2.3.6 Mechanisms

The experiments described above have usually been interpreted to mean that there is some competitive interaction in V1 between fibres from the two eyes. This is activity dependent [Stryker & Harris 1986], and depends on both the strength and the correlational structure of the incoming activity. If one eye is given a competitive disadvantage, there is a shift to the other eye. Relative rather than absolute strengths seem to be the important factor [Chapman et al 1986], and a competitive imbalance increases the degree of monocularity. If correlations between the two eyes are disrupted, the degree of monocularity is also increased. However, stripes can form naturally even when the two eyes are likely to be highly correlated (e.g. in monkeys).

Direct measurements have been made of the retinal correlations produced by spontaneous activity. [Mastronade 1989] found positive correlations between the firing of neighbouring cells of similar receptive field type in the cat. More recently [Meister et al 1991] studied the correlations in fetal cat retina *in vitro*, and found that spontaneous activity had the form of a wave of excitation sweeping across the retina in an arbitrary direction, lasting a few seconds, followed by one to two minutes silence. Both these experiments show that spontaneous activity is indeed locally correlated. However, there are no experimental results regarding the form of retinal correlations produced by normal patterned input. It is likely that these will be significantly different from the spontaneous case. In particular, one would not expect the two eyes to be correlated during spontaneous activity, whereas one would for the evoked activity case.

Two experiments which provide further evidence about mechanisms are as follows. [Reiter & Stryker 1988] used the easily-measurable effects of monocular occlusion to test the Hebbian hypothesis that both pre- and postsynaptic activity are required for changes in synaptic strengths. They blocked only postsynaptic activity in the cortex during the critical period while one eye was occluded, and found that there was a consistent shift in the responsiveness of the visual cortex in favour of the less-active, *closed eye*. This indicates that repeated pairing of presynaptic activity with zero postsynaptic activity leads to a competitive disadvantage for that eye compared to an occluded eye. Another experiment designed to test the effect of pre- and postsynaptic activity pairing was [Frégnac et al 1988]. Here, it was found that a cell dominant for eye 1 could be converted to a cell dominant for eye 2 by repeated artificial (i.e. direct current injection from an electrode) increase in the cell's response to input from eye 2, thus confirming the importance of temporal correlations in pre- and postsynaptic activity.

2.4 Conclusions

A large proportion of what is known experimentally about the mappings from retina to tectum and from LGN to V1 can be understood in terms of a sheet of presynaptic cells connected to a sheet of postsynaptic cells by fibres with variable connection strengths. In frogs and goldfish, experimental manipulations to this system have included removing or rotating parts of the pre- and/or postsynaptic sheet, fusing together parts of two or more presynaptic sheets, and introducing fibres from an additional presynaptic sheet to compete with the normal fibres for space on the postsynaptic sheet. In cats and monkeys, experiments have focused on the effects of monocular deprivation on patterns of ocular dominance as a way of examining the behaviour of the system under abnormal conditions.

The retinotectal and retinocortical systems are rather different in detail. However, they have the following important properties in common:

- There appears to be a polarity mechanism that provides an initial orientation for the map.
- An initially crude map on the postsynaptic sheet gradually refines during development.
- Ocular dominance stripes are formed when two presynaptic sheets compete for the same postsynaptic space.

Phenomena two and three are our primary interest in this thesis: in particular, how they can arise from the same mechanisms.

2.3.5 Experimental manipulations to dominance and the pattern of stripes

As in the retinotectal system, a large number of experiments can be performed in the retinocortical system to create abnormal circumstances during development. In the retinocortical system many of these experiments are concerned with the effect on ocular dominance stripes of disrupting the normal patterns of activity in one or both eyes. These results can shed light on the mechanisms underlying stripe formation in the normal system, and also provide extra constraints for computational models. Some of these results are now described.

- **Monocular suture:** One eye is occluded or sewn shut during the critical period. After a few weeks it is found that (a) a higher proportion of cells than normal are completely monocular, (b) substantially more of the cells in layer IV can be driven by the normal eye as compared to the deprived eye, and (c) ocular dominance stripes are now of different thicknesses for the two eyes. The stripes receiving input from the normal eye expand at the expense of the stripes from the deprived eye: however, the stripe periodicity remains the same (see e.g. [Shatz & Stryker 1978, Hubel et al 1977, LeVay et al 1980]). Even occlusion by the nictating membrane (which produces a much weaker decrease in light levels than suturing but has the effect of blurring the image) causes the same shifts in ocularity [Kuffler et al 1984, page 541].
- **Binocular suture / dark rearing:** Both eyes are sewn shut, with the result that ocular dominance columns form roughly as normal [Kuffler et al 1984, page 547]. In the paradigm of dark-rearing (i.e. lack of normal visual experience), it was originally found that stripes also formed as normal [Frégnac & Imbert 1978], although later [Swindale 1981] (also Swindale, personal communication) found no evidence of ocular dominance stripes in dark reared cats. However, Swindale's results are controversial (for instance [Swindale & Cynader 1986] reported differences between physiological and anatomical data in a similar experiment). Evidence from other experiments is that dark-rearing can extend the critical period almost indefinitely ([Cynader 1979, Mower et al 1983], for review see [Munro 1986]). Periods of visual experience as little as 6 hours long in dark-reared cats can cause the onset of the critical period, which then appears to run its course even if the animals are immediately returned to the dark [Kuffler et al 1984, pages 543–544].
- **Impulse blockade:** [Stryker & Harris 1986] removed even spontaneous activity by blocking impulses in the two eyes with TTX, and found that when both eyes were thus treated, stripes failed to form. A related experiment was performed in [Chapman et al 1986], who examined the consequences of competition between an occluded eye and one treated with TTX. The result was a shift in ocularity to the occluded eye.
- **Reverse suture:** Here one eye is shut for a time, then opened again and the other eye is shut. If this reversal takes place during the critical period, the impoverished ocular dominance stripes from the eye first deprived are able to expand and eventually (given sufficient time within the critical period) become wider than the stripes from the eye that was initially open [Movshon & Blakemore 1974].
- **Artificial strabismus:** Here the correlational structure of the inputs from the two eyes is disrupted by cutting the extra-ocular muscles, which prevents image registration in the two retinae [Hubel & Wiesel 1965]. This has the effect that almost all cells become entirely monocular, and the pattern of stripes becomes correspondingly sharper. However, these changes occur more slowly than the changes following monocular deprivation [Freeman et al 1982].
- **Alternating occlusion:** Various experiments have been performed to assess to exactly what degree activity in corresponding positions in the two eyes needs to be simultaneous to maintain binocularity. [Hubel & Wiesel 1965] investigated a regime of alternating occlusion on a time scale of one day per eye, from normal eye opening until 10 weeks after birth, and found that the shift towards monocularity was even greater than for the strabismatic cats. The effects of more rapid alternations in deprivation were investigated in [Blasdel & Pettigrew 1979] and [Altmann et al 1987]. Using mechanical and solid-state shutters respectively over the eyes, they found that alternation rates of a few seconds or even fractions of a second reduced cortical binocularity, and also disrupted normal depth discrimination in behavioural experiments [Altmann et al 1987].
- **Effect of eye movements:** Various experiments suggest that eye movements are essential for the plasticity effects described above to operate. [Freeman & Bonds 1979] found that monocular deprivation did not lead to a breakdown of binocularity in 4-week old kittens if the animals were paralysed. However, if either eye was moved mechanically, there was a shift to monocularity. A similar result has been found for plasticity with regard to orientation selectivity in [Buisseret et al 1978].

also arranged in a pattern of stripes, though the thickness of these stripes is several times less than that of ocular dominance stripes [Hubel & Wiesel 1977, **?**]. Again these extend through the whole thickness of the cortex.

From V1, fibres project mainly to V2, and then from V2 to V4 and V5. These projections are broadly topographic, but with a detailed fine structure (see e.g. [Thompson 1985, Ferrer et al 1988]). We do not consider these "association projections" further.

2.3.3 Detailed structure of ocular dominance stripes

A detailed account of the structure of ocular dominance stripes in macaque monkey is given in [LeVay et al 1985], who used computer-aided 3-D surface modelling techniques to reconstruct the cortical surface in V1 from a series of slices cut through the brain. Below we quote part of the abstract.

> As described in earlier studies, the stripes formed a system of parallel bands, with numerous branches and islands. They were roughly orthogonal to the V1/V2 border throughout the binocular segment of the cortex. In the lateral part of the operculum, where the fovea is represented, the stripes were less orderly than elsewhere. In the calcarine fissure the stripes ran directly across the striate cortex from its dorsal to its ventral margin. In the far periphery the stripes for the ipsilateral eye became progressively narrower, eventually fragmenting into small islands at the edge of the monocular segment. The overall periodicity (width of left- plus right-eye pair of stripes) averaged 0.88 mm but decreased by a factor of about 2 from center to periphery. This decrease was not accounted for solely by shrinkage of the ipsilateral eye stripes.

The fact that stripes have a tendency to run into the boundaries of V1 at right angles has been commented on by many authors. Also noted has been the tendency for stripe endings to be rounded rather than flat (see e.g. [Swindale 1980]).

An important step forward was taken in [Blasdel & Salama 1986], who used voltage-sensitive dyes to examine patterns of both ocular dominance and orientation selectivity in living macaque monkeys. They found ocular dominance stripes of the same thickness as those found by earlier methods, again intersecting the borders of V1 at right angles. Their technique allowed them to study ocularity and orientation domains in the same animal, and thus see how the discontinuities in the two maps compare. It was found that ocular dominance and orientation stripes do not intersect at a consistent angle, as was first suggested by Hubel and Wiesel (see e.g. [Hubel & Wiesel 1977]). They concluded that "...disruptions in the gradient of preferred orientation tend to coincide with reversals in the gradient of ocular dominance...". That is, orientation changes most rapidly when ocular dominance changes least rapidly. However, their conclusions regarding the structure of the orientation map have recently been contradicted by [Bonhoeffer & Grinvald 1991], who suggest that regions of iso-orientation are more patch-like than band-like.

2.3.4 Development of stripes and the critical period

Ocular dominance stripes develop from an initially unsegregated binocular projection. The stripes appear to form by retraction of exuberant axons, although in the final state it can still be the case that a single axon arborizes to contact two stripes. However, there are differences in the time course of this segregation between cats and monkeys. In cats, the stripes first begin to appear about one month after birth [Kuffler et al 1984, page 536], but in monkeys segregation begins before birth [Rakic 1976]. It is important to note that this prenatal segregation could be driven by spontaneous activity in the visual system (for evidence of spontaneous activity before birth see [Galli & Maffei 1988, Meister et al 1991]), and thus may not require a substantially different explanation from the case of segregation driven by postnatal visual experience, except for the difference in input correlations (see chapter 3).

Both cats and monkeys have a "critical period" for visual development: roughly the first six weeks after birth in monkeys, and from week 3 to week 6 in cats (see e.g. [Kuffler et al 1984, pages 543–544]). This is the period for which the system is plastic: procedures such as monocular deprivation (covering up one eye, as described below), even for a very short time, can have a dramatic effect on the structure of V1. After this period the structure is fixed, and for instance monocular deprivation (even for an extended period of time) has no effect. However, we note later that under some circumstances the critical period can be extended. There is evidence that certain chemicals play a role in determining when the system is plastic [Kuffler et al 1984, page 546].

(a) (b)

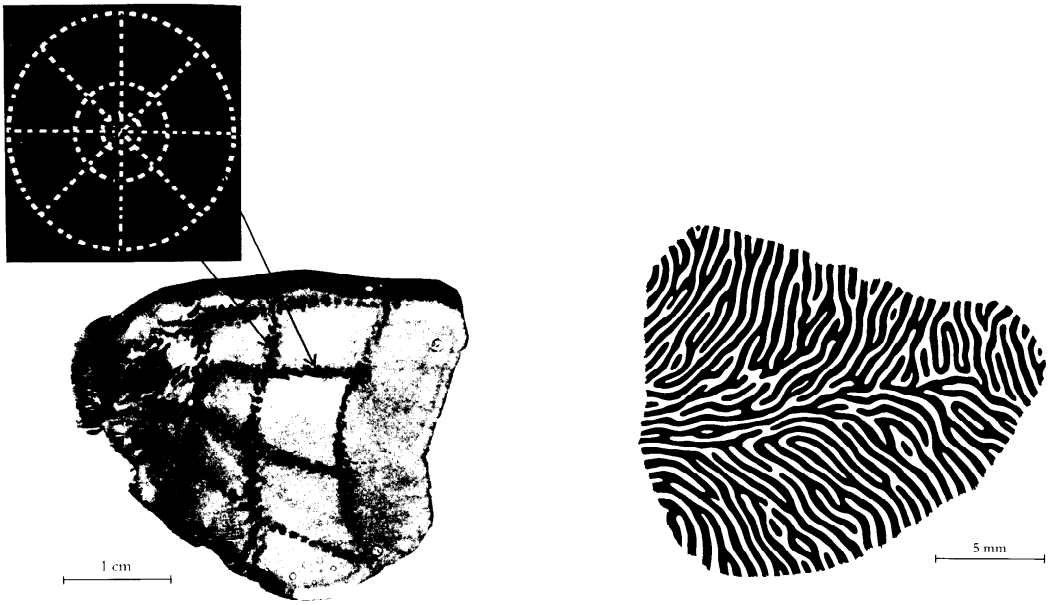

Figure 2.4: **(a)** Result of an experiment by Roger Tootell that demonstrates the topography of the map from retina via LGN to cortex. The stimulus shown was presented to an anesthetized macaque monkey for 45 minutes. V1 had previously been injected with a radioactively labelled chemical that concentrates where cells are most active. The resulting audioradiograph is of a section of V1 parallel to the surface. As can be seen, neighbourhoods in the retina are preserved in the cortex. The discontinuities in the image lines on the cortex represent shifts in ocular dominance: the pattern was shown to only one eye. **(b)** Ocular dominance stripes in V1 in the macaque as revealed by staining techniques. Both pictures taken from [**?**].

[Stryker & Harris 1986]. Recent work has shown that such stripes are also present in humans [Horton et al 1990]. These have a similar qualitative form, though are approximately twice as wide as in cats and monkeys.

The topography of the final map is illustrated in figure 2.4(a). In monkeys, cortical cells are almost entirely monocular in layer IV, so that an electrode traversing this region is driven by one eye and then the other in an alternating fashion (although there are some differences between species: for instance, New World monkeys do not possess ocular dominance stripes, and layer IV is entirely binocular [Hendrickson 1985]). A typical pattern of stripes is shown in 2.4(b): each stripe is approximately 400μm in width. In cats, there is a greater range of ocularities, and the stripes are less sharply defined [Shatz & Stryker 1978]. Hubel and Wiesel identified 7 degrees of dominance, so that a cell of degree 1 or 7 is completely dominant for one eye or the other respectively, and a cell of degree 4 can be driven equally by both eyes (see e.g. [Hubel & Wiesel 1965, **?**]). After recording from a number of cells, an ocular dominance histogram can be drawn, showing the number of cells falling into each category. For cats this is convex, i.e. the most common ocularity is degree 4 (binocular) dropping off on each side.[7] For monkeys it is concave, i.e. rising towards the ends so that the most common ocularity is complete dominance for one or other eye. Lower mammals such as mice have a very slight variation in dominance across the cortex: most cells can be driven equally by both eyes. For cats and monkeys in the layers above and below layer IV similar variations in dominance are present but to a lesser extent, so that an electrode penetrating orthogonal to the surface encounters cells which are dominant for the same eye as in layer IV. Thus the stripes seen on the surface are in fact columns extending through the thickness of the cortex. Although qualitatively similar, the detailed layout of the stripe pattern is different for each individual.

In addition to ocularity, other variables besides space are also mapped across V1 (for review see [Knudsen et al 1987]). One of these is orientation. The overall topography of the map ensures that position in the visual field progresses smoothly across V1. However, on a smaller scale there is smoothness of the orientation map: neighbouring cells respond to similar orientations in a smooth progression. Cells of the same orientation are

[7] Although this is the picture as presented in for instance [Kuffler et al 1984, page 537], it has been suggested [Shatz & Stryker 1978] that using greater care in determining whether cells lie in layer IV rather than deeper or more superficial layers, in which cells have a greater tendency towards binocularity, shows that in fact the ocular dominance histogram for layer IV of the normal cat is roughly flat.

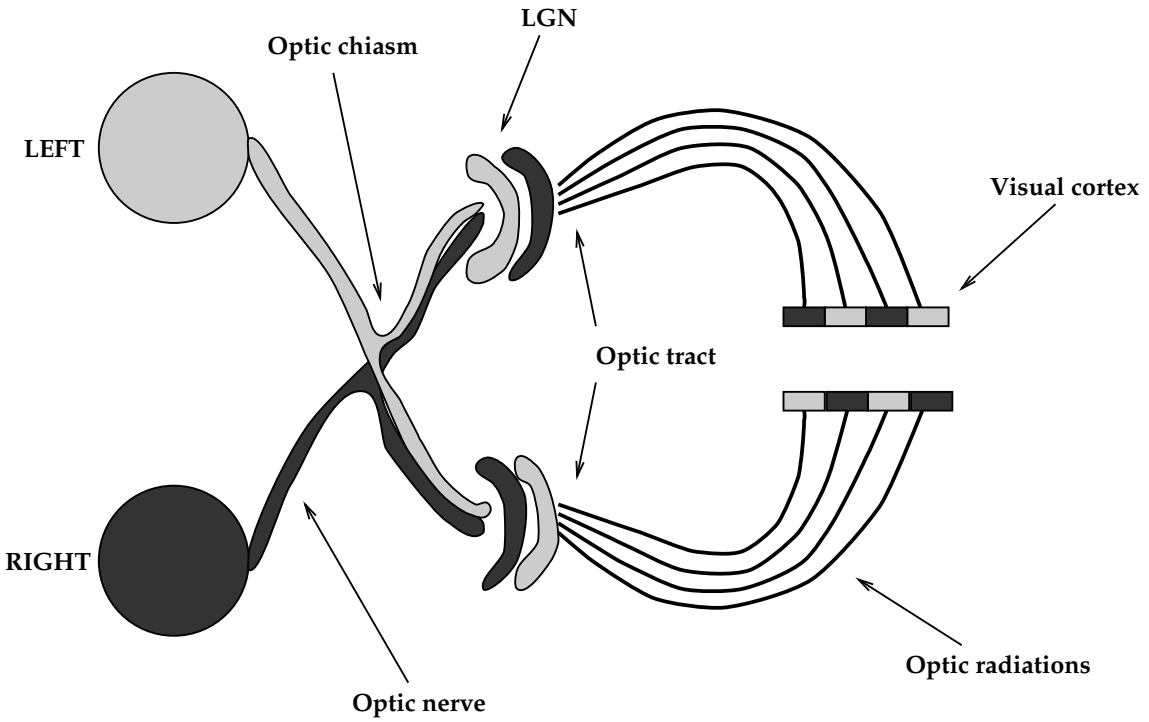

Figure 2.3: A simplified picture of the retinocortical system (after [Kuffler et al 1984]). Only two of the six layers of the LGN are shown.

optic nerve. There are also horizontal and amacrine cells, which make predominantly lateral connections. These layers perform some preliminary processing of the visual image. Retinal ganglion cells have centre-surround receptive fields,[5] and these axons project to the LGN. Although still controversial, many people believe that in cats the optic nerve is again quite disordered (e.g. [Horton et al 1979], also Glen Jeffreys, Personal Communication).

The LGN is a structure lying between the optic chiasm and V1: thus it receives inputs from both eyes. Inputs from the two eyes are initially intermixed during development: however they gradually segregate into a series of eye-specific layers, each of which receives input directly from the retina. This segregation is activity-dependent [Shatz & Stryker 1988]. In the cat there are three layers for each eye: each receives input across the whole visual field in an orderly map. These maps are aligned, so that an electrode penetrating orthogonal to the layers would encounter cells responding to a similar position in the visual field in each layer (even if the layers correspond to different eyes). The area over which each ganglion cell axon makes contacts varies depending on where in the retina that fibre originated from. Axons representing cells in the fovea of the retina arborize over a smaller area than cells in the periphery. There are also many more LGN cells representing the fovea than the periphery. In general LGN cells have centre-surround receptive fields. Each layer sends a projection to V1.

2.3.2 V1

Primary visual cortex lies at the back of the brain, slightly folded in towards the opposite hemisphere. It is also made up of several layers, some of which receive mostly direct inputs from the LGN, some mostly inputs from other layers, and some a mixture. However, the primary site of termination for LGN fibres is layer IV. In the monkey, the receptive fields of cells in this layer are primarily of centre-surround type, whereas in the cat they are mostly simple (oriented) cells.[6] Initially during development the projection from LGN to layer IV is diffuse with only crude topographic order, and cortical cells are binocular. The formation of this initial map is not activity dependent (reviewed in [Meister et al 1991]). Subsequently, topographic refinement and segregation into ocular dominance stripes occurs (see e.g. [Shatz & Stryker 1978], that is dependent on neural activity

[5]Cells with centre-surround receptive fields respond best either to an appropriately located dark spot on a light background or an appropriately located light spot on a dark background.

[6]Simple cells respond optimally to an oriented edge or bar at some particular position and angle.

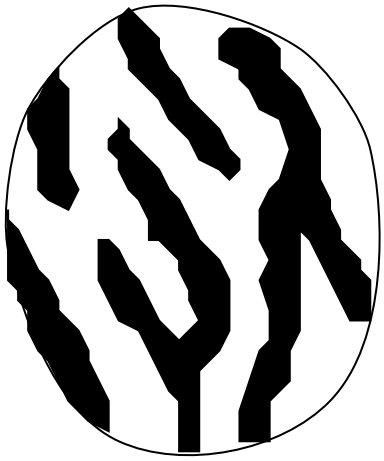

Figure 2.2: A typical pattern of stripes created in frog tectum by implant of a third eye (after [Constantine-Paton & Law 1982]).

- An activity-based mechanism that causes the crude map formed by the polarity mechanism to refine [Meyer 1983]: this is dependent on the activity of retinal cells being correlated, but not perfectly correlated [Cook & Rankin 1986].

Further conclusions for the case of ocular dominance stripes are:

- The mechanisms that form a topographic map for a single eye also form ocular dominance stripes (from an initially unsegregated map) for a double projection from two eyes [Constantine-Paton & Law 1978, Law & Constantine-Paton 1980, Law & Constantine-Paton 1981], or a compound eye where both halves attempt to innervate the same part of tectum [Fawcett & Willshaw 1982].
- Stripe formation is activity dependent [Meyer 1982(b), Boss & Schmidt 1984, Reh & Constantine-Paton 1985].
- It is unlikely that a global chemical difference between the two projections is the cause of ocular dominance segregation [Ide et al 1983].

We return to these points in the next chapter.

2.3 The retinocortical system

In mammals such as cats and monkeys the central brain structure receiving the first inputs from the two eyes is area V1 of visual cortex, also known as area 17, or primary or striate visual cortex. Connections from the retina are not direct: retinal ganglion cells synapse at the lateral geniculate nucleus (LGN) in an ordered map, and then geniculate cells project to V1, again forming an ordered map. Thus, visual space is mapped topographically across the cortex. An important difference with the retinotectal system is that V1 naturally receives inputs from both eyes. Fibres from the two eyes are only partially crossed at the optic chiasm: those representing the left visual field from each eye go to the left hemisphere and those representing the right visual field to the right hemisphere. Although terminations from the two eyes are initially evenly distributed in V1, segregation of the two projections occurs during development into an alternating pattern of ocular dominance stripes. This is summarized in figure 2.3. We now discuss this system in more detail (for a fuller account see for instance [Kuffler et al 1984, Lund 1988, Miller & Stryker 1990, Price 1991]). Note that this is a rather simplified description: for instance, we do not consider the large number of fibres carrying information back from cortex to LGN, the function of which is largely unknown.

2.3.1 Precortical stages

The retina is made up of three layers of cells: rods and cones, which convert incoming light into electrical signals, a middle layer of bipolar cells, and then finally retinal ganglion cells, the axons of which form the

However, if the lens is left intact, the map refines as normal in strobe light [Cook 1987]. Lastly, goldfish reared in the dark (i.e. with only spontaneous retinal activity) have maps as refined as goldfish reared under ordinary lighting conditions [Cook 1988, Cook & Becker 1990].

We return to discuss particular theoretical proposals regarding activity-based mechanisms in the next chapter.

2.2.3 Ocular dominance stripes

One of the most remarkable features of the retinotectal system is its behaviour in the unnatural situation of two retinae innervating the same tectum. Here a process of competition appears to take place, and from an initially binocular pattern of innervation a pattern of monocular stripes is formed. The basic results are as follows:

- Early experiments: [Cronly-Dillon & Glaizner 1974] stripped away optic fibres from the left tectum in goldfish, redirected them into the right tectum, and simultaneously removed the left tectum. After leaving the fish for one year they found that terminals from the two eyes lay in two segregated zones, with an overlapping zone in between. In a similar experiment [Levine & Jacobson 1975] found several segregated regions arranged in irregular patches.
- [Constantine-Paton & Law 1978, Law & Constantine-Paton 1981] created a binocularly innervated tectum by implanting an extra eye into embryonic frogs. Here, the fibres from the supernumerary eye grew into one or both tecta, creating regions of binocular innervation. Autoradiographic tracing revealed initially continuous labelling over the entire tectal surface, followed by segregation into a set of eye-specific stripes running rostro-caudally.
- [Law & Constantine-Paton 1980] found that when one tectum was totally or partially ablated, fibres which had lost their normal termination sites crossed to the other tectum and made connections in the appropriate region of tectum. Here, stripes were formed in those parts of the remaining tectum that were innervated by both eyes: invading ipsilateral fibres managed to displace the established connections of the normal contralateral fibres. All bands were highly uniform in width and oriented rostro-caudally.
- [Fawcett & Willshaw 1982] reported stripes from a single surgically reconstructed compound (e.g. double-nasal) eye, and [Straznicky & Tay 1982] found stripes when a compound eye competed for the same tectal space as a normal eye.
- In the so-called "isogenic eye experiment", [Ide et al 1983] took a nasal eye fragment and let it grow into a complete eye. They found that this initially formed a double-nasal map across the whole tectum, which gradually segregated into a pattern of stripes.
- Role of activity: Various experiments have shown that blocking retinal ganglion cell activity with TTX leads to a failure of double projections to segregate into stripes, for instance [Meyer 1982(b)] and [Boss & Schmidt 1984] in goldfish, and [Reh & Constantine-Paton 1985] in frogs.

A typical picture of stripes resulting from one of these experiments is shown in figure 2.2.

2.2.4 Summary

To summarize, the above results point to the existence of the following basic types of mechanisms of map formation in the retinotectal system:

- A polarity mechanism that crudely matches regions of the retina to regions of the tectum [Hunt & Jacobson 1972, Willshaw et al 1983, Fraser & Perkel 1990]. This is not activity dependent [Meyer 1983], and is enabled only after a certain stage of development [Hunt & Jacobson 1972].
- A mechanism that enables the map to expand or compress so as to form smooth order between a mismatched retina and tectum [Yoon 1971, Schmidt 1978, Udin & Fawcett 1988]. Under some circumstances the form of this map can be influenced by the history of the system [Schmidt 1978].
- An interaction between fibres causing them to align with their neighbours, which can sometimes outweigh the polarity mechanism [Jacobson & Levine 1975, Udin & Fawcett 1988].

2.2.1 Effect of various surgical manipulations

A large amount of data exist regarding the effect of various surgical manipulations on the retinotectal system. Studying the behaviour under abnormal conditions helps to illuminate the mechanisms of map formation under ordinary conditions,[2] and provides additional constraints for computational models. We first survey very briefly some of the data regarding manipulations to the single-eye projection: there are a large number of review papers that cover this material in greater detail (e.g. [Fraser & Hunt 1980, Meyer 1982(a), Trisler 1982, Schmidt 1985, Schmidt 1988, Udin & Fawcett 1988, Fraser & Perkel 1990, Hankin & Lund 1991]). In particular, where specific references for the results below are not shown, see [Udin & Fawcett 1988, Fraser & Perkel 1990].

- If a *Xenopus*[3] eye is rotated in situ during development, a normal map results if the rotation is carried out before a certain age, whereas an appropriately rotated map occurs if the rotation is carried out after that age [Hunt & Jacobson 1972].
- If the tectum is rotated during regeneration of the optic nerve, in some cases a normal map results whereas in other cases a rotated map results. Similar results follow if parts of the tectum are translocated: in some cases the cut retinal axons regrow to innervate their normal piece of tectum, and in other cases a map is formed that ignores the translocation.
- Compound eye experiments: When a whole eye is created by fusing together two half eyes, the two halves being of the same type (e.g. nasal, ventral or temporal), they each map across the whole tectum.
- Ablating half the tectum leads to a gradual compression of the regenerating map to fit into the remaining available space [Yoon 1971].
- The map formed after removal of half the retina initially covers half the tectum, but then gradually expands to fill the whole tectum [Schmidt 1978]. Axon terminal density remains the same [Schmidt et al 1978]. If the optic nerve is then made to regenerate again an expanded map is immediately formed [Schmidt 1978].
- Fibres innervating transplanted tissue show a strong tendency to align with fibres in the surrounding tectum, regardless of the orientation of the transplant [Jacobson & Levine 1975]. However, even in the absence of other optic nerve fibres, fibres can find their correct position in the tectum (reviewed in [Fraser & Perkel 1990]).

A number of models based on the matching of chemical markers between retina and tectum have been proposed to account for the above observations. These will be discussed in the next chapter.

2.2.2 Role of activity

There is also a body of data addressing the role of neural activity in map formation. The main results are as follows (for more detailed reviews see [Fawcett & O'Leary 1985, Constantine-Paton et al 1990])

- Spontaneous activity of neighbouring retinal ganglion cells is correlated [Arnett 1978, Ginsburg et al 1984].
- Topographic refinement of the map can be prevented by blocking impulse activity in retinal ganglion cells with Tetrodotoxin (TTX)[4] [Schmidt & Edwards 1983, Meyer 1983].
- Topographic refinement is also prevented by rearing in stroboscopic light [Schmidt & Eisele 1985, Cook & Rankin 1986]. More recent work has revealed some subtleties in these strobe experiments. Firstly, the effect of strobe light varies at different periods during optic nerve regeneration [Cook 1988]. Secondly, the strobe experiments described above had the lens of the goldfish *ablated*, thus creating a diffuse retinal image (with diurnal light the map forms normally under these conditions, i.e. a lack of patterned stimuli).

[2] Though in general it should be noted that regeneration results cannot always be generalized to the case of development.

[3] This is a species of amphibian commonly used in retinotectal mapping experiments.

[4] Tetrodotoxin is a potent neurotoxin that blocks sodium channels.

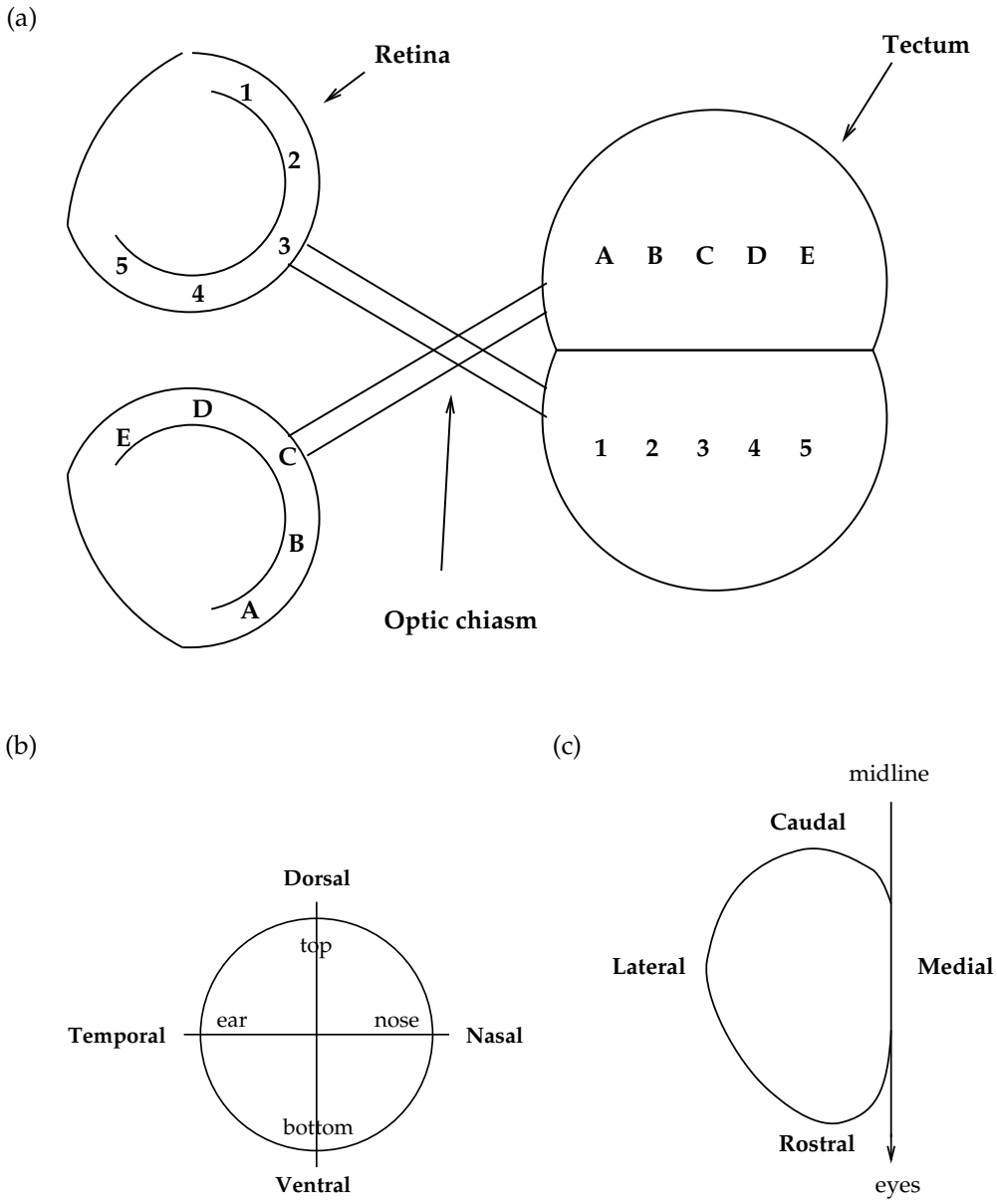

Figure 2.1: (a) A simplified picture of the retinotectal system (after [Meyer 1979]). (b) Terminology for referring to retinal positions. (c) Terminology for referring to tectal positions.

2.1 Introduction

One of the advantages of studying the vertebrate visual system is that, over the past several decades, a large amount of experimental data has been accumulated regarding how this system develops. This data is a vital resource for both constraining models of visual development and inspiring theoretical analysis.

In this chapter we introduce some aspects of the visual system of two different kinds of vertebrate: firstly amphibians and fish (in particular frogs and goldfish), and then higher mammals (in particular cats and monkeys). We note immediately that, although data from a number of different species will be referred to within each group, for our purposes the differences between species within each group are less important than the similarities. We also argue that, despite the many obvious differences between the two groups themselves, in certain key respects they are similar enough for a unified theoretical treatment of visual map formation.

The key points we emphasise are as follows:

- Topographic map development is an active process, rather than relying purely on the preservation of order from retina to cortex/tectum.
- There is evidence of a role for both chemically and activity based processes in topographic map formation, and correlations in activity are crucially important.
- Stripes can form when two eyes innervate the same target structure.

2.2 The retinotectal system

In animals such as frogs and goldfish the main visual centre is the optic tectum. During development, fibres grow from each retina to the opposite tectum,[1] crossing at the optic chiasm, to form a topographic map. This is oriented such that the nasal-temporal and dorsal-ventral axes of each retina map to the caudal-rostral and lateral-medial axes of each tectum respectively (see figure 2.1 for a diagram of the system and an explanation of this terminology). For many purposes, the system can be considered as a sheet of retinal ganglion cells connected to a sheet of tectal cells by a bundle of ganglion cell fibres [Meyer 1982(a)]. The density of ganglion cells over the retina is roughly uniform [Schmidt 1985], and most of these animals have a field of view of 180 degrees, which can be well approximated by a hemisphere centred on the eye. This mapping has the virtue of being a central brain system easy to access [Schmidt 1985] and manipulate [Edelman et al 1985] for a long period of time during development, and it has provided neuroscientists with a model system for studying a variety of phenomena [Fraser & Hunt 1980]. We now focus on the process of map formation.

There is clear evidence that topographic map formation in this system is an active process, rather than simply being due to fibres from the eye retaining their order while growing from retina to tectum. Some evidence relating to this is as follows:

- Although there is wide variation between species in the degree of order existing in the optic nerve, it is almost always the case that the final map in the tectum is ordered to a greater extent than is the optic nerve [Udin & Fawcett 1988].
- The map refines from crude to more precise order during development [Meyer 1983].
- In the frog, retina and tectum grow asymmetrically: the retina adds cells to its periphery in a series of annuli, whereas the tectum adds cells to its caudomedial edge. Despite this, at each stage of development an ordered retinotectal map exists (reviewed in [Gaze & Keating 1972]).
- If the optic nerve of an adult animal is cut, it can regrow to form a normal map, even if the original order of the fibres is artificially scrambled after optic nerve section (reviewed in [Sperry 1963]).

[1] For a recent review of how retinal axons are guided to the tectum see [Hankin & Lund 1991].

Chapter 2

Review of Biological Data