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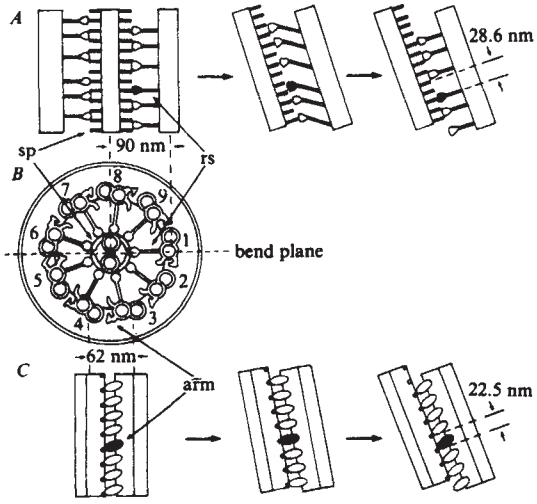

Fig. 4 Hypothetical changes in axonmal substructures in a bent cilium. *A*, doublet no. 1 (see *B*) in a segment of the cilium slides by 28.6 nm relative to the central tubules to complete one cycle of attachment-detachment between the radial spokes (rs) and the central sheath projections (sp)[12]. This causes the segment to change its direction by 0·32 rad. The vertical distance between the neutral lines of doublet no. 1 and the central tubules is 90 nm. *B*, A cross section of the cilium. *C*, Doublet no. 3 (see *B*) in the segment slides by 22.5 nm relative to doublet no. 4 to complete one cycle of attachment-detachment between the dynein arms (arm) of doublet no. 3 and the binding sites on the b-tubule of doublet no. 4 (ref. 11). This causes the segment to change direction by 0.36 rad. The vertical distance of the neutral lines of doublets nos 3 and 4 is 62 nm when measured in the direction of one bend plane. The changes in angular direction of the segment mentioned above are calculated by the equation: $\phi = u/d$ (see Fig. 1*B*). Dimensions are based on values reported by other authors[10–12].

detailed information about the relative positions of arms, spokes and their respective binding sites among different tubules, it is not fruitful to speculate further on this matter. However, it is worth noting that the theoretical minimum angle (for example, 0.32 rad for spokes) approximately matches the observed minimum angular step (0.2–0.3 rad). Further investigations, with single cilia such as those of sea urchin embryos[13], seem necessary to clarify whether the bend steps in the *Mytilus* compound cilia result from an inherent property of the axoneme rather than from interactions of many component cilia.

A preliminary report of this work has been presented elsewhere[14]. I thank Professor K. Takahashi for reading the manuscript and Professors Y. Hiramoto and P. Satir for discussion.

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Non-retinotopic arrangement of fibres in cat optic nerve

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Fibres in the mammalian optic nerve are generally thought to be organised retinotopically. Recording electrophysiologically from the cat optic nerve, we found little evidence to support this notion, which led us to investigate the problem by anatomical methods. We made a localised injection of horseradish peroxidase into the lateral geniculate body of the cat, labelling a small clump of retinal ganglion cells and their axons in the optic nerve. These fibres, emanating from neighbouring cells in the retina, became widely scattered through the optic nerve, indicating that retinotopic order is essentially lacking.

Perhaps no single fibre tract of the central nervous system has been so well studied as the optic nerve pathway from the eye to the brain. Nevertheless, the developmental mechanisms responsible for guiding incoming retinal ganglion cell axons to appropriate sites in their target nuclei, to achieve a precise topographical representation of the visual world, remain poorly understood. One theory, generally known as the 'chemo-affinity theory', states that each axon is attracted by a specific chemical signal to make its proper synaptic connection[1]. This proposal does not require retinotopic order in the optic nerve. An alternative theory suggests that fibres leave the retina in a strict retinotopic array and maintain their parallel alignment throughout the optic pathway, to be channelled to correct terminations by simple mechanical forces[2]. This explanation implies that information concerning specificity is embodied in the spatial arrangement of the fibres in the optic nerve and is thus predicated on the assumption that they are organised retinotopically.

The classical neuroanatomical literature is replete with studies reporting that fibres in the mammalian optic nerve are arranged retinotopically (see ref. 3 for summary and further references). These experiments involved making retinal lesions and looking for the pattern of subsequent degeneration in the optic nerve. Results obtained by this technique were difficult to interpret because the retinal lesion unavoidably damaged optic fibres passing across the retinal surface from more peripheral regions, and the degeneration stains were often unreliable. A few investigators actually failed to find evidence favouring retinotopy, but these negative reports received little attention[4,5]. The evidence available from physiological recordings made 20 yr ago in the spider monkey optic nerve suggested a scattered distribution of receptive fields[6]. Given this uncertainty over an issue of such importance to theories of neural development, it seemed worthwhile to re-examine the question of retinotopy in the mammalian optic nerve by physiological methods and modern anatomical techniques.

We began by repeating the physiological experiments in the cat. Recordings were made from three adult cats under thiopental anaesthesia according to standard procedures[6]. A tungsten microelectrode was passed vertically through the optic nerve at the point where it emerges from the optic canal to enter the cranial cavity (Horsley-Clarke V −4.00, A 15.75, L 3.75), and the location of each receptive field encountered was mapped in the animal's visual field. Our findings essentially confirmed the previous spider monkey study. In a typical penetration (Fig. 1) receptive fields of successively recorded fibres were located in widely separated areas of the visual field. Little hint of retino-

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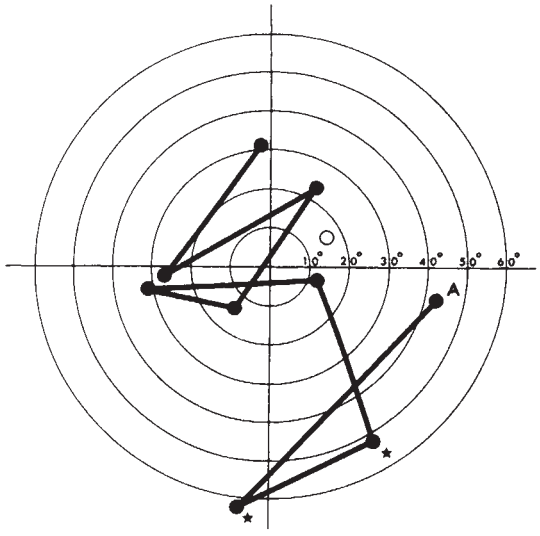

Fig. 1 Location in the visual field of nine receptive fields mapped in a vertical penetration through the right optic nerve beginning at A. The horizontal and vertical lines represent the horizontal and vertical meridians which cross at the area centralis. The open circle marks the projection of the optic disk. The two units marked with stars were recorded simultaneously.

topic order was apparent, although as the electrode descended through the nerve, receptive fields were more likely to be found higher and higher in the visual field. Receptive fields of simultaneously recorded units showed no particular tendency to be aggregated.

These physiological experiments seemed fairly persuasive but the possibility of artefact, due perhaps to uneven slippage or displacement of fibres by the electrode, could not be excluded. Therefore, we determined to corroborate the physiological evidence, by using the recently developed method of tracing anatomical projections by the retrograde transport of the enzyme horseradish peroxidase (HRP), as visualised by tetramethyl benzidine, a highly sensitive chromogen[7]. This technique avoids many of the problems inherent in the older degeneration methods, and it permits a much finer resolution of the fibre arrangement in the optic nerve. Results obtained from one cat will be presented; the findings have been confirmed in two other animals.

An anaesthetised cat was placed in a stereotaxic frame, and a site midway between the dorsal and ventral borders of lamina A of the right lateral geniculate body was located by recording with a tungsten electrode while stimulating with small spots of light in the visual field. The electrode was then replaced with a glass micropipette filled with a 20% solution of HRP in Tris–KCl buffer, the site was verified by recording again, and HRP was passed iontophoretically for 100 min to achieve a localised injection[8]. The animal was allowed to recover and after 44 h was re-anaesthetised and perfused with saline followed by 2.5% glutaraldehyde, 0.5% paraformaldehyde in 0.1 M phosphate buffer solution. A block containing the anterior half of the brain and the optic nerves was cut in serial coronal 100-μm frozen sections; the retinae were prepared for whole mounts. Tissue was reacted with tetramethyl benzidine and H_2O_2 for HRP activity and examined in the light microscope.

The injection site was centred in lamina A of the right lateral geniculate body, although the surrounding halo of the blue reaction product extended in every direction for about 1.5 mm. The zone of effective HRP uptake was restricted to the core of the injection site, judging from the pattern of cell labelling in the retinae. No HRP activity was present in the right retina; in the left retina (Fig. 2) a small patch of retinal ganglion cells containing HRP was observed. This region, which corresponded exactly to the injection site mapped physiologically in the lateral geniculate, occupied about 3.4 mm^2 or less than 1% of the entire retinal surface area. Granules of HRP product were detected in a total of 3,750 partially filled cells. In the heart of this labelled region eight virtually adjacent β cells were very heavily stained with HRP. Their cell bodies were completely filled and the dendritic tree could be followed out to the tertiary branches in the inner plexiform layer. From each of these eight cells an HRP-filled axon was visible streaming across the retina in a fairly direct course to the optic disk. The eight axons formed a loose bundle, occasionally crossing and intermingling; this made it difficult to be sure of the identity of each axon once it reached the optic disk. No axons could be followed more than 100 μm from the other more faintly labelled cell bodies.

These same eight axons were readily seen in the very first optic nerve section, just posterior to the optic disk, and followed section by section towards the chiasm. No other axons in the nerve, chiasm, or tract were labelled until a point in the optic tract a few millimetres before the injection site, except for a faint ninth fibre seen briefly for a short segment of the nerve. It proved possible by sketching every few sections to trace the course of each individual fibre from the optic disk through almost the full length of the nerve. Unfortunately, some of the fibres filled erratically for 1.1 mm just before the chiasm and their identities became confused. After the chiasm the eight fibres were assigned new labels and followed in the optic tract up to the lateral geniculate where they became lost in the injection site.

The arrangement of the eight fibres at several points in the optic pathway is shown in Fig. 3. Entering the nerve at the optic disk, the fibres were aggregated, although, relatively speaking, they were farther apart than one would expect from the close proximity of their cell bodies in the retina. For a short distance in the nerve they remained grouped, but with each consecutive section they quickly became more and more widely dispersed, until at 3 mm from the optic disk they were no longer confined to a single quadrant of the nerve. For the remaining 9 mm to the chiasm the fibres maintained a scattered disposition, with less rapid shifts in relative position. In the tract they were also dispersed (not illustrated), with some suggestion of reaggregation as they approached the lateral geniculate body.

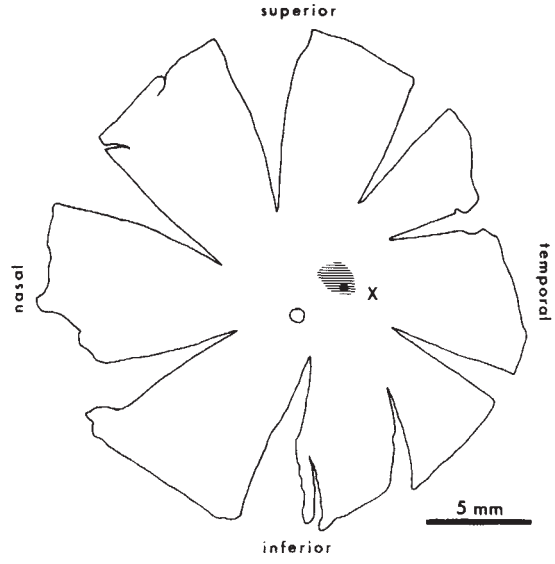

Fig. 2 Outline of a whole mount of the left retina. Cross-hatching indicates the region containing HRP-labelled cells; the black dot marks the location of the eight heavily filled cells. The open circle is the optic disk; the cross represents the position of the area centralis.

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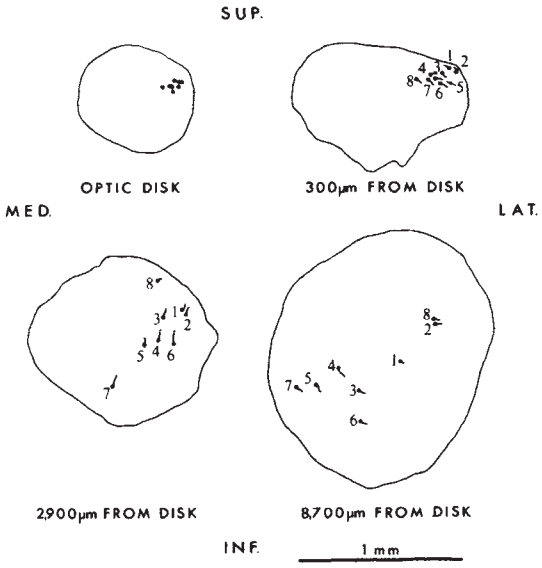

Fig. 3 Position of the eight HRP-labelled fibres at four stages in the optic pathway; their relative thickness has been exaggerated to make them visible. The optic chiasm begins 12,000 μm from the optic disk.

It is apparent that beyond the first few millimetres no strict retinotopy is present in the cat optic nerve although some crude topography may be preserved; axons of adjacent retinal ganglion cells do not generally travel side by side in the nerve. It might be argued that fibres from these adjacent cells are merely being reassorted in the nerve according to cell type, but we think this is unlikely, especially as in this particular experiment all eight labelled cells happened to be of the same cell type. The fibre pattern in the optic nerve is clearly not based on a system of simple retinal coordinates, although we do not conclude that the fibres are arranged haphazardly. They may be organised in some complicated fashion which is not yet clear. It is interesting, in this regard, that once the fibres diverge quickly in the initial portion of the nerve, they tend to maintain a more constant disposition, hinting that the scatter is somehow controlled.

In the light of our findings, it seems unlikely that the physical arrangement of fibres in the optic nerve and tract could alone account for the retinotopy present in the lateral geniculate body. Conceivably, however, retinotopic order is present as fibres first reach their targets, and their relative positions then shift during subsequent development. The critical information is lacking, namely, the temporal and spatial order of the nerve fibres on arrival at the lateral geniculate body in the embryo. It would further be interesting to know how the fibres of the optic nerve are organised and parcelled into their connective tissue fascicles. Finally, it is perplexing that fibres in the mammalian optic nerve should be scattered, in view of the evidence favouring retinotopic order in the optic nerves of fish and amphibia. One wonders if the non-retinotopic arrangement of fibres in the mammalian optic nerve may be of functional significance.

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Information processing of visual stimuli in an 'extinguished' field

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Lesions of the right parieto-occipital cortex in man produce a variety of behavioural disturbances which interfere with the detection of, and orientation to external stimuli[1]. One striking example is extinction to double simultaneous stimulation (DSS), in which presentation of a single stimulus in any area of the visual field results in its accurate description, but lateralised simultaneous presentation of two stimuli, one in each field, results in the verbal description of only the stimulus in the right visual field (RVF)[2]. While extinction to DSS can also be demonstrated in other (non-visual) sensory modalites[3], and is occasionally seen following left-hemisphere lesions[4] our concern here is with visual extinction to DSS following right parieto-occipital lesions whose precise nature is poorly understood although variety of theories have been proposed to account for it[5–7]. One of the critical, yet unexplored questions about extinction concerns the fate of the extinguished stimulus. The following observations demonstrate that although the extinguished stimulus often goes completely unnoticed by the patient, the patients are able to utilise the extinguished stimulus in an interfield comparison task. Accurate same/different judgments between the visual fields could be made in situations in which the patients did not know the identity of, and at times even denied the presence of, the left field stimulus.

The subjects were four right-handed female patients ranging in age from 56 to 70 years who were selected for study by routine neurologic examination. Although all patients had full visual field capacity when tested by a standard perimetry mapping with a single 1-cm, white object, each patient extinguished LVF stimuli on DSS, and left-sided touch stimuli under double simultaneous tactile stimulation. Each patient was alert and oriented and without language disturbance. Patients were tested on the third hospital day, before therapeutic manoeuvres (two cases). Patient no. 3 received steroids over the 36 hours before testing. Patient no. 4 had a persistent defect that remained unchanged during the weeks following surgery. Angiographic analysis and/or computerised tomography[8] revealed that all four patients had tumours in the right parietal lobe. (Cerebral angiography is a standard neuroradiologic procedure in which contrast material is injected into each discrete arterial system of the brain. This procedure aids the neurologist in diagnosis and the neurosurgeon in treatment. Computerised tomography is a brain imaging technique.) Neuropathologic analysis of tissue biopsies confirmed the clinical diagnosis of tumour in all patients.

Table 1 Single visual field naming

Patient no.	Visual field: Left	Visual field: Right
1	1.00 (15)	1.00 (12)
2	0.94 (16)	0.89 (9)
3	0.86 (14)	1.00 (15)
4	0.91 (33)	0.88 (33)

The proportion of trials that were correctly named by each patient in each visual field is shown. Numbers in parentheses represent total number of trials presented to each visual field. Performance differences between the visual fields were not significant ($t(3) = 1.12$, $P < 0.4$). Variation in total number of trials presented to each patient is described in the text.