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Measuring Subjective Visual Perception in the Nonhuman Primate

Abstract: *Understanding how activity in the brain leads to a subjective percept is of great interest to philosophers and neuroscientists alike. In the last years, neurophysiological experiments have approached this problem directly by measuring neural signals in animals as they experience well-defined visual percepts. Stimuli in these studies are often inherently ambiguous, and thus rely upon the subjective report, generally from trained monkeys, to provide a measure of perception. By correlating activity levels in the brain to this report, one can speculate on the role of individual neurons and groups of neurons in the formation and maintenance of a particular percept. However, in order to draw valid conclusions from such experiments, it is critical that the responses accurately and reliably reflect what is perceived. For this reason, a number of behavioural paradigms have been developed to control and evaluate the truthfulness of responses from behaving animals. Here we describe several approaches to optimizing the reliability of a monkey's perceptual report, and argue that their combination provides an invaluable approach in the study of subjective visual perception.*

Everybody's got something to hide except me and my monkey

John Lennon and Paul McCartney (1968)

Introduction

How the activity of neurons in the brain can give rise to a percept that is 'subjective' has been, and continues to be, one of the great mysteries of science. The faculty of vision has been central in approaching this question both experimentally and theoretically (Crick & Koch, 2003). Modern experimental approaches to understanding neural mechanisms of visual perception often rely on comparing

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two inherently different quantities. The first is one of many sorts of neurophysiological signals, typically collected from an electrode embedded among neurons in the brain itself. The second is the visual percept generated by the same brain, and is often provided by the report of a trained macaque monkey — a species whose visual abilities are in most respects identical to those of humans. Of these parallel measurements, the latter is often considerably more difficult to obtain, and its accuracy generally limits the validity of any conclusions drawn. Here we review a number of methods that have been applied to overcome the manifest problem of limited access to personal experiences, as well as the further complication of communicating with a different species.

In approaching this issue, it is important to realize that the brain's own action forces upon us a distinction between sensation and subjective perception. Visual 'sensation', as we use the term here, is the reception of a pattern of light on the retina and the automatic, indifferent cascade of neural responses that follows. 'Perception', on the other hand, we reserve for describing what we actually see — or at least what we think we see. Unlike sensation, perception it is an active and interpretive process, drawing upon the benign sensory traces and culminating in our ultimate subjective impression of the visual world. Of course, this dichotomy, like most, is far too simple to be useful. Our sensory machinery is most certainly not impartial to our perception, since it is evolutionarily tuned to facilitate particular percepts and exclude others. And our perception does not simply draw upon our sensory apparatus, but can also shape it according to expectations, the relevance of particular objects, or recent experience. However,

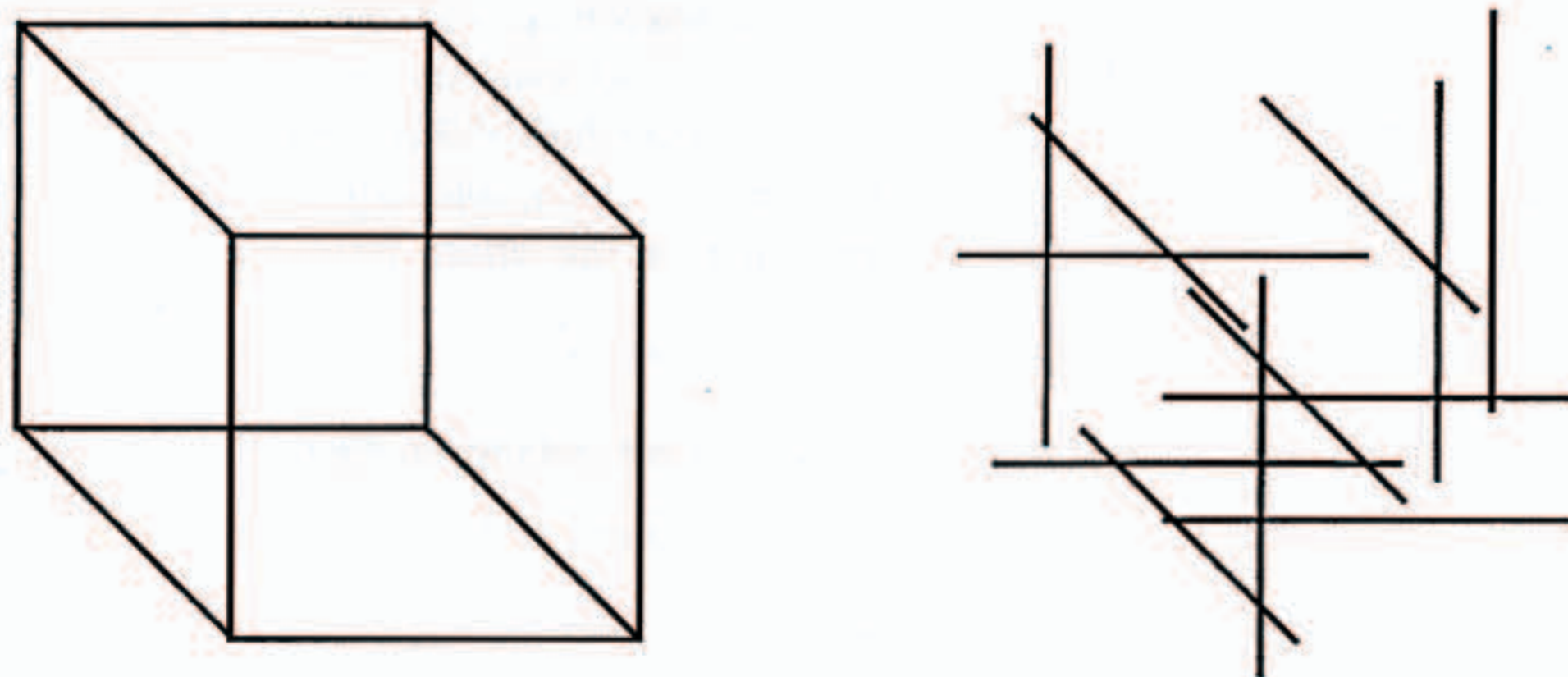


Figure 1

The specific placement of 12 line segments determines how each of them is perceived. (a) By configuring the lines into the well-known Necker cube, each line can take on exactly two perceived configurations. This is a notable reduction from a single line, appearing alone on the sheet, which can, in theory, give the appearance of any of an infinite number of angle/length combinations. (b) Arranging the same segments randomly gives an impression that is much more flat, as if the segments are lying on a flat piece of paper. In some respects, the percept in (b) thus is more veridical than that in (a).

despite these concessions, it is difficult to discard this dichotomy completely for one simple reason: subjective perception can, on occasion, be completely uncoupled from sensory events. One need only consider visual perception during dreaming.

This uncoupling serves as an entry point for research into perception, and visual scientists have therefore often exploited ambiguous patterns that offer more than one valid perceptual interpretation. The ambiguous, and often wavering, impression of these patterns, perhaps more than any other demonstration, illustrates the active and interpretive nature of perception. The famous Necker cube (Figure 1a), for example, offers exactly two valid configurations, with its front face aimed either upward or downward. But why is the Necker cube ambiguous? Careful consideration reveals that its specialized structure does not create ambiguity, but instead constrains it. Each of its 12 line segments, if considered alone, can be conceived in multiple geometries, since an infinity of angle/length combinations in three dimensions give rise to the same two-dimensional projection onto the receptors tiling the retina. Only when these line segments are positioned such that they begin to interact is the interpretation constrained further by the brain. In the case of the Necker cube, exactly two valid interpretations remain. Interestingly, neither of these interpretations can be described as 'veridical', which would hold the line segments to lie on a flat surface. Such a percept can be easily achieved when the same components are arranged in a different manner (Figure 1b). Why then does the brain reject the veridical (flat) interpretation of the Necker cube in favour of a virtual three-dimensional figure that is itself ambiguous? And where in the brain is the ultimate geometry decided? Intriguing questions such as these have been asked with increasing frequency by neurophysiologists, in the hopes that they will provide insight into fundamental mechanisms of visual perception. It is, for example, of great interest to learn how a 'sensory' neuron in the visual cortex (i.e., one whose activity is reliably modulated by the appearance and removal of a visual pattern) would respond under conditions in which the same pattern is *perceived* in two different ways. Does the ultimate perceptual interpretation of a stimulus depend upon (or perhaps contribute to) the activity of such visually responsive neurons? And if so, what types of neurons might show such perception-related activity? To test these questions experimentally in monkeys it is necessary to gain accurate knowledge of their perceptual state.

A number of important differences exist in the collection of psychophysical data from humans and monkeys. In addition to the well-established performance fluctuations and criterion changes that can cause difficulties in measuring human perception, monkeys pose an additional difficulty: they have no *a priori* desire to be 'truthful' in their responses. While the default assumption for humans is that they are responding as accurately as they can, that for monkeys is that they are responding inaccurately — and the investigator must continually prove otherwise. In performing tasks in the laboratory, monkeys are motivated by immediate reward, say a drink of apple juice or a marshmallow, and their main objective is to optimize the frequency of this reward. While this might seem benign, it

becomes a problem as soon as the monkey must report its internal, subjective percept with stimuli that are truly ambiguous, since it is no longer possible to differentially reward trials based on their 'truthfulness'. And a monkey who understands that there are no negative consequences for incorrect answers eventually loses motivation to respond accurately.

The present article thus focuses on various tricks and methods currently used to define and evaluate the perception of ambiguous patterns. The ultimate goal of many of these tricks is to shape and maintain an accurate subjective report on the part of the monkey, since this provides the ultimate access to the monkey's perceptual state. We consider two types of multistable stimuli that have been studied in our laboratory. The first is the phenomenon of binocular rivalry (BR), which can be elicited by simply presenting dissimilar stimuli to corresponding regions of the two eyes (Dutour, 1760). Normally the eyes see roughly (but not exactly)

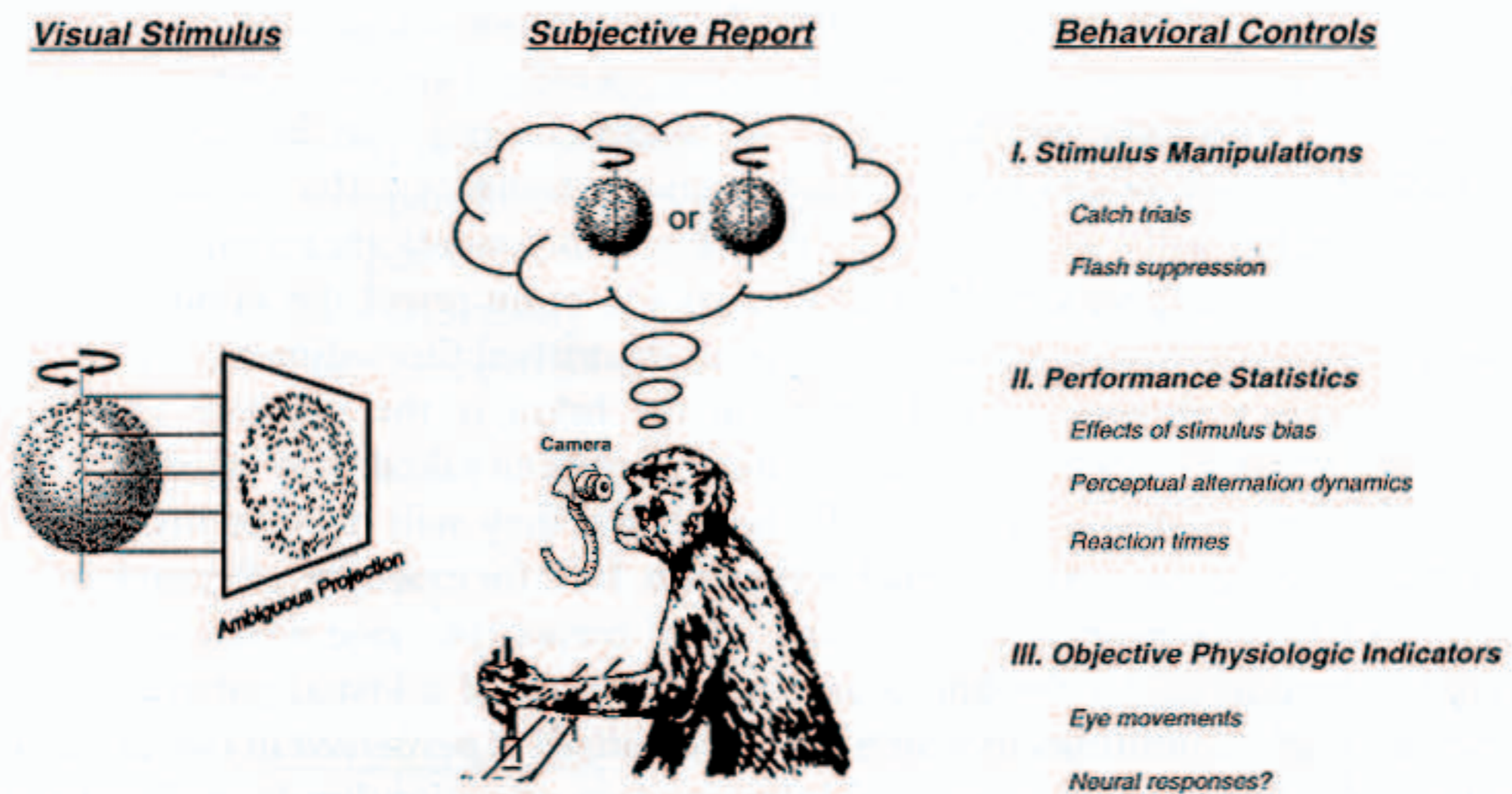


Figure 2

Monkeys are often trained to report their perception of an ambiguous pattern by means of pulling a lever, as shown here. In this example, the pattern is the two-dimensional (orthographic) projection of a transparent, textured sphere. When in motion, this stimulus gives the striking percept of a three-dimensional ball. However, the flat projection does not provide information as to whether the leftward or rightward moving dots represent the front face (e.g., if, as considered from above, the sphere is spinning in a clockwise or counter-clockwise manner). Thus, the brain imposes a particular depth organization onto this ambiguous pattern, ultimately generating the percept of a sphere spinning in one of the two possible directions. As in binocular rivalry and other multistable stimuli, continuous viewing of this pattern gives rise to a dynamic percept, where perceptual dominance (here: clockwise vs. counter-clockwise motion) alternates every few seconds between viable visual interpretations. Given the reliance on the subjective report, a number of approaches are used in order to evaluate and control the monkey's accuracy. These include manipulations biasing interpretation of the stimulus, statistical evaluation of the animal's reported percept, and using objective physiological measures such as eye movements. These approaches are discussed in detail in the text.

the same image of the world. However, when two very different monocular patterns are shown, the brain selects only one to reach conscious perception at any point in time. The second stimulus, shown in the left portion of Figure 2, is comprised of a circular region filled with random dots that, when set in coordinated motion, gives rise to the perception of an illusory three-dimensional rotating sphere (RS). This so-called structure-from-motion stimulus is a striking example of how the brain can use a single cue (relative motion in this case) to construct the impression of depth and three-dimensional shape (Wallach & O'Connell, 1953). The RS stimulus is inherently ambiguous, with either the leftward or rightward dots being perceived as moving on the front surface. Both the BR and RS stimulus, like virtually all ambiguous patterns, destabilize perception. The subjective impression alternates unpredictably between the two solutions as long as the stimulus is present.

We consider here three general approaches for shaping and evaluating the perception of these and related stimuli, outlined on the right in Figure 2. First, it is often possible to physically disambiguate such patterns to provide a coarse measure of the monkey's honesty or reliability. Next, a statistical analysis of the animal's perceptual report can often provide further evidence regarding the accuracy of the monkey's responses. Third, there exists a small number of objective physiological indicators that can provide a trial-by-trial evaluation of the monkey's subjective performance. Below, we give examples of each of these methods, and describe how we have combined these methods to evaluate the monkey's response accuracy in the perception of the RS pattern. We then present recent results in which eye movements serve as a tool for investigating perception-related brain states under general anaesthesia.

Disambiguating Stimulus Manipulations

In soliciting subjective responses from a monkey with stimuli that are either inherently ambiguous in nature, or near the perceptual threshold, it is essential to include the frequent presentation of control stimuli whose correct answer is clear to both the monkey and the experimenter. These so-called 'catch trials' provide a coarse measure of the monkey's performance, and comprise an essential part of nearly all studies in which the neural basis of perception is studied. In binocular rivalry, where monkeys are trained to report which of two stimuli they see at each point in time, unambiguous catch trials have been used in all studies to date (Leopold & Logothetis, 1996; Logothetis & Schall, 1989; Sheinberg & Logothetis, 1997). These generally consist of presenting the monocular stimuli alone, leading to an unambiguous response requirement, in the context of which inaccurate responses can be immediately identified. As a matter of course, provisions must be made to hide the identity of catch trials from the monkey, in our case by mimicking the smooth transitions of normal rivalry surrounding such trials. Such stimuli not only provide a means to monitor the performance, but also permit the experimenter to reward objectively based on response accuracy, and thus initially train and later continually remind the monkey not to stray from

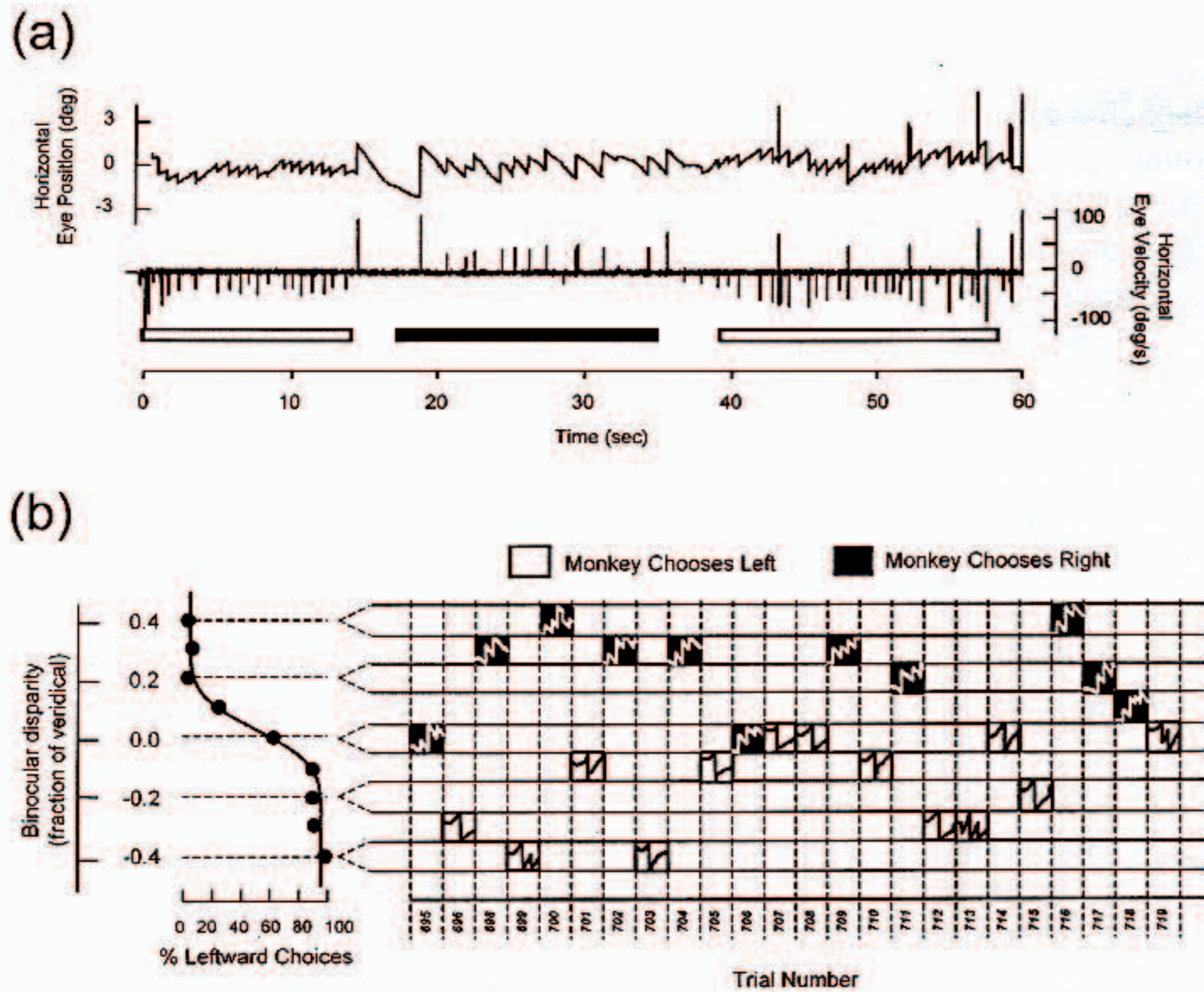


Figure 3

Behavioural controls used during monkey's viewing of the ambiguous rotating sphere shown in Figure 1. (a) Use of optokinetic nystagmus (OKN) responses as an objective indicator of perception. Eye position was measured during a one-minute period in which the monkey was viewing the ambiguous sphere. The upper trace is the horizontal eye position as a function of time, showing the characteristic sawtooth pattern of optokinetic movements. The change in the polarity of this pattern represents a change in the perceived spin direction of the rotating sphere. Immediately below is the eye velocity signal from the same period, whose vertical peaks (corresponding to the 'fast phase' of the OKN) show more clearly the perception-related state changes. Note that the change in the eye movements is not accompanied by a change in the stimulus, only a change in the perception. (b) Combination of several approaches used to evaluate response accuracy. In this experiment the monkey viewed brief periods of the rotating sphere, and was asked to report its direction each time by pulling one of two levers. To evaluate the response accuracy we used each of the approaches outlined in Figure 1. First, we applied a *stimulus manipulation* to bias the monkey's perception. We did this by applying binocular disparity (stereoscopic depth information) to the dots on the sphere. For large values of disparity, this disambiguated the percept sufficiently such that we could define a 'correct answer' for each trial. Second, we examined the *performance statistics* for disparity values that only slightly biased perception. This is shown in the left portion of the figure, where the fraction of leftward responses varies systematically as a function of the binocular disparity applied. Note that even with relatively small fractions of the 'correct' disparity (± 0.2), the perception was systematically biased. Finally, the accuracy of performance was additionally evaluated by comparing the *objective physiological indicator* of OKN during epochs in which the monkey reported leftward vs. rightward motion. This is shown for a representative sample of 24 subsequently performed trials on the right side of the figure. On each trial, the sphere was shown with a particular disparity, and the monkey's response and OKN were recorded. Note that the responses and OKN were both influenced by the disparity applied, but that, under conditions of true ambiguity (0.0 disparity), the OKN polarity continued to match the monkey's report.

reporting his subjective percept. As described in greater detail below, monkeys are notoriously cagey in this respect. If they discover that there are no consequences for incorrect responses, their performance will tend toward completely random.

For other stimuli, such as the RS shown in Figure 2, effective catch trials can often be created by the addition of disambiguating cues. In the RS, the perception of three-dimensional shape can be traced to the parallax motion of dots, sliding past each other more quickly in the centre than near the edges. However, as in the Necker cube, there remain two equally valid interpretations, with the ball moving either clockwise or counter-clockwise when considered from above. This seldom occurs in natural vision, as the structure of any such pattern is fortified by redundant cues for depth, including binocular disparity,¹ shading, texture gradients, perspective, occlusion, etc. (Cavanagh, 1987). Experimentally, it is possible to use these and other cues to bias perception of the sphere with any one of these cues to create an unambiguous stimulus that can be employed as a catch trial. In the laboratory, we have used the cues of binocular disparity and luminance gradients to bias perception of the RS in this manner.

An example using binocular disparity to this end is shown on the right side of Figure 3b. In this experiment, perception of one or the other direction of the rotating sphere was enhanced by adding binocular information, and the amount of positive or negative disparity is signified by the vertical position in the plot. Black boxes signify a monkey reporting a rightward moving front face, and white boxes a leftward moving front face (for the moment, the eye movement traces inside the boxes should be ignored). Note that positive disparities (upper portion of the grid) yield primarily rightward responses while negative disparities (lower portion) yield primarily leftward responses. The addition of significant disparity is thus an effective cue to bias perception of the RS stimulus, providing us with a valid catch trial stimulus with which to continually evaluate and refine the accuracy of the monkey's perceptual report. This approach has been recently applied in neurophysiological experiments in monkeys trained to report the direction of rotation (Bradley *et al.*, 1998; Grunewald *et al.*, 2002; Dodd *et al.*, 2001).

The addition of external cues to disambiguate perception is not used exclusively to hone behavioural accuracy. It has also been used effectively to create alternate perceptual contexts for a given stimulus (Duncan *et al.*, 2000; Zhou *et al.*, 2000; Baumann *et al.*, 1997; Rossi *et al.*, 1996; Bakin *et al.*, 2000; Andrews *et al.*, 2002; for a review, see Albright & Stoner, 2002). These experiments generally rely on global stimulus changes that alter the manner in which an ambiguous local feature is interpreted. While such stimulus manipulations do not allow for a complete isolation of perceptual mechanisms, they nonetheless provide a powerful means to investigate how global information shapes perception-related responses in the brain.

[1] Binocular disparity refers to the slight shift in the retinal projections on the two eyes of a point in three-dimensional space. This shift stems from the slightly different views that the two eyes have of a target, and serves as the basis for our stereoscopic perception. In the laboratory, such disparity cues can be manipulated to add different amounts of stereoscopic depth information to a stimulus.

In some cases, the perception of a pattern can be biased not only by changes in its overall structure, but also by the temporal sequence of stimulus presentation. A series of relatively new tricks have made it possible to gain further experimental control over the perception of a stimulus that is, in many respects, completely ambiguous. An example of such a bias that has been used extensively in neurophysiological experiments is the phenomenon of binocular rivalry flash suppression (Wolfe, 1984). In this paradigm, dissimilar stimuli are presented to the two eyes asynchronously — with an interval ≥ 500 ms between the first and second. This presentation sequence consistently results in perception being dominated by the second pattern, with complete perceptual suppression of the first (until spontaneous binocular rivalry alternation sets in). Given this experimental control over perception, the flash suppression paradigm has been used in several neurophysiological studies to bias perception during binocular rivalry (Sengpiel *et al.*, 1995; Sheinberg & Logothetis, 1997; Kreiman *et al.*, 2002; Leopold *et al.*, 2003). Interestingly, a recent study has suggested that flash suppression is not restricted to conditions of interocular conflict, but can be used effectively even if there is no spatial conflict between the first and second stimuli (Wilke *et al.*, 2002). This ‘generalized’ flash suppression is a powerful new technique that is currently being used to investigate the neural basis of stimulus visibility. Importantly, and in contrast to other disappearance phenomena, both types of flash suppression are effective in the face of even the strongest attention or deepest introspection.

Finally, a recently described technique provides an additional means of having control over a monkey’s percept during neurophysiological experiments. When ambiguous patterns are presented intermittently rather than continuously, perception can often become locked in a particular configuration for extended periods of time (Leopold *et al.*, 2002b). In the context of this stabilization, the subjective interpretation of successive presentations is not akin to tossing a coin, but is instead highly dependent upon the preceding interpretations. This differs markedly from continuous viewing of ambiguous patterns, where the perceptual history is thought to have little if any role in dictating the stimulus interpretation at any point in time. The degree of stabilization is a variable of the exact stimulus timing parameters, thus providing an additional means to evaluate the accuracy of the monkey’s perceptual responses. However, perhaps more importantly, this paradigm allows for the investigation of activity *between* stimulus presentations, where the perceptual interpretation of the upcoming presentation is, in fact, already determined (Maier *et al.*, 2002). Stabilization, like flash suppression, can be observed under a wide range of attentional states, and is experienced equally well by naïve subjects (who are unaware the stimulus is ambiguous) and experienced subjects.

Many of the above stimulus manipulations are powerful in biasing perception, and are critical to the arsenal of tools used by neurophysiologists seeking fundamental mechanisms of vision. However, alone they are often insufficient to draw conclusions regarding the neural underpinnings of subjective perception for at least two reasons. First, from a physiological perspective, such perception-

related changes are, by definition, confounded with a change in the visual stimulus. Often these changes need to be relatively large in order to provide an unambiguous interpretation for the monkey. The burden of proof lies with the investigator that perception-related modulation of neural activity is above and beyond that which might be expected based only on the sensory manipulation. Second, and more important for the current discussion, stimulus manipulations alone, in the form of catch trials, are often insufficient for enforcing accurate responses during truly ambiguous trials. This is because monkeys can often detect subtle changes in a stimulus, and may use that, rather than the intended global percept, to perform the task. The intelligence of monkeys is seldom clearer than when they find a shortcut or unintended cue to use in optimizing their reward. Their ability to discriminate ambiguous (uncontrolled) from unambiguous (controlled) trials is a particularly nefarious example of this. A monkey might, for example, modify his behaviour according to the ability of the experimenter to reward the accuracy of his response, reporting perfectly on unambiguous catch trials and randomly during the truly ambiguous trials (during which they are inevitably rewarded by chance, even if they report their percept inaccurately). While this might seem unlikely, monkeys commonly show such refined strategies in attempting to optimize their frequency of reward.

There are a number of commonly applied tricks to minimize the probability of the monkey making the association between stimulus appearance (unambiguous vs. ambiguous) and reward contingency (accurate feedback vs. no feedback). For example, one strategy, which is beyond the scope of the current discussion, is to employ a reward schedule that is variable, where the monkey always has a certain *probability* of obtaining reward with each correct response (a so-called variable-ratio schedule). Another trick, described below, is to restrict the disambiguating cues to low values, serving only to push perception of an ambiguous stimulus in a particular direction, without guaranteeing that it will follow 100% of the time. With such stimuli, it is often possible to create a biased stimulus that is nearly or even completely indiscriminable from the ambiguous pattern. But given that its bias is relatively weak, its effectiveness cannot be adequately judged on a trial-by-trial basis, but must rely on a statistical analysis. The next section thus focuses on how the performance and other statistics, when considered over many trials, can be used as evidence that a monkey is responding truthfully according to his subjective percept.

Statistical Analysis of Perception

A slight bias in an ambiguous pattern essentially affects the probability that it will be perceived in a particular configuration. The reason is that, while the stimulus is still lacking a large enough amount of disambiguating cues to be perceived in a unique fashion, the visual system can take into consideration even very small cues that favour one of the alternate stimulus interpretations. This happens more often the more salient these cues are, thus providing the possibility to parametrically vary the likelihood of a perceptual bias to occur. To return to

the RS example, the left portion of Figure 3b shows that varying the strength of a cue along a continuum serves to change this probability along a continuum. In this figure, disparity values of +1.0 and -1.0 can be seen to correspond to the 'correct' binocular disparity that would exist in an actual three-dimensional rotating sphere of the size depicted on the screen. Notice that, in the well-trained monkey from whom these data were derived, even a relatively small disparity value (± 0.2) was sufficient to impose a particular perceptual interpretation. Smaller disparities gave rise to intermediate levels of bias, with a value of 0.0 (no valid stereoscopic information) resulting in half the choices leftward and half rightward. Such performance statistics, giving rise to a psychometric function, have been used previously to demonstrate that the monkey is accurately reporting his perception of ambiguous or threshold-level stimuli (see, for example, Britten *et al.*, 1992; Dodd *et al.*, 2001). In the case of ambiguous or rivalrous patterns, it is important to acknowledge that there is no *a priori* reason to expect equal dominance of all competing percepts, since there are also subject-specific inherent biases in the manner in which stimuli are perceived (Sereno & Sereno, 1999).

Performance, in the sense of correct or 'correctly biased' responses, is but one statistical variable that can be monitored to establish the accuracy of the animal's report. In addition, one can monitor aspects of the temporal dynamics, a technique that has proven invaluable in the study of binocular rivalry. In rivalry the alternation between dominance of each eye's pattern is stochastic in time (Fox & Herrmann, 1967), with the duration of a particular dominance phase independent of the alternation history. However, despite the randomness in this process, the shape of the distribution of many dominance phases is entirely deterministic, and often modelled with a gamma function (Levelt, 1965). While the processes underlying these dynamics remain a topic of debate, they serve as a signature for rivalry and other forms of multistable perception (Borsellino *et al.*, 1972; Leopold & Logothetis, 1999). These dynamics also characterize monkeys' perception during rivalry (Myerson *et al.*, 1981; Leopold & Logothetis, 1996), and thus provide additional, although arduous, means to evaluate response accuracy during neurophysiological experiments. The mean or expected dominance time is also a parameter that can be manipulated in rivalry by adjusting the relative strength (e.g., contrast) of the competing monocular stimuli. This causes a stereotypic change in the relative balance of perception that was first described by Levelt (1965). Specifically, raising the contrast of one stimulus results in decreased mean dominance time of its rival. This result, besides raising the interesting question of why such a relationship might emerge, has been instrumental in neurophysiological studies of binocular rivalry (Leopold & Logothetis, 1996; Sheinberg & Logothetis, 1997), and has provided a powerful means of evaluating performance.

The use of statistical evaluation, in combination with stimulus manipulations, thus provides a set of tools by which one can systematically manipulate a stimulus, and compare the changes over many trials according to a set of well-defined expectations. In addition to performance, and the temporal dynamics mentioned above, one can also observe trends in other variables such as manual reaction

times for additional evidence that the monkey is responding correctly. Of course, none of these methods can effectively be used to monitor trial-by-trial responses during truly ambiguous presentations, for which an objective 'lie detector' would be invaluable. The next section demonstrates that such behavioural controls are actually possible in some instances, and that their use in the study of perception may play an increasingly prominent role.

Objective Physiologic Indicators of Perception

Sometimes the body betrays subjective states, a fact that serves as the basis for the polygraph or lie detector. Visual perception has a small number of objective physiologic indicators. The dilation of the pupil has, for example, been shown to change in accordance with periods of dominance and perception during binocular rivalry (Lowe & Ogle, 1966; Richards, 1966). Clearly, any such measures would be of great value in assessing and correcting the performance of a monkey who has little inherent motivation for responding accurately and 'honestly'. By far the most powerful type of objective indicator of perception used today is the pattern of eye movements automatically elicited upon viewing certain types of visual patterns. Of the different types of eye movements that might be exploited for this purpose, it is, perhaps ironically, an evolutionarily ancient system that has proven the most useful for gauging subjective perception — optokinetic nystagmus or OKN. These movements are elicited when a subject attempts to hold a steady gaze while viewing a moving surface. The eyes are typically forced into a sequence of drifts and jumps that, when viewed as a function of time, have a stereotypic sawtooth pattern (see, for example, Figure 3a). This well-studied phenomenon is robust, and can be elicited by many types of moving stimuli under a variety of conditions. Its reflexive nature has previously been exploited to evaluate, for example, aspects of perception in infants too young to report their percept (Manny & Fern, 1990; Fox *et al.*, 1979).

We have used this technique extensively with both BR and RS stimuli. Unlike the infant studies, our use of OKN has been to reinforce or refute a particular response provided by the monkey. Importantly, this is possible because not only can OKN reflect the direction of a moving visual pattern, but it can also accurately reflect the perceived direction of motion in an ambiguous stimulus. This has been shown previously for binocular rivalry in both humans (Enoksson, 1968) and monkeys (Logothetis & Schall, 1990). If, for example, rivalry is initiated between an upward- and downward-moving pattern, perception of the upward pattern will be accompanied by 'upward' OKN (with the slow phase moving upward). When, however, the perception switches to downward (with no change in the stimulus) so does the OKN polarity. This obligatory coupling between the direction of OKN and perception has provided an objective indicator of perception in a number of human rivalry studies (Fox *et al.*, 1975; Leopold *et al.*, 1995) and has also served as the basis for training and evaluating the accuracy of responses in neurophysiological studies (Logothetis & Schall, 1989).

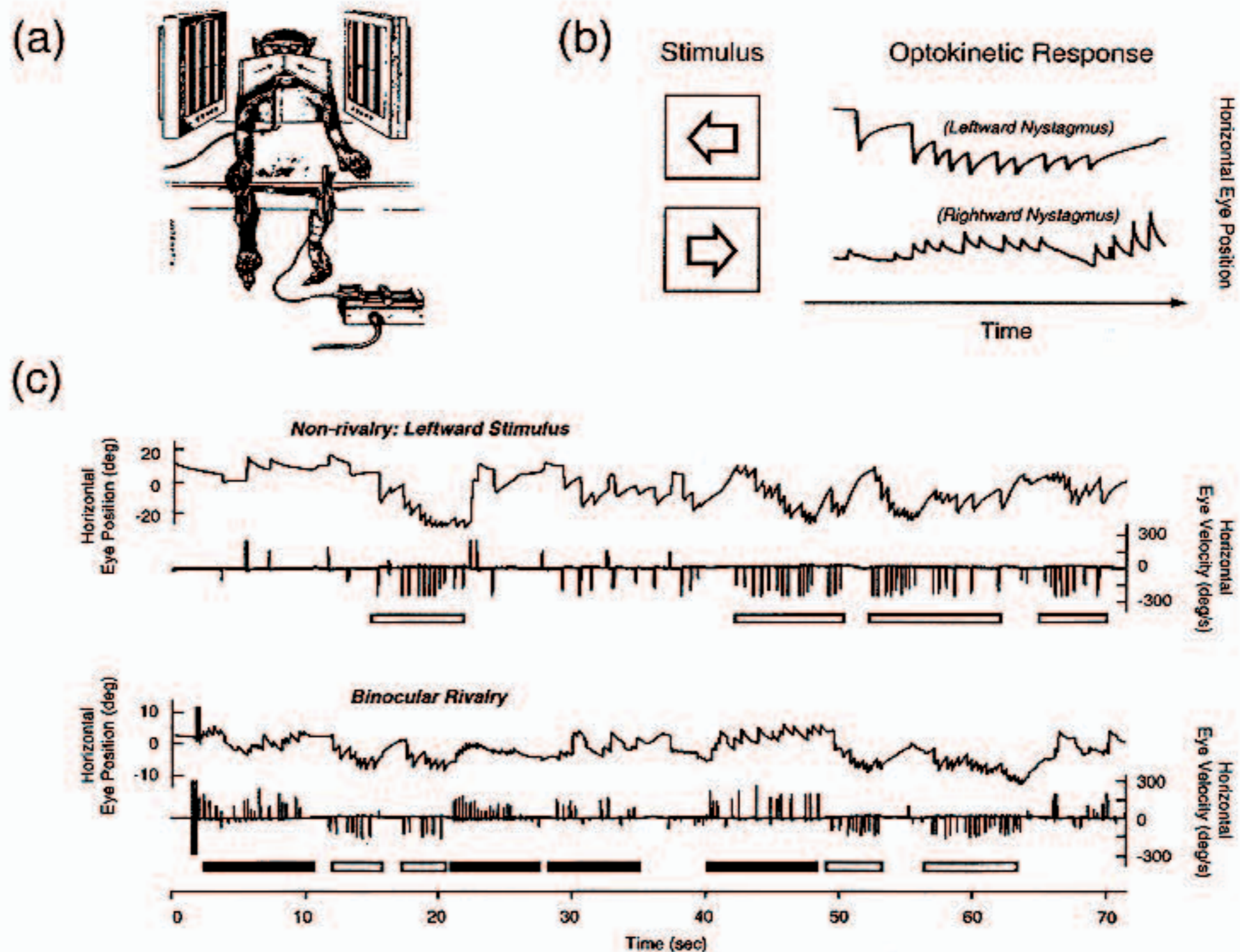


Figure 4

Perception-related optokinetic movements measured in a monkey in a state of dissociation anaesthesia brought about by the narcotic ketamine. (a) Setup designed to monitor physiological responses, including eye movements, during the gradual transition from wakefulness to anaesthesia. The setup is equipped with many features traditionally used to test alert monkeys, such as measurement of behavioural responses and eye position. In addition, the monkey has been trained to accept the insertion of an intravenous injection catheter during wakefulness, through which various agents, ketamine in this case, can be infused during the experiment. The visual stimulation apparatus is designed to present large-field motion patterns, with mirrors used to independently stimulate the two eyes. It was thus possible to present monocular, binocular, or binocularly rivalrous stimuli during both waking and anaesthesia. The dissociation anaesthesia brought about with ketamine results in the eyes remaining open, with the direction of gaze roughly straight ahead, permitting large-field stimulation with this apparatus. (b) Under low dose (1 mg/kg) ketamine anaesthesia, while the monkey is behaviourally dissociated from the environment, optokinetic movements can be elicited by moving stimuli, shown here by the different polarity traces for leftward vs. rightward stimulation. These OKN responses differ slightly in their structure from those elicited during waking, however, their polarity unambiguously reflects the direction of the inducing stimulus. (c) Examples of OKN patterns elicited during extended viewing of non-rivalrous and rivalrous moving patterns during ketamine dissociation. The format is the same as in Figure 2a. During non-rivalrous leftward stimulation, several trains of OKN movements were elicited with a polarity reflecting the stimulus (white bars). During binocular rivalry, below, the eye trace again shows trains of repetitive OKN movements induced by a stimulus. However, in this case, the leftward stimulus was presented to one eye while the rightward one was presented to the other one. In the waking state, this stimulus configuration normally gives rise to vigorous binocular rivalry, with perception continually alternating between rightward and leftward motion. As one can see from the figure, state changes in the OKN response were also present during ketamine anaesthesia. Given that the monkey was under a state of behavioural dissociation, and therefore unable to report any percept, it is interesting to speculate on the relationship of these state changes to conscious visual perception.

Recently, we have demonstrated that OKN is also a reliable indicator of perceived rotation for patterns like that shown in Figure 2a. An example of OKN movements during one minute of continuous, unrestricted viewing of the ambiguous rotating sphere is shown in Figure 3a. The top trace in this figure shows the horizontal eye position as a function of time. Note the characteristic sawtooth pattern, comprised of slow and fast phases, that is present throughout the trial. Close examination reveals that this pattern changed polarity after roughly 15 seconds, and then back again after roughly 38 seconds. These changes in polarity are more easily seen in the trace just underneath, which represents the instantaneous velocity at each time point. The fast phases (saccades) are shown by the spikes in this trace, with their sign showing a transition at the same time points. These phases of leftward and rightward OKN, further marked by the horizontal bars beneath, represent spontaneous state changes experienced by the monkey upon viewing this stimulus. These results are further supported by human psychophysical studies with superimposed patterns that are transparently moving in opposite directions. For these stimuli that are eliciting similar reversals of subjective depth, the evoked OKN were highly correlated with the perceived motion on the attended surface (Watanabe, 1999).

The eye movement traces shown in the grid on the right side of Figure 3b demonstrate that these optokinetic responses are in perfect agreement with the monkey's reported perception of the rotating sphere, just as is the case for binocular rivalry. Superimposed on the black squares, corresponding to trials in which the monkey pulled the lever signalling that the front face was perceived to the right, the OKN slow phases are moving rightward. On the white squares, however, the slow phases are moving leftward. This relationship is consistent even in the completely ambiguous condition (0.0 disparity). Thus, Figure 3b represents the convergence of each of the general techniques outlined in Figure 2, integrated to optimally control and evaluate the monkey's performance. Disambiguating cues were added to the pattern, a statistical analysis of performance was undertaken to verify the effect of subtle stimulus changes, and eye movements were monitored as an objective indicator of the monkey's perception.

Most recently, OKN has been used as an objective measure in monkeys whose perceptual state is not clearly defined (Figure 4). In these experiments, we investigated the possibility that optokinetic nystagmus could be used to investigate perception-related brain states in an animal in a state of 'dissociation' brought about by the anaesthetic ketamine (Leopold *et al.*, 2002a). This experiment was facilitated by a novel setup in which the state of consciousness could be continually modulated, by injecting ketamine through an intravenous line (Figure 4a). The animal sat in a chair and viewed two mirrors, angled in such a way to provide independent stimulation to the two eyes from flat monitors. For a range of doses, OKN movements could be reliably elicited, albeit slightly abnormal in form (Figure 4b), while the monkey was otherwise unresponsive to external stimuli. Under these conditions, we presented either non-rivalrous, monocular stimulation (Figure 4c, upper) or rivalrous stimulation, with opposite horizontal directions in the two eyes (Figure 4c, lower). Interestingly, during binocular rivalry,

we observed periods of leftward OKN interleaved with those of rightward OKN. During wakefulness such periods would correlate nearly perfectly with the monkey's perceptual experience. During ketamine dissociation, it is only possible to say that these OKN traces are objective indicators for brain-state changes that may bear a relationship to subjective perception. Thus, while it is interesting to speculate what such state changes might entail, further research is required to delve deeper into this difficult issue.

It is possible that objective indicators for perception will play an increasingly important role in brain research in the future, as our understanding of the brain's approach to vision becomes more refined. This might even take the form of using neural signals themselves as a means to 'decode' perception at each time point, and then using this signal to judge the accuracy of a subjective response. Physiological studies from our group and others have shown that, while many neurons in the early visual areas modulate with perception during ambiguous stimulation, these modulations are seldom reliable enough to serve as a behavioural control (for a review, see Leopold & Logothetis, 1999). Nonetheless, recordings from the temporal lobe visual areas suggest that with certain high-level neurons, such a scheme for monitoring perception may, in fact, be possible. During binocular rivalry flash suppression, neurons in monkeys, and more recently those in humans, reliably follow the subjective percept (Sheinberg & Logothetis, 1997; Kreiman *et al.*, 2002). Remarkably, some neurons in the human medial temporal lobe even respond when a stimulus is not physically presented at all, but only *imagined* using visual imagery (Kreiman *et al.*, 2000). The activity of these neurons thus appear to lie very close to very personal aspects of subjective perception, and experiments in the future may thus take an increasingly voyeuristic approach to exploring the neural underpinnings of visual perception.

Conclusions

The study of the neural basis of visual perception is a topic of great interest, and, while even its core remains poorly understood, considerable progress has been made. Ambiguous and rivalrous patterns serve as excellent tools for investigating principles of visual perception, and have been widely known and utilized long before the advent of alert monkey neurophysiology (von Helmholtz, 1925; Wertheimer, 1912; Koffka, 1935). Given their multiple perceptual interpretations, such patterns are a convenient tool for neurophysiologists seeking the neural basis of visual perception. They are diverse, appealing to many aspects of visual processing, easy to create, and a fascination for both visual scientists and the layman. One might then ask, why have there been so few studies that have specifically employed such patterns to study neural mechanisms of perceptual organization? The answer most certainly lies not in the difficulty of the physiological techniques, nor in the stimuli themselves, but rather in the great difficulty in obtaining a reliable measure of subjective visual perception from monkeys. The various tools outlined and elaborated here provide a concerted approach that we have used successfully to tackle this challenging problem. Further

elaboration of these techniques, as well as the introduction of new ones, will likely hold an important place for neurophysiologists eager to understand how that which we sense is transformed into that which we see.

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References

- Albright, T.D., Stoner, G.R. (2002), 'Contextual influences on visual processing', *Annual Review of Neuroscience*, **25**, pp. 339–79.
- Andrews, T.J., Schluppeck, D., Homfray, D., Blakemore, C., Blakemore, C. (2002), 'Activity in the fusiform gyrus predicts conscious perception of Rubin's vase-face illusion', *Neuroimage*, **17** (2), pp. 890–901.
- Bakin, J.S., Nakayama, K., Gilbert, C.D. (2000), 'Visual responses in monkey areas V1 and V2 to three-dimensional surface configurations', *Journal of Neuroscience*, **20** (21), pp. 8188–98.
- Baumann, R., van der Zwan, R., Peterhans, E. (1997), 'Figure-ground segregation at contours: a neural mechanism in the visual cortex of the alert monkey', *European Journal of Neuroscience*, **9** (6), pp. 1290–303.
- Borsellino, A., De Marco, A., Allazetta, A., Rinesi, S., Bartolini, B. (1972), 'Reversal time distribution in the perception of visual ambiguous stimuli', *Kybernetik*, **10** (3), pp. 139–44.
- Bradley, D.C., Chang, G.C., Andersen, R.A. (1998), 'Encoding of three-dimensional structure-from-motion by primate area MT neurons', *Nature*, **392** (6677), pp. 714–7.
- Britten, K.H., Shadlen, M.N., Newsome, W.T., Movshon, J.A. (1992), 'The analysis of visual motion: a comparison of neuronal and psychophysical performance', *Journal of Neuroscience*, **12** (12), pp. 4745–65.
- Cavanagh, P. (1987), 'Reconstructing the third dimension: interactions between color, texture, motion, binocular disparity and shape', *Computer Vision, Graphics, and Image Processing*, **37**, pp. 171–95.
- Crick, F., Koch, C. (2003), 'A framework for consciousness', *Nature Neuroscience*, **6** (2), pp. 119–26.
- Dodd, J.V., Krug, K., Cumming, B.G., Parker, A.J. (2001), 'Perceptually bistable three-dimensional figures evoke high choice probabilities in cortical area MT', *Journal of Neuroscience*, **21** (13), pp. 4809–21.
- Duncan, R.O., Albright, T.D., Stoner, G.R. (2000), 'Occlusion and the interpretation of visual motion: perceptual and neuronal effects of context', *Journal of Neuroscience*, **20** (15), pp. 5885–97.
- Dutour, E.F. (1760), 'Discussion d'une question d'optique [Discussion on a question of optics]', *l'Academie des Sciences. Memoires de Mathematique et de physique presentes par Divers Savants*, **3**, pp. 514–30.
- Enoksson, P. (1968), 'Studies in optokinetic binocular rivalry with a new device', *Acta Ophthalmologica*, **46** (1), pp. 71–4.
- Fox, R., Herrmann, J. (1967), 'Stochastic properties of binocular rivalry alternations', *Perception & Psychophysics*, **2**, pp. 432–6.
- Fox, R., Aslin, R.N., Shea, S.L., Dumais, S.T. (1979), 'Stereopsis in human infants', *Science*, **207**, pp. 323–4.
- Fox, R., Todd, S., Bettinger, L.A. (1975), 'Optokinetic nystagmus as an objective indicator of binocular rivalry', *Vision Research*, **15** (7), pp. 849–53.
- Grunewald, A., Bradley, D.C., Andersen, R.A. (2002), 'Neural correlates of structure-from-motion perception in macaque V1 and MT', *Journal of Neuroscience*, **22** (14), pp. 6195–207.
- Koffka, K. (1935), *Principles of Gestalt Psychology* (New York, Harcourt, Brace and World).
- Kreiman, G., Fried, I., Koch, C. (2002), 'Single-neuron correlates of subjective vision in the human medial temporal lobe', *Proceedings of the National Academy of Sciences of the United States of America*, **99** (12), pp. 8378–83.
- Kreiman, G., Koch, C., Fried, I. (2000), 'Imagery neurons in the human brain', *Nature*, **408** (6810), pp. 357–61.
- Leopold, D.A., Fitzgibbons, J.C., Logothetis, N.K. (1995), 'The role of attention in binocular rivalry as revealed through optokinetic nystagmus', A.I.Memo No.1554, C.B.C.L.Paper No.126, pp. 1–17.
- Leopold, D.A., Logothetis, N.K. (1996), 'Activity changes in early visual cortex reflect monkeys' percepts during binocular rivalry', *Nature*, **379** (6565), pp. 549–53.
- Leopold, D.A., Logothetis, N.K. (1999), 'Multistable phenomena: changing views in perception', *Trends in Cognitive Sciences*, **3** (7), pp. 254–64.

- Leopold, D.A., Maier, A., Wilke, M., Logothetis, N.K. (2003), 'Binocular rivalry and the illusion of monocular vision' in *Binocular Rivalry and Perceptual Ambiguity*, eds D. Alais and R. Blake (Cambridge, MA: MIT Press).
- Leopold, D.A., Plettenberg, H.K., Logothetis, N.K. (2002a), 'Visual processing in the ketamine-anesthetized monkey: optokinetic and blood oxygenation level-dependent responses', *Experimental Brain Research*, **143**, pp. 359–72.
- Leopold, D.A., Wilke, M., Maier, A., Logothetis, N.K. (2002b), 'Stable perception of visually ambiguous patterns', *Nature Neuroscience*, **5** (6), pp. 605–9.
- Levelt, W. (1965), *On binocular rivalry* (Soesterberg, The Netherlands: Institute for Perception RVO-TNO).
- Logothetis, N.K., Schall, J.D. (1989), 'Neuronal correlates of subjective visual perception.', *Science*, **245** (4919), pp. 761–3.
- Logothetis, N.K., Schall, J.D. (1990), 'Binocular motion rivalry in macaque monkeys: eye dominance and tracking eye movements', *Vision Research*, **30** (10), pp. 1409–19.
- Lowe, S.W., Ogle, K.N. (1966), 'Dynamics of the pupil during binocular rivalry', *Archives of Ophthalmology*, **75** (3), pp. 395–403.
- Maier, A., Leopold, D.A., Logothetis, N.K. (2002), 'Neural activity during stable perception of ambiguous displays in monkey visual cortex', *Soc. Neurosci. Abstr*, **161**, p. 13.
- Manny, R.E., Fern, K.D. (1990), 'Motion coherence in infants', *Vision Research*, **30** (9), pp. 1319–29.
- Myerson, J., Miezin, F., Allman, J. (1981), 'Binocular rivalry in macaque monkeys and humans: A comparative study in perception', *Behav. Anal. Lett.* **1**, pp. 149–56.
- Richards, W. (1966), 'Attenuation of the pupil response during binocular rivalry', *Vision Research*, **6** (3), pp. 239–40.
- Rossi, A.F., Rittenhouse, C.D., Paradiso, M.A. (1996), 'The representation of brightness in primary visual cortex', *Science*, **273** (5278), pp. 1104–7.
- Sengpiel, F., Blakemore, C., Harrad, R. (1995), 'Interocular suppression in the primary visual cortex: a possible neural basis of binocular rivalry', *Vision Research*, **35** (2), pp. 179–95.
- Sereno, M.E., Sereno, M.I. (1999), '2-D center-surround effects on 3-D structure-from-motion', *Journal of Experimental Psychology: Human Perception & Performance*, **25** (6), pp. 1834–54.
- Sheinberg, D.L., Logothetis, N.K. (1997), 'The role of temporal cortical areas in perceptual organization', *Proceedings of the National Academy of Sciences of the United States of America*, **94** (7), pp. 3408–13.
- von Helmholtz, H. (1925), *Treatise on Physiological Optics* [1826] (Dover, New York, Southall, J.P.).
- Wallach, H., O'Connell, D.N. (1953), 'The kinetic depth effect', *Journal of Experimental Psychology*, **45**, pp. 205–17.
- Watanabe, K. (1999), 'Optokinetic nystagmus with spontaneous reversal of transparent motion perception', *Experimental Brain Research*, **129** (1), pp. 156–60.
- Wertheimer, M. (1912), 'Experimentelle Studien über das Sehen von Bewegung', *Zeitschrift für Psychologie mit Zeitschrift für angewandte Psychologie*, **61** (161), p. 265.
- Wilke, M., Leopold, D.A., Logothetis, N.K. (2002), 'Flash suppression without interocular conflict', *Society for Neuroscience Abstracts*, **161**, p. 15.
- Wolfe, J.M. (1984), 'Reversing ocular dominance and suppression in a single flash', *Vision Research*, **24** (5), pp. 471–8.
- Zhou, H., Friedman, H.S., von der Heydt, R. (2000), 'Coding of border ownership in monkey visual cortex', *Journal of Neuroscience*, **20** (17), pp. 6594–611.