in feedback inhibition. This study uses a large-scale model of turtle

visual cortex [4] to investigate the roles of feedforward and feedback inhibition in controlling the activity of propagating waves in the visual cortex of freshwater turtles.

2. Methods

Simulations were carried out with a large-scale model of turtle visual cortex implemented in *Genesis*. The model was similar to that recently described by Nenadic et al. (2003), except that a population of subpial cells was added for the current study. In brief, the model consists of 788 cortical neurons and 201 geniculate neurons. The cortex contains 44 subpial cells, 45 stellate cells and 20 horizontal cells. Each cortical neuron is a multicompartmental model constructed using the known anatomy of a specific cell type. Biophysical characterizations of the passive properties of each cell type are available. The detailed kinetics of voltage-gated conductances are not known for turtle cortical neurons, but the firing pattern of each type of neuron was matched to the firing pattern of the same type of real neuron following intrasomatic current injections. Pyramidal cells and subpial cells show spike rate adaptation while stellate and horizontal cells show no spike rate adaptation. Inhibition of pyramidal cells by subpial, stellate and horizontal cells was by both $GABA_A$ and $GABA_B$ receptor-mediated inhibition. In addition, subpial and stellate cells inhibited each other. The propagation velocity of the waves produced by simultaneous activation of all of the geniculate neurons was measured by plotting the half height latency of the waves [7]. The duration of the wave was the time required for activity in the cortex to decline to its prestimulus level. The strength of $GABA_A$ -mediated inhibition on pyramidals cells postsynaptic to each population of inhibitory interneurons was systematically varied by changing the magnitude of the g_{max} factor in the postsynaptic current function.

3. Results

Wave velocity. A wave of depolarizing activity orginates near the rostral pole of visual cortex and propagates anisotropically across the cortex in both turtles and the model following real or simulated visual stimulation. The propagation velocity ranges from 7 μm/ms to 40 μm/ms. Figure 1 illustrates the effect of changing the magnitude of $GABA_A$ postsynaptic conductance of afferents from subpial cells on pyramidal cells. Increasing or decreasing the $GABA_A$ conductance of subpial cell afferents on pyramidal cells controls the formation of the wave. Low $GABA_A$ conductances result in a wave that propagates with a velocity of approximately 8 μm/ms. Conductances above 5 nS result in a depolarizing response, but no wave propagates. The wave, thus, has a propagation velocity of 0 μm/ms. By contrast, varying the $GABA_A$ conductance postsynaptic to stellate and horizontal cell afferents on pyramidal cells has no influence on the formation or propagation velocity of the wave.

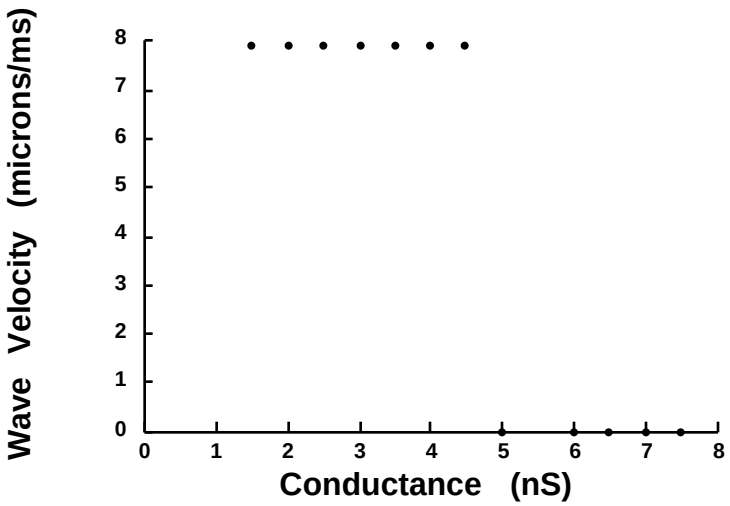

Fig. 1. Velocity of the cortical wave resulting from simultaneous activation of all of the geniculate neurons as a function of the strength of synapses effected by subpial cells on pyramidal cells.

Wave duration. It takes approximately 200 ms for the wave to propagate diagonally across the cortex from its rostrolateral to caudomedial poles. Some level of activity typically persists for an additional 600 ms, so the total duration of waves is approximately 800 ms. Figure 2 illustrates the effect of changing $GABA_A$ conductance postsynaptic to subpial (Fig. 2A), stellate (Fig. 2B) and horizontal (Fig. 2C) afferents. Low $GABA_A$ conductances postsynaptic to subpial afferents result in a wave with a duration of approximately 800 ms. Increasing the $GABA_A$ conductance above 4.5 nS results in a depolarization with a duration of about 300 ms, although a propagating wave is not generated. Increasing or decreasing the $GABA_A$ conductance postsynaptic to both stellate and horizontal cell afferents on pyramidal cells has a marked effect on wave duration. Conductances below 3.0 nS result in waves that last through the duration of the simulation (1,500 ms). Conductances above 3.0 nS result in waves that decrease in duration as the conductance increases. Conductances greater than 7.5 nS result in depolarizing responses that do not propagate.

3. **Discussion**

This study used a large-scale model of turtle visual cortex to study the relative contributions of different populations of inhibitory interneurons on the dynamics of propagating waves in the visual cortex of freshwater turtles. It indicates that feedforward inhibition, mediated by subpial

cells, plays a major role in controlling the formation of the wave. By contrast, feedback inhibition mediated by both stellate and horizontal cells is important in regulating the duration of the wave. Presumed pyramidal cells in turtle visual cortex respond preferentially to moving stimuli or two spots of light presented at different points in visual space with a temporal separation in an apparent motion paradigm, but respond poorly to simultaneous activation of two, spatially separated spots of light [2]. Cells in the outer half of layer 1, by contrast, respond preferentially to two simultaneously activated spots of light. This region of layer 1 is populated by subpial cells. Since subpial cells are inhibitory interneurons it is reasonable to hypothesize that they inhibit pyramidal cells when active, decreasing the probability that they respond to transient fluctuations in light intensity. This is a desired feature of cells involved in analyzing moving stimuli (Ulinski, 1999) that would bias the motion analysis system against fluctuations in light intensity caused by stationary stimuli. By contrast, the simulations presented here suggest that stellate and horizontal cells play little or no role in regulating the genesis of the wave, but do control the duration of the wave. This feature of the inhibitory feedback circuits of the cortex may not have a functional significance when the stimulus is a flash of light, but would be important in determining the frequency response properties of the cortical circuits when the system is presented with a temporally varying light intensity function.

Acknowledgement

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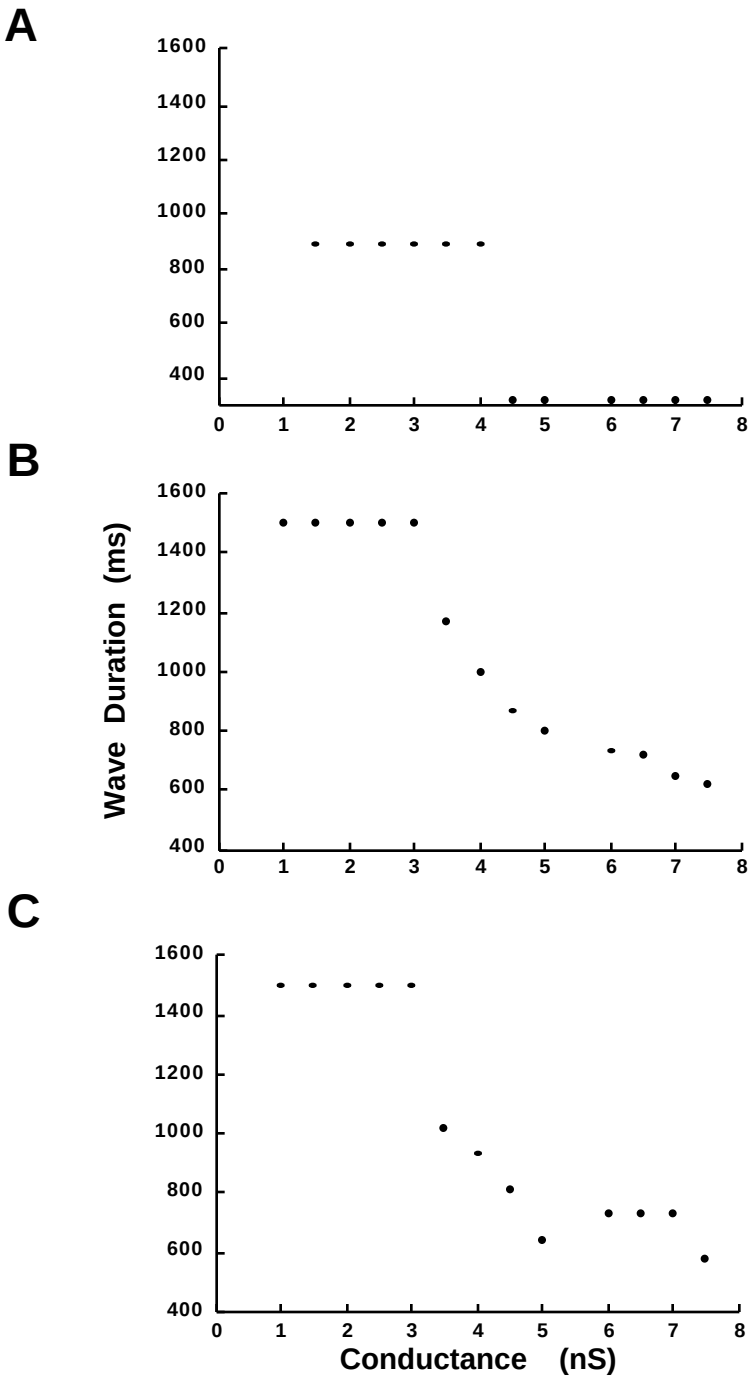

Fig. 2. Duration of the cortical wave resulting from simultaneous activation of all of the geniculate neurons as a function of the strength of synapses effected by subpial (A), stellate (B) and horizontal (C) cells on pyramidal cells.

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