

The discontinuous visual projections on the *Xenopus* optic tectum following regeneration after unilateral nerve section

D. J. WILLSHAW AND R. M. GAZE

*Department of Zoology, Edinburgh University, West Mains Road,
Edinburgh EH9 3JT, UK*

SUMMARY

The establishment of retinotectal projections following transection of one optic nerve in developing *Xenopus* has been investigated. Between 3 weeks and 11 months after the operation, the nerve fibre tracer horseradish peroxidase (HRP) was applied to either the operated or the unoperated nerve, and the brains were prepared for examination as whole mounts.

In most cases fibres from the operated nerve innervated both tecta, with the result that one tectum was doubly innervated and one tectum singly innervated. Two months after transection of the optic nerve in tadpole life, between stages 50 and 54, this nerve usually made a uniform projection on the contralateral tectum and a striped projection on the ipsilateral, doubly innervated, tectum. The projection made by the unoperated nerve on this tectum was a similar pattern of stripes, which ran generally rostrocaudally. Two months after transection of the optic nerve of newly metamorphosed animals, the projection formed by the operated nerve on the doubly innervated tectum was usually a pattern of spots or spots mixed together with stripes in no particular orientation superimposed on a roughly uniform background. In a small number of cases the projections made by the same nerve on the two tecta were approximately complementary; that is, the presence of label on one tectum corresponded with its absence on the other tectum.

The results are examined in the context of the development of the retina and of the tectum. It is suggested that the consistently oriented stripes which result from nerve transection at a stage at which only a small proportion of the retinal fibres had reached the tectum are formed by the interaction of two equally matched sets of developing fibres, stripe orientation being determined by the mode of growth of the optic tectum. The formation of patterns of spots or spots mixed together with stripes following nerve transection after the end of the main phase of tectal histogenesis, and when 50% of the optic fibres had already reached the tectum, is attributed to an unequal competition between the two sets of fibres.

INTRODUCTION

In this paper we discuss the patterns of connectivity made by two similar neural structures on a common target. We have used the visual system of *Xenopus laevis*, which is readily accessible to surgical manipulation and assessment at all developmental stages.

In the binocularly innervated parts of the brain, the sites of termination of the fibres originating from the two eyes tend to be segregated into stripes, bands or blotches. The best-known example is the set of ocular dominance bands found in

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the visual cortex of various mammals, which are particularly well developed in the monkey (Hubel & Wiesel, 1968, 1972; Hubel, Wiesel & LeVay, 1976; Wiesel, Hubel & Lam, 1974).

In anuran amphibians, fishes and birds the main visual centre is the optic tectum, which does not receive a direct binocular input. In these animals double projections have to be produced by experimental means (Levine & Jacobson, 1975). The development of double projections has been studied by the implantation of a third eye into the head of a frog embryo (Constantine-Paton & Law, 1978), by the removal of one tectum in frog tadpoles (Straznicky & Glastonbury, 1979; Law & Constantine-Paton, 1980), by the construction of 'compound eyes' in *Xenopus* embryos (Fawcett & Willshaw, 1982; Ide, Fraser & Meyer, 1983) and by surgical interference with the optic chiasma in chicks (Fawcett & Cowan, 1985). The establishment of double projections in adult goldfish has been achieved by the removal of one tectum (Sharma, 1973) and by the deflection of selected optic fibre fascicles onto the ipsilateral tectum (Meyer, 1983a), and in juvenile *Xenopus* by section of both optic nerves near the chiasma to induce bilateral tectal innervation by the cut nerves (Glastonbury & Straznicky, 1978; Straznicky, Tay & Hiscock, 1980).

Stripe formation involves an interaction between the two visual inputs, which leads to the local segregation of fibres from each source while overall retinotopic organization is preserved. It has been proposed that the formation of stripes involves competition between two opposing mechanisms involved in the establishment of the binocular projection. The effect of one would be to induce each set of afferent fibres to project in retinotopic order across the same target area, whereas the effect of the other would be to induce the members of one group of fibres to segregate out from the members of the other group (LeVay, Hubel & Wiesel, 1975). An alternative proposal (von der Malsburg & Willshaw, 1976; von der Malsburg, 1979) is that two mechanisms of this general type act consecutively, with the second mechanism acting by itself to redistribute the initial retinotopic arrangement of fibres.

What is the difference between the two fibre populations which underlies the segregation process? In frogs, stripes are not caused by markers signalling left/right differences, since they form when two eyes of similar laterality are induced to innervate one tectum (Law & Constantine-Paton, 1981). Stripe formation does not require the segregating fibres to come from anatomically separate eyes, since in *Xenopus* fibres from the two halves of a surgically made compound eye form stripes (Fawcett & Willshaw, 1982). It is also not necessary for the segregating inputs to come from genetically different pieces of retina, as is the case where the component halves of a compound eye are taken from different animals, since isogenic compound eyes in *Xenopus* will form stripes (Ide *et al.* 1983). It has been suggested that retinal fibres are able to recognize the fibres from ganglion cells neighbouring their parent ganglion cells, possibly by electrical means (Willshaw & von der Malsburg, 1976), and in this way terminate on the

tectum together with fibres from the same eye while avoiding those from the other eye (von der Malsburg & Willshaw, 1976; von der Malsburg, 1979; Meyer, 1982; Fawcett & Willshaw, 1982). It has long been known that interaction between the two eyes at a functional level does occur in the mammalian visual cortex (Hubel & Wiesel, 1962, 1963, 1965) and neural function could be involved in the establishment of visual projections in fishes and amphibians (Meyer, 1982, 1983*b*; Schmidt & Edwards, 1983; Boss & Schmidt, 1984; Reh & Constantine-Paton, 1985).

The tectal distribution of stripes in *Xenopus* under various conditions is the subject of this paper. Our starting point was the observation by Glastonbury & Straznicky (1978) that in adult *Xenopus* in which a double projection had been induced by cutting one of the nerves there was no segregation of the two projections into stripes. This suggested that there were differences between the development and the regeneration of double projections; in particular, that in *Xenopus* an already established projection could not be disturbed by the fibres of a newly regenerating nerve.

Previous work on stripe development in anuran amphibians has involved embryonic manipulation before the optic nerve connects with its target centres, or interference with the visual system in the juvenile or adult animal. Thus the system has been disturbed before the appearance of retinotectal connections, or very much later in life, when the rapid phase of visual system development is finished. We have taken advantage of the very extended period over which retinotectal connections form in *Xenopus* larvae to compare the effect of interference during larval life, when intensive growth of retina, tectum and retinotectal connections is occurring, with the effect of operation at a later stage. In our experiments, we cut one optic nerve intracranially, just rostral to the chiasma, to induce bilateral tectal innervation by the cut nerve. The result was a double projection on one tectum, where regenerating fibres terminated along with normal fibres from the other eye, and a single projection on the other tectum.

In the first series of experiments, the nerve was cut between stages 50 and 54 (Nieuwkoop & Faber, 1967). Since at this stage only a small proportion of the adult complement of optic nerve fibres has arrived at the tectum (Wilson, 1971), most of the fibres innervating the tecta after the nerve was cut will have come from newly developed retina. These fibres would be innervating the tectum at a stage of development when the main part of tectal growth was nearing completion, just before metamorphic climax (Straznicky & Gaze, 1972). In the second series, the nerve was cut one to five weeks after metamorphosis, when about 50 % of the full, adult complement of optic fibres would have reached the tectum. In this case a substantial proportion of the optic fibres reaching the tectum after the nerve was cut would be regenerating fibres and the main, premetamorphic, phase of tectal growth would be complete.

Between three weeks and eleven months after the operation we looked at the projections which had formed, using the neuroanatomical tracer horseradish peroxidase (HRP).



1A



1B



2A



2B

Figs 1, 2. *Camera-lucida* drawings (A) and photographs (B) of two whole mount brains showing the pattern of labelling in the ipsilateral tract and tectum following application of HRP to the operated optic nerve. Dorsolateral view; rostral tectum is towards the bottom of the picture, the lateral edge to the right. In both cases the left nerve had been cut at stage 53 and then filled with HRP 3 months later. The optic tract is very wide, with fibres innervating the tectum through both brachia and over the surface of the tectum. The areas of labelled tectal neuropil have well-defined orientations, particularly at the lateral and medial edges of the tectum. Scale bar, 500 μ m.

MATERIALS AND METHODS

In the experiments on tadpoles the optic nerve was cut either by severing the olfactory nerves and then lifting up the forebrain and diencephalon to expose the chiasma, or by penetrating the space between the brain case and the dorsolateral edge of the brain to cut the nerve intracranially. In postmetamorphic animals the optic nerve was cut through the roof of the mouth, between the chiasma and the nearby blood vessel. Tadpoles were reared on Boots' vegetable and liver baby food until metamorphosis and juveniles were fed on Tubifex worms. At times between 3 weeks and 11 months after nerve section, the animals were anaesthetized by immersion in 1:3000 MS222 (ethyl m-aminobenzoate, Sandoz) in Niu-Twitty solution. A small piece of HRP was then applied to the cut end of either the operated or the unoperated optic nerve. The animals were kept out of water for 20 min to facilitate the uptake of HRP by the nerve, and were then revived. 48 h later, they were reanaesthetized, perfused and fixed in 2.5% glutaraldehyde in 0.1 M-phosphate buffer. The brains were dissected out and reacted according to the method of Adams (1977). In most cases the brains were cleared in methyl salicylate and prepared as whole mounts. In some cases transverse sections of the brain were cut at 50 μ m and rereacted for HRP, to examine the depth of staining achieved in the whole mount method. To give a direct comparison, in some of the sectioned brains only alternate sections were rereacted.

For most figures, we show a *camera-lucida* drawing as well as a photograph, since no photograph can illustrate the distribution of fibres adequately.

RESULTS

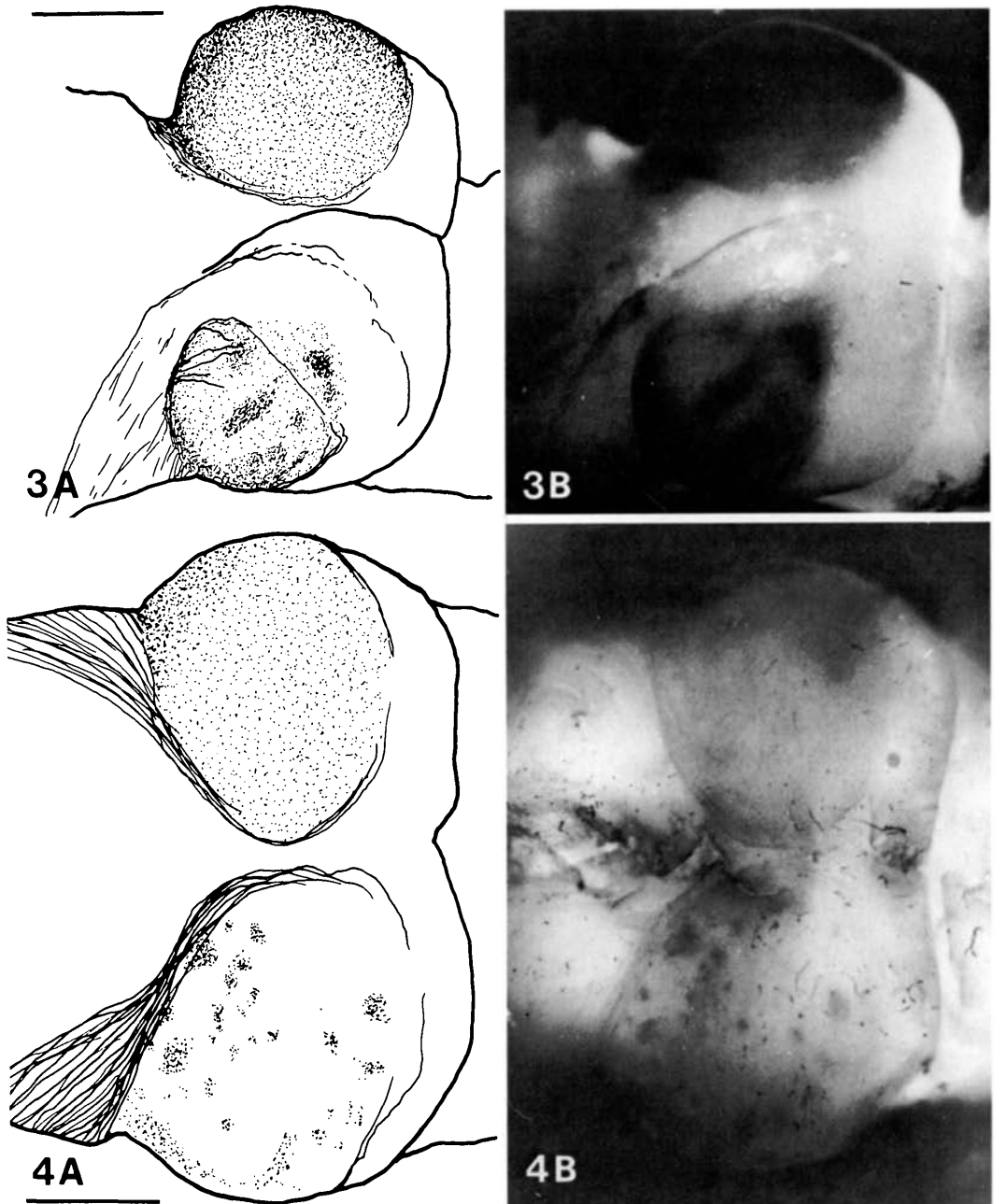
This analysis is based on 60 out of 124 experimental animals prepared as whole mounts. The cases which were not considered in detail were those in which there was no evidence that the nerve had been cut or that the cut nerve had reinnervated the brain. In addition, fifteen operated brains were analysed in transverse section and fifteen normal animals were prepared as whole mounts. In each brain the distribution of stained fibres and neuropil in the optic tract and on the optic tectum was assessed. The results are classified according to the stage at which the nerve was cut and the time allowed for regeneration to occur. These results are described below and are summarized in numerical form in Tables 1 and 2.

Following section of the nerve, fibres grew back to both tecta. The pattern of growth of the fibres, which included regenerating as well as newly growing fibres, was as described previously (Gaze & Fawcett, 1983; Taylor & Gaze, 1985). In particular, the distribution of labelled fibres in the tracts was generally less orderly and wider than that of normal fibres. At the tectum, particularly ipsilaterally, fibres tended to pass over the tectal roof, as well as around the edges of the tectum to form prominent brachia. In addition, fibres frequently swept wide round the lateral margin of the visually innervated part of the ipsilateral tectum. These characteristic behaviours of the fibres are shown in Figs 1, 2.

Early operations

The nerve was cut in tadpole life, between stages 50 and 54, and the projections were assessed between 5 weeks and 11 months after the operation.

When the cut nerve was labelled, the contralateral projection was uniform (Figs 3, 4) in 13 cases and non-uniform in 6. After a survival time shorter than 2 months the ipsilateral projection consisted of a set of poorly defined spots of stained neuropil on an otherwise empty background. After longer survival times



Figs 3, 4. Dorsal views of the two whole mount preparations showing the distribution of label on both tecta following application of HRP to the operated optic nerve. Rostral tectum is to the left. The left nerve was cut at stage 52, then filled with HRP 4 months later (Fig. 3), and 8 months later (Fig. 4). In both cases the tectum which is contralateral to the cut nerve is uniformly labelled. In Fig. 3 the ipsilateral projection is striped and restricted to the rostralateral part of the optic tectum. In Fig. 4 the ipsilateral projection comprises a set of spots. Scale bars, 500 μm .

Table 1. *Operated nerve filled*

	Total	Nature of the contralateral projection: uniform/non-uniform	Nature of the ipsilateral projection: stripes/spots
Early operation	19		
up to 2 months reinnervation	3	3/0	0/3
2–11 months reinnervation	16	10/6	10/4*
Late operation	25		
3.5 weeks reinnervation	3	3/0	(projections absent)
5 weeks reinnervation	2	2/0	0/1†
2 to 6.5 months reinnervation	20	17/3	7/11‡

* In the other 2 cases there was no ipsilateral projection.

† In the other case there was no ipsilateral projection.

‡ The projections categorized as stripes also had spots. In one further case (Fig. 11) the projection was a set of stripes running normal to the direction of the fibre trajectories; in the final case both ipsilateral and contralateral projections were incomplete.

Table 2. *Unoperated nerve filled*

	Total	Presence of contralateral projection only/presence of both projections	Nature of the contralateral projection: 'negative' stripes/spots
Early operation	10		
3–8 months reinnervation	10	7/3	10/0
Late operation	6		
5 weeks reinnervation	2	2/0	(both uniform)
3–6 months reinnervation	4	2/2	0/4

(up to 11 months) the ipsilateral projection formed a discontinuous pattern of areas of labelled neuropil scattered over the tectum. In 10 out of 14 cases the labelled areas were elongated, and so a definite orientation could be assigned to them (Figs 1, 2). On rostral tectum the direction of these stripes followed the overall (rostrocaudal) direction of the fibres entering the tectum from the optic tract. Stripes at or near the lateral or medial edges of the tectum ran parallel to the direction of the appropriate brachium, so some of them were curved. Caudally, the stripes ran around the edge of the tectum. Areas of stained neuropil in the central regions of the tectal surface tended to be smaller and more rounded and so no orientation could be given to them. In four cases the discontinuous ipsilateral label was in the form of spots or blotches (Fig. 4). In sections cut orthogonal to the direction of the stripes it could be seen that these regions of labelled tectum had the form of columnar structures extending throughout the depth of layers 8 and 9 (Lázár, 1984) of the tectum (Fig. 5).

In five cases the pattern of fibre trajectories effectively divided the tectum into two regions (Fig. 6; see also Fig. 1). The rostrolateral two-thirds of the innervated

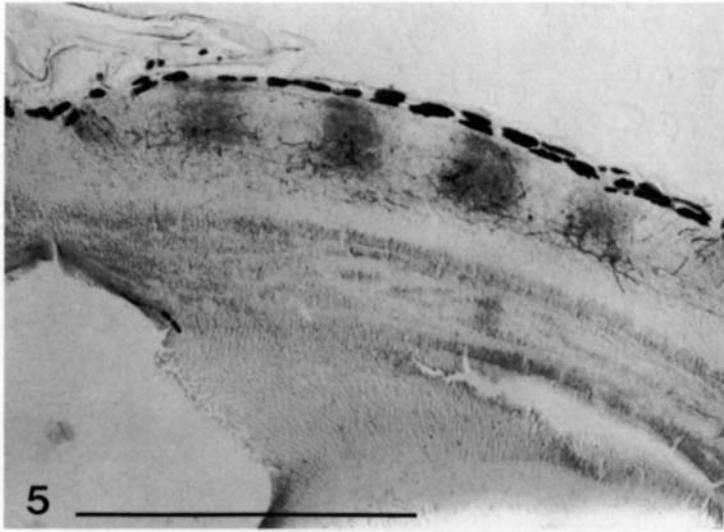


Fig. 5. Transverse section showing the distribution of label on the ipsilateral tectum following application of HRP to the operated optic nerve. The left nerve was cut at stage 50 and then filled with HRP 10 months later. The left tectum is shown, with medial tectum to the left. The areas of labelled neuropil extend as columns throughout the fibre layers of the tectum. Scale bar, 500 μm .

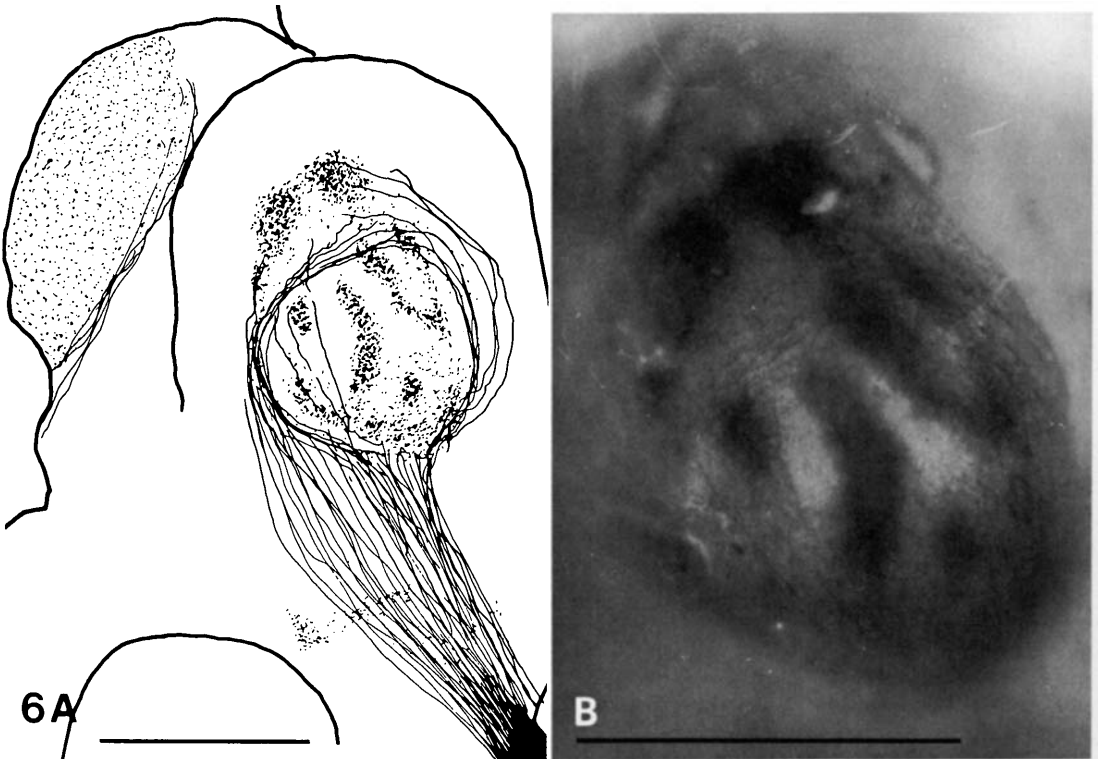


Fig. 6. *Camera-lucida* drawing (A) and photograph (B) showing the distribution of label over the ipsilateral tectum after application of HRP to the operated optic nerve. The left nerve of this animal had been cut at stage 51 and then filled with HRP 3 months later. The left tectum is shown from the dorsolateral viewpoint, with rostral tectum to the bottom, lateral to the right. The drawing shows a pattern of stripes across part of the ipsilateral tectum, intersected by a set of abnormally positioned labelled fibres which enclose the rostralateral two-thirds of the innervated region. The photograph is at a higher power and shows the abnormally positioned fibres. Scale bars, 500 μm .

tectum was separated from the caudomedial third by fibres which looped right across the tectum from the medial to the lateral brachium. The division of the tectum into two parts in these cases was also detectable in the pattern of labelled neuropil (Figs 1, 2).

It seemed likely that, in cases where the innervated tectum was subdivided in this fashion, the rostralateral part represented that part of the tectum present when the fibres first grew in following nerve section, whereas the caudomedial part represented tectum which had grown and became innervated subsequently. We therefore prepared normal projections in tadpoles at stages 51–53, representing the state of the system at the time the nerve cuts were made, and normal projections in tadpoles at stage 57, representing the state of the system at the time at which fibres might be expected to grow to the tectum after nerve section (Gaze & Grant, 1978). Fig. 7 compares the projections at these various larval stages with the discontinuous projection on the tectum illustrated in Fig. 1. As may be seen, the area of the normal stage 57 projection is comparable with the area of the rostralateral subdivision of the regenerated projection.

When the unoperated nerve was filled, in most cases there was labelling of the contralateral tectum only. The distribution of label was discontinuous and made a pattern which was approximately the 'negative' of that seen when the operated nerve had been filled; that is, there was a set of labelled neuropil in which a number of unlabelled regions could be seen. In cases where the relative amounts of unlabelled and labelled neuropil were comparable, 'figure' could no longer be

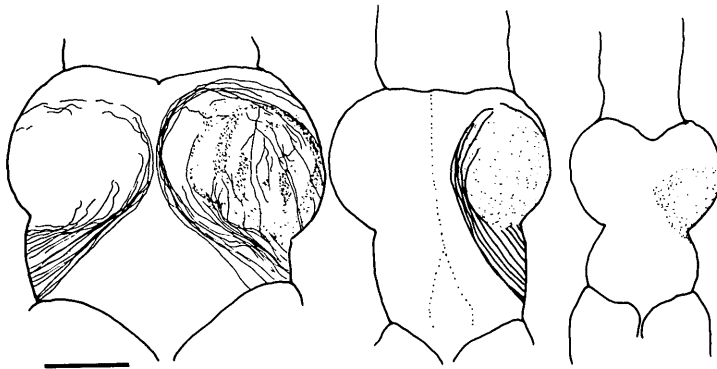


Fig. 7. Composite *camera-lucida* drawing showing three tecta in dorsal view, oriented with rostral brain to the bottom of the picture. In this figure are compared the normal pattern of tectal innervation by the contralateral optic nerve at stages 53 (right-hand drawing) and 57 (centre) with the postmetamorphic striped projection pattern illustrated in Fig. 1 (left-hand drawing; note that the innermost line of fibres shown in Fig. 1A has been omitted here, to aid clarity; furthermore that in Fig. 1 the brain is seen from the dorsolateral rather than the dorsal viewpoint). The stripes in this pattern seem to lie along the successively newly growing edge of the tectum. Scale bar, 500 μm .



Fig. 8. The distribution of labelled neuropil on the contralateral tectum following application of HRP to the *unoperated* optic nerve. The left nerve had been cut at stage 52 and HRP was applied to the right nerve 4 months later. Rostral tectum is towards the bottom left of the picture, lateral tectum to the right. Scale bar, 500 μm .

distinguished from 'ground', and thus the projection came to resemble one in which the operated nerve had been labelled (Fig. 8).

Late operations

In these animals the optic nerve was cut one to five weeks after metamorphosis.

Three and a half to five weeks after the operation, fills of the operated nerve showed that there was a faint and uniform projection over the contralateral tectum. On the ipsilateral tectum, fibres had reached either the brachia, predominantly the medial brachium, or the tectum to give an extremely faint uniform fill. In one case there was faint, diffuse labelling of the medial and lateral tectal margins, adjacent to the brachia. By eight weeks the tectal projections had acquired their characteristic form, as described below.

When the cut nerve was filled between 2 and 6.5 months after the operation, both optic tracts were filled with fibres, and were wider than those in the preparations where the nerve had been cut at the earlier stage. Both tecta were innervated by fibres running in both lateral and medial brachia, and also by many fibres running over rostral tectum. In some cases a few fibres had crossed from one tract to the other.

The contralateral projection was generally uniform, and resembled a normal regenerated projection. The pattern of labelling on the ipsilateral tectum was made up of a uniform background, of intensity equal to that on the contralateral side, on which was superimposed either a pattern of small spots of more densely labelled neuropil (Fig. 9) or a set of spots interspersed with stripes running in various different directions (Fig. 10). In one case there was a set of stripes running normal to the direction of ingrowth of the fibres (Fig. 11). The similarities between the projection patterns of animals that had had their nerves cut in the same batch of operations (some with different survival times) were in general much greater than those between the patterns from different batches of operations.

Fills of the uncut nerve resulted in non-uniform labelling of the contralateral tectum. The pattern resembled a uniform projection from which small round spots had been removed. The two cases where there was also labelled neuropil on the ipsilateral tectum are discussed below.

Sectioned material

One potential disadvantage of the whole mount method employed is that the chromogen may not penetrate to the entire depth of the tectal fibre layers. It could be argued, therefore, that the pattern of labelling revealed by this method reflects

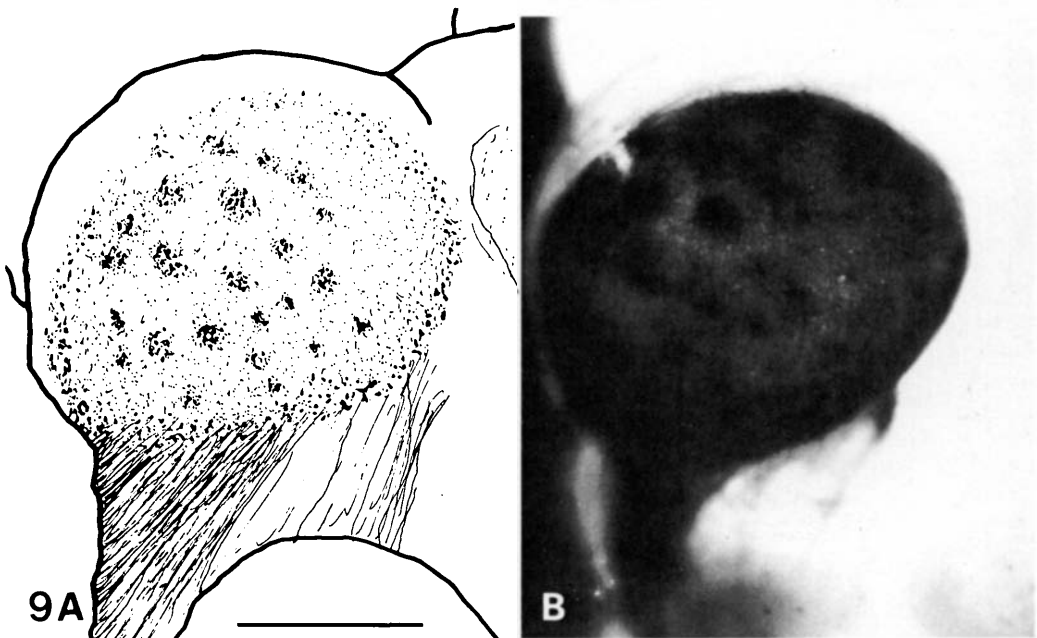
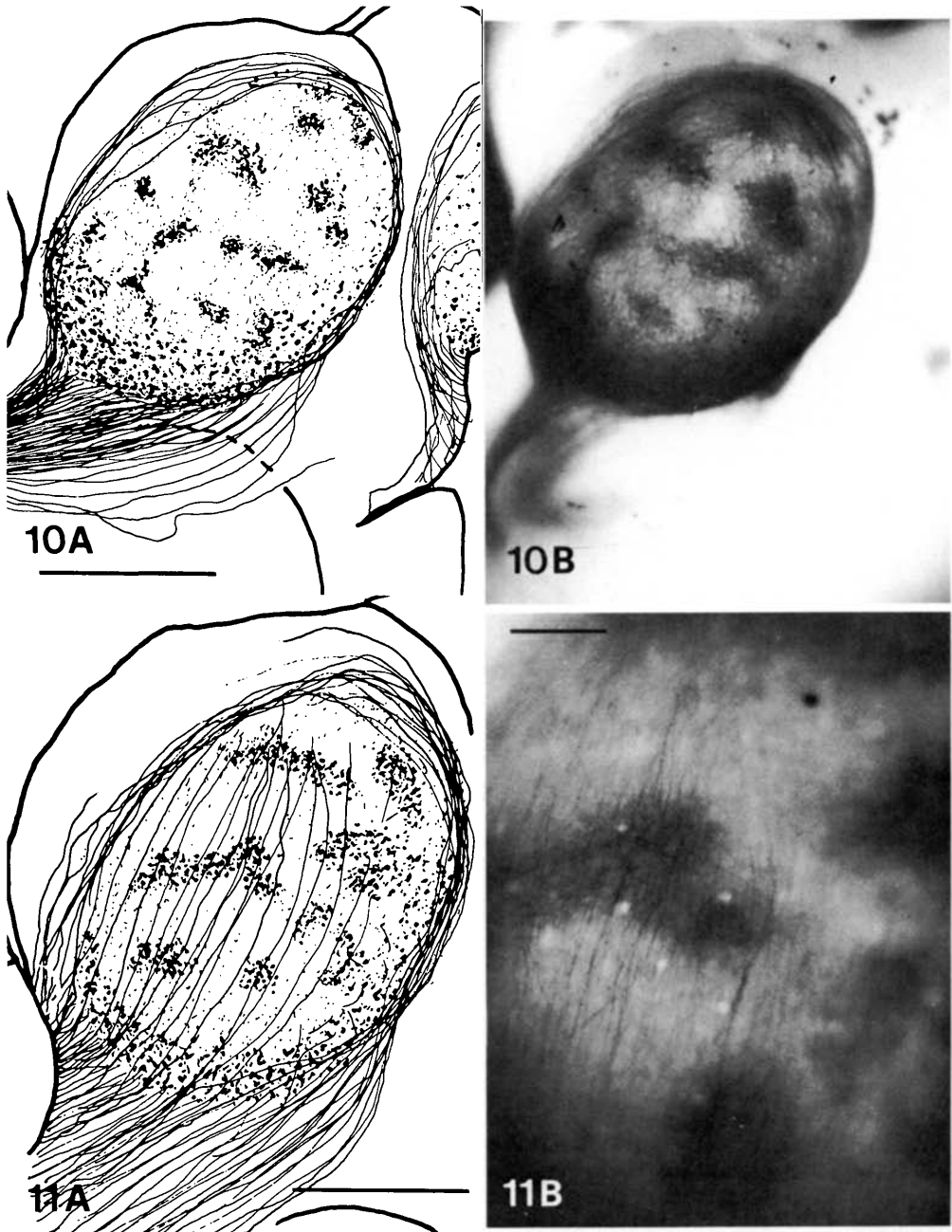


Fig. 9. The distribution of label on the ipsilateral tectum following application of HRP to the operated optic nerve. The right nerve had been sectioned 5 weeks after metamorphosis and was then filled 4 months later. Dorsal view of the right tectum, with rostral tectum to the bottom of the picture and lateral tectum to the left. The pattern of labelled neuropil is a set of spots on a uniform background. Scale bar, 500 μm .



Figs 10, 11. The distribution of label on the ipsilateral tectum following application of HRP to the operated optic nerve. In both cases the right nerve had been sectioned 3 weeks after metamorphosis and was then filled with HRP 6.5 months later. Dorsal view of the right tectum, with rostral tectum to the bottom of the picture and lateral tectum to the left. The labelled neuropil forms a pattern of spots interspersed with stripes (Fig. 10) or a pattern of stripes (Fig. 11). In Fig. 11, the photograph (B) is a higher magnification version of the *camera-lucida* drawing (A), showing that the stripes run at right angles to the direction of the fibres. These two preparations are from the same batch of operations; the preparation illustrated in Fig. 9 is from a different batch of operations. Scale bars, 500 μm for Figs 10, 11A, 100 μm for the higher magnification photograph Fig. 11B.

the superficial distribution of fibre terminations only. To check this we examined in transverse section the brains of experimental animals operated after metamorphosis in which there had been bilateral regeneration. The cut nerve was filled with HRP four months after the operation. In three cases where the brains had been reacted as whole mounts, transverse sections were compared with adjacent sections which had been rereacted after cutting. We found little difference in the depth of penetration between the two cases.

Bilateral innervation by the uncut nerve

In 14 animals, involving fills of either the uncut or the cut nerve, there was evidence that the uncut nerve had projected to both tecta. In the cases where the *cut* nerve had been filled, the presence of a non-uniform projection on the contralateral tectum indicated the presence of a double projection from the uncut nerve. Some of the projections were roughly complementary; that is, the presence of labelled neuropil in a particular position on one tectum corresponded with an absence of label in that position on the other tectum. In three cases there was a uniform projection on one tectum except for a few small holes, whilst the other tectum had just a few spots of labelled neuropil in the positions approximately complementary to the holes. In another three cases the region of label on one tectum was grossly complementary to the region on the other tectum but the two regions were themselves broken up into spots or bands.

DISCUSSION

These experiments provide possible explanations for the orientation of the stripes in certain cases, based on the observation that the positions of the stripes resulting from operation at an early developmental stage run in a generally rostrocaudal direction, closely following the lines adopted during development by the medial brachium and by the advancing caudal margin of the innervated region of the tectum (Straznicky & Gaze, 1972). We have also shown that the pattern of the discontinuous projections formed in larval *Xenopus* is very different from that formed after metamorphosis.

At the stage in larval life when the early operations were done, the rate of increase in the number of retinal fibres is approaching its maximum (Jacobson, 1976; Beach & Jacobson, 1979) and most of the fibres growing to the tectum after such nerve section will be new and uncut fibres. We suggest that in this situation there will be a competition between two comparable populations of fibres, giving a discontinuous double projection in the form of stripes with an orientation determined by the pattern of growth of the tectum, either directly or as a consequence of the relation between its mode of growth and that of the retina. It could be, for example, that the interaction between the two populations of retinal fibres to give stripes is facilitated at the growing edge of the tectum. Alternatively, the orientation of the stripes may reflect the shifting of connections which occurs in

developing *Xenopus*. The retina grows in roughly concentric annular rings while the main direction of growth of the tectum is rostralateral to caudomedial; yet throughout this period of growth there is an ordered projection of retina onto tectum (Straznicky & Gaze, 1972; Scott & Lazar, 1976; Gaze, Keating, Ostberg & Chung, 1979). Although in our results the orientation of the stripes tends to follow that of the fibre trajectories, it is unlikely that fibre trajectories themselves determine stripe orientation. Counter-examples include Fig. 11 of this paper, the case of the double-ventral projection (Fawcett & Willshaw, 1982) and stripe formation in the chick embryo (Fawcett & Cowan, 1985).

When one optic nerve is cut after metamorphosis, a large proportion of the fibres growing to the tecta from this nerve, over the period allowed before the projections are assessed, will be regenerating fibres. These fibres are growing onto a tectum which has passed the period of most rapid growth and the fibres have to compete with an established normal projection of fibres already present on the ipsilateral tectum. In this case the observed result tends to be a discontinuous projection in the form of spots or blotches. When stripes do occur, they tend to have no particular orientation. We suggest that there will now be an unequal competition between the two projections, based on either qualitative (regenerating *vs* resident projection) or quantitative differences (fibre number). In the absence of a rapidly growing tectum, the areas of labelled neuropil would have no orientation, or no consistent orientation. The similarities and differences observed between the patterns from different batches of operations from this experimental series suggest that the strength of the competition is determined by the fine details of the operation and that once the development of the tectum is complete there will be no radical change in the double projection pattern.

There is clear evidence that in mammals striped visual projections develop from a previous state of a complete superimposition of the two component inputs (Rakic, 1977). Stripes induced to form in an adult goldfish tectum segregate out from initially superimposed projections (Meyer, 1983*b*) and there is a suggestion that this is also the case in chick embryos (Fawcett & Cowan, 1985). Constantine-Paton & Law (1978) observed that, when striping was induced in three-eyed frogs, the caudal, newly growing part of the young tectum was uniformly labelled. This suggests that the banding seen in more developed rostral regions had segregated out from a uniform double projection. When both normal optic nerves of these three-eyed animals were cut, histological examination soon after the operation showed that the supernumerary projection was continuous. Examination of different animals at a later stage of development revealed a striped projection (Reh & Constantine-Paton, 1985). The present observations are compatible with the idea that the earliest state of a double projection is a uniform superimposition of fibres from the two eyes.

There are interesting differences, which are not yet understood, between the patterns of double innervation seen in different animal models. In both *Rana* (Constantine-Paton & Law, 1978) and *Xenopus* (Fawcett & Willshaw, 1982), the

patterns of stripes which are established during development are generally oriented rostrocaudally. However, in contrast to our findings of spots or stripes of no particular orientation following nerve section after metamorphosis, stripes can be induced in postmetamorphic *Rana pipiens*, by removal of one tectum, and these show a generally rostrocaudal orientation (Law & Constantine-Paton, 1980). Stripes induced in the chick by interference with the embryonic chiasma (Fawcett & Cowan, 1985) run more or less orthogonally to the direction of ingrowth of the fibres. There are certainly considerable differences in the developmental mechanisms involved in the establishment of the retinotectal projections in *Xenopus*, *Rana*, goldfish and chick. In *Xenopus* and goldfish, optic fibres can alter their tectal projections as the topology of the system changes with development (Straznický & Gaze, 1972; Gaze *et al.* 1979; Cook, Rankin & Stevens, 1983; Easter & Stuermer, 1984). In this respect the situation in *Rana* is equivocal since it has been suggested that fibre-shift on the tectum does not occur (Jacobson, 1977), whereas more recent work would indicate that terminal arborizations are also mobile in *Rana* (Reh & Constantine-Paton, 1984). In the chick, optic fibres seem to be unable to adjust their position at all (although this has recently been challenged: McLoon, 1985) and retinal cell death has been invoked to account for stripe formation (Fawcett & Cowan, 1985).

In a small number of cases the projections made by the same optic nerve on the two tecta show a degree of complementarity. Although these results are intriguing, in common with previous results on *Rana* (Law & Constantine-Paton, 1981) and chick (Fawcett & Cowan, 1985) they are insufficiently precise to warrant further comments.

At the time of nerve section in the early series of the present experiments, the projection from the eye to the tectum was confined to the rostrolateral corner of the developing optic tectum (Fig. 7). Somehow section of the nerve induces a considerable proportion of the regenerating (and the newly growing, uncut) fibres to grow to the ipsilateral rather than the contralateral tectum. The fibres involved in this early event, however, are but a small proportion of those that develop later; and the evidence from electrophysiological recordings, and from the extent of stripe formation, indicates that a considerable proportion of all the later-growing fibres continues to make the same mistake and grow ipsilaterally. At present the mechanisms underlying this intriguing observation are not understood.

Fibres from a cut optic nerve which grow to a tectum innervated by a normal projection interact with that projection to terminate discontinuously and this entails displacing some of the fibres already present to new sites. The form of the discontinuous projection pattern appears to be determined by the nature of the two sets of fibres involved in the interaction and the dynamics of tectal growth.

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