

# Cortical Adaptation to Aperiodic Tactile Stimuli

Kathy K. Miu<sup>1</sup>, Roxanna M. Webber<sup>2</sup>, and Garrett B. Stanley<sup>1</sup>

<sup>1</sup>*Division of Engineering and Applied Sciences, Harvard University; and* <sup>2</sup>*Harvard-Massachusetts Institute of Technology Division of Health Sciences and Technology, Cambridge, Massachusetts 02138*

**Miu, Kathy K., Roxanna M. Webber, and Garrett B. Stanley.** Cortical Adaptation to Aperiodic Tactile Stimuli. Adaptation of Sprague-Dawley rat neurons to repetitive vibrissa deflection was investigated with respect to the regularity of the applied stimulus. Neurons in the barrel cortex responded to whisker deflection trains of 2 natures: one beginning with 4 s of periodic pulses, and the other with pulses at irregular intervals. Following, cells were allowed a short rest, and then were probed by 2 s of periodic pulses. Cells were allowed a recovery period of 8 s between trials. In preliminary tests, cells responded generally the same to both classes of stimuli. Spiking rate was highest for the first pulse of each test and declined during successive pulses. Response heightened slightly on the first pulse following rest, only to adapt again to subsequent pulses. Differences between higher frequency stimuli evoked responses were more difficult to discriminate. Further data is necessary toward a more quantitative comparison.

## INTRODUCTION

Rats move their vibrissae, or whiskers, as a means to detect and differentiate the textures of their environment (Carvell and Simons, 1990). Vibrissae generally remain motionless when the rat is resting. In other situations, rats are found to whisk, or actively move their vibrissae, between 4 to 12 Hz, as observed when the animal is surveying its environment. Higher frequency motion can occur when a vibrissa resonates off a surface (Moore, 2004).

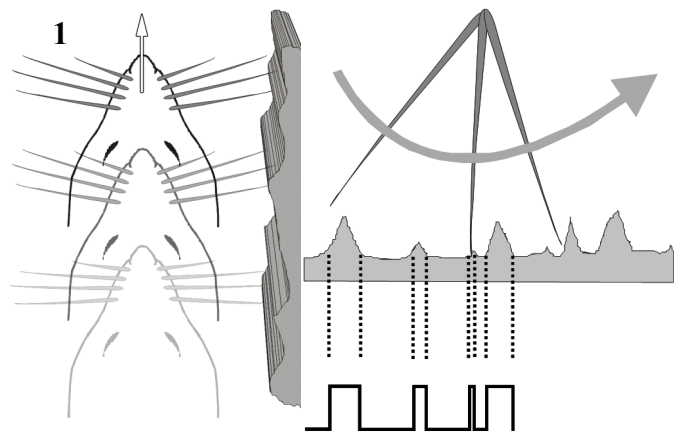
Adaptation, or a decline in action potential firing in the presence of a repetitive stimulus, occurs in cells of the somatosensory cortex when the vibrissae are stimulated at frequencies exceeding 1 Hz (Ahissar *et al.*, 2001; Chung *et al.*, 2002). Adaptation has been demonstrated in the thalamus and barrel cortex using periodic stimuli (Chung *et al.*, 2002; Hartings *et al.*, 2003; Khatri *et al.*, 2004). In the natural environment, textures are rarely found as regular (fig. 1) as they are simulated in the lab setting. In this study, adaptation was characterized using stimuli that were aperiodic. We questioned whether adaptation was a function of the regularity of the signal or if the phenomenon was

contingent upon the number of stimuli applied over a small time interval. Though adaptation was expected, the response to the periodic control and the aperiodic test stimuli were anticipated to be unequal. If it is found that the cells actually do respond differently based on temporal irregularity, the disparity between firing rates should be the most apparent with the lower frequency stimuli, perhaps suggesting that the cells take a longer time to adapt to a stimulus that deviates the greatest from the periodic control and that cells recover more readily from such a stimulus. More data is being collected to quantify the neuronal firing rates and to form a conclusion.

## METHODS

### *Animals and Surgical Preparation*

Three female adult Sprague-Dawley rats weighing 250–300 g (Charles River Facility, Wilmington, MA) were individually prepared as experimental subjects using previously described methods (Webber, 2004). 2% vaporized isoflurane was used to initially sedate the animal, which was then injected intraperitoneally with a sodium pentobarbital (50 mg/kg) anesthetic. Fur was shaved from the head to clear the surgical area. Teramycin ointment was applied to the animal's eyes. The animal was subcutaneously injected with 1 mL



**Figure 1.** Hypothetical aperiodic vibrissa deflection encountered by a rat while running across a texture.

lactated ringer's solution (Baxter Healthcare Corporation, Deerfield, IL) for hydration, and intramuscularly injected with atropine (0.09 mg/kg) to prevent secretions in the lung. The animal was transferred to a stereotaxic frame (Koph Instruments, Tujunga, CA), on top of a 38°C heating pad. Betadine was used to clean the area of incision, and lidocaine was injected as a local anesthetic. Skin, connective tissue, and left temporal muscle were surgically removed, allowing for a craniotomy on the left parietal bone, 3.0–7.0 mm lateral to the midline and 2.0–5.0 mm caudal to the bregma, to expose the barrel region of the primary somatosensory cortex (Paxinos and Watson, 1998). Exposed dura was covered in mineral oil. Throughout the experiment, respiratory rate and pinch reflexes were used to assess the animal's condition. The animal remained anesthetized with periodic injections of pentobarbital (12.5 mg/kg), and 0.5 mL euthasol was used to euthanize the animal at the end of the experiment. The protocol was approved by the Harvard University Animal Care and Use Committee and was in accordance with the guidelines set forth by the National Institutes of Health.

#### *Vibrissa stimulation and electrophysiological recordings*

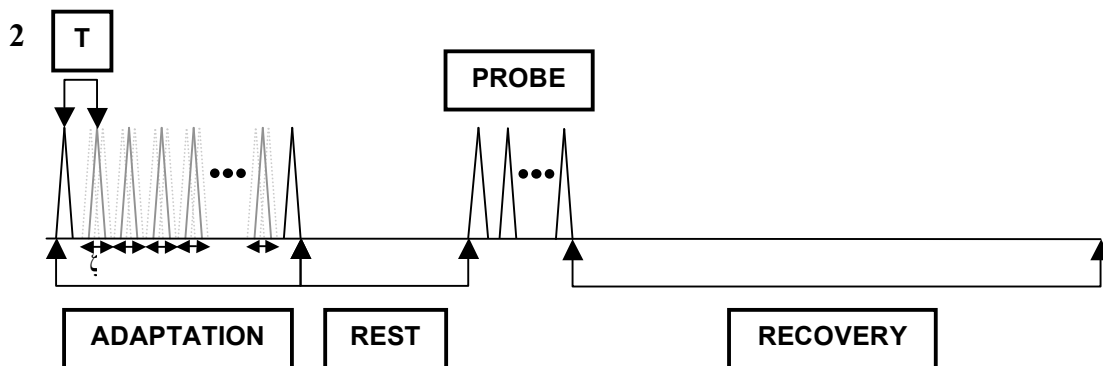
Controlled vibrissa deflections were implemented in the rostral-caudal direction with a multilayered piezoelectric bending actuator (Polytech PI, Auburn, MA), as described previously (Webber 2004). The principal whisker, or vibrissa that induced the greatest response from the cell when deflected, was inserted into a 20- $\mu$ L glass pipette attached to the actuator.

Stimulus trains were constructed using short pulses that deflected the vibrissa 700  $\mu$ m in the rostral direction and back in the caudal direction within 10 ms. In this study, stimuli (fig. 2) consisted of a 4 s adaptation period of either  $n$  periodic or

aperiodic pulses, a 1 s rest insufficient for full recovery from adaptation (Chung, 2002), a 2 s periodic probe period of  $n/2$  pulses, and an 8 s recovery period between trials. Aperiodic adaptation periods were generated by jittering the pulses in the 2 to  $n-1$  positions by  $\zeta$ , a random number taken from the Gaussian normal distribution, with mean 0 and either standard deviation 0.5 or 1, depending on the date of the stimulus generation, multiplied by  $\sigma$ , which was 10, 15, 20, or 35 percent of the period  $T$ . Trains were generated for 4, 6, 8, 16, 30, 40, and 64 Hz. Trains for each frequency and  $\zeta$  ran for 5 min, amounting to approximately 20 trials per unique stimulus. No particular sequence was used to run the stimulus trains in their entirety from cell to cell.

LabWindows software (National Instruments, Austin, TX) was used to handle the voltage output to the actuator and the data acquisition. A tungsten microelectrode (4–5 M $\Omega$ , FHC, Bowdoinham, ME) was inserted into the cortex in the area of the craniotomy, at a depth of 500 to 900  $\mu$ m. Signals were amplified (A-M Systems, Sequim, WA), band-pass filtered between 300–5000 Hz, and sampled at 20 k samples/s with 16-bit resolution. Upon discovering a cell for extracellular recording, the principal whisker was determined by trial and error. Recordings were taken from neurons that primarily responded to 1 whisker, and at most 2, suggesting that the electrode was located within the barrel cortex, as additionally supported by previous reports on the depth of the barrel region (Simons, 1978).

Raster plots and peristimulus time histograms (PSTHs) were generated to characterize the spiking rate of cells. The responses of the cell during the experiment were recorded as spike trains separated by each trial. For each stimulus applied, the cell's firing rate was averaged across all trials, and added into 1-ms bins that were plotted in the form of a PSTH.

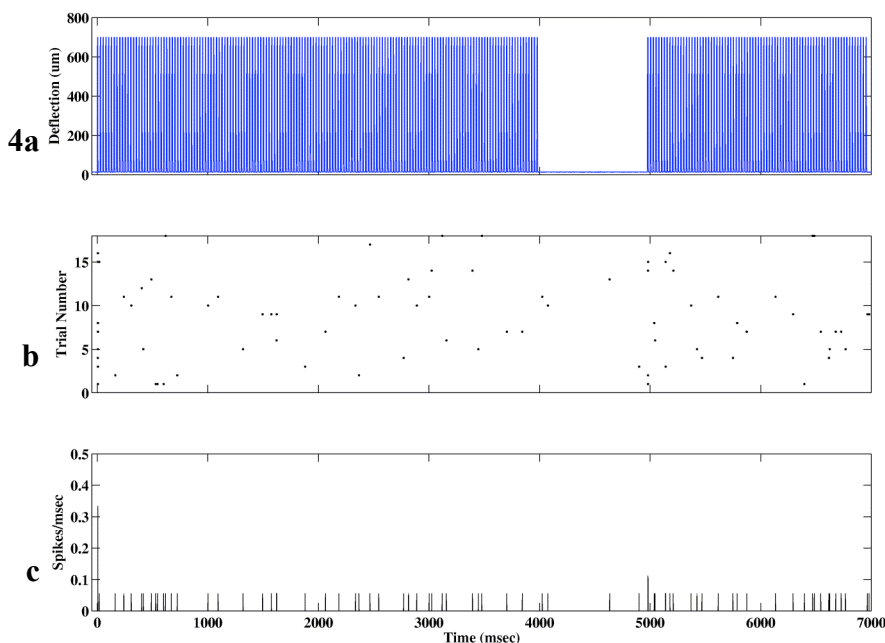


**Figure 2.** Stimulus train template. For control stimuli,  $\zeta = 0$ . For jittered stimuli,  $\zeta = \sigma * randn$ , where  $\sigma = \{.1T, .15T, .2T, .35T\}$ , and  $randn$  is a randomly generated number from the Gaussian normal distribution with mean 0 and standard deviation 0.5 or 1.

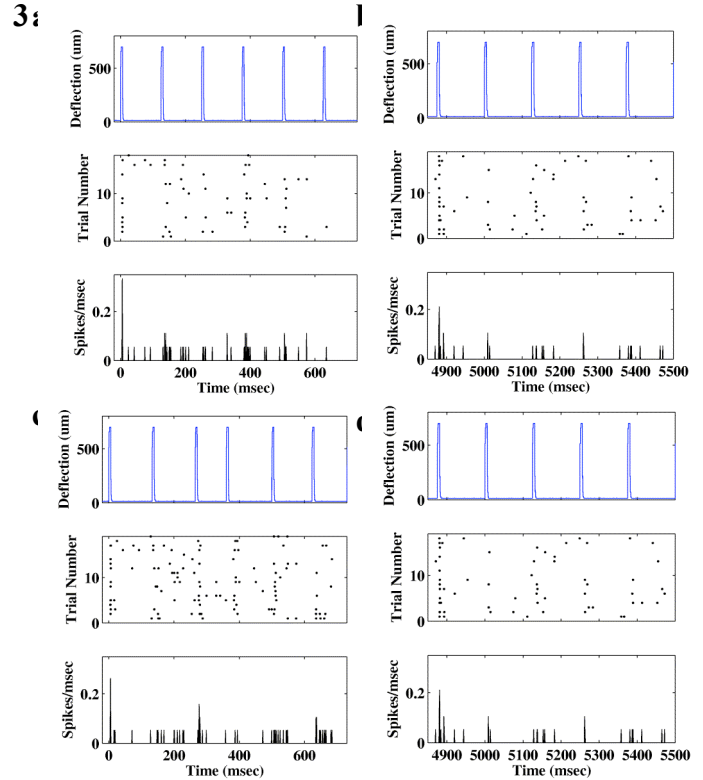
PRELIMINARY RESULTS AND DISCUSSION

In initial tests, cells responded qualitatively the same to both the periodic and aperiodic classes of stimuli (figs. 3a, b, c, d). The first pulse of each test elicited the greatest spiking rate, which exponentially declined after each successive pulse and plateaued to a spontaneous level of response. During rest, the cell recovered slightly from adaptation, as demonstrated by heightened response on the first pulse of the probe period. The initial response to the probe seemed to show that the cell did not experience full recovery during the 1 s rest, but the current stimulus in use is not sufficient enough for characterizing the effect of aperiodic stimuli on the rate of recovery. After prolonged exposure to the probe, the cell adapted as expected to the repeated pulses. The response rates during the probe periods have yet to be compared to each other or to the response during the earlier adaptation periods. There is not enough data yet to numerically contrast the response rates of the cells to the regular and jittered adaptation periods and to the probe periods that followed. This task is especially challenging because the spontaneous activity of individual cells has made the decay function difficult to estimate in this preliminary work.

Cells from the first experiment adapted almost immediately to the 64 Hz trains, which were removed altogether from the procedure due to the mechanical improbabilities of producing whisker deflections that deviated from the control by only 1–3 ms. Rapid adaptation to the 40 Hz stimulus was also witnessed, and data from the 40 Hz trains have been collected from all animals as an example of neuronal response



**Figure 4.** *a.* 40 Hz periodic deflections of a vibrissa during one stimulus train, excluding the 8 s recovery period. *b.* Corresponding raster plot of the cell's spiking activity for each trial. Points denote times when the cell fired an action potential. *c.* PSTH summarizing the cell's spiking rate in the presence of the 40 Hz periodic stimuli, consistent with the trends of other cells to stimuli of varying frequencies.



**Figure 3.** Recordings obtained from: *a.* the first 700 ms of an 8 Hz periodic stimulus; *b.* the first 600 ms of the probe period following the 8 Hz periodic adaptation; *c.* the first 700 ms of the 8 Hz jittered ( $\sigma = .20T$ ) stimulus; *d.* the first 600 ms of the probe period following the 8 Hz jittered adaptation.

to high frequency deflections (fig. 4). Data from midrange frequencies between 16–40 Hz, except for 30 Hz, have not been collected, and may be included in later study.

#### ACKNOWLEDGMENTS

We thank the members of the Harvard BioControls Laboratory, for their continual support and helpful comments, and the staff of the Harvard Biological Laboratories, for the care of our rats.

#### GRANTS

This work has been supported by the Herchel Smith Harvard Undergraduate Summer Research Fellowship and the National Science Foundation Research Experience for Undergraduates (REU) program.

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