# Effects of sleep and arousal on the processing of visual information in the cat

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*Single units in the cat lateral geniculate nucleus and primary visual cortex show changes in both spontaneous and visually evoked firing as a function of the state of wakefulness. On arousal spontaneous firing is smoother and often reduced, whereas evoked responses are usually enhanced; the result is an increase in the signal-to-noise ratio. Single- and double-label 2-deoxyglucose autoradiographs show further that slow-wave sleep differentially depresses visually evoked activity in the deeper layers of the visual cortex.*

SUBJECTIVELY it seems obvious that the way in which the brain handles sensory information must change radically between sleeping and waking. To examine these changes it is important to be able to influence the firing of neurones along a sensory pathway by natural stimulation. We have chosen the visual system to study neural activity as a function of the state of arousal because, in the pathway from the retina through the lateral geniculate body (LGB) to the primary visual cortex, the properties of the cells are well understood in terms of their optimum visual stimuli. In an animal that closes its eyes when asleep, additional mechanisms for blocking visual messages during sleep might seem unnecessary but, beyond the retina, such mechanisms do seem to exist. In the cat, spontaneous firing patterns of cells in the LGB[1,2] and primary visual cortex[3–6] show marked differences between sleeping and waking. In the LGB Coenen and Vendrik[7] have shown that responses to light stimulation are strongly enhanced on arousal in lightly anaesthetized cats. In the present study we have recorded from single cells in the LGB and striate cortex[8], examining the effects of the state of wakefulness on both the vigour and specificity of responses. We have also compared sleep and arousal using the 2-deoxyglucose method for labelling neurones according to activity[9,10].

## Single-cell recording

We compared spontaneous and visually evoked firing in sleeping and waking states in 130 cortical cells in 15 cats, and in 14 geniculate neurones in 2 cats.

Each cat was first sleep deprived overnight in a slowly revolving (0.5 r.p.m.) drum, and then prepared as if for chronic recording[1,4], under halothane anaesthesia. Four chlorided silver electroencephalogram (EEG) electrodes were cemented over the dura and a pedestal for holding a hydraulic microelectrode advancer was cemented to the skull. For cortical recording we positioned the pedestal over the postlateral gyrus. For geniculate recording the animal's head was put in a Horsley–Clarke headholder and the pedestal cemented stereotaxically above the LGB. The head was then freed, well before terminating the anaesthesia. We infiltrated skin incisions with Xylocaine, intubated the trachea, paralysed the animal with continuous intravenous succinylcholine and monitored levels of expired $CO_2$. The head was held firmly with adhesive tape and gauze pads. Pupils were dilated with homatropine, contact lenses were fitted so that images on a screen at 1.5 m distance produced a focused image on the retina, and the optic disk and area centralis of each eye were mapped by optical projection. When necessary we used an adjustable prism to bring the two centres of gaze into superposition.

The halothane was then discontinued, and in the EEG irregular high-voltage activity of the anaesthetized state gave way, in a few minutes, to the low-voltage rapid activity of the waking state. Most of the cats then slept spontaneously and frequently, as indicated by high-voltage slow waves. Arousal from slow-wave sleep was spontaneous or could be produced by a noise or tactile stimulus. Rapid eye movement (REM) sleep was recognized by episodes of large monophasic potentials recorded from the visual cortex (ponto-geniculo-occipital (PGO) waves), which could be suppressed by arousing the animal.

For each cell we first mapped receptive fields on the screen with a hand-held slide projector. For cortical cells a computer-driven optic bench was adjusted to produce moving-slit stimuli which were tailored for optimal position, orientation, shape and rate of movement. The stimuli for geniculate cells were stationary circular spots or annuli. Action potentials, EEGs and traces representing the presentations of the stimuli were recorded on a Grass polygraph and on magnetic tape for subsequent averaging. Every cell included in the series was followed over several transitions between waking and high-voltage slow-wave sleep.

## Recordings from lateral geniculate body

With the screen diffusely lit, geniculate cells showed an increase in spontaneous firing rate when the animal was aroused from slow-wave sleep, as expected from previous studies[7,11–13]. Moreover, the pattern of firing changed from high-frequency bursts of two to eight spikes to more regular firing[1,3,14].

In all 14 geniculate cells there were marked changes also in responsiveness to visual stimuli, as illustrated in Fig. 1. In Fig. 1*a*, during an otherwise wakeful period, there was a brief episode of high-voltage slow-wave sleep lasting about 30 s and ending spontaneously. The stimulus, which was repeated throughout, was a small (1/4°) spot of light covering the receptive field centre. During the slow waves there was a depression of the on-response, obvious in both the spike record and the average-response histograms. This change is most easily explained by supposing that the efficacy of optic nerve fibres in triggering the geniculate cell is enhanced on arousal[7]. All the effects of arousal cannot be explained in this way, however. In Fig. 1*b*, the stimulus was an annulus covering the surround of the cell's receptive field. Now spontaneous arousal was accompanied not only by an increase in the off discharge, but also by an enhanced suppression of firing while the annulus was on.

Figure 1*c* shows the enhancement of suppression for the same on-centre cell, in a slightly different way. In Fig. 1*c*, upper half, the screen was lit steadily and diffusely by a low-level background light. The tonic firing of the cell was obviously decreased during each of the two bursts of slow waves. In the lower half, an annulus covering the receptive field surround tonically sup-

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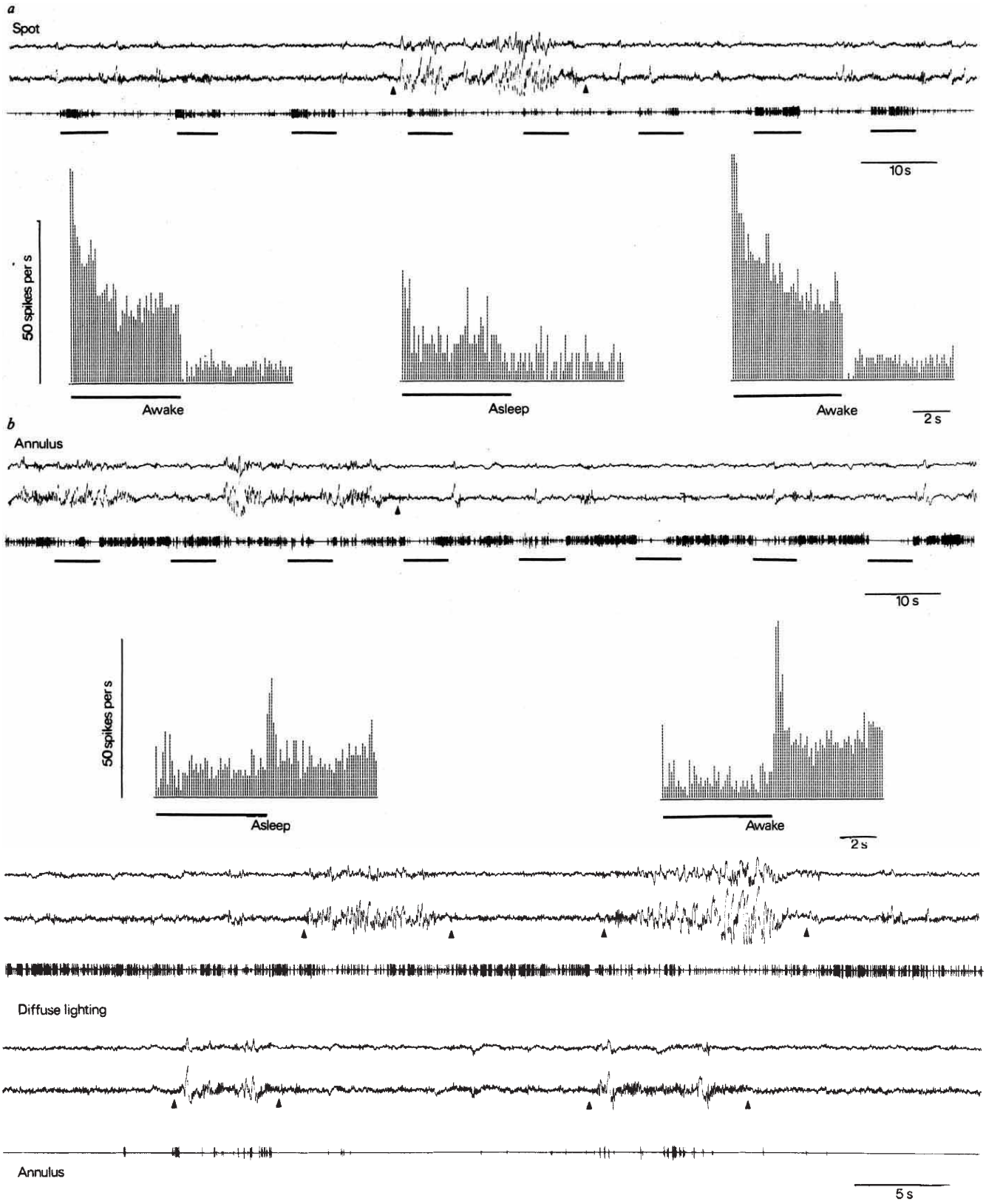


**Fig. 1** *a* and *b*, Responses of an on-centre cell from layer A of the lateral geniculate nucleus in a drowsy cat. In each polygraph record the upper two traces are the bipolar EEGs from anterior and posterior head regions; the third trace shows the spikes from the geniculate cell, converted into pulses, in these and subsequent polygraph records, by a Schmitt trigger circuit. Each record lasts ~2 min. Brief periods of sleep, which end spontaneously, are indicated by the slow waves in the middle of record *a* and (roughly) the left half of *b*. The approximate transitions between the flat waking EEG record and periods of slow-wave sleep are indicated by arrowheads. In *a* a spot covering the receptive field centre is flashed on and off. The relative weakness of the on responses during periods of slow waves can be seen in the record of spikes and in the three histograms. The left histogram is the average of 13 responses, of which the last 3 are shown. The middle histogram is an average of the 2 responses during the burst of slow waves, and the right histogram the average of the next 16 responses. In *b* the stimulus is an annulus covering the receptive-field surround. Both the suppression of firing during the stimulus and the off discharge are weaker during sleep. Histograms are the average of nine responses each, before and after the arrowhead. *c*, Effects of slow-wave sleep on steady-state firing of the same cell. In the upper set of three traces (50 s) the screen is diffusely lit by the background light. At each burst of slow waves in the cortical EEG (upper two traces) the rate of firing declines. In the lower set an annulus covers the receptive-field surround. In the aroused periods the discharges are almost completely suppressed, but each episode of slow waves is accompanied by bursts of impulses. Onset and end of slow-wave bursts are indicated by arrowheads.

pressed the firing. The suppression was almost complete when the EEG was flat, but during the slow waves there were bursts of impulses. Thus arousal could depress or elevate the cell's firing rate, depending on the visual stimulus used.

For off-centre cells there was a similar enhancement, both in the suppression of firing and off-discharge to a spot covering the receptive field centre, and in the on-response to an annulus. In both on-centre and off-centre cells diffuse light was less effective than a spot confined to the receptive field centre. This is characteristic of geniculate cells. The diffuse light responses of both on-centre and off-centre cells showed little or no enhancement on arousal from slow-wave sleep, presumably because the increase in the response from the field centre was counterbalanced by an increased opponent response from the surround. To understand the significance of this one must recall that a weaker response to a large spot than to a small one just covering the field centre is characteristic also of retinal ganglion cells[15,16]. But geniculate cells receiving their main excitatory optic input from a single retinal ganglion cell show a more pronounced reduction in response to stimuli including the field surround than do the retinal ganglion cells[14,17]: indeed, this is the main known contribution of the lateral geniculate to the processing of visual information. If the response enhancement on arousal were greater for a large spot than for a small one, one would have to conclude that arousal led to an impairment of this function.

Arousal from slow-wave sleep produced no obvious changes in geniculate receptive field sizes as mapped by small spots. As visual acuity is presumably related in geniculate cells to receptive field centre size, an increase in centre size on arousal[18] would have been perplexing if not dismaying.

In summary, arousal from slow-wave sleep increased the spontaneous firing rate of lateral geniculate cells and reduced or eliminated the high-frequency bursts (not resolved in the slow time scale of Fig. 1); both the excitatory and inhibitory components of responses to spatially restricted visual stimuli were enhanced; and, finally, responses from the receptive field centre and the antagonistic surround were both enhanced.

Presumably the mechanism of these effects depends on non-retinal projections to the LGB because in mammals there do not seem to be projections from brain to retina, and firing of retinal ganglion cells is unaffected by arousal[1]. The increase in the on- or off-discharges on arousal is known to reflect an increase in the proportion of optic nerve impulses that succeed in triggering geniculate impulses (the firing index)[7]. The enhanced suppression of discharge seen on arousal may reflect enhanced inhibition from other geniculate neurones that are excited by the stimulus and whose firing index is increased by arousal; or arousal may lead to an enhancement of both excitatory and inhibitory synapses. An increased firing during sleep might also be somehow related to the high-voltage cortical slow waves, which, if present in thalamus and cortex concurrently, could be associated with swings in membrane potential capable of triggering bursts of impulses. Suppressing these slow waves, on arousal, could then abolish the discharges.

## Visual cortex

In contrast to geniculate cells, cortical cells varied greatly from one to the next in the degree to which they were influenced by changes in arousal level. Marked differences were often seen between two cells simultaneously recorded from two electrodes spaced 1 mm or less apart, or between two cells simultaneously recorded from one electrode. Nevertheless, each individual cell showed a consistent type of change over several cycles of

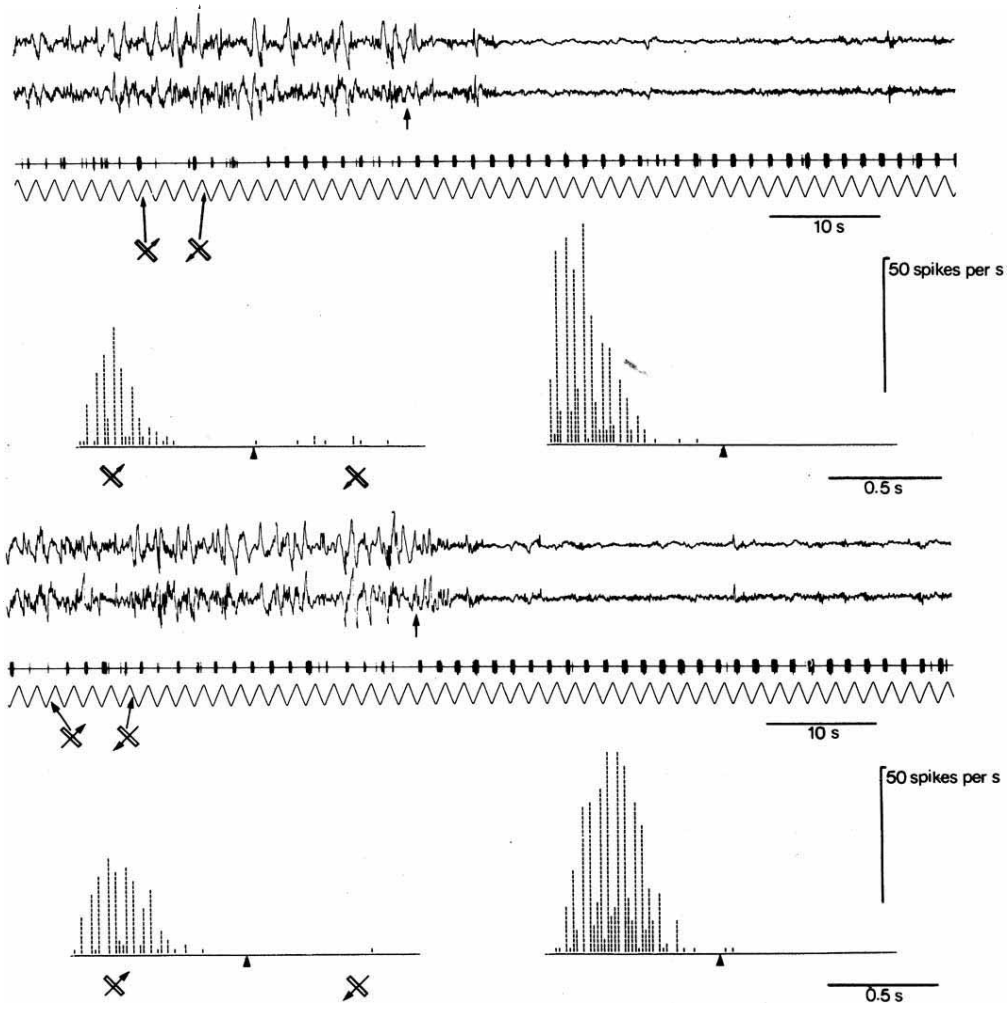


**Fig. 2** Effects of arousal on the responses of a cell in layer 6 of striate cortex. The record is 85 s long. Near the middle a noise (arrow) arouses the cat, as shown by the suppression of the EEG slow waves in the upper pairs of traces. Responses of the cell (third trace) are to a 1/2°×5° stimulus oriented 45° anticlockwise to vertical and swept up and to the right and down to the left (indicated in the fourth trace by up-and-down deflections). On arousal the responses are more consistent and on the whole stronger, as can be seen in the average response histograms. Each histogram is the average of 40 responses. The arrowhead below each histogram indicates when the stimulus reversed direction.

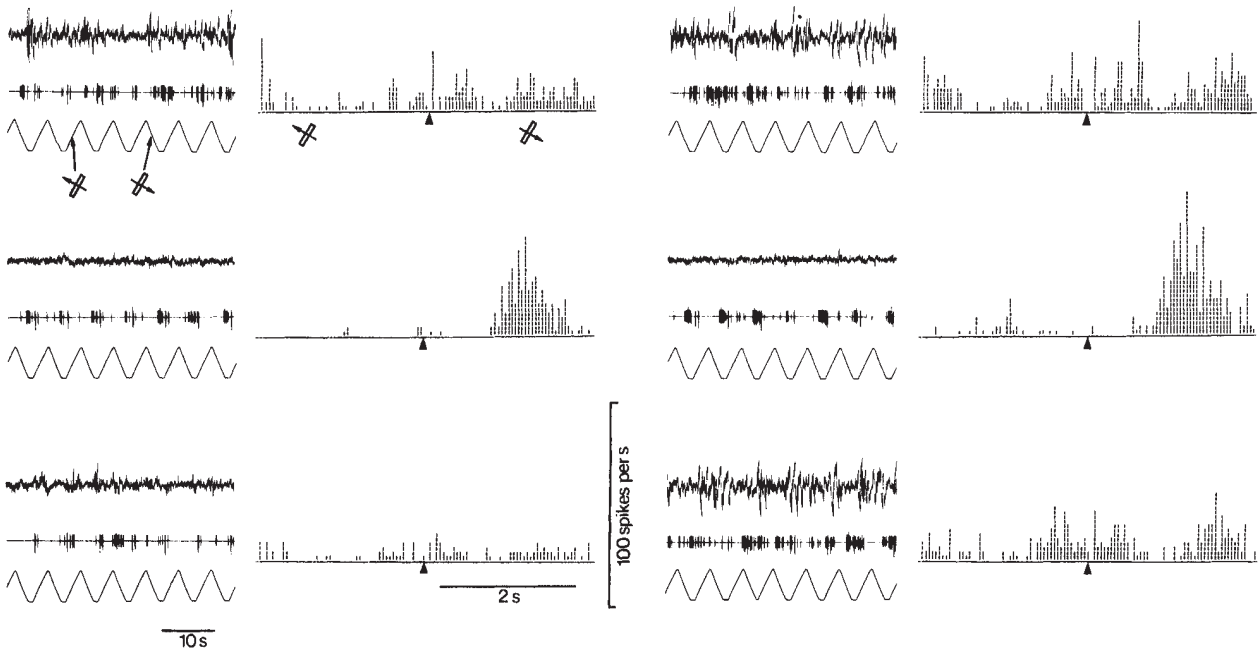


**Fig. 3** Responses of a cell in the striate cortex with the cat in various levels of arousal. Each record lasts 45 s and ~3 min elapse between records. As indicated by the EEG (upper trace), the three records on the left side are taken, from above downwards, in slow-wave sleep, awake and slow-wave sleep; those on the right are in slow-wave sleep, awake and slow-wave sleep. The middle trace shows impulse discharges, and lower trace indicates by up-and-down deflections left and right movement of a $1/4° \times 2°$ slit oriented 30° clockwise to vertical. In the alert state the cell responds briskly to rightward movement, but hardly at all to leftward movement. In drowsiness and sleep spontaneous firing is greatly increased, and responses to the moving slit are almost completely absent. Each histogram is the average of 12 responses.

sleeping and waking. Usually (in two-thirds of the 130 cells studied) an irregular burst of spontaneous firing in slow-wave sleep was reduced in overall rate and replaced by a smoother, more regular pattern on awakening. In 10 cells there was an increased firing rate and a smoothing. The rest of the cells showed no difference in spontaneous activity between sleeping and waking. Visually evoked responses were either unaffected or enhanced by awakening: in no cells were responses diminished. Roughly one-third of all cells showed an increase in evoked response that was obvious on the polygraph record; many more cells showed an enhancement of responses that were detected only by histogram averaging. Even in cells showing no increase in evoked response, the response was usually easier to observe against the more regular or reduced background firing.

Figure 2 shows an example of the effects of arousal on the responses of a cortical cell. The stimulus was an optimally oriented moving slit of light. The responses, which were weak and capricious during slow-wave sleep, became stronger and more consistent after arousal by a noise. Despite the increase in response to the optimum direction of movement (up and to the right), the reverse direction remained ineffective.

Figure 3 shows six extracts from a record of another cell, taken over a 15-min period during which the cat repeatedly slept and awoke. The visually evoked responses were drastically changed, from vigorous while awake to almost completely absent during sleep. The increase in the response in the awake state was especially obvious because the background firing was reduced.

Four of the cells showed a transient burst of smooth steady firing lasting for about 30 s when the animal awoke spontaneously or was aroused by a noise or touch. After the burst the firing remained regular, usually stabilizing at a rate about the same as that during sleep or slightly higher. Had these cells not been clearly and specifically driven by particular visual stimuli, they might have been classed as multimodal, given their tendency to respond to any stimulus capable of arousing the animal. We saw no cells in striate cortex that responded to sense modalities other than visual, except in association with arousal.

A fall in both orientation specificity and movement–direction selectivity has been reported following stimulation of the menencephalic reticular formation[19]. Our preliminary results with natural arousal do not, however, point to a loss of specificity; on the contrary there may sometimes be an improvement. Figure 4 shows that the response to an optimally oriented slit was clearly, though not dramatically, improved after arousal, caused in this case by a loud noise, while the background firing was reduced and smoother. Directional selectivity was slightly improved, in that the response to the less effective direction of movement declined. For most directionally selective cells, however, the responses to the two opposite directions changed roughly in proportion. If, as in Fig. 2, one direction of movement failed to evoke a response in sleep, the same was so after arousal. No cell lost directional selectivity after arousal from sleep.

In testing orientation selectivity with a hand-held visual stimulator, we usually found no change. A few cells showed a slight improvement, but to be certain of this it will be necessary to compare orientation tuning curves.

Finally, in several cells we studied the effects of awakening on end stopping—the decline in response that occurs in some cells, termed hypercomplex, when a slit, edge, or dark bar is made longer than optimal[20]; the degree of stopping did not vary with level of arousal. The enhanced excitation from the activating part of the receptive field is therefore presumably offset by an enhanced inhibition from the outlying areas.

These observations are consistent with previous ones[20–22] that deepening barbiturate anaesthesia suppresses responses but does not change their specificity or lead to other qualitative changes. They also confirm the finding of Wurtz[23] that cells in area 17 recorded from awake alert monkeys with chronic recording techniques show responses that are not obviously different from responses obtained under barbiturate anaesthesia.

Most of the cells we studied were complex in type. The few simple cells examined showed the same types of changes as the complex cells. Though we have too few cells to make reliable comparisons of laminar distribution, the most striking changes in responses seemed to be in deeper-layer cells.

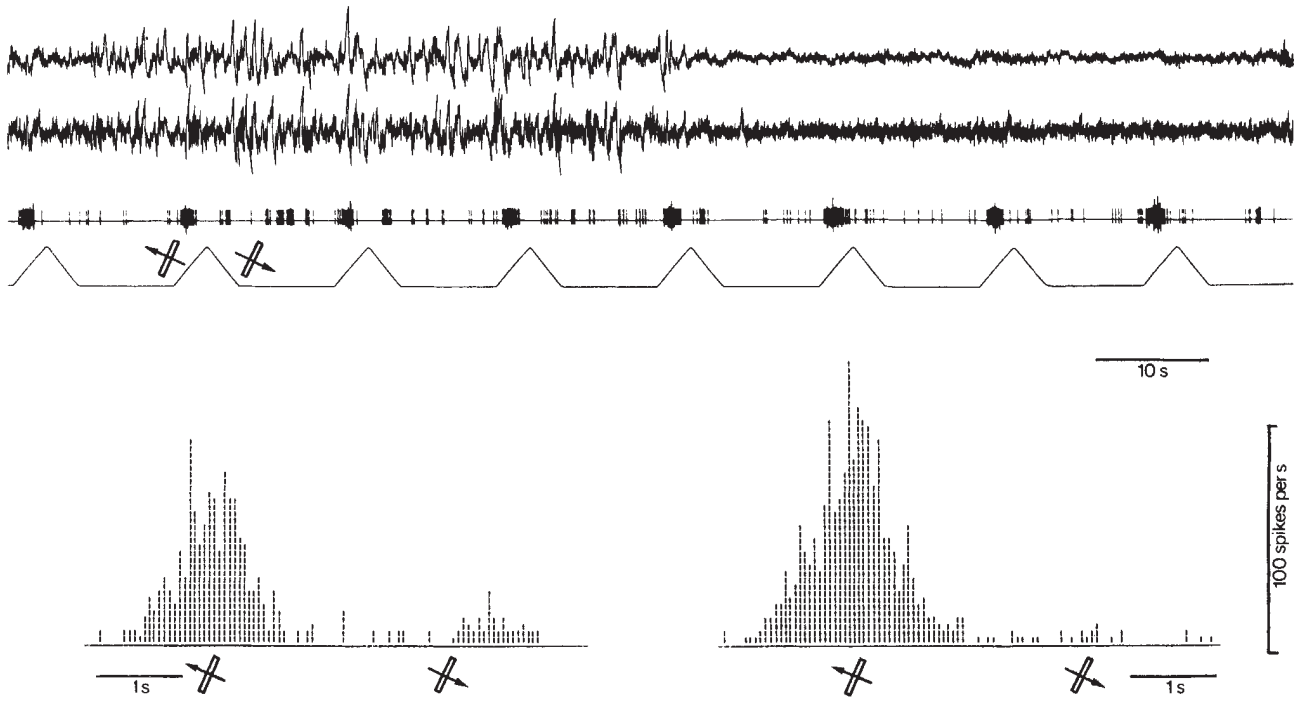


**Fig. 4** Effects of arousal from slow-wave sleep on responses and response selectivity of a cell in layer 2 of striate cortex. About halfway through the 2-min record the cat is aroused by a noise. An optimal slit, $1/2° \times 3°$, oriented 25° clockwise to vertical, evokes a response (third trace) that is much greater to movement up and to the left than down and to the right. Arousal results in a moderate increase in the response to leftward movement, and a virtual elimination of the response to rightward movement (see the histograms). Arousal also produces suppression and smoothing of the spontaneous firing.

## 2-Deoxyglucose studies

We examined deoxyglucose uptake as a function of waking state in eight cats. Four cats, two awake and two in slow-wave sleep, were stimulated with moving vertical stripes confined to the right visual field. The other four cats were half the time awake and half the time asleep (see below). The cats studied in slow-wave sleep were sleep deprived on a treadmill.

Cats were prepared in the same way as those used for physiological recordings, except that the microelectrode advancer was not installed. After discontinuing the anaesthetic we waited until the arrhythmic slow-wave pattern of halothane anaesthesia gave way to the low-voltage rapid activity characteristic of arousal. In the sleep-deprived animals this waking activity was soon replaced by the high-voltage slow waves of slow-wave sleep. A noise or tactile stimulus was sufficient to arouse the animals.

The visual stimulus was a moving set of irregularly spaced vertical black and white stripes projected on a screen by a slide projector and a motor-driven mirror, which produced a back-and-forth movement at $2° s^{-1}$. Stripe width was about 1/4° near the vertical midline, gradually increasing to 2–3° in the periphery. The stripes were confined to the right field of vision, and did not include the vertical midline but extended from 2–3° to the right of the midline, out to ~45°. The diffusely lit part of the screen (0.5 log cd $m^{-2}$) covered the vertical meridian and left visual field. We injected $^{14}$C-2-deoxyglucose in a single pulse over 5–10 s, began the stimulus immediately and continued it for 45 min.

The cats were then deeply anaesthetized with thiopental and perfused with normal saline followed by formol–saline. The brains were removed, frozen in liquid $N_2$–cooled Freon-25 at −100 °C and sectioned on a cryostatat at −30 °C. Sections were mounted on glass coverslips, heated to 75 °C to drive off water and exposed against X-ray film. We sometimes combined autoradiographs of 2–4 successive cortical sections by making enlargements on film and superimposing them, so that we could average the patterns seen in several single sections and obtain an enhancement of the overall pattern.

Though the two waking brains differed consistently from the two sleeping ones, we were worried that the differences might be due to variability between individual cats rather than to differences in their arousal state. In our first attempt to demonstrate differences in a single animal we alternated the stimuli, presenting stripes to the left visual field when the cat was awake and to the right field when it was asleep. The result was unsatisfactory, perhaps because each hemisphere was stimulated only half the time and any label associated with visual stimuli would be seen against a background representing both states of wakefulness.

To overcome these problems (and also with an eye to countless other applications), we developed a double-label 2-deoxyglucose technique, exploiting the differential sensitivity to $^{14}$C and $^{3}$H $\beta$-emissions of standard X-ray film and LKB Ultrofilm $^{3}$H. In standard X-ray film the emulsion is protected by a gelatin layer, ~1 μm thick, which acts as a partial barrier to the low-energy $^{3}$H emissions. The LKB film lacks this coating and is roughly 20 times more sensitive than X-ray film to $^{3}$H, whereas the two films are about equally sensitive to $^{14}$C. These ratios were determined by exposing both types of film to standards made by soaking pieces of filter paper in serial dilutions of $^{3}$H and $^{14}$C. In the autoradiographs shown here we increased the ratio of sensitivity to $^{14}$C to sensitivity to $^{3}$H of the X-ray film to about 100:1 by interposing an additional 10-μm layer of polyethylene film.

In the injections of deoxyglucose we tried to achieve a $^{14}$C/$^{3}$H ratio that would allow the $^{3}$H to overpower the $^{14}$C on the LKB film, and the $^{14}$C to predominate on the X-ray film.

Both double-label cats were sleep deprived on a treadmill and prepared as described for the single-label ($^{14}$C) cats. After the halothane was discontinued we waited until the EEG had shifted to a normal slow-wave sleep pattern from which the animal could easily be aroused. We then injected the $^{14}$C-2-deoxyglucose and stimulated the left visual field with vertical black and white stripes for 45 min, all the while praying that the animal would stay asleep. Next we aroused the cat, injected the $^{3}$H-deoxyglucose and stimulated the right visual field for 45 min,

keeping the cat awake by a general uproar and tactile stimuli as needed. To be certain of confining the stimulus to the contralateral hemisphere we avoided stimulating a strip of visual field 2–3° to either side of the vertical midline. The cat was perfused and the brain sectioned as already described. The histological sections (together with a set of filter paper standards) were exposed first to X-ray film protected by polyethylene film and then to LKB film.

## Lateral geniculate autoradiography

In the two single-label animals whose right visual fields were stimulated when awake, the left LGBs were heavily labelled. The region of dense label was confined to the part of the geniculate corresponding to the area of visual field stimulated, extending on coronal sections medially almost to the medial border, which corresponds to the vertical meridian, and laterally over half to two-thirds of the geniculate's width, corresponding to the 45° lateral extent of the stimulus (Fig. 5*a*). The right (unstimulated) LGB showed label only at background levels. In one of the two animals stimulated while in slow-wave sleep, both sides showed label only at background levels; in the other animal there was only very faint labelling on the stimulated side (not shown). In the double-label cat (Fig. 5*b*) only the $^{3}$H-sensitive film showed a left–right difference in geniculate labelling, and again the region with increased label (in the left geniculate) corresponded exactly to the part of the visual field stimulated. No difference was seen between the two sides on the polyethylene-protected X-ray film, except for slightly heightened labelling on the left, in exactly the same place as the label on the $^{3}$H film and doubtless due either to some unfiltered $^{3}$H or to some $^{14}$C-deoxyglucose still in the cat's bloodstream 45 min after the first injection, when the second, waking, $^{3}$H stimulus was begun. That the lack of $^{14}$C label on the right side was not due to failure of uptake of $^{14}$C is clear from the cortical autoradiographs in the same animal (see below). Considering the profound effects of slow-wave sleep on responses of the individual cells we studied, the pronounced differences in the autoradiography are not too surprising.

## Cortical autoradiography

A consistent and marked difference was also seen in the pattern of labelling in the visual cortex. Figure 5*c* shows representative overlaid sections from two single-label ($^{14}$C) cats, awake and in slow-wave sleep. These animals both had had their right visual fields stimulated, and in each there were conspicuous columns in the left hemisphere, and no hint of any periodic labelling pattern in the right hemisphere. In the awake animal the columns extended through the full thickness of cortex (except for layer 1) with roughly uniform density. In the cats stimulated during slow-wave sleep, the columns in the upper layers (above layer 4) were labelled about as densely as in the waking cats, but below layer 4 they were in most sections hardly visible against the background. In some cats layer 4 was continuously and densely labelled (Fig. 5*c*, waking) whereas in other cats it was not (Fig. 5*c*, slow-wave sleep). These differences in layer 4 labelling did not consistently correlate with sleep state and we cannot account for them.

The double-label cat gave the same result (Fig. 6). The upper pair of autoradiograph overlays are made from the same sets of sections as the lower pair, the only differences being in the type of film used and the interposition of a sheet of polyethylene film in the lower ($^{14}$C) set. Columns extended through the full thickness of cortex in the waking, $^{3}$H-labelled side, and for the most part only halfway down on the sleeping, $^{14}$C side. The figure also demonstrates how effectively this technique can distinguish between two different stimuli, as in each case only the appropriate hemisphere shows columns.

## Discussion

One might have imagined that when an animal awakens the neurones in its brain would simply become more active, as suggested by Sherrington[24]. While this may apply to some areas

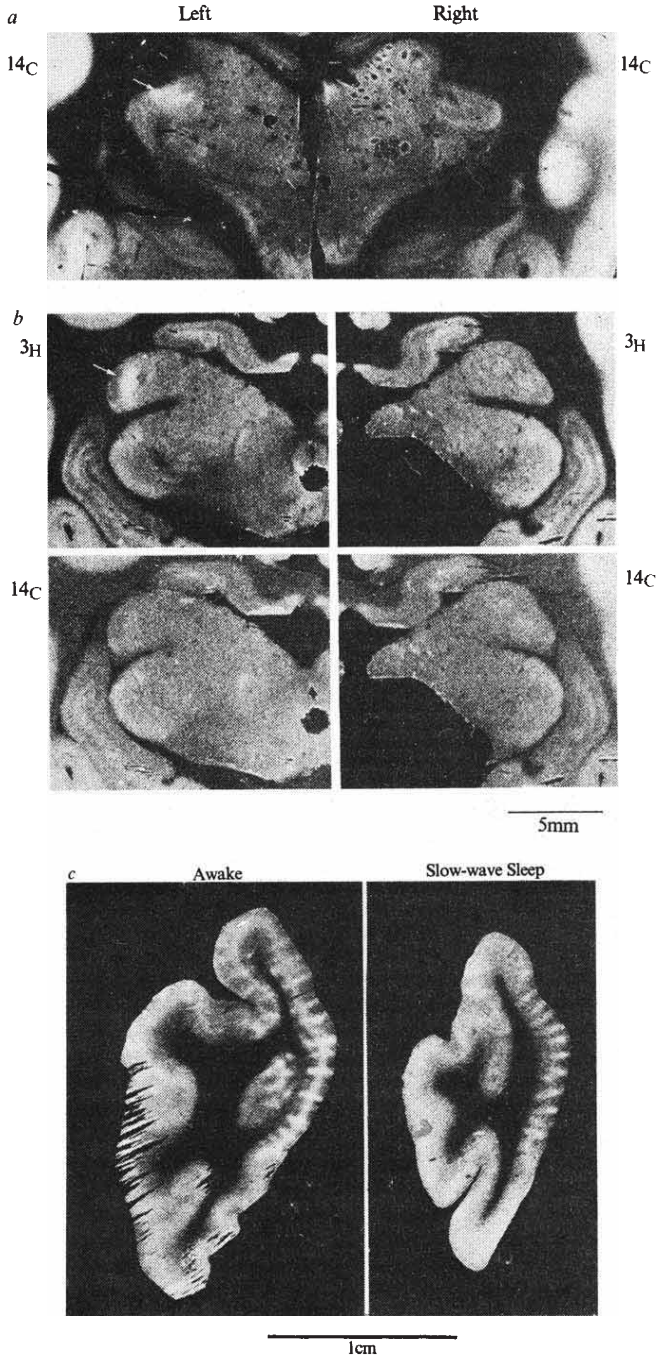


**Fig. 5** *a*, 2-Deoxyglucose labelling of lateral geniculate nucleus in an awake cat by a moving grating of vertical black and white stripes. Stimulus was confined to the right field of vision, coming to within 2° or 3° of the vertical midline. Label in the left LGB is indicated by the arrow. Another waking cat gave a similar result. Figs 5 and 6 are negatives; labelled regions show as bright areas. *b*, Four autoradiographs showing results of the sleep–waking double-label experiment. After the $^{14}$C-2-deoxyglucose injection (100 μCi kg$^{-1}$) the cat was stimulated while in slow-wave sleep for 45 min, the stimulus being confined to the left visual field. $^{3}$H-2-deoxyglucose (5 mCi kg$^{-1}$) was then given, and followed by 45 min of stimulation to the right visual field during which the cat was kept aroused. The same sets of sections were exposed to LKB Ultrofilm ($^{3}$H) and to polyethylene-protected X-ray film ($^{14}$C). The $^{14}$C autoradiographs of coronal sections show no obvious labelling; the $^{3}$H autoradiographs by contrast show a dense patch of label in the appropriate part of the left LGB. *c*, Deoxyglucose labelling of visual cortex in two cats, awake and in slow-wave sleep, stimulated with vertical stripes confined to the right visual field. Each part consists of three superimposed successive sections. Columns are labelled on the medial surface (to the right) in both coronal sections through the left hemispheres; the vertical midline projection (postlateral gyrus, at the top) is, as expected, not labelled. In the waking cat the columns (which appear bright in these negatives) extend through the full cortical thickness; in the slow-wave sleep cat they are well labelled in the superficial half of the cortex, but below that they are faint or absent.

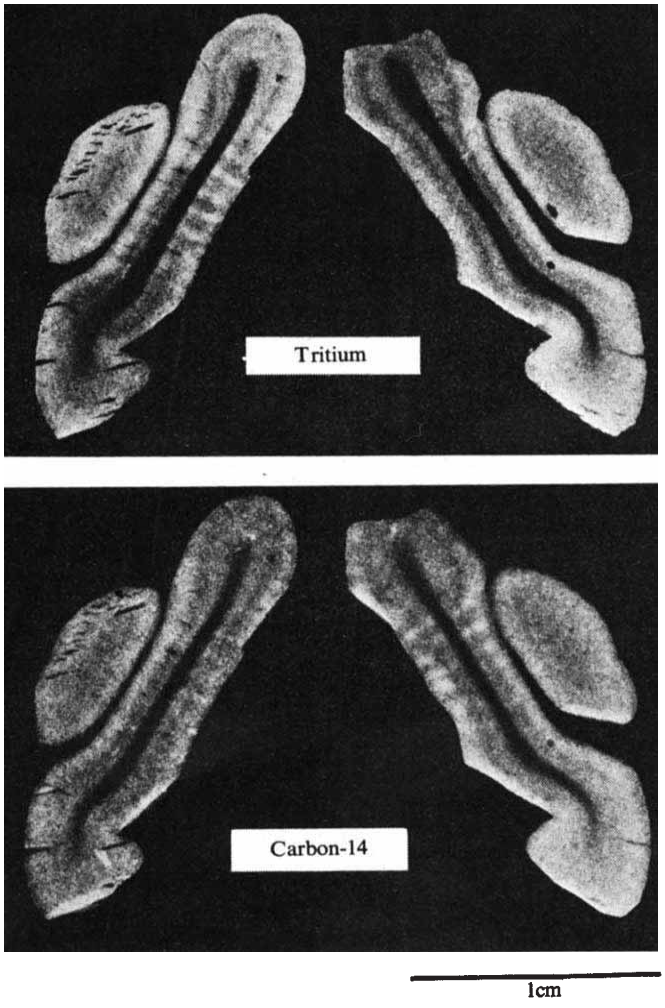


**Fig. 6** Double-label deoxyglucose labelling of cortex; three successive sections exposed to LKB film ($^{3}$H) and to protected X-ray film ($^{14}$C) are superimposed. In the upper, waking, $^{3}$H-labelled autoradiograph, columns are seen only in the left hemisphere and extend through the full cortical thickness. In the lower, sleeping, $^{14}$C-labelled autoradiograph they are more densely labelled in the upper layers than in the lower ones.

of the brain, for example to parts of the brain stem reticular formation, it does not fit well with what we know of the cerebral cortex. The EEG does not elucidate this question, because although it is a sensitive indicator of arousal, its interpretation in terms of underlying neuronal activity is equivocal: a flattening on arousal from slow-wave sleep can be due to a reduction of activity or a desynchronization; the waves themselves may represent summation of impulses or of graded potentials. Recordings from single cortical neurones have shown that the flattening of the EEG on arousal from slow-wave sleep is most often associated with a lowered rate of spontaneous neuronal firing[4,5,25]. Some cells, in our experience a minority, show a transient increase in firing rate. Usually high-frequency bursts are replaced by more regular firing.

Early studies of the effects of arousal on responses from the primary visual cortex used direct electrical stimulation at various points along the pathway, or diffuse light flashes. These stimuli have the disadvantage (compared with stimulation by small spots or lines) that they may evoke competing excitatory and inhibitory mechanisms with consequent loss of effectiveness. Nevertheless the responses they do evoke are facilitated by arousal from slow-wave sleep[26–28]. In studies much farther along in the visual pathway, in the inferotemporal region of nitrous oxide-anaesthetized monkeys, neurones have been observed to respond to complex stimuli more vigorously when the EEG is flat than during periods of high-voltage slow waves[29].

Our results suggest that arousal brings about an improvement in signal-to-noise ratio: geniculate cells showed enhanced evoked discharges and most cortical cells showed enhanced responses against a lowered or less chaotic background. (Similar effects were seen in somatosensory cortex of monkeys by Gücer[30].) But more than that, all components of the response were enhanced, suppression of firing as well as increases. Arousal may thus be attended by either depression or elevation of firing rate, depending on stimulus conditions. A cell in an awake animal is more the slave of incoming sensory inputs; in sleep it is more independent, less fettered by sensory constraints, but more at the mercy of events related to the still all-too-mysterious slow waves.

In normal life, even with the eyes open and surveying a complex scene, only a small fraction of cells in the visual cortex is likely to be engaged at any given instant because, for example, a light-dark contour can have only one orientation, can move only in one direction and at one velocity. For a few cells the discharge rate will probably be increased by the stimulus, but the remainder will continue to fire at their spontaneous rate, which will on the whole be depressed by arousal. If the visual cortex is representative of the rest of the brain, then in wakefulness most cells are not active but held in quiet readiness.

The effects of arousal in the small sample of geniculate cells studied were surprisingly strong, in contrast with the effects on cortical cells, most of which showed only a modest increase in response. This suggests that for some cortical cells the enhanced responsiveness of geniculate cells may be transmitted not as more vigorous firing but as more selective firing. Several cells showed a relatively greater enhancement to an optimal stimulus than to a suboptimal one, and consequently an improved selectivity for orientation or movement direction. We never saw a decline in selectivity.

In the cat the transition from the awake state to slow-wave sleep may be gradual, characterized in the EEG by bursts of high-voltage slow waves similar to those seen in continuous full-blown slow-wave sleep, alternating every few seconds with the low-voltage fast activity of arousal. The EEG alone cannot tell us whether this represents repeated transitory changes in arousal level or instead is a steady-state level of low arousal (drowsiness) characterized by a fluctuating EEG. Our single-cell recordings from geniculate and cortex support the former alternative, given the often tight correlation, within a few seconds, between a cell's behaviour and the onset or termination of an episode of slow waves.

Certain brain-stem neurones have long been known to show firing patterns that are closely correlated with levels of arousal[31–39]. Recently attention has focused increasingly on two monoaminergic brain-stem regions, the raphé nuclei and the locus coeruleus. Neurones in both these structures fire more rapidly during periods of increased alertness[40–43]. Like visual neurones, the brainstem neurones show a remarkably close correlation with the EEG, but in the brain stem, changes in firing rate usually precede the EEG changes by several seconds[43,44]. As both pharmacological and physiological studies have suggested that monoaminergic brain-stem neurones are important in controlling arousal, we compared, in a few cats, the effects on visual neurones of stimulating the locus coeruleus to the effects of spontaneous arousal and awakening induced by sensory stimuli. In each case they were the same. The effects of natural arousal from slow-wave sleep on spontaneous and evoked activity could be further exaggerated in an already awake animal by a loud noise or pinch; here again locus coeruleus stimulation had the same effect as a loud noise or a pinch.

The deoxyglucose autoradiographs showed clearly that the depression of activity in slow-wave sleep is different in different layers, being especially profound in 5 and 6. (This is consistent with an observation by Singer *et al.*[19], that cortical cells that could be antidromically activated from tectum or geniculate were particularly likely to be activated by brain-stem stimulation.) Our single-cell recordings had hinted at laminar differences, but it was certainly not true that in sleep suppression

of responses occurred in all of the deeper-layer cells, or in none of the upper-layer cells. The autoradiographic differences may not be due entirely to cell-body labelling: only electron microscopy will show whether the radioactivity is in cell bodies, axon terminals, dendrites, or all three.

The fact that some cells in layers 5 and 6 shut down in slow-wave sleep is pertinent to the functioning of the superior colliculus and LGB, for they are the respective major targets of these two layers. One guess might be that the source of the arousal effects observed in the LGB is the brain stem, because the locus coeruleus is known to send strong projections to the geniculate, and the dorsal raphé nucleus probably does[45,46]. Arousal could also act on the geniculate indirectly by reviving some otherwise dormant cells in layer 6 (ref. 19). This could be tested by cortical cooling or injection of local anaesthetics during examination of arousal effects in geniculate cells. It will be especially interesting to compare the responses of cells in the superior colliculus during waking and sleeping, because cooling and ablation of the visual cortex are known to abolish directionally selective responses to moving visual stimuli[47].

Our physiological findings imply either that the responses of many visual neurones in the central nervous system are enhanced on arousal, or that in sleep the responses are dulled. As the function of sleep is unknown, it is, of course, not clear whether a muffling of sensory input during sleep serves to insulate the animal from its environment to permit uninterrupted sleep or whether sensory systems also need to rest and the decreased responsiveness we see reflects whatever recuperative process the brain undergoes during sleep.

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# LETTERS TO NATURE

## Density power spectrum in the local interstellar medium

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**Since the identification of interstellar scintillation, the interstellar medium (ISM) has been known to contain electron density fluctuations having scales $\sim 10^9$ m. The scattering properties of these irregularities have been used in pulsar and continuum source studies and to investigate the small scale turbulence itself[1–11]. (We use 'turbulence' here to imply a disordered, irregular flow.) If the ISM turbulence extends over a broad enough range of fluctuation scales, it could have an important role in galactic cosmic ray transport and confinement[12–14]. Here we present observational evidence that electron density irregularities exist over a very wide range of scale sizes. Radio scattering observations associated with the wavenumber range $\sim 10^{-11}$–$10^{-6}$ m$^{-1}$ are consistent with a density spectrum of the form (wavenumber)$^{-3.7\pm0.6}$. At lower spatial wavenumbers ($10^{-16}$–$10^{-18}$ m$^{-1}$) the power spectrum can be estimated by computation of the density fluctuations near the 'outer' scale of the spectrum[15], comparison with density irregularities predicted by theoretical models of the ISM[16], and comparison with observations of the velocity structure function[13,17,18]. When combined with the high-wavenumber (radio) data, these low-wavenumber spectrum estimates are most simply interpreted in terms of a density spectrum behaving as (wavenumber)$^{-3.6\pm0.2}$ over a 12 decade scale size range ($\sim$100 pc to $\sim 10^7$ m). There may be theoretical difficulties[12,14,19] with such a spectrum, however. Alternatively, the low-wavenumber data could be associated with ISM clouds which are physically distinct from the small scale turbulence.**

The power spectrum describes the decomposition of a random field's variance into its various Fourier wavenumber components: it partitions the fluctuation 'power' of the field into eddies, with the characteristic size of an eddy being $\sim 2\pi$/wavenumber. The random field of interest here is the interstellar electron density. We assume that the density spectrum $P_{3N}$ (=Fourier transform of the three-dimensional density covariance function) depends only on the modulus of the wavenumber (isotropic statistics) and is independent of position within the ISM (homogeneous statistics). The homogeneity assumption is expected to break down at scale sizes comparable with the overall dimensions of the flow[4]. We have interpreted observations that are sensitive to particular scale sizes in terms of the density fluctuations required on those irregularity scales.

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