

16 to 20 hours at 60°C. Sections were then washed through 4× SSC, treated with ribonuclease A (20 µg/ml) in 10 mM tris-saline (pH 8) with 1 mM EDTA for 30 min at 45°C, washed through descending concentrations of SSC to 0.1× SSC at 60°C for 1 hour, mounted onto gelatin-coated slides, and air-dried. The distribution of hybridization was evaluated with both film (Amersham βmax) and emulsion (Kodak NTB2) autoradiographic techniques with exposure times of 3 to 5 days and 2 to 6 weeks, respectively. For densitometric analysis, film autoradiograms were calibrated relative to ³⁵S-labeled brain paste standards (exposed, with tissue, to each sheet of film) by using The Microcomputer Imaging Device (Imaging Research).

11. J. Scott *et al.*, *Nature* **302**, 538 (1983).
12. Antisense mouse NGF RNA probes (370 bases) were transcribed from Bam HI linearized pIB701 (Fig. 2A) with T3 RNA polymerase in the presence of [³⁵S]uridine 5'-(α-thio)triphosphate.
13. S. R. Whittemore *et al.*, *J. Neurosci. Res.* **20**, 403 (1988).
14. M. A. Schwarz *et al.*, *J. Neurochem.* **52**, 1203 (1989).
15. Control sense strand RNA probes (380 bases) for mouse NGF were transcribed from Hind III linearized pIB701 (Fig. 2A) with T7 RNA polymerase.
16. C. Ayer-LeLievre *et al.*, *Science* **240**, 1339 (1988); P. D. Rennett and G. Heinrich, *Biochem. Biophys. Res. Commun.* **138**, 813 (1986).
17. R. H. Edwards *et al.*, *Nature* **319**, 784 (1986).
18. M. J. Selby, R. Edwards, F. Sharp, W. J. Rutter, *Mol. Cell. Biol.* **7**, 3057 (1987).
19. S. R. Whittemore *et al.*, *J. Neurosci.* **7**, 244 (1987).
20. L. Larkfors, I. Stromberg, T. Ebendal, L. Olson, *J. Neurosci. Res.* **18**, 525 (1987).
21. R. H. Edwards, M. J. Selby, P. D. Garcia, W. J. Rutter, *J. Biol. Chem.* **263**, 6810 (1988).
22. J. I. Morgan, D. R. Cohen, J. L. Hempstead, T. Curran, *Science* **237**, 192 (1987); D. W. Saffen *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **85**, 7795 (1988); J. D. White and C. M. Gall, *Mol. Brain Res.* **3**, 21 (1987).
23. C. Gall, *J. Neurosci.* **8**, 1852 (1988); J. D. White, C. M. Gall, J. F. McKelvy, *ibid.* **7**, 753 (1987); C. M. Gall and J. D. White, in *The Hippocampus, New Vistas*, V. Chan-Palay, Ed. (Liss, New York, in press); G. L. Yont, C. M. Gall, J. D. White, *Soc. Neurosci. Abstr.*, in press.
24. B. J. Morris *et al.*, *Neurosci. Lett.* **80**, 298 (1987); B. J. Morris *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **85**, 3226 (1988).
25. C. R. Buck, H. J. Martinez, M. V. Chao, I. B. Black, *Dev. Brain Res.* **44**, 259 (1988).
26. M. E. Greenberg *et al.*, *Science* **234**, 80 (1986); J. I. Morgan and T. Curran, *Nature* **322**, 552 (1986).
27. J. M. Allen *et al.*, *Brain Res.* **427**, 1 (1987).
28. T. Sutula, X. X. He, J. Cavazos, G. Scott, *Science* **239**, 1147 (1988); M. Bundman *et al.*, *Soc. Neurosci. Abstr.* **14**, 833 (1988).
29. Total RNA was purified by the method of Chirgwin *et al.* (30) from pooled CA1-dentate gyrus and retrohippocampal cortex (including entorhinal cortex) samples from control and HL rats. RNA samples (usually 10 µg of total RNA) with 25 µg of wheat germ transfer RNA were annealed to an excess of ³²P-labeled DNA or RNA probe for 16 hours at 57°C in 80% formamide, 0.4M NaCl, 40 mM Pipes (pH 6.4), and 1 mM EDTA in a total volume of 10 µl. Samples were diluted to 200 µl with 0.25M NaCl, denatured salmon sperm DNA (200 µg/ml), 1 mM ZnSO₄, and 30 mM sodium acetate (pH 4.6) and digested with 200 units of S1 nuclease (Pharmacia) for 2 hours at 37°C. Ethanol-precipitated samples were separated by electrophoresis on 6% polyacrylamide:7M urea gels and exposed to Kodak XAR5 film 1 to 5 days.
30. J. M. Chirgwin *et al.*, *Biochemistry* **24**, 5294 (1979).
31. We thank J. Scott for providing the mouse β-NGF cDNA clone; S. Whittemore for providing the rat β-NGF cDNA clone; G. Lynch and R. Bradshaw for helpful comments; and J. Lauterborn, K. Murray, and D. Benson for technical assistance. Supported by NS26748 and NS00915 to C.M.G. and NS24747 and a grant from Alzheimer's Disease and Related Disorders Association to P.J.I.

14 February 1989; accepted 29 June 1989

Neuronal Correlates of Subjective Visual Perception

NIKOS K. LOGOTHETIS AND JEFFREY D. SCHALL*

Neuronal activity in the superior temporal sulcus of monkeys, a cortical region that plays an important role in analyzing visual motion, was related to the subjective perception of movement during a visual task. Single neurons were recorded while monkeys (*Macaca mulatta*) discriminated the direction of motion of stimuli that could be seen moving in either of two directions during binocular rivalry. The activity of many neurons was dictated by the retinal stimulus. Other neurons, however, reflected the monkeys' reported perception of motion direction, indicating that these neurons in the superior temporal sulcus may mediate the perceptual experience of a moving object.

NEURONS IN THE VISUAL CORTEX of higher mammals respond only to specific properties of visual stimuli (1). One way to distinguish neuronal activity related to perceptual processes rather than to physical stimulus characteristics is to expose the visual system to stimuli that allow more than one percept. When the visual cues provided are enough to dictate one description of the visual scene, perception is unique and stable. But when the sensory data are insufficient for just one interpretation, rival possibilities are entertained and perception becomes ambiguous, switching between the alternatives. Binocular rivalry, a percept that ensues when dissimilar stimuli are presented to the two eyes, is a typical instance of perceptual instability (2). Because such stimuli cannot be fused by the cyclopean visual system, the perception alternates between the stimulus seen by the right eye alone or the left eye alone. For example, when the right eye is presented with upward movement and the left eye with downward movement, the perceived motion alternates between up and down.

The middle temporal (MT) and medial superior temporal areas in the superior temporal sulcus (STS) contain neurons that analyze visual motion (3), but it is not known whether such activity can be directly

related to the conscious perception of movement. To investigate this possibility, we used rhesus monkeys because they experience binocular rivalry (4).

Three rhesus monkeys were trained in a motion discrimination task. Two vertically drifting horizontal gratings were generated on a video monitor and presented independently to the two eyes through a stereoscopic viewer. Eye movements were monitored with a scleral search coil, and a disparity calibration was performed to position the

Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology, Cambridge, MA 02139.

*Present address: Department of Psychology, Vanderbilt University, Nashville, TN 37240.

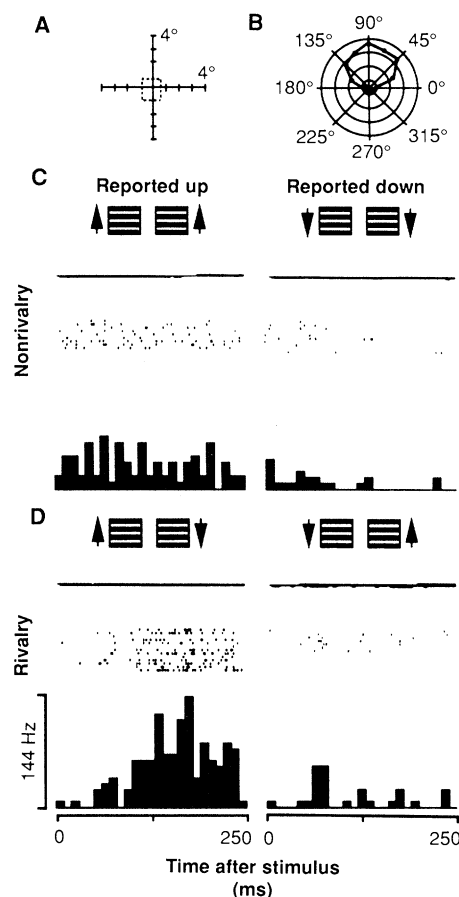


Fig. 1. Response of single unit in the STS to nonrivalrous and rivalrous stimuli. (A) Receptive field position. This cell had a small central receptive field. (B) Direction tuning curve. Each point represents the average discharge rate in response to drifting gratings. Each concentric circle represents 30 spikes per second. The cell preferred upward motion. (C and D) Responses during nonrivalrous (C) and rivalrous (D) grating presentation when the monkey reported seeing up (left) and down (right). The gratings depict the type of motion presented to each eye. Beneath the gratings, the vertical eye movement traces are superimposed for each trial. Single unit activity is illustrated by rasters and time histograms of the average firing rate. The eye position traces, rasters, and histograms are aligned on the onset of the nonrivalrous or rivalrous grating presentations.

gratings so that they overlapped (5). A trial began with the appearance of a fixation spot. After the monkey fixated on the spot, drifting gratings were presented for 400 to 1500 ms. The gratings were replaced by two spots on the left and right of the fixation spot. If the monkey perceived upward motion, he was required to execute a saccade (quick eye movement) to the right spot; a saccade to the left spot was required after downward movement. In half of the trials the gratings drifted in the same direction, and in the other half they were rivalrous, containing an equal number of up-down and down-up presentations. In the rivalrous trials the monkeys were rewarded for either response. Also, in half of the trials the fixation spot was removed when the gratings appeared to allow optokinetic responses. The various trial types were pseudorandomly interleaved.

Overall, the perceptual choice in rivalrous trials was as likely to correspond to the stimulus presented to one eye as to the other. As observed in humans (6), in 93% of the rivalry trials in which the monkeys exhibited measurable pursuit (7), its direction corresponded to the reported perceived

movement. The gain of pursuit during rivalry was significantly lower (mean $\pm$ SEM = 0.30 ± 0.01 for rivalry versus 1.00 ± 0.01 for nonrivalry), and the latency was significantly longer than normal (average of 296 ± 1.9 ms for rivalry versus 189 ± 2.5 ms for nonrivalry).

A total of 66 neurons were recorded from two monkeys (8). Seven had receptive fields that did not include the fovea; therefore, they were not used in this analysis. The remaining units exhibited directional specificity, and even if their preferred direction was not vertical on initial inspection, they had unequal responses for upward versus downward motion. Their receptive fields included the fovea, and their size was comparable to their eccentricity. According to these receptive field properties, these units were probably in MT. All of the neurons

analyzed in this report were binocular and approximately equally driven by stimulation of either eye.

A variety of neuronal responses was observed in STS, and different populations of neurons could be distinguished by comparing their modulation during nonrivalrous and rivalrous trials. The responses of one neuron with activity that was correlated with the perceived direction of motion during rivalry is shown in Fig. 1. When the gratings were moving in the same direction, the response of the cell reflected its upward preference. However, when the gratings presented to each eye were moving in opposite directions (that is, the grating presented to one eye moved downward and that presented to the other eye moved upward), then the cell discharged on those trials in which the monkey indicated that he per-

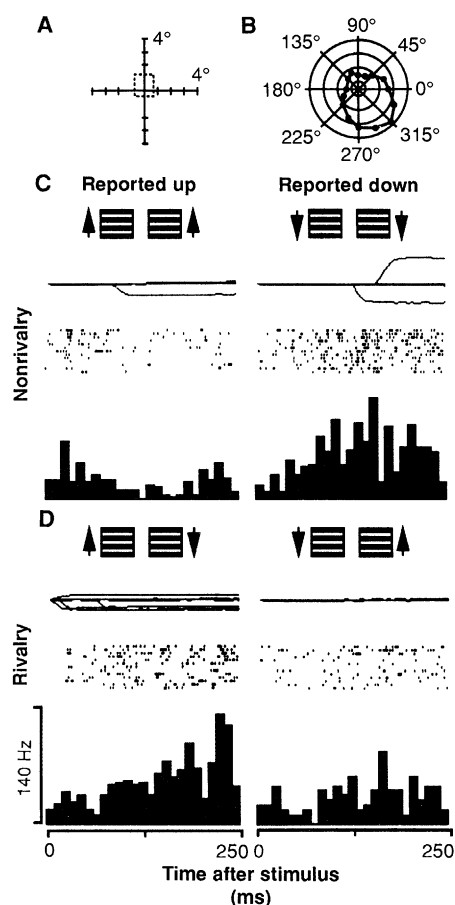
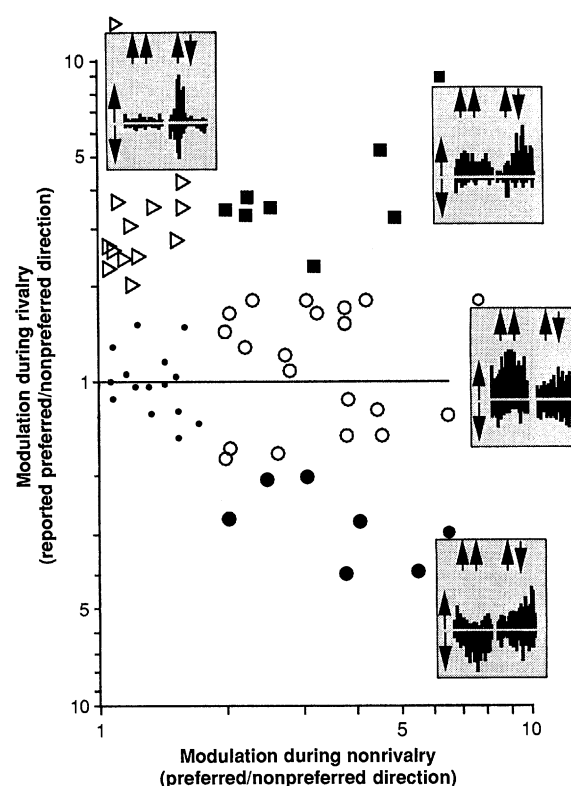


Fig. 2. Response of another STS unit during nonrivalrous and rivalrous grating presentation. Conventions are as in Fig. 1.

Fig. 3. Scatter plot of the directional modulation with nonrivalrous and rivalrous stimulus presentation. The response of each neuron ($n = 59$) was defined as the number of spikes discharged in the first 100 ms after grating presentation in each trial. The abscissa represents the ratio of the average response of a cell in a block of nonrivalrous trials to gratings in its preferred direction divided by the average response to gratings in its nonpreferred direction. The ordinate represents the modulation of the cell during rivalrous stimulus presentation. This modulation was defined as the ratio of the average response in trials in which the monkey reported seeing the direction of motion corresponding to the preferred direction of the cell divided by the average response in trials in which the monkey reported seeing the direction of motion in the nonpreferred direction. Values in the upper half indicate that the response of the cell was greater when the perceptual choice corresponded to the preferred direction. Values in the lower half indicate that the neuronal response was greater when the behavioral choice was in the nonpreferred direction. This analysis does not reflect the overall level of activity of the cells but rather the ratio of activities for the two directions. Lower half of the ordinate is a mirror image of the upper half and reflects movement preference in the opposite direction. A t test was used to determine whether the directional modulation of a cell was significant. All of the cells in the plot were derived from the same sample, but symbols illustrate the different types of modulation. Small solid dots (●) represent cells that were not directional in the vertical axis during either the nonrivalrous or the rivalrous trials. The open triangles (Δ) represent cells that were not significantly directional during the nonrivalrous presentation but were directional during rivalry. Hence, the assignment of these points to the upper half of the plot was arbitrary. The open circles (○) represent cells that exhibited significant directional modulation during the nonrivalrous presentation, but during rivalry their response was independent of the perceptual choice of the monkey. The solid squares (■) and circles (●) signify cells that exhibited significant directionality during both rivalrous and nonrivalrous trials. Cells designated by solid squares responded more during rivalry when the perceptual choice of the monkeys corresponded to the preferred direction of the cell, while those signified with solid circles responded when the perceptual choice corresponded to the nonpreferred direction. (Insets) Spike histograms of examples of the four modulated cell classes. The type of symbol at the upper left of each inset indicates the cell class. The arrows at the top of each panel indicate the nonrivalrous and rivalrous trial types, and the arrows on the left indicate trials in which the monkey reported upward or downward motion.



ceived upward movement. In contrast, this unit did not discharge on trials in which the monkey responded that he perceived downward motion, even though the optimal, upward-moving stimulus was being presented to one or the other eye. Although only 250 ms of activity is shown in Fig. 1, the differential activity was present as long as the gratings were presented (up to 1500 ms). The activity of another STS unit is shown in Fig. 2. This unit was more active in rivalry trials in which the monkey reported the direction of motion corresponding to the nonpreferred direction of the cell.

A quantitative analysis of the modulation of each neuron was performed (Fig. 3). Twenty-five percent of the neurons showed insignificant directionality in the vertical axis; another 21% of the cells, which had horizontal or oblique preferred directions, displayed directionality during rivalrous but not nonrivalrous trials. Thirty-two percent of the units exhibited directionality for non-rivalrous gratings, but their response during rivalry was independent of the perceptual choice of the monkeys; these units discharged whenever their optimal stimulus was present. Finally, 22% of the cells were modulated during rivalry according to their direction preference exhibited during nonrivalry. Half of these units responded when the perceptual choice of the monkey corresponded to the preferred direction of the cell (Fig. 1), and the other half responded when the preferred direction of motion was present in the suppressed eye (Fig. 2).

Because neuronal activity related to pursuit eye movements has been recorded in STS (9), the modulation of this last class of neuron could be a consequence of the pursuit eye movements, which are themselves correlated with the perceived direction of motion. Several arguments refute this interpretation. First, during trials in which the fixation spot was visible, the monkey did not exhibit measurable nystagmus, but the pattern of neuronal response was the same as that elicited in trials in which no fixation spot appeared. Second, the quantitative analysis of neuronal modulation (Fig. 3) included only the first 100 ms after grating presentation, well before pursuit was initiated. Finally, the relation of neuronal onset time to stimulus or pursuit onset was determined (10); this analysis confirmed that the neuronal discharge was related to stimulus presentation and not the execution of pursuit eye movements. Hence, the differential neuronal activity of these units during rivalry reflects a perceptual and not an oculomotor process. Studies reveal comparable prop-

erties of MT neurons in a different visual task (11).

During rivalry the stimulus presented to one eye is periodically invisible even though it still impinges on the retina. Psychoanatomical experiments have shown that this suppression occurs at a relatively advanced station in the visual pathway (12). Our results provide information about the site and mechanism of binocular rivalry by indicating that the STS contains elements that might mediate the periodic suppression and dominance characterizing binocular rivalry.

The neurons that discharged regardless of whether their optimal stimulus was in the suppressed or the dominant eye may be first-order neurons receiving afferents that are not inhibited during rivalry suppression. When the neurons that were differentially responsive in the vertical axis only during rivalry were mapped conventionally, they had a horizontal or oblique preferred direction. Thus, their directional tuning might be dynamic and adaptable to the perceptual requirements. The units that were specifically active when the optimal stimulus was present in the dominant eye (Fig. 1) could mediate the perception of motion that was expressed in the behavioral response of the monkeys. Finally, the neurons that were active when their optimal stimulus was present in the suppressed eye (Fig. 2) might provide the inhibition to lower or higher visual centers to suppress the view of one eye during rivalry.

This interpretation of the results is by no means conclusive. The differential modulation of these STS neurons in response to rivalrous stimuli was evident much earlier than subjects typically resolve the rivalrous perception. Thus, further processing is clearly involved, and the data do not exclude the possibility that the perception-related modulation observed in these neurons may be a result of feedback from higher centers.

In conclusion, the results of this study suggest the possibility of experimentally relating the activity of single neurons in the visual system to the internal perceptual state of the subjects. Such experiments may lead to a better understanding of how the processes that result in an internal representation of the visual world are instantiated in the structure and function of the visual pathways.

REFERENCES AND NOTES

1. D. H. Hubel and T. N. Wiesel, *J. Physiol. (London)* **195**, 215 (1968).
2. P. Walker, *Psychol. Bull.* **85**, 376 (1978); J. M. Wolfe, *Psychol. Rev.* **93**, 269 (1986); R. Blake, *ibid.* **96**, 145 (1989).
3. D. C. Van Essen, in *Cerebral Cortex*, vol. 3, *Visual Cortex*, A. Peters and E. G. Jones, Eds. (Plenum, New York, 1985), pp. 259–329; J. H. R. Maunsell and W. T. Newsome, *Annu. Rev. Neurosci.* **10**, 363 (1987); W. T. Newsome and R. H. Wurtz, *Trends Neurosci.* **11**, 394 (1988).
4. J. Myerson *et al.*, *Behav. Anal. Lett.* **1**, 149 (1981).
5. The monkey was required to fixate on a spot that was presented to each eye sequentially. The location of the spot was adjusted for each eye so that the monkey made no saccade to refixate on it when the presentation was changed from one eye to the other. This approach allowed us to align the fixation target within the limits of resolution of our system (0.4°). The gratings were centered on the fused points. Separate psychophysical tests with random dot stereograms revealed that each monkey had normal stereoscopic fusion.
6. R. Fox *et al.*, *Vision Res.* **15**, 849 (1975).
7. The onset and the gain of pursuit were determined by computer. All saccades were detected and excised. The onset of pursuit was computed by detecting a monotonic change in eye position of the appropriate speed (20 to 130% of the grating speed) and direction that moved the gaze at least 3 SD from the initial fixation position. The eye velocity was obtained by computing the slope of the regression line between the onset of pursuit and end of stimulus presentation. Eye velocity divided by the target velocity defined the pursuit gain.
8. The monkeys were prepared for recording with sterile surgical technique under pentobarbital anesthesia. Single units were recorded and isolated conventionally. Receptive fields were mapped with computer-generated gratings and spots that could be removed by hand with a joystick interface or that automatically drifted at different locations or directions while the monkey maintained fixation on a spot. A grating was positioned at the most sensitive region of the receptive field of a cell and drifted in 8 to 16 different directions to determine the directional tuning curve. After determination of the preferred direction, a grating was drifted in that direction in different locations of the monitor to map the borders of the receptive field.
9. W. T. Newsome *et al.*, *J. Neurophysiol.* **60**, 604 (1988).
10. The neuronal latencies were determined from spike density functions that were derived by convolving the spike train with a Gaussian filter [J. M. MacPherson and J. W. Aldridge, *Brain Res.* **175**, 183 (1979)]. The SD of the filter was the maximum of the video frame duration or the average interspike interval during the fixation period. The onset of activation was defined at the time when the spike density function deviated from the baseline before the stimulus by 3 SD. A statistical analysis of the relations between the neuronal response latency (NL), the pursuit latency (PL), and their difference (PL – NL) was performed [D. Commenges and J. Seal, *Brain Res.* **383**, 350 (1986)]. There was essentially no relation between NL and PL (the average slope $\pm$ SE for the $n = 10$ cells was -0.019 ± 0.021); in contrast there was a strong linear relation between PL – NL and PL (average slope $\pm$ SE = 1.132 ± 0.046 for the 10 cells). Furthermore, the ratio of the variance of NL to the variance of PL – NL was 17.84 ± 2.31 for $n = 10$ cells.
11. W. T. Newsome, K. H. Britten, J. A. Movshon, *Soc. Neurosci. Abstr.* **14**, 458 (1988); K. H. Britten, W. T. Newsome, J. A. Movshon, *ibid.*, p. 458.
12. R. Blake and R. Overton, *Perception (London)* **8**, 143 (1979).
13. We thank P. H. Schiller for his support; J. H. R. Maunsell, C. F. Stromeyer, J. Wu, J. M. Wolfe, and the reviewers for comments on the manuscript; E. Charles and D. Poeppel for participating in some recording; and M. E. Flynn-Sullivan for skilled technical assistance. N.K.L. was supported by NIH grant EY00676 and Office of Naval Research grant N00014-88-K-0164 to PHS, and J.D.S. was supported by NIH grant EY05959.

15 February 1989; accepted 31 May 1989