gion, which facilitates the formation of the open complex. Consequently, the recognition of a specific binding site and the formation of a stable (open) polymerase-DNA complex ready for initiation depends on the quality of the contact points and on the stability of the helix, thus providing a simple explanation why the correlation between frequencies of polymerase binding and localized DNA melting is not perfect (see Figs. 1 and 2). Therefore, the helix stability in a promoter and its flanking DNA regions may play an important role in setting the level of transcription and consequently may have a regulatory function in gene expression. In this regard, it may be significant that the nucleotide sequence with the lowest A + T content in Table 1 codes for an unusually weak promoter, namely $P_{lacI}$ (*5*).

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## Orientation Anisotropy of Visual Stimuli in Rhesus Monkey: A Behavioral Study

Abstract. *The contrast sensitivity of the rhesus monkey was tested, according to a modified reaction-time paradigm, for sine-wave grating targets at different orientations. The monkey possesses an oblique effect slightly larger than that of humans. A reaction time analysis showed the oblique effect to be a suprathreshold as well as a threshold phenomenon. The presence of this effect further strengthens the use of the monkey as a model for the human visual system.*

The human ability to resolve grating patterns with a vertical or horizontal orientation better than those with an oblique orientation has been well documented (*1*). We know that this orientation anisotropy or oblique effect is of neural origin, because it is present even if the optics of the eye are bypassed and laser interference fringes are formed directly on the retina (*2*). The oblique effect, present only for central vision, has many of the characteristics of meridional amblyopia, which is considered to be due to environmental factors during early development (*3*). Attempts to obtain supporting evidence for these environmental influences are contradictory since some investigators (*4*) have found evidence for an oblique effect in infants and others (*5*) have not, although recent evidence indicates that this discrepancy may be due to differences in measurement techniques (*6*). Attempts to determine the neural mechanism for an orientation anisotropy have also been contradictory (*7–9*). Mansfield has reported that in monkeys a preponderance of neurons in the striate cortex with receptive fields in the fovea respond optimally to vertical or horizontal stimuli. Additonally, visual evoked responses from the monkey indicate the presence of an oblique effect. However, Finlay *et al.* and Poggio *et al.* (*9*) have reported that there is not a significant orientation bias for monkey foveal striate neurons. There are, of course, several possible reasons for the discrepancy.

The first question to be answered before investigations into the neural mechanisms of the oblique effect become significant is: Does the monkey behaviorally demonstrate an oblique effect? We now present a behavioral demonstration of the oblique effect in two rhesus monkeys. We also show how the oblique effect varies as a function of the spatial frequency of the stimulus and provide behavioral data indicating that the oblique effect is a suprathreshold as well as a threshold phenomenon (*10*).

Monkeys were trained to detect sinusoidal grating patterns generated on a cathode-ray tube (CRT) according to the method described by Campbell and Green (*11*). The CRT was masked to subtend a 4° visual angle at 114 cm (the viewing distance). The mean luminance of the visual display, 67 cd/m$^2$, remained constant for all contrast levels and spatial frequencies. The oscilloscope was cradled in an apparatus that could be rotated about the center of the display in 10° increments from 0° through 170° with additional stops at 45° and 135°.

The behavioral procedures used for the data collection were a modification of the reaction time procedure used previously in increment threshold experiments (*12*). The monkeys were trained to press and hold a lever at the start of each trial, which was signaled by the onset of


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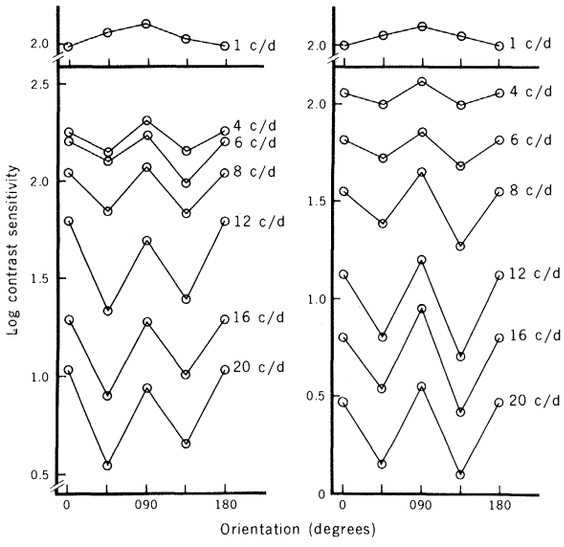


Fig. 1. Contrast sensitivity as a function of grating orientation for spatial frequencies of 0.5 to 20 cycles per degree (*c/d*). Data for two monkeys are shown.

an auditory cue. The lever press initiated a foreperiod of variable duration during which the grating was presented with a .02 probability at the end of any consecutive 100-msec period. Concurrent with the onset of the grating stimulus, a reaction-time counter and a 700-msec limited-hold reinforcement period were started. If the monkey released the lever within the limited-hold period, we considered that he had detected the stimulus change; the reaction time was recorded, and he was rewarded with a conditioned reinforcer (tone) after each trial and orange juice or water on a random .5 probability basis. A 4-second intertrial period followed each rewarded trial and trials for which the reaction time was longer than the limited-hold period. In order to discourage anticipatory responses, however, if the monkey released the lever before the onset of the grating stimulus, a 14-second intertrial interval occurred. Data were collected by a descending method of limits. Each series started with a grating contrast of 70 percent and was reduced in increments of 0.1 log unit after the rewarded trials only. Reaction times were recorded for each contrast level until the monkey failed to release the lever within the 700-msec hold period for two consecutive trials, which we considered to indicate that the monkey had not detected the stimulus change (*13*). The contrast value associated with these trials was taken as the threshold, and the attenuator was reset to start a new series.

Two rhesus monkeys (*Macaca mulatta*) approximately 18 months old were studied. The monkeys had been born in a colony and reared in cages since infancy. Their eyes were refracted by retinoscopy under cycloplegia, and lenses to correct their refractive errors were worn during the experiments. One monkey, whose suprathreshold data will be shown, exhibited a slight degree of spherical hyperopia of both eyes while the other was a simple myope. Restraints were positioned on both sides of the head to prevent head tilt, and the display was viewed through natural pupils.

In Fig. 1 contrast sensitivity data are shown for four grating orientations for each of several spatial frequencies. The data are the reciprocals of the mean threshold contrasts from 30 determinations. The standard errors of these values were typically about 0.02 log units of contrast sensitivity, which is smaller than the symbol size. With a grating stimulus of 20 cycles per degree (c/d), the difference in contrast sensitivity for horizontally and vertically oriented gratings versus obliquely oriented gratings is substantial (approximately 0.4 log unit). The magnitude of the oblique effect for these two monkeys was larger than we have found for human subjects tested on the same apparatus. The magnitude of the oblique effect systematically decreases for lower spatial frequencies; it is essentially absent for spatial frequencies of 1 c/d or less. These data are similar to those reported by Camisa *et al.* for humans (*14*).

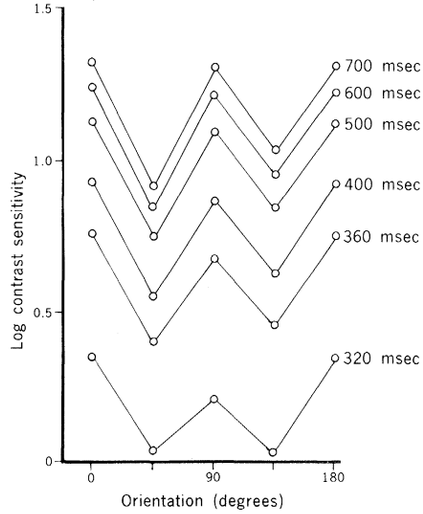


Fig. 2. Suprathreshold contrast sensitivity by a rhesus monkey for a 16-c/d grating seen at different orientations. The criterion reaction times are indicated next to each function.

The reaction-time data showed that the median reaction time increased as a simple monotonic function with a decrease in the physical contrast of the grating. This inverse relationship between reaction time and contrast is considered to reflect the relationship between physical and perceived contrast. In fact, simple reaction time is generally considered to be directly correlated with the perceptual latency of a stimulus so that stimuli with equal latencies have equal perceptual values (*15*). Therefore, it would seem reasonable that the oblique effect could be investigated for suprathreshold stimuli by determining at each of the four major stimulus orientations the contrast value necessary to obtain a criterion reaction time. Such data for several criterion reaction times for a 16 c/d stimulus are shown in Fig. 2. The contrast value for each criterion reaction time was determined by fitting a power function (by a least-squares method) to the median reaction times from 30 measurements at each stimulus contrast and orientation. The reciprocal of each contrast value, that is, contrast sensitivity, was then plotted as a function of grating orientation for several indicated criterion reaction times. Each function represents gratings of equal perceptual contrast; however, the shorter the criterion reaction time, the higher the physical contrast. The oblique effect is present with approximately the same magnitude over the entire range of suprathreshold contrast levels used in the experiments (Fig. 2). This property of orientation anisotropy, which to our knowledge has not been shown previously for either humans or monkeys, demonstrates that the mechanism responsible for the effect operates at both threshold and suprathreshold contrast levels. Preliminary data we have collected indicate that humans also exhibit the same type of suprathreshold oblique effect as that found in the monkeys.

Our data unequivocally demonstrate the presence of an oblique effect in the monkey. Since the subjects used in these experiments were reared in a man-made environment, finding an oblique effect in them does not eliminate the "carpen-

tered world'' hypothesis as the possible etiological agent. However, the data further validate the rhesus monkey as an animal model for the human visual system, since such a subtle effect is present for both species.

One possible explanation for the lack of agreement between the electrophysiological studies dealing with the distribution of preferred stimulus orientation for neurons in the monkey's striate cortex may stem from the fact that these studies have not analyzed orientation tuning for the various separate categories of cortical neurons. Although attempts to behaviorally demonstrate an oblique effect in cat have failed (*16*), Hirsch and Leventhal have shown that a significant orientation anisotropy exists in the cat's striate cortex for neurons that have small receptive fields and that require slow stimulus movement. These neurons presumably receive afferent input from the sustained or X cell population in the lateral geniculate nucleus and probably process information concerning high spatial frequency. Since the oblique effect is observed only for stimuli of high spatial frequency, the orientation tuning of cortical cells having high spatial-frequency tuning, small receptive fields, and preferring slow stimulus movement should be investigated in the monkey (*17*).

The demonstration of an oblique effect in monkeys provides additional information that the monkey processes spatial information as humans do and bridges the gap between the psychophysical data on humans and neurophysiological data on laboratory animals.

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## Stress and Coping Factors Influence Tumor Growth

Abstract. *Growth of syngeneic P815 mastocytoma in DBA/2J male mice was evaluated as a result of various stress regimens. A single session of inescapable shock resulted in earlier tumor appearance, exaggeration of tumor size, and decreased survival time in recipient animals. Escapable shock had no such effects. The effects of the inescapable shock were mitigated if mice received long-term shock treatment.*

Inconsistent and often contradictory results have been reported concerning the effects of stress on tumor growth. Whereas some investigators have reported stress-induced exacerbation of tumorigenicity (*1*, *2*), others have found stress to retard tumor growth (*3*). Interpretation of these results is complicated by the lack of between experiment consistency concerning the species, tumor system, and stressor used, as well as the methods of assessing tumor growth. Nevertheless, there is some suggestion that the severity and chronicity of the stress determine the effects on tumor development (*1*-*3*). Moreover, given the differential effects of controllable and uncontrollable stress on other physiological pathologies (*4*) as well as neurochemical activity (*5*), the possibility should be considered that coping processes may play a role in determining the stress effect on tumor development.

We have examined the effects of coping mechanisms and chronicity of stress on tumor development. A total of 90 DBA/2J male mice (20 to 23 g), housed five per cage and permitted unlimited food and water, were studied in the initial experiment to evaluate tumor development following a single session of inescapable shock. Mice received a subcutaneous injection in the left flank region of $6.25 \times 10^4$ viable syngeneic P815 mastocytoma cells suspended in 0.25 ml of RPMI-1640 medium. This dose was selected on the basis of earlier results showing that this number of cells resulted in tumor appearance (defined as 3 $mm^2$) within 7 to 9 days in all animals (*6*). The P815 cells, which were acquired from a donor mouse bearing an ascites tumor, were washed twice in RPMI-1640 after being extracted and then suspended in this medium for injection. Viability was assessed with trypan blue.

Twenty-four hours after tumor cell transplantation, the animals were individually placed in the shock apparatus for their only shock session. The shock apparatus consisted of six black Plexiglas chambers measuring 30 by 14 by 15 cm. Shock (a-c, 60 Hz) was delivered through a 3000-V source to the grid floor, which was composed of 0.32-cm stainless steel rods 1.0 cm apart and connected through neon bulbs (*7*).

Independent groups of mice received either 1.1, 2.2, or 3.3 hours of apparatus exposure. These groups were divided into subgroups of ten each such that animals in each group were exposed to shock of 75 or 150 $\mu$A, or no shock. Shock presentations 6 seconds long were delivered at 1-minute intervals. Tumor size was measured horizontally and vertically with vernier calipers over the 14-day period after cell transplantation. Since tumors grew in somewhat irregular shapes, the largest dimensions perpendicular to one another were chosen in all instances. An approximation of the area of each tumor was obtained by multiplying the two measurements for each animal. The reliability of this measure within and between raters exceeded .80,


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