

# The thalamus as a monitor of motor outputs

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Many of the ascending pathways to the thalamus have branches involved in movement control. In addition, the recently defined, rich innervation of 'higher' thalamic nuclei (such as the pulvinar) from pyramidal cells in layer five of the neocortex also comes from branches of long descending axons that supply motor structures. For many higher thalamic nuclei the clue to understanding the messages that are relayed to the cortex will depend on knowing the nature of these layer five motor outputs and on defining how messages from groups of functionally distinct output types are combined as inputs to higher cortical areas. Current evidence indicates that many and possibly all thalamic relays to the neocortex are about instructions that cortical and subcortical neurons are contributing to movement control. The perceptual functions of the cortex can thus be seen to represent abstractions from ongoing motor instructions.

**Keywords:** thalamic afferents; sensory; cerebellar; mamillary; cortical

## 1. INTRODUCTION

The discussion of thalamus and cortex in this volume and in much of the earlier literature has been largely concerned with the messages that reach the cerebral cortex from the thalamus, with the messages that the cortex sends back to the thalamus and with the processing that occurs in the cortex itself. However, what matters most for survival of the organism are the instructions that the cortex sends to lower centres and the peripheral effects of these instructions. Not only are these outputs essential components of the organism's behavioural repertoire, representing essentially the only route over which cortical computations can benefit the organism, but at any one moment, cortical computations that were not kept informed about current motor instructions would represent higher control centres dangerously out of touch with the machinery that they are controlling. These are relatively simple thoughts about mechanisms of motor control. However, they have played little or no role in the way we think about thalamocortical circuits other than those involving motor cortical areas and their interactions with cerebellar and striatal circuits.

Here, we review evidence that a great many of the afferent messages reaching the thalamus and then passed on to the cerebral cortex come from axons that branch, sending one branch to centres in the brain stem or spinal cord and the other to the thalamus (see figure 1). This is true of the axons that reach 'first-order' thalamic relays (defined by Sherman & Guillery 2001, 2002; Guillery & Sherman 2002; shown as FO on the left in figure 1*b*), and is also true of axons that arise in layer five of the cortex, and pass to 'higher-order' thalamic relays (HO in figure 1*b*). That is, the 'driving'<sup>1</sup> afferents going to the thalamus

along the classically recognized ascending pathways, and also the driving afferents coming from the cortex, send branches to lower centres in the brain stem or spinal cord. All cortical areas, as far as we know, have a layer five output going to lower centres, and we show that many of these output axons also contribute a branch to a higher-order thalamic relay. Also, because all cortical areas have a thalamic input, the process of monitoring outputs that are currently being sent to lower centres is not something that can be thought of as characteristic only of thalamic relays going to cortical 'motor' areas. It is something that is likely to be a continuing process characteristic of all thalamic relays.

One can think, for example, about the cells in layer five of the primary visual cortex. These send axons to the superior colliculus and other brain stem centres, with branches to higher-order thalamic relays in the pulvinar region (Bourassa & Deschênes 1995; Rockland 1998; Guillery *et al.* 2001), and these in turn project to several of the visual cortical areas associated with higher visual processing (Rezák & Benevento 1979; Standage & Benevento 1983; Abramson & Chalupa 1985). This 'trans-thalamic' corticocortical link, from area 17 to other visual cortical areas, then, should be seen as a pathway that is concerned, not *specifically* with sensory processing, with the identification and localization of objects 'out there' in visual space, but rather, with sending messages that represent current instructions going from the cortex to the superior colliculus and brain stem. These messages are likely, directly or indirectly, to relate to instructions about the head and eye movements that are controlled by the superior colliculus. It is these messages that are also being passed from one cortical area to another with a relay in the thalamus, and that must play a significant role in sensory processing. We need to think about how such copies of instructions to lower, brain stem and spinal centres contribute to higher cortical functions and perceptual processing.

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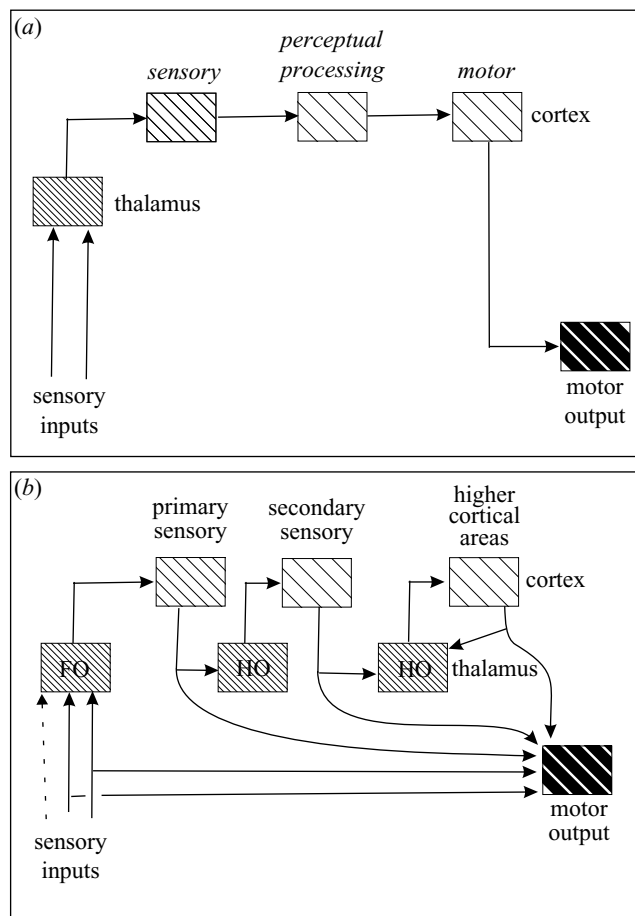


Figure 1. Two schematic representations of thalamocortical links of sensory and motor pathways. (a) The conventional view (for references see text) that sees sensory inputs relayed through the thalamus, passed from the thalamus to the cortex and then passed through a series of cortical areas concerned with perceptual processing (only one is shown here) to motor cortical areas for output to lower motor centres. (b) This shows the view of the connections represented here (the current view), which involves extensive branches from the sensory inputs directly to motor outputs and also includes the transthalamic connections between cortical areas described in the text. FO, first-order thalamic relays; HO, higher-order thalamic relays. Note that branches to motor centres may be given off by inputs to pre-thalamic relays (e.g. afferents to gracile, cuneate or lateral cervical nuclei), or by afferents to the first-order thalamic relays. In addition, there are branches to motor centres given off by corticofugal axons from cells in cortical layer five that innervate higher-order thalamic relays. The interrupted lines at the lower left of the figure illustrate a possible (but unproven) 'pure' sensory route to the cortex with no branches to any motor outputs (see text).

## 2. THE IMPLICATIONS OF BRANCHED AFFERENTS TO THE THALAMUS FOR SENSORY PROCESSING

Before considering the detailed evidence for the connectivity patterns shown in figure 1*b*, it is important to understand how they relate to contemporary views of thalamocortical and corticocortical communication, and to explore the implications they have for our understanding of sensory processing. Sensory processing through corticocortical pathways has in the past been thought of primarily

in terms of direct corticocortical connections (simplified in figure 1*a*; for details see Van Essen *et al.* (1992) and Kandel *et al.* (2000)).<sup>2</sup> The connections we show in figure 1 as the indirect corticothalamocortical pathways (see also Sherman & Guillery 2002), going through higher-order thalamic relays (HO in figure 1*b*) such as the pulvinar or mediodorsal nucleus, are generally not considered at all, or the thalamic contribution is thought of as playing a minor role, or a modulatory role in sensory processing (Olshausen *et al.* 1993). On this 'conventional' view one might wish to ignore the extent to which the many distinct sensory areas that characterize major modalities (e.g. visual, auditory, somatosensory) are receiving copies of motor instructions from thalamic afferents, rather than information from other cortical areas about objects and events in the real world 'out there'. That is, in the conventional view, corticocortical processing of sensory events is seen as a purely intracortical mechanism that is largely independent of corticofugal axons and the thalamic circuits that they innervate; it would represent sensory events rather than motor instructions. The motor instructions in this conventional view are issued once cortical processing of the sensory input is completed and passed to distinct areas concerned with motor control.

One example of the currently dominant approach to sensory processing, from among many studies of cortical functions, comes from Galletti *et al.* (2001), who traced corticocortical connections from cortical area V6 to several other cortical areas (but not to or from thalamus). In the abstract they state:

We suggest that V6 plays a pivotal role in the dorsal visual stream, by distributing the visual information coming from the occipital lobe to the sensorimotor areas of the parietal cortex. Given the functional characteristics of the cells of this network, we suggest that it could perform the fast form and motion analyses needed for the visual guiding of arm movements as well as their coordination with the eyes and the head.

This strategy, of tracing pathways that link cortical areas, without looking at descending outputs that are also sent from most or all of the relevant areas of the cortex to lower centres for motor actions, or to the thalamus for relay to other cortical areas, is currently widely employed (see Romanski *et al.* 1999; Andreas *et al.* 2001; Luppino *et al.* 2001; Nakamura *et al.* 2001; Rizzolatti & Luppino 2001). Now that the connections, shown in figure 1*b*, that involve axons from cortex to motor centres with branches to the thalamus are being revealed for many cortical areas, the conventional view can be seen as an oversimplification that is likely to miss much that is of critical importance in corticocortical processing.

Two points need to be made in a critique of the conventional view. The first (see also Sherman & Guillery 2002) is that there is essentially no experimental evidence to show the extent to which processing in higher cortical areas depends on direct corticocortical as opposed to transthalamic corticocortical pathways. One way of looking at this is to ask about the extent to which direct corticocortical pathways may be either modulators or drivers. Currently, we have no evidence about this, nor do we know how the two pathways interact in the cortex. These are relationships that need to be defined. Clearly, in order

to understand how any cortical area receives the information that is processed there, we need to look at all of the pathways that can carry the relevant information, we have to understand the contribution that each makes to processing in that cortical area, and we must know how the several inputs relate to each other. The importance of the thalamic routes to the cortex becomes clear as soon as it is recognized that no area of neocortex is without a thalamic input and that a thalamic input, even when numerically small, as it is in, for example, the primary visual cortex (Ahmed *et al.* 1994; Latawiec *et al.* 2000), can provide the major functional driving input to a cortical area.

The second point, summarized in later sections, is that many, possibly all, thalamocortical afferents can be regarded as relays to the cortex of copies of instructions that are concurrently being sent to lower centres, because, as noted above, most driver inputs to thalamus are branches of axons that also project to lower centres (see figure 1*b*; Guillery & Sherman 2002). Sensory processing in the cortex on a quite broad scale can then be seen to derive primarily from an analysis of ongoing efferent messages, and we may want to look at the nature of the messages that reach the cortex in a somewhat novel light, asking how sensory experiences are synthesized out of descending (motor) instructions instead of asking, as one is generally inclined to do in current studies, how motor instructions are synthesized out of sensory inputs.

In a practical sense, as the messages that are travelling along the two branches of the relevant axons, one going to the thalamus for transmission to the cortex, the other towards the brain stem or spinal cord, are the same, the choice for the observer is not a real choice at all about the nature of the information *received* by the lower centres on the one hand or by the cortex through the thalamus on the other. It is the action on the cells receiving the messages and the further processing of the messages that will differ. Further, and perhaps more importantly for the observer looking at the nature of the messages coming to the cortex from the thalamus, there is a real choice when the functional significance of these messages is under study. Should one categorize the pathway going to the thalamus from the visual, auditory or somatosensory periphery as functionally 'sensory', recording the activity along the pathway in terms of the perceptual qualities we associate with each? Or should we be looking for a different analysis of the messages that, as shown in figure 1, are also being passed to motor centres and categorize them on the basis of their actions on these centres? We return to this question in a later section.

To illustrate this very general point, it is worth looking again at a specific example from the visual system. However, it has to be stressed that the argument applies to most, possibly all of the afferents that are relayed through the thalamus to the cortex, even to pathways, like those going through medial dorsal or intralaminar thalamic nuclei, about whose function we have much less knowledge. The structure of the argument is clearest for pathways like the visual pathways where we understand the nature of the messages quite well, but is most important for pathways about which we know less, where we are still uncertain about just what is the nature of the message that is being sent to the cortex.

A retinofugal axon or a corticofugal axon from layer five of area 17, each innervating the thalamus (the lateral geniculate nucleus or pulvinar region, respectively) and also sending a branch to the midbrain, can be treated as a part of a sensory system on the way to the cortex, and when it is, the receptive field properties that relate to retinal coordinates, like centre-surround properties, will be studied. If, however, it is seen as an input to the midbrain, which is concerned with the control of head and eye movements, then one is likely to be interested in a different set of properties that relate to features like movement vectors, etc. In practice, the retinofugal axon is more likely to be viewed in terms of its retinal properties, whereas one might start to look for the motor properties of the corticofugal axon, even though the two have a great deal in common in terms of their branching patterns and the cell groups that they innervate (thalamus and colliculus). One can argue that it may be possible to translate the one set of sensory properties into the other, motor-set, but this will only be possible when both are well understood. For most of the afferent pathways to the thalamus we know far too little to be able to do this, and the functional properties that we ascribe to a pathway will depend on whether we see that pathway as a part of a sensory or a motor system.

For any thalamic relay we can ask whether we are likely to learn most about its function if we can define the nature of the 'sensory' messages that are transmitted to the cortex, or whether a different and perhaps more informative view could be obtained by defining how the non-thalamic (motor) branch acts at *its* terminal site(s). Defining the functional properties of any axon is a difficult task, and even where we seem to have an understanding of those functional properties, as for example in some parts of the visual system, the analysis in the past has often depended on a serendipitous selection of test stimuli,<sup>3</sup> or an inspired view about how the system might function.<sup>4</sup> We have to be able to think not only about the relationship between the messages that the retina sends to the brain and the behaviour that these messages produce, but we have to address a possibly more difficult issue, which is to think about how reports of visual perceptions relate to messages sent to the superior colliculus or, in general, how perceptual processes relate to the messages that are being passed to motor centres by axons that also lead to the cortical areas playing a role in perceptual processes.

From the point of view of the animal's survival, the action of the branch that has an immediate motor effect is more important, in the short term, than the action of the branch that leads through the thalamus to some cortical area. The latter will serve, in the long term, for learned responses that involve the cortical circuits concerned with perceptual processing. In the following, we look at the extent to which these cortical circuits depend for their inputs on pathways that also play a crucial role in the moment-to-moment responses to changes in the environment. That is, we try to define what is known about the branching patterns of the axons that provide the main driving afferents to thalamic relays. Where we see such branching patterns we can conclude that the pathways are not 'pure' sensory pathways, established to project images of the external world onto an internal, cerebral 'screen', to be processed before any motor responses (the

'conventional' cortical circuits considered above; see figure 1*a*). Functionally, the axons that give off branches to lower, motor centres and also innervate the thalamus are crucial for an immediate and completely different, behavioural role.

In principle, one might anticipate that as, in the evolutionary development of mammals, the role of the neocortex in the control of behaviour becomes of increasing importance, so there would be a greater likelihood of finding pure sensory pathways going to the thalamus for relay to the cortex (illustrated as dotted lines in the left part of figure 1*b*). That is, where the need for immediate reactions are taken care of by pathways that have branches going to the brain stem or spinal motor centres, cortical areas that are independent of such close motor connections and that are specialized for longer-term reactions, could reasonably be expected. However, we stress that currently there is no strong evidence that any afferent pathway to the thalamus lacks a branch to the brain stem or spinal cord. The negative evidence, that there are no branches, is of course, far less telling than the positive evidence, particularly as for many pathways there has been no systematic search for such branches. The following sections will serve to focus on pathways where evidence about branching patterns is needed, and this should be seen as the major function of this review: to emphasize the importance of more experimental information about the way in which afferents to the thalamus and cortex do or do not represent monitors of motor instructions.

### **3. DO AFFERENTS TO MOST, POSSIBLY ALL, THALAMIC NUCLEI CARRY INFORMATION THAT IS CONCURRENTLY GOING ALONG EFFERENT PATHWAYS TO THE BRAIN STEM AND SPINAL CORD?**

#### **(a) *General considerations***

The evidence concerning the extent to which afferents to the thalamus are carrying information that is also sent to other, brain stem or spinal, centres varies considerably. It depends on evidence about the branching patterns of individual axons, and this has been obtained primarily from three lines of evidence (see Lu & Willis (1999) for a detailed review). One involves the staining and tracing of individual axons. This is done either in Golgi preparations or with more recently developed methods that fill individual axons with marker molecules such as horseradish peroxidase or biocytin. A second involves the injection of two different retrogradely transported marker molecules into distinct presumed sites of axon termination and the subsequent demonstration of cell bodies carrying both markers. Finally, branching can also be demonstrated electrophysiologically, by antidromic activation of a recorded neuron from different terminal sites, but there are relatively few such studies of thalamic afferents.

No technique is guaranteed to display all the branches that exist. The Golgi method can fail, especially where axons are myelinated. Molecules can fail to be transported in sufficient quantity along one or another branch, which is particularly likely for finer branches when large molecules such as horseradish peroxidase are used, and conduction failures can also interfere with the electrophysiological demonstration of branching patterns,

particularly when antidromic conduction is being tested (Goldstein & Rall 1974). For these reasons, much of the following discussion is concerned with a first stage of defining thalamic inputs in terms of their branching patterns, aiming to show that branches exist, rather than demonstrating that all afferents branch or that a given proportion of afferents branch. A second stage of defining which, if any, of the input pathways to the thalamus are unbranched is largely beyond the reach of currently available knowledge, and will depend on experiments that are specifically designed to address this issue for each of the many pathways that go to the thalamus. The final resolution of this second stage may have to depend on methods that are less liable to false negative results than those that have been used so far.

Although the main aim of the following sections is to demonstrate that thalamic afferents often have branches to lower centres or are innervated by axons that have such branches, we stress that, in the long run, if it can be shown that only some axons in any one afferent category are branched, then a demonstration of the functional properties that distinguish the branched from the unbranched afferents will be important for understanding the nature of the relevant thalamic relays. Further, the clear demonstration of thalamic afferents that have no branches to brain stem or spinal centres and that arise from cells that are not innervated by axons having such branches, would be evidence for a 'pure' sensory pathway to the cortex. Such a pathway would serve to bring sensory messages to the cortex for cortical processing. Transmission to sub-cortical motor centres could then occur only after the sensory inputs had been passed through the cortex. As we have pointed out, a pathway like this would be in accord with many conventional views about sensory processing in the cortex, but currently we know of no evidence for such a pathway. Because of the difficulties of defining branching patterns and because in the past relatively few studies have focused on this issue, further studies of the problem with modern, or preferably, new methods are needed. Evidence of a pure sensory pathway whose functional characteristics could be compared with those of the more readily demonstrable branched pathways could prove to be of considerable interest, as it would demonstrate a pathway that produced no motor effects until after impulses had passed through the cortex and would be in contrast to many of the pathways considered below, which are producing motor effects at the same time as, or before, they send impulses to the cortex.

In the rest of this essay we look first at the ascending, first-order pathways afferent to the thalamus, starting with the visual pathways. The evidence on branching patterns is relatively extensive here, although not conclusive on some points. This section serves to illustrate some of the interpretative problems that apply to all thalamic afferents. The ascending somatosensory pathways raise several issues that are not apparent in the visual system, and we also look at these in some detail. These two sections serve to focus attention on the nature of the problems that still need to be addressed for understanding how afferents to the thalamus relate to motor instructions. Many of the problems addressed in these two sections arise again for all other ascending, first-order afferent pathways to the thalamus, and these are then sketched in more briefly.

Finally, we look at the higher-order afferents that come from layer five of the cerebral cortex and innervate the thalamus.

### (b) *First-order thalamic relays*

#### (i) *The retinthalamic pathway*

Axons from the retina innervate the lateral geniculate nucleus in a precise and well-defined pattern, and the lateral geniculate nucleus in turn projects mainly to the primary visual cortex (area 17). Many retinal ganglion cells also send axons to other centres, including the superior colliculus and the pretectum (references below), and there is evidence that many of these are branches of axons that also go to the lateral geniculate nucleus. Jhaveri *et al.* (1991) described the early innervation of the lateral geniculate nucleus formed by branches of retinotectal axons in hamsters, and Chalupa & Thompson (1980) reported that all retinal ganglion cells in hamsters project to the superior colliculus. Vaney *et al.* (1981) showed that almost all ganglion cells in the rabbit project to the superior colliculus, and Linden & Perry (1983) reported that more than 90% of retinal ganglion cells in the rat project to the superior colliculus (see also Dreher *et al.* 1985). This indicates that most, probably all retinogeniculate axons in these species are branches of axons going to the midbrain.

The evidence in the cat and the monkey is related to the subdivision of retinal ganglion cells into functionally distinct classes (in the cat, X, Y and W cells, which are also called beta, alpha and gamma, respectively; in primates, parvocellular, magnocellular and koniocellular cells). There is evidence that in the cat the largest ganglion cells (Y cells) all project to the lateral geniculate nucleus and the superior colliculus (Fukuda & Stone 1974; Wässle & Illing 1980; Leventhal *et al.* 1985), and the branches of the individual axons going to these centres have been demonstrated by filling single axons (Sur *et al.* 1987; Tamamaki *et al.* 1994). The smallest ganglion cells (W cells) also project to both cell groups. Wässle & Illing (1980), using a retrograde transport method, found that 80% of these cells project to the superior colliculus, and Leventhal *et al.* (1985) report that *ca.* 75% of this cell group is labelled after injections into the lateral geniculate nucleus, and *ca.* 80% after injections into the superior colliculus. This indicates that there must be a significant degree to which these cells have branched axons going to both centres. Because of the difficulties of the method it is possible that all of these small cells, which all have fine axons, have branching axons. However, because these smallest cells are a heterogeneous group, direct evidence for branching in all these cells is currently not available.

The intermediate group in the cat (X cells) has proved the most difficult for defining the axonal branching patterns. Early evidence based on antidromic stimulation of retinal ganglion cells from the superior colliculus and lateral geniculate nucleus showed the X cells projecting to the lateral geniculate nucleus only (Fukuda & Stone 1974). On the basis of retrograde transport experiments, Wässle & Illing (1980) reported that 10% of these cells project to the superior colliculus. Koontz *et al.* (1985) reported that X cells could be retrogradely labelled by injections into the pretectum, whereas Leventhal *et al.* (1985) found no X cell axons going to the superior colliculus and only *ca.* 1% going to the pretectum. Single cell

injections of horseradish peroxidase showed very few of the X cells with projections to the midbrain (Sur *et al.* 1987), but showed some with fine branches that could be traced into the brachium of the superior colliculus, at which point the the label became too weak to follow further. When the smaller molecule, biocytin, was used for the intracellular injections, those branches could be traced to terminal arbors in the pretectum for six out of six X cells (Tamamaki *et al.* 1994).

This evidence, for a cell group that is far more homogeneous than the W cells, highlights the difficulty of interpreting negative evidence about branching. Particularly where only a proportion of such a cell population shows branching, even when that proportion is quite small, one has to entertain the possibility that many branches were not revealed because of one or another of the difficulties outlined earlier. That is, the significance of exceptional observations has to be taken into account where a very small minority of cells in an otherwise homogeneous population show a particular branching pattern. Where the methods for studying the connections are less than completely secure, the small minority may represent all of the cells, as seems probable for the retinal X cells in the cat that have demonstrable fine branches going to the midbrain.

In the monkey, Bunt *et al.* (1975) using injections of horseradish peroxidase in the lateral geniculate nucleus or tectum found that essentially all retinal ganglion cells were labelled after injections into the lateral geniculate nucleus and that after tectal injections, cells of all size classes were labelled except for the central 10° of the retina where there was essentially no labelling. Because of the observations in the cat, and as central ganglion cells have thinner axons than more peripheral cells, this raises the possibility that in the monkey, as in the cat, all ganglion cells may have a midbrain branch. In contrast to this, Schiller & Malpel (1977) reported only one 'colour-opponent' (i.e. parvocellular) cell with an axon terminating in the superior colliculus, but did find such axons for the other two cell classes. Leventhal *et al.* (1981) reported that all three types of retinal ganglion cell could be retrogradely labelled by injections into the lateral geniculate nucleus, but that no labelled parvocellular ganglion cells were identifiable after injections into superior colliculus or pretectum. Perry & Cowey (1984) found that cells from the central retina could be labelled by injections of the superior colliculus, and that in the retina the soma sizes of labelled cells overlapped almost completely with the soma sizes of the parvocellular ganglion cells labelled after a geniculate injection. However, where the retrogradely labelled cells had a well-labelled dendritic arbor they were identified as koniocellular, not parvocellular elements. In addition, some magnocellular ganglion cells were labelled. Because for many cells the dendritic arbor was unstained, the possibility remains that parvocellular ganglion cells project to the midbrain, but that these axons have relatively poor retrograde transport mechanisms so that the dendrites are not well revealed.

In summary, it is reasonable to assume that for the cat, sufficiently sensitive methods are likely to show branching in most, possibly all retinofugal axons distributing to the thalamus and midbrain. That is, the pattern for the cat may be entirely like that in rabbits and rodents, with all

geniculate axons formed as branches of midbrain axons. Details regarding the branching patterns of retinofugal axons in the monkey remain to be resolved with suitable methods,<sup>5</sup> and are likely to be of particular interest. The partial evidence available so far indicates that there may well be fine branches to the midbrain from all retinofugal axons. However, as we have argued earlier, it is not unreasonable to expect that in species having the most neocortical control of neural functions, one might be most likely to find pure sensory pathways. This would then provide a pathway to the cortex that is not constrained by the concurrent messages that have to be sent along to motor pathways. Such an 'emancipation' of the sensory pathways would signal some possibly distinct functional relationships, but the nature of these relationships is at present unexplored. It has to be stressed that if there is a pure sensory pathway to the visual cortex in any species, there are two important relationships that should still be seen as providing a close link to motor outputs. One is that the pure sensory pathway runs in parallel with the other retinofugal pathways that are known definitely to have links with the tectum and pretectum. The second relates to the axons from layer five of primary visual cortex that send branches to the thalamus and brain stem (see above and figure 1), and have been found in all species studied (Rockland (1998) for the monkey; Bourassa & Deschênes (1995) for the rat; Guillery *et al.* (2001) for the cat). These, too, would point to a close link with motor outputs at very early stages of cortical processing. The issues of first demonstrating such pure pathways and then understanding their functions remain to be addressed.

We have looked at the evidence for branching for the retinofugal pathway in some detail because the issue has been studied more closely and by a greater variety of methods than is available for other afferents to the thalamus, and also because this evidence demonstrates the difficulties of coming to clear conclusions about branching patterns in the absence of a clear positive identification of the branches themselves. The possibility that all thalamic afferents may represent branches of other systems, which are primarily concerned with motor actions and not with the transmission of sensory messages to the cortex, has not played a significant role in earlier studies of pathways afferent to the thalamus, so that consideration of specific branching patterns has been erratic and generally less complete than for the visual pathways.

(ii) *Ascending pathways to the ventral posterior thalamic nucleus*

The pathways to the ventral posterior nucleus of the thalamus, concerned with touch, kinesthesia, pain and temperature, introduce an important organizational feature that is not seen in the visual pathways, but is present in all other systems afferent to the thalamus. Whereas the retinothalamic axons arise from cells, the retinal ganglion cells, whose inputs in mammals are not accessible to any other, non-retinal, pathways, most of the other afferents to the thalamus come from cells that are innervated by axons that already have had an opportunity for interactions with other systems at a pre-thalamic level. For example, the cells in the medulla (gracile, cuneate and lateral cervical nuclei), which send their axons to the ventral posterior thalamic nucleus, are innervated by axons that

also have spinal branches relating to the segmental reflexes of the spinal cord (Cajal 1911; Brown *et al.* 1977; Brown & Fyffe 1981). If we are looking at the extent to which the messages that reach the thalamus represent not just sensory inputs, but also represent information about ongoing motor instructions, we have to look not only at the axons that innervate the thalamus but also at the axons that innervate the gracile, cuneate and lateral cervical cells.

Apart from the axons that arise in the gracile and cuneate nuclei, other pathways that go to the ventral posterior thalamic nucleus include the smaller spinocervical pathway, with a relay in the lateral cervical nucleus, and the anterolateral pathway with relays in the posterior horn of the spinal cord. In addition there are pathways from the trigeminal nuclei in the brain stem. Although damage to the medial lemniscus, which represents the major afferent pathways to the ventral posterior nucleus, produces severe and often well localized sensory losses, so that the medial lemniscus must be regarded as a 'sensory' pathway, the axons that travel in the posterior columns of the spinal cord and innervate the gracile and cuneate nuclei are, as we have seen, branches of dorsal root axons that also have extensive ramifications in the spinal cord, and there they play a role in the control of spinal mechanisms relating to motor control. All textbooks stress that damage to these incoming dorsal root axons produces not only sensory, but also motor deficits. However, when we look at the activity of the thalamocortical part of this pathway, almost invariably the focus is on the sensory aspects, and the clear involvement of the incoming messages with motor mechanisms at spinal levels is left out of the functional picture.

The gracile and cuneate nuclei themselves send many axons to non-thalamic centres in the brain stem and hypothalamus (Berkley *et al.* 1980; Feldman & Kruger 1980; Berkley 1983), and we know about the branching patterns to some extent. Berkley (1975) found that axons from the gracile nucleus go to the inferior olive and also to the thalamus, but that experiments using two distinct retrogradely transported markers show them coming from different cell groups. In addition, there are projections from the gracile and cuneate nuclei to the tectum and pretectum (Bull & Berkley 1984). Again, there is evidence from retrogradely transported markers that the pretectal and tectal projections come from distinct cell populations, although a small proportion of cells showed double labelling, leaving some questions about the full extent to which afferents reaching the thalamus carry messages that also go to the tectum and pretectum.

A further point relevant for the projections from the gracile and cuneate nuclei is that where two distinct projections arise from more or less distinct cell groups in these nuclei, these cell groups are, as far as we know, both likely to be innervated by the dorsal root inputs. That is, they can, from the point of view of the present argument, also be seen as carrying comparable messages to the thalamus on the one hand and to tectal, pretectal or cerebellar circuits concerned with movement control on the other. Certainly, from the evidence of connectivity patterns currently available one has to regard the input to the thalamus from the gracile and cuneate nuclei as bearing a close relationship to messages that are concurrently being sent to spinal, cerebellar, tectal, pretectal and hypothalamic circuits.

The spinocervical pathway is a smaller pathway that carries messages from the spinal cord to a relay in the lateral cervical nucleus and from there to the ventral posterior nucleus. Djouhri *et al.* (1997) cite evidence that many spinocervical axons give off branches close to their spinal origin, innervating cells in laminae I to VI, and they also present evidence that spinocervical axons innervate cells whose axons distribute to the periaqueductal grey and the deep layers of the superior colliculus. Craig & Burton (1979), using retrogradely transported tracers, showed that 92–97% of the cells in the lateral cervical nucleus itself project to the contralateral thalamus and that 1–5% project to the ipsilateral thalamus, forcing the conclusion that any significant projection from the lateral cervical nucleus to other centres must be produced by branching axons. Giesler *et al.* (1988) described connections to the deep layers of the superior colliculus and to the periventricular grey of the midbrain in addition to the ones going to the thalamus. Berkley *et al.* (1980) showed that 40% or more of the lateral cervical neurons were double labelled after injections of tracers into the thalamus and tectum, and Djouhri *et al.* (1994), using antidromic stimulation found that 50% of neurons in the lateral cervical nucleus showed a projection to the tectum and thalamus. Here, again, we have to conclude that the pathway to the thalamus comes from axons that are also supplying centres concerned with motor control mechanisms: somatic control in the tectum as well as visceral control in the hypothalamus and periaqueductal grey.

In addition to the above there is a small group of cells (nucleus X) receiving ascending spinal afferents and sending axons to the cerebellum, inferior colliculus and the ventral posterior thalamic nucleus, with the thalamic axons formed by branches of the collicular afferents (Li & Mizuno 1997).

The dorsal root axons that enter the cord in the lateral division of the dorsal root innervate the spinal cells of the anterolateral pathway and these have extensive intraspinal branches. These dorsal horn cells play a role in innervating local, spinal reflexes, and also give rise to the long ascending anterolateral pathways. There is evidence for extensive branching in the ascending axons of the anterolateral pathway. Katter *et al.* (1996) using antidromic stimuli showed that 20% of spinothalamic cells in the sacral cord of rats also had branches going to the hypothalamus, and a fuller account of the branching patterns of the axons of dorsal horn cells has been provided by Lu & Willis (1999), who described locally arborizing axons as well as ascending branches of spinothalamic axons that distribute to the midbrain, including the tectum and the reticular formation.

For the trigeminal pathways, Veinante *et al.* (2000a) describe single filled axons going from the trigeminal nuclei to the ventral posteromedial thalamic nucleus, and also having branches going to the superior colliculus, the prerubral field, pretectum and the zona incerta.

In summary, there is a great deal of evidence about the extensive pre-thalamic branching patterns of axons that innervate the ventral posterior thalamic nucleus. When we teach students about the medial lemniscus we generally present them with evidence concerning stimuli that are specific for the peripheral receptors, classify the peripheral axons in terms of their size and conduction velocity, and

describe the sensory perceptions produced by stimulation or the losses produced by lesions. When we are looking at spinal mechanisms, some of the same dorsal root axons will be considered from the point of view of their local connections and their motor actions, but these actions and connections are rarely considered in relation to the pathways that relay information through the thalamus to the somatosensory cortex.

The connections summarized above raise a question about the information that is relayed in the thalamus and processed in the cortex. Is this information that can only be considered in terms of the categories used by the psychologist or the clinician? That is, is this hot or cold? Is your finger flexed or extended? Am I touching you with one point or two? Is this a dime or a quarter? Or does the cortex deal with information that relates more closely to the messages that concurrently are being transmitted by the spinal, olivary, tectal and hypothalamic connections of the incoming axons, and from these abstract the answers to the above questions?

### (iii) *Other first-order ascending pathways*

The summary overview of the visual and somatosensory pathways presented above demonstrates two points: one is that many of the axons that innervate first-order thalamic nuclei also send direct or indirect inputs to the motor circuitry of the brain stem and spinal cord, relating not only to somatic but also to visceral responses; and the second is that evidence about the full extent of the relevant branching is difficult to obtain by contemporary methods, and has, in many instances, not been sufficiently explored. To a large extent, the functional significance of these extrathalamic connections for understanding the messages that are relayed by the thalamus has not been fully appreciated. The same two points apply to other first-order afferents to the thalamus and in the following paragraphs we summarize evidence concerning some other ascending afferents to the thalamus only briefly.

For the auditory pathway, we know that ascending afferents reach the medial geniculate nucleus from the inferior colliculus, and that the inferior colliculus receives its auditory inputs from several parallel pathways through the brain stem: from the ventral and dorsal cochlear nuclei, the superior olivary complex and the lateral lemniscus. Although it is known that brainstem auditory relays send axons to the reticular formation, the periaqueductal gray and the superior colliculus (Henkel (1983) and Whitley & Henkel (1984) for the ventral nucleus of the lateral lemniscus, and Harting & Van Lieshout (2000) for the inferior colliculus) and that there are several other descending pathways from the inferior colliculus (Vetter *et al.* 1993; Shore & Moore 1998), we have no evidence about the extent to which the messages that are passed to the medial geniculate nucleus travel in axons that branch to innervate these other structures. In rodents, groups of nerve cells lying within the cochlear nerve, the cochlear root neurons (López *et al.* 1999), send thick axons to several brain stem centres, including the facial nucleus, likely to be concerned with the auditory startle response. These axons do not innervate any of the auditory relays on the route to the thalamus, so that their relationship to the thalamic relay can be questioned, except that the cochlear root neurons are innervated by branches of the cochlear nerve,

and the axons of the cochlear nerve that give rise to these branches are also likely to innervate the classical auditory brain stem relays on the way to the thalamus. However, details regarding the termination of these axons that branch to innervate the cochlear root neurons have not been defined. Whether some, perhaps even all, afferents to the medial geniculate nucleus reflect messages that the auditory pathway is concurrently sending to the brain stem or spinal centres is essentially undefined at present.

For the vestibulothalamic pathways of the cat, Matsuo *et al.* (1994) have described vestibular neurons that send branches to the thalamus and also to the interstitial nucleus of Cajal, and central grey substance. Isu *et al.* (1989) described cells in the descending vestibular nucleus of the cat that gave rise to vestibulothalamic axons and that could also be stimulated antidromically from the first cervical segment of the spinal cord.

The mamillothalamic and cerebellothalamic pathways both differ somewhat from the pathways considered above. Neither can be regarded as 'sensory', and each may be carrying messages that have already involved complex circuitry that includes neocortex or hippocampal cortex. We have not treated them as higher-order relays because we have previously defined higher-order relays as thalamic relays that receive their *driving* afferents directly from the cortex (Sherman & Guillery 2001, p. 231). The distinction that matters here is that a higher-order relay is sending messages to the cortex about the outputs of other cortical areas, whereas the mamillary and cerebellar afferents to the thalamus, which, on the basis of their synaptic relationships, must be regarded as the drivers at their thalamic termination (Harding 1973; Rinvik & Grofova 1974*a,b*; Somogyi *et al.* 1978; Kultas-Ilinsky & Ilinsky 1991), are carrying messages from lower, non-telencephalic centres.<sup>6</sup> One might expect that as these two pathways are already carrying information about motor control mechanisms, they might differ from the other ascending pathways and go straight to the thalamus without sending any branches to yet other parts of motor control circuitry. This may be so for some of these axons, but there is evidence for significant pre-thalamic branching in both systems.

The branching of the individual axons in the mamillothalamic tract was already recognized and illustrated by Kölliker (1896) and Cajal (1911). The mamillothalamic axons go to the three anterior thalamic nuclei (Cowan & Powell 1954) and the mamillotegmental axons, which are branches of the individual mamillothalamic axons, go to the dorsal and deep tegmental nucleus, to the rostral part of the pontine nuclei, and to an adjacent part of the pontine reticular formation (Guillery 1957; Cruce 1977; Torigoe *et al.* 1986). Cells in the smallest of the three anterior thalamic nuclei (the anterodorsal nucleus) of rats respond to particular orientations of the head in relation to the environment (Taube 1995). These 'head direction' units receive inputs from the tiny lateral mamillary nucleus (Stackman & Taube 1998), which in turn receives information about angular head velocity from the dorsal tegmental nucleus (Bassett & Taube 2001). That is, this pathway, destined for retrosplenial and postsubicular cortex, at first sight looks as though it is sending sensory information about head position to cortex, where it is likely to relate closely to the place cells seen in hippocam-

pal and adjacent cortex (Taube 1999). However, the anterior thalamic cells discharge *ca.* 40 ms before the appropriate head position is reached, and the mamillary cells are even earlier, indicating that the system is sending an efference copy to the cortex, not a pure sensory record about head position.<sup>7</sup> It is to be noted that the pontine termination of the mamillotegmental tract lies in the reticular formation close to the midline, which is a region known to be concerned with control of eye movements (Hess *et al.* 1989).

Axons from the largest of the deep cerebellar nuclei (the dentate nucleus) send projections to the thalamus and also to the pontine reticular formation and the red nucleus (Stanton 1980, 2001). These and other observations of the multiple projections from the deep cerebellar nuclei are based on methods that do not allow the identification of branching patterns. However, it is probable that many of the axons going to the ventral anterior and ventral lateral nuclei of the thalamus are branches of axons that also go to other brain stem centres. Cajal (1911) described the branching pattern of the cerebellofugal fibres on the basis of Golgi preparations, and there is more recent evidence from electrophysiological recording and from single cell injections that some of the axons going to the thalamus are branches of axons that also go to the red nucleus, where they synapse with rubrospinal neurons (Tsukahara *et al.* 1967; Shinoda *et al.* 1988). In addition, other cerebellar axons that go to the thalamus also send branches to the tegmental reticular nucleus of the pons and to the inferior olive (McCrea *et al.* 1978).

For the mamillothalamic and the cerebellothalamic axons it may be readily agreed that these are not sending pure 'sensory' information to the cortex, but rather are sending to cortex copies of messages providing current motor instructions to the brain stem. For the classical sensory pathways this is perhaps less obvious, but it has to be recognized that the patterns of connections formed by the branching afferents to the thalamus are closely comparable, and that perhaps it is only the mind-set of the observer that underlies the distinction between the sensory pathways on the one hand and mamillary and cerebellar pathways on the other.

### (c) *Higher-order thalamic relays*

Although evidence has been available for some time that there are driving afferents from the cerebral cortex going to higher-order thalamic relays (see Sherman & Guillery 2001; Guillery & Sherman 2002) and that there are also long descending pathways coming from the same cortical areas, evidence that some, possibly all of the thalamic afferents are branches of the long descending axons has been available only recently. This was based on single cell injections or injections of just a few cells with anterograde tracers. Many examples of layer five cells innervating thalamus and having descending branches to the brain stem or beyond are now available and they will be only briefly summarized here. It should be noted that this evidence is in sharp contrast to observations made after injections of tracers into layer six cortical cells. These cells send modulatory axons to the thalamus, and commonly, perhaps always, have branches to the thalamic reticular nucleus, but they do not appear to extend beyond the thalamus. In this respect, then, the axons from cortical

layer five to the thalamus resemble the ascending driver afferents to first-order thalamic relays considered in the previous section: that is, they have no branches going to the thalamic reticular nucleus, but many, possibly all, do have branches going beyond the thalamus to lower centres.

In terms of the development of our thoughts about the branching patterns of thalamic drivers, it is worth noting that it was not until several studies of corticothalamic axons showed that layer five cells commonly send a branch extending to the brain stem or spinal cord, that we began to look at the possibility that this feature, like the fine structure of the terminals and their synaptic relationships (see Sherman & Guillery 2001), might also be a property shared by all driver afferents to the thalamus. We have considered the branching patterns of first-order afferents first in this account, because this is a more logical approach, but the higher-order afferents came first in our appreciation of the functional implications of such branches. The important point to be stressed is that the basic functional relationships of cortical and subcortical driver afferents to the thalamus, with branches going directly or indirectly to motor centres, are strictly comparable. Whereas the branching patterns of the ascending afferents show that the first-order thalamic relays are receiving messages that have already contributed to subcortical and subthalamic motor outputs, for higher-order thalamic relays the branching patterns of the corticothalamic layer five afferents demonstrate that there are important transthalamic corticocortical links that are concerned with transmitting, from one cortical area to another, information about the concurrent descending motor outputs of the first cortical area.

Deschênes *et al.* (1994), Bourassa & Deschênes (1995), Bourassa *et al.* (1995) and Veinante *et al.* (2000b) showed that in the rat the axons that terminate in the thalamus and come from motor, somatosensory or visual cortex are branches of long descending axons that go to or through the brain stem, particularly to tectum and pons. Casanova (1993) showed that in the cat, axons projecting to the pulvinar from striate cortex also send branches to the tectum, and Guillery *et al.* (2001) showed a comparable branching pattern for axons going from the cat's cortical areas 17, 18 or 19 to the lateral posterior nucleus. Rockland (1998), for the macaque, described the characteristic layer five thalamic afferents coming from areas 17 and middle temporal area (area MT); these have terminals in the pulvinar and continue to the superior colliculus and the pretectal area. That is, the evidence available at present indicates that the pattern of layer five cortical cells having one branch with terminals in a thalamic relay nucleus and another branch that goes to more caudal areas of the brain stem, including tectum, pretectum or pons, is demonstrable for several different species, for several functionally distinct cortical areas and for all cortical areas studied, whether innervated by first or by higher-order thalamic relays. It may well be a general feature of layer five projections to the thalamus. A systematic investigation of these projection patterns, particularly with a more systematic focus on the details of the caudal termination sites, may prove highly informative about the relationships of the transthalamic corticocortical pathways to the long

descending (effector) axons that arise from cortical layer five.

#### 4. CONCLUSIONS

Information about axonal systems that send the same messages to two distinct neural centres can help to define how the functions of these two recipient centres may be related. We have shown that many of the messages that the thalamus relays to the cerebral cortex are also going to other centres in the brain stem that relate directly or indirectly to motor functions. For the classical sensory pathways to the cortex, this stresses the close relationship of the sensory messages to ongoing motor circuitry. For thalamocortical pathways with less clearly defined functions, an understanding of the links with motor pathways may throw new light on the function of these pathways.

The conclusions having the most immediate and straightforward practical significance concern the importance of, and the clear need for, more observations on the branching patterns of driver afferents that innervate the thalamus. For each afferent pathway, ascending from the brain stem and spinal cord, as well as descending from cortical layer five, we need to know whether these axons branch, we need to know which are the cell groups innervated by the non-thalamic branches and, above all, we need to find out about the functional role of these non-thalamic branches. For example, Sommer & Wurtz (2002) recently provided evidence suggesting that the mediodorsal thalamic neurons send corollary discharge messages about saccadic eye movements to cortex. They proposed that cells in the intermediate layers of the superior colliculus project downstream to centres concerned with saccade generation and also project upstream to the mediodorsal nucleus for relay of this information to the frontal cortex. Their study illustrates the importance of detailed information about the relevant pathways. Currently, we do not know how the descending axons from the colliculus relate to the ascending axons, nor do we know whether the ascending axons to the mediodorsal nucleus are drivers or modulators.<sup>8</sup> Other afferents coming either from the dorsal tegmental regions (Kuroda & Price 1991) or from the frontal cortex (Schwartz *et al.* 1991) could act as drivers providing input about saccade generation. In this situation the thalamic response could be linked to the motor action of the proposed descending branch, but this relationship is not clear for most of the descending branches that have been considered in this review. The point has generally not been addressed except in terms of functional roles defined by what is otherwise known about particular cell groups: for instance, that the hypothalamic connections are likely to relate to visceral functions, and tectal connections are likely to relate to movements of head and eyes, etc.

Lu & Willis (1999) have given a detailed account of branching patterns in the ascending somatosensory pathways, and they consider the methods as well as some of the major results. Their account and some of the observations we have summarized stress that for these patterns of branching, the old adage, that absence of evidence is not evidence for absence, must play a major role in an evaluation of current knowledge. There are two relevant points. One is that until quite recently, and with relatively

few exceptions, the problem has simply not been considered of interest. The second point is that many of the methods currently available all too readily lead to false negative results.

The most interesting conclusions arise from a recognition that much of the input to the thalamus is represented by branches of axons having functions quite distinct from those that are generally considered to characterize the thalamocortical pathways: that is, sensory functions leading through a group of interconnected cortical areas to perceptual functions and eventually to motor outputs. Understanding, for example, the extent to which messages that are passed from the thalamus to the somatosensory cortex relate to the functions of terminals within the spinal cord, inferior olive or hypothalamus, should lead to questions about perceptions of touch, kinesthesia or pain that relate more closely to the role of these centres in relation to ongoing behavioural patterns. To what extent would the messages passing from the thalamus to the cortex be changed if the actions produced by the motor branches of the relevant afferents were experimentally blocked or modified? Are there examples, comparable to those reported for the anterodorsal nucleus, of thalamocortical responses that anticipate the recorded 'receptive field'?

For thalamic relays whose function is reasonably well understood, for example the primary visual relay, in the lateral geniculate nucleus, viewing thalamocortical functions from the point of view of the related motor actions may not at present add greatly to our current understanding of the basic neuronal mechanisms themselves. It may, however, serve to stress that the currently dominant approaches, termed by Churchland *et al.* (1994) the 'theory of pure vision' and the 'doctrine of the receptive field', provide but a partial view of what they describe as 'interactive vision', that is visual processing in an alert, behaving animal.

For thalamic relays whose function we do not understand (the majority), recognition of the related motor connections may prove much more useful. Could we learn more about the messages that the pulvinar is sending to the temporal cortex, if we understood the nature of the motor instructions that the corticothalamic innervation of the pulvinar from layer five cells is concurrently sending to lower centres? And if the corticothalamic drivers that innervate the mediodorsal nucleus also have descending motor branches, may knowledge about the functional actions of these motor branches help us to understand the functions of the mediodorsal relay?

We have argued that the branching patterns demonstrated here, particularly the many corticothalamic connections that arise from long descending layer five output axons, force us to view perceptual processing as a product built up from messages that are essentially abstracts of motor instructions. This is not a retreat to a behaviourist view that denies or ignores perceptual processes, nor is it a verbal trick that dresses perceptual processing in a superficial set of new clothes taken from the motor system. It is, rather, an opportunity to ask a new set of questions about the nature of the messages that the thalamus transfers to the cortex.

The neuronal connections that we have described can change the way in which we think about sensory pro-

cessing. Instead of neuronal relays that pass messages about the external world through a series of cortical areas for analysis and subsequent motor action, we have described a set of connections that will provide information to the cortex about motor instructions that are being sent to motor centres (and in some instances may already have been executed). That is, we should look at thalamocortical messages, and by implication at our sensory experiences, as not representing the world that is currently out there at this moment, but as representing information that is based on, or synthesized from, behavioural responses to the external world that are planned or have already been executed.

## ENDNOTES

<sup>1</sup>The distinction between driver afferents and modulators has been discussed previously by Sherman & Guillery (1998, 2001). The drivers carry the primary message and in a sensory relay carry the information that specifies receptive field properties. The modulators can produce relatively small changes in receptive field properties, and generally change the discharge properties of relay cells without major modification of the receptive fields. In a sensory relay, destruction of the driver input removes the specific sensory response, whereas removal of a modulator does not.

<sup>2</sup>In a critique of this contemporary scheme of sensory mechanisms it was described by Churchland *et al.* (1994) as the 'conventional wisdom' or the 'theory of pure vision'.

<sup>3</sup>Hubel's autobiography (Hubel 1996) has a clear description of the extent to which defining receptive fields depends on the tools available and on the exploitation of fortunate accidents.

<sup>4</sup>When Maturana *et al.* (1960) categorized properties of retinotectal axons in the frog, they described neurons in terms of what the frog might see, although, as they recognized, each of their functional categories would actually produce a distinct motor response in the frog. They stated that for the frogs 'a form deprived of movement seems to be behaviourally meaningless', implying that the frog's response is the crucial variable for understanding the visual input.

<sup>5</sup>We have not considered evidence from transneuronal retrograde degeneration of retinal ganglion cells after cortical lesions, which affect the retinal X ganglion cells in the cat and the parvocellular ganglion cells in the monkey selectively (see, for example, Tong *et al.* 1982; Callahan *et al.* 1984; Johnson & Cowey 2000). This has been interpreted as evidence that these cells lack an extrageniculate branch. However, this is not really evidence about branching patterns; rather, it shows the extent to which a cell is or is not dependent upon the integrity of one or another of its branches, each of which may be transporting different combinations of trophic substances back to the cell body.

<sup>6</sup>It is possible to argue that, as the medial or the lateral lemnisci both take origin in cell groups that receive a cortical innervation, they are similar to the cerebellar and mamillary pathways. We recognize the similarity but have treated the two groups as distinct because the information transmitted by the two lemnisci is similar to the information that reaches their cells of origin from non-cortical sources. In this they differ from the cerebello- and mamillothalamic pathways, where it is much more difficult to relate the nature of the activity to any specific messages entering the nervous system. Possibly, when we understand these systems better, the distinction will be either clarified or lost.

<sup>7</sup>Hippocampal place cells in rats fire maximally before the place specific for that cell is reached (Muller & Kubie 1989), indicating that here, too, cortical cells are not responding just to sensory inputs about place but are recording ongoing instructions that anticipate the acquisition of a particular position in the environment.

<sup>8</sup>Evidence from the rat indicates that they resemble modulators in other thalamic relays (Kuroda & Price 1991).

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